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(54) Title: ORGANIC COMPOSITIONS TO TREAT KRAS-RELATED DISEASES

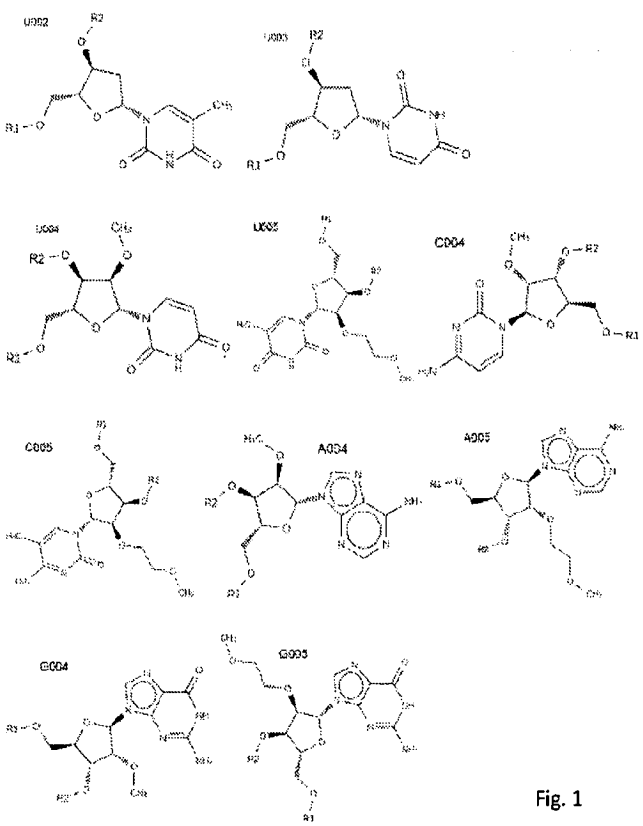


Fig. 1

(57) Abstract: The present disclosure relates to RNAi agents useful in methods of treating KRAS-related diseases such as a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to KRAS.

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ORGANIC COMPOSITIONS TO TREAT KRAS-RELATED DISEASES

BACKGROUND OF THE INVENTION

[001] KRAS is a member of the RAS subfamily of small GTPases. It is involved in cellular signal transduction, growth, differentiation, survival and other cellular functions. Over-expression or hyper-activity of KRAS, along with RAS family members HRAS and NRAS, have been associated with a number of diseases, including various cancers. RAS mutations are found in approximately one-third of all human malignancies. Bos et al. 1989. Cancer Res. 49: 4682-4689. KRAS accounts for most of the RAS mutations found in the majority of human malignancies, including 90% of RAS mutations in lung adenocarcinomas. Forbes et al. 2006. Br. J. Cancer 94: 318-322.

[002] Mutations, hyper-activity and/or over-expression of KRAS in particular has been associated with cancer, including adenocarcinoma, colorectal cancer (including advanced and metastatic colorectal cancer), colon cancer, lung (including non-small cell lung cancer and lung adenocarcinoma), acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases.

[003] There exists the need for treatments related to KRAS-related diseases.

[004]

[005] BRIEF SUMMARY OF THE INVENTION

[006] The present disclosure encompasses RNAi (RNA interference) agents to KRAS, which are useful in the treatment of KRAS-related diseases, such as cancer, cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases.

[007] The present disclosure also encompasses a method of treating a human subject having a pathological state mediated at least in part by KRAS expression, the method comprising the step of administering to the subject a therapeutically effective amount of a RNAi agent KRAS.

[008] The method also optionally further comprises the step of administering a second agent. In some embodiments, this second agent is another RNAi agent to KRAS. In other embodiments, the second agent is another treatment, such as one directed to another target, which is also hyper-active, mutated and/or over-expressed in the pathological state.

[009] The present disclosure provides specific RNAi agents and methods that are useful in reducing KRAS levels in a subject, e.g., a mammal, such as a human. The present disclosure specifically provides double-stranded RNAi agents comprising at least 15 to at least 19 or more contiguous nucleotides of KRAS. In particular, the present disclosure provides agents comprising sequences of 15 or more contiguous nucleotides differing by 0, 1, 2 or 3 from those of the RNAi agents provided, e.g., in Tables 1 to 6. The RNAi agents particularly can in one embodiment comprise less than 30 nucleotides per strand, e.g., such as 17 – 23 nucleotides, 15 – 19, 18-22 nucleotides, and/or 19-21 nucleotides, and/or such as those provided, e.g., in Tables 1 to 6, and modified and unmodified variants thereof (e.g., wherein the sense and/or anti-sense or first and/or second strand are modified or unmodified). The present disclosure also provides agents comprising a sense strand and an anti-sense strand, wherein the sense and/or the anti-sense strand comprise

sequences of 19 or more contiguous nucleotides differing by 0, 1, 2 or 3 from those of the RNAi agents provided, e.g., in Tables 1 to 6, and modified or unmodified variants thereof. The sense and anti-sense strand can be contiguous, or covalently bounds, e.g., via a loop or linker. The RNAi agents particularly can in one embodiment comprise less than 30 nucleotides per strand, e.g., such as 17 to 23 nucleotides, 18 to 22 nucleotides, and/or 19 to 21 nucleotides, and/or sequences such as those provided, e.g., in Tables 1 to 6.

[0010] The double-stranded RNAi agents can have 0, 1 or 2 blunt ends, and/or overhangs of 1, 2, 3 or 4 nucleotides (i.e., 1 to 4 nt) from one or both 3' and/or 5' ends. The double-stranded RNAi agents can also optionally comprise one or two 3' caps and/or one or more modified nucleotides. Modified variants of sequences as provided herein include those that are otherwise identical but contain substitutions of a naturally-occurring nucleotide for a corresponding modified nucleotide.

[0011] Furthermore, the RNAi agent can either contain only naturally-occurring nucleotide subunits (e.g., ribonucleotides), or one or more modifications to the sugar, phosphate or base of one or more of the replacement nucleotide subunits, whether they comprise ribonucleotide subunits or deoxyribonucleotide subunits or other related modified variants. In one embodiment, modified variants of the disclosed RNAi agents have a thymidine (as RNA, or, preferably, DNA) replacing a uridine, or have an inosine base. In some embodiments, the modified variants of the disclosed RNAi agents can have a nick in the passenger strand, mismatches between the guide and passenger strand, DNA replacing the RNA of a portion of both the guide and passenger strand (e.g., the seed region), and/or a shortened passenger strand (e.g., 15, 16, 17 or 18 nt). Once a functional guide strand is identified, modifications and variants of the RNAi agent can be readily made. Any combination of modifications which is not mutually exclusive can be (e.g., the combination of base modifications with shortened passenger strand; or nicked passenger strand and base modifications; or DNA replacing part or all of the seed region and base modifications in the remaining RNA; etc.).

[0012] In one embodiment, modified variants of the disclosed RNAi agents include RNAi agents with the same sequence (e.g., the same sequence of bases) as disclosed in Tables 1 to 6, but with one or more modifications to one or more of the sugar or phosphate of one or more of the nucleotide subunits. In one embodiment, the modifications improve efficacy, stability (e.g., against nucleases in, for example, blood serum or intestinal fluid), and/or reduce immunogenicity of the RNAi agent. One aspect of the present disclosure relates to a double-stranded oligonucleotide comprising at least one non-natural nucleobase. In certain embodiments, the non-natural nucleobase is difluorotolyl, nitroindolyl, nitropyrrolyl, or nitroimidazolyl. In a particular embodiment, the non-natural nucleobase is difluorotolyl. In certain embodiments, only one of the two oligonucleotide strands contains a non-natural nucleobase. In certain embodiments, both of the oligonucleotide strands contain a non-natural nucleobase.

[0013] The RNAi agent(s) can optionally be attached to a ligand selected to improve one or more characteristic, such as, e.g., stability, distribution and/or cellular uptake of the agent, e.g., cholesterol or a derivative thereof. The RNAi agent(s) can be isolated or be part of a pharmaceutical composition used for the methods described herein. Particularly, the pharmaceutical composition can be formulated for delivery to specific tissues (e.g., those afflicted with a KRAS-

related disease) or formulated for parenteral administration. The pharmaceutical composition can optionally comprise two or more RNAi agents, each one directed to the same or a different segment of the KRAS mRNA. Optionally, the pharmaceutical composition can further comprise or be used in conjunction with any known treatment for any KRAS-related disease.

[0014] The present disclosure further provides methods for reducing the level of KRAS mRNA in a cell, particularly in the case of a disease characterized by over-expression or hyper-activity of KRAS. Cells comprising an alteration such as a mutation, over-expression and/or hyperactivity of KRAS are termed "KRAS-defective" cells. Such methods comprise the step of administering one or more of the RNAi agents of the present disclosure to a cell, as further described below. The present methods utilize the cellular mechanisms involved in RNA interference to selectively degrade the target RNA in a cell and are comprised of the step of contacting a cell with one or more of the RNAi agents of the present disclosure.

[0015] The present disclosure further provides methods for reducing the level of KRAS mRNA in a cell, particularly in the case of a disease characterized by over-expression, mutation or hyper-activity of KRAS. Such methods comprise the step of administering one or more of the RNAi agents of the present disclosure to a cell, as further described below. The present methods utilize the cellular mechanisms involved in RNA interference to selectively degrade the target RNA in a cell and are comprised of the step of contacting a cell with one or more of the RNAi agents of the present disclosure.

[0016] The present disclosure also encompasses a method of treating a human subject having a pathological state mediated at least in part by KRAS expression, the method comprising the step of administering to the subject a therapeutically effective amount of a RNAi agent targeting KRAS. Additional methods involve preventing, treating, modulating and/or ameliorating a pathological state wherein disease progression (e.g., tumor growth) requires KRAS, although KRAS is not amplified, over-expressed or mis-localized. Such methods comprise the step of administering one or more of the RNAi agents of the present disclosure to a subject, as further described below. The present methods utilize the cellular mechanisms involved in RNA interference to selectively degrade the target RNA in a cell comprise the step of contacting a cell with one or more of the RNAi agents of the present disclosure. Such methods can be performed directly on a cell or can be performed on a mammalian subject by administering to a subject one or more of the RNAi agents/pharmaceutical compositions of the present disclosure. Reduction of target KRAS RNA in a cell results in a reduction in the amount of encoded KRAS protein produced. In an organism, this can result in restoration of balance in a pathway involving KRAS, and/or prevention of KRAS accumulation, and/or a reduction in KRAS activity and/or expression, and/or prevention of KRAS -mediated activation of other genes, and/or amelioration, treatment and/or prevention of a KRAS-related disease. In one embodiment, a reduction in KRAS expression, level or activity can limit tumor growth.

[0017] The methods and compositions of the present disclosure, e.g., the methods and KRAS RNAi agent compositions, can be used in any appropriate dosage and/or formulation described herein or known in the art, as well as with any suitable route of administration described herein or known in the art.

[0018] The details of one or more embodiments of the present disclosure are set forth in the accompanying drawings and the description below. Elements of the various embodiments (e.g., sequences, modifications, endcaps, combinations of RNAi agents, combination therapy involving a KRAS RNAi agent and another agent, etc.) which are not mutually-exclusive can be combined with each other as described herein and as known or developed in the art. For example, any RNAi agent sequence disclosed herein can be combined with any set of modifications or endcaps disclosed herein. Any combination of modifications, 5' end caps, and/or 3' end caps can be used with any RNAi agent sequence disclosed herein. Any RNAi agent disclosed herein (with any combination of modifications or endcaps or without either modifications or endcaps) can be combined with any other RNAi agent or other treatment composition or method disclosed herein.

[0019] Other features, objects, and advantages of the present disclosure will be apparent from this description, the drawings, and from the claims.

[0020]

[0021] BRIEF DESCRIPTION OF THE FIGURE

[0022] Figure 1 illustrates various modified nucleotides: U002, U003, U004, U005, C004, C005, A004, A005, G005, and G004, which can be used in the RNAi agents disclosed herein. U002 indicates a 2'- deoxy-thymidine which is DNA. U003 indicates 2'-deoxy uridine. U004 indicates a nucleotide with a Uridine ("U") base with a 2'-O-methyl modification. U005 indicates a U base with a 2'-O-methoxyethyl (MOE) modification. C004 indicates a Cysteine ("C") base with a 2'-O-methyl modification. C005 indicates a C base with 2'-O-methoxyethyl modification. A004 indicates an Adenosine ("A") base with a 2'-O-methyl modification. A005 indicates an A base with 2'-O-methoxyethyl modification. G005 indicates a Guanosine ("G") base with a 2'O-methyl modification. G004 indicates a G base with a 2'O-methyl modification.

DETAILED DESCRIPTION OF THE INVENTION

[0023] The present disclosure encompasses RNAi agents to KRAS, for targeting and inhibition of the KRAS gene, which are useful in treatment of KRAS-related diseases (e.g., diseases associated with mutations in and/or altered expression, level and/or activity of KRAS, and/or diseases which require KRAS, and/or diseases treatable by modulating the expression, level and/or activity of KRAS), such as a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver or hepatic, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases. The present disclosure also provides methods of treating a human subject having a pathological state mediated at least in part by KRAS expression or over-expression or hyper-activity, the method comprising the step of administering to the subject a therapeutically effective amount of a RNAi agent to KRAS.

[0024] Various embodiments of the present disclosure include the following.

[0025] In one embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS (or any set of overlapping RNAi agents specific to KRAS) provided, e.g., in any of Tables 1 to 6. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense and an anti-sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sense strand of a RNAi agent from any sequence provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the first strand, and the second strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the second strand of any RNAi agent provided herein.

[0026] Particular duplexes include the example unmodified (e.g., "generic") and example modified sequences listed in Table 1. In addition to the described example modifications, other modified variants are contemplated and can be made using the nucleotide sequences provided. In various embodiments, the first and/or second strand are modified or unmodified or a combination of one modified and one unmodified.

[0027] RNAi Agents comprising an antisense and a sense strand described herein

[0028] In one embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to KRAS selected from any sequence (or overlapping set of sequences) provided in a table herein (e.g., any of Tables 1 to 6). In one embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0 nucleotides from the antisense strand of a RNAi agent to KRAS selected from any sequence (or overlapping set of sequences) provided in a table here (e.g., any of Tables 1 to 6). In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense and an anti-sense strand, wherein the sequence of the anti-sense strand comprises the sequence of the anti-sense strand of a RNAi agent from any sequence provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the sequence of the first strand of any RNAi agent provided herein. Particular duplexes include those specific duplexes provided above and as listed in any one or more of Table 1. Additional modified sequences (e.g., sequences comprising one or more modified base) of each of the compositions above are also contemplated as part of the present disclosure.

[0029]

[0030] TABLE 1. SEQ ID NOs. for RNAi Agents to KRAS

[0031] Provided in Table 1 are the nickname of various KRAS RNAi duplexes; the SEQ ID NOs. of unmodified (e.g., "generic") sense and anti-sense sequences; and the SEQ ID NOs. for example sense and anti-sense strands.

[0032] Table 1, below, provides the SEQ ID NOs for the unmodified and an example modified sequence of the sense and an anti-sense strands of various RNAi agents to KRAS. The base composition of each sequence represented by a SEQ ID NO is provided in more detail in Tables 2 and 3. Table 4 shows overlapping groups of these KRAS RNAi agents. Tables 5 and 6 show efficacy of various KRAS RNAi agents.

Table 1. SEQ ID NOs for unmodified and example modified sequences of a first and a second strand (e.g., sense and anti-sense strand) for RNAi agents to KRAS

	UNMODIFIED SEQUENCES		EXAMPLE MODIFIED	SEQUENCES
Duplex	SENSE SEQ ID NO:	ANTI-SENSE SEQ ID NO:	SENSE SEQ ID NO:	ANTI-SENSE SEQ ID NO:
AD-35523.3	1	428	855	1282
AD-35529.1	2	429	856	1283
AD-35535.4	3	430	857	1284
AD-35541.4	4	431	858	1285
AD-35547.4	5	432	859	1286
AD-35553.4	6	433	860	1287
AD-35559.4	7	434	861	1288
AD-35565.4	8	435	862	1289
AD-35524.4	9	436	863	1290
AD-35530.4	10	437	864	1291
AD-35536.4	11	438	865	1292
AD-35542.4	12	439	866	1293
AD-35548.4	13	440	867	1294
AD-35554.4	14	441	868	1295
AD-35560.2	15	442	869	1296
AD-35566.4	16	443	870	1297
AD-35525.2	17	444	871	1298
AD-35531.4	18	445	872	1299
AD-35537.4	19	446	873	1300
AD-35543.2	20	447	874	1301
AD-35549.4	21	448	875	1302
AD-35555.4	22	449	876	1303
AD-35561.4	23	450	877	1304
AD-35567.4	24	451	878	1305
AD-35526.4	25	452	879	1306
AD-35532.4	26	453	880	1307
AD-35538.4	27	454	881	1308
AD-35544.4	28	455	882	1309
AD-35550.4	29	456	883	1310
AD-35556.4	30	457	884	1311
AD-35562.4	31	458	885	1312
AD-35568.4	32	459	886	1313
AD-35527.4	33	460	887	1314
AD-35533.4	34	461	888	1315
AD-35539.4	35	462	889	1316
AD-35545.4	36	463	890	1317
AD-35551.4	37	464	891	1318
AD-35563.4	38	465	892	1319
AD-35528.4	39	466	893	1320
AD-35540.4	40	467	894	1321
AD-35546.4	41	468	895	1322

AD-35552.4	42	469	896	1323
AD-35558.4	43	470	897	1324
AD-35564.4	44	471	898	1325
AD-35570.4	45	472	899	1326
AD-35571.4	46	473	900	1327
AD-35577.4	47	474	901	1328
AD-35583.4	48	475	902	1329
AD-35589.4	49	476	903	1330
AD-35595.4	50	477	904	1331
AD-35601.4	51	478	905	1332
AD-35607.4	52	479	906	1333
AD-35613.4	53	480	907	1334
AD-35572.4	54	481	908	1335
AD-35578.4	55	482	909	1336
AD-35584.4	56	483	910	1337
AD-35590.4	57	484	911	1338
AD-35596.4	58	485	912	1339
AD-35602.4	59	486	913	1340
AD-35608.4	60	487	914	1341
AD-35614.4	61	488	915	1342
AD-35573.4	62	489	916	1343
AD-35579.4	63	490	917	1344
AD-35585.4	64	491	918	1345
AD-35591.4	65	492	919	1346
AD-35597.4	66	493	920	1347
AD-35603.4	67	494	921	1348
AD-35609.4	68	495	922	1349
AD-35615.4	69	496	923	1350
AD-35574.4	70	497	924	1351
AD-35580.1	71	498	925	1352
AD-35586.4	72	499	926	1353
AD-35592.4	73	500	927	1354
AD-35598.4	74	501	928	1355
AD-35604.4	75	502	929	1356
AD-35610.4	76	503	930	1357
AD-35616.4	77	504	931	1358
AD-35575.4	78	505	932	1359
AD-35581.4	79	506	933	1360
AD-35587.4	80	507	934	1361
AD-35593.4	81	508	935	1362
AD-35599.4	82	509	936	1363
AD-35605.4	83	510	937	1364
AD-35611.4	84	511	938	1365
AD-35617.4	85	512	939	1366
AD-35576.4	86	513	940	1367
AD-35588.4	87	514	941	1368
AD-35667.1	88	515	942	1369
AD-35673.1	89	516	943	1370
AD-35679.1	90	517	944	1371
AD-35685.1	91	518	945	1372
AD-35691.1	92	519	946	1373
AD-35557.1	93	520	947	1374
AD-35618.1	94	521	948	1375
AD-35569.1	95	522	949	1376
AD-35534.1	96	523	950	1377
AD-35582.1	97	524	951	1378
AD-35594.1	98	525	952	1379
AD-35600.1	99	526	953	1380
AD-35606.1	100	527	954	1381
AD-35612.1	101	528	955	1382
AD-38127.1	102	529	956	1383
AD-38133.1	103	530	957	1384

AD-38139.1	104	531	958	1385
AD-38145.1	105	532	959	1386
AD-38151.1	106	533	960	1387
AD-38157.1	107	534	961	1388
AD-38163.1	108	535	962	1389
AD-38169.1	109	536	963	1390
AD-38128.1	110	537	964	1391
AD-38134.1	111	538	965	1392
AD-38140.1	112	539	966	1393
AD-38146.1	113	540	967	1394
AD-38152.1	114	541	968	1395
AD-38158.1	115	542	969	1396
AD-38164.1	116	543	970	1397
AD-38170.1	117	544	971	1398
AD-38129.1	118	545	972	1399
AD-38135.1	119	546	973	1400
AD-38141.1	120	547	974	1401
AD-38147.1	121	548	975	1402
AD-38153.1	122	549	976	1403
AD-38159.1	123	550	977	1404
AD-38165.1	124	551	978	1405
AD-38171.1	125	552	979	1406
AD-38130.1	126	553	980	1407
AD-38136.1	127	554	981	1408
AD-38142.1	128	555	982	1409
AD-38148.1	129	556	983	1410
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AD-38143.1	136	563	990	1417
AD-38149.1	137	564	991	1418
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AD-38161.1	139	566	993	1420
AD-38167.1	140	567	994	1421
AD-38173.1	141	568	995	1422
AD-38132.1	142	569	996	1423
AD-38138.1	143	570	997	1424
AD-38144.1	144	571	998	1425
AD-38150.1	145	572	999	1426
AD-38156.1	146	573	1000	1427
AD-38162.1	147	574	1001	1428
AD-38168.1	148	575	1002	1429
AD-38174.1	149	576	1003	1430
AD-39683.1	150	577	1004	1431
AD-39689.1	151	578	1005	1432
AD-39695.1	152	579	1006	1433
AD-39701.1	153	580	1007	1434
AD-39707.1	154	581	1008	1435
AD-39713.1	155	582	1009	1436
AD-39719.1	156	583	1010	1437
AD-39725.1	157	584	1011	1438
AD-39684.1	158	585	1012	1439
AD-39690.1	159	586	1013	1440
AD-39696.1	160	587	1014	1441
AD-39702.1	161	588	1015	1442
AD-39708.1	162	589	1016	1443
AD-39714.1	163	590	1017	1444
AD-39720.1	164	591	1018	1445
AD-39726.1	165	592	1019	1446

AD-39685.1	166	593	1020	1447
AD-39691.1	167	594	1021	1448
AD-39697.1	168	595	1022	1449
AD-39703.1	169	596	1023	1450
AD-39709.1	170	597	1024	1451
AD-39715.1	171	598	1025	1452
AD-39721.1	172	599	1026	1453
AD-39727.1	173	600	1027	1454
AD-39686.1	174	601	1028	1455
AD-39692.1	175	602	1029	1456
AD-39698.1	176	603	1030	1457
AD-39704.1	177	604	1031	1458
AD-39710.1	178	605	1032	1459
AD-39716.1	179	606	1033	1460
AD-39722.1	180	607	1034	1461
AD-39728.1	181	608	1035	1462
AD-39687.1	182	609	1036	1463
AD-39693.1	183	610	1037	1464
AD-39699.1	184	611	1038	1465
AD-39705.1	185	612	1039	1466
AD-39711.1	186	613	1040	1467
AD-39717.1	187	614	1041	1468
AD-39723.1	188	615	1042	1469
AD-39729.1	189	616	1043	1470
AD-39688.1	190	617	1044	1471
AD-39694.1	191	618	1045	1472
AD-39700.1	192	619	1046	1473
AD-39706.1	193	620	1047	1474
AD-39712.1	194	621	1048	1475
AD-39718.1	195	622	1049	1476
AD-39724.1	196	623	1050	1477
AD-39730.1	197	624	1051	1478
AD-39736.1	198	625	1052	1479
AD-39742.1	199	626	1053	1480
AD-39748.1	200	627	1054	1481
AD-39754.1	201	628	1055	1482
AD-39760.1	202	629	1056	1483
AD-39766.1	203	630	1057	1484
AD-39772.1	204	631	1058	1485
AD-39731.1	205	632	1059	1486
AD-39737.1	206	633	1060	1487
AD-39743.1	207	634	1061	1488
AD-39749.1	208	635	1062	1489
AD-39755.1	209	636	1063	1490
AD-39761.1	210	637	1064	1491
AD-39767.1	211	638	1065	1492
AD-39773.1	212	639	1066	1493
AD-39732.1	213	640	1067	1494
AD-39738.1	214	641	1068	1495
AD-39744.1	215	642	1069	1496
AD-39750.1	216	643	1070	1497
AD-39756.1	217	644	1071	1498
AD-39762.1	218	645	1072	1499
AD-39768.1	219	646	1073	1500
AD-39774.1	220	647	1074	1501
AD-39733.1	221	648	1075	1502
AD-39739.1	222	649	1076	1503
AD-39745.1	223	650	1077	1504
AD-39751.1	224	651	1078	1505
AD-39757.1	225	652	1079	1506
AD-39763.1	226	653	1080	1507
AD-39769.1	227	654	1081	1508

AD-39775.1	228	655	1082	1509
AD-39734.1	229	656	1083	1510
AD-39740.1	230	657	1084	1511
AD-39746.1	231	658	1085	1512
AD-39752.1	232	659	1086	1513
AD-39758.1	233	660	1087	1514
AD-39764.1	234	661	1088	1515
AD-39770.1	235	662	1089	1516
AD-39776.1	236	663	1090	1517
AD-39735.1	237	664	1091	1518
AD-39741.1	238	665	1092	1519
AD-39747.1	239	666	1093	1520
AD-39753.1	240	667	1094	1521
AD-39759.1	241	668	1095	1522
AD-39765.1	242	669	1096	1523
AD-39771.1	243	670	1097	1524
AD-39778.1	244	671	1098	1525
AD-39784.1	245	672	1099	1526
AD-39790.1	246	673	1100	1527
AD-39796.1	247	674	1101	1528
AD-39802.1	248	675	1102	1529
AD-39808.1	249	676	1103	1530
AD-39814.1	250	677	1104	1531
AD-39820.1	251	678	1105	1532
AD-39779.1	252	679	1106	1533
AD-39785.1	253	680	1107	1534
AD-39791.1	254	681	1108	1535
AD-39797.1	255	682	1109	1536
AD-39803.1	256	683	1110	1537
AD-39809.1	257	684	1111	1538
AD-39815.1	258	685	1112	1539
AD-39821.1	259	686	1113	1540
AD-39780.1	260	687	1114	1541
AD-39786.1	261	688	1115	1542
AD-39792.1	262	689	1116	1543
AD-39798.1	263	690	1117	1544
AD-39804.1	264	691	1118	1545
AD-39810.1	265	692	1119	1546
AD-39816.1	266	693	1120	1547
AD-39822.1	267	694	1121	1548
AD-39781.1	268	695	1122	1549
AD-39787.1	269	696	1123	1550
AD-39793.1	270	697	1124	1551
AD-39799.1	271	698	1125	1552
AD-39805.1	272	699	1126	1553
AD-39811.1	273	700	1127	1554
AD-39817.1	274	701	1128	1555
AD-39823.1	275	702	1129	1556
AD-39782.1	276	703	1130	1557
AD-39788.1	277	704	1131	1558
AD-39794.1	278	705	1132	1559
AD-39800.1	279	706	1133	1560
AD-39806.1	280	707	1134	1561
AD-39812.1	281	708	1135	1562
AD-39818.1	282	709	1136	1563
AD-39824.1	283	710	1137	1564
AD-39783.1	284	711	1138	1565
AD-39789.1	285	712	1139	1566
AD-39795.1	286	713	1140	1567
AD-39801.1	287	714	1141	1568
AD-39807.1	288	715	1142	1569
AD-39813.1	289	716	1143	1570

AD-39819.1	290	717	1144	1571
AD-39825.1	291	718	1145	1572
AD-39831.1	292	719	1146	1573
AD-39837.1	293	720	1147	1574
AD-39843.1	294	721	1148	1575
AD-39849.1	295	722	1149	1576
AD-39855.1	296	723	1150	1577
AD-39861.1	297	724	1151	1578
AD-39867.1	298	725	1152	1579
AD-39826.1	299	726	1153	1580
AD-39832.1	300	727	1154	1581
AD-39838.1	301	728	1155	1582
AD-39844.1	302	729	1156	1583
AD-39850.1	303	730	1157	1584
AD-39856.1	304	731	1158	1585
AD-39862.1	305	732	1159	1586
AD-39868.1	306	733	1160	1587
AD-39827.1	307	734	1161	1588
AD-39833.1	308	735	1162	1589
AD-39839.1	309	736	1163	1590
AD-39845.1	310	737	1164	1591
AD-39851.1	311	738	1165	1592
AD-39857.1	312	739	1166	1593
AD-39863.1	313	740	1167	1594
AD-39869.1	314	741	1168	1595
AD-39828.1	315	742	1169	1596
AD-39834.1	316	743	1170	1597
AD-39840.1	317	744	1171	1598
AD-39846.1	318	745	1172	1599
AD-39852.1	319	746	1173	1600
AD-39858.1	320	747	1174	1601
AD-39864.1	321	748	1175	1602
AD-39870.1	322	749	1176	1603
AD-39829.1	323	750	1177	1604
AD-39835.1	324	751	1178	1605
AD-39841.1	325	752	1179	1606
AD-39853.1	326	753	1180	1607
AD-39859.1	327	754	1181	1608
AD-39865.1	328	755	1182	1609
AD-39871.1	329	756	1183	1610
AD-39830.1	330	757	1184	1611
AD-39836.1	331	758	1185	1612
AD-39842.1	332	759	1186	1613
AD-39848.1	333	760	1187	1614
AD-39854.1	334	761	1188	1615
AD-39860.1	335	762	1189	1616
AD-39866.1	336	763	1190	1617
AD-39992.1	337	764	1191	1618
AD-39998.1	338	765	1192	1619
AD-40004.1	339	766	1193	1620
AD-40010.1	340	767	1194	1621
AD-40016.1	341	768	1195	1622
AD-40022.1	342	769	1196	1623
AD-40028.1	343	770	1197	1624
AD-40034.1	344	771	1198	1625
AD-39999.1	345	772	1199	1626
AD-40005.1	346	773	1200	1627
AD-40011.1	347	774	1201	1628
AD-40017.1	348	775	1202	1629
AD-40029.1	349	776	1203	1630
AD-40035.1	350	777	1204	1631
AD-39994.1	351	778	1205	1632

AD-40000.1	352	779	1206	1633
AD-40006.1	353	780	1207	1634
AD-40012.1	354	781	1208	1635
AD-40018.1	355	782	1209	1636
AD-40024.1	356	783	1210	1637
AD-40030.1	357	784	1211	1638
AD-40036.1	358	785	1212	1639
AD-39995.1	359	786	1213	1640
AD-40001.1	360	787	1214	1641
AD-40007.1	361	788	1215	1642
AD-40013.1	362	789	1216	1643
AD-40019.1	363	790	1217	1644
AD-40025.1	364	791	1218	1645
AD-40031.1	365	792	1219	1646
AD-40037.1	366	793	1220	1647
AD-39996.1	367	794	1221	1648
AD-40002.1	368	795	1222	1649
AD-40008.1	369	796	1223	1650
AD-40014.1	370	797	1224	1651
AD-40020.1	371	798	1225	1652
AD-40026.1	372	799	1226	1653
AD-40032.1	373	800	1227	1654
AD-40038.1	374	801	1228	1655
AD-39997.1	375	802	1229	1656
AD-40009.1	376	803	1230	1657
AD-40015.1	377	804	1231	1658
AD-40021.1	378	805	1232	1659
AD-40027.1	379	806	1233	1660
AD-40033.1	380	807	1234	1661
AD-40039.1	381	808	1235	1662
AD-40045.1	382	809	1236	1663
AD-40051.1	383	810	1237	1664
AD-40057.1	384	811	1238	1665
AD-40063.1	385	812	1239	1666
AD-40069.1	386	813	1240	1667
AD-40075.1	387	814	1241	1668
AD-40081.1	388	815	1242	1669
AD-40040.1	389	816	1243	1670
AD-40046.1	390	817	1244	1671
AD-40052.1	391	818	1245	1672
AD-40058.1	392	819	1246	1673
AD-40064.1	393	820	1247	1674
AD-40070.1	394	821	1248	1675
AD-40076.1	395	822	1249	1676
AD-40082.1	396	823	1250	1677
AD-40041.1	397	824	1251	1678
AD-40047.1	398	825	1252	1679
AD-40053.1	399	826	1253	1680
AD-40059.1	400	827	1254	1681
AD-40065.1	401	828	1255	1682
AD-40071.1	402	829	1256	1683
AD-40077.1	403	830	1257	1684
AD-40083.1	404	831	1258	1685
AD-40042.1	405	832	1259	1686
AD-40048.1	406	833	1260	1687
AD-40054.1	407	834	1261	1688
AD-40060.1	408	835	1262	1689
AD-40066.1	409	836	1263	1690
AD-40072.1	410	837	1264	1691
AD-40078.1	411	838	1265	1692
AD-40084.1	412	839	1266	1693
AD-40043.1	413	840	1267	1694

AD-40049.1	414	841	1268	1695
AD-40055.1	415	842	1269	1696
AD-40061.1	416	843	1270	1697
AD-40067.1	417	844	1271	1698
AD-40073.1	418	845	1272	1699
AD-40079.1	419	846	1273	1700
AD-40085.1	420	847	1274	1701
AD-40044.1	421	848	1275	1702
AD-40050.1	422	849	1276	1703
AD-40056.1	423	850	1277	1704
AD-40062.1	424	851	1278	1705
AD-40068.1	425	852	1279	1706
AD-40074.1	426	853	1280	1707
AD-40080.1	427	854	1281	1708
AD-39720.1	1716	1754	1792	1830
AD-39706.1	1717	1755	1793	1831
AD-39712.1	1718	1756	1794	1832
AD-39760.1	1719	1757	1795	1833
AD-39732.1	1720	1758	1796	1834
AD-35541.4	1721	1759	1797	1835
AD-39735.1	1722	1760	1798	1836
AD-39741.1	1723	1761	1799	1837
AD-39778.1	1724	1762	1800	1838
AD-39790.1	1725	1763	1801	1839
AD-39822.1	1726	1764	1802	1840
AD-35609.4	1727	1765	1803	1841
AD-35581.4	1728	1766	1804	1842
AD-39845.1	1729	1767	1805	1843
AD-39858.1	1730	1768	1806	1844
AD-39870.1	1731	1769	1807	1845
AD-35576.4	1732	1770	1808	1846
AD-35588.4	1733	1771	1809	1847
AD-35600.1	1734	1772	1810	1848
AD-35606.1	1735	1773	1811	1849
AD-38151.1	1736	1774	1812	1850
AD-38163.1	1737	1775	1813	1851
AD-39999.1	1738	1776	1814	1852
AD-38159.1	1739	1777	1815	1853
AD-38130.1	1740	1778	1816	1854
AD-38136.1	1741	1779	1817	1855
AD-40036.1	1742	1780	1818	1856
AD-40008.1	1743	1781	1819	1857
AD-40021.1	1744	1782	1820	1858
AD-40077.1	1745	1783	1821	1859
AD-40072.1	1746	1784	1822	1860
AD-40061.1	1747	1785	1823	1861
AD-40068.1	1748	1786	1824	1862
AD-38131.1	1749	1787	1825	1863
AD-38167.1	1750	1788	1826	1864
KRAS1273 31273_A22S 26	1751	1789	1827	1865
KRAS2892 2892_A37S2 6	1752	1790	1828	1866
KRAS4731 4731_A22S2 6	1753	1791	1829	1867
AD-39741.1	2770	2760		
AD-39735.1	2771	2761		
AD-38159.1	2772	2762		

NA	2773	2763		
AD-38130.1	2774	2764		
NA	2775	2765		
NA	2776	2766		
AD-38136.1	2777	2767		
AD-40061.1	2778	2768		
AD-35588.4	2779	2769		
AD-39845.1	2790	2780		
AD-39720.1	2791	2781		
AD-35581.4	2792	2782		
AD-40068.1	2793	2783		
AD-39778.1	2794	2784		
AD-35606.1	2795	2785		
AD-35609.4	2796	2786		
AD-38163.1	2797	2787		
AD-35600.1	2798	2788		
AD-40008.1	2799	2789		
AD-40036.1	2810	2800		
AD-39790.1	2811	2801		
AD-39870.1	2812	2802		
AD-38131.1	2813	2803		
AD-40077.1	2814	2804		
AD-38167.1	2815	2805		
AD-38151.1	2816	2806		
AD-39858.1	2817	2807		
AD-39706.1	2818	2808		
AD-40021.1	2819	2809		
AD-39760.1	2828	2820		
AD-39822.1	2829	2821		
AD-39999.1	2830	2822		
AD-40072.1	2831	2823		
AD-39732.1	2832	2824		
AD-35576.4	2833	2825		
AD-39712.1	2834	2826		
AD-35541.4	2835	2827		

[0033] Table 1 presents the SEQ ID identifiers of an example unmodified first and second strand of each KRAS RNAi agent; the Table also provides an example modified sequence for each KRAS RNAi agent. For example, in Table 1, the unmodified sequences of example KRAS RNAi agent nicknamed AD-35523.3 are SEQ ID NOs: 1 and 428. An example set of modified sequences for this duplex is represented by SEQ ID NOs: 855 and 1282. Also note that the "AD" prefix of the nickname is on occasion replaced by "ND". The name of the RNAi also sometimes has a suffix, such as .1. This indicates a particular variant of a duplex. Thus, AD-35523.1, AD-35523.2, AD-35523.3, ND-35523 and the like all indicate KRAS RNAi agents of the same sequence, although they may differ in how they are modified. In these cases, replacement of a U with a T is considered a modification that does not introduce a mismatch; thus, two otherwise identical sequences wherein one or more U bases are replaced by T are still considered to be identical and the same. Some

nicknames of RNAi agents also comprise the suffix "b1", indicating "batch 1." The various KRAS RNAi agents comprising the nickname AD-35523 thus all have the same base sequence (though not necessarily the same modification), and the suffix "b1" (or "b2" or the like) may indicate a particular batch, though these also have the same sequence.

[0034] Some RNAi agents in Table 1 have alternative names or nicknames. Some nicknames are derived from their position in the KRAS gene and, often, a code for the format for modifications. It is noted, however, that different methodologies are available for numbering the KRAS gene sequence. The numbering used herein for the KRAS gene is for illustration only. Alternative names of some duplexes are listed below:

[0035]

[0036] **Table 1.1. Alternative Names of some RNAi Agents**

Duplex Name	Nickname
AD-39741.1	hs_KRAS_322_A22S26
AD-38159.1	hs_KRAS_528_A22S26
AD-39735.1	hs_KRAS_321_A22S26
AD-38130.1	hs_KRAS_531_A22S26

[0037]

[0038] NA, not applicable.

[0039]

[0040] Additional alternative names are provided in Tables 1, 2 and 3. For example, hs_KRAS 1273_A22S26, hs_KRAS 2892_A37S26, and hs_KRAS 4731_A22S26 are also sometimes alternatively designated KRAS1273, KRAS2892, and KRAS4731, respectively.

Table 1.2. Additional Alternative Names of some RNAi Agents

Additional siRNAs disclosed herein also have alternative names. These names begin with AD. These alternative names, nicknames and sequences of the generic (unmodified) sequences are provided below. The target sequence (DNA) corresponding to the Guide and Sense strand are provided. siRNAs include, for example, double-stranded RNA corresponding to the DNA sequences provided (e.g., as RNA with or without any of the following or combination of any of the following: modification(s), terminal TT or other overhang(s), endcap(s), alternative base (LNA, PNA, etc.), and/or a few DNA bases interspersed among the RNA or other bases, etc.).

AD nick-name	Nickname siRNA	Guide 19mer generic	SEQ ID NO.	Sense 19mer generic	SEQ ID NO.
AD-39741.1	hs KRAS 322 A22S26	ATCAATTACTACTTGCTTC	2760	GAAGCAAGTAGTAATTGAT	2770
AD-39735.1	hs KRAS 321 A22S26	TCAATTACTACTTGCTTCC	2761	GGAAGCAAGTAGTAATTGA	2771
AD-	hs KRAS	TTTCCTACTAGGACCATAG	2762	CTATGGTCCTAGTAG	2772

38159.1	528 A22S26			GAAA	
NA	hs KRAS 1273 A22S26	TAACTTTACATTCATCAGG	2763	CCTGATGAATGTAAAGTTA	2773
AD-38130.1	hs KRAS 531 A22S26	TTATTTCCTACTAGGACCA	2764	TGGTCCTAGTAGGAAATAA	2774
NA	hs KRAS 4731 A22S26	AATCTAGTTATGACTATTC	2765	GAATAGTCATAACTAGATT	2775
NA	hs KRAS 2892 A37S26	TATCTTTATTAAATTCTCC	2766	GGAGAATTTAATAAAGATA	2776
AD-38136.1	NA	TTTATTTCCTACTAGGACC	2767	GGTCCTAGTAGGAAATAAA	2777
AD-40061.1	NA	AATTCCATAACTTCTTGCT	2768	AGCAAGAAGTTATGGAATT	2778
AD-35588.4	NA	TCTATAATGGTGAATATCT	2769	AGATATTCACCATTATAGA	2779
AD-39845.1	NA	GATTTAGTATTATTTATGG	2780	CCATAAATAATACTAAATC	2790
AD-39720.1	NA	AGCTCCAACTACCACAAGT	2781	ACTTGTGGTAGTTGGAGCT	2791
AD-35581.4	NA	TTATTTATGGCAAATACAC	2782	GTGTATTTGCCATAAATAA	2792
AD-40068.1	NA	AATAAAAGGAATTCCATAA	2783	TTATGGAATTCCTTTTATT	2793
AD-39778.1	NA	TTCTCCATCAATTACTACT	2784	AGTAGTAATTGATGGAGAA	2794
AD-35606.1	NA	TTCTCTATAATGGTGAATA	2785	TATTCACCATTATAGAGAA	2795
AD-35609.4	NA	AAATACACAAAGAAAGCCC	2786	GGGCTTTCTTTGTGTATTT	2796
AD-38163.1	NA	TTTAATTTGTTCTCTATAA	2787	TTATAGAGAACAAATTAAA	2797
AD-35600.1	NA	TCTCTATAATGGTGAATAT	2788	ATATTCACCATTATAGAGA	2798
AD-40008.1	NA	TCTAGAAGGCAAATCACAT	2789	ATGTGATTTGCCTTCTAGA	2799
AD-40036.1	NA	AATCACATTTATTTCCTAC	2800	GTAGGAAATAAATGTGATT	2810
AD-39790.1	NA	GTTTCTCCATCAATTACTA	2801	TAGTAATTGATGGAGAAAC	2811
AD-39870.	hs KRAS 459	ATATCTTCAAATGATTTAG	2802	CTAAATCATTTGAAGATAT	2812

1	A37S26				
AD-38131.1	NA	TTTCAATAAAAGGAATTCC	2803	GGAATTCCTTTTATTGAAA	2813
AD-40077.1	NA	CTTGCTAAGTCCTGAGCCT	2804	AGGCTCAGGACTTAGCAAG	2814
AD-38167.1	NA	CTGATGTTTCAATAAAAGG	2805	CCTTTTATTGAAACATCAG	2815
AD-38151.1	NA	TAATTTGTTCTCTATAATG	2806	CATTATAGAGAACAAATTA	2816
AD-39858.1	NA	ATCTTCAAATGATTTAGTA	2807	TACTAAATCATTTGAAGAT	2817
AD-39706.1	NA	ATCGTCAAGGCACTCTTGC	2808	GCAAGAGTGCCTTGACGAT	2818
AD-40021.1	NA	TGTCTACTGTTCTAGAAGG	2809	CCTTCTAGAACAGTAGACA	2819
AD-39760.1	NA	ATTAGCTGTATCGTCAAGG	2820	CCTTGACGATACAGCTAAT	2828
AD-39822.1	NA	TCGAGAATATCCAAGAGAC	2821	GTCTCTTGGATATTCTCGA	2829
AD-39999.1	NA	TCTTCAGAGTCCTTAACTC	2822	GAGTTAAGGACTCTGAAGA	2830
AD-40072.1	NA	ATAACTTCTTGCTAAGTCC	2823	GGACTTAGCAAGAAGTTAT	2831
AD-39732.1	NA	AATGATTCTGAATTAGCTG	2824	CAGCTAATTCAGAATCATT	2832
AD-35576.4	NA	TATAATGGTGAATATCTTC	2825	GAAGATATTCACCATTATA	2833
AD-39712.1	NA	TATCGTCAAGGCACTCTTG	2826	CAAGAGTGCCTTGACGATA	2834
AD-35541.4	NA	TATTGTTGGATCATATTCG	2827	CGAATATGATCCAACAATA	2835

Additional tables (e.g., Tables 1.1 and 1.2) are continuations of Table 1; thus, references to any Table or Tables include references to additional Tables. For example, references to Table 1 also include references to Tables 1.1 and 1.2; and references to Tables 1 to 6 include Tables 1.1, 1.2, 6.1, 6.2, etc.

[0041] Various Embodiments of the Present Disclosure

[0042] Various RNAi agents to KRAS are disclosed in Tables 1 to 6.

[0043] Tables 1, 2 and 3 provide the sequence, SEQ ID NOs and relative positions of various RNAi agents to KRAS, including both unmodified sequences (listed in Table 2) and example modified sequences (listed in Table 3).

[0044] In the sequences in Table 3, lower-case letters (e.g., c, u) indicate modified nucleotides while upper case letters (e.g., C, U, A, G) indicate unmodified nucleotides. In this Table, example modified versions of each of the sequences are shown. However, the present disclosure also contemplates and encompasses unmodified versions of these sequences and other versions which comprise additional or alternative modifications. Thus, for example, AD-35523.3 can optionally have the unmodified sequences of SEQ ID NO: 1 in the sense strand and SEQ ID NO: 428 in the anti-sense strand. The present disclosure also encompasses alternative modified versions of the duplex comprising the modified sequences of SEQ ID NO: 855 in the sense strand and SEQ ID NO: 1282 in the anti-sense strand. The present disclosure also encompasses different modified variants of SEQ ID NO: 1 in the sense strand and SEQ ID NO: 428 in the anti-sense strand. Similarly, the present disclosure also encompasses any modified variant of any unmodified sequence disclosed herein.

[0045] In the sequences in Tables 1 to 3, the modified and unmodified sequences can optionally comprise the sequence "TT", "dTdT", "dTsdT" or "UU" at the 3' end. Thus, in the example above, AD-35523.3 can optionally have the modified sequences of SEQ ID NO: 855 in the sense strand and SEQ ID NO: 1282 in the anti-sense strand. As noted in Table 3, below, SEQ ID NO: 855 and SEQ ID NO: 1282 include a terminal dTdT. dT is 2'-deoxy-thymidine-5'-phosphate and sdT is 2'-deoxy Thymidine 5'-phosphorothioate. In the disclosed sequences, terminal dinucleotide "UU" is 2'-OMe-U 2'-OMe-U, and neither the terminal TT nor the terminal UU are in the inverted/reverse orientation. The terminal dithymidine (or UU) is not part of the KRAS target sequence, but is a modified variant of the dithymidine dinucleotide commonly placed as an overhang to protect the ends of siRNAs from nucleases (see, for example, Elbashir et al. 2001 Nature 411: 494-498; Elbashir et al. 2001 EMBO J. 20: 6877-6888; and Kraynack et al. 2006 RNA 12:163-176). A terminal dinucleotide is known from these references to enhance nuclease resistance but not contribute to target recognition. Thus, the present disclosure also encompasses any modified or any unmodified sequence disclosed herein, wherein the modified sequence comprises a terminal TT, dTdT, sdT, dTsdT, sdTsdT, sdTdT, or the like which may be in either the inverted/reverse orientation or in the same 5' to 3' orientation as the KRAS specific sequence in the duplex. In addition, terminology used herein referring to "the KRAS portion of a RNAi agent sequence" and the like indicate the portion of the sequence of a RNAi agent which is derived from KRAS (thus "the KRAS portion of a RNAi agent sequence" does not include, for example, a terminal dTdT, TT, UU, or the like, but does include the portion of the RNAi agent that corresponds to or is complementary to a portion of the KRAS gene sequence or mRNA sequence.

[0046] On any modified or unmodified sequence, a 3' end cap, as is known in the art, can be used instead of or in addition to a terminal dinucleotide to stabilize the end from nuclease degradation provided that the 3' end cap is able to both stablize the RNAi agent (e.g., against nucleases) and not interfere excessively with siRNA activity. Thus, the present disclosure also encompasses any modified or any unmodified sequence disclosed herein, wherein the modified sequence further comprises a terminal 3' end cap.

[0047] Table 4 provides sets of overlapping RNAi agents to KRAS.

[0048] Activity levels of various KRAS RNAi agents are provided in Tables 5 and 6.

[0049]

[0050] **An RNAi agent comprising an anti-sense strand described herein**

[0051] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to KRAS selected from those anti-sense strands in the specific duplexes provided herein and as listed, e.g., in Tables 1 to 6.

[0052] Various specific embodiments of this embodiment are described below.

[0053] In one embodiment, the composition further comprises a second RNAi agent to KRAS. In various embodiments, the second RNAi agent is physically separate from the first, or the two KRAS RNAi agents are physically connected (e.g., covalently linked or otherwise conjugated) or combined in the same pharmaceutical composition, or are both elements in the same treatment regimen.

[0054] In one embodiment, the composition comprises a RNAi agent comprising a first and an second strand, wherein the sequence of the first strand and the sequence of the second strand are the sequences of the first and second strand, respectively, of any RNAi agent provided herein. In one embodiment, the composition comprises a RNAi agent comprising a first and an second strand, wherein the sequence of the first strand and the sequence of the second strand are the sequences of the first and second strand, respectively, of any RNAi agent provided herein, further comprising an additional about 6 to 20 nucleotides on one or both strands (e.g., about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 nt). In various embodiments, the first and second strands are the sense and anti-sense strands listed in the Tables herein, respectively. In various embodiments, the first and second strands are the anti-sense and sense strands listed in the Tables herein, respectively.

[0055] In one embodiment, the antisense strand is about 30 or fewer nt in length.

[0056] In one embodiment, the sense strand and the antisense strand form a duplex region of about 15 to about 30 nucleotide pairs in length.

[0057] In one embodiment, the antisense strand is about 15 to about 36 nt in length, including about 18 to about 30 nt in length, and further including about 19 to about 21 nt in length and about 19 to about 23 nt in length. In one embodiment, the antisense strand has at least the length selected from about 15 nt, about 16 nt, about 17 nt, about 18 nt, about 19 nt, about 20 nt, about 21 nt, about 22 nt, about 23 nt, about 24 nt, about 25 nt, about 26 nt, about 27 nt, about 28 nt, about 29 nt and about 30 nt.

[0058] In one embodiment, the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment, e.g., cytoplasm, interstitial fluids, blood serum, lung or intestinal lavage fluid.

[0059] In one embodiment, the RNAi agent comprises at least one sugar backbone modification (e.g., phosphorothioate linkage) and/or at least one 2'-modified nucleotide. In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0060] In one embodiment, the RNAi agent comprises: at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or at least

one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[0061] In one embodiment, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA). In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0062] In one embodiment, the RNAi agent comprises a blunt end.

[0063] In one embodiment, the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[0064] In one embodiment, the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[0065] In one embodiment, the RNAi agent is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[0066] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 60% at a concentration of 10 nM in RKO cells *in vitro*.

[0067] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 70% at a concentration of 10 nM in RKO cells *in vitro*.

[0068] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 80% at a concentration of 10 nM in RKO cells *in vitro*.

[0069] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 90% at a concentration of 10 nM in RKO cells *in vitro*.

[0070] In one embodiment, the RNAi agent has an EC50 of no more than about 0.1 nM in MiaPaca2 cells.

[0071] In one embodiment, the RNAi agent has an EC50 of no more than about 0.01 nM in MiaPaca2 cells.

[0072] In one embodiment, the RNAi agent has an EC50 of no more than about 0.001 nM in MiaPaca2 cells.

[0073] **A RNAi agent comprising a first and a second strand described herein**

[0074] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand strand comprises at least 15 contiguous nucleotides, differing by 0, 1, 2, or 3

nucleotides from the sequence of the first strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and listed, e.g., in Table 1.

[0075] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or second strand comprise at least 15 contiguous nucleotides, differing by 0, 1, 2, or 3 nucleotides from the sequence of the first and/or second strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and listed, e.g., in Table 1.

[0076] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or second strand comprise the sequence of the first and/or second strand, respectively, of a RNAi agent to KRAS selected from the specific duplexes provided herein and listed, e.g., in Table 1.

[0077] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or second strand are the sequence of the first and/or second strand, respectively, of a RNAi agent to KRAS selected from the specific duplexes provided herein and listed, e.g., in Table 1.

[0078] Various specific embodiments of these embodiments are described below.

[0079] In one embodiment, the composition further comprises a second RNAi agent to KRAS. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated).

[0080] In one embodiment, the antisense strand is about 30 or fewer nt in length.

[0081] In one embodiment, the sense strand and the antisense strand form a duplex region of about 15 to about 30 nt pairs in length.

[0082] In one embodiment, the antisense strand is about 15 to about 36 nt in length including about 18 to about 23 nt in length, and including about 19 to about 21 nt in length and about 19 to about 23 nt in length. In one embodiment, the antisense strand has at least the length selected from about 15 nt, about 16 nt, about 17 nt, about 18 nt, about 19 nt, about 20 nt, about 21 nt, about 22 nt, about 23 nt, about 24 nt, about 25 nt, about 26 nt, about 27 nt, about 28 nt, about 29 nt and about 30 nt.

[0083] In one embodiment, the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment, e.g., blood serum or intestinal lavage fluid.

[0084] In one embodiment, the RNAi agent comprises at least one sugar backbone modification (e.g., phosphorothioate linkage) and/or at least one 2'-modified nucleotide. In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0085] In one embodiment, the RNAi agent comprises: at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[0086] In one embodiment, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[0087] In one embodiment, the RNAi agent comprises a blunt end.

[0088] In one embodiment, the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[0089] In one embodiment, the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[0090] In one embodiment, the RNAi agent is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[0091] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 60% at a concentration of 10 nM in RKO cells *in vitro*.

[0092] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 70% at a concentration of 10 nM in RKO cells *in vitro*.

[0093] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 80% at a concentration of 10 nM in RKO cells *in vitro*.

[0094] In one embodiment, the RNAi agent is capable of inhibiting expression of KRAS by at least about 90% at a concentration of 10 nM in RKO cells *in vitro*.

[0095] In one embodiment, the RNAi agent has an EC50 of no more than about 0.1 nM in MiaPaca2 cells.

[0096] In one embodiment, the RNAi agent has an EC50 of no more than about 0.01 nM in MiaPaca2 cells.

[0097] In one embodiment, the RNAi agent has an EC50 of no more than about 0.001 nM in MiaPaca2 cells.

[0098] **A method of treatment using a RNAi agent described herein**

[0099] In one particular specific embodiment, the present disclosure relates to a method of treating a KRAS-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising at least an antisense strand, wherein the antisense strand comprises at least 15 to 19 contiguous

nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and as listed, e.g., in Table 1.

[00100] In another embodiment, the present disclosure relates to such a method, wherein the composition comprising a RNAi agent further comprises a sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sense strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and as listed, e.g., in Table 1.

[00101] In one embodiment of the method, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand is the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition further comprises a pharmaceutically effective formulation.

[00102] In one embodiment of the method, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand comprises the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition further comprises a pharmaceutically effective formulation.

[00103] Various particular specific embodiments of these embodiments are described below.

[00104] In one embodiment, the KRAS-related disease is a proliferative disease, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00105] In one embodiment, the KRAS-related disease is a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00106] In one embodiment, the method further comprises the administration of an additional treatment. In one embodiment, the additional treatment is a therapeutically effective amount of a composition.

[00107] In one embodiment, the additional treatment is a method (or procedure).

[00108] In one embodiment, the additional treatment and the RNAi agent can be administered in any order, or can be administered simultaneously.

[00109] In one embodiment, the method further comprises the step of administering an additional treatment for a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00110] In one embodiment, the method further comprises the step of administering an additional treatment or therapy selected from the list of an additional antagonist to a KRAS-related disease.

[00111] In one embodiment, the composition comprises a second RNAi agent to KRAS. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated).

[00112] In one embodiment, the method further comprises the step of administering an additional RNAi agent which comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and as listed, e.g., in Table 1.

[00113] A method of inhibiting the expression of KRAS using a RNAi agent described herein

[00114] In one particular specific embodiment, the present disclosure relates to a method of inhibiting the expression of KRAS in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent of the present disclosure.

[00115] In one embodiment of the method, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1.

[00116] In one embodiment of the method, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand is the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition is in a pharmaceutically effective formulation.

[00117] In one embodiment of the method, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand comprises the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition is in a pharmaceutically effective formulation.

[00118] Various particular embodiments of these embodiments are described below.

[00119] In one embodiment, the individual is afflicted with or susceptible to a KRAS-related disease.

[00120] In one embodiment, the KRAS-related disease is a proliferative disease, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00121] In one embodiment, the KRAS-related disease is a proliferative disease, including without limitation a solid or liquid cancer, e.g., adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00122] In one embodiment, the method further comprises the administration of an additional treatment. In one embodiment, the additional treatment is a therapeutically effective amount of a composition. In one embodiment, the additional treatment is a therapeutically relevant method (or procedure).

[00123] In one embodiment, the additional treatment and the RNAi agent can be administered in any order or can be administered simultaneously.

[00124] In one embodiment, the method further comprises the step of administering an additional treatment for a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00125] In one embodiment, the composition comprises a second RNAi agent to KRAS. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated).

[00126] In one embodiment, the method further comprises the step of administering an additional RNAi agent which comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to KRAS selected from the specific duplexes provided herein and as listed, e.g., in Table 1.

[00127] **Pharmaceutical compositions of a RNAi agent to KRAS**

[00128] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent of the present disclosure. In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition is in a pharmaceutically effective formulation.

[00129] In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand is the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition is in a pharmaceutically effective formulation.

[00130] In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the sequence of the sense and/or anti-sense strand comprises the sequence of the sense and/or the anti-sense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1, wherein the composition is in a pharmaceutically effective formulation.

[00131] In one embodiment, the present disclosure pertains to the use of a RNAi agent in the manufacture of a medicament for treatment of a KRAS-related disease, wherein the RNAi agent comprises a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to KRAS selected from those specific duplex provided herein and as listed, e.g., in Table 1.

[00132]

[00133] Specific Embodiments of RNAi Agents to KRAS comprising mismatches from the disclosed sequences

[00134] Various specific embodiments of a RNAi agent to KRAS are disclosed herein. The present disclosure encompasses the example modified sequences provided in Tables 1 to 6, and the corresponding unmodified sequences and other modified sequences (e.g., modified and unmodified variants). Specific embodiments of the present disclosure include RNAi agents which comprise sequences differing by 0, 1, 2, or 3 nt (nucleotides) or bp [basepair(s)] (e.g., with 0, 1, 2 or 3 mismatches) from any of the RNAi agents listed in Table 1, and modified and unmodified variants thereof. As described in additional detail below, a mismatch is defined herein as a difference between the base sequence (e.g., A instead of G) or length when two sequences are maximally aligned and compared. In addition, as described in more detail below, an "unmodified variant" is a variant in which the base sequence is identical, but none of the bases are modified; this includes, for example, a sequence identical to the corresponding portion of the wild-type KRAS mRNA or gene. A "modified variant" contains one or more modifications (or one or more fewer or different modifications) to a nucleotide, sugar, phosphate or backbone, and/or addition of one or more moieties; but without a change, substitution, addition, or deletion to the base sequence. A particular sequence and its modified or unmodified variants have 0 mismatches among them.

[00135] In one particular embodiment, the present disclosure comprises a RNAi agent comprising a sense and an anti-sense strand, wherein the sense and/or anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense and/or anti-sense strand of: any of the RNAi agents listed in Tables 1 to 6, and modified and unmodified variants thereof.

[00136] In another particular embodiment, the RNAi agent comprises a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sense strand of any of the RNAi agents listed in Tables 1 to 6, and modified and unmodified variants thereof.

[00137] Other embodiments

[00138] Various particular specific embodiments of this disclosure are described below.

[00139] In one embodiment, the disclosure pertains to a composition according to any of the embodiments described herein, for use in a method of treating a KRAS-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to any of the claims.

[00140] One embodiment of the disclosure is the use of a composition according to any of these embodiments, in the manufacture of a medicament for treatment of an KRAS-related disease.

[00141] In one embodiment, the KRAS-related disease is a proliferative disease, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome..

[00142] In one embodiment, the KRAS-related disease is a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma,

ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[00143] In one embodiment, the disclosure pertains to the composition of any of the above embodiments, for use in the treatment of an KRAS-related disease.

[00144] Definitions

[00145] For convenience, the meaning of certain terms and phrases used in the specification, examples, and appended claims, are provided below. If there is an apparent discrepancy between the usage of a term in other parts of this specification and its definition provided in this section, the definition in this section shall prevail.

[00146] KRAS

By "KRAS" is meant the gene, mRNA, and/or protein, or any nucleic acid encoding the protein, or any mutant, variant or modified version thereof, designated by the Approved Gene Symbol: KRAS; Cytogenetic location: 12p12.1; Genomic coordinates (GRCh37): 12:25,358,179 - 25,403,853 (from NCBI), which also variously designated: KRas, K-ras, K-RAS, GTPase KRas, and V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog, C-K-RAS; K-RAS2A; K-RAS2B; K-RAS4A; K-RAS4B; KI-RAS; KRAS2; RASK2; v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog [Source: MGI Symbol; Acc: MGI: 96680]; OMIM: 190070 MGI: 96680 HomoloGene: 37990 GeneCards: KRAS Gene; Species Human: Entrez 3845; Ensembl ENSG00000133703; UniProt P01116; RefSeq (mRNA) NM_004985.3; RefSeq (protein) NP_004976.2; Location (UCSC) Chr 12: 25.36 – 25.4 Mb; Species-Mouse: Entrez-16653; Ensembl-ENSMUSG00000030265; UniProt-O70564; RefSeq (mRNA)-NM_021284.6; RefSeq (protein)-NP_067259.4; Location (UCSC)-Chr 6: 145.17 – 145.2 Mb.

[00147] The Ras subfamily

[00148] The Ras subfamily (an abbreviation of RAt Sarcoma) is a protein subfamily of small GTPases that are involved in cellular signal transduction and other processes. Activation of Ras signaling causes cell growth, differentiation and survival.

[00149] Since Ras communicates signals from outside the cell to the nucleus, mutations in ras genes can cause permanent activation and inappropriate transmission inside the cell, even in the absence of extracellular signals. Because these signals result in cell growth and division, dysregulated or otherwise aberrant Ras signaling can ultimately lead to oncogenesis and cancer. Goodsell et al. 1999. Oncologist 4. 3: 263-4. Activating mutations in Ras are found in a third of all human tumors and up to 90% in specific tumor types. Downward. 2003. Nat. Rev. Cancer 3. 1: 11–22; Bos et al. 1989 Cancer Res. 49: 4682-4689; and Forbes et al. 2006 Br. J. Cancer 94: 318-322

[00150] The ras genes were first identified as the transforming oncogenes [Malumbres et al. 2003. Nat. Rev. Cancer 3. 6: 459–65] responsible for the cancer-causing activities of the Harvey (the HRAS oncogene) and Kirsten (KRAS) sarcoma viruses, by Scolnick and colleagues at the

National Institutes of Health (NIH). Chang et al. 1982. Proc. Natl. Acad. Sci. U.S.A. 79. 16: 4848–52. These viruses were discovered originally in rats during the 1960s by Jennifer Harvey [Harvey. 1964. Nature 204. 4963: 1104–5] and Werner Kirsten [Kirsten et al. 1970. Bibl Haematol. 36: 246–9], respectively. In 1982, activated and transforming human KRAS genes were discovered in human cancer cells [Santos et al. 1982. Nature 298. 5872: 343–7], [Parada et al. 1982. Nature 297. 5866: 474–8]. Subsequent studies identified a third human KRAS gene, designated NRAS, for its initial identification in human neuroblastoma cells.

[00151] The three human KRAS genes encode highly related 188 to 189 amino acid proteins, designated H-Ras, N-Ras and K-Ras4A and K-Ras4B (the two K-Ras proteins arise from alternative gene splicing). For additional information pertaining to KRAS cloning and isoforms, see, for example, Der et al. 1982 Proc. Nat. Acad. Sci. 79: 3637-3640; Chang et al. 1982 Proc. Nat. Acad. Sci. 79: 4848-4852; McCoy et al. 1983 Nature 302: 79-81; McGrath et al. 1983 Nature 304: 501-506; and Carta et al. 2006 Am. J. Hum. Genet. 79: 129-135.

[00152] Ras function

[00153] Ras proteins function as binary molecular switches that control intracellular signaling networks. Ras-regulated signal pathways, control such processes as actin cytoskeletal integrity, proliferation, differentiation, cell adhesion, apoptosis, and cell migration. Ras and ras-related proteins are often deregulated in cancers, leading to increased invasion and metastasis and decreased apoptosis.

[00154] Ras activates several pathways, of which the mitogen-activated protein (MAP) kinase cascade has been well-studied. This cascade transmits signals downstream and results in the transcription of genes involved in cell growth and division. There is a separate AKT pathway that inhibits apoptosis.

[00155] In various embodiments, the RNAi agents can be used to treat KRAS-related diseases in which any one or more of these pathways or functions is altered. In various embodiments, the present disclosure encompasses KRAS RNAi agents that modulate or alter Ras-regulated signal pathways, including the MAP kinase cascade, and/or modulate or alter processes such as actin cytoskeletal integrity, proliferation, differentiation, cell adhesion, apoptosis, and cell migration. Ras and ras-related proteins are often deregulated in cancers, leading to increased invasion and metastasis and decreased apoptosis.

[00156] Activation and deactivation

[00157] Ras is a G protein, or a guanosine-nucleotide-binding protein. Specifically, it is a single-subunit small GTPase, which is related in structure to the G_α subunit of heterotrimeric G proteins (large GTPases). G proteins function as binary signaling switches with "on" and "off" states. In the "off" state it is bound to the nucleotide guanosine diphosphate (GDP), while in the "on" state, Ras is bound to guanosine triphosphate (GTP), which has an extra phosphate group as compared to GDP. This extra phosphate holds the two switch regions in a "loaded-spring" configuration (specifically the Thr-35 and Gly-60). When released, the switch regions relax which causes a conformational change

into the inactivate state. Hence, activation and deactivation of Ras and other small G proteins are controlled by cycling between the active GTP-bound and inactive GDP-bound forms.

[00158] Critical regions of KRAS for oncogenic activity include codons 12, 13, 59, 60, 61, 63 and 153. Grimmond et al. 1992 Urol. Res. 20:121-126; Burmer et al. 1989 Proc. Natl. Acad. Sci. 86: 2403-2407. Mutations sometimes appear affecting these codons. Some KRAS mutations cause RAS to accumulate in the GTP-bound state by impairing intrinsic GTPase activity and conferring resistance to GTPase-activating proteins. Zenker et al. 2007 J. Med. Genet. 44: 131-135. In various embodiments, the sequence of the KRAS RNAi agent encompasses the portion of the coding segment corresponding to any of the above-listed codons. In various embodiments, the KRAS RNAi agent has a mismatch to the wild-type (wt) KRAS sequence, such that the sequence of the KRAS RNAi agent matches the sequence of a mutated portion of the KRAS gene. In various embodiments, the disclosure encompasses the administration to a patient of a KRAS RNAi agent with a sequence corresponding to that of a particular mutation found in the patient, optionally combined with the administration of a KRAS RNAi agent with a sequence encompassing the wt sequence. In some embodiments, the KRAS RNAi agents correspond to different portions of the KRAS mRNA. In some embodiments, the patient may have one or more mutations corresponding to particular codons of KRAS (e.g., codons 12, 13 and/or 59), but the remainder of the KRAS gene is wild type, and thus the patient can be administered a KRAS RNAi agent with a wild-type sequence which does not span the mutation, and/or administered a KRAS RNAi agent with a sequence corresponding to the one or more mutations.

[00159] In some embodiments, the disclosure encompasses a method involving the steps of identifying a patient with a KRAS-related disease, isolating a nucleic acid encoding or corresponding to the KRAS protein or gene from the patient, determining the sequence of the nucleic acid to determine if there is a mutation in the KRAS gene, and, if the sequence indicates a mutation in KRAS, producing a KRAS RNAi agent with a sequence which corresponds to the mutation, and administering the KRAS RNAi agent in a therapeutically effective amount to treat or ameliorate the KRAS-related disease. In some embodiments, the KRAS RNAi agent is administered along with or as part of a treatment regimen with another disease treatment appropriate to the KRAS-related disease.

[00160] The process of RAS exchanging the bound nucleotide is facilitated by guanine nucleotide exchange factors (GEFs) and GTPase activating proteins (GAPs). As per its classification, Ras has an intrinsic GTPase activity, which means that the protein on its own will hydrolyze a bound GTP molecule into GDP. However this process is too slow for efficient function, and hence the GAP for Ras, RasGAP, may bind to and stabilize the catalytic machinery of Ras, supplying additional catalytic residues ("arginine finger") such that a water molecule is optimally positioned for nucleophilic attack on the gamma-phosphate of GTP. An inorganic phosphate is released and the Ras molecule is now bound to a GDP. Since the GDP-bound form is "off" or "inactive" for signaling, GTPase Activating Protein inactivates Ras by activating its GTPase activity. Thus, GAPs accelerate Ras inactivation.

[00161] GEFs catalyze a "push and pull" reaction which releases GDP from Ras. They insert close to the P-loop and magnesium cation binding site and inhibit the interaction of these with the

gamma phosphate anion. Acidic (negative) residues in switch II "pull" a lysine in the P-loop away from the GDP, which "pushes" switch I away from the guanine. The contacts holding GDP in place are broken and it is released into the cytoplasm. Because intracellular GTP is abundant relative to GDP (approximately 10 fold more). GTP predominantly re-enters the nucleotide binding pocket of Ras and reloads the spring. Thus GEFs facilitate Ras activation. Well known GEFs include Son of Sevenless (Sos) and cdc25 which include the RasGEF domain.

[00162] The balance between GEF and GAP activity determines the guanine nucleotide status of Ras, thereby regulating Ras activity.

[00163] In the GTP-bound conformation, Ras has high affinity for numerous effectors which allow it to carry out its functions. These include PI3K. Other small GTPases may bind adaptors such as arfaptin or second messenger systems such as adenylyl cyclase. The Ras binding domain is found in many effectors and invariably binds to one of the switch regions, because these change conformation between the active and inactive forms. However, they may also bind to the rest of the protein surface.

[00164] In various embodiments, the present disclosure encompasses KRAS RNAi agents that modulate the amount of KRAS and/or the amount of activated KRAS in a cell. In various other embodiments, the present disclosure encompasses a composition or pharmaceutical composition comprising and/or a method of treatment involving one or more KRAS RNAi agents and a second agent (e.g., another RNAi agent, antibody, or small molecule) which targets a factor which interacts with KRAS (e.g., PI3K, GAP, etc.).

[00165] **Ras in cancer**

[00166] Mutations in the Ras family of proto-oncogenes are very common. A pharmacological approach that curtails Ras activity can inhibit certain cancer types. Ras point mutations are the single most common abnormality of human proto-oncogenes. Pathologic Basis of Disease 8th ed. 2010. p. 282. Ras inhibitor trans-farnesylthiosalicylic acid (FTS, Salirasib) exhibits profound anti-oncogenic effects in many cancer cell lines. Rotblat et al. 2008. Methods Enzymol 439: 467–89; and Blum et al. 2005. Cancer Research 65. 3: 999–1006.

[00167] In various embodiments, KRAS RNAi agents disclosed herein can be introduced into tumor cells with a point mutation in KRAS or other mutation causing an over-expression or hyper-activity of KRAS. Such cells are termed "KRAS-defective" cells.

[00168] Inappropriate activation of the gene has been shown to play a key role in signal transduction, proliferation and malignant transformation. Lodish et al. 2000. Chapter 25. Cancer. Molecular cell biology. 4th ed. San Francisco: W.H. Freeman.

[00169] Mutations in a number of different genes as well as KRAS itself can also have this effect. Oncogenes such as p210BCR-ABL or the growth receptor erbB are upstream of Ras, so if they are constitutively activated their signals will transduce through Ras.

[00170] The tumour suppressor gene NF1 encodes a Ras-GAP – its mutation in neurofibromatosis will mean that Ras is less likely to be inactivated. RNAi agents targeting KRAS can thus be used in conjunction with other agents (e.g., other RNAi agents) which target other factors which effect KRAS and its various pathways.

[00171] Finally, Ras oncogenes can be activated by point mutations so that the GTPase reaction can no longer be stimulated by GAP – this increases the half life of active Ras-GTP mutants.

[00172] In various embodiments, the KRAS RNAi agent can be administered to patients having a KRAS-related diseases involving a mutation outside KRAS, such as in p210BCR-ABL, erbB, or NF1. In various other embodiments, the present disclosure encompasses a composition or pharmaceutical composition or treatment method involving both one or more KRAS RNAi agents and one or more agents (e.g., a RNAi agent, antibody or small molecule) which targets another factor which causes inappropriate activation of KRAS, such as in p210BCR-ABL, erbB, or NF1.

[00173] **Constitutively active Ras**

[00174] Constitutively active Ras (Ras^D) is one which contains mutations that prevent GTP hydrolysis, thus locking Ras in a permanently 'On' state.

[00175] The most common mutations are found at residue G12 in the P-loop and the catalytic residue Q61.

[00176] The glycine to valine mutation at residue 12 renders the GTPase domain of Ras insensitive to inactivation by GAP and thus stuck in the "on state". Ras requires a GAP for inactivation as it is a relatively poor catalyst on its own, as opposed to other G-domain-containing proteins such as the alpha subunit of heterotrimeric G proteins.

[00177] Residue 61 is responsible for stabilizing the transition state for GTP hydrolysis. Because enzyme catalysis in general is achieved by lowering the energy barrier between substrate and product, mutation of Q61 to K necessarily reduces the rate of intrinsic Ras GTP hydrolysis to physiologically meaningless levels.

[00178] In various embodiments, the present disclosure pertains to a method of treatment of a patient having or susceptible to a KRAS-related disease, wherein the KRAS is constitutively active.

[00179] **KRAS sequences in various species**

[00180] The sequence of KRAS gene has determined for various species, including Human (HGNC: 6407; NM_004985.3); Mouse (MGI:96680); and Rat (RGD:2981). A RNAi agent specific to KRAS can be designed such that the sequence thereof completely matches that of the mRNA corresponding to the human KRAS gene and the homologous gene from a test animal. This is advantageous when developing a therapeutic RNAi agent since the same RNAi agent can be used in both a test animal (e.g., rat, mouse, or cynomolgus monkey, etc.) and a human.

[00181] The KRAS sequence in cynomolgus monkey (*Macaca fascicularis*, or "cyno") has been partially determined. Shown below are the partial cyno sequence and comparisons beween portions of the cyno and human KRAS sequences. NM_004985 KRAS, v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog consensus -- target length = 5312, consensus length = 4474, 23 contigs (longest is 775) 113 mismatches, 1651.87410068346 reads, coverage: max = 96, mean = 13.158; consensus consistency = 99.41%, target/consensus conservation 97.47%.

[00182]

[00183] KRAS cynomolgus sequence:

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 60

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNAGGCACTG 120

AAGGCGGCGG CGGGGCCAGA GGCTCAGCGG CTCCCCGGGG CGGGAGAGAG NNNNNNNNNN 180

NNNNNNNNNN NNNNNNNNNN NNNNAGTTGG AGCTGGTGGG GTAGGCAAGA GTGCCTTGAC 240

NNNNNNGCTA ATTCAGAATC ATTTTGTGGA CGAATATGAT CCAACAATAG AGGATTCCTA 300

CAGGAAGCAA GTAGTAATTG ATGGAGAAAC CTGTCTCTTG GATATTCTCG ACACAGCAGG 360

TCAAGAGGAG TACAGTGCAA TGAGGGACCA GTACATGAGG ACTGGGGAGG GCTTTCTTTG 420

TGTATTTGCC ATAAATAATA CTAAATCATT TGAAGATATT CACCATTATA GAGAACAAAT 480

TAAAAGAGTT AAGGACTCTG AAGATGTACC TATGGTCCTA GTAGGAAATA AATGTGATTT 540

GCCTTCTAGA ACAGTAGACA CAAAACAGGC TCAGGACTTA GCAAGAAGTT ACGGAATTCC 600

TTTTATTGAA ACATCAGCAA AGACAAGACA GGGTGTTGAT GATGCCTTCT ATACATTAGT 660

TCGAGAAATT CGAAAACATA AAGAAAAGAT GAGCAAAGAT GGTAAAAAGA AGAAAAAGAA 720

GTCAAAGACA AAGTGTGTAA TTATGTAAAT ACAATTTGTA CTTTTTTCTT AAGGCATACT 780

AGTAAAAGTG GTAATTTTTG TACATTACAC TAAATTATTA GCATTTGTTT TAGCATTACC 840

TAATTTTTTT CCTGCTCCAT GCAGACTGTT AGCTTTTACC TTAAATGCTT ATTTTAAAAT 900

GACAGTGGAA GCTTTTTTTT CCTCTAAGTG CCAGTATTCC CAGAGTTTTG ATTTTTGAAC 960

TAGCAATGCC TGTGAAAAAG AAACTGAATA CCTAAGATTT CTGTCTTGGG GTTTTTGGTG 1020

CNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNAATT 1080

AATGAAGCTT CTGAATCATC CCTATTCTGT GTTTTATCTA GTCACATAAA TGGATTAATT 1140

ACTAATTTCA GTTGAGACCT TCTAATTGGT TTTTACTGAA ACATTGAGGG AACACAAANN 1200

NNNNNNNNNN NNNNNNNNNN NNNNTCTAGG CATCATGTCC TATAGTTTGT CATCCCTGAT 1260

GAATGTAAAG TTACACTGTT CACAAAGGTT TTGTTCCCTT TCCACTGCTA TTAGTCATGG 1320

TCACTCTCCC CGNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNTGGAA AAAAATTACA 1380

AGTCAATGGA AACTATTATA AGGCCGTTTC CTTTTCACAT TAGATAAATT ACTATAAAGA 1440

CTCCTAATAG CTTTTCCTGT TAAGGCAGAC CCAGTATGAA ATGGGGATTN NNNNNNNNNN 1500

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TGACATTAAA AGATTATTTG GGCCAGTTAT AGCTTAGTAG GTGTTGAAGA GACCAAGGTT 1740

GCATGGCCAG GCCCTGTGTG AACCTTTGAG CTTTCATAGA GAGTTTCACA GCATGGACTG 1800

TGTCCCCATG GTCATCCAGT GTTGTCATGC ATTGGTTAGT CAAAATGGGG AGGGACTAGG 1860

ACAGTTTGGA TAGGTCAACA AGATACATTC TCACTCTGTG GTGGTCCTGC TGACAAATCA 1920

AGAGCATTGC TTTTGTTTTT TAAGAAAATG AACTCTTTTT TAAAAATTAC TTTTAAATAT 1980

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NNNNNNNNNN NNNAAGTTTT ACAATCTCTA GGTTTGGCTA GTTCTCTTAA CACTGGTTAA 2100

ATTAACATTT CATAAACACT TTTCAAGNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 2160

NNNNNNNNNN NNNNNNNNNN NNNATTTAAA ATGTTACTTA TTTTAAAATA TATGAAATGA 2220

GATGGCATGG TGAGGTGAAA GTATCACTGG ACTANNAAGA AGGTGACTTA GGTTCTAGAT 2280

AGTTGTCTTT TAGGACTCTG ATTTTGAGGA CATCACTTAC TATCCATTTC TTCATGTTAA 2340

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN TTTTTACAAC TATGTGATTT ATATTCCGTT 2400

TACATGAGGA TACACTTATT TGTCAAGCTC AGCACAATCT AAAAATTTTT AACCTATGTT 2460

ACACCATCTT CAGTGCCAAT CTTGGGCAAA ATTGTGCAAG AGGTGAAGTT TATATTTGAA 2520

TATCCATTCT CGTTTTAGGA CTCTCCTTCC ATGTTAGTGT CATCTTGCCT GCCTACCTTC 2580

CACATGCCCC ATGACTTGAT GCAGTTTTAA TACTTCTAAT TCCCCTAACC ATAAGATTTA 2640

CTGCTGCTAT GGATATCTCC ATGAAGTTTT CCCNNNNNNN NNNNNNNNNN NNNNNNNNNN 2700

NNNNNNNNNN NNNNNNNNNN NGAGAATCTG ACAGATACCA TAATGGGATT TGACCTAATC 2760

ACTAATTTTC AGGTGGTGGC CGATCCTTTG AAAATATCTC TGCTGCCCAA TCCATTAGCG 2820

ACAGTAGGAT TTTTCAGACC TGGTATGAAT AGACAGAACC CTATCCAGTG GAAGGAGAAT 2880

TTAATAAAGA TAGTACTGAA ATAATTCCTA AGGTAATCTA CAACTAGGAC TACTCCTGGT 2940

AACAGTAATA CATTCCATTG TTTTAGTAAC CAGAAATNNN NNNNNNNNNN NNNNNNNNNN 3000

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNCCAGGCTG 3060

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CGTGCCTCGG CATCCTGAGT AGCTGGGATT ACAGGCATGT GCCNCCACAC TCAACTAATT 3180

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NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 3600

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNTTACTGTA CACATTAAGG 3660

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TTTAACTGAG TCACACTGCA TAGGAATTTA GAACCTAACT TTTATAGGTT ATCAAAACTG 4320

TTGCCTCCAT TGCACAATTT TGTCCTAATA CATACATGGA GACTTTGTGG GGCATGTTAA 4380

GTTACAGTTT GCACAAGTTC ATCTCATTTG TATTCCATTG ATTTTTTTTT TCTTCTAAAC 4440

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NNTCTGACGA TTTCCATTTG TCAAAAAGTA ATGATTTCTT GATAATTATG TAGTAATGTT 4560

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AACATGCACA TTTTGTACAT TGTGCTTTCT TTTGTGGGAC ATATGCAGTG TGATCCAGTT 5100

GTTTTCCATC ATTTGGTTGC GCTGACCTAG GAATGTTGGT CATATCAAAC ATTAAAAATG 5160

ACCACTCTTT TAATTGAAAT TAACTTTTAA ATGTTTATAG GAGTATGTGC TGTGAAGTGA 5220

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[00184] AAAATAGTTA CAGTGACAAA AAAAAAAANN NN 5312 [SEQ ID NO: 1709].

[00185]

[00186] Comparisons between portions of the human sequence and the cyno sequence are presented below.

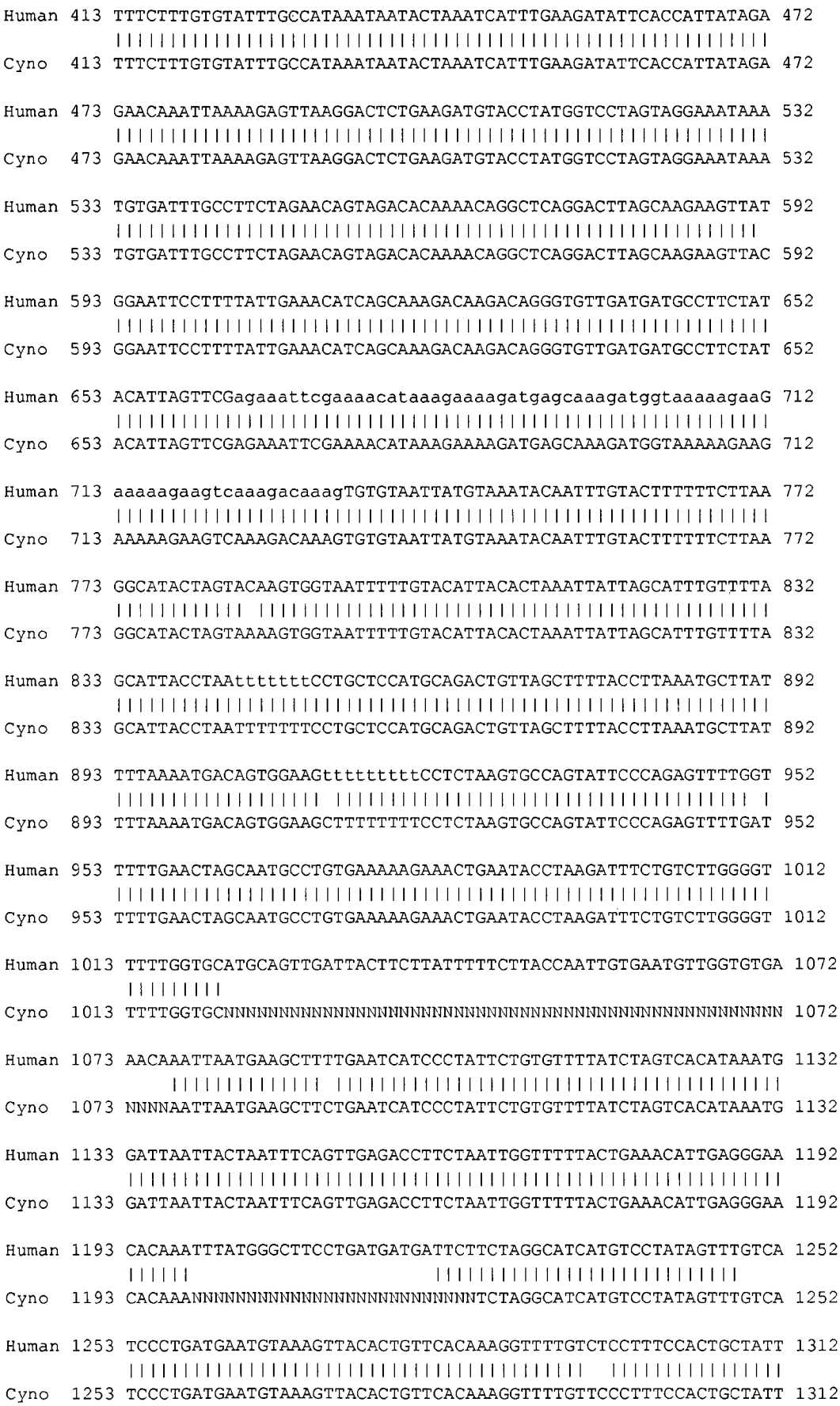
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Human 113 AGGCACTGAAGGCGGCGGCGGGGCCAGAGGCTCAGCGGCTCCCAGGTGCGGGAGAGAGGC 172
          ||||||||||||||||||||||||||||||||||||||||||||| || ||||||||||
Cyno  113 AGGCACTGAAGGCGGCGGCGGGGCCAGAGGCTCAGCGGCTCCCCGGGGCGGGAGAGAGNN 172

Human 173 CTGCTGAAAATGACTGAATATAAACTTGTGGTAGTTGGAGCTGGTGGCGTAGGCAAGAGT 232
                                    ||||||||||||||| ||||||||||||
Cyno  173 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAGTTGGAGCTGGTGGGGTAGGCAAGAGT 232

Human 233 GCCTTGACGATACAGCTAATTCAGAATCATTTTGTGGACGAATATGATCCAACAATAGAG 292
          ||||||||      ||||||||||||||||||||||||||||||||||||||||||||||
Cyno  233 GCCTTGACNNNNNNGCTAATTCAGAATCATTTTGTGGACGAATATGATCCAACAATAGAG 292

Human 293 GATTCCTACAGGAAGCAAGTAGTAATTGATGGAGAAACCTGTCTCTTGGATATTCTCGAC 352
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  293 GATTCCTACAGGAAGCAAGTAGTAATTGATGGAGAAACCTGTCTCTTGGATATTCTCGAC 352

Human 353 ACAGCAGGTCAAGAGGAGTACAGTGCAATGAGGGACCAGTACATGAGGACTGGGGAGGGC 412
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  353 ACAGCAGGTCAAGAGGAGTACAGTGCAATGAGGGACCAGTACATGAGGACTGGGGAGGGC 412
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Human 413 TTTCTTTGTGTATTTGCCATAAATAATACTAAATCATTTGAAGATATTCACCATTATAGA 472
Cyno 413 TTTCTTTGTGTATTTGCCATAAATAATACTAAATCATTTGAAGATATTCACCATTATAGA 472
Human 473 GAACAAATTAAAAGAGTTAAGGACTCTGAAGATGTACCTATGGTCCTAGTAGGAAATAAA 532
Cyno 473 GAACAAATTAAAAGAGTTAAGGACTCTGAAGATGTACCTATGGTCCTAGTAGGAAATAAA 532
Human 533 TGTGATTTGCCTTCTAGAACAGTAGACACAAAACAGGCTCAGGACTTAGCAAGAAGTTAT 592
Cyno 533 TGTGATTTGCCTTCTAGAACAGTAGACACAAAACAGGCTCAGGACTTAGCAAGAAGTTAC 592
Human 593 GGAATTCCTTTTATTGAAACATCAGCAAAGACAAGACAGGGTGTTGATGATGCCTTCTAT 652
Cyno 593 GGAATTCCTTTTATTGAAACATCAGCAAAGACAAGACAGGGTGTTGATGATGCCTTCTAT 652
Human 653 ACATTAGTTCGagaaattcgaaaacataaagaaaagatgagcaaagatggtaaaaagaaG 712
Cyno 653 ACATTAGTTCGAGAAATTCGAAAACATAAAGAAAAGATGAGCAAAGATGGTAAAAAGAAG 712
Human 713 aaaaagaagtcaaagacaaagTGTGTAATTATGTAAATACAATTTGTACTTTTTTCTTAA 772
Cyno 713 AAAAAGAAGTCAAAGACAAAGTGTGTAATTATGTAAATACAATTTGTACTTTTTTCTTAA 772
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Human 833 GCATTACCTAATttttttCCTGCTCCATGCAGACTGTTAGCTTTTACCTTAAATGCTTAT 892
Cyno 833 GCATTACCTAATTTTTTTCCTGCTCCATGCAGACTGTTAGCTTTTACCTTAAATGCTTAT 892
Human 893 TTTAAAATGACAGTGGAAGttttttttttCCTCTAAGTGCCAGTATTCCCAGAGTTTTGGT 952
Cyno 893 TTTAAAATGACAGTGGAAGCTTTTTTTTCCTCTAAGTGCCAGTATTCCCAGAGTTTTGAT 952
Human 953 TTTTGAACTAGCAATGCCTGTGAAAAAGAAACTGAATACCTAAGATTTCTGTCTTGGGGT 1012
Cyno 953 TTTTGAACTAGCAATGCCTGTGAAAAAGAAACTGAATACCTAAGATTTCTGTCTTGGGGT 1012
Human 1013 TTTTGGTGCATGCAGTTGATTACTTCTTATTTTTCTTACCAATTGTGAATGTTGGTGTGA 1072
Cyno 1013 TTTTGGTGCNNN

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Human 1313 AGTCATGGTCACTCTCCCCAAAATATTATATTTTTTCTATaaaaagaaaaaaatggaaaA 1372
           ||||||||||||||||||                                  |||||||
Cyno  1313 AGTCATGGTCACTCTCCCCGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNTGGAAAA 1372

Human 1373 aaaTTACAAGGCAATGGAAACTATTATAAGGCCATTTCCTTTTCACATTAGATAAATTAC 1432
           |||||||||| ||||||||||||||||||||| |||||||||||||||||||||||||||
Cyno  1373 AAATTACAAGTCAATGGAAACTATTATAAGGCCGTTTCCTTTTCACATTAGATAAATTAC 1432

Human 1433 TATAAAGACTCCTAATAGCTTTTCCTGTTAAGGCAGACCCAGTATGAAATGGGGATTATT 1492
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  1433 TATAAAGACTCCTAATAGCTTTTCCTGTTAAGGCAGACCCAGTATGAAATGGGGATTNNN 1492

Human 1493 ATAGCAACCATTTTGGGGCTATATTTACATGCTACTAAATTTTTATAATAATTGAAAAGA 1552
                                        ||||||||||||||||||||  |
Cyno  1493 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAATTTTTATAATAATTGAAATAA 1552

Human 1553 TTTTAACAAGTATAAAAAATTCTCATAGGAATTAAATGTAGTCTCCCTGTGTCAGACTGC 1612
           |||||||| |||||||||||||||||||||||||||||||||||||||||||||||| |||
Cyno  1553 TTTTAACATGTATAAAAAATTCTCATAGGAATTAAATGTAGTCTCCCTGTGTCAGATTGC 1612

Human 1613 TCTTTCATAGTATAACTTTAAATCTTTTCTTCAACTTGAGTCTTTGAAGATAGTTTTAAT 1672
           |||||||||||||||||||||||||||||||||||| |||||||||| |||||||||
Cyno  1613 TCTTTCATAGTATAACTTTAAATCTTTTCTTCAACTTCAGTCTTTGAAGGTAGTTTTAAT 1672

Human 1673 TCTGCTTGTGACATTAAAAGATTATTTGGGCCAGTTATAGCTTATTAGGTGTTGAAGAGA 1732
           |||||||||||||||||||||||||||||||||||||||||| ||||||||||||||
Cyno  1673 TCTGCTTGTGACATTAAAAGATTATTTGGGCCAGTTATAGCTTAGTAGGTGTTGAAGAGA 1732

Human 1733 CCAAGGTTGCAAGGCCAGGCCCTGTGTGAACCTTTGAGCTTTCATAGAGAGTTTCACAGC 1792
           |||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  1733 CCAAGGTTGCATGGCCAGGCCCTGTGTGAACCTTTGAGCTTTCATAGAGAGTTTCACAGC 1792

Human 1793 ATGGACTGTGTCCCCACGGTCATCCAGTGTTGTCATGCATTGGTTAGTCAAAATGGGGAG 1852
           |||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
Cyno  1793 ATGGACTGTGTCCCCATGGTCATCCAGTGTTGTCATGCATTGGTTAGTCAAAATGGGGAG 1852

Human 1853 GGACTAGGGCAGTTTGGATAGCTCAACAAGATACAATCTCACTCTGTGGTGGTCCTGCTG 1912
           |||||||| |||||||||||| |||||||||||| |||||||||||||||||||||||
Cyno  1853 GGACTAGGACAGTTTGGATAGGTCAACAAGATACATTCTCACTCTGTGGTGGTCCTGCTG 1912

Human 1913 ACAAATCAAGAGCATTGCTTTTGTTTCTTAAGAAAACAAACTCTTTTTTAAAAATTACTT 1972
           |||||||||||||||||||||||||| ||||||||| ||||||||||||||||||||||
Cyno  1913 ACAAATCAAGAGCATTGCTTTTGTTTTTTAAGAAAATGAACTCTTTTTTAAAAATTACTT 1972

Human 1973 TTAAATATTAACTCAAAAGTTGAGATTTTGGGGTGGTGGTGTGCCAAGACATTAAttttT 2032
           |||||||||||||||||||||||||||||||||| |||||| ||||||||||||||||||
Cyno  1973 TTAAATATTAACTCAAAAGTTGAGATTTTGGGGGGGTGGTATGCCAAGACATTAATTTTT 2032

Human 2033 tttttAAACAATGAAGTGAAAAAGTTTTACAATCTCTAGGTTTGGCTAGTTCTCTTAACA 2092
           ||                 |||||||||||||||||||||||||||||||||||||||
Cyno  2033 TTNNNNNNNNNNNNNNNNNNNAAGTTTTACAATCTCTAGGTTTGGCTAGTTCTCTTAACA 2092

Human 2093 CTGGTTAAATTAACATTGCATAAACACTTTTCAAG 2127 [SEQ ID NO: 1710]
           |||||||||||||||||| ||||||||||||||||||
Cyno  2093 CTGGTTAAATTAACATTTCATAAACACTTTTCAAG 2127 [SEQ ID NO: 1711]


Human 2184  atttaaaatgttacttattttaaaataaatGAAGTGAGATGGCATGGTGAGGTGAAAGTA 2243
            |||||||||||||||||||||||||||| ||||| ||||||||||||||||||||||||||
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Cyno  2184  ATTTAAAATGTTACTTATTTTAAAATATATGAAATGAGATGGCATGGTGAGGTGAAAGTA 2243

Human 2244  TCACTGGACTAGGAAGAAGGTGACTTAGGTTCTAGATAGGTGTCTTTTAGGACTCTGATT 2303
            ||||||||||| |||||||||||||||||||||||| ||||||||||||||||||||
Cyno  2244  TCACTGGACTANNAAGAAGGTGACTTAGGTTCTAGATAGTTGTCTTTTAGGACTCTGATT 2303

Human 2304  TTGAGGACATCACTTACTATCCATTTCTTCATGTTAAAAGAAGTCATCTCAAACTCTTAG 2363
            |||||||||||||||||||||||||||||||||||
Cyno  2304  TTGAGGACATCACTTACTATCCATTTCTTCATGTTAANNNNNNNNNNNNNNNNNNNNNN 2363

Human 2364  ttttttttttttACAACTATGTAATTTATATTCCATTTACATAAGGATACACTTATTTGT 2423
                    |||||||||||||| |||||||||| ||||||| ||||||||||||||||
Cyno  2364  NNNNNNNTTTTTACAACTATGTGATTTATATTCCGTTTACATGAGGATACACTTATTTGT 2423

Human 2424  CAAGCTCAGCACAATCTGTAAATTTTTAACCTATGTTACACCATCTTCAGTGCCAGTCTT 2483
            |||||||||||||||||  |||||||||||||||||||||||||||||||||| ||||
Cyno  2424  CAAGCTCAGCACAATCTAAAAATTTTTAACCTATGTTACACCATCTTCAGTGCCAATCTT 2483

Human 2484  GGGCAAAATTGTGCAAGAGGTGAAGTTTATATTTGAATATCCATTCTCGTTTTAGGACTC 2543
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  2484  GGGCAAAATTGTGCAAGAGGTGAAGTTTATATTTGAATATCCATTCTCGTTTTAGGACTC 2543

Human 2544  TTCTTCCATATTAGTGTCATCTTGCCTCCCTACCTTCCACATGCCCCATGACTTGATGCA 2603
            | ||||||| |||||||||||||||| |||||||||||||||||||||||||||||||
Cyno  2544  TCCTTCCATGTTAGTGTCATCTTGCCTGCCTACCTTCCACATGCCCCATGACTTGATGCA 2603

Human 2604  GTTTTAATACTTGTAATTCCCCTAACCATAAGATTTACTGCTGCTGTGGATATCTCCATG 2663
            ||||||||||| |||||||||||||||||||||||||||||||| ||||||||||||||
Cyno  2604  GTTTTAATACTTCTAATTCCCCTAACCATAAGATTTACTGCTGCTATGGATATCTCCATG 2663

Human 2664  AAGTTTTCCCACTGAGTCACATCAGAAATGCCCTACATCTTATTTCCTCAGGGCTCAAGA 2723
            |||||||||                                                ||
Cyno  2664  AAGTTTTCCCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGA 2723

Human 2724  GAATCTGACAGATACCATAAAGGGATTTGACCTAATCACTAATTTTCAGGTGGTGGCTGA 2783
            |||||||||||||||||| |||||||||||||||||||||||||||||||||||| ||
Cyno  2724  GAATCTGACAGATACCATAATGGGATTTGACCTAATCACTAATTTTCAGGTGGTGGCCGA 2783

Human 2784  TGCTTTGAACATCTCTTTGCTGCCCAATCCATTAGCGACAGTAGGATTTTTCAAACCTGG 2843
            | ||||||| || ||| ||||||||||||||||||||||||||||||||||| ||||||
Cyno  2784  TCCTTTGAAAATATCTCTGCTGCCCAATCCATTAGCGACAGTAGGATTTTTCAGACCTGG 2843

Human 2844  TATGAATAGACAGAACCCTATCCAGTGGAAGGAGAATTTAATAAAGATAGTGCTGAAAGA 2903
            |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||| |
Cyno  2844  TATGAATAGACAGAACCCTATCCAGTGGAAGGAGAATTTAATAAAGATAGTACTGAAATA 2903

Human 2904  ATTCCTTAGGTAATCTATAACTAGGACTACTCCTGGTAACAGTAATACATTCCATTGTTT 2963
            |||||| |||||||||| ||||||||||||||||||||||||||||||||||||||||
Cyno  2904  ATTCCTAAGGTAATCTACAACTAGGACTACTCCTGGTAACAGTAATACATTCCATTGTTT 2963

Human 2964  TAGTAACCAGAAAT 2977 [SEQ ID NO: 1712]
            |||||||||||||
Cyno  2964  TAGTAACCAGAAAT 2977 [SEQ ID NO: 1713]


Human 3053 CCAGGCTGGAATGCAGTGGCGCCATCTCAGCTCACTGCAACCTCCATCTCCCAGGTTCAA 3112
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  3053 CCAGGCTGGAATGCAGTGGCGCCATCTCAGCTCACTGCAACCTCCATCTCCCAGGTTCAA 3112
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Human 3113 GCGATTCTCGTGCCTCGGCCTCCTGAGTAGCTGGGATTACAGGCGTGTGCCACTACACTC 3172
Cyno  3113 GCGATTCTCGTGCCTCGGCATCCTGAGTAGCTGGGATTACAGGCATGTGCCNCCACACTC 3172

Human 3173 AACTAATTTTTGTATTTTTAGGAGAGACGGGGTTTCACCCTGTTGGCCAGGCTGGTCTCG 3232
Cyno  3173 AACTAATTTTTGTAGTTTTAGGAGAGACAGGGTTTCACCCTATTGGCCAGGCTGGTCTCG 3232

Human 3233 AACTCCTGACCTCAAGTGATTCACCCACCTTGGCCTCATAAACCTGTTTTGCAGAACTCA 3292
Cyno  3233 AACTCCTGACCTCAAGTGATTCACCCACCTNNNCCTCATAAAGCCGTTTTGCAGAACTCA 3292

Human 3293 TTTATTCAGCAAATATTTATTGAGTGCCTACCAGATGCCAGTCACCGCACAAGGCACTGG 3352
Cyno  3293 TTTATTCAGCAAATATTTATTGAGTGCCTACCAGATGCCAGTCATTTCACAAGGCACTGG 3352

Human 3353 GTATATGGTATCCCCAAACAAGAGACATAATCCCGGTCCTTAGGTAGTGCTAG 3405
Cyno  3353 GTATATGGTATCCCCAAACAAGAGACATAATCCTGGTCCTTAGCTAGTGCTAG 3405

Human 3643 TTACTGTACACATTAAGGTGTATGTCAGATATTCATATTGACCCAAATGTGTAATATTCC 3702
Cyno  3643 TTACTGTACACATTAAGGTGTATGTCAGATATCCATATTGAANNNNNNNNNNNNNNNNNN 3702

Human 3703 AGTTTTCTCTGCATAAGTAATTAAAATATACTTAAAAATTAATAGTTTTATCTGGGTACA 3762
Cyno  3703 NNNNNNNNNNNNNNNNATAATTAAAATATACTTAAAAATTAATAGTTTTATCTGGGTACA 3762

Human 3763 AATAAACAGGTGCCTGAACTAGTTCACAGACAAGGAAACTTCTATGTAAAAATCACTATG 3822
Cyno  3763 AACAAACAGGTGCCTGAACTAGTTCACAGACAAGGAAACTTCTATGTAAAAATCAGTATG 3822

Human 3823 ATTTCTGAATTGCTATGTGAAACTACAGATCTTTGGAACACTGTTTAGGTAGGGTGTTAA 3882
Cyno  3823 ATTTNNNNNNNNNNNNGTGAAACTACAGATCTTTGGAACATTGTTTAGATAGGGTGTTAA 3882

Human 3883 GACTTACACAGTACCTCGTTTCTACACAGAGAAAGAAATGGCCATACTTCAGGAACTGCA 3942
Cyno  3883 GACTTACACAGTACCACGTTTCTACACACAGAAAGAAATGGCCATACTTCAGGAACTGCA 3942

Human 3943 GTGCTTATGAGGGGATATTTAGGCCTCTTGAATTTTTGATGTAGATGGGCAttttttttAA 4002
Cyno  3943 GTGCTAATGAGGGGATATTTAGGCCTCTTGAATTTTTGATGTAGATGGGCATTTTTTTAA 4002

Human 4003 GGTAGTGGTTAATTACCTTTATGTGAACTTTGAATGGTTTAACAAAAGATTTGTTTTTGT 4062
Cyno  4003 GGTANNTGGTAATTACCTTTATGTGAACTTTGAATGGTTTAACAAAAGATTTGTTTTTGT 4062

Human 4063 AGAGATTTTAAAGGGGGAGAATTCTAGAAATAAATGTTACCTAATTATTACAGCCTTAAA 4122
Cyno  4063 AGAGATTTTAAAGGGGGAGAATGCTAGAAATAAATGTTATCTAANNNNNNNNCGCCTTAAA 4122

Human 4123 GACAAAAATCCTTGTTGAAGttttttttaaaaaaaGCTAAATTACATAGACTTAGGCATTA 4182
Cyno  4123 GATAAAAATCCTTGTTGAAGTTTTTTAAAAAAAAGCTAAATTACATAGTCTTAGGCATTA 4182

Human 4183 ACATGTTTGTGGAAGAATATAGCAGACGTATATTGTATCATTTGAGTGAATGTTCCCAAG 4242
Cyno  4183 ACATGTTTGTGGAAGAATATAGCACACATATATTGTATCATTTGAGTGAATATTCCCAAA 4242
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Human 4243 TAGGCATTCTAGGCTCTATTTAACTGAGTCACACTGCATAGGAATTTAGAACCTAACTTT 4302
Cyno  4243 TAGGCATTCTAGGCTCTATTTAACTGAGTCACACTGCATAGGAATTTAGAACCTAACTTT 4302

Human 4303 TATAGGTTATCAAAACTGTTGTCACCATTGCACAATTTTGTCCTAATATATACATAGAAA 4362
Cyno  4303 TATAGGTTATCAAAACTGTTGCCTCCATTGCACAATTTTGTCCTAATACATACATGGAGA 4362

Human 4363 CTTTGTGGGGCATGTTAAGTTACAGTTTGCACAAGTTCATCTCATTTGTATTCCATTGAT 4422
Cyno  4363 CTTTGTGGGGCATGTTAAGTTACAGTTTGCACAAGTTCATCTCATTTGTATTCCATTGAT 4422

Human 4423 ttttttttttcttctaaacatttttttcttcaaacagtatataacttttttttaggggatttT 4482
Cyno  4423 TTTTTTTTTCTTCTAAACATTTTTTCTTCAAACAGTATATAACTTTTTTTTAGGGGATTTT 4482

Human 4483 tttttAGACAGCAAAAACTATCTGAAGATTTCCATTTGTCAAAAAGTAATGATTTCTTGA 4542
Cyno  4483 TTTTNNNNNNNNNNNNNNNNTCTGACGATTTCCATTTGTCAAAAAGTAATGATTTCTTGA 4542

Human 4543 TAATTGTGTAGTAATGTTTTTTAGAACCCAGCAGTTACCTTAAAGCTGAATTTATATTTA 4602
Cyno  4543 TAATTATGTAGTAATGTTTTTAAGAACCCAGCAGTTACCTTAAAGCTGAATTTATATTTA 4602

Human 4603 GTAACTTCTGTGTTAATACTGGATAGCATGAATTCTGCATTGAGAAACTGAATAGCTGTC 4662
Cyno  4603 ATAACTTCTGTGTTAATACTGGATAGCATGAATTCTGCATTGAGAAACTGAATAGNNNNN 4662

Human 4663 ATAAAATGAAACTTTCTTTCTAAAGAAAGATACTCACATGAGTTCTTGAAGAATAGTCAT 4722
Cyno  4663 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCATGAGTTCTTGAAGAATAGTCAT 4722

Human 4723 AACTAGATTAAGATCTGTGTTTTAGTTTAATAGTTTGAAGTGCCTGTTTGGGATAATGAT 4782
Cyno  4723 AACTAGATTAAGATCTGTGTTTTAGTTTAATAGTTTGAAGTGCCTGTTTGGGATAATGAT 4782

Human 4783 AGGTAATTTAGATGAATTTAGGGGaaaaaaaaGTTATCTGCAGATATGTTGAGGGCCCAT 4842
Cyno  4783 AGGTAATTTAGATGAATTTAGGGGGAAAAAAAGTTATCTGCAGAAATGTTGAGGGCCCAT 4842

Human 4843 CTCTCCCCCCACACCCCCACAGAGCTAACTGGGTTACAGTGTTTTATCCGAAAGTTTCCA 4902
Cyno  4843 CTCTCCCCACACACCCACATAGAGCTAACTGGGTTACAGTGTTTTATCCGAAAGTTTCCA 4902

Human 4903 ATTCCACTGTCTTGTGTTTTCATGTTGAAAATACTTTTGCATTTTTCCTTTGAGTGCCAA 4962
Cyno  4903 ATTCCACTGTCTTGTGTTTTCATGTTGAAAATACTTTTGCATTTTTCCTTTGAGTGCCAA 4962

Human 4963 TTTCTTACTAGTACTATTTCTTAATGTAACATGTTTACCTGGAATGTATTTTAACTATTT 5022
Cyno  4963 TTTCTTACTAGTACTATTTCTTAATGTAACATGTTTACCTGGAATGTATTTTAACTATTT 5022

Human 5023 TTGTATAGTGTAAACTGAAACATGCACATTTTGTACATTGTGCTTTCTTTTGTGGGACAT 5082
Cyno  5023 TTGTATAGTGTAAACTGAAACATGCACATTTTGTACATTGTGCTTTCTTTTGTGGGACAT 5082

Human 5083 ATGCAGTGTGATCCAGTTGTTTTCCATCATTTGGTTGCGCTGACCTAGGAATGTTGGTCA 5142
Cyno  5083 ATGCAGTGTGATCCAGTTGTTTTCCATCATTTGGTTGCGCTGACCTAGGAATGTTGGTCA 5142
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Human 5143 TATCAAACATTAAAAATGACCACTCTTTTAATTGAAATTAACTTTTAAATGTTTATAGGA 5202
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  5143 TATCAAACATTAAAAATGACCACTCTTTTAATTGAAATTAACTTTTAAATGTTTATAGGA 5202

Human 5203 GTATGTGCTGTGAAGTGATCTAAAATTTGTAATATTTTTGTCATGAACTGTACTACTCCT 5262
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  5203 GTATGTGCTGTGAAGTGATCTAAAATTTGTAATATTTTTGTCATGAACTGTACTACTCCT 5262

Human 5263 AATTATTGTAATGTAATAAAAATAGTTACAGTGACaaaaaaaaaaA 5308
          ||||||||||||||||||||||||||||||||||||||||||||
Cyno  5263 AATTATTGTAATGTAATAAAAATAGTTACAGTGACAAAAAAAAAAA 5308

Human [SEQ ID NO: 1714]

Cyno  [SEQ ID NO: 1715]
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[00187]

[00188] The lowercase letters in the KRAS sequence are an NCBI convention for low-complexity sequences. The matching algorithm frequently excludes these when calculating match scores, as they tend to match against large numbers of things in the genome.

[00189]

[00190] In one embodiment, the KRAS RNAi agent of the present disclosure comprises a sequence which is identical in the all three of human, rat and cyno KRAS mRNAs. This sequence identity across species facilitates animal testing prior to human testing, since the sequence of the RNAi does not need to be modified due to species-specific differences in the target sequence. In one embodiment, the KRAS RNAi agent comprises a sequence which is identical in the human, mouse and cyno KRAS mRNAs. In various embodiments, the KRAS RNAi agent comprises a sequence which is identical in human and mouse, human and rat, and/or human and cyno.

[00191] Additional embodiments of a RNAi agent to KRAS

[00192] The present disclosure pertains to RNAi agents which target human KRAS. In one embodiment, the KRAS RNAi agent comprises a sequence which does not match that of any other mRNA or gene. In one embodiment, the KRAS RNAi agent comprises a sequence which differs from all other known non-KRAS mRNAs or genes by at least 0, 1, 2 or 3 nucleotides. An increase in the number of mismatches between the KRAS RNAi sequence and that of any other gene can decrease the amount of "off-target effects" or the RNAi agent targeting a non-target gene (e.g., a gene that is not KRAS).

[00193] In one embodiment, the KRAS RNAi agent of the present disclosure is administered to a patient in need thereof (e.g., a patient suffering from a KRAS-related disease).

[00194] The patient can also be administered more than one RNAi agent specific to KRAS. In one embodiment, the KRAS RNAi agent(s) of the present disclosure can optionally be administered along with one or more additional pharmaceutical agent appropriate for that disease. In one embodiment, the KRAS RNAi agent(s) of the present disclosure can be optionally administered along with any other appropriate additional treatment, wherein the additional treatment can be a composition (e.g., another agent that can treat a KRAS-related disease such as a cancer treatment) or a method (e.g., surgery to remove a tumor if the KRAS-related disease is a cancer).

[00195] The RNAi agent(s) and additional disease treatment(s) can be administered in any order, simultaneously, concurrently, separately, or sequentially, or in one or multiple doses over time.

[00196] **Additional Definitions**

[00197] For convenience, the meaning of certain terms and phrases used in the specification, examples, and appended claims, are provided below. If there is an apparent discrepancy between the usage of a term in other parts of this specification and its definition provided in this section, the definition in this section shall prevail.

[00198] As used throughout this disclosure, articles such as "a" and "an" refer to one or more than one (at least one) of the grammatical object of the article.

[00199] **RNAi Agent**

[00200] In one embodiment, the present disclosure pertains to a KRAS RNAi agent or other composition comprising at least an antisense nucleic acid sequence complementary to a KRAS nucleic acid (or portion thereof), or pertains to a recombinant expression vector encoding an shRNA or composition comprising the antisense nucleic acid that can function as an RNAi as defined below. As used herein, an "antisense" nucleic acid comprises a nucleotide sequence complementary to a "sense" nucleic acid encoding the KRAS protein (e.g., complementary to the coding strand of a double-stranded DNA, complementary to an mRNA or complementary to the coding strand of a KRAS gene or nucleic acid).

[00201] RNAi agents include, as non-limiting examples, siRNAs (small interfering RNAs), dsRNAs (double stranded RNAs), shRNAs (short hairpin RNAs) and miRNAs (micro RNAs).

[00202] In various embodiments, the present disclosure pertains to any RNAi agent comprising a RNA sequence corresponding to any DNA sequences disclosed herein (e.g., wherein the DNA nucleotides are replaced by the corresponding RNA nucleotide, for example, with T in DNA replaced by U in RNA, and with ribose instead of deoxyribose in the sugar-phosphate backbone).

[00203] In one embodiment, the RNAi comprises a single strand. This single-stranded RNAi agent oligonucleotide or polynucleotide can comprise the sense or antisense strand, as described by Sioud 2005 J. Mol. Biol. 348:1079-1090, and references therein. Thus the disclosure encompasses RNAi agents with a single strand comprising either the sense or antisense strand of an RNAi agent described herein. The disclosure also encompasses RNAi agents comprising a single strand, wherein the single strand comprises the sequences of both the antisense and sense strands of any RNAi agent disclosed herein, e.g., wherein the strands are contiguous, connected by a loop or otherwise linked. Examples of such molecules include those with a hairpin between the sense and anti-sense sequences (e.g., shRNA).

[00204] The RNAi agent(s) of the present disclosure target (e.g., bind to, anneal to, hybridize, etc.) the KRAS mRNA. The use of the RNAi agent specific to KRAS results in a decrease of KRAS activity, level and/or expression, e.g., a "knock-down" (KD) or "knock-out" of the target gene or target sequence. In one embodiment, in the case of a disease state characterized by over-expression or hyper-activity of KRAS, administration of a RNAi agent to KRAS knocks down the KRAS target enough to provide a more normal or therapeutic level of KRAS activity or expression.

[00205] In one embodiment, the RNAi comprises a single strand (such as an shRNA, as described herein).

[00206] In various embodiments, one or both strands contain one or more nicks, i.e., a break or missing bond in the phosphate backbone, such that at least one nucleotide subunit is not covalently linked to the adjacent nucleotide subunit in any given sequence. In some embodiments, the passenger strand is nicked (see, for example, WO 2007/107162). In various embodiments, one or both strands contain one or more gaps, e.g., wherein at least one entire nucleotide subunit is absent from the disclosed sequence. Where a sense or antisense sequence contains a gap, that strand is envisioned to comprise two separate oligonucleotides.

[00207] Particularly useful siRNAs include those which can bind specifically to those regions of the KRAS mRNA that have one or more of the following qualities: binding in the coding segment of KRAS; binding at or near the junction of the 5' untranslated region and the start of the coding segment; binding at or near the translational start site of the mRNA; binding at, across or near junctions of exons and introns; little or no binding to the mRNAs or transcripts of other genes (little or no "off-target effects"); binding to the KRAS mRNA in or near a region or regions that is not double-stranded or a stem region, e.g., those in a loop or single-stranded portion; eliciting little or no immunogenicity; binding in a segment of the KRAS mRNA sequence which is conserved among various animal species (including human, mouse, rat, cyno, etc.), as the presence of a conserved sequence facilitates testing using various laboratory animals; binding to double-stranded region(s) of the mRNA; binding to an AT-rich region (e.g., at least about 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60% AT-rich); and/or lacking particular sequences known or suspected to decrease siRNA activity, e.g., the presence of a GG sequence at the 5' end, which may decrease separation of the double-stranded portion of the siRNA. In one embodiment, the RNAi agent specific to KRAS can be a double-stranded RNA having any one or more of these qualities.

[00208] The term "double-stranded RNA" or "dsRNA," as used herein, refers to a RNAi agent comprising a first and a second strand; e.g., a composition that includes an RNA molecule or complex of molecules having a hybridized duplex region (i.e., a region where the nucleotide bases from the first strand and the second strand are paired) that comprises two anti-parallel and substantially complementary nucleic acid strands, which will be referred to as having "sense" and "antisense" orientations with respect to a target RNA. The antisense strand, with respect to the mRNA target, is also called the "guide" strand, and the sense strand is also called the "passenger" or "anti-guide" strand. The passenger strand can include at least one or more of the following: one or more extra nucleotides (e.g., a bulge or 1 nt loop) compared to the other strand, a nick, a gap, a mismatch, etc., compared to the other strand. In various embodiments, the RNAi agent comprises a first strand and a second strand. In various embodiments, and as used herein and as is clear by context, terminology referring to the first strand refers to the sense strand and the second strand refers to the anti-sense strand as listed in any Table herein. In other embodiments, and as used herein and as is clear by context, the first strand refers to the anti-sense strand, and the second strand refers to the sense strand as listed in any Table herein.

[00209] The duplex region can be of any length that permits specific degradation of a desired target RNA through a RISC pathway, but will typically range from 9 to 36 base pairs ("bp") in length,

e.g., 15-30 bp in length. Considering a duplex between 9 and 36 bp, the duplex can be any length in this range, for example, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 bp and any sub-range therebetween, including, but not limited to 15-30 bp, 15-26 bp, 15-23 bp, 15-22 bp, 15-21 bp, 15-20 bp, 15-19 bp, 15-18 bp, 15-17 bp, 18-30 bp, 18-26 bp, 18-23 bp, 18-22 bp, 18-21 bp, 18-20 bp, 19-30 bp, 19-26 bp, 19-23 bp, 19-22 bp, 19-21 bp, 19-20 bp, 19 bp, 20-30 bp, 20-26 bp, 20-25 bp, 20-24 bp, 20-23 bp, 20-22 bp, 20-21 bp, 20 basepairs, 21-30 bp, 21-26 bp, 21-25 bp, 21-24 bp, 21-23 bp, 21-22 bp, 21 bp, 22 bp, or 23 bp. The dsRNAs generated in the cell by processing with Dicer and similar enzymes are generally in the range of about 19 to about 22 bp in length. One strand of the duplex region of a dsRNA comprises a sequence that is substantially complementary to a region of a target RNA. The two strands forming the duplex structure can be from a single RNA molecule having at least one self-complementary duplex region, or can be formed from two or more separate RNA molecules that hybridize to form the duplex. Where the duplex region is formed from two self-complementary regions of a single molecule, the molecule can have a duplex region separated by a single-stranded chain of nucleotides (herein referred to as a "hairpin loop", e.g., such as found in an shRNA construct) between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure. The hairpin loop can comprise at least one unpaired nucleotide; in some embodiments the hairpin loop can comprise at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 23 or more unpaired nucleotides. Where the two substantially complementary strands of a dsRNA are comprised by separate RNA molecules, those molecules need not, but can, be covalently connected. Where the two strands are connected covalently by a hairpin loop, the construct is generally referred to herein and in the art as a "shRNA". Where the two strands are connected covalently by means other than a hairpin loop, the connecting structure is referred to as a "linker."

[00210]

[00211] RNAi Agents to KRAS comprising mismatches from the disclosed sequences

[00212] Various specific embodiments of a RNAi agent to KRAS are disclosed herein; example sequences are provided in Tables 1, 2 and 3. Specific embodiments of the present disclosure include RNAi agents which comprise sequences differing by 0, 1, 2, or 3 nt (nucleotides) or bp [basepair(s)] (e.g., with 0, 1, 2 or 3 mismatches) from any of the RNAi agents listed in Tables 1 to 6, and modified and unmodified variants thereof.

[00213] A mismatch is defined herein as a difference between the base sequence or length when two sequences are maximally aligned and compared. A mismatch is defined as a position wherein the base of one sequence does not match the base of the other sequence. Thus, a mismatch is counted, for example, if a position in one sequence has a particular base (e.g., A), and the corresponding position on the other sequence has a different base (e.g., G). Substitution of A, for example, with T, C, G or U would constitute a mismatch. Substitution of G with T, A, C or U would also constitute a mismatch. Substitution of C with T, G, A or U would also constitute a mismatch. Substitution of U with A, C or G would constitute a mismatch. Note, however, that on a given strand, a U can be replaced by T (either as RNA or, preferably, DNA, e.g., 2'-deoxy-thymidine); the replacement of a U with a T is not a mismatch as used herein, as either U or T can

pair with A on the opposite strand. The RNAi agent can thus comprise one or more DNA bases, e.g., T. In some cases, in a portion or portions of the RNAi agent, DNA can be used in place of RNA (e.g., in the seed region), to form a DNA-RNA hybrid. See, for example, Yamato et al. 2011 cancer Gene Ther. 18: 587-597. No mismatch is counted between a DNA portion(s) of the RNAi agent and the corresponding target mRNA if basepairing occurs (e.g., between A, G, C, or T in the DNA portion, and the corresponding U, C, G, or A, respectively in the mRNA).

[00214] A mismatch is also counted, e.g., if a position in one sequence has a base (e.g., A), and the corresponding position on the other sequence has no base (e.g., that position is an abasic nucleotide, which comprises a phosphate-sugar backbone but no base). A single-stranded nick in either sequence (or in the sense or anti-sense strand) is not counted as mismatch. Thus, as a non-limiting example, no mismatch would be counted if one sequence comprises the sequence AG, but the other sequence comprises the sequence AG with a single-stranded nick between the A and the G. A nucleotide modification in the sugar or phosphate is also not considered a mismatch. Thus, if one sequence comprises a C, and the other sequence comprises a modified C (e.g., 2'-modification) at the same position, no mismatch would be counted.

[00215] Thus, no mismatches are counted if modifications are made to the sugar, phosphate, or backbone of the RNAi agent without modifying the base. Thus, a sequence of GGACGAAUAUGAUCCAACA (SEQ ID NO: 1) as an RNA and the same sequence as a PNA (peptide nucleic acid) (or TNA or GNA or FANA) have 0 mismatches from each other.

[00216] It is also noted that the sequences of the RNAi agents in Tables 1 to 6 include sequences which comprise modifications, as detailed in Table 3. It is noted that dTdT (2'-deoxy-thymidine-5'-phosphate and 2'-deoxy-thymidine-5'-phosphate), or in some cases, TT or UU, is added as a cap or extension to both 3'-ends, but this cap or extension is not included in the calculation of the total number of mismatches. In addition, in Table 3, a modified sequence can comprise one or more modifications from the corresponding unmodified sequence. In this case, lowercase "c" represents 2'-O-methylcytidine-5'-phosphate, and lowercase "u" represents 2'-O-methyluridine-5'-phosphate. Uppercase "A", "C", "G" and "U" represent the un-modified adenosine-5'-phosphate, cytidine-5'-phosphate, guanosine-5'-phosphate, and uridine-5'-phosphate, respectively. The substitution of modified c for unmodified C does not count as a mismatch in numbering the 0, 1, 2, or 3 mismatches between sequences. This nomenclature is used for all sequences in Tables 1 to 6. Thus, an equal number of mismatches would be calculated (a) between a test sequence and a modified sequence, and (b) between the same test sequence and the corresponding unmodified sequence from the KRAS gene, and (c) between a modified sequence and a differently modified sequence which have the same base sequence.

[00217] In one particular embodiment, the present disclosure comprises a RNAi agent comprising a anti-sense strand comprising at least 15 to 19 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand of: any of the RNAi agents listed in Tables 1 to 6, and modified and unmodified variants thereof.

[00218] The present disclosure pertains to "modified and unmodified variants" of the disclosed sequences.

[00219] An "unmodified variant" of a particular sequence is the corresponding portion of KRAS

without any modifications. Example modified sequences are listed in Tables 1, 2 and 3. The "unmodified variants" of the sequences of Tables 1 to 6 have the identical sequence, without base modifications or terminal dTdT. A given sequence and an "unmodified variant" of it differ by 0 nt (and have no mismatches).

[00220] A "modified variant" of a particular sequence comprises one or more (or one or more fewer) modifications to the backbone, sugar, phosphate or base, but do not have any base substitutions (e.g., G for C, or A for G); thus a given sequence and a modified variant thereof differ by 0 nt (and have no mismatches). As another example, a given sequence as a RNA and the same sequence as a PNA are modified variants of each other and differ by 0 nt (and have no mismatches). Similarly, the same sequence (with no base substitutions) as a locked nucleic acid (LNA), Morpholino, threose nucleic acid (TNA), or glycol nucleic acid (GNA) would be a modified variant which has 0 mismatches.

[00221] As detailed below, substituting a single nucleotide at a given position with a modified version of the same nucleotide would produce a modified variant (with 0 mismatches).

[00222] In another particular embodiment, the RNAi agent comprises a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sense strand of any of the RNAi agents listed in Tables 1 to 6and modified and unmodified variants thereof.

[00223] RNAi agents to KRAS of the present disclosure can be used in RNA interference.

[00224] **Modifications of RNAi Agent Sequences**

[00225] The present disclosure encompasses both unmodified sequences and example modified sequences, such as those disclosed in Tables 1, 2 and 3.

[00226] The present disclosure further encompasses any other modification of a disclosed sequence (e.g., a modified variant).

[00227] For example, the disclosure encompasses a RNAi agent with a substitution of a single nucleotide at a given position with a modified version of the same nucleotide. Thus a nucleotide (A, G, C or U) can be replaced by the corresponding 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5- oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3) w, or 2,6-diaminopurine.

[00228] Additional modified variants include the addition of any other moiety (e.g., a radiolabel or other tag or conjugate) to the RNAi agent; provided that the base sequence is identical, the addition of other moieties produces a "modified variant" (with no mismatches).

[00229] Various sets of modifications can be used. These include the following formats, which

are used in various screens disclosed herein.

A22S26

A22 indicates that All UA as 2'-OMe-U A and all CA as 2'-OMe-C A

S26 indicates that All U as 2'-OMe-U and all C as 2'-OMe-C

All 3' overhangs as 2'-OMe-U 2'-OMe-U

[00230] In addition to these modifications and patterns (e.g, formats) for modifications, other modifications or sets of modifications of the sequences provided can be generated using common knowledge of nucleic acid modification.

[00231] RNA Interference

[00232] RNA interference (RNAi) is a post-transcriptional, targeted gene-silencing technique that uses double-stranded RNA (dsRNA) to degrade messenger RNA (mRNA) containing the same sequence as the dsRNA. The process of RNAi occurs when ribonuclease III (Dicer) cleaves the longer dsRNA into shorter fragments called siRNAs. siRNAs (small interfering RNAs) produced by Dicer are typically about 21 to 23 nucleotides long and comprise about 19 base pair duplexes (though artificial siRNAs or RNAi agents can be shorter or longer, and/or blunt-ended, and/or comprises one or more endcaps). The smaller RNA segments then mediate the degradation of the target mRNA. Dicer has also been implicated in the excision of 21- and 22-nucleotide small temporal RNAs (stRNAs) from precursor RNA of conserved structure that are implicated in translational control. Hutvagner et al. 2001 Science 293: 834. The RNAi response also features an endonuclease complex, commonly referred to as an RNA-induced silencing complex (RISC), which mediates cleavage of single-stranded mRNA complementary to the anti-sense strand of the RNAi agent. Cleavage of the target RNA takes place in the middle of the region complementary to the anti-sense strand of the siRNA duplex.

[00233] In one aspect, an RNA interference agent includes a single-stranded RNA that interacts with a target RNA sequence to direct the cleavage of the target RNA. Without wishing to be bound by theory, the present disclosure contemplates a long double-stranded RNA introduced into plants and invertebrate cells is broken down into siRNA by a Type III endonuclease known as Dicer. Sharp et al. 2001 Genes Dev. 15:485. Dicer, a ribonuclease-III-like enzyme, processes the dsRNA into 19-23 base pair short interfering RNAs with characteristic two base 3' overhangs. Bernstein, et al. 2001 Nature 409:363. The siRNAs are then incorporated into an RNA-induced silencing complex (RISC) where one or more helicases unwind the siRNA duplex, enabling one of the now unpaired siRNA strands to act as a "guide" strand to guide target recognition. Nykanen, et al. 2001 Cell 107:309. Upon binding of the antisense guide strand to the appropriate target mRNA, one or more endonucleases within the RISC cleaves the target to induce silencing. Elbashir, et al. 2001 Genes Dev. 15:188. Thus, in one aspect the present disclosure relates to a single-stranded RNA that promotes the formation of a RISC complex to effect silencing of the target gene.

[00234] Kits for RNAi synthesis are commercially available, e.g., from New England Biolabs and Ambion.

[00235] The RNAi agent(s) of the present disclosure target (e.g., bind to, anneal to, etc.) the KRAS mRNA. The use of the RNAi agent to KRAS results in a decrease of KRAS activity, level and/or expression, e.g., a "knock-down" or "knock-out" of the target gene or target sequence. Particularly, in one embodiment, in the case of a disease state characterized by over-expression or hyper-activity of KRAS, administration of a RNAi agent to KRAS knocks down the KRAS target enough to restore a normal level of KRAS activity.

[00236] A suitable RNAi agent can be selected by any process known in the art or conceivable by one of ordinary skill in the art. For example, the selection criteria can include one or more of the following steps: initial analysis of the KRAS gene sequence and design of RNAi agents; this design can take into consideration sequence similarity across species (human, cynomolgus, mouse, etc.) and dissimilarity to other (non-KRAS) genes; screening of RNAi agents *in vitro* (e.g., at 10 nM in RKO cells); determination of EC50 in RKO cells; determination of viability of cells treated with RNAi agents, including insensitive cells which do not require KRAS for survival, or sensitive cells, which do require KRAS for survival; testing with human PBMC (peripheral blood mononuclear cells), e.g., to test levels of TNF-alpha to estimate immunogenicity, wherein immunostimulatory sequences are less desired; testing in human whole blood assay, wherein fresh human blood is treated with an RNAi agent and cytokine/chemokine levels are determined [e.g., TNF-alpha (tumor necrosis factor-alpha) and/or MCP1 (monocyte chemotactic protein 1)], wherein Immunostimulatory sequences are less desired; determination of gene knockdown *in vivo* using subcutaneous tumors in test animals; KRAS target gene modulation analysis, e.g., using a pharmacodynamic (PD) marker, for example, other factors whose expression is affected by KRAS, wherein KRAS knockdown leads to a dose-dependent reduction of abundance of those components; and optimization of specific modifications of the RNAi agents.

[00237] The dsRNA molecules (RNAi agents) described herein are thus useful in RNA interference of KRAS.

[00238] Features of a RNAi Agent: Sense strand, Antisense Strand and (Optional) Overhangs

[00239] In various embodiments, the RNAi agents comprise a first strand and a second strand, e.g., a sense strand and an antisense strand (or an antisense and a sense strand) and, optionally, one or both ends of the duplex containing unpaired nucleotides referred to herein as overhangs.

[00240] The term "antisense strand" refers to the strand of a RNAi agent which includes a region that is substantially complementary to a target sequence. As used herein, the term "region of complementarity" refers to the region on the antisense strand that is substantially complementary to a sequence, for example a target sequence, as defined herein. Where the region of complementarity is not fully complementary to the target sequence, the mismatches may be in the internal or terminal regions of the molecule. Generally, the most tolerated mismatches are in the terminal regions, e.g., within 5, 4, 3, or 2 nucleotides of the 5' and/or 3' terminus.

[00241] The term "sense strand," as used herein, refers to the strand of a RNAi agent that includes a region that is substantially complementary to a region of the antisense strand as that term is defined herein.

[00242] The sequence of a gene may vary from individual to individual, especially at wobble positions within the coding segment, or in the untranslated region; individuals may also differ from each other in coding sequence, resulting in additional differences in mRNA. The sequence of the sense and antisense strands of the RNAi agent can thus be designed to correspond to that of an individual patient, if and where needed. RNAi agents can also be modified in sequence to reduce immunogenicity, binding to undesired mRNAs (e.g., "off-target effects") or to increase stability in the blood. These sequence variants are independent of chemical modification of the bases or 5' or 3' or other end-caps of the RNAi agents.

[00243] The RNAi agents can also have overhangs of 0, 1, or 2 overhangs; in the case of a 0 nt overhang, they are blunt-ended. A RNAi agent can have 0, 1 or 2 blunt ends. In a "blunt-ended RNAi agent" both strands terminate in a base-pair; thus a blunt-ended molecule lacks either 3' or 5' single-stranded nucleotide overhangs.

[00244] The RNAi agents can comprise overhang(s), blunt end(s), and/or 5' and 3' endcap(s).

[00245] As used herein, the term "overhang" or "nucleotide overhang" refer to at least one unpaired nucleotide that protrudes from the end of at least one of the two strands of the duplex structure of a RNAi agent. For example, when a 3'-end of one strand of a dsRNA extends beyond the 5'-end of the other strand, or vice versa, the unpaired nucleotide(s) form the overhang. A dsRNA can comprise an overhang of at least one nucleotide; alternatively the overhang can comprise at least two nucleotides, at least three nucleotides, at least four nucleotides, at least five nucleotides or more. An overhang can comprise or consist of a nucleotide/nucleoside analog, including a deoxynucleotide/nucleoside. The overhang(s) may be on the sense strand, the antisense strand or any combination thereof. Furthermore, the nucleotide(s) of an overhang can be present on the 5' end, 3' end or both ends of either an antisense or sense strand of a dsRNA.The RNAi agent can also optionally comprise a cap. The term "Cap" and the like include a chemical moiety attached to the end of a double-stranded nucleotide duplex, but is used herein to exclude a chemical moiety that is a nucleotide or nucleoside. A "3' Cap" is attached at the 3' end of a nucleotide or oligonucleotide and protects the molecule from degradation, e.g., from nucleases, such as those in blood serum or intestinal fluid. A 3' cap can replace a TT or UU dinucleotide at the end of a blunt-ended RNAi agent. In one embodiment, 3' end caps are as disclosed in, for example, WO 2005/021749 and WO 2007/128477. A "5' cap" is attached at the 5' end of a nucleotide or oligonucleotide. A cap should not interfere (or unduly interfere) with RNAi activity.

[00246]

[00247] The present disclosure thus contemplates a RNAi agent specific to KRAS comprising an antisense strand (which may be contiguous or connected via a linker or loop) in a RNAi agent. In a more specific embodiment, an RNAi agent comprises an antisense strand and a sense strand which together comprise a double-stranded or complementary region. In one embodiment, it can also optionally comprise one or two overhangs and/or one or two caps. The RNAi agent is used to induce RNA interference of the target gene, KRAS.

[00248] Target and complementary sequences

[00249] The RNAi agents of the present disclosure target (e.g., specifically bind to, anneal to, etc.) the mRNA encoding the gene KRAS. The use of the RNAi agent specific to KRAS results in a decrease of KRAS activity, level and/or expression, e.g., a "knock-down" or "knock-out" of the target gene or target sequence. Particularly in one embodiment, in the case of a disease state characterized by over-expression or hyper-activity of KRAS, administration of a RNAi agent to KRAS knocks down the KRAS gene enough to restore a normal level of KRAS activity or expression.

[00250] In one embodiment, the first or second strand of the RNAi comprises a sequence complementary to that of the target nucleic acid, KRAS.

[00251] As used herein, the term "strand comprising a sequence" refers to an oligonucleotide comprising a chain of nucleotides that is described by the sequence referred to using the standard nucleotide nomenclature.

[00252] As used herein, "target sequence" or "target gene" refer to a contiguous portion of the nucleotide sequence of an mRNA molecule formed during the transcription of a gene, e.g., a KRAS gene, including mRNA that is a product of RNA processing of a primary transcription product. The target portion of the sequence will be at least long enough to serve as a substrate for iRNA-directed cleavage at or near that portion. For example, the target sequence will generally be from 9-36 nucleotides ("nt") in length, e.g., 15-30 nt in length, including all sub-ranges therebetween. As non-limiting examples, the target sequence can be from 15-30 nt, 15-26 nt, 15-23 nt, 15-22 nt, 15-21 nt, 15-20 nt, 15-19 nt, 15-18 nt, 15-17 nt, 18-30 nt, 18-26 nt, 18-23 nt, 18-22 nt, 18-21 nt, 18-20 nt, 19-30 nt, 19-26 nt, 19-23 nt, 19-22 nt, 19-21 nt, 19-20 nt, 19 nt, 20-30 nt, 20-26 nt, 20-25 nt, 20-24 nt, 20-23 nt, 20-22 nt, 20-21 nt, 20 nt, 21-30 nt, 21-26 nt, 21-25 nt, 21-24 nt, 21-23 nt, or 21-22 nt, 21 nt, 22 nt, or 23 nt. The sense and antisense strands of the RNAi comprise a sequence complementary to that of the target nucleic acid, KRAS.

[00253] As used herein, and unless otherwise indicated, the term "complementary" refers to the ability of an oligonucleotide or polynucleotide comprising a first nucleotide sequence to hybridize and form a duplex structure under certain conditions with an oligonucleotide or polynucleotide comprising a second nucleotide sequence. Such conditions can, for example, be stringent, e.g., 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA, 50°C or 70°C for 12-16 hours followed by washing. Other conditions, such as physiologically relevant conditions as may be encountered inside an organism, can apply. The skilled person will be able to determine the set of conditions most appropriate for a test of complementarity of two sequences in accordance with the ultimate application of the hybridized nucleotides.

[00254] Complementary sequences within a RNAi agent, e.g., within a dsRNA as described herein, include base-paired oligonucleotides or polynucleotides comprising a first nucleotide sequence to an oligonucleotide or polynucleotide comprising a second nucleotide sequence over the entire length of one or both nucleotide sequences. Such sequences can be referred to as "fully complementary" with respect to each other herein. However, where a first sequence is referred to as "substantially complementary" with respect to a second sequence herein, the two sequences can be fully complementary, or they may form one or more, but generally not more than 5, 4, 3 or 2

mismatched base pairs upon hybridization for a duplex up to 30 base pairs, while retaining the ability to hybridize under the conditions most relevant to their ultimate application, e.g., inhibition of gene expression via a RISC pathway. However, where two oligonucleotides are designed to form, upon hybridization, one or more single-stranded overhangs, such overhangs shall not be regarded as mismatches with regard to the determination of complementarity. For example, a dsRNA comprising one oligonucleotide 21 nucleotides in length and another oligonucleotide 23 nucleotides in length, wherein the longer oligonucleotide comprises a sequence of 21 nucleotides that is fully complementary to the shorter oligonucleotide, may yet be referred to as "fully complementary" for the purposes described herein. The term "overhang" describes an unpaired nucleotide at the 3' or 5' end of a double-stranded nucleotide duplex, as described above. In one embodiment, the overhang is 1 to 4 nt long and is on the 3' end.

[00255] "Complementary" sequences, as used herein, may also include, or be formed entirely from, non-Watson-Crick base pairs and/or base pairs formed from non-natural and modified nucleotides, in as far as the above requirements with respect to their ability to hybridize are fulfilled. Such non-Watson-Crick base pairs includes, but are not limited to, Wobble or Hoogstein base pairing. The terms "complementary," "fully complementary" and "substantially complementary" herein may furthermore be used with respect to the base matching between the sense strand and the antisense strand of a dsRNA, or between the antisense strand of a RNAi agent and a target sequence, as will be understood from the context of their use. As used herein, a polynucleotide that is "substantially complementary to at least part of" a messenger RNA (mRNA) refers to a polynucleotide that is substantially complementary to a contiguous portion of the mRNA of interest (e.g., an mRNA encoding KRAS). For example, a polynucleotide is complementary to at least a part of a KRAS mRNA if the sequence is substantially complementary to a non-interrupted portion of an mRNA encoding KRAS.

[00256] Thus, the RNAi agent of the present disclosure is complimentary or substantially complimentary to a target sequence in the target KRAS and is double-stranded, comprising a sense and an antisense strand (which can be contiguous, linked via a loop, or otherwise joined), where the double-stranded region an be 9 to 36 bp long (particularly for example, 19-22 bp or 19-23 bp long), and can furthermore optionally comprise a 3' or 5' overhang, and the RNAi agent can furthermore comprise a 3' cap. The RNAi agent mediates RNA interference, down-regulating or inhibiting the level, expression and/or activity of KRAS, and/or establishing or re-establishing an approximately normal level of KRAS and/or KRAS activity, or other biological function related to KRAS.

[00257] Thus, the RNAi agent of the present disclosure is complimentary or substantially complimentary to a target sequence in the target KRAS and is double-stranded, comprising a sense and an antisense strand (which can be contiguous, linked via a loop, or otherwise joined), where the double-stranded region an be 9 to 36 bp long (particularly for example, 19-22 bp or 19-23 bp long), and can furthermore optionally comprise a 3' or 5' overhang, and the RNAi agent can furthermore comprise a 3' cap. The RNAi agent mediates RNA interference, down-regulating or inhibiting the level, expression and/or activity of KRAS, and/or establishing or re-establishing an approximately normal level of KRAS activity or expression.

[00258] The term "double-stranded RNA" or "dsRNA," as used herein, refers to an RNAi agent

comprising a first and a second strand; e.g., a composition that includes an RNA molecule or complex of molecules having a hybridized duplex region that comprises two anti-parallel and substantially complementary nucleic acid strands, which will be referred to as having "sense" and "antisense" orientations with respect to a target RNA. The antisense strand, with respect to the mRNA target, is also called the "guide" strand, and the sense strand is also called the "passenger" strand. As used herein, depending on the context, the "first" strand can be the guide or antisense strand, and the "second" strand can be the passenger or sense strand. Also as used herein, again depending on the context, the "first" strand can be the passenger or sense strand, and the "second" strand can be the guide or antisense. The passenger strand can include at least one or more of the following: one or more extra nucleotides (e.g., a bulge or 1 nt loop) compared to the other strand, a nick, a gap, etc., compared to the other strand. In various embodiments, the first strand is the sense strand and the second strand is the anti-sense strand. In other embodiments, the first strand is the anti-sense strand, and the second strand is the sense strand.

[00259] The duplex region can be of any length that permits loading into the RISC complex and subsequent specific degradation of a desired target RNA through a RISC pathway, but will typically range from 9 to 36 base pairs ("bp") in length, e.g., 15-30 base pairs in length. Considering a duplex between 9 and 36 base pairs, the duplex can be any length in this range, for example, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 bp and any sub-range therebetween, including, but not limited to 15-30 base pairs, 15-26 bp, 15-23 bp, 15-22 bp, 15-21 bp, 15-20 bp, 15-19 bp, 15-18 bp, 15-17 bp, 18-30 bp, 18-26 bp, 18-23 bp, 18-22 bp, 18-21 bp, 18-20 bp, 19-30 bp, 19-26 bp, 19-23 bp, 19-22 bp, 19-21 bp, 19-20 bp, 19 bp, 20-30 bp, 20-26 bp, 20-25 bp, 20-24 bp, 20-23 bp, 20-22 bp, 20-21 bp, 20 bp, 21-30 bp, 21-26 bp, 21-25 bp, 21-24 bp, 21-23 bp, 21-22 bp, 21 bp, 22 bp, or 23 bp.

[00260] The dsRNAs generated in the cell by processing with Dicer and similar enzymes are generally in the range of about 19 to about 22 base pairs in length, although artificial RNAi agents can be synethesized or made by any method known in the art. One strand of the duplex region of a dsRNA comprises a sequence that is substantially complementary to a region of a target RNA. The two strands forming the duplex structure can be from a single RNA molecule having at least one self-complementary duplex region, or can be formed from two or more separate RNA molecules that hybridize to form the duplex. Where the duplex region is formed from two self-complementary regions of a single molecule, the molecule can have a duplex region separated by a single stranded chain of nucleotides (herein referred to as a "hairpin loop", e.g., such as found in an shRNA construct) between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure. The hairpin loop can comprise at least one unpaired nucleotide; in some embodiments the hairpin loop can comprise at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 23 or more unpaired nucleotides. Where the two substantially complementary strands of a dsRNA are comprised by separate RNA molecules, those molecules need not, but can be covalently connected. Where the two strands are connected covalently by a hairpin loop, the construct is generally referred to herein and in the art as a "shRNA". Where the two strands are connected covalently by means other than a hairpin loop, the connecting structure is referred to as a "linker." The term "siRNA" is also used herein to refer to a dsRNA as

described above.

[00261] RNAi Agents Lowering or Normalizing KRAS Level, Expression And/Or Activity

[00262] RNAi agents for targeting KRAS include those which bind to a KRAS sequence provided herein and which work to reduce KRAS through a RNAi mechanism. Example RNAi agents (e.g., siRNAs) to KRAS are provided, e.g., in Table 1.

[00263] Any method known in the art can be use to measure changes in KRAS activity, level, and/or expression induced by a KRAS RNAi agent. Measurements can be performed at multiple timepoints, prior to, during and after administration of the RNAi agent, to determine the effect of the RNAi agent.

[00264] The RNAi agents of the present disclosure silence, inhibit the expression of, down-regulate the expression of, and/or suppress the expression of KRAS, such that an approximately normal level of KRAS activity or expression is restored.

[00265] In addition, in various embodiments, depending on the disease condition and biological context, it is acceptable to use the RNAi agents of the present disclosure to establish a level of KRAS expression, activity and/or level which is below the normal level, or above the normal level, depending on the therapeutic outcome that is desired.

[00266] Any method known in the art can be use to measure changes in KRAS activity, level and/or expression induced by a KRAS siRNA. Measurements can be performed at multiple timepoints, prior to, during and after administration of the siRNA, to determine the effect of the siRNA.

[00267] The terms "silence," "inhibit the expression of," "down-regulate the expression of," "suppress the expression of," and the like, in so far as they refer to a KRAS gene, herein refer to the at least partial suppression of the expression of a KRAS gene, as manifested by a reduction of the amount of KRAS mRNA which may be isolated from or detected in a first cell or group of cells in which a KRAS gene is transcribed and which has or have been treated such that the expression of a KRAS gene is inhibited, as compared to a second cell or group of cells substantially identical to the first cell or group of cells but which has or have not been so treated (control cells). The degree of inhibition is usually expressed in terms of

$$\frac{(\text{mRNA in control cells}) - (\text{mRNA in treated cells})}{(\text{mRNA in control cells})} \bullet 100\% \qquad \text{Equation 1}$$

[00268] Alternatively, the degree of inhibition may be given in terms of a reduction of a parameter that is functionally linked to KRAS gene expression, e.g., the amount of protein encoded by a KRAS gene, alteration in expression of a protein whose expression is dependent on KRAS, etc. In principle, KRAS gene silencing may be determined in any cell expressing KRAS, either constitutively or by genomic engineering, and by any appropriate assay. However, when a reference or control is needed in order to determine whether a given RNAi agent inhibits the expression of KRAS by a certain degree and therefore is encompassed by the instant disclosure, the assays provided in the Examples below shall serve as such reference.

[00269] For example, in certain instances, expression of KRAS is suppressed by at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% by administration of a RNAi agent featured in the present disclosure. In some embodiments, KRAS is suppressed by at least about 60%, 70%, or 80% by administration of a RNAi agent featured in the present disclosure. In some embodiments, KRAS is suppressed by at least about 85%, 90%, or 95% or more by administration of a RNAi agent, as described herein. In one embodiment, the degree of KRAS suppression is determined by loss of full length KRAS mRNA in a treated cell compared to an untreated cell. In one embodiment, the degree of KRAS suppression is determined with a phenotypic assay that monitors loss of proliferative activity and/or cell death. Other embodiments are as provided in the Examples.

[00270] The ability of a RNAi agent to suppress KRAS can be first tested *in vitro* (e.g., using test cells such as RKO).

[00271] RNAi agents which can suppress KRAS *in vitro* can then be tested for immunostimulation using, for example, a PBMC (peripheral blood mononuclear cell) assay. RNAi agents can also be tested in animal tests. Test and control animals include those which over-express or under-express KRAS, as described in, for example, Hummer et al. 2005 J. Am. Soc. Nephrol. 16: 3160-3166; Randrianarison et al. 2007 Am. J. Physiol. Lung Cell. Mol. Physiol. 294: 409-416; Cao et al. 2006 Am. J. Physiol. Renal Physiol., and references cited therein. RNAi agents which suppress or alter the level, activity and/or expression of KRAS can be used in medicaments to treat various KRAS-related diseases.

[00272] By "lower" in the context of KRAS or a symptom of a KRAS-related disease is meant a statistically significant decrease in such level. The decrease can be, for example, at least 10%, at least 20%, at least 30%, at least 40% or more. If, for a particular disease, or for an individual suffering from a particular disease, the levels or expression of KRAS are elevated, treatment with a KRAS RNAi agent of the present disclosure can particularly reduce the level or expression of KRAS to a level considered in the literature as within the range of normal for an individual without such disorder, or to a level that reduces or ameliorates symptoms of a disease. The level or expression of KRAS can be measured by evaluation of mRNA (e.g., via Northern blots or PCR), or protein (e.g., Western blots). The effect of a RNAi agent on KRAS expression can be determined by measuring KRAS gene transcription rates (e.g., via Northern blots; or reverse transcriptase polymerase chain reaction or real-time polymerase chain reaction).

[00273] As used herein, "down-regulates" refers to any statistically significant decrease in a biological activity and/or expression of KRAS, including full blocking of the activity (i.e., complete inhibition) and/or expression. For example, "down-regulation" can refer to a decrease of at least about 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 % in KRAS level, activity and/or expression.

[00274] As used herein, the term "inhibit" or "inhibiting" KRAS refers to any statistically significant decrease in biological level, activity and/or expression of KRAS, including full blocking of the activity and/or expression. For example, "inhibition" can refer to a decrease of at least about 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 % in KRAS level, activity and/or expression. As used herein, the term "inhibit" similarly refers to a significant decrease in level, activity and/or expression, while referring to any other biological agent or composition.

[00275] By "level", it is meant that the KRAS RNAi agent can alter the level of KRAS, e.g., the level of KRAS mRNA or the level of KRAS protein, or the level of activity of KRAS.

[00276] Some diseases, such as types of a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases, are characterized by a KRAS mutation or excessive KRAS abundance or activity. Particularly in one embodiment, in the case of a disease characterized by over-expression and/or hyper-activity of KRAS, administration of a RNAi agent to KRAS reduces the level, expression and/or activity of KRAS. Thus, in various embodiments, administration of a RNAi agent to KRAS particularly establishes or re-establishes a normal or approximately normal level of KRAS activity, expression and/or level.

[00277] By "normal" or "approximately normal" in terms of level, expression and/or activity, is meant at least: about 50%, about 60%, about 70%, about 80%, about 90%, and/or about 100%; and/or no more than: about 100%, about 120%, about 130%, about 140%, or about 150% of the level, expression or activity of KRAS in a healthy cell, tissue, or organ. This can be measured using, for example, lung or kidney homogenates, as described in Gambling et al. 2004 Kidney Intl. 65: 1774-1781. Particularly in one embodiment, administration of the appropriate amount of the appropriate KRAS RNAi agent restores KRAS level, activity and/or expression to about 50% to about 150%, more particularly about 60% to about 140%, more particularly to about 70% to about 130%, more particularly to about 80% to about 120%, more particularly to about 90% to about 110%, and most particularly to about 100% of that of a healthy cell, tissue or organ. Administration of a KRAS RNAi to a patient with a KRAS-related disease thus particularly restores the level, activity, and/or expression of KRAS and the level of Na^+ reabsorption to an approximately normal level, as determined by direct measurements of KRAS mRNA or protein levels, or indirect determinations. In addition, the preferred target amount of KRAS level, expression and/or activity after KRAS RNAi agent administration can be calculated to take into account any other perturbations in a KRAS-related pathway. For example, if another factor in a KRAS-related pathway is either over- or under-expressed, KRAS level, expression or activity may be modulated to attain a more normal state.

[00278] In addition, in various embodiments, depending on the disease condition and biological context, it is acceptable to use the RNAi agents of the present disclosure to establish a level of KRAS expression, activity and/or level which is below the normal level, or above the normal level.

[00279] **Types of RNAi Agents and Modification Thereof**

[00280] The use of RNAi agents or compositions comprising an antisense nucleic acid to down-modulate the expression of a particular protein in a cell is well known in the art. A RNAi agent comprises a sequence complementary to, and is capable of hydrogen bonding to, the coding strand of another nucleic acid (e.g., an mRNA). Thus, in various embodiments, the RNAi agents of the

present disclosure encompass any RNAi agents which target (e.g., are complementary, capable of hybridizing or hydrogen bonding to, etc.) any sequence presented, e.g., in any of Tables 1 to 6.

[00281] Once a functional guide strand has been identified, many variations to the guide and/or passenger strand can be made. For example, the RNAi agent may have modifications internally, or at one or both ends. The modifications at the ends can help stabilize the RNAi agent, protecting it from degradation by nucleases in the blood. The RNAi agents may optionally be directed to regions of the KRAS mRNA known or predicted to be near or at splice sites of the gene.

[00282] A RNAi agent can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, RNAi agent can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to decrease off-target effects, and/or increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used.

[00283] "G," "C," "A," "T" and "U" each generally stand for a nucleotide that contains guanine, cytosine, adenine, thymidine and uracil as a base, respectively. However, the terms "ribonucleotide", "deoxynucleotide", or "nucleotide" can also refer to a modified nucleotide or a surrogate replacement moiety. The skilled person is well aware that guanine, cytosine, adenine, and uracil may be replaced by other moieties without substantially altering the base pairing properties of an oligonucleotide comprising a nucleotide bearing such replacement moiety. For example, without limitation, a nucleotide comprising inosine as its base may base pair with nucleotides containing adenine, cytosine, or uracil. Hence, nucleotides containing uracil, guanine, or adenine may be replaced in the nucleotide sequences of dsRNA featured in the present disclosure by a nucleotide containing, for example, inosine. In another example, adenine and cytosine anywhere in the oligonucleotide can be replaced with guanine and uracil, respectively to form Wobble base pairing with the target mRNA. Sequences containing such replacement moieties are suitable for the compositions and methods featured in the present disclosure.

[00284] The skilled artisan will recognize that the term "RNA molecule" or "ribonucleic acid molecule" encompasses not only RNA molecules as expressed or found in nature (i.e., are naturally occurring), but also non-naturally occurring analogs and derivatives of RNA comprising one or more ribonucleotide/ribonucleoside analogs or derivatives as described herein or as known in the art.The RNA can be modified in the nucleobase structure or in the ribose-phosphate backbone structure, e.g., as described herein below. However, the molecules comprising ribonucleoside analogs or derivatives must retain the ability to form a duplex. As non-limiting examples, an RNA molecule can also include at least one modified ribonucleoside, including but not limited to a 2'-O-methyl modified nucleotide, a nucleoside comprising a 5' phosphorothioate group, a terminal nucleoside linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a locked nucleoside, an abasic nucleoside, a 2'-deoxy-2'-fluoro modified nucleoside, a 2'-amino-modified nucleoside, 2'-alkyl-modified nucleoside, morpholino nucleoside, an unlocked ribonucleotide (e.g., an acyclic nucleotide monomer, as described in WO 2008/147824), a phosphoramidate or a non-natural base comprising nucleoside, or any combination thereof. Alternatively, an RNA molecule can comprise at least two modified ribonucleosides, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9,

at least 10, at least 15, at least 20 or more, up to the entire length of the dsRNA molecule. The modifications need not be the same for each of such a plurality of modified ribonucleosides in an RNA molecule. In one embodiment, modified RNAs contemplated for use in methods and compositions described herein are peptide nucleic acids (PNAs) that have the ability to form the required duplex structure and that permit or mediate the specific degradation of a target RNA via a RISC pathway.

[00285] Examples of modified nucleotides which can be used to generate the RNAi agent include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5- oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

[00286] A "modified variant" of a sequence disclosed herein includes any variant comprising the same sequence, but with a modification in the base, sugar, phosphate or backbone (but not a base substitution, e.g., A for G, or C for U). Thus, a modified variant can comprise any modified nucleotide described above (e.g., 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, etc.). When a base is replaced by a corresponding modified base (e.g., A for modified A), these modified nucleotides do not constitute a mismatch or base difference. Thus a given sequence with a U at a particular position and a modified variant comprising a 5-fluorouracil, 5-bromouracil, 5-chlorouracil, or 5-iodouracil at the same sequence would differ by 0 nt (or have no mismatches); however, a given sequence with a C at a particular position and a different sequence with a 5-fluorouracil (wherein the two sequences are otherwise identical) would differ by 1 nt (1 mismatch).

[00287] Replacing the 3'-terminal nucleotide overhanging segments of a 21-mer siRNA duplex having two-nucleotide 3'-overhangs with deoxyribonucleotides does not have an adverse effect on RNAi activity. Replacing up to four nucleotides on each end of the siRNA with deoxyribonucleotides has been well tolerated, whereas complete substitution with deoxyribonucleotides results in no RNAi activity. International PCT Publication No. WO 00/44914, and Beach et al. International PCT Publication No. WO 01/68836 preliminarily suggest that siRNA may include modifications to either the phosphate-sugar backbone or the nucleoside to include at least one of a nitrogen or sulfur heteroatom. Kreutzer et al. Canadian Patent Application No. 2,359,180, also describe certain chemical modifications for use in dsRNA constructs in order to counteract activation of double-stranded RNA-dependent protein kinase PKR, specifically 2'-amino or 2'-O-methyl nucleotides, and nucleotides containing a 2'-O or 4'-C methylene bridge. Additional 3'-terminal nucleotide overhangs include dT (deoxythimidine), 2'-O,4'-C-ethylene thymidine (eT), and 2-hydroxyethyl phosphate (hp).

4-thiouracil and 5-bromouracil substitutions can also be made. Parrish et al. 2000 Molecular Cell 6: 1077-1087.

[00288] Those skilled in the art will appreciate that it is possible to synthesize and modify the siRNA as desired, using any conventional method known in the art (see Henschel et al. 2004 DEQOR: a web-based tool for the design and quality control of siRNAs. Nucleic Acids Research 32 (Web Server Issue): W113-W120). In addition, if the RNAi agent is a shRNA, it will be apparent to those skilled in the art that there are a variety of regulatory sequences (for example, constitutive or inducible promoters, tissue- specific promoters or functional fragments thereof, etc.) which are useful for shRNA expression construct/vector.

[00289] There are several examples in the art describing sugar, base, phosphate and backbone modifications that can be introduced into nucleic acid molecules with significant enhancement in their nuclease stability and efficacy. For example, oligonucleotides are modified to enhance stability and/or enhance biological activity by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-flouro, 2'-O-methyl, 2'-O-allyl, 2'-H, nucleotide base modifications (for a review see Usman and Cedergren 1992 TIBS. 17: 34; Usman et al. 1994 Nucleic Acids Symp. Ser. 31: 163; Burgin et al. 1996 Biochemistry 35: 14090). Sugar modification of nucleic acid molecules are extensively described in the art.

[00290] In various embodiments, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00291] Additional modifications and conjugations of RNAi agents have been described. Soutschek et al. 2004 Nature 432: 173-178 presented conjugation of cholesterol to the 3'-end of the sense strand of a siRNA molecule by means of a pyrrolidine linker, thereby generating a covalent and irreversible conjugate. Chemical modifications (including conjugation with other molecules) of RNAi agents may also be made to improve the *in vivo* pharmacokinetic retention time and efficiency.

[00292] In various embodiments, the RNAi agent to KRAS comprises at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide. In certain embodiments, the RNAi agent can comprise a non-natural nucleobase, wherein the non-natural nucleobase is difluorotolyl, nitroindolyl, nitropyrrolyl, or nitroimidazolyl. In a particular embodiment, the non-natural nucleobase is difluorotolyl. In certain embodiments, only one of the two oligonucleotide strands contains a non-natural nucleobase. In certain embodiments, both of the oligonucleotide strands contain a non-natural nucleobase.

[00293] In another embodiment, the RNAi comprises a gap or contains mismatch comprising an abasic nucleotide.

[00294] In another embodiment, the RNAi agent has a single-stranded nick (e.g., a break or missing bond in the backbone). In various embodiments, a single-stranded nick can be in either the sense or anti-sense strand, or both.

[00295] This nick can be, for example, in the sense strand, producing a small internally segmented interfering RNA, or sisiRNA, which may have less off-target effects than the corresponding RNAi agent without a nick. See, for example, WO 2007/107162 to Wengels and Kjems.

[00296] The antisense nucleic acid or RNAi agent can also have an alternative backbone such as locked nucleic acids (LNA), Morpholinos, peptidic nucleic acids (PNA), threose nucleic acid (TNA), or glycol nucleic acid (GNA), or FANA and/or it can be labeled (e.g., radiolabeled or otherwise tagged). FANA are described in Dowler et al. 2006 Nucl. Acids Res. 34: 1669-1675.

[00297] One or both strands can comprise an alternative backbone.

[00298] In yet another embodiment, the RNAi agent employed by the methods of the present disclosure can include an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other. Gaultier et al. 1987 Nucleic Acids. Res. 15: 6625-6641.

[00299] The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. 1987 Nucleic Acids Res. 15: 6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. 1987 FEBS Lett. 215: 327-330).

[00300] Other modifications and/or other changes can be made to the RNAi agent. A portion of the RNAi agent can be double-stranded DNA, while another portion is double-stranded RNA, forming a DNA-RNA chimera (See, for example, Yamato et al. 2011. Cancer Gene Ther. 18: 587-597). Mismatches between the guide and passenger stand can also be introduced, though some positions may be better suited than others (See, for example, U.S. Patent App. No. 2009/0209626 to Khvorova). The passenger strand can also be shortened, to as short as 15 or 16 nt, while the guide strand remains 19 nt or longer (See, for example, Sun et al. 2008 Nature Biotech. 26: 1379-1382; and Chu and Rana 2008 RNA 14: 1714-1719). This can increase incorporation of the guide strand into the RNA-induced Silence Complex (RISC), and decrease incorporation of the passenger strand, than reducing off-target effects. In some cases, the passenger strand may be more amenable to modification (e.g., single-stranded nicking, nucleotide modifications, and shortening) than the guide strand.

[00301] These and many other modifications can be made once a functional guide strand is identified.

[00302] **Pharmaceutical Compositions of RNAi Agents**

[00303] As used here, a "pharmaceutical composition" comprises a pharmaceutically effective amount of one or more KRAS RNAi agent, a pharmaceutically acceptable carrier, and, optionally, an additional disease treatment which works synergistically with the RNAi agent. As used herein, "pharmacologically effective amount," "therapeutically effective amount" or simply "effective amount" refers to that amount of a RNAi agent effective to produce the intended pharmacological,

therapeutic or preventive result. For example, if a given clinical treatment is considered effective where there is at least a 10% reduction in a measurable parameter associated with a disease or disorder, a therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 10% reduction in that parameter. In this embodiment, a therapeutically effective amount of a RNAi agent targeting KRAS can reduce KRAS protein levels by at least 10%. In additional embodiments, a given clinical treatment is considered effective where there is at least a 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90 or 95% reduction in a measurable parameter associated with a disease or disorder, and the therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90 or 95% reduction, respectively, in that parameter.

[00304] The term "pharmaceutically acceptable carrier" refers to a carrier for administration of a therapeutic agent. Such carriers include, but are not limited to, lipid nanoparticles, saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The term specifically excludes cell culture medium. Any appropriate phamaceutical carrier known in the art can be used in conjunction with the RNAi agents disclosed herein.

[00305] **Pharmaceutical Composition Comprising a RNAi Agent to KRAS**

[00306] Additional components of a pharmaceutical composition comprising a RNAi Agent to KRAS are contemplated to aid in delivery, stability, efficacy, or reduction of immunogenicity.

[00307] Liposomes have been used previously for drug delivery (e.g., delivery of a chemotherapeutic). Liposomes (e.g., cationic liposomes) are described in PCT publications WO02/100435A1, WO03/015757A1, WO04029213A2; and WO/2011/076807; U.S. Pat. Nos. 5,962,016; 5,030,453; and 6,680,068; and U.S. Patent Application 2004/0208921. A process of making liposomes is also described in WO04/002453A1. Furthermore, neutral lipids have been incorporated into cationic liposomes (e.g., Farhood et al. 1995), as well as PEGylated lipids.

[00308] Cationic liposomes have been used to deliver RNAi agent to various cell types (Sioud and Sorensen 2003; U.S. Patent Application 2004/0204377; Duxbury et al., 2004; Donze and Picard, 2002).

[00309] Use of neutral liposomes disclosed in Miller et al. 1998, and U.S. Patent Application 2003/0012812.

[00310] As used herein, the term "SNALP" refers to a stable nucleic acid-lipid particle. A SNALP represents a vesicle of lipids coating a reduced aqueous interior comprising a nucleic acid such as an iRNA or a plasmid from which an iRNA is transcribed. SNALPs are described, e.g., in U.S. Patent Application Publication Nos. 20060240093, 20070135372, and in International Application No. WO 2009082817.

[00311] Chemical transfection using lipid-based, amine-based and polymer-based techniques, is disclosed in products from Ambion Inc., Austin, Tex.; and Novagen, EMD Biosciences, Inc, an Affiliate of Merck KGaA, Darmstadt, Germany); Ovcharenko D (2003) "Efficient delivery of siRNAs to human primary cells." Ambion TechNotes 10 (5): 15-16). Additionally, Song et al. (Nat Med. published online (Feb I 0, 2003) doi: 10.1038/nm828) and others [Caplen et al. 2001 Proc. Natl.

Acad. Sci. (USA), 98: 9742-9747; and McCaffrey et al. Nature 414: 34-39] disclose that liver cells can be efficiently transfected by injection of the siRNA into a mammal's circulatory system.

[00312] A variety of molecules have been used for cell-specific RNAi agent delivery. See, for example, WO/2011/076807. For example, the nucleic acid-condensing property of protamine has been combined with specific antibodies to deliver siRNAs. Song et al. 2005 Nat Biotech. 23: 709-717. The self-assembly PEGylated polycation polyethylenimine (PEI) has also been used to condense and protect siRNAs. Schiffelers et al. 2004 Nucl. Acids Res. 32: el49, 141-1 10.

[00313] The RNAi agents of the present disclosure can be delivered via, for example, Lipid nanoparticles (LNP); neutral liposomes (NL); polymer nanoparticles; double-stranded RNA binding motifs (dsRBMs); or via modification of the RNAi agent (e.g., covalent attachment to the dsRNA) or by any method known in the art for delivery of a RNAi agent comprising nucleic acids.

[00314] Lipid nanoparticles (LNP) are self-assembling cationic lipid based systems. These can comprise, for example, a neutral lipid (the liposome base); a cationic lipid (for siRNA loading); cholesterol (for stabilizing the liposomes); and PEG-lipid (for stabilizing the formulation, charge shielding and extended circulation in the bloodstream).

[00315] The cationic lipid can comprise, for example, a headgroup, a linker, a tail and a cholesterol tail. The LNP can have, for example, good tumor delivery, extended circulation in the blood, small particles (e.g., less than 100 nm), and stability in the tumor microenvironment (which has low pH and is hypoxic).

[00316] **Neutral liposomes (NL) are non-cationic lipid based particles.**

[00317] Polymer nanoparticles are self-assembling polymer-based particles.

[00318] Double-stranded RNA binding motifs (dsRBMs) are self-assembling RNA binding proteins, which will need modifications.

[00319] In various embodiments, the RNAi agent to KRAS is packaged as a monotherapy into a delivery vehicle, or may be further ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00320] The RNAi agents of the present disclosure can be prepared in a pharmaceutical composition comprising various components appropriate for the particular method of administration of the RNAi agent.

[00321] **KRAS-Related Diseases**

[00322] The present disclosure encompasses RNAi agents to KRAS and administration of the RNAi agents to humans and non-human animals to treat various KRAS-related diseases.

[00323] By "KRAS-related disease" is meant any disease related to a dysfunction in the level, expression and/or activity of KRAS, and/or any disease which can be treated and/or ameliorated by

modulating the level, expression and/or activity of KRAS. In particular, it includes a proliferative disease, including without limitation a solid or liquid cancer, e.g., adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases.

[00324] For additional information on KRAS-related diseases, see, for example: Bos. 1989. Cancer Res. 49. 17: 4682–9; Engelman et al. 2008. Nature Med. 14: 1351-1356; Haigis et al. 2008 Nature Gen. 40: 600-608; Karapetis et al. 2008 N. E. J. Med. 359: 1757-1765; Kiaris et al. 1995. Int. J. Oncol. 7: 413-421; Liu et al. 1987 Nature 330: 186-188; Riely et al. 2008 Clin. Cancer Res. 14: 5731; and Riely et al. 2009. Proc. Am. Thorac. Soc. 6: 201-205. KRAS mutation, hyperactivity or over-expression is also associated with cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome. Adachi et al. 2012 Seizure: Eur. J. Epilepsy 21: 55-60; Kim et al. 2011. J. Korean Soc. Neonatol. 18: 374-378.

[00325] RNAi agents to KRAS can thus be used to treat KRAS-related diseases, particularly those diseases associated with altered expression, activity and/or levels of KRAS.

[00326] Use of RNAi Agents for Treatment of KRAS-Related Diseases

[00327] The RNAi agents to KRAS described herein can be formulated into pharmaceutical compositions which can be administered to humans or non-human animals. These compositions can comprise one or more RNAi agents, and, optionally, additional treatments useful for treating KRAS-related diseases. They can be administered as part of an early/preventative treatment, and can be administered in a therapeutically-effective dosage. The pharmaceutical composition can comprise a pharmaceutical carrier and can be administered by any method known in the art. These various aspects of the present disclosure are described in additional detail below.

[00328] RNAi agents to KRAS can be administered to humans and non-human animals for treatment of KRAS-related diseases.

[00329] In one embodiment of the present disclosure, the compositions comprising a KRAS RNAi agent can be administered to non-human animals. For example, the compositions can be given to chickens, turkeys, livestock animals (such as sheep, pigs, horses, cattle, etc.), companion animals (e.g., cats and dogs) and can have efficacy in treatment of proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome, and similar diseases. In each case, the RNAi agent to KRAS would be selected to match the sequence of the KRAS of the genome of the animal, and to, particularly, contain at least 1 nt mismatch from all other genes in that animal's genome. The RNAi agents of the present disclosure can thus be used in treatment of KRAS-related diseases in humans and non-human animals.

[00330] As used herein in the context of KRAS expression, the terms "treat," "treatment," and the like, refer to relief from or alleviation of pathological processes mediated by KRAS expression. In the context of the present disclosure insofar as it relates to any of the other conditions recited herein below (other than pathological processes mediated by KRAS expression), the terms "treat,"

"treatment," and the like mean to relieve or alleviate at least one symptom associated with such condition, or to slow or reverse the progression or anticipated progression of such condition, such as slowing the progression of a lipid disorder, such as atherosclerosis.

[00331] By "treatment" is also meant prophylaxis, therapy, cure, or any other change in a patient's condition indicating improvement or absence of degradation of physical condition. By "treatment" is meant treatment of KRAS-related disease (e.g., a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome), or any appropriate treatment of any other ailment the patient has. As used herein, the terms "treatment" and "treat" refer to both prophylactic and preventative treatment and curative or disease-modifying treatment, including treatment of patients at risk of contracting a disease or suspected of having a disease, as well as patients already ill or diagnosed as suffering from a condition. The terms "treatment" and "treat" also refer to the maintenance and/or promotion of health in an individual not suffering from a disease but who may be susceptible to developing an unhealthy condition, such as nitrogen imbalance or muscle loss. In one embodiment, "treatment" does not encompass prevention of a disease state. Thus, the present disclosure is useful for suppressing expression of KRAS and/or treating a KRAS-related disease in an individual afflicted by a KRAS-related disease, or an individual susceptible to a KRAS-related disease. An individual "afflicted" by a KRAS-related disease has demonstrated detectable symptoms characteristics of the disease, or had otherwise been shown clinically to have been exposed to or to carry KRAS-related disease pathogens or markers. As non-limiting examples, an individual afflicted by a KRAS-related disease can show outward symptoms; or can show no outward symptoms but can be shown with a clinical test to carry protein markers associated with a KRAS-related disease, or proteins or genetic material associated with a pathogen in the blood.

[00332] Early treatment of some KRAS-related diseases may be more efficacious if administered early rather than later. Thus, in one particular embodiment, the RNAi agent to KRAS is administered early, prior to disease manifestation, and/or as a preventative agent, rather than administered after disease establishment.

[00333] Treatments of KRAS-related diseases can comprise various treatments, comprising a KRAS RNAi agent, and optionally further comprising an additional treatment, which can be a method (or procedure), or an additional composition (e.g., an agent or additional RNAi agent).

[00334] **Dosages and Effective Amounts of RNAi Agents**

[00335] The RNAi agents of the present disclosure are administered in a dosage of a therapeutically effective amount to a patient in need thereof.

[00336] An "effective amount" or a "therapeutically effective amount" is an amount that treats a disease or medical condition of an individual, or, more generally, provides a nutritional, physiological or medical benefit to an individual. As used herein, the phrases "therapeutically effective amount"

and "prophylactically effective amount" refer to an amount that provides a therapeutic benefit in the treatment, prevention, or management of pathological processes mediated by KRAS expression or an overt symptom of pathological processes mediated by KRAS expression. The specific amount that is therapeutically effective can be readily determined by an ordinary medical practitioner, and may vary depending on factors known in the art, such as, for example, the type of pathological processes mediated by KRAS expression, the patient's history and age, the stage of pathological processes mediated by KRAS expression, and the administration of other agents that inhibit pathological processes mediated by KRAS expression.

[00337] In various embodiments of the present disclosure, the patient is at least about 1, 3, 6, or 9 months, or 1, 5, 10, 20, 30, 40, 50, 55, 60, 65, 70, or 75 years of age. In various embodiments, the patient is no more than about 1, 3, 6, or 9 months, or 1, 5, 10, 20, 30, 40, 50, 55, 60, 65, 70, 75, 80, 90, or 100 years of age. In various embodiments the patient has a body weight of at least about 5, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380 or 400 lbs. In various embodiments, the patient has a body weight of no more than about 5, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380 or 400 lbs.

[00338] In various embodiments of the present disclosure, the dosage [measuring only the active ingredient(s)] can be at least about 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 ng, 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 micrograms, 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 mg. In various embodiments, the dosage can be no more than about 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 mg. In various embodiments, the dosage can be administered at least more than once a day, daily, more than once a weekly, weekly, bi-weekly, monthly, and/or every 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 months, or a combination thereof.

[00339] In various embodiments, the dosage is correlated to the body weight or body surface area of the individual. The actual dosage level can be varied to obtain an amount of active agent which is effective for a particular patient, composition and mode of administration, without being toxic to the patient. The selected dose will depend on a variety of pharmacokinetic factors, including the activity of the particular RNAi agent employed, the route of administration, the rate of excretion of the RNAi agent, the duration of the treatment, other drugs, compounds and/or materials used in combination with the RNAi agent, the age, sex, weight, condition, general health and prior medical history of the patient, and like factors well known in the medical arts. A physician or veterinarian having ordinary skill in the art can readily determine the effective amount of the RNAi agent required. A suitable dose will be that amount which is the lowest dose effective to produce a therapeutic effect, or a dose low enough to produce a therapeutic effect without causing side effects.

[00340]

[00341] RNAi Agents to KRAS in Combination with Other Therapies

[00342] In addition to a therapeutically-effective dosage of one or more RNAi agents to KRAS, the pharmaceutical compositions of the present disclosure can comprise or be used in conjunction with an additional disease treatment which works synergistically with the RNAi agent.

[00343] In addition, many tumors contain mutations in both KRAS and one or more other genes. For example, some lung cancer or colorectal tumor cells or other types of cancer can have mutations in both KRAS and one or more of: EGFR, GLUT1, PI3K, RAF, and APC. Haigis et al. 2008 Nature Gen. 40: 600-608; Karapetis et al. 2008 N. E. J. Med. 359: 1757-1765; and Yun et al. 2009 Science 325: 1555-1559. Effective combination therapy can comprise a KRAS RNAi agent combined with an agent which targets the other mutated hyper-active or overexpressed protein, or which is an approved therapy for the cancer type being treated.

[00344] RNAi agents to KRAS can thus be effective when used in a regimen involving other disease treatments. Some of these treatments are not effective when the patient has an activating mutation in KRAS. However, the RNAi agent to KRAS can reduce the overall amount of KRAS, improving the efficacy of disease treatments which are not effective in the presence of an activating KRAS mutation.

[00345] Furthermore, proliferation, survival and/or apoptosis resistance of KRAS-defective tumor cells may require another factor such as NF-kappa-B or I-kappa-B kinase TBK1. Meylan et al. 2009 Nature 462: 104-107; and Barbie et al. 2009 Nature 462: 108-112. Thus, in some embodiments, effective combination therapy can comprise administration of a KRAS RNAi agent and administration (or co-administration) of a treatment which targets the other factor (e.g., a siRNA, antibody or small molecule which targets NF-kappa-B or TBK1).

[00346] Thus, the KRAS RNAi agent can be used in a combination therapy along with any other therapeutic composition or method or therapy, including those which specifically target another factor, or which are otherwise known to be effective in treatment of a KRAS-related disease.

[00347] In the treatment of these KRAS-related diseases, the RNAi agent(s) and additional disease treatment(s) can be administered in any order, simultaneously or sequentially, or in multiple doses over time. Administration of the RNAi agent and the additional treatment can be, for example, simultaneous, concurrent, separate or sequential.

[00348] Simultaneous administration may, e.g., take place in the form of one fixed combination with two or more active ingredients, or by simultaneously administering two or more active ingredients that are formulated independently. Sequential use (administration) preferably means administration of one (or more) components of a combination at one time point, other components at a different time point, that is, in a chronically staggered manner, preferably such that the combination shows more efficiency than the single compounds administered independently (especially showing synergism). Separate use (administration) preferably means administration of the components of the combination independently of each other at different time points, preferably meaning that the components (a) and (b) are administered such that no overlap of significant measurable blood levels of both compounds are present in an overlapping manner (at the same time).

[00349] Also combinations of two or more of sequential, separate and simultaneous administration are possible, preferably such that the combination component-drugs show a joint

therapeutic effect that exceeds the effect found when the combination component-drugs are used independently at time intervals so large that no mutual effect on their therapeutic efficiency can be found, a synergistic effect being especially preferred.

[00350] The term "delay of progression" as used herein means administration of the combination to patients being in a pre-stage or in an early phase, of the first manifestation or a relapse of the disease to be treated, in which patients, e.g., a pre-form of the corresponding disease is diagnosed or which patients are in a condition, e.g., during a medical treatment or a condition resulting from an accident, under which it is likely that a corresponding disease will develop.

[00351] "Jointly therapeutically active" or "joint therapeutic effect" means that the compounds may be given separately (in a chronically staggered manner, especially a sequence-specific manner) in such time intervals that they preferably, in the warm-blooded animal, especially human, to be treated, still show a (preferably synergistic) interaction (joint therapeutic effect). Whether this is the case, can inter alia be determined by following the blood levels, showing that both compounds are present in the blood of the human to be treated at least during certain time intervals.

[00352] The present disclosure thus encompasses a combination therapy comprising both a KRAS RNAi agent and one or more additional therapies for KRAS-related diseases known in the art.

[00353] The use of known treatments for any of KRAS-related diseases is within the capabilities of one of ordinary skill in the art. Any such additional treatment can be used in conjunction with a RNAi agent to KRAS.

[00354] The dosages of the additional treatments and RNAi agents can be easily determined by one of ordinary skill in the art, and as described herein.

[00355]

[00356] Embodiments comprising one or more efficacious RNAi agents to KRAS

[00357] In various embodiments of the present disclosure, the present disclosure comprises a RNAi agent demonstrating at least about 40, 50, 60, 70, 80, 90 or 95% knockdown (KD) (i.e., no more than about 60, 50, 40, 30, 20, 10, or 5% residual gene activity, respectively) of the KRAS gene at an *in vitro* concentration of 10 or 0.1 nM as assayed in RKO cells.

[00358] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of a Fold-Change at 10 nM at 24 hr of < 0.05, < 0.10, < 0.20, < 0.30, < 0.40 (indicating a KRAS gene knock-down of at least 95, 90, 80, 70, or 60%, respectively, at a concentration of 10 nM at 24 hrs in RKO cells). RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00359] Embodiments comprising one or more efficacious RNAi agents to KRAS

[00360] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of a Fold-Change at 0.1 nM at 120 hr of < 0.30, < 0.20, or < 0.10 (indicating a KRAS gene knock-down of at least 70, 80, or 90%, respectively, at a concentration of 0.1 nM at 120 hrs in RKO cells). RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00361] Various embodiments comprising one or more RNAi agents to KRAS with low EC50

[00362] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of mediating a 50% gene knockdown (EC50) of KRAS at a low concentration in RKO cells. For many of the RNAi agents listed herein, an estimated EC50 is calculated. Cells are treated at 10nM, 1nM, 0.1nM, 0.01nM, and 0.001nM of RNAi agent, and the data fit to a curve. The indicated EC50 is an estimated EC50 calculated from available data that is expected to give 50% gene knock-down of KRAS in RKO cells. In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of mediating a 50% gene knockdown (EC50) at 100, 75, 50, 25, 10, 5, 2.5, 1, 0.75, 0.5, 0.25, 0.2, 0.12, 0.1, 0.09, 0.08, 0.07, 0.06, 0.05, 0.04, 0.03, or 0.02 nM or less in RKO cells. RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00363] Specific embodiments of RNAi agents to KRAS

[00364] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a sense strand and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of: any RNAi agent from any of Tables 1 to 6 and modified or unmodified variants thereof.

[00365] In one embodiment, the composition comprises any one or more of: a RNAi agent comprising a sense strand and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0 nucleotides from the anti-sense strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00366] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00367] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising an anti-sense strand comprising the sequence of the anti-sense strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00368] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprises an anti-sense strand consisting of the sequence of the anti-sense strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00369] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the second of the first strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00370] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the

first and the second strand are the sequences of the first and second strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof.

[00371] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the second of the first strand of any RNAi agent from any of Tables 1 to 6, and modified and unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[00372]

[00373]

[00374] Specific embodiments of RNAi agents to KRAS

[00375] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first strand of: any RNAi agent from any of Tables 1 to 6 or modified or unmodified variants thereof.

[00376] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from the first strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[00377] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the sequence of a first strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[00378] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strands of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[00379] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the first and the second strand are the sequences of the first and second strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[00380] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[00381] Specific embodiments comprising at least 15 contiguous nucleotides differing from 0 to 3 nt from RNAi agents disclosed herein

[00382] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides (nt) differing by 0, 1, 2, or 3 nt from a first strand of:

any RNAi agent from any of Tables 1 to 6 or modified or unmodified variants thereof.

[00383] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[00384] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35523.3 (SEQ ID NO: 428), or a modified or unmodified variant thereof.

[00385] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35529.1 (SEQ ID NO: 429), or a modified or unmodified variant thereof.

[00386] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35535.4 (SEQ ID NO: 430), or a modified or unmodified variant thereof.

[00387] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35541.4 (SEQ ID NO: 431), or a modified or unmodified variant thereof.

[00388] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35547.4 (SEQ ID NO: 432), or a modified or unmodified variant thereof.

[00389] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35553.4 (SEQ ID NO: 433), or a modified or unmodified variant thereof.

[00390] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35559.4 (SEQ ID NO: 434), or a modified or unmodified variant thereof.

[00391] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35565.4 (SEQ ID NO: 435), or a modified or unmodified variant thereof.

[00392] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35524.4 (SEQ ID NO: 436), or a modified or unmodified variant thereof.

[00393] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35530.4 (SEQ ID NO: 437), or a modified or unmodified variant thereof.

[00394] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35536.4 (SEQ ID NO: 438), or a modified or unmodified variant thereof.

[00395] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35542.4 (SEQ ID NO: 439), or a modified or unmodified variant thereof.

[00396] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35548.4 (SEQ ID NO:

440), or a modified or unmodified variant thereof.

[00397] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35554.4 (SEQ ID NO: 441), or a modified or unmodified variant thereof.

[00398] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35560.2 (SEQ ID NO: 442), or a modified or unmodified variant thereof.

[00399] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35566.4 (SEQ ID NO: 443), or a modified or unmodified variant thereof.

[00400] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35525.2 (SEQ ID NO: 444), or a modified or unmodified variant thereof.

[00401] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35531.4 (SEQ ID NO: 445), or a modified or unmodified variant thereof.

[00402] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35537.4 (SEQ ID NO: 446), or a modified or unmodified variant thereof.

[00403] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35543.2 (SEQ ID NO: 447), or a modified or unmodified variant thereof.

[00404] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35549.4 (SEQ ID NO: 448), or a modified or unmodified variant thereof.

[00405] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35555.4 (SEQ ID NO: 449), or a modified or unmodified variant thereof.

[00406] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35561.4 (SEQ ID NO: 450), or a modified or unmodified variant thereof.

[00407] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35567.4 (SEQ ID NO: 451), or a modified or unmodified variant thereof.

[00408] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35526.4 (SEQ ID NO: 452), or a modified or unmodified variant thereof.

[00409] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35532.4 (SEQ ID NO: 453), or a modified or unmodified variant thereof.

[00410] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35538.4 (SEQ ID NO: 454), or a modified or unmodified variant thereof.

[00411] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35544.4 (SEQ ID NO: 455), or a modified or unmodified variant thereof.

[00412] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35550.4 (SEQ ID NO: 456), or a modified or unmodified variant thereof.

[00413] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35556.4 (SEQ ID NO: 457), or a modified or unmodified variant thereof.

[00414] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35562.4 (SEQ ID NO: 458), or a modified or unmodified variant thereof.

[00415] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35568.4 (SEQ ID NO: 459), or a modified or unmodified variant thereof.

[00416] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35527.4 (SEQ ID NO: 460), or a modified or unmodified variant thereof.

[00417] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35533.4 (SEQ ID NO: 461), or a modified or unmodified variant thereof.

[00418] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35539.4 (SEQ ID NO: 462), or a modified or unmodified variant thereof.

[00419] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35545.4 (SEQ ID NO: 463), or a modified or unmodified variant thereof.

[00420] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35551.4 (SEQ ID NO: 464), or a modified or unmodified variant thereof.

[00421] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35563.4 (SEQ ID NO: 465), or a modified or unmodified variant thereof.

[00422] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35528.4 (SEQ ID NO: 466), or a modified or unmodified variant thereof.

[00423] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35540.4 (SEQ ID NO: 467), or a modified or unmodified variant thereof.

[00424] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35546.4 (SEQ ID NO: 468), or a modified or unmodified variant thereof.

[00425] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35552.4 (SEQ ID NO: 469), or a modified or unmodified variant thereof.

[00426] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35558.4 (SEQ ID NO: 470), or a modified or unmodified variant thereof.

[00427] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35564.4 (SEQ ID NO: 471), or a modified or unmodified variant thereof.

[00428] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35570.4 (SEQ ID NO: 472), or a modified or unmodified variant thereof.

[00429] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35571.4 (SEQ ID NO: 473), or a modified or unmodified variant thereof.

[00430] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35577.4 (SEQ ID NO: 474), or a modified or unmodified variant thereof.

[00431] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35583.4 (SEQ ID NO: 475), or a modified or unmodified variant thereof.

[00432] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35589.4 (SEQ ID NO: 476), or a modified or unmodified variant thereof.

[00433] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35595.4 (SEQ ID NO: 477), or a modified or unmodified variant thereof.

[00434] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35601.4 (SEQ ID NO: 478), or a modified or unmodified variant thereof.

[00435] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35607.4 (SEQ ID NO: 479), or a modified or unmodified variant thereof.

[00436] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35613.4 (SEQ ID NO: 480), or a modified or unmodified variant thereof.

[00437] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35572.4 (SEQ ID NO:

481), or a modified or unmodified variant thereof.

[00438] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35578.4 (SEQ ID NO: 482), or a modified or unmodified variant thereof.

[00439] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35584.4 (SEQ ID NO: 483), or a modified or unmodified variant thereof.

[00440] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35590.4 (SEQ ID NO: 484), or a modified or unmodified variant thereof.

[00441] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35596.4 (SEQ ID NO: 485), or a modified or unmodified variant thereof.

[00442] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35602.4 (SEQ ID NO: 486), or a modified or unmodified variant thereof.

[00443] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35608.4 (SEQ ID NO: 487), or a modified or unmodified variant thereof.

[00444] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35614.4 (SEQ ID NO: 488), or a modified or unmodified variant thereof.

[00445] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35573.4 (SEQ ID NO: 489), or a modified or unmodified variant thereof.

[00446] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35579.4 (SEQ ID NO: 490), or a modified or unmodified variant thereof.

[00447] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35585.4 (SEQ ID NO: 491), or a modified or unmodified variant thereof.

[00448] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35591.4 (SEQ ID NO: 492), or a modified or unmodified variant thereof.

[00449] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35597.4 (SEQ ID NO: 493), or a modified or unmodified variant thereof.

[00450] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35603.4 (SEQ ID NO: 494), or a modified or unmodified variant thereof.

[00451] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35609.4 (SEQ ID NO: 495), or a modified or unmodified variant thereof.

[00452] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35615.4 (SEQ ID NO: 496), or a modified or unmodified variant thereof.

[00453] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35574.4 (SEQ ID NO: 497), or a modified or unmodified variant thereof.

[00454] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35580.1 (SEQ ID NO: 498), or a modified or unmodified variant thereof.

[00455] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35586.4 (SEQ ID NO: 499), or a modified or unmodified variant thereof.

[00456] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35592.4 (SEQ ID NO: 500), or a modified or unmodified variant thereof.

[00457] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35598.4 (SEQ ID NO: 501), or a modified or unmodified variant thereof.

[00458] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35604.4 (SEQ ID NO: 502), or a modified or unmodified variant thereof.

[00459] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35610.4 (SEQ ID NO: 503), or a modified or unmodified variant thereof.

[00460] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35616.4 (SEQ ID NO: 504), or a modified or unmodified variant thereof.

[00461] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35575.4 (SEQ ID NO: 505), or a modified or unmodified variant thereof.

[00462] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35581.4 (SEQ ID NO: 506), or a modified or unmodified variant thereof.

[00463] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35587.4 (SEQ ID NO: 507), or a modified or unmodified variant thereof.

[00464] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35593.4 (SEQ ID NO: 508), or a modified or unmodified variant thereof.

[00465] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35599.4 (SEQ ID NO: 509), or a modified or unmodified variant thereof.

[00466] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35605.4 (SEQ ID NO: 510), or a modified or unmodified variant thereof.

[00467] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35611.4 (SEQ ID NO: 511), or a modified or unmodified variant thereof.

[00468] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35617.4 (SEQ ID NO: 512), or a modified or unmodified variant thereof.

[00469] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35576.4 (SEQ ID NO: 513), or a modified or unmodified variant thereof.

[00470] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35588.4 (SEQ ID NO: 514), or a modified or unmodified variant thereof.

[00471] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35667.1 (SEQ ID NO: 515), or a modified or unmodified variant thereof.

[00472] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35673.1 (SEQ ID NO: 516), or a modified or unmodified variant thereof.

[00473] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35679.1 (SEQ ID NO: 517), or a modified or unmodified variant thereof.

[00474] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35685.1 (SEQ ID NO: 518), or a modified or unmodified variant thereof.

[00475] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35691.1 (SEQ ID NO: 519), or a modified or unmodified variant thereof.

[00476] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35557.1 (SEQ ID NO: 520), or a modified or unmodified variant thereof.

[00477] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35618.1 (SEQ ID NO: 521), or a modified or unmodified variant thereof.

[00478] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35569.1 (SEQ ID NO:

522), or a modified or unmodified variant thereof.

[00479] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35534.1 (SEQ ID NO: 523), or a modified or unmodified variant thereof.

[00480] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35582.1 (SEQ ID NO: 524), or a modified or unmodified variant thereof.

[00481] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35594.1 (SEQ ID NO: 525), or a modified or unmodified variant thereof.

[00482] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35600.1 (SEQ ID NO: 526), or a modified or unmodified variant thereof.

[00483] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35606.1 (SEQ ID NO: 527), or a modified or unmodified variant thereof.

[00484] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35612.1 (SEQ ID NO: 528), or a modified or unmodified variant thereof.

[00485] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38127.1 (SEQ ID NO: 529), or a modified or unmodified variant thereof.

[00486] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38133.1 (SEQ ID NO: 530), or a modified or unmodified variant thereof.

[00487] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38139.1 (SEQ ID NO: 531), or a modified or unmodified variant thereof.

[00488] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38145.1 (SEQ ID NO: 532), or a modified or unmodified variant thereof.

[00489] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38151.1 (SEQ ID NO: 533), or a modified or unmodified variant thereof.

[00490] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38157.1 (SEQ ID NO: 534), or a modified or unmodified variant thereof.

[00491] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38163.1 (SEQ ID NO: 535), or a modified or unmodified variant thereof.

[00492] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38169.1 (SEQ ID NO: 536), or a modified or unmodified variant thereof.

[00493] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38128.1 (SEQ ID NO: 537), or a modified or unmodified variant thereof.

[00494] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38134.1 (SEQ ID NO: 538), or a modified or unmodified variant thereof.

[00495] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38140.1 (SEQ ID NO: 539), or a modified or unmodified variant thereof.

[00496] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38146.1 (SEQ ID NO: 540), or a modified or unmodified variant thereof.

[00497] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38152.1 (SEQ ID NO: 541), or a modified or unmodified variant thereof.

[00498] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38158.1 (SEQ ID NO: 542), or a modified or unmodified variant thereof.

[00499] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38164.1 (SEQ ID NO: 543), or a modified or unmodified variant thereof.

[00500] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38170.1 (SEQ ID NO: 544), or a modified or unmodified variant thereof.

[00501] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38129.1 (SEQ ID NO: 545), or a modified or unmodified variant thereof.

[00502] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38135.1 (SEQ ID NO: 546), or a modified or unmodified variant thereof.

[00503] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38141.1 (SEQ ID NO: 547), or a modified or unmodified variant thereof.

[00504] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38147.1 (SEQ ID NO: 548), or a modified or unmodified variant thereof.

[00505] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38153.1 (SEQ ID NO: 549), or a modified or unmodified variant thereof.

[00506] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38159.1 (SEQ ID NO: 550), or a modified or unmodified variant thereof.

[00507] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38165.1 (SEQ ID NO: 551), or a modified or unmodified variant thereof.

[00508] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38171.1 (SEQ ID NO: 552), or a modified or unmodified variant thereof.

[00509] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38130.1 (SEQ ID NO: 553), or a modified or unmodified variant thereof.

[00510] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38136.1 (SEQ ID NO: 554), or a modified or unmodified variant thereof.

[00511] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38142.1 (SEQ ID NO: 555), or a modified or unmodified variant thereof.

[00512] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38148.1 (SEQ ID NO: 556), or a modified or unmodified variant thereof.

[00513] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38154.1 (SEQ ID NO: 557), or a modified or unmodified variant thereof.

[00514] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38160.1 (SEQ ID NO: 558), or a modified or unmodified variant thereof.

[00515] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38166.1 (SEQ ID NO: 559), or a modified or unmodified variant thereof.

[00516] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38172.1 (SEQ ID NO: 560), or a modified or unmodified variant thereof.

[00517] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38131.1 (SEQ ID NO: 561), or a modified or unmodified variant thereof.

[00518] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38137.1 (SEQ ID NO: 562), or a modified or unmodified variant thereof.

[00519] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38143.1 (SEQ ID NO:

563), or a modified or unmodified variant thereof.

[00520] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38149.1 (SEQ ID NO: 564), or a modified or unmodified variant thereof.

[00521] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38155.1 (SEQ ID NO: 565), or a modified or unmodified variant thereof.

[00522] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38161.1 (SEQ ID NO: 566), or a modified or unmodified variant thereof.

[00523] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38167.1 (SEQ ID NO: 567), or a modified or unmodified variant thereof.

[00524] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38173.1 (SEQ ID NO: 568), or a modified or unmodified variant thereof.

[00525] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38132.1 (SEQ ID NO: 569), or a modified or unmodified variant thereof.

[00526] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38138.1 (SEQ ID NO: 570), or a modified or unmodified variant thereof.

[00527] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38144.1 (SEQ ID NO: 571), or a modified or unmodified variant thereof.

[00528] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38150.1 (SEQ ID NO: 572), or a modified or unmodified variant thereof.

[00529] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38156.1 (SEQ ID NO: 573), or a modified or unmodified variant thereof.

[00530] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38162.1 (SEQ ID NO: 574), or a modified or unmodified variant thereof.

[00531] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38168.1 (SEQ ID NO: 575), or a modified or unmodified variant thereof.

[00532] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38174.1 (SEQ ID NO: 576), or a modified or unmodified variant thereof.

[00533] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39683.1 (SEQ ID NO: 577), or a modified or unmodified variant thereof.

[00534] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39689.1 (SEQ ID NO: 578), or a modified or unmodified variant thereof.

[00535] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39695.1 (SEQ ID NO: 579), or a modified or unmodified variant thereof.

[00536] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39701.1 (SEQ ID NO: 580), or a modified or unmodified variant thereof.

[00537] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39707.1 (SEQ ID NO: 581), or a modified or unmodified variant thereof.

[00538] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39713.1 (SEQ ID NO: 582), or a modified or unmodified variant thereof.

[00539] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39719.1 (SEQ ID NO: 583), or a modified or unmodified variant thereof.

[00540] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39725.1 (SEQ ID NO: 584), or a modified or unmodified variant thereof.

[00541] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39684.1 (SEQ ID NO: 585), or a modified or unmodified variant thereof.

[00542] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39690.1 (SEQ ID NO: 586), or a modified or unmodified variant thereof.

[00543] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39696.1 (SEQ ID NO: 587), or a modified or unmodified variant thereof.

[00544] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39702.1 (SEQ ID NO: 588), or a modified or unmodified variant thereof.

[00545] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39708.1 (SEQ ID NO: 589), or a modified or unmodified variant thereof.

[00546] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39714.1 (SEQ ID NO: 590), or a modified or unmodified variant thereof.

[00547] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39720.1 (SEQ ID NO: 591), or a modified or unmodified variant thereof.

[00548] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39726.1 (SEQ ID NO: 592), or a modified or unmodified variant thereof.

[00549] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39685.1 (SEQ ID NO: 593), or a modified or unmodified variant thereof.

[00550] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39691.1 (SEQ ID NO: 594), or a modified or unmodified variant thereof.

[00551] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39697.1 (SEQ ID NO: 595), or a modified or unmodified variant thereof.

[00552] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39703.1 (SEQ ID NO: 596), or a modified or unmodified variant thereof.

[00553] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39709.1 (SEQ ID NO: 597), or a modified or unmodified variant thereof.

[00554] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39715.1 (SEQ ID NO: 598), or a modified or unmodified variant thereof.

[00555] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39721.1 (SEQ ID NO: 599), or a modified or unmodified variant thereof.

[00556] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39727.1 (SEQ ID NO: 600), or a modified or unmodified variant thereof.

[00557] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39686.1 (SEQ ID NO: 601), or a modified or unmodified variant thereof.

[00558] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39692.1 (SEQ ID NO: 602), or a modified or unmodified variant thereof.

[00559] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39698.1 (SEQ ID NO: 603), or a modified or unmodified variant thereof.

[00560] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39704.1 (SEQ ID NO:

604), or a modified or unmodified variant thereof.

[00561] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39710.1 (SEQ ID NO: 605), or a modified or unmodified variant thereof.

[00562] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39716.1 (SEQ ID NO: 606), or a modified or unmodified variant thereof.

[00563] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39722.1 (SEQ ID NO: 607), or a modified or unmodified variant thereof.

[00564] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39728.1 (SEQ ID NO: 608), or a modified or unmodified variant thereof.

[00565] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39687.1 (SEQ ID NO: 609), or a modified or unmodified variant thereof.

[00566] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39693.1 (SEQ ID NO: 610), or a modified or unmodified variant thereof.

[00567] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39699.1 (SEQ ID NO: 611), or a modified or unmodified variant thereof.

[00568] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39705.1 (SEQ ID NO: 612), or a modified or unmodified variant thereof.

[00569] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39711.1 (SEQ ID NO: 613), or a modified or unmodified variant thereof.

[00570] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39717.1 (SEQ ID NO: 614), or a modified or unmodified variant thereof.

[00571] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39723.1 (SEQ ID NO: 615), or a modified or unmodified variant thereof.

[00572] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39729.1 (SEQ ID NO: 616), or a modified or unmodified variant thereof.

[00573] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39688.1 (SEQ ID NO: 617), or a modified or unmodified variant thereof.

[00574] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39694.1 (SEQ ID NO: 618), or a modified or unmodified variant thereof.

[00575] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39700.1 (SEQ ID NO: 619), or a modified or unmodified variant thereof.

[00576] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39706.1 (SEQ ID NO: 620), or a modified or unmodified variant thereof.

[00577] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39712.1 (SEQ ID NO: 621), or a modified or unmodified variant thereof.

[00578] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39718.1 (SEQ ID NO: 622), or a modified or unmodified variant thereof.

[00579] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39724.1 (SEQ ID NO: 623), or a modified or unmodified variant thereof.

[00580] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39730.1 (SEQ ID NO: 624), or a modified or unmodified variant thereof.

[00581] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39736.1 (SEQ ID NO: 625), or a modified or unmodified variant thereof.

[00582] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39742.1 (SEQ ID NO: 626), or a modified or unmodified variant thereof.

[00583] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39748.1 (SEQ ID NO: 627), or a modified or unmodified variant thereof.

[00584] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39754.1 (SEQ ID NO: 628), or a modified or unmodified variant thereof.

[00585] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39760.1 (SEQ ID NO: 629), or a modified or unmodified variant thereof.

[00586] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39766.1 (SEQ ID NO: 630), or a modified or unmodified variant thereof.

[00587] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39772.1 (SEQ ID NO: 631), or a modified or unmodified variant thereof.

[00588] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39731.1 (SEQ ID NO: 632), or a modified or unmodified variant thereof.

[00589] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39737.1 (SEQ ID NO: 633), or a modified or unmodified variant thereof.

[00590] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39743.1 (SEQ ID NO: 634), or a modified or unmodified variant thereof.

[00591] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39749.1 (SEQ ID NO: 635), or a modified or unmodified variant thereof.

[00592] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39755.1 (SEQ ID NO: 636), or a modified or unmodified variant thereof.

[00593] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39761.1 (SEQ ID NO: 637), or a modified or unmodified variant thereof.

[00594] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39767.1 (SEQ ID NO: 638), or a modified or unmodified variant thereof.

[00595] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39773.1 (SEQ ID NO: 639), or a modified or unmodified variant thereof.

[00596] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39732.1 (SEQ ID NO: 640), or a modified or unmodified variant thereof.

[00597] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39738.1 (SEQ ID NO: 641), or a modified or unmodified variant thereof.

[00598] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39744.1 (SEQ ID NO: 642), or a modified or unmodified variant thereof.

[00599] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39750.1 (SEQ ID NO: 643), or a modified or unmodified variant thereof.

[00600] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39756.1 (SEQ ID NO: 644), or a modified or unmodified variant thereof.

[00601] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39762.1 (SEQ ID NO:

645), or a modified or unmodified variant thereof.

[00602] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39768.1 (SEQ ID NO: 646), or a modified or unmodified variant thereof.

[00603] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39774.1 (SEQ ID NO: 647), or a modified or unmodified variant thereof.

[00604] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39733.1 (SEQ ID NO: 648), or a modified or unmodified variant thereof.

[00605] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39739.1 (SEQ ID NO: 649), or a modified or unmodified variant thereof.

[00606] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39745.1 (SEQ ID NO: 650), or a modified or unmodified variant thereof.

[00607] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39751.1 (SEQ ID NO: 651), or a modified or unmodified variant thereof.

[00608] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39757.1 (SEQ ID NO: 652), or a modified or unmodified variant thereof.

[00609] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39763.1 (SEQ ID NO: 653), or a modified or unmodified variant thereof.

[00610] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39769.1 (SEQ ID NO: 654), or a modified or unmodified variant thereof.

[00611] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39775.1 (SEQ ID NO: 655), or a modified or unmodified variant thereof.

[00612] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39734.1 (SEQ ID NO: 656), or a modified or unmodified variant thereof.

[00613] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39740.1 (SEQ ID NO: 657), or a modified or unmodified variant thereof.

[00614] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39746.1 (SEQ ID NO: 658), or a modified or unmodified variant thereof.

[00615] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39752.1 (SEQ ID NO: 659), or a modified or unmodified variant thereof.

[00616] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39758.1 (SEQ ID NO: 660), or a modified or unmodified variant thereof.

[00617] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39764.1 (SEQ ID NO: 661), or a modified or unmodified variant thereof.

[00618] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39770.1 (SEQ ID NO: 662), or a modified or unmodified variant thereof.

[00619] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39776.1 (SEQ ID NO: 663), or a modified or unmodified variant thereof.

[00620] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39735.1 (SEQ ID NO: 664), or a modified or unmodified variant thereof.

[00621] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39741.1 (SEQ ID NO: 665), or a modified or unmodified variant thereof.

[00622] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39747.1 (SEQ ID NO: 666), or a modified or unmodified variant thereof.

[00623] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39753.1 (SEQ ID NO: 667), or a modified or unmodified variant thereof.

[00624] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39759.1 (SEQ ID NO: 668), or a modified or unmodified variant thereof.

[00625] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39765.1 (SEQ ID NO: 669), or a modified or unmodified variant thereof.

[00626] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39771.1 (SEQ ID NO: 670), or a modified or unmodified variant thereof.

[00627] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39778.1 (SEQ ID NO: 671), or a modified or unmodified variant thereof.

[00628] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39784.1 (SEQ ID NO: 672), or a modified or unmodified variant thereof.

[00629] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39790.1 (SEQ ID NO: 673), or a modified or unmodified variant thereof.

[00630] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39796.1 (SEQ ID NO: 674), or a modified or unmodified variant thereof.

[00631] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39802.1 (SEQ ID NO: 675), or a modified or unmodified variant thereof.

[00632] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39808.1 (SEQ ID NO: 676), or a modified or unmodified variant thereof.

[00633] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39814.1 (SEQ ID NO: 677), or a modified or unmodified variant thereof.

[00634] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39820.1 (SEQ ID NO: 678), or a modified or unmodified variant thereof.

[00635] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39779.1 (SEQ ID NO: 679), or a modified or unmodified variant thereof.

[00636] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39785.1 (SEQ ID NO: 680), or a modified or unmodified variant thereof.

[00637] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39791.1 (SEQ ID NO: 681), or a modified or unmodified variant thereof.

[00638] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39797.1 (SEQ ID NO: 682), or a modified or unmodified variant thereof.

[00639] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39803.1 (SEQ ID NO: 683), or a modified or unmodified variant thereof.

[00640] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39809.1 (SEQ ID NO: 684), or a modified or unmodified variant thereof.

[00641] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39815.1 (SEQ ID NO: 685), or a modified or unmodified variant thereof.

[00642] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39821.1 (SEQ ID NO:

686), or a modified or unmodified variant thereof.

[00643] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39780.1 (SEQ ID NO: 687), or a modified or unmodified variant thereof.

[00644] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39786.1 (SEQ ID NO: 688), or a modified or unmodified variant thereof.

[00645] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39792.1 (SEQ ID NO: 689), or a modified or unmodified variant thereof.

[00646] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39798.1 (SEQ ID NO: 690), or a modified or unmodified variant thereof.

[00647] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39804.1 (SEQ ID NO: 691), or a modified or unmodified variant thereof.

[00648] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39810.1 (SEQ ID NO: 692), or a modified or unmodified variant thereof.

[00649] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39816.1 (SEQ ID NO: 693), or a modified or unmodified variant thereof.

[00650] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39822.1 (SEQ ID NO: 694), or a modified or unmodified variant thereof.

[00651] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39781.1 (SEQ ID NO: 695), or a modified or unmodified variant thereof.

[00652] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39787.1 (SEQ ID NO: 696), or a modified or unmodified variant thereof.

[00653] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39793.1 (SEQ ID NO: 697), or a modified or unmodified variant thereof.

[00654] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39799.1 (SEQ ID NO: 698), or a modified or unmodified variant thereof.

[00655] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39805.1 (SEQ ID NO: 699), or a modified or unmodified variant thereof.

[00656] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39811.1 (SEQ ID NO: 700), or a modified or unmodified variant thereof.

[00657] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39817.1 (SEQ ID NO: 701), or a modified or unmodified variant thereof.

[00658] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39823.1 (SEQ ID NO: 702), or a modified or unmodified variant thereof.

[00659] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39782.1 (SEQ ID NO: 703), or a modified or unmodified variant thereof.

[00660] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39788.1 (SEQ ID NO: 704), or a modified or unmodified variant thereof.

[00661] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39794.1 (SEQ ID NO: 705), or a modified or unmodified variant thereof.

[00662] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39800.1 (SEQ ID NO: 706), or a modified or unmodified variant thereof.

[00663] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39806.1 (SEQ ID NO: 707), or a modified or unmodified variant thereof.

[00664] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39812.1 (SEQ ID NO: 708), or a modified or unmodified variant thereof.

[00665] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39818.1 (SEQ ID NO: 709), or a modified or unmodified variant thereof.

[00666] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39824.1 (SEQ ID NO: 710), or a modified or unmodified variant thereof.

[00667] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39783.1 (SEQ ID NO: 711), or a modified or unmodified variant thereof.

[00668] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39789.1 (SEQ ID NO: 712), or a modified or unmodified variant thereof.

[00669] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39795.1 (SEQ ID NO: 713), or a modified or unmodified variant thereof.

[00670] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39801.1 (SEQ ID NO: 714), or a modified or unmodified variant thereof.

[00671] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39807.1 (SEQ ID NO: 715), or a modified or unmodified variant thereof.

[00672] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39813.1 (SEQ ID NO: 716), or a modified or unmodified variant thereof.

[00673] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39819.1 (SEQ ID NO: 717), or a modified or unmodified variant thereof.

[00674] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39825.1 (SEQ ID NO: 718), or a modified or unmodified variant thereof.

[00675] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39831.1 (SEQ ID NO: 719), or a modified or unmodified variant thereof.

[00676] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39837.1 (SEQ ID NO: 720), or a modified or unmodified variant thereof.

[00677] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39843.1 (SEQ ID NO: 721), or a modified or unmodified variant thereof.

[00678] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39849.1 (SEQ ID NO: 722), or a modified or unmodified variant thereof.

[00679] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39855.1 (SEQ ID NO: 723), or a modified or unmodified variant thereof.

[00680] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39861.1 (SEQ ID NO: 724), or a modified or unmodified variant thereof.

[00681] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39867.1 (SEQ ID NO: 725), or a modified or unmodified variant thereof.

[00682] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39826.1 (SEQ ID NO: 726), or a modified or unmodified variant thereof.

[00683] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39832.1 (SEQ ID NO:

727), or a modified or unmodified variant thereof.

[00684] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39838.1 (SEQ ID NO: 728), or a modified or unmodified variant thereof.

[00685] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39844.1 (SEQ ID NO: 729), or a modified or unmodified variant thereof.

[00686] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39850.1 (SEQ ID NO: 730), or a modified or unmodified variant thereof.

[00687] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39856.1 (SEQ ID NO: 731), or a modified or unmodified variant thereof.

[00688] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39862.1 (SEQ ID NO: 732), or a modified or unmodified variant thereof.

[00689] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39868.1 (SEQ ID NO: 733), or a modified or unmodified variant thereof.

[00690] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39827.1 (SEQ ID NO: 734), or a modified or unmodified variant thereof.

[00691] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39833.1 (SEQ ID NO: 735), or a modified or unmodified variant thereof.

[00692] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39839.1 (SEQ ID NO: 736), or a modified or unmodified variant thereof.

[00693] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39845.1 (SEQ ID NO: 737), or a modified or unmodified variant thereof.

[00694] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39851.1 (SEQ ID NO: 738), or a modified or unmodified variant thereof.

[00695] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39857.1 (SEQ ID NO: 739), or a modified or unmodified variant thereof.

[00696] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39863.1 (SEQ ID NO: 740), or a modified or unmodified variant thereof.

[00697] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39869.1 (SEQ ID NO: 741), or a modified or unmodified variant thereof.

[00698] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39828.1 (SEQ ID NO: 742), or a modified or unmodified variant thereof.

[00699] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39834.1 (SEQ ID NO: 743), or a modified or unmodified variant thereof.

[00700] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39840.1 (SEQ ID NO: 744), or a modified or unmodified variant thereof.

[00701] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39846.1 (SEQ ID NO: 745), or a modified or unmodified variant thereof.

[00702] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39852.1 (SEQ ID NO: 746), or a modified or unmodified variant thereof.

[00703] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39858.1 (SEQ ID NO: 747), or a modified or unmodified variant thereof.

[00704] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39864.1 (SEQ ID NO: 748), or a modified or unmodified variant thereof.

[00705] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39870.1 (SEQ ID NO: 749), or a modified or unmodified variant thereof.

[00706] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39829.1 (SEQ ID NO: 750), or a modified or unmodified variant thereof.

[00707] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39835.1 (SEQ ID NO: 751), or a modified or unmodified variant thereof.

[00708] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39841.1 (SEQ ID NO: 752), or a modified or unmodified variant thereof.

[00709] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39853.1 (SEQ ID NO: 753), or a modified or unmodified variant thereof.

[00710] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39859.1 (SEQ ID NO: 754), or a modified or unmodified variant thereof.

[00711] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39865.1 (SEQ ID NO: 755), or a modified or unmodified variant thereof.

[00712] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39871.1 (SEQ ID NO: 756), or a modified or unmodified variant thereof.

[00713] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39830.1 (SEQ ID NO: 757), or a modified or unmodified variant thereof.

[00714] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39836.1 (SEQ ID NO: 758), or a modified or unmodified variant thereof.

[00715] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39842.1 (SEQ ID NO: 759), or a modified or unmodified variant thereof.

[00716] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39848.1 (SEQ ID NO: 760), or a modified or unmodified variant thereof.

[00717] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39854.1 (SEQ ID NO: 761), or a modified or unmodified variant thereof.

[00718] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39860.1 (SEQ ID NO: 762), or a modified or unmodified variant thereof.

[00719] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39866.1 (SEQ ID NO: 763), or a modified or unmodified variant thereof.

[00720] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39992.1 (SEQ ID NO: 764), or a modified or unmodified variant thereof.

[00721] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39998.1 (SEQ ID NO: 765), or a modified or unmodified variant thereof.

[00722] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40004.1 (SEQ ID NO: 766), or a modified or unmodified variant thereof.

[00723] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40010.1 (SEQ ID NO: 767), or a modified or unmodified variant thereof.

[00724] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40016.1 (SEQ ID NO:

768), or a modified or unmodified variant thereof.

[00725] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40022.1 (SEQ ID NO: 769), or a modified or unmodified variant thereof.

[00726] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40028.1 (SEQ ID NO: 770), or a modified or unmodified variant thereof.

[00727] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40034.1 (SEQ ID NO: 771), or a modified or unmodified variant thereof.

[00728] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39999.1 (SEQ ID NO: 772), or a modified or unmodified variant thereof.

[00729] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40005.1 (SEQ ID NO: 773), or a modified or unmodified variant thereof.

[00730] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40011.1 (SEQ ID NO: 774), or a modified or unmodified variant thereof.

[00731] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40017.1 (SEQ ID NO: 775), or a modified or unmodified variant thereof.

[00732] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40029.1 (SEQ ID NO: 776), or a modified or unmodified variant thereof.

[00733] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40035.1 (SEQ ID NO: 777), or a modified or unmodified variant thereof.

[00734] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39994.1 (SEQ ID NO: 778), or a modified or unmodified variant thereof.

[00735] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40000.1 (SEQ ID NO: 779), or a modified or unmodified variant thereof.

[00736] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40006.1 (SEQ ID NO: 780), or a modified or unmodified variant thereof.

[00737] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40012.1 (SEQ ID NO: 781), or a modified or unmodified variant thereof.

[00738] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40018.1 (SEQ ID NO: 782), or a modified or unmodified variant thereof.

[00739] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40024.1 (SEQ ID NO: 783), or a modified or unmodified variant thereof.

[00740] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40030.1 (SEQ ID NO: 784), or a modified or unmodified variant thereof.

[00741] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40036.1 (SEQ ID NO: 785), or a modified or unmodified variant thereof.

[00742] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39995.1 (SEQ ID NO: 786), or a modified or unmodified variant thereof.

[00743] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40001.1 (SEQ ID NO: 787), or a modified or unmodified variant thereof.

[00744] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40007.1 (SEQ ID NO: 788), or a modified or unmodified variant thereof.

[00745] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40013.1 (SEQ ID NO: 789), or a modified or unmodified variant thereof.

[00746] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40019.1 (SEQ ID NO: 790), or a modified or unmodified variant thereof.

[00747] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40025.1 (SEQ ID NO: 791), or a modified or unmodified variant thereof.

[00748] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40031.1 (SEQ ID NO: 792), or a modified or unmodified variant thereof.

[00749] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40037.1 (SEQ ID NO: 793), or a modified or unmodified variant thereof.

[00750] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39996.1 (SEQ ID NO: 794), or a modified or unmodified variant thereof.

[00751] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40002.1 (SEQ ID NO: 795), or a modified or unmodified variant thereof.

[00752] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40008.1 (SEQ ID NO: 796), or a modified or unmodified variant thereof.

[00753] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40014.1 (SEQ ID NO: 797), or a modified or unmodified variant thereof.

[00754] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40020.1 (SEQ ID NO: 798), or a modified or unmodified variant thereof.

[00755] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40026.1 (SEQ ID NO: 799), or a modified or unmodified variant thereof.

[00756] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40032.1 (SEQ ID NO: 800), or a modified or unmodified variant thereof.

[00757] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40038.1 (SEQ ID NO: 801), or a modified or unmodified variant thereof.

[00758] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39997.1 (SEQ ID NO: 802), or a modified or unmodified variant thereof.

[00759] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40009.1 (SEQ ID NO: 803), or a modified or unmodified variant thereof.

[00760] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40015.1 (SEQ ID NO: 804), or a modified or unmodified variant thereof.

[00761] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40021.1 (SEQ ID NO: 805), or a modified or unmodified variant thereof.

[00762] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40027.1 (SEQ ID NO: 806), or a modified or unmodified variant thereof.

[00763] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40033.1 (SEQ ID NO: 807), or a modified or unmodified variant thereof.

[00764] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40039.1 (SEQ ID NO: 808), or a modified or unmodified variant thereof.

[00765] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40045.1 (SEQ ID NO:

809), or a modified or unmodified variant thereof.

[00766] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40051.1 (SEQ ID NO: 810), or a modified or unmodified variant thereof.

[00767] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40057.1 (SEQ ID NO: 811), or a modified or unmodified variant thereof.

[00768] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40063.1 (SEQ ID NO: 812), or a modified or unmodified variant thereof.

[00769] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40069.1 (SEQ ID NO: 813), or a modified or unmodified variant thereof.

[00770] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40075.1 (SEQ ID NO: 814), or a modified or unmodified variant thereof.

[00771] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40081.1 (SEQ ID NO: 815), or a modified or unmodified variant thereof.

[00772] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40040.1 (SEQ ID NO: 816), or a modified or unmodified variant thereof.

[00773] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40046.1 (SEQ ID NO: 817), or a modified or unmodified variant thereof.

[00774] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40052.1 (SEQ ID NO: 818), or a modified or unmodified variant thereof.

[00775] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40058.1 (SEQ ID NO: 819), or a modified or unmodified variant thereof.

[00776] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40064.1 (SEQ ID NO: 820), or a modified or unmodified variant thereof.

[00777] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40070.1 (SEQ ID NO: 821), or a modified or unmodified variant thereof.

[00778] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40076.1 (SEQ ID NO: 822), or a modified or unmodified variant thereof.

[00779] A RNAi agent comprising a first and a second strand, wherein the first strand comprises

at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40082.1 (SEQ ID NO: 823), or a modified or unmodified variant thereof.

[00780] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40041.1 (SEQ ID NO: 824), or a modified or unmodified variant thereof.

[00781] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40047.1 (SEQ ID NO: 825), or a modified or unmodified variant thereof.

[00782] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40053.1 (SEQ ID NO: 826), or a modified or unmodified variant thereof.

[00783] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40059.1 (SEQ ID NO: 827), or a modified or unmodified variant thereof.

[00784] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40065.1 (SEQ ID NO: 828), or a modified or unmodified variant thereof.

[00785] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40071.1 (SEQ ID NO: 829), or a modified or unmodified variant thereof.

[00786] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40077.1 (SEQ ID NO: 830), or a modified or unmodified variant thereof.

[00787] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40083.1 (SEQ ID NO: 831), or a modified or unmodified variant thereof.

[00788] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40042.1 (SEQ ID NO: 832), or a modified or unmodified variant thereof.

[00789] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40048.1 (SEQ ID NO: 833), or a modified or unmodified variant thereof.

[00790] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40054.1 (SEQ ID NO: 834), or a modified or unmodified variant thereof.

[00791] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40060.1 (SEQ ID NO: 835), or a modified or unmodified variant thereof.

[00792] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40066.1 (SEQ ID NO: 836), or a modified or unmodified variant thereof.

[00793] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40072.1 (SEQ ID NO: 837), or a modified or unmodified variant thereof.

[00794] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40078.1 (SEQ ID NO: 838), or a modified or unmodified variant thereof.

[00795] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40084.1 (SEQ ID NO: 839), or a modified or unmodified variant thereof.

[00796] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40043.1 (SEQ ID NO: 840), or a modified or unmodified variant thereof.

[00797] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40049.1 (SEQ ID NO: 841), or a modified or unmodified variant thereof.

[00798] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40055.1 (SEQ ID NO: 842), or a modified or unmodified variant thereof.

[00799] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40061.1 (SEQ ID NO: 843), or a modified or unmodified variant thereof.

[00800] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40067.1 (SEQ ID NO: 844), or a modified or unmodified variant thereof.

[00801] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40073.1 (SEQ ID NO: 845), or a modified or unmodified variant thereof.

[00802] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40079.1 (SEQ ID NO: 846), or a modified or unmodified variant thereof.

[00803] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40085.1 (SEQ ID NO: 847), or a modified or unmodified variant thereof.

[00804] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40044.1 (SEQ ID NO: 848), or a modified or unmodified variant thereof.

[00805] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40050.1 (SEQ ID NO: 849), or a modified or unmodified variant thereof.

[00806] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40056.1 (SEQ ID NO:

850), or a modified or unmodified variant thereof.

[00807] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40062.1 (SEQ ID NO: 851), or a modified or unmodified variant thereof.

[00808] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40068.1 (SEQ ID NO: 852), or a modified or unmodified variant thereof.

[00809] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40074.1 (SEQ ID NO: 853), or a modified or unmodified variant thereof.

[00810] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40080.1 (SEQ ID NO: 854), or a modified or unmodified variant thereof.

[00811] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39720.1 (SEQ ID NO: 1754), or a modified or unmodified variant thereof.

[00812] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39706.1 (SEQ ID NO: 1755), or a modified or unmodified variant thereof.

[00813] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39712.1 (SEQ ID NO: 1756), or a modified or unmodified variant thereof.

[00814] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39760.1 (SEQ ID NO: 1757), or a modified or unmodified variant thereof.

[00815] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39732.1 (SEQ ID NO: 1758), or a modified or unmodified variant thereof.

[00816] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35541.4 (SEQ ID NO: 1759), or a modified or unmodified variant thereof.

[00817] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NO: 1760), or a modified or unmodified variant thereof.

[00818] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39741.1, or modified or unmodified variants thereof.

[00819] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: hs_KRAS_ 322_A22S26 (SEQ ID NO: 1761), or a modified or unmodified variant thereof.

[00820] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39778.1 (SEQ ID NO: 1762), or a modified or unmodified variant thereof.

[00821] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39790.1 (SEQ ID NO: 1763), or a modified or unmodified variant thereof.

[00822] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39822.1 (SEQ ID NO: 1764), or a modified or unmodified variant thereof.

[00823] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35609.4 (SEQ ID NO: 1765), or a modified or unmodified variant thereof.

[00824] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35581.4 (SEQ ID NO: 1766), or a modified or unmodified variant thereof.

[00825] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39845.1 (SEQ ID NO: 1767), or a modified or unmodified variant thereof.

[00826] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39858.1 (SEQ ID NO: 1768), or a modified or unmodified variant thereof.

[00827] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39870.1 (SEQ ID NO: 1769), or a modified or unmodified variant thereof.

[00828] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35576.4 (SEQ ID NO: 1770), or a modified or unmodified variant thereof.

[00829] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35588.4 (SEQ ID NO: 1771), or a modified or unmodified variant thereof.

[00830] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35600.1 (SEQ ID NO: 1772), or a modified or unmodified variant thereof.

[00831] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-35606.1 (SEQ ID NO: 1773), or a modified or unmodified variant thereof.

[00832] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38151.1 (SEQ ID NO: 1774), or a modified or unmodified variant thereof.

[00833] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38163.1 (SEQ ID NO: 1775), or a modified or unmodified variant thereof.

[00834] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-39999.1 (SEQ ID NO: 1776), or a modified or unmodified variant thereof.

[00835] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38159.1 or hs_KRAS_ 528_A22S26 (SEQ ID NO: 1777), or a modified or unmodified variant thereof.

[00836] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38130.1 or hs_KRAS_ 531_A22S26 (SEQ ID NO: 1778), or a modified or unmodified variant thereof.

[00837] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38136.1 (SEQ ID NO: 1779), or a modified or unmodified variant thereof.

[00838] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40036.1 (SEQ ID NO: 1780), or a modified or unmodified variant thereof.

[00839] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40008.1 (SEQ ID NO: 1781), or a modified or unmodified variant thereof.

[00840] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40021.1 (SEQ ID NO: 1782), or a modified or unmodified variant thereof.

[00841] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40077.1 (SEQ ID NO: 1783), or a modified or unmodified variant thereof.

[00842] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40072.1 (SEQ ID NO: 1784), or a modified or unmodified variant thereof.

[00843] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40061.1 (SEQ ID NO: 1785), or a modified or unmodified variant thereof.

[00844] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-40068.1 (SEQ ID NO: 1786), or a modified or unmodified variant thereof.

[00845] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38131.1 (SEQ ID NO: 1787), or a modified or unmodified variant thereof.

[00846] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: AD-38167.1 (SEQ ID NO: 1788), or a modified or unmodified variant thereof.

[00847] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: hs_KRAS 1273_A22S26 (SEQ ID NO: 1789), or a modified or unmodified variant thereof.

[00848] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: hs_KRAS 2892_A37S26 (SEQ ID NO: 1790), or a modified or unmodified variant thereof.

[00849] A RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nt differing by 0, 1, 2, or 3 nt from a first strand of: hs_KRAS 4731_A22S26 (SEQ ID NO: 1791), or a modified or unmodified variant thereof.

[00850] Specific embodiments comprising at least 15 contiguous nucleotides of any RNAi agent disclosed herein

[00851] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides (differing by 0 nucleotides) from a first strand of: any RNAi agent from any of Tables 1 to 6 or modified or unmodified variants thereof.

[00852] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[00853] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35523.3 (SEQ ID NO: 428), or a modified or unmodified variant thereof.

[00854] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35529.1 (SEQ ID NO: 429), or a modified or unmodified variant thereof.

[00855] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35535.4 (SEQ ID NO: 430), or a modified or unmodified variant thereof.

[00856] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35541.4 (SEQ ID NO: 431), or a modified or unmodified variant thereof.

[00857] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35547.4 (SEQ ID NO: 432), or a modified or unmodified variant thereof.

[00858] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35553.4 (SEQ ID NO: 433), or a modified or unmodified variant thereof.

[00859] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-35559.4 (SEQ ID NO: 434), or a modified or unmodified variant thereof.

[00860] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35565.4 (SEQ ID NO: 435), or a modified or unmodified variant thereof.

[00861] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35524.4 (SEQ ID NO: 436), or a modified or unmodified variant thereof.

[00862] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35530.4 (SEQ ID NO: 437), or a modified or unmodified variant thereof.

[00863] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35536.4 (SEQ ID NO: 438), or a modified or unmodified variant thereof.

[00864] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35542.4 (SEQ ID NO: 439), or a modified or unmodified variant thereof.

[00865] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35548.4 (SEQ ID NO: 440), or a modified or unmodified variant thereof.

[00866] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35554.4 (SEQ ID NO: 441), or a modified or unmodified variant thereof.

[00867] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35560.2 (SEQ ID NO: 442), or a modified or unmodified variant thereof.

[00868] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35566.4 (SEQ ID NO: 443), or a modified or unmodified variant thereof.

[00869] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35525.2 (SEQ ID NO: 444), or a modified or unmodified variant thereof.

[00870] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35531.4 (SEQ ID NO: 445), or a modified or unmodified variant thereof.

[00871] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35537.4 (SEQ ID NO: 446), or a modified or unmodified variant thereof.

[00872] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35543.2 (SEQ ID NO: 447), or a modified or unmodified variant thereof.

[00873] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35549.4 (SEQ ID NO: 448), or a modified or unmodified variant thereof.

[00874] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35555.4 (SEQ ID NO: 449), or a modified or unmodified variant thereof.

[00875] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35561.4 (SEQ ID NO: 450), or a modified or unmodified variant thereof.

[00876] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35567.4 (SEQ ID NO: 451), or a modified or unmodified variant thereof.

[00877] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35526.4 (SEQ ID NO: 452), or a modified or unmodified variant thereof.

[00878] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35532.4 (SEQ ID NO: 453), or a modified or unmodified variant thereof.

[00879] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35538.4 (SEQ ID NO: 454), or a modified or unmodified variant thereof.

[00880] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35544.4 (SEQ ID NO: 455), or a modified or unmodified variant thereof.

[00881] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35550.4 (SEQ ID NO: 456), or a modified or unmodified variant thereof.

[00882] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35556.4 (SEQ ID NO: 457), or a modified or unmodified variant thereof.

[00883] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35562.4 (SEQ ID NO: 458), or a modified or unmodified variant thereof.

[00884] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35568.4 (SEQ ID NO: 459), or a modified or unmodified variant thereof.

[00885] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35527.4 (SEQ ID NO: 460), or a modified or unmodified variant thereof.

[00886] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35533.4 (SEQ ID NO: 461),

or a modified or unmodified variant thereof.

[00887] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35539.4 (SEQ ID NO: 462), or a modified or unmodified variant thereof.

[00888] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35545.4 (SEQ ID NO: 463), or a modified or unmodified variant thereof.

[00889] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35551.4 (SEQ ID NO: 464), or a modified or unmodified variant thereof.

[00890] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35563.4 (SEQ ID NO: 465), or a modified or unmodified variant thereof.

[00891] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35528.4 (SEQ ID NO: 466), or a modified or unmodified variant thereof.

[00892] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35540.4 (SEQ ID NO: 467), or a modified or unmodified variant thereof.

[00893] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35546.4 (SEQ ID NO: 468), or a modified or unmodified variant thereof.

[00894] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35552.4 (SEQ ID NO: 469), or a modified or unmodified variant thereof.

[00895] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35558.4 (SEQ ID NO: 470), or a modified or unmodified variant thereof.

[00896] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35564.4 (SEQ ID NO: 471), or a modified or unmodified variant thereof.

[00897] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35570.4 (SEQ ID NO: 472), or a modified or unmodified variant thereof.

[00898] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35571.4 (SEQ ID NO: 473), or a modified or unmodified variant thereof.

[00899] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35577.4 (SEQ ID NO: 474), or a modified or unmodified variant thereof.

[00900] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-35583.4 (SEQ ID NO: 475), or a modified or unmodified variant thereof.

[00901] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35589.4 (SEQ ID NO: 476), or a modified or unmodified variant thereof.

[00902] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35595.4 (SEQ ID NO: 477), or a modified or unmodified variant thereof.

[00903] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35601.4 (SEQ ID NO: 478), or a modified or unmodified variant thereof.

[00904] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35607.4 (SEQ ID NO: 479), or a modified or unmodified variant thereof.

[00905] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35613.4 (SEQ ID NO: 480), or a modified or unmodified variant thereof.

[00906] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35572.4 (SEQ ID NO: 481), or a modified or unmodified variant thereof.

[00907] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35578.4 (SEQ ID NO: 482), or a modified or unmodified variant thereof.

[00908] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35584.4 (SEQ ID NO: 483), or a modified or unmodified variant thereof.

[00909] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35590.4 (SEQ ID NO: 484), or a modified or unmodified variant thereof.

[00910] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35596.4 (SEQ ID NO: 485), or a modified or unmodified variant thereof.

[00911] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35602.4 (SEQ ID NO: 486), or a modified or unmodified variant thereof.

[00912] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35608.4 (SEQ ID NO: 487), or a modified or unmodified variant thereof.

[00913] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35614.4 (SEQ ID NO: 488), or a modified or unmodified variant thereof.

[00914] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35573.4 (SEQ ID NO: 489), or a modified or unmodified variant thereof.

[00915] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35579.4 (SEQ ID NO: 490), or a modified or unmodified variant thereof.

[00916] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35585.4 (SEQ ID NO: 491), or a modified or unmodified variant thereof.

[00917] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35591.4 (SEQ ID NO: 492), or a modified or unmodified variant thereof.

[00918] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35597.4 (SEQ ID NO: 493), or a modified or unmodified variant thereof.

[00919] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35603.4 (SEQ ID NO: 494), or a modified or unmodified variant thereof.

[00920] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35609.4 (SEQ ID NO: 495), or a modified or unmodified variant thereof.

[00921] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35615.4 (SEQ ID NO: 496), or a modified or unmodified variant thereof.

[00922] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35574.4 (SEQ ID NO: 497), or a modified or unmodified variant thereof.

[00923] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35580.1 (SEQ ID NO: 498), or a modified or unmodified variant thereof.

[00924] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35586.4 (SEQ ID NO: 499), or a modified or unmodified variant thereof.

[00925] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35592.4 (SEQ ID NO: 500), or a modified or unmodified variant thereof.

[00926] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35598.4 (SEQ ID NO: 501), or a modified or unmodified variant thereof.

[00927] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35604.4 (SEQ ID NO: 502),

or a modified or unmodified variant thereof.

[00928] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35610.4 (SEQ ID NO: 503), or a modified or unmodified variant thereof.

[00929] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35616.4 (SEQ ID NO: 504), or a modified or unmodified variant thereof.

[00930] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35575.4 (SEQ ID NO: 505), or a modified or unmodified variant thereof.

[00931] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35581.4 (SEQ ID NO: 506), or a modified or unmodified variant thereof.

[00932] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35587.4 (SEQ ID NO: 507), or a modified or unmodified variant thereof.

[00933] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35593.4 (SEQ ID NO: 508), or a modified or unmodified variant thereof.

[00934] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35599.4 (SEQ ID NO: 509), or a modified or unmodified variant thereof.

[00935] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35605.4 (SEQ ID NO: 510), or a modified or unmodified variant thereof.

[00936] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35611.4 (SEQ ID NO: 511), or a modified or unmodified variant thereof.

[00937] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35617.4 (SEQ ID NO: 512), or a modified or unmodified variant thereof.

[00938] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35576.4 (SEQ ID NO: 513), or a modified or unmodified variant thereof.

[00939] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35588.4 (SEQ ID NO: 514), or a modified or unmodified variant thereof.

[00940] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35667.1 (SEQ ID NO: 515), or a modified or unmodified variant thereof.

[00941] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-35673.1 (SEQ ID NO: 516), or a modified or unmodified variant thereof.

[00942] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35679.1 (SEQ ID NO: 517), or a modified or unmodified variant thereof.

[00943] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35685.1 (SEQ ID NO: 518), or a modified or unmodified variant thereof.

[00944] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35691.1 (SEQ ID NO: 519), or a modified or unmodified variant thereof.

[00945] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35557.1 (SEQ ID NO: 520), or a modified or unmodified variant thereof.

[00946] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35618.1 (SEQ ID NO: 521), or a modified or unmodified variant thereof.

[00947] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35569.1 (SEQ ID NO: 522), or a modified or unmodified variant thereof.

[00948] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35534.1 (SEQ ID NO: 523), or a modified or unmodified variant thereof.

[00949] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35582.1 (SEQ ID NO: 524), or a modified or unmodified variant thereof.

[00950] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35594.1 (SEQ ID NO: 525), or a modified or unmodified variant thereof.

[00951] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35600.1 (SEQ ID NO: 526), or a modified or unmodified variant thereof.

[00952] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35606.1 (SEQ ID NO: 527), or a modified or unmodified variant thereof.

[00953] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35612.1 (SEQ ID NO: 528), or a modified or unmodified variant thereof.

[00954] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38127.1 (SEQ ID NO: 529), or a modified or unmodified variant thereof.

[00955] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38133.1 (SEQ ID NO: 530), or a modified or unmodified variant thereof.

[00956] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38139.1 (SEQ ID NO: 531), or a modified or unmodified variant thereof.

[00957] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38145.1 (SEQ ID NO: 532), or a modified or unmodified variant thereof.

[00958] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38151.1 (SEQ ID NO: 533), or a modified or unmodified variant thereof.

[00959] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38157.1 (SEQ ID NO: 534), or a modified or unmodified variant thereof.

[00960] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38163.1 (SEQ ID NO: 535), or a modified or unmodified variant thereof.

[00961] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38169.1 (SEQ ID NO: 536), or a modified or unmodified variant thereof.

[00962] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38128.1 (SEQ ID NO: 537), or a modified or unmodified variant thereof.

[00963] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38134.1 (SEQ ID NO: 538), or a modified or unmodified variant thereof.

[00964] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38140.1 (SEQ ID NO: 539), or a modified or unmodified variant thereof.

[00965] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38146.1 (SEQ ID NO: 540), or a modified or unmodified variant thereof.

[00966] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38152.1 (SEQ ID NO: 541), or a modified or unmodified variant thereof.

[00967] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38158.1 (SEQ ID NO: 542), or a modified or unmodified variant thereof.

[00968] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38164.1 (SEQ ID NO: 543),

or a modified or unmodified variant thereof.

[00969] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38170.1 (SEQ ID NO: 544), or a modified or unmodified variant thereof.

[00970] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38129.1 (SEQ ID NO: 545), or a modified or unmodified variant thereof.

[00971] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38135.1 (SEQ ID NO: 546), or a modified or unmodified variant thereof.

[00972] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38141.1 (SEQ ID NO: 547), or a modified or unmodified variant thereof.

[00973] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38147.1 (SEQ ID NO: 548), or a modified or unmodified variant thereof.

[00974] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38153.1 (SEQ ID NO: 549), or a modified or unmodified variant thereof.

[00975] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38159.1 (SEQ ID NO: 550), or a modified or unmodified variant thereof.

[00976] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38165.1 (SEQ ID NO: 551), or a modified or unmodified variant thereof.

[00977] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38171.1 (SEQ ID NO: 552), or a modified or unmodified variant thereof.

[00978] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38130.1 (SEQ ID NO: 553), or a modified or unmodified variant thereof.

[00979] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38136.1 (SEQ ID NO: 554), or a modified or unmodified variant thereof.

[00980] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38142.1 (SEQ ID NO: 555), or a modified or unmodified variant thereof.

[00981] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38148.1 (SEQ ID NO: 556), or a modified or unmodified variant thereof.

[00982] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-38154.1 (SEQ ID NO: 557), or a modified or unmodified variant thereof.

[00983] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38160.1 (SEQ ID NO: 558), or a modified or unmodified variant thereof.

[00984] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38166.1 (SEQ ID NO: 559), or a modified or unmodified variant thereof.

[00985] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38172.1 (SEQ ID NO: 560), or a modified or unmodified variant thereof.

[00986] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38131.1 (SEQ ID NO: 561), or a modified or unmodified variant thereof.

[00987] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38137.1 (SEQ ID NO: 562), or a modified or unmodified variant thereof.

[00988] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38143.1 (SEQ ID NO: 563), or a modified or unmodified variant thereof.

[00989] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38149.1 (SEQ ID NO: 564), or a modified or unmodified variant thereof.

[00990] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38155.1 (SEQ ID NO: 565), or a modified or unmodified variant thereof.

[00991] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38161.1 (SEQ ID NO: 566), or a modified or unmodified variant thereof.

[00992] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38167.1 (SEQ ID NO: 567), or a modified or unmodified variant thereof.

[00993] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38173.1 (SEQ ID NO: 568), or a modified or unmodified variant thereof.

[00994] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38132.1 (SEQ ID NO: 569), or a modified or unmodified variant thereof.

[00995] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38138.1 (SEQ ID NO: 570), or a modified or unmodified variant thereof.

[00996] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38144.1 (SEQ ID NO: 571), or a modified or unmodified variant thereof.

[00997] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38150.1 (SEQ ID NO: 572), or a modified or unmodified variant thereof.

[00998] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38156.1 (SEQ ID NO: 573), or a modified or unmodified variant thereof.

[00999] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38162.1 (SEQ ID NO: 574), or a modified or unmodified variant thereof.

[001000] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38168.1 (SEQ ID NO: 575), or a modified or unmodified variant thereof.

[001001] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38174.1 (SEQ ID NO: 576), or a modified or unmodified variant thereof.

[001002] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39683.1 (SEQ ID NO: 577), or a modified or unmodified variant thereof.

[001003] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39689.1 (SEQ ID NO: 578), or a modified or unmodified variant thereof.

[001004] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39695.1 (SEQ ID NO: 579), or a modified or unmodified variant thereof.

[001005] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39701.1 (SEQ ID NO: 580), or a modified or unmodified variant thereof.

[001006] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39707.1 (SEQ ID NO: 581), or a modified or unmodified variant thereof.

[001007] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39713.1 (SEQ ID NO: 582), or a modified or unmodified variant thereof.

[001008] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39719.1 (SEQ ID NO: 583), or a modified or unmodified variant thereof.

[001009] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39725.1 (SEQ ID NO: 584),

or a modified or unmodified variant thereof.

[001010] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39684.1 (SEQ ID NO: 585), or a modified or unmodified variant thereof.

[001011] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39690.1 (SEQ ID NO: 586), or a modified or unmodified variant thereof.

[001012] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39696.1 (SEQ ID NO: 587), or a modified or unmodified variant thereof.

[001013] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39702.1 (SEQ ID NO: 588), or a modified or unmodified variant thereof.

[001014] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39708.1 (SEQ ID NO: 589), or a modified or unmodified variant thereof.

[001015] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39714.1 (SEQ ID NO: 590), or a modified or unmodified variant thereof.

[001016] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39720.1 (SEQ ID NO: 591), or a modified or unmodified variant thereof.

[001017] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39726.1 (SEQ ID NO: 592), or a modified or unmodified variant thereof.

[001018] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39685.1 (SEQ ID NO: 593), or a modified or unmodified variant thereof.

[001019] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39691.1 (SEQ ID NO: 594), or a modified or unmodified variant thereof.

[001020] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39697.1 (SEQ ID NO: 595), or a modified or unmodified variant thereof.

[001021] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39703.1 (SEQ ID NO: 596), or a modified or unmodified variant thereof.

[001022] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39709.1 (SEQ ID NO: 597), or a modified or unmodified variant thereof.

[001023] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-39715.1 (SEQ ID NO: 598), or a modified or unmodified variant thereof.

[001024] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39721.1 (SEQ ID NO: 599), or a modified or unmodified variant thereof.

[001025] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39727.1 (SEQ ID NO: 600), or a modified or unmodified variant thereof.

[001026] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39686.1 (SEQ ID NO: 601), or a modified or unmodified variant thereof.

[001027] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39692.1 (SEQ ID NO: 602), or a modified or unmodified variant thereof.

[001028] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39698.1 (SEQ ID NO: 603), or a modified or unmodified variant thereof.

[001029] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39704.1 (SEQ ID NO: 604), or a modified or unmodified variant thereof.

[001030] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39710.1 (SEQ ID NO: 605), or a modified or unmodified variant thereof.

[001031] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39716.1 (SEQ ID NO: 606), or a modified or unmodified variant thereof.

[001032] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39722.1 (SEQ ID NO: 607), or a modified or unmodified variant thereof.

[001033] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39728.1 (SEQ ID NO: 608), or a modified or unmodified variant thereof.

[001034] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39687.1 (SEQ ID NO: 609), or a modified or unmodified variant thereof.

[001035] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39693.1 (SEQ ID NO: 610), or a modified or unmodified variant thereof.

[001036] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39699.1 (SEQ ID NO: 611), or a modified or unmodified variant thereof.

[001037] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39705.1 (SEQ ID NO: 612), or a modified or unmodified variant thereof.

[001038] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39711.1 (SEQ ID NO: 613), or a modified or unmodified variant thereof.

[001039] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39717.1 (SEQ ID NO: 614), or a modified or unmodified variant thereof.

[001040] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39723.1 (SEQ ID NO: 615), or a modified or unmodified variant thereof.

[001041] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39729.1 (SEQ ID NO: 616), or a modified or unmodified variant thereof.

[001042] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39688.1 (SEQ ID NO: 617), or a modified or unmodified variant thereof.

[001043] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39694.1 (SEQ ID NO: 618), or a modified or unmodified variant thereof.

[001044] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39700.1 (SEQ ID NO: 619), or a modified or unmodified variant thereof.

[001045] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39706.1 (SEQ ID NO: 620), or a modified or unmodified variant thereof.

[001046] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39712.1 (SEQ ID NO: 621), or a modified or unmodified variant thereof.

[001047] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39718.1 (SEQ ID NO: 622), or a modified or unmodified variant thereof.

[001048] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39724.1 (SEQ ID NO: 623), or a modified or unmodified variant thereof.

[001049] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39730.1 (SEQ ID NO: 624), or a modified or unmodified variant thereof.

[001050] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39736.1 (SEQ ID NO: 625),

or a modified or unmodified variant thereof.

[001051] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39742.1 (SEQ ID NO: 626), or a modified or unmodified variant thereof.

[001052] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39748.1 (SEQ ID NO: 627), or a modified or unmodified variant thereof.

[001053] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39754.1 (SEQ ID NO: 628), or a modified or unmodified variant thereof.

[001054] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39760.1 (SEQ ID NO: 629), or a modified or unmodified variant thereof.

[001055] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39766.1 (SEQ ID NO: 630), or a modified or unmodified variant thereof.

[001056] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39772.1 (SEQ ID NO: 631), or a modified or unmodified variant thereof.

[001057] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39731.1 (SEQ ID NO: 632), or a modified or unmodified variant thereof.

[001058] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39737.1 (SEQ ID NO: 633), or a modified or unmodified variant thereof.

[001059] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39743.1 (SEQ ID NO: 634), or a modified or unmodified variant thereof.

[001060] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39749.1 (SEQ ID NO: 635), or a modified or unmodified variant thereof.

[001061] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39755.1 (SEQ ID NO: 636), or a modified or unmodified variant thereof.

[001062] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39761.1 (SEQ ID NO: 637), or a modified or unmodified variant thereof.

[001063] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39767.1 (SEQ ID NO: 638), or a modified or unmodified variant thereof.

[001064] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-39773.1 (SEQ ID NO: 639), or a modified or unmodified variant thereof.

[001065] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39732.1 (SEQ ID NO: 640), or a modified or unmodified variant thereof.

[001066] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39738.1 (SEQ ID NO: 641), or a modified or unmodified variant thereof.

[001067] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39744.1 (SEQ ID NO: 642), or a modified or unmodified variant thereof.

[001068] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39750.1 (SEQ ID NO: 643), or a modified or unmodified variant thereof.

[001069] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39756.1 (SEQ ID NO: 644), or a modified or unmodified variant thereof.

[001070] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39762.1 (SEQ ID NO: 645), or a modified or unmodified variant thereof.

[001071] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39768.1 (SEQ ID NO: 646), or a modified or unmodified variant thereof.

[001072] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39774.1 (SEQ ID NO: 647), or a modified or unmodified variant thereof.

[001073] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39733.1 (SEQ ID NO: 648), or a modified or unmodified variant thereof.

[001074] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39739.1 (SEQ ID NO: 649), or a modified or unmodified variant thereof.

[001075] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39745.1 (SEQ ID NO: 650), or a modified or unmodified variant thereof.

[001076] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39751.1 (SEQ ID NO: 651), or a modified or unmodified variant thereof.

[001077] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39757.1 (SEQ ID NO: 652), or a modified or unmodified variant thereof.

[001078] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39763.1 (SEQ ID NO: 653), or a modified or unmodified variant thereof.

[001079] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39769.1 (SEQ ID NO: 654), or a modified or unmodified variant thereof.

[001080] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39775.1 (SEQ ID NO: 655), or a modified or unmodified variant thereof.

[001081] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39734.1 (SEQ ID NO: 656), or a modified or unmodified variant thereof.

[001082] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39740.1 (SEQ ID NO: 657), or a modified or unmodified variant thereof.

[001083] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39746.1 (SEQ ID NO: 658), or a modified or unmodified variant thereof.

[001084] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39752.1 (SEQ ID NO: 659), or a modified or unmodified variant thereof.

[001085] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39758.1 (SEQ ID NO: 660), or a modified or unmodified variant thereof.

[001086] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39764.1 (SEQ ID NO: 661), or a modified or unmodified variant thereof.

[001087] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39770.1 (SEQ ID NO: 662), or a modified or unmodified variant thereof.

[001088] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39776.1 (SEQ ID NO: 663), or a modified or unmodified variant thereof.

[001089] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39735.1 (SEQ ID NO: 664), or a modified or unmodified variant thereof.

[001090] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39741.1 (SEQ ID NO: 665), or a modified or unmodified variant thereof.

[001091] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39747.1 (SEQ ID NO: 666),

or a modified or unmodified variant thereof.

[001092] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39753.1 (SEQ ID NO: 667), or a modified or unmodified variant thereof.

[001093] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39759.1 (SEQ ID NO: 668), or a modified or unmodified variant thereof.

[001094] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39765.1 (SEQ ID NO: 669), or a modified or unmodified variant thereof.

[001095] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39771.1 (SEQ ID NO: 670), or a modified or unmodified variant thereof.

[001096] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39778.1 (SEQ ID NO: 671), or a modified or unmodified variant thereof.

[001097] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39784.1 (SEQ ID NO: 672), or a modified or unmodified variant thereof.

[001098] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39790.1 (SEQ ID NO: 673), or a modified or unmodified variant thereof.

[001099] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39796.1 (SEQ ID NO: 674), or a modified or unmodified variant thereof.

[001100] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39802.1 (SEQ ID NO: 675), or a modified or unmodified variant thereof.

[001101] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39808.1 (SEQ ID NO: 676), or a modified or unmodified variant thereof.

[001102] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39814.1 (SEQ ID NO: 677), or a modified or unmodified variant thereof.

[001103] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39820.1 (SEQ ID NO: 678), or a modified or unmodified variant thereof.

[001104] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39779.1 (SEQ ID NO: 679), or a modified or unmodified variant thereof.

[001105] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-39785.1 (SEQ ID NO: 680), or a modified or unmodified variant thereof.

[001106] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39791.1 (SEQ ID NO: 681), or a modified or unmodified variant thereof.

[001107] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39797.1 (SEQ ID NO: 682), or a modified or unmodified variant thereof.

[001108] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39803.1 (SEQ ID NO: 683), or a modified or unmodified variant thereof.

[001109] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39809.1 (SEQ ID NO: 684), or a modified or unmodified variant thereof.

[001110] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39815.1 (SEQ ID NO: 685), or a modified or unmodified variant thereof.

[001111] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39821.1 (SEQ ID NO: 686), or a modified or unmodified variant thereof.

[001112] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39780.1 (SEQ ID NO: 687), or a modified or unmodified variant thereof.

[001113] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39786.1 (SEQ ID NO: 688), or a modified or unmodified variant thereof.

[001114] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39792.1 (SEQ ID NO: 689), or a modified or unmodified variant thereof.

[001115] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39798.1 (SEQ ID NO: 690), or a modified or unmodified variant thereof.

[001116] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39804.1 (SEQ ID NO: 691), or a modified or unmodified variant thereof.

[001117] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39810.1 (SEQ ID NO: 692), or a modified or unmodified variant thereof.

[001118] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39816.1 (SEQ ID NO: 693), or a modified or unmodified variant thereof.

[001119] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39822.1 (SEQ ID NO: 694), or a modified or unmodified variant thereof.

[001120] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39781.1 (SEQ ID NO: 695), or a modified or unmodified variant thereof.

[001121] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39787.1 (SEQ ID NO: 696), or a modified or unmodified variant thereof.

[001122] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39793.1 (SEQ ID NO: 697), or a modified or unmodified variant thereof.

[001123] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39799.1 (SEQ ID NO: 698), or a modified or unmodified variant thereof.

[001124] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39805.1 (SEQ ID NO: 699), or a modified or unmodified variant thereof.

[001125] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39811.1 (SEQ ID NO: 700), or a modified or unmodified variant thereof.

[001126] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39817.1 (SEQ ID NO: 701), or a modified or unmodified variant thereof.

[001127] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39823.1 (SEQ ID NO: 702), or a modified or unmodified variant thereof.

[001128] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39782.1 (SEQ ID NO: 703), or a modified or unmodified variant thereof.

[001129] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39788.1 (SEQ ID NO: 704), or a modified or unmodified variant thereof.

[001130] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39794.1 (SEQ ID NO: 705), or a modified or unmodified variant thereof.

[001131] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39800.1 (SEQ ID NO: 706), or a modified or unmodified variant thereof.

[001132] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39806.1 (SEQ ID NO: 707),

or a modified or unmodified variant thereof.

[001133] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39812.1 (SEQ ID NO: 708), or a modified or unmodified variant thereof.

[001134] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39818.1 (SEQ ID NO: 709), or a modified or unmodified variant thereof.

[001135] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39824.1 (SEQ ID NO: 710), or a modified or unmodified variant thereof.

[001136] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39783.1 (SEQ ID NO: 711), or a modified or unmodified variant thereof.

[001137] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39789.1 (SEQ ID NO: 712), or a modified or unmodified variant thereof.

[001138] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39795.1 (SEQ ID NO: 713), or a modified or unmodified variant thereof.

[001139] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39801.1 (SEQ ID NO: 714), or a modified or unmodified variant thereof.

[001140] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39807.1 (SEQ ID NO: 715), or a modified or unmodified variant thereof.

[001141] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39813.1 (SEQ ID NO: 716), or a modified or unmodified variant thereof.

[001142] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39819.1 (SEQ ID NO: 717), or a modified or unmodified variant thereof.

[001143] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39825.1 (SEQ ID NO: 718), or a modified or unmodified variant thereof.

[001144] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39831.1 (SEQ ID NO: 719), or a modified or unmodified variant thereof.

[001145] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39837.1 (SEQ ID NO: 720), or a modified or unmodified variant thereof.

[001146] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-39843.1 (SEQ ID NO: 721), or a modified or unmodified variant thereof.

[001147] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39849.1 (SEQ ID NO: 722), or a modified or unmodified variant thereof.

[001148] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39855.1 (SEQ ID NO: 723), or a modified or unmodified variant thereof.

[001149] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39861.1 (SEQ ID NO: 724), or a modified or unmodified variant thereof.

[001150] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39867.1 (SEQ ID NO: 725), or a modified or unmodified variant thereof.

[001151] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39826.1 (SEQ ID NO: 726), or a modified or unmodified variant thereof.

[001152] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39832.1 (SEQ ID NO: 727), or a modified or unmodified variant thereof.

[001153] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39838.1 (SEQ ID NO: 728), or a modified or unmodified variant thereof.

[001154] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39844.1 (SEQ ID NO: 729), or a modified or unmodified variant thereof.

[001155] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39850.1 (SEQ ID NO: 730), or a modified or unmodified variant thereof.

[001156] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39856.1 (SEQ ID NO: 731), or a modified or unmodified variant thereof.

[001157] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39862.1 (SEQ ID NO: 732), or a modified or unmodified variant thereof.

[001158] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39868.1 (SEQ ID NO: 733), or a modified or unmodified variant thereof.

[001159] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39827.1 (SEQ ID NO: 734), or a modified or unmodified variant thereof.

[001160] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39833.1 (SEQ ID NO: 735), or a modified or unmodified variant thereof.

[001161] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39839.1 (SEQ ID NO: 736), or a modified or unmodified variant thereof.

[001162] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39845.1 (SEQ ID NO: 737), or a modified or unmodified variant thereof.

[001163] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39851.1 (SEQ ID NO: 738), or a modified or unmodified variant thereof.

[001164] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39857.1 (SEQ ID NO: 739), or a modified or unmodified variant thereof.

[001165] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39863.1 (SEQ ID NO: 740), or a modified or unmodified variant thereof.

[001166] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39869.1 (SEQ ID NO: 741), or a modified or unmodified variant thereof.

[001167] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39828.1 (SEQ ID NO: 742), or a modified or unmodified variant thereof.

[001168] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39834.1 (SEQ ID NO: 743), or a modified or unmodified variant thereof.

[001169] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39840.1 (SEQ ID NO: 744), or a modified or unmodified variant thereof.

[001170] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39846.1 (SEQ ID NO: 745), or a modified or unmodified variant thereof.

[001171] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39852.1 (SEQ ID NO: 746), or a modified or unmodified variant thereof.

[001172] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39858.1 (SEQ ID NO: 747), or a modified or unmodified variant thereof.

[001173] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39864.1 (SEQ ID NO: 748),

or a modified or unmodified variant thereof.

[001174] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39870.1 (SEQ ID NO: 749), or a modified or unmodified variant thereof.

[001175] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39829.1 (SEQ ID NO: 750), or a modified or unmodified variant thereof.

[001176] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39835.1 (SEQ ID NO: 751), or a modified or unmodified variant thereof.

[001177] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39841.1 (SEQ ID NO: 752), or a modified or unmodified variant thereof.

[001178] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39853.1 (SEQ ID NO: 753), or a modified or unmodified variant thereof.

[001179] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39859.1 (SEQ ID NO: 754), or a modified or unmodified variant thereof.

[001180] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39865.1 (SEQ ID NO: 755), or a modified or unmodified variant thereof.

[001181] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39871.1 (SEQ ID NO: 756), or a modified or unmodified variant thereof.

[001182] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39830.1 (SEQ ID NO: 757), or a modified or unmodified variant thereof.

[001183] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39836.1 (SEQ ID NO: 758), or a modified or unmodified variant thereof.

[001184] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39842.1 (SEQ ID NO: 759), or a modified or unmodified variant thereof.

[001185] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39848.1 (SEQ ID NO: 760), or a modified or unmodified variant thereof.

[001186] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39854.1 (SEQ ID NO: 761), or a modified or unmodified variant thereof.

[001187] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-39860.1 (SEQ ID NO: 762), or a modified or unmodified variant thereof.

[001188] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39866.1 (SEQ ID NO: 763), or a modified or unmodified variant thereof.

[001189] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39992.1 (SEQ ID NO: 764), or a modified or unmodified variant thereof.

[001190] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39998.1 (SEQ ID NO: 765), or a modified or unmodified variant thereof.

[001191] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40004.1 (SEQ ID NO: 766), or a modified or unmodified variant thereof.

[001192] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40010.1 (SEQ ID NO: 767), or a modified or unmodified variant thereof.

[001193] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40016.1 (SEQ ID NO: 768), or a modified or unmodified variant thereof.

[001194] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40022.1 (SEQ ID NO: 769), or a modified or unmodified variant thereof.

[001195] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40028.1 (SEQ ID NO: 770), or a modified or unmodified variant thereof.

[001196] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40034.1 (SEQ ID NO: 771), or a modified or unmodified variant thereof.

[001197] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39999.1 (SEQ ID NO: 772), or a modified or unmodified variant thereof.

[001198] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40005.1 (SEQ ID NO: 773), or a modified or unmodified variant thereof.

[001199] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40011.1 (SEQ ID NO: 774), or a modified or unmodified variant thereof.

[001200] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40017.1 (SEQ ID NO: 775), or a modified or unmodified variant thereof.

[001201] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40029.1 (SEQ ID NO: 776), or a modified or unmodified variant thereof.

[001202] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40035.1 (SEQ ID NO: 777), or a modified or unmodified variant thereof.

[001203] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39994.1 (SEQ ID NO: 778), or a modified or unmodified variant thereof.

[001204] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40000.1 (SEQ ID NO: 779), or a modified or unmodified variant thereof.

[001205] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40006.1 (SEQ ID NO: 780), or a modified or unmodified variant thereof.

[001206] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40012.1 (SEQ ID NO: 781), or a modified or unmodified variant thereof.

[001207] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40018.1 (SEQ ID NO: 782), or a modified or unmodified variant thereof.

[001208] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40024.1 (SEQ ID NO: 783), or a modified or unmodified variant thereof.

[001209] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40030.1 (SEQ ID NO: 784), or a modified or unmodified variant thereof.

[001210] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40036.1 (SEQ ID NO: 785), or a modified or unmodified variant thereof.

[001211] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39995.1 (SEQ ID NO: 786), or a modified or unmodified variant thereof.

[001212] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40001.1 (SEQ ID NO: 787), or a modified or unmodified variant thereof.

[001213] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40007.1 (SEQ ID NO: 788), or a modified or unmodified variant thereof.

[001214] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40013.1 (SEQ ID NO: 789),

or a modified or unmodified variant thereof.

[001215] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40019.1 (SEQ ID NO: 790), or a modified or unmodified variant thereof.

[001216] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40025.1 (SEQ ID NO: 791), or a modified or unmodified variant thereof.

[001217] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40031.1 (SEQ ID NO: 792), or a modified or unmodified variant thereof.

[001218] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40037.1 (SEQ ID NO: 793), or a modified or unmodified variant thereof.

[001219] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39996.1 (SEQ ID NO: 794), or a modified or unmodified variant thereof.

[001220] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40002.1 (SEQ ID NO: 795), or a modified or unmodified variant thereof.

[001221] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40008.1 (SEQ ID NO: 796), or a modified or unmodified variant thereof.

[001222] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40014.1 (SEQ ID NO: 797), or a modified or unmodified variant thereof.

[001223] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40020.1 (SEQ ID NO: 798), or a modified or unmodified variant thereof.

[001224] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40026.1 (SEQ ID NO: 799), or a modified or unmodified variant thereof.

[001225] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40032.1 (SEQ ID NO: 800), or a modified or unmodified variant thereof.

[001226] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40038.1 (SEQ ID NO: 801), or a modified or unmodified variant thereof.

[001227] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39997.1 (SEQ ID NO: 802), or a modified or unmodified variant thereof.

[001228] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-40009.1 (SEQ ID NO: 803), or a modified or unmodified variant thereof.

[001229] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40015.1 (SEQ ID NO: 804), or a modified or unmodified variant thereof.

[001230] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40021.1 (SEQ ID NO: 805), or a modified or unmodified variant thereof.

[001231] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40027.1 (SEQ ID NO: 806), or a modified or unmodified variant thereof.

[001232] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40033.1 (SEQ ID NO: 807), or a modified or unmodified variant thereof.

[001233] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40039.1 (SEQ ID NO: 808), or a modified or unmodified variant thereof.

[001234] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40045.1 (SEQ ID NO: 809), or a modified or unmodified variant thereof.

[001235] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40051.1 (SEQ ID NO: 810), or a modified or unmodified variant thereof.

[001236] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40057.1 (SEQ ID NO: 811), or a modified or unmodified variant thereof.

[001237] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40063.1 (SEQ ID NO: 812), or a modified or unmodified variant thereof.

[001238] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40069.1 (SEQ ID NO: 813), or a modified or unmodified variant thereof.

[001239] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40075.1 (SEQ ID NO: 814), or a modified or unmodified variant thereof.

[001240] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40081.1 (SEQ ID NO: 815), or a modified or unmodified variant thereof.

[001241] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40040.1 (SEQ ID NO: 816), or a modified or unmodified variant thereof.

[001242] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40046.1 (SEQ ID NO: 817), or a modified or unmodified variant thereof.

[001243] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40052.1 (SEQ ID NO: 818), or a modified or unmodified variant thereof.

[001244] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40058.1 (SEQ ID NO: 819), or a modified or unmodified variant thereof.

[001245] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40064.1 (SEQ ID NO: 820), or a modified or unmodified variant thereof.

[001246] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40070.1 (SEQ ID NO: 821), or a modified or unmodified variant thereof.

[001247] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40076.1 (SEQ ID NO: 822), or a modified or unmodified variant thereof.

[001248] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40082.1 (SEQ ID NO: 823), or a modified or unmodified variant thereof.

[001249] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40041.1 (SEQ ID NO: 824), or a modified or unmodified variant thereof.

[001250] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40047.1 (SEQ ID NO: 825), or a modified or unmodified variant thereof.

[001251] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40053.1 (SEQ ID NO: 826), or a modified or unmodified variant thereof.

[001252] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40059.1 (SEQ ID NO: 827), or a modified or unmodified variant thereof.

[001253] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40065.1 (SEQ ID NO: 828), or a modified or unmodified variant thereof.

[001254] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40071.1 (SEQ ID NO: 829), or a modified or unmodified variant thereof.

[001255] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40077.1 (SEQ ID NO: 830),

or a modified or unmodified variant thereof.

[001256] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40083.1 (SEQ ID NO: 831), or a modified or unmodified variant thereof.

[001257] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40042.1 (SEQ ID NO: 832), or a modified or unmodified variant thereof.

[001258] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40048.1 (SEQ ID NO: 833), or a modified or unmodified variant thereof.

[001259] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40054.1 (SEQ ID NO: 834), or a modified or unmodified variant thereof.

[001260] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40060.1 (SEQ ID NO: 835), or a modified or unmodified variant thereof.

[001261] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40066.1 (SEQ ID NO: 836), or a modified or unmodified variant thereof.

[001262] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40072.1 (SEQ ID NO: 837), or a modified or unmodified variant thereof.

[001263] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40078.1 (SEQ ID NO: 838), or a modified or unmodified variant thereof.

[001264] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40084.1 (SEQ ID NO: 839), or a modified or unmodified variant thereof.

[001265] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40043.1 (SEQ ID NO: 840), or a modified or unmodified variant thereof.

[001266] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40049.1 (SEQ ID NO: 841), or a modified or unmodified variant thereof.

[001267] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40055.1 (SEQ ID NO: 842), or a modified or unmodified variant thereof.

[001268] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40061.1 (SEQ ID NO: 843), or a modified or unmodified variant thereof.

[001269] A RNAi agent comprising a first strand and a second strand, wherein the first strand

comprises at least 15 contiguous nucleotides from a first strand of: AD-40067.1 (SEQ ID NO: 844), or a modified or unmodified variant thereof.

[001270] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40073.1 (SEQ ID NO: 845), or a modified or unmodified variant thereof.

[001271] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40079.1 (SEQ ID NO: 846), or a modified or unmodified variant thereof.

[001272] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40085.1 (SEQ ID NO: 847), or a modified or unmodified variant thereof.

[001273] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40044.1 (SEQ ID NO: 848), or a modified or unmodified variant thereof.

[001274] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40050.1 (SEQ ID NO: 849), or a modified or unmodified variant thereof.

[001275] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40056.1 (SEQ ID NO: 850), or a modified or unmodified variant thereof.

[001276] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40062.1 (SEQ ID NO: 851), or a modified or unmodified variant thereof.

[001277] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40068.1 (SEQ ID NO: 852), or a modified or unmodified variant thereof.

[001278] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40074.1 (SEQ ID NO: 853), or a modified or unmodified variant thereof.

[001279] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40080.1 (SEQ ID NO: 854), or a modified or unmodified variant thereof.

[001280] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39720.1 (SEQ ID NOs: 1754), or a modified or unmodified variant thereof.

[001281] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39706.1 (SEQ ID NOs: 1755), or a modified or unmodified variant thereof.

[001282] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39712.1 (SEQ ID NOs: 1756), or a modified or unmodified variant thereof.

[001283] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39760.1 (SEQ ID NOs: 1757), or a modified or unmodified variant thereof.

[001284] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39732.1 (SEQ ID NOs: 1758), or a modified or unmodified variant thereof.

[001285] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35541.4 (SEQ ID NOs: 1759), or a modified or unmodified variant thereof.

[001286] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NOs: 1760), or a modified or unmodified variant thereof.

[001287] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39741.1, or modified or unmodified variants thereof.

[001288] hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1761), or a modified or unmodified variant thereof.

[001289] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39778.1 (SEQ ID NOs: 1762), or a modified or unmodified variant thereof.

[001290] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39790.1 (SEQ ID NOs: 1763), or a modified or unmodified variant thereof.

[001291] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39822.1 (SEQ ID NOs: 1764), or a modified or unmodified variant thereof.

[001292] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35609.4 (SEQ ID NOs: 1765), or a modified or unmodified variant thereof.

[001293] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35581.4 (SEQ ID NOs: 1766), or a modified or unmodified variant thereof.

[001294] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39845.1 (SEQ ID NOs: 1767), or a modified or unmodified variant thereof.

[001295] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39858.1 (SEQ ID NOs: 1768), or a modified or unmodified variant thereof.

[001296] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39870.1 (SEQ ID NOs: 1769), or a modified or unmodified variant thereof.

[001297] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35576.4 (SEQ ID NOs: 1770), or a modified or unmodified variant thereof.

[001298] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35588.4 (SEQ ID NOs: 1771), or a modified or unmodified variant thereof.

[001299] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35600.1 (SEQ ID NOs: 1772), or a modified or unmodified variant thereof.

[001300] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-35606.1 (SEQ ID NOs: 1773), or a modified or unmodified variant thereof.

[001301] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38151.1 (SEQ ID NOs: 1774), or a modified or unmodified variant thereof.

[001302] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38163.1 (SEQ ID NOs: 1775), or a modified or unmodified variant thereof.

[001303] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-39999.1 (SEQ ID NOs: 1776), or a modified or unmodified variant thereof.

[001304] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38159.1 or hs_KRAS_528_A22S26 (SEQ ID NOs: 1777), or a modified or unmodified variant thereof.

[001305] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38130.1 or hs_KRAS_531_A22S26 (SEQ ID NOs: 1778), or a modified or unmodified variant thereof.

[001306] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38136.1 (SEQ ID NOs: 1779), or a modified or unmodified variant thereof.

[001307] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40036.1 (SEQ ID NOs: 1780), or a modified or unmodified variant thereof.

[001308] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40008.1 (SEQ ID NOs: 1781), or a modified or unmodified variant thereof.

[001309] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40021.1 (SEQ ID NOs: 1782), or a modified or unmodified variant thereof.

[001310] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40077.1 (SEQ ID NOs: 1783), or a modified or unmodified variant thereof.

[001311] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40072.1 (SEQ ID NOs: 1784), or a modified or unmodified variant thereof.

[001312] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40061.1 (SEQ ID NOs: 1785), or a modified or unmodified variant thereof.

[001313] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-40068.1 (SEQ ID NOs: 1786), or a modified or unmodified variant thereof.

[001314] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38131.1 (SEQ ID NOs: 1787), or a modified or unmodified variant thereof.

[001315] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: AD-38167.1 (SEQ ID NOs: 1788), or a modified or unmodified variant thereof.

[001316] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1789), or a modified or unmodified variant thereof.

[001317] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1790), or a modified or unmodified variant thereof.

[001318] A RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides from a first strand of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1791), or a modified or unmodified variant thereof.

[001319] **Specific embodiments comprising a first strand of a RNAi agent disclosed herein**

[001320] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[001321] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[001322] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35523.3 (SEQ ID NO: 428), or a modified or unmodified variant thereof.

[001323] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35529.1 (SEQ ID NO: 429), or a modified or

unmodified variant thereof.

[001324] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35535.4 (SEQ ID NO: 430), or a modified or unmodified variant thereof.

[001325] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35541.4 (SEQ ID NO: 431), or a modified or unmodified variant thereof.

[001326] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35547.4 (SEQ ID NO: 432), or a modified or unmodified variant thereof.

[001327] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35553.4 (SEQ ID NO: 433), or a modified or unmodified variant thereof.

[001328] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35559.4 (SEQ ID NO: 434), or a modified or unmodified variant thereof.

[001329] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35565.4 (SEQ ID NO: 435), or a modified or unmodified variant thereof.

[001330] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35524.4 (SEQ ID NO: 436), or a modified or unmodified variant thereof.

[001331] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35530.4 (SEQ ID NO: 437), or a modified or unmodified variant thereof.

[001332] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35536.4 (SEQ ID NO: 438), or a modified or unmodified variant thereof.

[001333] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35542.4 (SEQ ID NO: 439), or a modified or unmodified variant thereof.

[001334] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35548.4 (SEQ ID NO: 440), or a modified or unmodified variant thereof.

[001335] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35554.4 (SEQ ID NO: 441), or a modified or unmodified variant thereof.

[001336] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35560.2 (SEQ ID NO: 442), or a modified or unmodified variant thereof.

[001337] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-35566.4 (SEQ ID NO: 443), or a modified or unmodified variant thereof.

[001338] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35525.2 (SEQ ID NO: 444), or a modified or unmodified variant thereof.

[001339] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35531.4 (SEQ ID NO: 445), or a modified or unmodified variant thereof.

[001340] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35537.4 (SEQ ID NO: 446), or a modified or unmodified variant thereof.

[001341] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35543.2 (SEQ ID NO: 447), or a modified or unmodified variant thereof.

[001342] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35549.4 (SEQ ID NO: 448), or a modified or unmodified variant thereof.

[001343] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35555.4 (SEQ ID NO: 449), or a modified or unmodified variant thereof.

[001344] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35561.4 (SEQ ID NO: 450), or a modified or unmodified variant thereof.

[001345] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35567.4 (SEQ ID NO: 451), or a modified or unmodified variant thereof.

[001346] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35526.4 (SEQ ID NO: 452), or a modified or unmodified variant thereof.

[001347] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35532.4 (SEQ ID NO: 453), or a modified or unmodified variant thereof.

[001348] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35538.4 (SEQ ID NO: 454), or a modified or unmodified variant thereof.

[001349] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35544.4 (SEQ ID NO: 455), or a modified or unmodified variant thereof.

[001350] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35550.4 (SEQ ID NO: 456), or a modified or unmodified variant thereof.

[001351] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35556.4 (SEQ ID NO: 457), or a modified or unmodified variant thereof.

[001352] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35562.4 (SEQ ID NO: 458), or a modified or unmodified variant thereof.

[001353] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35568.4 (SEQ ID NO: 459), or a modified or unmodified variant thereof.

[001354] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35527.4 (SEQ ID NO: 460), or a modified or unmodified variant thereof.

[001355] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35533.4 (SEQ ID NO: 461), or a modified or unmodified variant thereof.

[001356] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35539.4 (SEQ ID NO: 462), or a modified or unmodified variant thereof.

[001357] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35545.4 (SEQ ID NO: 463), or a modified or unmodified variant thereof.

[001358] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35551.4 (SEQ ID NO: 464), or a modified or unmodified variant thereof.

[001359] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35563.4 (SEQ ID NO: 465), or a modified or unmodified variant thereof.

[001360] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35528.4 (SEQ ID NO: 466), or a modified or unmodified variant thereof.

[001361] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35540.4 (SEQ ID NO: 467), or a modified or unmodified variant thereof.

[001362] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35546.4 (SEQ ID NO: 468), or a modified or unmodified variant thereof.

[001363] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35552.4 (SEQ ID NO: 469), or a modified or unmodified variant thereof.

[001364] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35558.4 (SEQ ID NO: 470), or a modified or

unmodified variant thereof.

[001365] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35564.4 (SEQ ID NO: 471), or a modified or unmodified variant thereof.

[001366] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35570.4 (SEQ ID NO: 472), or a modified or unmodified variant thereof.

[001367] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35571.4 (SEQ ID NO: 473), or a modified or unmodified variant thereof.

[001368] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35577.4 (SEQ ID NO: 474), or a modified or unmodified variant thereof.

[001369] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35583.4 (SEQ ID NO: 475), or a modified or unmodified variant thereof.

[001370] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35589.4 (SEQ ID NO: 476), or a modified or unmodified variant thereof.

[001371] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35595.4 (SEQ ID NO: 477), or a modified or unmodified variant thereof.

[001372] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35601.4 (SEQ ID NO: 478), or a modified or unmodified variant thereof.

[001373] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35607.4 (SEQ ID NO: 479), or a modified or unmodified variant thereof.

[001374] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35613.4 (SEQ ID NO: 480), or a modified or unmodified variant thereof.

[001375] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35572.4 (SEQ ID NO: 481), or a modified or unmodified variant thereof.

[001376] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35578.4 (SEQ ID NO: 482), or a modified or unmodified variant thereof.

[001377] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35584.4 (SEQ ID NO: 483), or a modified or unmodified variant thereof.

[001378] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-35590.4 (SEQ ID NO: 484), or a modified or unmodified variant thereof.

[001379] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35596.4 (SEQ ID NO: 485), or a modified or unmodified variant thereof.

[001380] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35602.4 (SEQ ID NO: 486), or a modified or unmodified variant thereof.

[001381] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35608.4 (SEQ ID NO: 487), or a modified or unmodified variant thereof.

[001382] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35614.4 (SEQ ID NO: 488), or a modified or unmodified variant thereof.

[001383] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35573.4 (SEQ ID NO: 489), or a modified or unmodified variant thereof.

[001384] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35579.4 (SEQ ID NO: 490), or a modified or unmodified variant thereof.

[001385] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35585.4 (SEQ ID NO: 491), or a modified or unmodified variant thereof.

[001386] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35591.4 (SEQ ID NO: 492), or a modified or unmodified variant thereof.

[001387] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35597.4 (SEQ ID NO: 493), or a modified or unmodified variant thereof.

[001388] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35603.4 (SEQ ID NO: 494), or a modified or unmodified variant thereof.

[001389] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35609.4 (SEQ ID NO: 495), or a modified or unmodified variant thereof.

[001390] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35615.4 (SEQ ID NO: 496), or a modified or unmodified variant thereof.

[001391] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35574.4 (SEQ ID NO: 497), or a modified or unmodified variant thereof.

[001392] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35580.1 (SEQ ID NO: 498), or a modified or unmodified variant thereof.

[001393] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35586.4 (SEQ ID NO: 499), or a modified or unmodified variant thereof.

[001394] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35592.4 (SEQ ID NO: 500), or a modified or unmodified variant thereof.

[001395] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35598.4 (SEQ ID NO: 501), or a modified or unmodified variant thereof.

[001396] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35604.4 (SEQ ID NO: 502), or a modified or unmodified variant thereof.

[001397] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35610.4 (SEQ ID NO: 503), or a modified or unmodified variant thereof.

[001398] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35616.4 (SEQ ID NO: 504), or a modified or unmodified variant thereof.

[001399] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35575.4 (SEQ ID NO: 505), or a modified or unmodified variant thereof.

[001400] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35581.4 (SEQ ID NO: 506), or a modified or unmodified variant thereof.

[001401] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35587.4 (SEQ ID NO: 507), or a modified or unmodified variant thereof.

[001402] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35593.4 (SEQ ID NO: 508), or a modified or unmodified variant thereof.

[001403] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35599.4 (SEQ ID NO: 509), or a modified or unmodified variant thereof.

[001404] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35605.4 (SEQ ID NO: 510), or a modified or unmodified variant thereof.

[001405] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35611.4 (SEQ ID NO: 511), or a modified or

unmodified variant thereof.

[001406] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35617.4 (SEQ ID NO: 512), or a modified or unmodified variant thereof.

[001407] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35576.4 (SEQ ID NO: 513), or a modified or unmodified variant thereof.

[001408] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35588.4 (SEQ ID NO: 514), or a modified or unmodified variant thereof.

[001409] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35667.1 (SEQ ID NO: 515), or a modified or unmodified variant thereof.

[001410] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35673.1 (SEQ ID NO: 516), or a modified or unmodified variant thereof.

[001411] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35679.1 (SEQ ID NO: 517), or a modified or unmodified variant thereof.

[001412] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35685.1 (SEQ ID NO: 518), or a modified or unmodified variant thereof.

[001413] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35691.1 (SEQ ID NO: 519), or a modified or unmodified variant thereof.

[001414] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35557.1 (SEQ ID NO: 520), or a modified or unmodified variant thereof.

[001415] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35618.1 (SEQ ID NO: 521), or a modified or unmodified variant thereof.

[001416] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35569.1 (SEQ ID NO: 522), or a modified or unmodified variant thereof.

[001417] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35534.1 (SEQ ID NO: 523), or a modified or unmodified variant thereof.

[001418] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35582.1 (SEQ ID NO: 524), or a modified or unmodified variant thereof.

[001419] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-35594.1 (SEQ ID NO: 525), or a modified or unmodified variant thereof.

[001420] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35600.1 (SEQ ID NO: 526), or a modified or unmodified variant thereof.

[001421] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35606.1 (SEQ ID NO: 527), or a modified or unmodified variant thereof.

[001422] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35612.1 (SEQ ID NO: 528), or a modified or unmodified variant thereof.

[001423] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38127.1 (SEQ ID NO: 529), or a modified or unmodified variant thereof.

[001424] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38133.1 (SEQ ID NO: 530), or a modified or unmodified variant thereof.

[001425] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38139.1 (SEQ ID NO: 531), or a modified or unmodified variant thereof.

[001426] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38145.1 (SEQ ID NO: 532), or a modified or unmodified variant thereof.

[001427] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38151.1 (SEQ ID NO: 533), or a modified or unmodified variant thereof.

[001428] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38157.1 (SEQ ID NO: 534), or a modified or unmodified variant thereof.

[001429] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38163.1 (SEQ ID NO: 535), or a modified or unmodified variant thereof.

[001430] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38169.1 (SEQ ID NO: 536), or a modified or unmodified variant thereof.

[001431] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38128.1 (SEQ ID NO: 537), or a modified or unmodified variant thereof.

[001432] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38134.1 (SEQ ID NO: 538), or a modified or unmodified variant thereof.

[001433] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38140.1 (SEQ ID NO: 539), or a modified or unmodified variant thereof.

[001434] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38146.1 (SEQ ID NO: 540), or a modified or unmodified variant thereof.

[001435] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38152.1 (SEQ ID NO: 541), or a modified or unmodified variant thereof.

[001436] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38158.1 (SEQ ID NO: 542), or a modified or unmodified variant thereof.

[001437] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38164.1 (SEQ ID NO: 543), or a modified or unmodified variant thereof.

[001438] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38170.1 (SEQ ID NO: 544), or a modified or unmodified variant thereof.

[001439] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38129.1 (SEQ ID NO: 545), or a modified or unmodified variant thereof.

[001440] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38135.1 (SEQ ID NO: 546), or a modified or unmodified variant thereof.

[001441] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38141.1 (SEQ ID NO: 547), or a modified or unmodified variant thereof.

[001442] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38147.1 (SEQ ID NO: 548), or a modified or unmodified variant thereof.

[001443] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38153.1 (SEQ ID NO: 549), or a modified or unmodified variant thereof.

[001444] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38159.1 (SEQ ID NO: 550), or a modified or unmodified variant thereof.

[001445] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38165.1 (SEQ ID NO: 551), or a modified or unmodified variant thereof.

[001446] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38171.1 (SEQ ID NO: 552), or a modified or

unmodified variant thereof.

[001447] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38130.1 (SEQ ID NO: 553), or a modified or unmodified variant thereof.

[001448] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38136.1 (SEQ ID NO: 554), or a modified or unmodified variant thereof.

[001449] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38142.1 (SEQ ID NO: 555), or a modified or unmodified variant thereof.

[001450] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38148.1 (SEQ ID NO: 556), or a modified or unmodified variant thereof.

[001451] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38154.1 (SEQ ID NO: 557), or a modified or unmodified variant thereof.

[001452] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38160.1 (SEQ ID NO: 558), or a modified or unmodified variant thereof.

[001453] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38166.1 (SEQ ID NO: 559), or a modified or unmodified variant thereof.

[001454] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38172.1 (SEQ ID NO: 560), or a modified or unmodified variant thereof.

[001455] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38131.1 (SEQ ID NO: 561), or a modified or unmodified variant thereof.

[001456] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38137.1 (SEQ ID NO: 562), or a modified or unmodified variant thereof.

[001457] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38143.1 (SEQ ID NO: 563), or a modified or unmodified variant thereof.

[001458] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38149.1 (SEQ ID NO: 564), or a modified or unmodified variant thereof.

[001459] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38155.1 (SEQ ID NO: 565), or a modified or unmodified variant thereof.

[001460] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-38161.1 (SEQ ID NO: 566), or a modified or unmodified variant thereof.

[001461] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38167.1 (SEQ ID NO: 567), or a modified or unmodified variant thereof.

[001462] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38173.1 (SEQ ID NO: 568), or a modified or unmodified variant thereof.

[001463] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38132.1 (SEQ ID NO: 569), or a modified or unmodified variant thereof.

[001464] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38138.1 (SEQ ID NO: 570), or a modified or unmodified variant thereof.

[001465] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38144.1 (SEQ ID NO: 571), or a modified or unmodified variant thereof.

[001466] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38150.1 (SEQ ID NO: 572), or a modified or unmodified variant thereof.

[001467] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38156.1 (SEQ ID NO: 573), or a modified or unmodified variant thereof.

[001468] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38162.1 (SEQ ID NO: 574), or a modified or unmodified variant thereof.

[001469] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38168.1 (SEQ ID NO: 575), or a modified or unmodified variant thereof.

[001470] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38174.1 (SEQ ID NO: 576), or a modified or unmodified variant thereof.

[001471] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39683.1 (SEQ ID NO: 577), or a modified or unmodified variant thereof.

[001472] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39689.1 (SEQ ID NO: 578), or a modified or unmodified variant thereof.

[001473] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39695.1 (SEQ ID NO: 579), or a modified or unmodified variant thereof.

[001474] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39701.1 (SEQ ID NO: 580), or a modified or unmodified variant thereof.

[001475] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39707.1 (SEQ ID NO: 581), or a modified or unmodified variant thereof.

[001476] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39713.1 (SEQ ID NO: 582), or a modified or unmodified variant thereof.

[001477] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39719.1 (SEQ ID NO: 583), or a modified or unmodified variant thereof.

[001478] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39725.1 (SEQ ID NO: 584), or a modified or unmodified variant thereof.

[001479] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39684.1 (SEQ ID NO: 585), or a modified or unmodified variant thereof.

[001480] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39690.1 (SEQ ID NO: 586), or a modified or unmodified variant thereof.

[001481] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39696.1 (SEQ ID NO: 587), or a modified or unmodified variant thereof.

[001482] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39702.1 (SEQ ID NO: 588), or a modified or unmodified variant thereof.

[001483] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39708.1 (SEQ ID NO: 589), or a modified or unmodified variant thereof.

[001484] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39714.1 (SEQ ID NO: 590), or a modified or unmodified variant thereof.

[001485] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39720.1 (SEQ ID NO: 591), or a modified or unmodified variant thereof.

[001486] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39726.1 (SEQ ID NO: 592), or a modified or unmodified variant thereof.

[001487] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39685.1 (SEQ ID NO: 593), or a modified or

unmodified variant thereof.

[001488] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39691.1 (SEQ ID NO: 594), or a modified or unmodified variant thereof.

[001489] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39697.1 (SEQ ID NO: 595), or a modified or unmodified variant thereof.

[001490] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39703.1 (SEQ ID NO: 596), or a modified or unmodified variant thereof.

[001491] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39709.1 (SEQ ID NO: 597), or a modified or unmodified variant thereof.

[001492] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39715.1 (SEQ ID NO: 598), or a modified or unmodified variant thereof.

[001493] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39721.1 (SEQ ID NO: 599), or a modified or unmodified variant thereof.

[001494] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39727.1 (SEQ ID NO: 600), or a modified or unmodified variant thereof.

[001495] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39686.1 (SEQ ID NO: 601), or a modified or unmodified variant thereof.

[001496] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39692.1 (SEQ ID NO: 602), or a modified or unmodified variant thereof.

[001497] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39698.1 (SEQ ID NO: 603), or a modified or unmodified variant thereof.

[001498] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39704.1 (SEQ ID NO: 604), or a modified or unmodified variant thereof.

[001499] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39710.1 (SEQ ID NO: 605), or a modified or unmodified variant thereof.

[001500] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39716.1 (SEQ ID NO: 606), or a modified or unmodified variant thereof.

[001501] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-39722.1 (SEQ ID NO: 607), or a modified or unmodified variant thereof.

[001502] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39728.1 (SEQ ID NO: 608), or a modified or unmodified variant thereof.

[001503] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39687.1 (SEQ ID NO: 609), or a modified or unmodified variant thereof.

[001504] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39693.1 (SEQ ID NO: 610), or a modified or unmodified variant thereof.

[001505] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39699.1 (SEQ ID NO: 611), or a modified or unmodified variant thereof.

[001506] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39705.1 (SEQ ID NO: 612), or a modified or unmodified variant thereof.

[001507] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39711.1 (SEQ ID NO: 613), or a modified or unmodified variant thereof.

[001508] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39717.1 (SEQ ID NO: 614), or a modified or unmodified variant thereof.

[001509] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39723.1 (SEQ ID NO: 615), or a modified or unmodified variant thereof.

[001510] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39729.1 (SEQ ID NO: 616), or a modified or unmodified variant thereof.

[001511] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39688.1 (SEQ ID NO: 617), or a modified or unmodified variant thereof.

[001512] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39694.1 (SEQ ID NO: 618), or a modified or unmodified variant thereof.

[001513] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39700.1 (SEQ ID NO: 619), or a modified or unmodified variant thereof.

[001514] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39706.1 (SEQ ID NO: 620), or a modified or unmodified variant thereof.

[001515] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39712.1 (SEQ ID NO: 621), or a modified or unmodified variant thereof.

[001516] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39718.1 (SEQ ID NO: 622), or a modified or unmodified variant thereof.

[001517] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39724.1 (SEQ ID NO: 623), or a modified or unmodified variant thereof.

[001518] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39730.1 (SEQ ID NO: 624), or a modified or unmodified variant thereof.

[001519] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39736.1 (SEQ ID NO: 625), or a modified or unmodified variant thereof.

[001520] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39742.1 (SEQ ID NO: 626), or a modified or unmodified variant thereof.

[001521] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39748.1 (SEQ ID NO: 627), or a modified or unmodified variant thereof.

[001522] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39754.1 (SEQ ID NO: 628), or a modified or unmodified variant thereof.

[001523] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39760.1 (SEQ ID NO: 629), or a modified or unmodified variant thereof.

[001524] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39766.1 (SEQ ID NO: 630), or a modified or unmodified variant thereof.

[001525] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39772.1 (SEQ ID NO: 631), or a modified or unmodified variant thereof.

[001526] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39731.1 (SEQ ID NO: 632), or a modified or unmodified variant thereof.

[001527] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39737.1 (SEQ ID NO: 633), or a modified or unmodified variant thereof.

[001528] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39743.1 (SEQ ID NO: 634), or a modified or

unmodified variant thereof.

[001529] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39749.1 (SEQ ID NO: 635), or a modified or unmodified variant thereof.

[001530] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39755.1 (SEQ ID NO: 636), or a modified or unmodified variant thereof.

[001531] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39761.1 (SEQ ID NO: 637), or a modified or unmodified variant thereof.

[001532] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39767.1 (SEQ ID NO: 638), or a modified or unmodified variant thereof.

[001533] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39773.1 (SEQ ID NO: 639), or a modified or unmodified variant thereof.

[001534] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39732.1 (SEQ ID NO: 640), or a modified or unmodified variant thereof.

[001535] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39738.1 (SEQ ID NO: 641), or a modified or unmodified variant thereof.

[001536] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39744.1 (SEQ ID NO: 642), or a modified or unmodified variant thereof.

[001537] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39750.1 (SEQ ID NO: 643), or a modified or unmodified variant thereof.

[001538] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39756.1 (SEQ ID NO: 644), or a modified or unmodified variant thereof.

[001539] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39762.1 (SEQ ID NO: 645), or a modified or unmodified variant thereof.

[001540] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39768.1 (SEQ ID NO: 646), or a modified or unmodified variant thereof.

[001541] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39774.1 (SEQ ID NO: 647), or a modified or unmodified variant thereof.

[001542] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-39733.1 (SEQ ID NO: 648), or a modified or unmodified variant thereof.

[001543] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39739.1 (SEQ ID NO: 649), or a modified or unmodified variant thereof.

[001544] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39745.1 (SEQ ID NO: 650), or a modified or unmodified variant thereof.

[001545] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39751.1 (SEQ ID NO: 651), or a modified or unmodified variant thereof.

[001546] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39757.1 (SEQ ID NO: 652), or a modified or unmodified variant thereof.

[001547] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39763.1 (SEQ ID NO: 653), or a modified or unmodified variant thereof.

[001548] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39769.1 (SEQ ID NO: 654), or a modified or unmodified variant thereof.

[001549] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39775.1 (SEQ ID NO: 655), or a modified or unmodified variant thereof.

[001550] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39734.1 (SEQ ID NO: 656), or a modified or unmodified variant thereof.

[001551] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39740.1 (SEQ ID NO: 657), or a modified or unmodified variant thereof.

[001552] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39746.1 (SEQ ID NO: 658), or a modified or unmodified variant thereof.

[001553] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39752.1 (SEQ ID NO: 659), or a modified or unmodified variant thereof.

[001554] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39758.1 (SEQ ID NO: 660), or a modified or unmodified variant thereof.

[001555] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39764.1 (SEQ ID NO: 661), or a modified or unmodified variant thereof.

[001556] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39770.1 (SEQ ID NO: 662), or a modified or unmodified variant thereof.

[001557] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39776.1 (SEQ ID NO: 663), or a modified or unmodified variant thereof.

[001558] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39735.1 (SEQ ID NO: 664), or a modified or unmodified variant thereof.

[001559] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39741.1 (SEQ ID NO: 665), or a modified or unmodified variant thereof.

[001560] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39747.1 (SEQ ID NO: 666), or a modified or unmodified variant thereof.

[001561] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39753.1 (SEQ ID NO: 667), or a modified or unmodified variant thereof.

[001562] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39759.1 (SEQ ID NO: 668), or a modified or unmodified variant thereof.

[001563] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39765.1 (SEQ ID NO: 669), or a modified or unmodified variant thereof.

[001564] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39771.1 (SEQ ID NO: 670), or a modified or unmodified variant thereof.

[001565] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39778.1 (SEQ ID NO: 671), or a modified or unmodified variant thereof.

[001566] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39784.1 (SEQ ID NO: 672), or a modified or unmodified variant thereof.

[001567] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39790.1 (SEQ ID NO: 673), or a modified or unmodified variant thereof.

[001568] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39796.1 (SEQ ID NO: 674), or a modified or unmodified variant thereof.

[001569] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39802.1 (SEQ ID NO: 675), or a modified or

unmodified variant thereof.

[001570] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39808.1 (SEQ ID NO: 676), or a modified or unmodified variant thereof.

[001571] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39814.1 (SEQ ID NO: 677), or a modified or unmodified variant thereof.

[001572] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39820.1 (SEQ ID NO: 678), or a modified or unmodified variant thereof.

[001573] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39779.1 (SEQ ID NO: 679), or a modified or unmodified variant thereof.

[001574] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39785.1 (SEQ ID NO: 680), or a modified or unmodified variant thereof.

[001575] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39791.1 (SEQ ID NO: 681), or a modified or unmodified variant thereof.

[001576] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39797.1 (SEQ ID NO: 682), or a modified or unmodified variant thereof.

[001577] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39803.1 (SEQ ID NO: 683), or a modified or unmodified variant thereof.

[001578] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39809.1 (SEQ ID NO: 684), or a modified or unmodified variant thereof.

[001579] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39815.1 (SEQ ID NO: 685), or a modified or unmodified variant thereof.

[001580] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39821.1 (SEQ ID NO: 686), or a modified or unmodified variant thereof.

[001581] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39780.1 (SEQ ID NO: 687), or a modified or unmodified variant thereof.

[001582] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39786.1 (SEQ ID NO: 688), or a modified or unmodified variant thereof.

[001583] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-39792.1 (SEQ ID NO: 689), or a modified or unmodified variant thereof.

[001584] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39798.1 (SEQ ID NO: 690), or a modified or unmodified variant thereof.

[001585] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39804.1 (SEQ ID NO: 691), or a modified or unmodified variant thereof.

[001586] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39810.1 (SEQ ID NO: 692), or a modified or unmodified variant thereof.

[001587] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39816.1 (SEQ ID NO: 693), or a modified or unmodified variant thereof.

[001588] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39822.1 (SEQ ID NO: 694), or a modified or unmodified variant thereof.

[001589] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39781.1 (SEQ ID NO: 695), or a modified or unmodified variant thereof.

[001590] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39787.1 (SEQ ID NO: 696), or a modified or unmodified variant thereof.

[001591] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39793.1 (SEQ ID NO: 697), or a modified or unmodified variant thereof.

[001592] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39799.1 (SEQ ID NO: 698), or a modified or unmodified variant thereof.

[001593] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39805.1 (SEQ ID NO: 699), or a modified or unmodified variant thereof.

[001594] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39811.1 (SEQ ID NO: 700), or a modified or unmodified variant thereof.

[001595] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39817.1 (SEQ ID NO: 701), or a modified or unmodified variant thereof.

[001596] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39823.1 (SEQ ID NO: 702), or a modified or unmodified variant thereof.

[001597] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39782.1 (SEQ ID NO: 703), or a modified or unmodified variant thereof.

[001598] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39788.1 (SEQ ID NO: 704), or a modified or unmodified variant thereof.

[001599] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39794.1 (SEQ ID NO: 705), or a modified or unmodified variant thereof.

[001600] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39800.1 (SEQ ID NO: 706), or a modified or unmodified variant thereof.

[001601] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39806.1 (SEQ ID NO: 707), or a modified or unmodified variant thereof.

[001602] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39812.1 (SEQ ID NO: 708), or a modified or unmodified variant thereof.

[001603] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39818.1 (SEQ ID NO: 709), or a modified or unmodified variant thereof.

[001604] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39824.1 (SEQ ID NO: 710), or a modified or unmodified variant thereof.

[001605] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39783.1 (SEQ ID NO: 711), or a modified or unmodified variant thereof.

[001606] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39789.1 (SEQ ID NO: 712), or a modified or unmodified variant thereof.

[001607] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39795.1 (SEQ ID NO: 713), or a modified or unmodified variant thereof.

[001608] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39801.1 (SEQ ID NO: 714), or a modified or unmodified variant thereof.

[001609] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39807.1 (SEQ ID NO: 715), or a modified or unmodified variant thereof.

[001610] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39813.1 (SEQ ID NO: 716), or a modified or

unmodified variant thereof.

[001611] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39819.1 (SEQ ID NO: 717), or a modified or unmodified variant thereof.

[001612] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39825.1 (SEQ ID NO: 718), or a modified or unmodified variant thereof.

[001613] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39831.1 (SEQ ID NO: 719), or a modified or unmodified variant thereof.

[001614] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39837.1 (SEQ ID NO: 720), or a modified or unmodified variant thereof.

[001615] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39843.1 (SEQ ID NO: 721), or a modified or unmodified variant thereof.

[001616] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39849.1 (SEQ ID NO: 722), or a modified or unmodified variant thereof.

[001617] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39855.1 (SEQ ID NO: 723), or a modified or unmodified variant thereof.

[001618] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39861.1 (SEQ ID NO: 724), or a modified or unmodified variant thereof.

[001619] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39867.1 (SEQ ID NO: 725), or a modified or unmodified variant thereof.

[001620] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39826.1 (SEQ ID NO: 726), or a modified or unmodified variant thereof.

[001621] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39832.1 (SEQ ID NO: 727), or a modified or unmodified variant thereof.

[001622] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39838.1 (SEQ ID NO: 728), or a modified or unmodified variant thereof.

[001623] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39844.1 (SEQ ID NO: 729), or a modified or unmodified variant thereof.

[001624] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-39850.1 (SEQ ID NO: 730), or a modified or unmodified variant thereof.

[001625] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39856.1 (SEQ ID NO: 731), or a modified or unmodified variant thereof.

[001626] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39862.1 (SEQ ID NO: 732), or a modified or unmodified variant thereof.

[001627] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39868.1 (SEQ ID NO: 733), or a modified or unmodified variant thereof.

[001628] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39827.1 (SEQ ID NO: 734), or a modified or unmodified variant thereof.

[001629] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39833.1 (SEQ ID NO: 735), or a modified or unmodified variant thereof.

[001630] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39839.1 (SEQ ID NO: 736), or a modified or unmodified variant thereof.

[001631] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39845.1 (SEQ ID NO: 737), or a modified or unmodified variant thereof.

[001632] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39851.1 (SEQ ID NO: 738), or a modified or unmodified variant thereof.

[001633] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39857.1 (SEQ ID NO: 739), or a modified or unmodified variant thereof.

[001634] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39863.1 (SEQ ID NO: 740), or a modified or unmodified variant thereof.

[001635] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39869.1 (SEQ ID NO: 741), or a modified or unmodified variant thereof.

[001636] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39828.1 (SEQ ID NO: 742), or a modified or unmodified variant thereof.

[001637] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39834.1 (SEQ ID NO: 743), or a modified or unmodified variant thereof.

[001638] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39840.1 (SEQ ID NO: 744), or a modified or unmodified variant thereof.

[001639] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39846.1 (SEQ ID NO: 745), or a modified or unmodified variant thereof.

[001640] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39852.1 (SEQ ID NO: 746), or a modified or unmodified variant thereof.

[001641] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39858.1 (SEQ ID NO: 747), or a modified or unmodified variant thereof.

[001642] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39864.1 (SEQ ID NO: 748), or a modified or unmodified variant thereof.

[001643] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39870.1 (SEQ ID NO: 749), or a modified or unmodified variant thereof.

[001644] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39829.1 (SEQ ID NO: 750), or a modified or unmodified variant thereof.

[001645] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39835.1 (SEQ ID NO: 751), or a modified or unmodified variant thereof.

[001646] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39841.1 (SEQ ID NO: 752), or a modified or unmodified variant thereof.

[001647] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39853.1 (SEQ ID NO: 753), or a modified or unmodified variant thereof.

[001648] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39859.1 (SEQ ID NO: 754), or a modified or unmodified variant thereof.

[001649] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39865.1 (SEQ ID NO: 755), or a modified or unmodified variant thereof.

[001650] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39871.1 (SEQ ID NO: 756), or a modified or unmodified variant thereof.

[001651] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39830.1 (SEQ ID NO: 757), or a modified or

unmodified variant thereof.

[001652] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39836.1 (SEQ ID NO: 758), or a modified or unmodified variant thereof.

[001653] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39842.1 (SEQ ID NO: 759), or a modified or unmodified variant thereof.

[001654] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39848.1 (SEQ ID NO: 760), or a modified or unmodified variant thereof.

[001655] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39854.1 (SEQ ID NO: 761), or a modified or unmodified variant thereof.

[001656] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39860.1 (SEQ ID NO: 762), or a modified or unmodified variant thereof.

[001657] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39866.1 (SEQ ID NO: 763), or a modified or unmodified variant thereof.

[001658] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39992.1 (SEQ ID NO: 764), or a modified or unmodified variant thereof.

[001659] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39998.1 (SEQ ID NO: 765), or a modified or unmodified variant thereof.

[001660] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40004.1 (SEQ ID NO: 766), or a modified or unmodified variant thereof.

[001661] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40010.1 (SEQ ID NO: 767), or a modified or unmodified variant thereof.

[001662] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40016.1 (SEQ ID NO: 768), or a modified or unmodified variant thereof.

[001663] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40022.1 (SEQ ID NO: 769), or a modified or unmodified variant thereof.

[001664] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40028.1 (SEQ ID NO: 770), or a modified or unmodified variant thereof.

[001665] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-40034.1 (SEQ ID NO: 771), or a modified or unmodified variant thereof.

[001666] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39999.1 (SEQ ID NO: 772), or a modified or unmodified variant thereof.

[001667] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40005.1 (SEQ ID NO: 773), or a modified or unmodified variant thereof.

[001668] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40011.1 (SEQ ID NO: 774), or a modified or unmodified variant thereof.

[001669] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40017.1 (SEQ ID NO: 775), or a modified or unmodified variant thereof.

[001670] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40029.1 (SEQ ID NO: 776), or a modified or unmodified variant thereof.

[001671] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40035.1 (SEQ ID NO: 777), or a modified or unmodified variant thereof.

[001672] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39994.1 (SEQ ID NO: 778), or a modified or unmodified variant thereof.

[001673] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40000.1 (SEQ ID NO: 779), or a modified or unmodified variant thereof.

[001674] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40006.1 (SEQ ID NO: 780), or a modified or unmodified variant thereof.

[001675] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40012.1 (SEQ ID NO: 781), or a modified or unmodified variant thereof.

[001676] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40018.1 (SEQ ID NO: 782), or a modified or unmodified variant thereof.

[001677] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40024.1 (SEQ ID NO: 783), or a modified or unmodified variant thereof.

[001678] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40030.1 (SEQ ID NO: 784), or a modified or unmodified variant thereof.

[001679] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40036.1 (SEQ ID NO: 785), or a modified or unmodified variant thereof.

[001680] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39995.1 (SEQ ID NO: 786), or a modified or unmodified variant thereof.

[001681] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40001.1 (SEQ ID NO: 787), or a modified or unmodified variant thereof.

[001682] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40007.1 (SEQ ID NO: 788), or a modified or unmodified variant thereof.

[001683] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40013.1 (SEQ ID NO: 789), or a modified or unmodified variant thereof.

[001684] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40019.1 (SEQ ID NO: 790), or a modified or unmodified variant thereof.

[001685] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40025.1 (SEQ ID NO: 791), or a modified or unmodified variant thereof.

[001686] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40031.1 (SEQ ID NO: 792), or a modified or unmodified variant thereof.

[001687] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40037.1 (SEQ ID NO: 793), or a modified or unmodified variant thereof.

[001688] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39996.1 (SEQ ID NO: 794), or a modified or unmodified variant thereof.

[001689] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40002.1 (SEQ ID NO: 795), or a modified or unmodified variant thereof.

[001690] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40008.1 (SEQ ID NO: 796), or a modified or unmodified variant thereof.

[001691] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40014.1 (SEQ ID NO: 797), or a modified or unmodified variant thereof.

[001692] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40020.1 (SEQ ID NO: 798), or a modified or

unmodified variant thereof.

[001693] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40026.1 (SEQ ID NO: 799), or a modified or unmodified variant thereof.

[001694] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40032.1 (SEQ ID NO: 800), or a modified or unmodified variant thereof.

[001695] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40038.1 (SEQ ID NO: 801), or a modified or unmodified variant thereof.

[001696] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39997.1 (SEQ ID NO: 802), or a modified or unmodified variant thereof.

[001697] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40009.1 (SEQ ID NO: 803), or a modified or unmodified variant thereof.

[001698] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40015.1 (SEQ ID NO: 804), or a modified or unmodified variant thereof.

[001699] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40021.1 (SEQ ID NO: 805), or a modified or unmodified variant thereof.

[001700] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40027.1 (SEQ ID NO: 806), or a modified or unmodified variant thereof.

[001701] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40033.1 (SEQ ID NO: 807), or a modified or unmodified variant thereof.

[001702] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40039.1 (SEQ ID NO: 808), or a modified or unmodified variant thereof.

[001703] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40045.1 (SEQ ID NO: 809), or a modified or unmodified variant thereof.

[001704] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40051.1 (SEQ ID NO: 810), or a modified or unmodified variant thereof.

[001705] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40057.1 (SEQ ID NO: 811), or a modified or unmodified variant thereof.

[001706] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-40063.1 (SEQ ID NO: 812), or a modified or unmodified variant thereof.

[001707] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40069.1 (SEQ ID NO: 813), or a modified or unmodified variant thereof.

[001708] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40075.1 (SEQ ID NO: 814), or a modified or unmodified variant thereof.

[001709] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40081.1 (SEQ ID NO: 815), or a modified or unmodified variant thereof.

[001710] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40040.1 (SEQ ID NO: 816), or a modified or unmodified variant thereof.

[001711] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40046.1 (SEQ ID NO: 817), or a modified or unmodified variant thereof.

[001712] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40052.1 (SEQ ID NO: 818), or a modified or unmodified variant thereof.

[001713] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40058.1 (SEQ ID NO: 819), or a modified or unmodified variant thereof.

[001714] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40064.1 (SEQ ID NO: 820), or a modified or unmodified variant thereof.

[001715] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40070.1 (SEQ ID NO: 821), or a modified or unmodified variant thereof.

[001716] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40076.1 (SEQ ID NO: 822), or a modified or unmodified variant thereof.

[001717] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40082.1 (SEQ ID NO: 823), or a modified or unmodified variant thereof.

[001718] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40041.1 (SEQ ID NO: 824), or a modified or unmodified variant thereof.

[001719] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40047.1 (SEQ ID NO: 825), or a modified or unmodified variant thereof.

[001720] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40053.1 (SEQ ID NO: 826), or a modified or unmodified variant thereof.

[001721] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40059.1 (SEQ ID NO: 827), or a modified or unmodified variant thereof.

[001722] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40065.1 (SEQ ID NO: 828), or a modified or unmodified variant thereof.

[001723] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40071.1 (SEQ ID NO: 829), or a modified or unmodified variant thereof.

[001724] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40077.1 (SEQ ID NO: 830), or a modified or unmodified variant thereof.

[001725] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40083.1 (SEQ ID NO: 831), or a modified or unmodified variant thereof.

[001726] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40042.1 (SEQ ID NO: 832), or a modified or unmodified variant thereof.

[001727] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40048.1 (SEQ ID NO: 833), or a modified or unmodified variant thereof.

[001728] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40054.1 (SEQ ID NO: 834), or a modified or unmodified variant thereof.

[001729] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40060.1 (SEQ ID NO: 835), or a modified or unmodified variant thereof.

[001730] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40066.1 (SEQ ID NO: 836), or a modified or unmodified variant thereof.

[001731] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40072.1 (SEQ ID NO: 837), or a modified or unmodified variant thereof.

[001732] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40078.1 (SEQ ID NO: 838), or a modified or unmodified variant thereof.

[001733] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40084.1 (SEQ ID NO: 839), or a modified or

unmodified variant thereof.

[001734] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40043.1 (SEQ ID NO: 840), or a modified or unmodified variant thereof.

[001735] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40049.1 (SEQ ID NO: 841), or a modified or unmodified variant thereof.

[001736] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40055.1 (SEQ ID NO: 842), or a modified or unmodified variant thereof.

[001737] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40061.1 (SEQ ID NO: 843), or a modified or unmodified variant thereof.

[001738] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40067.1 (SEQ ID NO: 844), or a modified or unmodified variant thereof.

[001739] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40073.1 (SEQ ID NO: 845), or a modified or unmodified variant thereof.

[001740] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40079.1 (SEQ ID NO: 846), or a modified or unmodified variant thereof.

[001741] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40085.1 (SEQ ID NO: 847), or a modified or unmodified variant thereof.

[001742] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40044.1 (SEQ ID NO: 848), or a modified or unmodified variant thereof.

[001743] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40050.1 (SEQ ID NO: 849), or a modified or unmodified variant thereof.

[001744] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40056.1 (SEQ ID NO: 850), or a modified or unmodified variant thereof.

[001745] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40062.1 (SEQ ID NO: 851), or a modified or unmodified variant thereof.

[001746] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40068.1 (SEQ ID NO: 852), or a modified or unmodified variant thereof.

[001747] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

strand is the sequence of a first strand of: AD-40074.1 (SEQ ID NO: 853), or a modified or unmodified variant thereof.

[001748] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40080.1 (SEQ ID NO: 854), or a modified or unmodified variant thereof.

[001749] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39720.1 (SEQ ID NOs: 1716 and 1754), or a modified or unmodified variant thereof.

[001750] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39706.1 (SEQ ID NOs: 1717 and 1755), or a modified or unmodified variant thereof.

[001751] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39712.1 (SEQ ID NOs: 1718 and 1756), or a modified or unmodified variant thereof.

[001752] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39760.1 (SEQ ID NOs: 1719 and 1757), or a modified or unmodified variant thereof.

[001753] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39732.1 (SEQ ID NOs: 1720 and 1758), or a modified or unmodified variant thereof.

[001754] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35541.4 (SEQ ID NOs: 1721 and 1759), or a modified or unmodified variant thereof.

[001755] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NOs: 1722 and 1760), or a modified or unmodified variant thereof.

[001756] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39741.1, or modified or unmodified variants thereof.

[001757] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1723 and 1761), or a modified or unmodified variant thereof.

[001758] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39778.1 (SEQ ID NOs: 1724 and 1762), or a modified or unmodified variant thereof.

[001759] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39790.1 (SEQ ID NOs: 1725 and 1763), or a modified or unmodified variant thereof.

[001760] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39822.1 (SEQ ID NOs: 1726 and 1764), or a modified or unmodified variant thereof.

[001761] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35609.4 (SEQ ID NOs: 1727 and 1765), or a modified or unmodified variant thereof.

[001762] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35581.4 (SEQ ID NOs: 1728 and 1766), or a modified or unmodified variant thereof.

[001763] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39845.1 (SEQ ID NOs: 1729 and 1767), or a modified or unmodified variant thereof.

[001764] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39858.1 (SEQ ID NOs: 1730 and 1768), or a modified or unmodified variant thereof.

[001765] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39870.1 (SEQ ID NOs: 1731 and 1769), or a modified or unmodified variant thereof.

[001766] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35576.4 (SEQ ID NOs: 1732 and 1770), or a modified or unmodified variant thereof.

[001767] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35588.4 (SEQ ID NOs: 1733 and 1771), or a modified or unmodified variant thereof.

[001768] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35600.1 (SEQ ID NOs: 1734 and 1772), or a modified or unmodified variant thereof.

[001769] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-35606.1 (SEQ ID NOs: 1735 and 1773), or a modified or unmodified variant thereof.

[001770] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38151.1 (SEQ ID NOs: 1736 and 1774), or a modified or unmodified variant thereof.

[001771] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38163.1 (SEQ ID NOs: 1737 and 1775), or a modified or unmodified variant thereof.

[001772] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-39999.1 (SEQ ID NOs: 1738 and 1776), or a modified or unmodified variant thereof.

[001773] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38159.1 or hs_KRAS_ 528_A22S26 (SEQ ID NOs: 1739 and 1777), or a modified or unmodified variant thereof.

[001774] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38130.1 or hs_KRAS_ 531_A22S26 (SEQ ID NOs: 1740 and 1778), or a modified or unmodified variant thereof.

[001775] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38136.1 (SEQ ID NOs: 1741 and 1779), or a modified or unmodified variant thereof.

[001776] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40036.1 (SEQ ID NOs: 1742 and 1780), or a modified or unmodified variant thereof.

[001777] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40008.1 (SEQ ID NOs: 1743 and 1781), or a modified or unmodified variant thereof.

[001778] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40021.1 (SEQ ID NOs: 1744 and 1782), or a modified or unmodified variant thereof.

[001779] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40077.1 (SEQ ID NOs: 1745 and 1783), or a modified or unmodified variant thereof.

[001780] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40072.1 (SEQ ID NOs: 1746 and 1784), or a modified or unmodified variant thereof.

[001781] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40061.1 (SEQ ID NOs: 1747 and 1785), or a modified or unmodified variant thereof.

[001782] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-40068.1 (SEQ ID NOs: 1748 and 1786), or a modified or unmodified variant thereof.

[001783] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38131.1 (SEQ ID NOs: 1749 and 1787), or a modified or unmodified variant thereof.

[001784] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: AD-38167.1 (SEQ ID NOs: 1750 and 1788), or a modified or unmodified variant thereof.

[001785] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1751 and 1789), or a modified or unmodified variant thereof.

[001786] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1752 and 1790), or a modified or unmodified variant thereof.

[001787] A RNAi agent comprising a first and a second strand, wherein the sequence of the first strand is the sequence of a first strand of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1753 and 1791), or a modified or unmodified variant thereof.

[001788]

[001789] Specific embodiments comprising the first and/or second strands of a RNAi agent disclosed herein

[001790] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[001791] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[001792] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35523.3 (SEQ ID NOs: 1 and 428), or a modified or unmodified variant thereof.

[001793] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35529.1 (SEQ ID NOs: 2 and 429), or a modified or unmodified variant thereof.

[001794] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35535.4 (SEQ ID NOs: 3 and 430), or a modified or unmodified variant thereof.

[001795] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 4 and 431), or a modified or unmodified variant thereof.

[001796] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35547.4 (SEQ ID NOs: 5 and 432), or a modified or unmodified variant thereof.

[001797] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35553.4 (SEQ ID NOs: 6 and 433), or a modified or unmodified variant thereof.

[001798] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35559.4 (SEQ ID NOs: 7 and 434), or a modified or unmodified variant thereof.

[001799] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35565.4 (SEQ ID NOs: 8 and 435), or a modified or unmodified variant thereof.

[001800] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35524.4 (SEQ ID NOs: 9 and 436), or a modified or unmodified variant thereof.

[001801] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-35530.4 (SEQ ID NOs: 10 and 437), or a modified or unmodified variant thereof.

[001802] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35536.4 (SEQ ID NOs: 11 and 438), or a modified or unmodified variant thereof.

[001803] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35542.4 (SEQ ID NOs: 12 and 439), or a modified or unmodified variant thereof.

[001804] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35548.4 (SEQ ID NOs: 13 and 440), or a modified or unmodified variant thereof.

[001805] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35554.4 (SEQ ID NOs: 14 and 441), or a modified or unmodified variant thereof.

[001806] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35560.2 (SEQ ID NOs: 15 and 442), or a modified or unmodified variant thereof.

[001807] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35566.4 (SEQ ID NOs: 16 and 443), or a modified or unmodified variant thereof.

[001808] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35525.2 (SEQ ID NOs: 17 and 444), or a modified or unmodified variant thereof.

[001809] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35531.4 (SEQ ID NOs: 18 and 445), or a modified or unmodified variant thereof.

[001810] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35537.4 (SEQ ID NOs: 19 and 446), or a modified or unmodified variant thereof.

[001811] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35543.2 (SEQ ID NOs: 20 and 447), or a modified or unmodified variant thereof.

[001812] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35549.4 (SEQ ID NOs: 21 and 448), or a modified or unmodified variant thereof.

[001813] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35555.4 (SEQ ID NOs: 22 and 449), or a modified or unmodified variant thereof.

[001814] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35561.4 (SEQ ID NOs: 23 and 450), or a modified or unmodified variant thereof.

[001815] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35567.4 (SEQ ID NOs: 24 and 451), or a modified or unmodified variant thereof.

[001816] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35526.4 (SEQ ID NOs: 25 and 452), or a modified or unmodified variant thereof.

[001817] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35532.4 (SEQ ID NOs: 26 and 453), or a modified or unmodified variant thereof.

[001818] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35538.4 (SEQ ID NOs: 27 and 454), or a modified or unmodified variant thereof.

[001819] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35544.4 (SEQ ID NOs: 28 and 455), or a modified or unmodified variant thereof.

[001820] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35550.4 (SEQ ID NOs: 29 and 456), or a modified or unmodified variant thereof.

[001821] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35556.4 (SEQ ID NOs: 30 and 457), or a modified or unmodified variant thereof.

[001822] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35562.4 (SEQ ID NOs: 31 and 458), or a modified or unmodified variant thereof.

[001823] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35568.4 (SEQ ID NOs: 32 and 459), or a modified or unmodified variant thereof.

[001824] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35527.4 (SEQ ID NOs: 33 and 460), or a modified or unmodified variant thereof.

[001825] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35533.4 (SEQ ID NOs: 34 and 461), or a modified or unmodified variant thereof.

[001826] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35539.4 (SEQ ID NOs: 35 and 462), or a modified or unmodified variant thereof.

[001827] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35545.4 (SEQ ID NOs: 36 and 463), or a modified or unmodified variant thereof.

[001828] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35551.4 (SEQ

ID NOs: 37 and 464), or a modified or unmodified variant thereof.

[001829] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35563.4 (SEQ ID NOs: 38 and 465), or a modified or unmodified variant thereof.

[001830] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35528.4 (SEQ ID NOs: 39 and 466), or a modified or unmodified variant thereof.

[001831] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35540.4 (SEQ ID NOs: 40 and 467), or a modified or unmodified variant thereof.

[001832] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35546.4 (SEQ ID NOs: 41 and 468), or a modified or unmodified variant thereof.

[001833] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35552.4 (SEQ ID NOs: 42 and 469), or a modified or unmodified variant thereof.

[001834] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35558.4 (SEQ ID NOs: 43 and 470), or a modified or unmodified variant thereof.

[001835] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35564.4 (SEQ ID NOs: 44 and 471), or a modified or unmodified variant thereof.

[001836] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35570.4 (SEQ ID NOs: 45 and 472), or a modified or unmodified variant thereof.

[001837] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35571.4 (SEQ ID NOs: 46 and 473), or a modified or unmodified variant thereof.

[001838] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35577.4 (SEQ ID NOs: 47 and 474), or a modified or unmodified variant thereof.

[001839] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35583.4 (SEQ ID NOs: 48 and 475), or a modified or unmodified variant thereof.

[001840] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35589.4 (SEQ ID NOs: 49 and 476), or a modified or unmodified variant thereof.

[001841] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35595.4 (SEQ ID NOs: 50 and 477), or a modified or unmodified variant thereof.

[001842] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-35601.4 (SEQ ID NOs: 51 and 478), or a modified or unmodified variant thereof.

[001843] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35607.4 (SEQ ID NOs: 52 and 479), or a modified or unmodified variant thereof.

[001844] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35613.4 (SEQ ID NOs: 53 and 480), or a modified or unmodified variant thereof.

[001845] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35572.4 (SEQ ID NOs: 54 and 481), or a modified or unmodified variant thereof.

[001846] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35578.4 (SEQ ID NOs: 55 and 482), or a modified or unmodified variant thereof.

[001847] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35584.4 (SEQ ID NOs: 56 and 483), or a modified or unmodified variant thereof.

[001848] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35590.4 (SEQ ID NOs: 57 and 484), or a modified or unmodified variant thereof.

[001849] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35596.4 (SEQ ID NOs: 58 and 485), or a modified or unmodified variant thereof.

[001850] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35602.4 (SEQ ID NOs: 59 and 486), or a modified or unmodified variant thereof.

[001851] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35608.4 (SEQ ID NOs: 60 and 487), or a modified or unmodified variant thereof.

[001852] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35614.4 (SEQ ID NOs: 61 and 488), or a modified or unmodified variant thereof.

[001853] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35573.4 (SEQ ID NOs: 62 and 489), or a modified or unmodified variant thereof.

[001854] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35579.4 (SEQ ID NOs: 63 and 490), or a modified or unmodified variant thereof.

[001855] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35585.4 (SEQ ID NOs: 64 and 491), or a modified or unmodified variant thereof.

[001856] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35591.4 (SEQ ID NOs: 65 and 492), or a modified or unmodified variant thereof.

[001857] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35597.4 (SEQ ID NOs: 66 and 493), or a modified or unmodified variant thereof.

[001858] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35603.4 (SEQ ID NOs: 67 and 494), or a modified or unmodified variant thereof.

[001859] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 68 and 495), or a modified or unmodified variant thereof.

[001860] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35615.4 (SEQ ID NOs: 69 and 496), or a modified or unmodified variant thereof.

[001861] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35574.4 (SEQ ID NOs: 70 and 497), or a modified or unmodified variant thereof.

[001862] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35580.1 (SEQ ID NOs: 71 and 498), or a modified or unmodified variant thereof.

[001863] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35586.4 (SEQ ID NOs: 72 and 499), or a modified or unmodified variant thereof.

[001864] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35592.4 (SEQ ID NOs: 73 and 500), or a modified or unmodified variant thereof.

[001865] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35598.4 (SEQ ID NOs: 74 and 501), or a modified or unmodified variant thereof.

[001866] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35604.4 (SEQ ID NOs: 75 and 502), or a modified or unmodified variant thereof.

[001867] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35610.4 (SEQ ID NOs: 76 and 503), or a modified or unmodified variant thereof.

[001868] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35616.4 (SEQ ID NOs: 77 and 504), or a modified or unmodified variant thereof.

[001869] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35575.4 (SEQ

ID NOs: 78 and 505), or a modified or unmodified variant thereof.

[001870] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 79 and 506), or a modified or unmodified variant thereof.

[001871] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35587.4 (SEQ ID NOs: 80 and 507), or a modified or unmodified variant thereof.

[001872] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35593.4 (SEQ ID NOs: 81 and 508), or a modified or unmodified variant thereof.

[001873] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35599.4 (SEQ ID NOs: 82 and 509), or a modified or unmodified variant thereof.

[001874] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35605.4 (SEQ ID NOs: 83 and 510), or a modified or unmodified variant thereof.

[001875] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35611.4 (SEQ ID NOs: 84 and 511), or a modified or unmodified variant thereof.

[001876] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35617.4 (SEQ ID NOs: 85 and 512), or a modified or unmodified variant thereof.

[001877] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 86 and 513), or a modified or unmodified variant thereof.

[001878] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 87 and 514), or a modified or unmodified variant thereof.

[001879] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35667.1 (SEQ ID NOs: 88 and 515), or a modified or unmodified variant thereof.

[001880] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35673.1 (SEQ ID NOs: 89 and 516), or a modified or unmodified variant thereof.

[001881] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35679.1 (SEQ ID NOs: 90 and 517), or a modified or unmodified variant thereof.

[001882] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35685.1 (SEQ ID NOs: 91 and 518), or a modified or unmodified variant thereof.

[001883] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-35691.1 (SEQ ID NOs: 92 and 519), or a modified or unmodified variant thereof.

[001884] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35557.1 (SEQ ID NOs: 93 and 520), or a modified or unmodified variant thereof.

[001885] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35618.1 (SEQ ID NOs: 94 and 521), or a modified or unmodified variant thereof.

[001886] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35569.1 (SEQ ID NOs: 95 and 522), or a modified or unmodified variant thereof.

[001887] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35534.1 (SEQ ID NOs: 96 and 523), or a modified or unmodified variant thereof.

[001888] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35582.1 (SEQ ID NOs: 97 and 524), or a modified or unmodified variant thereof.

[001889] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35594.1 (SEQ ID NOs: 98 and 525), or a modified or unmodified variant thereof.

[001890] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 99 and 526), or a modified or unmodified variant thereof.

[001891] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35606.1 (SEQ ID NOs: 100 and 527), or a modified or unmodified variant thereof.

[001892] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35612.1 (SEQ ID NOs: 101 and 528), or a modified or unmodified variant thereof.

[001893] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38127.1 (SEQ ID NOs: 102 and 529), or a modified or unmodified variant thereof.

[001894] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38133.1 (SEQ ID NOs: 103 and 530), or a modified or unmodified variant thereof.

[001895] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38139.1 (SEQ ID NOs: 104 and 531), or a modified or unmodified variant thereof.

[001896] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38145.1 (SEQ ID NOs: 105 and 532), or a modified or unmodified variant thereof.

[001897] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 106 and 533), or a modified or unmodified variant thereof.

[001898] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38157.1 (SEQ ID NOs: 107 and 534), or a modified or unmodified variant thereof.

[001899] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 108 and 535), or a modified or unmodified variant thereof.

[001900] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38169.1 (SEQ ID NOs: 109 and 536), or a modified or unmodified variant thereof.

[001901] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38128.1 (SEQ ID NOs: 110 and 537), or a modified or unmodified variant thereof.

[001902] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38134.1 (SEQ ID NOs: 111 and 538), or a modified or unmodified variant thereof.

[001903] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38140.1 (SEQ ID NOs: 112 and 539), or a modified or unmodified variant thereof.

[001904] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38146.1 (SEQ ID NOs: 113 and 540), or a modified or unmodified variant thereof.

[001905] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38152.1 (SEQ ID NOs: 114 and 541), or a modified or unmodified variant thereof.

[001906] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38158.1 (SEQ ID NOs: 115 and 542), or a modified or unmodified variant thereof.

[001907] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38164.1 (SEQ ID NOs: 116 and 543), or a modified or unmodified variant thereof.

[001908] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38170.1 (SEQ ID NOs: 117 and 544), or a modified or unmodified variant thereof.

[001909] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38129.1 (SEQ ID NOs: 118 and 545), or a modified or unmodified variant thereof.

[001910] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38135.1 (SEQ

ID NOs: 119 and 546), or a modified or unmodified variant thereof.

[001911] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38141.1 (SEQ ID NOs: 120 and 547), or a modified or unmodified variant thereof.

[001912] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38147.1 (SEQ ID NOs: 121 and 548), or a modified or unmodified variant thereof.

[001913] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38153.1 (SEQ ID NOs: 122 and 549), or a modified or unmodified variant thereof.

[001914] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38159.1 (SEQ ID NOs: 123 and 550), or a modified or unmodified variant thereof.

[001915] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38165.1 (SEQ ID NOs: 124 and 551), or a modified or unmodified variant thereof.

[001916] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38171.1 (SEQ ID NOs: 125 and 552), or a modified or unmodified variant thereof.

[001917] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38130.1 (SEQ ID NOs: 126 and 553), or a modified or unmodified variant thereof.

[001918] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 127 and 554), or a modified or unmodified variant thereof.

[001919] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38142.1 (SEQ ID NOs: 128 and 555), or a modified or unmodified variant thereof.

[001920] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38148.1 (SEQ ID NOs: 129 and 556), or a modified or unmodified variant thereof.

[001921] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38154.1 (SEQ ID NOs: 130 and 557), or a modified or unmodified variant thereof.

[001922] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38160.1 (SEQ ID NOs: 131 and 558), or a modified or unmodified variant thereof.

[001923] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38166.1 (SEQ ID NOs: 132 and 559), or a modified or unmodified variant thereof.

[001924] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-38172.1 (SEQ ID NOs: 133 and 560), or a modified or unmodified variant thereof.

[001925] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 134 and 561), or a modified or unmodified variant thereof.

[001926] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38137.1 (SEQ ID NOs: 135 and 562), or a modified or unmodified variant thereof.

[001927] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38143.1 (SEQ ID NOs: 136 and 563), or a modified or unmodified variant thereof.

[001928] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38149.1 (SEQ ID NOs: 137 and 564), or a modified or unmodified variant thereof.

[001929] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38155.1 (SEQ ID NOs: 138 and 565), or a modified or unmodified variant thereof.

[001930] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38161.1 (SEQ ID NOs: 139 and 566), or a modified or unmodified variant thereof.

[001931] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 140 and 567), or a modified or unmodified variant thereof.

[001932] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38173.1 (SEQ ID NOs: 141 and 568), or a modified or unmodified variant thereof.

[001933] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38132.1 (SEQ ID NOs: 142 and 569), or a modified or unmodified variant thereof.

[001934] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38138.1 (SEQ ID NOs: 143 and 570), or a modified or unmodified variant thereof.

[001935] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38144.1 (SEQ ID NOs: 144 and 571), or a modified or unmodified variant thereof.

[001936] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38150.1 (SEQ ID NOs: 145 and 572), or a modified or unmodified variant thereof.

[001937] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38156.1 (SEQ ID NOs: 146 and 573), or a modified or unmodified variant thereof.

[001938] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38162.1 (SEQ ID NOs: 147 and 574), or a modified or unmodified variant thereof.

[001939] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38168.1 (SEQ ID NOs: 148 and 575), or a modified or unmodified variant thereof.

[001940] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38174.1 (SEQ ID NOs: 149 and 576), or a modified or unmodified variant thereof.

[001941] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39683.1 (SEQ ID NOs: 150 and 577), or a modified or unmodified variant thereof.

[001942] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39689.1 (SEQ ID NOs: 151 and 578), or a modified or unmodified variant thereof.

[001943] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39695.1 (SEQ ID NOs: 152 and 579), or a modified or unmodified variant thereof.

[001944] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39701.1 (SEQ ID NOs: 153 and 580), or a modified or unmodified variant thereof.

[001945] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39707.1 (SEQ ID NOs: 154 and 581), or a modified or unmodified variant thereof.

[001946] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39713.1 (SEQ ID NOs: 155 and 582), or a modified or unmodified variant thereof.

[001947] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39719.1 (SEQ ID NOs: 156 and 583), or a modified or unmodified variant thereof.

[001948] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39725.1 (SEQ ID NOs: 157 and 584), or a modified or unmodified variant thereof.

[001949] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39684.1 (SEQ ID NOs: 158 and 585), or a modified or unmodified variant thereof.

[001950] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39690.1 (SEQ ID NOs: 159 and 586), or a modified or unmodified variant thereof.

[001951] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39696.1 (SEQ

ID NOs: 160 and 587), or a modified or unmodified variant thereof.

[001952] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39702.1 (SEQ ID NOs: 161 and 588), or a modified or unmodified variant thereof.

[001953] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39708.1 (SEQ ID NOs: 162 and 589), or a modified or unmodified variant thereof.

[001954] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39714.1 (SEQ ID NOs: 163 and 590), or a modified or unmodified variant thereof.

[001955] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39720.1 (SEQ ID NOs: 164 and 591), or a modified or unmodified variant thereof.

[001956] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39726.1 (SEQ ID NOs: 165 and 592), or a modified or unmodified variant thereof.

[001957] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39685.1 (SEQ ID NOs: 166 and 593), or a modified or unmodified variant thereof.

[001958] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39691.1 (SEQ ID NOs: 167 and 594), or a modified or unmodified variant thereof.

[001959] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39697.1 (SEQ ID NOs: 168 and 595), or a modified or unmodified variant thereof.

[001960] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39703.1 (SEQ ID NOs: 169 and 596), or a modified or unmodified variant thereof.

[001961] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39709.1 (SEQ ID NOs: 170 and 597), or a modified or unmodified variant thereof.

[001962] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39715.1 (SEQ ID NOs: 171 and 598), or a modified or unmodified variant thereof.

[001963] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39721.1 (SEQ ID NOs: 172 and 599), or a modified or unmodified variant thereof.

[001964] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39727.1 (SEQ ID NOs: 173 and 600), or a modified or unmodified variant thereof.

[001965] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-39686.1 (SEQ ID NOs: 174 and 601), or a modified or unmodified variant thereof.

[001966] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39692.1 (SEQ ID NOs: 175 and 602), or a modified or unmodified variant thereof.

[001967] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39698.1 (SEQ ID NOs: 176 and 603), or a modified or unmodified variant thereof.

[001968] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39704.1 (SEQ ID NOs: 177 and 604), or a modified or unmodified variant thereof.

[001969] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39710.1 (SEQ ID NOs: 178 and 605), or a modified or unmodified variant thereof.

[001970] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39716.1 (SEQ ID NOs: 179 and 606), or a modified or unmodified variant thereof.

[001971] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39722.1 (SEQ ID NOs: 180 and 607), or a modified or unmodified variant thereof.

[001972] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39728.1 (SEQ ID NOs: 181 and 608), or a modified or unmodified variant thereof.

[001973] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39687.1 (SEQ ID NOs: 182 and 609), or a modified or unmodified variant thereof.

[001974] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39693.1 (SEQ ID NOs: 183 and 610), or a modified or unmodified variant thereof.

[001975] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39699.1 (SEQ ID NOs: 184 and 611), or a modified or unmodified variant thereof.

[001976] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39705.1 (SEQ ID NOs: 185 and 612), or a modified or unmodified variant thereof.

[001977] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39711.1 (SEQ ID NOs: 186 and 613), or a modified or unmodified variant thereof.

[001978] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39717.1 (SEQ ID NOs: 187 and 614), or a modified or unmodified variant thereof.

[001979] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39723.1 (SEQ ID NOs: 188 and 615), or a modified or unmodified variant thereof.

[001980] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39729.1 (SEQ ID NOs: 189 and 616), or a modified or unmodified variant thereof.

[001981] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39688.1 (SEQ ID NOs: 190 and 617), or a modified or unmodified variant thereof.

[001982] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39694.1 (SEQ ID NOs: 191 and 618), or a modified or unmodified variant thereof.

[001983] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39700.1 (SEQ ID NOs: 192 and 619), or a modified or unmodified variant thereof.

[001984] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 193 and 620), or a modified or unmodified variant thereof.

[001985] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 194 and 621), or a modified or unmodified variant thereof.

[001986] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39718.1 (SEQ ID NOs: 195 and 622), or a modified or unmodified variant thereof.

[001987] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39724.1 (SEQ ID NOs: 196 and 623), or a modified or unmodified variant thereof.

[001988] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39730.1 (SEQ ID NOs: 197 and 624), or a modified or unmodified variant thereof.

[001989] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39736.1 (SEQ ID NOs: 198 and 625), or a modified or unmodified variant thereof.

[001990] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39742.1 (SEQ ID NOs: 199 and 626), or a modified or unmodified variant thereof.

[001991] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39748.1 (SEQ ID NOs: 200 and 627), or a modified or unmodified variant thereof.

[001992] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39754.1 (SEQ

ID NOs: 201 and 628), or a modified or unmodified variant thereof.

[001993] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 202 and 629), or a modified or unmodified variant thereof.

[001994] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39766.1 (SEQ ID NOs: 203 and 630), or a modified or unmodified variant thereof.

[001995] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39772.1 (SEQ ID NOs: 204 and 631), or a modified or unmodified variant thereof.

[001996] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39731.1 (SEQ ID NOs: 205 and 632), or a modified or unmodified variant thereof.

[001997] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39737.1 (SEQ ID NOs: 206 and 633), or a modified or unmodified variant thereof.

[001998] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39743.1 (SEQ ID NOs: 207 and 634), or a modified or unmodified variant thereof.

[001999] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39749.1 (SEQ ID NOs: 208 and 635), or a modified or unmodified variant thereof.

[002000] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39755.1 (SEQ ID NOs: 209 and 636), or a modified or unmodified variant thereof.

[002001] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39761.1 (SEQ ID NOs: 210 and 637), or a modified or unmodified variant thereof.

[002002] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39767.1 (SEQ ID NOs: 211 and 638), or a modified or unmodified variant thereof.

[002003] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39773.1 (SEQ ID NOs: 212 and 639), or a modified or unmodified variant thereof.

[002004] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39732.1 (SEQ ID NOs: 213 and 640), or a modified or unmodified variant thereof.

[002005] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39738.1 (SEQ ID NOs: 214 and 641), or a modified or unmodified variant thereof.

[002006] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-39744.1 (SEQ ID NOs: 215 and 642), or a modified or unmodified variant thereof.

[002007] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39750.1 (SEQ ID NOs: 216 and 643), or a modified or unmodified variant thereof.

[002008] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39756.1 (SEQ ID NOs: 217 and 644), or a modified or unmodified variant thereof.

[002009] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39762.1 (SEQ ID NOs: 218 and 645), or a modified or unmodified variant thereof.

[002010] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39768.1 (SEQ ID NOs: 219 and 646), or a modified or unmodified variant thereof.

[002011] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39774.1 (SEQ ID NOs: 220 and 647), or a modified or unmodified variant thereof.

[002012] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39733.1 (SEQ ID NOs: 221 and 648), or a modified or unmodified variant thereof.

[002013] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39739.1 (SEQ ID NOs: 222 and 649), or a modified or unmodified variant thereof.

[002014] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39745.1 (SEQ ID NOs: 223 and 650), or a modified or unmodified variant thereof.

[002015] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39751.1 (SEQ ID NOs: 224 and 651), or a modified or unmodified variant thereof.

[002016] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39757.1 (SEQ ID NOs: 225 and 652), or a modified or unmodified variant thereof.

[002017] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39763.1 (SEQ ID NOs: 226 and 653), or a modified or unmodified variant thereof.

[002018] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39769.1 (SEQ ID NOs: 227 and 654), or a modified or unmodified variant thereof.

[002019] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39775.1 (SEQ ID NOs: 228 and 655), or a modified or unmodified variant thereof.

[002020] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39734.1 (SEQ ID NOs: 229 and 656), or a modified or unmodified variant thereof.

[002021] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39740.1 (SEQ ID NOs: 230 and 657), or a modified or unmodified variant thereof.

[002022] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39746.1 (SEQ ID NOs: 231 and 658), or a modified or unmodified variant thereof.

[002023] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39752.1 (SEQ ID NOs: 232 and 659), or a modified or unmodified variant thereof.

[002024] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39758.1 (SEQ ID NOs: 233 and 660), or a modified or unmodified variant thereof.

[002025] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39764.1 (SEQ ID NOs: 234 and 661), or a modified or unmodified variant thereof.

[002026] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39770.1 (SEQ ID NOs: 235 and 662), or a modified or unmodified variant thereof.

[002027] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39776.1 (SEQ ID NOs: 236 and 663), or a modified or unmodified variant thereof.

[002028] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39735.1 (SEQ ID NOs: 237 and 664), or a modified or unmodified variant thereof.

[002029] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39741.1 (SEQ ID NOs: 238 and 665), or a modified or unmodified variant thereof.

[002030] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39747.1 (SEQ ID NOs: 239 and 666), or a modified or unmodified variant thereof.

[002031] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39753.1 (SEQ ID NOs: 240 and 667), or a modified or unmodified variant thereof.

[002032] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39759.1 (SEQ ID NOs: 241 and 668), or a modified or unmodified variant thereof.

[002033] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39765.1 (SEQ

ID NOs: 242 and 669), or a modified or unmodified variant thereof.

[002034] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39771.1 (SEQ ID NOs: 243 and 670), or a modified or unmodified variant thereof.

[002035] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 244 and 671), or a modified or unmodified variant thereof.

[002036] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39784.1 (SEQ ID NOs: 245 and 672), or a modified or unmodified variant thereof.

[002037] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39790.1 (SEQ ID NOs: 246 and 673), or a modified or unmodified variant thereof.

[002038] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39796.1 (SEQ ID NOs: 247 and 674), or a modified or unmodified variant thereof.

[002039] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39802.1 (SEQ ID NOs: 248 and 675), or a modified or unmodified variant thereof.

[002040] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39808.1 (SEQ ID NOs: 249 and 676), or a modified or unmodified variant thereof.

[002041] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39814.1 (SEQ ID NOs: 250 and 677), or a modified or unmodified variant thereof.

[002042] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39820.1 (SEQ ID NOs: 251 and 678), or a modified or unmodified variant thereof.

[002043] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39779.1 (SEQ ID NOs: 252 and 679), or a modified or unmodified variant thereof.

[002044] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39785.1 (SEQ ID NOs: 253 and 680), or a modified or unmodified variant thereof.

[002045] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39791.1 (SEQ ID NOs: 254 and 681), or a modified or unmodified variant thereof.

[002046] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39797.1 (SEQ ID NOs: 255 and 682), or a modified or unmodified variant thereof.

[002047] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-39803.1 (SEQ ID NOs: 256 and 683), or a modified or unmodified variant thereof.

[002048] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39809.1 (SEQ ID NOs: 257 and 684), or a modified or unmodified variant thereof.

[002049] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39815.1 (SEQ ID NOs: 258 and 685), or a modified or unmodified variant thereof.

[002050] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39821.1 (SEQ ID NOs: 259 and 686), or a modified or unmodified variant thereof.

[002051] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39780.1 (SEQ ID NOs: 260 and 687), or a modified or unmodified variant thereof.

[002052] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39786.1 (SEQ ID NOs: 261 and 688), or a modified or unmodified variant thereof.

[002053] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39792.1 (SEQ ID NOs: 262 and 689), or a modified or unmodified variant thereof.

[002054] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39798.1 (SEQ ID NOs: 263 and 690), or a modified or unmodified variant thereof.

[002055] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39804.1 (SEQ ID NOs: 264 and 691), or a modified or unmodified variant thereof.

[002056] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39810.1 (SEQ ID NOs: 265 and 692), or a modified or unmodified variant thereof.

[002057] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39816.1 (SEQ ID NOs: 266 and 693), or a modified or unmodified variant thereof.

[002058] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 267 and 694), or a modified or unmodified variant thereof.

[002059] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39781.1 (SEQ ID NOs: 268 and 695), or a modified or unmodified variant thereof.

[002060] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39787.1 (SEQ ID NOs: 269 and 696), or a modified or unmodified variant thereof.

[002061] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39793.1 (SEQ ID NOs: 270 and 697), or a modified or unmodified variant thereof.

[002062] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39799.1 (SEQ ID NOs: 271 and 698), or a modified or unmodified variant thereof.

[002063] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39805.1 (SEQ ID NOs: 272 and 699), or a modified or unmodified variant thereof.

[002064] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39811.1 (SEQ ID NOs: 273 and 700), or a modified or unmodified variant thereof.

[002065] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39817.1 (SEQ ID NOs: 274 and 701), or a modified or unmodified variant thereof.

[002066] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39823.1 (SEQ ID NOs: 275 and 702), or a modified or unmodified variant thereof.

[002067] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39782.1 (SEQ ID NOs: 276 and 703), or a modified or unmodified variant thereof.

[002068] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39788.1 (SEQ ID NOs: 277 and 704), or a modified or unmodified variant thereof.

[002069] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39794.1 (SEQ ID NOs: 278 and 705), or a modified or unmodified variant thereof.

[002070] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39800.1 (SEQ ID NOs: 279 and 706), or a modified or unmodified variant thereof.

[002071] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39806.1 (SEQ ID NOs: 280 and 707), or a modified or unmodified variant thereof.

[002072] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39812.1 (SEQ ID NOs: 281 and 708), or a modified or unmodified variant thereof.

[002073] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39818.1 (SEQ ID NOs: 282 and 709), or a modified or unmodified variant thereof.

[002074] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39824.1 (SEQ

ID NOs: 283 and 710), or a modified or unmodified variant thereof.

[002075] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39783.1 (SEQ ID NOs: 284 and 711), or a modified or unmodified variant thereof.

[002076] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39789.1 (SEQ ID NOs: 285 and 712), or a modified or unmodified variant thereof.

[002077] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39795.1 (SEQ ID NOs: 286 and 713), or a modified or unmodified variant thereof.

[002078] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39801.1 (SEQ ID NOs: 287 and 714), or a modified or unmodified variant thereof.

[002079] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39807.1 (SEQ ID NOs: 288 and 715), or a modified or unmodified variant thereof.

[002080] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39813.1 (SEQ ID NOs: 289 and 716), or a modified or unmodified variant thereof.

[002081] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39819.1 (SEQ ID NOs: 290 and 717), or a modified or unmodified variant thereof.

[002082] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39825.1 (SEQ ID NOs: 291 and 718), or a modified or unmodified variant thereof.

[002083] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39831.1 (SEQ ID NOs: 292 and 719), or a modified or unmodified variant thereof.

[002084] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39837.1 (SEQ ID NOs: 293 and 720), or a modified or unmodified variant thereof.

[002085] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39843.1 (SEQ ID NOs: 294 and 721), or a modified or unmodified variant thereof.

[002086] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39849.1 (SEQ ID NOs: 295 and 722), or a modified or unmodified variant thereof.

[002087] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39855.1 (SEQ ID NOs: 296 and 723), or a modified or unmodified variant thereof.

[002088] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-39861.1 (SEQ ID NOs: 297 and 724), or a modified or unmodified variant thereof.

[002089] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39867.1 (SEQ ID NOs: 298 and 725), or a modified or unmodified variant thereof.

[002090] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39826.1 (SEQ ID NOs: 299 and 726), or a modified or unmodified variant thereof.

[002091] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39832.1 (SEQ ID NOs: 300 and 727), or a modified or unmodified variant thereof.

[002092] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39838.1 (SEQ ID NOs: 301 and 728), or a modified or unmodified variant thereof.

[002093] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39844.1 (SEQ ID NOs: 302 and 729), or a modified or unmodified variant thereof.

[002094] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39850.1 (SEQ ID NOs: 303 and 730), or a modified or unmodified variant thereof.

[002095] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39856.1 (SEQ ID NOs: 304 and 731), or a modified or unmodified variant thereof.

[002096] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39862.1 (SEQ ID NOs: 305 and 732), or a modified or unmodified variant thereof.

[002097] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39868.1 (SEQ ID NOs: 306 and 733), or a modified or unmodified variant thereof.

[002098] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39827.1 (SEQ ID NOs: 307 and 734), or a modified or unmodified variant thereof.

[002099] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39833.1 (SEQ ID NOs: 308 and 735), or a modified or unmodified variant thereof.

[002100] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39839.1 (SEQ ID NOs: 309 and 736), or a modified or unmodified variant thereof.

[002101] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 310 and 737), or a modified or unmodified variant thereof.

[002102] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39851.1 (SEQ ID NOs: 311 and 738), or a modified or unmodified variant thereof.

[002103] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39857.1 (SEQ ID NOs: 312 and 739), or a modified or unmodified variant thereof.

[002104] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39863.1 (SEQ ID NOs: 313 and 740), or a modified or unmodified variant thereof.

[002105] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39869.1 (SEQ ID NOs: 314 and 741), or a modified or unmodified variant thereof.

[002106] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39828.1 (SEQ ID NOs: 315 and 742), or a modified or unmodified variant thereof.

[002107] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39834.1 (SEQ ID NOs: 316 and 743), or a modified or unmodified variant thereof.

[002108] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39840.1 (SEQ ID NOs: 317 and 744), or a modified or unmodified variant thereof.

[002109] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39846.1 (SEQ ID NOs: 318 and 745), or a modified or unmodified variant thereof.

[002110] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39852.1 (SEQ ID NOs: 319 and 746), or a modified or unmodified variant thereof.

[002111] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 320 and 747), or a modified or unmodified variant thereof.

[002112] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39864.1 (SEQ ID NOs: 321 and 748), or a modified or unmodified variant thereof.

[002113] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 322 and 749), or a modified or unmodified variant thereof.

[002114] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39829.1 (SEQ ID NOs: 323 and 750), or a modified or unmodified variant thereof.

[002115] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39835.1 (SEQ

ID NOs: 324 and 751), or a modified or unmodified variant thereof.

[002116] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39841.1 (SEQ ID NOs: 325 and 752), or a modified or unmodified variant thereof.

[002117] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39853.1 (SEQ ID NOs: 326 and 753), or a modified or unmodified variant thereof.

[002118] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39859.1 (SEQ ID NOs: 327 and 754), or a modified or unmodified variant thereof.

[002119] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39865.1 (SEQ ID NOs: 328 and 755), or a modified or unmodified variant thereof.

[002120] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39871.1 (SEQ ID NOs: 329 and 756), or a modified or unmodified variant thereof.

[002121] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39830.1 (SEQ ID NOs: 330 and 757), or a modified or unmodified variant thereof.

[002122] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39836.1 (SEQ ID NOs: 331 and 758), or a modified or unmodified variant thereof.

[002123] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39842.1 (SEQ ID NOs: 332 and 759), or a modified or unmodified variant thereof.

[002124] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39848.1 (SEQ ID NOs: 333 and 760), or a modified or unmodified variant thereof.

[002125] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39854.1 (SEQ ID NOs: 334 and 761), or a modified or unmodified variant thereof.

[002126] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39860.1 (SEQ ID NOs: 335 and 762), or a modified or unmodified variant thereof.

[002127] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39866.1 (SEQ ID NOs: 336 and 763), or a modified or unmodified variant thereof.

[002128] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39992.1 (SEQ ID NOs: 337 and 764), or a modified or unmodified variant thereof.

[002129] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-39998.1 (SEQ ID NOs: 338 and 765), or a modified or unmodified variant thereof.

[002130] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40004.1 (SEQ ID NOs: 339 and 766), or a modified or unmodified variant thereof.

[002131] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40010.1 (SEQ ID NOs: 340 and 767), or a modified or unmodified variant thereof.

[002132] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40016.1 (SEQ ID NOs: 341 and 768), or a modified or unmodified variant thereof.

[002133] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40022.1 (SEQ ID NOs: 342 and 769), or a modified or unmodified variant thereof.

[002134] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40028.1 (SEQ ID NOs: 343 and 770), or a modified or unmodified variant thereof.

[002135] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40034.1 (SEQ ID NOs: 344 and 771), or a modified or unmodified variant thereof.

[002136] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 345 and 772), or a modified or unmodified variant thereof.

[002137] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40005.1 (SEQ ID NOs: 346 and 773), or a modified or unmodified variant thereof.

[002138] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40011.1 (SEQ ID NOs: 347 and 774), or a modified or unmodified variant thereof.

[002139] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40017.1 (SEQ ID NOs: 348 and 775), or a modified or unmodified variant thereof.

[002140] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40029.1 (SEQ ID NOs: 349 and 776), or a modified or unmodified variant thereof.

[002141] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40035.1 (SEQ ID NOs: 350 and 777), or a modified or unmodified variant thereof.

[002142] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39994.1 (SEQ ID NOs: 351 and 778), or a modified or unmodified variant thereof.

[002143] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40000.1 (SEQ ID NOs: 352 and 779), or a modified or unmodified variant thereof.

[002144] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40006.1 (SEQ ID NOs: 353 and 780), or a modified or unmodified variant thereof.

[002145] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40012.1 (SEQ ID NOs: 354 and 781), or a modified or unmodified variant thereof.

[002146] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40018.1 (SEQ ID NOs: 355 and 782), or a modified or unmodified variant thereof.

[002147] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40024.1 (SEQ ID NOs: 356 and 783), or a modified or unmodified variant thereof.

[002148] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40030.1 (SEQ ID NOs: 357 and 784), or a modified or unmodified variant thereof.

[002149] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 358 and 785), or a modified or unmodified variant thereof.

[002150] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39995.1 (SEQ ID NOs: 359 and 786), or a modified or unmodified variant thereof.

[002151] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40001.1 (SEQ ID NOs: 360 and 787), or a modified or unmodified variant thereof.

[002152] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40007.1 (SEQ ID NOs: 361 and 788), or a modified or unmodified variant thereof.

[002153] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40013.1 (SEQ ID NOs: 362 and 789), or a modified or unmodified variant thereof.

[002154] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40019.1 (SEQ ID NOs: 363 and 790), or a modified or unmodified variant thereof.

[002155] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40025.1 (SEQ ID NOs: 364 and 791), or a modified or unmodified variant thereof.

[002156] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40031.1 (SEQ

ID NOs: 365 and 792), or a modified or unmodified variant thereof.

[002157] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40037.1 (SEQ ID NOs: 366 and 793), or a modified or unmodified variant thereof.

[002158] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39996.1 (SEQ ID NOs: 367 and 794), or a modified or unmodified variant thereof.

[002159] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40002.1 (SEQ ID NOs: 368 and 795), or a modified or unmodified variant thereof.

[002160] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 369 and 796), or a modified or unmodified variant thereof.

[002161] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40014.1 (SEQ ID NOs: 370 and 797), or a modified or unmodified variant thereof.

[002162] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40020.1 (SEQ ID NOs: 371 and 798), or a modified or unmodified variant thereof.

[002163] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40026.1 (SEQ ID NOs: 372 and 799), or a modified or unmodified variant thereof.

[002164] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40032.1 (SEQ ID NOs: 373 and 800), or a modified or unmodified variant thereof.

[002165] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40038.1 (SEQ ID NOs: 374 and 801), or a modified or unmodified variant thereof.

[002166] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39997.1 (SEQ ID NOs: 375 and 802), or a modified or unmodified variant thereof.

[002167] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40009.1 (SEQ ID NOs: 376 and 803), or a modified or unmodified variant thereof.

[002168] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40015.1 (SEQ ID NOs: 377 and 804), or a modified or unmodified variant thereof.

[002169] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 378 and 805), or a modified or unmodified variant thereof.

[002170] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-40027.1 (SEQ ID NOs: 379 and 806), or a modified or unmodified variant thereof.

[002171] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40033.1 (SEQ ID NOs: 380 and 807), or a modified or unmodified variant thereof.

[002172] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40039.1 (SEQ ID NOs: 381 and 808), or a modified or unmodified variant thereof.

[002173] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40045.1 (SEQ ID NOs: 382 and 809), or a modified or unmodified variant thereof.

[002174] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40051.1 (SEQ ID NOs: 383 and 810), or a modified or unmodified variant thereof.

[002175] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40057.1 (SEQ ID NOs: 384 and 811), or a modified or unmodified variant thereof.

[002176] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40063.1 (SEQ ID NOs: 385 and 812), or a modified or unmodified variant thereof.

[002177] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40069.1 (SEQ ID NOs: 386 and 813), or a modified or unmodified variant thereof.

[002178] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40075.1 (SEQ ID NOs: 387 and 814), or a modified or unmodified variant thereof.

[002179] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40081.1 (SEQ ID NOs: 388 and 815), or a modified or unmodified variant thereof.

[002180] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40040.1 (SEQ ID NOs: 389 and 816), or a modified or unmodified variant thereof.

[002181] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40046.1 (SEQ ID NOs: 390 and 817), or a modified or unmodified variant thereof.

[002182] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40052.1 (SEQ ID NOs: 391 and 818), or a modified or unmodified variant thereof.

[002183] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40058.1 (SEQ ID NOs: 392 and 819), or a modified or unmodified variant thereof.

[002184] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40064.1 (SEQ ID NOs: 393 and 820), or a modified or unmodified variant thereof.

[002185] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40070.1 (SEQ ID NOs: 394 and 821), or a modified or unmodified variant thereof.

[002186] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40076.1 (SEQ ID NOs: 395 and 822), or a modified or unmodified variant thereof.

[002187] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40082.1 (SEQ ID NOs: 396 and 823), or a modified or unmodified variant thereof.

[002188] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40041.1 (SEQ ID NOs: 397 and 824), or a modified or unmodified variant thereof.

[002189] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40047.1 (SEQ ID NOs: 398 and 825), or a modified or unmodified variant thereof.

[002190] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40053.1 (SEQ ID NOs: 399 and 826), or a modified or unmodified variant thereof.

[002191] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40059.1 (SEQ ID NOs: 400 and 827), or a modified or unmodified variant thereof.

[002192] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40065.1 (SEQ ID NOs: 401 and 828), or a modified or unmodified variant thereof.

[002193] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40071.1 (SEQ ID NOs: 402 and 829), or a modified or unmodified variant thereof.

[002194] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40077.1 (SEQ ID NOs: 403 and 830), or a modified or unmodified variant thereof.

[002195] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40083.1 (SEQ ID NOs: 404 and 831), or a modified or unmodified variant thereof.

[002196] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40042.1 (SEQ ID NOs: 405 and 832), or a modified or unmodified variant thereof.

[002197] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40048.1 (SEQ

ID NOs: 406 and 833), or a modified or unmodified variant thereof.

[002198] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40054.1 (SEQ ID NOs: 407 and 834), or a modified or unmodified variant thereof.

[002199] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40060.1 (SEQ ID NOs: 408 and 835), or a modified or unmodified variant thereof.

[002200] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40066.1 (SEQ ID NOs: 409 and 836), or a modified or unmodified variant thereof.

[002201] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 410 and 837), or a modified or unmodified variant thereof.

[002202] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40078.1 (SEQ ID NOs: 411 and 838), or a modified or unmodified variant thereof.

[002203] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40084.1 (SEQ ID NOs: 412 and 839), or a modified or unmodified variant thereof.

[002204] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40043.1 (SEQ ID NOs: 413 and 840), or a modified or unmodified variant thereof.

[002205] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40049.1 (SEQ ID NOs: 414 and 841), or a modified or unmodified variant thereof.

[002206] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40055.1 (SEQ ID NOs: 415 and 842), or a modified or unmodified variant thereof.

[002207] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 416 and 843), or a modified or unmodified variant thereof.

[002208] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40067.1 (SEQ ID NOs: 417 and 844), or a modified or unmodified variant thereof.

[002209] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40073.1 (SEQ ID NOs: 418 and 845), or a modified or unmodified variant thereof.

[002210] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40079.1 (SEQ ID NOs: 419 and 846), or a modified or unmodified variant thereof.

[002211] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands comprise the sequences of a first and/or second strand of: AD-40085.1 (SEQ ID NOs: 420 and 847), or a modified or unmodified variant thereof.

[002212] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40044.1 (SEQ ID NOs: 421 and 848), or a modified or unmodified variant thereof.

[002213] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40050.1 (SEQ ID NOs: 422 and 849), or a modified or unmodified variant thereof.

[002214] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40056.1 (SEQ ID NOs: 423 and 850), or a modified or unmodified variant thereof.

[002215] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40062.1 (SEQ ID NOs: 424 and 851), or a modified or unmodified variant thereof.

[002216] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 425 and 852), or a modified or unmodified variant thereof.

[002217] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40074.1 (SEQ ID NOs: 426 and 853), or a modified or unmodified variant thereof.

[002218] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40080.1 (SEQ ID NOs: 427 and 854), or a modified or unmodified variant thereof.

[002219] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39720.1 (SEQ ID NOs: 1716 and 1754), or a modified or unmodified variant thereof.

[002220] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 1717 and 1755), or a modified or unmodified variant thereof.

[002221] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 1718 and 1756), or a modified or unmodified variant thereof.

[002222] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 1719 and 1757), or a modified or unmodified variant thereof.

[002223] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39732.1 (SEQ ID NOs: 1720 and 1758), or a modified or unmodified variant thereof.

[002224] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 1721 and 1759), or a modified or unmodified variant thereof.

[002225] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NOs: 1722 and 1760), or a modified or unmodified variant thereof.

[002226] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39741.1, or modified or unmodified variants thereof.

[002227] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1723 and 1761), or a modified or unmodified variant thereof.

[002228] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 1724 and 1762), or a modified or unmodified variant thereof.

[002229] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39790.1 (SEQ ID NOs: 1725 and 1763), or a modified or unmodified variant thereof.

[002230] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 1726 and 1764), or a modified or unmodified variant thereof.

[002231] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 1727 and 1765), or a modified or unmodified variant thereof.

[002232] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 1728 and 1766), or a modified or unmodified variant thereof.

[002233] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 1729 and 1767), or a modified or unmodified variant thereof.

[002234] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 1730 and 1768), or a modified or unmodified variant thereof.

[002235] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 1731 and 1769), or a modified or unmodified variant thereof.

[002236] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 1732 and 1770), or a modified or unmodified variant thereof.

[002237] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 1733 and 1771), or a modified or unmodified variant thereof.

[002238] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 1734 and 1772), or a modified or unmodified variant thereof.

[002239] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-35606.1 (SEQ ID NOs: 1735 and 1773), or a modified or unmodified variant thereof.

[002240] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 1736 and 1774), or a modified or unmodified variant thereof.

[002241] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 1737 and 1775), or a modified or unmodified variant thereof.

[002242] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 1738 and 1776), or a modified or unmodified variant thereof.

[002243] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38159.1 or hs_KRAS_ 528_A22S26 (SEQ ID NOs: 1739 and 1777), or a modified or unmodified variant thereof.

[002244] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38130.1 or hs_KRAS_ 531_A22S26 (SEQ ID NOs: 1740 and 1778), or a modified or unmodified variant thereof.

[002245] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 1741 and 1779), or a modified or unmodified variant thereof.

[002246] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 1742 and 1780), or a modified or unmodified variant thereof.

[002247] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 1743 and 1781), or a modified or unmodified variant thereof.

[002248] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 1744 and 1782), or a modified or unmodified variant thereof.

[002249] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40077.1 (SEQ ID NOs: 1745 and 1783), or a modified or unmodified variant thereof.

[002250] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 1746 and 1784), or a modified or unmodified variant thereof.

[002251] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 1747 and 1785), or a modified or unmodified variant thereof.

[002252] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 1748 and 1786), or a modified or unmodified variant thereof.

[002253] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 1749 and 1787), or a modified or unmodified variant thereof.

[002254] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 1750 and 1788), or a modified or unmodified variant thereof.

[002255] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1751 and 1789), or a modified or unmodified variant thereof.

[002256] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1752 and 1790), or a modified or unmodified variant thereof.

[002257] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of a first and/or second strand of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1753 and 1791), or a modified or unmodified variant thereof.

[002258] Specific embodiments wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of a RNAi agent disclosed herein

[002259] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[002260] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[002261] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35523.3 (SEQ ID NOs: 1 and 428), or a modified or unmodified variant thereof.

[002262] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35529.1 (SEQ ID NOs: 2 and 429), or a modified or unmodified variant thereof.

[002263] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35535.4 (SEQ ID NOs: 3 and 430), or a modified or unmodified variant thereof.

[002264] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-35541.4 (SEQ ID NOs: 4 and 431), or a modified or unmodified variant thereof.

[002265] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35547.4 (SEQ ID NOs: 5 and 432), or a modified or unmodified variant thereof.

[002266] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35553.4 (SEQ ID NOs: 6 and 433), or a modified or unmodified variant thereof.

[002267] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35559.4 (SEQ ID NOs: 7 and 434), or a modified or unmodified variant thereof.

[002268] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35565.4 (SEQ ID NOs: 8 and 435), or a modified or unmodified variant thereof.

[002269] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35524.4 (SEQ ID NOs: 9 and 436), or a modified or unmodified variant thereof.

[002270] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35530.4 (SEQ ID NOs: 10 and 437), or a modified or unmodified variant thereof.

[002271] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35536.4 (SEQ ID NOs: 11 and 438), or a modified or unmodified variant thereof.

[002272] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35542.4 (SEQ ID NOs: 12 and 439), or a modified or unmodified variant thereof.

[002273] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35548.4 (SEQ ID NOs: 13 and 440), or a modified or unmodified variant thereof.

[002274] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35554.4 (SEQ ID NOs: 14 and 441), or a modified or unmodified variant thereof.

[002275] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35560.2 (SEQ ID NOs: 15 and 442), or a modified or unmodified variant thereof.

[002276] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35566.4 (SEQ ID NOs: 16 and 443), or a modified or unmodified variant thereof.

[002277] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35525.2 (SEQ ID NOs: 17 and 444), or a modified or unmodified variant thereof.

[002278] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35531.4 (SEQ ID NOs: 18 and 445), or a modified or unmodified variant thereof.

[002279] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35537.4 (SEQ ID NOs: 19 and 446), or a modified or unmodified variant thereof.

[002280] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35543.2 (SEQ ID NOs: 20 and 447), or a modified or unmodified variant thereof.

[002281] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35549.4 (SEQ ID NOs: 21 and 448), or a modified or unmodified variant thereof.

[002282] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35555.4 (SEQ ID NOs: 22 and 449), or a modified or unmodified variant thereof.

[002283] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35561.4 (SEQ ID NOs: 23 and 450), or a modified or unmodified variant thereof.

[002284] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35567.4 (SEQ ID NOs: 24 and 451), or a modified or unmodified variant thereof.

[002285] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35526.4 (SEQ ID NOs: 25 and 452), or a modified or unmodified variant thereof.

[002286] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35532.4 (SEQ ID NOs: 26 and 453), or a modified or unmodified variant thereof.

[002287] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35538.4 (SEQ ID NOs: 27 and 454), or a modified or unmodified variant thereof.

[002288] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35544.4 (SEQ ID NOs: 28 and 455), or a modified or unmodified variant thereof.

[002289] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35550.4 (SEQ ID NOs: 29 and 456), or a modified or unmodified variant thereof.

[002290] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35556.4 (SEQ ID NOs: 30 and 457), or a modified or unmodified variant thereof.

[002291] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35562.4 (SEQ ID

NOs: 31 and 458), or a modified or unmodified variant thereof.

[002292] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35568.4 (SEQ ID NOs: 32 and 459), or a modified or unmodified variant thereof.

[002293] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35527.4 (SEQ ID NOs: 33 and 460), or a modified or unmodified variant thereof.

[002294] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35533.4 (SEQ ID NOs: 34 and 461), or a modified or unmodified variant thereof.

[002295] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35539.4 (SEQ ID NOs: 35 and 462), or a modified or unmodified variant thereof.

[002296] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35545.4 (SEQ ID NOs: 36 and 463), or a modified or unmodified variant thereof.

[002297] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35551.4 (SEQ ID NOs: 37 and 464), or a modified or unmodified variant thereof.

[002298] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35563.4 (SEQ ID NOs: 38 and 465), or a modified or unmodified variant thereof.

[002299] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35528.4 (SEQ ID NOs: 39 and 466), or a modified or unmodified variant thereof.

[002300] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35540.4 (SEQ ID NOs: 40 and 467), or a modified or unmodified variant thereof.

[002301] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35546.4 (SEQ ID NOs: 41 and 468), or a modified or unmodified variant thereof.

[002302] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35552.4 (SEQ ID NOs: 42 and 469), or a modified or unmodified variant thereof.

[002303] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35558.4 (SEQ ID NOs: 43 and 470), or a modified or unmodified variant thereof.

[002304] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35564.4 (SEQ ID NOs: 44 and 471), or a modified or unmodified variant thereof.

[002305] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-35570.4 (SEQ ID NOs: 45 and 472), or a modified or unmodified variant thereof.

[002306] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35571.4 (SEQ ID NOs: 46 and 473), or a modified or unmodified variant thereof.

[002307] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35577.4 (SEQ ID NOs: 47 and 474), or a modified or unmodified variant thereof.

[002308] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35583.4 (SEQ ID NOs: 48 and 475), or a modified or unmodified variant thereof.

[002309] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35589.4 (SEQ ID NOs: 49 and 476), or a modified or unmodified variant thereof.

[002310] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35595.4 (SEQ ID NOs: 50 and 477), or a modified or unmodified variant thereof.

[002311] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35601.4 (SEQ ID NOs: 51 and 478), or a modified or unmodified variant thereof.

[002312] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35607.4 (SEQ ID NOs: 52 and 479), or a modified or unmodified variant thereof.

[002313] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35613.4 (SEQ ID NOs: 53 and 480), or a modified or unmodified variant thereof.

[002314] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35572.4 (SEQ ID NOs: 54 and 481), or a modified or unmodified variant thereof.

[002315] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35578.4 (SEQ ID NOs: 55 and 482), or a modified or unmodified variant thereof.

[002316] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35584.4 (SEQ ID NOs: 56 and 483), or a modified or unmodified variant thereof.

[002317] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35590.4 (SEQ ID NOs: 57 and 484), or a modified or unmodified variant thereof.

[002318] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35596.4 (SEQ ID NOs: 58 and 485), or a modified or unmodified variant thereof.

[002319] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35602.4 (SEQ ID NOs: 59 and 486), or a modified or unmodified variant thereof.

[002320] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35608.4 (SEQ ID NOs: 60 and 487), or a modified or unmodified variant thereof.

[002321] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35614.4 (SEQ ID NOs: 61 and 488), or a modified or unmodified variant thereof.

[002322] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35573.4 (SEQ ID NOs: 62 and 489), or a modified or unmodified variant thereof.

[002323] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35579.4 (SEQ ID NOs: 63 and 490), or a modified or unmodified variant thereof.

[002324] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35585.4 (SEQ ID NOs: 64 and 491), or a modified or unmodified variant thereof.

[002325] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35591.4 (SEQ ID NOs: 65 and 492), or a modified or unmodified variant thereof.

[002326] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35597.4 (SEQ ID NOs: 66 and 493), or a modified or unmodified variant thereof.

[002327] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35603.4 (SEQ ID NOs: 67 and 494), or a modified or unmodified variant thereof.

[002328] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35609.4 (SEQ ID NOs: 68 and 495), or a modified or unmodified variant thereof.

[002329] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35615.4 (SEQ ID NOs: 69 and 496), or a modified or unmodified variant thereof.

[002330] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35574.4 (SEQ ID NOs: 70 and 497), or a modified or unmodified variant thereof.

[002331] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35580.1 (SEQ ID NOs: 71 and 498), or a modified or unmodified variant thereof.

[002332] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35586.4 (SEQ ID

NOs: 72 and 499), or a modified or unmodified variant thereof.

[002333] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35592.4 (SEQ ID NOs: 73 and 500), or a modified or unmodified variant thereof.

[002334] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35598.4 (SEQ ID NOs: 74 and 501), or a modified or unmodified variant thereof.

[002335] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35604.4 (SEQ ID NOs: 75 and 502), or a modified or unmodified variant thereof.

[002336] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35610.4 (SEQ ID NOs: 76 and 503), or a modified or unmodified variant thereof.

[002337] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35616.4 (SEQ ID NOs: 77 and 504), or a modified or unmodified variant thereof.

[002338] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35575.4 (SEQ ID NOs: 78 and 505), or a modified or unmodified variant thereof.

[002339] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35581.4 (SEQ ID NOs: 79 and 506), or a modified or unmodified variant thereof.

[002340] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35587.4 (SEQ ID NOs: 80 and 507), or a modified or unmodified variant thereof.

[002341] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35593.4 (SEQ ID NOs: 81 and 508), or a modified or unmodified variant thereof.

[002342] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35599.4 (SEQ ID NOs: 82 and 509), or a modified or unmodified variant thereof.

[002343] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35605.4 (SEQ ID NOs: 83 and 510), or a modified or unmodified variant thereof.

[002344] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35611.4 (SEQ ID NOs: 84 and 511), or a modified or unmodified variant thereof.

[002345] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35617.4 (SEQ ID NOs: 85 and 512), or a modified or unmodified variant thereof.

[002346] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-35576.4 (SEQ ID NOs: 86 and 513), or a modified or unmodified variant thereof.

[002347] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35588.4 (SEQ ID NOs: 87 and 514), or a modified or unmodified variant thereof.

[002348] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35667.1 (SEQ ID NOs: 88 and 515), or a modified or unmodified variant thereof.

[002349] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35673.1 (SEQ ID NOs: 89 and 516), or a modified or unmodified variant thereof.

[002350] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35679.1 (SEQ ID NOs: 90 and 517), or a modified or unmodified variant thereof.

[002351] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35685.1 (SEQ ID NOs: 91 and 518), or a modified or unmodified variant thereof.

[002352] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35691.1 (SEQ ID NOs: 92 and 519), or a modified or unmodified variant thereof.

[002353] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35557.1 (SEQ ID NOs: 93 and 520), or a modified or unmodified variant thereof.

[002354] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35618.1 (SEQ ID NOs: 94 and 521), or a modified or unmodified variant thereof.

[002355] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35569.1 (SEQ ID NOs: 95 and 522), or a modified or unmodified variant thereof.

[002356] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35534.1 (SEQ ID NOs: 96 and 523), or a modified or unmodified variant thereof.

[002357] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35582.1 (SEQ ID NOs: 97 and 524), or a modified or unmodified variant thereof.

[002358] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35594.1 (SEQ ID NOs: 98 and 525), or a modified or unmodified variant thereof.

[002359] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35600.1 (SEQ ID NOs: 99 and 526), or a modified or unmodified variant thereof.

[002360] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35606.1 (SEQ ID NOs: 100 and 527), or a modified or unmodified variant thereof.

[002361] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35612.1 (SEQ ID NOs: 101 and 528), or a modified or unmodified variant thereof.

[002362] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38127.1 (SEQ ID NOs: 102 and 529), or a modified or unmodified variant thereof.

[002363] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38133.1 (SEQ ID NOs: 103 and 530), or a modified or unmodified variant thereof.

[002364] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38139.1 (SEQ ID NOs: 104 and 531), or a modified or unmodified variant thereof.

[002365] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38145.1 (SEQ ID NOs: 105 and 532), or a modified or unmodified variant thereof.

[002366] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38151.1 (SEQ ID NOs: 106 and 533), or a modified or unmodified variant thereof.

[002367] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38157.1 (SEQ ID NOs: 107 and 534), or a modified or unmodified variant thereof.

[002368] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38163.1 (SEQ ID NOs: 108 and 535), or a modified or unmodified variant thereof.

[002369] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38169.1 (SEQ ID NOs: 109 and 536), or a modified or unmodified variant thereof.

[002370] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38128.1 (SEQ ID NOs: 110 and 537), or a modified or unmodified variant thereof.

[002371] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38134.1 (SEQ ID NOs: 111 and 538), or a modified or unmodified variant thereof.

[002372] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38140.1 (SEQ ID NOs: 112 and 539), or a modified or unmodified variant thereof.

[002373] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38146.1 (SEQ ID

NOs: 113 and 540), or a modified or unmodified variant thereof.

[002374] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38152.1 (SEQ ID NOs: 114 and 541), or a modified or unmodified variant thereof.

[002375] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38158.1 (SEQ ID NOs: 115 and 542), or a modified or unmodified variant thereof.

[002376] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38164.1 (SEQ ID NOs: 116 and 543), or a modified or unmodified variant thereof.

[002377] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38170.1 (SEQ ID NOs: 117 and 544), or a modified or unmodified variant thereof.

[002378] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38129.1 (SEQ ID NOs: 118 and 545), or a modified or unmodified variant thereof.

[002379] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38135.1 (SEQ ID NOs: 119 and 546), or a modified or unmodified variant thereof.

[002380] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38141.1 (SEQ ID NOs: 120 and 547), or a modified or unmodified variant thereof.

[002381] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38147.1 (SEQ ID NOs: 121 and 548), or a modified or unmodified variant thereof.

[002382] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38153.1 (SEQ ID NOs: 122 and 549), or a modified or unmodified variant thereof.

[002383] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38159.1 (SEQ ID NOs: 123 and 550), or a modified or unmodified variant thereof.

[002384] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38165.1 (SEQ ID NOs: 124 and 551), or a modified or unmodified variant thereof.

[002385] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38171.1 (SEQ ID NOs: 125 and 552), or a modified or unmodified variant thereof.

[002386] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38130.1 (SEQ ID NOs: 126 and 553), or a modified or unmodified variant thereof.

[002387] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-38136.1 (SEQ ID NOs: 127 and 554), or a modified or unmodified variant thereof.

[002388] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38142.1 (SEQ ID NOs: 128 and 555), or a modified or unmodified variant thereof.

[002389] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38148.1 (SEQ ID NOs: 129 and 556), or a modified or unmodified variant thereof.

[002390] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38154.1 (SEQ ID NOs: 130 and 557), or a modified or unmodified variant thereof.

[002391] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38160.1 (SEQ ID NOs: 131 and 558), or a modified or unmodified variant thereof.

[002392] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38166.1 (SEQ ID NOs: 132 and 559), or a modified or unmodified variant thereof.

[002393] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38172.1 (SEQ ID NOs: 133 and 560), or a modified or unmodified variant thereof.

[002394] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38131.1 (SEQ ID NOs: 134 and 561), or a modified or unmodified variant thereof.

[002395] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38137.1 (SEQ ID NOs: 135 and 562), or a modified or unmodified variant thereof.

[002396] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38143.1 (SEQ ID NOs: 136 and 563), or a modified or unmodified variant thereof.

[002397] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38149.1 (SEQ ID NOs: 137 and 564), or a modified or unmodified variant thereof.

[002398] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38155.1 (SEQ ID NOs: 138 and 565), or a modified or unmodified variant thereof.

[002399] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38161.1 (SEQ ID NOs: 139 and 566), or a modified or unmodified variant thereof.

[002400] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38167.1 (SEQ ID NOs: 140 and 567), or a modified or unmodified variant thereof.

[002401] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38173.1 (SEQ ID NOs: 141 and 568), or a modified or unmodified variant thereof.

[002402] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38132.1 (SEQ ID NOs: 142 and 569), or a modified or unmodified variant thereof.

[002403] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38138.1 (SEQ ID NOs: 143 and 570), or a modified or unmodified variant thereof.

[002404] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38144.1 (SEQ ID NOs: 144 and 571), or a modified or unmodified variant thereof.

[002405] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38150.1 (SEQ ID NOs: 145 and 572), or a modified or unmodified variant thereof.

[002406] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38156.1 (SEQ ID NOs: 146 and 573), or a modified or unmodified variant thereof.

[002407] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38162.1 (SEQ ID NOs: 147 and 574), or a modified or unmodified variant thereof.

[002408] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38168.1 (SEQ ID NOs: 148 and 575), or a modified or unmodified variant thereof.

[002409] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38174.1 (SEQ ID NOs: 149 and 576), or a modified or unmodified variant thereof.

[002410] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39683.1 (SEQ ID NOs: 150 and 577), or a modified or unmodified variant thereof.

[002411] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39689.1 (SEQ ID NOs: 151 and 578), or a modified or unmodified variant thereof.

[002412] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39695.1 (SEQ ID NOs: 152 and 579), or a modified or unmodified variant thereof.

[002413] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39701.1 (SEQ ID NOs: 153 and 580), or a modified or unmodified variant thereof.

[002414] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39707.1 (SEQ ID

NOs: 154 and 581), or a modified or unmodified variant thereof.

[002415] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39713.1 (SEQ ID NOs: 155 and 582), or a modified or unmodified variant thereof.

[002416] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39719.1 (SEQ ID NOs: 156 and 583), or a modified or unmodified variant thereof.

[002417] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39725.1 (SEQ ID NOs: 157 and 584), or a modified or unmodified variant thereof.

[002418] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39684.1 (SEQ ID NOs: 158 and 585), or a modified or unmodified variant thereof.

[002419] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39690.1 (SEQ ID NOs: 159 and 586), or a modified or unmodified variant thereof.

[002420] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39696.1 (SEQ ID NOs: 160 and 587), or a modified or unmodified variant thereof.

[002421] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39702.1 (SEQ ID NOs: 161 and 588), or a modified or unmodified variant thereof.

[002422] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39708.1 (SEQ ID NOs: 162 and 589), or a modified or unmodified variant thereof.

[002423] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39714.1 (SEQ ID NOs: 163 and 590), or a modified or unmodified variant thereof.

[002424] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39720.1 (SEQ ID NOs: 164 and 591), or a modified or unmodified variant thereof.

[002425] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39726.1 (SEQ ID NOs: 165 and 592), or a modified or unmodified variant thereof.

[002426] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39685.1 (SEQ ID NOs: 166 and 593), or a modified or unmodified variant thereof.

[002427] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39691.1 (SEQ ID NOs: 167 and 594), or a modified or unmodified variant thereof.

[002428] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-39697.1 (SEQ ID NOs: 168 and 595), or a modified or unmodified variant thereof.

[002429] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39703.1 (SEQ ID NOs: 169 and 596), or a modified or unmodified variant thereof.

[002430] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39709.1 (SEQ ID NOs: 170 and 597), or a modified or unmodified variant thereof.

[002431] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39715.1 (SEQ ID NOs: 171 and 598), or a modified or unmodified variant thereof.

[002432] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39721.1 (SEQ ID NOs: 172 and 599), or a modified or unmodified variant thereof.

[002433] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39727.1 (SEQ ID NOs: 173 and 600), or a modified or unmodified variant thereof.

[002434] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39686.1 (SEQ ID NOs: 174 and 601), or a modified or unmodified variant thereof.

[002435] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39692.1 (SEQ ID NOs: 175 and 602), or a modified or unmodified variant thereof.

[002436] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39698.1 (SEQ ID NOs: 176 and 603), or a modified or unmodified variant thereof.

[002437] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39704.1 (SEQ ID NOs: 177 and 604), or a modified or unmodified variant thereof.

[002438] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39710.1 (SEQ ID NOs: 178 and 605), or a modified or unmodified variant thereof.

[002439] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39716.1 (SEQ ID NOs: 179 and 606), or a modified or unmodified variant thereof.

[002440] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39722.1 (SEQ ID NOs: 180 and 607), or a modified or unmodified variant thereof.

[002441] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39728.1 (SEQ ID NOs: 181 and 608), or a modified or unmodified variant thereof.

[002442] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39687.1 (SEQ ID NOs: 182 and 609), or a modified or unmodified variant thereof.

[002443] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39693.1 (SEQ ID NOs: 183 and 610), or a modified or unmodified variant thereof.

[002444] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39699.1 (SEQ ID NOs: 184 and 611), or a modified or unmodified variant thereof.

[002445] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39705.1 (SEQ ID NOs: 185 and 612), or a modified or unmodified variant thereof.

[002446] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39711.1 (SEQ ID NOs: 186 and 613), or a modified or unmodified variant thereof.

[002447] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39717.1 (SEQ ID NOs: 187 and 614), or a modified or unmodified variant thereof.

[002448] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39723.1 (SEQ ID NOs: 188 and 615), or a modified or unmodified variant thereof.

[002449] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39729.1 (SEQ ID NOs: 189 and 616), or a modified or unmodified variant thereof.

[002450] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39688.1 (SEQ ID NOs: 190 and 617), or a modified or unmodified variant thereof.

[002451] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39694.1 (SEQ ID NOs: 191 and 618), or a modified or unmodified variant thereof.

[002452] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39700.1 (SEQ ID NOs: 192 and 619), or a modified or unmodified variant thereof.

[002453] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39706.1 (SEQ ID NOs: 193 and 620), or a modified or unmodified variant thereof.

[002454] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39712.1 (SEQ ID NOs: 194 and 621), or a modified or unmodified variant thereof.

[002455] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39718.1 (SEQ ID

NOs: 195 and 622), or a modified or unmodified variant thereof.

[002456] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39724.1 (SEQ ID NOs: 196 and 623), or a modified or unmodified variant thereof.

[002457] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39730.1 (SEQ ID NOs: 197 and 624), or a modified or unmodified variant thereof.

[002458] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39736.1 (SEQ ID NOs: 198 and 625), or a modified or unmodified variant thereof.

[002459] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39742.1 (SEQ ID NOs: 199 and 626), or a modified or unmodified variant thereof.

[002460] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39748.1 (SEQ ID NOs: 200 and 627), or a modified or unmodified variant thereof.

[002461] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39754.1 (SEQ ID NOs: 201 and 628), or a modified or unmodified variant thereof.

[002462] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39760.1 (SEQ ID NOs: 202 and 629), or a modified or unmodified variant thereof.

[002463] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39766.1 (SEQ ID NOs: 203 and 630), or a modified or unmodified variant thereof.

[002464] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39772.1 (SEQ ID NOs: 204 and 631), or a modified or unmodified variant thereof.

[002465] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39731.1 (SEQ ID NOs: 205 and 632), or a modified or unmodified variant thereof.

[002466] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39737.1 (SEQ ID NOs: 206 and 633), or a modified or unmodified variant thereof.

[002467] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39743.1 (SEQ ID NOs: 207 and 634), or a modified or unmodified variant thereof.

[002468] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39749.1 (SEQ ID NOs: 208 and 635), or a modified or unmodified variant thereof.

[002469] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-39755.1 (SEQ ID NOs: 209 and 636), or a modified or unmodified variant thereof.

[002470] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39761.1 (SEQ ID NOs: 210 and 637), or a modified or unmodified variant thereof.

[002471] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39767.1 (SEQ ID NOs: 211 and 638), or a modified or unmodified variant thereof.

[002472] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39773.1 (SEQ ID NOs: 212 and 639), or a modified or unmodified variant thereof.

[002473] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39732.1 (SEQ ID NOs: 213 and 640), or a modified or unmodified variant thereof.

[002474] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39738.1 (SEQ ID NOs: 214 and 641), or a modified or unmodified variant thereof.

[002475] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39744.1 (SEQ ID NOs: 215 and 642), or a modified or unmodified variant thereof.

[002476] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39750.1 (SEQ ID NOs: 216 and 643), or a modified or unmodified variant thereof.

[002477] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39756.1 (SEQ ID NOs: 217 and 644), or a modified or unmodified variant thereof.

[002478] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39762.1 (SEQ ID NOs: 218 and 645), or a modified or unmodified variant thereof.

[002479] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39768.1 (SEQ ID NOs: 219 and 646), or a modified or unmodified variant thereof.

[002480] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39774.1 (SEQ ID NOs: 220 and 647), or a modified or unmodified variant thereof.

[002481] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39733.1 (SEQ ID NOs: 221 and 648), or a modified or unmodified variant thereof.

[002482] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39739.1 (SEQ ID NOs: 222 and 649), or a modified or unmodified variant thereof.

[002483] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39745.1 (SEQ ID NOs: 223 and 650), or a modified or unmodified variant thereof.

[002484] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39751.1 (SEQ ID NOs: 224 and 651), or a modified or unmodified variant thereof.

[002485] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39757.1 (SEQ ID NOs: 225 and 652), or a modified or unmodified variant thereof.

[002486] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39763.1 (SEQ ID NOs: 226 and 653), or a modified or unmodified variant thereof.

[002487] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39769.1 (SEQ ID NOs: 227 and 654), or a modified or unmodified variant thereof.

[002488] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39775.1 (SEQ ID NOs: 228 and 655), or a modified or unmodified variant thereof.

[002489] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39734.1 (SEQ ID NOs: 229 and 656), or a modified or unmodified variant thereof.

[002490] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39740.1 (SEQ ID NOs: 230 and 657), or a modified or unmodified variant thereof.

[002491] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39746.1 (SEQ ID NOs: 231 and 658), or a modified or unmodified variant thereof.

[002492] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39752.1 (SEQ ID NOs: 232 and 659), or a modified or unmodified variant thereof.

[002493] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39758.1 (SEQ ID NOs: 233 and 660), or a modified or unmodified variant thereof.

[002494] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39764.1 (SEQ ID NOs: 234 and 661), or a modified or unmodified variant thereof.

[002495] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39770.1 (SEQ ID NOs: 235 and 662), or a modified or unmodified variant thereof.

[002496] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39776.1 (SEQ ID

NOs: 236 and 663), or a modified or unmodified variant thereof.

[002497] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39735.1 (SEQ ID NOs: 237 and 664), or a modified or unmodified variant thereof.

[002498] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39741.1 (SEQ ID NOs: 238 and 665), or a modified or unmodified variant thereof.

[002499] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39747.1 (SEQ ID NOs: 239 and 666), or a modified or unmodified variant thereof.

[002500] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39753.1 (SEQ ID NOs: 240 and 667), or a modified or unmodified variant thereof.

[002501] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39759.1 (SEQ ID NOs: 241 and 668), or a modified or unmodified variant thereof.

[002502] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39765.1 (SEQ ID NOs: 242 and 669), or a modified or unmodified variant thereof.

[002503] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39771.1 (SEQ ID NOs: 243 and 670), or a modified or unmodified variant thereof.

[002504] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39778.1 (SEQ ID NOs: 244 and 671), or a modified or unmodified variant thereof.

[002505] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39784.1 (SEQ ID NOs: 245 and 672), or a modified or unmodified variant thereof.

[002506] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39790.1 (SEQ ID NOs: 246 and 673), or a modified or unmodified variant thereof.

[002507] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39796.1 (SEQ ID NOs: 247 and 674), or a modified or unmodified variant thereof.

[002508] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39802.1 (SEQ ID NOs: 248 and 675), or a modified or unmodified variant thereof.

[002509] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39808.1 (SEQ ID NOs: 249 and 676), or a modified or unmodified variant thereof.

[002510] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-39814.1 (SEQ ID NOs: 250 and 677), or a modified or unmodified variant thereof.

[002511] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39820.1 (SEQ ID NOs: 251 and 678), or a modified or unmodified variant thereof.

[002512] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39779.1 (SEQ ID NOs: 252 and 679), or a modified or unmodified variant thereof.

[002513] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39785.1 (SEQ ID NOs: 253 and 680), or a modified or unmodified variant thereof.

[002514] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39791.1 (SEQ ID NOs: 254 and 681), or a modified or unmodified variant thereof.

[002515] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39797.1 (SEQ ID NOs: 255 and 682), or a modified or unmodified variant thereof.

[002516] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39803.1 (SEQ ID NOs: 256 and 683), or a modified or unmodified variant thereof.

[002517] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39809.1 (SEQ ID NOs: 257 and 684), or a modified or unmodified variant thereof.

[002518] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39815.1 (SEQ ID NOs: 258 and 685), or a modified or unmodified variant thereof.

[002519] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39821.1 (SEQ ID NOs: 259 and 686), or a modified or unmodified variant thereof.

[002520] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39780.1 (SEQ ID NOs: 260 and 687), or a modified or unmodified variant thereof.

[002521] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39786.1 (SEQ ID NOs: 261 and 688), or a modified or unmodified variant thereof.

[002522] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39792.1 (SEQ ID NOs: 262 and 689), or a modified or unmodified variant thereof.

[002523] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39798.1 (SEQ ID NOs: 263 and 690), or a modified or unmodified variant thereof.

[002524] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39804.1 (SEQ ID NOs: 264 and 691), or a modified or unmodified variant thereof.

[002525] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39810.1 (SEQ ID NOs: 265 and 692), or a modified or unmodified variant thereof.

[002526] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39816.1 (SEQ ID NOs: 266 and 693), or a modified or unmodified variant thereof.

[002527] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39822.1 (SEQ ID NOs: 267 and 694), or a modified or unmodified variant thereof.

[002528] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39781.1 (SEQ ID NOs: 268 and 695), or a modified or unmodified variant thereof.

[002529] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39787.1 (SEQ ID NOs: 269 and 696), or a modified or unmodified variant thereof.

[002530] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39793.1 (SEQ ID NOs: 270 and 697), or a modified or unmodified variant thereof.

[002531] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39799.1 (SEQ ID NOs: 271 and 698), or a modified or unmodified variant thereof.

[002532] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39805.1 (SEQ ID NOs: 272 and 699), or a modified or unmodified variant thereof.

[002533] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39811.1 (SEQ ID NOs: 273 and 700), or a modified or unmodified variant thereof.

[002534] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39817.1 (SEQ ID NOs: 274 and 701), or a modified or unmodified variant thereof.

[002535] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39823.1 (SEQ ID NOs: 275 and 702), or a modified or unmodified variant thereof.

[002536] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39782.1 (SEQ ID NOs: 276 and 703), or a modified or unmodified variant thereof.

[002537] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39788.1 (SEQ ID

NOs: 277 and 704), or a modified or unmodified variant thereof.

[002538] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39794.1 (SEQ ID NOs: 278 and 705), or a modified or unmodified variant thereof.

[002539] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39800.1 (SEQ ID NOs: 279 and 706), or a modified or unmodified variant thereof.

[002540] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39806.1 (SEQ ID NOs: 280 and 707), or a modified or unmodified variant thereof.

[002541] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39812.1 (SEQ ID NOs: 281 and 708), or a modified or unmodified variant thereof.

[002542] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39818.1 (SEQ ID NOs: 282 and 709), or a modified or unmodified variant thereof.

[002543] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39824.1 (SEQ ID NOs: 283 and 710), or a modified or unmodified variant thereof.

[002544] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39783.1 (SEQ ID NOs: 284 and 711), or a modified or unmodified variant thereof.

[002545] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39789.1 (SEQ ID NOs: 285 and 712), or a modified or unmodified variant thereof.

[002546] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39795.1 (SEQ ID NOs: 286 and 713), or a modified or unmodified variant thereof.

[002547] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39801.1 (SEQ ID NOs: 287 and 714), or a modified or unmodified variant thereof.

[002548] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39807.1 (SEQ ID NOs: 288 and 715), or a modified or unmodified variant thereof.

[002549] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39813.1 (SEQ ID NOs: 289 and 716), or a modified or unmodified variant thereof.

[002550] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39819.1 (SEQ ID NOs: 290 and 717), or a modified or unmodified variant thereof.

[002551] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-39825.1 (SEQ ID NOs: 291 and 718), or a modified or unmodified variant thereof.

[002552] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39831.1 (SEQ ID NOs: 292 and 719), or a modified or unmodified variant thereof.

[002553] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39837.1 (SEQ ID NOs: 293 and 720), or a modified or unmodified variant thereof.

[002554] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39843.1 (SEQ ID NOs: 294 and 721), or a modified or unmodified variant thereof.

[002555] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39849.1 (SEQ ID NOs: 295 and 722), or a modified or unmodified variant thereof.

[002556] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39855.1 (SEQ ID NOs: 296 and 723), or a modified or unmodified variant thereof.

[002557] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39861.1 (SEQ ID NOs: 297 and 724), or a modified or unmodified variant thereof.

[002558] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39867.1 (SEQ ID NOs: 298 and 725), or a modified or unmodified variant thereof.

[002559] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39826.1 (SEQ ID NOs: 299 and 726), or a modified or unmodified variant thereof.

[002560] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39832.1 (SEQ ID NOs: 300 and 727), or a modified or unmodified variant thereof.

[002561] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39838.1 (SEQ ID NOs: 301 and 728), or a modified or unmodified variant thereof.

[002562] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39844.1 (SEQ ID NOs: 302 and 729), or a modified or unmodified variant thereof.

[002563] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39850.1 (SEQ ID NOs: 303 and 730), or a modified or unmodified variant thereof.

[002564] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39856.1 (SEQ ID NOs: 304 and 731), or a modified or unmodified variant thereof.

[002565] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39862.1 (SEQ ID NOs: 305 and 732), or a modified or unmodified variant thereof.

[002566] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39868.1 (SEQ ID NOs: 306 and 733), or a modified or unmodified variant thereof.

[002567] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39827.1 (SEQ ID NOs: 307 and 734), or a modified or unmodified variant thereof.

[002568] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39833.1 (SEQ ID NOs: 308 and 735), or a modified or unmodified variant thereof.

[002569] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39839.1 (SEQ ID NOs: 309 and 736), or a modified or unmodified variant thereof.

[002570] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39845.1 (SEQ ID NOs: 310 and 737), or a modified or unmodified variant thereof.

[002571] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39851.1 (SEQ ID NOs: 311 and 738), or a modified or unmodified variant thereof.

[002572] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39857.1 (SEQ ID NOs: 312 and 739), or a modified or unmodified variant thereof.

[002573] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39863.1 (SEQ ID NOs: 313 and 740), or a modified or unmodified variant thereof.

[002574] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39869.1 (SEQ ID NOs: 314 and 741), or a modified or unmodified variant thereof.

[002575] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39828.1 (SEQ ID NOs: 315 and 742), or a modified or unmodified variant thereof.

[002576] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39834.1 (SEQ ID NOs: 316 and 743), or a modified or unmodified variant thereof.

[002577] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39840.1 (SEQ ID NOs: 317 and 744), or a modified or unmodified variant thereof.

[002578] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39846.1 (SEQ ID

NOs: 318 and 745), or a modified or unmodified variant thereof.

[002579] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39852.1 (SEQ ID NOs: 319 and 746), or a modified or unmodified variant thereof.

[002580] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39858.1 (SEQ ID NOs: 320 and 747), or a modified or unmodified variant thereof.

[002581] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39864.1 (SEQ ID NOs: 321 and 748), or a modified or unmodified variant thereof.

[002582] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39870.1 (SEQ ID NOs: 322 and 749), or a modified or unmodified variant thereof.

[002583] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39829.1 (SEQ ID NOs: 323 and 750), or a modified or unmodified variant thereof.

[002584] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39835.1 (SEQ ID NOs: 324 and 751), or a modified or unmodified variant thereof.

[002585] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39841.1 (SEQ ID NOs: 325 and 752), or a modified or unmodified variant thereof.

[002586] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39853.1 (SEQ ID NOs: 326 and 753), or a modified or unmodified variant thereof.

[002587] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39859.1 (SEQ ID NOs: 327 and 754), or a modified or unmodified variant thereof.

[002588] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39865.1 (SEQ ID NOs: 328 and 755), or a modified or unmodified variant thereof.

[002589] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39871.1 (SEQ ID NOs: 329 and 756), or a modified or unmodified variant thereof.

[002590] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39830.1 (SEQ ID NOs: 330 and 757), or a modified or unmodified variant thereof.

[002591] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39836.1 (SEQ ID NOs: 331 and 758), or a modified or unmodified variant thereof.

[002592] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-39842.1 (SEQ ID NOs: 332 and 759), or a modified or unmodified variant thereof.

[002593] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39848.1 (SEQ ID NOs: 333 and 760), or a modified or unmodified variant thereof.

[002594] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39854.1 (SEQ ID NOs: 334 and 761), or a modified or unmodified variant thereof.

[002595] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39860.1 (SEQ ID NOs: 335 and 762), or a modified or unmodified variant thereof.

[002596] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39866.1 (SEQ ID NOs: 336 and 763), or a modified or unmodified variant thereof.

[002597] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39992.1 (SEQ ID NOs: 337 and 764), or a modified or unmodified variant thereof.

[002598] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39998.1 (SEQ ID NOs: 338 and 765), or a modified or unmodified variant thereof.

[002599] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40004.1 (SEQ ID NOs: 339 and 766), or a modified or unmodified variant thereof.

[002600] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40010.1 (SEQ ID NOs: 340 and 767), or a modified or unmodified variant thereof.

[002601] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40016.1 (SEQ ID NOs: 341 and 768), or a modified or unmodified variant thereof.

[002602] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40022.1 (SEQ ID NOs: 342 and 769), or a modified or unmodified variant thereof.

[002603] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40028.1 (SEQ ID NOs: 343 and 770), or a modified or unmodified variant thereof.

[002604] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40034.1 (SEQ ID NOs: 344 and 771), or a modified or unmodified variant thereof.

[002605] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39999.1 (SEQ ID NOs: 345 and 772), or a modified or unmodified variant thereof.

[002606] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40005.1 (SEQ ID NOs: 346 and 773), or a modified or unmodified variant thereof.

[002607] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40011.1 (SEQ ID NOs: 347 and 774), or a modified or unmodified variant thereof.

[002608] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40017.1 (SEQ ID NOs: 348 and 775), or a modified or unmodified variant thereof.

[002609] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40029.1 (SEQ ID NOs: 349 and 776), or a modified or unmodified variant thereof.

[002610] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40035.1 (SEQ ID NOs: 350 and 777), or a modified or unmodified variant thereof.

[002611] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39994.1 (SEQ ID NOs: 351 and 778), or a modified or unmodified variant thereof.

[002612] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40000.1 (SEQ ID NOs: 352 and 779), or a modified or unmodified variant thereof.

[002613] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40006.1 (SEQ ID NOs: 353 and 780), or a modified or unmodified variant thereof.

[002614] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40012.1 (SEQ ID NOs: 354 and 781), or a modified or unmodified variant thereof.

[002615] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40018.1 (SEQ ID NOs: 355 and 782), or a modified or unmodified variant thereof.

[002616] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40024.1 (SEQ ID NOs: 356 and 783), or a modified or unmodified variant thereof.

[002617] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40030.1 (SEQ ID NOs: 357 and 784), or a modified or unmodified variant thereof.

[002618] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40036.1 (SEQ ID NOs: 358 and 785), or a modified or unmodified variant thereof.

[002619] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39995.1 (SEQ ID

NOs: 359 and 786), or a modified or unmodified variant thereof.

[002620] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40001.1 (SEQ ID NOs: 360 and 787), or a modified or unmodified variant thereof.

[002621] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40007.1 (SEQ ID NOs: 361 and 788), or a modified or unmodified variant thereof.

[002622] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40013.1 (SEQ ID NOs: 362 and 789), or a modified or unmodified variant thereof.

[002623] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40019.1 (SEQ ID NOs: 363 and 790), or a modified or unmodified variant thereof.

[002624] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40025.1 (SEQ ID NOs: 364 and 791), or a modified or unmodified variant thereof.

[002625] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40031.1 (SEQ ID NOs: 365 and 792), or a modified or unmodified variant thereof.

[002626] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40037.1 (SEQ ID NOs: 366 and 793), or a modified or unmodified variant thereof.

[002627] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39996.1 (SEQ ID NOs: 367 and 794), or a modified or unmodified variant thereof.

[002628] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40002.1 (SEQ ID NOs: 368 and 795), or a modified or unmodified variant thereof.

[002629] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40008.1 (SEQ ID NOs: 369 and 796), or a modified or unmodified variant thereof.

[002630] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40014.1 (SEQ ID NOs: 370 and 797), or a modified or unmodified variant thereof.

[002631] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40020.1 (SEQ ID NOs: 371 and 798), or a modified or unmodified variant thereof.

[002632] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40026.1 (SEQ ID NOs: 372 and 799), or a modified or unmodified variant thereof.

[002633] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-40032.1 (SEQ ID NOs: 373 and 800), or a modified or unmodified variant thereof.

[002634] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40038.1 (SEQ ID NOs: 374 and 801), or a modified or unmodified variant thereof.

[002635] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39997.1 (SEQ ID NOs: 375 and 802), or a modified or unmodified variant thereof.

[002636] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40009.1 (SEQ ID NOs: 376 and 803), or a modified or unmodified variant thereof.

[002637] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40015.1 (SEQ ID NOs: 377 and 804), or a modified or unmodified variant thereof.

[002638] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40021.1 (SEQ ID NOs: 378 and 805), or a modified or unmodified variant thereof.

[002639] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40027.1 (SEQ ID NOs: 379 and 806), or a modified or unmodified variant thereof.

[002640] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40033.1 (SEQ ID NOs: 380 and 807), or a modified or unmodified variant thereof.

[002641] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40039.1 (SEQ ID NOs: 381 and 808), or a modified or unmodified variant thereof.

[002642] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40045.1 (SEQ ID NOs: 382 and 809), or a modified or unmodified variant thereof.

[002643] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40051.1 (SEQ ID NOs: 383 and 810), or a modified or unmodified variant thereof.

[002644] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40057.1 (SEQ ID NOs: 384 and 811), or a modified or unmodified variant thereof.

[002645] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40063.1 (SEQ ID NOs: 385 and 812), or a modified or unmodified variant thereof.

[002646] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40069.1 (SEQ ID NOs: 386 and 813), or a modified or unmodified variant thereof.

[002647] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40075.1 (SEQ ID NOs: 387 and 814), or a modified or unmodified variant thereof.

[002648] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40081.1 (SEQ ID NOs: 388 and 815), or a modified or unmodified variant thereof.

[002649] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40040.1 (SEQ ID NOs: 389 and 816), or a modified or unmodified variant thereof.

[002650] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40046.1 (SEQ ID NOs: 390 and 817), or a modified or unmodified variant thereof.

[002651] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40052.1 (SEQ ID NOs: 391 and 818), or a modified or unmodified variant thereof.

[002652] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40058.1 (SEQ ID NOs: 392 and 819), or a modified or unmodified variant thereof.

[002653] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40064.1 (SEQ ID NOs: 393 and 820), or a modified or unmodified variant thereof.

[002654] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40070.1 (SEQ ID NOs: 394 and 821), or a modified or unmodified variant thereof.

[002655] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40076.1 (SEQ ID NOs: 395 and 822), or a modified or unmodified variant thereof.

[002656] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40082.1 (SEQ ID NOs: 396 and 823), or a modified or unmodified variant thereof.

[002657] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40041.1 (SEQ ID NOs: 397 and 824), or a modified or unmodified variant thereof.

[002658] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40047.1 (SEQ ID NOs: 398 and 825), or a modified or unmodified variant thereof.

[002659] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40053.1 (SEQ ID NOs: 399 and 826), or a modified or unmodified variant thereof.

[002660] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40059.1 (SEQ ID

NOs: 400 and 827), or a modified or unmodified variant thereof.

[002661] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40065.1 (SEQ ID NOs: 401 and 828), or a modified or unmodified variant thereof.

[002662] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40071.1 (SEQ ID NOs: 402 and 829), or a modified or unmodified variant thereof.

[002663] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40077.1 (SEQ ID NOs: 403 and 830), or a modified or unmodified variant thereof.

[002664] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40083.1 (SEQ ID NOs: 404 and 831), or a modified or unmodified variant thereof.

[002665] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40042.1 (SEQ ID NOs: 405 and 832), or a modified or unmodified variant thereof.

[002666] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40048.1 (SEQ ID NOs: 406 and 833), or a modified or unmodified variant thereof.

[002667] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40054.1 (SEQ ID NOs: 407 and 834), or a modified or unmodified variant thereof.

[002668] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40060.1 (SEQ ID NOs: 408 and 835), or a modified or unmodified variant thereof.

[002669] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40066.1 (SEQ ID NOs: 409 and 836), or a modified or unmodified variant thereof.

[002670] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40072.1 (SEQ ID NOs: 410 and 837), or a modified or unmodified variant thereof.

[002671] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40078.1 (SEQ ID NOs: 411 and 838), or a modified or unmodified variant thereof.

[002672] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40084.1 (SEQ ID NOs: 412 and 839), or a modified or unmodified variant thereof.

[002673] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40043.1 (SEQ ID NOs: 413 and 840), or a modified or unmodified variant thereof.

[002674] A RNAi agent comprising a first and a second strand, wherein the sequences of the first

and/or second strands are the sequences of the first and/or second strands of: AD-40049.1 (SEQ ID NOs: 414 and 841), or a modified or unmodified variant thereof.

[002675] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40055.1 (SEQ ID NOs: 415 and 842), or a modified or unmodified variant thereof.

[002676] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40061.1 (SEQ ID NOs: 416 and 843), or a modified or unmodified variant thereof.

[002677] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40067.1 (SEQ ID NOs: 417 and 844), or a modified or unmodified variant thereof.

[002678] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40073.1 (SEQ ID NOs: 418 and 845), or a modified or unmodified variant thereof.

[002679] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40079.1 (SEQ ID NOs: 419 and 846), or a modified or unmodified variant thereof.

[002680] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40085.1 (SEQ ID NOs: 420 and 847), or a modified or unmodified variant thereof.

[002681] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40044.1 (SEQ ID NOs: 421 and 848), or a modified or unmodified variant thereof.

[002682] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40050.1 (SEQ ID NOs: 422 and 849), or a modified or unmodified variant thereof.

[002683] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40056.1 (SEQ ID NOs: 423 and 850), or a modified or unmodified variant thereof.

[002684] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40062.1 (SEQ ID NOs: 424 and 851), or a modified or unmodified variant thereof.

[002685] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40068.1 (SEQ ID NOs: 425 and 852), or a modified or unmodified variant thereof.

[002686] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40074.1 (SEQ ID NOs: 426 and 853), or a modified or unmodified variant thereof.

[002687] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40080.1 (SEQ ID NOs: 427 and 854), or a modified or unmodified variant thereof.

[002688] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39720.1 (SEQ ID NOs: 1716 and 1754), or a modified or unmodified variant thereof.

[002689] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39706.1 (SEQ ID NOs: 1717 and 1755), or a modified or unmodified variant thereof.

[002690] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39712.1 (SEQ ID NOs: 1718 and 1756), or a modified or unmodified variant thereof.

[002691] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39760.1 (SEQ ID NOs: 1719 and 1757), or a modified or unmodified variant thereof.

[002692] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39732.1 (SEQ ID NOs: 1720 and 1758), or a modified or unmodified variant thereof.

[002693] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35541.4 (SEQ ID NOs: 1721 and 1759), or a modified or unmodified variant thereof.

[002694] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NOs: 1722 and 1760), or a modified or unmodified variant thereof.

[002695] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39741.1, or modified or unmodified variants thereof.

[002696] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1723 and 1761), or a modified or unmodified variant thereof.

[002697] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39778.1 (SEQ ID NOs: 1724 and 1762), or a modified or unmodified variant thereof.

[002698] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39790.1 (SEQ ID NOs: 1725 and 1763), or a modified or unmodified variant thereof.

[002699] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39822.1 (SEQ ID NOs: 1726 and 1764), or a modified or unmodified variant thereof.

[002700] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35609.4 (SEQ ID NOs: 1727 and 1765), or a modified or unmodified variant thereof.

[002701] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35581.4 (SEQ ID NOs: 1728 and 1766), or a modified or unmodified variant thereof.

[002702] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39845.1 (SEQ ID NOs: 1729 and 1767), or a modified or unmodified variant thereof.

[002703] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39858.1 (SEQ ID NOs: 1730 and 1768), or a modified or unmodified variant thereof.

[002704] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39870.1 (SEQ ID NOs: 1731 and 1769), or a modified or unmodified variant thereof.

[002705] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35576.4 (SEQ ID NOs: 1732 and 1770), or a modified or unmodified variant thereof.

[002706] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35588.4 (SEQ ID NOs: 1733 and 1771), or a modified or unmodified variant thereof.

[002707] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35600.1 (SEQ ID NOs: 1734 and 1772), or a modified or unmodified variant thereof.

[002708] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-35606.1 (SEQ ID NOs: 1735 and 1773), or a modified or unmodified variant thereof.

[002709] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38151.1 (SEQ ID NOs: 1736 and 1774), or a modified or unmodified variant thereof.

[002710] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38163.1 (SEQ ID NOs: 1737 and 1775), or a modified or unmodified variant thereof.

[002711] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-39999.1 (SEQ ID NOs: 1738 and 1776), or a modified or unmodified variant thereof.

[002712] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38159.1 or hs_KRAS_ 528_A22S26 (SEQ ID NOs: 1739 and 1777), or a modified or unmodified variant thereof.

[002713] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38130.1 or hs_KRAS_ 531_A22S26 (SEQ ID NOs: 1740 and 1778), or a modified or unmodified variant thereof.

[002714] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38136.1 (SEQ ID NOs: 1741 and 1779), or a modified or unmodified variant thereof.

[002715] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40036.1 (SEQ ID NOs: 1742 and 1780), or a modified or unmodified variant thereof.

[002716] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40008.1 (SEQ ID NOs: 1743 and 1781), or a modified or unmodified variant thereof.

[002717] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40021.1 (SEQ ID NOs: 1744 and 1782), or a modified or unmodified variant thereof.

[002718] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40077.1 (SEQ ID NOs: 1745 and 1783), or a modified or unmodified variant thereof.

[002719] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40072.1 (SEQ ID NOs: 1746 and 1784), or a modified or unmodified variant thereof.

[002720] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40061.1 (SEQ ID NOs: 1747 and 1785), or a modified or unmodified variant thereof.

[002721] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-40068.1 (SEQ ID NOs: 1748 and 1786), or a modified or unmodified variant thereof.

[002722] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38131.1 (SEQ ID NOs: 1749 and 1787), or a modified or unmodified variant thereof.

[002723] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: AD-38167.1 (SEQ ID NOs: 1750 and 1788), or a modified or unmodified variant thereof.

[002724] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1751 and 1789), or a modified or unmodified variant thereof.

[002725] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1752 and 1790), or a modified or unmodified variant thereof.

[002726] A RNAi agent comprising a first and a second strand, wherein the sequences of the first and/or second strands are the sequences of the first and/or second strands of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1753 and 1791), or a modified or unmodified variant thereof.

[002727] Specific embodiments wherein the sequences of the first and/or second strands are the sequences of the first and/or second strand of a RNAi agent disclosed herein, further comprising up to about 20 additional nucleotides

[002728] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002729] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[002730] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35523.3 (SEQ ID NOs: 1 and 428), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002731] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35529.1 (SEQ ID NOs: 2 and 429), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002732] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35535.4 (SEQ ID NOs: 3 and 430), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002733] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 4 and 431), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002734] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35547.4 (SEQ ID NOs: 5 and 432), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002735] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35553.4 (SEQ ID NOs: 6 and 433), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002736] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35559.4 (SEQ ID NOs: 7 and 434), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002737] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35565.4 (SEQ ID NOs:

8 and 435), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002738] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35524.4 (SEQ ID NOs: 9 and 436), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002739] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35530.4 (SEQ ID NOs: 10 and 437), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002740] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35536.4 (SEQ ID NOs: 11 and 438), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002741] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35542.4 (SEQ ID NOs: 12 and 439), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002742] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35548.4 (SEQ ID NOs: 13 and 440), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002743] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35554.4 (SEQ ID NOs: 14 and 441), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002744] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35560.2 (SEQ ID NOs: 15 and 442), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002745] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35566.4 (SEQ ID NOs: 16 and 443), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002746] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35525.2 (SEQ ID NOs: 17 and 444), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002747] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35531.4 (SEQ ID NOs: 18 and 445), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002748] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35537.4 (SEQ ID NOs: 19 and 446), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002749] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35543.2 (SEQ ID NOs: 20 and 447), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002750] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35549.4 (SEQ ID NOs: 21 and 448), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002751] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35555.4 (SEQ ID NOs: 22 and 449), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002752] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35561.4 (SEQ ID NOs: 23 and 450), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002753] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35567.4 (SEQ ID NOs: 24 and 451), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002754] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35526.4 (SEQ ID NOs: 25 and 452), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002755] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35532.4 (SEQ ID NOs: 26 and 453), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002756] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35538.4 (SEQ ID NOs: 27 and 454), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002757] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35544.4 (SEQ ID NOs: 28 and 455), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002758] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35550.4 (SEQ ID NOs: 29 and 456), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002759] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35556.4 (SEQ ID NOs: 30 and 457), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002760] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35562.4 (SEQ ID NOs: 31 and 458), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002761] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35568.4 (SEQ ID NOs: 32 and 459), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002762] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35527.4 (SEQ ID NOs: 33 and 460), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002763] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35533.4 (SEQ ID NOs: 34 and 461), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002764] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35539.4 (SEQ ID NOs: 35 and 462), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002765] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35545.4 (SEQ ID NOs: 36 and 463), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002766] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35551.4 (SEQ ID NOs: 37 and 464), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002767] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35563.4 (SEQ ID NOs: 38 and 465), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002768] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-35528.4 (SEQ ID NOs: 39 and 466), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002769] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35540.4 (SEQ ID NOs: 40 and 467), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002770] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35546.4 (SEQ ID NOs: 41 and 468), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002771] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35552.4 (SEQ ID NOs: 42 and 469), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002772] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35558.4 (SEQ ID NOs: 43 and 470), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002773] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35564.4 (SEQ ID NOs: 44 and 471), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002774] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35570.4 (SEQ ID NOs: 45 and 472), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002775] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35571.4 (SEQ ID NOs: 46 and 473), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002776] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35577.4 (SEQ ID NOs: 47 and 474), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002777] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35583.4 (SEQ ID NOs: 48 and 475), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002778] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35589.4 (SEQ ID NOs:

49 and 476), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002779] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35595.4 (SEQ ID NOs: 50 and 477), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002780] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35601.4 (SEQ ID NOs: 51 and 478), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002781] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35607.4 (SEQ ID NOs: 52 and 479), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002782] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35613.4 (SEQ ID NOs: 53 and 480), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002783] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35572.4 (SEQ ID NOs: 54 and 481), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002784] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35578.4 (SEQ ID NOs: 55 and 482), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002785] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35584.4 (SEQ ID NOs: 56 and 483), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002786] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35590.4 (SEQ ID NOs: 57 and 484), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002787] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35596.4 (SEQ ID NOs: 58 and 485), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002788] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35602.4 (SEQ ID NOs: 59 and 486), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002789] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35608.4 (SEQ ID NOs: 60 and 487), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002790] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35614.4 (SEQ ID NOs: 61 and 488), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002791] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35573.4 (SEQ ID NOs: 62 and 489), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002792] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35579.4 (SEQ ID NOs: 63 and 490), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002793] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35585.4 (SEQ ID NOs: 64 and 491), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002794] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35591.4 (SEQ ID NOs: 65 and 492), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002795] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35597.4 (SEQ ID NOs: 66 and 493), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002796] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35603.4 (SEQ ID NOs: 67 and 494), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002797] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 68 and 495), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002798] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35615.4 (SEQ ID NOs: 69 and 496), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002799] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35574.4 (SEQ ID NOs: 70 and 497), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002800] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35580.1 (SEQ ID NOs: 71 and 498), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002801] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35586.4 (SEQ ID NOs: 72 and 499), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002802] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35592.4 (SEQ ID NOs: 73 and 500), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002803] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35598.4 (SEQ ID NOs: 74 and 501), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002804] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35604.4 (SEQ ID NOs: 75 and 502), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002805] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35610.4 (SEQ ID NOs: 76 and 503), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002806] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35616.4 (SEQ ID NOs: 77 and 504), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002807] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35575.4 (SEQ ID NOs: 78 and 505), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002808] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 79 and 506), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002809] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-35587.4 (SEQ ID NOs: 80 and 507), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002810] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35593.4 (SEQ ID NOs: 81 and 508), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002811] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35599.4 (SEQ ID NOs: 82 and 509), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002812] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35605.4 (SEQ ID NOs: 83 and 510), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002813] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35611.4 (SEQ ID NOs: 84 and 511), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002814] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35617.4 (SEQ ID NOs: 85 and 512), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002815] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 86 and 513), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002816] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 87 and 514), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002817] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35667.1 (SEQ ID NOs: 88 and 515), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002818] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35673.1 (SEQ ID NOs: 89 and 516), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002819] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35679.1 (SEQ ID NOs:

90 and 517), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002820] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35685.1 (SEQ ID NOs: 91 and 518), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002821] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35691.1 (SEQ ID NOs: 92 and 519), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002822] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35557.1 (SEQ ID NOs: 93 and 520), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002823] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35618.1 (SEQ ID NOs: 94 and 521), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002824] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35569.1 (SEQ ID NOs: 95 and 522), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002825] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35534.1 (SEQ ID NOs: 96 and 523), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002826] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35582.1 (SEQ ID NOs: 97 and 524), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002827] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35594.1 (SEQ ID NOs: 98 and 525), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002828] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 99 and 526), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002829] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35606.1 (SEQ ID NOs: 100 and 527), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002830] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35612.1 (SEQ ID NOs: 101 and 528), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002831] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38127.1 (SEQ ID NOs: 102 and 529), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002832] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38133.1 (SEQ ID NOs: 103 and 530), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002833] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38139.1 (SEQ ID NOs: 104 and 531), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002834] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38145.1 (SEQ ID NOs: 105 and 532), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002835] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 106 and 533), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002836] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38157.1 (SEQ ID NOs: 107 and 534), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002837] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 108 and 535), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002838] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38169.1 (SEQ ID NOs: 109 and 536), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002839] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38128.1 (SEQ ID NOs: 110 and 537), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002840] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38134.1 (SEQ ID NOs: 111 and 538), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002841] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38140.1 (SEQ ID NOs: 112 and 539), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002842] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38146.1 (SEQ ID NOs: 113 and 540), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002843] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38152.1 (SEQ ID NOs: 114 and 541), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002844] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38158.1 (SEQ ID NOs: 115 and 542), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002845] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38164.1 (SEQ ID NOs: 116 and 543), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002846] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38170.1 (SEQ ID NOs: 117 and 544), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002847] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38129.1 (SEQ ID NOs: 118 and 545), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002848] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38135.1 (SEQ ID NOs: 119 and 546), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002849] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38141.1 (SEQ ID NOs: 120 and 547), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002850] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-38147.1 (SEQ ID NOs: 121 and 548), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002851] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38153.1 (SEQ ID NOs: 122 and 549), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002852] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38159.1 (SEQ ID NOs: 123 and 550), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002853] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38165.1 (SEQ ID NOs: 124 and 551), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002854] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38171.1 (SEQ ID NOs: 125 and 552), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002855] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38130.1 (SEQ ID NOs: 126 and 553), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002856] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 127 and 554), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002857] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38142.1 (SEQ ID NOs: 128 and 555), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002858] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38148.1 (SEQ ID NOs: 129 and 556), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002859] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38154.1 (SEQ ID NOs: 130 and 557), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002860] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38160.1 (SEQ ID NOs:

131 and 558), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002861] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38166.1 (SEQ ID NOs: 132 and 559), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002862] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38172.1 (SEQ ID NOs: 133 and 560), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002863] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 134 and 561), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002864] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38137.1 (SEQ ID NOs: 135 and 562), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002865] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38143.1 (SEQ ID NOs: 136 and 563), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002866] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38149.1 (SEQ ID NOs: 137 and 564), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002867] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38155.1 (SEQ ID NOs: 138 and 565), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002868] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38161.1 (SEQ ID NOs: 139 and 566), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002869] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 140 and 567), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002870] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38173.1 (SEQ ID NOs: 141 and 568), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002871] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38132.1 (SEQ ID NOs: 142 and 569), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002872] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38138.1 (SEQ ID NOs: 143 and 570), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002873] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38144.1 (SEQ ID NOs: 144 and 571), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002874] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38150.1 (SEQ ID NOs: 145 and 572), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002875] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38156.1 (SEQ ID NOs: 146 and 573), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002876] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38162.1 (SEQ ID NOs: 147 and 574), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002877] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38168.1 (SEQ ID NOs: 148 and 575), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002878] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38174.1 (SEQ ID NOs: 149 and 576), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002879] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39683.1 (SEQ ID NOs: 150 and 577), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002880] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39689.1 (SEQ ID NOs: 151 and 578), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002881] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39695.1 (SEQ ID NOs: 152 and 579), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002882] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39701.1 (SEQ ID NOs: 153 and 580), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002883] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39707.1 (SEQ ID NOs: 154 and 581), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002884] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39713.1 (SEQ ID NOs: 155 and 582), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002885] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39719.1 (SEQ ID NOs: 156 and 583), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002886] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39725.1 (SEQ ID NOs: 157 and 584), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002887] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39684.1 (SEQ ID NOs: 158 and 585), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002888] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39690.1 (SEQ ID NOs: 159 and 586), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002889] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39696.1 (SEQ ID NOs: 160 and 587), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002890] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39702.1 (SEQ ID NOs: 161 and 588), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002891] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39708.1 (SEQ ID NOs: 162 and 589), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002892] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39714.1 (SEQ ID NOs: 163 and 590), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002893] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39720.1 (SEQ ID NOs: 164 and 591), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002894] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39726.1 (SEQ ID NOs: 165 and 592), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002895] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39685.1 (SEQ ID NOs: 166 and 593), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002896] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39691.1 (SEQ ID NOs: 167 and 594), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002897] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39697.1 (SEQ ID NOs: 168 and 595), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002898] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39703.1 (SEQ ID NOs: 169 and 596), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002899] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39709.1 (SEQ ID NOs: 170 and 597), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002900] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39715.1 (SEQ ID NOs: 171 and 598), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002901] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39721.1 (SEQ ID NOs:

172 and 599), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002902] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39727.1 (SEQ ID NOs: 173 and 600), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002903] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39686.1 (SEQ ID NOs: 174 and 601), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002904] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39692.1 (SEQ ID NOs: 175 and 602), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002905] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39698.1 (SEQ ID NOs: 176 and 603), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002906] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39704.1 (SEQ ID NOs: 177 and 604), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002907] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39710.1 (SEQ ID NOs: 178 and 605), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002908] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39716.1 (SEQ ID NOs: 179 and 606), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002909] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39722.1 (SEQ ID NOs: 180 and 607), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002910] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39728.1 (SEQ ID NOs: 181 and 608), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002911] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39687.1 (SEQ ID NOs: 182 and 609), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002912] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39693.1 (SEQ ID NOs: 183 and 610), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002913] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39699.1 (SEQ ID NOs: 184 and 611), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002914] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39705.1 (SEQ ID NOs: 185 and 612), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002915] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39711.1 (SEQ ID NOs: 186 and 613), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002916] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39717.1 (SEQ ID NOs: 187 and 614), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002917] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39723.1 (SEQ ID NOs: 188 and 615), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002918] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39729.1 (SEQ ID NOs: 189 and 616), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002919] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39688.1 (SEQ ID NOs: 190 and 617), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002920] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39694.1 (SEQ ID NOs: 191 and 618), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002921] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39700.1 (SEQ ID NOs: 192 and 619), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002922] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 193 and 620), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002923] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 194 and 621), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002924] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39718.1 (SEQ ID NOs: 195 and 622), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002925] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39724.1 (SEQ ID NOs: 196 and 623), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002926] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39730.1 (SEQ ID NOs: 197 and 624), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002927] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39736.1 (SEQ ID NOs: 198 and 625), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002928] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39742.1 (SEQ ID NOs: 199 and 626), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002929] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39748.1 (SEQ ID NOs: 200 and 627), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002930] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39754.1 (SEQ ID NOs: 201 and 628), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002931] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 202 and 629), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002932] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39766.1 (SEQ ID NOs: 203 and 630), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002933] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39772.1 (SEQ ID NOs: 204 and 631), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002934] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39731.1 (SEQ ID NOs: 205 and 632), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002935] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39737.1 (SEQ ID NOs: 206 and 633), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002936] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39743.1 (SEQ ID NOs: 207 and 634), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002937] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39749.1 (SEQ ID NOs: 208 and 635), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002938] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39755.1 (SEQ ID NOs: 209 and 636), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002939] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39761.1 (SEQ ID NOs: 210 and 637), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002940] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39767.1 (SEQ ID NOs: 211 and 638), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002941] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39773.1 (SEQ ID NOs: 212 and 639), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002942] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39732.1 (SEQ ID NOs:

213 and 640), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002943] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39738.1 (SEQ ID NOs: 214 and 641), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002944] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39744.1 (SEQ ID NOs: 215 and 642), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002945] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39750.1 (SEQ ID NOs: 216 and 643), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002946] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39756.1 (SEQ ID NOs: 217 and 644), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002947] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39762.1 (SEQ ID NOs: 218 and 645), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002948] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39768.1 (SEQ ID NOs: 219 and 646), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002949] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39774.1 (SEQ ID NOs: 220 and 647), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002950] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39733.1 (SEQ ID NOs: 221 and 648), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002951] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39739.1 (SEQ ID NOs: 222 and 649), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002952] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39745.1 (SEQ ID NOs: 223 and 650), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002953] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39751.1 (SEQ ID NOs: 224 and 651), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002954] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39757.1 (SEQ ID NOs: 225 and 652), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002955] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39763.1 (SEQ ID NOs: 226 and 653), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002956] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39769.1 (SEQ ID NOs: 227 and 654), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002957] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39775.1 (SEQ ID NOs: 228 and 655), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002958] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39734.1 (SEQ ID NOs: 229 and 656), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002959] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39740.1 (SEQ ID NOs: 230 and 657), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002960] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39746.1 (SEQ ID NOs: 231 and 658), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002961] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39752.1 (SEQ ID NOs: 232 and 659), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002962] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39758.1 (SEQ ID NOs: 233 and 660), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002963] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39764.1 (SEQ ID NOs: 234 and 661), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002964] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39770.1 (SEQ ID NOs: 235 and 662), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002965] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39776.1 (SEQ ID NOs: 236 and 663), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002966] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39735.1 (SEQ ID NOs: 237 and 664), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002967] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39741.1 (SEQ ID NOs: 238 and 665), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002968] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39747.1 (SEQ ID NOs: 239 and 666), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002969] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39753.1 (SEQ ID NOs: 240 and 667), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002970] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39759.1 (SEQ ID NOs: 241 and 668), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002971] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39765.1 (SEQ ID NOs: 242 and 669), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002972] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39771.1 (SEQ ID NOs: 243 and 670), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002973] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 244 and 671), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002974] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39784.1 (SEQ ID NOs: 245 and 672), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002975] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39790.1 (SEQ ID NOs: 246 and 673), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002976] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39796.1 (SEQ ID NOs: 247 and 674), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002977] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39802.1 (SEQ ID NOs: 248 and 675), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002978] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39808.1 (SEQ ID NOs: 249 and 676), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002979] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39814.1 (SEQ ID NOs: 250 and 677), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002980] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39820.1 (SEQ ID NOs: 251 and 678), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002981] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39779.1 (SEQ ID NOs: 252 and 679), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002982] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39785.1 (SEQ ID NOs: 253 and 680), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002983] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39791.1 (SEQ ID NOs:

254 and 681), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002984] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39797.1 (SEQ ID NOs: 255 and 682), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002985] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39803.1 (SEQ ID NOs: 256 and 683), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002986] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39809.1 (SEQ ID NOs: 257 and 684), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002987] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39815.1 (SEQ ID NOs: 258 and 685), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002988] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39821.1 (SEQ ID NOs: 259 and 686), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002989] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39780.1 (SEQ ID NOs: 260 and 687), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002990] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39786.1 (SEQ ID NOs: 261 and 688), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002991] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39792.1 (SEQ ID NOs: 262 and 689), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002992] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39798.1 (SEQ ID NOs: 263 and 690), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002993] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39804.1 (SEQ ID NOs: 264 and 691), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[002994] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39810.1 (SEQ ID NOs: 265 and 692), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002995] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39816.1 (SEQ ID NOs: 266 and 693), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002996] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 267 and 694), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002997] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39781.1 (SEQ ID NOs: 268 and 695), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002998] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39787.1 (SEQ ID NOs: 269 and 696), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[002999] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39793.1 (SEQ ID NOs: 270 and 697), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003000] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39799.1 (SEQ ID NOs: 271 and 698), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003001] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39805.1 (SEQ ID NOs: 272 and 699), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003002] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39811.1 (SEQ ID NOs: 273 and 700), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003003] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39817.1 (SEQ ID NOs: 274 and 701), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003004] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39823.1 (SEQ ID NOs: 275 and 702), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003005] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39782.1 (SEQ ID NOs: 276 and 703), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003006] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39788.1 (SEQ ID NOs: 277 and 704), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003007] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39794.1 (SEQ ID NOs: 278 and 705), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003008] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39800.1 (SEQ ID NOs: 279 and 706), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003009] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39806.1 (SEQ ID NOs: 280 and 707), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003010] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39812.1 (SEQ ID NOs: 281 and 708), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003011] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39818.1 (SEQ ID NOs: 282 and 709), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003012] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39824.1 (SEQ ID NOs: 283 and 710), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003013] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39783.1 (SEQ ID NOs: 284 and 711), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003014] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39789.1 (SEQ ID NOs: 285 and 712), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003015] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39795.1 (SEQ ID NOs: 286 and 713), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003016] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39801.1 (SEQ ID NOs: 287 and 714), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003017] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39807.1 (SEQ ID NOs: 288 and 715), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003018] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39813.1 (SEQ ID NOs: 289 and 716), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003019] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39819.1 (SEQ ID NOs: 290 and 717), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003020] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39825.1 (SEQ ID NOs: 291 and 718), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003021] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39831.1 (SEQ ID NOs: 292 and 719), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003022] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39837.1 (SEQ ID NOs: 293 and 720), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003023] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39843.1 (SEQ ID NOs: 294 and 721), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003024] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39849.1 (SEQ ID NOs:

295 and 722), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003025] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39855.1 (SEQ ID NOs: 296 and 723), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003026] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39861.1 (SEQ ID NOs: 297 and 724), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003027] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39867.1 (SEQ ID NOs: 298 and 725), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003028] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39826.1 (SEQ ID NOs: 299 and 726), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003029] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39832.1 (SEQ ID NOs: 300 and 727), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003030] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39838.1 (SEQ ID NOs: 301 and 728), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003031] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39844.1 (SEQ ID NOs: 302 and 729), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003032] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39850.1 (SEQ ID NOs: 303 and 730), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003033] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39856.1 (SEQ ID NOs: 304 and 731), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003034] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39862.1 (SEQ ID NOs: 305 and 732), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[003035] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39868.1 (SEQ ID NOs: 306 and 733), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003036] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39827.1 (SEQ ID NOs: 307 and 734), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003037] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39833.1 (SEQ ID NOs: 308 and 735), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003038] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39839.1 (SEQ ID NOs: 309 and 736), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003039] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 310 and 737), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003040] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39851.1 (SEQ ID NOs: 311 and 738), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003041] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39857.1 (SEQ ID NOs: 312 and 739), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003042] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39863.1 (SEQ ID NOs: 313 and 740), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003043] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39869.1 (SEQ ID NOs: 314 and 741), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003044] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39828.1 (SEQ ID NOs: 315 and 742), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003045] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39834.1 (SEQ ID NOs: 316 and 743), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003046] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39840.1 (SEQ ID NOs: 317 and 744), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003047] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39846.1 (SEQ ID NOs: 318 and 745), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003048] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39852.1 (SEQ ID NOs: 319 and 746), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003049] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 320 and 747), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003050] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39864.1 (SEQ ID NOs: 321 and 748), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003051] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 322 and 749), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003052] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39829.1 (SEQ ID NOs: 323 and 750), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003053] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39835.1 (SEQ ID NOs: 324 and 751), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003054] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39841.1 (SEQ ID NOs: 325 and 752), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003055] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39853.1 (SEQ ID NOs: 326 and 753), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003056] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39859.1 (SEQ ID NOs: 327 and 754), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003057] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39865.1 (SEQ ID NOs: 328 and 755), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003058] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39871.1 (SEQ ID NOs: 329 and 756), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003059] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39830.1 (SEQ ID NOs: 330 and 757), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003060] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39836.1 (SEQ ID NOs: 331 and 758), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003061] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39842.1 (SEQ ID NOs: 332 and 759), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003062] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39848.1 (SEQ ID NOs: 333 and 760), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003063] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39854.1 (SEQ ID NOs: 334 and 761), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003064] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39860.1 (SEQ ID NOs: 335 and 762), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003065] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39866.1 (SEQ ID NOs:

336 and 763), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003066] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39992.1 (SEQ ID NOs: 337 and 764), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003067] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39998.1 (SEQ ID NOs: 338 and 765), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003068] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40004.1 (SEQ ID NOs: 339 and 766), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003069] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40010.1 (SEQ ID NOs: 340 and 767), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003070] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40016.1 (SEQ ID NOs: 341 and 768), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003071] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40022.1 (SEQ ID NOs: 342 and 769), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003072] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40028.1 (SEQ ID NOs: 343 and 770), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003073] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40034.1 (SEQ ID NOs: 344 and 771), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003074] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 345 and 772), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003075] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40005.1 (SEQ ID NOs: 346 and 773), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[003076] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40011.1 (SEQ ID NOs: 347 and 774), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003077] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40017.1 (SEQ ID NOs: 348 and 775), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003078] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40029.1 (SEQ ID NOs: 349 and 776), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003079] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40035.1 (SEQ ID NOs: 350 and 777), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003080] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39994.1 (SEQ ID NOs: 351 and 778), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003081] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40000.1 (SEQ ID NOs: 352 and 779), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003082] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40006.1 (SEQ ID NOs: 353 and 780), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003083] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40012.1 (SEQ ID NOs: 354 and 781), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003084] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40018.1 (SEQ ID NOs: 355 and 782), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003085] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40024.1 (SEQ ID NOs: 356 and 783), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003086] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40030.1 (SEQ ID NOs: 357 and 784), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003087] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 358 and 785), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003088] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39995.1 (SEQ ID NOs: 359 and 786), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003089] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40001.1 (SEQ ID NOs: 360 and 787), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003090] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40007.1 (SEQ ID NOs: 361 and 788), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003091] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40013.1 (SEQ ID NOs: 362 and 789), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003092] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40019.1 (SEQ ID NOs: 363 and 790), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003093] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40025.1 (SEQ ID NOs: 364 and 791), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003094] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40031.1 (SEQ ID NOs: 365 and 792), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003095] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40037.1 (SEQ ID NOs: 366 and 793), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003096] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-39996.1 (SEQ ID NOs: 367 and 794), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003097] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40002.1 (SEQ ID NOs: 368 and 795), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003098] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 369 and 796), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003099] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40014.1 (SEQ ID NOs: 370 and 797), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003100] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40020.1 (SEQ ID NOs: 371 and 798), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003101] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40026.1 (SEQ ID NOs: 372 and 799), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003102] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40032.1 (SEQ ID NOs: 373 and 800), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003103] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40038.1 (SEQ ID NOs: 374 and 801), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003104] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39997.1 (SEQ ID NOs: 375 and 802), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003105] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40009.1 (SEQ ID NOs: 376 and 803), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003106] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40015.1 (SEQ ID NOs:

377 and 804), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003107] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 378 and 805), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003108] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40027.1 (SEQ ID NOs: 379 and 806), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003109] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40033.1 (SEQ ID NOs: 380 and 807), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003110] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40039.1 (SEQ ID NOs: 381 and 808), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003111] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40045.1 (SEQ ID NOs: 382 and 809), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003112] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40051.1 (SEQ ID NOs: 383 and 810), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003113] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40057.1 (SEQ ID NOs: 384 and 811), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003114] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40063.1 (SEQ ID NOs: 385 and 812), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003115] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40069.1 (SEQ ID NOs: 386 and 813), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003116] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40075.1 (SEQ ID NOs: 387 and 814), or modified or unmodified variants thereof, wherein the first and/or second strand

further comprise up to about 20 additional nucleotides.

[003117] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40081.1 (SEQ ID NOs: 388 and 815), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003118] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40040.1 (SEQ ID NOs: 389 and 816), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003119] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40046.1 (SEQ ID NOs: 390 and 817), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003120] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40052.1 (SEQ ID NOs: 391 and 818), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003121] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40058.1 (SEQ ID NOs: 392 and 819), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003122] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40064.1 (SEQ ID NOs: 393 and 820), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003123] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40070.1 (SEQ ID NOs: 394 and 821), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003124] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40076.1 (SEQ ID NOs: 395 and 822), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003125] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40082.1 (SEQ ID NOs: 396 and 823), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003126] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40041.1 (SEQ ID NOs: 397 and 824), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003127] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40047.1 (SEQ ID NOs: 398 and 825), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003128] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40053.1 (SEQ ID NOs: 399 and 826), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003129] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40059.1 (SEQ ID NOs: 400 and 827), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003130] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40065.1 (SEQ ID NOs: 401 and 828), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003131] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40071.1 (SEQ ID NOs: 402 and 829), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003132] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40077.1 (SEQ ID NOs: 403 and 830), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003133] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40083.1 (SEQ ID NOs: 404 and 831), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003134] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40042.1 (SEQ ID NOs: 405 and 832), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003135] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40048.1 (SEQ ID NOs: 406 and 833), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003136] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40054.1 (SEQ ID NOs: 407 and 834), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003137] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand is the sequence of a first and/or second strand of: AD-40060.1 (SEQ ID NOs: 408 and 835), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003138] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40066.1 (SEQ ID NOs: 409 and 836), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003139] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 410 and 837), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003140] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40078.1 (SEQ ID NOs: 411 and 838), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003141] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40084.1 (SEQ ID NOs: 412 and 839), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003142] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40043.1 (SEQ ID NOs: 413 and 840), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003143] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40049.1 (SEQ ID NOs: 414 and 841), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003144] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40055.1 (SEQ ID NOs: 415 and 842), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003145] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 416 and 843), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003146] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40067.1 (SEQ ID NOs: 417 and 844), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003147] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40073.1 (SEQ ID NOs:

418 and 845), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003148] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40079.1 (SEQ ID NOs: 419 and 846), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003149] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40085.1 (SEQ ID NOs: 420 and 847), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003150] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40044.1 (SEQ ID NOs: 421 and 848), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003151] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40050.1 (SEQ ID NOs: 422 and 849), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003152] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40056.1 (SEQ ID NOs: 423 and 850), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003153] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40062.1 (SEQ ID NOs: 424 and 851), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003154] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 425 and 852), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003155] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40074.1 (SEQ ID NOs: 426 and 853), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003156] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40080.1 (SEQ ID NOs: 427 and 854), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003157] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39720.1 (SEQ ID NOs:

1716 and 1754), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003158] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 1717 and 1755), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003159] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 1718 and 1756), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003160] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 1719 and 1757), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003161] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39732.1 (SEQ ID NOs: 1720 and 1758), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003162] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 1721 and 1759), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003163] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39735.1 or hs_KRAS_321_A22S26 (SEQ ID NOs: 1722 and 1760), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003164] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39741.1, or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003165] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1723 and 1761), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003166] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 1724 and 1762), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003167] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39790.1 (SEQ ID NOs:

1725 and 1763), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003168] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 1726 and 1764), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003169] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 1727 and 1765), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003170] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 1728 and 1766), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003171] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 1729 and 1767), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003172] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 1730 and 1768), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003173] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 1731 and 1769), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003174] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 1732 and 1770), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003175] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 1733 and 1771), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003176] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 1734 and 1772), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003177] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-35606.1 (SEQ ID NOs:

1735 and 1773), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003178] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 1736 and 1774), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003179] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 1737 and 1775), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003180] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 1738 and 1776), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003181] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38159.1 or hs_KRAS_528_A22S26 (SEQ ID NOs: 1739 and 1777), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003182] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38130.1 or hs_KRAS_531_A22S26 (SEQ ID NOs: 1740 and 1778), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003183] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 1741 and 1779), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003184] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 1742 and 1780), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003185] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 1743 and 1781), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003186] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 1744 and 1782), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003187] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40077.1 (SEQ ID NOs:

1745 and 1783), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003188] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 1746 and 1784), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003189] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 1747 and 1785), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003190] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 1748 and 1786), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003191] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 1749 and 1787), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003192] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 1750 and 1788), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003193] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1751 and 1789), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003194] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1752 and 1790), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003195] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand is the sequence of a first and/or second strand of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1753 and 1791), or modified or unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[003196]

[003197] In various embodiments, the disclosure comprises a RNAi agent comprising a sense and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the antisense strand of any RNAi agent disclosed herein, or modified or unmodified variants thereof, wherein the antisense strand optionally further comprises 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more nt (or any range thereof, e.g., 0-1, 1-2, 1-3, 1-4 nt, etc.).

[003198] In one embodiment, the disclosure comprises any one or more RNAi agent listed herein.

[003199] Specific embodiments wherein the sequences of the first and/or second strands are the sequences of the first and/or second strand of a RNAi agent disclosed herein, further comprising up to about 20 additional nucleotides

[003200] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of any RNAi agent from any of Tables 1 to 6, or modified and unmodified variants thereof.

[003201] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[003202] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35523.3 (SEQ ID NOs: 1 and 428), or a modified or unmodified variant thereof.

[003203] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35529.1 (SEQ ID NOs: 2 and 429), or a modified or unmodified variant thereof.

[003204] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35535.4 (SEQ ID NOs: 3 and 430), or a modified or unmodified variant thereof.

[003205] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 4 and 431), or a modified or unmodified variant thereof.

[003206] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35547.4 (SEQ ID NOs: 5 and 432), or a modified or unmodified variant thereof.

[003207] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35553.4 (SEQ ID NOs: 6 and 433), or a modified or unmodified variant thereof.

[003208] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35559.4 (SEQ ID NOs: 7 and 434), or a modified or unmodified variant thereof.

[003209] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35565.4 (SEQ ID NOs: 8 and 435), or a modified or unmodified variant thereof.

[003210] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35524.4 (SEQ ID NOs: 9 and 436), or a modified or unmodified variant thereof.

[003211] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35530.4 (SEQ ID NOs: 10 and 437), or a modified or unmodified variant thereof.

[003212] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35536.4 (SEQ ID NOs: 11 and 438), or a modified or unmodified variant thereof.

[003213] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35542.4 (SEQ ID NOs: 12 and 439), or a modified or unmodified variant thereof.

[003214] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35548.4 (SEQ ID NOs: 13 and 440), or a modified or unmodified variant thereof.

[003215] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35554.4 (SEQ ID NOs: 14 and 441), or a modified or unmodified variant thereof.

[003216] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35560.2 (SEQ ID NOs: 15 and 442), or a modified or unmodified variant thereof.

[003217] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35566.4 (SEQ ID NOs: 16 and 443), or a modified or unmodified variant thereof.

[003218] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35525.2 (SEQ ID NOs: 17 and 444), or a modified or unmodified variant thereof.

[003219] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35531.4 (SEQ ID NOs: 18 and 445), or a modified or unmodified variant thereof.

[003220] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35537.4 (SEQ ID NOs: 19 and 446), or a modified or unmodified variant thereof.

[003221] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35543.2 (SEQ ID NOs: 20 and 447), or a modified or unmodified variant thereof.

[003222] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35549.4 (SEQ ID NOs: 21 and 448), or a modified or unmodified variant thereof.

[003223] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35555.4 (SEQ ID NOs: 22 and 449), or a modified or unmodified variant thereof.

[003224] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35561.4 (SEQ ID NOs: 23 and 450), or a modified or unmodified variant thereof.

[003225] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35567.4 (SEQ ID NOs: 24 and 451), or a modified or unmodified variant thereof.

[003226] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35526.4 (SEQ ID NOs: 25 and 452), or a modified or unmodified variant thereof.

[003227] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35532.4 (SEQ ID NOs: 26 and 453), or a modified or unmodified variant thereof.

[003228] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35538.4 (SEQ ID NOs: 27 and 454), or a modified or unmodified variant thereof.

[003229] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-35544.4 (SEQ ID NOs: 28 and 455), or a modified or unmodified variant thereof.

[003230] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35550.4 (SEQ ID NOs: 29 and 456), or a modified or unmodified variant thereof.

[003231] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35556.4 (SEQ ID NOs: 30 and 457), or a modified or unmodified variant thereof.

[003232] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35562.4 (SEQ ID NOs: 31 and 458), or a modified or unmodified variant thereof.

[003233] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35568.4 (SEQ ID NOs: 32 and 459), or a modified or unmodified variant thereof.

[003234] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35527.4 (SEQ ID NOs: 33 and 460), or a modified or unmodified variant thereof.

[003235] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35533.4 (SEQ ID NOs: 34 and 461), or a modified or unmodified variant thereof.

[003236] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35539.4 (SEQ ID NOs: 35 and 462), or a modified or unmodified variant thereof.

[003237] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35545.4 (SEQ ID NOs: 36 and 463), or a modified or unmodified variant thereof.

[003238] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35551.4 (SEQ ID NOs: 37 and 464), or a modified or unmodified variant thereof.

[003239] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35563.4 (SEQ ID NOs: 38 and 465), or a modified or unmodified variant

thereof.

[003240] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35528.4 (SEQ ID NOs: 39 and 466), or a modified or unmodified variant thereof.

[003241] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35540.4 (SEQ ID NOs: 40 and 467), or a modified or unmodified variant thereof.

[003242] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35546.4 (SEQ ID NOs: 41 and 468), or a modified or unmodified variant thereof.

[003243] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35552.4 (SEQ ID NOs: 42 and 469), or a modified or unmodified variant thereof.

[003244] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35558.4 (SEQ ID NOs: 43 and 470), or a modified or unmodified variant thereof.

[003245] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35564.4 (SEQ ID NOs: 44 and 471), or a modified or unmodified variant thereof.

[003246] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35570.4 (SEQ ID NOs: 45 and 472), or a modified or unmodified variant thereof.

[003247] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35571.4 (SEQ ID NOs: 46 and 473), or a modified or unmodified variant thereof.

[003248] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35577.4 (SEQ ID NOs: 47 and 474), or a modified or unmodified variant thereof.

[003249] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35583.4 (SEQ ID NOs: 48 and 475), or a modified or unmodified variant thereof.

[003250] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35589.4 (SEQ ID NOs: 49 and 476), or a modified or unmodified variant thereof.

[003251] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35595.4 (SEQ ID NOs: 50 and 477), or a modified or unmodified variant thereof.

[003252] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35601.4 (SEQ ID NOs: 51 and 478), or a modified or unmodified variant thereof.

[003253] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35607.4 (SEQ ID NOs: 52 and 479), or a modified or unmodified variant thereof.

[003254] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35613.4 (SEQ ID NOs: 53 and 480), or a modified or unmodified variant thereof.

[003255] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35572.4 (SEQ ID NOs: 54 and 481), or a modified or unmodified variant thereof.

[003256] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35578.4 (SEQ ID NOs: 55 and 482), or a modified or unmodified variant thereof.

[003257] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35584.4 (SEQ ID NOs: 56 and 483), or a modified or unmodified variant thereof.

[003258] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35590.4 (SEQ ID NOs: 57 and 484), or a modified or unmodified variant thereof.

[003259] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35596.4 (SEQ ID NOs: 58 and 485), or a modified or unmodified variant thereof.

[003260] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35602.4 (SEQ ID NOs: 59 and 486), or a modified or unmodified variant thereof.

[003261] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35608.4 (SEQ ID NOs: 60 and 487), or a modified or unmodified variant thereof.

[003262] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35614.4 (SEQ ID NOs: 61 and 488), or a modified or unmodified variant thereof.

[003263] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35573.4 (SEQ ID NOs: 62 and 489), or a modified or unmodified variant thereof.

[003264] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35579.4 (SEQ ID NOs: 63 and 490), or a modified or unmodified variant thereof.

[003265] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35585.4 (SEQ ID NOs: 64 and 491), or a modified or unmodified variant thereof.

[003266] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35591.4 (SEQ ID NOs: 65 and 492), or a modified or unmodified variant thereof.

[003267] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35597.4 (SEQ ID NOs: 66 and 493), or a modified or unmodified variant thereof.

[003268] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35603.4 (SEQ ID NOs: 67 and 494), or a modified or unmodified variant thereof.

[003269] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 68 and 495), or a modified or unmodified variant thereof.

[003270] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-35615.4 (SEQ ID NOs: 69 and 496), or a modified or unmodified variant thereof.

[003271] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35574.4 (SEQ ID NOs: 70 and 497), or a modified or unmodified variant thereof.

[003272] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35580.1 (SEQ ID NOs: 71 and 498), or a modified or unmodified variant thereof.

[003273] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35586.4 (SEQ ID NOs: 72 and 499), or a modified or unmodified variant thereof.

[003274] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35592.4 (SEQ ID NOs: 73 and 500), or a modified or unmodified variant thereof.

[003275] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35598.4 (SEQ ID NOs: 74 and 501), or a modified or unmodified variant thereof.

[003276] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35604.4 (SEQ ID NOs: 75 and 502), or a modified or unmodified variant thereof.

[003277] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35610.4 (SEQ ID NOs: 76 and 503), or a modified or unmodified variant thereof.

[003278] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35616.4 (SEQ ID NOs: 77 and 504), or a modified or unmodified variant thereof.

[003279] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35575.4 (SEQ ID NOs: 78 and 505), or a modified or unmodified variant thereof.

[003280] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 79 and 506), or a modified or unmodified variant

thereof.

[003281] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35587.4 (SEQ ID NOs: 80 and 507), or a modified or unmodified variant thereof.

[003282] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35593.4 (SEQ ID NOs: 81 and 508), or a modified or unmodified variant thereof.

[003283] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35599.4 (SEQ ID NOs: 82 and 509), or a modified or unmodified variant thereof.

[003284] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35605.4 (SEQ ID NOs: 83 and 510), or a modified or unmodified variant thereof.

[003285] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35611.4 (SEQ ID NOs: 84 and 511), or a modified or unmodified variant thereof.

[003286] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35617.4 (SEQ ID NOs: 85 and 512), or a modified or unmodified variant thereof.

[003287] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 86 and 513), or a modified or unmodified variant thereof.

[003288] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 87 and 514), or a modified or unmodified variant thereof.

[003289] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35667.1 (SEQ ID NOs: 88 and 515), or a modified or unmodified variant thereof.

[003290] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35673.1 (SEQ ID NOs: 89 and 516), or a modified or unmodified variant thereof.

[003291] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35679.1 (SEQ ID NOs: 90 and 517), or a modified or unmodified variant thereof.

[003292] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35685.1 (SEQ ID NOs: 91 and 518), or a modified or unmodified variant thereof.

[003293] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35691.1 (SEQ ID NOs: 92 and 519), or a modified or unmodified variant thereof.

[003294] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35557.1 (SEQ ID NOs: 93 and 520), or a modified or unmodified variant thereof.

[003295] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35618.1 (SEQ ID NOs: 94 and 521), or a modified or unmodified variant thereof.

[003296] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35569.1 (SEQ ID NOs: 95 and 522), or a modified or unmodified variant thereof.

[003297] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35534.1 (SEQ ID NOs: 96 and 523), or a modified or unmodified variant thereof.

[003298] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35582.1 (SEQ ID NOs: 97 and 524), or a modified or unmodified variant thereof.

[003299] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35594.1 (SEQ ID NOs: 98 and 525), or a modified or unmodified variant thereof.

[003300] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 99 and 526), or a modified or unmodified variant thereof.

[003301] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35606.1 (SEQ ID NOs: 100 and 527), or a modified or unmodified variant thereof.

[003302] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35612.1 (SEQ ID NOs: 101 and 528), or a modified or unmodified variant thereof.

[003303] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38127.1 (SEQ ID NOs: 102 and 529), or a modified or unmodified variant thereof.

[003304] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38133.1 (SEQ ID NOs: 103 and 530), or a modified or unmodified variant thereof.

[003305] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38139.1 (SEQ ID NOs: 104 and 531), or a modified or unmodified variant thereof.

[003306] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38145.1 (SEQ ID NOs: 105 and 532), or a modified or unmodified variant thereof.

[003307] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 106 and 533), or a modified or unmodified variant thereof.

[003308] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38157.1 (SEQ ID NOs: 107 and 534), or a modified or unmodified variant thereof.

[003309] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 108 and 535), or a modified or unmodified variant thereof.

[003310] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38169.1 (SEQ ID NOs: 109 and 536), or a modified or unmodified variant thereof.

[003311] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-38128.1 (SEQ ID NOs: 110 and 537), or a modified or unmodified variant thereof.

[003312] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38134.1 (SEQ ID NOs: 111 and 538), or a modified or unmodified variant thereof.

[003313] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38140.1 (SEQ ID NOs: 112 and 539), or a modified or unmodified variant thereof.

[003314] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38146.1 (SEQ ID NOs: 113 and 540), or a modified or unmodified variant thereof.

[003315] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38152.1 (SEQ ID NOs: 114 and 541), or a modified or unmodified variant thereof.

[003316] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38158.1 (SEQ ID NOs: 115 and 542), or a modified or unmodified variant thereof.

[003317] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38164.1 (SEQ ID NOs: 116 and 543), or a modified or unmodified variant thereof.

[003318] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38170.1 (SEQ ID NOs: 117 and 544), or a modified or unmodified variant thereof.

[003319] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38129.1 (SEQ ID NOs: 118 and 545), or a modified or unmodified variant thereof.

[003320] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38135.1 (SEQ ID NOs: 119 and 546), or a modified or unmodified variant thereof.

[003321] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38141.1 (SEQ ID NOs: 120 and 547), or a modified or unmodified variant

thereof.

[003322] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38147.1 (SEQ ID NOs: 121 and 548), or a modified or unmodified variant thereof.

[003323] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38153.1 (SEQ ID NOs: 122 and 549), or a modified or unmodified variant thereof.

[003324] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38159.1 (SEQ ID NOs: 123 and 550), or a modified or unmodified variant thereof.

[003325] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38165.1 (SEQ ID NOs: 124 and 551), or a modified or unmodified variant thereof.

[003326] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38171.1 (SEQ ID NOs: 125 and 552), or a modified or unmodified variant thereof.

[003327] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38130.1 (SEQ ID NOs: 126 and 553), or a modified or unmodified variant thereof.

[003328] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 127 and 554), or a modified or unmodified variant thereof.

[003329] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38142.1 (SEQ ID NOs: 128 and 555), or a modified or unmodified variant thereof.

[003330] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38148.1 (SEQ ID NOs: 129 and 556), or a modified or unmodified variant thereof.

[003331] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38154.1 (SEQ ID NOs: 130 and 557), or a modified or unmodified variant thereof.

[003332] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38160.1 (SEQ ID NOs: 131 and 558), or a modified or unmodified variant thereof.

[003333] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38166.1 (SEQ ID NOs: 132 and 559), or a modified or unmodified variant thereof.

[003334] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38172.1 (SEQ ID NOs: 133 and 560), or a modified or unmodified variant thereof.

[003335] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 134 and 561), or a modified or unmodified variant thereof.

[003336] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38137.1 (SEQ ID NOs: 135 and 562), or a modified or unmodified variant thereof.

[003337] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38143.1 (SEQ ID NOs: 136 and 563), or a modified or unmodified variant thereof.

[003338] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38149.1 (SEQ ID NOs: 137 and 564), or a modified or unmodified variant thereof.

[003339] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38155.1 (SEQ ID NOs: 138 and 565), or a modified or unmodified variant thereof.

[003340] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38161.1 (SEQ ID NOs: 139 and 566), or a modified or unmodified variant thereof.

[003341] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 140 and 567), or a modified or unmodified variant thereof.

[003342] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38173.1 (SEQ ID NOs: 141 and 568), or a modified or unmodified variant thereof.

[003343] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38132.1 (SEQ ID NOs: 142 and 569), or a modified or unmodified variant thereof.

[003344] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38138.1 (SEQ ID NOs: 143 and 570), or a modified or unmodified variant thereof.

[003345] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38144.1 (SEQ ID NOs: 144 and 571), or a modified or unmodified variant thereof.

[003346] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38150.1 (SEQ ID NOs: 145 and 572), or a modified or unmodified variant thereof.

[003347] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38156.1 (SEQ ID NOs: 146 and 573), or a modified or unmodified variant thereof.

[003348] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38162.1 (SEQ ID NOs: 147 and 574), or a modified or unmodified variant thereof.

[003349] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38168.1 (SEQ ID NOs: 148 and 575), or a modified or unmodified variant thereof.

[003350] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38174.1 (SEQ ID NOs: 149 and 576), or a modified or unmodified variant thereof.

[003351] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39683.1 (SEQ ID NOs: 150 and 577), or a modified or unmodified variant thereof.

[003352] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39689.1 (SEQ ID NOs: 151 and 578), or a modified or unmodified variant thereof.

[003353] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39695.1 (SEQ ID NOs: 152 and 579), or a modified or unmodified variant thereof.

[003354] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39701.1 (SEQ ID NOs: 153 and 580), or a modified or unmodified variant thereof.

[003355] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39707.1 (SEQ ID NOs: 154 and 581), or a modified or unmodified variant thereof.

[003356] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39713.1 (SEQ ID NOs: 155 and 582), or a modified or unmodified variant thereof.

[003357] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39719.1 (SEQ ID NOs: 156 and 583), or a modified or unmodified variant thereof.

[003358] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39725.1 (SEQ ID NOs: 157 and 584), or a modified or unmodified variant thereof.

[003359] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39684.1 (SEQ ID NOs: 158 and 585), or a modified or unmodified variant thereof.

[003360] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39690.1 (SEQ ID NOs: 159 and 586), or a modified or unmodified variant thereof.

[003361] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39696.1 (SEQ ID NOs: 160 and 587), or a modified or unmodified variant thereof.

[003362] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39702.1 (SEQ ID NOs: 161 and 588), or a modified or unmodified variant

thereof.

[003363] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39708.1 (SEQ ID NOs: 162 and 589), or a modified or unmodified variant thereof.

[003364] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39714.1 (SEQ ID NOs: 163 and 590), or a modified or unmodified variant thereof.

[003365] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39720.1 (SEQ ID NOs: 164 and 591), or a modified or unmodified variant thereof.

[003366] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39726.1 (SEQ ID NOs: 165 and 592), or a modified or unmodified variant thereof.

[003367] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39685.1 (SEQ ID NOs: 166 and 593), or a modified or unmodified variant thereof.

[003368] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39691.1 (SEQ ID NOs: 167 and 594), or a modified or unmodified variant thereof.

[003369] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39697.1 (SEQ ID NOs: 168 and 595), or a modified or unmodified variant thereof.

[003370] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39703.1 (SEQ ID NOs: 169 and 596), or a modified or unmodified variant thereof.

[003371] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39709.1 (SEQ ID NOs: 170 and 597), or a modified or unmodified variant thereof.

[003372] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39715.1 (SEQ ID NOs: 171 and 598), or a modified or unmodified variant thereof.

[003373] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39721.1 (SEQ ID NOs: 172 and 599), or a modified or unmodified variant thereof.

[003374] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39727.1 (SEQ ID NOs: 173 and 600), or a modified or unmodified variant thereof.

[003375] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39686.1 (SEQ ID NOs: 174 and 601), or a modified or unmodified variant thereof.

[003376] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39692.1 (SEQ ID NOs: 175 and 602), or a modified or unmodified variant thereof.

[003377] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39698.1 (SEQ ID NOs: 176 and 603), or a modified or unmodified variant thereof.

[003378] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39704.1 (SEQ ID NOs: 177 and 604), or a modified or unmodified variant thereof.

[003379] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39710.1 (SEQ ID NOs: 178 and 605), or a modified or unmodified variant thereof.

[003380] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39716.1 (SEQ ID NOs: 179 and 606), or a modified or unmodified variant thereof.

[003381] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39722.1 (SEQ ID NOs: 180 and 607), or a modified or unmodified variant thereof.

[003382] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39728.1 (SEQ ID NOs: 181 and 608), or a modified or unmodified variant thereof.

[003383] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39687.1 (SEQ ID NOs: 182 and 609), or a modified or unmodified variant thereof.

[003384] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39693.1 (SEQ ID NOs: 183 and 610), or a modified or unmodified variant thereof.

[003385] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39699.1 (SEQ ID NOs: 184 and 611), or a modified or unmodified variant thereof.

[003386] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39705.1 (SEQ ID NOs: 185 and 612), or a modified or unmodified variant thereof.

[003387] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39711.1 (SEQ ID NOs: 186 and 613), or a modified or unmodified variant thereof.

[003388] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39717.1 (SEQ ID NOs: 187 and 614), or a modified or unmodified variant thereof.

[003389] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39723.1 (SEQ ID NOs: 188 and 615), or a modified or unmodified variant thereof.

[003390] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39729.1 (SEQ ID NOs: 189 and 616), or a modified or unmodified variant thereof.

[003391] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39688.1 (SEQ ID NOs: 190 and 617), or a modified or unmodified variant thereof.

[003392] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39694.1 (SEQ ID NOs: 191 and 618), or a modified or unmodified variant thereof.

[003393] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39700.1 (SEQ ID NOs: 192 and 619), or a modified or unmodified variant thereof.

[003394] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 193 and 620), or a modified or unmodified variant thereof.

[003395] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 194 and 621), or a modified or unmodified variant thereof.

[003396] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39718.1 (SEQ ID NOs: 195 and 622), or a modified or unmodified variant thereof.

[003397] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39724.1 (SEQ ID NOs: 196 and 623), or a modified or unmodified variant thereof.

[003398] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39730.1 (SEQ ID NOs: 197 and 624), or a modified or unmodified variant thereof.

[003399] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39736.1 (SEQ ID NOs: 198 and 625), or a modified or unmodified variant thereof.

[003400] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39742.1 (SEQ ID NOs: 199 and 626), or a modified or unmodified variant thereof.

[003401] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39748.1 (SEQ ID NOs: 200 and 627), or a modified or unmodified variant thereof.

[003402] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39754.1 (SEQ ID NOs: 201 and 628), or a modified or unmodified variant thereof.

[003403] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 202 and 629), or a modified or unmodified variant

thereof.

[003404] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39766.1 (SEQ ID NOs: 203 and 630), or a modified or unmodified variant thereof.

[003405] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39772.1 (SEQ ID NOs: 204 and 631), or a modified or unmodified variant thereof.

[003406] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39731.1 (SEQ ID NOs: 205 and 632), or a modified or unmodified variant thereof.

[003407] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39737.1 (SEQ ID NOs: 206 and 633), or a modified or unmodified variant thereof.

[003408] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39743.1 (SEQ ID NOs: 207 and 634), or a modified or unmodified variant thereof.

[003409] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39749.1 (SEQ ID NOs: 208 and 635), or a modified or unmodified variant thereof.

[003410] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39755.1 (SEQ ID NOs: 209 and 636), or a modified or unmodified variant thereof.

[003411] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39761.1 (SEQ ID NOs: 210 and 637), or a modified or unmodified variant thereof.

[003412] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39767.1 (SEQ ID NOs: 211 and 638), or a modified or unmodified variant thereof.

[003413] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39773.1 (SEQ ID NOs: 212 and 639), or a modified or unmodified variant thereof.

[003414] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39732.1 (SEQ ID NOs: 213 and 640), or a modified or unmodified variant thereof.

[003415] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39738.1 (SEQ ID NOs: 214 and 641), or a modified or unmodified variant thereof.

[003416] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39744.1 (SEQ ID NOs: 215 and 642), or a modified or unmodified variant thereof.

[003417] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39750.1 (SEQ ID NOs: 216 and 643), or a modified or unmodified variant thereof.

[003418] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39756.1 (SEQ ID NOs: 217 and 644), or a modified or unmodified variant thereof.

[003419] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39762.1 (SEQ ID NOs: 218 and 645), or a modified or unmodified variant thereof.

[003420] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39768.1 (SEQ ID NOs: 219 and 646), or a modified or unmodified variant thereof.

[003421] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39774.1 (SEQ ID NOs: 220 and 647), or a modified or unmodified variant thereof.

[003422] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39733.1 (SEQ ID NOs: 221 and 648), or a modified or unmodified variant thereof.

[003423] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39739.1 (SEQ ID NOs: 222 and 649), or a modified or unmodified variant thereof.

[003424] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39745.1 (SEQ ID NOs: 223 and 650), or a modified or unmodified variant thereof.

[003425] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39751.1 (SEQ ID NOs: 224 and 651), or a modified or unmodified variant thereof.

[003426] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39757.1 (SEQ ID NOs: 225 and 652), or a modified or unmodified variant thereof.

[003427] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39763.1 (SEQ ID NOs: 226 and 653), or a modified or unmodified variant thereof.

[003428] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39769.1 (SEQ ID NOs: 227 and 654), or a modified or unmodified variant thereof.

[003429] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39775.1 (SEQ ID NOs: 228 and 655), or a modified or unmodified variant thereof.

[003430] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39734.1 (SEQ ID NOs: 229 and 656), or a modified or unmodified variant thereof.

[003431] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39740.1 (SEQ ID NOs: 230 and 657), or a modified or unmodified variant thereof.

[003432] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39746.1 (SEQ ID NOs: 231 and 658), or a modified or unmodified variant thereof.

[003433] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39752.1 (SEQ ID NOs: 232 and 659), or a modified or unmodified variant thereof.

[003434] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39758.1 (SEQ ID NOs: 233 and 660), or a modified or unmodified variant thereof.

[003435] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39764.1 (SEQ ID NOs: 234 and 661), or a modified or unmodified variant thereof.

[003436] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39770.1 (SEQ ID NOs: 235 and 662), or a modified or unmodified variant thereof.

[003437] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39776.1 (SEQ ID NOs: 236 and 663), or a modified or unmodified variant thereof.

[003438] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39735.1 (SEQ ID NOs: 237 and 664), or a modified or unmodified variant thereof.

[003439] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39741.1 (SEQ ID NOs: 238 and 665), or a modified or unmodified variant thereof.

[003440] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39747.1 (SEQ ID NOs: 239 and 666), or a modified or unmodified variant thereof.

[003441] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39753.1 (SEQ ID NOs: 240 and 667), or a modified or unmodified variant thereof.

[003442] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39759.1 (SEQ ID NOs: 241 and 668), or a modified or unmodified variant thereof.

[003443] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39765.1 (SEQ ID NOs: 242 and 669), or a modified or unmodified variant thereof.

[003444] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39771.1 (SEQ ID NOs: 243 and 670), or a modified or unmodified variant

thereof.

[003445] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 244 and 671), or a modified or unmodified variant thereof.

[003446] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39784.1 (SEQ ID NOs: 245 and 672), or a modified or unmodified variant thereof.

[003447] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39790.1 (SEQ ID NOs: 246 and 673), or a modified or unmodified variant thereof.

[003448] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39796.1 (SEQ ID NOs: 247 and 674), or a modified or unmodified variant thereof.

[003449] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39802.1 (SEQ ID NOs: 248 and 675), or a modified or unmodified variant thereof.

[003450] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39808.1 (SEQ ID NOs: 249 and 676), or a modified or unmodified variant thereof.

[003451] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39814.1 (SEQ ID NOs: 250 and 677), or a modified or unmodified variant thereof.

[003452] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39820.1 (SEQ ID NOs: 251 and 678), or a modified or unmodified variant thereof.

[003453] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39779.1 (SEQ ID NOs: 252 and 679), or a modified or unmodified variant thereof.

[003454] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39785.1 (SEQ ID NOs: 253 and 680), or a modified or unmodified variant thereof.

[003455] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39791.1 (SEQ ID NOs: 254 and 681), or a modified or unmodified variant thereof.

[003456] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39797.1 (SEQ ID NOs: 255 and 682), or a modified or unmodified variant thereof.

[003457] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39803.1 (SEQ ID NOs: 256 and 683), or a modified or unmodified variant thereof.

[003458] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39809.1 (SEQ ID NOs: 257 and 684), or a modified or unmodified variant thereof.

[003459] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39815.1 (SEQ ID NOs: 258 and 685), or a modified or unmodified variant thereof.

[003460] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39821.1 (SEQ ID NOs: 259 and 686), or a modified or unmodified variant thereof.

[003461] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39780.1 (SEQ ID NOs: 260 and 687), or a modified or unmodified variant thereof.

[003462] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39786.1 (SEQ ID NOs: 261 and 688), or a modified or unmodified variant thereof.

[003463] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39792.1 (SEQ ID NOs: 262 and 689), or a modified or unmodified variant thereof.

[003464] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39798.1 (SEQ ID NOs: 263 and 690), or a modified or unmodified variant thereof.

[003465] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39804.1 (SEQ ID NOs: 264 and 691), or a modified or unmodified variant thereof.

[003466] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39810.1 (SEQ ID NOs: 265 and 692), or a modified or unmodified variant thereof.

[003467] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39816.1 (SEQ ID NOs: 266 and 693), or a modified or unmodified variant thereof.

[003468] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 267 and 694), or a modified or unmodified variant thereof.

[003469] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39781.1 (SEQ ID NOs: 268 and 695), or a modified or unmodified variant thereof.

[003470] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39787.1 (SEQ ID NOs: 269 and 696), or a modified or unmodified variant thereof.

[003471] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39793.1 (SEQ ID NOs: 270 and 697), or a modified or unmodified variant thereof.

[003472] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39799.1 (SEQ ID NOs: 271 and 698), or a modified or unmodified variant thereof.

[003473] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39805.1 (SEQ ID NOs: 272 and 699), or a modified or unmodified variant thereof.

[003474] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39811.1 (SEQ ID NOs: 273 and 700), or a modified or unmodified variant thereof.

[003475] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39817.1 (SEQ ID NOs: 274 and 701), or a modified or unmodified variant thereof.

[003476] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39823.1 (SEQ ID NOs: 275 and 702), or a modified or unmodified variant thereof.

[003477] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39782.1 (SEQ ID NOs: 276 and 703), or a modified or unmodified variant thereof.

[003478] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39788.1 (SEQ ID NOs: 277 and 704), or a modified or unmodified variant thereof.

[003479] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39794.1 (SEQ ID NOs: 278 and 705), or a modified or unmodified variant thereof.

[003480] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39800.1 (SEQ ID NOs: 279 and 706), or a modified or unmodified variant thereof.

[003481] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39806.1 (SEQ ID NOs: 280 and 707), or a modified or unmodified variant thereof.

[003482] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39812.1 (SEQ ID NOs: 281 and 708), or a modified or unmodified variant thereof.

[003483] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39818.1 (SEQ ID NOs: 282 and 709), or a modified or unmodified variant thereof.

[003484] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39824.1 (SEQ ID NOs: 283 and 710), or a modified or unmodified variant thereof.

[003485] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39783.1 (SEQ ID NOs: 284 and 711), or a modified or unmodified variant

thereof.

[003486] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39789.1 (SEQ ID NOs: 285 and 712), or a modified or unmodified variant thereof.

[003487] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39795.1 (SEQ ID NOs: 286 and 713), or a modified or unmodified variant thereof.

[003488] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39801.1 (SEQ ID NOs: 287 and 714), or a modified or unmodified variant thereof.

[003489] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39807.1 (SEQ ID NOs: 288 and 715), or a modified or unmodified variant thereof.

[003490] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39813.1 (SEQ ID NOs: 289 and 716), or a modified or unmodified variant thereof.

[003491] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39819.1 (SEQ ID NOs: 290 and 717), or a modified or unmodified variant thereof.

[003492] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39825.1 (SEQ ID NOs: 291 and 718), or a modified or unmodified variant thereof.

[003493] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39831.1 (SEQ ID NOs: 292 and 719), or a modified or unmodified variant thereof.

[003494] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39837.1 (SEQ ID NOs: 293 and 720), or a modified or unmodified variant thereof.

[003495] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39843.1 (SEQ ID NOs: 294 and 721), or a modified or unmodified variant thereof.

[003496] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39849.1 (SEQ ID NOs: 295 and 722), or a modified or unmodified variant thereof.

[003497] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39855.1 (SEQ ID NOs: 296 and 723), or a modified or unmodified variant thereof.

[003498] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39861.1 (SEQ ID NOs: 297 and 724), or a modified or unmodified variant thereof.

[003499] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39867.1 (SEQ ID NOs: 298 and 725), or a modified or unmodified variant thereof.

[003500] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39826.1 (SEQ ID NOs: 299 and 726), or a modified or unmodified variant thereof.

[003501] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39832.1 (SEQ ID NOs: 300 and 727), or a modified or unmodified variant thereof.

[003502] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39838.1 (SEQ ID NOs: 301 and 728), or a modified or unmodified variant thereof.

[003503] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39844.1 (SEQ ID NOs: 302 and 729), or a modified or unmodified variant thereof.

[003504] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39850.1 (SEQ ID NOs: 303 and 730), or a modified or unmodified variant thereof.

[003505] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39856.1 (SEQ ID NOs: 304 and 731), or a modified or unmodified variant thereof.

[003506] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39862.1 (SEQ ID NOs: 305 and 732), or a modified or unmodified variant thereof.

[003507] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39868.1 (SEQ ID NOs: 306 and 733), or a modified or unmodified variant thereof.

[003508] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39827.1 (SEQ ID NOs: 307 and 734), or a modified or unmodified variant thereof.

[003509] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39833.1 (SEQ ID NOs: 308 and 735), or a modified or unmodified variant thereof.

[003510] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39839.1 (SEQ ID NOs: 309 and 736), or a modified or unmodified variant thereof.

[003511] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 310 and 737), or a modified or unmodified variant thereof.

[003512] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39851.1 (SEQ ID NOs: 311 and 738), or a modified or unmodified variant thereof.

[003513] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39857.1 (SEQ ID NOs: 312 and 739), or a modified or unmodified variant thereof.

[003514] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39863.1 (SEQ ID NOs: 313 and 740), or a modified or unmodified variant thereof.

[003515] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39869.1 (SEQ ID NOs: 314 and 741), or a modified or unmodified variant thereof.

[003516] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39828.1 (SEQ ID NOs: 315 and 742), or a modified or unmodified variant thereof.

[003517] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39834.1 (SEQ ID NOs: 316 and 743), or a modified or unmodified variant thereof.

[003518] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39840.1 (SEQ ID NOs: 317 and 744), or a modified or unmodified variant thereof.

[003519] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39846.1 (SEQ ID NOs: 318 and 745), or a modified or unmodified variant thereof.

[003520] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39852.1 (SEQ ID NOs: 319 and 746), or a modified or unmodified variant thereof.

[003521] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 320 and 747), or a modified or unmodified variant thereof.

[003522] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39864.1 (SEQ ID NOs: 321 and 748), or a modified or unmodified variant thereof.

[003523] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 322 and 749), or a modified or unmodified variant thereof.

[003524] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39829.1 (SEQ ID NOs: 323 and 750), or a modified or unmodified variant thereof.

[003525] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39835.1 (SEQ ID NOs: 324 and 751), or a modified or unmodified variant thereof.

[003526] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39841.1 (SEQ ID NOs: 325 and 752), or a modified or unmodified variant

thereof.

[003527] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39853.1 (SEQ ID NOs: 326 and 753), or a modified or unmodified variant thereof.

[003528] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39859.1 (SEQ ID NOs: 327 and 754), or a modified or unmodified variant thereof.

[003529] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39865.1 (SEQ ID NOs: 328 and 755), or a modified or unmodified variant thereof.

[003530] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39871.1 (SEQ ID NOs: 329 and 756), or a modified or unmodified variant thereof.

[003531] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39830.1 (SEQ ID NOs: 330 and 757), or a modified or unmodified variant thereof.

[003532] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39836.1 (SEQ ID NOs: 331 and 758), or a modified or unmodified variant thereof.

[003533] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39842.1 (SEQ ID NOs: 332 and 759), or a modified or unmodified variant thereof.

[003534] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39848.1 (SEQ ID NOs: 333 and 760), or a modified or unmodified variant thereof.

[003535] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39854.1 (SEQ ID NOs: 334 and 761), or a modified or unmodified variant thereof.

[003536] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39860.1 (SEQ ID NOs: 335 and 762), or a modified or unmodified variant thereof.

[003537] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39866.1 (SEQ ID NOs: 336 and 763), or a modified or unmodified variant thereof.

[003538] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39992.1 (SEQ ID NOs: 337 and 764), or a modified or unmodified variant thereof.

[003539] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39998.1 (SEQ ID NOs: 338 and 765), or a modified or unmodified variant thereof.

[003540] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40004.1 (SEQ ID NOs: 339 and 766), or a modified or unmodified variant thereof.

[003541] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40010.1 (SEQ ID NOs: 340 and 767), or a modified or unmodified variant thereof.

[003542] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40016.1 (SEQ ID NOs: 341 and 768), or a modified or unmodified variant thereof.

[003543] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40022.1 (SEQ ID NOs: 342 and 769), or a modified or unmodified variant thereof.

[003544] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40028.1 (SEQ ID NOs: 343 and 770), or a modified or unmodified variant thereof.

[003545] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40034.1 (SEQ ID NOs: 344 and 771), or a modified or unmodified variant thereof.

[003546] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 345 and 772), or a modified or unmodified variant thereof.

[003547] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40005.1 (SEQ ID NOs: 346 and 773), or a modified or unmodified variant thereof.

[003548] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40011.1 (SEQ ID NOs: 347 and 774), or a modified or unmodified variant thereof.

[003549] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40017.1 (SEQ ID NOs: 348 and 775), or a modified or unmodified variant thereof.

[003550] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40029.1 (SEQ ID NOs: 349 and 776), or a modified or unmodified variant thereof.

[003551] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40035.1 (SEQ ID NOs: 350 and 777), or a modified or unmodified variant thereof.

[003552] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39994.1 (SEQ ID NOs: 351 and 778), or a modified or unmodified variant thereof.

[003553] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40000.1 (SEQ ID NOs: 352 and 779), or a modified or unmodified variant thereof.

[003554] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40006.1 (SEQ ID NOs: 353 and 780), or a modified or unmodified variant thereof.

[003555] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40012.1 (SEQ ID NOs: 354 and 781), or a modified or unmodified variant thereof.

[003556] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40018.1 (SEQ ID NOs: 355 and 782), or a modified or unmodified variant thereof.

[003557] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-40024.1 (SEQ ID NOs: 356 and 783), or a modified or unmodified variant thereof.

[003558] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40030.1 (SEQ ID NOs: 357 and 784), or a modified or unmodified variant thereof.

[003559] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 358 and 785), or a modified or unmodified variant thereof.

[003560] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39995.1 (SEQ ID NOs: 359 and 786), or a modified or unmodified variant thereof.

[003561] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40001.1 (SEQ ID NOs: 360 and 787), or a modified or unmodified variant thereof.

[003562] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40007.1 (SEQ ID NOs: 361 and 788), or a modified or unmodified variant thereof.

[003563] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40013.1 (SEQ ID NOs: 362 and 789), or a modified or unmodified variant thereof.

[003564] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40019.1 (SEQ ID NOs: 363 and 790), or a modified or unmodified variant thereof.

[003565] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40025.1 (SEQ ID NOs: 364 and 791), or a modified or unmodified variant thereof.

[003566] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40031.1 (SEQ ID NOs: 365 and 792), or a modified or unmodified variant thereof.

[003567] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40037.1 (SEQ ID NOs: 366 and 793), or a modified or unmodified variant

thereof.

[003568] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39996.1 (SEQ ID NOs: 367 and 794), or a modified or unmodified variant thereof.

[003569] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40002.1 (SEQ ID NOs: 368 and 795), or a modified or unmodified variant thereof.

[003570] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 369 and 796), or a modified or unmodified variant thereof.

[003571] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40014.1 (SEQ ID NOs: 370 and 797), or a modified or unmodified variant thereof.

[003572] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40020.1 (SEQ ID NOs: 371 and 798), or a modified or unmodified variant thereof.

[003573] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40026.1 (SEQ ID NOs: 372 and 799), or a modified or unmodified variant thereof.

[003574] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40032.1 (SEQ ID NOs: 373 and 800), or a modified or unmodified variant thereof.

[003575] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40038.1 (SEQ ID NOs: 374 and 801), or a modified or unmodified variant thereof.

[003576] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39997.1 (SEQ ID NOs: 375 and 802), or a modified or unmodified variant thereof.

[003577] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40009.1 (SEQ ID NOs: 376 and 803), or a modified or unmodified variant thereof.

[003578] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40015.1 (SEQ ID NOs: 377 and 804), or a modified or unmodified variant thereof.

[003579] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 378 and 805), or a modified or unmodified variant thereof.

[003580] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40027.1 (SEQ ID NOs: 379 and 806), or a modified or unmodified variant thereof.

[003581] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40033.1 (SEQ ID NOs: 380 and 807), or a modified or unmodified variant thereof.

[003582] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40039.1 (SEQ ID NOs: 381 and 808), or a modified or unmodified variant thereof.

[003583] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40045.1 (SEQ ID NOs: 382 and 809), or a modified or unmodified variant thereof.

[003584] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40051.1 (SEQ ID NOs: 383 and 810), or a modified or unmodified variant thereof.

[003585] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40057.1 (SEQ ID NOs: 384 and 811), or a modified or unmodified variant thereof.

[003586] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40063.1 (SEQ ID NOs: 385 and 812), or a modified or unmodified variant thereof.

[003587] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40069.1 (SEQ ID NOs: 386 and 813), or a modified or unmodified variant thereof.

[003588] A RNAi agent comprising a first and a second strand, wherein the sequence of the first

and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40075.1 (SEQ ID NOs: 387 and 814), or a modified or unmodified variant thereof.

[003589] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40081.1 (SEQ ID NOs: 388 and 815), or a modified or unmodified variant thereof.

[003590] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40040.1 (SEQ ID NOs: 389 and 816), or a modified or unmodified variant thereof.

[003591] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40046.1 (SEQ ID NOs: 390 and 817), or a modified or unmodified variant thereof.

[003592] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40052.1 (SEQ ID NOs: 391 and 818), or a modified or unmodified variant thereof.

[003593] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40058.1 (SEQ ID NOs: 392 and 819), or a modified or unmodified variant thereof.

[003594] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40064.1 (SEQ ID NOs: 393 and 820), or a modified or unmodified variant thereof.

[003595] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40070.1 (SEQ ID NOs: 394 and 821), or a modified or unmodified variant thereof.

[003596] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40076.1 (SEQ ID NOs: 395 and 822), or a modified or unmodified variant thereof.

[003597] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40082.1 (SEQ ID NOs: 396 and 823), or a modified or unmodified variant thereof.

[003598] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-40041.1 (SEQ ID NOs: 397 and 824), or a modified or unmodified variant thereof.

[003599] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40047.1 (SEQ ID NOs: 398 and 825), or a modified or unmodified variant thereof.

[003600] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40053.1 (SEQ ID NOs: 399 and 826), or a modified or unmodified variant thereof.

[003601] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40059.1 (SEQ ID NOs: 400 and 827), or a modified or unmodified variant thereof.

[003602] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40065.1 (SEQ ID NOs: 401 and 828), or a modified or unmodified variant thereof.

[003603] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40071.1 (SEQ ID NOs: 402 and 829), or a modified or unmodified variant thereof.

[003604] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40077.1 (SEQ ID NOs: 403 and 830), or a modified or unmodified variant thereof.

[003605] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40083.1 (SEQ ID NOs: 404 and 831), or a modified or unmodified variant thereof.

[003606] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40042.1 (SEQ ID NOs: 405 and 832), or a modified or unmodified variant thereof.

[003607] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40048.1 (SEQ ID NOs: 406 and 833), or a modified or unmodified variant thereof.

[003608] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40054.1 (SEQ ID NOs: 407 and 834), or a modified or unmodified variant

thereof.

[003609] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40060.1 (SEQ ID NOs: 408 and 835), or a modified or unmodified variant thereof.

[003610] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40066.1 (SEQ ID NOs: 409 and 836), or a modified or unmodified variant thereof.

[003611] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 410 and 837), or a modified or unmodified variant thereof.

[003612] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40078.1 (SEQ ID NOs: 411 and 838), or a modified or unmodified variant thereof.

[003613] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40084.1 (SEQ ID NOs: 412 and 839), or a modified or unmodified variant thereof.

[003614] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40043.1 (SEQ ID NOs: 413 and 840), or a modified or unmodified variant thereof.

[003615] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40049.1 (SEQ ID NOs: 414 and 841), or a modified or unmodified variant thereof.

[003616] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40055.1 (SEQ ID NOs: 415 and 842), or a modified or unmodified variant thereof.

[003617] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 416 and 843), or a modified or unmodified variant thereof.

[003618] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40067.1 (SEQ ID NOs: 417 and 844), or a modified or unmodified variant thereof.

[003619] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40073.1 (SEQ ID NOs: 418 and 845), or a modified or unmodified variant thereof.

[003620] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40079.1 (SEQ ID NOs: 419 and 846), or a modified or unmodified variant thereof.

[003621] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40085.1 (SEQ ID NOs: 420 and 847), or a modified or unmodified variant thereof.

[003622] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40044.1 (SEQ ID NOs: 421 and 848), or a modified or unmodified variant thereof.

[003623] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40050.1 (SEQ ID NOs: 422 and 849), or a modified or unmodified variant thereof.

[003624] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40056.1 (SEQ ID NOs: 423 and 850), or a modified or unmodified variant thereof.

[003625] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40062.1 (SEQ ID NOs: 424 and 851), or a modified or unmodified variant thereof.

[003626] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 425 and 852), or a modified or unmodified variant thereof.

[003627] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40074.1 (SEQ ID NOs: 426 and 853), or a modified or unmodified variant thereof.

[003628] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40080.1 (SEQ ID NOs: 427 and 854), or a modified or unmodified variant thereof.

[003629] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39720.1 (SEQ ID NOs: 1716 and 1754), or a modified or unmodified variant thereof.

[003630] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39706.1 (SEQ ID NOs: 1717 and 1755), or a modified or unmodified variant thereof.

[003631] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39712.1 (SEQ ID NOs: 1718 and 1756), or a modified or unmodified variant thereof.

[003632] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39760.1 (SEQ ID NOs: 1719 and 1757), or a modified or unmodified variant thereof.

[003633] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39732.1 (SEQ ID NOs: 1720 and 1758), or a modified or unmodified variant thereof.

[003634] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35541.4 (SEQ ID NOs: 1721 and 1759), or a modified or unmodified variant thereof.

[003635] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39735.1 or hs_KRAS_ 321_A22S26 (SEQ ID NOs: 1722 and 1760), or a modified or unmodified variant thereof.

[003636] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39741.1, or a modified or unmodified variant thereof.

[003637] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: hs_KRAS_ 322_A22S26 (SEQ ID NOs: 1723 and 1761), or a modified or unmodified variant thereof.

[003638] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39778.1 (SEQ ID NOs: 1724 and 1762), or a modified or unmodified variant thereof.

[003639] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-39790.1 (SEQ ID NOs: 1725 and 1763), or a modified or unmodified variant thereof.

[003640] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39822.1 (SEQ ID NOs: 1726 and 1764), or a modified or unmodified variant thereof.

[003641] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35609.4 (SEQ ID NOs: 1727 and 1765), or a modified or unmodified variant thereof.

[003642] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35581.4 (SEQ ID NOs: 1728 and 1766), or a modified or unmodified variant thereof.

[003643] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39845.1 (SEQ ID NOs: 1729 and 1767), or a modified or unmodified variant thereof.

[003644] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39858.1 (SEQ ID NOs: 1730 and 1768), or a modified or unmodified variant thereof.

[003645] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39870.1 (SEQ ID NOs: 1731 and 1769), or a modified or unmodified variant thereof.

[003646] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35576.4 (SEQ ID NOs: 1732 and 1770), or a modified or unmodified variant thereof.

[003647] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35588.4 (SEQ ID NOs: 1733 and 1771), or a modified or unmodified variant thereof.

[003648] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-35600.1 (SEQ ID NOs: 1734 and 1772), or a modified or unmodified variant thereof.

[003649] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-35606.1 (SEQ ID NOs: 1735 and 1773), or a modified or unmodified variant thereof.

[003650] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38151.1 (SEQ ID NOs: 1736 and 1774), or a modified or unmodified variant thereof.

[003651] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38163.1 (SEQ ID NOs: 1737 and 1775), or a modified or unmodified variant thereof.

[003652] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-39999.1 (SEQ ID NOs: 1738 and 1776), or a modified or unmodified variant thereof.

[003653] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38159.1 or hs_KRAS_ 528_A22S26 (SEQ ID NOs: 1739 and 1777), or a modified or unmodified variant thereof.

[003654] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38130.1 or hs_KRAS_ 531_A22S26 (SEQ ID NOs: 1740 and 1778), or a modified or unmodified variant thereof.

[003655] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38136.1 (SEQ ID NOs: 1741 and 1779), or a modified or unmodified variant thereof.

[003656] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40036.1 (SEQ ID NOs: 1742 and 1780), or a modified or unmodified variant thereof.

[003657] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40008.1 (SEQ ID NOs: 1743 and 1781), or a modified or unmodified variant thereof.

[003658] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40021.1 (SEQ ID NOs: 1744 and 1782), or a modified or unmodified variant thereof.

[003659] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or

second strand of: AD-40077.1 (SEQ ID NOs: 1745 and 1783), or a modified or unmodified variant thereof.

[003660] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40072.1 (SEQ ID NOs: 1746 and 1784), or a modified or unmodified variant thereof.

[003661] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40061.1 (SEQ ID NOs: 1747 and 1785), or a modified or unmodified variant thereof.

[003662] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-40068.1 (SEQ ID NOs: 1748 and 1786), or a modified or unmodified variant thereof.

[003663] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38131.1 (SEQ ID NOs: 1749 and 1787), or a modified or unmodified variant thereof.

[003664] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: AD-38167.1 (SEQ ID NOs: 1750 and 1788), or a modified or unmodified variant thereof.

[003665] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: hs_KRAS 1273_A22S26 (SEQ ID NOs: 1751 and 1789), or a modified or unmodified variant thereof.

[003666] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: hs_KRAS 2892_A37S26 (SEQ ID NOs: 1752 and 1790), or a modified or unmodified variant thereof.

[003667] A RNAi agent comprising a first and a second strand, wherein the sequence of the first and/or second strand comprise a sequence of 15 contiguous nt from the sequence of a first and/or second strand of: hs_KRAS 4731_A22S26 (SEQ ID NOs: 1753 and 1791), or a modified or unmodified variant thereof.

[003668]

[003669] In various embodiments, the disclosure comprises a RNAi agent comprising a sense and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the antisense strand of any RNAi agent disclosed herein, or a modified or unmodified variant thereof, wherein the antisense strand optionally further comprises 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more nt (or any range thereof, e.g., 0-1, 1-2, 1-3, 1-4 nt, etc.).

[003670] In one embodiment, the disclosure comprises any one or more RNAi agent listed herein.

[003671] **Overlapping sets of RNAi agents to KRAS**

[003672] In various embodiments, the present disclosure relates to groups of RNAi agents to KRAS with overlapping sequences. Thus, the present disclosure encompasses groups of RNAi agents wherein each RNAi agent in the group overlaps with each other RNAi agent in the same group by at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more nucleotides. Particularly, in one embodiment, the overlap is at least 12 nt.

[003673] Some of the RNAi agents listed herein overlap each other in sequence. Table 2 presents a compilation of some of these groups of overlapping RNAi agents, wherein each member of a group overlaps with each other member of the same group by at least 12 nt. A 12-nt portion of the overlap of the sense and anti-sense strand are presented.

[003674] Thus, for example, as shown in Table 4, the sequences of duplexes AD-39695.1, AD-39689.1,AD-39707.1, AD-39683.1, and AD-39701.1 all overlap, wherein the overlap in sense strand comprises the sequence CUGAAUAUAAAC (SEQ ID NO: 1874) and the overlap in the anti-sense strand comprises the sequence GUUUAUAUUCAG (SEQ ID NO: 1875).

[003675] However, in the present disclosure encompasses any set or subset or group or subgroup of KRAS RNAi agents which share the common technical feature of a sequence overlap (e.g., by at least 12 nt). Thus the present disclosure also encompasses the example groups of AD-39695.1, AD-39689.1, AD-39707.1, AD-39683.1, and AD-39701.1, but also these subgroups: AD-39695.1 and AD-39689.1; AD-39695.1 and AD-39707.1; AD-39695.1, AD-39689.1, and AD-39701.1; AD-39689.1, AD-39707.1, and AD-39701.1; AD-39707.1 and AD-39683.1; AD-39707.1, AD-39683.1, and AD-39701.1; etc, and any other group of overlapping KRAS RNAi agents.

[003676] Thus, these and other various sets of overlapping RNAi agents presented in Table 4 share common technical features, for example, the overlap in the sense and anti-sense strand.

[003677] Particular sets of overlapping RNAi agents to KRAS are provided below in Table 4.

[003678] The present disclosure thus encompasses any group or subgroup of RNAi agents comprising a common technical feature, wherein the common technical feature is an overlap (e.g., of at least 12 nt) of a sequence in the sense or anti-sense strand.

[003679] Thus:

[003680] The present disclosure encompasses a RNAi agent comprising a first and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the first strand of, and/or the second strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the second strand, of any of the group or subgroup or set or subset of overlapping RNAi agents presented in Table 4.

[003681] The present disclosure similarly encompasses various embodiments encompassing groups of overlapping RNAi agents presented in Table 4.

[003682] Additional Definitions

[003683] Unless defined otherwise, the technical and scientific terms used herein have the same meaning as that usually understood by a specialist familiar with the field to which the present disclosure belongs.

[003684] Unless indicated otherwise, all methods, steps, techniques and manipulations that are not specifically described in detail can be performed and have been performed in a manner known per se, as will be clear to the skilled person. Reference is for example again made to the standard handbooks and the general background art mentioned herein and to the further references cited therein.

[003685] Claims to the present disclosure are non-limiting and are provided below.

[003686] Although particular embodiments and claims have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, or the scope of subject matter of claims of any corresponding future application. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the present disclosure without departing from the spirit and scope of the present disclosure as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims. Redrafting of claim scope in later-filed corresponding applications may be due to limitations by the patent laws of various countries and should not be interpreted as giving up subject matter of the claims.

[003687] Various additional formulations and obvious variants of the described RNAi agents to KRAS can be devised by those of ordinary skill in the art. Non-limiting example RNAi agents to KRAS are described in the Examples below, which do not limit the scope of the present disclosure as described in the claims.

EXAMPLES

EXAMPLE 1

Bioinformatics and KRAS RNAi Agent (siRNA) sequences

[003688] The sequences of unmodifed and example modified KRAS RNAi agent sequences are provided in Tables 2 and 3, below.

[003689] KRAS oligonucleotide design is carried out to identify siRNAs targeting mRNAs encoding the KRAS gene.

[003690] Experimental Methods

[003691] Bioinformatics

[003692] Transcripts

[003693] siRNA design is carried out to identify RNAi agents (e.g., siRNAs) targeting the human Kirsten rat sarcoma viral oncogene (KRAS). Design uses the following transcripts from the NCBI

RefSeq collection: KRAS - NM_033360.2, NM_004985.3. For KRAS, the requirement of perfect matching to the non-human primate *Macaca fascicularis is* waived.

[003694] siRNA Design and Specificity Prediction

[003695] The predicted specificity of all possible 19mers is predicted from each sequence. Candidate 19mers are then selected as matching Coding Sequence ("CDS") or Untranslated Regions ("UTRs"). The candidate siRNAs for each gene (KRAS, 432 from CDS) are used in a comprehensive search against the human transcriptome (defined as the set of NM_ and XM_ records within the human NCBI Refseq set) using the FASTA algorithm. The perl script 'parseFasta.pl' is then used to parse the alignments and generate a score based on the position and number of mismatches between the siRNA and any potential 'off-target' transcript. The off-target score is weighted to emphasize differences in the 'seed' region of siRNAs, in positions 2-9 from the 5' end of the molecule. Each oligo-transcript pair from the FASTA search is given a mismatch score by summing the individual mismatch scores; mismatches in the position 2-9 are counted as 2.8, mismatches in the cleavage site positions 10-11 are counted as 1.2, and mismatches in region 12-19 counted as 1.0. An additional off-target prediction is carried out by comparing the frequency of heptamers and octomers derived from 3 distinct, seed-derived hexamers of each oligo. The hexamers from positions 2-7 relative to the 5' start is used to create 2 heptamers and one octomer. We create 'heptamer1' by adding a 3' A to the hexamer; we create heptamer2 by adding a 5' A to the hexamer; we create the octomer by adding an A to both 5' and 3' ends of the hexamer. The frequency of octomers and heptamers in the human 3'UTRome (defined as the subsequence of the transcriptome from NCBI's Refseq database where the end of the coding region, the 'CDS', is clearly defined) is pre-calculated. The octomer frequency is normalized to the heptamer frequency using the median value from the range of octomer frequencies. A 'mirSeedScore' is then calculated by calculating the sum of [(3 X normalized octomer count) + (2 X heptamer2 count) + (1 X heptamer1 count)].

[003696] Both siRNAs strands are assigned to a category of specificity according to the calculated scores: a score above 3 qualifies as highly specific, equal to 3 as specific and between 2.2 and 2.8 as moderately specific. We sorted by the specificity of the antisense strand.

[003697] siRNA sequence selection

[003698] Sense and antisense derived siRNA oligos are synthesized and formed into duplexes. The total numbers of duplexes per gene were: KRAS, 432.

[003699] **Synthesis of KRAS sequences**

[003700] Synthesis:

[003701] KRAS sequences are synthesized on MerMade 192 synthesizer at 1μmol scale. A total of 864 single strands (432 duplexes) for KRAS are synthesized for the human KRAS gene. For all the sequences, 'endolight' chemistry is applied as detailed below.

- All pyrimidines (cytosine and uridine) in the sense strand are replaced with corresponding 2'-O-Methyl bases (2' O-Methyl C and 2'-O-Methyl U)
- In the antisense strand, pyrimidines (C and U) adjacent to (towards 5' position) ribo A nucleoside are replaced with their corresponding 2-O-Methyl nucleosides
- A two base dTdT extension at 3' end of both sense and anti sense sequences is introduced. This two base overhang has a phosphodiester linkage
- The sequence file is converted to a text file to make it compatible for loading in the MerMade 192 synthesis software
- A unique ID is generated for each single strand and these are shown in Tables 1 to 3.

[003702] The synthesis of KRAS sequences used solid supported oligonucleotide synthesis using phosphoramidite chemistry

[003703] The synthesis of the above sequences is performed at 1μm scale in 96 well plates and 192 sequences are made per run. The amidite solutions are prepared at 0.1M concentration and ethyl thio tetrazole (0.6M in Acetonitrile) is used as activator.

[003704] Cleavage and Deprotection:

[003705] The synthesized sequences are cleaved and deprotected in 96 well plates, using a mixture of aqueous and ethanolic methylamine (3:1 ratio) in the first step and triethylamine ^{3}HF in the second step. The crude sequences thus obtained are precipitated using acetone: ethanol mix and the pellet are re-suspended in 0.02M sodium acetate buffer. Samples from each sequence are analyzed by LC-MS and the resulting mass data confirmed the identity of the sequences. A selected set of samples are also analyzed by IEX chromatography.

[003706] Purification and Desalting:

[003707] All single strands are isolated as desalted solutions in water prior to annealing step. Sequences are purified on AKTA explorer purification system using Source 15Q column. Purification is performed using a column and in-line buffer heater set at 60°C. A single peak corresponding to the full length sequence is collected in the eluant and is subsequently analyzed for purity by ion exchange chromatography.

[003708] The purified sequences are desalted on a Sephadex G25 column using AKTA purifier. The desalted KRAS sequences are analyzed for concentration and purity. The single strands are annealed on an automated platform to form siRNA duplexes. Each duplex is made at a concentration of 10μM in 1x PBS and are analyzed for purity by capillary gel electrophoresis. Details on individual duplexes are provided in Tables 1 to 3. Some sequences in Table 2, and other tables herein, represent the DNA target of the recited RNAi agent (these DNA targets comprise DNA sequences, comprising T, rather than RNA sequences, which comprise U).

Table 2. KRAS duplexes with unmodified sequences

Duplex	Sense Seq	SEQ ID NO:	Antisense Seq	SEQ ID NO:

AD-35523.3	GGACGAAUAUGAUCCAACA	1	UGUUGGAUCAUAUUCGUCC	428
AD-35529.1	GACGAAUAUGAUCCAACAA	2	UUGUUGGAUCAUAUUCGUC	429
AD-35535.4	ACGAAUAUGAUCCAACAAU	3	AUUGUUGGAUCAUAUUCGU	430
AD-35541.4	CGAAUAUGAUCCAACAAUA	4	UAUUGUUGGAUCAUAUUCG	431
AD-35547.4	GAAUAUGAUCCAACAAUAG	5	CUAUUGUUGGAUCAUAUUC	432
AD-35553.4	AAUAUGAUCCAACAAUAGA	6	UCUAUUGUUGGAUCAUAUU	433
AD-35559.4	AUAUGAUCCAACAAUAGAG	7	CUCUAUUGUUGGAUCAUAU	434
AD-35565.4	UAUGAUCCAACAAUAGAGG	8	CCUCUAUUGUUGGAUCAUA	435
AD-35524.4	AUGAUCCAACAAUAGAGGA	9	UCCUCUAUUGUUGGAUCAU	436
AD-35530.4	UGAUCCAACAAUAGAGGAU	10	AUCCUCUAUUGUUGGAUCA	437
AD-35536.4	GAUCCAACAAUAGAGGAUU	11	AAUCCUCUAUUGUUGGAUC	438
AD-35542.4	AUCCAACAAUAGAGGAUUC	12	GAAUCCUCUAUUGUUGGAU	439
AD-35548.4	UCCAACAAUAGAGGAUUCC	13	GGAAUCCUCUAUUGUUGGA	440
AD-35554.4	CCAACAAUAGAGGAUUCCU	14	AGGAAUCCUCUAUUGUUGG	441
AD-35560.2	CAACAAUAGAGGAUUCCUA	15	UAGGAAUCCUCUAUUGUUG	442
AD-35566.4	AACAAUAGAGGAUUCCUAC	16	GUAGGAAUCCUCUAUUGUU	443
AD-35525.2	ACAAUAGAGGAUUCCUACA	17	UGUAGGAAUCCUCUAUUGU	444
AD-35531.4	CAAUAGAGGAUUCCUACAG	18	CUGUAGGAAUCCUCUAUUG	445
AD-35537.4	AAUAGAGGAUUCCUACAGG	19	CCUGUAGGAAUCCUCUAUU	446
AD-35543.2	AUAGAGGAUUCCUACAGGA	20	UCCUGUAGGAAUCCUCUAU	447
AD-35549.4	UAGAGGAUUCCUACAGGAA	21	UUCCUGUAGGAAUCCUCUA	448
AD-35555.4	AGAGGAUUCCUACAGGAAG	22	CUUCCUGUAGGAAUCCUCU	449
AD-35561.4	GAGGAUUCCUACAGGAAGC	23	GCUUCCUGUAGGAAUCCUC	450
AD-35567.4	AGGAUUCCUACAGGAAGCA	24	UGCUUCCUGUAGGAAUCCU	451
AD-35526.4	GGAUUCCUACAGGAAGCAA	25	UUGCUUCCUGUAGGAAUCC	452
AD-35532.4	GAUUCCUACAGGAAGCAAG	26	CUUGCUUCCUGUAGGAAUC	453
AD-35538.4	AUUCCUACAGGAAGCAAGU	27	ACUUGCUUCCUGUAGGAAU	454
AD-35544.4	UUCCUACAGGAAGCAAGUA	28	UACUUGCUUCCUGUAGGAA	455
AD-35550.4	UCCUACAGGAAGCAAGUAG	29	CUACUUGCUUCCUGUAGGA	456
AD-35556.4	CCUACAGGAAGCAAGUAGU	30	ACUACUUGCUUCCUGUAGG	457
AD-35562.4	CUACAGGAAGCAAGUAGUA	31	UACUACUUGCUUCCUGUAG	458
AD-35568.4	UACAGGAAGCAAGUAGUAA	32	UUACUACUUGCUUCCUGUA	459
AD-35527.4	ACAGGAAGCAAGUAGUAAU	33	AUUACUACUUGCUUCCUGU	460
AD-35533.4	CAGGAAGCAAGUAGUAAUU	34	AAUUACUACUUGCUUCCUG	461
AD-35539.4	UUGGAUAUUCUCGACACAG	35	CUGUGUCGAGAAUAUCCAA	462
AD-35545.4	UGGAUAUUCUCGACACAGC	36	GCUGUGUCGAGAAUAUCCA	463
AD-35551.4	GGAUAUUCUCGACACAGCA	37	UGCUGUGUCGAGAAUAUCC	464
AD-35563.4	AUAUUCUCGACACAGCAGG	38	CCUGCUGUGUCGAGAAUAU	465
AD-35528.4	AUUCUCGACACAGCAGGUC	39	GACCUGCUGUGUCGAGAAU	466
AD-35540.4	UCUCGACACAGCAGGUCAA	40	UUGACCUGCUGUGUCGAGA	467
AD-35546.4	CUCGACACAGCAGGUCAAG	41	CUUGACCUGCUGUGUCGAG	468
AD-35552.4	UCGACACAGCAGGUCAAGA	42	UCUUGACCUGCUGUGUCGA	469
AD-35558.4	CGACACAGCAGGUCAAGAG	43	CUCUUGACCUGCUGUGUCG	470
AD-35564.4	GACACAGCAGGUCAAGAGG	44	CCUCUUGACCUGCUGUGUC	471
AD-35570.4	ACACAGCAGGUCAAGAGGA	45	UCCUCUUGACCUGCUGUGU	472

AD-35571.4	CACAGCAGGUCAAGAGGAG	46	CUCCUCUUGACCUGCUGUG	473
AD-35577.4	ACAGCAGGUCAAGAGGAGU	47	ACUCCUCUUGACCUGCUGU	474
AD-35583.4	CAGCAGGUCAAGAGGAGUA	48	UACUCCUCUUGACCUGCUG	475
AD-35589.4	AGCAGGUCAAGAGGAGUAC	49	GUACUCCUCUUGACCUGCU	476
AD-35595.4	GCAGGUCAAGAGGAGUACA	50	UGUACUCCUCUUGACCUGC	477
AD-35601.4	CAGGUCAAGAGGAGUACAG	51	CUGUACUCCUCUUGACCUG	478
AD-35607.4	AGGUCAAGAGGAGUACAGU	52	ACUGUACUCCUCUUGACCU	479
AD-35613.4	GGUCAAGAGGAGUACAGUG	53	CACUGUACUCCUCUUGACC	480
AD-35572.4	GUCAAGAGGAGUACAGUGC	54	GCACUGUACUCCUCUUGAC	481
AD-35578.4	UCAAGAGGAGUACAGUGCA	55	UGCACUGUACUCCUCUUGA	482
AD-35584.4	CAAGAGGAGUACAGUGCAA	56	UUGCACUGUACUCCUCUUG	483
AD-35590.4	AAGAGGAGUACAGUGCAAU	57	AUUGCACUGUACUCCUCUU	484
AD-35596.4	AGAGGAGUACAGUGCAAUG	58	CAUUGCACUGUACUCCUCU	485
AD-35602.4	GAGGAGUACAGUGCAAUGA	59	UCAUUGCACUGUACUCCUC	486
AD-35608.4	AGGAGUACAGUGCAAUGAG	60	CUCAUUGCACUGUACUCCU	487
AD-35614.4	GGAGUACAGUGCAAUGAGG	61	CCUCAUUGCACUGUACUCC	488
AD-35573.4	GAGUACAGUGCAAUGAGGG	62	CCCUCAUUGCACUGUACUC	489
AD-35579.4	GGGGAGGGCUUUCUUUGUG	63	CACAAAGAAAGCCCUCCCC	490
AD-35585.4	GGGAGGGCUUUCUUUGUGU	64	ACACAAAGAAAGCCCUCCC	491
AD-35591.4	GGAGGGCUUUCUUUGUGUA	65	UACACAAAGAAAGCCCUCC	492
AD-35597.4	GAGGGCUUUCUUUGUGUAU	66	AUACACAAAGAAAGCCCUC	493
AD-35603.4	AGGGCUUUCUUUGUGUAUU	67	AAUACACAAAGAAAGCCCU	494
AD-35609.4	GGGCUUUCUUUGUGUAUUU	68	AAAUACACAAAGAAAGCCC	495
AD-35615.4	GGCUUUCUUUGUGUAUUUG	69	CAAAUACACAAAGAAAGCC	496
AD-35574.4	GCUUUCUUUGUGUAUUUGC	70	GCAAAUACACAAAGAAAGC	497
AD-35580.1	CUUUCUUUGUGUAUUUGCC	71	GGCAAAUACACAAAGAAAG	498
AD-35586.4	UUUCUUUGUGUAUUUGCCA	72	UGGCAAAUACACAAAGAAA	499
AD-35592.4	UUCUUUGUGUAUUUGCCAU	73	AUGGCAAAUACACAAAGAA	500
AD-35598.4	UCUUUGUGUAUUUGCCAUA	74	UAUGGCAAAUACACAAAGA	501
AD-35604.4	CUUUGUGUAUUUGCCAUAA	75	UUAUGGCAAAUACACAAAG	502
AD-35610.4	UUUGUGUAUUUGCCAUAAA	76	UUUAUGGCAAAUACACAAA	503
AD-35616.4	UUGUGUAUUUGCCAUAAAU	77	AUUUAUGGCAAAUACACAA	504
AD-35575.4	UGUGUAUUUGCCAUAAAUA	78	UAUUUAUGGCAAAUACACA	505
AD-35581.4	GUGUAUUUGCCAUAAAUAA	79	UUAUUUAUGGCAAAUACAC	506
AD-35587.4	UGUAUUUGCCAUAAAUAAU	80	AUUAUUUAUGGCAAAUACA	507
AD-35593.4	GUAUUUGCCAUAAAUAAUA	81	UAUUAUUUAUGGCAAAUAC	508
AD-35599.4	UAUUUGCCAUAAAUAAUAC	82	GUAUUAUUUAUGGCAAAUA	509
AD-35605.4	AUUUGCCAUAAAUAAUACU	83	AGUAUUAUUUAUGGCAAAU	510
AD-35611.4	UUUGCCAUAAAUAAUACUA	84	UAGUAUUAUUUAUGGCAAA	511
AD-35617.4	UGAAGAUAUUCACCAUUAU	85	AUAAUGGUGAAUAUCUUCA	512
AD-35576.4	GAAGAUAUUCACCAUUAUA	86	UAUAAUGGUGAAUAUCUUC	513
AD-35588.4	AGAUAUUCACCAUUAUAGA	87	UCUAUAAUGGUGAAUAUCU	514
AD-35667.1	AAACAUCAGCAAAGACAAG	88	CUUGUCUUUGCUGAUGUUU	515
AD-35673.1	AACAUCAGCAAAGACAAGA	89	UCUUGUCUUUGCUGAUGUU	516
AD-35679.1	ACAUCAGCAAAGACAAGAC	90	GUCUUGUCUUUGCUGAUGU	517

AD-35685.1	CAUCAGCAAAGACAAGACA	91	UGUCUUGUCUUUGCUGAUG	518
AD-35691.1	AUCAGCAAAGACAAGACAG	92	CUGUCUUGUCUUUGCUGAU	519
AD-35557.1	GAUAUUCUCGACACAGCAG	93	CUGCUGUGUCGAGAAUAUC	520
AD-35618.1	UUCACCAUUAUAGAGAACA	94	UGUUCUCUAUAAUGGUGAA	521
AD-35569.1	UAUUCUCGACACAGCAGGU	95	ACCUGCUGUGUCGAGAAUA	522
AD-35534.1	UUCUCGACACAGCAGGUCA	96	UGACCUGCUGUGUCGAGAA	523
AD-35582.1	AAGAUAUUCACCAUUAUAG	97	CUAUAAUGGUGAAUAUCUU	524
AD-35594.1	GAUAUUCACCAUUAUAGAG	98	CUCUAUAAUGGUGAAUAUC	525
AD-35600.1	AUAUUCACCAUUAUAGAGA	99	UCUCUAUAAUGGUGAAUAU	526
AD-35606.1	UAUUCACCAUUAUAGAGAA	100	UUCUCUAUAAUGGUGAAUA	527
AD-35612.1	AUUCACCAUUAUAGAGAAC	101	GUUCUCUAUAAUGGUGAAU	528
AD-38127.1	UCACCAUUAUAGAGAACAA	102	UUGUUCUCUAUAAUGGUGA	529
AD-38133.1	CACCAUUAUAGAGAACAAA	103	UUUGUUCUCUAUAAUGGUG	530
AD-38139.1	ACCAUUAUAGAGAACAAAU	104	AUUUGUUCUCUAUAAUGGU	531
AD-38145.1	CCAUUAUAGAGAACAAAUU	105	AAUUUGUUCUCUAUAAUGG	532
AD-38151.1	CAUUAUAGAGAACAAAUUA	106	UAAUUUGUUCUCUAUAAUG	533
AD-38157.1	AUUAUAGAGAACAAAUUAA	107	UUAAUUUGUUCUCUAUAAU	534
AD-38163.1	UUAUAGAGAACAAAUUAAA	108	UUUAAUUUGUUCUCUAUAA	535
AD-38169.1	UAUAGAGAACAAAUUAAAA	109	UUUUAAUUUGUUCUCUAUA	536
AD-38128.1	AUAGAGAACAAAUUAAAAG	110	CUUUUAAUUUGUUCUCUAU	537
AD-38134.1	UAGAGAACAAAUUAAAAGA	111	UCUUUUAAUUUGUUCUCUA	538
AD-38140.1	AGAGAACAAAUUAAAAGAG	112	CUCUUUUAAUUUGUUCUCU	539
AD-38146.1	GAAGAUGUACCUAUGGUCC	113	GGACCAUAGGUACAUCUUC	540
AD-38152.1	AAGAUGUACCUAUGGUCCU	114	AGGACCAUAGGUACAUCUU	541
AD-38158.1	AGAUGUACCUAUGGUCCUA	115	UAGGACCAUAGGUACAUCU	542
AD-38164.1	GAUGUACCUAUGGUCCUAG	116	CUAGGACCAUAGGUACAUC	543
AD-38170.1	AUGUACCUAUGGUCCUAGU	117	ACUAGGACCAUAGGUACAU	544
AD-38129.1	UGUACCUAUGGUCCUAGUA	118	UACUAGGACCAUAGGUACA	545
AD-38135.1	GUACCUAUGGUCCUAGUAG	119	CUACUAGGACCAUAGGUAC	546
AD-38141.1	UACCUAUGGUCCUAGUAGG	120	CCUACUAGGACCAUAGGUA	547
AD-38147.1	ACCUAUGGUCCUAGUAGGA	121	UCCUACUAGGACCAUAGGU	548
AD-38153.1	CCUAUGGUCCUAGUAGGAA	122	UUCCUACUAGGACCAUAGG	549
AD-38159.1	CUAUGGUCCUAGUAGGAAA	123	UUUCCUACUAGGACCAUAG	550
AD-38165.1	UAUGGUCCUAGUAGGAAAU	124	AUUUCCUACUAGGACCAUA	551
AD-38171.1	AUGGUCCUAGUAGGAAAUA	125	UAUUUCCUACUAGGACCAU	552
AD-38130.1	UGGUCCUAGUAGGAAAUAA	126	UUAUUUCCUACUAGGACCA	553
AD-38136.1	GGUCCUAGUAGGAAAUAAA	127	UUUAUUUCCUACUAGGACC	554
AD-38142.1	GUCCUAGUAGGAAAUAAAU	128	AUUUAUUUCCUACUAGGAC	555
AD-38148.1	UCCUAGUAGGAAAUAAAUG	129	CAUUUAUUUCCUACUAGGA	556
AD-38154.1	CCUAGUAGGAAAUAAAUGU	130	ACAUUUAUUUCCUACUAGG	557
AD-38160.1	CUAGUAGGAAAUAAAUGUG	131	CACAUUUAUUUCCUACUAG	558
AD-38166.1	UAGUAGGAAAUAAAUGUGA	132	UCACAUUUAUUUCCUACUA	559
AD-38172.1	AGUAGGAAAUAAAUGUGAU	133	AUCACAUUUAUUUCCUACU	560
AD-38131.1	GGAAUUCCUUUUAUUGAAA	134	UUUCAAUAAAAGGAAUUCC	561
AD-38137.1	GAAUUCCUUUUAUUGAAAC	135	GUUUCAAUAAAAGGAAUUC	562

AD-38143.1	AAUUCCUUUUAUUGAAACA	136	UGUUUCAAUAAAAGGAAUU	563
AD-38149.1	AUUCCUUUUAUUGAAACAU	137	AUGUUUCAAUAAAAGGAAU	564
AD-38155.1	UUCCUUUUAUUGAAACAUC	138	GAUGUUUCAAUAAAAGGAA	565
AD-38161.1	UCCUUUUAUUGAAACAUCA	139	UGAUGUUUCAAUAAAAGGA	566
AD-38167.1	CCUUUUAUUGAAACAUCAG	140	CUGAUGUUUCAAUAAAAGG	567
AD-38173.1	CUUUUAUUGAAACAUCAGC	141	GCUGAUGUUUCAAUAAAAG	568
AD-38132.1	UUUUAUUGAAACAUCAGCA	142	UGCUGAUGUUUCAAUAAAA	569
AD-38138.1	UUUAUUGAAACAUCAGCAA	143	UUGCUGAUGUUUCAAUAAA	570
AD-38144.1	UUAUUGAAACAUCAGCAAA	144	UUUGCUGAUGUUUCAAUAA	571
AD-38150.1	UAUUGAAACAUCAGCAAAG	145	CUUUGCUGAUGUUUCAAUA	572
AD-38156.1	AUUGAAACAUCAGCAAAGA	146	UCUUUGCUGAUGUUUCAAU	573
AD-38162.1	UUGAAACAUCAGCAAAGAC	147	GUCUUUGCUGAUGUUUCAA	574
AD-38168.1	UGAAACAUCAGCAAAGACA	148	UGUCUUUGCUGAUGUUUCA	575
AD-38174.1	GAAACAUCAGCAAAGACAA	149	UUGUCUUUGCUGAUGUUUC	576
AD-39683.1	AUGACUGAAUAUAAACUUG	150	CAAGUUUAUAUUCAGUCAU	577
AD-39689.1	UGACUGAAUAUAAACUUGU	151	ACAAGUUUAUAUUCAGUCA	578
AD-39695.1	GACUGAAUAUAAACUUGUG	152	CACAAGUUUAUAUUCAGUC	579
AD-39701.1	ACUGAAUAUAAACUUGUGG	153	CCACAAGUUUAUAUUCAGU	580
AD-39707.1	CUGAAUAUAAACUUGUGGU	154	ACCACAAGUUUAUAUUCAG	581
AD-39713.1	UGAAUAUAAACUUGUGGUA	155	UACCACAAGUUUAUAUUCA	582
AD-39719.1	GAAUAUAAACUUGUGGUAG	156	CUACCACAAGUUUAUAUUC	583
AD-39725.1	AAUAUAAACUUGUGGUAGU	157	ACUACCACAAGUUUAUAUU	584
AD-39684.1	AUAUAAACUUGUGGUAGUU	158	AACUACCACAAGUUUAUAU	585
AD-39690.1	UAUAAACUUGUGGUAGUUG	159	CAACUACCACAAGUUUAUA	586
AD-39696.1	AUAAACUUGUGGUAGUUGG	160	CCAACUACCACAAGUUUAU	587
AD-39702.1	UAAACUUGUGGUAGUUGGA	161	UCCAACUACCACAAGUUUA	588
AD-39708.1	AAACUUGUGGUAGUUGGAG	162	CUCCAACUACCACAAGUUU	589
AD-39714.1	AACUUGUGGUAGUUGGAGC	163	GCUCCAACUACCACAAGUU	590
AD-39720.1	ACUUGUGGUAGUUGGAGCU	164	AGCUCCAACUACCACAAGU	591
AD-39726.1	CUUGUGGUAGUUGGAGCUG	165	CAGCUCCAACUACCACAAG	592
AD-39685.1	UUGUGGUAGUUGGAGCUGG	166	CCAGCUCCAACUACCACAA	593
AD-39691.1	UGUGGUAGUUGGAGCUGGU	167	ACCAGCUCCAACUACCACA	594
AD-39697.1	GUGGUAGUUGGAGCUGGUG	168	CACCAGCUCCAACUACCAC	595
AD-39703.1	UGGUAGUUGGAGCUGGUGG	169	CCACCAGCUCCAACUACCA	596
AD-39709.1	GGUAGUUGGAGCUGGUGGC	170	GCCACCAGCUCCAACUACC	597
AD-39715.1	GUAGUUGGAGCUGGUGGCG	171	CGCCACCAGCUCCAACUAC	598
AD-39721.1	UAGUUGGAGCUGGUGGCGU	172	ACGCCACCAGCUCCAACUA	599
AD-39727.1	AGUUGGAGCUGGUGGCGUA	173	UACGCCACCAGCUCCAACU	600
AD-39686.1	GUUGGAGCUGGUGGCGUAG	174	CUACGCCACCAGCUCCAAC	601
AD-39692.1	UUGGAGCUGGUGGCGUAGG	175	CCUACGCCACCAGCUCCAA	602
AD-39698.1	UGGAGCUGGUGGCGUAGGC	176	GCCUACGCCACCAGCUCCA	603
AD-39704.1	GGAGCUGGUGGCGUAGGCA	177	UGCCUACGCCACCAGCUCC	604
AD-39710.1	GAGCUGGUGGCGUAGGCAA	178	UUGCCUACGCCACCAGCUC	605
AD-39716.1	AGCUGGUGGCGUAGGCAAG	179	CUUGCCUACGCCACCAGCU	606
AD-39722.1	GCUGGUGGCGUAGGCAAGA	180	UCUUGCCUACGCCACCAGC	607

AD-39728.1	CUGGUGGCGUAGGCAAGAG	181	CUCUUGCCUACGCCACCAG	608
AD-39687.1	UGGUGGCGUAGGCAAGAGU	182	ACUCUUGCCUACGCCACCA	609
AD-39693.1	GGUGGCGUAGGCAAGAGUG	183	CACUCUUGCCUACGCCACC	610
AD-39699.1	GUGGCGUAGGCAAGAGUGC	184	GCACUCUUGCCUACGCCAC	611
AD-39705.1	UGGCGUAGGCAAGAGUGCC	185	GGCACUCUUGCCUACGCCA	612
AD-39711.1	GGCGUAGGCAAGAGUGCCU	186	AGGCACUCUUGCCUACGCC	613
AD-39717.1	GCGUAGGCAAGAGUGCCUU	187	AAGGCACUCUUGCCUACGC	614
AD-39723.1	CGUAGGCAAGAGUGCCUUG	188	CAAGGCACUCUUGCCUACG	615
AD-39729.1	GUAGGCAAGAGUGCCUUGA	189	UCAAGGCACUCUUGCCUAC	616
AD-39688.1	UAGGCAAGAGUGCCUUGAC	190	GUCAAGGCACUCUUGCCUA	617
AD-39694.1	AGGCAAGAGUGCCUUGACG	191	CGUCAAGGCACUCUUGCCU	618
AD-39700.1	GGCAAGAGUGCCUUGACGA	192	UCGUCAAGGCACUCUUGCC	619
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AD-39712.1	CAAGAGUGCCUUGACGAUA	194	UAUCGUCAAGGCACUCUUG	621
AD-39718.1	AAGAGUGCCUUGACGAUAC	195	GUAUCGUCAAGGCACUCUU	622
AD-39724.1	AGAGUGCCUUGACGAUACA	196	UGUAUCGUCAAGGCACUCU	623
AD-39730.1	GAGUGCCUUGACGAUACAG	197	CUGUAUCGUCAAGGCACUC	624
AD-39736.1	AGUGCCUUGACGAUACAGC	198	GCUGUAUCGUCAAGGCACU	625
AD-39742.1	GUGCCUUGACGAUACAGCU	199	AGCUGUAUCGUCAAGGCAC	626
AD-39748.1	UGCCUUGACGAUACAGCUA	200	UAGCUGUAUCGUCAAGGCA	627
AD-39754.1	GCCUUGACGAUACAGCUAA	201	UUAGCUGUAUCGUCAAGGC	628
AD-39760.1	CCUUGACGAUACAGCUAAU	202	AUUAGCUGUAUCGUCAAGG	629
AD-39766.1	CUUGACGAUACAGCUAAUU	203	AAUUAGCUGUAUCGUCAAG	630
AD-39772.1	UUGACGAUACAGCUAAUUC	204	GAAUUAGCUGUAUCGUCAA	631
AD-39731.1	UGACGAUACAGCUAAUUCA	205	UGAAUUAGCUGUAUCGUCA	632
AD-39737.1	GACGAUACAGCUAAUUCAG	206	CUGAAUUAGCUGUAUCGUC	633
AD-39743.1	ACGAUACAGCUAAUUCAGA	207	UCUGAAUUAGCUGUAUCGU	634
AD-39749.1	CGAUACAGCUAAUUCAGAA	208	UUCUGAAUUAGCUGUAUCG	635
AD-39755.1	GAUACAGCUAAUUCAGAAU	209	AUUCUGAAUUAGCUGUAUC	636
AD-39761.1	AUACAGCUAAUUCAGAAUC	210	GAUUCUGAAUUAGCUGUAU	637
AD-39767.1	UACAGCUAAUUCAGAAUCA	211	UGAUUCUGAAUUAGCUGUA	638
AD-39773.1	ACAGCUAAUUCAGAAUCAU	212	AUGAUUCUGAAUUAGCUGU	639
AD-39732.1	CAGCUAAUUCAGAAUCAUU	213	AAUGAUUCUGAAUUAGCUG	640
AD-39738.1	AGCUAAUUCAGAAUCAUUU	214	AAAUGAUUCUGAAUUAGCU	641
AD-39744.1	GCUAAUUCAGAAUCAUUUU	215	AAAAUGAUUCUGAAUUAGC	642
AD-39750.1	CUAAUUCAGAAUCAUUUUG	216	CAAAAUGAUUCUGAAUUAG	643
AD-39756.1	UAAUUCAGAAUCAUUUUGU	217	ACAAAAUGAUUCUGAAUUA	644
AD-39762.1	AAUUCAGAAUCAUUUUGUG	218	CACAAAAUGAUUCUGAAUU	645
AD-39768.1	AUUCAGAAUCAUUUUGUGG	219	CCACAAAAUGAUUCUGAAU	646
AD-39774.1	UUCAGAAUCAUUUUGUGGA	220	UCCACAAAAUGAUUCUGAA	647
AD-39733.1	UCAGAAUCAUUUUGUGGAC	221	GUCCACAAAAUGAUUCUGA	648
AD-39739.1	CAGAAUCAUUUUGUGGACG	222	CGUCCACAAAAUGAUUCUG	649
AD-39745.1	AGAAUCAUUUUGUGGACGA	223	UCGUCCACAAAAUGAUUCU	650
AD-39751.1	GAAUCAUUUUGUGGACGAA	224	UUCGUCCACAAAAUGAUUC	651
AD-39757.1	AAUCAUUUUGUGGACGAAU	225	AUUCGUCCACAAAAUGAUU	652

AD-39763.1	AUCAUUUUGUGGACGAAUA	226	UAUUCGUCCACAAAAUGAU	653
AD-39769.1	UCAUUUUGUGGACGAAUAU	227	AUAUUCGUCCACAAAAUGA	654
AD-39775.1	CAUUUUGUGGACGAAUAUG	228	CAUAUUCGUCCACAAAAUG	655
AD-39734.1	AUUUUGUGGACGAAUAUGA	229	UCAUAUUCGUCCACAAAAU	656
AD-39740.1	UUUUGUGGACGAAUAUGAU	230	AUCAUAUUCGUCCACAAAA	657
AD-39746.1	UUUGUGGACGAAUAUGAUC	231	GAUCAUAUUCGUCCACAAA	658
AD-39752.1	UUGUGGACGAAUAUGAUCC	232	GGAUCAUAUUCGUCCACAA	659
AD-39758.1	UGUGGACGAAUAUGAUCCA	233	UGGAUCAUAUUCGUCCACA	660
AD-39764.1	GUGGACGAAUAUGAUCCAA	234	UUGGAUCAUAUUCGUCCAC	661
AD-39770.1	UGGACGAAUAUGAUCCAAC	235	GUUGGAUCAUAUUCGUCCA	662
AD-39776.1	AGGAAGCAAGUAGUAAUUG	236	CAAUUACUACUUGCUUCCU	663
AD-39735.1	GGAAGCAAGUAGUAAUUGA	237	UCAAUUACUACUUGCUUCC	664
AD-39741.1	GAAGCAAGUAGUAAUUGAU	238	AUCAAUUACUACUUGCUUC	665
AD-39747.1	AAGCAAGUAGUAAUUGAUG	239	CAUCAAUUACUACUUGCUU	666
AD-39753.1	AGCAAGUAGUAAUUGAUGG	240	CCAUCAAUUACUACUUGCU	667
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AD-39765.1	CAAGUAGUAAUUGAUGGAG	242	CUCCAUCAAUUACUACUUG	669
AD-39771.1	AAGUAGUAAUUGAUGGAGA	243	UCUCCAUCAAUUACUACUU	670
AD-39778.1	AGUAGUAAUUGAUGGAGAA	244	UUCUCCAUCAAUUACUACU	671
AD-39784.1	GUAGUAAUUGAUGGAGAAA	245	UUUCUCCAUCAAUUACUAC	672
AD-39790.1	UAGUAAUUGAUGGAGAAAC	246	GUUUCUCCAUCAAUUACUA	673
AD-39796.1	AGUAAUUGAUGGAGAAACC	247	GGUUUCUCCAUCAAUUACU	674
AD-39802.1	GUAAUUGAUGGAGAAACCU	248	AGGUUUCUCCAUCAAUUAC	675
AD-39808.1	UAAUUGAUGGAGAAACCUG	249	CAGGUUUCUCCAUCAAUUA	676
AD-39814.1	AAUUGAUGGAGAAACCUGU	250	ACAGGUUUCUCCAUCAAUU	677
AD-39820.1	AUUGAUGGAGAAACCUGUC	251	GACAGGUUUCUCCAUCAAU	678
AD-39779.1	UUGAUGGAGAAACCUGUCU	252	AGACAGGUUUCUCCAUCAA	679
AD-39785.1	UGAUGGAGAAACCUGUCUC	253	GAGACAGGUUUCUCCAUCA	680
AD-39791.1	GAUGGAGAAACCUGUCUCU	254	AGAGACAGGUUUCUCCAUC	681
AD-39797.1	AUGGAGAAACCUGUCUCUU	255	AAGAGACAGGUUUCUCCAU	682
AD-39803.1	UGGAGAAACCUGUCUCUUG	256	CAAGAGACAGGUUUCUCCA	683
AD-39809.1	GGAGAAACCUGUCUCUUGG	257	CCAAGAGACAGGUUUCUCC	684
AD-39815.1	GAGAAACCUGUCUCUUGGA	258	UCCAAGAGACAGGUUUCUC	685
AD-39821.1	AGAAACCUGUCUCUUGGAU	259	AUCCAAGAGACAGGUUUCU	686
AD-39780.1	GAAACCUGUCUCUUGGAUA	260	UAUCCAAGAGACAGGUUUC	687
AD-39786.1	AAACCUGUCUCUUGGAUAU	261	AUAUCCAAGAGACAGGUUU	688
AD-39792.1	AACCUGUCUCUUGGAUAUU	262	AAUAUCCAAGAGACAGGUU	689
AD-39798.1	ACCUGUCUCUUGGAUAUUC	263	GAAUAUCCAAGAGACAGGU	690
AD-39804.1	CCUGUCUCUUGGAUAUUCU	264	AGAAUAUCCAAGAGACAGG	691
AD-39810.1	CUGUCUCUUGGAUAUUCUC	265	GAGAAUAUCCAAGAGACAG	692
AD-39816.1	UGUCUCUUGGAUAUUCUCG	266	CGAGAAUAUCCAAGAGACA	693
AD-39822.1	GUCUCUUGGAUAUUCUCGA	267	UCGAGAAUAUCCAAGAGAC	694
AD-39781.1	UCUCUUGGAUAUUCUCGAC	268	GUCGAGAAUAUCCAAGAGA	695
AD-39787.1	CUCUUGGAUAUUCUCGACA	269	UGUCGAGAAUAUCCAAGAG	696
AD-39793.1	UCUUGGAUAUUCUCGACAC	270	GUGUCGAGAAUAUCCAAGA	697

AD-39799.1	CUUGGAUAUUCUCGACACA	271	UGUGUCGAGAAUAUCCAAG	698
AD-39805.1	AGUACAGUGCAAUGAGGGA	272	UCCCUCAUUGCACUGUACU	699
AD-39811.1	GUACAGUGCAAUGAGGGAC	273	GUCCCUCAUUGCACUGUAC	700
AD-39817.1	UACAGUGCAAUGAGGGACC	274	GGUCCCUCAUUGCACUGUA	701
AD-39823.1	ACAGUGCAAUGAGGGACCA	275	UGGUCCCUCAUUGCACUGU	702
AD-39782.1	CAGUGCAAUGAGGGACCAG	276	CUGGUCCCUCAUUGCACUG	703
AD-39788.1	AGUGCAAUGAGGGACCAGU	277	ACUGGUCCCUCAUUGCACU	704
AD-39794.1	GUGCAAUGAGGGACCAGUA	278	UACUGGUCCCUCAUUGCAC	705
AD-39800.1	UGCAAUGAGGGACCAGUAC	279	GUACUGGUCCCUCAUUGCA	706
AD-39806.1	GCAAUGAGGGACCAGUACA	280	UGUACUGGUCCCUCAUUGC	707
AD-39812.1	CAAUGAGGGACCAGUACAU	281	AUGUACUGGUCCCUCAUUG	708
AD-39818.1	AAUGAGGGACCAGUACAUG	282	CAUGUACUGGUCCCUCAUU	709
AD-39824.1	AUGAGGGACCAGUACAUGA	283	UCAUGUACUGGUCCCUCAU	710
AD-39783.1	UGAGGGACCAGUACAUGAG	284	CUCAUGUACUGGUCCCUCA	711
AD-39789.1	GAGGGACCAGUACAUGAGG	285	CCUCAUGUACUGGUCCCUC	712
AD-39795.1	AGGGACCAGUACAUGAGGA	286	UCCUCAUGUACUGGUCCCU	713
AD-39801.1	GGGACCAGUACAUGAGGAC	287	GUCCUCAUGUACUGGUCCC	714
AD-39807.1	GGACCAGUACAUGAGGACU	288	AGUCCUCAUGUACUGGUCC	715
AD-39813.1	GACCAGUACAUGAGGACUG	289	CAGUCCUCAUGUACUGGUC	716
AD-39819.1	ACCAGUACAUGAGGACUGG	290	CCAGUCCUCAUGUACUGGU	717
AD-39825.1	CCAGUACAUGAGGACUGGG	291	CCCAGUCCUCAUGUACUGG	718
AD-39831.1	CAGUACAUGAGGACUGGGG	292	CCCCAGUCCUCAUGUACUG	719
AD-39837.1	AGUACAUGAGGACUGGGGA	293	UCCCCAGUCCUCAUGUACU	720
AD-39843.1	GUACAUGAGGACUGGGGAG	294	CUCCCCAGUCCUCAUGUAC	721
AD-39849.1	UACAUGAGGACUGGGGAGG	295	CCUCCCCAGUCCUCAUGUA	722
AD-39855.1	ACAUGAGGACUGGGGAGGG	296	CCCUCCCCAGUCCUCAUGU	723
AD-39861.1	CAUGAGGACUGGGGAGGGC	297	GCCCUCCCCAGUCCUCAUG	724
AD-39867.1	AUGAGGACUGGGGAGGGCU	298	AGCCCUCCCCAGUCCUCAU	725
AD-39826.1	UGAGGACUGGGGAGGGCUU	299	AAGCCCUCCCCAGUCCUCA	726
AD-39832.1	GAGGACUGGGGAGGGCUUU	300	AAAGCCCUCCCCAGUCCUC	727
AD-39838.1	AGGACUGGGGAGGGCUUUC	301	GAAAGCCCUCCCCAGUCCU	728
AD-39844.1	GGACUGGGGAGGGCUUUCU	302	AGAAAGCCCUCCCCAGUCC	729
AD-39850.1	GACUGGGGAGGGCUUUCUU	303	AAGAAAGCCCUCCCCAGUC	730
AD-39856.1	ACUGGGGAGGGCUUUCUUU	304	AAAGAAAGCCCUCCCCAGU	731
AD-39862.1	CUGGGGAGGGCUUUCUUUG	305	CAAAGAAAGCCCUCCCCAG	732
AD-39868.1	UGGGGAGGGCUUUCUUUGU	306	ACAAAGAAAGCCCUCCCCA	733
AD-39827.1	UUGCCAUAAAUAAUACUAA	307	UUAGUAUUAUUUAUGGCAA	734
AD-39833.1	UGCCAUAAAUAAUACUAAA	308	UUUAGUAUUAUUUAUGGCA	735
AD-39839.1	GCCAUAAAUAAUACUAAAU	309	AUUUAGUAUUAUUUAUGGC	736
AD-39845.1	CCAUAAAUAAUACUAAAUC	310	GAUUUAGUAUUAUUUAUGG	737
AD-39851.1	CAUAAAUAAUACUAAAUCA	311	UGAUUUAGUAUUAUUUAUG	738
AD-39857.1	AUAAAUAAUACUAAAUCAU	312	AUGAUUUAGUAUUAUUUAU	739
AD-39863.1	UAAAUAAUACUAAAUCAUU	313	AAUGAUUUAGUAUUAUUUA	740
AD-39869.1	AAAUAAUACUAAAUCAUUU	314	AAAUGAUUUAGUAUUAUUU	741
AD-39828.1	AAUAAUACUAAAUCAUUUG	315	CAAAUGAUUUAGUAUUAUU	742

AD-39834.1	AUAAUACUAAAUCAUUUGA	316	UCAAAUGAUUUAGUAUUAU	743
AD-39840.1	UAAUACUAAAUCAUUUGAA	317	UUCAAAUGAUUUAGUAUUA	744
AD-39846.1	AAUACUAAAUCAUUUGAAG	318	CUUCAAAUGAUUUAGUAUU	745
AD-39852.1	AUACUAAAUCAUUUGAAGA	319	UCUUCAAAUGAUUUAGUAU	746
AD-39858.1	UACUAAAUCAUUUGAAGAU	320	AUCUUCAAAUGAUUUAGUA	747
AD-39864.1	ACUAAAUCAUUUGAAGAUA	321	UAUCUUCAAAUGAUUUAGU	748
AD-39870.1	CUAAAUCAUUUGAAGAUAU	322	AUAUCUUCAAAUGAUUUAG	749
AD-39829.1	UAAAUCAUUUGAAGAUAUU	323	AAUAUCUUCAAAUGAUUUA	750
AD-39835.1	AAAUCAUUUGAAGAUAUUC	324	GAAUAUCUUCAAAUGAUUU	751
AD-39841.1	AAUCAUUUGAAGAUAUUCA	325	UGAAUAUCUUCAAAUGAUU	752
AD-39853.1	UCAUUUGAAGAUAUUCACC	326	GGUGAAUAUCUUCAAAUGA	753
AD-39859.1	CAUUUGAAGAUAUUCACCA	327	UGGUGAAUAUCUUCAAAUG	754
AD-39865.1	AUUUGAAGAUAUUCACCAU	328	AUGGUGAAUAUCUUCAAAU	755
AD-39871.1	UUUGAAGAUAUUCACCAUU	329	AAUGGUGAAUAUCUUCAAA	756
AD-39830.1	UUGAAGAUAUUCACCAUUA	330	UAAUGGUGAAUAUCUUCAA	757
AD-39836.1	GAGAACAAAUUAAAAGAGU	331	ACUCUUUUAAUUUGUUCUC	758
AD-39842.1	AGAACAAAUUAAAAGAGUU	332	AACUCUUUUAAUUUGUUCU	759
AD-39848.1	GAACAAAUUAAAAGAGUUA	333	UAACUCUUUUAAUUUGUUC	760
AD-39854.1	AACAAAUUAAAAGAGUUAA	334	UUAACUCUUUUAAUUUGUU	761
AD-39860.1	ACAAAUUAAAAGAGUUAAG	335	CUUAACUCUUUUAAUUUGU	762
AD-39866.1	CAAAUUAAAAGAGUUAAGG	336	CCUUAACUCUUUUAAUUUG	763
AD-39992.1	AAAUUAAAAGAGUUAAGGA	337	UCCUUAACUCUUUUAAUUU	764
AD-39998.1	AAUUAAAAGAGUUAAGGAC	338	GUCCUUAACUCUUUUAAUU	765
AD-40004.1	AUUAAAAGAGUUAAGGACU	339	AGUCCUUAACUCUUUUAAU	766
AD-40010.1	UUAAAAGAGUUAAGGACUC	340	GAGUCCUUAACUCUUUUAA	767
AD-40016.1	UAAAAGAGUUAAGGACUCU	341	AGAGUCCUUAACUCUUUUA	768
AD-40022.1	AAAAGAGUUAAGGACUCUG	342	CAGAGUCCUUAACUCUUUU	769
AD-40028.1	AAAGAGUUAAGGACUCUGA	343	UCAGAGUCCUUAACUCUUU	770
AD-40034.1	AAGAGUUAAGGACUCUGAA	344	UUCAGAGUCCUUAACUCUU	771
AD-39999.1	GAGUUAAGGACUCUGAAGA	345	UCUUCAGAGUCCUUAACUC	772
AD-40005.1	AGUUAAGGACUCUGAAGAU	346	AUCUUCAGAGUCCUUAACU	773
AD-40011.1	GUUAAGGACUCUGAAGAUG	347	CAUCUUCAGAGUCCUUAAC	774
AD-40017.1	UUAAGGACUCUGAAGAUGU	348	ACAUCUUCAGAGUCCUUAA	775
AD-40029.1	AAGGACUCUGAAGAUGUAC	349	GUACAUCUUCAGAGUCCUU	776
AD-40035.1	AGGACUCUGAAGAUGUACC	350	GGUACAUCUUCAGAGUCCU	777
AD-39994.1	GGACUCUGAAGAUGUACCU	351	AGGUACAUCUUCAGAGUCC	778
AD-40000.1	GACUCUGAAGAUGUACCUA	352	UAGGUACAUCUUCAGAGUC	779
AD-40006.1	ACUCUGAAGAUGUACCUAU	353	AUAGGUACAUCUUCAGAGU	780
AD-40012.1	CUCUGAAGAUGUACCUAUG	354	CAUAGGUACAUCUUCAGAG	781
AD-40018.1	UCUGAAGAUGUACCUAUGG	355	CCAUAGGUACAUCUUCAGA	782
AD-40024.1	CUGAAGAUGUACCUAUGGU	356	ACCAUAGGUACAUCUUCAG	783
AD-40030.1	UGAAGAUGUACCUAUGGUC	357	GACCAUAGGUACAUCUUCA	784
AD-40036.1	GUAGGAAAUAAAUGUGAUU	358	AAUCACAUUUAUUUCCUAC	785
AD-39995.1	UAGGAAAUAAAUGUGAUUU	359	AAAUCACAUUUAUUUCCUA	786
AD-40001.1	AGGAAAUAAAUGUGAUUUG	360	CAAAUCACAUUUAUUUCCU	787

AD-40007.1	GGAAAUAAAUGUGAUUUGC	361	GCAAAUCACAUUUAUUUCC	788
AD-40013.1	GAAAUAAAUGUGAUUUGCC	362	GGCAAAUCACAUUUAUUUC	789
AD-40019.1	AAAUAAAUGUGAUUUGCCU	363	AGGCAAAUCACAUUUAUUU	790
AD-40025.1	AAUAAAUGUGAUUUGCCUU	364	AAGGCAAAUCACAUUUAUU	791
AD-40031.1	AUAAAUGUGAUUUGCCUUC	365	GAAGGCAAAUCACAUUUAU	792
AD-40037.1	UAAAUGUGAUUUGCCUUCU	366	AGAAGGCAAAUCACAUUUA	793
AD-39996.1	AAAUGUGAUUUGCCUUCUA	367	UAGAAGGCAAAUCACAUUU	794
AD-40002.1	AAUGUGAUUUGCCUUCUAG	368	CUAGAAGGCAAAUCACAUU	795
AD-40008.1	AUGUGAUUUGCCUUCUAGA	369	UCUAGAAGGCAAAUCACAU	796
AD-40014.1	UGUGAUUUGCCUUCUAGAA	370	UUCUAGAAGGCAAAUCACA	797
AD-40020.1	GUGAUUUGCCUUCUAGAAC	371	GUUCUAGAAGGCAAAUCAC	798
AD-40026.1	UGAUUUGCCUUCUAGAACA	372	UGUUCUAGAAGGCAAAUCA	799
AD-40032.1	GAUUUGCCUUCUAGAACAG	373	CUGUUCUAGAAGGCAAAUC	800
AD-40038.1	AUUUGCCUUCUAGAACAGU	374	ACUGUUCUAGAAGGCAAAU	801
AD-39997.1	UUUGCCUUCUAGAACAGUA	375	UACUGUUCUAGAAGGCAAA	802
AD-40009.1	UGCCUUCUAGAACAGUAGA	376	UCUACUGUUCUAGAAGGCA	803
AD-40015.1	GCCUUCUAGAACAGUAGAC	377	GUCUACUGUUCUAGAAGGC	804
AD-40021.1	CCUUCUAGAACAGUAGACA	378	UGUCUACUGUUCUAGAAGG	805
AD-40027.1	CUUCUAGAACAGUAGACAC	379	GUGUCUACUGUUCUAGAAG	806
AD-40033.1	UUCUAGAACAGUAGACACA	380	UGUGUCUACUGUUCUAGAA	807
AD-40039.1	UCUAGAACAGUAGACACAA	381	UUGUGUCUACUGUUCUAGA	808
AD-40045.1	CUAGAACAGUAGACACAAA	382	UUUGUGUCUACUGUUCUAG	809
AD-40051.1	UAGAACAGUAGACACAAAA	383	UUUUGUGUCUACUGUUCUA	810
AD-40057.1	AGAACAGUAGACACAAAAC	384	GUUUUGUGUCUACUGUUCU	811
AD-40063.1	GAACAGUAGACACAAAACA	385	UGUUUUGUGUCUACUGUUC	812
AD-40069.1	AACAGUAGACACAAAACAG	386	CUGUUUUGUGUCUACUGUU	813
AD-40075.1	ACAGUAGACACAAAACAGG	387	CCUGUUUUGUGUCUACUGU	814
AD-40081.1	CAGUAGACACAAAACAGGC	388	GCCUGUUUUGUGUCUACUG	815
AD-40040.1	AGUAGACACAAAACAGGCU	389	AGCCUGUUUUGUGUCUACU	816
AD-40046.1	GUAGACACAAAACAGGCUC	390	GAGCCUGUUUUGUGUCUAC	817
AD-40052.1	UAGACACAAAACAGGCUCA	391	UGAGCCUGUUUUGUGUCUA	818
AD-40058.1	AGACACAAAACAGGCUCAG	392	CUGAGCCUGUUUUGUGUCU	819
AD-40064.1	GACACAAAACAGGCUCAGG	393	CCUGAGCCUGUUUUGUGUC	820
AD-40070.1	ACACAAAACAGGCUCAGGA	394	UCCUGAGCCUGUUUUGUGU	821
AD-40076.1	CACAAAACAGGCUCAGGAC	395	GUCCUGAGCCUGUUUUGUG	822
AD-40082.1	ACAAAACAGGCUCAGGACU	396	AGUCCUGAGCCUGUUUUGU	823
AD-40041.1	CAAAACAGGCUCAGGACUU	397	AAGUCCUGAGCCUGUUUUG	824
AD-40047.1	AAAACAGGCUCAGGACUUA	398	UAAGUCCUGAGCCUGUUUU	825
AD-40053.1	AAACAGGCUCAGGACUUAG	399	CUAAGUCCUGAGCCUGUUU	826
AD-40059.1	AACAGGCUCAGGACUUAGC	400	GCUAAGUCCUGAGCCUGUU	827
AD-40065.1	ACAGGCUCAGGACUUAGCA	401	UGCUAAGUCCUGAGCCUGU	828
AD-40071.1	CAGGCUCAGGACUUAGCAA	402	UUGCUAAGUCCUGAGCCUG	829
AD-40077.1	AGGCUCAGGACUUAGCAAG	403	CUUGCUAAGUCCUGAGCCU	830
AD-40083.1	GGCUCAGGACUUAGCAAGA	404	UCUUGCUAAGUCCUGAGCC	831
AD-40042.1	GCUCAGGACUUAGCAAGAA	405	UUCUUGCUAAGUCCUGAGC	832

AD-40048.1	CUCAGGACUUAGCAAGAAG	406	CUUCUUGCUAAGUCCUGAG	833
AD-40054.1	UCAGGACUUAGCAAGAAGU	407	ACUUCUUGCUAAGUCCUGA	834
AD-40060.1	CAGGACUUAGCAAGAAGUU	408	AACUUCUUGCUAAGUCCUG	835
AD-40066.1	AGGACUUAGCAAGAAGUUA	409	UAACUUCUUGCUAAGUCCU	836
AD-40072.1	GGACUUAGCAAGAAGUUAU	410	AUAACUUCUUGCUAAGUCC	837
AD-40078.1	GACUUAGCAAGAAGUUAUG	411	CAUAACUUCUUGCUAAGUC	838
AD-40084.1	ACUUAGCAAGAAGUUAUGG	412	CCAUAACUUCUUGCUAAGU	839
AD-40043.1	CUUAGCAAGAAGUUAUGGA	413	UCCAUAACUUCUUGCUAAG	840
AD-40049.1	UUAGCAAGAAGUUAUGGAA	414	UUCCAUAACUUCUUGCUAA	841
AD-40055.1	UAGCAAGAAGUUAUGGAAU	415	AUUCCAUAACUUCUUGCUA	842
AD-40061.1	AGCAAGAAGUUAUGGAAUU	416	AAUUCCAUAACUUCUUGCU	843
AD-40067.1	GCAAGAAGUUAUGGAAUUC	417	GAAUUCCAUAACUUCUUGC	844
AD-40073.1	CAAGAAGUUAUGGAAUUCC	418	GGAAUUCCAUAACUUCUUG	845
AD-40079.1	AAGAAGUUAUGGAAUUCCU	419	AGGAAUUCCAUAACUUCUU	846
AD-40085.1	AGAAGUUAUGGAAUUCCUU	420	AAGGAAUUCCAUAACUUCU	847
AD-40044.1	GAAGUUAUGGAAUUCCUUU	421	AAAGGAAUUCCAUAACUUC	848
AD-40050.1	AAGUUAUGGAAUUCCUUUU	422	AAAAGGAAUUCCAUAACUU	849
AD-40056.1	AGUUAUGGAAUUCCUUUUA	423	UAAAAGGAAUUCCAUAACU	850
AD-40062.1	GUUAUGGAAUUCCUUUUAU	424	AUAAAAGGAAUUCCAUAAC	851
AD-40068.1	UUAUGGAAUUCCUUUUAUU	425	AAUAAAAGGAAUUCCAUAA	852
AD-40074.1	UAUGGAAUUCCUUUUAUUG	426	CAAUAAAAGGAAUUCCAUA	853
AD-40080.1	AUGGAAUUCCUUUUAUUGA	427	UCAAUAAAAGGAAUUCCAU	854
AD-39720.1	ACTTGTGGTAGTTGGAGCT	1716	AGCTCCAACTACCACAAGT	1754
AD-39706.1	GCAAGAGTGCCTTGACGAT	1717	ATCGTCAAGGCACTCTTGC	1755
AD-39712.1	CAAGAGTGCCTTGACGATA	1718	TATCGTCAAGGCACTCTTG	1756
AD-39760.1	CCTTGACGATACAGCTAAT	1719	ATTAGCTGTATCGTCAAGG	1757
AD-39732.1	CAGCTAATTCAGAATCATT	1720	AATGATTCTGAATTAGCTG	1758
AD-35541.4	CGAATATGATCCAACAATA	1721	TATTGTTGGATCATATTCG	1759
AD-39735.1 or hs_KRAS_ 321_A22S26	GGAAGCAAGTAGTAATTGA	1722	TCAATTACTACTTGCTTCC	1760
AD-39741.1 or hs_KRAS_ 322_A22S26	GAAGCAAGTAGTAATTGAT	1723	ATCAATTACTACTTGCTTC	1761
AD-39778.1	AGTAGTAATTGATGGAGAA	1724	TTCTCCATCAATTACTACT	1762
AD-39790.1	TAGTAATTGATGGAGAAAC	1725	GTTTCTCCATCAATTACTA	1763
AD-39822.1	GTCTCTTGGATATTCTCGA	1726	TCGAGAATATCCAAGAGAC	1764
AD-35609.4	GGGCTTTCTTTGTGTATTT	1727	AAATACACAAAGAAAGCCC	1765
AD-35581.4	GTGTATTTGCCATAAATAA	1728	TTATTTATGGCAAATACAC	1766
AD-39845.1	CCATAAATAATACTAAATC	1729	GATTTAGTATTATTTATGG	1767
AD-39858.1	TACTAAATCATTTGAAGAT	1730	ATCTTCAAATGATTTAGTA	1768
AD-39870.1	CTAAATCATTTGAAGATAT	1731	ATATCTTCAAATGATTTAG	1769
AD-35576.4	GAAGATATTCACCATTATA	1732	TATAATGGTGAATATCTTC	1770
AD-35588.4	AGATATTCACCATTATAGA	1733	TCTATAATGGTGAATATCT	1771
AD-35600.1	ATATTCACCATTATAGAGA	1734	TCTCTATAATGGTGAATAT	1772
AD-35606.1	TATTCACCATTATAGAGAA	1735	TTCTCTATAATGGTGAATA	1773
AD-38151.1	CATTATAGAGAACAAATTA	1736	TAATTTGTTCTCTATAATG	1774

AD-38163.1	TTATAGAGAACAAATTAAA	1737	TTTAATTTGTTCTCTATAA	1775
AD-39999.1	GAGTTAAGGACTCTGAAGA	1738	TCTTCAGAGTCCTTAACTC	1776
AD-38159.1 or hs_KRAS_528_A22S26	CTATGGTCCTAGTAGGAAA	1739	TTTCCTACTAGGACCATAG	1777
AD-38130.1 or hs_KRAS_531_A22S26	TGGTCCTAGTAGGAAATAA	1740	TTATTTCCTACTAGGACCA	1778
AD-38136.1	GGTCCTAGTAGGAAATAAA	1741	TTTATTTCCTACTAGGACC	1779
AD-40036.1	GTAGGAAATAAATGTGATT	1742	AATCACATTTATTTCCTAC	1780
AD-40008.1	ATGTGATTTGCCTTCTAGA	1743	TCTAGAAGGCAAATCACAT	1781
AD-40021.1	CCTTCTAGAACAGTAGACA	1744	TGTCTACTGTTCTAGAAGG	1782
AD-40077.1	AGGCTCAGGACTTAGCAAG	1745	CTTGCTAAGTCCTGAGCCT	1783
AD-40072.1	GGACTTAGCAAGAAGTTAT	1746	ATAACTTCTTGCTAAGTCC	1784
AD-40061.1	AGCAAGAAGTTATGGAATT	1747	AATTCCATAACTTCTTGCT	1785
AD-40068.1	TTATGGAATTCCTTTTATT	1748	AATAAAAGGAATTCCATAA	1786
AD-38131.1	GGAATTCCTTTTATTGAAA	1749	TTTCAATAAAAGGAATTCC	1787
AD-38167.1	CCTTTTATTGAAACATCAG	1750	CTGATGTTTCAATAAAAGG	1788
hs_KRAS 1273_A22S26	CCTGATGAATGTAAAGTTA	1751	TAACTTTACATTCATCAGG	1789
hs_KRAS 2892_A37S26	GGAGAATTTAATAAAGATA	1752	TATCTTTATTAAATTCTCC	1790
hs_KRAS 4731_A22S26	GAATAGTCATAACTAGATT	1753	AATCTAGTTATGACTATTC	1791

Table 3. KRAS duplexes with modified sequences

Duplex	Sense Sequence	Seq SEQ ID NO:	Anti sense Sequence	Seq SEQ ID NO:
AD-35523.3	GGAcGAAuAuGAuccAAcAdTdT	855	UGUUGGAUcAuAUUCGUCCdTdT	1282
AD-35529.1	GAcGAAuAuGAuccAAcAAdTdT	856	UUGUUGGAUcAuAUUCGUCdTdT	1283
AD-35535.4	AcGAAuAuGAuccAAcAAudTdT	857	AUUGUUGGAUcAuAUUCGUdTdT	1284
AD-35541.4	cGAAuAuGAuccAAcAAuAdTdT	858	uAUUGUUGGAUcAuAUUCGdTdT	1285
AD-35547.4	GAAuAuGAuccAAcAAuAGdTdT	859	CuAUUGUUGGAUcAuAUUCdTdT	1286
AD-35553.4	AAuAuGAuccAAcAAuAGAdTdT	860	UCuAUUGUUGGAUcAuAUUdTdT	1287
AD-35559.4	AuAuGAuccAAcAAuAGAGdTdT	861	CUCuAUUGUUGGAUcAuAUdTdT	1288
AD-35565.4	uAuGAuccAAcAAuAGAGGdTdT	862	CCUCuAUUGUUGGAUcAuAdTdT	1289
AD-35524.4	AuGAuccAAcAAuAGAGGAdTdT	863	UCCUCuAUUGUUGGAUcAUdTdT	1290
AD-35530.4	uGAuccAAcAAuAGAGGAudTdT	864	AUCCUCuAUUGUUGGAUcAdTdT	1291
AD-35536.4	GAuccAAcAAuAGAGGAuudTdT	865	AAUCCUCuAUUGUUGGAUCdTdT	1292
AD-35542.4	AuccAAcAAuAGAGGAuucdTdT	866	GAAUCCUCuAUUGUUGGAUdTdT	1293
AD-35548.4	uccAAcAAuAGAGGAuuccdTdT	867	GGAAUCCUCuAUUGUUGGAdTdT	1294
AD-35554.4	ccAAcAAuAGAGGAuuccudTdT	868	AGGAAUCCUCuAUUGUUGGdTdT	1295
AD-35560.2	cAAcAAuAGAGGAuuccuAdTdT	869	uAGGAAUCCUCuAUUGUUGdTdT	1296
AD-35566.4	AAcAAuAGAGGAuuccuAcdTdT	870	GuAGGAAUCCUCuAUUGUUdTdT	1297
AD-35525.2	AcAAuAGAGGAuuccuAcAdTdT	871	UGuAGGAAUCCUCuAUUGUdTdT	1298
AD-35531.4	cAAuAGAGGAuuccuAcAGdTdT	872	CUGuAGGAAUCCUCuAUUGdTdT	1299
AD-35537.4	AAuAGAGGAuuccuAcAGGdTdT	873	CCUGuAGGAAUCCUCuAUUdTdT	1300

AD-35543.2	AuAGAGGAuuccuAcAGGAdTdT	874	UCCUGuAGGAAUCCUCuAUdTdT	1301
AD-35549.4	uAGAGGAuuccuAcAGGAAdTdT	875	UUCCUGuAGGAAUCCUCuAdTdT	1302
AD-35555.4	AGAGGAuuccuAcAGGAAGdTdT	876	CUUCCUGuAGGAAUCCUCUdTdT	1303
AD-35561.4	GAGGAuuccuAcAGGAAGcdTdT	877	GCUUCCUGuAGGAAUCCUCdTdT	1304
AD-35567.4	AGGAuuccuAcAGGAAGcAdTdT	878	UGCUUCCUGuAGGAAUCCUdTdT	1305
AD-35526.4	GGAuuccuAcAGGAAGcAAdTdT	879	UUGCUUCCUGuAGGAAUCCdTdT	1306
AD-35532.4	GAuuccuAcAGGAAGcAAGdTdT	880	CUUGCUUCCUGuAGGAAUCdTdT	1307
AD-35538.4	AuuccuAcAGGAAGcAAGudTdT	881	ACUUGCUUCCUGuAGGAAUdTdT	1308
AD-35544.4	uuccuAcAGGAAGcAAGuAdTdT	882	uACUUGCUUCCUGuAGGAAdTdT	1309
AD-35550.4	uccuAcAGGAAGcAAGuAGdTdT	883	CuACUUGCUUCCUGuAGGAdTdT	1310
AD-35556.4	ccuAcAGGAAGcAAGuAGudTdT	884	ACuACUUGCUUCCUGuAGGdTdT	1311
AD-35562.4	cuAcAGGAAGcAAGuAGuAdTdT	885	uACuACUUGCUUCCUGuAGdTdT	1312
AD-35568.4	uAcAGGAAGcAAGuAGuAAdTdT	886	UuACuACUUGCUUCCUGuAdTdT	1313
AD-35527.4	AcAGGAAGcAAGuAGuAAudTdT	887	AUuACuACUUGCUUCCUGUdTdT	1314
AD-35533.4	cAGGAAGcAAGuAGuAAuudTdT	888	AAUuACuACUUGCUUCCUGdTdT	1315
AD-35539.4	uuGGAuAuucucGAcAcAGdTdT	889	CUGUGUCGAGAAuAUCcAAdTdT	1316
AD-35545.4	uGGAuAuucucGAcAcAGcdTdT	890	GCUGUGUCGAGAAuAUCcAdTdT	1317
AD-35551.4	GGAuAuucucGAcAcAGcAdTdT	891	UGCUGUGUCGAGAAuAUCCdTdT	1318
AD-35563.4	AuAuucucGAcAcAGcAGGdTdT	892	CCUGCUGUGUCGAGAAuAUdTdT	1319
AD-35528.4	AuucucGAcAcAGcAGGucdTdT	893	GACCUGCUGUGUCGAGAAUdTdT	1320
AD-35540.4	ucucGAcAcAGcAGGucAAdTdT	894	UUGACCUGCUGUGUCGAGAdTdT	1321
AD-35546.4	cucGAcAcAGcAGGucAAGdTdT	895	CUUGACCUGCUGUGUCGAGdTdT	1322
AD-35552.4	ucGAcAcAGcAGGucAAGAdTdT	896	UCUUGACCUGCUGUGUCGAdTdT	1323
AD-35558.4	cGAcAcAGcAGGucAAGAGdTdT	897	CUCUUGACCUGCUGUGUCGdTdT	1324
AD-35564.4	GAcAcAGcAGGucAAGAGGdTdT	898	CCUCUUGACCUGCUGUGUCdTdT	1325
AD-35570.4	AcAcAGcAGGucAAGAGGAdTdT	899	UCCUCUUGACCUGCUGUGUdTdT	1326
AD-35571.4	cAcAGcAGGucAAGAGGAGdTdT	900	CUCCUCUUGACCUGCUGUGdTdT	1327
AD-35577.4	AcAGcAGGucAAGAGGAGudTdT	901	ACUCCUCUUGACCUGCUGUdTdT	1328
AD-35583.4	cAGcAGGucAAGAGGAGuAdTdT	902	uACUCCUCUUGACCUGCUGdTdT	1329
AD-35589.4	AGcAGGucAAGAGGAGuAcdTdT	903	GuACUCCUCUUGACCUGCUdTdT	1330
AD-35595.4	GcAGGucAAGAGGAGuAcAdTdT	904	UGuACUCCUCUUGACCUGCdTdT	1331
AD-35601.4	cAGGucAAGAGGAGuAcAGdTdT	905	CUGuACUCCUCUUGACCUGdTdT	1332
AD-35607.4	AGGucAAGAGGAGuAcAGudTdT	906	ACUGuACUCCUCUUGACCUdTdT	1333
AD-35613.4	GGucAAGAGGAGuAcAGuGdTdT	907	cACUGuACUCCUCUUGACCdTdT	1334
AD-35572.4	GucAAGAGGAGuAcAGuGcdTdT	908	GcACUGuACUCCUCUUGACdTdT	1335
AD-35578.4	ucAAGAGGAGuAcAGuGcAdTdT	909	UGcACUGuACUCCUCUUGAdTdT	1336
AD-35584.4	cAAGAGGAGuAcAGuGcAAdTdT	910	UUGcACUGuACUCCUCUUGdTdT	1337
AD-35590.4	AAGAGGAGuAcAGuGcAAudTdT	911	AUUGcACUGuACUCCUCUUdTdT	1338
AD-35596.4	AGAGGAGuAcAGuGcAAuGdTdT	912	cAUUGcACUGuACUCCUCUdTdT	1339
AD-35602.4	GAGGAGuAcAGuGcAAuGAdTdT	913	UcAUUGcACUGuACUCCUCdTdT	1340
AD-35608.4	AGGAGuAcAGuGcAAuGAGdTdT	914	CUcAUUGcACUGuACUCCUdTdT	1341
AD-35614.4	GGAGuAcAGuGcAAuGAGGdTdT	915	CCUcAUUGcACUGuACUCCdTdT	1342
AD-35573.4	GAGuAcAGuGcAAuGAGGGdTdT	916	CCCUcAUUGcACUGuACUCdTdT	1343
AD-35579.4	GGGGAGGGcuuucuuuGuGdTdT	917	cAcAAAGAAAGCCCUCCCCdTdT	1344
AD-35585.4	GGGAGGGcuuucuuuGuGudTdT	918	AcAcAAAGAAAGCCCUCCCdTdT	1345

AD-35591.4	GGAGGGcuuucuuuGuGuAdTdT	919	uAcAcAAAGAAAGCCCUCCdTdT	1346
AD-35597.4	GAGGGcuuucuuuGuGuAudTdT	920	AuAcAcAAAGAAAGCCCUCdTdT	1347
AD-35603.4	AGGGcuuucuuuGuGuAuudTdT	921	AAuAcAcAAAGAAAGCCCUdTdT	1348
AD-35609.4	GGGcuuucuuuGuGuAuuudTdT	922	AAAuAcAcAAAGAAAGCCCdTdT	1349
AD-35615.4	GGcuuucuuuGuGuAuuuGdTdT	923	cAAAuAcAcAAAGAAAGCCdTdT	1350
AD-35574.4	GcuuucuuuGuGuAuuuGcdTdT	924	GcAAAuAcAcAAAGAAAGCdTdT	1351
AD-35580.1	cuuucuuuGuGuAuuuGccdTdT	925	GGcAAAuAcAcAAAGAAAGdTdT	1352
AD-35586.4	uuucuuuGuGuAuuuGccAdTdT	926	UGGcAAAuAcAcAAAGAAAdTdT	1353
AD-35592.4	uucuuuGuGuAuuuGccAudTdT	927	AUGGcAAAuAcAcAAAGAAdTdT	1354
AD-35598.4	ucuuuGuGuAuuuGccAuAdTdT	928	uAUGGcAAAuAcAcAAAGAdTdT	1355
AD-35604.4	cuuuGuGuAuuuGccAuAAdTdT	929	UuAUGGcAAAuAcAcAAAGdTdT	1356
AD-35610.4	uuuGuGuAuuuGccAuAAAdTdT	930	UUuAUGGcAAAuAcAcAAAdTdT	1357
AD-35616.4	uuGuGuAuuuGccAuAAAudTdT	931	AUUuAUGGcAAAuAcAcAAdTdT	1358
AD-35575.4	uGuGuAuuuGccAuAAAuAdTdT	932	uAUUuAUGGcAAAuAcAcAdTdT	1359
AD-35581.4	GuGuAuuuGccAuAAAuAAdTdT	933	UuAUUuAUGGcAAAuAcACdTdT	1360
AD-35587.4	uGuAuuuGccAuAAAuAAudTdT	934	AUuAUUuAUGGcAAAuAcAdTdT	1361
AD-35593.4	GuAuuuGccAuAAAuAAuAdTdT	935	uAUuAUUuAUGGcAAAuACdTdT	1362
AD-35599.4	uAuuuGccAuAAAuAAuAcdTdT	936	GuAUuAUUuAUGGcAAAuAdTdT	1363
AD-35605.4	AuuuGccAuAAAuAAuAcudTdT	937	AGuAUuAUUuAUGGcAAAUdTdT	1364
AD-35611.4	uuuGccAuAAAuAAuAcuAdTdT	938	uAGuAUuAUUuAUGGcAAAdTdT	1365
AD-35617.4	uGAAGAuAuucAccAuuAudTdT	939	AuAAUGGUGAAuAUCUUcAdTdT	1366
AD-35576.4	GAAGAuAuucAccAuuAuAdTdT	940	uAuAAUGGUGAAuAUCUUCdTdT	1367
AD-35588.4	AGAuAuucAccAuuAuAGAdTdT	941	UCuAuAAUGGUGAAuAUCUdTdT	1368
AD-35667.1	AAAcAucAGcAAAGAcAAGdTdT	942	CUUGUCUUUGCUGAUGUUUdTdT	1369
AD-35673.1	AAcAucAGcAAAGAcAAGAdTdT	943	UCUUGUCUUUGCUGAUGUUdTdT	1370
AD-35679.1	AcAucAGcAAAGAcAAGAcdTdT	944	GUCUUGUCUUUGCUGAUGUdTdT	1371
AD-35685.1	cAucAGcAAAGAcAAGAcAdTdT	945	UGUCUUGUCUUUGCUGAUGdTdT	1372
AD-35691.1	AucAGcAAAGAcAAGAcAGdTdT	946	CUGUCUUGUCUUUGCUGAUdTdT	1373
AD-35557.1	GAuAuucucGAcAcAGcAGdTdT	947	CUGCUGUGUCGAGAAuAUCdTdT	1374
AD-35618.1	uucAccAuuAuAGAGAAcAdTdT	948	UGUUCUCuAuAAUGGUGAAdTdT	1375
AD-35569.1	uAuucucGAcAcAGcAGGudTdT	949	ACCUGCUGUGUCGAGAAuAdTdT	1376
AD-35534.1	uucucGAcAcAGcAGGucAdTdT	950	UGACCUGCUGUGUCGAGAAdTdT	1377
AD-35582.1	AAGAuAuucAccAuuAuAGdTdT	951	CuAuAAUGGUGAAuAUCUUdTdT	1378
AD-35594.1	GAuAuucAccAuuAuAGAGdTdT	952	CUCuAuAAUGGUGAAuAUCdTdT	1379
AD-35600.1	AuAuucAccAuuAuAGAGAdTdT	953	UCUCuAuAAUGGUGAAuAUdTdT	1380
AD-35606.1	uAuucAccAuuAuAGAGAAdTdT	954	UUCUCuAuAAUGGUGAAuAdTdT	1381
AD-35612.1	AuucAccAuuAuAGAGAAcdTdT	955	GUUCUCuAuAAUGGUGAAUdTdT	1382
AD-38127.1	ucAccAuuAuAGAGAAcAAdTdT	956	UUGUUCUCuAuAAUGGUGAdTdT	1383
AD-38133.1	cAccAuuAuAGAGAAcAAAdTdT	957	UUUGUUCUCuAuAAUGGUGdTdT	1384
AD-38139.1	AccAuuAuAGAGAAcAAAudTdT	958	AUUUGUUCUCuAuAAUGGUdTdT	1385
AD-38145.1	ccAuuAuAGAGAAcAAAuudTdT	959	AAUUUGUUCUCuAuAAUGGdTdT	1386
AD-38151.1	cAuuAuAGAGAAcAAAuuAdTdT	960	uAAUUUGUUCUCuAuAAUGdTdT	1387
AD-38157.1	AuuAuAGAGAAcAAAuuAAdTdT	961	UuAAUUUGUUCUCuAuAAUdTdT	1388
AD-38163.1	uuAuAGAGAAcAAAuuAAAdTdT	962	UUuAAUUUGUUCUCuAuAAdTdT	1389
AD-38169.1	uAuAGAGAAcAAAuuAAAAdTdT	963	UUUuAAUUUGUUCUCuAuAdTdT	1390

AD-38128.1	AuAGAGAAcAAAuuAAAAGdTdT	964	CUUUuAAUUUGUUCUCuAUdTdT	1391
AD-38134.1	uAGAGAAcAAAuuAAAAGAdTdT	965	UCUUUuAAUUUGUUCUCuAdTdT	1392
AD-38140.1	AGAGAAcAAAuuAAAAGAGdTdT	966	CUCUUUuAAUUUGUUCUCUdTdT	1393
AD-38146.1	GAAGAuGuAccuAuGGuccdTdT	967	GGACcAuAGGuAcAUCUUCdTdT	1394
AD-38152.1	AAGAuGuAccuAuGGuccudTdT	968	AGGACcAuAGGuAcAUCUUdTdT	1395
AD-38158.1	AGAuGuAccuAuGGuccuAdTdT	969	uAGGACcAuAGGuAcAUCUdTdT	1396
AD-38164.1	GAuGuAccuAuGGuccuAGdTdT	970	CuAGGACcAuAGGuAcAUCdTdT	1397
AD-38170.1	AuGuAccuAuGGuccuAGudTdT	971	ACuAGGACcAuAGGuAcAUdTdT	1398
AD-38129.1	uGuAccuAuGGuccuAGuAdTdT	972	uACuAGGACcAuAGGuAcAdTdT	1399
AD-38135.1	GuAccuAuGGuccuAGuAGdTdT	973	CuACuAGGACcAuAGGuACdTdT	1400
AD-38141.1	uAccuAuGGuccuAGuAGGdTdT	974	CCuACuAGGACcAuAGGuAdTdT	1401
AD-38147.1	AccuAuGGuccuAGuAGGAdTdT	975	UCCuACuAGGACcAuAGGUdTdT	1402
AD-38153.1	ccuAuGGuccuAGuAGGAAdTdT	976	UUCCuACuAGGACcAuAGGdTdT	1403
AD-38159.1	cuAuGGuccuAGuAGGAAAdTdT	977	UUUCCuACuAGGACcAuAGdTdT	1404
AD-38165.1	uAuGGuccuAGuAGGAAAudTdT	978	AUUUCCuACuAGGACcAuAdTdT	1405
AD-38171.1	AuGGuccuAGuAGGAAAuAdTdT	979	uAUUUCCuACuAGGACcAUdTdT	1406
AD-38130.1	uGGuccuAGuAGGAAAuAAdTdT	980	UuAUUUCCuACuAGGACcAdTdT	1407
AD-38136.1	GGuccuAGuAGGAAAuAAAdTdT	981	UUuAUUUCCuACuAGGACCdTdT	1408
AD-38142.1	GuccuAGuAGGAAAuAAAudTdT	982	AUUuAUUUCCuACuAGGACdTdT	1409
AD-38148.1	uccuAGuAGGAAAuAAAuGdTdT	983	cAUUuAUUUCCuACuAGGAdTdT	1410
AD-38154.1	ccuAGuAGGAAAuAAAuGudTdT	984	AcAUUuAUUUCCuACuAGGdTdT	1411
AD-38160.1	cuAGuAGGAAAuAAAuGuGdTdT	985	cAcAUUuAUUUCCuACuAGdTdT	1412
AD-38166.1	uAGuAGGAAAuAAAuGuGAdTdT	986	UcAcAUUuAUUUCCuACuAdTdT	1413
AD-38172.1	AGuAGGAAAuAAAuGuGAudTdT	987	AUcAcAUUuAUUUCCuACUdTdT	1414
AD-38131.1	GGAAuuccuuuuAuuGAAAdTdT	988	UUUcAAuAAAAGGAAUUCCdTdT	1415
AD-38137.1	GAAuuccuuuuAuuGAAAcdTdT	989	GUUUcAAuAAAAGGAAUUCdTdT	1416
AD-38143.1	AAuuccuuuuAuuGAAAcAdTdT	990	UGUUUcAAuAAAAGGAAUUdTdT	1417
AD-38149.1	AuuccuuuuAuuGAAAcAudTdT	991	AUGUUUcAAuAAAAGGAAUdTdT	1418
AD-38155.1	uuccuuuuAuuGAAAcAucdTdT	992	GAUGUUUcAAuAAAAGGAAdTdT	1419
AD-38161.1	uccuuuuAuuGAAAcAucAdTdT	993	UGAUGUUUcAAuAAAAGGAdTdT	1420
AD-38167.1	ccuuuuAuuGAAAcAucAGdTdT	994	CUGAUGUUUcAAuAAAAGGdTdT	1421
AD-38173.1	cuuuuAuuGAAAcAucAGcdTdT	995	GCUGAUGUUUcAAuAAAAGdTdT	1422
AD-38132.1	uuuuAuuGAAAcAucAGcAdTdT	996	UGCUGAUGUUUcAAuAAAAdTdT	1423
AD-38138.1	uuuAuuGAAAcAucAGcAAdTdT	997	UUGCUGAUGUUUcAAuAAAdTdT	1424
AD-38144.1	uuAuuGAAAcAucAGcAAAdTdT	998	UUUGCUGAUGUUUcAAuAAdTdT	1425
AD-38150.1	uAuuGAAAcAucAGcAAAGdTdT	999	CUUUGCUGAUGUUUcAAuAdTdT	1426
AD-38156.1	AuuGAAAcAucAGcAAAGAdTdT	1000	UCUUUGCUGAUGUUUcAAUdTdT	1427
AD-38162.1	uuGAAAcAucAGcAAAGAcdTdT	1001	GUCUUUGCUGAUGUUUcAAdTdT	1428
AD-38168.1	uGAAAcAucAGcAAAGAcAdTdT	1002	UGUCUUUGCUGAUGUUUcAdTdT	1429
AD-38174.1	GAAAcAucAGcAAAGAcAAdTdT	1003	UUGUCUUUGCUGAUGUUUCdTdT	1430
AD-39683.1	AuGAcuGAAuAuAAAcuuGdTdT	1004	cAAGUUuAuAUUcAGUcAUdTdT	1431
AD-39689.1	uGAcuGAAuAuAAAcuuGudTdT	1005	AcAAGUUuAuAUUcAGUcAdTdT	1432
AD-39695.1	GAcuGAAuAuAAAcuuGuGdTdT	1006	cAcAAGUUuAuAUUcAGUCdTdT	1433
AD-39701.1	AcuGAAuAuAAAcuuGuGGdTdT	1007	CcAcAAGUUuAuAUUcAGUdTdT	1434
AD-39707.1	cuGAAuAuAAAcuuGuGGudTdT	1008	ACcAcAAGUUuAuAUUcAGdTdT	1435

AD-39713.1	uGAAuAuAAAcuuGuGGuAdTdT	1009	uACcAcAAGUUuAuAUUcAdTdT	1436
AD-39719.1	GAAuAuAAAcuuGuGGuAGdTdT	1010	CuACcAcAAGUUuAuAUUCdTdT	1437
AD-39725.1	AAuAuAAAcuuGuGGuAGudTdT	1011	ACuACcAcAAGUUuAuAUUdTdT	1438
AD-39684.1	AuAuAAAcuuGuGGuAGuudTdT	1012	AACuACcAcAAGUUuAuAUdTdT	1439
AD-39690.1	uAuAAAcuuGuGGuAGuuGdTdT	1013	cAACuACcAcAAGUUuAuAdTdT	1440
AD-39696.1	AuAAAcuuGuGGuAGuuGGdTdT	1014	CcAACuACcAcAAGUUuAUdTdT	1441
AD-39702.1	uAAAcuuGuGGuAGuuGGAdTdT	1015	UCcAACuACcAcAAGUUuAdTdT	1442
AD-39708.1	AAAcuuGuGGuAGuuGGAGdTdT	1016	CUCcAACuACcAcAAGUUUdTdT	1443
AD-39714.1	AAcuuGuGGuAGuuGGAGcdTdT	1017	GCUCcAACuACcAcAAGUUdTdT	1444
AD-39720.1	AcuuGuGGuAGuuGGAGcudTdT	1018	AGCUCcAACuACcAcAAGUdTdT	1445
AD-39726.1	cuuGuGGuAGuuGGAGcuGdTdT	1019	cAGCUCcAACuACcAcAAGdTdT	1446
AD-39685.1	uuGuGGuAGuuGGAGcuGGdTdT	1020	CcAGCUCcAACuACcAcAAdTdT	1447
AD-39691.1	uGuGGuAGuuGGAGcuGGudTdT	1021	ACcAGCUCcAACuACcAcAdTdT	1448
AD-39697.1	GuGGuAGuuGGAGcuGGuGdTdT	1022	cACcAGCUCcAACuACcACdTdT	1449
AD-39703.1	uGGuAGuuGGAGcuGGuGGdTdT	1023	CcACcAGCUCcAACuACcAdTdT	1450
AD-39709.1	GGuAGuuGGAGcuGGuGGcdTdT	1024	GCcACcAGCUCcAACuACCdTdT	1451
AD-39715.1	GuAGuuGGAGcuGGuGGcGdTdT	1025	CGCcACcAGCUCcAACuACdTdT	1452
AD-39721.1	uAGuuGGAGcuGGuGGcGudTdT	1026	ACGCcACcAGCUCcAACuAdTdT	1453
AD-39727.1	AGuuGGAGcuGGuGGcGuAdTdT	1027	uACGCcACcAGCUCcAACUdTdT	1454
AD-39686.1	GuuGGAGcuGGuGGcGuAGdTdT	1028	CuACGCcACcAGCUCcAACdTdT	1455
AD-39692.1	uuGGAGcuGGuGGcGuAGGdTdT	1029	CCuACGCcACcAGCUCcAAdTdT	1456
AD-39698.1	uGGAGcuGGuGGcGuAGGcdTdT	1030	GCCuACGCcACcAGCUCcAdTdT	1457
AD-39704.1	GGAGcuGGuGGcGuAGGcAdTdT	1031	UGCCuACGCcACcAGCUCCdTdT	1458
AD-39710.1	GAGcuGGuGGcGuAGGcAAdTdT	1032	UUGCCuACGCcACcAGCUCdTdT	1459
AD-39716.1	AGcuGGuGGcGuAGGcAAGdTdT	1033	CUUGCCuACGCcACcAGCUdTdT	1460
AD-39722.1	GcuGGuGGcGuAGGcAAGAdTdT	1034	UCUUGCCuACGCcACcAGCdTdT	1461
AD-39728.1	cuGGuGGcGuAGGcAAGAGdTdT	1035	CUCUUGCCuACGCcACcAGdTdT	1462
AD-39687.1	uGGuGGcGuAGGcAAGAGudTdT	1036	ACUCUUGCCuACGCcACcAdTdT	1463
AD-39693.1	GGuGGcGuAGGcAAGAGuGdTdT	1037	cACUCUUGCCuACGCcACCdTdT	1464
AD-39699.1	GuGGcGuAGGcAAGAGuGcdTdT	1038	GcACUCUUGCCuACGCcACdTdT	1465
AD-39705.1	uGGcGuAGGcAAGAGuGccdTdT	1039	GGcACUCUUGCCuACGCcAdTdT	1466
AD-39711.1	GGcGuAGGcAAGAGuGccudTdT	1040	AGGcACUCUUGCCuACGCCdTdT	1467
AD-39717.1	GcGuAGGcAAGAGuGccuudTdT	1041	AAGGcACUCUUGCCuACGCdTdT	1468
AD-39723.1	cGuAGGcAAGAGuGccuuGdTdT	1042	cAAGGcACUCUUGCCuACGdTdT	1469
AD-39729.1	GuAGGcAAGAGuGccuuGAdTdT	1043	UcAAGGcACUCUUGCCuACdTdT	1470
AD-39688.1	uAGGcAAGAGuGccuuGAcdTdT	1044	GUcAAGGcACUCUUGCCuAdTdT	1471
AD-39694.1	AGGcAAGAGuGccuuGAcGdTdT	1045	CGUcAAGGcACUCUUGCCUdTdT	1472
AD-39700.1	GGcAAGAGuGccuuGAcGAdTdT	1046	UCGUcAAGGcACUCUUGCCdTdT	1473
AD-39706.1	GcAAGAGuGccuuGAcGAudTdT	1047	AUCGUcAAGGcACUCUUGCdTdT	1474
AD-39712.1	cAAGAGuGccuuGAcGAuAdTdT	1048	uAUCGUcAAGGcACUCUUGdTdT	1475
AD-39718.1	AAGAGuGccuuGAcGAuAcdTdT	1049	GuAUCGUcAAGGcACUCUUdTdT	1476
AD-39724.1	AGAGuGccuuGAcGAuAcAdTdT	1050	UGuAUCGUcAAGGcACUCUdTdT	1477
AD-39730.1	GAGuGccuuGAcGAuAcAGdTdT	1051	CUGuAUCGUcAAGGcACUCdTdT	1478
AD-39736.1	AGuGccuuGAcGAuAcAGcdTdT	1052	GCUGuAUCGUcAAGGcACUdTdT	1479
AD-39742.1	GuGccuuGAcGAuAcAGcudTdT	1053	AGCUGuAUCGUcAAGGcACdTdT	1480

AD-39748.1	uGccuuGAcGAuAcAGcuAdTdT	1054	uAGCUGuAUCGUcAAGGcAdTdT	1481
AD-39754.1	GccuuGAcGAuAcAGcuAAdTdT	1055	UuAGCUGuAUCGUcAAGGCdTdT	1482
AD-39760.1	ccuuGAcGAuAcAGcuAAudTdT	1056	AUuAGCUGuAUCGUcAAGGdTdT	1483
AD-39766.1	cuuGAcGAuAcAGcuAAuudTdT	1057	AAUuAGCUGuAUCGUcAAGdTdT	1484
AD-39772.1	uuGAcGAuAcAGcuAAuucdTdT	1058	GAAUuAGCUGuAUCGUcAAdTdT	1485
AD-39731.1	uGAcGAuAcAGcuAAuucAdTdT	1059	UGAAUuAGCUGuAUCGUcAdTdT	1486
AD-39737.1	GAcGAuAcAGcuAAuucAGdTdT	1060	CUGAAUuAGCUGuAUCGUCdTdT	1487
AD-39743.1	AcGAuAcAGcuAAuucAGAdTdT	1061	UCUGAAUuAGCUGuAUCGUdTdT	1488
AD-39749.1	cGAuAcAGcuAAuucAGAAdTdT	1062	UUCUGAAUuAGCUGuAUCGdTdT	1489
AD-39755.1	GAuAcAGcuAAuucAGAAudTdT	1063	AUUCUGAAUuAGCUGuAUCdTdT	1490
AD-39761.1	AuAcAGcuAAuucAGAAucdTdT	1064	GAUUCUGAAUuAGCUGuAUdTdT	1491
AD-39767.1	uAcAGcuAAuucAGAAucAdTdT	1065	UGAUUCUGAAUuAGCUGuAdTdT	1492
AD-39773.1	AcAGcuAAuucAGAAucAudTdT	1066	AUGAUUCUGAAUuAGCUGUdTdT	1493
AD-39732.1	cAGcuAAuucAGAAucAuudTdT	1067	AAUGAUUCUGAAUuAGCUGdTdT	1494
AD-39738.1	AGcuAAuucAGAAucAuuudTdT	1068	AAAUGAUUCUGAAUuAGCUdTdT	1495
AD-39744.1	GcuAAuucAGAAucAuuuudTdT	1069	AAAAUGAUUCUGAAUuAGCdTdT	1496
AD-39750.1	cuAAuucAGAAucAuuuuGdTdT	1070	cAAAAUGAUUCUGAAUuAGdTdT	1497
AD-39756.1	uAAuucAGAAucAuuuuGudTdT	1071	AcAAAAUGAUUCUGAAUuAdTdT	1498
AD-39762.1	AAuucAGAAucAuuuuGuGdTdT	1072	cAcAAAAUGAUUCUGAAUUdTdT	1499
AD-39768.1	AuucAGAAucAuuuuGuGGdTdT	1073	CcAcAAAAUGAUUCUGAAUdTdT	1500
AD-39774.1	uucAGAAucAuuuuGuGGAdTdT	1074	UCcAcAAAAUGAUUCUGAAdTdT	1501
AD-39733.1	ucAGAAucAuuuuGuGGAcdTdT	1075	GUCcAcAAAAUGAUUCUGAdTdT	1502
AD-39739.1	cAGAAucAuuuuGuGGAcGdTdT	1076	CGUCcAcAAAAUGAUUCUGdTdT	1503
AD-39745.1	AGAAucAuuuuGuGGAcGAdTdT	1077	UCGUCcAcAAAAUGAUUCUdTdT	1504
AD-39751.1	GAAucAuuuuGuGGAcGAAdTdT	1078	UUCGUCcAcAAAAUGAUUCdTdT	1505
AD-39757.1	AAucAuuuuGuGGAcGAAudTdT	1079	AUUCGUCcAcAAAAUGAUUdTdT	1506
AD-39763.1	AucAuuuuGuGGAcGAAuAdTdT	1080	uAUUCGUCcAcAAAAUGAUdTdT	1507
AD-39769.1	ucAuuuuGuGGAcGAAuAudTdT	1081	AuAUUCGUCcAcAAAAUGAdTdT	1508
AD-39775.1	cAuuuuGuGGAcGAAuAuGdTdT	1082	cAuAUUCGUCcAcAAAAUGdTdT	1509
AD-39734.1	AuuuuGuGGAcGAAuAuGAdTdT	1083	UcAuAUUCGUCcAcAAAAUdTdT	1510
AD-39740.1	uuuuGuGGAcGAAuAuGAudTdT	1084	AUcAuAUUCGUCcAcAAAAdTdT	1511
AD-39746.1	uuuGuGGAcGAAuAuGAucdTdT	1085	GAUcAuAUUCGUCcAcAAAdTdT	1512
AD-39752.1	uuGuGGAcGAAuAuGAuccdTdT	1086	GGAUcAuAUUCGUCcAcAAdTdT	1513
AD-39758.1	uGuGGAcGAAuAuGAuccAdTdT	1087	UGGAUcAuAUUCGUCcAcAdTdT	1514
AD-39764.1	GuGGAcGAAuAuGAuccAAdTdT	1088	UUGGAUcAuAUUCGUCcACdTdT	1515
AD-39770.1	uGGAcGAAuAuGAuccAAcdTdT	1089	GUUGGAUcAuAUUCGUCcAdTdT	1516
AD-39776.1	AGGAAGcAAGuAGuAAuuGdTdT	1090	cAAUuACuACUUGCUUCCUdTdT	1517
AD-39735.1	GGAAGcAAGuAGuAAuuGAdTdT	1091	UcAAUuACuACUUGCUUCCdTdT	1518
AD-39741.1	GAAGcAAGuAGuAAuuGAudTdT	1092	AUcAAUuACuACUUGCUUCdTdT	1519
AD-39747.1	AAGcAAGuAGuAAuuGAuGdTdT	1093	cAUcAAUuACuACUUGCUUdTdT	1520
AD-39753.1	AGcAAGuAGuAAuuGAuGGdTdT	1094	CcAUcAAUuACuACUUGCUdTdT	1521
AD-39759.1	GcAAGuAGuAAuuGAuGGAdTdT	1095	UCcAUcAAUuACuACUUGCdTdT	1522
AD-39765.1	cAAGuAGuAAuuGAuGGAGdTdT	1096	CUCcAUcAAUuACuACUUGdTdT	1523
AD-39771.1	AAGuAGuAAuuGAuGGAGAdTdT	1097	UCUCcAUcAAUuACuACUUdTdT	1524
AD-39778.1	AGuAGuAAuuGAuGGAGAAdTdT	1098	UUCUCcAUcAAUuACuACUdTdT	1525

AD-39784.1	GuAGuAAuuGAuGGAGAAAdTdT	1099	UUUCUCcAUcAAUuACuACdTdT	1526
AD-39790.1	uAGuAAuuGAuGGAGAAAcdTdT	1100	GUUUCUCcAUcAAUuACuAdTdT	1527
AD-39796.1	AGuAAuuGAuGGAGAAAccdTdT	1101	GGUUUCUCcAUcAAUuACUdTdT	1528
AD-39802.1	GuAAuuGAuGGAGAAAccudTdT	1102	AGGUUUCUCcAUcAAUuACdTdT	1529
AD-39808.1	uAAuuGAuGGAGAAAccuGdTdT	1103	cAGGUUUCUCcAUcAAUuAdTdT	1530
AD-39814.1	AAuuGAuGGAGAAAccuGudTdT	1104	AcAGGUUUCUCcAUcAAUUdTdT	1531
AD-39820.1	AuuGAuGGAGAAAccuGucdTdT	1105	GAcAGGUUUCUCcAUcAAUdTdT	1532
AD-39779.1	uuGAuGGAGAAAccuGucudTdT	1106	AGAcAGGUUUCUCcAUcAAdTdT	1533
AD-39785.1	uGAuGGAGAAAccuGucucdTdT	1107	GAGAcAGGUUUCUCcAUcAdTdT	1534
AD-39791.1	GAuGGAGAAAccuGucucudTdT	1108	AGAGAcAGGUUUCUCcAUCdTdT	1535
AD-39797.1	AuGGAGAAAccuGucucuudTdT	1109	AAGAGAcAGGUUUCUCcAUdTdT	1536
AD-39803.1	uGGAGAAAccuGucucuuGdTdT	1110	cAAGAGAcAGGUUUCUCcAdTdT	1537
AD-39809.1	GGAGAAAccuGucucuuGGdTdT	1111	CcAAGAGAcAGGUUUCUCCdTdT	1538
AD-39815.1	GAGAAAccuGucucuuGGAdTdT	1112	UCcAAGAGAcAGGUUUCUCdTdT	1539
AD-39821.1	AGAAAccuGucucuuGGAudTdT	1113	AUCcAAGAGAcAGGUUUCUdTdT	1540
AD-39780.1	GAAAccuGucucuuGGAuAdTdT	1114	uAUCcAAGAGAcAGGUUUCdTdT	1541
AD-39786.1	AAAccuGucucuuGGAuAudTdT	1115	AuAUCcAAGAGAcAGGUUUdTdT	1542
AD-39792.1	AAccuGucucuuGGAuAuudTdT	1116	AAuAUCcAAGAGAcAGGUUdTdT	1543
AD-39798.1	AccuGucucuuGGAuAuucdTdT	1117	GAAuAUCcAAGAGAcAGGUdTdT	1544
AD-39804.1	ccuGucucuuGGAuAuucudTdT	1118	AGAAuAUCcAAGAGAcAGGdTdT	1545
AD-39810.1	cuGucucuuGGAuAuucucdTdT	1119	GAGAAuAUCcAAGAGAcAGdTdT	1546
AD-39816.1	uGucucuuGGAuAuucucGdTdT	1120	CGAGAAuAUCcAAGAGAcAdTdT	1547
AD-39822.1	GucucuuGGAuAuucucGAdTdT	1121	UCGAGAAuAUCcAAGAGACdTdT	1548
AD-39781.1	ucucuuGGAuAuucucGAcdTdT	1122	GUCGAGAAuAUCcAAGAGAdTdT	1549
AD-39787.1	cucuuGGAuAuucucGAcAdTdT	1123	UGUCGAGAAuAUCcAAGAGdTdT	1550
AD-39793.1	ucuuGGAuAuucucGAcAcdTdT	1124	GUGUCGAGAAuAUCcAAGAdTdT	1551
AD-39799.1	cuuGGAuAuucucGAcAcAdTdT	1125	UGUGUCGAGAAuAUCcAAGdTdT	1552
AD-39805.1	AGuAcAGuGcAAuGAGGGAdTdT	1126	UCCCUcAUUGcACUGuACUdTdT	1553
AD-39811.1	GuAcAGuGcAAuGAGGGAcdTdT	1127	GUCCCUcAUUGcACUGuACdTdT	1554
AD-39817.1	uAcAGuGcAAuGAGGGAccdTdT	1128	GGUCCCUcAUUGcACUGuAdTdT	1555
AD-39823.1	AcAGuGcAAuGAGGGAccAdTdT	1129	UGGUCCCUcAUUGcACUGUdTdT	1556
AD-39782.1	cAGuGcAAuGAGGGAccAGdTdT	1130	CUGGUCCCUcAUUGcACUGdTdT	1557
AD-39788.1	AGuGcAAuGAGGGAccAGudTdT	1131	ACUGGUCCCUcAUUGcACUdTdT	1558
AD-39794.1	GuGcAAuGAGGGAccAGuAdTdT	1132	uACUGGUCCCUcAUUGcACdTdT	1559
AD-39800.1	uGcAAuGAGGGAccAGuAcdTdT	1133	GuACUGGUCCCUcAUUGcAdTdT	1560
AD-39806.1	GcAAuGAGGGAccAGuAcAdTdT	1134	UGuACUGGUCCCUcAUUGCdTdT	1561
AD-39812.1	cAAuGAGGGAccAGuAcAudTdT	1135	AUGuACUGGUCCCUcAUUGdTdT	1562
AD-39818.1	AAuGAGGGAccAGuAcAuGdTdT	1136	cAUGuACUGGUCCCUcAUUdTdT	1563
AD-39824.1	AuGAGGGAccAGuAcAuGAdTdT	1137	UcAUGuACUGGUCCCUcAUdTdT	1564
AD-39783.1	uGAGGGAccAGuAcAuGAGdTdT	1138	CUcAUGuACUGGUCCCUcAdTdT	1565
AD-39789.1	GAGGGAccAGuAcAuGAGGdTdT	1139	CCUcAUGuACUGGUCCCUCdTdT	1566
AD-39795.1	AGGGAccAGuAcAuGAGGAdTdT	1140	UCCUcAUGuACUGGUCCCUdTdT	1567
AD-39801.1	GGGAccAGuAcAuGAGGAcdTdT	1141	GUCCUcAUGuACUGGUCCCdTdT	1568
AD-39807.1	GGAccAGuAcAuGAGGAcudTdT	1142	AGUCCUcAUGuACUGGUCCdTdT	1569
AD-39813.1	GAccAGuAcAuGAGGAcuGdTdT	1143	cAGUCCUcAUGuACUGGUCdTdT	1570

AD-39819.1	AccAGuAcAuGAGGAcuGGdTdT	1144	CcAGUCCUcAUGuACUGGUdTdT	1571
AD-39825.1	ccAGuAcAuGAGGAcuGGGdTdT	1145	CCcAGUCCUcAUGuACUGGdTdT	1572
AD-39831.1	cAGuAcAuGAGGAcuGGGGdTdT	1146	CCCcAGUCCUcAUGuACUGdTdT	1573
AD-39837.1	AGuAcAuGAGGAcuGGGGAdTdT	1147	UCCCcAGUCCUcAUGuACUdTdT	1574
AD-39843.1	GuAcAuGAGGAcuGGGGAGdTdT	1148	CUCCCcAGUCCUcAUGuACdTdT	1575
AD-39849.1	uAcAuGAGGAcuGGGGAGGdTdT	1149	CCUCCCcAGUCCUcAUGuAdTdT	1576
AD-39855.1	AcAuGAGGAcuGGGGAGGGdTdT	1150	CCCUCCCcAGUCCUcAUGUdTdT	1577
AD-39861.1	cAuGAGGAcuGGGGAGGGcdTdT	1151	GCCCUCCCcAGUCCUcAUGdTdT	1578
AD-39867.1	AuGAGGAcuGGGGAGGGcudTdT	1152	AGCCCUCCCcAGUCCUcAUdTdT	1579
AD-39826.1	uGAGGAcuGGGGAGGGcuudTdT	1153	AAGCCCUCCCcAGUCCUcAdTdT	1580
AD-39832.1	GAGGAcuGGGGAGGGcuuudTdT	1154	AAAGCCCUCCCcAGUCCUCdTdT	1581
AD-39838.1	AGGAcuGGGGAGGGcuuucdTdT	1155	GAAAGCCCUCCCcAGUCCUdTdT	1582
AD-39844.1	GGAcuGGGGAGGGcuuucudTdT	1156	AGAAAGCCCUCCCcAGUCCdTdT	1583
AD-39850.1	GAcuGGGGAGGGcuuucuudTdT	1157	AAGAAAGCCCUCCCcAGUCdTdT	1584
AD-39856.1	AcuGGGGAGGGcuuucuuudTdT	1158	AAAGAAAGCCCUCCCcAGUdTdT	1585
AD-39862.1	cuGGGGAGGGcuuucuuuGdTdT	1159	cAAAGAAAGCCCUCCCcAGdTdT	1586
AD-39868.1	uGGGGAGGGcuuucuuuGudTdT	1160	AcAAAGAAAGCCCUCCCcAdTdT	1587
AD-39827.1	uuGccAuAAAuAAuAcuAAdTdT	1161	UuAGuAUuAUUuAUGGcAAdTdT	1588
AD-39833.1	uGccAuAAAuAAuAcuAAAdTdT	1162	UUuAGuAUuAUUuAUGGcAdTdT	1589
AD-39839.1	GccAuAAAuAAuAcuAAAudTdT	1163	AUUuAGuAUuAUUuAUGGCdTdT	1590
AD-39845.1	ccAuAAAuAAuAcuAAAucdTdT	1164	GAUUuAGuAUuAUUuAUGGdTdT	1591
AD-39851.1	cAuAAAuAAuAcuAAAucAdTdT	1165	UGAUUuAGuAUuAUUuAUGdTdT	1592
AD-39857.1	AuAAAuAAuAcuAAAucAudTdT	1166	AUGAUUuAGuAUuAUUuAUdTdT	1593
AD-39863.1	uAAAuAAuAcuAAAucAuudTdT	1167	AAUGAUUuAGuAUuAUUuAdTdT	1594
AD-39869.1	AAAuAAuAcuAAAucAuuudTdT	1168	AAAUGAUUuAGuAUuAUUUdTdT	1595
AD-39828.1	AAuAAuAcuAAAucAuuuGdTdT	1169	cAAAUGAUUuAGuAUuAUUdTdT	1596
AD-39834.1	AuAAuAcuAAAucAuuuGAdTdT	1170	UcAAAUGAUUuAGuAUuAUdTdT	1597
AD-39840.1	uAAuAcuAAAucAuuuGAAdTdT	1171	UUcAAAUGAUUuAGuAUuAdTdT	1598
AD-39846.1	AAuAcuAAAucAuuuGAAGdTdT	1172	CUUcAAAUGAUUuAGuAUUdTdT	1599
AD-39852.1	AuAcuAAAucAuuuGAAGAdTdT	1173	UCUUcAAAUGAUUuAGuAUdTdT	1600
AD-39858.1	uAcuAAAucAuuuGAAGAudTdT	1174	AUCUUcAAAUGAUUuAGuAdTdT	1601
AD-39864.1	AcuAAAucAuuuGAAGAuAdTdT	1175	uAUCUUcAAAUGAUUuAGUdTdT	1602
AD-39870.1	cuAAAucAuuuGAAGAuAudTdT	1176	AuAUCUUcAAAUGAUUuAGdTdT	1603
AD-39829.1	uAAAucAuuuGAAGAuAuudTdT	1177	AAuAUCUUcAAAUGAUUuAdTdT	1604
AD-39835.1	AAAucAuuuGAAGAuAuucdTdT	1178	GAAuAUCUUcAAAUGAUUUdTdT	1605
AD-39841.1	AAucAuuuGAAGAuAuucAdTdT	1179	UGAAuAUCUUcAAAUGAUUdTdT	1606
AD-39853.1	ucAuuuGAAGAuAuucAccdTdT	1180	GGUGAAuAUCUUcAAAUGAdTdT	1607
AD-39859.1	cAuuuGAAGAuAuucAccAdTdT	1181	UGGUGAAuAUCUUcAAAUGdTdT	1608
AD-39865.1	AuuuGAAGAuAuucAccAudTdT	1182	AUGGUGAAuAUCUUcAAAUdTdT	1609
AD-39871.1	uuuGAAGAuAuucAccAuudTdT	1183	AAUGGUGAAuAUCUUcAAAdTdT	1610
AD-39830.1	uuGAAGAuAuucAccAuuAdTdT	1184	uAAUGGUGAAuAUCUUcAAdTdT	1611
AD-39836.1	GAGAAcAAAuuAAAAGAGudTdT	1185	ACUCUUUuAAUUUGUUCUCdTdT	1612
AD-39842.1	AGAAcAAAuuAAAAGAGuudTdT	1186	AACUCUUUuAAUUUGUUCUdTdT	1613
AD-39848.1	GAAcAAAuuAAAAGAGuuAdTdT	1187	uAACUCUUUuAAUUUGUUCdTdT	1614
AD-39854.1	AAcAAAuuAAAAGAGuuAAdTdT	1188	UuAACUCUUUuAAUUUGUUdTdT	1615

AD-39860.1	AcAAAuuAAAAGAGuuAAGdTdT	1189	CUuAACUCUUUuAAUUUGUdTdT	1616
AD-39866.1	cAAAuuAAAAGAGuuAAGGdTdT	1190	CCUuAACUCUUUuAAUUUGdTdT	1617
AD-39992.1	AAAuuAAAAGAGuuAAGGAdTdT	1191	UCCUuAACUCUUUuAAUUUdTdT	1618
AD-39998.1	AAuuAAAAGAGuuAAGGAcdTdT	1192	GUCCUuAACUCUUUuAAUUdTdT	1619
AD-40004.1	AuuAAAAGAGuuAAGGAcudTdT	1193	AGUCCUuAACUCUUUuAAUdTdT	1620
AD-40010.1	uuAAAAGAGuuAAGGAcucdTdT	1194	GAGUCCUuAACUCUUUuAAdTdT	1621
AD-40016.1	uAAAAGAGuuAAGGAcucudTdT	1195	AGAGUCCUuAACUCUUUuAdTdT	1622
AD-40022.1	AAAAGAGuuAAGGAcucuGdTdT	1196	cAGAGUCCUuAACUCUUUUdTdT	1623
AD-40028.1	AAAGAGuuAAGGAcucuGAdTdT	1197	UcAGAGUCCUuAACUCUUUdTdT	1624
AD-40034.1	AAGAGuuAAGGAcucuGAAdTdT	1198	UUcAGAGUCCUuAACUCUUdTdT	1625
AD-39999.1	GAGuuAAGGAcucuGAAGAdTdT	1199	UCUUcAGAGUCCUuAACUCdTdT	1626
AD-40005.1	AGuuAAGGAcucuGAAGAudTdT	1200	AUCUUcAGAGUCCUuAACUdTdT	1627
AD-40011.1	GuuAAGGAcucuGAAGAuGdTdT	1201	cAUCUUcAGAGUCCUuAACdTdT	1628
AD-40017.1	uuAAGGAcucuGAAGAuGudTdT	1202	AcAUCUUcAGAGUCCUuAAdTdT	1629
AD-40029.1	AAGGAcucuGAAGAuGuAcdTdT	1203	GuAcAUCUUcAGAGUCCUUdTdT	1630
AD-40035.1	AGGAcucuGAAGAuGuAccdTdT	1204	GGuAcAUCUUcAGAGUCCUdTdT	1631
AD-39994.1	GGAcucuGAAGAuGuAccudTdT	1205	AGGuAcAUCUUcAGAGUCCdTdT	1632
AD-40000.1	GAcucuGAAGAuGuAccuAdTdT	1206	uAGGuAcAUCUUcAGAGUCdTdT	1633
AD-40006.1	AcucuGAAGAuGuAccuAudTdT	1207	AuAGGuAcAUCUUcAGAGUdTdT	1634
AD-40012.1	cucuGAAGAuGuAccuAuGdTdT	1208	cAuAGGuAcAUCUUcAGAGdTdT	1635
AD-40018.1	ucuGAAGAuGuAccuAuGGdTdT	1209	CcAuAGGuAcAUCUUcAGAdTdT	1636
AD-40024.1	cuGAAGAuGuAccuAuGGudTdT	1210	ACcAuAGGuAcAUCUUcAGdTdT	1637
AD-40030.1	uGAAGAuGuAccuAuGGucdTdT	1211	GACcAuAGGuAcAUCUUcAdTdT	1638
AD-40036.1	GuAGGAAAuAAAuGuGAuudTdT	1212	AAUcAcAUUuAUUUCCuACdTdT	1639
AD-39995.1	uAGGAAAuAAAuGuGAuuudTdT	1213	AAAUcAcAUUuAUUUCCuAdTdT	1640
AD-40001.1	AGGAAAuAAAuGuGAuuuGdTdT	1214	cAAAUcAcAUUuAUUUCCUdTdT	1641
AD-40007.1	GGAAAuAAAuGuGAuuuGcdTdT	1215	GcAAAUcAcAUUuAUUUCCdTdT	1642
AD-40013.1	GAAAuAAAuGuGAuuuGccdTdT	1216	GGcAAAUcAcAUUuAUUUCdTdT	1643
AD-40019.1	AAAuAAAuGuGAuuuGccudTdT	1217	AGGcAAAUcAcAUUuAUUUdTdT	1644
AD-40025.1	AAuAAAuGuGAuuuGccuudTdT	1218	AAGGcAAAUcAcAUUuAUUdTdT	1645
AD-40031.1	AuAAAuGuGAuuuGccuucdTdT	1219	GAAGGcAAAUcAcAUUuAUdTdT	1646
AD-40037.1	uAAAuGuGAuuuGccuucudTdT	1220	AGAAGGcAAAUcAcAUUuAdTdT	1647
AD-39996.1	AAAuGuGAuuuGccuucuAdTdT	1221	uAGAAGGcAAAUcAcAUUUdTdT	1648
AD-40002.1	AAuGuGAuuuGccuucuAGdTdT	1222	CuAGAAGGcAAAUcAcAUUdTdT	1649
AD-40008.1	AuGuGAuuuGccuucuAGAdTdT	1223	UCuAGAAGGcAAAUcAcAUdTdT	1650
AD-40014.1	uGuGAuuuGccuucuAGAAdTdT	1224	UUCuAGAAGGcAAAUcAcAdTdT	1651
AD-40020.1	GuGAuuuGccuucuAGAAcdTdT	1225	GUUCuAGAAGGcAAAUcACdTdT	1652
AD-40026.1	uGAuuuGccuucuAGAAcAdTdT	1226	UGUUCuAGAAGGcAAAUcAdTdT	1653
AD-40032.1	GAuuuGccuucuAGAAcAGdTdT	1227	CUGUUCuAGAAGGcAAAUCdTdT	1654
AD-40038.1	AuuuGccuucuAGAAcAGudTdT	1228	ACUGUUCuAGAAGGcAAAUdTdT	1655
AD-39997.1	uuuGccuucuAGAAcAGuAdTdT	1229	uACUGUUCuAGAAGGcAAAdTdT	1656
AD-40009.1	uGccuucuAGAAcAGuAGAdTdT	1230	UCuACUGUUCuAGAAGGcAdTdT	1657
AD-40015.1	GccuucuAGAAcAGuAGAcdTdT	1231	GUCuACUGUUCuAGAAGGCdTdT	1658
AD-40021.1	ccuucuAGAAcAGuAGAcAdTdT	1232	UGUCuACUGUUCuAGAAGGdTdT	1659
AD-40027.1	cuucuAGAAcAGuAGAcAcdTdT	1233	GUGUCuACUGUUCuAGAAGdTdT	1660

AD-40033.1	uucuAGAAcAGuAGAcAcAdTdT	1234	UGUGUCuACUGUUCuAGAAdTdT	1661
AD-40039.1	ucuAGAAcAGuAGAcAcAAdTdT	1235	UUGUGUCuACUGUUCuAGAdTdT	1662
AD-40045.1	cuAGAAcAGuAGAcAcAAAdTdT	1236	UUUGUGUCuACUGUUCuAGdTdT	1663
AD-40051.1	uAGAAcAGuAGAcAcAAAAdTdT	1237	UUUUGUGUCuACUGUUCuAdTdT	1664
AD-40057.1	AGAAcAGuAGAcAcAAAAcdTdT	1238	GUUUUGUGUCuACUGUUCUdTdT	1665
AD-40063.1	GAAcAGuAGAcAcAAAAcAdTdT	1239	UGUUUUGUGUCuACUGUUCdTdT	1666
AD-40069.1	AAcAGuAGAcAcAAAAcAGdTdT	1240	CUGUUUUGUGUCuACUGUUdTdT	1667
AD-40075.1	AcAGuAGAcAcAAAAcAGGdTdT	1241	CCUGUUUUGUGUCuACUGUdTdT	1668
AD-40081.1	cAGuAGAcAcAAAAcAGGcdTdT	1242	GCCUGUUUUGUGUCuACUGdTdT	1669
AD-40040.1	AGuAGAcAcAAAAcAGGcudTdT	1243	AGCCUGUUUUGUGUCuACUdTdT	1670
AD-40046.1	GuAGAcAcAAAAcAGGcucdTdT	1244	GAGCCUGUUUUGUGUCuACdTdT	1671
AD-40052.1	uAGAcAcAAAAcAGGcucAdTdT	1245	UGAGCCUGUUUUGUGUCuAdTdT	1672
AD-40058.1	AGAcAcAAAAcAGGcucAGdTdT	1246	CUGAGCCUGUUUUGUGUCUdTdT	1673
AD-40064.1	GAcAcAAAAcAGGcucAGGdTdT	1247	CCUGAGCCUGUUUUGUGUCdTdT	1674
AD-40070.1	AcAcAAAAcAGGcucAGGAdTdT	1248	UCCUGAGCCUGUUUUGUGUdTdT	1675
AD-40076.1	cAcAAAAcAGGcucAGGAcdTdT	1249	GUCCUGAGCCUGUUUUGUGdTdT	1676
AD-40082.1	AcAAAAcAGGcucAGGAcudTdT	1250	AGUCCUGAGCCUGUUUUGUdTdT	1677
AD-40041.1	cAAAAcAGGcucAGGAcuudTdT	1251	AAGUCCUGAGCCUGUUUUGdTdT	1678
AD-40047.1	AAAAcAGGcucAGGAcuuAdTdT	1252	uAAGUCCUGAGCCUGUUUUdTdT	1679
AD-40053.1	AAAcAGGcucAGGAcuuAGdTdT	1253	CuAAGUCCUGAGCCUGUUUdTdT	1680
AD-40059.1	AAcAGGcucAGGAcuuAGcdTdT	1254	GCuAAGUCCUGAGCCUGUUdTdT	1681
AD-40065.1	AcAGGcucAGGAcuuAGcAdTdT	1255	UGCuAAGUCCUGAGCCUGUdTdT	1682
AD-40071.1	cAGGcucAGGAcuuAGcAAdTdT	1256	UUGCuAAGUCCUGAGCCUGdTdT	1683
AD-40077.1	AGGcucAGGAcuuAGcAAGdTdT	1257	CUUGCuAAGUCCUGAGCCUdTdT	1684
AD-40083.1	GGcucAGGAcuuAGcAAGAdTdT	1258	UCUUGCuAAGUCCUGAGCCdTdT	1685
AD-40042.1	GcucAGGAcuuAGcAAGAAdTdT	1259	UUCUUGCuAAGUCCUGAGCdTdT	1686
AD-40048.1	cucAGGAcuuAGcAAGAAGdTdT	1260	CUUCUUGCuAAGUCCUGAGdTdT	1687
AD-40054.1	ucAGGAcuuAGcAAGAAGudTdT	1261	ACUUCUUGCuAAGUCCUGAdTdT	1688
AD-40060.1	cAGGAcuuAGcAAGAAGuudTdT	1262	AACUUCUUGCuAAGUCCUGdTdT	1689
AD-40066.1	AGGAcuuAGcAAGAAGuuAdTdT	1263	uAACUUCUUGCuAAGUCCUdTdT	1690
AD-40072.1	GGAcuuAGcAAGAAGuuAudTdT	1264	AuAACUUCUUGCuAAGUCCdTdT	1691
AD-40078.1	GAcuuAGcAAGAAGuuAuGdTdT	1265	cAuAACUUCUUGCuAAGUCdTdT	1692
AD-40084.1	AcuuAGcAAGAAGuuAuGGdTdT	1266	CcAuAACUUCUUGCuAAGUdTdT	1693
AD-40043.1	cuuAGcAAGAAGuuAuGGAdTdT	1267	UCcAuAACUUCUUGCuAAGdTdT	1694
AD-40049.1	uuAGcAAGAAGuuAuGGAAdTdT	1268	UUCcAuAACUUCUUGCuAAdTdT	1695
AD-40055.1	uAGcAAGAAGuuAuGGAAudTdT	1269	AUUCcAuAACUUCUUGCuAdTdT	1696
AD-40061.1	AGcAAGAAGuuAuGGAAuudTdT	1270	AAUUCcAuAACUUCUUGCUdTdT	1697
AD-40067.1	GcAAGAAGuuAuGGAAuucdTdT	1271	GAAUUCcAuAACUUCUUGCdTdT	1698
AD-40073.1	cAAGAAGuuAuGGAAuuccdTdT	1272	GGAAUUCcAuAACUUCUUGdTdT	1699
AD-40079.1	AAGAAGuuAuGGAAuuccudTdT	1273	AGGAAUUCcAuAACUUCUUdTdT	1700
AD-40085.1	AGAAGuuAuGGAAuuccuudTdT	1274	AAGGAAUUCcAuAACUUCUdTdT	1701
AD-40044.1	GAAGuuAuGGAAuuccuuudTdT	1275	AAAGGAAUUCcAuAACUUCdTdT	1702
AD-40050.1	AAGuuAuGGAAuuccuuuudTdT	1276	AAAAGGAAUUCcAuAACUUdTdT	1703
AD-40056.1	AGuuAuGGAAuuccuuuuAdTdT	1277	uAAAAGGAAUUCcAuAACUdTdT	1704
AD-40062.1	GuuAuGGAAuuccuuuuAudTdT	1278	AuAAAAGGAAUUCcAuAACdTdT	1705

AD-40068.1	uuAuGGAAuuccuuuuAuudTdT	1279	AAuAAAAGGAAUUCcAuAAdTdT	1706
AD-40074.1	uAuGGAAuuccuuuuAuuGdTdT	1280	cAAuAAAAGGAAUUCcAuAdTdT	1707
AD-40080.1	AuGGAAuuccuuuuAuuGAdTdT	1281	UcAAuAAAAGGAAUUCcAUdTdT	1708
AD-39720.1	ActtGtGGtAGttGGAGcttt	1792	AGCTCcAACtACcAcAAGTtt	1830
AD-39706.1	GcAAGAGtGccttGAcGAttt	1793	ATCGTcAAGGcACTCTTGCtt	1831
AD-39712.1	cAAGAGtGccttGAcGAtAtt	1794	tATCGTcAAGGcACTCTTGtt	1832
AD-39760.1	ccttGAcGAtAcAGctAAttt	1795	ATtAGCTGtATCGTcAAGGtt	1833
AD-39732.1	cAGctAAttcAGAAtcAtttt	1796	AATGATTCTGAATtAGCTGtt	1834
AD-35541.4	cGAAtAtGAtccAAcAAtAtt	1797	tATTGTTGGATcAtATTCGtt	1835
AD-39735.1 or hs_KRAS 321_A22S26	GGAAGcAAGtAGtAAttGAuu	1798	TcAATtACtACTTGCTTCCuu	1836
AD-39741.1 or hs_KRAS 322_A22S26	GAAGcAAGtAGtAAttGAtuu	1799	ATcAATtACtACTTGCTTCuu	1837
AD-39778.1	AGtAGtAAttGAtGGAGAAtt	1800	TTCTCcATcAATtACtACTtt	1838
AD-39790.1	tAGtAAttGAtGGAGAAActt	1801	GTTTCTCcATcAATtACtAtt	1839
AD-39822.1	GtctcttGGAtAttctcGAtt	1802	TCGAGAAtATCcAAGAGACtt	1840
AD-35609.4	GGGctttctttGtGtAttttt	1803	AAAtAcAcAAAGAAAGCCCtt	1841
AD-35581.4	GtGtAtttGccAtAAAtAAtt	1804	TtATTtATGGcAAAtAcACtt	1842
AD-39845.1	ccAtAAAtAAtActAAAtctt	1805	GATTtAGtATtATTtATGGtt	1843
AD-39858.1	tActAAAtcAtttGAAGAttt	1806	ATCTTcAAATGATTtAGtAtt	1844
AD-39870.1	ctAAAtcAtttGAAGAtAtuu	1807	AtATCTTcAAATGATTtAGuu	1845
AD-35576.4	GAAGAtAttcAccAttAtAtt	1808	tAtAATGGTGAAtATCTTCtt	1846
AD-35588.4	AGAtAttcAccAttAtAGAtt	1809	TCtAtAATGGTGAAtATCTtt	1847
AD-35600.1	AtAttcAccAttAtAGAGAtt	1810	TCTCtAtAATGGTGAAtATtt	1848
AD-35606.1	tAttcAccAttAtAGAGAAtt	1811	TTCTCtAtAATGGTGAAtAtt	1849
AD-38151.1	cAttAtAGAGAAcAAAttAtt	1812	tAATTTGTTCTCtAtAATGtt	1850
AD-38163.1	ttAtAGAGAAcAAAttAAAtt	1813	TTtAATTTGTTCTCtAtAAtt	1851
AD-39999.1	GAGttAAGGActctGAAGAtt	1814	TCTTcAGAGTCCTtAACTCtt	1852
AD-38159.1 or hs_KRAS 528_A22S26	ctAtGGtcctAGtAGGAAAuu	1815	TTTCCtACtAGGACcAtAGuu	1853
AD-38130.1 or hs_KRAS 531_A22S26	tGGtcctAGtAGGAAAtAAuu	1816	TtATTTCCtACtAGGACcAuu	1854
AD-38136.1	GGtcctAGtAGGAAAtAAAtt	1817	TTtATTTCCtACtAGGACCtt	1855
AD-40036.1	GtAGGAAAtAAAtGtGAtttt	1818	AATcAcATTtATTTCCtACtt	1856
AD-40008.1	AtGtGAtttGccttctAGAtt	1819	TCtAGAAGGcAAATcAcATtt	1857
AD-40021.1	ccttctAGAAcAGtAGAcAtt	1820	TGTCtACTGTTCtAGAAGGtt	1858
AD-40077.1	AGGctcAGGActtAGcAAGtt	1821	CTTGCtAAGTCCTGAGCCTtt	1859
AD-40072.1	GGActtAGcAAGAAGttAttt	1822	AtAACTTCTTGCtAAGTCCtt	1860
AD-40061.1	AGcAAGAAGttAtGGAAtttt	1823	AATTCcAtAACTTCTTGCTtt	1861
AD-40068.1	ttAtGGAAttccttttAtttt	1824	AAtAAAAGGAATTCcAtAAtt	1862
AD-38131.1	GGAAttccttttAttGAAAtt	1825	TTTcAAtAAAAGGAATTCCtt	1863
AD-38167.1	cctttttAttGAAAcAtcAGtt	1826	CTGATGTTTcAAtAAAAGGtt	1864
hs_KRAS 1273_A22S26	cctGAtGAAtGtAAAGttAuu	1827	tAACTTtAcATTcATcAGGuu	1865
hs_KRAS 2892_A37S26	GGAGAAtttAAtAAAGAtAuu	1828	TATCTTtATtAAATTCTCCuu	1866

hs_KRAS 4731_A22S26	GAAtAGtcAtAActAGAttuu	1829	AATCtAGTtATGACtATTCuu	1867

[003709] Modifications of the sequences of RNAi agents are easily conceived by one of skill in the art. Examples and non-limiting modifications of these sequences are conceived and are also listed in Table 3. Note for example, that many sequences end with a terminal dTdT. This is a variant of the TT terminal overhang known to protect siRNAs from nuclease degradation (e.g., in blood serum or intestinal fluid). The dTdT or TT terminal overhangs are optional; they can be replaced by various types of 3' end caps, provided that the 3' end caps are capable of both mediating nuclease resistance and allowing siRNA activity.

[003710] Some modifications are placed at sites predicted to be sensitive to endonucleases. Some modifications are designed to eliminate an immune response to the siRNA while preserving activity. In general, the sense strand is heavily modified, and the antisense strand lightly modified. Some modifications serve more than one purpose.

[003711] The sequences in Table s 1 to 3 are represented by these abbreviations:

TABLE 1A. ABBREVIATIONS

Abbreviation	Nucleotide(s)
A	adenosine-5'-phosphate
C	cytidine-5'-phosphate
G	guanosine-5'-phosphate
dT	2'-deoxy-thymidine-5'-phosphate
U	uridine-5'-phosphate
c	2'-O-methylcytidine-5'-phosphate
u	2'-O-methyluridine-5'-phosphate
sdT	2'-deoxy Thymidine 5'-phosphorothioate

[003712] **siRNA sequence selection**

[003713] Sense and antisense human SCNNB1-derived siRNA oligos (RNAi agents to KRAS) are synthesized, as described herein. The sense and their respective antisense oligos are annealed into duplexes.

[003714] **EXAMPLE 2**

[003715] Overlapping sets of KRAS RNAi Agents

[003716] The present disclosure also relates to groups of RNAi agents to KRAS with overlapping sequences. Thus, the present disclosure encompasses groups of RNAi agents wherein each RNAi agent in the group overlaps with each other RNAi agent in the same group by at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more nucleotides. Particularly, in one embodiment, the overlap is at least 12 nt.

[003717] Some of the RNAi agents listed herein overlap each other in sequence. Table 4 presents a compilation of some of these groups of overlapping RNAi agents, wherein each member of a group overlaps with each other member of the same group by at least 12 nt. A 12-nt portion of the overlap of the sense and anti-sense strand are presented.

[003718] Thus, for example, as shown in Table 4, the sequences of duplexes AD-39695.1, AD-39689.1,AD-39707.1, AD-39683.1, and AD-39701.1 all overlap, wherein the overlap in sense strand comprises the sequence CUGAAUAUAAAC (SEQ ID NO: 1874) and the overlap in the anti-sense strand comprises the sequence GUUUAUAUUCAG (SEQ ID NO: 1875).

[003719] However, in the present disclosure encompasses any set or subset or group or subgroup of KRAS RNAi agents which share the common technical feature of a sequence overlap (e.g., by at least 12 nt). Thus the present disclosure also encompasses the example groups of AD-39695.1, AD-39689.1, AD-39707.1, AD-39683.1, and AD-39701.1, but also these subgroups: AD-39695.1 and AD-39689.1; AD-39695.1 and AD-39707.1; AD-39695.1, AD-39689.1, and AD-39701.1; AD-39689.1, AD-39707.1, and AD-39701.1; AD-39707.1 and AD-39683.1; AD-39707.1, AD-39683.1, and AD-39701.1; etc, and any other group of overlapping KRAS RNAi agents.

Table 4. Overlapping sets of KRAS RNAi agents

Sense overlap	SEQ ID NO:	Anti-sense overlap	SEQ ID NO:	Overlapping RNAi agents to KRAS
UGACUGAAUAUA	1868	UAUAUUCAGUCA	1869	AD-39689.1,AD-39683.1
GACUGAAUAUAA	1870	UUAUAUUCAGUC	1871	AD-39695.1,AD-39689.1,AD-39683.1
ACUGAAUAUAAA	1872	UUUAUAUUCAGU	1873	AD-39695.1,AD-39689.1,AD-39683.1,AD-39701.1
CUGAAUAUAAAC	1874	GUUUAUAUUCAG	1875	AD-39695.1,AD-39689.1,AD-39707.1,AD-39683.1,AD-39701.1
UGAAUAUAAACU	1876	AGUUUAUAUUCA	1877	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1
GAAUAUAAACUU	1878	AAGUUUAUAUUC	1879	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1,AD-39719.1
AAUAUAAACUUG	1880	CAAGUUUAUAUU	1881	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1,AD-39725.1,AD-39719.1
AUAUAAACUUGU	1882	ACAAGUUUAUAU	1883	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1
UAUAAACUUGUG	1884	CACAAGUUUAUA	1885	AD-39690.1,AD-39695.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1
AUAAACUUGUGG	1886	CCACAAGUUUAU	1887	AD-39690.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1,AD-39696.1
UAAACUUGUGGU	1888	ACCACAAGUUUA	1889	AD-39690.1,AD-39713.1,AD-39707.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39696.1
AAACUUGUGGUA	1890	UACCACAAGUUU	1891	AD-39690.1,AD-39713.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39696.1,AD-39708.1
AACUUGUGGUAG	1892	CUACCACAAGUU	1893	AD-39690.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1
ACUUGUGGUAGU	1894	ACUACCACAAGU	1895	AD-39690.1,AD-39725.1,AD-39702.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1
CUUGUGGUAGUU	1896	AACUACCACAAG	1897	AD-39690.1,AD-39702.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1
UUGUGGUAGUUG	1898	CAACUACCACAA	1899	AD-39690.1,AD-39702.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1

UGUGGUAGUUGG	**1900**	CCAACUACCACA	**1901**	AD-39691.1,AD-39702.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
GUGGUAGUUGGA	**1902**	UCCAACUACCAC	**1903**	AD-39691.1,AD-39697.1,AD-39702.1,AD-39714.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
UGGUAGUUGGAG	**1904**	CUCCAACUACCA	**1905**	AD-39703.1,AD-39691.1,AD-39697.1,AD-39714.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
GGUAGUUGGAGC	**1906**	GCUCCAACUACC	**1907**	AD-39703.1,AD-39691.1,AD-39697.1,AD-39714.1,AD-39709.1,AD-39720.1,AD-39726.1,AD-39685.1
GUAGUUGGAGCU	**1908**	AGCUCCAACUAC	**1909**	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39720.1,AD-39726.1,AD-39685.1
UAGUUGGAGCUG	**1910**	CAGCUCCAACUA	**1911**	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39726.1,AD-39685.1
AGUUGGAGCUGG	**1912**	CCAGCUCCAACU	**1913**	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1,AD-39685.1
GUUGGAGCUGGU	**1914**	ACCAGCUCCAAC	**1915**	AD-39703.1,AD-39691.1,AD-39686.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1
UUGGAGCUGGUG	**1916**	CACCAGCUCCAA	**1917**	AD-39703.1,AD-39686.1,AD-39697.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1
UGGAGCUGGUGG	**1918**	CCACCAGCUCCA	**1919**	AD-39703.1,AD-39686.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39698.1,AD-39721.1,AD-39727.1
GGAGCUGGUGGC	**1920**	GCCACCAGCUCC	**1921**	AD-39686.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
GAGCUGGUGGCG	**1922**	CGCCACCAGCUC	**1923**	AD-39710.1,AD-39686.1,AD-39692.1,AD-39715.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
AGCUGGUGGCGU	**1924**	ACGCCACCAGCU	**1925**	AD-39710.1,AD-39686.1,AD-39692.1,AD-39716.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
GCUGGUGGCGUA	**1926**	UACGCCACCAGC	**1927**	AD-39710.1,AD-39686.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39698.1,AD-39704.1,AD-39727.1
CUGGUGGCGUAG	**1928**	CUACGCCACCAG	**1929**	AD-39710.1,AD-39686.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1
UGGUGGCGUAGG	**1930**	CCUACGCCACCA	**1931**	AD-39710.1,AD-39687.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1
GGUGGCGUAGGC	**1932**	GCCUACGCCACC	**1933**	AD-39693.1,AD-39710.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1
GUGGCGUAGGCA	**1934**	UGCCUACGCCAC	**1935**	AD-39693.1,AD-39710.1,AD-39699.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39704.1
UGGCGUAGGCAA	**1936**	UUGCCUACGCCA	**1937**	AD-39693.1,AD-39710.1,AD-39699.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39705.1,AD-39728.1
GGCGUAGGCAAG	**1938**	CUUGCCUACGCC	**1939**	AD-39693.1,AD-39699.1,AD-39687.1,AD-39711.1,AD-39722.1,AD-39716.1,AD-39705.1,AD-39728.1
GCGUAGGCAAGA	**1940**	UCUUGCCUACGC	**1941**	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-39722.1,AD-39705.1,AD-39728.1
CGUAGGCAAGAG	**1942**	CUCUUGCCUACG	**1943**	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-39705.1,AD-39728.1,AD-39723.1
GUAGGCAAGAGU	**1944**	ACUCUUGCCUAC	**1945**	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-

				39729.1,AD-39705.1,AD-39723.1
UAGGCAAGAGUG	**1946**	CACUCUUGCCUA	**1947**	AD-39693.1,AD-39699.1,AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39723.1
AGGCAAGAGUGC	**1948**	GCACUCUUGCCU	**1949**	AD-39699.1,AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39694.1,AD-39723.1
GGCAAGAGUGCC	**1950**	GGCACUCUUGCC	**1951**	AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39694.1,AD-39700.1,AD-39723.1
GCAAGAGUGCCU	**1952**	AGGCACUCUUGC	**1953**	AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
CAAGAGUGCCUU	**1954**	AAGGCACUCUUG	**1955**	AD-39712.1,AD-39717.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
AAGAGUGCCUUG	**1956**	CAAGGCACUCUU	**1957**	AD-39718.1,AD-39712.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
AGAGUGCCUUGA	**1958**	UCAAGGCACUCU	**1959**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1
GAGUGCCUUGAC	**1960**	GUCAAGGCACUC	**1961**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39688.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39730.1
AGUGCCUUGACG	**1962**	CGUCAAGGCACU	**1963**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39706.1,AD-39694.1,AD-39736.1,AD-39700.1,AD-39730.1
GUGCCUUGACGA	**1964**	UCGUCAAGGCAC	**1965**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39706.1,AD-39736.1,AD-39700.1,AD-39730.1
UGCCUUGACGAU	**1966**	AUCGUCAAGGCA	**1967**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39706.1,AD-39736.1,AD-39748.1,AD-39730.1
GCCUUGACGAUA	**1968**	UAUCGUCAAGGC	**1969**	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39730.1
CCUUGACGAUAC	**1970**	GUAUCGUCAAGG	**1971**	AD-39718.1,AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1
CUUGACGAUACA	**1972**	UGUAUCGUCAAG	**1973**	AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1,AD-39766.1
UUGACGAUACAG	**1974**	CUGUAUCGUCAA	**1975**	AD-39742.1,AD-39772.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1,AD-39766.1
UGACGAUACAGC	**1976**	GCUGUAUCGUCA	**1977**	AD-39742.1,AD-39772.1,AD-39754.1,AD-39736.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1
GACGAUACAGCU	**1978**	AGCUGUAUCGUC	**1979**	AD-39737.1,AD-39742.1,AD-39772.1,AD-39754.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1
ACGAUACAGCUA	**1980**	UAGCUGUAUCGU	**1981**	AD-39737.1,AD-39772.1,AD-39754.1,AD-39743.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1
CGAUACAGCUAA	**1982**	UUAGCUGUAUCG	**1983**	AD-39737.1,AD-39772.1,AD-39754.1,AD-39743.1,AD-39731.1,AD-39760.1,AD-39749.1,AD-39766.1
GAUACAGCUAAU	**1984**	AUUAGCUGUAUC	**1985**	AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39760.1,AD-39749.1,AD-39755.1,AD-39766.1
AUACAGCUAAUU	**1986**	AAUUAGCUGUAU	**1987**	AD-39761.1,AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39749.1,AD-39755.1,AD-39766.1
UACAGCUAAUUC	**1988**	GAAUUAGCUGUA	**1989**	AD-39767.1,AD-39761.1,AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39749.1,AD-39755.1

ACAGCUAAUUCA	1990	UGAAUUAGCUGU	1991	AD-39767.1,AD-39761.1,AD-39737.1,AD-39743.1,AD-39731.1,AD-39773.1,AD-39749.1,AD-39755.1
CAGCUAAUUCAG	1992	CUGAAUUAGCUG	1993	AD-39767.1,AD-39761.1,AD-39737.1,AD-39732.1,AD-39743.1,AD-39773.1,AD-39749.1,AD-39755.1
AGCUAAUUCAGA	1994	UCUGAAUUAGCU	1995	AD-39767.1,AD-39761.1,AD-39732.1,AD-39743.1,AD-39738.1,AD-39773.1,AD-39749.1,AD-39755.1
GCUAAUUCAGAA	1996	UUCUGAAUUAGC	1997	AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39738.1,AD-39773.1,AD-39749.1,AD-39755.1
CUAAUUCAGAAU	1998	AUUCUGAAUUAG	1999	AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1,AD-39755.1
UAAUUCAGAAUC	2000	GAUUCUGAAUUA	2001	AD-39756.1,AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1
AAUUCAGAAUCA	2002	UGAUUCUGAAUU	2003	AD-39756.1,AD-39767.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1
AUUCAGAAUCAU	2004	AUGAUUCUGAAU	2005	AD-39756.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39768.1,AD-39750.1,AD-39738.1,AD-39773.1
UUCAGAAUCAUU	2006	AAUGAUUCUGAA	2007	AD-39756.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39768.1,AD-39750.1,AD-39738.1
UCAGAAUCAUUU	2008	AAAUGAUUCUGA	2009	AD-39756.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1,AD-39738.1
CAGAAUCAUUUU	2010	AAAAUGAUUCUG	2011	AD-39756.1,AD-39739.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1
AGAAUCAUUUUG	2012	CAAAAUGAUUCU	2013	AD-39745.1,AD-39756.1,AD-39739.1,AD-39774.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1
GAAUCAUUUUGU	2014	ACAAAAUGAUUC	2015	AD-39745.1,AD-39756.1,AD-39739.1,AD-39774.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39751.1
AAUCAUUUUGUG	2016	CACAAAAUGAUU	2017	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39751.1
AUCAUUUUGUGG	2018	CCACAAAAUGAU	2019	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39733.1,AD-39768.1,AD-39751.1,AD-39763.1
UCAUUUUGUGGA	2020	UCCACAAAAUGA	2021	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39733.1,AD-39751.1,AD-39769.1,AD-39763.1
CAUUUUGUGGAC	2022	GUCCACAAAAUG	2023	AD-39745.1,AD-39739.1,AD-39775.1,AD-39757.1,AD-39733.1,AD-39751.1,AD-39769.1,AD-39763.1
AUUUUGUGGACG	2024	CGUCCACAAAAU	2025	AD-39745.1,AD-39739.1,AD-39775.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39763.1,AD-39734.1
UUUUGUGGACGA	2026	UCGUCCACAAAA	2027	AD-39745.1,AD-39775.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UUUGUGGACGAA	2028	UUCGUCCACAAA	2029	AD-39775.1,AD-39746.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UUGUGGACGAAU	2030	AUUCGUCCACAA	2031	AD-39752.1,AD-39775.1,AD-39746.1,AD-39757.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UGUGGACGAAUA	2032	UAUUCGUCCACA	2033	AD-39752.1,AD-39775.1,AD-39746.1,AD-39758.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
GUGGACGAAUAU	2034	AUAUUCGUCCAC	2035	AD-39752.1,AD-39775.1,AD-39764.1,AD-39746.1,AD-39758.1,AD-

				39769.1,AD-39740.1,AD-39734.1
UGGACGAAUAUG	2036	CAUAUUCGUCCA	2037	AD-39752.1,AD-39775.1,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1,AD-39734.1
GGACGAAUAUGA	2038	UCAUAUUCGUCC	2039	AD-39752.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1,AD-39734.1
GACGAAUAUGAU	2040	AUCAUAUUCGUC	2041	AD-39752.1,AD-35529.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1
ACGAAUAUGAUC	2042	GAUCAUAUUCGU	2043	AD-39752.1,AD-35529.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-35535.4,AD-39770.1,AD-39758.1
CGAAUAUGAUCC	2044	GGAUCAUAUUCG	2045	AD-39752.1,AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-39758.1
GAAUAUGAUCCA	2046	UGGAUCAUAUUC	2047	AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-39758.1,AD-35547.4
AAUAUGAUCCAA	2048	UUGGAUCAUAUU	2049	AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-35553.4,AD-35547.4
AUAUGAUCCAAC	2050	GUUGGAUCAUAU	2051	AD-35529.1,AD-35523.3,AD-35541.4,AD-35559.4,AD-35535.4,AD-39770.1,AD-35553.4,AD-35547.4
UAUGAUCCAACA	2052	UGUUGGAUCAUA	2053	AD-35529.1,AD-35523.3,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4
AUGAUCCAACAA	2054	UUGUUGGAUCAU	2055	AD-35529.1,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4,AD-35524.4
UGAUCCAACAAU	2056	AUUGUUGGAUCA	2057	AD-35530.4,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4,AD-35524.4
GAUCCAACAAUA	2058	UAUUGUUGGAUC	2059	AD-35530.4,AD-35541.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35536.4,AD-35547.4,AD-35524.4
AUCCAACAAUAG	2060	CUAUUGUUGGAU	2061	AD-35530.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35542.4,AD-35536.4,AD-35547.4,AD-35524.4
UCCAACAAUAGA	2062	UCUAUUGUUGGA	2063	AD-35530.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35524.4
CCAACAAUAGAG	2064	CUCUAUUGUUGG	2065	AD-35554.4,AD-35530.4,AD-35565.4,AD-35559.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35524.4
CAACAAUAGAGG	2066	CCUCUAUUGUUG	2067	AD-35554.4,AD-35530.4,AD-35565.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2,AD-35524.4
AACAAUAGAGGA	2068	UCCUCUAUUGUU	2069	AD-35554.4,AD-35530.4,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2,AD-35524.4
ACAAUAGAGGAU	2070	AUCCUCUAUUGU	2071	AD-35554.4,AD-35530.4,AD-35525.2,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2
CAAUAGAGGAUU	2072	AAUCCUCUAUUG	2073	AD-35554.4,AD-35525.2,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35531.4,AD-35560.2
AAUAGAGGAUUC	2074	GAAUCCUCUAUU	2075	AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35548.4,AD-35542.4,AD-35531.4,AD-35560.2
AUAGAGGAUUCC	2076	GGAAUCCUCUAU	2077	AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35548.4,AD-35531.4,AD-35560.2,AD-35543.2
UAGAGGAUUCCU	2078	AGGAAUCCUCUA	2079	AD-35549.4,AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35560.2,AD-35543.2

AGAGGAUUCCUA	2080	UAGGAAUCCUCU	2081	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35560.2,AD-35543.2
GAGGAUUCCUAC	2082	GUAGGAAUCCUC	2083	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35561.4,AD-35543.2
AGGAUUCCUACA	2084	UGUAGGAAUCCU	2085	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35531.4,AD-35561.4,AD-35543.2,AD-35567.4
GGAUUCCUACAG	2086	CUGUAGGAAUCC	2087	AD-35549.4,AD-35555.4,AD-35526.4,AD-35537.4,AD-35531.4,AD-35561.4,AD-35543.2,AD-35567.4
GAUUCCUACAGG	2088	CCUGUAGGAAUC	2089	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35537.4,AD-35561.4,AD-35543.2,AD-35567.4
AUUCCUACAGGA	2090	UCCUGUAGGAAU	2091	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35538.4,AD-35561.4,AD-35543.2,AD-35567.4
UUCCUACAGGAA	2092	UUCCUGUAGGAA	2093	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
UCCUACAGGAAG	2094	CUUCCUGUAGGA	2095	AD-35555.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
CCUACAGGAAGC	2096	GCUUCCUGUAGG	2097	AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
CUACAGGAAGCA	2098	UGCUUCCUGUAG	2099	AD-35562.4,AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35567.4
UACAGGAAGCAA	2100	UUGCUUCCUGUA	2101	AD-35562.4,AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4
ACAGGAAGCAAG	2102	CUUGCUUCCUGU	2103	AD-35562.4,AD-35556.4,AD-35532.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4,AD-35527.4
CAGGAAGCAAGU	2104	ACUUGCUUCCUG	2105	AD-35562.4,AD-35556.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4,AD-35533.4,AD-35527.4
AGGAAGCAAGUA	2106	UACUUGCUUCCU	2107	AD-35562.4,AD-35556.4,AD-35550.4,AD-39776.1,AD-35568.4,AD-35544.4,AD-35533.4,AD-35527.4
GGAAGCAAGUAG	2108	CUACUUGCUUCC	2109	AD-35562.4,AD-39735.1,AD-35556.4,AD-35550.4,AD-39776.1,AD-35568.4,AD-35533.4,AD-35527.4
GAAGCAAGUAGU	2110	ACUACUUGCUUC	2111	AD-35562.4,AD-39735.1,AD-35556.4,AD-39776.1,AD-35568.4,AD-35533.4,AD-35527.4,AD-39741.1
AAGCAAGUAGUA	2112	UACUACUUGCUU	2113	AD-35562.4,AD-39735.1,AD-39776.1,AD-35568.4,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
AGCAAGUAGUAA	2114	UUACUACUUGCU	2115	AD-39735.1,AD-39753.1,AD-39776.1,AD-35568.4,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
GCAAGUAGUAAU	2116	AUUACUACUUGC	2117	AD-39735.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
CAAGUAGUAAUU	2118	AAUUACUACUUG	2119	AD-39735.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-35533.4,AD-39765.1,AD-39741.1
AAGUAGUAAUUG	2120	CAAUUACUACUU	2121	AD-39735.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-39765.1,AD-39741.1
AGUAGUAAUUGA	2122	UCAAUUACUACU	2123	AD-39735.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39747.1,AD-39765.1,AD-39741.1
GUAGUAAUUGAU	2124	AUCAAUUACUAC	2125	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-

				39747.1,AD-39765.1,AD-39741.1
UAGUAAUUGAUG	**2126**	CAUCAAUUACUA	**2127**	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39747.1,AD-39765.1,AD-39790.1
AGUAAUUGAUGG	**2128**	CCAUCAAUUACU	**2129**	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39796.1,AD-39765.1,AD-39790.1
GUAAUUGAUGGA	**2130**	UCCAUCAAUUAC	**2131**	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39796.1,AD-39765.1,AD-39802.1,AD-39790.1
UAAUUGAUGGAG	**2132**	CUCCAUCAAUUA	**2133**	AD-39784.1,AD-39778.1,AD-39808.1,AD-39771.1,AD-39796.1,AD-39765.1,AD-39802.1,AD-39790.1
AAUUGAUGGAGA	**2134**	UCUCCAUCAAUU	**2135**	AD-39784.1,AD-39814.1,AD-39778.1,AD-39808.1,AD-39771.1,AD-39796.1,AD-39802.1,AD-39790.1
AUUGAUGGAGAA	**2136**	UUCUCCAUCAAU	**2137**	AD-39784.1,AD-39814.1,AD-39778.1,AD-39808.1,AD-39820.1,AD-39796.1,AD-39802.1,AD-39790.1
UUGAUGGAGAAA	**2138**	UUUCUCCAUCAA	**2139**	AD-39784.1,AD-39814.1,AD-39808.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1,AD-39790.1
UGAUGGAGAAAC	**2140**	GUUUCUCCAUCA	**2141**	AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1,AD-39790.1
GAUGGAGAAACC	**2142**	GGUUUCUCCAUC	**2143**	AD-39791.1,AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1
AUGGAGAAACCU	**2144**	AGGUUUCUCCAU	**2145**	AD-39791.1,AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39797.1,AD-39802.1
UGGAGAAACCUG	**2146**	CAGGUUUCUCCA	**2147**	AD-39791.1,AD-39814.1,AD-39808.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39797.1
GGAGAAACCUGU	**2148**	ACAGGUUUCUCC	**2149**	AD-39791.1,AD-39814.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39809.1,AD-39779.1,AD-39797.1
GAGAAACCUGUC	**2150**	GACAGGUUUCUC	**2151**	AD-39815.1,AD-39791.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39809.1,AD-39779.1,AD-39797.1
AGAAACCUGUCU	**2152**	AGACAGGUUUCU	**2153**	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39785.1,AD-39809.1,AD-39779.1,AD-39797.1
GAAACCUGUCUC	**2154**	GAGACAGGUUUC	**2155**	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39785.1,AD-39809.1,AD-39780.1,AD-39797.1
AAACCUGUCUCU	**2156**	AGAGACAGGUUU	**2157**	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39780.1,AD-39797.1,AD-39786.1
AACCUGUCUCUU	**2158**	AAGAGACAGGUU	**2159**	AD-39815.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39780.1,AD-39797.1,AD-39786.1
ACCUGUCUCUUG	**2160**	CAAGAGACAGGU	**2161**	AD-39815.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39780.1,AD-39798.1,AD-39786.1
CCUGUCUCUUGG	**2162**	CCAAGAGACAGG	**2163**	AD-39815.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39804.1,AD-39780.1,AD-39798.1,AD-39786.1
CUGUCUCUUGGA	**2164**	UCCAAGAGACAG	**2165**	AD-39815.1,AD-39821.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39798.1,AD-39786.1
UGUCUCUUGGAU	**2166**	AUCCAAGAGACA	**2167**	AD-39816.1,AD-39821.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39798.1,AD-39786.1
GUCUCUUGGAUA	**2168**	UAUCCAAGAGAC	**2169**	AD-39816.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39822.1,AD-39798.1,AD-39786.1

UCUCUUGGAUAU	2170	AUAUCCAAGAGA	2171	AD-39816.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1,AD-39786.1
CUCUUGGAUAUU	2172	AAUAUCCAAGAG	2173	AD-39816.1,AD-39792.1,AD-39804.1,AD-39787.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1
UCUUGGAUAUUC	2174	GAAUAUCCAAGA	2175	AD-39816.1,AD-39793.1,AD-39804.1,AD-39787.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1
CUUGGAUAUUCU	2176	AGAAUAUCCAAG	2177	AD-39799.1,AD-39816.1,AD-39793.1,AD-39804.1,AD-39787.1,AD-39810.1,AD-39781.1,AD-39822.1
UUGGAUAUUCUC	2178	GAGAAUAUCCAA	2179	AD-39799.1,AD-39816.1,AD-39793.1,AD-39787.1,AD-35539.4,AD-39810.1,AD-39781.1,AD-39822.1
UGGAUAUUCUCG	2180	CGAGAAUAUCCA	2181	AD-39799.1,AD-39816.1,AD-39793.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1,AD-39822.1
GGAUAUUCUCGA	2182	UCGAGAAUAUCC	2183	AD-39799.1,AD-35551.4,AD-39793.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1,AD-39822.1
GAUAUUCUCGAC	2184	GUCGAGAAUAUC	2185	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1
AUAUUCUCGACA	2186	UGUCGAGAAUAU	2187	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-35563.4
UAUUCUCGACAC	2188	GUGUCGAGAAUA	2189	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-35539.4,AD-35545.4,AD-35569.1,AD-35563.4
AUUCUCGACACA	2190	UGUGUCGAGAAU	2191	AD-39799.1,AD-35528.4,AD-35551.4,AD-35557.1,AD-35539.4,AD-35545.4,AD-35569.1,AD-35563.4
UUCUCGACACAG	2192	CUGUGUCGAGAA	2193	AD-35528.4,AD-35551.4,AD-35557.1,AD-35539.4,AD-35534.1,AD-35545.4,AD-35569.1,AD-35563.4
UCUCGACACAGC	2194	GCUGUGUCGAGA	2195	AD-35528.4,AD-35551.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35545.4,AD-35569.1,AD-35563.4
CUCGACACAGCA	2196	UGCUGUGUCGAG	2197	AD-35528.4,AD-35551.4,AD-35546.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4
UCGACACAGCAG	2198	CUGCUGUGUCGA	2199	AD-35552.4,AD-35528.4,AD-35546.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4
CGACACAGCAGG	2200	CCUGCUGUGUCG	2201	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4
GACACAGCAGGU	2202	ACCUGCUGUGUC	2203	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35534.1,AD-35564.4,AD-35569.1
ACACAGCAGGUC	2204	GACCUGCUGUGU	2205	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35534.1,AD-35564.4
CACAGCAGGUCA	2206	UGACCUGCUGUG	2207	AD-35552.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35534.1,AD-35564.4,AD-35571.4
ACAGCAGGUCAA	2208	UUGACCUGCUGU	2209	AD-35577.4,AD-35552.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35564.4,AD-35571.4
CAGCAGGUCAAG	2210	CUUGACCUGCUG	2211	AD-35577.4,AD-35552.4,AD-35558.4,AD-35546.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35571.4
AGCAGGUCAAGA	2212	UCUUGACCUGCU	2213	AD-35577.4,AD-35552.4,AD-35558.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35589.4,AD-35571.4
GCAGGUCAAGAG	2214	CUCUUGACCUGC	2215	AD-35577.4,AD-35595.4,AD-35558.4,AD-35583.4,AD-35570.4,AD-

				35564.4,AD-35589.4,AD-35571.4
CAGGUCAAGAGG	2216	CCUCUUGACCUG	2217	AD-35577.4,AD-35595.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35589.4,AD-35571.4,AD-35601.4
AGGUCAAGAGGA	2218	UCCUCUUGACCU	2219	AD-35577.4,AD-35595.4,AD-35583.4,AD-35570.4,AD-35589.4,AD-35607.4,AD-35571.4,AD-35601.4
GGUCAAGAGGAG	2220	CUCCUCUUGACC	2221	AD-35577.4,AD-35595.4,AD-35583.4,AD-35589.4,AD-35607.4,AD-35571.4,AD-35613.4,AD-35601.4
GUCAAGAGGAGU	2222	ACUCCUCUUGAC	2223	AD-35577.4,AD-35595.4,AD-35583.4,AD-35572.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
UCAAGAGGAGUA	2224	UACUCCUCUUGA	2225	AD-35595.4,AD-35583.4,AD-35578.4,AD-35572.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
CAAGAGGAGUAC	2226	GUACUCCUCUUG	2227	AD-35595.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
AAGAGGAGUACA	2228	UGUACUCCUCUU	2229	AD-35590.4,AD-35595.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35607.4,AD-35613.4,AD-35601.4
AGAGGAGUACAG	2230	CUGUACUCCUCU	2231	AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35607.4,AD-35613.4,AD-35601.4
GAGGAGUACAGU	2232	ACUGUACUCCUC	2233	AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35602.4,AD-35584.4,AD-35607.4,AD-35613.4
AGGAGUACAGUG	2234	CACUGUACUCCU	2235	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35602.4,AD-35584.4,AD-35613.4
GGAGUACAGUGC	2236	GCACUGUACUCC	2237	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35614.4,AD-35602.4,AD-35584.4
GAGUACAGUGCA	2238	UGCACUGUACUC	2239	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35614.4,AD-35602.4,AD-35584.4,AD-35573.4
AGUACAGUGCAA	2240	UUGCACUGUACU	2241	AD-39805.1,AD-35608.4,AD-35596.4,AD-35590.4,AD-35614.4,AD-35602.4,AD-35584.4,AD-35573.4
GUACAGUGCAAU	2242	AUUGCACUGUAC	2243	AD-39805.1,AD-35608.4,AD-35596.4,AD-35590.4,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
UACAGUGCAAUG	2244	CAUUGCACUGUA	2245	AD-39805.1,AD-35608.4,AD-35596.4,AD-39817.1,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
ACAGUGCAAUGA	2246	UCAUUGCACUGU	2247	AD-39805.1,AD-35608.4,AD-39823.1,AD-39817.1,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
CAGUGCAAUGAG	2248	CUCAUUGCACUG	2249	AD-39805.1,AD-35608.4,AD-39823.1,AD-39817.1,AD-39811.1,AD-35614.4,AD-35573.4,AD-39782.1
AGUGCAAUGAGG	2250	CCUCAUUGCACU	2251	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-35614.4,AD-35573.4,AD-39782.1
GUGCAAUGAGGG	2252	CCCUCAUUGCAC	2253	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-35573.4,AD-39782.1,AD-39794.1
UGCAAUGAGGGA	2254	UCCCUCAUUGCA	2255	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-39782.1,AD-39794.1,AD-39800.1
GCAAUGAGGGAC	2256	GUCCCUCAUUGC	2257	AD-39806.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-39782.1,AD-39794.1,AD-39800.1
CAAUGAGGGACC	2258	GGUCCCUCAUUG	2259	AD-39806.1,AD-39823.1,AD-39812.1,AD-39817.1,AD-39788.1,AD-39782.1,AD-39794.1,AD-39800.1

AAUGAGGGACCA	2260	UGGUCCCUCAUU	2261	AD-39806.1,AD-39823.1,AD-39812.1,AD-39788.1,AD-39782.1,AD-39794.1,AD-39818.1,AD-39800.1
AUGAGGGACCAG	2262	CUGGUCCCUCAU	2263	AD-39806.1,AD-39812.1,AD-39788.1,AD-39824.1,AD-39782.1,AD-39794.1,AD-39818.1,AD-39800.1
UGAGGGACCAGU	2264	ACUGGUCCCUCA	2265	AD-39806.1,AD-39812.1,AD-39788.1,AD-39824.1,AD-39783.1,AD-39794.1,AD-39818.1,AD-39800.1
GAGGGACCAGUA	2266	UACUGGUCCCUC	2267	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39783.1,AD-39794.1,AD-39818.1,AD-39800.1
AGGGACCAGUAC	2268	GUACUGGUCCCU	2269	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39818.1,AD-39800.1
GGGACCAGUACA	2270	UGUACUGGUCCC	2271	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39818.1
GGACCAGUACAU	2272	AUGUACUGGUCC	2273	AD-39789.1,AD-39807.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39818.1
GACCAGUACAUG	2274	CAUGUACUGGUC	2275	AD-39789.1,AD-39807.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39818.1
ACCAGUACAUGA	2276	UCAUGUACUGGU	2277	AD-39789.1,AD-39807.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39819.1
CCAGUACAUGAG	2278	CUCAUGUACUGG	2279	AD-39789.1,AD-39807.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39819.1
CAGUACAUGAGG	2280	CCUCAUGUACUG	2281	AD-39789.1,AD-39807.1,AD-39795.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1
AGUACAUGAGGA	2282	UCCUCAUGUACU	2283	AD-39807.1,AD-39837.1,AD-39795.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1
GUACAUGAGGAC	2284	GUCCUCAUGUAC	2285	AD-39807.1,AD-39837.1,AD-39843.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1
UACAUGAGGACU	2286	AGUCCUCAUGUA	2287	AD-39807.1,AD-39837.1,AD-39843.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39849.1,AD-39819.1
ACAUGAGGACUG	2288	CAGUCCUCAUGU	2289	AD-39837.1,AD-39843.1,AD-39813.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39849.1,AD-39819.1
CAUGAGGACUGG	2290	CCAGUCCUCAUG	2291	AD-39861.1,AD-39837.1,AD-39843.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39849.1,AD-39819.1
AUGAGGACUGGG	2292	CCCAGUCCUCAU	2293	AD-39861.1,AD-39837.1,AD-39843.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39867.1,AD-39849.1
UGAGGACUGGGG	2294	CCCCAGUCCUCA	2295	AD-39861.1,AD-39837.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39831.1,AD-39867.1,AD-39849.1
GAGGACUGGGGA	2296	UCCCCAGUCCUC	2297	AD-39861.1,AD-39832.1,AD-39837.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1
AGGACUGGGGAG	2298	CUCCCCAGUCCU	2299	AD-39861.1,AD-39832.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1,AD-39838.1
GGACUGGGGAGG	2300	CCUCCCCAGUCC	2301	AD-39844.1,AD-39861.1,AD-39832.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1,AD-39838.1
GACUGGGGAGGG	2302	CCCUCCCCAGUC	2303	AD-39850.1,AD-39844.1,AD-39861.1,AD-39832.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39838.1
ACUGGGGAGGGC	2304	GCCCUCCCCAGU	2305	AD-39850.1,AD-39844.1,AD-39861.1,AD-39832.1,AD-39856.1,AD-

				39826.1,AD-39867.1,AD-39838.1
CUGGGGAGGGCU	2306	AGCCCUCCCCAG	2307	AD-39850.1,AD-39844.1,AD-39862.1,AD-39832.1,AD-39856.1,AD-39826.1,AD-39867.1,AD-39838.1
UGGGGAGGGCUU	2308	AAGCCCUCCCCA	2309	AD-39850.1,AD-39844.1,AD-39868.1,AD-39862.1,AD-39832.1,AD-39856.1,AD-39826.1,AD-39838.1
GGGGAGGGCUUU	2310	AAAGCCCUCCCC	2311	AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39832.1,AD-39856.1,AD-39838.1
GGGAGGGCUUUC	2312	GAAAGCCCUCCC	2313	AD-35585.4,AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39856.1,AD-39838.1
GGAGGGCUUUCU	2314	AGAAAGCCCUCC	2315	AD-35585.4,AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39856.1,AD-35591.4
GAGGGCUUUCUU	2316	AAGAAAGCCCUC	2317	AD-35585.4,AD-39850.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-39856.1,AD-35591.4
AGGGCUUUCUUU	2318	AAAGAAAGCCCU	2319	AD-35585.4,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-39856.1,AD-35591.4,AD-35603.4
GGGCUUUCUUUG	2320	CAAAGAAAGCCC	2321	AD-35585.4,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4
GGCUUUCUUUGU	2322	ACAAAGAAAGCC	2323	AD-35585.4,AD-39868.1,AD-35579.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4
GCUUUCUUUGUG	2324	CACAAAGAAAGC	2325	AD-35585.4,AD-35579.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35574.4
CUUUCUUUGUGU	2326	ACACAAAGAAAG	2327	AD-35585.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35580.1,AD-35574.4
UUUCUUUGUGUA	2328	UACACAAAGAAA	2329	AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35586.4,AD-35580.1,AD-35574.4
UUCUUUGUGUAU	2330	AUACACAAAGAA	2331	AD-35615.4,AD-35597.4,AD-35609.4,AD-35592.4,AD-35603.4,AD-35586.4,AD-35580.1,AD-35574.4
UCUUUGUGUAUU	2332	AAUACACAAAGA	2333	AD-35615.4,AD-35609.4,AD-35592.4,AD-35603.4,AD-35586.4,AD-35598.4,AD-35580.1,AD-35574.4
CUUUGUGUAUUU	2334	AAAUACACAAAG	2335	AD-35604.4,AD-35615.4,AD-35609.4,AD-35592.4,AD-35586.4,AD-35598.4,AD-35580.1,AD-35574.4
UUUGUGUAUUUG	2336	CAAAUACACAAA	2337	AD-35604.4,AD-35615.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35580.1,AD-35574.4
UUGUGUAUUUGC	2338	GCAAAUACACAA	2339	AD-35604.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35580.1,AD-35574.4
UGUGUAUUUGCC	2340	GGCAAAUACACA	2341	AD-35604.4,AD-35575.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35580.1
GUGUAUUUGCCA	2342	UGGCAAAUACAC	2343	AD-35604.4,AD-35575.4,AD-35581.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4
UGUAUUUGCCAU	2344	AUGGCAAAUACA	2345	AD-35604.4,AD-35575.4,AD-35581.4,AD-35592.4,AD-35587.4,AD-35610.4,AD-35598.4,AD-35616.4
GUAUUUGCCAUA	2346	UAUGGCAAAUAC	2347	AD-35604.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35593.4
UAUUUGCCAUAA	2348	UUAUGGCAAAUA	2349	AD-35604.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35616.4,AD-35593.4,AD-35599.4

AUUUGCCAUAAA	2350	UUUAUGGCAAAU	2351	AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35605.4,AD-35616.4,AD-35593.4,AD-35599.4
UUUGCCAUAAAU	2352	AUUUAUGGCAAA	2353	AD-35611.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35605.4,AD-35616.4,AD-35593.4,AD-35599.4
UUGCCAUAAAUA	2354	UAUUUAUGGCAA	2355	AD-35611.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
UGCCAUAAAUAA	2356	UUAUUUAUGGCA	2357	AD-35611.4,AD-35581.4,AD-35587.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
GCCAUAAAUAAU	2358	AUUAUUUAUGGC	2359	AD-39839.1,AD-35611.4,AD-35587.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
CCAUAAAUAAUA	2360	UAUUAUUUAUGG	2361	AD-39839.1,AD-35611.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4,AD-39845.1
CAUAAAUAAUAC	2362	GUAUUAUUUAUG	2363	AD-39839.1,AD-35611.4,AD-39833.1,AD-35605.4,AD-39851.1,AD-39827.1,AD-35599.4,AD-39845.1
AUAAAUAAUACU	2364	AGUAUUAUUUAU	2365	AD-39839.1,AD-35611.4,AD-39857.1,AD-39833.1,AD-35605.4,AD-39851.1,AD-39827.1,AD-39845.1
UAAAUAAUACUA	2366	UAGUAUUAUUUA	2367	AD-39839.1,AD-35611.4,AD-39857.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39827.1,AD-39845.1
AAAUAAUACUAA	2368	UUAGUAUUAUUU	2369	AD-39839.1,AD-39857.1,AD-39869.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39827.1,AD-39845.1
AAUAAUACUAAA	2370	UUUAGUAUUAUU	2371	AD-39828.1,AD-39839.1,AD-39857.1,AD-39869.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39845.1
AUAAUACUAAAU	2372	AUUUAGUAUUAU	2373	AD-39828.1,AD-39839.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39851.1,AD-39863.1,AD-39845.1
UAAUACUAAAUC	2374	GAUUUAGUAUUA	2375	AD-39828.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39851.1,AD-39863.1,AD-39845.1
AAUACUAAAUCA	2376	UGAUUUAGUAUU	2377	AD-39828.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39851.1,AD-39863.1,AD-39846.1
AUACUAAAUCAU	2378	AUGAUUUAGUAU	2379	AD-39828.1,AD-39852.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39863.1,AD-39846.1
UACUAAAUCAUU	2380	AAUGAUUUAGUA	2381	AD-39828.1,AD-39852.1,AD-39834.1,AD-39858.1,AD-39869.1,AD-39840.1,AD-39863.1,AD-39846.1
ACUAAAUCAUUU	2382	AAAUGAUUUAGU	2383	AD-39828.1,AD-39852.1,AD-39834.1,AD-39858.1,AD-39869.1,AD-39840.1,AD-39864.1,AD-39846.1
CUAAAUCAUUUG	2384	CAAAUGAUUUAG	2385	AD-39828.1,AD-39852.1,AD-39870.1,AD-39834.1,AD-39858.1,AD-39840.1,AD-39864.1,AD-39846.1
UAAAUCAUUUGA	2386	UCAAAUGAUUUA	2387	AD-39852.1,AD-39870.1,AD-39829.1,AD-39834.1,AD-39858.1,AD-39840.1,AD-39864.1,AD-39846.1
AAAUCAUUUGAA	2388	UUCAAAUGAUUU	2389	AD-39852.1,AD-39870.1,AD-39829.1,AD-39858.1,AD-39840.1,AD-39835.1,AD-39864.1,AD-39846.1
AAUCAUUUGAAG	2390	CUUCAAAUGAUU	2391	AD-39852.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-39864.1,AD-39846.1
AUCAUUUGAAGA	2392	UCUUCAAAUGAU	2393	AD-39852.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-39864.1
UCAUUUGAAGAU	2394	AUCUUCAAAUGA	2395	AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-

				39864.1,AD-39853.1
CAUUUGAAGAUA	2396	UAUCUUCAAAUG	2397	AD-39870.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39864.1,AD-39853.1
AUUUGAAGAUAU	2398	AUAUCUUCAAAU	2399	AD-39865.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39853.1
UUUGAAGAUAUU	2400	AAUAUCUUCAAA	2401	AD-39871.1,AD-39865.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39853.1
UUGAAGAUAUUC	2402	GAAUAUCUUCAA	2403	AD-39871.1,AD-39865.1,AD-39841.1,AD-39830.1,AD-39835.1,AD-39859.1,AD-39853.1
UGAAGAUAUUCA	2404	UGAAUAUCUUCA	2405	AD-39871.1,AD-39865.1,AD-39841.1,AD-39830.1,AD-35617.4,AD-39859.1,AD-39853.1
GAAGAUAUUCAC	2406	GUGAAUAUCUUC	2407	AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-39853.1
AAGAUAUUCACC	2408	GGUGAAUAUCUU	2409	AD-35582.1,AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-39853.1
AGAUAUUCACCA	2410	UGGUGAAUAUCU	2411	AD-35582.1,AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-35588.4
GAUAUUCACCAU	2412	AUGGUGAAUAUC	2413	AD-35582.1,AD-39871.1,AD-39865.1,AD-35594.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4
AUAUUCACCAUU	2414	AAUGGUGAAUAU	2415	AD-35582.1,AD-39871.1,AD-35594.1,AD-35600.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4
UAUUCACCAUUA	2416	UAAUGGUGAAUA	2417	AD-35582.1,AD-35606.1,AD-35594.1,AD-35600.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4
AUUCACCAUUAU	2418	AUAAUGGUGAAU	2419	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35617.4,AD-35576.4,AD-35588.4
UUCACCAUUAUA	2420	UAUAAUGGUGAA	2421	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35576.4,AD-35618.1,AD-35588.4
UCACCAUUAUAG	2422	CUAUAAUGGUGA	2423	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35618.1,AD-35588.4,AD-38127.1
CACCAUUAUAGA	2424	UCUAUAAUGGUG	2425	AD-38133.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35618.1,AD-35588.4,AD-38127.1
ACCAUUAUAGAG	2426	CUCUAUAAUGGU	2427	AD-38133.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-38139.1,AD-35618.1,AD-38127.1
CCAUUAUAGAGA	2428	UCUCUAUAAUGG	2429	AD-38133.1,AD-35606.1,AD-35612.1,AD-35600.1,AD-38145.1,AD-38139.1,AD-35618.1,AD-38127.1
CAUUAUAGAGAA	2430	UUCUCUAUAAUG	2431	AD-38133.1,AD-35606.1,AD-35612.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-35618.1,AD-38127.1
AUUAUAGAGAAC	2432	GUUCUCUAUAAU	2433	AD-38133.1,AD-35612.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-35618.1,AD-38127.1
UUAUAGAGAACA	2434	UGUUCUCUAUAA	2435	AD-38133.1,AD-38163.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-35618.1,AD-38127.1
UAUAGAGAACAA	2436	UUGUUCUCUAUA	2437	AD-38133.1,AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38127.1
AUAGAGAACAAA	2438	UUUGUUCUCUAU	2439	AD-38133.1,AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38128.1

UAGAGAACAAAU	2440	AUUUGUUCUCUA	2441	AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-38134.1
AGAGAACAAAUU	2442	AAUUUGUUCUCU	2443	AD-38163.1,AD-38145.1,AD-38140.1,AD-38169.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-38134.1
GAGAACAAAUUA	2444	UAAUUUGUUCUC	2445	AD-38163.1,AD-38140.1,AD-38169.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-39836.1,AD-38134.1
AGAACAAAUUAA	2446	UUAAUUUGUUCU	2447	AD-38163.1,AD-38140.1,AD-38169.1,AD-38157.1,AD-38128.1,AD-39842.1,AD-39836.1,AD-38134.1
GAACAAAUUAAA	2448	UUUAAUUUGUUC	2449	AD-38163.1,AD-38140.1,AD-38169.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
AACAAAUUAAAA	2450	UUUUAAUUUGUU	2451	AD-38140.1,AD-38169.1,AD-39854.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
ACAAAUUAAAAG	2452	CUUUUAAUUUGU	2453	AD-39860.1,AD-38140.1,AD-39854.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
CAAAUUAAAAGA	2454	UCUUUUAAUUUG	2455	AD-39860.1,AD-38140.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1,AD-38134.1
AAAUUAAAAGAG	2456	CUCUUUUAAUUU	2457	AD-39992.1,AD-39860.1,AD-38140.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1
AAUUAAAAGAGU	2458	ACUCUUUUAAUU	2459	AD-39992.1,AD-39860.1,AD-39998.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1
AUUAAAAGAGUU	2460	AACUCUUUUAAU	2461	AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1
UUAAAAGAGUUA	2462	UAACUCUUUUAA	2463	AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-40010.1,AD-39848.1,AD-39866.1
UAAAAGAGUUAA	2464	UUAACUCUUUUA	2465	AD-40016.1,AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-40010.1,AD-39866.1
AAAAGAGUUAAG	2466	CUUAACUCUUUU	2467	AD-40016.1,AD-39992.1,AD-39860.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1,AD-39866.1
AAAGAGUUAAGG	2468	CCUUAACUCUUU	2469	AD-40016.1,AD-40028.1,AD-39992.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1,AD-39866.1
AAGAGUUAAGGA	2470	UCCUUAACUCUU	2471	AD-40016.1,AD-40028.1,AD-40034.1,AD-39992.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1
AGAGUUAAGGAC	2472	GUCCUUAACUCU	2473	AD-40016.1,AD-40028.1,AD-40034.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1
GAGUUAAGGACU	2474	AGUCCUUAACUC	2475	AD-40016.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40004.1,AD-40010.1
AGUUAAGGACUC	2476	GAGUCCUUAACU	2477	AD-40016.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1,AD-40010.1
GUUAAGGACUCU	2478	AGAGUCCUUAAC	2479	AD-40016.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1
UUAAGGACUCUG	2480	CAGAGUCCUUAA	2481	AD-40017.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1
UAAGGACUCUGA	2482	UCAGAGUCCUUA	2483	AD-40017.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40005.1
AAGGACUCUGAA	2484	UUCAGAGUCCUU	2485	AD-40017.1,AD-40029.1,AD-40011.1,AD-40034.1,AD-39999.1,AD-

				40005.1
AGGACUCUGAAG	**2486**	CUUCAGAGUCCU	**2487**	AD-40017.1,AD-40029.1,AD-40011.1,AD-39999.1,AD-40005.1,AD-40035.1
GGACUCUGAAGA	**2488**	UCUUCAGAGUCC	**2489**	AD-40017.1,AD-40029.1,AD-40011.1,AD-39994.1,AD-39999.1,AD-40005.1,AD-40035.1
GACUCUGAAGAU	**2490**	AUCUUCAGAGUC	**2491**	AD-40017.1,AD-40029.1,AD-40011.1,AD-40000.1,AD-39994.1,AD-40005.1,AD-40035.1
ACUCUGAAGAUG	**2492**	CAUCUUCAGAGU	**2493**	AD-40017.1,AD-40029.1,AD-40011.1,AD-40000.1,AD-39994.1,AD-40006.1,AD-40035.1
CUCUGAAGAUGU	**2494**	ACAUCUUCAGAG	**2495**	AD-40017.1,AD-40029.1,AD-40000.1,AD-39994.1,AD-40012.1,AD-40006.1,AD-40035.1
UCUGAAGAUGUA	**2496**	UACAUCUUCAGA	**2497**	AD-40029.1,AD-40000.1,AD-39994.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
CUGAAGAUGUAC	**2498**	GUACAUCUUCAG	**2499**	AD-40029.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
UGAAGAUGUACC	**2500**	GGUACAUCUUCA	**2501**	AD-40030.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
GAAGAUGUACCU	**2502**	AGGUACAUCUUC	**2503**	AD-40030.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38146.1,AD-40018.1
AAGAUGUACCUA	**2504**	UAGGUACAUCUU	**2505**	AD-40030.1,AD-40000.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38146.1,AD-40018.1,AD-38152.1
AGAUGUACCUAU	**2506**	AUAGGUACAUCU	**2507**	AD-40030.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1
GAUGUACCUAUG	**2508**	CAUAGGUACAUC	**2509**	AD-40030.1,AD-40024.1,AD-40012.1,AD-38164.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1
AUGUACCUAUGG	**2510**	CCAUAGGUACAU	**2511**	AD-40030.1,AD-40024.1,AD-38164.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1
UGUACCUAUGGU	**2512**	ACCAUAGGUACA	**2513**	AD-40030.1,AD-40024.1,AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38152.1
GUACCUAUGGUC	**2514**	GACCAUAGGUAC	**2515**	AD-40030.1,AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38152.1,AD-38135.1
UACCUAUGGUCC	**2516**	GGACCAUAGGUA	**2517**	AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38141.1,AD-38152.1,AD-38135.1
ACCUAUGGUCCU	**2518**	AGGACCAUAGGU	**2519**	AD-38164.1,AD-38129.1,AD-38170.1,AD-38147.1,AD-38158.1,AD-38141.1,AD-38152.1,AD-38135.1
CCUAUGGUCCUA	**2520**	UAGGACCAUAGG	**2521**	AD-38164.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38158.1,AD-38141.1,AD-38135.1
CUAUGGUCCUAG	**2522**	CUAGGACCAUAG	**2523**	AD-38164.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38141.1,AD-38135.1
UAUGGUCCUAGU	**2524**	ACUAGGACCAUA	**2525**	AD-38165.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38141.1,AD-38135.1
AUGGUCCUAGUA	**2526**	UACUAGGACCAU	**2527**	AD-38165.1,AD-38171.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38135.1
UGGUCCUAGUAG	**2528**	CUACUAGGACCA	**2529**	AD-38165.1,AD-38171.1,AD-38159.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38130.1,AD-38135.1

GGUCCUAGUAGG	2530	CCUACUAGGACC	2531	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38130.1
GUCCUAGUAGGA	2532	UCCUACUAGGAC	2533	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38153.1,AD-38147.1,AD-38142.1,AD-38130.1
UCCUAGUAGGAA	2534	UUCCUACUAGGA	2535	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38148.1,AD-38153.1,AD-38142.1,AD-38130.1
CCUAGUAGGAAA	2536	UUUCCUACUAGG	2537	AD-38165.1,AD-38171.1,AD-38154.1,AD-38159.1,AD-38136.1,AD-38148.1,AD-38142.1,AD-38130.1
CUAGUAGGAAAU	2538	AUUUCCUACUAG	2539	AD-38165.1,AD-38171.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38160.1,AD-38142.1,AD-38130.1
UAGUAGGAAAUA	2540	UAUUUCCUACUA	2541	AD-38171.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38166.1,AD-38160.1,AD-38142.1,AD-38130.1
AGUAGGAAAUAA	2542	UUAUUUCCUACU	2543	AD-38154.1,AD-38136.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1,AD-38130.1
GUAGGAAAUAAA	2544	UUUAUUUCCUAC	2545	AD-40036.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1
UAGGAAAUAAAU	2546	AUUUAUUUCCUA	2547	AD-39995.1,AD-40036.1,AD-38154.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1
AGGAAAUAAAUG	2548	CAUUUAUUUCCU	2549	AD-39995.1,AD-40036.1,AD-38154.1,AD-40001.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1
GGAAAUAAAUGU	2550	ACAUUUAUUUCC	2551	AD-39995.1,AD-40036.1,AD-38154.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-40007.1
GAAAUAAAUGUG	2552	CACAUUUAUUUC	2553	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-40007.1
AAAUAAAUGUGA	2554	UCACAUUUAUUU	2555	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-40007.1,AD-40019.1
AAUAAAUGUGAU	2556	AUCACAUUUAUU	2557	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-40025.1,AD-38172.1,AD-40007.1,AD-40019.1
AUAAAUGUGAUU	2558	AAUCACAUUUAU	2559	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-40019.1
UAAAUGUGAUUU	2560	AAAUCACAUUUA	2561	AD-39995.1,AD-40013.1,AD-40037.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-40019.1
AAAUGUGAUUUG	2562	CAAAUCACAUUU	2563	AD-40013.1,AD-40037.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-39996.1,AD-40019.1
AAUGUGAUUUGC	2564	GCAAAUCACAUU	2565	AD-40013.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40007.1,AD-39996.1,AD-40019.1
AUGUGAUUUGCC	2566	GGCAAAUCACAU	2567	AD-40008.1,AD-40013.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-39996.1,AD-40019.1
UGUGAUUUGCCU	2568	AGGCAAAUCACA	2569	AD-40008.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1,AD-40019.1
GUGAUUUGCCUU	2570	AAGGCAAAUCAC	2571	AD-40008.1,AD-40037.1,AD-40020.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1
UGAUUUGCCUUC	2572	GAAGGCAAAUCA	2573	AD-40026.1,AD-40008.1,AD-40037.1,AD-40020.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1
GAUUUGCCUUCU	2574	AGAAGGCAAAUC	2575	AD-40026.1,AD-40008.1,AD-40032.1,AD-40037.1,AD-40020.1,AD-

				40002.1,AD-40014.1,AD-39996.1
AUUUGCCUUCUA	2576	UAGAAGGCAAAU	2577	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-40002.1,AD-40014.1,AD-39996.1
UUUGCCUUCUAG	2578	CUAGAAGGCAAA	2579	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-40002.1,AD-39997.1,AD-40014.1
UUGCCUUCUAGA	2580	UCUAGAAGGCAA	2581	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-39997.1,AD-40014.1
UGCCUUCUAGAA	2582	UUCUAGAAGGCA	2583	AD-40038.1,AD-40026.1,AD-40032.1,AD-40020.1,AD-40009.1,AD-39997.1,AD-40014.1
GCCUUCUAGAAC	2584	GUUCUAGAAGGC	2585	AD-40038.1,AD-40026.1,AD-40015.1,AD-40032.1,AD-40020.1,AD-40009.1,AD-39997.1
CCUUCUAGAACA	2586	UGUUCUAGAAGG	2587	AD-40038.1,AD-40026.1,AD-40015.1,AD-40021.1,AD-40032.1,AD-40009.1,AD-39997.1
CUUCUAGAACAG	2588	CUGUUCUAGAAG	2589	AD-40038.1,AD-40027.1,AD-40015.1,AD-40021.1,AD-40032.1,AD-40009.1,AD-39997.1
UUCUAGAACAGU	2590	ACUGUUCUAGAA	2591	AD-40038.1,AD-40027.1,AD-40015.1,AD-40021.1,AD-40009.1,AD-40033.1,AD-39997.1
UCUAGAACAGUA	2592	UACUGUUCUAGA	2593	AD-40027.1,AD-40015.1,AD-40021.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-39997.1
CUAGAACAGUAG	2594	CUACUGUUCUAG	2595	AD-40027.1,AD-40015.1,AD-40021.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-40045.1
UAGAACAGUAGA	2596	UCUACUGUUCUA	2597	AD-40027.1,AD-40015.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-40045.1
AGAACAGUAGAC	2598	GUCUACUGUUCU	2599	AD-40027.1,AD-40057.1,AD-40015.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40033.1,AD-40045.1
GAACAGUAGACA	2600	UGUCUACUGUUC	2601	AD-40027.1,AD-40057.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1
AACAGUAGACAC	2602	GUGUCUACUGUU	2603	AD-40027.1,AD-40057.1,AD-40051.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1,AD-40069.1
ACAGUAGACACA	2604	UGUGUCUACUGU	2605	AD-40057.1,AD-40051.1,AD-40075.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1,AD-40069.1
CAGUAGACACAA	2606	UUGUGUCUACUG	2607	AD-40057.1,AD-40051.1,AD-40075.1,AD-40039.1,AD-40081.1,AD-40063.1,AD-40045.1,AD-40069.1
AGUAGACACAAA	2608	UUUGUGUCUACU	2609	AD-40057.1,AD-40051.1,AD-40075.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40045.1,AD-40069.1
GUAGACACAAAA	2610	UUUUGUGUCUAC	2611	AD-40057.1,AD-40051.1,AD-40075.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
UAGACACAAAAC	2612	GUUUUGUGUCUA	2613	AD-40057.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
AGACACAAAACA	2614	UGUUUUGUGUCU	2615	AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
GACACAAAACAG	2616	CUGUUUUGUGUC	2617	AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40064.1,AD-40069.1
ACACAAAACAGG	2618	CCUGUUUUGUGU	2619	AD-40070.1,AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40064.1

CACAAAACAGGC	2620	GCCUGUUUUGUG	2621	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40040.1,AD-40081.1,AD-40064.1
ACAAAACAGGCU	2622	AGCCUGUUUUGU	2623	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40040.1,AD-40082.1,AD-40064.1
CAAAACAGGCUC	2624	GAGCCUGUUUUG	2625	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40064.1
AAAACAGGCUCA	2626	UGAGCCUGUUUU	2627	AD-40070.1,AD-40058.1,AD-40052.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40064.1,AD-40047.1
AAACAGGCUCAG	2628	CUGAGCCUGUUU	2629	AD-40070.1,AD-40058.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40064.1,AD-40047.1
AACAGGCUCAGG	2630	CCUGAGCCUGUU	2631	AD-40059.1,AD-40070.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40064.1,AD-40047.1
ACAGGCUCAGGA	2632	UCCUGAGCCUGU	2633	AD-40059.1,AD-40070.1,AD-40065.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40047.1
CAGGCUCAGGAC	2634	GUCCUGAGCCUG	2635	AD-40059.1,AD-40065.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40071.1,AD-40053.1,AD-40047.1
AGGCUCAGGACU	2636	AGUCCUGAGCCU	2637	AD-40059.1,AD-40065.1,AD-40041.1,AD-40082.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40047.1
GGCUCAGGACUU	2638	AAGUCCUGAGCC	2639	AD-40059.1,AD-40065.1,AD-40041.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1,AD-40047.1
GCUCAGGACUUA	2640	UAAGUCCUGAGC	2641	AD-40059.1,AD-40065.1,AD-40042.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1,AD-40047.1
CUCAGGACUUAG	2642	CUAAGUCCUGAG	2643	AD-40059.1,AD-40065.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1
UCAGGACUUAGC	2644	GCUAAGUCCUGA	2645	AD-40059.1,AD-40065.1,AD-40054.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
CAGGACUUAGCA	2646	UGCUAAGUCCUG	2647	AD-40065.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
AGGACUUAGCAA	2648	UUGCUAAGUCCU	2649	AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
GGACUUAGCAAG	2650	CUUGCUAAGUCC	2651	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40077.1,AD-40083.1
GACUUAGCAAGA	2652	UCUUGCUAAGUC	2653	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40078.1,AD-40083.1
ACUUAGCAAGAA	2654	UUCUUGCUAAGU	2655	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40084.1,AD-40078.1
CUUAGCAAGAAG	2656	CUUCUUGCUAAG	2657	AD-40072.1,AD-40054.1,AD-40060.1,AD-40066.1,AD-40043.1,AD-40048.1,AD-40084.1,AD-40078.1
UUAGCAAGAAGU	2658	ACUUCUUGCUAA	2659	AD-40072.1,AD-40054.1,AD-40060.1,AD-40066.1,AD-40043.1,AD-40084.1,AD-40049.1,AD-40078.1
UAGCAAGAAGUU	2660	AACUUCUUGCUA	2661	AD-40072.1,AD-40060.1,AD-40066.1,AD-40055.1,AD-40043.1,AD-40084.1,AD-40049.1,AD-40078.1
AGCAAGAAGUUA	2662	UAACUUCUUGCU	2663	AD-40072.1,AD-40066.1,AD-40055.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40049.1,AD-40078.1
GCAAGAAGUUAU	2664	AUAACUUCUUGC	2665	AD-40072.1,AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-

				40084.1,AD-40049.1,AD-40078.1
CAAGAAGUUAUG	2666	CAUAACUUCUUG	2667	AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40073.1,AD-40049.1,AD-40078.1
AAGAAGUUAUGG	2668	CCAUAACUUCUU	2669	AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40073.1,AD-40079.1,AD-40049.1
AGAAGUUAUGGA	2670	UCCAUAACUUCU	2671	AD-40085.1,AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40073.1,AD-40079.1,AD-40049.1
GAAGUUAUGGAA	2672	UUCCAUAACUUC	2673	AD-40085.1,AD-40044.1,AD-40055.1,AD-40067.1,AD-40061.1,AD-40073.1,AD-40079.1,AD-40049.1
AAGUUAUGGAAU	2674	AUUCCAUAACUU	2675	AD-40085.1,AD-40044.1,AD-40055.1,AD-40067.1,AD-40061.1,AD-40050.1,AD-40073.1,AD-40079.1
AGUUAUGGAAUU	2676	AAUUCCAUAACU	2677	AD-40085.1,AD-40044.1,AD-40067.1,AD-40056.1,AD-40061.1,AD-40050.1,AD-40073.1,AD-40079.1
GUUAUGGAAUUC	2678	GAAUUCCAUAAC	2679	AD-40062.1,AD-40085.1,AD-40044.1,AD-40067.1,AD-40056.1,AD-40050.1,AD-40073.1,AD-40079.1
UUAUGGAAUUCC	2680	GGAAUUCCAUAA	2681	AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1,AD-40073.1,AD-40079.1
UAUGGAAUUCCU	2682	AGGAAUUCCAUA	2683	AD-40074.1,AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1,AD-40079.1
AUGGAAUUCCUU	2684	AAGGAAUUCCAU	2685	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1
UGGAAUUCCUUU	2686	AAAGGAAUUCCA	2687	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40044.1,AD-40056.1,AD-40050.1
GGAAUUCCUUUU	2688	AAAAGGAAUUCC	2689	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40056.1,AD-40050.1,AD-38131.1
GAAUUCCUUUUA	2690	UAAAAGGAAUUC	2691	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-38137.1,AD-40056.1,AD-38131.1
AAUUCCUUUUAU	2692	AUAAAAGGAAUU	2693	AD-40080.1,AD-38143.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-38137.1,AD-38131.1
AUUCCUUUUAUU	2694	AAUAAAAGGAAU	2695	AD-40080.1,AD-38149.1,AD-38143.1,AD-40074.1,AD-40068.1,AD-38137.1,AD-38131.1
UUCCUUUUAUUG	2696	CAAUAAAAGGAA	2697	AD-40080.1,AD-38149.1,AD-38143.1,AD-40074.1,AD-38137.1,AD-38155.1,AD-38131.1
UCCUUUUAUUGA	2698	UCAAUAAAAGGA	2699	AD-40080.1,AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38155.1,AD-38131.1
CCUUUUAUUGAA	2700	UUCAAUAAAAGG	2701	AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38167.1,AD-38155.1,AD-38131.1
CUUUUAUUGAAA	2702	UUUCAAUAAAAG	2703	AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38173.1,AD-38167.1,AD-38155.1,AD-38131.1
UUUUAUUGAAAC	2704	GUUUCAAUAAAA	2705	AD-38149.1,AD-38143.1,AD-38132.1,AD-38137.1,AD-38161.1,AD-38173.1,AD-38167.1,AD-38155.1
UUUAUUGAAACA	2706	UGUUUCAAUAAA	2707	AD-38149.1,AD-38143.1,AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1
UUAUUGAAACAU	2708	AUGUUUCAAUAA	2709	AD-38149.1,AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1,AD-38144.1

UAUUGAAACAUC	2710	GAUGUUUCAAUA	2711	AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1,AD-38150.1,AD-38144.1
AUUGAAACAUCA	2712	UGAUGUUUCAAU	2713	AD-38132.1,AD-38156.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38150.1,AD-38144.1
UUGAAACAUCAG	2714	CUGAUGUUUCAA	2715	AD-38132.1,AD-38162.1,AD-38156.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38150.1,AD-38144.1
UGAAACAUCAGC	2716	GCUGAUGUUUCA	2717	AD-38132.1,AD-38162.1,AD-38156.1,AD-38168.1,AD-38173.1,AD-38138.1,AD-38150.1,AD-38144.1
GAAACAUCAGCA	2718	UGCUGAUGUUUC	2719	AD-38174.1,AD-38132.1,AD-38162.1,AD-38156.1,AD-38168.1,AD-38138.1,AD-38150.1,AD-38144.1
AAACAUCAGCAA	2720	UUGCUGAUGUUU	2721	AD-38174.1,AD-38162.1,AD-35667.1,AD-38156.1,AD-38168.1,AD-38138.1,AD-38150.1,AD-38144.1
AACAUCAGCAAA	2722	UUUGCUGAUGUU	2723	AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-38156.1,AD-38168.1,AD-38150.1,AD-38144.1
ACAUCAGCAAAG	2724	CUUUGCUGAUGU	2725	AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38156.1,AD-38168.1,AD-38150.1
CAUCAGCAAAGA	2726	UCUUUGCUGAUG	2727	AD-35685.1,AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38156.1,AD-38168.1
AUCAGCAAAGAC	2728	GUCUUUGCUGAU	2729	AD-35685.1,AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38168.1,AD-35691.1
UCAGCAAAGACA	2730	UGUCUUUGCUGA	2731	AD-35685.1,AD-38174.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-38168.1,AD-35691.1
CAGCAAAGACAA	2732	UUGUCUUUGCUG	2733	AD-35685.1,AD-38174.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-35691.1
AGCAAAGACAAG	2734	CUUGUCUUUGCU	2735	AD-35685.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-35691.1
GCAAAGACAAGA	2736	UCUUGUCUUUGC	2737	AD-35685.1,AD-35673.1,AD-35679.1,AD-35691.1
CAAAGACAAGAC	2738	GUCUUGUCUUUG	2739	AD-35685.1,AD-35679.1,AD-35691.1
AAAGACAAGACA	2740	UGUCUUGUCUUU	2741	AD-35685.1,AD-35691.1

[003720] The position ("Pos") in NM_000336.2 is indicated. 12 examplary nt of the overlap in the sense and anti-sense strand are presented; in many cases, the overlap is actually longer.

EXAMPLE 3
EFFICACY OF KRAS RNAi AGENTS

[003721] KRAS RNAi agents were tested for efficacy, and the results are shown in Tables 5 and 6, below.

[003722] **In vitro screening**:

[003723] Cell culture and transfections:

[003724] RKO cells (ATCC, Manassas, VA) are grown to near confluence at 37°C in an atmosphere of 5% CO_2 in McCoy's Medium (ATCC) supplemented with 10% FBS, streptomycin, and glutamine (ATCC) before being released from the plate by trypsinization. Transfection is carried

out by adding 14.8µl of Opti-MEM plus 0.2µl of Lipofectamine RNAiMax per well (Invitrogen, Carlsbad, CA, cat # 13778-150) to 5µl of siRNA duplexes per well into a 96-well plate and incubated at room temperature for 15 minutes. 80µl of complete growth media without antibiotic containing ~2 x10^4 RKO cells are then added to the siRNA mixture. Cells are incubated for either 24 hours prior to RNA purification. Single dose experiments are performed at 10nM and in some cases 0.1nM final duplex concentration and dose response experiments are done at 10, 1, 0.5, 0.1,0.05, 0.01, 0.005, 0.001, 0.0005, 0.0001, 0.00005, 0.00001 nM final duplex concentration.

[003725] Total RNA isolation using DYNABEADS mRNA Isolation Kit (Invitrogen, part #: 610-12):

[003726] Cells are harvested and lysed in 150µl of Lysis/Binding Buffer then mixed for 5 minute at 850rpm using an Eppendorf Thermomixer (the mixing speed is the same throughout the process). Ten microliters of magnetic beads and 80µl Lysis/Binding Buffer mixture are added to a round bottom plate and mixed for 1 minute. Magnetic beads are captured using magnetic stand and the supernatant is removed without disturbing the beads. After removing supernatant, the lysed cells are added to the remaining beads and mixed for 5 minutes. After removing supernatant, magnetic beads are washed 2 times with 150µl Wash Buffer A and mixed for 1 minute. Beads are capture again and supernatant removed. Beads are then washed with 150µl Wash Buffer B, captured and supernatant is removed. Beads are next washed with 150µl Elution Buffer, captured and supernatant removed. Beads are allowed to dry for 2 minutes. After drying, 50µl of Elution Buffer is added and mixed for 5 minutes at 70°C. Beads are captured on magnet for 5 minutes. 40µl of supernatant is removed and added to another 96 well plate.

[003727] cDNA synthesis using ABI High capacity cDNA reverse transcription kit (Applied Biosystems, Foster City, CA, Cat #4368813):

[003728] A master mix of 2µl 10X Buffer, 0.8µl 25X dNTPs, 2µl Random primers, 1µl Reverse Transcriptase, 1µl RNase inhibitor and 3.2µl of H2O per reaction are added into 10µl total RNA. cDNA is generated using a Bio-Rad C-1000 or S-1000 thermal cycler (Hercules, CA) through the following steps: 25°C 10 min, 37°C 120 min, 85°C 5 sec, 4°C hold.

[003729] Real time PCR:

[003730] 2µl of cDNA are added to a master mix containing 1µl 18S TaqMan Probe (Applied Biosystems Cat # 4319413E), 1µl KRAS TaqMan probe (Applied Biosystems cat # HS00180035_m1, HS00932330_m1, or HS00610483) and 10µl TaqMan Universal PCR Master Mix (Applied Biosystems Cat #4324018) per well in a MicroAmp Optical 96 well plate (Applied Biosystems cat # 4326659). Real time PCR is done in an ABI 7900HT Real Time PCR system (Applied Biosystems) using the ΔΔCt(RQ) assay. Each duplex is tested in two independent transfections and each transfection is assayed in duplicate, unless otherwise noted in the summary tables.

[003731] Real time data are analyzed using the ΔΔCt method and normalized to assays performed with cells transfected with 10nM AD-1955 to calculate relative fold change.

Table 5. KRAS RNAi agents, 0.1 and 10nM KD at 24 hrs

SD = standard deviation, AVG = average

	10nM KRAS		.1nM KRAS		10nM	.1nM	10nM	.1nM
Duplex ID	bio1	bio2	bio1	bio2	SD	SD	AVG	AVG
AD-35613.4	0.332	0.542	1.814	1.365	0.1484	0.3177	0.437	1.589
AD-35572.4	0.403	0.666	1.850	1.571	0.1859	0.1975	0.535	1.711
AD-35578.4	0.194	0.905	0.622	0.485	0.5030	0.0965	0.550	0.554
AD-35584.4	0.171	0.239	0.953	0.654	0.0480	0.2115	0.205	0.803
AD-35590.4	0.167	0.296	0.988	0.832	0.0919	0.1105	0.231	0.910
AD-35596.4	0.782	0.837	1.540	1.263	0.0392	0.1962	0.809	1.402
AD-35602.4	1.013	0.915	1.264	0.934	0.0694	0.2334	0.964	1.099
AD-35608.4	0.818	0.631	1.120	1.093	0.1321	0.0191	0.725	1.106
AD-35614.4	0.898	1.025	1.929	1.195	0.0898	0.5194	0.961	1.562
AD-35573.4	0.920	0.809	1.412	0.957	0.0785	0.3219	0.865	1.185
AD-35579.4	0.794	0.946	1.694	1.244	0.1072	0.3189	0.870	1.469
AD-35585.4	0.861	0.738	3.016	2.552	0.0870	0.3281	0.800	2.784
AD-35591.4	0.458	0.325	1.238	1.073	0.0938	0.1162	0.392	1.156
AD-35597.4	0.948	0.897	1.523	0.864	0.0358	0.4657	0.922	1.194
AD-35603.4	0.401	0.405	0.817	0.618	0.0025	0.1402	0.403	0.718
AD-35609.4	0.168	0.165	0.503	0.320	0.0022	0.1295	0.167	0.411
AD-35615.4	0.555	0.620	1.397	0.818	0.0460	0.4099	0.587	1.108
AD-35574.4	0.762	0.650	1.009	0.643	0.0790	0.2590	0.706	0.826
AD-35580.1	0.436	0.398	1.334	0.768	0.0275	0.4003	0.417	1.051
AD-35586.4	0.242	0.266	0.908	0.577	0.0175	0.2337	0.254	0.743
AD-35592.4	0.212	0.166	0.600	0.504	0.0324	0.0685	0.189	0.552
AD-35598.4	0.828	0.893	1.318	1.147	0.0461	0.1205	0.861	1.232
AD-35604.4	0.070	0.179	0.594	0.496	0.0770	0.0692	0.124	0.545
AD-35610.4	0.415	0.633	1.068	0.887	0.1537	0.1275	0.524	0.977
AD-35616.4	0.159	0.342	0.300	0.213	0.1288	0.0610	0.251	0.256
AD-35575.4	0.470	0.689	0.789	0.749	0.1547	0.0284	0.579	0.769
AD-35581.4	0.137	0.288	0.220	0.196	0.1064	0.0170	0.212	0.208
AD-35587.4	0.637	0.670	1.059	0.975	0.0231	0.0591	0.653	1.017
AD-35593.4	0.200	0.463	0.724	0.489	0.1859	0.1661	0.332	0.607
AD-35599.4	0.685	1.281	1.273	0.952	0.4217	0.2266	0.983	1.113
AD-35605.4	0.564	0.798	1.423	0.897	0.1649	0.3718	0.681	1.160
AD-35611.4	0.644	0.844	1.189	0.922	0.1418	0.1887	0.744	1.055
AD-35617.4	0.219	0.213	0.594	0.625	0.0047	0.0220	0.216	0.609
AD-35576.4	0.451	0.365	1.167	0.928	0.0604	0.1693	0.408	1.047
AD-35588.4	0.185	0.290	0.442	0.323	0.0736	0.0841	0.237	0.383
AD-35667.1	0.497	0.623	1.030	0.857	0.0897	0.1228	0.560	0.943

AD-35673.1	0.367	0.405	0.771	0.693	0.0268	0.0547	0.386	0.732
AD-35679.1	0.217	0.330	0.329	0.293	0.0798	0.0258	0.274	0.311
AD-35685.1	0.310	0.255	0.345	0.339	0.0390	0.0045	0.283	0.342
AD-35691.1	0.258	0.257	0.955	0.535	0.0005	0.2968	0.258	0.745
AD-35557.1	0.843	0.624	1.056	0.947	0.1547	0.0766	0.734	1.002
AD-35618.1	0.447	0.425	0.611	0.439	0.0157	0.1218	0.436	0.525
AD-35569.1	0.319	0.404	0.805	0.715	0.0605	0.0636	0.362	0.760
AD-35534.1	0.578	0.582	0.877	0.944	0.0028	0.0475	0.580	0.910
AD-35582.1	0.518	0.974	0.982	0.977	0.3223	0.0035	0.746	0.980
AD-35594.1	0.441	0.317	0.884	0.679	0.0877	0.1451	0.379	0.782
AD-35600.1	0.207	0.394	0.309	0.233	0.1322	0.0539	0.301	0.271
AD-35606.1	0.285	0.177	0.384	0.346	0.0770	0.0272	0.231	0.365
AD-35612.1	1.070	0.947	1.027	0.827	0.0870	0.1415	1.009	0.927
AD-38127.1	0.217	0.162	0.594	0.491	0.0388	0.0728	0.189	0.542
AD-38128.1	0.157	0.146	0.521	0.366	0.0072	0.1095	0.151	0.443
AD-38164.1	1.112	1.993	1.213	0.982	0.6224	0.1633	1.553	1.097
AD-38165.1	0.619	0.731	1.002	0.837	0.0790	0.1173	0.675	0.920
AD-38160.1	1.159	1.129	1.300	0.920	0.0216	0.2685	1.144	1.110
AD-38161.1	0.144	0.125	0.355	0.319	0.0130	0.0256	0.134	0.337
AD-38133.1	0.164	0.142	0.574	0.590	0.0154	0.0113	0.153	0.582
AD-38170.1	0.147	0.191	0.734	0.487	0.0311	0.1744	0.169	0.611
AD-38171.1	0.858	1.067	1.408	1.101	0.1480	0.2168	0.962	1.254
AD-38166.1	0.319	0.486	0.846	0.848	0.1184	0.0016	0.402	0.847
AD-38167.1	0.119	0.182	0.740	0.546	0.0440	0.1368	0.150	0.643
AD-38139.1	0.148	0.085	0.259	0.198	0.0445	0.0433	0.116	0.229
AD-38134.1	0.117	0.190	0.248	0.380	0.0514	0.0936	0.154	0.314
AD-38129.1	0.776	0.860	1.038	1.089	0.0596	0.0356	0.818	1.064
AD-38130.1	0.528	0.820	0.900	0.846	0.2064	0.0386	0.674	0.873
AD-38172.1	0.076	0.094	0.289	0.247	0.0127	0.0298	0.085	0.268
AD-38145.1	0.150	0.128	0.440	0.371	0.0154	0.0488	0.139	0.406
AD-38135.1	0.959	1.429	0.965	0.900	0.3321	0.0459	1.194	0.932
AD-38131.1	0.135	0.173	0.414	0.279	0.0267	0.0955	0.154	0.347
AD-38173.1	0.609	0.988	1.132	1.373	0.2681	0.1707	0.798	1.253
AD-38151.1	0.211	0.181	0.378	0.554	0.0218	0.1246	0.196	0.466
AD-38140.1	0.652	0.794	1.087	1.045	0.1004	0.0298	0.723	1.066
AD-38141.1	0.450	0.512	1.002	0.840	0.0433	0.1147	0.481	0.921
AD-38136.1	0.053	0.096	0.150	0.121	0.0301	0.0199	0.074	0.136
AD-38137.1	0.283	0.259	0.677	0.580	0.0169	0.0687	0.271	0.628
AD-38132.1	0.256	0.333	0.669	0.726	0.0543	0.0404	0.294	0.697
AD-38157.1	0.760	0.543	0.768	0.900	0.1536	0.0937	0.651	0.834
AD-38146.1	0.249	0.240	0.617	0.584	0.0065	0.0237	0.245	0.600
AD-38147.1	0.271	0.361	0.858	0.909	0.0638	0.0365	0.316	0.883
AD-38142.1	0.389	0.634	0.971	0.712	0.1732	0.1831	0.512	0.841

AD-38143.1	0.378	0.657	0.920	0.808	0.1966	0.0791	0.518	0.864
AD-38163.1	0.088	0.083	0.143	0.172	0.0036	0.0206	0.085	0.158
AD-38152.1	0.755	0.580	1.057	0.897	0.1238	0.1134	0.667	0.977
AD-38153.1	0.727	0.781	0.855	1.006	0.0380	0.1067	0.754	0.930
AD-38148.1	0.553	0.522	0.784	0.831	0.0215	0.0333	0.537	0.807
AD-38149.1	0.269	0.295	0.607	0.641	0.0186	0.0242	0.282	0.624
AD-38138.1	0.330	0.417	0.402	0.448	0.0615	0.0321	0.373	0.425
AD-38169.1	0.380	0.248	0.626	0.540	0.0929	0.0607	0.314	0.583
AD-38158.1	0.699	0.611	0.800	1.250	0.0619	0.3184	0.655	1.025
AD-38159.1	0.161	0.122	0.210	0.227	0.0274	0.0123	0.142	0.219
AD-38154.1	0.212	0.172	0.628	0.507	0.0286	0.0858	0.192	0.567
AD-38155.1	0.198	0.215	0.331	0.309	0.0122	0.0153	0.207	0.320
AD-39683.1	0.471	0.536	1.135	0.812	0.0461	0.2283	0.504	0.973
AD-39689.1	0.630	0.627	1.148	0.979	0.0025	0.1194	0.629	1.064
AD-39695.1	0.659	0.557	1.222	1.022	0.0723	0.1414	0.608	1.122
AD-39701.1	1.218	1.231	0.704	0.724	0.0092	0.0141	1.225	0.714
AD-39707.1	0.384	0.160	1.387	1.087	0.1584	0.2121	0.272	1.237
AD-39713.1	1.157	0.481	1.128	1.228	0.4778	0.0707	0.819	1.178
AD-39719.1	0.885	0.631	1.178	1.189	0.1791	0.0073	0.758	1.183
AD-39725.1	1.105	1.074	1.203	1.751	0.0222	0.3878	1.089	1.477
AD-39684.1	0.321	0.186	0.954	1.222	0.0952	0.1895	0.253	1.088
AD-39690.1	0.825	0.828	0.832	0.852	0.0019	0.0139	0.826	0.842
AD-39696.1	1.071	0.996	1.087	0.883	0.0532	0.1443	1.034	0.985
AD-39702.1	0.360	0.334	1.050	1.285	0.0179	0.1660	0.347	1.167
AD-39708.1	0.757	0.969	1.049	1.091	0.1494	0.0299	0.863	1.070
AD-39714.1	0.953	1.056	0.779	0.639	0.0731	0.0995	1.004	0.709
AD-39720.1	0.210	0.182	0.404	0.691	0.0199	0.2030	0.196	0.548
AD-39726.1	0.774	0.968	0.921	1.068	0.1372	0.1037	0.871	0.995
AD-39685.1	1.022	1.358	1.053	0.997	0.2378	0.0399	1.190	1.025
AD-39691.1	0.494	0.380	0.913	0.967	0.0806	0.0379	0.437	0.940
AD-39697.1	0.892	1.333	0.937	1.344	0.3125	0.2883	1.113	1.140
AD-39703.1	1.071	1.141	0.983	0.864	0.0497	0.0842	1.106	0.924
AD-39709.1	0.905	1.086	0.944	1.079	0.1284	0.0953	0.995	1.011
AD-39715.1	0.347	0.385	1.398	1.013	0.0265	0.2722	0.366	1.205
AD-39721.1	0.911	0.781	1.128	1.119	0.0918	0.0066	0.846	1.123
AD-39727.1	0.267	0.271	0.911	1.038	0.0028	0.0894	0.269	0.975
AD-39686.1	0.897	0.490	0.781	0.633	0.2877	0.1044	0.694	0.707
AD-39692.1	0.936	0.879	0.814	0.802	0.0403	0.0083	0.908	0.808
AD-39698.1	1.257	1.375	0.829	0.876	0.0834	0.0333	1.316	0.853
AD-39704.1	1.211	1.189	0.909	0.735	0.0155	0.1234	1.200	0.822
AD-39710.1	1.389	1.136	0.881	0.862	0.1789	0.0130	1.263	0.871
AD-39716.1	0.787	0.943	0.991	0.963	0.1099	0.0199	0.865	0.977
AD-39722.1	1.147	1.049	0.872	0.716	0.0688	0.1108	1.098	0.794

AD-39728.1	0.846	0.974	0.891	0.928	0.0902	0.0264	0.910	0.909
AD-39683.1	0.374	0.307	0.996	0.982	0.0469	0.0098	0.341	0.989
AD-39687.1	1.015	0.775	1.035	1.642	0.1695	0.4296	0.895	1.338
AD-39689.1	0.340	0.328	0.769	0.762	0.0090	0.0047	0.334	0.765
AD-39693.1	1.262	0.832	0.855	0.967	0.3040	0.0791	1.047	0.911
AD-39699.1	1.173	1.113	1.113	1.307	0.0423	0.1375	1.143	1.210
AD-39705.1	0.622	0.582	0.730	0.807	0.0282	0.0542	0.602	0.768
AD-39711.1	1.996	0.864	0.720	0.829	0.8006	0.0770	1.430	0.774
AD-39717.1	0.551	0.523	1.136	1.064	0.0197	0.0511	0.537	1.100
AD-39723.1	1.179	0.695	0.877	0.873	0.3428	0.0025	0.937	0.875
AD-39729.1	1.083	0.864	0.898	0.873	0.1547	0.0178	0.973	0.885
AD-39688.1	0.341	0.492	0.700	0.782	0.1064	0.0577	0.416	0.741
AD-39694.1	0.230	0.327	0.923	1.087	0.0685	0.1164	0.279	1.005
AD-39700.1	0.529	0.760	0.600	0.671	0.1631	0.0497	0.645	0.635
AD-39706.1	0.180	0.217	0.447	0.522	0.0263	0.0528	0.198	0.484
AD-39712.1	0.330	0.394	0.798	0.777	0.0452	0.0147	0.362	0.787
AD-39718.1	0.672	0.798	0.688	0.724	0.0889	0.0255	0.735	0.706
AD-39724.1	0.599	1.136	0.643	0.680	0.3804	0.0261	0.868	0.661
AD-39730.1	0.996	1.459	0.848	0.784	0.3271	0.0448	1.228	0.816
AD-39736.1	1.085	1.121	0.733	0.883	0.0254	0.1064	1.103	0.808
AD-39742.1	0.518	0.561	0.651	0.703	0.0308	0.0374	0.539	0.677
AD-39748.1	0.445	0.609	0.772	0.788	0.1163	0.0113	0.527	0.780
AD-39754.1	0.549	0.823	0.691	0.894	0.1942	0.1438	0.686	0.793
AD-39760.1	0.233	0.210	0.417	0.747	0.0158	0.2332	0.221	0.582
AD-39766.1	0.700	0.882	0.849	0.836	0.1291	0.0095	0.791	0.843
AD-39772.1	0.323	0.379	0.797	0.870	0.0393	0.0519	0.351	0.833
AD-39731.1	0.804	0.222	0.452	0.417	0.4116	0.0251	0.513	0.434
AD-39737.1	0.450	0.347	0.737	0.768	0.0726	0.0219	0.399	0.753
AD-39743.1	0.375	0.533	0.794	0.852	0.1112	0.0415	0.454	0.823
AD-39695.1	0.610	0.492	0.831	0.821	0.0836	0.0070	0.551	0.826
AD-39749.1	0.292	0.121	0.545	0.695	0.1205	0.1059	0.206	0.620
AD-39755.1	0.226	0.275	0.874	1.170	0.0350	0.2093	0.251	1.022
AD-39761.1	0.821	0.841	0.942	1.101	0.0141	0.1124	0.831	1.022
AD-39767.1	0.360	0.374	0.730	0.711	0.0097	0.0134	0.367	0.720
AD-39773.1	0.223	0.236	0.802	1.159	0.0096	0.2520	0.229	0.980
AD-39732.1	0.446	0.662	1.593	1.181	0.1532	0.2914	0.554	1.387
AD-39738.1	0.257	0.147	1.369	1.482	0.0776	0.0801	0.202	1.426
AD-39744.1	0.259	0.200	1.097	0.871	0.0414	0.1592	0.230	0.984
AD-39750.1	0.182	0.302	0.642	0.782	0.0853	0.0988	0.242	0.712
AD-39756.1	0.568	0.548	0.808	0.993	0.0144	0.1308	0.558	0.900
AD-39762.1	0.684	0.916	0.783	0.929	0.1641	0.1031	0.800	0.856
AD-39768.1	0.929	1.239	1.000	1.033	0.2194	0.0239	1.084	1.016
AD-39774.1	0.391	0.447	1.087	1.087	0.0399	0.0003	0.419	1.087

AD-39733.1	0.605	0.569	1.020	1.212	0.0251	0.1355	0.587	1.116
AD-39739.1	0.950	1.271	0.959	1.030	0.2265	0.0501	1.111	0.994
AD-39701.1	0.798	1.193	1.221	1.018	0.2794	0.1437	0.996	1.120
AD-39745.1	0.257	0.212	1.116	1.226	0.0317	0.0779	0.234	1.171
AD-39751.1	0.260	0.248	1.037	2.286	0.0085	0.8828	0.254	1.662
AD-39757.1	0.319	0.566	1.098	0.949	0.1753	0.1053	0.443	1.023
AD-39763.1	0.235	0.300	0.667	0.531	0.0463	0.0961	0.267	0.599
AD-39769.1	0.637	0.531	0.526	0.826	0.0749	0.2120	0.584	0.676
AD-39775.1	0.472	0.526	0.760	1.002	0.0382	0.1711	0.499	0.881
AD-39734.1	0.915	0.920	0.751	0.837	0.0035	0.0606	0.917	0.794
AD-39740.1	0.323	0.302	0.406	0.632	0.0145	0.1593	0.312	0.519
AD-39746.1	0.553	0.702	0.949	1.145	0.1058	0.1382	0.627	1.047
AD-39752.1	0.440	0.577	0.855	0.860	0.0965	0.0030	0.509	0.857
AD-39758.1	1.129	1.095	0.952	0.830	0.0238	0.0863	1.112	0.891
AD-39764.1	1.125	0.898	1.205	1.405	0.1606	0.1409	1.011	1.305
AD-39770.1	0.647	0.314	0.672	0.461	0.2356	0.1486	0.480	0.566
AD-39776.1	1.013	0.970	1.035	0.739	0.0304	0.2092	0.992	0.887
AD-39735.1	0.284	0.201	0.613	0.976	0.0588	0.2564	0.242	0.794
AD-39741.1	0.177	0.188	0.526	0.806	0.0074	0.1977	0.182	0.666
AD-39747.1	1.047	0.926	1.247	1.483	0.0854	0.1666	0.986	1.365
AD-39753.1	1.082	0.823	1.034	1.662	0.1833	0.4437	0.953	1.348
AD-39759.1	0.327	0.292	0.638	0.412	0.0252	0.1600	0.309	0.525
AD-39765.1	1.099	0.596	1.270	1.027	0.3554	0.1714	0.847	1.148
AD-39771.1	0.238	0.334	0.801	0.460	0.0679	0.2407	0.286	0.631
AD-39778.1	0.217	0.250	0.502	0.354	0.0235	0.1042	0.233	0.428
AD-39784.1	0.698	0.598	1.036	0.944	0.0708	0.0655	0.648	0.990
AD-39790.1	0.150	0.260	0.614	0.787	0.0777	0.1221	0.205	0.700
AD-39796.1	0.635	0.610	0.731	0.846	0.0178	0.0813	0.622	0.788
AD-39802.1	0.349	0.150	0.898	0.970	0.1408	0.0509	0.249	0.934
AD-39808.1	0.734	0.972	1.079	0.955	0.1680	0.0881	0.853	1.017
AD-39814.1	1.070	1.294	0.979	0.968	0.1588	0.0074	1.182	0.974
AD-39820.1	0.381	0.209	0.786	0.687	0.1218	0.0701	0.295	0.737
AD-39779.1	0.744	0.889	1.038	0.942	0.1020	0.0683	0.817	0.990
AD-39785.1	0.182	0.218	0.509	0.506	0.0255	0.0022	0.200	0.507
AD-39791.1	0.214	0.308	0.556	0.519	0.0667	0.0260	0.261	0.537
AD-39797.1	0.341	0.326	0.788	0.543	0.0100	0.1730	0.333	0.665
AD-39803.1	0.229	0.210	0.808	0.648	0.0135	0.1133	0.220	0.728
AD-39809.1	0.624	0.829	1.060	1.031	0.1450	0.0211	0.727	1.046
AD-39815.1	0.441	0.449	0.862	0.852	0.0057	0.0072	0.445	0.857
AD-39821.1	0.582	0.592	0.722	0.608	0.0071	0.0806	0.587	0.665
AD-39780.1	0.748	0.784	0.973	0.976	0.0252	0.0025	0.766	0.974
AD-39786.1	0.376	0.455	0.466	0.640	0.0557	0.1226	0.416	0.553
AD-39792.1	1.195	1.019	0.908	1.168	0.1249	0.1835	1.107	1.038

AD-39798.1	0.429	0.342	0.933	0.936	0.0615	0.0020	0.386	0.934
AD-39804.1	0.551	0.588	0.942	0.959	0.0259	0.0119	0.570	0.950
AD-39810.1	0.605	0.532	0.989	0.956	0.0518	0.0236	0.568	0.972
AD-39764.1	1.112	1.027	0.961	0.746	0.0602	0.1522	1.070	0.854
AD-39816.1	0.805	0.645	1.014	0.839	0.1130	0.1236	0.725	0.927
AD-39770.1	0.420	0.371	0.858	0.887	0.0345	0.0201	0.396	0.873
AD-39822.1	0.288	0.313	0.589	0.494	0.0178	0.0671	0.301	0.542
AD-39781.1	0.276	0.379	0.404	0.305	0.0725	0.0701	0.328	0.354
AD-39787.1	0.982	1.065	0.675	0.803	0.0584	0.0909	1.024	0.739
AD-39793.1	0.165	0.291	0.487	0.488	0.0893	0.0007	0.228	0.487
AD-39799.1	0.444	0.540	0.686	0.746	0.0675	0.0423	0.492	0.716
AD-39805.1	0.295	0.250	0.474	0.421	0.0320	0.0371	0.273	0.448
AD-39811.1	0.646	0.792	0.892	0.882	0.1030	0.0070	0.719	0.887
AD-39817.1	0.583	0.824	0.848	0.846	0.1708	0.0012	0.703	0.847
AD-39823.1	1.229	1.075	1.080	0.859	0.1083	0.1564	1.152	0.970
AD-39782.1	0.605	0.757	1.162	0.883	0.1076	0.1972	0.681	1.022
AD-39788.1	0.257	0.289	0.665	0.534	0.0227	0.0926	0.273	0.599
AD-39794.1	0.667	0.699	1.196	1.102	0.0229	0.0668	0.683	1.149
AD-39800.1	0.888	0.734	1.201	0.908	0.1092	0.2072	0.811	1.054
AD-39806.1	0.505	0.637	0.630	0.849	0.0935	0.1549	0.571	0.739
AD-39812.1	0.281	0.390	0.521	0.597	0.0771	0.0538	0.335	0.559
AD-39818.1	0.999	1.049	0.789	0.936	0.0347	0.1044	1.024	0.863
AD-39824.1	1.086	1.053	1.370	1.034	0.0235	0.2377	1.070	1.202
AD-39783.1	0.460	0.731	0.736	0.822	0.1916	0.0609	0.595	0.779
AD-39789.1	0.859	1.454	1.139	1.308	0.4213	0.1195	1.157	1.224
AD-39795.1	1.165	0.901	1.015	0.916	0.1866	0.0698	1.033	0.965
AD-39801.1	1.222	1.191	1.098	0.843	0.0216	0.1801	1.207	0.971
AD-39807.1	0.776	0.807	1.007	1.002	0.0215	0.0036	0.791	1.004
AD-39813.1	0.923	1.206	1.008	0.901	0.1998	0.0753	1.065	0.955
AD-39819.1	0.952	1.021	1.024	0.916	0.0484	0.0765	0.986	0.970
AD-39825.1	0.648	0.864	1.028	0.981	0.1529	0.0336	0.756	1.004
AD-39776.1	0.795	1.019	0.891	1.046	0.1581	0.1094	0.907	0.969
AD-39831.1	0.648	0.601	1.018	1.034	0.0334	0.0119	0.624	1.026
AD-39837.1	0.799	0.984	0.969	0.903	0.1308	0.0463	0.891	0.936
AD-39843.1	0.325	0.385	0.695	0.572	0.0427	0.0866	0.355	0.634
AD-39849.1	0.702	1.075	0.903	0.969	0.2638	0.0469	0.889	0.936
AD-39855.1	0.309	0.490	1.202	0.800	0.1280	0.2840	0.399	1.001
AD-39861.1	0.762	1.162	1.020	1.000	0.2825	0.0141	0.962	1.010
AD-39867.1	0.873	1.162	1.219	0.918	0.2040	0.2126	1.017	1.069
AD-39826.1	1.358	1.043	1.148	0.961	0.2226	0.1320	1.201	1.055
AD-39832.1	0.792	1.337	1.214	0.873	0.3849	0.2413	1.065	1.043
AD-39838.1	0.429	0.270	0.793	0.530	0.1128	0.1859	0.349	0.661
AD-39844.1	0.572	0.789	0.833	0.692	0.1536	0.0997	0.680	0.762

AD-39850.1	0.535	0.231	0.505	0.529	0.2152	0.0169	0.383	0.517
AD-39856.1	0.323	0.377	0.835	0.784	0.0384	0.0359	0.350	0.810
AD-39862.1	0.405	0.429	0.835	0.615	0.0167	0.1552	0.417	0.725
AD-39868.1	0.386	0.484	0.683	0.643	0.0697	0.0284	0.435	0.663
AD-39735.1	0.168	0.255	0.439	0.294	0.0616	0.1026	0.211	0.366
AD-39827.1	0.202	0.313	0.616	0.413	0.0787	0.1432	0.258	0.515
AD-39833.1	0.190	0.492	1.007	1.026	0.2134	0.0135	0.341	1.017
AD-39839.1	0.790	1.002	1.227	1.327	0.1503	0.0708	0.896	1.277
AD-39845.1	0.192	0.213	0.391	0.218	0.0147	0.1220	0.202	0.304
AD-39851.1	0.779	0.493	1.243	0.929	0.2022	0.2220	0.636	1.086
AD-39857.1	0.602	1.444	0.992	0.692	0.5960	0.2120	1.023	0.842
AD-39863.1	0.482	0.135	0.906	0.632	0.2449	0.1937	0.308	0.769
AD-39869.1	0.357	0.025	0.799	0.558	0.2347	0.1708	0.191	0.678
AD-39828.1	1.185	1.085	1.176	0.952	0.0707	0.1585	1.135	1.064
AD-39834.1	1.140	1.273	1.315	1.075	0.0938	0.1698	1.207	1.195
AD-39840.1	0.251	0.541	0.766	0.591	0.2050	0.1239	0.396	0.679
AD-39846.1	0.635	0.646	1.044	0.984	0.0077	0.0425	0.641	1.014
AD-39852.1	0.434	0.555	0.707	0.719	0.0857	0.0085	0.494	0.713
AD-39858.1	0.169	0.192	0.363	0.268	0.0160	0.0670	0.180	0.316
AD-39864.1	1.612	1.161	0.825	0.919	0.3189	0.0665	1.387	0.872
AD-39870.1	0.321	0.186	0.072	0.170	0.0952	0.0695	0.253	0.121
AD-39829.1	0.283	0.133	0.353	0.266	0.1060	0.0611	0.208	0.310
AD-39835.1	1.265	0.792	0.460	0.641	0.3343	0.1277	1.029	0.551
AD-39841.1	0.345	0.267	0.416	0.369	0.0552	0.0335	0.306	0.392
AD-39853.1	0.257	0.268	0.640	0.527	0.0081	0.0799	0.262	0.584
AD-39859.1	0.316	0.290	0.773	0.886	0.0182	0.0801	0.303	0.830
AD-39865.1	0.228	0.216	0.456	0.424	0.0084	0.0231	0.222	0.440
AD-39871.1	0.218	0.338	0.502	0.571	0.0849	0.0489	0.278	0.537
AD-39830.1	0.284	0.293	0.770	0.716	0.0063	0.0379	0.289	0.743
AD-39836.1	0.267	0.232	0.615	0.580	0.0249	0.0254	0.250	0.598
AD-39842.1	0.242	0.259	0.707	0.654	0.0121	0.0373	0.250	0.681
AD-39848.1	0.515	0.591	1.071	1.012	0.0536	0.0416	0.553	1.042
AD-39854.1	0.853	1.128	1.035	1.059	0.1943	0.0169	0.991	1.047
AD-39860.1	0.969	1.119	0.965	0.833	0.1058	0.0936	1.044	0.899
AD-39866.1	0.247	0.395	0.733	0.834	0.1045	0.0711	0.321	0.784
AD-39992.1	0.507	0.837	0.985	0.990	0.2334	0.0032	0.672	0.988
AD-39998.1	0.384	0.549	0.745	0.676	0.1167	0.0486	0.466	0.711
AD-40004.1	0.509	0.664	1.090	1.042	0.1096	0.0340	0.587	1.066
AD-40010.1	0.212	0.245	0.954	0.885	0.0232	0.0487	0.228	0.919
AD-40016.1	0.261	0.514	0.731	1.050	0.1790	0.2254	0.387	0.891
AD-40022.1	0.784	1.221	0.955	0.939	0.3089	0.0112	1.003	0.947
AD-40028.1	0.907	1.194	1.062	0.976	0.2026	0.0608	1.050	1.019
AD-40034.1	0.367	0.483	0.902	0.718	0.0819	0.1298	0.425	0.810

AD-39999.1	0.227	0.339	0.910	0.837	0.0789	0.0511	0.283	0.873
AD-40005.1	0.219	0.202	0.419	0.421	0.0121	0.0012	0.211	0.420
AD-40011.1	0.470	0.529	0.731	0.637	0.0413	0.0663	0.499	0.684
AD-40017.1	0.209	0.402	0.873	0.806	0.1364	0.0475	0.306	0.839
AD-40029.1	0.793	0.821	0.904	0.834	0.0199	0.0496	0.807	0.869
AD-39846.1	0.591	0.468	0.690	0.823	0.0867	0.0942	0.529	0.757
AD-40035.1	0.872	1.166	1.079	1.090	0.2083	0.0081	1.019	1.085
AD-39852.1	0.439	0.346	0.784	0.995	0.0659	0.1492	0.393	0.890
AD-39994.1	0.396	0.517	0.936	1.097	0.0854	0.1137	0.457	1.016
AD-40000.1	0.574	0.734	1.100	1.100	0.1133	0.0004	0.654	1.100
AD-40006.1	0.402	0.389	0.831	0.800	0.0094	0.0223	0.395	0.815
AD-40012.1	0.211	0.435	0.704	0.929	0.1588	0.1593	0.323	0.816
AD-40018.1	0.692	1.163	0.808	0.933	0.3325	0.0883	0.928	0.871
AD-40024.1	0.182	0.428	0.772	0.716	0.1739	0.0399	0.305	0.744
AD-40030.1	0.437	0.651	0.825	0.874	0.1516	0.0344	0.544	0.849
AD-40036.1	0.092	0.216	0.452	0.532	0.0876	0.0567	0.154	0.492
AD-39995.1	0.290	0.686	0.918	0.618	0.2803	0.2122	0.488	0.768
AD-40001.1	0.672	0.758	0.709	1.090	0.0607	0.2698	0.715	0.899
AD-40007.1	0.785	0.477	0.780	0.928	0.2177	0.1048	0.631	0.854
AD-40013.1	0.503	0.901	0.782	1.056	0.2814	0.1936	0.702	0.919
AD-40019.1	0.264	0.125	0.615	0.731	0.0979	0.0818	0.194	0.673
AD-40025.1	0.864	1.208	0.968	1.047	0.2430	0.0562	1.036	1.007
AD-40031.1	0.268	0.286	0.995	0.805	0.0124	0.1344	0.277	0.900
AD-40037.1	0.579	0.647	0.689	1.211	0.0484	0.3693	0.613	0.950
AD-39996.1	0.338	0.400	0.618	0.680	0.0438	0.0442	0.369	0.649
AD-40002.1	0.993	0.812	0.746	0.851	0.1281	0.0747	0.903	0.798
AD-40008.1	0.227	0.154	0.309	0.434	0.0516	0.0879	0.190	0.372
AD-40014.1	0.612	0.631	0.702	0.613	0.0136	0.0630	0.622	0.658
AD-40020.1	0.386	0.409	0.962	1.008	0.0164	0.0324	0.398	0.985
AD-40026.1	0.229	0.130	0.370	0.498	0.0702	0.0901	0.180	0.434
AD-40032.1	0.421	0.454	0.979	0.954	0.0232	0.0176	0.437	0.966
AD-40038.1	0.491	0.674	0.851	1.008	0.1291	0.1106	0.582	0.930
AD-39997.1	0.644	0.860	0.749	0.878	0.1531	0.0917	0.752	0.814
AD-39858.1	0.146	0.293	0.681	0.569	0.1043	0.0792	0.219	0.625
AD-40009.1	0.191	0.382	0.912	1.055	0.1351	0.1012	0.287	0.984
AD-40015.1	0.897	0.856	0.778	1.065	0.0292	0.2034	0.876	0.922
AD-40021.1	0.225	0.282	0.850	0.658	0.0401	0.1358	0.254	0.754
AD-40027.1	0.466	1.083	0.916	0.854	0.4358	0.0437	0.774	0.885
AD-40033.1	0.278	0.311	0.426	0.588	0.0230	0.1150	0.295	0.507
AD-40039.1	0.257	0.447	0.666	0.739	0.1348	0.0511	0.352	0.703
AD-40045.1	0.263	0.147	0.526	0.945	0.0821	0.2962	0.205	0.735
AD-40051.1	0.162	0.126	0.665	0.837	0.0255	0.1209	0.144	0.751
AD-40057.1	0.150	0.176	0.641	0.791	0.0178	0.1066	0.163	0.716

AD-40063.1	0.220	0.287	0.650	0.977	0.0468	0.2311	0.253	0.813
AD-40069.1	0.431	0.559	0.729	0.922	0.0907	0.1363	0.495	0.825
AD-40075.1	0.399	0.613	0.834	0.972	0.1511	0.0971	0.506	0.903
AD-40081.1	0.287	0.351	0.499	0.612	0.0453	0.0795	0.319	0.556
AD-40040.1	0.861	0.850	0.888	1.077	0.0077	0.1337	0.856	0.983
AD-40046.1	0.386	0.397	0.607	0.634	0.0083	0.0191	0.392	0.621
AD-39864.1	0.930	0.933	0.810	1.018	0.0022	0.1468	0.931	0.914
AD-40052.1	0.272	0.216	0.526	0.852	0.0396	0.2299	0.244	0.689
AD-40058.1	0.398	0.305	0.928	1.079	0.0655	0.1071	0.351	1.003
AD-40064.1	0.460	0.208	0.909	1.083	0.1777	0.1230	0.334	0.996
AD-40070.1	0.116	0.454	0.447	0.885	0.2390	0.3095	0.285	0.666
AD-40076.1	0.396	1.498	0.634	1.054	0.7792	0.2969	0.947	0.844
AD-40082.1	0.584	0.553	0.760	1.053	0.0218	0.2073	0.569	0.906
AD-40041.1	0.196	0.241	0.862	0.978	0.0322	0.0819	0.218	0.920
AD-40047.1	0.289	0.214	0.699	1.096	0.0535	0.2806	0.251	0.897
AD-40053.1	0.973	1.094	0.717	1.079	0.0854	0.2560	1.033	0.898
AD-40059.1	1.064	0.985	0.720	1.088	0.0562	0.2601	1.025	0.904
AD-40065.1	0.855	0.863	0.589	1.020	0.0057	0.3048	0.859	0.805
AD-40071.1	0.242	0.346	0.846	0.826	0.0739	0.0142	0.294	0.836
AD-40077.1	0.249	0.187	0.649	0.738	0.0437	0.0633	0.218	0.693
AD-40083.1	0.286	0.339	0.807	1.130	0.0373	0.2279	0.312	0.968
AD-40042.1	0.549	0.288	1.205	1.288	0.1845	0.0587	0.418	1.246
AD-40048.1	0.413	0.345	0.713	0.940	0.0483	0.1610	0.379	0.826
AD-40054.1	0.278	0.258	0.685	0.825	0.0146	0.0989	0.268	0.755
AD-40060.1	0.288	0.230	0.781	0.811	0.0410	0.0217	0.259	0.796
AD-40066.1	0.779	0.829	0.950	1.284	0.0357	0.2361	0.804	1.117
AD-40072.1	0.273	0.169	0.579	0.963	0.0738	0.2716	0.221	0.771
AD-40078.1	0.747	0.841	1.177	1.410	0.0666	0.1645	0.794	1.294
AD-40084.1	1.064	0.972	0.944	1.036	0.0647	0.0651	1.018	0.990
AD-40043.1	0.340	0.313	0.804	0.795	0.0190	0.0065	0.327	0.800
AD-40049.1	0.179	0.159	0.339	0.312	0.0141	0.0191	0.169	0.326
AD-40055.1	0.243	0.248	0.811	0.817	0.0034	0.0044	0.245	0.814
AD-40061.1	0.153	0.229	0.357	0.519	0.0537	0.1146	0.191	0.438
AD-40067.1	0.260	0.141	0.715	0.692	0.0837	0.0156	0.201	0.703
AD-40073.1	0.241	0.156	0.833	0.858	0.0597	0.0180	0.199	0.846
AD-40079.1	0.236	0.236	0.694	0.991	0.0002	0.2099	0.236	0.842
AD-40085.1	0.188	0.210	0.558	0.519	0.0155	0.0276	0.199	0.539
AD-40044.1	0.229	0.126	0.342	0.506	0.0728	0.1157	0.178	0.424
AD-40050.1	1.016	0.566	0.933	1.088	0.3183	0.1097	0.791	1.011
AD-40056.1	0.274	0.244	0.801	1.155	0.0215	0.2506	0.259	0.978
AD-40062.1	0.536	0.653	0.900	1.143	0.0822	0.1719	0.595	1.022
AD-40068.1	0.175	0.131	0.218	0.438	0.0313	0.1551	0.153	0.328
AD-40074.1	0.366	0.462	0.911	0.734	0.0674	0.1256	0.414	0.823

AD-40080.1	0.273	0.296	0.844	0.932	0.0166	0.0623	0.284	0.888
AD-40071.1	0.341	0.214	0.691	0.912	0.0902	0.1562	0.277	0.801
AD-40077.1	0.192	0.180	0.483	0.404	0.0083	0.0563	0.186	0.444
AD-40083.1	0.145	0.238	0.514	0.872	0.0657	0.2536	0.192	0.693
AD-40042.1	0.403	0.288	0.626	0.747	0.0814	0.0856	0.346	0.686
AD-35523.3	0.228	0.350	1.165	1.104	0.0862	0.0434	0.289	1.135
AD-35529.1	0.367	0.368	1.099	0.831	0.0004	0.1893	0.368	0.965
AD-35535.4	0.466	0.362	0.563	0.600	0.0735	0.0264	0.414	0.582
AD-35541.4	0.585	0.358	1.003	0.713	0.1606	0.2052	0.472	0.858
AD-35547.4	0.491	0.546	0.732	0.626	0.0393	0.0753	0.518	0.679
AD-35553.4	0.785	0.690	1.043	0.744	0.0677	0.2115	0.738	0.893
AD-35559.4	0.387	0.437	0.779	0.776	0.0357	0.0021	0.412	0.778
AD-35565.4	0.549	0.568	0.930	1.163	0.0132	0.1647	0.559	1.046
AD-35524.4	0.358	0.399	0.997	0.915	0.0289	0.0576	0.379	0.956
AD-35530.4	0.212	0.406	1.129	0.981	0.1374	0.1046	0.309	1.055
AD-35536.4	0.463	0.272	1.028	1.131	0.1352	0.0727	0.368	1.080
AD-35542.4	0.573	0.537	0.804	0.919	0.0255	0.0808	0.555	0.861
AD-35548.4	0.944	0.574	0.886	0.728	0.2619	0.1113	0.759	0.807
AD-35554.4	0.490	0.393	1.021	0.679	0.0682	0.2416	0.442	0.850
AD-35560.2	1.199	0.386	0.796	0.610	0.5748	0.1310	0.793	0.703
AD-35566.4	1.082	0.981	0.747	0.840	0.0714	0.0652	1.031	0.794
AD-35525.2	0.645	0.767	0.956	0.627	0.0864	0.2323	0.706	0.792
AD-35531.4	0.425	0.328	0.755	0.776	0.0683	0.0144	0.376	0.765
AD-35537.4	0.824	0.823	0.710	0.628	0.0004	0.0578	0.824	0.669
AD-35543.2	0.232	0.367	0.980	0.845	0.0954	0.0949	0.300	0.912
AD-35549.4	1.492	0.378	1.057	0.665	0.7877	0.2769	0.935	0.861
AD-35555.4	0.382	0.460	1.133	1.096	0.0554	0.0260	0.421	1.115
AD-35561.4	1.037	0.685	1.036	0.854	0.2488	0.1285	0.861	0.945
AD-35567.4	1.437	0.698	1.098	0.909	0.5222	0.1337	1.068	1.004
AD-35526.4	1.354	0.995	0.597	0.754	0.2540	0.1111	1.174	0.675
AD-35532.4	0.645	0.312	1.117	0.944	0.2357	0.1222	0.479	1.031
AD-35535.4	0.694	0.362	0.856	1.093	0.2353	0.1672	0.528	0.974
AD-35538.4	0.280	0.358	1.121	0.733	0.0551	0.2744	0.319	0.927
AD-35544.4	1.562	0.806	0.895	1.104	0.5351	0.1477	1.184	1.000
AD-35550.4	0.988	0.683	0.745	1.159	0.2155	0.2926	0.836	0.952
AD-35556.4	0.597	0.298	1.087	0.890	0.2119	0.1388	0.448	0.989
AD-35562.4	0.412	0.652	0.796	0.857	0.1700	0.0436	0.532	0.826
AD-35568.4	0.324	0.544	0.986	1.171	0.1556	0.1304	0.434	1.079
AD-35527.4	0.218	0.272	1.079	1.097	0.0380	0.0122	0.245	1.088
AD-35533.4	0.488	0.226	1.236	1.089	0.1848	0.1038	0.357	1.162
AD-35539.4	0.821	0.660	1.065	1.155	0.1140	0.0637	0.740	1.110
AD-35545.4	1.206	0.787	0.990	1.097	0.2968	0.0755	0.997	1.043
AD-35551.4	0.860	0.404	1.011	1.078	0.3220	0.0473	0.632	1.044

AD-35563.4	1.183	0.977	0.908	1.277	0.1461	0.2606	1.080	1.092
AD-35528.4	0.955	0.770	1.094	0.757	0.1309	0.2387	0.863	0.926
AD-35540.4	0.560	0.541	1.061	1.052	0.0132	0.0065	0.550	1.056
AD-35546.4	0.716	0.605	1.121	0.996	0.0789	0.0886	0.660	1.058
AD-35541.4	0.847	0.358	1.046	1.002	0.3458	0.0314	0.603	1.024
AD-35552.4	0.468	0.529	1.057	1.002	0.0431	0.0391	0.499	1.029
AD-35558.4	0.424	0.342	1.241	1.045	0.0578	0.1385	0.383	1.143
AD-35564.4	0.485	0.438	0.980	0.968	0.0329	0.0085	0.461	0.974
AD-35570.4	0.579	0.413	0.839	1.108	0.1175	0.1900	0.496	0.973
AD-35571.4	0.476	0.348	0.818	0.951	0.0907	0.0943	0.412	0.885
AD-35577.4	0.300	0.393	0.844	0.882	0.0660	0.0267	0.347	0.863
AD-35583.4	1.305	0.679	0.970	1.085	0.4424	0.0813	0.992	1.027
AD-35589.4	1.799	1.425	1.223	1.155	0.2646	0.0480	1.612	1.189
AD-35595.4	0.504	0.417	0.976	1.013	0.0619	0.0261	0.461	0.995
AD-35601.4	0.834	0.338	1.076	0.938	0.3513	0.0973	0.586	1.007
AD-35607.4	0.597	0.419	1.000	1.074	0.1256	0.0523	0.508	1.037

Table 6. IC50 data: KRAS fold change values

SD = standard deviation, Avg = average

Duplex	IC50_bio1	IC50_bio2	AvgIC50	SD
AD-39731.1	0.020	0.003	0.012	0.0122
AD-39706.1	0.004	0.000	0.002	0.0028
AD-39720.1	0.012	0.002	0.007	0.0070
AD-39741.1	0.002	0.000	0.001	0.0015
AD-39738.1	0.002	0.001	0.002	0.0008
AD-39870.1	0.159	0.069	0.114	0.0636
AD-39845.1	0.056	0.015	0.036	0.0294
AD-39829.1	0.133	0.027	0.080	0.0750
AD-39778.1	0.135	0.040	0.088	0.0670
AD-39865.1	0.179	0.038	0.109	0.0996
AD-39793.1	0.003	0.078	0.041	0.0526
AD-39785.1	0.004	0.014	0.009	0.0068
AD-40068.1	0.010	0.002	0.006	0.0052
AD-40008.1	0.041	0.011	0.026	0.0217
AD-40026.1	0.014	0.009	0.012	0.0036
AD-40061.1	0.014	0.004	0.009	0.0068
AD-40036.1	0.040	0.013	0.027	0.0196
AD-40057.1	0.030	0.111	0.071	0.0577
AD-35581.4	0.017	0.027	0.022	0.0071
AD-35616.4	0.032	0.044	0.038	0.0091
AD-35588.4	0.036	0.060	0.048	0.0164
AD-35604.4	0.088	0.373	0.231	0.2015

AD-35592.4	0.086	0.266	0.176	0.1270
AD-35685.1	0.036	0.019	0.027	0.0120
AD-38159.1	0.093	0.096	0.095	0.0027
AD-38139.1	0.092	0.354	0.223	0.1849
AD-38172.1	0.130	0.180	0.155	0.0352
AD-38134.1	0.120	0.199	0.159	0.0557
AD-38161.1	0.109	0.173	0.141	0.0448
AD-38131.1	0.134	0.374	0.254	0.1699
AD-38128.1	0.014	0.070	0.042	0.0394
AD-38151.1	0.093	0.315	0.204	0.1571
AD-38127.1	0.064	0.089	0.077	0.0177
AD-38154.1	0.041	0.284	0.163	0.1721
AD-38133.1	0.036	0.203	0.120	0.1182
AD-38170.1	0.140	0.332	0.236	0.1352
AD-38167.1	0.247	0.262	0.255	0.0104
AD-39735.1	0.060	0.034	0.047	0.0186
AD-39858.1	0.040	0.037	0.039	0.0016
AD-39781.1	0.009	0.016	0.013	0.0043
AD-39841.1	0.420	0.242	0.331	0.1255
AD-39805.1	0.057	0.073	0.065	0.0114
AD-39869.1	0.182	0.142	0.162	0.0281
AD-39790.1	0.143	0.059	0.101	0.0595
AD-40044.1	0.019	0.057	0.038	0.0265
AD-40049.1	0.017	0.039	0.028	0.0154
AD-40005.1	0.013	0.066	0.039	0.0372
AD-40077.1	0.049	0.241	0.145	0.1358
AD-40085.1	0.039	0.488	0.264	0.3173
AD-40019.1	0.103	0.340	0.222	0.1677
AD-40083.1	0.108	0.426	0.267	0.2253
AD-35609.4	0.055	0.055	0.055	0.0001
AD-35679.1	0.113	0.209	0.161	0.0673
AD-35600.1	0.046	0.027	0.037	0.0134
AD-35606.1	0.045	0.043	0.044	0.0018
AD-38136.1	0.035	0.043	0.039	0.0061
AD-38163.1	0.019	0.016	0.018	0.0017
AD-38155.1	0.236	0.220	0.228	0.0118
AD-38145.1	0.111	0.230	0.171	0.0842
AD-38138.1	0.260	0.675	0.468	0.2933

Bio1: biological replicates 1 and 2; residual mRNA level relative to control.

TABLE 6.1. Efficacy of particular KRAS siRNAs.

Various KRAS siRNAs were tested for efficacy in RKO cells in vitro. Results are provided in Table 6.1, below. Provided are the residual gene activity at 10 nM (Column 2) and 0.1 nM (Column 3). For example, for AD-39720.1, there was a residual gene activity of 0.2, or 20% (indicating 80% gene knockdown) at 10 nM, and 0.55 or 55% (45% gene knockdown) at 0.1 nM. IC50 of knockdown in nM in MiaPaca 2 cells is also provided.

K-RAS siRNA	10nM RKO	0.1nM RKO	knockdown IC50 MiaPaca 2
AD-35600.1	0.3	0.27	0.0934
AD-35609.4	0.17	0.41	0.037049
AD-38136.1	0.07	0.14	0.0346
AD-38159.1	0.14	0.22	0.01861
AD-38163.1	0.09	0.16	0.0383
AD-39720.1	0.2	0.55	0.005496
AD-39735.1	0.21	0.37	0.0473
AD-39741.1	0.18	0.67	0.0394
AD-39760.1			0.0806
AD-39778.1	0.23	0.43	0.040545
AD-39822.1			1.3242
AD-39845.1	0.2	0.3	0.020622
AD-39870.1	0.25	0.12	0.026542
AD-40008.1	0.19	0.37	0.033536
AD-40021.1			0.1217
AD-40061.1	0.19	0.44	0.009348
AD-40068.1	0.15	0.33	0.009477
AD-40072.1			0.2838

TABLE 6.2. Efficacy of particular KRAS siRNAs.

Table 6.2, below, provides additional data pertaining to activity of particular KRAS siRNAs. The generic target sequence is provided. Proliferation was tested in vitro in MiaPaca2 cells, which are KRAS mutant and are therefore K-RAS dependent. IC50 was studied, using test concentrations from 0 to 10 nM. IC50 data are provided. For example, in the first row, siRNA AD-39822.1 has an IC50 of 1.3242 nM.

Proliferation was tested in both BXPC3 and NCIH28 cells, which are both Wild type for KRAS and are therefore KRAS independent. IC50 was studied, using test concentrations of 0 to 10 nM. In these studies, >10 nM IC50 indicates that the efficacy of KRAS siRNAs was specific to KRAS (little or no substantial off-target effects).

AlnyID	Nicknames	Guide 19mer generic	SEQ ID NO:	Proli-feration BXPC3	Proli-feration NCIH28	IC50 MiaPaca 2
AD-35600.1	NA	TCTCTATAATGGTGAATAT	2742	>10	>10	0.0934
AD-35609.	NA	AAATACACAAAGAAAGCCC	2743	>10	>10	0.037049395

4						
AD-38136.1	NA	TTTATTTCCTACTAGGACC	2744	>10	>10	0.0346
AD-38159.1	hs KRAS 528 A22S26	TTTCCTACTAGGACCATAG	2745	>10	>10	0.01861
AD-38163.1	NA	TTTAATTTGTTCTCTATAA	2746	>10	>10	0.0383
AD-39720.1	NA	AGCTCCAACTACCACAAGT	2747	>10	>10	0.005495521
AD-39735.1	hs KRAS 321 A22S26	TCAATTACTACTTGCTTCC	2748	>10	>10	0.0473
AD-39741.1	hs KRAS 322 A22S26	ATCAATTACTACTTGCTTC	2749	>10	>10	0.0394
AD-39760.1	NA	ATTAGCTGTATCGTCAAGG	2750	>10	>10	0.0806
AD-39778.1	NA	TTCTCCATCAATTACTACT	2751	>10	>10	0.040544532
AD-39822.1	NA	TCGAGAATATCCAAGAGAC	2752	>10	>10	1.3242
AD-39845.1	NA	GATTTAGTATTATTTATGG	2753	>10	>10	0.020622331
AD-39870.1	NA	ATATCTTCAAATGATTTAG	2754	>10	>10	0.026542015
AD-40008.1	NA	TCTAGAAGGCAAATCACAT	2755	>10	>10	0.033536261
AD-40021.1	NA	TGTCTACTGTTCTAGAAGG	2756	>10	>10	0.1217
AD-40061.1	NA	AATTCCATAACTTCTTGCT	2757	>10	>10	0.00934829
AD-40068.1	NA	AATAAAAGGAATTCCATAA	2758	>10	>10	0.009476662
AD-40072.1	NA	ATAACTTCTTGCTAAGTCC	2759	>10	>10	0.2838

[003732] EQUIVALENTS

[003733] A composition of embodiment 1 is a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

[003734] The composition of embodiment 1, wherein the composition further comprises a second RNAi agent to KRAS.

[003735] The composition of embodiment 1, wherein the antisense strand is 30 or fewer nucleotides in length.

[003736] The composition of embodiment 1, wherein the sense strand and the antisense strand form a duplex region 15 to 30 nucleotide pairs in length.

[003737] The composition of embodiment 1, wherein the antisense strand and the sense strand are independently 19 to 23 nucleotides in length.

[003738] The composition of embodiment 1, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[003739] The composition of embodiment 1, wherein the RNAi agent comprises at least one modified backbone and/or at least one 2'-modified nucleotide.

[003740] The composition of embodiment 1, wherein the RNAi agent comprises:

a) at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or

b) at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or

c) at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or

d) at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[003741] The composition of embodiment 1, wherein the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[003742] The composition of embodiment 1, wherein the RNAi agent comprises a blunt end.

[003743] The composition of embodiment 1, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[003744] The composition of embodiment 1, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[003745] The composition of embodiment 1, wherein the RNAi agent is ligated to one or more agent selected from: one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[003746] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 60% at a concentration of 10 nM in RKO cells in vitro.

[003747] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 70% at a concentration of 10 nM in RKO cells in vitro.

[003748] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 80% at a concentration of 10 nM in RKO cells in vitro.

[003749] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 90% at a concentration of 10 nM in RKO cells in vitro.

[003750] The composition of embodiment 1, wherein the RNAi agent has an EC50 of no more than about 0.1 nM.

[003751] The composition of embodiment 1, wherein the RNAi agent has an EC50 of no more than about 0.01 nM.

[003752] The composition of embodiment 1, wherein the RNAi agent has an EC50 of no more than about 0.001 nM.

[003753] A composition of embodiment 2 comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent specific to KRAS provided in Table 1.

[003754] The composition of embodiment 2, wherein the composition comprises a second RNAi agent to KRAS.

[003755] The composition of embodiment 2, wherein the second strand is 30 or fewer nucleotides in length.

[003756] The composition of embodiment 2, wherein the first strand and the second strand form a duplex region 15 to 30 nucleotide pairs in length.

[003757] The composition of embodiment 2, wherein the first strand and the second strand are independently 19 to 23 nucleotides in length.

[003758] The composition of embodiment 2, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[003759] The composition of embodiment 2, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

[003760] The composition of embodiment 2, wherein the RNAi agent comprises:

at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide;

and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

The composition of embodiment 2, wherein the RNAi agent comprises one or more 2'-modifications selected from the group consisting of:

2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[003761] The composition of embodiment 2, wherein the RNAi agent comprises a blunt end.

[003762] The composition of embodiment 2, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[003763] The composition of embodiment 2, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand.

[003764] The composition of embodiment 2, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[003765] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 60% at a concentration of 10 nM in RKO cells in vitro.

[003766] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 70% at a concentration of 10 nM in RKO cells in vitro.

[003767] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 80% at a concentration of 10 nM in RKO cells in vitro.

[003768] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 90% at a concentration of 10 nM in RKO cells in vitro.

[003769] The composition of embodiment 2, wherein the RNAi agent has an EC50 of no more than about 0.1 nM.

[003770] The composition of embodiment 2, wherein the RNAi agent has an EC50 of no more than about 0.01 nM in MiaPaca2 cells.

[003771] The composition of embodiment 2, wherein the RNAi agent has an EC50 of no more than about 0.001 nM in MiaPaca2 cells.

[003772] A method of embodiment 3 is a method comprising a method of treating a KRAS-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

[003773] The method of embodiment 3, wherein the KRAS-related disease is a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome..

[003774] The method of embodiment 3, wherein the KRAS-related disease is a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003775] The method of embodiment 3, wherein the method further comprises the step of administering an additional treatment for a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003776] The method of embodiment 3, wherein the method further comprises the step of administering an additional treatment for a proliferative disease, including without limitation a solid or

liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003777] The method of embodiment 3, wherein the composition comprises a second RNAi agent to KRAS.

[003778] The method of embodiment 3, wherein the method further comprises the step of administering an additional RNAi agent to KRAS.

[003779] The method of embodiment 3, further comprising the administration of an additional treatment.

[003780] The method of embodiment 3, wherein the additional treatment is a composition.

[003781] The method of embodiment 3, wherein the additional treatment is a method.

[003782] The method of embodiment 3, wherein the additional treatment and the RNAi agent can be administered in any order.

[003783] A method of embodiment 4 is a method comprising a method of inhibiting the expression of KRAS in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

[003784] The method of embodiment 4, wherein the individual is afflicted with or susceptible to a KRAS-related disease.

[003785] The method of embodiment 4, wherein the KRAS-related disease is a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003786] The method of embodiment 4, wherein the KRAS-related disease is a proliferative disease.

[003787] The method of embodiment 4, wherein the KRAS-related disease is a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome

[003788] The method of embodiment 4, further comprising the administration of an additional treatment.

[003789] The method of embodiment 4, wherein the additional treatment is a composition.

[003790] The method of embodiment 4, wherein the additional treatment is a method.

[003791] The method of embodiment 4, wherein the additional treatment and the RNAi agent can be administered in any order.

[003792] A composition of embodiment 5 is a composition comprising a medicament for use in an RNAi formulation comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

[003793] Any composition above in a pharmaceutically effective formulation.

[003794] The composition according to embodiment 5, for use in a method of treating a KRAS-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to embodiment 1.

[003795] The use of a composition according to embodiment 5, in the manufacture of a medicament for the treatment of a KRAS-related disease.

[003796] The use of a composition according to embodiment 5, in the manufacture of a medicament for the treatment of a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, or cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003797] The use of embodiment 5, wherein the KRAS-related disease is a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

[003798] The composition of embodiment 1, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

[003799] The composition of embodiment 1, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

[003800] Unless defined otherwise, the technical and scientific terms used herein have the same meaning as that usually understood by a specialist familiar with the field to which the disclosure belongs.

[003801] Unless indicated otherwise, all methods, steps, techniques and manipulations that are not specifically described in detail can be performed and have been performed in a manner known per se, as will be clear to the skilled person. Reference is for example again made to the standard handbooks and the general background art mentioned herein and to the further references cited therein. Unless indicated otherwise, each of the references cited herein is incorporated in its entirety by reference.

[003802] Claims are non-limiting and are provided below.

[003803] Although particular embodiments and claims have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, or the scope of subject matter of claims of any corresponding future application. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the disclosure without departing from the spirit and scope of the disclosure as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary

skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims. Those skilled in the art will recognize or be able to ascertain, using no more than routine experimentation, many equivalents of the specific embodiments of the disclosure described herein. Such equivalents are intended to be encompassed by the following claims. Redrafting of claim scope in later filed corresponding applications may be due to limitations by the patent laws of various countries and should not be interpreted as giving up subject matter of the claims.

Claims

We claim:

1. A composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

2. The composition of claim 1, wherein the composition further comprises a second RNAi agent to KRAS.

3. The composition of claim 1, wherein the RNAi agent comprises at least one modified backbone and/or at least one 2'-modified nucleotide.

4. The composition of claim 1, wherein the RNAi agent is ligated to one or more agent selected from: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

5. A composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent specific to KRAS provided in Table 1.

6. The composition of claim 1, wherein the composition comprises a second RNAi agent to KRAS.

7. The composition of claim 1, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

8. The composition of claim 1, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

9. A method of treating a KRAS-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

10. The method of claim 9, wherein the KRAS-related disease is a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

11. The method of claim 9, wherein the method further comprises the step of administering an additional treatment for a proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

12. The method of claim 11, wherein the method further comprises the step of administering an additional RNAi agent to KRAS.

13. A method of inhibiting the expression of KRAS in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

14. The method of claim 13, wherein the KRAS-related disease isa proliferative disease, cardio-facio-cutaneous (CFC) syndrome or Noonan syndrome.

15. A medicament for use in an RNAi formulation comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to KRAS provided in Table 1.

16. Any composition above in a pharmaceutically effective formulation.

17. The composition according to claim 1, for use in a method of treating a KRAS-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to claim 1.

18. The use of a composition according to claim 1, in the manufacture of a medicament for the treatment of a KRAS-related disease.

19. The composition of claim 1, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

20. The composition of claim 5, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

21. The composition of claim 1, wherein the RNAi agent has an EC50 of no more than about 1 nM in MiaPaca2 cells.

22. The composition of claim 1, wherein the RNAi agent is capable of inhibiting expression of KRAS by at least about 70% at a concentration of 10 nM in RKO cells in vitro.

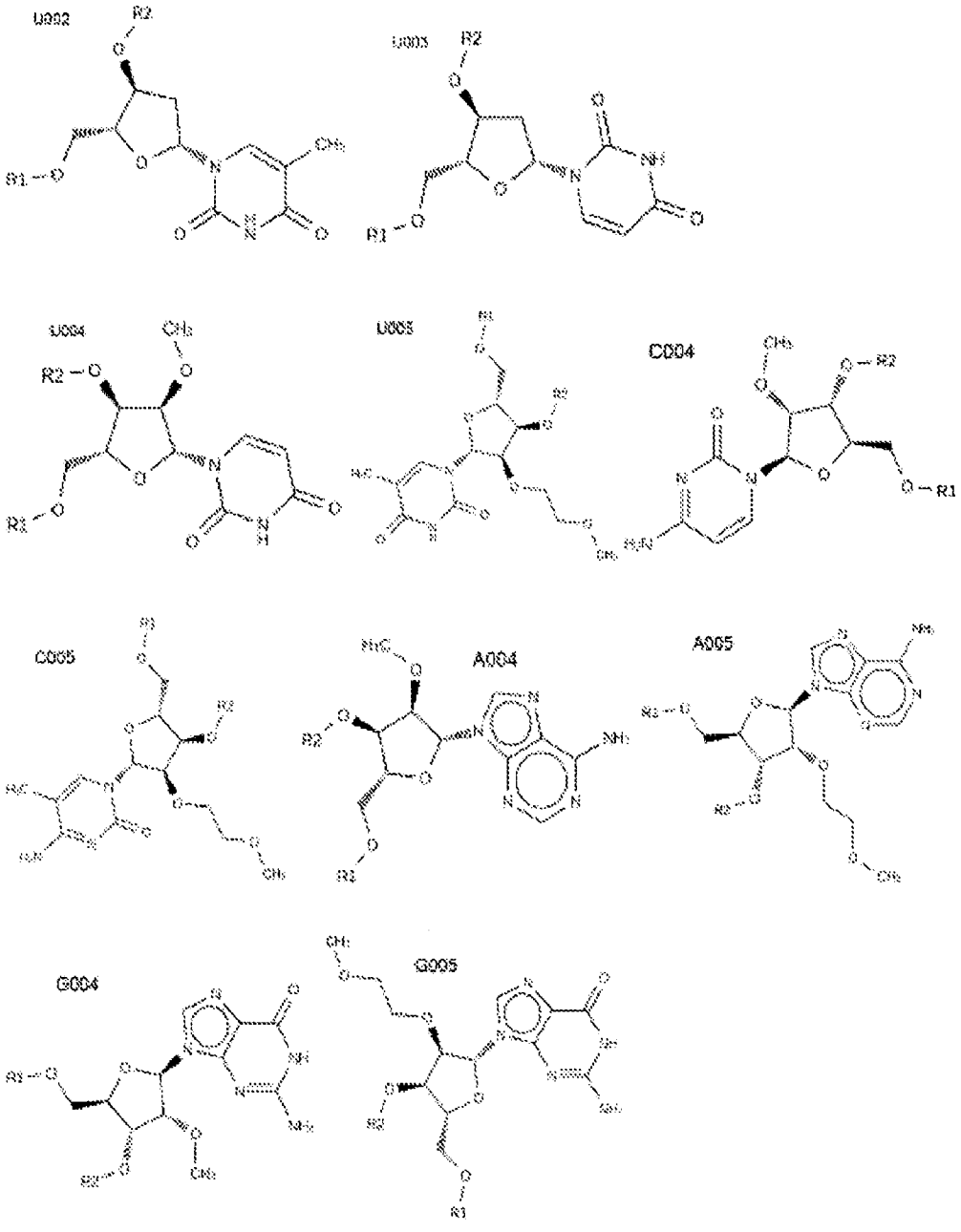


Fig. 1

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[Continued on next page]

(54) Title: ORGANIC COMPOSITIONS TO TREAT KRAS-RELATED DISEASES

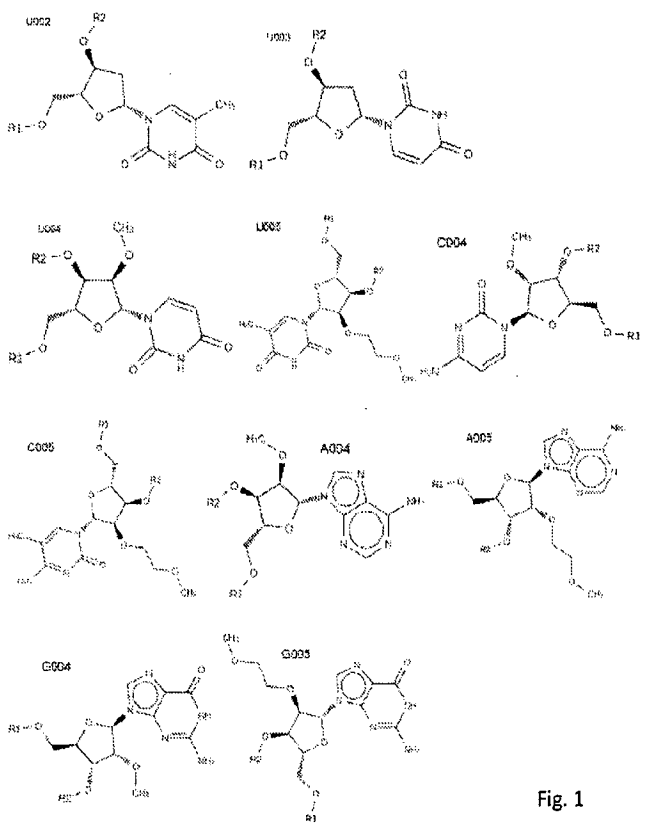


Fig. 1

(57) Abstract: The present disclosure relates to RNAi agents useful in methods of treating KRAS-related diseases such as a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to KRAS.

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/108217 A2 (INTRADIGM CORP [US]; XIE FRANK Y [US]; YANG XIAODONG [US]; LIU YING [U) 3 September 2009 (2009-09-03) the whole document	1-22
X	WO 2010/115206 A2 (DICERNA PHARMACEUTICALS INC [US]; BROWN BOB D [US]) 7 October 2010 (2010-10-07) the whole document	1-22
X	WO 2010/115202 A2 (DICERNA PHARMACEUTICALS INC [US]; BROWN BOB D [US]) 7 October 2010 (2010-10-07) the whole document	1-22

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 July 2013	28/10/2013

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Spindler, Mark-Peter

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/038847

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/109516 A2 (MDRNA INC [US]; QUAY STEVEN C [US]; MCSWIGGEN JAMES [US]; VAISH NAREND) 12 September 2008 (2008-09-12) the whole document	1-22
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1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/038847

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-22(partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-22(partially)

composition comprising an RNAi agent targeting KRAS wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 428 (optionally the sense strand of said RNAi agent comprises at least 15 contiguous differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 1); medical implementations of said RNAi agent

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2-433. claims: 1-22(partially)

as in 1) but wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 429-854, 1789-1791, 2763, 2765 or 2766, respectively (RNAi agents of tables 1, 1a and 1b having the same AD-identifier but different SEQ ID NOs were counted as one invention)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2013/038847

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INTERNATIONAL SEARCH REPORT

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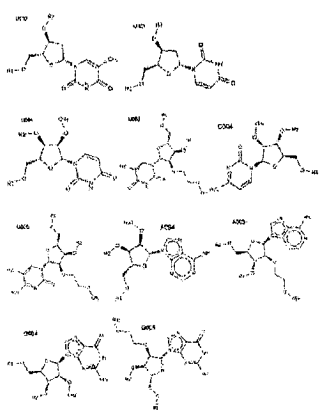
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(54)发明名称

治疗KRAS相关疾病的有机组合物

(57)摘要

本公开涉及RNAi剂，所述RNAi剂可用于使用治疗有效量的针对KRAS的RNAi剂治疗KRAS相关疾病方法中，所述疾病为例如增殖性疾病，包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和/或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、和心面皮肤(CFC)综合征和努南综合征，以及类似和相关的疾病。



CN 104583406 A

1. 一种组合物，其包含含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

2. 根据权利要求 1 所述的组合物，其中组合物还包含针对 KRAS 的第二 RNAi 剂。

3. 根据权利要求 1 所述的组合物，其中 RNAi 剂包含至少一条修饰的主链和 / 或至少一个 2' 修饰的核苷酸。

4. 根据权利要求 1 所述的组合物，其中 RNAi 剂连接至选自以下的一种或多种物质 :诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

5. 一种组合物，其包含含有第一链和第二链的 RNAi 剂，其中第一链和第二链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的第一链和第二链分别差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

6. 根据权利要求 1 所述的组合物，其中组合物包含针对 KRAS 的第二 RNAi 剂。

7. 根据权利要求 1 所述的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2' - 修饰的核苷酸。

8. 根据权利要求 1 所述的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自 :诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

9. 一种治疗个体中 KRAS 相关疾病的方法，该方法包括向所述个体施用治疗有效量的组合物的步骤，所述组合物包含含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

10. 根据权利要求 9 所述的方法，其中的 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征。

11. 根据权利要求 9 所述的方法，其中该方法还包括施用针对增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的额外治疗的步骤。

12. 根据权利要求 11 所述的方法，其中该方法还包括施用针对 KRAS 的另外的 RNAi 剂的步骤。

13. 一种抑制个体中 KRAS 表达的方法，该方法包括向所述个体施用治疗有效量的组合物的步骤，所述组合物包含含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

14. 根据权利要求 13 所述的方法，其中的 KRAS 相关疾病是增殖性疾病、心面皮肤

(CFC) 综合征或努南综合征。

15. 一种用于 RNAi 制剂中的药物，所述 RNAi 制剂包含含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

16. 位于药学有效的制剂中的以上的任何组合物。

17. 用于治疗个体中 KRAS 相关疾病的方法中的权利要求 1 所述的组合物，所述方法包括向所述个体施用治疗有效量的权利要求 1 所述的组合物的步骤。

18. 根据权利要求 1 所述的组合物用于生产治疗 KRAS 相关疾病的药物的用途。

19. 根据权利要求 1 所述的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

20. 根据权利要求 5 所述的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

21. 根据权利要求 1 所述的组合物，其中的 RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 1nM。

22. 根据权利要求 1 所述的组合物，其中的 RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 70%。

治疗 KRAS 相关疾病的有机组合物

[0001] 发明背景

[0002] KRAS 是小分子 GTP 酶的 RAS 亚族中的一员。它参与细胞信号转导、细胞的生长、分化、存活以及其它细胞功能。KRAS 以及 RAS 家族成员 HRAS 和 NRAS 的过度表达或活性过高与包括各种癌症在内的多种疾病有关。在约三分之一的全部人类恶性肿瘤中发现了 RAS 突变 (Bos 等人，1989. Cancer Res. 49:4682-4689)。KRAS 占了大多数人类恶性肿瘤中所发现的 RAS 突变的大部分，包括在肺腺癌中发现的 RAS 突变的 90% (Forbes 等人，2006. Br. J. Cancer 94:318-322)。

[0003] KRAS 的突变、活性过高和 / 或过度表达与癌症有关，包括腺癌、结肠直肠癌 (包括晚期和转移的结肠直肠癌)、结肠癌、肺癌 (包括非小细胞肺癌和肺腺癌)、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、心面皮肤 (CFC) 综合征和努南综合征，以及类似和相关的疾病。

[0004] 需要与 KRAS 相关疾病相关的治疗。

[0005] 发明概述

[0006] 本公开涵盖针对 KRAS 的 RNAi(RNA 干扰) 剂，其可用于治疗 KRAS 相关疾病，例如癌症、心面皮肤 (CFC) 综合征和努南综合征，以及类似和相关的疾病。

[0007] 本公开还涵盖一种治疗患有至少部分由 KRAS 表达介导的病理状态的人类个体的方法，所述方法包括向所述个体施用治疗有效量的针对 KRAS 的 RNAi 剂的步骤。

[0008] 该方法还任选地进一步包括施用第二种活性剂的步骤。在一些实施方案中，所述第二种活性剂是针对 KRAS 的另一种 RNAi 剂。在另一些实施方案中，第二种活性剂是另一种治疗，例如针对另一种也在病理状态中活性过高、突变和 / 或过度表达的靶点的治疗。

[0009] 本公开提供可用于减少个体 (例如哺乳动物，如人) 中 KRAS 水平的特异性 RNAi 剂和方法。本公开特别地提供包含 KRAS 的至少 15 个到至少 19 个或更多个连续核苷酸的双链 RNAi 剂。具体而言，本公开提供包含与例如表 1 至 6 中提供的 RNAi 剂的那些序列差异 0、1、2 或 3 个核苷酸的 15 个或更多个连续核苷酸的序列的活性剂。在一个实施方案中，RNAi 剂特别可以包含每条链小于 30 个核苷酸，例如，17 至 23 个核苷酸，15 至 19 个核苷酸，18 至 22 个核苷酸，和 / 或 19 至 21 个核苷酸，和 / 或如例如在表 1 至 6 中提供的那些，及其修饰变体和未修饰变体 (例如其中的有义链和 / 或反义链或第一链和 / 或第二链是修饰的或未修饰的)。本公开还提供包含有义链和反义链的活性剂，其中所述有义链和 / 或反义链包含与例如表 1 至 6 中提供的 RNAi 剂及其修饰变体和未修饰变体的那些序列差异 0、1、2 或 3 个核苷酸的 19 个或更多个连续核苷酸的序列。有义链和反义链可以是连续的，或共价结合，例如，借助环或接头共价结合。在一个实施方案中，RNAi 剂特别可以包含每条链小于 30 个核苷酸，例如，17 至 23 个核苷酸，18 至 22 个核苷酸和 / 或 19 至 21 个核苷酸，和 / 或如例如在表 1 至 6 中提供的序列。

[0010] 双链 RNAi 剂可以具有 0、1 或 2 个平末端，和 / 或从一个末端或 3' 末端和 / 或 5' 末端具有含 1、2、3 个或 4 个核苷酸 (即，1 至 4 个核苷酸) 的突出端。双链 RNAi 剂也可以

任选地包含一个或两个 3' 帽结构和 / 或一个或多个修饰的核苷酸。本文所提供的序列的修饰变体包括那些除了天然核苷酸被相应的修饰的核苷酸置换外其它均相同的变体。

[0011] 此外，RNAi 剂可以仅包含天然的核苷酸亚单位（例如核糖核苷酸），或包含针对一个或多个替换核苷酸亚单位的糖、磷酸酯或碱基的一个或多个修饰，无论它们是否包含核糖核苷酸亚单位或脱氧核糖核苷酸亚单位或其它相关的修饰变体。在一个实施方案中，公开的 RNAi 剂的修饰变体具有替换尿苷的胸苷（作为 RNA，或优选地，DNA），或具有肌苷碱基。在一些实施方案中，公开的 RNAi 剂的修饰变体可以具有位于过客链中的切口、引导链与过客链之间的错配、替代引导链和过客链的一部分（例如种子区）中的 RNA 的 DNA、和 / 或缩短的过客链（例如 15、16、17 或 18 个核苷酸）。一旦确定了功能性引导链，就可以容易地制备 RNAi 剂的修饰和变体。任何不相互排斥的修饰的组合均是可行的（例如碱基修饰与缩短的过客链的组合；有切口的过客链与碱基修饰的组合；或 DNA 替代部分或全部种子区与剩余 RNA 的碱基修饰的组合等）。

[0012] 在一个实施方案中，公开的 RNAi 剂的修饰变体包括具有与表 1 至 6 中所公开的序列相同的序列（例如，相同碱基序列）、但是具有针对一个或多个核苷酸亚基的糖或磷酸酯中一者或多者的一个或多个修饰的 RNAi 剂。在一个实施方案中，所述修饰改善 RNAi 剂的功效、稳定性（例如，针对血清和 / 或肠液中的核酸酶）和 / 或降低免疫原性。本公开的一个方面涉及包含至少一个非天然核碱基的双链寡核苷酸。在某些实施方案中，非天然核碱基是二氟甲苯基、硝基吲哚基、硝基吡咯基或硝基咪唑基。在一个特定实施方案中，非天然核碱基是二氟甲苯基。在某些实施方案中，两条寡核苷酸链中仅一条链含有非天然核碱基。在某些实施方案中，两条寡核苷酸链均含有非天然核碱基。

[0013] RNAi 剂可以任选地连接至被选择用来改善 RNAi 剂的一种或多种特征，例如，稳定性、分布和 / 或细胞摄入的配体，例如胆固醇或其衍生物。RNAi 剂可以是分离的或是用于本文所述方法的药物组合物的一部分。特别地，药物组合物可以被配制成用于向特定的组织（例如，KRAS- 相关疾病的患病组织）递送或配制成用于胃肠外给药。药物组合物可以任选地包含两种或更多种 RNAi 剂，每一种涉及 KRAS mRNA 的相同或不同区段。任选地，药物组合物还可以包含用于任何 KRAS 相关疾病的任何已知治疗或与其联合使用。

[0014] 本公开还提供了用于降低细胞中 KRAS mRNA 水平的方法，特别是在以 KRAS 过度表达或活性过高为特征的疾病情况下。包含 KRAS 的改变例如突变、过度表达和 / 或活性过高的细胞被称为“KRAS 缺陷型”细胞。所述方法包括向细胞施用一种或多种本公开的 RNAi 剂的步骤，如下文进一步所述。本发明的方法利用参与 RNA 干扰的细胞机制来选择性地降解细胞中的靶 RNA，并且包括使细胞与本公开的一种或多种 RNAi 剂接触的步骤。

[0015] 本公开还提供了用于降低细胞中 KRAS mRNA 水平的方法，特别是在以 KRAS 过度表达、突变或活性过高为特征的疾病情况下。所述方法包括向细胞施用一种或多种本公开的 RNAi 剂的步骤，如下文进一步所述。本发明的方法利用参与 RNA 干扰的细胞机制来选择性地降解细胞中的靶 RNA，并且包括使细胞与本公开的一种或多种 RNAi 剂接触的步骤。

[0016] 本公开还涵盖一种治疗患有至少部分由 KRAS 表达介导的病理状态的人类个体的方法，所述方法包括向所述个体施用治疗有效量的靶向 KRAS 的 RNAi 剂的步骤。额外的方法涉及预防、治疗、调节和 / 或改善其中疾病的进展（例如，肿瘤生长）需要 KRAS（虽然 KRAS 未扩增、过度表达或错误定位）的病理状态。所述方法包括向个体施用一种或多种本公开

的 RNAi 剂的步骤，如下文进一步所述。本发明的方法利用参与 RNA 干扰的细胞机制来选择性地降解细胞中的靶 RNA，并且包括使细胞与本公开的一种或多种 RNAi 剂接触的步骤。所述方法可以对细胞直接进行，或者可以通过向个体施用本公开的一种或多种 RNAi 剂 / 药物组合物而对哺乳动物个体进行。减少细胞中的靶 KRAS RNA 导致所产生的编码的 KRAS 蛋白的量减少。在生物体中，这可以导致恢复涉及 KRAS 的途径中的平衡、和 / 或阻止 KRAS 积累、和 / 或降低 KRAS 活性和 / 或表达、和 / 或阻止 KRAS 介导的其它基因激活、和 / 或改善、治疗和 / 或预防 KRAS 相关疾病。在一个实施方案中，KRAS 表达、水平或活性的降低可以限制肿瘤生长。

[0017] 本公开的方法和组合物，例如，该方法和 KRAS RNAi 剂组合物，可以以本文所述的或本领域已知的任何适宜剂量和 / 或制剂、以本文所述的或本领域已知的任何适宜的施用途径使用。

[0018] 在附图和下文描述中阐述本公开的一个或多个实施方案的详细内容。多种实施方案的不相互排斥的要素（例如，RNAi 剂的序列、修饰、末端帽结构、组合、涉及 KRAS RNAi 剂和另一种活性剂的组合疗法等）可以彼此组合，其如本文所述并且是本领域已知的或被开发的。例如，本文中公开的任何 RNAi 剂序列可以与本文中公开的任何修饰或末端帽结构的集合相组合。修饰、5' 末端帽结构和 / 或 3' 末端帽结构的任何组合可以随本文中公开的任何 RNAi 剂序列一起使用。本文中公开的任何 RNAi 剂（具有修饰或末端帽结构的任何组合或者不具有修饰或末端帽结构）可以与本文中公开的任何其它 RNAi 剂或其它治疗组合物或方法组合。

[0019] 从本说明书、附图和权利要求书中可以明显看出本公开的其它特征、目的和优点。

[0020] 附图简述

[0021] 图 1 显示各种修饰的核苷酸：可以在本文中公开的 RNAi 剂中使用的 U002、U003、U004、U005、C004、C005、A004、A005、G005 和 G004。U002 表示作为 DNA 的 2' - 脱氧胸苷。U003 表示 2' - 脱氧尿苷。U004 表示具有带 2' -O- 甲基修饰的尿苷（“U”）碱基的核苷酸。U005 表示带 2' -O- 甲氧基乙基 (MOE) 修饰的 U 碱基。C004 表示带 2' -O- 甲基修饰的半胱氨酸（“C”）碱基。C005 表示带 2' -O- 甲氧基乙基修饰的 C 碱基。A004 表示带 2' -O- 甲基修饰的腺苷（“A”）碱基。A005 表示带 2' -O- 甲氧基乙基修饰的 A 碱基。G005 表示带 2' O- 甲基修饰的鸟苷（“G”）碱基。G004 表示带 2' O- 甲基修饰的 G 碱基。

[0022] 发明详述

[0023] 本公开涵盖用于靶向和抑制 KRAS 基因的针对 KRAS 的 RNAi 剂，所述 RNAi 剂可用于治疗 KRAS 相关疾病（例如，与 KRAS 中的突变和 / 或 KRAS 表达、水平和 / 或活性改变相关的疾病，和 / 或需要 KRAS 的疾病，和 / 或通过调节 KRAS 的表达、水平和 / 或活性可治疗的疾病），例如增殖性疾病，包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、心面皮肤 (CFC) 综合征和努南综合征，以及类似和相关的疾病。本公开还提供了治疗患有至少部分由 KRAS 表达或过度表达或活性过高介导的病理状态的人类个体的方法，所述方法包括向所述个体施用治疗有效量的针对 KRAS 的 RNAi 剂的步骤。

[0024] 本公开的多种实施方案包括：

[0025] 在一个实施方案中，本公开涉及一种组合物，其包含含有有义链和反义链的 RNAi 剂，其中反义链包含与例如表 1 至 6 中任意一个所提供的针对 KRAS 特异性的 RNAi 剂（或对 KRAS 特异性的重叠性 RNAi 剂的任何集合）的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含含有有义链和反义链的 RNAi 剂，其中有义链包含与来自本文提供的任何序列中的 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含含有第一链和第二链的 RNAi 剂，其中第一链包含与本文提供的任何 RNAi 剂的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，并且第二链包含与本文提供的任何 RNAi 剂的第二链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0026] 特定的双链体包括表 1 中列出的示例性未修饰的序列（“通用序列 (generic)”）和示例性修饰序列。除所描述的示例性修饰之外，其它修饰的变体也在考虑的范围内并且可以使用提供的核苷酸序列来制备这些修饰的变体。在多种实施方案中，第一链和 / 或第二链是修饰的或未修饰的或是一个是修饰的、另一个是未修饰的组合。

[0027] 包含本文所述的反义链和有义链的 RNAi 剂

[0028] 在一个实施方案中，本公开涉及一种组合物，其包含含有反义链的 RNAi 剂，其中反义链包含与选自本文的表（例如表 1 至 6 中的任意一个）中所提供的任何序列（或序列的重叠组）的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在一个实施方案中，本公开涉及一种组合物，其包含含有有义链和反义链的 RNAi 剂，其中反义链包含与选自本文的表（例如表 1 至 6 中的任意一个）中所提供的任何序列（或序列的重叠组）的针对 KRAS 的 RNAi 剂的反义链差异 0 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含含有有义链和反义链的 RNAi 剂，其中反义链的序列包含选自本文提供的任何序列的 RNAi 剂的反义链序列。在另一个实施方案中，本公开涉及一种组合物，其包含含有第一链和第二链的 RNAi 剂，其中第一链的序列是本文提供的任何 RNAi 剂的第一链的序列。特定的双链体包括以上提供的以及在表 1 的一处或多处所列的那些特定的双链体。各个组合物的其它修饰的序列（例如包含一个或多个修饰的碱基的序列）也被看作是本公开的一部分。

[0029] 表 1. 针对 KRAS 的 RNAi 剂的 SEQ ID NOs

[0030] 在表 1 中提供的是各种 KRAS RNAi 双链体的别名；未修饰的（例如“通用的”）有义序列和反义序列的 SEQ ID NOs；示例性修饰的有义序列和反义序列的 SEQ ID NOs。

[0031] 下表 1 提供了针对 KRAS 的各种 RNAi 剂的有义链和反义链的未修饰和示例性修饰的序列的 SEQ ID NOs。在表 2 和表 3 中更详细地提供了 SEQ ID NO 所代表的各序列的碱基组成。表 4 显示了这些 KRAS RNAi 剂的重叠组。表 5 和 6 显示了各种 KRAS RNAi 剂的效力。

[0032] 表 1. 针对 KRAS 的 RNAi 剂的第一链和第二链（例如有义链和反义链）的未修饰和示例性修饰的序列的 SEQ ID NOs

[0033]

	未修饰的序列		示例性修饰的序列	
双链体	有义 SEQ ID NO:	反义 SEQ ID NO:	有义 SEQ ID NO:	反义 SEQ ID NO:
AD-35523.3	1	428	855	1282
AD-35529.1	2	429	856	1283
AD-35535.4	3	430	857	1284
AD-35541.4	4	431	858	1285
AD-35547.4	5	432	859	1286
AD-35553.4	6	433	860	1287
AD-35559.4	7	434	861	1288
AD-35565.4	8	435	862	1289
AD-35524.4	9	436	863	1290
AD-35530.4	10	437	864	1291
AD-35536.4	11	438	865	1292
AD-35542.4	12	439	866	1293
AD-35548.4	13	440	867	1294
AD-35554.4	14	441	868	1295
AD-35560.2	15	442	869	1296
AD-35566.4	16	443	870	1297
AD-35525.2	17	444	871	1298
AD-35531.4	18	445	872	1299
AD-35537.4	19	446	873	1300
AD-35543.2	20	447	874	1301
AD-35549.4	21	448	875	1302
AD-35555.4	22	449	876	1303
AD-35561.4	23	450	877	1304
AD-35567.4	24	451	878	1305
AD-35526.4	25	452	879	1306
AD-35532.4	26	453	880	1307
AD-35538.4	27	454	881	1308
AD-35544.4	28	455	882	1309
AD-35550.4	29	456	883	1310
AD-35556.4	30	457	884	1311
AD-35562.4	31	458	885	1312
AD-35568.4	32	459	886	1313
AD-35527.4	33	460	887	1314
AD-35533.4	34	461	888	1315
AD-35539.4	35	462	889	1316
AD-35545.4	36	463	890	1317
AD-35551.4	37	464	891	1318
AD-35563.4	38	465	892	1319

[0034]

AD-35528.4	39	466	893	1320
AD-35540.4	40	467	894	1321
AD-35546.4	41	468	895	1322
AD-35552.4	42	469	896	1323
AD-35558.4	43	470	897	1324
AD-35564.4	44	471	898	1325
AD-35570.4	45	472	899	1326
AD-35571.4	46	473	900	1327
AD-35577.4	47	474	901	1328
AD-35583.4	48	475	902	1329
AD-35589.4	49	476	903	1330
AD-35595.4	50	477	904	1331
AD-35601.4	51	478	905	1332
AD-35607.4	52	479	906	1333
AD-35613.4	53	480	907	1334
AD-35572.4	54	481	908	1335
AD-35578.4	55	482	909	1336
AD-35584.4	56	483	910	1337
AD-35590.4	57	484	911	1338
AD-35596.4	58	485	912	1339
AD-35602.4	59	486	913	1340
AD-35608.4	60	487	914	1341
AD-35614.4	61	488	915	1342
AD-35573.4	62	489	916	1343
AD-35579.4	63	490	917	1344
AD-35585.4	64	491	918	1345
AD-35591.4	65	492	919	1346
AD-35597.4	66	493	920	1347
AD-35603.4	67	494	921	1348
AD-35609.4	68	495	922	1349
AD-35615.4	69	496	923	1350
AD-35574.4	70	497	924	1351
AD-35580.1	71	498	925	1352
AD-35586.4	72	499	926	1353
AD-35592.4	73	500	927	1354
AD-35598.4	74	501	928	1355
AD-35604.4	75	502	929	1356
AD-35610.4	76	503	930	1357
AD-35616.4	77	504	931	1358
AD-35575.4	78	505	932	1359
AD-35581.4	79	506	933	1360
AD-35587.4	80	507	934	1361

[0035]

AD-35593.4	81	508	935	1362
AD-35599.4	82	509	936	1363
AD-35605.4	83	510	937	1364
AD-35611.4	84	511	938	1365
AD-35617.4	85	512	939	1366
AD-35576.4	86	513	940	1367
AD-35588.4	87	514	941	1368
AD-35667.1	88	515	942	1369
AD-35673.1	89	516	943	1370
AD-35679.1	90	517	944	1371
AD-35685.1	91	518	945	1372
AD-35691.1	92	519	946	1373
AD-35557.1	93	520	947	1374
AD-35618.1	94	521	948	1375
AD-35569.1	95	522	949	1376
AD-35534.1	96	523	950	1377
AD-35582.1	97	524	951	1378
AD-35594.1	98	525	952	1379
AD-35600.1	99	526	953	1380
AD-35606.1	100	527	954	1381
AD-35612.1	101	528	955	1382
AD-38127.1	102	529	956	1383
AD-38133.1	103	530	957	1384
AD-38139.1	104	531	958	1385
AD-38145.1	105	532	959	1386
AD-38151.1	106	533	960	1387
AD-38157.1	107	534	961	1388
AD-38163.1	108	535	962	1389
AD-38169.1	109	536	963	1390
AD-38128.1	110	537	964	1391
AD-38134.1	111	538	965	1392
AD-38140.1	112	539	966	1393
AD-38146.1	113	540	967	1394
AD-38152.1	114	541	968	1395
AD-38158.1	115	542	969	1396
AD-38164.1	116	543	970	1397
AD-38170.1	117	544	971	1398
AD-38129.1	118	545	972	1399
AD-38135.1	119	546	973	1400
AD-38141.1	120	547	974	1401
AD-38147.1	121	548	975	1402
AD-38153.1	122	549	976	1403

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AD-38159.1	123	550	977	1404
AD-38165.1	124	551	978	1405
AD-38171.1	125	552	979	1406
AD-38130.1	126	553	980	1407
AD-38136.1	127	554	981	1408
AD-38142.1	128	555	982	1409
AD-38148.1	129	556	983	1410
AD-38154.1	130	557	984	1411
AD-38160.1	131	558	985	1412
AD-38166.1	132	559	986	1413
AD-38172.1	133	560	987	1414
AD-38131.1	134	561	988	1415
AD-38137.1	135	562	989	1416
AD-38143.1	136	563	990	1417
AD-38149.1	137	564	991	1418
AD-38155.1	138	565	992	1419
AD-38161.1	139	566	993	1420
AD-38167.1	140	567	994	1421
AD-38173.1	141	568	995	1422
AD-38132.1	142	569	996	1423
AD-38138.1	143	570	997	1424
AD-38144.1	144	571	998	1425
AD-38150.1	145	572	999	1426
AD-38156.1	146	573	1000	1427
AD-38162.1	147	574	1001	1428
AD-38168.1	148	575	1002	1429
AD-38174.1	149	576	1003	1430
AD-39683.1	150	577	1004	1431
AD-39689.1	151	578	1005	1432
AD-39695.1	152	579	1006	1433
AD-39701.1	153	580	1007	1434
AD-39707.1	154	581	1008	1435
AD-39713.1	155	582	1009	1436
AD-39719.1	156	583	1010	1437
AD-39725.1	157	584	1011	1438
AD-39684.1	158	585	1012	1439
AD-39690.1	159	586	1013	1440
AD-39696.1	160	587	1014	1441
AD-39702.1	161	588	1015	1442
AD-39708.1	162	589	1016	1443
AD-39714.1	163	590	1017	1444
AD-39720.1	164	591	1018	1445

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AD-39726.1	165	592	1019	1446
AD-39685.1	166	593	1020	1447
AD-39691.1	167	594	1021	1448
AD-39697.1	168	595	1022	1449
AD-39703.1	169	596	1023	1450
AD-39709.1	170	597	1024	1451
AD-39715.1	171	598	1025	1452
AD-39721.1	172	599	1026	1453
AD-39727.1	173	600	1027	1454
AD-39686.1	174	601	1028	1455
AD-39692.1	175	602	1029	1456
AD-39698.1	176	603	1030	1457
AD-39704.1	177	604	1031	1458
AD-39710.1	178	605	1032	1459
AD-39716.1	179	606	1033	1460
AD-39722.1	180	607	1034	1461
AD-39728.1	181	608	1035	1462
AD-39687.1	182	609	1036	1463
AD-39693.1	183	610	1037	1464
AD-39699.1	184	611	1038	1465
AD-39705.1	185	612	1039	1466
AD-39711.1	186	613	1040	1467
AD-39717.1	187	614	1041	1468
AD-39723.1	188	615	1042	1469
AD-39729.1	189	616	1043	1470
AD-39688.1	190	617	1044	1471
AD-39694.1	191	618	1045	1472
AD-39700.1	192	619	1046	1473
AD-39706.1	193	620	1047	1474
AD-39712.1	194	621	1048	1475
AD-39718.1	195	622	1049	1476
AD-39724.1	196	623	1050	1477
AD-39730.1	197	624	1051	1478
AD-39736.1	198	625	1052	1479
AD-39742.1	199	626	1053	1480
AD-39748.1	200	627	1054	1481
AD-39754.1	201	628	1055	1482
AD-39760.1	202	629	1056	1483
AD-39766.1	203	630	1057	1484
AD-39772.1	204	631	1058	1485
AD-39731.1	205	632	1059	1486
AD-39737.1	206	633	1060	1487

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AD-39743.1	207	634	1061	1488
AD-39749.1	208	635	1062	1489
AD-39755.1	209	636	1063	1490
AD-39761.1	210	637	1064	1491
AD-39767.1	211	638	1065	1492
AD-39773.1	212	639	1066	1493
AD-39732.1	213	640	1067	1494
AD-39738.1	214	641	1068	1495
AD-39744.1	215	642	1069	1496
AD-39750.1	216	643	1070	1497
AD-39756.1	217	644	1071	1498
AD-39762.1	218	645	1072	1499
AD-39768.1	219	646	1073	1500
AD-39774.1	220	647	1074	1501
AD-39733.1	221	648	1075	1502
AD-39739.1	222	649	1076	1503
AD-39745.1	223	650	1077	1504
AD-39751.1	224	651	1078	1505
AD-39757.1	225	652	1079	1506
AD-39763.1	226	653	1080	1507
AD-39769.1	227	654	1081	1508
AD-39775.1	228	655	1082	1509
AD-39734.1	229	656	1083	1510
AD-39740.1	230	657	1084	1511
AD-39746.1	231	658	1085	1512
AD-39752.1	232	659	1086	1513
AD-39758.1	233	660	1087	1514
AD-39764.1	234	661	1088	1515
AD-39770.1	235	662	1089	1516
AD-39776.1	236	663	1090	1517
AD-39735.1	237	664	1091	1518
AD-39741.1	238	665	1092	1519
AD-39747.1	239	666	1093	1520
AD-39753.1	240	667	1094	1521
AD-39759.1	241	668	1095	1522
AD-39765.1	242	669	1096	1523
AD-39771.1	243	670	1097	1524
AD-39778.1	244	671	1098	1525
AD-39784.1	245	672	1099	1526
AD-39790.1	246	673	1100	1527
AD-39796.1	247	674	1101	1528
AD-39802.1	248	675	1102	1529

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AD-39808.1	249	676	1103	1530
AD-39814.1	250	677	1104	1531
AD-39820.1	251	678	1105	1532
AD-39779.1	252	679	1106	1533
AD-39785.1	253	680	1107	1534
AD-39791.1	254	681	1108	1535
AD-39797.1	255	682	1109	1536
AD-39803.1	256	683	1110	1537
AD-39809.1	257	684	1111	1538
AD-39815.1	258	685	1112	1539
AD-39821.1	259	686	1113	1540
AD-39780.1	260	687	1114	1541
AD-39786.1	261	688	1115	1542
AD-39792.1	262	689	1116	1543
AD-39798.1	263	690	1117	1544
AD-39804.1	264	691	1118	1545
AD-39810.1	265	692	1119	1546
AD-39816.1	266	693	1120	1547
AD-39822.1	267	694	1121	1548
AD-39781.1	268	695	1122	1549
AD-39787.1	269	696	1123	1550
AD-39793.1	270	697	1124	1551
AD-39799.1	271	698	1125	1552
AD-39805.1	272	699	1126	1553
AD-39811.1	273	700	1127	1554
AD-39817.1	274	701	1128	1555
AD-39823.1	275	702	1129	1556
AD-39782.1	276	703	1130	1557
AD-39788.1	277	704	1131	1558
AD-39794.1	278	705	1132	1559
AD-39800.1	279	706	1133	1560
AD-39806.1	280	707	1134	1561
AD-39812.1	281	708	1135	1562
AD-39818.1	282	709	1136	1563
AD-39824.1	283	710	1137	1564
AD-39783.1	284	711	1138	1565
AD-39789.1	285	712	1139	1566
AD-39795.1	286	713	1140	1567
AD-39801.1	287	714	1141	1568
AD-39807.1	288	715	1142	1569
AD-39813.1	289	716	1143	1570
AD-39819.1	290	717	1144	1571

[0040]

AD-39825.1	291	718	1145	1572
AD-39831.1	292	719	1146	1573
AD-39837.1	293	720	1147	1574
AD-39843.1	294	721	1148	1575
AD-39849.1	295	722	1149	1576
AD-39855.1	296	723	1150	1577
AD-39861.1	297	724	1151	1578
AD-39867.1	298	725	1152	1579
AD-39826.1	299	726	1153	1580
AD-39832.1	300	727	1154	1581
AD-39838.1	301	728	1155	1582
AD-39844.1	302	729	1156	1583
AD-39850.1	303	730	1157	1584
AD-39856.1	304	731	1158	1585
AD-39862.1	305	732	1159	1586
AD-39868.1	306	733	1160	1587
AD-39827.1	307	734	1161	1588
AD-39833.1	308	735	1162	1589
AD-39839.1	309	736	1163	1590
AD-39845.1	310	737	1164	1591
AD-39851.1	311	738	1165	1592
AD-39857.1	312	739	1166	1593
AD-39863.1	313	740	1167	1594
AD-39869.1	314	741	1168	1595
AD-39828.1	315	742	1169	1596
AD-39834.1	316	743	1170	1597
AD-39840.1	317	744	1171	1598
AD-39846.1	318	745	1172	1599
AD-39852.1	319	746	1173	1600
AD-39858.1	320	747	1174	1601
AD-39864.1	321	748	1175	1602
AD-39870.1	322	749	1176	1603
AD-39829.1	323	750	1177	1604
AD-39835.1	324	751	1178	1605
AD-39841.1	325	752	1179	1606
AD-39853.1	326	753	1180	1607
AD-39859.1	327	754	1181	1608
AD-39865.1	328	755	1182	1609
AD-39871.1	329	756	1183	1610
AD-39830.1	330	757	1184	1611
AD-39836.1	331	758	1185	1612
AD-39842.1	332	759	1186	1613

[0041]

AD-39848.1	333	760	1187	1614
AD-39854.1	334	761	1188	1615
AD-39860.1	335	762	1189	1616
AD-39866.1	336	763	1190	1617
AD-39992.1	337	764	1191	1618
AD-39998.1	338	765	1192	1619
AD-40004.1	339	766	1193	1620
AD-40010.1	340	767	1194	1621
AD-40016.1	341	768	1195	1622
AD-40022.1	342	769	1196	1623
AD-40028.1	343	770	1197	1624
AD-40034.1	344	771	1198	1625
AD-39999.1	345	772	1199	1626
AD-40005.1	346	773	1200	1627
AD-40011.1	347	774	1201	1628
AD-40017.1	348	775	1202	1629
AD-40029.1	349	776	1203	1630
AD-40035.1	350	777	1204	1631
AD-39994.1	351	778	1205	1632
AD-40000.1	352	779	1206	1633
AD-40006.1	353	780	1207	1634
AD-40012.1	354	781	1208	1635
AD-40018.1	355	782	1209	1636
AD-40024.1	356	783	1210	1637
AD-40030.1	357	784	1211	1638
AD-40036.1	358	785	1212	1639
AD-39995.1	359	786	1213	1640
AD-40001.1	360	787	1214	1641
AD-40007.1	361	788	1215	1642
AD-40013.1	362	789	1216	1643
AD-40019.1	363	790	1217	1644
AD-40025.1	364	791	1218	1645
AD-40031.1	365	792	1219	1646
AD-40037.1	366	793	1220	1647
AD-39996.1	367	794	1221	1648
AD-40002.1	368	795	1222	1649
AD-40008.1	369	796	1223	1650
AD-40014.1	370	797	1224	1651
AD-40020.1	371	798	1225	1652
AD-40026.1	372	799	1226	1653
AD-40032.1	373	800	1227	1654
AD-40038.1	374	801	1228	1655

[0042]

AD-39997.1	375	802	1229	1656
AD-40009.1	376	803	1230	1657
AD-40015.1	377	804	1231	1658
AD-40021.1	378	805	1232	1659
AD-40027.1	379	806	1233	1660
AD-40033.1	380	807	1234	1661
AD-40039.1	381	808	1235	1662
AD-40045.1	382	809	1236	1663
AD-40051.1	383	810	1237	1664
AD-40057.1	384	811	1238	1665
AD-40063.1	385	812	1239	1666
AD-40069.1	386	813	1240	1667
AD-40075.1	387	814	1241	1668
AD-40081.1	388	815	1242	1669
AD-40040.1	389	816	1243	1670
AD-40046.1	390	817	1244	1671
AD-40052.1	391	818	1245	1672
AD-40058.1	392	819	1246	1673
AD-40064.1	393	820	1247	1674
AD-40070.1	394	821	1248	1675
AD-40076.1	395	822	1249	1676
AD-40082.1	396	823	1250	1677
AD-40041.1	397	824	1251	1678
AD-40047.1	398	825	1252	1679
AD-40053.1	399	826	1253	1680
AD-40059.1	400	827	1254	1681
AD-40065.1	401	828	1255	1682
AD-40071.1	402	829	1256	1683
AD-40077.1	403	830	1257	1684
AD-40083.1	404	831	1258	1685
AD-40042.1	405	832	1259	1686
AD-40048.1	406	833	1260	1687
AD-40054.1	407	834	1261	1688
AD-40060.1	408	835	1262	1689
AD-40066.1	409	836	1263	1690
AD-40072.1	410	837	1264	1691
AD-40078.1	411	838	1265	1692
AD-40084.1	412	839	1266	1693
AD-40043.1	413	840	1267	1694
AD-40049.1	414	841	1268	1695
AD-40055.1	415	842	1269	1696
AD-40061.1	416	843	1270	1697

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AD-40067.1	417	844	1271	1698
AD-40073.1	418	845	1272	1699
AD-40079.1	419	846	1273	1700
AD-40085.1	420	847	1274	1701
AD-40044.1	421	848	1275	1702
AD-40050.1	422	849	1276	1703
AD-40056.1	423	850	1277	1704
AD-40062.1	424	851	1278	1705
AD-40068.1	425	852	1279	1706
AD-40074.1	426	853	1280	1707
AD-40080.1	427	854	1281	1708
AD-39720.1	1716	1754	1792	1830
AD-39706.1	1717	1755	1793	1831
AD-39712.1	1718	1756	1794	1832
AD-39760.1	1719	1757	1795	1833
AD-39732.1	1720	1758	1796	1834
AD-35541.4	1721	1759	1797	1835
AD-39735.1 或 hs_KRAS_321_A22S26	1722	1760	1798	1836
AD-39741.1 或 hs_KRAS_322_A22S26	1723	1761	1799	1837
AD-39778.1	1724	1762	1800	1838
AD-39790.1	1725	1763	1801	1839
AD-39822.1	1726	1764	1802	1840
AD-35609.4	1727	1765	1803	1841
AD-35581.4	1728	1766	1804	1842
AD-39845.1	1729	1767	1805	1843
AD-39858.1	1730	1768	1806	1844
AD-39870.1	1731	1769	1807	1845
AD-35576.4	1732	1770	1808	1846
AD-35588.4	1733	1771	1809	1847
AD-35600.1	1734	1772	1810	1848
AD-35606.1	1735	1773	1811	1849
AD-38151.1	1736	1774	1812	1850
AD-38163.1	1737	1775	1813	1851
AD-39999.1	1738	1776	1814	1852
AD-38159.1 或 hs_KRAS_528_A22S26	1739	1777	1815	1853
AD-38130.1 或 hs_KRAS_531_A22S26	1740	1778	1816	1854
AD-38136.1	1741	1779	1817	1855
AD-40036.1	1742	1780	1818	1856

[0044]

AD-40008.1	1743	1781	1819	1857
AD-40021.1	1744	1782	1820	1858
AD-40077.1	1745	1783	1821	1859
AD-40072.1	1746	1784	1822	1860
AD-40061.1	1747	1785	1823	1861
AD-40068.1	1748	1786	1824	1862
AD-38131.1	1749	1787	1825	1863
AD-38167.1	1750	1788	1826	1864
KRAS1273 31273_A22S26	1751	1789	1827	1865
KRAS2892 2892_A37S26	1752	1790	1828	1866
KRAS4731 4731_A22S26	1753	1791	1829	1867
AD-39741.1	2770	2760		
AD-39735.1	2771	2761		
AD-38159.1	2772	2762		
NA	2773	2763		
AD-38130.1	2774	2764		
NA	2775	2765		
NA	2776	2766		
AD-38136.1	2777	2767		
AD-40061.1	2778	2768		
AD-35588.4	2779	2769		
AD-39845.1	2790	2780		
AD-39720.1	2791	2781		
AD-35581.4	2792	2782		
AD-40068.1	2793	2783		
AD-39778.1	2794	2784		
AD-35606.1	2795	2785		
AD-35609.4	2796	2786		
AD-38163.1	2797	2787		
AD-35600.1	2798	2788		
AD-40008.1	2799	2789		
AD-40036.1	2810	2800		
AD-39790.1	2811	2801		
AD-39870.1	2812	2802		
AD-38131.1	2813	2803		
AD-40077.1	2814	2804		
AD-38167.1	2815	2805		
AD-38151.1	2816	2806		
AD-39858.1	2817	2807		

[0045]

AD-39706.1	2818	2808		
AD-40021.1	2819	2809		
AD-39760.1	2828	2820		
AD-39822.1	2829	2821		
AD-39999.1	2830	2822		
AD-40072.1	2831	2823		
AD-39732.1	2832	2824		
AD-35576.4	2833	2825		
AD-39712.1	2834	2826		
AD-35541.4	2835	2827		

[0046] 表 1 给出了各 KRAS RNAi 剂的示例性未修饰的第一链和第二链的 SEQ ID 标识符；该表还提供了各 KRAS RNAi 剂的示例性修饰的序列。例如，在表 1 中，别名为 AD-35523.3 的示例性 KRAS RNAi 剂的未修饰的序列是 SEQ ID NOs:1 和 428。该双链体的一组示例性修饰序列由 SEQ ID NOs:855 和 1282 表示。还需要注意的是，别名的“AD”前缀有时会用“ND”代替。RNAi 的名称有时还有后缀，例如 .1。其表示双链体的一种特定变体。因此，AD-35523.1、AD-35523.2、AD-35523.3、ND-35523 等均表示相同序列的 KRAS RNAi 剂，尽管它们可能在如何被修饰上有所不同。在这些情况下，将 U 用 T 替换被认为是不会引起错配的修饰；因此，其中有一个或多个 U 碱基被 T 替换但其它部分相同的两个序列仍被认为是等同并且相同的。某些 RNAi 剂的别名还包含后缀“b1”，表示“批次 1”。因此，包含别名 AD-35523 的各种 KRAS RNAi 剂均具有相同的碱基序列（尽管不一定具有相同的修饰），而后缀“b1”（或“b2”等）表示特定的批次，尽管它们可能具有相同的序列。

[0047] 表 1 中的某些 RNAi 剂具有可替换的名称或别名。某些别名是从它们在 KRAS 基因中的位置得来的，并且通常是修饰形式的代码。然而，需要注意的是，对于 KRAS 基因序列的计数，有多种不同的方法。本文所用的对 KRAS 基因的计数仅用于举例说明。以下列出了一些双链体的可替换名称：

[0048] 表 1.1. 一些 RNAi 剂的可替换名称

[0049]

双链体名称	别名
AD-39741.1	hs_KRAS_322_A22S26
AD-38159.1	hs_KRAS_528_A22S26
AD-39735.1	hs_KRAS_321_A22S26
AD-38130.1	hs_KRAS_531_A22S26

[0050] NA，不适用。

[0051] 在表 1、2 和 3 中提供了另外的可替换名称。例如，hs_KRAS1273_A22S26、hs_KRAS2892_A37S26 和 hs_KRAS 4731_A22S26 有时分别被可替换地定名为 KRAS1273、KRAS2892 和 KRAS4731。

[0052] 表 1.2. 一些 RNAi 剂的另外的可替换名称

[0053] 本文所公开的其它 siRNAs 也具有可替换名称。这些名称以 AD 开头。以下提供通用的（未修饰的）序列的可替换的名称、别名和序列。提供了对应于引导链和有义链的靶序列 (DNA)。siRNAs 包括，例如对应于所提供的 DNA 序列的双链 RNA（例如，含或不含如下的任何一种或如下的任何一种的组合的 RNA：修饰、末端 TT 或其它突出端、末端帽结构、可替换碱基 (LNA、PNA 等)，和 / 或少量穿插在 RNA 中的 DNA 碱基或其它碱基等）。

[0054]

AD 别名	别名 siRNA	引导链 19 聚物 通用	SEQ ID NO.	有义链 19 聚物 通用	SEQ ID NO.
AD-39741.1	hs KRAS 322 A22S26	ATCAATTACTACTTGCTTC	2760	GAAGCAAGTAGTAATTGAT	2770
AD-39735.1	hs KRAS 321 A22S26	TCAATTACTACTTGCTTCC	2761	GGAAGCAAGTAGTAATTGA	2771

[0055]

AD-38159.1	hs KRAS 528 A22S26	TTTCCTACTAGGACCATAG	2762	CTATGGTCCTAGTAGGAAA	2772
NA	hs KRAS 1273 A22S26	TAACTTTACATTCATCAGG	2763	CCTGATGAATGTAAAGTTA	2773
AD-38130.1	hs KRAS 531 A22S26	TTATTTCCTACTAGGACCA	2764	TGGTCCTAGTAGGAAATAA	2774
NA	hs KRAS 4731 A22S26	AATCTAGTTATGACTATTC	2765	GAATAGTCATAACTAGATT	2775
NA	hs KRAS 2892 A37S26	TATCTTTATTAAATTCTCC	2766	GGAGAATTTAATAAAGATA	2776
AD-38136.1	NA	TTTATTTCCTACTAGGACC	2767	GGTCCTAGTAGGAAATAAA	2777
AD-40061.1	NA	AATTCCATAACTTCTTGCT	2768	AGCAAGAAGTTATGGAATT	2778
AD-35588.4	NA	TCTATAATGGTGAATATCT	2769	AGATATTCACCATTATAGA	2779
AD-39845.1	NA	GATTTAGTATTATTTATGG	2780	CCATAAATAATACTAAATC	2790
AD-39720.1	NA	AGCTCCAACTACCACAAGT	2781	ACTTGTGGTAGTTGGAGCT	2791
AD-35581.4	NA	TTATTTATGGCAAATACAC	2782	GTGTATTTGCCATAAATAA	2792
AD-40068.1	NA	AATAAAAGGAATTCCATAA	2783	TTATGGAATTCCTTTTATT	2793
AD-39778.1	NA	TTCTCCATCAATTACTACT	2784	AGTAGTAATTGATGGAGAA	2794
AD-35606.1	NA	TTCTCTATAATGGTGAATA	2785	TATTCACCATTATAGAGAA	2795
AD-35609.4	NA	AAATACACAAAGAAAGCCC	2786	GGGCTTTCTTTGTGTATTT	2796

[0056]

AD-38163.1	NA	TTTAATTTGTTCTCTATAA	2787	TTATAGAGAACAAATTAAA	2797
AD-35600.1	NA	TCTCTATAATGGTGAATAT	2788	ATATTCACCATTATAGAGA	2798
AD-40008.1	NA	TCTAGAAGGCAAATCACAT	2789	ATGTGATTTGCCTTCTAGA	2799
AD-40036.1	NA	AATCACATTTATTTCCTAC	2800	GTAGGAAATAAATGTGATT	2810
AD-39790.1	NA	GTTTCTCCATCAATTACTA	2801	TAGTAATTGATGGAGAAAC	2811
AD-39870.1	hs KRAS 459 A37S26	ATATCTTCAAATGATTTAG	2802	CTAAATCATTTGAAGATAT	2812
AD-38131.1	NA	TTTCAATAAAAGGAATTCC	2803	GGAATTCCTTTTATTGAAA	2813
AD-40077.1	NA	CTTGCTAAGTCCTGAGCCT	2804	AGGCTCAGGACTTAGCAAG	2814
AD-38167.1	NA	CTGATGTTTCAATAAAAGG	2805	CCTTTTATTGAAACATCAG	2815
AD-38151.1	NA	TAATTTGTTCTCTATAATG	2806	CATTATAGAGAACAAATTA	2816
AD-39858.1	NA	ATCTTCAAATGATTTAGTA	2807	TACTAAATCATTTGAAGAT	2817
AD-39706.1	NA	ATCGTCAAGGCACTCTTGC	2808	GCAAGAGTGCCTTGACGAT	2818
AD-40021.1	NA	TGTCTACTGTTCTAGAAGG	2809	CCTTCTAGAACAGTAGACA	2819
AD-39760.1	NA	ATTAGCTGTATCGTCAAGG	2820	CCTTGACGATACAGCTAAT	2828
AD-39822.1	NA	TCGAGAATATCCAAGAGAC	2821	GTCTCTTGGATATTCTCGA	2829
AD-39999.1	NA	TCTTCAGAGTCCTTAACTC	2822	GAGTTAAGGACTCTGAAGA	2830
AD-40072.1	NA	ATAACTTCTTGCTAAGTCC	2823	GGACTTAGCAAGAAGTTAT	2831

[0057]

AD-39732.1	NA	AATGATTCTGAATTAGCTG	2824	CAGCTAATTCAGAATCATT	2832
AD-35576.4	NA	TATAATGGTGAATATCTTC	2825	GAAGATATTCACCATTATA	2833
AD-39712.1	NA	TATCGTCAAGGCACTCTTG	2826	CAAGAGTGCCTTGACGATA	2834
AD-35541.4	NA	TATTGTTGGATCATATTCG	2827	CGAATATGATCCAACAATA	2835

[0058] 附加的表（例如表 1.1 和 1.2）是表 1 的续表；因此，在提到任何表时均包括附加的表。例如，在提到表 1 时也包括对表 1.1 和 1.2 的提及；在提到表 1 至 6 时也包括对表 1.1、1.2、6.1、6.2 等的提及。

[0059] 本公开的多种实施方案

[0060] 针对 KRAS 的各种 RNAi 剂在表 1 至 6 中公开。

[0061] 表 1、表 2 和表 3 提供多种针对 KRAS 的 RNAi 剂的序列、SEQ ID NOs 和相对位置，包括未修饰的序列（列于表 2）和示例性修饰的序列（列于表 3）。

[0062] 在表 3 的序列中，小写字母（例如，c、u）表示修饰的核苷酸，而大写字母（例如，C、U、A、G）表示未修饰的核苷酸。在该表中，显示每个序列的示例性修饰的形式。然而，本公开还考虑并且涵盖这些序列的未修饰形式和包含额外或替代性修饰的其它形式。因而，例如，AD-35523.3 可以任选地在有义链中具有未修饰的序列 SEQ ID NO:1 并且在反义链中具有 SEQ ID NO:428。本公开还涵盖双链体的替代性修饰形式，其在有义链中包含修饰的序列 SEQ ID NO:855 并且在反义链中包含 SEQ ID NO:1282。本公开还涵盖有义链中的 SEQ ID NO:1 和反义链中的 SEQ ID NO:428 的不同修饰形式。类似地，本公开还涵盖本文所公开的任何未修饰的序列的任何修饰的形式。

[0063] 在表 1 至 3 的序列中，修饰的和未修饰的序列可以任选地在 3' 末端包含序列“TT”、“dTdT”、“dTsdT”或“UU”。因此，在上述实例中，AD-35523.3 可以任选地在有义链中具有修饰的序列 SEQ ID NO:855 并且在反义链中具有 SEQ ID NO:1282。如下表 3 中所示，SEQ ID NO:855 和 SEQ ID NO:1282 包含末端 dTdT。dT 是 2'-脱氧-胸苷-5'-磷酸，sdT 是 2'-脱氧胸苷 5'-硫代磷酸酯。在公开的序列中，末端二核苷酸“UU”是 2'-OMe-U 2'-OMe-U，并且末端 TT 和末端 UU 均不处于倒转/反方向。末端二胸苷（或 UU）不是 KRAS 靶序列的部分，而是常作为突出端安置以保护 siRNA 末端免受核酸酶作用的二胸苷二核苷酸的修饰变体（见，例如，Elbashir 等人，2001 Nature 411:494-498；Elbashir 等人，2001 EMBO J.20:6877-6888；和 Kraynack 等人，2006 RNA 12:163-176）。从这些参考文献中已知末端二核苷酸增强核酸酶抗性但不有助于靶识别。因此，本公开还涵盖本文所公开的任何修饰的或任何未修饰的序列，其中修饰的序列包含末端 TT、dTdT、sdT、dTsdT、sdTsdT、sdTdT 等，它们可以处于倒转/反方向或与双链体中的 KRAS 特异性序列具有相同的 5'至 3'方向。此外，本文中关于“RNAi 剂序列的 KRAS 部分”等所用的术语是指得自 KRAS 的 RNAi 剂序列的部分（因此，“RNAi 剂序列的 KRAS 部分”不包括例如末端 dTdT、TT、UU 等，但包括对应于

KRAS 基因序列或 mRNA 序列的部分或与其互补的 RNAi 剂的部分。）

[0064] 在任何修饰或未修饰的序列上，如本领域已知，可以使用 3’ 末端帽结构代替末端二核苷酸或在末端二核苷酸上增加 3’ 末端帽结构以稳定末端，使其免遭核酸酶降解，条件是 3’ 末端帽结构能够稳定 RNAi 剂（例如，抵抗核酸酶）并且不会过度干扰 siRNA 活性。因此，本公开还涵盖本文所公开的任何修饰的或任何未修饰的序列，其中修饰的序列进一步包含末端的 3’ 末端帽结构。

[0065] 表 4 提供了针对 KRAS 的重叠性 RNAi 剂的集合。

[0066] 表 5 和表 6 提供了各种 KRAS RNAi 剂的活性水平。

[0067] 包含本文所述的反义链的 RNAi 剂

[0068] 在一个特定的具体实施方案中，本公开涉及一种包含 RNAi 剂的组合物，所述 RNAi 剂包含反义链，其中反义链包含与针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述反义链选自那些在本文提供和在例如表 1 至 6 中列出的特定双链体中的反义链。

[0069] 下文描述这些实施方案的各种具体实施方案。

[0070] 在一个实施方案中，组合物还包含针对 KRAS 的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂分离，或这两种 KRASRNAi 剂物理地连接（例如，共价连接或缀合），或组合在相同的药物组合物中，或是同一治疗方案中的两种成分。

[0071] 在一个实施方案中，该组合物包含含有第一链和第二链的 RNAi 剂，其中第一链的序列和第二链的序列分别是本文提供的任何 RNAi 剂的第一链和第二链的序列。在一个实施方案中，该组合物包含含有第一链和第二链的 RNAi 剂，其中第一链的序列和第二链的序列分别是本文提供的任何 RNAi 剂的第一链和第二链的序列，还在一条链或两条链上包含额外的约 6 至 20 个核苷酸（例如，约 6、7、8、9、10、11、12、13、14、15、16、17、18、19 或 20 个核苷酸）。在多种实施方案中，所述第一链和第二链分别是本文的表中所列的有义链和反义链。在多种实施方案中，所述第一链和第二链分别是本文的表中所列的反义链和有义链。

[0072] 在一个实施方案中，反义链具有约 30 个或更少个核苷酸长度。

[0073] 在一个实施方案中，有义链和反义链形成长度约 15 至约 30 个核苷酸对的双链体区。

[0074] 在一个实施方案中，反义链具有约 15 至约 36 个核苷酸长度，包括约 18 至约 30 个核苷酸长度，进一步包括约 19 至约 21 个核苷酸长度和约 19 至约 23 个核苷酸长度。在一个实施方案中，反义链具有至少选自约 15 个核苷酸、约 16 个核苷酸、约 17 个核苷酸、约 18 个核苷酸、约 19 个核苷酸、约 20 个核苷酸、约 21 个核苷酸、约 22 个核苷酸、约 23 个核苷酸、约 24 个核苷酸、约 25 个核苷酸、约 26 个核苷酸、约 27 个核苷酸、约 28 个核苷酸、约 29 个核苷酸和约 30 个核苷酸的长度。

[0075] 在一个实施方案中，RNAi 剂包含引起 RNAi 剂在生物样品或环境（例如，细胞质、肠液、血清、肺或肠灌洗液）中具有增加的稳定性的修饰。

[0076] 在一个实施方案中，RNAi 剂包含至少一个糖主链修饰（例如，硫代磷酸酯键）和 / 或至少一个 2’ 修饰的核苷酸。在一个实施方案中，全部嘧啶均是 2’ 0- 甲基修饰的核苷酸。

[0077] 在一个实施方案中，RNAi 剂包含 :至少一个 5’- 尿苷 - 腺嘌呤 -3’(5’-ua-3’) 二

核苷酸，其中尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 鸟嘌呤 -3'(5'-ug-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 胞苷 - 腺嘌呤 -3'(5'-ca-3') 二核苷酸，其中 5'- 胞苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 尿苷 -3'(5'-uu-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸。

[0078] 在一个实施方案中，RNAi 剂包含选自以下的 2'- 修饰：2'- 脱氧、2'- 脱氧 -2'- 氟、2'-O- 甲基、2'-O- 甲氧基乙基 (2'-O-MOE)、2'-O- 氨基丙基 (2'-O-AP)、2'-O- 二甲基氨基乙基 (2'-O-DMAOE)、2'-O- 二甲氨基丙基 (2'-O-DMAP)、2'-O- 二甲基氨基乙氧基乙基 (2'-O-DMAEOE) 和 2'-O-N- 甲基乙酰氨基 (2'-O-NMA)。在一个实施方案中，全部嘧啶均是 2'O- 甲基修饰的核苷酸。

[0079] 在一个实施方案中，RNAi 剂包含平末端。

[0080] 在一个实施方案中，RNAi 剂包含具有 1 至 4 个非配对核苷酸的突出端。

[0081] 在一个实施方案中，RNAi 剂包含在 RNAi 剂的反义链的 3' 末端处的突出端。

[0082] 在一个实施方案中，RNAi 剂连接至一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基 (hecigenin)、薯蓣皂苷配基、萜、三萜、菝葜皂苷元 (sarsasapogenin)、无羁萜、表木栓烷醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[0083] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 60%。

[0084] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 70%。

[0085] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 80%。

[0086] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 90%。

[0087] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.1nM。

[0088] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.01nM。

[0089] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.001nM。

[0090] 包含本文所述的第一链和第二链的 RNAi 剂

[0091] 在一个特定的具体实施方案中，本公开涉及一种包含 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列包含与针对 KRAS 的 RNAi 剂的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 KRAS 的 RNAi 剂。

[0092] 在一个特定的具体实施方案中，本公开涉及一种包含 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列包含与针对 KRAS 的 RNAi 剂的第一链和 / 或第二链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 KRAS 的 RNAi 剂选自本文中提供的和例如在表 1 中列出的特定双链体。

[0093] 在一个特定的具体实施方案中，本公开涉及一种包含 RNAi 剂的组合物，所述 RNAi

剂包含第一链和第二链，其中第一链和 / 或第二链的序列分别包含选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的第一链和 / 或第二链的序列。

[0094] 在一个特定的具体实施方案中，本公开涉及一种包含 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列分别是选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的第一链和 / 或第二链的序列。

[0095] 下文描述这些实施方案的多种具体实施方案。

[0096] 在一个实施方案中，组合物还包含针对 KRAS 的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂分离，或这两者物理地连接（例如，共价连接或缀合）。

[0097] 在一个实施方案中，反义链具有约 30 个或更少个核苷酸长度。

[0098] 在一个实施方案中，有义链和反义链形成长度约 15 至约 30 个核苷酸对的双链体区。

[0099] 在一个实施方案中，反义链具有约 15 至约 36 个核苷酸长度，包括约 18 至约 23 个核苷酸长度，并且包括约 19 至约 21 个核苷酸长度和约 19 至约 23 个核苷酸长度。在一个实施方案中，反义链具有至少选自约 15 个核苷酸、约 16 个核苷酸、约 17 个核苷酸、约 18 个核苷酸、约 19 个核苷酸、约 20 个核苷酸、约 21 个核苷酸、约 22 个核苷酸、约 23 个核苷酸、约 24 个核苷酸、约 25 个核苷酸、约 26 个核苷酸、约 27 个核苷酸、约 28 个核苷酸、约 29 个核苷酸和约 30 个核苷酸的长度。

[0100] 在一个实施方案中，RNAi 剂包含引起 RNAi 剂在生物样品或环境（例如，血清或肠道灌洗液）中具有增加的稳定性的修饰。

[0101] 在一个实施方案中，RNAi 剂包含至少一个糖主链修饰（例如，硫代磷酸酯键）和 / 或至少一个 2’ 修饰的核苷酸。在一个实施方案中，全部嘧啶均是 2’ O- 甲基修饰的核苷酸。

[0102] 在一个实施方案中，RNAi 剂包含：至少一个 5’- 尿苷 - 腺嘌呤 -3’(5’-ua-3’) 二核苷酸，其中尿苷是 2’- 修饰的核苷酸；和 / 或至少一个 5’- 尿苷 - 鸟嘌呤 -3’(5’-ug-3’) 二核苷酸，其中 5’- 尿苷是 2’- 修饰的核苷酸；和 / 或至少一个 5’- 胞苷 - 腺嘌呤 -3’(5’-ca-3’) 二核苷酸，其中 5’- 胞苷是 2’- 修饰的核苷酸；和 / 或至少一个 5’- 尿苷 - 尿苷 -3’(5’-uu-3’) 二核苷酸，其中 5’- 尿苷是 2’- 修饰的核苷酸。

[0103] 在一个实施方案中，RNAi 剂包含选自以下的 2’- 修饰：2’- 脱氧、2’- 脱氧 -2’- 氟、2’-O- 甲基、2’-O- 甲氧基乙基 (2’-O-MOE)、2’-O- 氨基丙基 (2’-O-AP)、2’-O- 二甲基氨基乙基 (2’-O-DMAOE)、2’-O- 二甲氨基丙基 (2’-O-DMAP)、2’-O- 二甲基氨基乙氧基乙基 (2’-O-DMAEOE) 和 2’-O-N- 甲基乙酰氨基 (2’-O-NMA)。

[0104] 在一个实施方案中，RNAi 剂包含平末端。

[0105] 在一个实施方案中，RNAi 剂包含具有 1 至 4 个非配对核苷酸的突出端。

[0106] 在一个实施方案中，RNAi 剂包含在 RNAi 剂的反义链的 3’ 末端处的突出端。

[0107] 在一个实施方案中，RNAi 剂连接至一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、

整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和/或转铁蛋白。

[0108] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 60%。

[0109] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 70%。

[0110] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 80%。

[0111] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 90%。

[0112] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.1nM。

[0113] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.01nM。

[0114] 在一个实施方案中，RNAi 剂在 MiaPaca2 细胞中的 EC50 不超过约 0.001nM。

[0115] 使用本文所述的 RNAi 剂治疗的方法

[0116] 在一个特定的具体实施方案中，本公开涉及在个体中治疗 KRAS 相关疾病的方法，该方法包括向个体施用治疗有效量的包含 RNAi 剂的组合物的步骤，所述 RNAi 剂至少包含一条反义链，其中的反义链包含与针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 至 19 个连续核苷酸，所述针对 KRAS 的 RNAi 剂选自在本文提供和在例如表 1 中列出的特定双链体。

[0117] 在另一个实施方案中，本公开涉及这样一种方法，其中的组合物所包含的 RNAi 剂还包括一条有义链，其中的有义链包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0118] 在该方法的一个实施方案中，RNAi 剂包含至少一条反义链，和/或包含一条有义链和一条反义链，其中有义链和/或反义链的序列是选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和/或反义链的序列，其中组合物还包括药学有效的制剂。

[0119] 在该方法的一个实施方案中，RNAi 剂包含至少一条反义链，和/或包含一条有义链和一条反义链，其中有义链和/或反义链的序列包含选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和/或反义链的序列，其中组合物还包括药学有效的制剂。

[0120] 下文描述这些实施方案的多种具体实施方案。

[0121] 在一个实施方案中，KRAS 相关疾病是增殖性疾病，或心面皮肤 (CFC) 综合征或努南综合征。

[0122] 在一个实施方案中，KRAS 相关疾病是增殖性疾病，包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和/或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌，或心面皮肤 (CFC) 综合征或努南综合征。

[0123] 在一个实施方案中，该方法还包括施用额外治疗。在一个实施方案中，额外治疗是治疗有效量的组合物。

[0124] 在一个实施方案中，额外治疗是一种方法（或手术操作）。

[0125] 在一个实施方案中，额外治疗和 RNAi 剂可以按任意顺序施用，或可以同时施用。

[0126] 在一个实施方案中，该方法还包括施用针对增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的额外治疗的步骤。

[0127] 在一个实施方案中，该方法还包括施用选自针对 KRAS 相关疾病的另外的拮抗剂的列表的额外治疗或疗法的步骤。

[0128] 在一个实施方案中，组合物包含针对 KRAS 的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂分离，或这两者物理地连接（例如，共价连接或缀合）。

[0129] 在一个实施方案中，该方法还包括施用另外的 RNAi 剂的步骤，所述另外的 RNAi 剂包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0130] 使用本文所述的 RNAi 剂抑制 KRAS 表达的方法

[0131] 在一个特定的具体实施方案中，本公开涉及在个体中抑制 KRAS 表达的方法，该方法包括向个体施用治疗有效量的包含本公开的 RNAi 剂的组合物的步骤。

[0132] 在该方法的一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中的反义链包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0133] 在该方法的一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中有义链和 / 或反义链的序列是选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和 / 或反义链的序列，其中的组合物位于药学有效的制剂中。

[0134] 在该方法的一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中有义链和 / 或反义链的序列包含选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和 / 或反义链的序列，其中的组合物位于药学有效的制剂中。

[0135] 下文描述这些实施方案的多种具体实施方案。

[0136] 在一个实施方案中，个体罹患或易患 KRAS 相关疾病。

[0137] 在一个实施方案中，KRAS 相关疾病是增殖性疾病，或心面皮肤 (CFC) 综合征或努南综合征。

[0138] 在一个实施方案中，KRAS 相关疾病是增殖性疾病，包括但不限于固体或液体癌，例如腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌，或心面皮肤 (CFC) 综合征或努南综合征。

[0139] 在一个实施方案中，该方法还包括施用额外治疗。在一个实施方案中，额外治疗是治疗有效量的组合物。在一个实施方案中，额外治疗是治疗相关的方法（或手术操作）。

[0140] 在一个实施方案中，额外治疗和 RNAi 剂可以按任意顺序施用，或可以同时施用。

[0141] 在一个实施方案中，该方法还包括施用针对增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的额外治疗的步骤。

[0142] 在一个实施方案中，组合物包含针对 KRAS 的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂分离，或这两者物理地连接（例如，共价连接或缀合）。

[0143] 在一个实施方案中，该方法还包括施用另外的 RNAi 剂的步骤，所述另外的 RNAi 剂包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0144] 针对 KRAS 的 RNAi 剂的药物组合物

[0145] 在一个特定的具体实施方案中，本公开涉及包含本公开的 RNAi 剂的组合物。在一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中的反义链包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中该组合物位于药学有效的制剂中。

[0146] 在一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中有义链和 / 或反义链的序列是选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和 / 或反义链的序列，其中的组合物位于药学有效的制剂中。

[0147] 在一个实施方案中，RNAi 剂包含至少一条反义链，和 / 或包含一条有义链和一条反义链，其中有义链和 / 或反义链的序列包含选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的有义链和 / 或反义链的序列，其中的组合物位于药学有效的制剂中。

[0148] 在一个实施方案中，本公开涉及 RNAi 剂在生产用于治疗 KRAS 相关疾病的药物中的用途，其中的 RNAi 剂包含一条有义链和一条反义链，其中的反义链包含与选自本文中提供的和例如在表 1 中列出的特定双链体的针对 KRAS 的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0149] 包含不同于所公开序列的错配的针对 KRAS 的 RNAi 剂的具体实施方案

[0150] 本文中公开了针对 KRAS 的 RNAi 剂的多种具体实施方案。本公开涵盖表 1 至 6 中提供的示例性修饰序列，和相应的未修饰序列和其它修饰的序列（例如，修饰的变体和未修饰的变体）。本公开的具体实施方案包括了包含下述序列的 RNAi 剂及其修饰变体和未修饰变体，所述序列与表 1 中所列的任一 RNAi 剂差异 0、1、2 或 3 个核苷酸或 bp（碱基对）（例如，0、1、2 或 3 错配）。如下文以额外细节描述，错配在本文中被定义为将两个序列最大限度地对齐并比较时碱基序列（例如，A 替代 G）或长度之间的差异。此外，如下文更详细地描述，“未修饰的变体”是其中碱基序列相同，但是没有一个碱基被修饰的变体；这种变体例如包括与野生型 KRAS mRNA 或基因的相应部分一致的序列。“修饰的变体”含有对核苷酸、糖、磷酸酯或主链的一个或多个修饰（或一个或多个减少或不同的修饰），和 / 或一个或多个部分的添加；但是对碱基序列无改变、置换、添加或缺失。特定序列及其修饰变体或未修饰变体具有彼此之间 0 个错配。

[0151] 在一个特定的实施方案中，本公开包含 RNAi 剂，所述 RNAi 剂包含有义链和反义链，其中的有义链和 / 或反义链包含与表 1 至 6 中列出的任一 RNAi 剂的有义链和 / 或反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0152] 在另一个具体实施方案中，RNAi 剂包含有义链，所述有义链包含与表 1 至 6 中列

出的任一 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0153] 其它实施方案

[0154] 下文描述本公开的多种特定的具体实施方案。

[0155] 在一个实施方案中，本公开涉及用于在个体中治疗 KRAS 相关疾病的方法的本文所述的任一实施方案的组合物，所述方法包括向个体施用治疗有效量的权利要求任意一项所述的组合物的步骤。

[0156] 本公开的一个实施方案是这些实施方案任意一项所述的组合物在生产用于治疗 KRAS 相关疾病的药物中的用途。

[0157] 在一个实施方案中，KRAS 相关疾病是增殖性疾病或心面皮肤 (CFC) 综合征或努南综合征。

[0158] 在一个实施方案中，KRAS 相关疾病是增殖性疾病或心面皮肤 (CFC) 综合征或努南综合征，所述增殖性疾病包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌。

[0159] 在一个实施方案中，本公开涉及用于治疗 KRAS 相关疾病的以上任一实施方案所述的组合物。

[0160] 定义

[0161] 出于便利，下文提供在本说明书、实施例和所附权利要求中使用的某些术语和短语的含义。如果本说明书的其它部分中某术语的用途和这一部分中所提供的其定义之间存在明显的不一致性，则这一部分中的定义应当占优。

[0162] KRAS

[0163] “KRAS”是指由公认的基因符号 KRAS 所指定的基因、mRNA 和 / 或蛋白质，或编码该蛋白质的任何核酸，或其任何突变体、变体或修饰的形式；细胞遗传定位：12p12.1；基因组坐标 (GRCh37)：12：25,358,179-25,403,853(来自 NCBI)，其还被不同地指定为：KRas、K-ras、K-RAS、GTP 酶 Kras 和 V-Ki-ras2Kirsten 大鼠肉瘤病毒癌基因同源物、C-K-RAS；K-RAS2A；K-RAS2B；K-RAS4A；K-RAS4B；KI-RAS；KRAS2；RASK2；v-Ki-ras2Kirsten 大鼠肉瘤病毒癌基因同源物 [来源：MGI 符号；Acc:MGI:96680]；OMIM:190070 MGI:96680 HomoloGene:37990 GeneCards:KRAS Gene；物种 - 人类：Entrez 3845；Ensembl ENSG00000133703；UniProt P01116；RefSeq(mRNA)NM_004985.3；RefSeq(蛋白)NP_004976.2；坐标 (UCSC)Chr 12:25.36 - 25.4Mb；物种 - 小鼠：Entrez-16653；Ensembl-ENSMUSG00000030265；UniProt-070564；RefSeq(mRNA)-NM_021284.6；RefSeq(蛋白)-NP_067259.4；坐标 (UCSC)-Chr 6:145.17 - 145.2Mb。

[0164] Ras 亚族

[0165] Ras 亚族 (大鼠肉瘤 (RAt Sarcoma) 的缩写) 是参与细胞信号转导和其它过程的小分子 GTP 酶的蛋白亚族。Ras 信号的激活或引起细胞生长、分化和存活。

[0166] 由于 Ras 将细胞外的信号传达到细胞核，因此，ras 基因的突变会造成永久性的活化以及即使在缺乏细胞外信号的情况下的不恰当的向细胞内的信号传递。由于这些信号会

导致细胞生长和分化，Ras 信号的失调或其它异常会最终导致肿瘤形成和癌症。Goodsell 等人，1999. Oncologist 4. 3:263-4。在三分之一的全部人类肿瘤和高达 90％的特定肿瘤类型中发现了 Ras 的激活突变。Downward. 2003. Nat. Rev. Cancer 3. 1:11 - 22 ;Bos 等人 1989 Cancer Res. 49:4682-4689 ;和 Forbes 等人 2006 Br. J. Cancer 94:318-322。

[0167] Ras 基因最初被美国国家健康研究院 (NIH) 的 Scolnick 及其同事鉴定为转化致癌基因 [Malumbres 等人 2003. Nat. Rev. Cancer 3. 6:459 - 65]，负责 Harvey(HRAS 致癌基因）和 Kirsten(KRAS) 肉瘤病毒的致癌活性。Chang 等人 1982. Proc. Natl. Acad. Sci. U. S. A. 79. 16:4848 - 52。这些病毒最初分别由 Jennifer Harvey[Harvey. 1964. Nature 204. 4963:1104 - 5] 和 Werner Kirsten[Kirsten 等人 1970. Bibl Haematol. 36:246 - 9] 在 20 世纪 60 年代在大鼠中发现。1982 年，在人类癌细胞中发现了激活的转化人 KRAS 基因 [Santos 等人 1982. Nature 298. 5872:343 - 7]、[Parada 等人 1982. Nature 297. 5866:474 - 8]。随后的研究发现了第三种人类 KRAS 基因，其被指定为 NRAS，因为它最初是在人成神经细胞瘤细胞中发现的。

[0168] 三种人类 KRAS 基因编码高度相关的 188 至 189 个氨基酸的蛋白，分别被指定为 H-Ras、N-Ras 以及 K-Ras4A 和 K-Ras4B（两种 K-Ras 蛋白来自选择性基因剪接）。关于 KRAS 克隆和亚型的其它信息，参见例如 Der 等人 1982 Proc. Nat. Acad. Sci. 79:3637-3640 ; Chang 等人 1982 Proc. Nat. Acad. Sci. 79:4848-4852 ;McCoy 等人 1983 Nature 302:79-81 ;McGrath 等人 1983 Nature 304:501-506 ; 和 Carta 等人 2006 Am. J. Hum. Genet. 79:129-135。

[0169] Ras 功能

[0170] Ras 蛋白起着二元分子开关的作用，控制着细胞内的信号网络。受 Ras 调控的信号途径控制着肌动蛋白细胞骨架完整性、增殖、分化、细胞粘附、细胞凋亡以及细胞迁移等过程。Ras 和 ras 相关蛋白在癌症中经常出现失调，导致侵入和转移的增加以及细胞凋亡的减少。

[0171] Ras 激活多种途径，其中的丝裂原活化蛋白 (MAP) 激酶级联已得到深入研究。该级联向下游传递信号并导致细胞生长和分裂中所涉及的基因的转录。这是抑制细胞凋亡的一条独立的 AKT 途径。

[0172] 在多种实施方案中，RNAi 剂可用于治疗其中这些途径或功能中的任何一个或多个发生了改变的 KRAS 相关疾病。在多种实施方案中，本公开涵盖了可以调节或改变受 Ras 调控的信号途径、包括 MAP 激酶级联和 / 或调节或改变肌动蛋白细胞骨架完整性、增殖、分化、细胞粘附、细胞凋亡和细胞迁移等过程的 KRAS RNAi 剂。Ras 和 ras 相关蛋白在癌症中经常出现失调，导致侵入和转移的增加以及细胞凋亡的减少。

[0173] 激活和失活

[0174] Ras 是一种 G 蛋白，或称为鸟嘌呤核苷酸结合蛋白。具体地讲，它是一种单亚基的小分子 GTP 酶，在结构上与异三聚体 G 蛋白（大分子 GTP 酶）的 G_{α} 亚基相关。G 蛋白起二元分子开关的作用，具有“开”和“关”两种状态。在“关”的状态，其与核苷酸二磷酸鸟苷 (GDP) 结合，在“开”的状态，Ras 与三磷酸鸟苷 (GTP) 结合，与 GDP 相比，GTP 具有一个额外的磷酸根基团。该额外的磷酸根将两个转换区保持在“加载的弹簧”构型（特别是 Thr-35 和 Gly-60)。当放松时，转换区松弛，使构象改变为失活状态。因此，Ras 和其它小分子 G 蛋

白的激活和失活是由活性的 GTP- 结合的形式和失活的 GDP- 结合的形式之间的循环控制的。

[0175] KRAS 的致癌活性的关键区域包括密码子 12、13、59、60、61、63 和 153。Grimmond 等人 1992 Urol. Res. 20:121-126 ;Burmer 等人 1989 Proc. Natl. Acad. Sci. 86:2403-2407。突变有时似乎会影响这些密码子。某些 KRAS 突变会通过破坏固有的 GTP 酶活性和使 GTP 酶活化蛋白产生抗性而造成 RAS 聚积在 GTP- 结合的状态。Zenker 等人 2007 J. Med. Genet. 44:131-135。在多种实施方案中,KRAS RNAi 剂的序列包括与任何以上列出的密码子相对应的编码段的部分。在多种实施方案中,KRAS RNAi 剂具有对野生型 (wt)KRAS 序列的错配,从而 KRAS RNAi 剂的序列与 KRAS 基因的突变部分的序列匹配。在多种实施方案中,本公开包括向患者施用具有与患者中所发现的特定突变的序列相对应的序列的 KRAS RNAi 剂,并任选地联合施用具有包含野生型序列的序列的 KRAS RNAi 剂。在某些实施方案中,KRAS RNAi 剂对应于 KRAS mRNA 的不同部分。在某些实施方案中,患者可具有对应于 KRAS 的特定密码子 (例如密码子 12、13 和 / 或 59) 的一个或多个突变,但 KRAS 基因的其余部分是野生型的,因此可以向患者施用具有不包含突变的野生型序列的 KRAS RNAi 剂,和 / 或施用具有对应于一个或多个突变的序列的 KRAS RNAi 剂。

[0176] 在某些实施方案中,本公开包括涉及如下步骤的方法 :鉴别患有 KRAS 相关疾病的患者,从患者中分离编码或对应于 KRAS 蛋白或基因的核酸,测定核酸序列以确定在 KRAS 基因中是否有突变,以及,如果序列显示 KRAS 的突变,生产具有与突变相对应的序列的 KRAS RNAi 剂,并以治疗有效量施用 KRAS RNAi 剂以治疗或改善 KRAS 相关疾病。在某些实施方案中,KRAS RNAi 剂单独施用或作为治疗方案的一部分与适于 KRAS 相关疾病的另一种疾病治疗方法一起施用。

[0177] 鸟嘌呤核苷酸交换因子 (GEFs) 和 GTP 酶活化蛋白 (GAPs) 对 RAS 交换结合的核苷酸的过程有促进作用。按照其分类,Ras 具有固有的 GTP 酶活性,这意味着该蛋白本身可使结合的 GTP 分子水解成 GDP。然而,该过程过于缓慢而无法产生有效的功能,因此,Ras 的 GAP(RasGAP) 会与 Ras 的催化机器结合并使其稳定,提供额外的催化残基 (“精氨酸指”) 以使水分子最佳地处于对 GTP 的 γ 磷酸根亲核进攻的位置。此时,无机磷酸盐被释放,Ras 分子与 GDP 结合。由于 GDP- 结合的形式对信号传导而言是“关”或“失活的”,GTP 酶活化蛋白通过激活其 GTP 酶活性而使 Ras 失活。因此,GAP 加速 Ras 失活。

[0178] GEF 催化从 Ras 释放 GDP 的“推拉”反应。它们插入到 P 环和镁阳离子结合位点附近并抑制其与 γ 磷酸根阴离子的相互作用。开关 II 中的酸性 (负性) 残基将 P 环中的赖氨酸“拉”离 GDP,后者将开关 I “推”离鸟嘌呤。将 GDP 固定在位的联系被破坏,使 GPD 释放到细胞质中。由于细胞内的 GTP 相对于 GDP 较为丰富 (约多 10 倍),GTP 大部分重新进入到 Ras 的核苷酸结合口袋并重新上紧弹簧。因此,GEF 促进 Ras 激活。公知的 GEF 包括包含 RasGEF 结构域的 Son of Sevenless(Sos) 和 cdc25。

[0179] GEF 和 GAP 活性之间的平衡决定了 Ras 的鸟嘌呤核苷酸状况,由此调节 Ras 活性。

[0180] 当处于 GTP- 结合的构象时,Ras 对多种效应物具有高亲和力,从而使其能够完成其功能。这其中包括 PI3K。其它小分子 GTP 酶可与连接物例如 Arfaptin 或第二信使系统例如腺苷酸环化酶结合。在许多效应物中发现了 Ras 结合结构域并且其总是与转换区之一结合,因为它们使构象在活性形式和无活性形式之间变化。但是,它们也可与其它蛋白表面

结合。

[0181] 在多种实施方案中，本公开涵盖调节细胞中 KRAS 的量和 / 或活化的 KRAS 的量的 KRAS RNAi 剂。在多种其它实施方案中，本公开涵盖涉及一种或多种 KRAS RNAi 剂和靶向于与 KRAS 相互作用的因子（例如 PI3K、GAP 等）的第二种活性剂（例如另一种 RNAi 剂、抗体或小分子）的组合物或药物组合物和 / 或治疗方法。

[0182] 癌症中的 Ras

[0183] 原癌基因的 Ras 家族的突变是非常常见的。消除 Ras 活性的药理学途径可抑制某些癌症类型。Ras 点突变是人原癌基因中唯一最常见的异常 (Pathologic Basis of Disease, 第 8 版，2010. 第 282 页）。Ras 抑制剂反 - 法尼基硫代水杨酸 (FTS, Salirasib) 在许多癌细胞系中显示显著的抗癌效果 (Rotblat 等人 2008. Methods Enzymol 439:467 - 89 ；和 Blum 等人 2005. Cancer Research 65. 3:999 - 1006)。

[0184] 在多种实施方案中，本文公开的 KRAS RNAi 剂可被引入到具有 KRAS 的点突变或造成 KRAS 过度表达或活性过高的其它突变的肿瘤细胞中。所述细胞被称为“KRAS- 缺陷型”细胞。

[0185] 已证实，基因的不恰当激活在信号转导、增殖和恶性转化中起关键作用 (Lodish 等人 2000. Chapter 25. Cancer. Molecular cell biology. 第 4 版，San Francisco:W. H. Freeman)。

[0186] 在多种不同基因以及 KRAS 本身中的突变也具有其作用。癌基因例如 p210BCR-ABL 或生长因子受体 erbB 是 Ras 的上游，因此，如果它们被组成性激活，它们的信号将通过 Ras 转导。

[0187] 肿瘤抑制基因 NF1 编码 Ras-GAP，其在神经纤维瘤病中的突变将意味着 Ras 不太可能被灭活。因此，靶向于 KRAS 的 RNAi 剂可与靶向于影响 KRAS 及其各种途径的其它因子的其它活性剂（例如其它 RNAi 剂）结合使用。

[0188] 最后，Ras 癌基因可通过点突变被激活，从而使 GTP 酶反应不再受 GAP 的刺激，这增加了活性的 Ras-GTP 突变体的半衰期。

[0189] 在多种实施方案中，KRAS RNAi 剂可施用给患有涉及 KRAS 之外的突变、例如 p210BCR-ABL、erbB 或 NF1 中的突变的 KRAS 相关疾病的患者。在多种其它实施方案中，本公开涵盖涉及一种或多种 KRAS RNAi 剂和一种或多种靶向于造成 KRAS 的不恰当激活的其它因子、例如 p210BCR-ABL、erbB 或 NF1 的活性剂（例如 RNAi 剂、抗体或小分子）的组合物或药物组合物或治疗方法。

[0190] 组成性活性的 Ras

[0191] 组成性活性的 Ras(Ras^D) 是一种包含阻止 GTP 水解的突变的形式，其使 Ras 锁定在永久性的“开”状态。

[0192] 最常见的突变发现于 P 环中的残基 G12 和催化残基 Q61。

[0193] 残基 12 处的甘氨酸到缬氨酸的突变使得 Ras 的 GTP 酶结构域对 GAP 引起的失活不敏感，因此始终处于“开”状态。Ras 需要 GAP 来灭活，因为与其它包含 G 结构域的蛋白例如异三聚体 G 蛋白的 α 亚基相反，Ras 对自身的催化作用相对较弱。

[0194] 残基 61 负责稳定 GTP 水解的过渡态。由于酶催化通常是通过降低底物和产物间的能垒来实现的，Q61 向 K 的突变必然使固有的 Ras GTP 水解的速率降低至无生理学意义

的水平。

[0195] 在多种实施方案中，本公开涉及对患有或易患其中的 KRAS 是组成性活化的 KRAS 相关疾病的患者进行治疗的方法。

[0196] 各物种的 KRAS 序列

[0197] 已经测定了多个物种的 KRAS 基因的序列，包括人 (HGNC:6407 ;NM_004985.3) ;小鼠 (MGI:96680) ;和大鼠 (RGD:2981)。可以如此设计对 KRAS 特异的 RNAi 剂，从而其序列完全匹配与人 KRAS 基因和来自试验动物的同源基因相对应的 mRNA 的序列。这在开发治疗性 RNAi 剂时是有利的，因为相同的 RNAi 剂可以同时用于试验动物（例如，大鼠、小鼠或食蟹猴等）和人中。

[0198] 已部分测定了食蟹猴 (Macaca fascicularis 或“cyno”) 中的 KRAS 序列。下文显示部分 Cyno 序列以及部分 Cyno 和人 KRAS 序列的比对结果。NM_004985 KRAS, v-Ki-ras2 Kirsten 大鼠肉瘤病毒癌基因同源物的共有序列 -- 靶长度＝ 5312，共有序列长度＝ 4474，23 个邻接片段（最长是 775) 113 个错配，1651.87410068346 读数，覆盖 :最大＝ 96，平均＝ 13.158 ;共有序列一致性＝ 99.41％，靶 / 共有序列保守性 97.47％。

[0199] KRAS 食蟹猴序列 :

[0200]

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 60

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNAGGCACTG 120

AAGGCGGCGG CGGGGCCAGA GGCTCAGCGG CTCCCCGGGG CGGGAGAGAG NNNNNNNNNN 180

NNNNNNNNNN NNNNNNNNNN NNNNAGTTGG AGCTGGTGGG GTAGGCAAGA GTGCCTTGAC 240

NNNNNNGCTA ATTCAGAATC ATTTTGTGGA CGAATATGAT CCAACAATAG AGGATTCCTA 300

CAGGAAGCAA GTAGTAATTG ATGGAGAAAC CTGTCTCTTG GATATTCTCG ACACAGCAGG 360

TCAAGAGGAG TACAGTGCAA TGAGGGACCA GTACATGAGG ACTGGGGAGG GCTTTCTTTG 420

TGTATTTGCC ATAAATAATA CTAAATCATT TGAAGATATT CACCATTATA GAGAACAAAT 480

TAAAAGAGTT AAGGACTCTG AAGATGTACC TATGGTCCTA GTAGGAAATA AATGTGATTT 540

GCCTTCTAGA ACAGTAGACA CAAAACAGGC TCAGGACTTA GCAAGAAGTT ACGGAATTCC 600

TTTTATTGAA ACATCAGCAA AGACAACACA GGGTGTTGAT GATGCCTTCT ATACATTAGT 660

TCGAGAAATT CGAAAACATA AAGAAAAGAT GAGCAAAGAT GGTAAAAAGA AGAAAAAGAA 720

GTCAAAGACA AAGTGTGTAA TTATGTAAAT ACAATTTGTA CTTTTTTCTT AAGGCATACT 780

AGTAAAAGTG GTAATTTTTG TACATTACAC TAAATTATTA GCATTTGTTT TAGCATTACC 840

TAATTTTTTT CCTCCTCCAT GCAGACTGTT ACCTTTTACC TTAAATGCTT ATTTTAAAAT 900

GACAGTGGAA GCTTTTTTTT CCTCTAAGTG CCAGTATTCC CAGAGTTTTG ATTTTTGAAC 960

TAGCAATGCC TGTGAAAAAG AAACTGAATA CCTAAGATTT CTGTCTTGGG GTTTTTGGTG 1020

CNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNAATT 1080

AATGAAGCTT CTGAATCATC CCTATTCTGT GTTTTATCTA GTCACATAAA TGGATTAATT 1140

ACTAATTTCA GTTGAGACCT TCTAATTGGT TTTTACTGAA ACATTGAGGG AACACAAANN 1200

NNNNNNNNNN NNNNNNNNNN NNNNTCTAGG CATCATGTCC TATAGTTTGT CATCCCTGAT 1260

GAATGTAAAG TTACACTGTT CACAAAGGTT TTGTTCCCTT TCCACTGCTA TTAGTCATGG 1320

TCACTCTCCC CGNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNTGGAA AAAAATTACA 1380

AGTCAATGGA AACTATTATA AGGCCGTTTC GTTTTCAGAT TACATAAATT ACTATAAAGA 1440

CTCCTAATAG GTTTTCCTGT TAAGGCAGAC CCAGTATGAA ATGGGGATTN NNNNNNNNNN 1500

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNA ATTTTTATAA TAATTGAAAT AATTTTAACA 1560

TGTATAAAAA ATTCTCATAG GAATTAAATG TAGTCTCCCT GTGTCAGATT GCTCTTTCAT 1620

AGTATAACTT TAAATCTTTT CTTCAAGTTC AGTCTTTGAA GGTAGTTTTA ATTCTGCTTG 1680

TGACATTAAA AGATTATTTG GGCCAGTTAT AGCTTAGTAG GTGTTGAAGA GACCAAGGTT 1740

GCATGGCCAG GCCCTGTGTG AACCTTTGAG CTTTCATAGA GAGTTTCACA GCATGGACTG 1800

TGTCCCCATG GTCATCCAGT GTTGTCATGC ATTGGTTAGT CAAAATGGGG AGGGACTAGG 1860

ACAGTTTGGA TAGGTCAACA AGATACATTC TCACTCTGTG GTGGTCCTGC TGACAAATCA 1920

AGAGCATTGC TTTTGTTTTT TAAGAAAATG AACTCTTTTT TAAAAATTAC TTTTAAATAT 1980

TAACTCAAAA GTTGAGATTT TGGGGGGGTG GTATGCCAAG ACATTAATTT TTTNNNNNNN 2040

[0201]

NNNNNNNNNN NNNAAGTTTT ACAATCTCTA GGTTTGGCTA GTTCTCTTAA CACTGGTTAA 2100

ATTAACATTT CATAAACACT TTTCAAGNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 2160

NNNNNNNNNN NNNNNNNNNN NNNATTTAAA ATGTTACTTA TTTTAAAATA TATCAAATCA 2220

GATGGCATGG TGAGGTGAAA GTATCACTGG ACTANNAAGA AGGTGACTTA GGTTCTAGAT 2280

AGTTCTCTTT TACCACTCTC ATTTTGACCA CATCACTTAC TATCCATTTC TTCATCTTAA 2340

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN TTTTTACAAC TATGTGATTT ATATTCCGTT 2400

TACATGAGGA TACACTTATT TGTCAAGCTC AGCACAATCT AAAAATTTTT AACCTATGTT 2460

ACACCATCTT CAGTGCCAAT CTTGGGCAAA ATTGTGCAAG AGGTGAAGTT TATATTTGAA 2520

TATCCATTCT CGTTTTAGGA CTCTCCTTCC ATGTTAGTGT CATCTTGCCT GCCTACCTTC 2580

CACATGCCCC ATGACTTGAT GCAGTTTTAA TACTTCTAAT TCCCCTAACC ATAAGATTTA 2640

CTGCTGCTAT GGATATCTCC ATGAAGTTTT CCCNNNNNNN NNNNNNNNNN NNNNNNNNNN 2700

NNNNNNNNNN NNNNNNNNNN NGAGAATCTG ACAGATACCA TAATGGGATT TGACCTAATC 2760

ACTAATTTTC AGGTGGTGGC CGATCCTTTG AAAATATCTC TGCTGCCCAA TCCATTAGCG 2820

ACAGTAGGAT TTTTCAGACC TGGTATGAAT AGACAGAACC CTATCCAGTG GAAGGAGAAT 2880

TTAATAAAGA TAGTACTGAA ATAATTCCTA AGGTAATCTA CAACTAGGAC TACTCCTGGT 2940

AACAGTAATA CATTCCATTG TTTTAGTAAC CAGAAATNNN NNNNNNNNNN NNNNNNNNNN 3000

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNCCAGGCTG 3060

GAATGCAGTG GCGCCATCTC AGCTCACTGC AACCTCCATC TCCCAGGTTC AAGCGATTCT 3120

CGTGCCTCGG CATCCTGAGT AGCTGGGATT ACAGGCATGT GCCNCCACAC TGAACTAATT 3180

TTTGTAGTTT TAGGAGAGAC AGGGTTTCAC CGTATTGGCC AGGCTGGTCT CGAACTCCTG 3240

ACCTCAAGTG ATTCACCCAC CTNNNCCTCA TAAAGCCGTT TTGCAGAACT CATTTATTCA 3300

GCAAATATTT ATTGAGTGCC TACCAGATGC CAGTCATTTC ACAAGGCACT GGGTATATGG 3360

TATCGCCAAA CAAGAGACAT AATCCTGGTC CTTAGGTAGT GCTAGCNNNN NNNNNNNNNN 3420

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 3480

NNNNGGGGTT TGGTCCCTGT GCCTGCTCTA TAATTGTTTT GCTATGATTC CAGTGAAANN 3540

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN 3600

NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNNN NNTTACTGTA CACATTAAGG 3660

TGTATGTCAG ATATCCATAT TGAANNNNNN NNNNNNNNNN NNNNNNNNNN NNNNNNNNAT 3720

AATTAAAATA TACTTAAAAA TTAATAGTTT TATCTGGGTA CAAACAAACA GGTGGCTGAA 3780

CTAGTTCACA GACAAGGAAA CTTCTATGTA AAAATCAGTA TGATTTNNNN NNNNNNNNGT 3840

GAAACTACAG ATCTTTGGAA CATTGTTTAG ATAGGGTGTT AAGACTTACA CAGTACCACG 3900

TTTCTACACA CAGAAAGAAA TGGCCATAGT TCAGGAACTG CAGTGCTAAT GAGGGGATAT 3960

TTAGGCCTCT TGAATTTTTG ATGTAGATGG GCATTTTTTT AAGGTANNTG GTAATTACCT 4020

TTATGTGAAC TTTGAATGGT TTAACAAAAG ATTTGTTTTT GTACAGATTT TAAAGGGGGA 4080

[0202]

GAATGCTAGA AATAAATGTT ATCTAANNNN NNNCGCCTTA AAGATAAAAA TCCTTGTTGA 4140

AGTTTTTTAA AAAAAAGCTA AATTACATAG TCTTAGGCAT TAACATGTTT GTGGAAGAAT 4200

ATAGCACACA TATATTGTAT CATTTGAGTG AATATTCCCA AATAGGCATT CTAGGCTCTA 4260

TTTAACTGAG TCACACTGCA TAGGAATTTA GAACCTAACT TTTATAGGTT ATCAAAACTG 4320

TTGCCTCCAT TGCACAATTT TGTCCTAATA CATACATGGA GACTTTGTGG GGCATGTTAA 4380

GTTACAGTTT GCACAAGTTC ATCTCATTTG TATTCCATTG ATTTTTTTTT TGTTCTAAAC 4440

ATTTTTTCTT CAAACAGTAT ATAACTTTTT TTAGGGGATT TTTTTTNNNN NNNNNNNNNN 4500

NNTCTGACGA TTTCCATTTG TCAAAAAGTA ATGATTTCTT GATAATTATG TAGTAATGTT 4560

TTTAAGAACC CAGCAGTTAC CTTAAAGCTG AATTTATATT TAATAACTTC TGTGTTAATA 4620

CTGGATAGCA TGAATTCTGC ATTGAGAAAC TGAATAGNNN NNNNNNNNNN NNNNNNNNNN 4680

NNNNNNNNNN NNNNNNNNCA TGAGTTCTTG AAGAATAGTC ATAACTAGAT TAAGATCTGT 4740

GTTTTAGTTT AATAGTTTGA AGTGCCTGTT TGGGATAATG ATAGGTAATT TAGATGAATT 4800

TAGGGGGAAA AAAAGTTATC TGCAGAAATG TTGAGGGCCC ATCTCTCCCC ACACACCCAC 4860

ATAGAGCTAA CTGGGTTACA GTGTTTTATC CGAAAGTTTC CAATTCCACT GTCTTGTGTT 4920

TTCATGTTGA AAATACTTTT GCATTTTTCC TTTGAGTGCC AATTTCTTAC TAGTACTATT 4980

TCTTAATGTA ACATGTTTAC CTGGAATGTA TTTTAACTAT TTTTGTATAG TGTAAACTGA 5040

AACATGCACA TTTTGTACAT TGTGCTTTCT TTTGTGGGAC ATATGCAGTG TGATCCAGTT 5100

GTTTTCCATC ATTTGGTTGC GCTGACCTAG GAATGTTGGT CATATCAAAC ATTAAAAATG 5160

ACCACTCTTT TAATTGAAAT TAACTTTTAA ATGTTTATAG GAGTATGTGC TGTGAAGTGA 5220

TCTAAAATTT GTAATATTTT TGTCATGAAC TGTACTACTC CTAATTATTG TAATGTAATA 5280

AAAATAGTTA CAGTGACAAA AAAAAAAANN NN 5312 [SEQ ID NO: 1709]。

[0203] 下文显示部分人序列和 Cyno 序列之间的比对结果。

[0204]

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Human 113 AGGCACTGAAGGCGGCGGCGGGGCCAGAGGCTCAGCGGCTCCCAGGTGCGGGAGAGAGGC 172
          ||||||||||||||||||||||||||||||||||||||||||||| || ||||||||||
Cyno  113 AGGCACTGAAGGCGGCGGCGGGGCCAGAGGCTCAGCGGCTCCCCGGGGCGGGAGAGAGNN 172

Human 173 CTGCTGAAAATGACTGAATATAAACTTGTGGTAGTTGGAGCTGGTGGCGTAGGCAAGAGT 232
                                    ||||||||||||||| ||||||||||||
Cyno  173 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAGTTGGAGCTGGTGGGGTAGGCAAGAGT 232

Human 233 GCCTTGACGATACAGCTAATTCAGAATCATTTTGTGGACGAATATGATCCAACAATAGAG 292
          ||||||||      ||||||||||||||||||||||||||||||||||||||||||||
Cyno  233 GCCTTGACNNNNNNGCTAATTCAGAATCATTTTGTGGACGAATATGATCCAACAATAGAG 292

Human 293 GATTCCTACAGGAAGCAAGTAGTAATTGATGGAGAAACCTGTCTCTTGGATATTCTCGAC 352
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  293 GATTCCTACAGGAAGCAAGTAGTAATTGATGGAGAAACCTGTCTCTTGGATATTCTCGAC 352

Human 353 ACAGCAGGTCAAGAGGAGTACAGTGCAATGAGGGACCAGTACATGAGGACTGGGGAGGGC 412
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  353 ACAGCAGGTCAAGAGGAGTACAGTGCAATGAGGGACCAGTACATGAGGACTGGGGAGGGC 412
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[0205]

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Human 413 TTTCTTTGTGTATTTGCCATAAATAATACTAAATCATTTGAAGATATTCACCATTATAGA 472
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  413 TTTCTTTGTGTATTTGCCATAAATAATACTAAATCATTTGAAGATATTCACCATTATAGA 472

Human 473 GAACAAATTAAAAGAGTTAAGGACTCTGAAGATGTACCTATGGTCCTAGTAGGAAATAAA 532
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  473 GAACAAATTAAAAGAGTTAAGGACTCTGAAGATGTACCTATGGTCCTAGTAGGAAATAAA 532

Human 533 TGTGATTTGCCTTCTAGAACAGTAGACACAAAACAGGCTCAGGACTTAGCAAGAAGTTAT 592
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  533 TGTGATTTGCCTTCTAGAACAGTAGACACAAAACAGGCTCAGGACTTAGCAAGAAGTTAC 592

Human 593 GGAATTCCTTTTATTGAAACATCAGCAAAGACAAGACAGGGTGTTGATGATGCCTTCTAT 652
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  593 GGAATTCCTTTTATTGAAACATCAGCAAAGACAAGACAGGGTGTTGATGATGCCTTCTAT 652

Human 653 ACATTAGTTCGagaaattcgaaaacataaagaaaagatgagcaaagatggtaaaaagaaG 712
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  653 ACATTAGTTCGAGAAATTCGAAAACATAAAGAAAAGATGAGCAAAGATGGTAAAAAGAAG 712

Human 713 aaaaagaagtcaaagacaaagTGTGTAATTATGTAAATACAATTTGTACTTTTTTCTTAA 772
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  713 AAAAAGAAGTCAAAGACAAAGTGTGTAATTATGTAAATACAATTTGTACTTTTTTCTTAA 772

Human 773 GGCATACTAGTACAAGTGGTAATTTTTGTACATTACACTAAATTATTAGCATTTGTTTTA 832
          ||||||||||||  ||||||||||||||||||||||||||||||||||||||||||||
Cyno  773 GGCATACTAGTAAAAGTGGTAATTTTTGTACATTACACTAAATTATTAGCATTTGTTTTA 832

Human 833 GCATTACCTAAttttttttCCTGCTCCATGCAGACTGTTAGCTTTTACCTTAAATGCTTAT 892
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  833 GCATTACCTAATTTTTTTCCTGCTCCATGCAGACTGTTAGCTTTTACCTTAAATGCTTAT 892

Human 893 TTTAAAATGACAGTGGAAGtttttttttCCTCTAAGTGCCAGTATTCCCAGAGTTTTGGT 952
          ||||||||||||||||||  ||||||||||||||||||||||||||||||||||||| |
Cyno  893 TTTAAAATGACAGTGGAAGCTTTTTTTCCTCTAAGTGCCAGTATTCCCAGAGTTTTGAT 952

Human 953 TTTTGAACTAGCAATGCCTGTGAAAAAGAAACTGAATACCTAAGATTTCTGTCTTGGGGT 1012
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  953 TTTTGAACTAGCAATGCCTGTGAAAAAGAAACTGAATACCTAAGATTTCTGTCTTGGGGT 1012

Human 1013 TTTTGGTGCATGCAGTTGATTACTTCTTATTTTTCTTACCAATTGTGAATGTTGGTGTGA 1072
           |||||||||
Cyno  1013 TTTTGGTGCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 1072

Human 1073 AACAAATTAATGAAGCTTTTGAATCATCCCTATTCTGTGTTTTATCTAGTCACATAAATG 1132
               |||||||||||||| ||||||||||||||||||||||||||||||||||||||||
Cyno  1073 NNNNAATTAATGAAGCTTCTGAATCATCCCTATTCTGTGTTTTATCTAGTCACATAAATG 1132

Human 1133 GATTAATTACTAATTTCAGTTGAGACCTTCTAATTGGTTTTTACTGAAACATTGAGGGAA 1192
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  1133 GATTAATTACTAATTTCAGTTGAGACCTTCTAATTGGTTTTTACTGAAACATTGAGGGAA 1192

Human 1193 CACAAATTTATGGGCTTCCTGATGATGATTCTTCTAGGCATCATGTCCTATAGTTTGTCA 1252
           ||||||                          ||||||||||||||||||||||||||||
Cyno  1193 CACAAANNNNNNNNNNNNNNNNNNNNNNNNNNTCTAGGCATCATGTCCTATAGTTTGTCA 1252

Human 1253 TCCCTGATGAATGTAAAGTTACACTGTTCACAAAGGTTTTGTCTCCTTTCCACTGCTATT 1312
           ||||||||||||||||||||||||||||||||||||||||||  ||||||||||||||||
Cyno  1253 TCCCTGATGAATGTAAAGTTACACTGTTCACAAAGGTTTTGTTCCCTTTCCACTGCTATT 1312
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[0206]

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Human 1313 AGTCATGGTCACTCTCCCCAAAATATTATATTTTTTCTATaaaaagaaaaaaatggaaaA 1372
           ||||||||||||||||||                                  |||||||
Cyno  1313 AGTCATGGTCACTCTCCCCGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNTGGAAAA 1372

Human 1373 aaaTTACAAGGCAATGGAAACTATTATAAGGCCATTTCCTTTTCACATTAGATAAATTAC 1432
           |||||||||| |||||||||||||||||||||| |||||||||||||||||||||||||
Cyno  1373 AAATTACAAGTCAATGGAAACTATTATAAGGCCGTTTCCTTTTCACATTAGATAAATTAC 1432

Human 1433 TATAAAGACTCCTAATAGCTTTTCCTGTTAAGGCAGACCCAGTATGAAATGGGGATTATT 1492
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  1433 TATAAAGACTCCTAATAGCTTTTCCTGTTAAGGCAGACCCAGTATGAAATGGGGATTNNN 1492

Human 1493 ATAGCAACCATTTTGGGGCTATATTTACATGCTACTAAATTTTTATAATAATTGAAAAGA 1552
                                               ||||||||||||||||||| 1
Cyno  1493 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAATTTTTATAATAATTGAAATAA 1552

Human 1553 TTTTAACAAGTATAAAAAATTCTCATAGGAATTAAATGTAGTCTCCCTGTGTCAGACTGC 1612
           |||||||| ||||||||||||||||||||||||||||||||||||||||||||||| |||
Cyno  1553 TTTTAACATGTATAAAAAATTCTCATAGGAATTAAATGTAGTCTCCCTGTGTCAGATTGC 1612

Human 1613 TCTTTCATAGTATAACTTTAAATCTTTTCTTCAACTTGAGTCTTTGAAGATAGTTTTAAT 1672
           |||||||||||||||||||||||||||||||||||| |||||||||| ||||||||||
Cyno  1613 TCTTTCATAGTATAACTTTAAATCTTTTCTTCAACTTCAGTCTTTGAAGGTAGTTTTAAT 1672

Human 1673 TCTGCTTGTGACATTAAAAGATTATTTGGGCCAGTTATAGCTTATTAGGTGTTGAAGAGA 1732
           |||||||||||||||||||||||||||||||||||||||||||| ||||||||||||||
Cyno  1673 TCTGCTTGTGACATTAAAAGATTATTTGGGCCAGTTATAGCTTAGTAGGTGTTGAAGAGA 1732

Human 1733 CCAAGGTTGCAAGGCCAGGCCCTGTGTGAACCTTTGAGCTTTCATAGAGAGTTTCACAGC 1792
           |||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  1733 CCAAGGTTGCATGGCCAGGCCCTGTGTGAACCTTTGAGCTTTCATAGAGAGTTTCACAGC 1792

Human 1793 ATGGACTGTGTCCCCACGGTCATCCAGTGTTGTCATGCATTGGTTAGTCAAAATGGGGAG 1852
           |||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
Cyno  1793 ATGGACTGTGTCCCCATGGTCATCCAGTGTTGTCATGCATTGGTTAGTCAAAATGGGGAG 1852

Human 1853 GGACTAGGGCAGTTTGGATAGCTCAACAAGATACAATCTCACTCTGTGGTGGTCCTGCTG 1912
           |||||||| |||||||||||| |||||||||||| |||||||||||||||||||||||
Cyno  1853 GGACTAGGACAGTTTGGATAGGTCAACAAGATACATTCTCACTCTGTGGTGGTCCTGCTG 1912

Human 1913 ACAAATCAAGAGCATTGCTTTTGTTTCTTAAGAAAACAAACTCTTTTTTAAAAATTACTT 1972
           |||||||||||||||||||||||||| |||||||| ||||||||||||||||||||||
Cyno  1913 ACAAATCAAGAGCATTGCTTTTGTTTTTTAAGAAAATGAACTCTTTTTTAAAAATTACTT 1972

Human 1973 TTAAATATTAACTCAAAAGTTGAGATTTTGGGGTGGTGGTGTGCCAAGACATTAAttttT 2032
           |||||||||||||||||||||||||||||||| |||||| ||||||||||||||||||
Cyno  1973 TTAAATATTAACTCAAAAGTTGAGATTTTGGGGGGGTGGTATGCCAAGACATTAATTTTT 2032

Human 2033 ttttAAACAATGAAGTGAAAAAGTTTTACAATCTCTAGGTTTGGCTAGTTCTCTTAACA 2092
           ||                 ||||||||||||||||||||||||||||||||||||
Cyno  2033 TTNNNNNNNNNNNNNNNNNNAAGTTTTACAATCTCTAGGTTTGGCTAGTTCTCTTAACA 2092

Human 2093 CTGGTTAAATTAACATTGCATAAACACTTTTCAAG 2127 [SEQ ID NO: 1710]
           |||||||||||||||||| ||||||||||||||||
Cyno  2093 CTGGTTAAATTAACATTTCATAAACACTTTTCAAG 2127 [SEQ ID NO: 1711]


Human 2184  atttaaaatgttacttatttttaaaataaatGAAGTGAGATGGCATGGTGAGGTGAAAGTA 2243
            ||||||||||||||||||||||||||||| ||||| ||||||||||||||||||||||||||
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[0207]

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Cyno   2184  ATTTAAAATGTTACTTATTTTAAAATATATGAAATGAGATGGCATGGTGAGGTGAAAGTA 2243

Human  2244  TCACTGGACTAGGAAGAAGGTGACTTAGGTTCTAGATAGGTGTCTTTTAGGACTCTGATT 2303
              ||||||||||| |||||||||||||||||||||||||| ||||||||||||||||||||
Cyno   2244  TCACTGGACTANNAAGAAGGTGACTTAGGTTCTAGATAGTTGTCTTTTAGGACTCTGATT 2303

Human  2304  TTGAGGACATCACTTACTATCCATTTCTTCATGTTAAAAGAAGTCATCTCAAACTCTTAG 2363
              ||||||||||||||||||||||||||||||||||||||
Cyno   2304  TTGAGGACATCACTTACTATCCATTTCTTCATGTTAANNNNNNNNNNNNNNNNNNNNNN 2363

Human  2364  tttttttttttttACAACTATGTAATTTATATTCCATTTACATAAGGATACACTTATTTGT 2423
                     |||||||||||||||| |||||||||| ||||||| ||||||||||||||||||
Cyno   2364  NNNNNNNTTTTTACAACTATGTGATTTATATTCCGTTTACATGAGGATACACTTATTTGT 2423

Human  2424  CAAGCTCAGCACAATCTGTAAATTTTTAACCTATGTTACACCATCTTCAGTGCCAGTCTT 2483
              |||||||||||||||||  ||||||||||||||||||||||||||||||||||| ||||
Cyno   2424  CAAGCTCAGCACAATCTAAAAATTTTTAACCTATGTTACACCATCTTCAGTGCCAATCTT 2483

Human  2484  GGGCAAAATTGTGCAAGAGGTGAAGTTTATATTTGAATATCCATTCTCGTTTTAGGACTC 2543
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno   2484  GGGCAAAATTGTGCAAGAGGTGAAGTTTATATTTGAATATCCATTCTCGTTTTAGGACTC 2543

Human  2544  TTCTTCCATATTAGTGTCATCTTGCCTCCCTACCTTCCACATGCCCCATGACTTGATGCA 2603
              | ||||||| |||||||||||||||| ||||||||||||||||||||||||||||||||
Cyno   2544  TCCTTCCATGTTAGTGTCATCTTGCCTGCCTACCTTCCACATGCCCCATGACTTGATGCA 2603

Human  2604  GTTTTAATACTTGTAATTCCCCTAACCATAAGATTTACTGCTGCTGTGGATATCTCCATG 2663
              |||||||||||| |||||||||||||||||||||||||||||| ||||||||||||||
Cyno   2604  GTTTTAATACTTCTAATTCCCCTAACCATAAGATTTACTGCTGCTATGGATATCTCCATG 2663

Human  2664  AAGTTTTCCCACTGAGTCACATCAGAAATGCCCTACATCTTATTTCCTCAGGGCTCAAGA 2723
              ||||||||||                                              ||
Cyno   2664  AAGTTTTCCCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGA 2723

Human  2724  GAATCTGACAGATACCATAAAGGGATTTGACCTAATCACTAATTTTCAGGTGGTGGCTGA 2783
              |||||||||||||||||||| |||||||||||||||||||||||||||||||||| ||
Cyno   2724  GAATCTGACAGATACCATAATGGGATTTGACCTAATCACTAATTTTCAGGTGGTGGCCGA 2783

Human  2784  TGCTTTGAACATCTCTTTGCTGCCCAATCCATTAGCGACAGTAGGATTTTTCAAACCTGG 2843
              | ||||||| || ||| ||||||||||||||||||||||||||||||||||| ||||||
Cyno   2784  TCCTTTGAAAATATCTCTGCTGCCCAATCCATTAGCGACAGTAGGATTTTTCAGACCTGG 2843

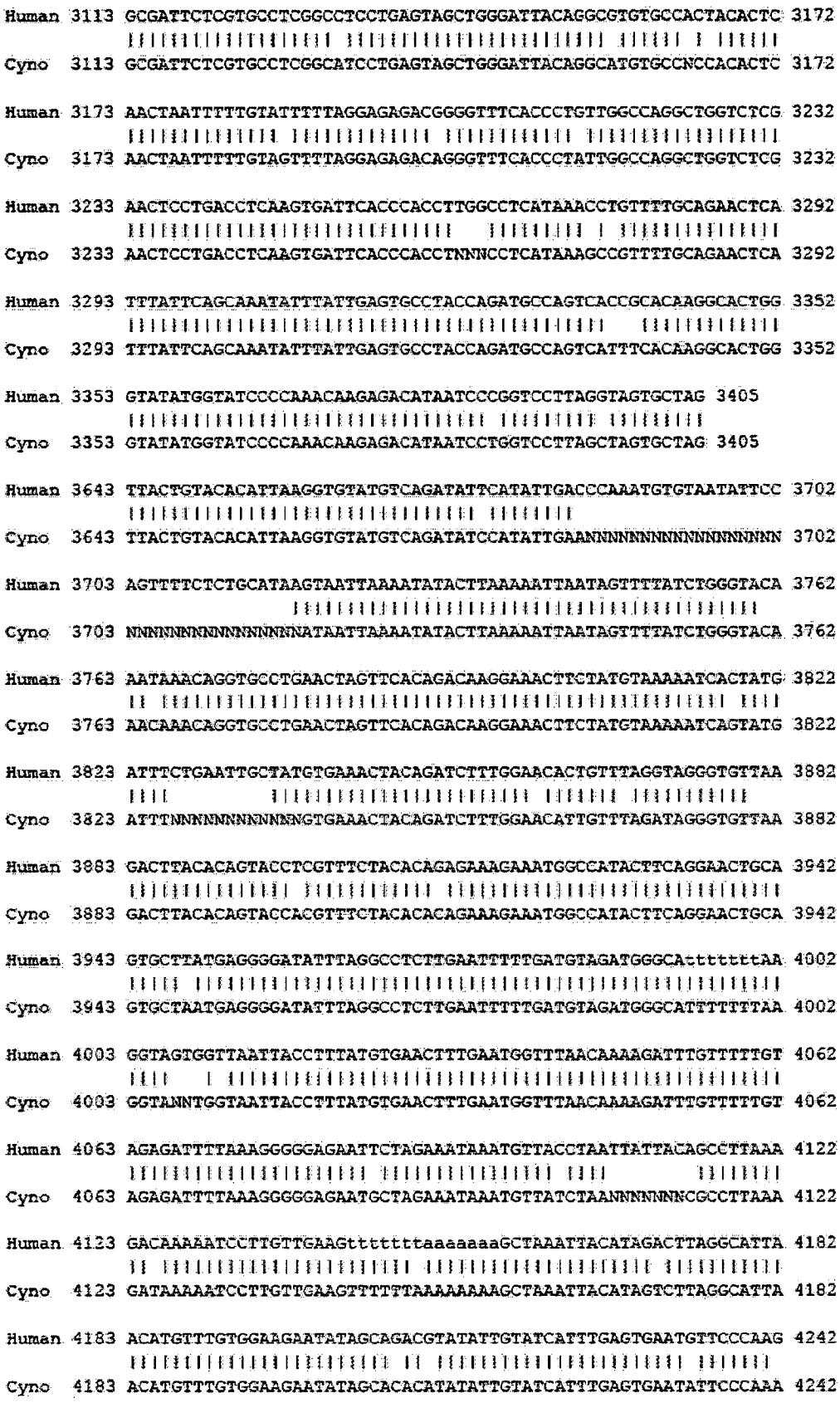
Human  2844  TATGAATAGACAGAACCCTATCCAGTGGAAGGAGAATTTAATAAAGATAGTGCTGAAAGA 2903
              |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||| |
Cyno   2844  TATGAATAGACAGAACCCTATCCAGTGGAAGGAGAATTTAATAAAGATAGTACTGAAATA 2903

Human  2904  ATTCCTTAGGTAATCTATAACTAGGACTACTCCTGGTAACAGTAATACATTCCATTGTTT 2963
              |||||| |||||||||| ||||||||||||||||||||||||||||||||||||||||
Cyno   2904  ATTCCTAAGGTAATCTACAACTAGGACTACTCCTGGTAACAGTAATACATTCCATTGTTT 2963

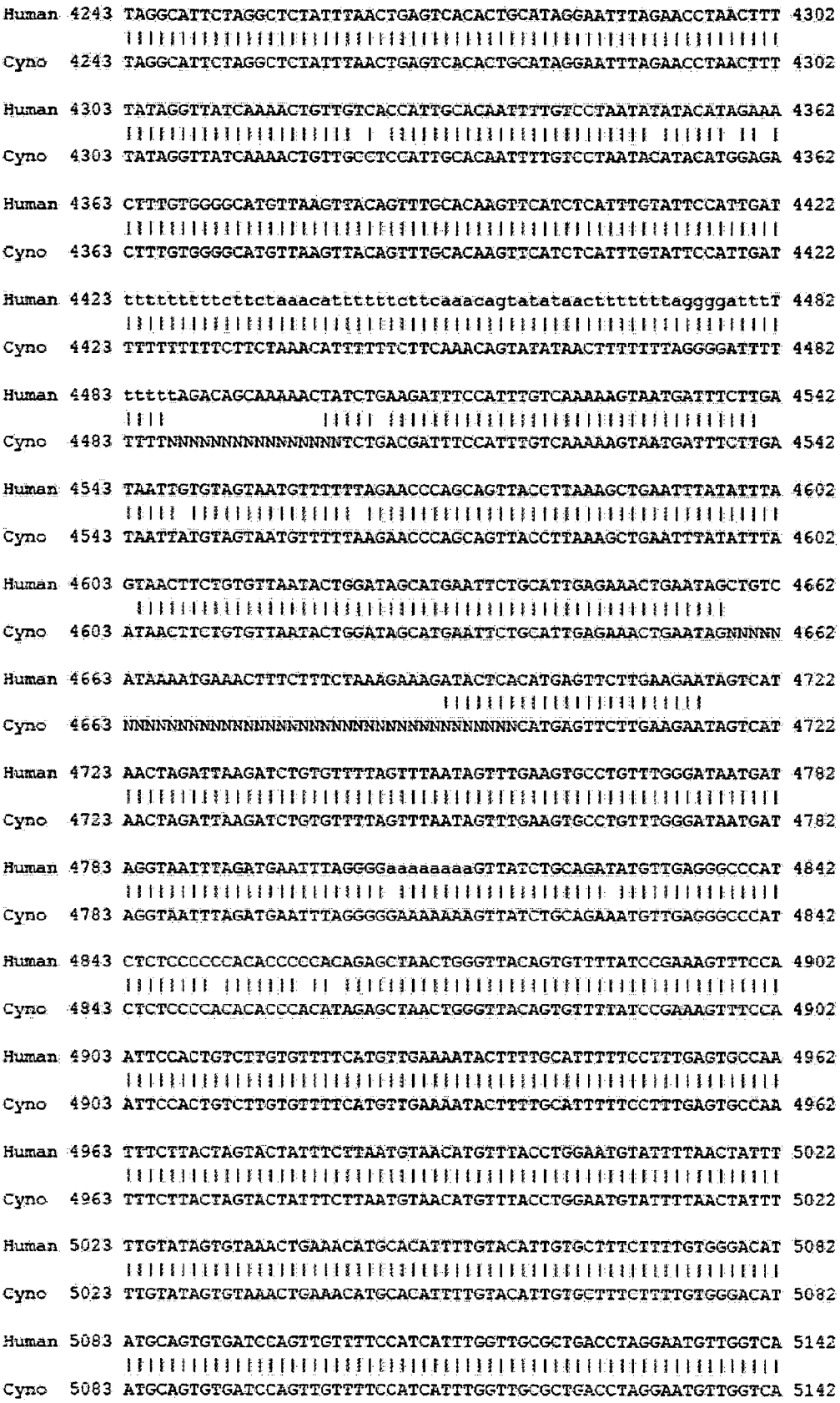
Human  2964  TAGTAACCAGAAAT 2977 [SEQ ID NO: 1712]
              |||||||||||||
Cyno   2964  TAGTAACCAGAAAT 2977 [SEQ ID NO: 1713]


Human  3053  CCAGGCTGGAATGCAGTGGCGCCATCTCAGCTCACTGCAACCTCCATCTCCCAGGTTCAA 3112
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno   3053  CCAGGCTGGAATGCAGTGGCGCCATCTCAGCTCACTGCAACCTCCATCTCCCAGGTTCAA 3112
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[0208]


Human 3113 GCGATTCTCGTGCCTCGGCCTCCTGAGTAGCTGGGATTACAGGCGTGTGCCACTACACTC 3172
Cyno 3113 GCGATTCTCGTGCCTCGGCATCCTGAGTAGCTGGGATTACAGGCATGTGCCNCCACACTC 3172
Human 3173 AACTAATTTTTGTATTTTTAGGAGAGACGGGGTTTCACCCTGTTGGCCAGGCTGGTCTCG 3232
Cyno 3173 AACTAATTTTTGTAGTTTTAGGAGAGACAGGGTTTCACCCTATTGGCCAGGCTGGTCTCG 3232
Human 3233 AACTCCTGACCTCAAGTGATTCACCCACCTTGGCCTCATAAACCTGTTTTGCAGAACTCA 3292
Cyno 3233 AACTCCTGACCTCAAGTGATTCACCCACCTNNNCCTCATAAAGCCGTTTTGCAGAACTCA 3292
Human 3293 TTTATTCAGCAAATATTTATTGAGTGCCTACCAGATGCCAGTCACCGCACAAGGCACTGG 3352
Cyno 3293 TTTATTCAGCAAATATTTATTGAGTGCCTACCAGATGCCAGTCATTTCACAAGGCACTGG 3352
Human 3353 GTATATGGTATCCCCAAACAAGAGACATAATCCCGGTCCTTAGGTAGTGCTAG 3405
Cyno 3353 GTATATGGTATCCCCAAACAAGAGACATAATCCTGGTCCTTAGCTAGTGCTAG 3405
Human 3643 TTACTGTACACATTAAGGTGTATGTCAGATATTCATATTGACCCAAATGTGTAATATTCC 3702
Cyno 3643 TTACTGTACACATTAAGGTGTATGTCAGATATCCATATTGAANNNNNNNNNNNNNNNNNN 3702
Human 3703 AGTTTTCTCTGCATAAGTAATTAAAATATACTTAAAAATTAATAGTTTTATCTGGGTACA 3762
Cyno 3703 NNNNNNNNNNNNNNNNATAATTAAAATATACTTAAAAATTAATAGTTTTATCTGGGTACA 3762
Human 3763 AATAAACAGGTGCCTGAACTAGTTCACAGACAAGGAAACTTCTATGTAAAAATCACTATG 3822
Cyno 3763 AACAAACAGGTGCCTGAACTAGTTCACAGACAAGGAAACTTCTATGTAAAAATCAGTATG 3822
Human 3823 ATTTCTGAATTGCTATGTGAAACTACAGATCTTTGGAACACTGTTTAGGTAGGGTGTTAA 3882
Cyno 3823 ATTTNNNNNNNNNNNNGTGAAACTACAGATCTTTGGAACATTGTTTAGATAGGGTGTTAA 3882
Human 3883 GACTTACACAGTACCTCGTTTCTACACAGAGAAAGAAATGGCCATACTTCAGGAACTGCA 3942
Cyno 3883 GACTTACACAGTACCACGTTTCTACACACAGAAAGAAATGGCCATACTTCAGGAACTGCA 3942
Human 3943 GTGCTTATGAGGGGATATTTAGGCCTCTTGAATTTTTGATGTAGATGGGCAttttttttAA 4002
Cyno 3943 GTGCTAATGAGGGGATATTTAGGCCTCTTGAATTTTTGATGTAGATGGGCATTTTTTTTAA 4002
Human 4003 GGTAGTGGTTAATTACCTTTATGTGAACTTTGAATGGTTTAACAAAAGATTTGTTTTTGT 4062
Cyno 4003 GGTANNTGGTAATTACCTTTATGTGAACTTTGAATGGTTTAACAAAAGATTTGTTTTTGT 4062
Human 4063 AGAGATTTTAAAGGGGGAGAATTCTAGAAATAAATGTTACCTAATTATTACAGCCTTAAA 4122
Cyno 4063 AGAGATTTTAAAGGGGGAGAATGCTAGAAATAAATGTTATCTAANNNNNNNCGCCTTAAA 4122
Human 4123 GACAAAAATCCTTGTTGAAGttttttaaaaaaaGCTAAATTACATAGACTTAGGCATTA 4182
Cyno 4123 GATAAAAATCCTTGTTGAAGTTTTTTAAAAAAAAGCTAAATTACATAGTCTTAGGCATTA 4182
Human 4183 ACATGTTTGTGGAAGAATATAGCAGACGTATATTGTATCATTTGAGTGAATGTTCCCAAG 4242
Cyno 4183 ACATGTTTGTGGAAGAATATAGCACACATATATTGTATCATTTGAGTGAATATTCCCAAA 4242

[0209]


Human 4243 TAGGCATTCTAGGCTCTATTTAACTGAGTCACACTGCATAGGAATTTAGAACCTAACTTT 4302
Cyno 4243 TAGGCATTCTAGGCTCTATTTAACTGAGTCACACTGCATAGGAATTTAGAACCTAACTTT 4302
Human 4303 TATAGGTTATCAAAACTGTTGTCACCATTGCACAATTTTGTCCTAATATATACATAGAAA 4362
Cyno 4303 TATAGGTTATCAAAACTGTTGCCTCCATTGCACAATTTTGTCCTAATACATACATGGAGA 4362
Human 4363 CTTTGTGGGGCATGTTAAGTTACAGTTTGCACAAGTTCATCTCATTTGTATTCCATTGAT 4422
Cyno 4363 CTTTGTGGGGCATGTTAAGTTACAGTTTGCACAAGTTCATCTCATTTGTATTCCATTGAT 4422
Human 4423 ttttttttttcttctaaacatttttttcttcaaacagtatataacttttttttaggggatttT 4482
Cyno 4423 TTTTTTTTTTCTTCTAAACATTTTTTCTTCAAACAGTATATAACTTTTTTTTAGGGGATTTT 4482
Human 4483 tttttAGACAGCAAAAACTATCTGAAGATTTCCATTTGTCAAAAAGTAATGATTTCTTGA 4542
Cyno 4483 TTTTNNNNNNNNNNNNNNNNTCTGACGATTTCCATTTGTCAAAAAGTAATGATTTCTTGA 4542
Human 4543 TAATTGTGTAGTAATGTTTTTTAGAACCCAGCAGTTACCTTAAAGCTGAATTTATATTTA 4602
Cyno 4543 TAATTATGTAGTAATGTTTTTTAAGAACCCAGCAGTTACCTTAAAGCTGAATTTATATTTA 4602
Human 4603 GTAACTTCTGTGTTAATACTGGATAGCATGAATTCTGCATTGAGAAACTGAATAGCTGTC 4662
Cyno 4603 ATAACTTCTGTGTTAATACTGGATAGCATGAATTCTGCATTGAGAAACTGAATAGNNNNN 4662
Human 4663 ATAAAATGAAACTTTCTTTCTAAAGAAAGATACTCACATGAGTTCTTGAAGAATAGTCAT 4722
Cyno 4663 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCATGAGTTCTTGAAGAATAGTCAT 4722
Human 4723 AACTAGATTAAGATCTGTGTTTTAGTTTAATAGTTTGAAGTGCCTGTTTGGGATAATGAT 4782
Cyno 4723 AACTAGATTAAGATCTGTGTTTTAGTTTAATAGTTTGAAGTGCCTGTTTGGGATAATGAT 4782
Human 4783 AGGTAATTTAGATGAATTTAGGGGaaaaaaaaGTTATCTGCAGATATGTTGAGGGCCCAT 4842
Cyno 4783 AGGTAATTTAGATGAATTTAGGGGGAAAAAAAGTTATCTGCAGAAATGTTGAGGGCCCAT 4842
Human 4843 CTCTCCCCCCACACCCCCACAGAGCTAACTGGGTTACAGTGTTTTATCCGAAAGTTTCCA 4902
Cyno 4843 CTCTCCCCACACACCCACATAGAGCTAACTGGGTTACAGTGTTTTATCCGAAAGTTTCCA 4902
Human 4903 ATTCCACTGTCTTGTGTTTTCATGTTGAAAATACTTTTGCATTTTTCCTTTGAGTGCCAA 4962
Cyno 4903 ATTCCACTGTCTTGTGTTTTCATGTTGAAAATACTTTTGCATTTTTCCTTTGAGTGCCAA 4962
Human 4963 TTTCTTACTAGTACTATTTCTTAATGTAACATGTTTACCTGGAATGTATTTTAACTATTT 5022
Cyno 4963 TTTCTTACTAGTACTATTTCTTAATGTAACATGTTTACCTGGAATGTATTTTAACTATTT 5022
Human 5023 TTGTATAGTGTAAACTGAAACATGCACATTTTGTACATTGTGCTTTCTTTTGTGGGACAT 5082
Cyno 5023 TTGTATAGTGTAAACTGAAACATGCACATTTTGTACATTGTGCTTTCTTTTGTGGGACAT 5082
Human 5083 ATGCAGTGTGATCCAGTTGTTTTCCATCATTTGGTTGCGCTGACCTAGGAATGTTGGTCA 5142
Cyno 5083 ATGCAGTGTGATCCAGTTGTTTTCCATCATTTGGTTGCGCTGACCTAGGAATGTTGGTCA 5142

[0210]

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Human 5143 TATCAAACATTAAAAATGACCACTCTTTTAATTGAAATTAACTTTTAAATGTTTATAGGA 5202
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  5143 TATCAAACATTAAAAATGACCACTCTTTTAATTGAAATTAACTTTTAAATGTTTATAGGA 5202

Human 5203 GTATGTGCTGTGAAGTGATCTAAAATTTGTAATATTTTTGTCATGAACTGTACTACTCCT 5262
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Cyno  5203 GTATGTGCTGTGAAGTGATCTAAAATTTGTAATATTTTTGTCATGAACTGTACTACTCCT 5262

Human 5263 AATTATTGTAATGTAATAAAAATAGTTACAGTGACaaaaaaaaaaA 5308
           ||||||||||||||||||||||||||||||||||||||||||||
Cyno  5263 AATTATTGTAATGTAATAAAAATAGTTACAGTGACAAAAAAAAAAA 5308

Human [SEQ ID NO: 1714]

Cyno  [SEQ ID NO: 1715]
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[0211] KRAS 序列中的小写字母是关于低复杂性序列的 NCBI 惯例。匹配算法在计算匹配分值时通常会排除这些序列，因为它们趋向于同基因组中的大量事务匹配。

[0212] 在一个实施方案中，本公开的KRAS RNAi剂包含在人、大鼠和食蟹猴这所有三种的KRAS mRNA中相同的序列。这种物种间的序列同一性有利于在人类试验之前的动物试验，因为无需因靶序列的物种间差异而对 RNAi 的序列进行修饰。在一个实施方案中，KRAS RNAi剂包含在人、小鼠和食蟹猴 KRAS mRNA 中相同的序列。在多种实施方案中，KRAS RNAi 剂包含在人和小鼠、人和大鼠和 / 或人和食蟹猴中相同的序列。

[0213] 针对 KRAS 的 RNAi 剂的额外实施方案

[0214] 本公开涉及靶向于人 KRAS 的 RNAi 剂。在一个实施方案中，KRAS RNAi 剂包含不匹配任何其它 mRNA 或基因序列的序列。在一个实施方案中，KRAS RNAi 剂包含与全部其它已知的非 KRAS mRNA 或基因差异至少 0、1、2 或 3 个核苷酸的序列。KRAS RNAi 序列与任何其它基因序列间错配数量的增加可以降低“脱靶效应”或靶向于非靶基因（例如，不是 KRAS 的基因）的 RNAi 剂的数量。

[0215] 在一个实施方案中，本公开的 KRAS RNAi 剂被施用给需要其的患者（例如，患有 KRAS 相关疾病的患者）。

[0216] 还可以向患者施用一种以上的对 KRAS 特异性的 RNAi 剂。在一个实施方案中，本公开的 KRAS RNAi 剂可任选地与一种或多种适于该疾病的额外的药剂一起施用。在一个实施方案中，本公开的KRAS RNAi剂可任选地与任何其它适宜的额外治疗一起施用，其中所述的额外治疗可以是组合物（例如，可治疗 KRAS 相关疾病例如癌症的治疗的另一种活性剂）或方法（例如，如果 KRAS 相关疾病是癌症的话，除去肿瘤的手术）。

[0217] RNAi 剂和额外的疾病疗法可以按任意顺序、同时、并行、分别或依次地施用，或随时间推移以一个或多个剂量施用。

[0218] 额外的定义

[0219] 出于便利，下文提供在本说明书、实施例和所附权利要求中使用的某些术语和短语的含义。如果本说明书的其它部分中某术语的用途和这个章节中所提供的其定义之间存在明显的不一致性，则这个章节中的定义应当占优。

[0220] 在整个申请文件中所用的冠词例如“一个”和“一种”是指一个或一个以上（至少一个）该冠词的语法宾语。

[0221] RNAi 剂

[0222] 在一个实施方案中，本公开涉及 KRAS RNAi 剂或包含至少一种与 KRAS 核酸（或其部分）互补的反义核酸序列的其它组合物，或编码 shRNA 的重组表达载体或包含可以作为如下文定义的 RNAi 发挥作用的反义核酸的组合物。

[0223] 如本文所用，“反义”核酸包含与编码 KRAS 蛋白的“有义”核酸互补（例如与双链 DNA 分子的编码链互补、与 mRNA 互补或与 KRAS 基因或核酸的编码链互补）的核苷酸序列。

[0224] RNAi 剂包括但不限于 siRNA（小干扰性 RNA）、dsRNA（双链 RNA）、shRNA（短发夹 RNA）和 miRNA（微 RNA）。

[0225] 在多种实施方案中，本公开涉及任何包含与本文所公开的任何 DNA 序列相对应的 RNA 序列的 RNAi 剂（例如，其中的 DNA 核苷酸被相应的 RNA 核苷酸代替，例如 DNA 中的 T 被 RNA 中的 U 代替，并且在糖 - 磷酸酯主链中用核糖代替脱氧核糖）。

[0226] 在一个实施方案中，RNAi 包含单链。这种单链 RNAi 剂寡核苷酸或多核苷酸可以包含有义链或反义链，如 Sioud 2005 J.Mol.Biol.348:1079-1090 及其中的参考文献所描述。因此，本公开涵盖具有单链的 RNAi 剂，所述单链包含本文所公开的 RNAi 剂的有义链或反义链。本公开还涵盖包含单链的 RNAi 剂，其中的单链同时包含本文所公开的 RNAi 剂的有义链和反义链，例如，其中的链是连续的、由环连接的或通过其它方式连接的。这样的分子的例子包括具有在有义序列和反义序列之间的发夹的那些（例如 shRNA）。

[0227] 本公开的 RNAi 剂靶向（例如，结合于、复性至、杂交等）KRAS mRNA。对 KRAS 特异性的 RNAi 剂的使用导致 KRAS 活性、水平和 / 或表达的减少，例如，靶基因或靶序列的“敲减”或“敲除”。在一个实施方案中，在病理状态以 KRAS 的过度表达或活性过高为特征的情况下，针对 KRAS 的 RNAi 剂的施用可敲减 KRAS 靶至足以提供更为正常的或治疗性的 KRAS 活性或表达水平。

[0228] 在一个实施方案中，RNAi 包含单链（如 shRNA，如本文所述）。

[0229] 在多种实施方案中，一条链或两条链包含切口，即磷酸酯主链中断裂或缺失的键，从而使至少有一个核苷酸亚基没有与给定序列中相邻的核苷酸亚基共价连接。在某些实施方案中，过客链包含切口（参见，例如 WO2007/107162）。在多种实施方案中，一条链或两条链包含一个或多个缺口，例如，其中至少有一个完整的核苷酸亚基从所公开的序列中缺失了。当有义序列或反义序列包含缺口时，该链被想像为包含两个独立的寡核苷酸。

[0230] 特别有用的 siRNA 包括可以与 KRAS mRNA 的某些区域特异性结合并且具有以下一种或多种性质的那些：在 KRAS 的编码区段结合；在 5’非翻译区和编码区段的起始密码子的交界处或其附近结合；在 mRNA 的翻译起始位点处或其附近结合；在外显子和内含子的交界处或其附近结合；与其它基因的 mRNA 或转录体少量结合或不结合（少量或无“脱靶效应”）；在不是双链区或茎区（例如，在环部分或单链部分中）的一个区域或多个区域内或其附近与 KRAS mRNA 结合；激发少量免疫原性或不激发免疫原性；在 KRAS mRNA 序列中各个动物物种（包括人、小鼠、大鼠、食蟹猴等）之间保守的区段内结合，原因是保守序列的存在有利于使用各种实验室动物进行试验；与 mRNA 的双链区域结合；与 AT 丰富区域结合（例如，至少约 50％、51％、52％、53％、54％、55％、56％、57％、58％、59 或 60％ AT 丰度）；和 / 或缺少已知或疑似减低 siRNA 活性的特定序列，例如，GG 序列在 5’ 末端的存在，这可以减少 siRNA 的双链部分的分离。在一个实施方案中，对 KRAS 特异性的 RNAi 剂可以是具有这些性质中的任何一种或多种的双链 RNA。

[0231] 如本文所用，术语“双链 RNA”或“dsRNA”是指包含第一链和第二链的 RNAi 剂；例如，包含具有杂交双链体区（即，其中来自第一链和第二链的核苷酸碱基配对的区域）的 RNA 分子或分子复合物的组合物，其中所述杂交双链体区包含两条反平行的和基本上互补的核酸链，其被称作具有相对于靶 RNA 的“有义”方向”和“反义”方向。相对于 mRNA 靶，反义链也称作“引导”链，有义链也称作“过客”链或“反引导”链。过客链可以包含以下至少一种或更多种情况：与另一条链相比有一个或多个额外的核苷酸（例如，凸出或 1 核苷酸环）、与另一条链相比的切口、缺口、错配等。在多种实施方案中，RNAi 剂包含第一链和第二链。在多种实施方案中，如本文所用的以及可以从上下文明显看出的，术语第一链是指如本文的任何表中所列的有义链并且第二链是指反义链。在其它实施方案中，如本文所用的以及可以从上下文明显看出的，第一链是指如本文的任何表中所列的反义链并且第二链是指有义链。

[0232] 双链体区可以具有允许经 RISC 途径特异性降解所期望的靶 RNA 的任何长度，但是一般范围是从 9 至 36 碱基对（“bp”）的长度，例如，15-30 个碱基对长度。考虑一个在 9 和 36 个碱基对之间的双链体，该双链体可以具有这个范围内的任何长度，例如，9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35 或 36 碱基对 (bp) 及其之间的任何子范围，包括但不限于 15-30 个碱基对、15-26 个碱基对、15-23 个碱基对、15-22 个碱基对、15-21 个碱基对、15-20 个碱基对、15-19 个碱基对、15-18 个碱基对、15-17 个碱基对、18-30 个碱基对、18-26 个碱基对、18-23 个碱基对、18-22 个碱基对、18-21 个碱基对、18-20 个碱基对、19-30 个碱基对、19-26 个碱基对、19-23 个碱基对、19-22 个碱基对、19-21 个碱基对、19-20 个碱基对、19 个碱基对、20-30 个碱基对、20-26 个碱基对、20-25 个碱基对、20-24 个碱基对、20-23 个碱基对、20-22 个碱基对、20-21 个碱基对、20 个碱基对、21-30 个碱基对、21-26 个碱基对、21-25 个碱基对、21-24 个碱基对、21-23 个碱基对、21-22 个碱基对、21 个碱基对、22 个碱基对或 23 个碱基对。细胞中通过 Dicer 和相似酶加工产生的 dsRNA 通常具有 19-22 的碱基对长度。dsRNA 的双链体区的一条链包含与靶 RNA 的区域基本上互补的序列。形成双链体结构的两条链可以来自具有至少一个自身互补双链体区域的单个 RNA 分子，或可以由杂交以形成该双链体的两个或更多个独立 RNA 分子组成。在双链体区是由单个分子的两个自身互补区域形成的情况下，该分子可以具有由形成双链体结构的一条链的 3’ - 端和相应另一条链的 5’ - 端之间的单链核苷酸链（本文中称作“发夹环”，例如，如存在于 shRNA 构建体中）分隔的双链体区。发夹环可以包含至少一个非配对核苷酸；在一些实施方案中，发夹环可以包含至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 20 个、至少 23 个或更多个非配对核苷酸。在 dsRNA 的两条基本上互补的链是由独立的 RNA 分子构成的情况下，这些分子不需要共价连接，但是可以共价连接。在两条链由发夹环共价连接的情况下，构建体通常在本文中和本领域中称作“shRNA”。在两条链借助发夹环之外的方式共价连接的情况下，连接结构称作“接头”。

[0233] 包含不同于所公开序列的错配的针对 KRAS 的 RNAi 剂

[0234] 本文中公开了针对 KRAS 的 RNAi 剂的各种具体实施方案；在表 1、2 和 3 中提供示例序列。本公开的具体实施方案包括了包含下述序列的 RNAi 剂及其修饰变体和未修饰变体，所述序列与表 1 至 6 中所列的任一 RNAi 剂差异 0、1、2 或 3 个核苷酸或碱基对（例如，

0、1、2 或 3 错配）。

[0235] 错配在本文中被定义为将两个序列最大限度地对齐并比较时碱基序列或长度之间的差异。将错配定义为一个位置，其中一个序列的碱基不匹配另一个序列的碱基。因此例如，如果一个序列中的某个位置具有特定碱基（例如，A）并且另一个序列上的相应位置具有不同的碱基（例如，G），则计为错配。例如，用 T、C、G 或 U 置换 A 将构成错配。用 T、A、C 或 U 置换 G 也将构成错配。用 T、G、A 或 U 置换 C 也将构成错配。用 A、C 或 G 置换 U 将构成错配。然而注意，在给定的链上，U 可以由 T 替换（作为 RNA 或，优选地，DNA，例如，2'-脱氧-胸苷）；用 T 替换 U 不是本文所述的错配，因为 U 或 T 均可以与对侧链上的 A 配对。RNAi 剂因此可以包含一个或多个 DNA 碱基，例如，T。在某些情况下，在 RNAi 剂的一个或多个部分，可用 DNA 代替 RNA（例如在种子区），以形成 DNA-RNA 杂合体。参见，例如 Yamato 等人 2011, cancer Gene Ther. 18:587-597。如果出现了碱基配对（例如 DNA 部分的 A、G、C 或 T 分别与 mRNA 的相应的 U、C、G 或 A 之间），RNAi 剂的 DNA 部分和相应的靶 mRNA 之间不计错配。

[0236] 例如，如果一个序列中的某个位置具有碱基（例如，A），而另一个序列中的相应位置没有碱基（例如，该位置是包含磷酸酯-糖主链但是不包含碱基的非碱基核苷酸），则计为错配。任何一个序列中（或有义链或反义链中）的单链切口不计为错配。因此，作为一个非限制性例子，如果一个序列包含序列 AG，而另一个序列包含在 A 和 G 之间具有单链切口的序列 AG，则将不计为错配。在糖或磷酸酯中的核苷酸修饰也不被认为是错配。因此，如果一个序列包含 C 并且另一个序列在相同位置包含修饰的 C（例如，2'-修饰），则将不计为错配。

[0237] 因此，如果在不修饰碱基的情况下对 RNAi 剂的糖、磷酸酯或主链进行修饰，则不计为错配。因而，作为 RNA 的序列 GGACGAAUAUGAUCCAACA(SEQ ID NO:1) 和作为 PNA（肽核酸）（或 TNA 或 GNA 或 FANA）的相同序列彼此具有 0 个错配。

[0238] 还应指出，表 1 至 6 中的 RNAi 剂的序列包括包含修饰的序列，如表 3 中详述。应当指出，将 dTdT(2'-脱氧胸苷-5'-磷酸和 2'-脱氧胸苷-5'-磷酸）或在一些情况下将 TT 或 UU 作为帽结构或延长物添加至两个 3' 末端，但是在计算错配总数时不包括这种帽结构或延长物。此外，在表 3 中，修饰的序列可包含一个或多个来自相应未修饰序列的修饰。在这种情况下，小写体"c"表示 2'-O- 甲基胞苷-5'-磷酸，并且小写体"u"表示 2'-O- 甲基尿苷-5'-磷酸。大写体"A"、"C"、"G"和"U"分别表示未修饰的腺苷-5'-磷酸、胞苷-5'-磷酸、鸟苷-5'-磷酸和尿苷-5'-磷酸。对序列之间的 0、1、2 或 3 个错配计数时，修饰的 c 置换未修饰的 C 不计为错配。对于表 1 至 6 中的全部序列均采用该命名法。因而，将 (a) 在测试序列和修饰的序列之间，和 (b) 在相同测试序列和来自 KRAS 基因的相应未修饰序列之间和 (c) 在修饰的序列和具有相同碱基序列的差异性修饰的序列之间计算相等数目的错配。

[0239] 在一个具体实施方案中，本公开包含 RNAi 剂及其修饰变体和未修饰变体，所述 RNAi 剂包含反义链，所述反义链包含与表 1 至 6 中列出的任一 RNAi 剂的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 至 19 个连续核苷酸。

[0240] 本公开涉及所公开序列的"修饰变体和未修饰变体"。

[0241] 特定序列的"未修饰变体"是 KRAS 的不带任何修饰的相应部分。表 1、2 和 3 列出了示例性修饰序列。表 1 至 6 的序列的"未修饰变体"具有不带碱基修饰或末端 dTdT 的相

同序列。一个给出的序列及其“未修饰变体”差异 0 个核苷酸（并且没有错配）.

[0242] 特定序列的“修饰变体”包含对主链、糖、磷酸酯或碱基的一个或多个（或一个或多个更少）修饰，但是没有任何碱基置换（例如，G 置换为 C，或 A 置换为 G）；因此一个给出的序列及其修饰变体差异 0 个核苷酸（并且没有错配）。作为另一个例子，作为 RNA 的给出序列和作为 PNA 的相同序列彼此是修饰变体并且差异 0 个核苷酸（并且没有错配）。类似地，作为锁核酸 (LNA)、吗啉代、苏糖核酸 (TNA) 或二醇核酸 (GNA) 的相同序列（没有碱基置换）将是具有 0 个错配的修饰变体。

[0243] 如下文详述，将给定位置处的单个核苷酸用修饰形式的相同核苷酸置换将产生修饰变体（具有 0 个错配）。

[0244] 在另一个具体实施方案中，RNAi 剂包含有义链，所述有义链包含与表 1 至 6 中列出的任一 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0245] 本公开的针对 KRAS 的 RNAi 剂可以用于 RNA 干扰。

[0246] RNAi 剂序列的修饰

[0247] 本公开涵盖未修饰的序列和示例性修饰序列，如在表 1、2 和 3 中公开的那些。

[0248] 本公开还涵盖所公开的序列的任何其它修饰（例如，修饰变体）。

[0249] 例如，本公开涵盖了给定位置处的单个核苷酸用修饰形式的相同核苷酸置换的 RNAi 剂。因而，核苷酸 (A、G、C 或 U) 可以由相应的 5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶、次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶、5- 羧甲基氨基甲基 -2- 硫代尿苷、5- 羧甲基氨基甲基尿嘧啶、二氢尿嘧啶、β -D- 半乳糖基 Q 核苷 (beta-D-galactosylqueosine)、肌苷、N6- 异戊烯基腺嘌呤、1- 甲基鸟嘌呤、1- 甲基肌苷、2,2- 二甲基鸟嘌呤、2- 甲基腺嘌呤、2- 甲基鸟嘌呤、3- 甲基胞嘧啶、5- 甲基胞嘧啶、N6- 腺嘌呤、7- 甲基鸟嘌呤、5- 甲氨基甲基尿嘧啶、5- 甲氧氨基甲基 -2- 硫尿嘧啶、β -D- 甘露糖基 Q 核苷 (beta-D-mannosylqueosine)、5’- 甲氧基羧基甲基尿嘧啶、5- 甲氧基尿嘧啶、2- 甲基硫代 -N6- 异戊烯基腺嘌呤、尿嘧啶 -5- 羟基乙酸 (v)、wybutoxosine、假尿嘧啶、Q 核苷 (queosine)、2- 硫胞嘧啶、5- 甲基 -2- 硫尿嘧啶、2- 硫尿嘧啶、4- 硫尿嘧啶、5- 甲基尿嘧啶、尿嘧啶 -5- 羟基乙酸甲酯 (oxyacetic acid methylester)、尿嘧啶 -5- 羟基乙酸 (v)、5- 甲基 -2- 硫尿嘧啶、3-(3- 氨基 -3-N-2- 羧丙基）尿嘧啶、(acp3)w 或 2,6- 二氨基嘌呤替换。

[0250] 额外的修饰变体包括向 RNAi 剂添加任何其它部分（例如，放射标记物或其它标签或缀合物）；只要碱基序列相同，其它部分的添加将产生“修饰变体”（无错配）。

[0251] 可以使用各种修饰集合。这些包括以下式样，所述样式用于本文中公开的各种筛选中。

[0252] A22S26

[0253] A22 表示全部 UA 为 2’-OMe-U A 并且全部 CA 为 2’-OMe-C A

[0254] S26 表示全部 U 为 2’-OMe-U 并且全部 C 为 2’-OMe-C

[0255] 全部 3’ 突出端为 2’-OMe-U 2’-OMe-U

[0256] 除这些修饰和修饰样式（例如，式样）之外，可以使用核酸修饰的公知常识产生所提供序列的其它修饰或修饰集合。

[0257] RNA 干扰

[0258] RNA 干扰 (RNAi) 是一项转录后定向基因沉默技术，该技术使用双链 RNA(dsRNA) 以降解含有与 dsRNA 相同的序列的信使 RNA(mRNA)。当核糖核酸酶 III(Dicer) 将较长 dsRNA 切割成称作 siRNA 的较短片段时，RNAi 的过程出现。由 Dicer 产生的 siRNA(小干扰性 RNA) 一般长约 21 至 23 个核苷酸并且包含约 19 个碱基对双链体 (不过人工 siRNA 或 RNAi 剂可以更短或更长，和 / 或平末端化，和 / 或包含一个或多个末端帽结构)。较小的 RNA 区段随后介导靶 mRNA 的降解。Dicer 还参与从结构保守的前体 RNA 中切出 21- 和 22- 个核苷酸的小时序 RNA(stRNA)，这些小时序 RNA 参与翻译性控制。Hutvagner 等人，2001 Science 293:834。RNAi 反应的特征还在于常称作 RNA 诱导性沉默复合物 (RISC) 的核酸内切酶复合物，其介导切割与 RNAi 剂的反义链互补的单链 mRNA。靶 RNA 的切割在与 siRNA 双链体的反义链互补的区域的中部发生。

[0259] 在一个方面，RNA 干扰剂包括与靶 RNA 序列相互作用以指导切割靶 RNA 的单链 RNA。不希望受理论约束，引入植物和无脊椎动物细胞中的长双链 RNA 被称作 Dicer 的 III 型核酸内切酶分解成 siRNA。Sharp 等人，2001 Genes Dev. 15:485。核糖核酸酶 III 型样酶 Dicer 将 dsRNA 加工成具有特征性双碱基 3' 突出端的 19-23 碱基对短干扰性 RNA。Bernstein 等人，2001 Nature 409:363。siRNA 随后被掺入 RNA 诱导性沉默复合物 (RISC) 中，在那里，一种或多种解旋酶解开 siRNA 双链体，从而使得现在未配对的 siRNA 链之一充当引导靶识别的“引导链”成为可能。Nykanen 等人，2001 Cell 107:309。一旦反义引导链与适宜的靶 mRNA 结合，RISC 内部的一种或多种核酸内切酶切割靶以引起沉默。Elbashir 等人，2001 Genes Dev. 15:188。因此，在一个方面，本公开涉及了促进实现靶基因沉默的 RISC 复合物形成的单链 RNA。

[0260] 用于 RNAi 合成的试剂盒是可商业获得的，例如，从 New England Biolabs 和 Ambion 获得。

[0261] 本公开的 RNAi 剂靶向 (例如，结合于、复性至等)KRAS mRNA。针对 KRAS 的 RNAi 剂的使用导致 KRAS 活性、水平和 / 或表达的减少，例如，靶基因或靶序列的“敲减”或“敲除”。特别地，在一个实施方案中，在病理状态以 KRAS 的过度表达或活性过高为特征的情况下，针对 KRAS 的 RNAi 剂的施用敲减 KRAS 靶，足以恢复 KRAS 活性的正常水平。

[0262] 合适的 RNAi 剂可以通过本领域已知的任何方法选择或是本领域普通技术人员可构思的。例如，选择标准可以包括以下一个或多个步骤：初始分析 KRAS 基因序列和设计 RNAi 剂；这种设计可以考虑跨物种的序列相似性 (人、食蟹猴、小鼠等) 和与其它 (非 KRAS) 基因的不相似性；体外筛选 RNAi 剂 (例如，在 RKO 细胞中以 10nM 的浓度)；在 RKO 细胞中确定 EC_{50}；确定用 RNAi 剂处理的细胞的生存力，所述细胞包括不需要 KRAS 用于存活的不敏感细胞或需要 KRAS 用于存活的敏感细胞；用例如人 PBMC(外周血单核细胞) 检验以测试 TNF-α 水平以估计免疫原性，其中免疫刺激性序列是不太想要的；在人全血测定法中检验，其中新鲜人血液用 RNAi 剂处理并且确定细胞因子 / 趋化因子水平 [例如，TNF-α (肿瘤坏死因子 -α) 和 / 或 MCP1(单核细胞趋化蛋白 1)]，其中免疫刺激性序列是不太想要的；在试验动物中使用皮下肿瘤在体内确定基因敲减；KRAS 靶基因调节作用分析，例如，使用药效动力学 (PD) 标志物，例如其表达受 KRAS 影响的其它因子，其中 KRAS 敲减导致这些组分的丰度剂量依赖性地减少；并且优化 RNAi 剂的特定修饰。

[0263] 本文所述的 dsRNA 分子（RNAi 剂）因此可用于 KRAS 基因的 RNA 干扰。

[0264] RNAi 剂的特征：有义链、反义链和（任选的）突出端

[0265] 在多种实施方案中，RNAi 剂包含第一链和第二链，例如，有义链和反义链（或反义链和有义链），并且任选地，双链体的一个或两个末端含有非配对核苷酸，在本文中称作“突出端”。

[0266] 术语“反义链”指 RNAi 剂的包含与靶序列基本上互补的区域的链。如本文所用，术语“互补区域”指反义链上与序列（例如，如本文定义的靶序列）基本上互补的区域。在互补区域不与靶序列完全互补的情况下，错配可以存在于分子的内部或末端区域内。通常，最耐受的错配存在于末端区域内，例如，在 5’ 和 / 或 3’ 末端的 5、4、3 或 2 个核苷酸内部。

[0267] 如本文所用，术语“有义链”指 RNAi 的链，所述链包含与本文中所定义的反义链的区域基本上互补的区域。

[0268] 基因的序列可以在个体之间变动，特别地在编码区段内部的摇摆位置处或在非翻译区中；个体也可以在编码序列方面彼此不同，导致 mRNA 中额外的差异。如果有并且在需要的情况下，RNAi 剂的有义链和反义链的序列因此可以设计成对应于个体患者的序列。也可以在序列方面修饰 RNAi 剂以降低免疫原性、减少与非预期 mRNA 的结合（例如，“脱靶效应”）或增加血液中的稳定性。这些序列变体与 RNAi 剂的碱基或 5’ 或 3’ 或其它末端帽结构的化学修饰无关。

[0269] RNAi 剂可以具有 0、1 或 2 个突出端；在 0 个核苷酸突出端情况下，它们平末端化。RNAi 剂可以具有 0、1 或 2 个平末端。在“平末端化 RNAi 剂”中，两条链以碱基配对方式终止；因此平末端化分子缺少 3’ 或 5’ 单链核苷酸突出端。

[0270] RNAi 剂可以包含突出端、平末端和 / 或 5’ 或 3’ 末端帽结构。

[0271] 如本文所用，术语“突出端”或“核苷酸突出端”指至少一个非配对核苷酸，其从 RNAi 剂的双链体结构的两条链的至少一条链的末端突出。例如，当 dsRNA 的一条链的 3’- 端延伸超过另一条链的 5’- 端时（反之亦然），未配对的核苷酸形成突出端。dsRNA 可以包含至少一个核苷酸的突出端；或者，该突出端可以包含至少 2 个核苷酸、至少 3 个核苷酸、至少 4 个核苷酸、至少 5 个或更多个核苷酸。突出端可以包含核苷酸 / 核苷类似物（包括脱氧核苷酸 / 核苷）或由其组成。突出端可以在有义链、反义链或其任意组合上。另外，突出端的核苷酸可以存在于 dsRNA 的反义或有义链的 5’ 末端、3’ 末端或两个末端上。RNAi 剂也可以任选地包含帽结构。术语“帽结构”等包括与双链核苷酸双链体的末端连接的化学部分，但是在本文中用来排除核苷酸或核苷形式的化学部分。“3’ 帽结构”连接在核苷酸或寡核苷酸的 3’ 末端处并保护分子例如免遭核酸酶（如血清或肠液中的那些核酸酶）的降解。3’ 帽结构可代替平末端 RNAi 剂末端的 TT 或 UU 二核苷酸。在一个实施方案中，3’ 末端帽结构如例如在 WO 2005/021749 和 WO 2007/128477 中公开的那样。“5’ 帽结构”连接在核苷酸或寡核苷酸的 5’ 末端处。帽结构不应当干扰（或过度干扰）RNAi 活性。

[0272] 本公开因此构思了对 KRAS 特异性的 RNAi 剂，其在 RNAi 剂中包含反义链（其可以是连续的或经接头或环连接）。在一个更具体的实施方案中，所述 RNAi 剂包含反义链和有义链，它们一起包含双链区或互补区。在一个实施方案中，其可以还任选地包含一个或两个突出端，和 / 或一个或两个帽结构。所述 RNAi 剂用来引起靶基因 KRAS 的 RNA 干扰。

[0273] 靶和互补序列

[0274] 本公开的 RNAi 剂靶向（例如，特异性结合于、复性至等）编码 KRAS 基因的 mRNA。对 KRAS 特异性的 RNAi 剂的使用导致 KRAS 活性、水平和 / 或表达的减少，例如，靶基因或靶序列的“敲减”或“敲除”。特别地，在一个实施方案中，在病理状态以 KRAS 的过度表达或活性过高为特征的情况下，针对 KRAS 的 RNAi 剂的施用敲减 KRAS 基因，足以恢复 KRAS 活性或表达的正常水平。

[0275] 在一个实施方案中，RNAi 的第一链或第二链包含与靶核酸 KRAS 的序列互补的序列。

[0276] 如本文所用，术语“包含某序列的链”是指寡核苷酸，其包含由使用标准核苷酸命名所指的序列描述的核苷酸链。

[0277] 如本文所用，“靶序列”或“靶基因”指基因转录期间形成的 mRNA 分子（例如，KRAS 基因）的核苷酸序列的连续部分，包括作为初级转录物产物的 RNA 加工的产物的 mRNA。该序列的靶部分将至少长到足以充当 iRNA 指导在这个部分或其附近切割的底物。例如，靶序列通常为 9-36 个核苷酸 (nt) 长度，例如，15-30 个核苷酸长度，包括在此之间的全部子范围。作为一个非限制性实例，靶序列可以具有 15-30 个核苷酸、15-26 个核苷酸、15-23 个核苷酸、15-22 个核苷酸、15-21 个核苷酸、15-20 个核苷酸、15-19 个核苷酸、15-18 个核苷酸、15-17 个核苷酸、18-30 个核苷酸、18-26 个核苷酸、18-23 个核苷酸、18-22 个核苷酸、18-21 个核苷酸、18-20 个核苷酸、19-30 个核苷酸、19-26 个核苷酸、19-23 个核苷酸、19-22 个核苷酸、19-21 个核苷酸、19-20 个核苷酸、19 个核苷酸、20-30 个核苷酸、20-26 个核苷酸、20-25 个核苷酸、20-24 个核苷酸、20-23 个核苷酸、20-22 个核苷酸、20-21 个核苷酸、20 个核苷酸、21-30 个核苷酸、21-26 个核苷酸、21-25 个核苷酸、21-24 个核苷酸、21-23 个核苷酸、或者 21-22 个核苷酸、21 个核苷酸、22 个核苷酸或 23 个核苷酸。RNAi 的有义链和反义链包含与靶核酸 (KRAS) 的序列互补的序列。

[0278] 除非另有说明，否则本文所用的术语“互补的”是指包含第一核苷酸序列的寡核苷酸或多核苷酸在某些条件下与包含第二核苷酸序列的寡核苷酸或多核苷酸杂交和形成双链体结构的能力。这类条件可以例如是严格的，例如，400mM NaCl，40mM PIPES pH 6.4，1mM EDTA，50℃或 70℃持续 12-16 小时，随后洗涤。可以使用其它条件，如在如生物体内部可能遭遇的生理相关条件。技术人员将能够根据杂交核苷酸的最终应用，确定最适宜检验两个序列的互补性的条件集合。

[0279] 在 RNAi 剂内部（例如，如本文所述的 dsRNA 内部）的互补序列包括针对一个或两个核苷酸序列的整个长度范围内与包含第二核苷酸序列的寡核苷酸或多核苷酸碱基配对的包含了第一核苷酸序列的寡核苷酸或多核苷酸。这类序列可以在本文中称作彼此“完全互补”。然而，在第一序列相对于本文中的第二序列称作“基本上互补”的情况下，这两个序列可以是完全互补的，或在杂交成至多 30 个碱基对的双链体时，它们可以形成 1 个或多个、但通常不多于 5、4、3 或 2 个错配碱基对，并且仍保留在与其最终应用（例如，通过 RISC 途径抑制基因表达）最相关的条件下杂交的能力。然而，在两个寡核苷酸被设计成在杂交时形成一个或多个单链突出端的情况下，就互补性的确定而言，这类突出端不应当被视作错配。例如，出于本文所述的目的，仍可以将包含长 21 个核苷酸的一个寡核苷酸和长 23 个核苷酸的另一个寡核苷酸、其中较长的寡核苷酸包含与较短寡核苷酸完全互补的 21 个核苷酸的序列的 dsRNA 称作“完全互补的”。如上文所述，术语“突出端”描述在双链核苷酸双链

体的 3' 或 5' 末端处的非配对核苷酸。在一个实施方案中，突出端为 1 至 4 个核苷酸长并且在 3' 末端上。

[0280] 如本文所用，“互补”序列也可以包含非 Watson-Crick 碱基对和 / 或由非天然和修饰的核苷酸形成的碱基对或完全由其形成，只要以上关于它们杂交能力的要求得到满足。这类非 Watson-Crick 碱基对包括但不限于摇摆或 Hoogstein 碱基配对。术语“互补的”、“完全互补的”和“基本上互补的”在此可以进一步用于 dsRNA 的有义链和反义链之间或 RNAi 剂的反义链和靶序列之间的碱基匹配，这可以从它们使用的上下文来理解。如本文所用，“与信使 RNA(mRNA) 的至少部分基本上互补”的多核苷酸指与目的 mRNA(例如，编码 KRAS 的 mRNA) 的连续部分基本上互补的多核苷酸。例如，如果一种多核苷酸的序列与编码 KRAS 的 mRNA 的非间断部分基本上互补，则该多核苷酸与 KRAS mRNA 的至少一部分互补。

[0281] 因此，本公开的 RNAi 剂互补于或基本上互补于靶 KRAS 中的靶序列并且是双链的，包含有义链和反义链 (其可以是连续的、经环连接或是接合的)，其中双链区域可以为 9 至 36bp 长 (特别地，例如 19 至 22bp 或 19 至 23bp 长)，并且可以进一步任选地包含 3' 突出端或 5' 突出端，并且该 RNAi 剂可以进一步包含 3' 帽结构。RNAi 剂介导 RNA 干扰，下调或抑制 KRAS 的水平、表达和 / 或活性，和 / 或建立或重建近似正常水平的 KRAS 和 / 或 KRAS 活性，或与 KRAS 相关的其它生物学功能。

[0282] 因此，本公开的 RNAi 剂互补于或基本上互补于靶 KRAS 中的靶序列并且是双链的，包含有义链和反义链 (其可以是连续的、经环连接或是接合的)，其中双链区域可以为 9 至 36bp 长 (特别地，例如 19 至 22bp 或 19 至 23bp 长)，并且可以进一步任选地包含 3' 突出端或 5' 突出端，并且该 RNAi 剂可以进一步包含 3' 帽结构。RNAi 剂介导 RNA 干扰，下调或抑制 KRAS 的水平、表达和 / 或活性，和 / 或建立或重建近似正常水平的 KRAS 活性或表达。

[0283] 如本文所用，术语“双链 RNA”或“dsRNA”指包含第一链和第二链的 RNAi 剂；例如包含具有杂交双链体区的 RNA 分子或分子复合物的组合物，所述杂交双链体区包含两条反平行的和基本上互补的核酸链，其将被称作具有相对于靶 RNA 的“有义”方向和“反义”方向。相对于 mRNA 靶，反义链也称作“引导”链，有义链也称作“过客”链。如本文所用，取决于上下文，“第一”链可以是引导链或反义链，“第二”链可以是过客链或有义链。同样如本文所用并且再次取决于上下文，“第一”链可以是过客链或有义链，“第二”链可以是引导链或反义链。过客链可以包含以下至少一种或更多种情况：与另一条链相比有一个或多个额外的核苷酸 (例如，凸出或 1 核苷酸环)、与另一条链相比的切口、缺口等。在多种实施方案中，第一链是有义链并且第二链是反义链。在其它实施方案中，第一链是反义链，并且第二链是有义链。

[0284] 双链体区可以具有允许负载进入 RISC 复合物并随后经 RISC 途径特异性降解所需靶 RNA 的任何长度，但是一般范围是从 9 至 36 碱基对 (“bp”) 的长度，例如，15-30 个碱基对长度。考虑一个在 9 和 36 个碱基对之间的双链体，该双链体可以具有这个范围内的任何长度，例如，9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35 或 36bp 及其之间的任何子范围，包括但不限于 15-30 个碱基对、15-26bp、15-23bp、15-22bp、15-21bp、15-20bp、15-19bp、15-18bp、15-17bp、18-30bp、18-26bp、18-23bp、18-22bp、18-21bp、18-20bp、19-30bp、19-26bp、19-23bp、19-22bp、19-21bp、19-20bp、19bp、20-30bp、20-26bp、20-25bp、20-24bp、20-23bp、20-22bp、20-21bp、

20bp、21-30bp、21-26bp、21-25bp、21-24bp、21-23bp、21-22bp、21bp、22bp 或 23bp。

[0285] 细胞中通过 Dicer 和相似酶加工产生的 dsRNA 通常具有约 19 至约 22 个碱基对范围内的长度，尽管可以合成或通过本领域的任何已知方法制备人工 RNAi 剂。dsRNA 的双链体区的一条链包含与靶 RNA 的一个区域基本上互补的序列。形成双链体结构的两条链可以来自具有至少一个自身互补双链体区的单个 RNA 分子，或者可以由两个或更多个可杂交形成双链体的独立 RNA 分子形成。在双链体区由单个分子的两个自身互补区形成的情况下，该分子可以具有由形成双链体结构的一条链的 3'-端和相应另一条链的 5'-端之间的单链核苷酸链（本文中称作“发夹环”，例如，如存在于 shRNA 构建体中）分隔的双链体区。发夹环可以包含至少一个非配对核苷酸；在一些实施方案中，发夹环可以包含至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 20 个、至少 23 个或更多个非配对核苷酸。在 dsRNA 的两条基本上互补的链由单独 RNA 分子构成的情况下，这些分子不需要共价连接，但是可以共价连接。在两条链由发夹环共价连接的情况下，构建体通常在本文中和本领域中称作“shRNA”。在两条链借助发夹环之外的方式共价连接的情况下，连接结构称作“接头”。术语“siRNA”也在本文中用来指如上文所述的 dsRNA。

[0286] 降低或正常化 KRAS 水平、表达和 / 或活性的 RNAi 剂

[0287] 用于靶向 KRAS 的 RNAi 剂包括那些与本文提供的 KRAS 序列结合并且通过 RNAi 机制起降低 KRAS 作用的 RNAi 剂。在例如表 1 中提供了针对 KRAS 的示例性 RNAi 剂（例如 siRNA）。

[0288] 可以用本领域已知的任何方法来测量由 KRAS RNAi 剂引起的 KRAS 活性、水平和 / 或表达的变化。测量可以在施用 RNAi 剂之前、施用期间和施用之后的多个时间点进行，以确定 RNAi 剂的作用。

[0289] 本公开的 RNAi 剂沉默、抑制、下调和 / 或阻抑 KRAS 的表达，从而恢复近似正常水平的 KRAS 活性或表达。

[0290] 此外，在多种实施方案中，取决于疾病状况和生物学背景，可接受的是，根据所需的治疗结果，使用本公开的 RNAi 剂建立低于正常水平或高于正常水平的 KRAS 表达、活性和 / 或水平。

[0291] 可以用本领域已知的任何方法来测量由 KRAS siRNA 引起的 KRAS 活性、水平和 / 或表达的变化。测量可以在施用 siRNA 之前、施用期间和施用之后的多个时间点进行，以确定 siRNA 的作用。

[0292] 术语“沉默”、“抑制……的表达”、“下调……的表达”、“阻抑……的表达”等，只要它们涉及 KRAS 基因，在此均指至少部分地阻抑 KRAS 基因的表达，其表现为可以从第一细胞或细胞群中分离或在其中检测到的 KRAS mRNA 的量的减少，其中，在所述第一细胞或细胞群中，KRAS 基因转录并且所述第一细胞或细胞群已经被处理，从而与基本上与第一细胞或细胞群相同的但尚未如此处理的第二细胞或细胞群（对照细胞）相比，KRAS 基因的表达被抑制。抑制程度通常以下式表述

[0293]

$$\frac{\text{(对照细胞中的 mRNA)- (处理细胞中的 mRNA)}}{\text{(对照细胞中的 mRNA)}} *100\%$$

[0294] 或者，抑制的程度可以用与 KRAS 基因表达功能性联系的参数（例如，KRAS 基因编码的蛋白质的量）的降低、其表达依赖于 KRAS 的蛋白质表达的改变等来给出。原则上，可以在以组成型方式或通过基因组工程化而表达 KRAS 的任何细胞中并且通过任何适宜的测定法确定 KRAS 基因沉默。然而，当需要参考或对照以确定给定的 RNAi 剂是否能够以一定程度抑制 KRAS 基因表达并且因此所述参考或对照属于本公开的范围内时，下文实施例中提供的测定法将充当该参照。

[0295] 例如，在某些情况下，通过施用本公开中表征的 RNAi 剂阻抑 KRAS 的表达至少约 10%、15%、20%、25%、30%、35%、40%、45%或 50%。在一些实施方案中，通过施用本公开中表征的 RNAi 剂阻抑 KRAS 至少约 60%、70%或 80%。在一些实施方案中，通过施用如本文所述的 RNAi 剂阻抑 KRAS 至少约 85%、90%或 95%或更多。在一个实施方案中，KRAS 的阻抑程度通过处理的细胞与未处理的细胞相比，全长 KRAS mRNA 的减少来测定。在一个实施方案中，KRAS 的阻抑程度通过监测增殖活性降低和 / 或细胞死亡的表型分析来测定。在实施例中提供了其它实施方案。

[0296] 可以首先在体外（例如，使用测试细胞如 RKO）测试 RNAi 剂抑制 KRAS 的能力。

[0297] 随后可以例如使用 PBMC（外周血单核细胞）测定法，对可在体外抑制 KRAS 的 RNAi 剂测试免疫刺激作用。也可以在动物试验中测试 RNAi 剂。试验动物和对照动物包括过度表达或不足表达 KRAS 的那些，例如，如 Hummer 等人 2005 J. Am. Soc. Nephrol. 16:3160-3166；Randrianarison 等人 2007 Am. J. Physiol. Lung Cell. Mol. Physiol. 294:409-416；Cao 等人 2006 Am. J. Physiol. Renal Physiol. 以及其中所引用的参考文献中所述。抑制或改变 KRAS 水平、活性和 / 或表达的 RNAi 剂可以用于治疗多种 KRAS 相关疾病的药物中。

[0298] 在 KRAS 或 KRAS 相关疾病的症状的语境中，“降低”意指这类水平的统计学显著地减少。减少可以例如是至少 10%、至少 20%、至少 30%、至少 40%或更多。如果一种具体疾病或患有一种具体疾病的个体的 KRAS 的水平或表达升高，用本公开的 KRAS RNAi 剂治疗则可以特别地使 KRAS 的水平或表达降低至文献中视为对未患这种疾病的个体而言的正常范围内的水平，或降低至减少或缓解疾病症状的水平。可以通过评价 mRNA（例如，借助 RNA 印迹或 PCR）或蛋白质（例如，蛋白质印迹法）测量 KRAS 的水平或表达。可以通过测量 KRAS 基因转录速率（例如，借助 RNA 印迹；或逆转录酶聚合酶链反应或实时聚合酶链反应）确定 RNAi 剂对 KRAS 表达的影响。

[0299] 如本文所用，“下调”指 KRAS 的生物活性和 / 或表达的任何统计学显著的减少，包括完全阻断活性（即，完全抑制）和 / 或表达。例如，“下调”可以指 KRAS 水平、活性和 / 或表达减少至少约 10%、20%、30%、40%、50%、60%、70%、80%、90%或 100%。

[0300] 如本文所用，术语“抑制”KRAS 指 KRAS 的生物学水平、活性和 / 或表达的任何统计学显著的减少，包括完全阻断活性和 / 或表达。例如，“抑制”可以指 KRAS 水平，活性和 / 或表达减少至少约 10%、20%、30%、40%、50%、60%、70%、80%、90%或 100%。如本文所用，当提到任何其它生物活性剂或组合物时，术语“抑制”类似地指水平、活性和 / 或表达的明显减少。

[0301] “水平”意指 KRAS RNAi 剂可以改变 KRAS 的水平，例如，KRAS mRNA 的水平或 KRAS 蛋白的水平或 KRAS 的活性水平。

[0302] 一些疾病，例如各种增殖性疾病、包括但不限于固体或液体癌、腺癌、结肠直肠癌、

晚期和/或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、心面皮肤(CFC)综合征和努南综合征，以及类似和相关的疾病，以KRAS突变或过高的KRAS丰度或活性为特征。特别是，在一个实施方案中，在疾病的特征在于KRAS的过度表达和/或活性过高的情况下，施用针对KRAS的RNAi剂以降低KRAS的水平、表达和/或活性。因此，在多种实施方案中，施用针对KRAS的RNAi剂特别地建立或重新建立KRAS活性、表达和/或浓度的正常水平或大致正常水平。

[0303] 就水平、表达和/或活性而言，“正常”或“大致正常”意指健康细胞、组织或器官中的KRAS的水平、表达或活性的约50%、约60%、约70%、约80%、约90%、和/或约100%；和/或不多于约100%、约120%、约130%、约140%或约150%。这可以按照Gambling等人2004 Kidney Intl.65:1774-1781中的描述，用例如肺或肾匀浆来测定。特别地，在一个实施方案中，施用适宜量的适宜KRAS RNAi剂将KRAS水平、活性和/或表达恢复到健康细胞、组织或器官的KRAS水平、活性和/或表达的约50%至约150%、更具体地约60%至约140%、更具体地至约70%至约130%、更具体地至约80%至约120%、更具体地至约90%至约110%和最具体地至约100%。因此，向患有KRAS相关疾病的患者施用KRAS RNAi特别地将KRAS的水平、活性和/或表达以及Na^+重吸收的水平恢复到大约正常的水平，如通过直接测量KRAS mRNA或蛋白质水平或间接测定所测定的。此外，施用KRAS RNAi剂后的KRAS水平、表达和/或活性的目标量的计算可以考虑KRAS-相关途径中的任何其它干扰。例如，如果KRAS-相关途径中的另一种因子过度表达或不足表达，可以对KRAS水平、表达或活性进行调控以达到更为正常的状态。

[0304] 此外，在多种实施方案中，取决于疾病状况和生物学背景，可接受的是，使用本公开的RNAi剂建立低于正常水平或高于正常水平的KRAS表达、活性和/或浓度水平。

[0305] RNAi剂及其修饰的类型

[0306] 包含反义核酸的RNAi剂或组合物下调细胞中特定蛋白质表达的用途是本领域熟知的。RNAi剂包含与另一个核酸(例如，mRNA)的编码链互补并且能够与之形成氢键的序列。因此，在多种实施方案中，本公开的RNAi剂涵盖了靶向(例如，互补于、能够与之杂交或通过氢键结合等)例如表1至6中所提出的任何序列的任何RNAi剂。

[0307] 一旦确定了一种有功能的引导链，就可以对引导链和/或过客链进行多种改变。例如，RNAi剂可以在内部或在一个或两个末端处具有修饰。在末端处的修饰可以帮助稳定RNAi剂，保护它免遭血液中的核酸酶降解。RNAi剂也可以任选地针对KRAS mRNA中已知或预期靠近或位于基因剪接位点的区域。

[0308] 可以使用化学合成和酶连接反应，利用本领域已知的方法构建RNAi剂。例如，可以使用天然存在的核苷酸或多种修饰的核苷酸化学合成RNAi剂，其中所述修饰的核苷酸被涉及用于降低脱靶效应，和/或增加分子的生物稳定性或增加反义核酸与有义核酸之间所形成的双链体的物理稳定性，例如，可以使用硫代磷酸酯衍生物和吖啶取代的核苷酸。

[0309] “G”、“C”、“A”、“T”和“U”各自通常表示分别含有鸟嘌呤、胞嘧啶、腺嘌呤、胸苷和尿嘧啶作为碱基的核苷酸。然而，术语“核糖核苷酸”、“脱氧核糖核苷酸”或“核苷酸”也可以指修饰的核苷酸或代用替换部分。技术人员充分了解，鸟嘌呤、胞嘧啶、腺嘌呤和尿嘧啶可

以由其它部分替换而基本上不改变包含携带这类替换部分的核苷酸的寡核苷酸的碱基配对特性。例如（但不限于），包含肌苷作为其碱基的核苷酸可以与含有腺嘌呤、胞嘧啶或尿嘧啶的核苷酸发生碱基配对。因此，含有尿嘧啶、鸟嘌呤或腺嘌呤的核苷酸可以在本公开中表征的 dsRNA 的核苷酸序列中由含有例如肌苷的核苷酸替换。在另一个实例中，寡核苷酸中任何地方的腺嘌呤和胞嘧啶可以分别地替换为鸟嘌呤和尿嘧啶，以形成与靶 mRNA 的 G-U 摇摆碱基配对。含有这类替换部分的序列适用于本公开中表征的组合物和方法。

[0310] 技术人员将认识到，术语“RNA 分子”或“核糖核酸分子”不仅包括如自然界中表达或存在（即天然存在）的 RNA 分子，还包括如本文所述或如本领域已知的包含一个或多个核糖核苷酸 / 核糖核苷类似物或衍生物的非天然存在的 RNA 类似物和衍生物。例如，如下文所述，可以在核碱基结构或在核糖 - 磷酸酯主链结构方面修饰 RNA。然而，包含核糖核苷类似物或衍生物的分子必须保留形成双链体的能力。作为非限制性的例子，RNA 分子也可以包含至少一个修饰的核糖核苷，其包括但不限于 2’-O- 甲基修饰的核苷酸、包含 5’ 硫代磷酸酯基的核苷、与胆甾烯基衍生物或十二烷酸双癸酰胺基连接的末端核苷、锁核苷 (locked nucleoside)、非碱基核苷、2’- 脱氧 -2’- 氟修饰的核苷、2’- 氨基修饰的核苷、2’- 烷基修饰的核苷、吗啉代核苷、非锁核糖核苷酸（例如，无环核苷酸单体，如 WO 2008/147824 中所述）、磷酰胺酯或包含非天然碱基的核苷，或其任意组合。或者，RNA 分子可以包含至少两个修饰的核糖核苷、至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 15 个、至少 20 个或更多个修饰的核糖核苷，直到 dsRNA 分子的整个长度。对于 RNA 分子中这些多个修饰的核糖核苷中的每一个，修饰不需要是相同的。在一个实施方案中，被构思用于本文所述方法和组合物中的修饰的 RNA 是具有形成所需双链体结构的能力并且允许或介导经 RISC 途径的靶 RNA 特异性降解的肽核酸 (PNA)。

[0311] 可以用来产生 RNAi 剂的修饰核苷酸的例子包括 5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶、次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶、5- 羧甲基氨基甲基 -2- 硫代尿苷、5- 羧甲基氨基甲基尿嘧啶、二氢尿嘧啶、β -D- 半乳糖基 Q 核苷、肌苷、N6- 异戊烯基腺嘌呤、1- 甲基鸟嘌呤、1- 甲基肌苷、2,2- 二甲基鸟嘌呤、2- 甲基腺嘌呤、2- 甲基鸟嘌呤、3- 甲基胞嘧啶、5- 甲基胞嘧啶、N6- 腺嘌呤、7- 甲基鸟嘌呤、5- 甲氨基甲基尿嘧啶、5- 甲氧氨基甲基 -2- 硫尿嘧啶、β -D- 甘露糖基 Q 核苷、5’- 甲氧基羧基甲基尿嘧啶、5- 甲氧基尿嘧啶、2- 甲基硫代 -N6- 异戊烯基腺嘌呤、尿嘧啶 -5- 羟基乙酸 (v)、wybutoxosine、假尿嘧啶、Q 核苷、2- 硫胞嘧啶、5- 甲基 -2- 硫尿嘧啶、2- 硫尿嘧啶、4- 硫尿嘧啶、5- 甲基尿嘧啶、尿嘧啶 -5- 羟基乙酸甲酯、尿嘧啶 -5- 羟基乙酸 (v)、5- 甲基 -2- 硫尿嘧啶、3-(3- 氨基 -3-N-2- 羧丙基）尿嘧啶、(acp3)w 和 2,6- 二氨基嘌呤。

[0312] 本文中公开的序列的“修饰变体”包括包含相同序列，但是在碱基、糖、磷酸酯或主链中具有修饰（但不是碱基置换，例如，A 置换为 G，或 C 置换为 U）的任何变体。因而，修饰的变体可以包含上文描述的任何修饰的核苷酸（例如，5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶，次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶等）。当碱基由相应的修饰碱基替换（例如，A 替换为修饰的 A）时，这些修饰的核苷酸不构成错配或碱基差异。因此，在特定位置处具有 U 的给定序列和在相同序列的相应位置处包含 5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶或 5- 碘尿嘧啶的修饰变体将差异 0 个核苷酸（或没有错配）；然而，在特定位置处具有 C 的给定序列和具有 5- 氟尿嘧啶的不同序列（其中除此之外，两

个序列相同）将差异 1 个核苷酸（1 个错配）。

[0313] 用脱氧核糖核苷酸替换具有双核苷酸 3’ 突出端的 21 聚 siRNA 双链体的 3’ 端核苷酸突出区段不会对 RNAi 活性产生不良作用。用脱氧核糖核苷酸替换 siRNA 的每个末端上的至多 4 个核苷酸已被良好耐受，而用脱氧核糖核苷酸完全置换导致无 RNAi 活性。国际 PCT 公开号 WO 00/44914 和 Beach 等人的国际 PCT 公开号 WO 01/68836 初步表明，siRNA 可以包括针对磷酸酯 - 糖主链或核苷的修饰以包含至少一个氮杂原子或硫杂原子。Kreutzer 等人的加拿大专利申请号 2,359,180 还描述了为了对抗双链 RNA 依赖性蛋白激酶 PKR 激活而用于 dsRNA 构建体中的某些化学修饰，特别是 2’ - 氨基核苷酸或 2’ -O- 甲基核苷酸和含有 2’ -O 亚甲基桥或 4’ -C 亚甲基桥的核苷酸。额外的 3’ 端核苷酸突出端包括 dT（脱氧胸苷）、2’ -O, 4’ -C- 亚乙基胸苷 (eT) 和 2- 羟乙基磷酸酯 (hp)。也可以制备 4- 硫尿嘧啶和 5- 溴尿嘧啶。Parrish 等人 2000 Molecular Cell 6:1077-1087。

[0314] 本领域技术人员将理解，可以使用本领域已知的任何常规方法合成并根据需要修饰 siRNA（见 Henschel 等人，2004 DEQOR:a web-based tool for the design and quality control of siRNAs. Nucleic Acids Research 32（网络服务器发行）:W113-W120）。另外，如果 RNAi 剂是 shRNA，本领域技术人员将显而易见的是，存在可用于 shRNA 表达构建体 / 载体的多种调节序列（例如，组成型或诱导型启动子、组织特异性启动子或其功能性片段等）。

[0315] 本领域中存在多种描述可以引入核酸分子中的糖修饰、碱基修饰、磷酸酯修饰和主链修饰并伴随核酸分子的核酸酶稳定性和功效显著增强的例子。例如，通过用抗核酸酶基团修饰，例如，2’ - 氨基、2’ -C- 烯丙基、2’ - 氟、2’ -O- 甲基、2’ -O- 烯丙基、2’ -H、核苷酸碱基修饰对寡核苷酸进行修饰以增强稳定性和 / 或增强生物活性（综述见 Usman 和 Cedergren 1992 TIBS. 17:34 ;Usman 等人，1994 Nucleic Acids Symp. Ser. 31:163 ;Burgin 等人，1996 Biochemistry 35:14090）。本领域中广泛描述了核酸分子的糖修饰。

[0316] 在多种实施方案中，RNAi 剂包含选自以下的 2’ - 修饰 :2’ - 脱氧、2’ - 脱氧 -2’ - 氟、2’ -O- 甲基、2’ -O- 甲氧基乙基 (2’ -O-MOE)、2’ -O- 氨基丙基 (2’ -O-AP)、2’ -O- 二甲基氨基乙基 (2’ -O-DMAOE)、2’ -O- 二甲氨基丙基 (2’ -O-DMAP)、2’ -O- 二甲基氨基乙氧基乙基 (2’ -O-DMAEOE) 和 2’ -O-N- 甲基乙酰氨基 (2’ -O-NMA)。

[0317] RNAi 剂的额外修饰和缀合已有记载。Soutschek 等人 2004 Nature 432:173-178 提出将胆固醇借助吡咯烷接头与 siRNA 分子的有义链的 3’ 末端缀合，由此产生共价的和不可逆的缀合物。也可以对 RNAi 剂进行化学修饰（包括与其它分子缀合）以改善体内药物动力学停留时间和效力。

[0318] 在多种实施方案中，针对 KRAS 的 RNAi 剂包含至少一个 5’ - 尿苷 - 腺嘌呤 -3’ (5’ -ua-3’) 二核苷酸，其中尿苷是 2’ - 修饰的核苷酸 ;至少一个 5’ - 尿苷 - 鸟嘌呤 -3’ (5’ -ug-3’) 二核苷酸，其中 5’ - 尿苷是 2’ - 修饰的核苷酸 ;至少一个 5’ - 胞苷 - 腺嘌呤 -3’ (5’ -ca-3’) 二核苷酸，其中 5’ - 胞苷是 2’ - 修饰的核苷酸 ;和 / 或至少一个 5’ - 尿苷 - 尿苷 -3’ (5’ -uu-3’) 二核苷酸，其中 5’ - 尿苷是 2’ - 修饰的核苷酸。在某些实施方案中，RNAi 剂可包含非天然核碱基，其中所述的非天然核碱基是二氟甲苯基、硝基吲哚基、硝基吡咯基或硝基咪唑基。在一个特定实施方案中，非天然核碱基是二氟甲苯基。在某些实施方案中，两条寡核苷酸链中仅一条链含有非天然核碱基。在某些实施方案中，两条

寡核苷酸链均含有非天然核碱基。

[0319] 在另一个实施方案中，RNAi 包含缺口或包含含有非碱基核苷酸的错配。

[0320] 在另一个实施方案中，RNAi 剂具有单链切口（例如，主链中的断裂或缺失的键）。在多种实施方案中，单链切口可以在有义链或反义链或这两种链中。

[0321] 这种切口可以例如在有义链中，产生内部分段的小干扰性 RNA 或 sisiRNA，其可以比没有切口的相应 RNAi 剂具有更少的脱靶效应。参见，例如 Wengels 和 Kjems 的申请 WO 2007/107162。

[0322] 反义核酸或 RNAi 剂也可以具有可替换主链如锁核酸 (LNA)、吗啉代、肽核酸 (PNA)、苏糖核酸 (TNA) 或二醇核酸 (GNA)、或 FANA 和 / 或其可以是标记的（例如，放射标记或其它标记）。FANA 记载于 Dowler 等人 2006Nucl. Acids Res. 34:1669-1675。

[0323] 一条链或两条链可以包含可替换主链。

[0324] 在又一个实施方案中，本公开的方法所使用的 RNAi 剂可以包括 α - 端基异构的核酸分子。α - 端基异构的核酸分子与互补性 RNA 形成特定双链杂交分子，其中与常见的 β - 单元相反，所述链相互平行地分布。Gaultier 等人，1987 Nucleic Acids. Res. 15:6625-6641。

[0325] 反义核酸分子也可以包含 2'-O- 甲基核糖核苷酸 (Inoue 等人，1987Nucleic Acids Res. 15:6131-6148) 或嵌合 RNA-DNA 类似物 (Inoue 等人，1987 FEBS Lett. 215:327-330)。

[0326] 可以对 RNAi 剂进行其它修饰和 / 或其它改变。RNAi 剂的一部分可以是双链 DNA，而另一部分是双链 RNA，从而形成 DNA-RNA 嵌合体（参见，例如 Yamato 等人，2011. Cancer Gene Ther. 18:587-597）。也可以引入引导链和过客链之间的错配，尽管某些位置可能比其它位置更为适合（参见，例如 Khvorova 的申请 U. S. Patent App. No. 2009/0209626）。过客链还可以被缩短至例如 15 或 16 个核苷酸，而引导链仍保持 19 个核苷酸或更长（参见，例如 Sun 等人，2008 Nature Biotech. 26:1379-1382；以及 Chu 和 Rana，2008 RNA 14:1714-1719）。这可以增加引导链向 RNA 诱导的沉默复合物 (RISC) 中的掺入，并减少过客链的掺入，减少脱靶效应。在某些情况下，过客链可能比引导链更经得起修饰（例如，单链切口、核苷酸修饰和缩短）。

[0327] 一旦确定了功能性引导链，就可以进行这些以及许多其它的修饰。

[0328] RNAi 剂的药物组合物

[0329] 如本文中使用，“药物组合物”包含药学有效量的一种或多种 KRASRNAi 剂、可药用载体和任选的与 RNAi 剂协同发挥作用的额外的疾病治疗。如本文所用，“药理学有效量”、“治疗有效量”或简单的“有效量”指有效产生预期的药理学、治疗或预防结果的 RNAi 剂的量。例如，如果与疾病或病症相关的可度量参数存在至少 10％的下降时认为给定的临床治疗有效，则用于治疗这种疾病或病症的药物的治疗有效量是实现该参数下降至少 10％所需要的量。在这个实施方案中，治疗有效量的靶向 KRAS 的 RNAi 剂可以减少 KRAS 蛋白质水平至少 10％。在另外的实施方案中，当与疾病或病症相关的可度量参数有至少 15％、20％、25％、30％、35％、40％、45％、50％、55％、60％、65％、70％、75％、80％、85％、90 或 95％的下降时，给定的临床治疗被视为有效，并且用于治疗该疾病或病症的药物的治疗有效量是分别实现该参数下降至少 15％、20％、25％、30％、35％、40％、45％、50％、55％、60％、65％、

70%、75%、80%、85%、90 或 95%所需的量。

[0330] 术语“可药用载体”指用于施用治疗剂的载体。这类载体包括但不限于脂质体纳米颗粒、盐水、缓冲盐水、右旋糖、水、甘油、乙醇及它们的组合。该术语特别地排除细胞培养基。本领域已知的任何适宜的药物载体均可与本文所公开的 RNAi 剂一起使用。

[0331] 包含针对 KRAS 的 RNAi 剂的药物组合物

[0332] 可以添加包含针对 KRAS 的 RNAi 剂的药物组合物的额外组分以有助于递送、稳定性、功效或降低免疫原性。

[0333] 先前已经使用脂质体用于药物递送（例如，递送化疗药）。脂质体（例如，阳离子脂质体）在 PCT 公开 WO 02/100435A1、WO 03/015757A1、WO 04029213A2 和 WO/2011/076807；美国专利号 5,962,016；5,030,453；和 6,680,068；以及美国专利申请 2004/0208921 中有记载。在 WO 04/002453A1 中还描述了产生脂质体的方法。另外，已经将中性脂质掺入阳离子脂质体中（例如，Farhood 等人，1995），还有聚乙二醇化的脂质。

[0334] 阳离子脂质体已经用于递送 RNAi 剂至各种细胞类型（Sioud 和 Sorensen，2003；美国专利申请 2004/0204377；Duxbury 等人，2004；Donze 和 Picard，2002）。

[0335] 中性脂质体的用途公开于 Miller 等人，1998 和美国专利申请 2003/0012812。

[0336] 如本文所用，术语“SNALP”指稳定的核酸 - 脂质粒子。SNALP 代表包被压缩的含水内部的脂质囊泡，其中所述含水内部包含核酸如 iRNA 或从中转录出 iRNA 的质粒。SNALP 例如在美国专利申请公开号 20060240093、20070135372 以及国际申请号 WO 2009082817 中有描述。

[0337] 采用基于脂质、基于胺和基于聚合物的技术的化学转染公开于 Ambion Inc.，Austin，Tex.；和 Novagen，EMD Biosciences，Inc，Merck KGaA 分公司，Darmstadt，德国）的产品；Ovcharenko D(2003) “Efficient delivery of siRNAs to human primary cells.” Ambion TechNotes 10(5):15-16)。另外，Song 等人 (Nat Med. 在线发表 (Feb 10,2003) doi :10.1038/nm828) 和其它人 [Caplen 等人，2001 Proc. Natl. Acad. Sci. (USA), 98:9742-9747；和 McCaffrey 等人，Nature 414:34-39] 公开了可以通过注射 siRNA 至哺乳动物的循环系统中高效地转染肝脏细胞。

[0338] 已经有多种分子被用于细胞特异性递送 RNAi 剂。参见，例如 WO/2011/076807。例如，已将鱼精蛋白的核酸浓缩特性与特异性抗体组合以递送 siRNA。Song 等人，2005 Nat Biotech. 23:709-717。自装配聚乙二醇化聚阳离子聚乙烯亚胺 (PEI) 也已经用于浓缩并保护 siRNA。Schiffelers 等人，2004 Nucl. Acids Res. 32:e149, 141-110。

[0339] 可以借助例如脂质纳米颗粒 (LNP)；中性脂质体 (NL)；聚合物纳米颗粒；双链 RNA 结合基序 (dsRBM)；或借助对 RNAi 剂的修饰（例如，与 dsRNA 共价接合）或通过本领域已知的用于递送包含核酸的 RNAi 剂的任何方法来递送本公开的 RNAi 剂。

[0340] 脂质纳米颗粒 (LNP) 是基于阳离子脂质的自装配系统。这些纳米颗粒可以包含例如中性脂质（脂质体基体）；阳离子脂质（用于加载 siRNA）；胆固醇（用于稳定脂质体）；和 PEG- 脂质（用于稳定制剂、电荷屏蔽和延长血流中的循环）。

[0341] 阳离子脂质可以包括例如头部基团、接头、尾部和胆固醇尾。LNP 可以具有例如良好的肿瘤递送、延长的血液中循环、小粒子（例如，小于 100nm）和在肿瘤微环境（其具有低 pH 并且低氧）中的稳定性。

[0342] 中性脂质体 (NL) 是非阳离子脂质类的粒子。

[0343] 聚合物纳米颗粒是自装配聚合物类的粒子。

[0344] 双链 RNA 结合基序 (dsRBMs) 是将需要修饰的自装配 RNA 结合蛋白。

[0345] 在本公开的多种实施方案中，针对 KRAS 的 RNAi 剂被作为单一疗法包装在递送载体中，或者可进一步连接至一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[0346] 可以将本公开的 RNAi 剂制成药物组合物，所述药物组合物包含适于施用 RNAi 剂的特定方法的多种组分。

[0347] KRAS 相关疾病

[0348] 本公开涵盖针对 KRAS 的 RNAi 剂和向人和非人动物施用该 RNAi 剂以治疗各种 KRAS 相关疾病。

[0349] “KRAS 相关疾病”意指与 KRAS 的水平、表达和 / 或活性的功能障碍相关的任何疾病，和 / 或可以通过调节 KRAS 的水平、表达和 / 或活性进行治疗和 / 或改善的任何疾病。具体地讲，其包括增殖性疾病，包括但不限于固体或液体癌，例如腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、心面皮肤 (CFC) 综合征和努南综合征，以及类似和相关的疾病。

[0350] 关于 KRAS 相关疾病的更多信息可参见，例如 :Bos. 1989. Cancer Res. 49. 17:4682 - 9 ;Engelman 等 人，2008. Nature Med. 14:1351-1356 ;Haigis 等 人，2008 Nature Gen. 40:600-608 ;Karapetis 等人，2008 N. E. J. Med. 359:1757-1765 ;Kiaris 等 人，1995. Int. J. Oncol. 7:413-421 ;Liu 等 人，1987Nature 330:186-188 ;Riely 等 人，2008 Clin. Cancer Res. 14:5731 ;和 Riely 等人，2009. Proc. Am. Thorac. Soc. 6:201-205。KRAS 突变、活性过高和过度表达还与心面皮肤 (CFC) 综合征和努南综合征有关。Adachi 等 人，2012Seizure:Eur. J. Epilepsy 21:55-60 ;Kim 等 人，2011. J. Korean Soc. Neonatol. 18:374-378。

[0351] 针对 KRAS 的 RNAi 剂因此可以用来治疗 KRAS 相关疾病，特别是与 KRAS 表达、活性和 / 或水平的改变有关的那些疾病。

[0352] RNAi 剂用于治疗 KRAS 相关疾病的用途

[0353] 可以将本文所述的针对 KRAS 的 RNAi 剂配制成可以施用于人或非人动物的药物组合物。这些组合物可以包含一种或多种 RNAi 剂，和任选地，可用于治疗 KRAS 相关疾病的额外治疗。它们可以作为早期 / 预防性疗法的一部分施用，并且可以按治疗有效的剂量施用。药物组合物可以包含药用载体并且可以通过本领域已知的任何方法施用。以下进一步详细描述本公开的这些各个方面。

[0354] 针对 KRAS 的 RNAi 剂可以施用给人和非人动物用于治疗 KRAS 相关疾病。

[0355] 在本公开的一个实施方案中，包含KRAS RNAi剂的组合物可以施用给非人动物。例如，可将组合物给予鸡、火鸡、家畜动物（如绵羊、猪、马、牛等）、伴侣动物（例如，猫和犬）并且可以在治疗增殖性疾病、心面皮肤（CFC）综合征或努南综合征以及类似疾病中具有功效。在每种情况下，将选择针对KRAS的RNAi剂以匹配该动物基因组的KRAS序列，并且尤其是含有来自该动物基因组的全部其它基因中的至少1个核苷酸错配。本公开的RNAi剂因此可以用于治疗人和非人动物中的KRAS相关疾病。

[0356] 本文中在KRAS表达的语境下所用的术语“治疗”、“疗法”等指减弱或减轻KRAS表达所介导的病理过程。在本公开的上下文中，当谈及下文描述的任何其它病况时（除KRAS表达所介导的病理过程之外），术语“治疗”、“疗法”等意指减弱或减轻与这种病况相关的至少一种症状，或减缓或逆转这种病况的进展或预期的进展，例如减缓脂质异常例如动脉粥样硬化的进展。

[0357] “治疗”还意指预防、治疗、治愈患者病况或患者病况的任何其它变化，所述变化表明身体状况的改善或不存在身体状况变劣。“治疗”意指对KRAS相关疾病（例如，增殖性疾病，包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和/或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌、或心面皮肤（CFC）综合征或努南综合征）的治疗或对患者具有的任何其它病痛的任何适宜治疗。如本文所用，术语“治疗”和“疗法”指预防性或阻止性治疗和治愈性或病情改善性治疗，包括治疗存在感染疾病风险或疑似患有疾病的患者，以及已经生病或诊断为患有疾病的患者。术语“治疗”和“疗法”还指在未患有疾病但是可能易于出现不健康状况、例如氮失衡或肌肉减少的个体中维持和/或促进健康。在一个实施方案中，“治疗”不涵盖疾病状态的预防。因此，本公开可用于在罹患KRAS相关疾病的个体或易患KRAS相关疾病的个体中抑制KRAS基因的表达和/或治疗KRAS相关疾病。“罹患”KRAS相关疾病的个体已经展示可检测的该疾病的特征性症状，或者已经在临床上证实暴露于或携带KRAS相关疾病的病原体或标志物。作为非限制性例子，罹患KRAS相关疾病的个体可以显示外在症状；或可以不显示外在症状，但是可以用临床试验证实在血液中携带与KRAS相关疾病相关的蛋白质标志物或与病原体相关的蛋白质或遗传物质。

[0358] 某些KRAS相关疾病的早治疗比晚治疗更有效。因此，在一个特定的实施方案中，针对KRAS的RNAi剂在疾病表现出来之前提早施用，和/或作为预防剂施用，而不是在疾病已经确立后施用。

[0359] KRAS相关疾病的治疗可以包括各种治疗，包括KRAS RNAi剂，并且任选地还包括额外治疗，其可以是方法（或操作），和/或额外的组合物（例如，药剂或额外的RNAi剂）。

[0360] RNAi剂的剂量和有效量

[0361] 本公开的RNAi剂以治疗有效量的剂量施用于有需要的患者。

[0362] “有效量”或“治疗有效量”是治疗个体的疾病或医学状况，或更一般地说，向个体提供营养、生理或医学益处的量。如本文所用，短语“治疗有效量”和“预防有效量”指在治疗、预防或管理由KRAS表达介导的病理过程或由KRAS表达介导的病理过程的明显症状时提供治疗益处的量。治疗有效的具体量可以由普通医疗执业者轻易地确定，并且可以根据本领域已知的因素变动，例如，由KRAS表达介导的病理过程的类型、患者病史和年龄、由

KRAS 表达介导的病理过程的阶段以及施用抑制由 KRAS 表达介导的病理过程的其它药物。

[0363] 在本公开的多种实施方案中，患者的年龄至少为约 1、3、6 或 9 个月、或 1、5、10、20、30、40、50、55、60、65、70 或 75 岁。在多种实施方案中，患者的年龄不超过约 1、3、6 或 9 个月、或 1、5、10、20、30、40、50、55、60、65、70、75、80、90 或 100 岁。在多种实施方案中，患者具有至少 约 5、10、15、20、30、40、50、60、70、80、90、100、120、140、160、180、200、220、240、260、280、300、320、340、360、380 或 400lbs 的体重。在多种实施方案中，患者具有不超过约 5、10、15、20、30、40、50、60、70、80、90、100、120、140、160、180、200、220、240、260、280、300、320、340、360、380 或 400lbs 的体重。

[0364] 在本公开的多种实施方案中，剂量 [仅计量有效成分] 可以是至少约 1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000ng、1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000 微克、1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000mg。在多种实施方案中，剂量可以是不超过约 10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000mg。在多种实施方案中，可以将该剂量施用每日至少多于 1 次、每日 1 次、每周多于 1 次、每周 1 次、每两周 1 次、每月 1 次和 / 或每 2、3、4、5、6、7、8、9、10、11 或 12 个月施用 1 次或其组合。

[0365] 在多种实施方案中，剂量与个体的体重或身体表面积相关。可以变动实际剂量水平以获得对特定的患者、组合物和施用方式而言是有效的并且对患者无毒的活性剂的量。选择的剂量水平取决于多种药物代谢动力学因素，包括所用的特定 RNAi 剂的活性、施用途径、RNAi 剂的排泄速率、治疗的持续时间、与 RNAi 剂组合使用的其它药物、化合物和 / 或材料、患者的年龄、性别、重量、状况、总体健康和既往医史等医学领域熟知的因素。具有本领域普通技术的医师或兽医师可以轻易地确定所需要的 RNAi 的有效量。合适的剂量将是有效产生治疗效果的最低剂量或低到足以在不造成副作用的情况下产生治疗效果的剂量。

[0366] 针对 KRAS 的 RNAi 剂与其它疗法组合

[0367] 除治疗有效剂量的一种或多种针对 KRAS 的 RNAi 剂外，本公开的药物组合物还可以包含与 RNAi 剂协同发挥作用的额外的疾病治疗或与之联合使用。

[0368] 此外，许多肿瘤同时包含 KRAS 的突变以及一种或多种其它基因的突变。例如，某些肺癌或结肠直肠肿瘤细胞或其它类型的癌症可同时具有 KRAS 的突变以及一种或多种如下的突变 :EGFR、GLUT1、PI3K、RAF 和 APC。Haigis 等人，2008 Nature Gen. 40:600-608 ;Karapetis 等 人，2008N. E. J. Med. 359:1757-1765 ; 和 Yun 等 人，2009 Science 325:1555-1559。有效的组合治疗可以包含 KRAS RNAi 剂与靶向于其它突变的活性过高或过度表达的蛋白的活性剂或已被批准用于所治疗的癌症类型的疗法组合。

[0369] 因此，当用于涉及其它疾病治疗的治疗方案时，针对 KRAS 的 RNAi 剂可以是有效的。当患者具有 KRAS 的激活突变时，这些治疗中的一些治疗是无效的。但是，针对 KRAS 的 RNAi 剂可以降低 KRAS 的总量，改善那些在存在 KRAS 激活突变的条件下是无效的疾病治疗的效力。

[0370] 此外，KRAS 缺陷型肿瘤细胞的增殖、存活和 / 或对细胞凋亡的抗性可能需要其它因子，例如 NF-κ-B 或 I-κ-B 激酶 TBK1。Meylan 等人，2009Nature 462:104-107 ;和 Barbie

等人，2009 Nature 462:108-112。因此，在某些实施方案中，有效的组合疗法可以包括施用KRAS RNAi 剂以及施用（或共同施用）靶向于其它因子的治疗（例如 siRNA、抗体或靶向于NF-κ-B 或 TBK1 的小分子）。

[0371] 因此，KRAS RNAi 剂可与任何其它治疗组合物或方法或疗法一起用于组合疗法，包括那些特异性地靶向于另一种因子或已知在治疗 KRAS 相关疾病中是有效的组合物或方法或疗法。

[0372] 在治疗这些 KRAS 相关疾病时，RNAi 剂和额外的疾病治疗可以按任意顺序、同时或依次地施用或随时间推移以多个剂量施用。RNAi 剂和额外治疗的施用可以例如是同时的，并行的、分别的或依次的。

[0373] 同时施用可以例如以与两种或更多种有效成分的一个固定组合的形式进行，或通过同时施用独立配制的两种或更多种有效成分进行。依次使用（施用）优选是指在一个时间点施用组合的一种（或多种）组分，在不同的时间点施用其它组分，即，以时间交错方式施用，优选能够使该组合比独立施用的单一化合物显示出更高的效力（特别是显示协同作用）。分别使用（施用）优选是意指在不同时间点彼此独立地施用该组合的各个组分，优选意指组分 (a) 和 (b) 以这两种化合物的明显可测量血液水平没有重叠（在相同的时间）的方式施用。

[0374] 另外，两种或更多种依次、分别和同时施用的组合也是可能的，优选组合的组分 - 药物显示联合治疗效果，该联合治疗效果超过当组合的组分 - 药物以如此大的时间间隔分别使用以至于无法观察到对其治疗效力的相互影响时所观察到的效果，协同效应是特别优选的。

[0375] 如本文所用的术语“延迟进展”意指将该组合施用给处于待治疗疾病的首次表现或复发的初级阶段或早期的患者，在所述患者中例如诊断出了相应疾病的前期形式，或者所述患者处于某种状况，例如在医学治疗期间，或处于因意外而产生的某种状况，在所述状况下相应疾病有可能形成。

[0376] “联合治疗活性”或“联合治疗效果”意指可以将化合物按一定的时间间隔（以时间交错方式，特别是以序列特异性方式）分别给予，从而它们优选在待治疗的温血动物（特别是人）中仍显示相互作用（优选显示协同的相互作用）（联合治疗效果）。可以通过监测血液水平、证实至少在某些时间区间内在待治疗的人的血液中同时存在两种化合物来确定是否为这种情形。

[0377] 因此，本公开涵盖包含 KRAS RNAi 剂和一种或多种本领域已知的治疗 KRAS 相关疾病的额外的治疗的组合疗法。

[0378] 针对任何 KRAS 相关疾病的已知疗法的应用处于本领域普通技术人员的能力范围内。任何这类额外的治疗均可以与针对 KRAS 的 RNAi 剂联合使用。

[0379] 额外治疗和 RNAi 剂的剂量可以由本领域普通技术人员并且如本文所述那样容易地确定。

[0380] 包含一种或多种针对 KRAS 的有效 RNAi 剂的实施方案

[0381] 在本公开的多种实施方案中，本公开包括 RNAi 剂，所述 RNAi 剂在 RKO 细胞中进行的体外测定中，在 10 或 0.1nM 的浓度下显示至少约 40%、50%、60%、70%、80%、90%或 95%的 KRAS 基因敲减 (KD)（即，分别不超过约 60%、50%、40%、30%、20%、10%或 5%的

残余基因活性）。

[0382] 在本公开的多种实施方案中，组合物包含一种或多种 RNAi 剂，所述 RNAi 剂能够在 24 小时在 10nM 实现 <0.05、<0.10、<0.20、<0.30、<0.40 的倍数变化（分别表示在 RKO 细胞中在 24 小时在 10nM 浓度时至少 95%、90%、80%、70%或 60%的 KRAS 基因敲减作用）。本文的表中公开了能够实现这些活性水平的 RNAi 剂。

[0383] 包含一种或多种针对 KRAS 的有效 RNAi 剂的实施方案

[0384] 在本公开的多种实施方案中，该组合物包含一种或多种 RNAi 剂，所述 RNAi 剂能够在 120 小时在 0.1nM 实现 <0.30、<0.20 或 <0.10 的倍数变化（分别表示在 RKO 细胞中在 120 小时在 0.1nM 浓度时至少 70%、80%或 90%的 KRAS 基因敲减作用）。本文的表中公开了能够实现这些活性水平的 RNAi 剂。

[0385] 包含一种或多种具有低 EC_{50}的针对 KRAS 的 RNAi 剂的多种实施方案

[0386] 在本公开的多种实施方案中，组合物包含能够在 RKO 细胞中以低浓度介导 KRAS 的 50%基因敲减作用（EC_{50}）的一种或多种 RNAi 剂。对于本文中列出的许多 RNAi 剂，计算估计的 EC_{50}。细胞用 10nM、1nM、0.1nM、0.01nM 和 0.001nM RNAi 剂处理，并将数据拟合成曲线。所示的 EC_{50}是从可用数据计算出的估计的 EC_{50}，预期其在 RKO 细胞中产生 KRAS 的 50%基因敲减。在本公开的多种实施方案中，组合物包含能够在 RKO 细胞中以 100、75、50、25、10、5、2.5、1、0.75、0.5、0.25、0.2、0.12、0.1、0.09、0.08、0.07、0.06、0.05、0.04、0.03 或 0.02nM 或更小的浓度介导 50%基因敲减作用（EC_{50}）的一种或多种 RNAi 剂。本文的表中公开了能够实现这些活性水平的 RNAi 剂。

[0387] 针对 KRAS 的 RNAi 剂的具体实施方案

[0388] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含有义链和反义链，其中反义链包含与来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体或未修饰变体的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0389] 在一个实施方案中，该组合物包含任意一种或多种包含有义链和反义链的 RNAi 剂，其中反义链包含与来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链差异 0 个核苷酸的至少 15 个连续核苷酸。

[0390] 在一个实施方案中，本公开涉及一种组合物，其包含任意一种或多种来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体。

[0391] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含反义链，所述反义链包含来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链的序列。

[0392] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含反义链，所述反义链由来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链的序列组成。

[0393] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体的第一链的序列。

[0394] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和第二链的序列是来自表 1 至 6 的任何一个的任

一种 RNAi 剂及其修饰变体和未修饰变体的第一链和第二链的序列。

[0395] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂及其修饰变体和未修饰变体的第一链的序列，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[0396] 针对 KRAS 的 RNAi 剂的具体实施方案

[0397] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链包含与来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体或未修饰变体的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0398] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链包含来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链的至少 15 个连续核苷酸。

[0399] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链的序列。

[0400] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列包含来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和 / 或第二链的序列。

[0401] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和第二链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和第二链的序列。

[0402] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和 / 或第二链的序列，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[0403] 包含与本文公开的 RNAi 剂差异 0 至 3 个核苷酸的至少 15 个连续核苷酸的具体实施方案

[0404] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链包含与来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体或未修饰变体的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0405] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[0406] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35523.3(SEQ ID NO:428)，或其修饰变体或未修饰变体。

[0407] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35529.1(SEQ ID NO:429)，或其修饰变体或未修饰变体。

[0408] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35535.4(SEQ ID NO:430),或其修饰变体或未修饰变体。

[0409] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35541.4(SEQ ID NO:431),或其修饰变体或未修饰变体。

[0410] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35547.4(SEQ ID NO:432),或其修饰变体或未修饰变体。

[0411] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35553.4(SEQ ID NO:433),或其修饰变体或未修饰变体。

[0412] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35559.4(SEQ ID NO:434),或其修饰变体或未修饰变体。

[0413] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35565.4(SEQ ID NO:435),或其修饰变体或未修饰变体。

[0414] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35524.4(SEQ ID NO:436),或其修饰变体或未修饰变体。

[0415] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35530.4(SEQ ID NO:437),或其修饰变体或未修饰变体。

[0416] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35536.4(SEQ ID NO:438),或其修饰变体或未修饰变体。

[0417] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35542.4(SEQ ID NO:439),或其修饰变体或未修饰变体。

[0418] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35548.4(SEQ ID NO:440),或其修饰变体或未修饰变体。

[0419] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35554.4(SEQ ID NO:441),或其修饰变体或未修饰变体。

[0420] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35560.2(SEQ ID NO:442),或其修饰变体或未修饰变体。

[0421] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35566.4(SEQ ID NO:443),或其修饰变体或未修饰变体。

[0422] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35525.2(SEQ ID NO:444),或其修饰变体或未修饰变体。

[0423] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35531.4(SEQ ID NO:445),或其修饰变体或未修饰变体。

[0424] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35537.4(SEQ ID NO:446),或其修饰变体或未修饰变体。

[0425] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35543.2(SEQ ID NO:447),或其修饰变体或未修饰变体。

[0426] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35549.4(SEQ ID NO:448),或其修饰变体或未修饰变体。

[0427] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35555.4(SEQ ID NO:449),或其修饰变体或未修饰变体。

[0428] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35561.4(SEQ ID NO:450),或其修饰变体或未修饰变体。

[0429] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35567.4(SEQ ID NO:451),或其修饰变体或未修饰变体。

[0430] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35526.4(SEQ ID NO:452),或其修饰变体或未修饰变体。

[0431] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35532.4(SEQ ID NO:453),或其修饰变体或未修饰变体。

[0432] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35538.4(SEQ ID NO:454),或其修饰变体或未修饰变体。

[0433] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35544.4(SEQ ID NO:455),或其修饰变体或未修饰变体。

[0434] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35550.4(SEQ ID NO:456),或其修饰变体或未修饰变体。

[0435] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35556.4(SEQ ID NO:457),或其修饰变体或未修饰变体。

[0436] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35562.4(SEQ ID NO:458),或其修饰变体或未修饰变体。

[0437] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35568.4(SEQ ID NO:459),或其修饰变体或未修饰变体。

[0438] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35527.4(SEQ ID NO:460),或其修饰变体或未修饰变体。

[0439] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35533.4(SEQ ID NO:461),或其修饰变体或未修饰变体。

[0440] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35539.4(SEQ ID NO:462),或其修饰变体或未修饰变体。

[0441] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35545.4(SEQ ID NO:463),或其修饰变体或未修饰变体。

[0442] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35551.4(SEQ ID NO:464),或其修饰变体或未修饰变体。

[0443] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35563.4(SEQ ID NO:465),或其修饰变体或未修饰变体。

[0444] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35528.4(SEQ ID NO:466),或其修饰变体或未修饰变体。

[0445] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35540.4(SEQ ID NO:467),或其修饰变体或未修饰变体。

[0446] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35546.4(SEQ ID NO:468),或其修饰变体或未修饰变体。

[0447] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35552.4(SEQ ID NO:469),或其修饰变体或未修饰变体。

[0448] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35558.4(SEQ ID NO:470),或其修饰变体或未修饰变体。

[0449] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35564.4(SEQ ID NO:471),或其修饰变体或未修饰变体。

[0450] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35570.4(SEQ ID NO:472),或其修饰变体或未修饰变体。

[0451] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35571.4(SEQ ID NO:473),或其修饰变体或未修饰变体。

[0452] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35577.4(SEQ ID NO:474),或其修饰变体或未修饰变体。

[0453] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35583.4(SEQ ID NO:475),或其修饰变体或未修饰变体。

[0454] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35589.4(SEQ ID NO:476),或其修饰变体或未修饰变体。

[0455] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35595.4(SEQ ID NO:477),或其修饰变体或未修饰变体。

[0456] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35601.4(SEQ ID NO:478),或其修饰变体或未修饰变体。

[0457] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35607.4(SEQ ID NO:479),或其修饰变体或未修饰变体。

[0458] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35613.4(SEQ ID NO:480),或其修饰变体或未修饰变体。

[0459] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35572.4(SEQ ID NO:481),或其修饰变体或未修饰变体。

[0460] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35578.4(SEQ ID NO:482),或其修饰变体或未修饰变体。

[0461] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35584.4(SEQ ID NO:483),或其修饰变体或未修饰变体。

[0462] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35590.4(SEQ ID NO:484),或其修饰变体或未修饰变体。

[0463] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35596.4(SEQ ID NO:485),或其修饰变体或未修饰变体。

[0464] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35602.4(SEQ ID NO:486),或其修饰变体或未修饰变体。

[0465] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35608.4(SEQ ID NO:487),或其修饰变体或未修饰变体。

[0466] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35614.4(SEQ ID NO:488),或其修饰变体或未修饰变体。

[0467] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35573.4(SEQ ID NO:489),或其修饰变体或未修饰变体。

[0468] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35579.4(SEQ ID NO:490),或其修饰变体或未修饰变体。

[0469] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35585.4(SEQ ID NO:491),或其修饰变体或未修饰变体。

[0470] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35591.4(SEQ ID NO:492),或其修饰变体或未修饰变体。

[0471] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35597.4(SEQ ID NO:493),或其修饰变体或未修饰变体。

[0472] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35603.4(SEQ ID NO:494),或其修饰变体或未修饰变体。

[0473] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35609.4(SEQ ID NO:495),或其修饰变体或未修饰变体。

[0474] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35615.4(SEQ ID NO:496),或其修饰变体或未修饰变体。

[0475] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35574.4(SEQ ID NO:497),或其修饰变体或未修饰变体。

[0476] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35580.1(SEQ ID NO:498),或其修饰变体或未修饰变体。

[0477] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35586.4(SEQ ID NO:499),或其修饰变体或未修饰变体。

[0478] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35592.4(SEQ ID NO:500),或其修饰变体或未修饰变体。

[0479] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35598.4(SEQ ID NO:501),或其修饰变体或未修饰变体。

[0480] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35604.4(SEQ ID NO:502),或其修饰变体或未修饰变体。

[0481] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35610.4(SEQ ID NO:503),或其修饰变体或未修饰变体。

[0482] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35616.4(SEQ ID NO:504),或其修饰变体或未修饰变体。

[0483] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35575.4(SEQ ID NO:505),或其修饰变体或未修饰变体。

[0484] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35581.4(SEQ ID NO:506),或其修饰变体或未修饰变体。

[0485] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35587.4(SEQ ID NO:507),或其修饰变体或未修饰变体。

[0486] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35593.4(SEQ ID NO:508),或其修饰变体或未修饰变体。

[0487] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35599.4(SEQ ID NO:509),或其修饰变体或未修饰变体。

[0488] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35605.4(SEQ ID NO:510),或其修饰变体或未修饰变体。

[0489] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35611.4(SEQ ID NO:511),或其修饰变体或未修饰变体。

[0490] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35617.4(SEQ ID NO:512),或其修饰变体或未修饰变体。

[0491] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35576.4(SEQ ID NO:513),或其修饰变体或未修饰变体。

[0492] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35588.4(SEQ ID NO:514),或其修饰变体或未修饰变体。

[0493] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35667.1(SEQ ID NO:515),或其修饰变体或未修饰变体。

[0494] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35673.1(SEQ ID NO:516),或其修饰变体或未修饰变体。

[0495] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35679.1(SEQ ID NO:517),或其修饰变体或未修饰变体。

[0496] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35685.1(SEQ ID NO:518),或其修饰变体或未修饰变体。

[0497] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35691.1(SEQ ID NO:519),或其修饰变体或未修饰变体。

[0498] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35557.1(SEQ ID NO:520),或其修饰变体或未修饰变体。

[0499] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35618.1(SEQ ID NO:521),或其修饰变体或未修饰变体。

[0500] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35569.1(SEQ ID NO:522),或其修饰变体或未修饰变体。

[0501] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35534.1(SEQ ID NO:523),或其修饰变体或未修饰变体。

[0502] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35582.1(SEQ ID NO:524),或其修饰变体或未修饰变体。

[0503] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35594.1(SEQ ID NO:525),或其修饰变体或未修饰变体。

[0504] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35600.1(SEQ ID NO:526),或其修饰变体或未修饰变体。

[0505] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35606.1(SEQ ID NO:527),或其修饰变体或未修饰变体。

[0506] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35612.1(SEQ ID NO:528),或其修饰变体或未修饰变体。

[0507] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38127.1(SEQ ID NO:529),或其修饰变体或未修饰变体。

[0508] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38133.1(SEQ ID NO:530),或其修饰变体或未修饰变体。

[0509] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38139.1(SEQ ID NO:531),或其修饰变体或未修饰变体。

[0510] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38145.1(SEQ ID NO:532),或其修饰变体或未修饰变体。

[0511] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38151.1(SEQ ID NO:533),或其修饰变体或未修饰变体。

[0512] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38157.1(SEQ ID NO:534),或其修饰变体或未修饰变体。

[0513] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38163.1(SEQ ID NO:535),或其修饰变体或未修饰变体。

[0514] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38169.1(SEQ ID NO:536),或其修饰变体或未修饰变体。

[0515] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38128.1(SEQ ID NO:537),或其修饰变体或未修饰变体。

[0516] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38134.1(SEQ ID NO:538),或其修饰变体或未修饰变体。

[0517] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38140.1(SEQ ID NO:539),或其修饰变体或未修饰变体。

[0518] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38146.1(SEQ ID NO:540),或其修饰变体或未修饰变体。

[0519] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38152.1(SEQ ID NO:541),或其修饰变体或未修饰变体。

[0520] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38158.1(SEQ ID NO:542),或其修饰变体或未修饰变体。

[0521] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38164.1(SEQ ID NO:543),或其修饰变体或未修饰变体。

[0522] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38170.1(SEQ ID NO:544),或其修饰变体或未修饰变体。

[0523] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38129.1(SEQ ID NO:545),或其修饰变体或未修饰变体。

[0524] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38135.1(SEQ ID NO:546),或其修饰变体或未修饰变体。

[0525] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38141.1(SEQ ID NO:547),或其修饰变体或未修饰变体。

[0526] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38147.1(SEQ ID NO:548),或其修饰变体或未修饰变体。

[0527] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38153.1(SEQ ID NO:549),或其修饰变体或未修饰变体。

[0528] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38159.1(SEQ ID NO:550),或其修饰变体或未修饰变体。

[0529] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38165.1(SEQ ID NO:551),或其修饰变体或未修饰变体。

[0530] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38171.1(SEQ ID NO:552),或其修饰变体或未修饰变体。

[0531] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38130.1(SEQ ID NO:553),或其修饰变体或未修饰变体。

[0532] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38136.1(SEQ ID NO:554),或其修饰变体或未修饰变体。

[0533] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38142.1(SEQ ID NO:555),或其修饰变体或未修饰变体。

[0534] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38148.1(SEQ ID NO:556),或其修饰变体或未修饰变体。

[0535] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38154.1(SEQ ID NO:557),或其修饰变体或未修饰变体。

[0536] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38160.1(SEQ ID NO:558),或其修饰变体或未修饰变体。

[0537] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38166.1(SEQ ID NO:559),或其修饰变体或未修饰变体。

[0538] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38172.1(SEQ ID NO:560),或其修饰变体或未修饰变体。

[0539] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38131.1(SEQ ID NO:561),或其修饰变体或未修饰变体。

[0540] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38137.1(SEQ ID NO:562),或其修饰变体或未修饰变体。

[0541] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38143.1(SEQ ID NO:563),或其修饰变体或未修饰变体。

[0542] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38149.1(SEQ ID NO:564),或其修饰变体或未修饰变体。

[0543] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38155.1(SEQ ID NO:565),或其修饰变体或未修饰变体。

[0544] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38161.1(SEQ ID NO:566),或其修饰变体或未修饰变体。

[0545] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38167.1(SEQ ID NO:567),或其修饰变体或未修饰变体。

[0546] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38173.1(SEQ ID NO:568),或其修饰变体或未修饰变体。

[0547] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38132.1(SEQ ID NO:569),或其修饰变体或未修饰变体。

[0548] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38138.1(SEQ ID NO:570),或其修饰变体或未修饰变体。

[0549] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38144.1(SEQ ID NO:571),或其修饰变体或未修饰变体。

[0550] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38150.1(SEQ ID NO:572),或其修饰变体或未修饰变体。

[0551] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38156.1(SEQ ID NO:573),或其修饰变体或未修饰变体。

[0552] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38162.1(SEQ ID NO:574),或其修饰变体或未修饰变体。

[0553] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38168.1(SEQ ID NO:575),或其修饰变体或未修饰变体。

[0554] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-38174.1(SEQ ID NO:576),或其修饰变体或未修饰变体。

[0555] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39683.1(SEQ ID NO:577),或其修饰变体或未修饰变体。

[0556] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39689.1(SEQ ID NO:578),或其修饰变体或未修饰变体。

[0557] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39695.1(SEQ ID NO:579),或其修饰变体或未修饰变体。

[0558] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39701.1(SEQ ID NO:580),或其修饰变体或未修饰变体。

[0559] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39707.1(SEQ ID NO:581),或其修饰变体或未修饰变体。

[0560] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39713.1(SEQ ID NO:582),或其修饰变体或未修饰变体。

[0561] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39719.1(SEQ ID NO:583),或其修饰变体或未修饰变体。

[0562] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39725.1(SEQ ID NO:584),或其修饰变体或未修饰变体。

[0563] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39684.1(SEQ ID NO:585),或其修饰变体或未修饰变体。

[0564] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39690.1(SEQ ID NO:586),或其修饰变体或未修饰变体。

[0565] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39696.1(SEQ ID NO:587),或其修饰变体或未修饰变体。

[0566] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39702.1(SEQ ID NO:588),或其修饰变体或未修饰变体。

[0567] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39708.1(SEQ ID NO:589),或其修饰变体或未修饰变体。

[0568] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39714.1(SEQ ID NO:590),或其修饰变体或未修饰变体。

[0569] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39720.1(SEQ ID NO:591),或其修饰变体或未修饰变体。

[0570] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39726.1(SEQ ID NO:592),或其修饰变体或未修饰变体。

[0571] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39685.1(SEQ ID NO:593),或其修饰变体或未修饰变体。

[0572] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39691.1(SEQ ID NO:594),或其修饰变体或未修饰变体。

[0573] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39697.1(SEQ ID NO:595),或其修饰变体或未修饰变体。

[0574] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39703.1(SEQ ID NO:596),或其修饰变体或未修饰变体。

[0575] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39709.1(SEQ ID NO:597),或其修饰变体或未修饰变体。

[0576] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39715.1(SEQ ID NO:598),或其修饰变体或未修饰变体。

[0577] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39721.1(SEQ ID NO:599),或其修饰变体或未修饰变体。

[0578] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39727.1(SEQ ID NO:600),或其修饰变体或未修饰变体。

[0579] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39686.1(SEQ ID NO:601),或其修饰变体或未修饰变体。

[0580] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39692.1(SEQ ID NO:602),或其修饰变体或未修饰变体。

[0581] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39698.1(SEQ ID NO:603),或其修饰变体或未修饰变体。

[0582] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39704.1(SEQ ID NO:604),或其修饰变体或未修饰变体。

[0583] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39710.1(SEQ ID NO:605),或其修饰变体或未修饰变体。

[0584] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39716.1(SEQ ID NO:606),或其修饰变体或未修饰变体。

[0585] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39722.1(SEQ ID NO:607),或其修饰变体或未修饰变体。

[0586] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39728.1(SEQ ID NO:608),或其修饰变体或未修饰变体。

[0587] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39687.1(SEQ ID NO:609),或其修饰变体或未修饰变体。

[0588] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39693.1(SEQ ID NO:610),或其修饰变体或未修饰变体。

[0589] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39699.1(SEQ ID NO:611),或其修饰变体或未修饰变体。

[0590] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39705.1(SEQ ID NO:612),或其修饰变体或未修饰变体。

[0591] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39711.1(SEQ ID NO:613),或其修饰变体或未修饰变体。

[0592] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39717.1(SEQ ID NO:614),或其修饰变体或未修饰变体。

[0593] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39723.1(SEQ ID NO:615),或其修饰变体或未修饰变体。

[0594] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39729.1(SEQ ID NO:616),或其修饰变体或未修饰变体。

[0595] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39688.1(SEQ ID NO:617),或其修饰变体或未修饰变体。

[0596] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39694.1(SEQ ID NO:618),或其修饰变体或未修饰变体。

[0597] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39700.1(SEQ ID NO:619),或其修饰变体或未修饰变体。

[0598] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39706.1(SEQ ID NO:620),或其修饰变体或未修饰变体。

[0599] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39712.1(SEQ ID NO:621),或其修饰变体或未修饰变体。

[0600] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39718.1(SEQ ID NO:622),或其修饰变体或未修饰变体。

[0601] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39724.1(SEQ ID NO:623),或其修饰变体或未修饰变体。

[0602] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39730.1(SEQ ID NO:624),或其修饰变体或未修饰变体。

[0603] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39736.1(SEQ ID NO:625),或其修饰变体或未修饰变体。

[0604] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39742.1(SEQ ID NO:626),或其修饰变体或未修饰变体。

[0605] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39748.1(SEQ ID NO:627),或其修饰变体或未修饰变体。

[0606] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39754.1(SEQ ID NO:628),或其修饰变体或未修饰变体。

[0607] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39760.1(SEQ ID NO:629),或其修饰变体或未修饰变体。

[0608] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39766.1(SEQ ID NO:630),或其修饰变体或未修饰变体。

[0609] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39772.1(SEQ ID NO:631),或其修饰变体或未修饰变体。

[0610] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39731.1(SEQ ID NO:632),或其修饰变体或未修饰变体。

[0611] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39737.1(SEQ ID NO:633),或其修饰变体或未修饰变体。

[0612] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39743.1(SEQ ID NO:634),或其修饰变体或未修饰变体。

[0613] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39749.1(SEQ ID NO:635),或其修饰变体或未修饰变体。

[0614] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39755.1(SEQ ID NO:636),或其修饰变体或未修饰变体。

[0615] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39761.1(SEQ ID NO:637),或其修饰变体或未修饰变体。

[0616] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39767.1(SEQ ID NO:638),或其修饰变体或未修饰变体。

[0617] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39773.1(SEQ ID NO:639),或其修饰变体或未修饰变体。

[0618] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39732.1(SEQ ID NO:640),或其修饰变体或未修饰变体。

[0619] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39738.1(SEQ ID NO:641),或其修饰变体或未修饰变体。

[0620] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39744.1(SEQ ID NO:642),或其修饰变体或未修饰变体。

[0621] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39750.1(SEQ ID NO:643),或其修饰变体或未修饰变体。

[0622] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39756.1(SEQ ID NO:644),或其修饰变体或未修饰变体。

[0623] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39762.1(SEQ ID NO:645),或其修饰变体或未修饰变体。

[0624] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39768.1(SEQ ID NO:646),或其修饰变体或未修饰变体。

[0625] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39774.1(SEQ ID NO:647),或其修饰变体或未修饰变体。

[0626] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39733.1(SEQ ID NO:648),或其修饰变体或未修饰变体。

[0627] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39739.1(SEQ ID NO:649),或其修饰变体或未修饰变体。

[0628] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39745.1(SEQ ID NO:650),或其修饰变体或未修饰变体。

[0629] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39751.1(SEQ ID NO:651),或其修饰变体或未修饰变体。

[0630] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39757.1(SEQ ID NO:652),或其修饰变体或未修饰变体。

[0631] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39763.1(SEQ ID NO:653),或其修饰变体或未修饰变体。

[0632] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39769.1(SEQ ID NO:654),或其修饰变体或未修饰变体。

[0633] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39775.1(SEQ ID NO:655),或其修饰变体或未修饰变体。

[0634] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39734.1(SEQ ID NO:656),或其修饰变体或未修饰变体。

[0635] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39740.1(SEQ ID NO:657),或其修饰变体或未修饰变体。

[0636] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39746.1(SEQ ID NO:658),或其修饰变体或未修饰变体。

[0637] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39752.1(SEQ ID NO:659),或其修饰变体或未修饰变体。

[0638] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39758.1(SEQ ID NO:660),或其修饰变体或未修饰变体。

[0639] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39764.1(SEQ ID NO:661),或其修饰变体或未修饰变体。

[0640] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39770.1(SEQ ID NO:662),或其修饰变体或未修饰变体。

[0641] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39776.1(SEQ ID NO:663),或其修饰变体或未修饰变体。

[0642] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39735.1(SEQ ID NO:664),或其修饰变体或未修饰变体。

[0643] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39741.1(SEQ ID NO:665),或其修饰变体或未修饰变体。

[0644] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39747.1(SEQ ID NO:666),或其修饰变体或未修饰变体。

[0645] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39753.1(SEQ ID NO:667),或其修饰变体或未修饰变体。

[0646] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39759.1(SEQ ID NO:668),或其修饰变体或未修饰变体。

[0647] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39765.1(SEQ ID NO:669),或其修饰变体或未修饰变体。

[0648] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39771.1(SEQ ID NO:670),或其修饰变体或未修饰变体。

[0649] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39778.1(SEQ ID NO:671),或其修饰变体或未修饰变体。

[0650] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39784.1(SEQ ID NO:672),或其修饰变体或未修饰变体。

[0651] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39790.1(SEQ ID NO:673),或其修饰变体或未修饰变体。

[0652] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39796.1(SEQ ID NO:674),或其修饰变体或未修饰变体。

[0653] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39802.1(SEQ ID NO:675),或其修饰变体或未修饰变体。

[0654] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39808.1(SEQ ID NO:676),或其修饰变体或未修饰变体。

[0655] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39814.1(SEQ ID NO:677),或其修饰变体或未修饰变体。

[0656] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39820.1(SEQ ID NO:678),或其修饰变体或未修饰变体。

[0657] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39779.1(SEQ ID NO:679),或其修饰变体或未修饰变体。

[0658] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39785.1(SEQ ID NO:680),或其修饰变体或未修饰变体。

[0659] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39791.1(SEQ ID NO:681),或其修饰变体或未修饰变体。

[0660] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39797.1(SEQ ID NO:682),或其修饰变体或未修饰变体。

[0661] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39803.1(SEQ ID NO:683),或其修饰变体或未修饰变体。

[0662] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39809.1(SEQ ID NO:684),或其修饰变体或未修饰变体。

[0663] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39815.1(SEQ ID NO:685),或其修饰变体或未修饰变体。

[0664] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39821.1(SEQ ID NO:686),或其修饰变体或未修饰变体。

[0665] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39780.1(SEQ ID NO:687),或其修饰变体或未修饰变体。

[0666] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39786.1(SEQ ID NO:688),或其修饰变体或未修饰变体。

[0667] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39792.1(SEQ ID NO:689),或其修饰变体或未修饰变体。

[0668] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39798.1(SEQ ID NO:690),或其修饰变体或未修饰变体。

[0669] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39804.1(SEQ ID NO:691),或其修饰变体或未修饰变体。

[0670] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39810.1(SEQ ID NO:692),或其修饰变体或未修饰变体。

[0671] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39816.1(SEQ ID NO:693),或其修饰变体或未修饰变体。

[0672] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39822.1(SEQ ID NO:694),或其修饰变体或未修饰变体。

[0673] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39781.1(SEQ ID NO:695),或其修饰变体或未修饰变体。

[0674] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39787.1(SEQ ID NO:696),或其修饰变体或未修饰变体。

[0675] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39793.1(SEQ ID NO:697),或其修饰变体或未修饰变体。

[0676] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39799.1(SEQ ID NO:698),或其修饰变体或未修饰变体。

[0677] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39805.1(SEQ ID NO:699),或其修饰变体或未修饰变体。

[0678] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39811.1(SEQ ID NO:700),或其修饰变体或未修饰变体。

[0679] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39817.1(SEQ ID NO:701),或其修饰变体或未修饰变体。

[0680] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39823.1(SEQ ID NO:702),或其修饰变体或未修饰变体。

[0681] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39782.1(SEQ ID NO:703),或其修饰变体或未修饰变体。

[0682] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39788.1(SEQ ID NO:704),或其修饰变体或未修饰变体。

[0683] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39794.1(SEQ ID NO:705),或其修饰变体或未修饰变体。

[0684] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39800.1(SEQ ID NO:706),或其修饰变体或未修饰变体。

[0685] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39806.1(SEQ ID NO:707),或其修饰变体或未修饰变体。

[0686] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39812.1(SEQ ID NO:708),或其修饰变体或未修饰变体。

[0687] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39818.1(SEQ ID NO:709),或其修饰变体或未修饰变体。

[0688] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39824.1(SEQ ID NO:710),或其修饰变体或未修饰变体。

[0689] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39783.1(SEQ ID NO:711),或其修饰变体或未修饰变体。

[0690] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39789.1(SEQ ID NO:712),或其修饰变体或未修饰变体。

[0691] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39795.1(SEQ ID NO:713),或其修饰变体或未修饰变体。

[0692] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39801.1(SEQ ID NO:714),或其修饰变体或未修饰变体。

[0693] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39807.1(SEQ ID NO:715),或其修饰变体或未修饰变体。

[0694] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39813.1(SEQ ID NO:716),或其修饰变体或未修饰变体。

[0695] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39819.1(SEQ ID NO:717),或其修饰变体或未修饰变体。

[0696] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39825.1(SEQ ID NO:718),或其修饰变体或未修饰变体。

[0697] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39831.1(SEQ ID NO:719),或其修饰变体或未修饰变体。

[0698] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39837.1(SEQ ID NO:720),或其修饰变体或未修饰变体。

[0699] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39843.1(SEQ ID NO:721),或其修饰变体或未修饰变体。

[0700] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39849.1(SEQ ID NO:722),或其修饰变体或未修饰变体。

[0701] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39855.1(SEQ ID NO:723),或其修饰变体或未修饰变体。

[0702] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39861.1(SEQ ID NO:724),或其修饰变体或未修饰变体。

[0703] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39867.1(SEQ ID NO:725),或其修饰变体或未修饰变体。

[0704] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39826.1(SEQ ID NO:726),或其修饰变体或未修饰变体。

[0705] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39832.1(SEQ ID NO:727),或其修饰变体或未修饰变体。

[0706] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39838.1(SEQ ID NO:728),或其修饰变体或未修饰变体。

[0707] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39844.1(SEQ ID NO:729),或其修饰变体或未修饰变体。

[0708] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39850.1(SEQ ID NO:730),或其修饰变体或未修饰变体。

[0709] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39856.1(SEQ ID NO:731),或其修饰变体或未修饰变体。

[0710] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39862.1(SEQ ID NO:732),或其修饰变体或未修饰变体。

[0711] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39868.1(SEQ ID NO:733),或其修饰变体或未修饰变体。

[0712] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39827.1(SEQ ID NO:734),或其修饰变体或未修饰变体。

[0713] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39833.1(SEQ ID NO:735),或其修饰变体或未修饰变体。

[0714] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39839.1(SEQ ID NO:736),或其修饰变体或未修饰变体。

[0715] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39845.1(SEQ ID NO:737),或其修饰变体或未修饰变体。

[0716] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39851.1(SEQ ID NO:738),或其修饰变体或未修饰变体。

[0717] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39857.1(SEQ ID NO:739),或其修饰变体或未修饰变体。

[0718] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39863.1(SEQ ID NO:740),或其修饰变体或未修饰变体。

[0719] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39869.1(SEQ ID NO:741),或其修饰变体或未修饰变体。

[0720] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39828.1(SEQ ID NO:742),或其修饰变体或未修饰变体。

[0721] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39834.1(SEQ ID NO:743),或其修饰变体或未修饰变体。

[0722] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39840.1(SEQ ID NO:744),或其修饰变体或未修饰变体。

[0723] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39846.1(SEQ ID NO:745),或其修饰变体或未修饰变体。

[0724] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39852.1(SEQ ID NO:746),或其修饰变体或未修饰变体。

[0725] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39858.1(SEQ ID NO:747),或其修饰变体或未修饰变体。

[0726] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39864.1(SEQ ID NO:748),或其修饰变体或未修饰变体。

[0727] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39870.1(SEQ ID NO:749),或其修饰变体或未修饰变体。

[0728] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39829.1(SEQ ID NO:750),或其修饰变体或未修饰变体。

[0729] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39835.1(SEQ ID NO:751),或其修饰变体或未修饰变体。

[0730] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39841.1(SEQ ID NO:752),或其修饰变体或未修饰变体。

[0731] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39853.1(SEQ ID NO:753),或其修饰变体或未修饰变体。

[0732] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39859.1(SEQ ID NO:754),或其修饰变体或未修饰变体。

[0733] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39865.1(SEQ ID NO:755),或其修饰变体或未修饰变体。

[0734] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39871.1(SEQ ID NO:756),或其修饰变体或未修饰变体。

[0735] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39830.1(SEQ ID NO:757),或其修饰变体或未修饰变体。

[0736] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39836.1(SEQ ID NO:758),或其修饰变体或未修饰变体。

[0737] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39842.1(SEQ ID NO:759),或其修饰变体或未修饰变体。

[0738] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39848.1(SEQ ID NO:760),或其修饰变体或未修饰变体。

[0739] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39854.1(SEQ ID NO:761),或其修饰变体或未修饰变体。

[0740] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39860.1(SEQ ID NO:762),或其修饰变体或未修饰变体。

[0741] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39866.1(SEQ ID NO:763),或其修饰变体或未修饰变体。

[0742] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39992.1(SEQ ID NO:764),或其修饰变体或未修饰变体。

[0743] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39998.1(SEQ ID NO:765),或其修饰变体或未修饰变体。

[0744] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40004.1(SEQ ID NO:766),或其修饰变体或未修饰变体。

[0745] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40010.1(SEQ ID NO:767),或其修饰变体或未修饰变体。

[0746] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40016.1(SEQ ID NO:768),或其修饰变体或未修饰变体。

[0747] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40022.1(SEQ ID NO:769),或其修饰变体或未修饰变体。

[0748] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40028.1(SEQ ID NO:770),或其修饰变体或未修饰变体。

[0749] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40034.1(SEQ ID NO:771),或其修饰变体或未修饰变体。

[0750] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39999.1(SEQ ID NO:772),或其修饰变体或未修饰变体。

[0751] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40005.1(SEQ ID NO:773),或其修饰变体或未修饰变体。

[0752] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40011.1(SEQ ID NO:774),或其修饰变体或未修饰变体。

[0753] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40017.1(SEQ ID NO:775),或其修饰变体或未修饰变体。

[0754] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40029.1(SEQ ID NO:776),或其修饰变体或未修饰变体。

[0755] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40035.1(SEQ ID NO:777),或其修饰变体或未修饰变体。

[0756] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39994.1(SEQ ID NO:778),或其修饰变体或未修饰变体。

[0757] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40000.1(SEQ ID NO:779),或其修饰变体或未修饰变体。

[0758] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40006.1(SEQ ID NO:780),或其修饰变体或未修饰变体。

[0759] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40012.1(SEQ ID NO:781),或其修饰变体或未修饰变体。

[0760] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40018.1(SEQ ID NO:782),或其修饰变体或未修饰变体。

[0761] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40024.1(SEQ ID NO:783),或其修饰变体或未修饰变体。

[0762] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40030.1(SEQ ID NO:784),或其修饰变体或未修饰变体。

[0763] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40036.1(SEQ ID NO:785),或其修饰变体或未修饰变体。

[0764] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39995.1(SEQ ID NO:786),或其修饰变体或未修饰变体。

[0765] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40001.1(SEQ ID NO:787),或其修饰变体或未修饰变体。

[0766] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40007.1(SEQ ID NO:788),或其修饰变体或未修饰变体。

[0767] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40013.1(SEQ ID NO:789),或其修饰变体或未修饰变体。

[0768] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40019.1(SEQ ID NO:790),或其修饰变体或未修饰变体。

[0769] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40025.1(SEQ ID NO:791),或其修饰变体或未修饰变体。

[0770] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40031.1(SEQ ID NO:792),或其修饰变体或未修饰变体。

[0771] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40037.1(SEQ ID NO:793),或其修饰变体或未修饰变体。

[0772] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39996.1(SEQ ID NO:794),或其修饰变体或未修饰变体。

[0773] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40002.1(SEQ ID NO:795),或其修饰变体或未修饰变体。

[0774] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40008.1(SEQ ID NO:796),或其修饰变体或未修饰变体。

[0775] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40014.1(SEQ ID NO:797),或其修饰变体或未修饰变体。

[0776] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40020.1(SEQ ID NO:798),或其修饰变体或未修饰变体。

[0777] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40026.1(SEQ ID NO:799),或其修饰变体或未修饰变体。

[0778] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40032.1(SEQ ID NO:800),或其修饰变体或未修饰变体。

[0779] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40038.1(SEQ ID NO:801),或其修饰变体或未修饰变体。

[0780] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39997.1(SEQ ID NO:802),或其修饰变体或未修饰变体。

[0781] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40009.1(SEQ ID NO:803),或其修饰变体或未修饰变体。

[0782] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40015.1(SEQ ID NO:804),或其修饰变体或未修饰变体。

[0783] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40021.1(SEQ ID NO:805),或其修饰变体或未修饰变体。

[0784] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40027.1(SEQ ID NO:806),或其修饰变体或未修饰变体。

[0785] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40033.1(SEQ ID NO:807),或其修饰变体或未修饰变体。

[0786] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40039.1(SEQ ID NO:808),或其修饰变体或未修饰变体。

[0787] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40045.1(SEQ ID NO:809),或其修饰变体或未修饰变体。

[0788] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40051.1(SEQ ID NO:810),或其修饰变体或未修饰变体。

[0789] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40057.1(SEQ ID NO:811),或其修饰变体或未修饰变体。

[0790] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40063.1(SEQ ID NO:812),或其修饰变体或未修饰变体。

[0791] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40069.1(SEQ ID NO:813),或其修饰变体或未修饰变体。

[0792] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40075.1(SEQ ID NO:814),或其修饰变体或未修饰变体。

[0793] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40081.1(SEQ ID NO:815),或其修饰变体或未修饰变体。

[0794] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40040.1(SEQ ID NO:816),或其修饰变体或未修饰变体。

[0795] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40046.1(SEQ ID NO:817),或其修饰变体或未修饰变体。

[0796] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40052.1(SEQ ID NO:818),或其修饰变体或未修饰变体。

[0797] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40058.1(SEQ ID NO:819),或其修饰变体或未修饰变体。

[0798] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40064.1(SEQ ID NO:820),或其修饰变体或未修饰变体。

[0799] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40070.1(SEQ ID NO:821),或其修饰变体或未修饰变体。

[0800] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40076.1(SEQ ID NO:822),或其修饰变体或未修饰变体。

[0801] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40082.1(SEQ ID NO:823),或其修饰变体或未修饰变体。

[0802] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40041.1(SEQ ID NO:824),或其修饰变体或未修饰变体。

[0803] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40047.1(SEQ ID NO:825),或其修饰变体或未修饰变体。

[0804] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40053.1(SEQ ID NO:826),或其修饰变体或未修饰变体。

[0805] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40059.1(SEQ ID NO:827),或其修饰变体或未修饰变体。

[0806] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40065.1(SEQ ID NO:828),或其修饰变体或未修饰变体。

[0807] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40071.1(SEQ ID NO:829),或其修饰变体或未修饰变体。

[0808] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40077.1(SEQ ID NO:830),或其修饰变体或未修饰变体。

[0809] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40083.1(SEQ ID NO:831),或其修饰变体或未修饰变体。

[0810] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40042.1(SEQ ID NO:832),或其修饰变体或未修饰变体。

[0811] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40048.1(SEQ ID NO:833),或其修饰变体或未修饰变体。

[0812] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40054.1(SEQ ID NO:834),或其修饰变体或未修饰变体。

[0813] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40060.1(SEQ ID NO:835),或其修饰变体或未修饰变体。

[0814] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40066.1(SEQ ID NO:836),或其修饰变体或未修饰变体。

[0815] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40072.1(SEQ ID NO:837),或其修饰变体或未修饰变体。

[0816] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40078.1(SEQ ID NO:838),或其修饰变体或未修饰变体。

[0817] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40084.1(SEQ ID NO:839),或其修饰变体或未修饰变体。

[0818] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40043.1(SEQ ID NO:840),或其修饰变体或未修饰变体。

[0819] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40049.1(SEQ ID NO:841),或其修饰变体或未修饰变体。

[0820] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40055.1(SEQ ID NO:842),或其修饰变体或未修饰变体。

[0821] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40061.1(SEQ ID NO:843),或其修饰变体或未修饰变体。

[0822] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40067.1(SEQ ID NO:844),或其修饰变体或未修饰变体。

[0823] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40073.1(SEQ ID NO:845),或其修饰变体或未修饰变体。

[0824] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40079.1(SEQ ID NO:846),或其修饰变体或未修饰变体。

[0825] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40085.1(SEQ ID NO:847),或其修饰变体或未修饰变体。

[0826] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40044.1(SEQ ID NO:848),或其修饰变体或未修饰变体。

[0827] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40050.1(SEQ ID NO:849),或其修饰变体或未修饰变体。

[0828] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40056.1(SEQ ID NO:850),或其修饰变体或未修饰变体。

[0829] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40062.1(SEQ ID NO:851),或其修饰变体或未修饰变体。

[0830] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40068.1(SEQ ID NO:852),或其修饰变体或未修饰变体。

[0831] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40074.1(SEQ ID NO:853),或其修饰变体或未修饰变体。

[0832] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-40080.1(SEQ ID NO:854),或其修饰变体或未修饰变体。

[0833] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39720.1(SEQ ID NO:1754),或其修饰变体或未修饰变体。

[0834] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39706.1(SEQ ID NO:1755),或其修饰变体或未修饰变体。

[0835] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39712.1(SEQ ID NO:1756),或其修饰变体或未修饰变体。

[0836] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39760.1(SEQ ID NO:1757),或其修饰变体或未修饰变体。

[0837] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、

1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39732.1(SEQ ID NO:1758),或其修饰变体或未修饰变体。

[0838] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35541.4(SEQ ID NO:1759),或其修饰变体或未修饰变体。

[0839] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NO:1760),或其修饰变体或未修饰变体。

[0840] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39741.1,或其修饰变体或未修饰变体。

[0841] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :hs_KRAS_322_A22S26(SEQ ID NO:1761),或其修饰变体或未修饰变体。

[0842] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39778.1(SEQ ID NO:1762),或其修饰变体或未修饰变体。

[0843] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39790.1(SEQ ID NO:1763),或其修饰变体或未修饰变体。

[0844] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39822.1(SEQ ID NO:1764),或其修饰变体或未修饰变体。

[0845] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35609.4(SEQ ID NO:1765),或其修饰变体或未修饰变体。

[0846] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35581.4(SEQ ID NO:1766),或其修饰变体或未修饰变体。

[0847] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39845.1(SEQ ID NO:1767),或其修饰变体或未修饰变体。

[0848] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39858.1(SEQ ID NO:1768),或其修饰变体或未修饰变体。

[0849] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-39870.1(SEQ ID NO:1769),或其修饰变体或未修饰变体。

[0850] 包含第一链和第二链的 RNAi 剂,其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-35576.4(SEQ ID NO:1770),或其修饰变体

或未修饰变体。

[0851] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-35588.4(SEQ ID NO:1771)，或其修饰变体或未修饰变体。

[0852] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-35600.1(SEQ ID NO:1772)，或其修饰变体或未修饰变体。

[0853] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-35606.1(SEQ ID NO:1773)，或其修饰变体或未修饰变体。

[0854] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38151.1(SEQ ID NO:1774)，或其修饰变体或未修饰变体。

[0855] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38163.1(SEQ ID NO:1775)，或其修饰变体或未修饰变体。

[0856] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-39999.1(SEQ ID NO:1776)，或其修饰变体或未修饰变体。

[0857] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NO:1777)，或其修饰变体或未修饰变体。

[0858] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NO:1778)，或其修饰变体或未修饰变体。

[0859] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38136.1(SEQ ID NO:1779)，或其修饰变体或未修饰变体。

[0860] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40036.1(SEQ ID NO:1780)，或其修饰变体或未修饰变体。

[0861] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40008.1(SEQ ID NO:1781)，或其修饰变体或未修饰变体。

[0862] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40021.1(SEQ ID NO:1782)，或其修饰变体或未修饰变体。

[0863] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40077.1(SEQ ID NO:1783)，或其修饰变体

或未修饰变体。

[0864] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40072.1(SEQ ID NO:1784)，或其修饰变体或未修饰变体。

[0865] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40061.1(SEQ ID NO:1785)，或其修饰变体或未修饰变体。

[0866] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-40068.1(SEQ ID NO:1786)，或其修饰变体或未修饰变体。

[0867] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38131.1(SEQ ID NO:1787)，或其修饰变体或未修饰变体。

[0868] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-38167.1(SEQ ID NO:1788)，或其修饰变体或未修饰变体。

[0869] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：hs_KRAS1273_A22S26(SEQ ID NO:1789)，或其修饰变体或未修饰变体。

[0870] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：hs_KRAS2892_A37S26(SEQ ID NO:1790)，或其修饰变体或未修饰变体。

[0871] 包含第一链和第二链的 RNAi 剂，其中第一链包含与如下 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：hs_KRAS4731_A22S26(SEQ ID NO:1791)，或其修饰变体或未修饰变体。

[0872] 包含本文公开的任何 RNAi 剂的至少 15 个连续核苷酸的具体实施方案

[0873] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链包含来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体或未修饰变体的第一链的至少 15 个连续核苷酸（差异 0 个核苷酸）。

[0874] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[0875] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35523.3(SEQ ID NO:428)，或其修饰变体或未修饰变体。

[0876] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35529.1(SEQ ID NO:429)，或其修饰变体或未修饰变体。

[0877] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35535.4(SEQ ID NO:430)，或其修饰变体或未修饰变体。

[0878] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35541.4(SEQ ID NO:431)，或其修饰变体或未修饰变体。

[0879] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35547.4(SEQ ID NO:432)，或其修饰变体或未修饰变体。

[0880] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35553.4(SEQ ID NO:433)，或其修饰变体或未修饰变体。

[0881] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35559.4(SEQ ID NO:434)，或其修饰变体或未修饰变体。

[0882] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35565.4(SEQ ID NO:435)，或其修饰变体或未修饰变体。

[0883] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35524.4(SEQ ID NO:436)，或其修饰变体或未修饰变体。

[0884] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35530.4(SEQ ID NO:437)，或其修饰变体或未修饰变体。

[0885] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35536.4(SEQ ID NO:438)，或其修饰变体或未修饰变体。

[0886] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35542.4(SEQ ID NO:439)，或其修饰变体或未修饰变体。

[0887] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35548.4(SEQ ID NO:440)，或其修饰变体或未修饰变体。

[0888] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35554.4(SEQ ID NO:441)，或其修饰变体或未修饰变体。

[0889] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35560.2(SEQ ID NO:442)，或其修饰变体或未修饰变体。

[0890] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35566.4(SEQ ID NO:443)，或其修饰变体或未修饰变体。

[0891] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35525.2(SEQ ID NO:444)，或其修饰变体或未修饰变体。

[0892] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35531.4(SEQ ID NO:445)，或其修饰变体或未修饰变体。

[0893] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35537.4(SEQ ID NO:446)，或其修饰变体或未修饰变体。

[0894] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35543.2(SEQ ID NO:447)，或其修饰变体或未修饰变体。

[0895] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35549.4(SEQ ID NO:448)，或其修饰变体或未修饰变体。

[0896] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35555.4(SEQ ID NO:449)，或其修饰变体或未修饰变体。

[0897] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35561.4(SEQ ID NO:450)，或其修饰变体或未修饰变体。

[0898] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-35567.4(SEQ ID NO:451),或其修饰变体或未修饰变体。

[0899] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35526.4(SEQ ID NO:452),或其修饰变体或未修饰变体。

[0900] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35532.4(SEQ ID NO:453),或其修饰变体或未修饰变体。

[0901] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35538.4(SEQ ID NO:454),或其修饰变体或未修饰变体。

[0902] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35544.4(SEQ ID NO:455),或其修饰变体或未修饰变体。

[0903] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35550.4(SEQ ID NO:456),或其修饰变体或未修饰变体。

[0904] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35556.4(SEQ ID NO:457),或其修饰变体或未修饰变体。

[0905] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35562.4(SEQ ID NO:458),或其修饰变体或未修饰变体。

[0906] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35568.4(SEQ ID NO:459),或其修饰变体或未修饰变体。

[0907] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35527.4(SEQ ID NO:460),或其修饰变体或未修饰变体。

[0908] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35533.4(SEQ ID NO:461),或其修饰变体或未修饰变体。

[0909] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35539.4(SEQ ID NO:462),或其修饰变体或未修饰变体。

[0910] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35545.4(SEQ ID NO:463),或其修饰变体或未修饰变体。

[0911] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35551.4(SEQ ID NO:464),或其修饰变体或未修饰变体。

[0912] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35563.4(SEQ ID NO:465),或其修饰变体或未修饰变体。

[0913] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35528.4(SEQ ID NO:466),或其修饰变体或未修饰变体。

[0914] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35540.4(SEQ ID NO:467),或其修饰变体或未修饰变体。

[0915] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35546.4(SEQ ID NO:468),或其修饰变体或未修饰变体。

[0916] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35552.4(SEQ ID NO:469),或其修饰变体或未修饰变体。

[0917] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35558.4(SEQ ID NO:470),或其修饰变体或未修饰变体。

[0918] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35564.4(SEQ ID NO:471)，或其修饰变体或未修饰变体。

[0919] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35570.4(SEQ ID NO:472)，或其修饰变体或未修饰变体。

[0920] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35571.4(SEQ ID NO:473)，或其修饰变体或未修饰变体。

[0921] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35577.4(SEQ ID NO:474)，或其修饰变体或未修饰变体。

[0922] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35583.4(SEQ ID NO:475)，或其修饰变体或未修饰变体。

[0923] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35589.4(SEQ ID NO:476)，或其修饰变体或未修饰变体。

[0924] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35595.4(SEQ ID NO:477)，或其修饰变体或未修饰变体。

[0925] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35601.4(SEQ ID NO:478)，或其修饰变体或未修饰变体。

[0926] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35607.4(SEQ ID NO:479)，或其修饰变体或未修饰变体。

[0927] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35613.4(SEQ ID NO:480)，或其修饰变体或未修饰变体。

[0928] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35572.4(SEQ ID NO:481)，或其修饰变体或未修饰变体。

[0929] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35578.4(SEQ ID NO:482)，或其修饰变体或未修饰变体。

[0930] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35584.4(SEQ lD NO:483)，或其修饰变体或未修饰变体。

[0931] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35590.4(SEQ ID NO:484)，或其修饰变体或未修饰变体。

[0932] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35596.4(SEQ ID NO:485)，或其修饰变体或未修饰变体。

[0933] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35602.4(SEQ ID NO:486)，或其修饰变体或未修饰变体。

[0934] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35608.4(SEQ ID NO:487)，或其修饰变体或未修饰变体。

[0935] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35614.4(SEQ ID NO:488)，或其修饰变体或未修饰变体。

[0936] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35573.4(SEQ ID NO:489)，或其修饰变体或未修饰变体。

[0937] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-35579.4(SEQ ID NO:490),或其修饰变体或未修饰变体。

[0938] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35585.4(SEQ ID NO:491),或其修饰变体或未修饰变体。

[0939] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35591.4(SEQ ID NO:492),或其修饰变体或未修饰变体。

[0940] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35597.4(SEQ ID NO:493),或其修饰变体或未修饰变体。

[0941] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35603.4(SEQ ID NO:494),或其修饰变体或未修饰变体。

[0942] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35609.4(SEQ ID NO:495),或其修饰变体或未修饰变体。

[0943] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35615.4(SEQ ID NO:496),或其修饰变体或未修饰变体。

[0944] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35574.4(SEQ ID NO:497),或其修饰变体或未修饰变体。

[0945] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35580.1(SEQ ID NO:498),或其修饰变体或未修饰变体。

[0946] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35586.4(SEQ ID NO:499),或其修饰变体或未修饰变体。

[0947] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35592.4(SEQ ID NO:500),或其修饰变体或未修饰变体。

[0948] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35598.4(SEQ ID NO:501),或其修饰变体或未修饰变体。

[0949] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35604.4(SEQ ID NO:502),或其修饰变体或未修饰变体。

[0950] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35610.4(SEQ ID NO:503),或其修饰变体或未修饰变体。

[0951] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35616.4(SEQ ID NO:504),或其修饰变体或未修饰变体。

[0952] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35575.4(SEQ ID NO:505),或其修饰变体或未修饰变体。

[0953] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35581.4(SEQ ID NO:506),或其修饰变体或未修饰变体。

[0954] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35587.4(SEQ ID NO:507),或其修饰变体或未修饰变体。

[0955] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35593.4(SEQ ID NO:508),或其修饰变体或未修饰变体。

[0956] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35599.4(SEQ ID NO:509),或其修饰变体或未修饰变体。

[0957] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35605.4(SEQ ID NO:510)，或其修饰变体或未修饰变体。

[0958] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35611.4(SEQ ID NO:511)，或其修饰变体或未修饰变体。

[0959] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35617.4(SEQ ID NO:512)，或其修饰变体或未修饰变体。

[0960] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35576.4(SEQ ID NO:513)，或其修饰变体或未修饰变体。

[0961] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35588.4(SEQ ID NO:514)，或其修饰变体或未修饰变体。

[0962] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35667.1(SEQ ID NO:515)，或其修饰变体或未修饰变体。

[0963] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35673.1(SEQ ID NO:516)，或其修饰变体或未修饰变体。

[0964] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35679.1(SEQ ID NO:517)，或其修饰变体或未修饰变体。

[0965] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35685.1(SEQ ID NO:518)，或其修饰变体或未修饰变体。

[0966] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35691.1(SEQ ID NO:519)，或其修饰变体或未修饰变体。

[0967] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35557.1(SEQ ID NO:520)，或其修饰变体或未修饰变体。

[0968] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35618.1(SEQ ID NO:521)，或其修饰变体或未修饰变体。

[0969] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35569.1(SEQ ID NO:522)，或其修饰变体或未修饰变体。

[0970] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35534.1(SEQ ID NO:523)，或其修饰变体或未修饰变体。

[0971] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35582.1(SEQ ID NO:524)，或其修饰变体或未修饰变体。

[0972] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35594.1(SEQ ID NO:525)，或其修饰变体或未修饰变体。

[0973] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35600.1(SEQ ID NO:526)，或其修饰变体或未修饰变体。

[0974] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35606.1(SEQ ID NO:527)，或其修饰变体或未修饰变体。

[0975] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35612.1(SEQ ID NO:528)，或其修饰变体或未修饰变体。

[0976] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-38127.1(SEQ ID NO:529),或其修饰变体或未修饰变体。

[0977] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38133.1(SEQ ID NO:530),或其修饰变体或未修饰变体。

[0978] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38139.1(SEQ ID NO:531),或其修饰变体或未修饰变体。

[0979] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38145.1(SEQ ID NO:532),或其修饰变体或未修饰变体。

[0980] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38151.1(SEQ ID NO:533),或其修饰变体或未修饰变体。

[0981] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38157.1(SEQ ID NO:534),或其修饰变体或未修饰变体。

[0982] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38163.1(SEQ ID NO:535),或其修饰变体或未修饰变体。

[0983] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38169.1(SEQ ID NO:536),或其修饰变体或未修饰变体。

[0984] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38128.1(SEQ ID NO:537),或其修饰变体或未修饰变体。

[0985] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38134.1(SEQ ID NO:538),或其修饰变体或未修饰变体。

[0986] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38140.1(SEQ ID NO:539),或其修饰变体或未修饰变体。

[0987] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38146.1(SEQ ID NO:540),或其修饰变体或未修饰变体。

[0988] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38152.1(SEQ ID NO:541),或其修饰变体或未修饰变体。

[0989] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38158.1(SEQ ID NO:542),或其修饰变体或未修饰变体。

[0990] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38164.1(SEQ ID NO:543),或其修饰变体或未修饰变体。

[0991] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38170.1(SEQ ID NO:544),或其修饰变体或未修饰变体。

[0992] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38129.1(SEQ ID NO:545),或其修饰变体或未修饰变体。

[0993] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38135.1(SEQ ID NO:546),或其修饰变体或未修饰变体。

[0994] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38141.1(SEQ ID NO:547),或其修饰变体或未修饰变体。

[0995] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38147.1(SEQ ID NO:548),或其修饰变体或未修饰变体。

[0996] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38153.1(SEQ ID NO:549)，或其修饰变体或未修饰变体。

[0997] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38159.1(SEQ ID NO:550)，或其修饰变体或未修饰变体。

[0998] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38165.1(SEQ ID NO:551)，或其修饰变体或未修饰变体。

[0999] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38171.1(SEQ ID NO:552)，或其修饰变体或未修饰变体。

[1000] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38130.1(SEQ ID NO:553)，或其修饰变体或未修饰变体。

[1001] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38136.1(SEQ ID NO:554)，或其修饰变体或未修饰变体。

[1002] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38142.1(SEQ ID NO:555)，或其修饰变体或未修饰变体。

[1003] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38148.1(SEQ ID NO:556)，或其修饰变体或未修饰变体。

[1004] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38154.1(SEQ ID NO:557)，或其修饰变体或未修饰变体。

[1005] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38160.1(SEQ ID NO:558)，或其修饰变体或未修饰变体。

[1006] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38166.1(SEQ ID NO:559)，或其修饰变体或未修饰变体。

[1007] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38172.1(SEQ ID NO:560)，或其修饰变体或未修饰变体。

[1008] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38131.1(SEQ ID NO:561)，或其修饰变体或未修饰变体。

[1009] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38137.1(SEQ ID NO:562)，或其修饰变体或未修饰变体。

[1010] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38143.1(SEQ ID NO:563)，或其修饰变体或未修饰变体。

[1011] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38149.1(SEQ ID NO:564)，或其修饰变体或未修饰变体。

[1012] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38155.1(SEQ ID NO:565)，或其修饰变体或未修饰变体。

[1013] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38161.1(SEQ ID NO:566)，或其修饰变体或未修饰变体。

[1014] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38167.1(SEQ ID NO:567)，或其修饰变体或未修饰变体。

[1015] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-38173.1(SEQ ID NO:568),或其修饰变体或未修饰变体。

[1016] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38132.1(SEQ ID NO:569),或其修饰变体或未修饰变体。

[1017] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38138.1(SEQ ID NO:570),或其修饰变体或未修饰变体。

[1018] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38144.1(SEQ ID NO:571),或其修饰变体或未修饰变体。

[1019] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38150.1(SEQ ID NO:572),或其修饰变体或未修饰变体。

[1020] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38156.1(SEQ ID NO:573),或其修饰变体或未修饰变体。

[1021] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38162.1(SEQ ID NO:574),或其修饰变体或未修饰变体。

[1022] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38168.1(SEQ ID NO:575),或其修饰变体或未修饰变体。

[1023] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-38174.1(SEQ ID NO:576),或其修饰变体或未修饰变体。

[1024] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39683.1(SEQ ID NO:577),或其修饰变体或未修饰变体。

[1025] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39689.1(SEQ ID NO:578),或其修饰变体或未修饰变体。

[1026] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39695.1(SEQ ID NO:579),或其修饰变体或未修饰变体。

[1027] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39701.1(SEQ ID NO:580),或其修饰变体或未修饰变体。

[1028] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39707.1(SEQ ID NO:581),或其修饰变体或未修饰变体。

[1029] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39713.1(SEQ ID NO:582),或其修饰变体或未修饰变体。

[1030] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39719.1(SEQ ID NO:583),或其修饰变体或未修饰变体。

[1031] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39725.1(SEQ ID NO:584),或其修饰变体或未修饰变体。

[1032] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39684.1(SEQ ID NO:585),或其修饰变体或未修饰变体。

[1033] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39690.1(SEQ ID NO:586),或其修饰变体或未修饰变体。

[1034] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39696.1(SEQ ID NO:587),或其修饰变体或未修饰变体。

[1035] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39702.1(SEQ ID NO:588)，或其修饰变体或未修饰变体。

[1036] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39708.1(SEQ ID NO:589)，或其修饰变体或未修饰变体。

[1037] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39714.1(SEQ ID NO:590)，或其修饰变体或未修饰变体。

[1038] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39720.1(SEQ ID NO:591)，或其修饰变体或未修饰变体。

[1039] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39726.1(SEQ ID NO:592)，或其修饰变体或未修饰变体。

[1040] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39685.1(SEQ ID NO:593)，或其修饰变体或未修饰变体。

[1041] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39691.1(SEQ ID NO:594)，或其修饰变体或未修饰变体。

[1042] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39697.1(SEQ ID NO:595)，或其修饰变体或未修饰变体。

[1043] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39703.1(SEQ ID NO:596)，或其修饰变体或未修饰变体。

[1044] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39709.1(SEQ ID NO:597)，或其修饰变体或未修饰变体。

[1045] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39715.1(SEQ ID NO:598)，或其修饰变体或未修饰变体。

[1046] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39721.1(SEQ ID NO:599)，或其修饰变体或未修饰变体。

[1047] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39727.1(SEQ ID NO:600)，或其修饰变体或未修饰变体。

[1048] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39686.1(SEQ ID NO:601)，或其修饰变体或未修饰变体。

[1049] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39692.1(SEQ ID NO:602)，或其修饰变体或未修饰变体。

[1050] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39698.1(SEQ ID NO:603)，或其修饰变体或未修饰变体。

[1051] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39704.1(SEQ ID NO:604)，或其修饰变体或未修饰变体。

[1052] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39710.1(SEQ ID NO:605)，或其修饰变体或未修饰变体。

[1053] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39716.1(SEQ ID NO:606)，或其修饰变体或未修饰变体。

[1054] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39722.1(SEQ ID NO:607),或其修饰变体或未修饰变体。

[1055] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39728.1(SEQ ID NO:608),或其修饰变体或未修饰变体。

[1056] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39687.1(SEQ ID NO:609),或其修饰变体或未修饰变体。

[1057] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39693.1(SEQ ID NO:610),或其修饰变体或未修饰变体。

[1058] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39699.1(SEQ ID NO:611),或其修饰变体或未修饰变体。

[1059] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39705.1(SEQ ID NO:612),或其修饰变体或未修饰变体。

[1060] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39711.1(SEQ ID NO:613),或其修饰变体或未修饰变体。

[1061] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39717.1(SEQ ID NO:614),或其修饰变体或未修饰变体。

[1062] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39723.1(SEQ ID NO:615),或其修饰变体或未修饰变体。

[1063] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39729.1(SEQ ID NO:616),或其修饰变体或未修饰变体。

[1064] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39688.1(SEQ ID NO:617),或其修饰变体或未修饰变体。

[1065] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39694.1(SEQ ID NO:618),或其修饰变体或未修饰变体。

[1066] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39700.1(SEQ ID NO:619),或其修饰变体或未修饰变体。

[1067] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39706.1(SEQ ID NO:620),或其修饰变体或未修饰变体。

[1068] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39712.1(SEQ ID NO:621),或其修饰变体或未修饰变体。

[1069] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39718.1(SEQ ID NO:622),或其修饰变体或未修饰变体。

[1070] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39724.1(SEQ ID NO:623),或其修饰变体或未修饰变体。

[1071] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39730.1(SEQ ID NO:624),或其修饰变体或未修饰变体。

[1072] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39736.1(SEQ ID NO:625),或其修饰变体或未修饰变体。

[1073] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39742.1(SEQ ID NO:626),或其修饰变体或未修饰变体。

[1074] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39748.1(SEQ ID NO:627)，或其修饰变体或未修饰变体。

[1075] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39754.1(SEQ ID NO:628)，或其修饰变体或未修饰变体。

[1076] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39760.1(SEQ ID NO:629)，或其修饰变体或未修饰变体。

[1077] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39766.1(SEQ ID NO:630)，或其修饰变体或未修饰变体。

[1078] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39772.1(SEQ ID NO:631)，或其修饰变体或未修饰变体。

[1079] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39731.1(SEQ ID NO:632)，或其修饰变体或未修饰变体。

[1080] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39737.1(SEQ ID NO:633)，或其修饰变体或未修饰变体。

[1081] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39743.1(SEQ ID NO:634)，或其修饰变体或未修饰变体。

[1082] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39749.1(SEQ ID NO:635)，或其修饰变体或未修饰变体。

[1083] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39755.1(SEQ ID NO:636)，或其修饰变体或未修饰变体。

[1084] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39761.1(SEQ ID NO:637)，或其修饰变体或未修饰变体。

[1085] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39767.1(SEQ ID NO:638)，或其修饰变体或未修饰变体。

[1086] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39773.1(SEQ ID NO:639)，或其修饰变体或未修饰变体。

[1087] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39732.1(SEQ ID NO:640)，或其修饰变体或未修饰变体。

[1088] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39738.1(SEQ ID NO:641)，或其修饰变体或未修饰变体。

[1089] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39744.1(SEQ ID NO:642)，或其修饰变体或未修饰变体。

[1090] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39750.1(SEQ ID NO:643)，或其修饰变体或未修饰变体。

[1091] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39756.1(SEQ ID NO:644)，或其修饰变体或未修饰变体。

[1092] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39762.1(SEQ ID NO:645)，或其修饰变体或未修饰变体。

[1093] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39768.1(SEQ ID NO:646),或其修饰变体或未修饰变体。

[1094] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39774.1(SEQ ID NO:647),或其修饰变体或未修饰变体。

[1095] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39733.1(SEQ ID NO:648),或其修饰变体或未修饰变体。

[1096] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39739.1(SEQ ID NO:649),或其修饰变体或未修饰变体。

[1097] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39745.1(SEQ ID NO:650),或其修饰变体或未修饰变体。

[1098] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39751.1(SEQ ID NO:651),或其修饰变体或未修饰变体。

[1099] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39757.1(SEQ ID NO:652),或其修饰变体或未修饰变体。

[1100] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39763.1(SEQ ID NO:653),或其修饰变体或未修饰变体。

[1101] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39769.1(SEQ ID NO:654),或其修饰变体或未修饰变体。

[1102] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39775.1(SEQ ID NO:655),或其修饰变体或未修饰变体。

[1103] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39734.1(SEQ ID NO:656),或其修饰变体或未修饰变体。

[1104] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39740.1(SEQ ID NO:657),或其修饰变体或未修饰变体。

[1105] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39746.1(SEQ ID NO:658),或其修饰变体或未修饰变体。

[1106] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39752.1(SEQ ID NO:659),或其修饰变体或未修饰变体。

[1107] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39758.1(SEQ ID NO:660),或其修饰变体或未修饰变体。

[1108] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39764.1(SEQ ID NO:661),或其修饰变体或未修饰变体。

[1109] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39770.1(SEQ ID NO:662),或其修饰变体或未修饰变体。

[1110] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39776.1(SEQ ID NO:663),或其修饰变体或未修饰变体。

[1111] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39735.1(SEQ ID NO:664),或其修饰变体或未修饰变体。

[1112] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39741.1(SEQ ID NO:665),或其修饰变体或未修饰变体。

[1113] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39747.1(SEQ ID NO:666)，或其修饰变体或未修饰变体。

[1114] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39753.1(SEQ ID NO:667)，或其修饰变体或未修饰变体。

[1115] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39759.1(SEQ ID NO:668)，或其修饰变体或未修饰变体。

[1116] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39765.1(SEQ ID NO:669)，或其修饰变体或未修饰变体。

[1117] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39771.1(SEQ ID NO:670)，或其修饰变体或未修饰变体。

[1118] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39778.1(SEQ ID NO:671)，或其修饰变体或未修饰变体。

[1119] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39784.1(SEQ ID NO:672)，或其修饰变体或未修饰变体。

[1120] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39790.1(SEQ ID NO:673)，或其修饰变体或未修饰变体。

[1121] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39796.1(SEQ ID NO:674)，或其修饰变体或未修饰变体。

[1122] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39802.1(SEQ ID NO:675)，或其修饰变体或未修饰变体。

[1123] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39808.1(SEQ ID NO:676)，或其修饰变体或未修饰变体。

[1124] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39814.1(SEQ ID NO:677)，或其修饰变体或未修饰变体。

[1125] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39820.1(SEQ ID NO:678)，或其修饰变体或未修饰变体。

[1126] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39779.1(SEQ ID NO:679)，或其修饰变体或未修饰变体。

[1127] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39785.1(SEQ ID NO:680)，或其修饰变体或未修饰变体。

[1128] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39791.1(SEQ ID NO:681)，或其修饰变体或未修饰变体。

[1129] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39797.1(SEQ ID NO:682)，或其修饰变体或未修饰变体。

[1130] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39803.1(SEQ ID NO:683)，或其修饰变体或未修饰变体。

[1131] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39809.1(SEQ ID NO:684)，或其修饰变体或未修饰变体。

[1132] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39815.1(SEQ ID NO:685),或其修饰变体或未修饰变体。

[1133] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39821.1(SEQ ID NO:686),或其修饰变体或未修饰变体。

[1134] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39780.1(SEQ ID NO:687),或其修饰变体或未修饰变体。

[1135] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39786.1(SEQ ID NO:688),或其修饰变体或未修饰变体。

[1136] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39792.1(SEQ ID NO:689),或其修饰变体或未修饰变体。

[1137] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39798.1(SEQ ID NO:690),或其修饰变体或未修饰变体。

[1138] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39804.1(SEQ ID NO:691),或其修饰变体或未修饰变体。

[1139] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39810.1(SEQ ID NO:692),或其修饰变体或未修饰变体。

[1140] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39816.1(SEQ ID NO:693),或其修饰变体或未修饰变体。

[1141] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39822.1(SEQ ID NO:694),或其修饰变体或未修饰变体。

[1142] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39781.1(SEQ ID NO:695),或其修饰变体或未修饰变体。

[1143] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39787.1(SEQ ID NO:696),或其修饰变体或未修饰变体。

[1144] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39793.1(SEQ ID NO:697),或其修饰变体或未修饰变体。

[1145] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39799.1(SEQ ID NO:698),或其修饰变体或未修饰变体。

[1146] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39805.1(SEQ ID NO:699),或其修饰变体或未修饰变体。

[1147] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39811.1(SEQ ID NO:700),或其修饰变体或未修饰变体。

[1148] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39817.1(SEQ ID NO:701),或其修饰变体或未修饰变体。

[1149] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39823.1(SEQ ID NO:702),或其修饰变体或未修饰变体。

[1150] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39782.1(SEQ ID NO:703),或其修饰变体或未修饰变体。

[1151] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39788.1(SEQ ID NO:704),或其修饰变体或未修饰变体。

[1152] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39794.1(SEQ ID NO:705)，或其修饰变体或未修饰变体。

[1153] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39800.1(SEQ ID NO:706)，或其修饰变体或未修饰变体。

[1154] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39806.1(SEQ ID NO:707)，或其修饰变体或未修饰变体。

[1155] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39812.1(SEQ ID NO:708)，或其修饰变体或未修饰变体。

[1156] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39818.1(SEQ ID NO:709)，或其修饰变体或未修饰变体。

[1157] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39824.1(SEQ ID NO:710)，或其修饰变体或未修饰变体。

[1158] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39783.1(SEQ ID NO:711)，或其修饰变体或未修饰变体。

[1159] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39789.1(SEQ ID NO:712)，或其修饰变体或未修饰变体。

[1160] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39795.1(SEQ ID NO:713)，或其修饰变体或未修饰变体。

[1161] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39801.1(SEQ ID NO:714)，或其修饰变体或未修饰变体。

[1162] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39807.1(SEQ ID NO:715)，或其修饰变体或未修饰变体。

[1163] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39813.1(SEQ ID NO:716)，或其修饰变体或未修饰变体。

[1164] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39819.1(SEQ ID NO:717)，或其修饰变体或未修饰变体。

[1165] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39825.1(SEQ ID NO:718)，或其修饰变体或未修饰变体。

[1166] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39831.1(SEQ ID NO:719)，或其修饰变体或未修饰变体。

[1167] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39837.1(SEQ ID NO:720)，或其修饰变体或未修饰变体。

[1168] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39843.1(SEQ ID NO:721)，或其修饰变体或未修饰变体。

[1169] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39849.1(SEQ ID NO:722)，或其修饰变体或未修饰变体。

[1170] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39855.1(SEQ ID NO:723)，或其修饰变体或未修饰变体。

[1171] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39861.1(SEQ ID NO:724),或其修饰变体或未修饰变体。

[1172] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39867.1(SEQ ID NO:725),或其修饰变体或未修饰变体。

[1173] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39826.1(SEQ ID NO:726),或其修饰变体或未修饰变体。

[1174] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39832.1(SEQ ID NO:727),或其修饰变体或未修饰变体。

[1175] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39838.1(SEQ ID NO:728),或其修饰变体或未修饰变体。

[1176] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39844.1(SEQ ID NO:729),或其修饰变体或未修饰变体。

[1177] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39850.1(SEQ ID NO:730),或其修饰变体或未修饰变体。

[1178] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39856.1(SEQ ID NO:731),或其修饰变体或未修饰变体。

[1179] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39862.1(SEQ ID NO:732),或其修饰变体或未修饰变体。

[1180] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39868.1(SEQ ID NO:733),或其修饰变体或未修饰变体。

[1181] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39827.1(SEQ ID NO:734),或其修饰变体或未修饰变体。

[1182] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39833.1(SEQ ID NO:735),或其修饰变体或未修饰变体。

[1183] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39839.1(SEQ ID NO:736),或其修饰变体或未修饰变体。

[1184] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39845.1(SEQ ID NO:737),或其修饰变体或未修饰变体。

[1185] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39851.1(SEQ ID NO:738),或其修饰变体或未修饰变体。

[1186] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39857.1(SEQ ID NO:739),或其修饰变体或未修饰变体。

[1187] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39863.1(SEQ ID NO:740),或其修饰变体或未修饰变体。

[1188] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39869.1(SEQ ID NO:741),或其修饰变体或未修饰变体。

[1189] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39828.1(SEQ ID NO:742),或其修饰变体或未修饰变体。

[1190] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39834.1(SEQ ID NO:743),或其修饰变体或未修饰变体。

[1191] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39840.1(SEQ ID NO:744)，或其修饰变体或未修饰变体。

[1192] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39846.1(SEQ ID NO:745)，或其修饰变体或未修饰变体。

[1193] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39852.1(SEQ ID NO:746)，或其修饰变体或未修饰变体。

[1194] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39858.1(SEQ ID NO:747)，或其修饰变体或未修饰变体。

[1195] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39864.1(SEQ ID NO:748)，或其修饰变体或未修饰变体。

[1196] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39870.1(SEQ ID NO:749)，或其修饰变体或未修饰变体。

[1197] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39829.1(SEQ ID NO:750)，或其修饰变体或未修饰变体。

[1198] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39835.1(SEQ ID NO:751)，或其修饰变体或未修饰变体。

[1199] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39841.1(SEQ ID NO:752)，或其修饰变体或未修饰变体。

[1200] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39853.1(SEQ ID NO:753)，或其修饰变体或未修饰变体。

[1201] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39859.1(SEQ ID NO:754)，或其修饰变体或未修饰变体。

[1202] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39865.1(SEQ ID NO:755)，或其修饰变体或未修饰变体。

[1203] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39871.1(SEQ ID NO:756)，或其修饰变体或未修饰变体。

[1204] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39830.1(SEQ ID NO:757)，或其修饰变体或未修饰变体。

[1205] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39836.1(SEQ ID NO:758)，或其修饰变体或未修饰变体。

[1206] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39842.1(SEQ ID NO:759)，或其修饰变体或未修饰变体。

[1207] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39848.1(SEQ ID NO:760)，或其修饰变体或未修饰变体。

[1208] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39854.1(SEQ ID NO:761)，或其修饰变体或未修饰变体。

[1209] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39860.1(SEQ ID NO:762)，或其修饰变体或未修饰变体。

[1210] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39866.1(SEQ ID NO:763),或其修饰变体或未修饰变体。

[1211] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39992.1(SEQ ID NO:764),或其修饰变体或未修饰变体。

[1212] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39998.1(SEQ ID NO:765),或其修饰变体或未修饰变体。

[1213] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40004.1(SEQ ID NO:766),或其修饰变体或未修饰变体。

[1214] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40010.1(SEQ ID NO:767),或其修饰变体或未修饰变体。

[1215] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40016.1(SEQ ID NO:768),或其修饰变体或未修饰变体。

[1216] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40022.1(SEQ ID NO:769),或其修饰变体或未修饰变体。

[1217] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40028.1(SEQ ID NO:770),或其修饰变体或未修饰变体。

[1218] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40034.1(SEQ ID NO:771),或其修饰变体或未修饰变体。

[1219] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39999.1(SEQ ID NO:772),或其修饰变体或未修饰变体。

[1220] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40005.1(SEQ ID NO:773),或其修饰变体或未修饰变体。

[1221] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40011.1(SEQ ID NO:774),或其修饰变体或未修饰变体。

[1222] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40017.1(SEQ ID NO:775),或其修饰变体或未修饰变体。

[1223] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40029.1(SEQ ID NO:776),或其修饰变体或未修饰变体。

[1224] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40035.1(SEQ ID NO:777),或其修饰变体或未修饰变体。

[1225] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39994.1(SEQ ID NO:778),或其修饰变体或未修饰变体。

[1226] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40000.1(SEQ ID NO:779),或其修饰变体或未修饰变体。

[1227] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40006.1(SEQ ID NO:780),或其修饰变体或未修饰变体。

[1228] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40012.1(SEQ ID NO:781),或其修饰变体或未修饰变体。

[1229] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40018.1(SEQ ID NO:782),或其修饰变体或未修饰变体。

[1230] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40024.1(SEQ ID NO:783)，或其修饰变体或未修饰变体。

[1231] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40030.1(SEQ ID NO:784)，或其修饰变体或未修饰变体。

[1232] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40036.1(SEQ ID NO:785)，或其修饰变体或未修饰变体。

[1233] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39995.1(SEQ ID NO:786)，或其修饰变体或未修饰变体。

[1234] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40001.1(SEQ ID NO:787)，或其修饰变体或未修饰变体。

[1235] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40007.1(SEQ ID NO:788)，或其修饰变体或未修饰变体。

[1236] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40013.1(SEQ ID NO:789)，或其修饰变体或未修饰变体。

[1237] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40019.1(SEQ ID NO:790)，或其修饰变体或未修饰变体。

[1238] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40025.1(SEQ ID NO:791)，或其修饰变体或未修饰变体。

[1239] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40031.1(SEQ ID NO:792)，或其修饰变体或未修饰变体。

[1240] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40037.1(SEQ ID NO:793)，或其修饰变体或未修饰变体。

[1241] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39996.1(SEQ ID NO:794)，或其修饰变体或未修饰变体。

[1242] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40002.1(SEQ lD NO:795)，或其修饰变体或未修饰变体。

[1243] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40008.1(SEQ ID NO:796)，或其修饰变体或未修饰变体。

[1244] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40014.1(SEQ ID NO:797)，或其修饰变体或未修饰变体。

[1245] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40020.1(SEQ ID NO:798)，或其修饰变体或未修饰变体。

[1246] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40026.1(SEQ ID NO:799)，或其修饰变体或未修饰变体。

[1247] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40032.1(SEQ ID NO:800)，或其修饰变体或未修饰变体。

[1248] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40038.1(SEQ ID NO:801)，或其修饰变体或未修饰变体。

[1249] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-39997.1(SEQ ID NO:802),或其修饰变体或未修饰变体。

[1250] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40009.1(SEQ ID NO:803),或其修饰变体或未修饰变体。

[1251] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40015.1(SEQ ID NO:804),或其修饰变体或未修饰变体。

[1252] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40021.1(SEQ ID NO:805),或其修饰变体或未修饰变体。

[1253] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40027.1(SEQ ID NO:806),或其修饰变体或未修饰变体。

[1254] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40033.1(SEQ ID NO:807),或其修饰变体或未修饰变体。

[1255] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40039.1(SEQ ID NO:808),或其修饰变体或未修饰变体。

[1256] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40045.1(SEQ ID NO:809),或其修饰变体或未修饰变体。

[1257] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40051.1(SEQ ID NO:810),或其修饰变体或未修饰变体。

[1258] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40057.1(SEQ ID NO:811),或其修饰变体或未修饰变体。

[1259] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40063.1(SEQ ID NO:812),或其修饰变体或未修饰变体。

[1260] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40069.1(SEQ ID NO:813),或其修饰变体或未修饰变体。

[1261] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40075.1(SEQ ID NO:814),或其修饰变体或未修饰变体。

[1262] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40081.1(SEQ ID NO:815),或其修饰变体或未修饰变体。

[1263] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40040.1(SEQ ID NO:816),或其修饰变体或未修饰变体。

[1264] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40046.1(SEQ ID NO:817),或其修饰变体或未修饰变体。

[1265] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40052.1(SEQ ID NO:818),或其修饰变体或未修饰变体。

[1266] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40058.1(SEQ ID NO:819),或其修饰变体或未修饰变体。

[1267] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40064.1(SEQ ID NO:820),或其修饰变体或未修饰变体。

[1268] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40070.1(SEQ ID NO:821),或其修饰变体或未修饰变体。

[1269] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40076.1(SEQ ID NO:822)，或其修饰变体或未修饰变体。

[1270] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40082.1(SEQ ID NO:823)，或其修饰变体或未修饰变体。

[1271] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40041.1(SEQ ID NO:824)，或其修饰变体或未修饰变体。

[1272] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40047.1(SEQ ID NO:825)，或其修饰变体或未修饰变体。

[1273] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40053.1(SEQ ID NO:826)，或其修饰变体或未修饰变体。

[1274] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40059.1(SEQ ID NO:827)，或其修饰变体或未修饰变体。

[1275] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40065.1(SEQ ID NO:828)，或其修饰变体或未修饰变体。

[1276] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40071.1(SEQ ID NO:829)，或其修饰变体或未修饰变体。

[1277] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40077.1(SEQ ID NO:830)，或其修饰变体或未修饰变体。

[1278] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40083.1(SEQ ID NO:831)，或其修饰变体或未修饰变体。

[1279] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40042.1(SEQ ID NO:832)，或其修饰变体或未修饰变体。

[1280] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40048.1(SEQ ID NO:833)，或其修饰变体或未修饰变体。

[1281] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40054.1(SEQ ID NO:834)，或其修饰变体或未修饰变体。

[1282] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40060.1(SEQ ID NO:835)，或其修饰变体或未修饰变体。

[1283] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40066.1(SEQ ID NO:836)，或其修饰变体或未修饰变体。

[1284] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40072.1(SEQ ID NO:837)，或其修饰变体或未修饰变体。

[1285] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40078.1(SEQ ID NO:838)，或其修饰变体或未修饰变体。

[1286] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40084.1(SEQ ID NO:839)，或其修饰变体或未修饰变体。

[1287] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40043.1(SEQ ID NO:840)，或其修饰变体或未修饰变体。

[1288] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的

至少 15 个连续核苷酸 :AD-40049.1(SEQ ID NO:841),或其修饰变体或未修饰变体。

[1289] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40055.1(SEQ ID NO:842),或其修饰变体或未修饰变体。

[1290] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40061.1(SEQ ID NO:843),或其修饰变体或未修饰变体。

[1291] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40067.1(SEQ ID NO:844),或其修饰变体或未修饰变体。

[1292] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40073.1(SEQ ID NO:845),或其修饰变体或未修饰变体。

[1293] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40079.1(SEQ ID NO:846),或其修饰变体或未修饰变体。

[1294] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40085.1(SEQ ID NO:847),或其修饰变体或未修饰变体。

[1295] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40044.1(SEQ ID NO:848),或其修饰变体或未修饰变体。

[1296] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40050.1(SEQ ID NO:849),或其修饰变体或未修饰变体。

[1297] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40056.1(SEQ ID NO:850),或其修饰变体或未修饰变体。

[1298] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40062.1(SEQ ID NO:851),或其修饰变体或未修饰变体。

[1299] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40068.1(SEQ ID NO:852),或其修饰变体或未修饰变体。

[1300] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40074.1(SEQ ID NO:853),或其修饰变体或未修饰变体。

[1301] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-40080.1(SEQ ID NO:854),或其修饰变体或未修饰变体。

[1302] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39720.1(SEQ ID NOs:1754),或其修饰变体或未修饰变体。

[1303] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39706.1(SEQ ID NOs:1755),或其修饰变体或未修饰变体。

[1304] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39712.1(SEQ ID NOs:1756),或其修饰变体或未修饰变体。

[1305] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39760.1(SEQ ID NOs:1757),或其修饰变体或未修饰变体。

[1306] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-39732.1(SEQ ID NOs:1758),或其修饰变体或未修饰变体。

[1307] 包含第一链和第二链的 RNAi 剂,其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸 :AD-35541.4(SEQ ID NOs:1759),或其修饰变体或未修饰变体。

[1308] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NOs:1760)，或其修饰变体或未修饰变体。

[1309] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39741.1，或其修饰变体或未修饰变体。

[1310] hs_KRAS_322_A22S26(SEQ ID NOs:1761)，或其修饰变体或未修饰变体。

[1311] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39778.1(SEQ ID NOs:1762)，或其修饰变体或未修饰变体。

[1312] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39790.1(SEQ ID NOs:1763)，或其修饰变体或未修饰变体。

[1313] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39822.1(SEQ ID NOs:1764)，或其修饰变体或未修饰变体。

[1314] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35609.4(SEQ ID NOs:1765)，或其修饰变体或未修饰变体。

[1315] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35581.4(SEQ ID NOs:1766)，或其修饰变体或未修饰变体。

[1316] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39845.1(SEQ ID NOs:1767)，或其修饰变体或未修饰变体。

[1317] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39858.1(SEQ ID NOs:1768)，或其修饰变体或未修饰变体。

[1318] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39870.1(SEQ ID NOs:1769)，或其修饰变体或未修饰变体。

[1319] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35576.4(SEQ ID NOs:1770)，或其修饰变体或未修饰变体。

[1320] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35588.4(SEQ ID NOs:1771)，或其修饰变体或未修饰变体。

[1321] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35600.1(SEQ ID NOs:1772)，或其修饰变体或未修饰变体。

[1322] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-35606.1(SEQ ID NOs:1773)，或其修饰变体或未修饰变体。

[1323] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38151.1(SEQ ID NOs:1774)，或其修饰变体或未修饰变体。

[1324] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38163.1(SEQ ID NOs:1775)，或其修饰变体或未修饰变体。

[1325] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-39999.1(SEQ ID NOs:1776)，或其修饰变体或未修饰变体。

[1326] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1777)，或其修饰变体或未修饰变体。

[1327] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1778)，或其修饰变体或未修饰变体。

[1328] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38136.1(SEQ ID NOs:1779)，或其修饰变体或未修饰变体。

[1329] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40036.1(SEQ ID NOs:1780)，或其修饰变体或未修饰变体。

[1330] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40008.1(SEQ ID NOs:1781)，或其修饰变体或未修饰变体。

[1331] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40021.1(SEQ ID NOs:1782)，或其修饰变体或未修饰变体。

[1332] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40077.1(SEQ ID NOs:1783)，或其修饰变体或未修饰变体。

[1333] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40072.1(SEQ ID NOs:1784)，或其修饰变体或未修饰变体。

[1334] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40061.1(SEQ ID NOs:1785)，或其修饰变体或未修饰变体。

[1335] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-40068.1(SEQ ID NOs:1786)，或其修饰变体或未修饰变体。

[1336] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38131.1(SEQ ID NOs:1787)，或其修饰变体或未修饰变体。

[1337] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：AD-38167.1(SEQ ID NOs:1788)，或其修饰变体或未修饰变体。

[1338] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：hs_KRAS 1273_A22S26(SEQ ID NOs:1789)，或其修饰变体或未修饰变体。

[1339] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：hs_KRAS 2892_A37S26(SEQ ID NOs:1790)，或其修饰变体或未修饰变体。

[1340] 包含第一链和第二链的 RNAi 剂，其中的第一链包含来自如下 RNAi 剂的第一链的至少 15 个连续核苷酸：hs_KRAS 4731_A22S26(SEQ ID NOs:1791)，或其修饰变体或未修饰变体。

[1341] 包含本文公开的 RNAi 剂的第一链的具体实施方案

[1342] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链的序列。

[1343] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[1344] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-35523.3(SEQ ID NO:428),或其修饰变体或未修饰变体。

[1345] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35529.1(SEQ ID NO:429),或其修饰变体或未修饰变体。

[1346] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35535.4(SEQ ID NO:430),或其修饰变体或未修饰变体。

[1347] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35541.4(SEQ ID NO:431),或其修饰变体或未修饰变体。

[1348] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35547.4(SEQ ID NO:432),或其修饰变体或未修饰变体。

[1349] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35553.4(SEQ ID NO:433),或其修饰变体或未修饰变体。

[1350] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35559.4(SEQ ID NO:434),或其修饰变体或未修饰变体。

[1351] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35565.4(SEQ ID NO:435),或其修饰变体或未修饰变体。

[1352] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35524.4(SEQ ID NO:436),或其修饰变体或未修饰变体。

[1353] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35530.4(SEQ ID NO:437),或其修饰变体或未修饰变体。

[1354] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35536.4(SEQ ID NO:438),或其修饰变体或未修饰变体。

[1355] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35542.4(SEQ ID NO:439),或其修饰变体或未修饰变体。

[1356] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35548.4(SEQ ID NO:440),或其修饰变体或未修饰变体。

[1357] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35554.4(SEQ ID NO:441),或其修饰变体或未修饰变体。

[1358] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35560.2(SEQ ID NO:442),或其修饰变体或未修饰变体。

[1359] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35566.4(SEQ ID NO:443),或其修饰变体或未修饰变体。

[1360] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35525.2(SEQ ID NO:444),或其修饰变体或未修饰变体。

[1361] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35531.4(SEQ ID NO:445),或其修饰变体或未修饰变体。

[1362] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35537.4(SEQ ID NO:446),或其修饰变体或未修饰变体。

[1363] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35543.2(SEQ ID NO:447),或其修饰变体或未修饰变体。

[1364] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35549.4(SEQ ID NO:448)，或其修饰变体或未修饰变体。

[1365] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35555.4(SEQ ID NO:449)，或其修饰变体或未修饰变体。

[1366] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35561.4(SEQ ID NO:450)，或其修饰变体或未修饰变体。

[1367] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35567.4(SEQ ID NO:451)，或其修饰变体或未修饰变体。

[1368] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35526.4(SEQ ID NO:452)，或其修饰变体或未修饰变体。

[1369] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35532.4(SEQ ID NO:453)，或其修饰变体或未修饰变体。

[1370] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35538.4(SEQ ID NO:454)，或其修饰变体或未修饰变体。

[1371] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35544.4(SEQ ID NO:455)，或其修饰变体或未修饰变体。

[1372] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35550.4(SEQ ID NO:456)，或其修饰变体或未修饰变体。

[1373] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35556.4(SEQ ID NO:457)，或其修饰变体或未修饰变体。

[1374] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35562.4(SEQ ID NO:458)，或其修饰变体或未修饰变体。

[1375] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35568.4(SEQ ID NO:459)，或其修饰变体或未修饰变体。

[1376] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35527.4(SEQ ID NO:460)，或其修饰变体或未修饰变体。

[1377] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35533.4(SEQ ID NO:461)，或其修饰变体或未修饰变体。

[1378] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35539.4(SEQ ID NO:462)，或其修饰变体或未修饰变体。

[1379] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35545.4(SEQ ID NO:463)，或其修饰变体或未修饰变体。

[1380] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35551.4(SEQ ID NO:464)，或其修饰变体或未修饰变体。

[1381] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35563.4(SEQ ID NO:465)，或其修饰变体或未修饰变体。

[1382] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35528.4(SEQ ID NO:466)，或其修饰变体或未修饰变体。

[1383] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-35540.4(SEQ ID NO:467),或其修饰变体或未修饰变体。

[1384] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35546.4(SEQ ID NO:468),或其修饰变体或未修饰变体。

[1385] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35552.4(SEQ ID NO:469),或其修饰变体或未修饰变体。

[1386] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35558.4(SEQ ID NO:470),或其修饰变体或未修饰变体。

[1387] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35564.4(SEQ ID NO:471),或其修饰变体或未修饰变体。

[1388] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35570.4(SEQ ID NO:472),或其修饰变体或未修饰变体。

[1389] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35571.4(SEQ ID NO:473),或其修饰变体或未修饰变体。

[1390] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35577.4(SEQ ID NO:474),或其修饰变体或未修饰变体。

[1391] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35583.4(SEQ ID NO:475),或其修饰变体或未修饰变体。

[1392] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35589.4(SEQ ID NO:476),或其修饰变体或未修饰变体。

[1393] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35595.4(SEQ ID NO:477),或其修饰变体或未修饰变体。

[1394] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35601.4(SEQ ID NO:478),或其修饰变体或未修饰变体。

[1395] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35607.4(SEQ ID NO:479),或其修饰变体或未修饰变体。

[1396] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35613.4(SEQ ID NO:480),或其修饰变体或未修饰变体。

[1397] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35572.4(SEQ ID NO:481),或其修饰变体或未修饰变体。

[1398] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35578.4(SEQ ID NO:482),或其修饰变体或未修饰变体。

[1399] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35584.4(SEQ ID NO:483),或其修饰变体或未修饰变体。

[1400] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35590.4(SEQ ID NO:484),或其修饰变体或未修饰变体。

[1401] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35596.4(SEQ ID NO:485),或其修饰变体或未修饰变体。

[1402] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35602.4(SEQ ID NO:486),或其修饰变体或未修饰变体。

[1403] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35608.4(SEQ ID NO:487)，或其修饰变体或未修饰变体。

[1404] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35614.4(SEQ ID NO:488)，或其修饰变体或未修饰变体。

[1405] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35573.4(SEQ ID NO:489)，或其修饰变体或未修饰变体。

[1406] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35579.4(SEQ ID NO:490)，或其修饰变体或未修饰变体。

[1407] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35585.4(SEQ ID NO:491)，或其修饰变体或未修饰变体。

[1408] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35591.4(SEQ ID NO:492)，或其修饰变体或未修饰变体。

[1409] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35597.4(SEQ ID NO:493)，或其修饰变体或未修饰变体。

[1410] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35603.4(SEQ ID NO:494)，或其修饰变体或未修饰变体。

[1411] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35609.4(SEQ ID NO:495)，或其修饰变体或未修饰变体。

[1412] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35615.4(SEQ ID NO:496)，或其修饰变体或未修饰变体。

[1413] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35574.4(SEQ ID NO:497)，或其修饰变体或未修饰变体。

[1414] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35580.1(SEQ ID NO:498)，或其修饰变体或未修饰变体。

[1415] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35586.4(SEQ ID NO:499)，或其修饰变体或未修饰变体。

[1416] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35592.4(SEQ ID NO:500)，或其修饰变体或未修饰变体。

[1417] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35598.4(SEQ ID NO:501)，或其修饰变体或未修饰变体。

[1418] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35604.4(SEQ ID NO:502)，或其修饰变体或未修饰变体。

[1419] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35610.4(SEQ ID NO:503)，或其修饰变体或未修饰变体。

[1420] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35616.4(SEQ ID NO:504)，或其修饰变体或未修饰变体。

[1421] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35575.4(SEQ ID NO:505)，或其修饰变体或未修饰变体。

[1422] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-35581.4(SEQ ID NO:506),或其修饰变体或未修饰变体。

[1423] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35587.4(SEQ ID NO:507),或其修饰变体或未修饰变体。

[1424] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35593.4(SEQ ID NO:508),或其修饰变体或未修饰变体。

[1425] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35599.4(SEQ ID NO:509),或其修饰变体或未修饰变体。

[1426] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35605.4(SEQ ID NO:510),或其修饰变体或未修饰变体。

[1427] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35611.4(SEQ ID NO:511),或其修饰变体或未修饰变体。

[1428] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35617.4(SEQ ID NO:512),或其修饰变体或未修饰变体。

[1429] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35576.4(SEQ ID NO:513),或其修饰变体或未修饰变体。

[1430] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35588.4(SEQ ID NO:514),或其修饰变体或未修饰变体。

[1431] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35667.1(SEQ ID NO:515),或其修饰变体或未修饰变体。

[1432] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35673.1(SEQ ID NO:516),或其修饰变体或未修饰变体。

[1433] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35679.1(SEQ ID NO:517),或其修饰变体或未修饰变体。

[1434] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35685.1(SEQ ID NO:518),或其修饰变体或未修饰变体。

[1435] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35691.1(SEQ ID NO:519),或其修饰变体或未修饰变体。

[1436] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35557.1(SEQ ID NO:520),或其修饰变体或未修饰变体。

[1437] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35618.1(SEQ ID NO:521),或其修饰变体或未修饰变体。

[1438] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35569.1(SEQ ID NO:522),或其修饰变体或未修饰变体。

[1439] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35534.1(SEQ ID NO:523),或其修饰变体或未修饰变体。

[1440] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35582.1(SEQ ID NO:524),或其修饰变体或未修饰变体。

[1441] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35594.1(SEQ ID NO:525),或其修饰变体或未修饰变体。

[1442] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35600.1(SEQ ID NO:526)，或其修饰变体或未修饰变体。

[1443] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35606.1(SEQ ID NO:527)，或其修饰变体或未修饰变体。

[1444] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35612.1(SEQ ID NO:528)，或其修饰变体或未修饰变体。

[1445] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38127.1(SEQ ID NO:529)，或其修饰变体或未修饰变体。

[1446] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38133.1(SEQ ID NO:530)，或其修饰变体或未修饰变体。

[1447] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38139.1(SEQ ID NO:531)，或其修饰变体或未修饰变体。

[1448] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38145.1(SEQ ID NO:532)，或其修饰变体或未修饰变体。

[1449] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38151.1(SEQ ID NO:533)，或其修饰变体或未修饰变体。

[1450] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38157.1(SEQ ID NO:534)，或其修饰变体或未修饰变体。

[1451] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38163.1(SEQ ID NO:535)，或其修饰变体或未修饰变体。

[1452] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38169.1(SEQ ID NO:536)，或其修饰变体或未修饰变体。

[1453] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38128.1(SEQ ID NO:537)，或其修饰变体或未修饰变体。

[1454] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38134.1(SEQ ID NO:538)，或其修饰变体或未修饰变体。

[1455] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38140.1(SEQ ID NO:539)，或其修饰变体或未修饰变体。

[1456] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38146.1(SEQ ID NO:540)，或其修饰变体或未修饰变体。

[1457] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38152.1(SEQ ID NO:541)，或其修饰变体或未修饰变体。

[1458] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38158.1(SEQ ID NO:542)，或其修饰变体或未修饰变体。

[1459] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38164.1(SEQ ID NO:543)，或其修饰变体或未修饰变体。

[1460] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38170.1(SEQ ID NO:544)，或其修饰变体或未修饰变体。

[1461] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-38129.1(SEQ ID NO:545),或其修饰变体或未修饰变体。

[1462] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38135.1(SEQ ID NO:546),或其修饰变体或未修饰变体。

[1463] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38141.1(SEQ ID NO:547),或其修饰变体或未修饰变体。

[1464] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38147.1(SEQ ID NO:548),或其修饰变体或未修饰变体。

[1465] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38153.1(SEQ ID NO:549),或其修饰变体或未修饰变体。

[1466] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38159.1(SEQ ID NO:550),或其修饰变体或未修饰变体。

[1467] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38165.1(SEQ ID NO:551),或其修饰变体或未修饰变体。

[1468] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38171.1(SEQ ID NO:552),或其修饰变体或未修饰变体。

[1469] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38130.1(SEQ ID NO:553),或其修饰变体或未修饰变体。

[1470] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38136.1(SEQ ID NO:554),或其修饰变体或未修饰变体。

[1471] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38142.1(SEQ ID NO:555),或其修饰变体或未修饰变体。

[1472] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38148.1(SEQ ID NO:556),或其修饰变体或未修饰变体。

[1473] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38154.1(SEQ ID NO:557),或其修饰变体或未修饰变体。

[1474] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38160.1(SEQ ID NO:558),或其修饰变体或未修饰变体。

[1475] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38166.1(SEQ ID NO:559),或其修饰变体或未修饰变体。

[1476] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38172.1(SEQ ID NO:560),或其修饰变体或未修饰变体。

[1477] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38131.1(SEQ ID NO:561),或其修饰变体或未修饰变体。

[1478] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38137.1(SEQ ID NO:562),或其修饰变体或未修饰变体。

[1479] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38143.1(SEQ ID NO:563),或其修饰变体或未修饰变体。

[1480] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38149.1(SEQ ID NO:564),或其修饰变体或未修饰变体。

[1481] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38155.1(SEQ ID NO:565)，或其修饰变体或未修饰变体。

[1482] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38161.1(SEQ ID NO:566)，或其修饰变体或未修饰变体。

[1483] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38167.1(SEQ ID NO:567)，或其修饰变体或未修饰变体。

[1484] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38173.1(SEQ ID NO:568)，或其修饰变体或未修饰变体。

[1485] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38132.1(SEQ ID NO:569)，或其修饰变体或未修饰变体。

[1486] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38138.1(SEQ ID NO:570)，或其修饰变体或未修饰变体。

[1487] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38144.1(SEQ ID NO:571)，或其修饰变体或未修饰变体。

[1488] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38150.1(SEQ ID NO:572)，或其修饰变体或未修饰变体。

[1489] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38156.1(SEQ ID NO:573)，或其修饰变体或未修饰变体。

[1490] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38162.1(SEQ ID NO:574)，或其修饰变体或未修饰变体。

[1491] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38168.1(SEQ ID NO:575)，或其修饰变体或未修饰变体。

[1492] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38174.1(SEQ ID NO:576)，或其修饰变体或未修饰变体。

[1493] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39683.1(SEQ ID NO:577)，或其修饰变体或未修饰变体。

[1494] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39689.1(SEQ ID NO:578)，或其修饰变体或未修饰变体。

[1495] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39695.1(SEQ ID NO:579)，或其修饰变体或未修饰变体。

[1496] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39701.1(SEQ ID NO:580)，或其修饰变体或未修饰变体。

[1497] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39707.1(SEQ ID NO:581)，或其修饰变体或未修饰变体。

[1498] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39713.1(SEQ ID NO:582)，或其修饰变体或未修饰变体。

[1499] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39719.1(SEQ ID NO:583)，或其修饰变体或未修饰变体。

[1500] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39725.1(SEQ ID NO:584),或其修饰变体或未修饰变体。

[1501] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39684.1(SEQ ID NO:585),或其修饰变体或未修饰变体。

[1502] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39690.1(SEQ ID NO:586),或其修饰变体或未修饰变体。

[1503] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39696.1(SEQ ID NO:587),或其修饰变体或未修饰变体。

[1504] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39702.1(SEQ ID NO:588),或其修饰变体或未修饰变体。

[1505] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39708.1(SEQ ID NO:589),或其修饰变体或未修饰变体。

[1506] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39714.1(SEQ ID NO:590),或其修饰变体或未修饰变体。

[1507] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39720.1(SEQ ID NO:591),或其修饰变体或未修饰变体。

[1508] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39726.1(SEQ ID NO:592),或其修饰变体或未修饰变体。

[1509] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39685.1(SEQ ID NO:593),或其修饰变体或未修饰变体。

[1510] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39691.1(SEQ ID NO:594),或其修饰变体或未修饰变体。

[1511] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39697.1(SEQ ID NO:595),或其修饰变体或未修饰变体。

[1512] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39703.1(SEQ ID NO:596),或其修饰变体或未修饰变体。

[1513] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39709.1(SEQ ID NO:597),或其修饰变体或未修饰变体。

[1514] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39715.1(SEQ ID NO:598),或其修饰变体或未修饰变体。

[1515] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39721.1(SEQ ID NO:599),或其修饰变体或未修饰变体。

[1516] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39727.1(SEQ ID NO:600),或其修饰变体或未修饰变体。

[1517] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39686.1(SEQ ID NO:601),或其修饰变体或未修饰变体。

[1518] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39692.1(SEQ ID NO:602),或其修饰变体或未修饰变体。

[1519] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39698.1(SEQ ID NO:603),或其修饰变体或未修饰变体。

[1520] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39704.1(SEQ ID NO:604)，或其修饰变体或未修饰变体。

[1521] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39710.1(SEQ ID NO:605)，或其修饰变体或未修饰变体。

[1522] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39716.1(SEQ ID NO:606)，或其修饰变体或未修饰变体。

[1523] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39722.1(SEQ ID NO:607)，或其修饰变体或未修饰变体。

[1524] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39728.1(SEQ ID NO:608)，或其修饰变体或未修饰变体。

[1525] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39687.1(SEQ ID NO:609)，或其修饰变体或未修饰变体。

[1526] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39693.1(SEQ ID NO:610)，或其修饰变体或未修饰变体。

[1527] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39699.1(SEQ ID NO:611)，或其修饰变体或未修饰变体。

[1528] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39705.1(SEQ ID NO:612)，或其修饰变体或未修饰变体。

[1529] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39711.1(SEQ ID NO:613)，或其修饰变体或未修饰变体。

[1530] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39717.1(SEQ ID NO:614)，或其修饰变体或未修饰变体。

[1531] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39723.1(SEQ ID NO:615)，或其修饰变体或未修饰变体。

[1532] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39729.1(SEQ ID NO:616)，或其修饰变体或未修饰变体。

[1533] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39688.1(SEQ ID NO:617)，或其修饰变体或未修饰变体。

[1534] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39694.1(SEQ ID NO:618)，或其修饰变体或未修饰变体。

[1535] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39700.1(SEQ ID NO:619)，或其修饰变体或未修饰变体。

[1536] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39706.1(SEQ ID NO:620)，或其修饰变体或未修饰变体。

[1537] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39712.1(SEQ ID NO:621)，或其修饰变体或未修饰变体。

[1538] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39718.1(SEQ ID NO:622)，或其修饰变体或未修饰变体。

[1539] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39724.1(SEQ ID NO:623),或其修饰变体或未修饰变体。

[1540] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39730.1(SEQ ID NO:624),或其修饰变体或未修饰变体。

[1541] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39736.1(SEQ ID NO:625),或其修饰变体或未修饰变体。

[1542] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39742.1(SEQ ID NO:626),或其修饰变体或未修饰变体。

[1543] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39748.1(SEQ ID NO:627),或其修饰变体或未修饰变体。

[1544] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39754.1(SEQ ID NO:628),或其修饰变体或未修饰变体。

[1545] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39760.1(SEQ ID NO:629),或其修饰变体或未修饰变体。

[1546] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39766.1(SEQ ID NO:630),或其修饰变体或未修饰变体。

[1547] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39772.1(SEQ ID NO:631),或其修饰变体或未修饰变体。

[1548] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39731.1(SEQ ID NO:632),或其修饰变体或未修饰变体。

[1549] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39737.1(SEQ ID NO:633),或其修饰变体或未修饰变体。

[1550] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39743.1(SEQ ID NO:634),或其修饰变体或未修饰变体。

[1551] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39749.1(SEQ ID NO:635),或其修饰变体或未修饰变体。

[1552] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39755.1(SEQ ID NO:636),或其修饰变体或未修饰变体。

[1553] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39761.1(SEQ ID NO:637),或其修饰变体或未修饰变体。

[1554] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39767.1(SEQ ID NO:638),或其修饰变体或未修饰变体。

[1555] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39773.1(SEQ ID NO:639),或其修饰变体或未修饰变体。

[1556] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39732.1(SEQ ID NO:640),或其修饰变体或未修饰变体。

[1557] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39738.1(SEQ ID NO:641),或其修饰变体或未修饰变体。

[1558] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39744.1(SEQ ID NO:642),或其修饰变体或未修饰变体。

[1559] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39750.1(SEQ ID NO:643)，或其修饰变体或未修饰变体。

[1560] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39756.1(SEQ ID NO:644)，或其修饰变体或未修饰变体。

[1561] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39762.1(SEQ ID NO:645)，或其修饰变体或未修饰变体。

[1562] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39768.1(SEQ ID NO:646)，或其修饰变体或未修饰变体。

[1563] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39774.1(SEQ ID NO:647)，或其修饰变体或未修饰变体。

[1564] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39733.1(SEQ ID NO:648)，或其修饰变体或未修饰变体。

[1565] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39739.1(SEQ ID NO:649)，或其修饰变体或未修饰变体。

[1566] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39745.1(SEQ ID NO:650)，或其修饰变体或未修饰变体。

[1567] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39751.1(SEQ ID NO:651)，或其修饰变体或未修饰变体。

[1568] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39757.1(SEQ ID NO:652)，或其修饰变体或未修饰变体。

[1569] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39763.1(SEQ ID NO:653)，或其修饰变体或未修饰变体。

[1570] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39769.1(SEQ ID NO:654)，或其修饰变体或未修饰变体。

[1571] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39775.1(SEQ ID NO:655)，或其修饰变体或未修饰变体。

[1572] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39734.1(SEQ ID NO:656)，或其修饰变体或未修饰变体。

[1573] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39740.1(SEQ ID NO:657)，或其修饰变体或未修饰变体。

[1574] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39746.1(SEQ ID NO:658)，或其修饰变体或未修饰变体。

[1575] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39752.1(SEQ ID NO:659)，或其修饰变体或未修饰变体。

[1576] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39758.1(SEQ ID NO:660)，或其修饰变体或未修饰变体。

[1577] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39764.1(SEQ ID NO:661)，或其修饰变体或未修饰变体。

[1578] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39770.1(SEQ ID NO:662),或其修饰变体或未修饰变体。

[1579] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39776.1(SEQ ID NO:663),或其修饰变体或未修饰变体。

[1580] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39735.1(SEQ ID NO:664),或其修饰变体或未修饰变体。

[1581] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39741.1(SEQ ID NO:665),或其修饰变体或未修饰变体。

[1582] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39747.1(SEQ ID NO:666),或其修饰变体或未修饰变体。

[1583] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39753.1(SEQ ID NO:667),或其修饰变体或未修饰变体。

[1584] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39759.1(SEQ ID NO:668),或其修饰变体或未修饰变体。

[1585] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39765.1(SEQ ID NO:669),或其修饰变体或未修饰变体。

[1586] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39771.1(SEQ ID NO:670),或其修饰变体或未修饰变体。

[1587] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39778.1(SEQ ID NO:671),或其修饰变体或未修饰变体。

[1588] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39784.1(SEQ ID NO:672),或其修饰变体或未修饰变体。

[1589] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39790.1(SEQ ID NO:673),或其修饰变体或未修饰变体。

[1590] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39796.1(SEQ ID NO:674),或其修饰变体或未修饰变体。

[1591] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39802.1(SEQ ID NO:675),或其修饰变体或未修饰变体。

[1592] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39808.1(SEQ ID NO:676),或其修饰变体或未修饰变体。

[1593] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39814.1(SEQ ID NO:677),或其修饰变体或未修饰变体。

[1594] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39820.1(SEQ ID NO:678),或其修饰变体或未修饰变体。

[1595] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39779.1(SEQ ID NO:679),或其修饰变体或未修饰变体。

[1596] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39785.1(SEQ ID NO:680),或其修饰变体或未修饰变体。

[1597] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39791.1(SEQ ID NO:681),或其修饰变体或未修饰变体。

[1598] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39797.1(SEQ ID NO:682)，或其修饰变体或未修饰变体。

[1599] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39803.1(SEQ ID NO:683)，或其修饰变体或未修饰变体。

[1600] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39809.1(SEQ ID NO:684)，或其修饰变体或未修饰变体。

[1601] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39815.1(SEQ ID NO:685)，或其修饰变体或未修饰变体。

[1602] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39821.1(SEQ ID NO:686)，或其修饰变体或未修饰变体。

[1603] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39780.1(SEQ ID NO:687)，或其修饰变体或未修饰变体。

[1604] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39786.1(SEQ ID NO:688)，或其修饰变体或未修饰变体。

[1605] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39792.1(SEQ ID NO:689)，或其修饰变体或未修饰变体。

[1606] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39798.1(SEQ ID NO:690)，或其修饰变体或未修饰变体。

[1607] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39804.1(SEQ ID NO:691)，或其修饰变体或未修饰变体。

[1608] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39810.1(SEQ ID NO:692)，或其修饰变体或未修饰变体。

[1609] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39816.1(SEQ ID NO:693)，或其修饰变体或未修饰变体。

[1610] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39822.1(SEQ ID NO:694)，或其修饰变体或未修饰变体。

[1611] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39781.1(SEQ ID NO:695)，或其修饰变体或未修饰变体。

[1612] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39787.1(SEQ ID NO:696)，或其修饰变体或未修饰变体。

[1613] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39793.1(SEQ ID NO:697)，或其修饰变体或未修饰变体。

[1614] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39799.1(SEQ ID NO:698)，或其修饰变体或未修饰变体。

[1615] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39805.1(SEQ ID NO:699)，或其修饰变体或未修饰变体。

[1616] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39811.1(SEQ ID NO:700)，或其修饰变体或未修饰变体。

[1617] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39817.1(SEQ ID NO:701),或其修饰变体或未修饰变体。

[1618] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39823.1(SEQ ID NO:702),或其修饰变体或未修饰变体。

[1619] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39782.1(SEQ ID NO:703),或其修饰变体或未修饰变体。

[1620] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39788.1(SEQ ID NO:704),或其修饰变体或未修饰变体。

[1621] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39794.1(SEQ ID NO:705),或其修饰变体或未修饰变体。

[1622] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39800.1(SEQ ID NO:706),或其修饰变体或未修饰变体。

[1623] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39806.1(SEQ ID NO:707),或其修饰变体或未修饰变体。

[1624] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39812.1(SEQ ID NO:708),或其修饰变体或未修饰变体。

[1625] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39818.1(SEQ ID NO:709),或其修饰变体或未修饰变体。

[1626] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39824.1(SEQ ID NO:710),或其修饰变体或未修饰变体。

[1627] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39783.1(SEQ ID NO:711),或其修饰变体或未修饰变体。

[1628] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39789.1(SEQ ID NO:712),或其修饰变体或未修饰变体。

[1629] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39795.1(SEQ ID NO:713),或其修饰变体或未修饰变体。

[1630] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39801.1(SEQ ID NO:714),或其修饰变体或未修饰变体。

[1631] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39807.1(SEQ ID NO:715),或其修饰变体或未修饰变体。

[1632] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39813.1(SEQ ID NO:716),或其修饰变体或未修饰变体。

[1633] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39819.1(SEQ ID NO:717),或其修饰变体或未修饰变体。

[1634] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39825.1(SEQ ID NO:718),或其修饰变体或未修饰变体。

[1635] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39831.1(SEQ ID NO:719),或其修饰变体或未修饰变体。

[1636] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39837.1(SEQ ID NO:720),或其修饰变体或未修饰变体。

[1637] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39843.1(SEQ ID NO:721)，或其修饰变体或未修饰变体。

[1638] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39849.1(SEQ ID NO:722)，或其修饰变体或未修饰变体。

[1639] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39855.1(SEQ ID NO:723)，或其修饰变体或未修饰变体。

[1640] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39861.1(SEQ ID NO:724)，或其修饰变体或未修饰变体。

[1641] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39867.1(SEQ ID NO:725)，或其修饰变体或未修饰变体。

[1642] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39826.1(SEQ ID NO:726)，或其修饰变体或未修饰变体。

[1643] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39832.1(SEQ ID NO:727)，或其修饰变体或未修饰变体。

[1644] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39838.1(SEQ ID NO:728)，或其修饰变体或未修饰变体。

[1645] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39844.1(SEQ ID NO:729)，或其修饰变体或未修饰变体。

[1646] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39850.1(SEQ ID NO:730)，或其修饰变体或未修饰变体。

[1647] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39856.1(SEQ ID NO:731)，或其修饰变体或未修饰变体。

[1648] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39862.1(SEQ ID NO:732)，或其修饰变体或未修饰变体。

[1649] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39868.1(SEQ ID NO:733)，或其修饰变体或未修饰变体。

[1650] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39827.1(SEQ ID NO:734)，或其修饰变体或未修饰变体。

[1651] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39833.1(SEQ ID NO:735)，或其修饰变体或未修饰变体。

[1652] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39839.1(SEQ ID NO:736)，或其修饰变体或未修饰变体。

[1653] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39845.1(SEQ ID NO:737)，或其修饰变体或未修饰变体。

[1654] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39851.1(SEQ ID NO:738)，或其修饰变体或未修饰变体。

[1655] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39857.1(SEQ ID NO:739)，或其修饰变体或未修饰变体。

[1656] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39863.1(SEQ ID NO:740),或其修饰变体或未修饰变体。

[1657] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39869.1(SEQ ID NO:741),或其修饰变体或未修饰变体。

[1658] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39828.1(SEQ ID NO:742),或其修饰变体或未修饰变体。

[1659] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39834.1(SEQ ID NO:743),或其修饰变体或未修饰变体。

[1660] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39840.1(SEQ ID NO:744),或其修饰变体或未修饰变体。

[1661] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39846.1(SEQ ID NO:745),或其修饰变体或未修饰变体。

[1662] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39852.1(SEQ ID NO:746),或其修饰变体或未修饰变体。

[1663] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39858.1(SEQ ID NO:747),或其修饰变体或未修饰变体。

[1664] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39864.1(SEQ ID NO:748),或其修饰变体或未修饰变体。

[1665] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39870.1(SEQ ID NO:749),或其修饰变体或未修饰变体。

[1666] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39829.1(SEQ ID NO:750),或其修饰变体或未修饰变体。

[1667] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39835.1(SEQ ID NO:751),或其修饰变体或未修饰变体。

[1668] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39841.1(SEQ ID NO:752),或其修饰变体或未修饰变体。

[1669] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39853.1(SEQ ID NO:753),或其修饰变体或未修饰变体。

[1670] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39859.1(SEQ ID NO:754),或其修饰变体或未修饰变体。

[1671] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39865.1(SEQ ID NO:755),或其修饰变体或未修饰变体。

[1672] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39871.1(SEQ ID NO:756),或其修饰变体或未修饰变体。

[1673] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39830.1(SEQ ID NO:757),或其修饰变体或未修饰变体。

[1674] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39836.1(SEQ ID NO:758),或其修饰变体或未修饰变体。

[1675] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39842.1(SEQ ID NO:759),或其修饰变体或未修饰变体。

[1676] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39848.1(SEQ ID NO:760)，或其修饰变体或未修饰变体。

[1677] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39854.1(SEQ ID NO:761)，或其修饰变体或未修饰变体。

[1678] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39860.1(SEQ ID NO:762)，或其修饰变体或未修饰变体。

[1679] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39866.1(SEQ ID NO:763)，或其修饰变体或未修饰变体。

[1680] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39992.1(SEQ ID NO:764)，或其修饰变体或未修饰变体。

[1681] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39998.1(SEQ ID NO:765)，或其修饰变体或未修饰变体。

[1682] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40004.1(SEQ ID NO:766)，或其修饰变体或未修饰变体。

[1683] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40010.1(SEQ ID NO:767)，或其修饰变体或未修饰变体。

[1684] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40016.1(SEQ ID NO:768)，或其修饰变体或未修饰变体。

[1685] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40022.1(SEQ ID NO:769)，或其修饰变体或未修饰变体。

[1686] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40028.1(SEQ ID NO:770)，或其修饰变体或未修饰变体。

[1687] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40034.1(SEQ ID NO:771)，或其修饰变体或未修饰变体。

[1688] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39999.1(SEQ ID NO:772)，或其修饰变体或未修饰变体。

[1689] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40005.1(SEQ ID NO:773)，或其修饰变体或未修饰变体。

[1690] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40011.1(SEQ ID NO:774)，或其修饰变体或未修饰变体。

[1691] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40017.1(SEQ ID NO:775)，或其修饰变体或未修饰变体。

[1692] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40029.1(SEQ ID NO:776)，或其修饰变体或未修饰变体。

[1693] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40035.1(SEQ ID NO:777)，或其修饰变体或未修饰变体。

[1694] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39994.1(SEQ ID NO:778)，或其修饰变体或未修饰变体。

[1695] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-40000.1(SEQ ID NO:779),或其修饰变体或未修饰变体。

[1696] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40006.1(SEQ ID NO:780),或其修饰变体或未修饰变体。

[1697] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40012.1(SEQ ID NO:781),或其修饰变体或未修饰变体。

[1698] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40018.1(SEQ ID NO:782),或其修饰变体或未修饰变体。

[1699] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40024.1(SEQ ID NO:783),或其修饰变体或未修饰变体。

[1700] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40030.1(SEQ ID NO:784),或其修饰变体或未修饰变体。

[1701] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40036.1(SEQ ID NO:785),或其修饰变体或未修饰变体。

[1702] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39995.1(SEQ ID NO:786),或其修饰变体或未修饰变体。

[1703] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40001.1(SEQ ID NO:787),或其修饰变体或未修饰变体。

[1704] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40007.1(SEQ ID NO:788),或其修饰变体或未修饰变体。

[1705] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40013.1(SEQ ID NO:789),或其修饰变体或未修饰变体。

[1706] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40019.1(SEQ ID NO:790),或其修饰变体或未修饰变体。

[1707] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40025.1(SEQ ID NO:791),或其修饰变体或未修饰变体。

[1708] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40031.1(SEQ ID NO:792),或其修饰变体或未修饰变体。

[1709] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40037.1(SEQ ID NO:793),或其修饰变体或未修饰变体。

[1710] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39996.1(SEQ ID NO:794),或其修饰变体或未修饰变体。

[1711] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40002.1(SEQ ID NO:795),或其修饰变体或未修饰变体。

[1712] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40008.1(SEQ ID NO:796),或其修饰变体或未修饰变体。

[1713] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40014.1(SEQ ID NO:797),或其修饰变体或未修饰变体。

[1714] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40020.1(SEQ ID NO:798),或其修饰变体或未修饰变体。

[1715] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40026.1(SEQ ID NO:799)，或其修饰变体或未修饰变体。

[1716] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40032.1(SEQ ID NO:800)，或其修饰变体或未修饰变体。

[1717] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40038.1(SEQ ID NO:801)，或其修饰变体或未修饰变体。

[1718] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39997.1(SEQ ID NO:802)，或其修饰变体或未修饰变体。

[1719] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40009.1(SEQ ID NO:803)，或其修饰变体或未修饰变体。

[1720] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40015.1(SEQ ID NO:804)，或其修饰变体或未修饰变体。

[1721] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40021.1(SEQ ID NO:805)，或其修饰变体或未修饰变体。

[1722] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40027.1(SEQ ID NO:806)，或其修饰变体或未修饰变体。

[1723] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40033.1(SEQ ID NO:807)，或其修饰变体或未修饰变体。

[1724] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40039.1(SEQ ID NO:808)，或其修饰变体或未修饰变体。

[1725] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40045.1(SEQ ID NO:809)，或其修饰变体或未修饰变体。

[1726] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40051.1(SEQ ID NO:810)，或其修饰变体或未修饰变体。

[1727] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40057.1(SEQ ID NO:811)，或其修饰变体或未修饰变体。

[1728] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40063.1(SEQ ID NO:812)，或其修饰变体或未修饰变体。

[1729] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40069.1(SEQ ID NO:813)，或其修饰变体或未修饰变体。

[1730] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40075.1(SEQ ID NO:814)，或其修饰变体或未修饰变体。

[1731] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40081.1(SEQ ID NO:815)，或其修饰变体或未修饰变体。

[1732] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40040.1(SEQ ID NO:816)，或其修饰变体或未修饰变体。

[1733] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40046.1(SEQ ID NO:817)，或其修饰变体或未修饰变体。

[1734] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-40052.1(SEQ ID NO:818),或其修饰变体或未修饰变体。

[1735] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40058.1(SEQ ID NO:819),或其修饰变体或未修饰变体。

[1736] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40064.1(SEQ ID NO:820),或其修饰变体或未修饰变体。

[1737] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40070.1(SEQ ID NO:821),或其修饰变体或未修饰变体。

[1738] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40076.1(SEQ ID NO:822),或其修饰变体或未修饰变体。

[1739] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40082.1(SEQ ID NO:823),或其修饰变体或未修饰变体。

[1740] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40041.1(SEQ ID NO:824),或其修饰变体或未修饰变体。

[1741] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40047.1(SEQ ID NO:825),或其修饰变体或未修饰变体。

[1742] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40053.1(SEQ ID NO:826),或其修饰变体或未修饰变体。

[1743] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40059.1(SEQ ID NO:827),或其修饰变体或未修饰变体。

[1744] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40065.1(SEQ ID NO:828),或其修饰变体或未修饰变体。

[1745] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40071.1(SEQ ID NO:829),或其修饰变体或未修饰变体。

[1746] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40077.1(SEQ ID NO:830),或其修饰变体或未修饰变体。

[1747] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40083.1(SEQ ID NO:831),或其修饰变体或未修饰变体。

[1748] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40042.1(SEQ ID NO:832),或其修饰变体或未修饰变体。

[1749] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40048.1(SEQ ID NO:833),或其修饰变体或未修饰变体。

[1750] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40054.1(SEQ ID NO:834),或其修饰变体或未修饰变体。

[1751] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40060.1(SEQ ID NO:835),或其修饰变体或未修饰变体。

[1752] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40066.1(SEQ ID NO:836),或其修饰变体或未修饰变体。

[1753] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40072.1(SEQ ID NO:837),或其修饰变体或未修饰变体。

[1754] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40078.1(SEQ ID NO:838)，或其修饰变体或未修饰变体。

[1755] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40084.1(SEQ ID NO:839)，或其修饰变体或未修饰变体。

[1756] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40043.1(SEQ ID NO:840)，或其修饰变体或未修饰变体。

[1757] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40049.1(SEQ ID NO:841)，或其修饰变体或未修饰变体。

[1758] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40055.1(SEQ ID NO:842)，或其修饰变体或未修饰变体。

[1759] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40061.1(SEQ ID NO:843)，或其修饰变体或未修饰变体。

[1760] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40067.1(SEQ ID NO:844)，或其修饰变体或未修饰变体。

[1761] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40073.1(SEQ ID NO:845)，或其修饰变体或未修饰变体。

[1762] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40079.1(SEQ ID NO:846)，或其修饰变体或未修饰变体。

[1763] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40085.1(SEQ ID NO:847)，或其修饰变体或未修饰变体。

[1764] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40044.1(SEQ ID NO:848)，或其修饰变体或未修饰变体。

[1765] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40050.1(SEQ ID NO:849)，或其修饰变体或未修饰变体。

[1766] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40056.1(SEQ ID NO:850)，或其修饰变体或未修饰变体。

[1767] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40062.1(SEQ ID NO:851)，或其修饰变体或未修饰变体。

[1768] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40068.1(SEQ ID NO:852)，或其修饰变体或未修饰变体。

[1769] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40074.1(SEQ ID NO:853)，或其修饰变体或未修饰变体。

[1770] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40080.1(SEQ ID NO:854)，或其修饰变体或未修饰变体。

[1771] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39720.1(SEQ ID NOs:1716 和 1754)，或其修饰变体或未修饰变体。

[1772] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39706.1(SEQ ID NOs:1717 和 1755)，或其修饰变体或未修饰变体。

[1773] 包含第一链和第二链的 RNAi 剂，其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-39712.1(SEQ ID NOs:1718 和 1756),或其修饰变体或未修饰变体。

[1774] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39760.1(SEQ ID NOs:1719 和 1757),或其修饰变体或未修饰变体。

[1775] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39732.1(SEQ ID NOs:1720 和 1758),或其修饰变体或未修饰变体。

[1776] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35541.4(SEQ ID NOs:1721 和 1759),或其修饰变体或未修饰变体。

[1777] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NOs:1722 和 1760),或其修饰变体或未修饰变体。

[1778] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39741.1,或其修饰变体或未修饰变体。

[1779] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :hs_KRAS_322_A22S26(SEQ ID NOs:1723 和 1761),或其修饰变体或未修饰变体。

[1780] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39778.1(SEQ ID NOs:1724 和 1762),或其修饰变体或未修饰变体。

[1781] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39790.1(SEQ ID NOs:1725 和 1763),或其修饰变体或未修饰变体。

[1782] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39822.1(SEQ ID NOs:1726 和 1764),或其修饰变体或未修饰变体。

[1783] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35609.4(SEQ ID NOs:1727 和 1765),或其修饰变体或未修饰变体。

[1784] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35581.4(SEQ ID NOs:1728 和 1766),或其修饰变体或未修饰变体。

[1785] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39845.1(SEQ ID NOs:1729 和 1767),或其修饰变体或未修饰变体。

[1786] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39858.1(SEQ ID NOs:1730 和 1768),或其修饰变体或未修饰变体。

[1787] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39870.1(SEQ ID NOs:1731 和 1769),或其修饰变体或未修饰变体。

[1788] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35576.4(SEQ ID NOs:1732 和 1770),或其修饰变体或未修饰变体。

[1789] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35588.4(SEQ ID NOs:1733 和 1771),或其修饰变体或未修饰变体。

[1790] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35600.1(SEQ ID NOs:1734 和 1772),或其修饰变体或未修饰变体。

[1791] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-35606.1(SEQ ID NOs:1735 和 1773),或其修饰变体或未修饰变体。

[1792] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序

列 :AD-38151.1(SEQ ID NOs:1736 和 1774),或其修饰变体或未修饰变体。

[1793] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38163.1(SEQ ID NOs:1737 和 1775),或其修饰变体或未修饰变体。

[1794] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-39999.1(SEQ ID NOs:1738 和 1776),或其修饰变体或未修饰变体。

[1795] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1739 和 1777),或其修饰变体或未修饰变体。

[1796] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1740 和 1778),或其修饰变体或未修饰变体。

[1797] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38136.1(SEQ ID NOs:1741 和 1779),或其修饰变体或未修饰变体。

[1798] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40036.1(SEQ ID NOs:1742 和 1780),或其修饰变体或未修饰变体。

[1799] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40008.1(SEQ ID NOs:1743 和 1781),或其修饰变体或未修饰变体。

[1800] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40021.1(SEQ ID NOs:1744 和 1782),或其修饰变体或未修饰变体。

[1801] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40077.1(SEQ ID NOs:1745 和 1783),或其修饰变体或未修饰变体。

[1802] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40072.1(SEQ ID NOs:1746 和 1784),或其修饰变体或未修饰变体。

[1803] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40061.1(SEQ ID NOs:1747 和 1785),或其修饰变体或未修饰变体。

[1804] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-40068.1(SEQ ID NOs:1748 和 1786),或其修饰变体或未修饰变体。

[1805] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38131.1(SEQ ID NOs:1749 和 1787),或其修饰变体或未修饰变体。

[1806] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :AD-38167.1(SEQ ID NOs:1750 和 1788),或其修饰变体或未修饰变体。

[1807] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :hs_KRAS 1273_A22S26(SEQ ID NOs:1751 和 1789),或其修饰变体或未修饰变体。

[1808] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :hs_KRAS 2892_A37S26(SEQ ID NOs:1752 和 1790),或其修饰变体或未修饰变体。

[1809] 包含第一链和第二链的 RNAi 剂,其中第一链的序列是如下 RNAi 剂的第一链的序列 :hs_KRAS 4731_A22S26(SEQ ID NOs:1753 和 1791),或其修饰变体或未修饰变体。

[1810] 包含本文公开的 RNAi 剂的第一链和 / 或第二链的具体实施方案

[1811] 在一个实施方案中,本公开涉及一种包含任意一种或多种 RNAi 剂的组合物,所述

RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列包含来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和 / 或第二链的序列。

[1812] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[1813] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35523.3(SEQ ID NOs:1 和 428)，或其修饰变体或未修饰变体。

[1814] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35529.1(SEQ ID NOs:2 和 429)，或其修饰变体或未修饰变体。

[1815] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35535.4(SEQ ID NOs:3 和 430)，或其修饰变体或未修饰变体。

[1816] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35541.4(SEQ ID NOs:4 和 431)，或其修饰变体或未修饰变体。

[1817] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35547.4(SEQ ID NOs:5 和 432)，或其修饰变体或未修饰变体。

[1818] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35553.4(SEQ ID NOs:6 和 433)，或其修饰变体或未修饰变体。

[1819] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35559.4(SEQ ID NOs:7 和 434)，或其修饰变体或未修饰变体。

[1820] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35565.4(SEQ ID NOs:8 和 435)，或其修饰变体或未修饰变体。

[1821] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35524.4(SEQ ID NOs:9 和 436)，或其修饰变体或未修饰变体。

[1822] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35530.4(SEQ ID NOs:10 和 437)，或其修饰变体或未修饰变体。

[1823] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35536.4(SEQ ID NOs:11 和 438)，或其修饰变体或未修饰变体。

[1824] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35542.4(SEQ ID NOs:12 和 439)，或其修饰变体或未

修饰变体。

[1825] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35548.4(SEQ ID NOs:13 和 440)，或其修饰变体或未修饰变体。

[1826] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35554.4(SEQ ID NOs:14 和 441)，或其修饰变体或未修饰变体。

[1827] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35560.2(SEQ ID NOs:15 和 442)，或其修饰变体或未修饰变体。

[1828] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35566.4(SEQ ID NOs:16 和 443)，或其修饰变体或未修饰变体。

[1829] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35525.2(SEQ ID NOs:17 和 444)，或其修饰变体或未修饰变体。

[1830] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35531.4(SEQ ID NOs:18 和 445)，或其修饰变体或未修饰变体。

[1831] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35537.4(SEQ ID NOs:19 和 446)，或其修饰变体或未修饰变体。

[1832] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35543.2(SEQ ID NOs:20 和 447)，或其修饰变体或未修饰变体。

[1833] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35549.4(SEQ ID NOs:21 和 448)，或其修饰变体或未修饰变体。

[1834] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35555.4(SEQ ID NOs:22 和 449)，或其修饰变体或未修饰变体。

[1835] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35561.4(SEQ ID NOs:23 和 450)，或其修饰变体或未修饰变体。

[1836] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35567.4(SEQ ID NOs:24 和 451)，或其修饰变体或未修饰变体。

[1837] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35526.4(SEQ ID NOs:25 和 452)，或其修饰变体或未

修饰变体。

[1838] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35532.4(SEQ ID NOs:26 和 453)，或其修饰变体或未修饰变体。

[1839] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35538.4(SEQ ID NOs:27 和 454)，或其修饰变体或未修饰变体。

[1840] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35544.4(SEQ ID NOs:28 和 455)，或其修饰变体或未修饰变体。

[1841] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35550.4(SEQ ID NOs:29 和 456)，或其修饰变体或未修饰变体。

[1842] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35556.4(SEQ ID NOs:30 和 457)，或其修饰变体或未修饰变体。

[1843] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35562.4(SEQ ID NOs:31 和 458)，或其修饰变体或未修饰变体。

[1844] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35568.4(SEQ ID NOs:32 和 459)，或其修饰变体或未修饰变体。

[1845] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35527.4(SEQ ID NOs:33 和 460)，或其修饰变体或未修饰变体。

[1846] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35533.4(SEQ ID NOs:34 和 461)，或其修饰变体或未修饰变体。

[1847] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35539.4(SEQ ID NOs:35 和 462)，或其修饰变体或未修饰变体。

[1848] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35545.4(SEQ ID NOs:36 和 463)，或其修饰变体或未修饰变体。

[1849] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35551.4(SEQ ID NOs:37 和 464)，或其修饰变体或未修饰变体。

[1850] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35563.4(SEQ ID NOs:38 和 465)，或其修饰变体或未

修饰变体。

[1851] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35528.4(SEQ ID NOs:39 和 466)，或其修饰变体或未修饰变体。

[1852] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35540.4(SEQ ID NOs:40 和 467)，或其修饰变体或未修饰变体。

[1853] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35546.4(SEQ ID NOs:41 和 468)，或其修饰变体或未修饰变体。

[1854] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35552.4(SEQ ID NOs:42 和 469)，或其修饰变体或未修饰变体。

[1855] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35558.4(SEQ ID NOs:43 和 470)，或其修饰变体或未修饰变体。

[1856] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35564.4(SEQ ID NOs:44 和 471)，或其修饰变体或未修饰变体。

[1857] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35570.4(SEQ ID NOs:45 和 472)，或其修饰变体或未修饰变体。

[1858] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35571.4(SEQ ID NOs:46 和 473)，或其修饰变体或未修饰变体。

[1859] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35577.4(SEQ ID NOs:47 和 474)，或其修饰变体或未修饰变体。

[1860] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35583.4(SEQ ID NOs:48 和 475)，或其修饰变体或未修饰变体。

[1861] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35589.4(SEQ ID NOs:49 和 476)，或其修饰变体或未修饰变体。

[1862] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35595.4(SEQ ID NOs:50 和 477)，或其修饰变体或未修饰变体。

[1863] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35601.4(SEQ ID NOs:51 和 478)，或其修饰变体或未

修饰变体。

[1864] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35607.4(SEQ ID NOs:52 和 479)，或其修饰变体或未修饰变体。

[1865] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35613.4(SEQ ID NOs:53 和 480)，或其修饰变体或未修饰变体。

[1866] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35572.4(SEQ ID NOs:54 和 481)，或其修饰变体或未修饰变体。

[1867] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35578.4(SEQ ID NOs:55 和 482)，或其修饰变体或未修饰变体。

[1868] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35584.4(SEQ ID NOs:56 和 483)，或其修饰变体或未修饰变体。

[1869] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35590.4(SEQ ID NOs:57 和 484)，或其修饰变体或未修饰变体。

[1870] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35596.4(SEQ ID NOs:58 和 485)，或其修饰变体或未修饰变体。

[1871] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35602.4(SEQ ID NOs:59 和 486)，或其修饰变体或未修饰变体。

[1872] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35608.4(SEQ ID NOs:60 和 487)，或其修饰变体或未修饰变体。

[1873] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35614.4(SEQ ID NOs:61 和 488)，或其修饰变体或未修饰变体。

[1874] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35573.4(SEQ ID NOs:62 和 489)，或其修饰变体或未修饰变体。

[1875] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35579.4(SEQ ID NOs:63 和 490)，或其修饰变体或未修饰变体。

[1876] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35585.4(SEQ ID NOs:64 和 491)，或其修饰变体或未

修饰变体。

[1877] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35591.4(SEQ ID NOs:65 和 492)，或其修饰变体或未修饰变体。

[1878] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35597.4(SEQ ID NOs:66 和 493)，或其修饰变体或未修饰变体。

[1879] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35603.4(SEQ ID NOs:67 和 494)，或其修饰变体或未修饰变体。

[1880] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35609.4(SEQ ID NOs:68 和 495)，或其修饰变体或未修饰变体。

[1881] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35615.4(SEQ ID NOs:69 和 496)，或其修饰变体或未修饰变体。

[1882] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35574.4(SEQ ID NOs:70 和 497)，或其修饰变体或未修饰变体。

[1883] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35580.1(SEQ ID NOs:71 和 498)，或其修饰变体或未修饰变体。

[1884] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35586.4(SEQ ID NOs:72 和 499)，或其修饰变体或未修饰变体。

[1885] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35592.4(SEQ ID NOs:73 和 500)，或其修饰变体或未修饰变体。

[1886] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35598.4(SEQ ID NOs:74 和 501)，或其修饰变体或未修饰变体。

[1887] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35604.4(SEQ ID NOs:75 和 502)，或其修饰变体或未修饰变体。

[1888] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35610.4(SEQ ID NOs:76 和 503)，或其修饰变体或未修饰变体。

[1889] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35616.4(SEQ ID NOs:77 和 504)，或其修饰变体或未

修饰变体。

[1890] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35575.4(SEQ ID NOs:78 和 505)，或其修饰变体或未修饰变体。

[1891] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:79 和 506)，或其修饰变体或未修饰变体。

[1892] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35587.4(SEQ ID NOs:80 和 507)，或其修饰变体或未修饰变体。

[1893] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35593.4(SEQ ID NOs:81 和 508)，或其修饰变体或未修饰变体。

[1894] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35599.4(SEQ ID NOs:82 和 509)，或其修饰变体或未修饰变体。

[1895] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35605.4(SEQ ID NOs:83 和 510)，或其修饰变体或未修饰变体。

[1896] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35611.4(SEQ ID NOs:84 和 511)，或其修饰变体或未修饰变体。

[1897] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35617.4(SEQ ID NOs:85 和 512)，或其修饰变体或未修饰变体。

[1898] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:86 和 513)，或其修饰变体或未修饰变体。

[1899] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:87 和 514)，或其修饰变体或未修饰变体。

[1900] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35667.1(SEQ ID NOs:88 和 515)，或其修饰变体或未修饰变体。

[1901] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35673.1(SEQ ID NOs:89 和 516)，或其修饰变体或未修饰变体。

[1902] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35679.1(SEQ ID NOs:90 和 517)，或其修饰变体或未

修饰变体。

[1903] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35685.1(SEQ ID NOs:91 和 518)，或其修饰变体或未修饰变体。

[1904] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35691.1(SEQ ID NOs:92 和 519)，或其修饰变体或未修饰变体。

[1905] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35557.1(SEQ ID NOs:93 和 520)，或其修饰变体或未修饰变体。

[1906] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35618.1(SEQ ID NOs:94 和 521)，或其修饰变体或未修饰变体。

[1907] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35569.1(SEQ ID NOs:95 和 522)，或其修饰变体或未修饰变体。

[1908] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35534.1(SEQ ID NOs:96 和 523)，或其修饰变体或未修饰变体。

[1909] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35582.1(SEQ ID NOs:97 和 524)，或其修饰变体或未修饰变体。

[1910] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35594.1(SEQ ID NOs:98 和 525)，或其修饰变体或未修饰变体。

[1911] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:99 和 526)，或其修饰变体或未修饰变体。

[1912] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:100 和 527)，或其修饰变体或未修饰变体。

[1913] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35612.1(SEQ ID NOs:101 和 528)，或其修饰变体或未修饰变体。

[1914] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38127.1(SEQ ID NOs:102 和 529)，或其修饰变体或未修饰变体。

[1915] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38133.1(SEQ ID NOs:103 和 530)，或其修饰变体或未

修饰变体。

[1916] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38139.1(SEQ ID NOs:104 和 531)，或其修饰变体或未修饰变体。

[1917] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38145.1(SEQ ID NOs:105 和 532)，或其修饰变体或未修饰变体。

[1918] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38151.1(SEQ ID NOs:106 和 533)，或其修饰变体或未修饰变体。

[1919] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38157.1(SEQ ID NOs:107 和 534)，或其修饰变体或未修饰变体。

[1920] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38163.1(SEQ ID NOs:108 和 535)，或其修饰变体或未修饰变体。

[1921] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38169.1(SEQ ID NOs:109 和 536)，或其修饰变体或未修饰变体。

[1922] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38128.1(SEQ ID NOs:110 和 537)，或其修饰变体或未修饰变体。

[1923] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38134.1(SEQ ID NOs:111 和 538)，或其修饰变体或未修饰变体。

[1924] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38140.1(SEQ ID NOs:112 和 539)，或其修饰变体或未修饰变体。

[1925] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38146.1(SEQ ID NOs:113 和 540)，或其修饰变体或未修饰变体。

[1926] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38152.1(SEQ ID NOs:114 和 541)，或其修饰变体或未修饰变体。

[1927] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38158.1(SEQ ID NOs:115 和 542)，或其修饰变体或未修饰变体。

[1928] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38164.1(SEQ ID NOs:116 和 543)，或其修饰变体或未

修饰变体。

[1929] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38170.1(SEQ ID NOs:117 和 544)，或其修饰变体或未修饰变体。

[1930] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38129.1(SEQ ID NOs:118 和 545)，或其修饰变体或未修饰变体。

[1931] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38135.1(SEQ ID NOs:119 和 546)，或其修饰变体或未修饰变体。

[1932] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38141.1(SEQ ID NOs:120 和 547)，或其修饰变体或未修饰变体。

[1933] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38147.1(SEQ ID NOs:121 和 548)，或其修饰变体或未修饰变体。

[1934] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38153.1(SEQ ID NOs:122 和 549)，或其修饰变体或未修饰变体。

[1935] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38159.1(SEQ ID NOs:123 和 550)，或其修饰变体或未修饰变体。

[1936] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38165.1(SEQ ID NOs:124 和 551)，或其修饰变体或未修饰变体。

[1937] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38171.1(SEQ ID NOs:125 和 552)，或其修饰变体或未修饰变体。

[1938] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38130.1(SEQ ID NOs:126 和 553)，或其修饰变体或未修饰变体。

[1939] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38136.1(SEQ ID NOs:127 和 554)，或其修饰变体或未修饰变体。

[1940] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38142.1(SEQ ID NOs:128 和 555)，或其修饰变体或未修饰变体。

[1941] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38148.1(SEQ ID NOs:129 和 556)，或其修饰变体或未

修饰变体。

[1942] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38154.1(SEQ ID NOs:130 和 557)，或其修饰变体或未修饰变体。

[1943] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38160.1(SEQ ID NOs:131 和 558)，或其修饰变体或未修饰变体。

[1944] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38166.1(SEQ ID NOs:132 和 559)，或其修饰变体或未修饰变体。

[1945] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38172.1(SEQ ID NOs:133 和 560)，或其修饰变体或未修饰变体。

[1946] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38131.1(SEQ ID NOs:134 和 561)，或其修饰变体或未修饰变体。

[1947] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38137.1(SEQ ID NOs:135 和 562)，或其修饰变体或未修饰变体。

[1948] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38143.1(SEQ ID NOs:136 和 563)，或其修饰变体或未修饰变体。

[1949] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38149.1(SEQ ID NOs:137 和 564)，或其修饰变体或未修饰变体。

[1950] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38155.1(SEQ ID NOs:138 和 565)，或其修饰变体或未修饰变体。

[1951] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38161.1(SEQ ID NOs:139 和 566)，或其修饰变体或未修饰变体。

[1952] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38167.1(SEQ ID NOs:140 和 567)，或其修饰变体或未修饰变体。

[1953] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38173.1(SEQ ID NOs:141 和 568)，或其修饰变体或未修饰变体。

[1954] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38132.1(SEQ ID NOs:142 和 569)，或其修饰变体或未

修饰变体。

[1955] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38138.1(SEQ ID NOs:143 和 570)，或其修饰变体或未修饰变体。

[1956] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38144.1(SEQ ID NOs:144 和 571)，或其修饰变体或未修饰变体。

[1957] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38150.1(SEQ ID NOs:145 和 572)，或其修饰变体或未修饰变体。

[1958] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38156.1(SEQ ID NOs:146 和 573)，或其修饰变体或未修饰变体。

[1959] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38162.1(SEQ ID NOs:147 和 574)，或其修饰变体或未修饰变体。

[1960] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38168.1(SEQ ID NOs:148 和 575)，或其修饰变体或未修饰变体。

[1961] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38174.1(SEQ ID NOs:149 和 576)，或其修饰变体或未修饰变体。

[1962] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39683.1(SEQ ID NOs:150 和 577)，或其修饰变体或未修饰变体。

[1963] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39689.1(SEQ ID NOs:151 和 578)，或其修饰变体或未修饰变体。

[1964] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39695.1(SEQ ID NOs:152 和 579)，或其修饰变体或未修饰变体。

[1965] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39701.1(SEQ ID NOs:153 和 580)，或其修饰变体或未修饰变体。

[1966] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39707.1(SEQ ID NOs:154 和 581)，或其修饰变体或未修饰变体。

[1967] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39713.1(SEQ ID NOs:155 和 582)，或其修饰变体或未

修饰变体。

[1968] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39719.1(SEQ ID NOs:156 和 583)，或其修饰变体或未修饰变体。

[1969] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39725.1(SEQ ID NOs:157 和 584)，或其修饰变体或未修饰变体。

[1970] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39684.1(SEQ ID NOs:158 和 585)，或其修饰变体或未修饰变体。

[1971] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39690.1(SEQ ID NOs:159 和 586)，或其修饰变体或未修饰变体。

[1972] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39696.1(SEQ ID NOs:160 和 587)，或其修饰变体或未修饰变体。

[1973] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39702.1(SEQ ID NOs:161 和 588)，或其修饰变体或未修饰变体。

[1974] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39708.1(SEQ ID NOs:162 和 589)，或其修饰变体或未修饰变体。

[1975] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39714.1(SEQ ID NOs:163 和 590)，或其修饰变体或未修饰变体。

[1976] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39720.1(SEQ ID NOs:164 和 591)，或其修饰变体或未修饰变体。

[1977] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39726.1(SEQ ID NOs:165 和 592)，或其修饰变体或未修饰变体。

[1978] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39685.1(SEQ ID NOs:166 和 593)，或其修饰变体或未修饰变体。

[1979] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39691.1(SEQ ID NOs:167 和 594)，或其修饰变体或未修饰变体。

[1980] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39697.1(SEQ ID NOs:168 和 595)，或其修饰变体或未

修饰变体。

[1981] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39703.1(SEQ ID NOs:169 和 596)，或其修饰变体或未修饰变体。

[1982] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39709.1(SEQ ID NOs:170 和 597)，或其修饰变体或未修饰变体。

[1983] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39715.1(SEQ ID NOs:171 和 598)，或其修饰变体或未修饰变体。

[1984] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39721.1(SEQ ID NOs:172 和 599)，或其修饰变体或未修饰变体。

[1985] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39727.1(SEQ ID NOs:173 和 600)，或其修饰变体或未修饰变体。

[1986] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39686.1(SEQ ID NOs:174 和 601)，或其修饰变体或未修饰变体。

[1987] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39692.1(SEQ ID NOs:175 和 602)，或其修饰变体或未修饰变体。

[1988] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39698.1(SEQ ID NOs:176 和 603)，或其修饰变体或未修饰变体。

[1989] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39704.1(SEQ ID NOs:177 和 604)，或其修饰变体或未修饰变体。

[1990] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39710.1(SEQ ID NOs:178 和 605)，或其修饰变体或未修饰变体。

[1991] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39716.1(SEQ ID NOs:179 和 606)，或其修饰变体或未修饰变体。

[1992] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39722.1(SEQ ID NOs:180 和 607)，或其修饰变体或未修饰变体。

[1993] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39728.1(SEQ ID NOs:181 和 608)，或其修饰变体或未

修饰变体。

[1994] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39687.1(SEQ ID NOs:182 和 609)，或其修饰变体或未修饰变体。

[1995] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39693.1(SEQ ID NOs:183 和 610)，或其修饰变体或未修饰变体。

[1996] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39699.1(SEQ ID NOs:184 和 611)，或其修饰变体或未修饰变体。

[1997] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39705.1(SEQ ID NOs:185 和 612)，或其修饰变体或未修饰变体。

[1998] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39711.1(SEQ ID NOs:186 和 613)，或其修饰变体或未修饰变体。

[1999] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39717.1(SEQ ID NOs:187 和 614)，或其修饰变体或未修饰变体。

[2000] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39723.1(SEQ ID NOs:188 和 615)，或其修饰变体或未修饰变体。

[2001] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39729.1(SEQ ID NOs:189 和 616)，或其修饰变体或未修饰变体。

[2002] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39688.1(SEQ ID NOs:190 和 617)，或其修饰变体或未修饰变体。

[2003] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39694.1(SEQ ID NOs:191 和 618)，或其修饰变体或未修饰变体。

[2004] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39700.1(SEQ ID NOs:192 和 619)，或其修饰变体或未修饰变体。

[2005] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39706.1(SEQ ID NOs:193 和 620)，或其修饰变体或未修饰变体。

[2006] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39712.1(SEQ ID NOs:194 和 621)，或其修饰变体或未

修饰变体。

[2007] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39718.1(SEQ ID NOs:195 和 622)，或其修饰变体或未修饰变体。

[2008] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39724.1(SEQ ID NOs:196 和 623)，或其修饰变体或未修饰变体。

[2009] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39730.1(SEQ ID NOs:197 和 624)，或其修饰变体或未修饰变体。

[2010] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39736.1(SEQ ID NOs:198 和 625)，或其修饰变体或未修饰变体。

[2011] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39742.1(SEQ ID NOs:199 和 626)，或其修饰变体或未修饰变体。

[2012] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39748.1(SEQ ID NOs:200 和 627)，或其修饰变体或未修饰变体。

[2013] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39754.1(SEQ ID NOs:201 和 628)，或其修饰变体或未修饰变体。

[2014] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39760.1(SEQ ID NOs:202 和 629)，或其修饰变体或未修饰变体。

[2015] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39766.1(SEQ ID NOs:203 和 630)，或其修饰变体或未修饰变体。

[2016] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39772.1(SEQ ID NOs:204 和 631)，或其修饰变体或未修饰变体。

[2017] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39731.1(SEQ ID NOs:205 和 632)，或其修饰变体或未修饰变体。

[2018] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39737.1(SEQ ID NOs:206 和 633)，或其修饰变体或未修饰变体。

[2019] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39743.1(SEQ ID NOs:207 和 634)，或其修饰变体或未

修饰变体。

[2020] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39749.1(SEQ ID NOs:208 和 635)，或其修饰变体或未修饰变体。

[2021] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39755.1(SEQ ID NOs:209 和 636)，或其修饰变体或未修饰变体。

[2022] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39761.1(SEQ ID NOs:210 和 637)，或其修饰变体或未修饰变体。

[2023] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39767.1(SEQ ID NOs:211 和 638)，或其修饰变体或未修饰变体。

[2024] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39773.1(SEQ ID NOs:212 和 639)，或其修饰变体或未修饰变体。

[2025] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39732.1(SEQ ID NOs:213 和 640)，或其修饰变体或未修饰变体。

[2026] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39738.1(SEQ ID NOs:214 和 641)，或其修饰变体或未修饰变体。

[2027] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39744.1(SEQ ID NOs:215 和 642)，或其修饰变体或未修饰变体。

[2028] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39750.1(SEQ ID NOs:216 和 643)，或其修饰变体或未修饰变体。

[2029] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39756.1(SEQ ID NOs:217 和 644)，或其修饰变体或未修饰变体。

[2030] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39762.1(SEQ ID NOs:218 和 645)，或其修饰变体或未修饰变体。

[2031] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39768.1(SEQ ID NOs:219 和 646)，或其修饰变体或未修饰变体。

[2032] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39774.1(SEQ ID NOs:220 和 647)，或其修饰变体或未

修饰变体。

[2033] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39733.1(SEQ ID NOs:221 和 648)，或其修饰变体或未修饰变体。

[2034] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39739.1(SEQ ID NOs:222 和 649)，或其修饰变体或未修饰变体。

[2035] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39745.1(SEQ ID NOs:223 和 650)，或其修饰变体或未修饰变体。

[2036] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39751.1(SEQ ID NOs:224 和 651)，或其修饰变体或未修饰变体。

[2037] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39757.1(SEQ ID NOs:225 和 652)，或其修饰变体或未修饰变体。

[2038] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39763.1(SEQ ID NOs:226 和 653)，或其修饰变体或未修饰变体。

[2039] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39769.1(SEQ ID NOs:227 和 654)，或其修饰变体或未修饰变体。

[2040] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39775.1(SEQ ID NOs:228 和 655)，或其修饰变体或未修饰变体。

[2041] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39734.1(SEQ ID NOs:229 和 656)，或其修饰变体或未修饰变体。

[2042] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39740.1(SEQ ID NOs:230 和 657)，或其修饰变体或未修饰变体。

[2043] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39746.1(SEQ ID NOs:231 和 658)，或其修饰变体或未修饰变体。

[2044] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39752.1(SEQ ID NOs:232 和 659)，或其修饰变体或未修饰变体。

[2045] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39758.1(SEQ ID NOs:233 和 660)，或其修饰变体或未

修饰变体。

[2046] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39764.1(SEQ ID NOs:234 和 661)，或其修饰变体或未修饰变体。

[2047] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39770.1(SEQ ID NOs:235 和 662)，或其修饰变体或未修饰变体。

[2048] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39776.1(SEQ ID NOs:236 和 663)，或其修饰变体或未修饰变体。

[2049] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39735.1(SEQ ID NOs:237 和 664)，或其修饰变体或未修饰变体。

[2050] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39741.1(SEQ ID NOs:238 和 665)，或其修饰变体或未修饰变体。

[2051] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39747.1(SEQ ID NOs:239 和 666)，或其修饰变体或未修饰变体。

[2052] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39753.1(SEQ ID NOs:240 和 667)，或其修饰变体或未修饰变体。

[2053] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39759.1(SEQ ID NOs:241 和 668)，或其修饰变体或未修饰变体。

[2054] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39765.1(SEQ ID NOs:242 和 669)，或其修饰变体或未修饰变体。

[2055] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39771.1(SEQ ID NOs:243 和 670)，或其修饰变体或未修饰变体。

[2056] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39778.1(SEQ ID NOs:244 和 671)，或其修饰变体或未修饰变体。

[2057] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39784.1(SEQ ID NOs:245 和 672)，或其修饰变体或未修饰变体。

[2058] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39790.1(SEQ ID NOs:246 和 673)，或其修饰变体或未

修饰变体。

[2059] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39796.1(SEQ ID NOs:247 和 674)，或其修饰变体或未修饰变体。

[2060] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39802.1(SEQ ID NOs:248 和 675)，或其修饰变体或未修饰变体。

[2061] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39808.1(SEQ ID NOs:249 和 676)，或其修饰变体或未修饰变体。

[2062] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39814.1(SEQ ID NOs:250 和 677)，或其修饰变体或未修饰变体。

[2063] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39820.1(SEQ ID NOs:251 和 678)，或其修饰变体或未修饰变体。

[2064] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39779.1(SEQ ID NOs:252 和 679)，或其修饰变体或未修饰变体。

[2065] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39785.1(SEQ ID NOs:253 和 680)，或其修饰变体或未修饰变体。

[2066] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39791.1(SEQ ID NOs:254 和 681)，或其修饰变体或未修饰变体。

[2067] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39797.1(SEQ ID NOs:255 和 682)，或其修饰变体或未修饰变体。

[2068] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39803.1(SEQ ID NOs:256 和 683)，或其修饰变体或未修饰变体。

[2069] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39809.1(SEQ ID NOs:257 和 684)，或其修饰变体或未修饰变体。

[2070] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39815.1(SEQ ID NOs:258 和 685)，或其修饰变体或未修饰变体。

[2071] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39821.1(SEQ ID NOs:259 和 686)，或其修饰变体或未

修饰变体。

[2072] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39780.1(SEQ ID NOs:260 和 687)，或其修饰变体或未修饰变体。

[2073] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39786.1(SEQ ID NOs:261 和 688)，或其修饰变体或未修饰变体。

[2074] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39792.1(SEQ ID NOs:262 和 689)，或其修饰变体或未修饰变体。

[2075] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39798.1(SEQ ID NOs:263 和 690)，或其修饰变体或未修饰变体。

[2076] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39804.1(SEQ ID NOs:264 和 691)，或其修饰变体或未修饰变体。

[2077] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39810.1(SEQ ID NOs:265 和 692)，或其修饰变体或未修饰变体。

[2078] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39816.1(SEQ ID NOs:266 和 693)，或其修饰变体或未修饰变体。

[2079] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39822.1(SEQ ID NOs:267 和 694)，或其修饰变体或未修饰变体。

[2080] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39781.1(SEQ ID NOs:268 和 695)，或其修饰变体或未修饰变体。

[2081] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39787.1(SEQ ID NOs:269 和 696)，或其修饰变体或未修饰变体。

[2082] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39793.1(SEQ ID NOs:270 和 697)，或其修饰变体或未修饰变体。

[2083] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39799.1(SEQ ID NOs:271 和 698)，或其修饰变体或未修饰变体。

[2084] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39805.1(SEQ ID NOs:272 和 699)，或其修饰变体或未

修饰变体。

[2085] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39811.1(SEQ ID NOs:273 和 700)，或其修饰变体或未修饰变体。

[2086] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39817.1(SEQ ID NOs:274 和 701)，或其修饰变体或未修饰变体。

[2087] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39823.1(SEQ ID NOs:275 和 702)，或其修饰变体或未修饰变体。

[2088] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39782.1(SEQ ID NOs:276 和 703)，或其修饰变体或未修饰变体。

[2089] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39788.1(SEQ ID NOs:277 和 704)，或其修饰变体或未修饰变体。

[2090] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39794.1(SEQ ID NOs:278 和 705)，或其修饰变体或未修饰变体。

[2091] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39800.1(SEQ ID NOs:279 和 706)，或其修饰变体或未修饰变体。

[2092] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39806.1(SEQ ID NOs:280 和 707)，或其修饰变体或未修饰变体。

[2093] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39812.1(SEQ ID NOs:281 和 708)，或其修饰变体或未修饰变体。

[2094] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39818.1(SEQ ID NOs:282 和 709)，或其修饰变体或未修饰变体。

[2095] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39824.1(SEQ ID NOs:283 和 710)，或其修饰变体或未修饰变体。

[2096] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39783.1(SEQ ID NOs:284 和 711)，或其修饰变体或未修饰变体。

[2097] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39789.1(SEQ ID NOs:285 和 712)，或其修饰变体或未

修饰变体。

[2098] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39795.1(SEQ ID NOs:286 和 713)，或其修饰变体或未修饰变体。

[2099] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39801.1(SEQ ID NOs:287 和 714)，或其修饰变体或未修饰变体。

[2100] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39807.1(SEQ ID NOs:288 和 715)，或其修饰变体或未修饰变体。

[2101] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39813.1(SEQ ID NOs:289 和 716)，或其修饰变体或未修饰变体。

[2102] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39819.1(SEQ ID NOs:290 和 717)，或其修饰变体或未修饰变体。

[2103] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39825.1(SEQ ID NOs:291 和 718)，或其修饰变体或未修饰变体。

[2104] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39831.1(SEQ ID NOs:292 和 719)，或其修饰变体或未修饰变体。

[2105] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39837.1(SEQ ID NOs:293 和 720)，或其修饰变体或未修饰变体。

[2106] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39843.1(SEQ ID NOs:294 和 721)，或其修饰变体或未修饰变体。

[2107] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39849.1(SEQ ID NOs:295 和 722)，或其修饰变体或未修饰变体。

[2108] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39855.1(SEQ ID NOs:296 和 723)，或其修饰变体或未修饰变体。

[2109] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39861.1(SEQ ID NOs:297 和 724)，或其修饰变体或未修饰变体。

[2110] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39867.1(SEQ ID NOs:298 和 725)，或其修饰变体或未

修饰变体。

[2111] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39826.1(SEQ ID NOs:299 和 726)，或其修饰变体或未修饰变体。

[2112] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39832.1(SEQ ID NOs:300 和 727)，或其修饰变体或未修饰变体。

[2113] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39838.1(SEQ ID NOs:301 和 728)，或其修饰变体或未修饰变体。

[2114] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39844.1(SEQ ID NOs:302 和 729)，或其修饰变体或未修饰变体。

[2115] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39850.1(SEQ ID NOs:303 和 730)，或其修饰变体或未修饰变体。

[2116] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39856.1(SEQ ID NOs:304 和 731)，或其修饰变体或未修饰变体。

[2117] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39862.1(SEQ ID NOs:305 和 732)，或其修饰变体或未修饰变体。

[2118] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39868.1(SEQ ID NOs:306 和 733)，或其修饰变体或未修饰变体。

[2119] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39827.1(SEQ ID NOs:307 和 734)，或其修饰变体或未修饰变体。

[2120] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39833.1(SEQ ID NOs:308 和 735)，或其修饰变体或未修饰变体。

[2121] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39839.1(SEQ ID NOs:309 和 736)，或其修饰变体或未修饰变体。

[2122] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39845.1(SEQ ID NOs:310 和 737)，或其修饰变体或未修饰变体。

[2123] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39851.1(SEQ ID NOs:311 和 738)，或其修饰变体或未

修饰变体。

[2124] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39857.1(SEQ ID NOs:312 和 739)，或其修饰变体或未修饰变体。

[2125] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39863.1(SEQ ID NOs:313 和 740)，或其修饰变体或未修饰变体。

[2126] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39869.1(SEQ ID NOs:314 和 741)，或其修饰变体或未修饰变体。

[2127] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39828.1(SEQ ID NOs:315 和 742)，或其修饰变体或未修饰变体。

[2128] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39834.1(SEQ ID NOs:316 和 743)，或其修饰变体或未修饰变体。

[2129] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39840.1(SEQ ID NOs:317 和 744)，或其修饰变体或未修饰变体。

[2130] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39846.1(SEQ ID NOs:318 和 745)，或其修饰变体或未修饰变体。

[2131] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39852.1(SEQ ID NOs:319 和 746)，或其修饰变体或未修饰变体。

[2132] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39858.1(SEQ ID NOs:320 和 747)，或其修饰变体或未修饰变体。

[2133] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39864.1(SEQ ID NOs:321 和 748)，或其修饰变体或未修饰变体。

[2134] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39870.1(SEQ ID NOs:322 和 749)，或其修饰变体或未修饰变体。

[2135] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39829.1(SEQ ID NOs:323 和 750)，或其修饰变体或未修饰变体。

[2136] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39835.1(SEQ ID NOs:324 和 751)，或其修饰变体或未

修饰变体。

[2137] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39841.1(SEQ ID NOs:325 和 752)，或其修饰变体或未修饰变体。

[2138] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39853.1(SEQ ID NOs:326 和 753)，或其修饰变体或未修饰变体。

[2139] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39859.1(SEQ ID NOs:327 和 754)，或其修饰变体或未修饰变体。

[2140] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39865.1(SEQ ID NOs:328 和 755)，或其修饰变体或未修饰变体。

[2141] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39871.1(SEQ ID NOs:329 和 756)，或其修饰变体或未修饰变体。

[2142] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39830.1(SEQ ID NOs:330 和 757)，或其修饰变体或未修饰变体。

[2143] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39836.1(SEQ ID NOs:331 和 758)，或其修饰变体或未修饰变体。

[2144] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39842.1(SEQ ID NOs:332 和 759)，或其修饰变体或未修饰变体。

[2145] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39848.1(SEQ ID NOs:333 和 760)，或其修饰变体或未修饰变体。

[2146] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39854.1(SEQ ID NOs:334 和 761)，或其修饰变体或未修饰变体。

[2147] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39860.1(SEQ ID NOs:335 和 762)，或其修饰变体或未修饰变体。

[2148] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39866.1(SEQ ID NOs:336 和 763)，或其修饰变体或未修饰变体。

[2149] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39992.1(SEQ ID NOs:337 和 764)，或其修饰变体或未

修饰变体。

[2150] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39998.1(SEQ ID NOs:338 和 765)，或其修饰变体或未修饰变体。

[2151] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40004.1(SEQ ID NOs:339 和 766)，或其修饰变体或未修饰变体。

[2152] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40010.1(SEQ ID NOs:340 和 767)，或其修饰变体或未修饰变体。

[2153] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40016.1(SEQ ID NOs:341 和 768)，或其修饰变体或未修饰变体。

[2154] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40022.1(SEQ ID NOs:342 和 769)，或其修饰变体或未修饰变体。

[2155] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40028.1(SEQ ID NOs:343 和 770)，或其修饰变体或未修饰变体。

[2156] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40034.1(SEQ ID NOs:344 和 771)，或其修饰变体或未修饰变体。

[2157] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39999.1(SEQ ID NOs:345 和 772)，或其修饰变体或未修饰变体。

[2158] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40005.1(SEQ ID NOs:346 和 773)，或其修饰变体或未修饰变体。

[2159] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40011.1(SEQ ID NOs:347 和 774)，或其修饰变体或未修饰变体。

[2160] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40017.1(SEQ ID NOs:348 和 775)，或其修饰变体或未修饰变体。

[2161] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40029.1(SEQ ID NOs:349 和 776)，或其修饰变体或未修饰变体。

[2162] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40035.1(SEQ ID NOs:350 和 777)，或其修饰变体或未

修饰变体。

[2163] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39994.1(SEQ ID NOs:351 和 778)，或其修饰变体或未修饰变体。

[2164] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40000.1(SEQ ID NOs:352 和 779)，或其修饰变体或未修饰变体。

[2165] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40006.1(SEQ ID NOs:353 和 780)，或其修饰变体或未修饰变体。

[2166] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40012.1(SEQ ID NOs:354 和 781)，或其修饰变体或未修饰变体。

[2167] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40018.1(SEQ ID NOs:355 和 782)，或其修饰变体或未修饰变体。

[2168] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40024.1(SEQ ID NOs:356 和 783)，或其修饰变体或未修饰变体。

[2169] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40030.1(SEQ ID NOs:357 和 784)，或其修饰变体或未修饰变体。

[2170] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40036.1(SEQ ID NOs:358 和 785)，或其修饰变体或未修饰变体。

[2171] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39995.1(SEQ ID NOs:359 和 786)，或其修饰变体或未修饰变体。

[2172] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40001.1(SEQ ID NOs:360 和 787)，或其修饰变体或未修饰变体。

[2173] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40007.1(SEQ ID NOs:361 和 788)，或其修饰变体或未修饰变体。

[2174] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40013.1(SEQ ID NOs:362 和 789)，或其修饰变体或未修饰变体。

[2175] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40019.1(SEQ ID NOs:363 和 790)，或其修饰变体或未

修饰变体。

[2176] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40025.1(SEQ ID NOs:364 和 791)，或其修饰变体或未修饰变体。

[2177] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40031.1(SEQ ID NOs:365 和 792)，或其修饰变体或未修饰变体。

[2178] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40037.1(SEQ ID NOs:366 和 793)，或其修饰变体或未修饰变体。

[2179] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39996.1(SEQ ID NOs:367 和 794)，或其修饰变体或未修饰变体。

[2180] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40002.1(SEQ ID NOs:368 和 795)，或其修饰变体或未修饰变体。

[2181] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40008.1(SEQ ID NOs:369 和 796)，或其修饰变体或未修饰变体。

[2182] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40014.1(SEQ ID NOs:370 和 797)，或其修饰变体或未修饰变体。

[2183] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40020.1(SEQ ID NOs:371 和 798)，或其修饰变体或未修饰变体。

[2184] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40026.1(SEQ ID NOs:372 和 799)，或其修饰变体或未修饰变体。

[2185] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40032.1(SEQ ID NOs:373 和 800)，或其修饰变体或未修饰变体。

[2186] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40038.1(SEQ ID NOs:374 和 801)，或其修饰变体或未修饰变体。

[2187] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39997.1(SEQ ID NOs:375 和 802)，或其修饰变体或未修饰变体。

[2188] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40009.1(SEQ ID NOs:376 和 803)，或其修饰变体或未

修饰变体。

[2189] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40015.1(SEQ ID NOs:377 和 804)，或其修饰变体或未修饰变体。

[2190] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40021.1(SEQ ID NOs:378 和 805)，或其修饰变体或未修饰变体。

[2191] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40027.1(SEQ ID NOs:379 和 806)，或其修饰变体或未修饰变体。

[2192] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40033.1(SEQ ID NOs:380 和 807)，或其修饰变体或未修饰变体。

[2193] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40039.1(SEQ ID NOs:381 和 808)，或其修饰变体或未修饰变体。

[2194] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40045.1(SEQ ID NOs:382 和 809)，或其修饰变体或未修饰变体。

[2195] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40051.1(SEQ ID NOs:383 和 810)，或其修饰变体或未修饰变体。

[2196] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40057.1(SEQ ID NOs:384 和 811)，或其修饰变体或未修饰变体。

[2197] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40063.1(SEQ ID NOs:385 和 812)，或其修饰变体或未修饰变体。

[2198] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40069.1(SEQ ID NOs:386 和 813)，或其修饰变体或未修饰变体。

[2199] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40075.1(SEQ ID NOs:387 和 814)，或其修饰变体或未修饰变体。

[2200] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40081.1(SEQ ID NOs:388 和 815)，或其修饰变体或未修饰变体。

[2201] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40040.1(SEQ ID NOs:389 和 816)，或其修饰变体或未

修饰变体。

[2202] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40046.1(SEQ ID NOs:390 和 817)，或其修饰变体或未修饰变体。

[2203] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40052.1(SEQ ID NOs:391 和 818)，或其修饰变体或未修饰变体。

[2204] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40058.1(SEQ ID NOs:392 和 819)，或其修饰变体或未修饰变体。

[2205] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40064.1(SEQ ID NOs:393 和 820)，或其修饰变体或未修饰变体。

[2206] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40070.1(SEQ ID NOs:394 和 821)，或其修饰变体或未修饰变体。

[2207] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40076.1(SEQ ID NOs:395 和 822)，或其修饰变体或未修饰变体。

[2208] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40082.1(SEQ ID NOs:396 和 823)，或其修饰变体或未修饰变体。

[2209] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40041.1(SEQ ID NOs:397 和 824)，或其修饰变体或未修饰变体。

[2210] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40047.1(SEQ ID NOs:398 和 825)，或其修饰变体或未修饰变体。

[2211] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40053.1(SEQ ID NOs:399 和 826)，或其修饰变体或未修饰变体。

[2212] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40059.1(SEQ ID NOs:400 和 827)，或其修饰变体或未修饰变体。

[2213] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40065.1(SEQ ID NOs:401 和 828)，或其修饰变体或未修饰变体。

[2214] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40071.1(SEQ ID NOs:402 和 829)，或其修饰变体或未

修饰变体。

[2215] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40077.1(SEQ ID NOs:403 和 830)，或其修饰变体或未修饰变体。

[2216] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40083.1(SEQ ID NOs:404 和 831)，或其修饰变体或未修饰变体。

[2217] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40042.1(SEQ ID NOs:405 和 832)，或其修饰变体或未修饰变体。

[2218] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40048.1(SEQ ID NOs:406 和 833)，或其修饰变体或未修饰变体。

[2219] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40054.1(SEQ ID NOs:407 和 834)，或其修饰变体或未修饰变体。

[2220] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40060.1(SEQ ID NOs:408 和 835)，或其修饰变体或未修饰变体。

[2221] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40066.1(SEQ ID NOs:409 和 836)，或其修饰变体或未修饰变体。

[2222] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40072.1(SEQ ID NOs:410 和 837)，或其修饰变体或未修饰变体。

[2223] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40078.1(SEQ ID NOs:411 和 838)，或其修饰变体或未修饰变体。

[2224] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40084.1(SEQ ID NOs:412 和 839)，或其修饰变体或未修饰变体。

[2225] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40043.1(SEQ ID NOs:413 和 840)，或其修饰变体或未修饰变体。

[2226] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40049.1(SEQ ID NOs:414 和 841)，或其修饰变体或未修饰变体。

[2227] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40055.1(SEQ ID NOs:415 和 842)，或其修饰变体或未

修饰变体。

[2228] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40061.1(SEQ ID NOs:416 和 843)，或其修饰变体或未修饰变体。

[2229] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40067.1(SEQ ID NOs:417 和 844)，或其修饰变体或未修饰变体。

[2230] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40073.1(SEQ ID NOs:418 和 845)，或其修饰变体或未修饰变体。

[2231] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40079.1(SEQ ID NOs:419 和 846)，或其修饰变体或未修饰变体。

[2232] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40085.1(SEQ ID NOs:420 和 847)，或其修饰变体或未修饰变体。

[2233] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40044.1(SEQ ID NOs:421 和 848)，或其修饰变体或未修饰变体。

[2234] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40050.1(SEQ ID NOs:422 和 849)，或其修饰变体或未修饰变体。

[2235] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40056.1(SEQ ID NOs:423 和 850)，或其修饰变体或未修饰变体。

[2236] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40062.1(SEQ ID NOs:424 和 851)，或其修饰变体或未修饰变体。

[2237] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40068.1(SEQ ID NOs:425 和 852)，或其修饰变体或未修饰变体。

[2238] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40074.1(SEQ ID NOs:426 和 853)，或其修饰变体或未修饰变体。

[2239] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40080.1(SEQ ID NOs:427 和 854)，或其修饰变体或未修饰变体。

[2240] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39720.1(SEQ ID NOs:1716 和 1754)，或其修饰变体或

未修饰变体。

[2241] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39706.1(SEQ ID NOs:1717 和 1755)，或其修饰变体或未修饰变体。

[2242] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39712.1(SEQ ID NOs:1718 和 1756)，或其修饰变体或未修饰变体。

[2243] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39760.1(SEQ ID NOs:1719 和 1757)，或其修饰变体或未修饰变体。

[2244] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39732.1(SEQ ID NOs:1720 和 1758)，或其修饰变体或未修饰变体。

[2245] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35541.4(SEQ ID NOs:1721 和 1759)，或其修饰变体或未修饰变体。

[2246] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NOs:1722 和 1760)，或其修饰变体或未修饰变体。

[2247] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39741.1，或其修饰变体或未修饰变体。

[2248] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS_322_A22S26(SEQ ID NOs:1723 和 1761)，或其修饰变体或未修饰变体。

[2249] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39778.1(SEQ ID NOs:1724 和 1762)，或其修饰变体或未修饰变体。

[2250] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39790.1(SEQ ID NOs:1725 和 1763)，或其修饰变体或未修饰变体。

[2251] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39822.1(SEQ ID NOs:1726 和 1764)，或其修饰变体或未修饰变体。

[2252] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35609.4(SEQ ID NOs:1727 和 1765)，或其修饰变体或未修饰变体。

[2253] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:1728 和 1766)，或其修饰变体或未修饰变体。

[2254] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39845.1(SEQ ID NOs:1729 和 1767)，或其修饰变体或未修饰变体。

[2255] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39858.1(SEQ ID NOs:1730 和 1768)，或其修饰变体或未修饰变体。

[2256] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39870.1(SEQ ID NOs:1731 和 1769)，或其修饰变体或未修饰变体。

[2257] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:1732 和 1770)，或其修饰变体或未修饰变体。

[2258] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:1733 和 1771)，或其修饰变体或未修饰变体。

[2259] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:1734 和 1772)，或其修饰变体或未修饰变体。

[2260] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:1735 和 1773)，或其修饰变体或未修饰变体。

[2261] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38151.1(SEQ ID NOs:1736 和 1774)，或其修饰变体或未修饰变体。

[2262] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38163.1(SEQ ID NOs:1737 和 1775)，或其修饰变体或未修饰变体。

[2263] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39999.1(SEQ ID NOs:1738 和 1776)，或其修饰变体或未修饰变体。

[2264] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1739 和 1777)，或其修饰变体或未修饰变体。

[2265] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1740 和 1778)，或其修饰变体或未修饰变体。

[2266] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38136.1(SEQ ID NOs:1741 和 1779)，或其修饰变体或未修饰变体。

[2267] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40036.1(SEQ ID NOs:1742 和 1780)，或其修饰变体或未修饰变体。

[2268] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40008.1(SEQ ID NOs:1743 和 1781)，或其修饰变体或未修饰变体。

[2269] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40021.1(SEQ ID NOs:1744 和 1782)，或其修饰变体或未修饰变体。

[2270] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40077.1(SEQ ID NOs:1745 和 1783)，或其修饰变体或未修饰变体。

[2271] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40072.1(SEQ ID NOs:1746 和 1784)，或其修饰变体或未修饰变体。

[2272] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40061.1(SEQ ID NOs:1747 和 1785)，或其修饰变体或未修饰变体。

[2273] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40068.1(SEQ ID NOs:1748 和 1786)，或其修饰变体或未修饰变体。

[2274] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38131.1(SEQ ID NOs:1749 和 1787)，或其修饰变体或未修饰变体。

[2275] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38167.1(SEQ ID NOs:1750 和 1788)，或其修饰变体或未修饰变体。

[2276] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 1273_A22S26(SEQ IDNOs:1751 和 1789)，或其修饰变体或未修饰变体。

[2277] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 2892_A37S26(SEQ IDNOs:1752 和 1790)，或其修饰变体或未修饰变体。

[2278] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 4731_A22S26(SEQ IDNOs:1753 和 1791)，或其修饰变体或未修饰变体。

[2279] 其中第一链和 / 或第二链的序列是本文公开的 RNAi 剂的第一链和 / 或第二链的序列的具体实施方案

[2280] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述

RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和 / 或第二链的序列。

[2281] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[2282] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35523.3(SEQ ID NOs:1 和 428)，或其修饰变体或未修饰变体。

[2283] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35529.1(SEQ ID NOs:2 和 429)，或其修饰变体或未修饰变体。

[2284] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35535.4(SEQ ID NOs:3 和 430)，或其修饰变体或未修饰变体。

[2285] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35541.4(SEQ ID NOs:4 和 431)，或其修饰变体或未修饰变体。

[2286] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35547.4(SEQ ID NOs:5 和 432)，或其修饰变体或未修饰变体。

[2287] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35553.4(SEQ ID NOs:6 和 433)，或其修饰变体或未修饰变体。

[2288] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35559.4(SEQ ID NOs:7 和 434)，或其修饰变体或未修饰变体。

[2289] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35565.4(SEQ ID NOs:8 和 435)，或其修饰变体或未修饰变体。

[2290] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35524.4(SEQ ID NOs:9 和 436)，或其修饰变体或未修饰变体。

[2291] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35530.4(SEQ ID NOs:10 和 437)，或其修饰变体或未修饰变体。

[2292] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35536.4(SEQ ID NOs:11 和 438)，或其修饰变体或未修饰变体。

[2293] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35542.4(SEQ ID NOs:12 和 439)，或其修饰变体或未修

饰变体。

[2294] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35548.4(SEQ ID NOs:13 和 440)，或其修饰变体或未修饰变体。

[2295] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35554.4(SEQ ID NOs:14 和 441)，或其修饰变体或未修饰变体。

[2296] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35560.2(SEQ ID NOs:15 和 442)，或其修饰变体或未修饰变体。

[2297] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35566.4(SEQ ID NOs:16 和 443)，或其修饰变体或未修饰变体。

[2298] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35525.2(SEQ ID NOs:17 和 444)，或其修饰变体或未修饰变体。

[2299] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35531.4(SEQ ID NOs:18 和 445)，或其修饰变体或未修饰变体。

[2300] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35537.4(SEQ ID NOs:19 和 446)，或其修饰变体或未修饰变体。

[2301] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35543.2(SEQ ID NOs:20 和 447)，或其修饰变体或未修饰变体。

[2302] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35549.4(SEQ ID NOs:21 和 448)，或其修饰变体或未修饰变体。

[2303] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35555.4(SEQ ID NOs:22 和 449)，或其修饰变体或未修饰变体。

[2304] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35561.4(SEQ ID NOs:23 和 450)，或其修饰变体或未修饰变体。

[2305] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35567.4(SEQ ID NOs:24 和 451)，或其修饰变体或未修饰变体。

[2306] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35526.4(SEQ ID NOs:25 和 452)，或其修饰变体或未修

饰变体。

[2307] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35532.4(SEQ ID NOs:26 和 453)，或其修饰变体或未修饰变体。

[2308] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35538.4(SEQ ID NOs:27 和 454)，或其修饰变体或未修饰变体。

[2309] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35544.4(SEQ ID NOs:28 和 455)，或其修饰变体或未修饰变体。

[2310] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35550.4(SEQ ID NOs:29 和 456)，或其修饰变体或未修饰变体。

[2311] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35556.4(SEQ ID NOs:30 和 457)，或其修饰变体或未修饰变体。

[2312] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35562.4(SEQ ID NOs:31 和 458)，或其修饰变体或未修饰变体。

[2313] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35568.4(SEQ ID NOs:32 和 459)，或其修饰变体或未修饰变体。

[2314] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35527.4(SEQ ID NOs:33 和 460)，或其修饰变体或未修饰变体。

[2315] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35533.4(SEQ ID NOs:34 和 461)，或其修饰变体或未修饰变体。

[2316] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35539.4(SEQ ID NOs:35 和 462)，或其修饰变体或未修饰变体。

[2317] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35545.4(SEQ ID NOs:36 和 463)，或其修饰变体或未修饰变体。

[2318] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35551.4(SEQ ID NOs:37 和 464)，或其修饰变体或未修饰变体。

[2319] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35563.4(SEQ ID NOs:38 和 465)，或其修饰变体或未修

饰变体。

[2320] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35528.4(SEQ ID NOs:39 和 466)，或其修饰变体或未修饰变体。

[2321] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35540.4(SEQ ID NOs:40 和 467)，或其修饰变体或未修饰变体。

[2322] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35546.4(SEQ ID NOs:41 和 468)，或其修饰变体或未修饰变体。

[2323] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35552.4(SEQ ID NOs:42 和 469)，或其修饰变体或未修饰变体。

[2324] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35558.4(SEQ ID NOs:43 和 470)，或其修饰变体或未修饰变体。

[2325] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35564.4(SEQ ID NOs:44 和 471)，或其修饰变体或未修饰变体。

[2326] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35570.4(SEQ ID NOs:45 和 472)，或其修饰变体或未修饰变体。

[2327] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35571.4(SEQ ID NOs:46 和 473)，或其修饰变体或未修饰变体。

[2328] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35577.4(SEQ ID NOs:47 和 474)，或其修饰变体或未修饰变体。

[2329] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35583.4(SEQ ID NOs:48 和 475)，或其修饰变体或未修饰变体。

[2330] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35589.4(SEQ ID NOs:49 和 476)，或其修饰变体或未修饰变体。

[2331] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35595.4(SEQ ID NOs:50 和 477)，或其修饰变体或未修饰变体。

[2332] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35601.4(SEQ ID NOs:51 和 478)，或其修饰变体或未修

饰变体。

[2333] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35607.4(SEQ ID NOs:52 和 479)，或其修饰变体或未修饰变体。

[2334] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35613.4(SEQ ID NOs:53 和 480)，或其修饰变体或未修饰变体。

[2335] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35572.4(SEQ ID NOs:54 和 481)，或其修饰变体或未修饰变体。

[2336] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35578.4(SEQ ID NOs:55 和 482)，或其修饰变体或未修饰变体。

[2337] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35584.4(SEQ ID NOs:56 和 483)，或其修饰变体或未修饰变体。

[2338] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35590.4(SEQ ID NOs:57 和 484)，或其修饰变体或未修饰变体。

[2339] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35596.4(SEQ ID NOs:58 和 485)，或其修饰变体或未修饰变体。

[2340] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35602.4(SEQ ID NOs:59 和 486)，或其修饰变体或未修饰变体。

[2341] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35608.4(SEQ ID NOs:60 和 487)，或其修饰变体或未修饰变体。

[2342] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35614.4(SEQ ID NOs:61 和 488)，或其修饰变体或未修饰变体。

[2343] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35573.4(SEQ ID NOs:62 和 489)，或其修饰变体或未修饰变体。

[2344] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35579.4(SEQ ID NOs:63 和 490)，或其修饰变体或未修饰变体。

[2345] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35585.4(SEQ ID NOs:64 和 491)，或其修饰变体或未修

饰变体。

[2346] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35591.4(SEQ ID NOs:65 和 492)，或其修饰变体或未修饰变体。

[2347] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35597.4(SEQ ID NOs:66 和 493)，或其修饰变体或未修饰变体。

[2348] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35603.4(SEQ ID NOs:67 和 494)，或其修饰变体或未修饰变体。

[2349] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35609.4(SEQ ID NOs:68 和 495)，或其修饰变体或未修饰变体。

[2350] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35615.4(SEQ ID NOs:69 和 496)，或其修饰变体或未修饰变体。

[2351] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35574.4(SEQ ID NOs:70 和 497)，或其修饰变体或未修饰变体。

[2352] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35580.1(SEQ ID NOs:71 和 498)，或其修饰变体或未修饰变体。

[2353] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35586.4(SEQ ID NOs:72 和 499)，或其修饰变体或未修饰变体。

[2354] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35592.4(SEQ ID NOs:73 和 500)，或其修饰变体或未修饰变体。

[2355] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35598.4(SEQ ID NOs:74 和 501)，或其修饰变体或未修饰变体。

[2356] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35604.4(SEQ ID NOs:75 和 502)，或其修饰变体或未修饰变体。

[2357] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35610.4(SEQ ID NOs:76 和 503)，或其修饰变体或未修饰变体。

[2358] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35616.4(SEQ ID NOs:77 和 504)，或其修饰变体或未修

饰变体。

[2359] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35575.4(SEQ ID NOs:78 和 505)，或其修饰变体或未修饰变体。

[2360] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:79 和 506)，或其修饰变体或未修饰变体。

[2361] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35587.4(SEQ ID NOs:80 和 507)，或其修饰变体或未修饰变体。

[2362] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35593.4(SEQ ID NOs:81 和 508)，或其修饰变体或未修饰变体。

[2363] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35599.4(SEQ ID NOs:82 和 509)，或其修饰变体或未修饰变体。

[2364] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35605.4(SEQ ID NOs:83 和 510)，或其修饰变体或未修饰变体。

[2365] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35611.4(SEQ ID NOs:84 和 511)，或其修饰变体或未修饰变体。

[2366] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35617.4(SEQ ID NOs:85 和 512)，或其修饰变体或未修饰变体。

[2367] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:86 和 513)，或其修饰变体或未修饰变体。

[2368] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:87 和 514)，或其修饰变体或未修饰变体。

[2369] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35667.1(SEQ ID NOs:88 和 515)，或其修饰变体或未修饰变体。

[2370] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35673.1(SEQ ID NOs:89 和 516)，或其修饰变体或未修饰变体。

[2371] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35679.1(SEQ ID NOs:90 和 517)，或其修饰变体或未修

饰变体。

[2372] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35685.1(SEQ ID NOs:91 和 518)，或其修饰变体或未修饰变体。

[2373] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35691.1(SEQ ID NOs:92 和 519)，或其修饰变体或未修饰变体。

[2374] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35557.1(SEQ ID NOs:93 和 520)，或其修饰变体或未修饰变体。

[2375] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35618.1(SEQ ID NOs:94 和 521)，或其修饰变体或未修饰变体。

[2376] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35569.1(SEQ ID NOs:95 和 522)，或其修饰变体或未修饰变体。

[2377] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35534.1(SEQ ID NOs:96 和 523)，或其修饰变体或未修饰变体。

[2378] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35582.1(SEQ ID NOs:97 和 524)，或其修饰变体或未修饰变体。

[2379] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35594.1(SEQ ID NOs:98 和 525)，或其修饰变体或未修饰变体。

[2380] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:99 和 526)，或其修饰变体或未修饰变体。

[2381] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:100 和 527)，或其修饰变体或未修饰变体。

[2382] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35612.1(SEQ ID NOs:101 和 528)，或其修饰变体或未修饰变体。

[2383] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38127.1(SEQ ID NOs:102 和 529)，或其修饰变体或未修饰变体。

[2384] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38133.1(SEQ ID NOs:103 和 530)，或其修饰变体或未修

饰变体。

[2385] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38139.1(SEQ ID NOs:104 和 531)，或其修饰变体或未修饰变体。

[2386] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38145.1(SEQ ID NOs:105 和 532)，或其修饰变体或未修饰变体。

[2387] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38151.1(SEQ ID NOs:106 和 533)，或其修饰变体或未修饰变体。

[2388] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38157.1(SEQ ID NOs:107 和 534)，或其修饰变体或未修饰变体。

[2389] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38163.1(SEQ ID NOs:108 和 535)，或其修饰变体或未修饰变体。

[2390] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38169.1(SEQ ID NOs:109 和 536)，或其修饰变体或未修饰变体。

[2391] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38128.1(SEQ ID NOs:110 和 537)，或其修饰变体或未修饰变体。

[2392] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38134.1(SEQ ID NOs:111 和 538)，或其修饰变体或未修饰变体。

[2393] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38140.1(SEQ ID NOs:112 和 539)，或其修饰变体或未修饰变体。

[2394] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38146.1(SEQ ID NOs:113 和 540)，或其修饰变体或未修饰变体。

[2395] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38152.1(SEQ ID NOs:114 和 541)，或其修饰变体或未修饰变体。

[2396] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38158.1(SEQ ID NOs:115 和 542)，或其修饰变体或未修饰变体。

[2397] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38164.1(SEQ ID NOs:116 和 543)，或其修饰变体或未修

饰变体。

[2398] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38170.1(SEQ ID NOs:117 和 544)，或其修饰变体或未修饰变体。

[2399] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38129.1(SEQ ID NOs:118 和 545)，或其修饰变体或未修饰变体。

[2400] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38135.1(SEQ ID NOs:119 和 546)，或其修饰变体或未修饰变体。

[2401] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38141.1(SEQ ID NOs:120 和 547)，或其修饰变体或未修饰变体。

[2402] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38147.1(SEQ ID NOs:121 和 548)，或其修饰变体或未修饰变体。

[2403] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38153.1(SEQ ID NOs:122 和 549)，或其修饰变体或未修饰变体。

[2404] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38159.1(SEQ ID NOs:123 和 550)，或其修饰变体或未修饰变体。

[2405] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38165.1(SEQ ID NOs:124 和 551)，或其修饰变体或未修饰变体。

[2406] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38171.1(SEQ ID NOs:125 和 552)，或其修饰变体或未修饰变体。

[2407] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38130.1(SEQ ID NOs:126 和 553)，或其修饰变体或未修饰变体。

[2408] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38136.1(SEQ ID NOs:127 和 554)，或其修饰变体或未修饰变体。

[2409] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38142.1(SEQ ID NOs:128 和 555)，或其修饰变体或未修饰变体。

[2410] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38148.1(SEQ ID NOs:129 和 556)，或其修饰变体或未修

饰变体。

[2411] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38154.1(SEQ ID NOs:130 和 557)，或其修饰变体或未修饰变体。

[2412] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38160.1(SEQ ID NOs:131 和 558)，或其修饰变体或未修饰变体。

[2413] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38166.1(SEQ ID NOs:132 和 559)，或其修饰变体或未修饰变体。

[2414] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38172.1(SEQ ID NOs:133 和 560)，或其修饰变体或未修饰变体。

[2415] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38131.1(SEQ ID NOs:134 和 561)，或其修饰变体或未修饰变体。

[2416] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38137.1(SEQ ID NOs:135 和 562)，或其修饰变体或未修饰变体。

[2417] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38143.1(SEQ ID NOs:136 和 563)，或其修饰变体或未修饰变体。

[2418] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38149.1(SEQ ID NOs:137 和 564)，或其修饰变体或未修饰变体。

[2419] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38155.1(SEQ ID NOs:138 和 565)，或其修饰变体或未修饰变体。

[2420] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38161.1(SEQ ID NOs:139 和 566)，或其修饰变体或未修饰变体。

[2421] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38167.1(SEQ ID NOs:140 和 567)，或其修饰变体或未修饰变体。

[2422] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38173.1(SEQ ID NOs:141 和 568)，或其修饰变体或未修饰变体。

[2423] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38132.1(SEQ ID NOs:142 和 569)，或其修饰变体或未修

饰变体。

[2424] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38138.1(SEQ ID NOs:143 和 570)，或其修饰变体或未修饰变体。

[2425] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38144.1(SEQ ID NOs:144 和 571)，或其修饰变体或未修饰变体。

[2426] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38150.1(SEQ ID NOs:145 和 572)，或其修饰变体或未修饰变体。

[2427] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38156.1(SEQ ID NOs:146 和 573)，或其修饰变体或未修饰变体。

[2428] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38162.1(SEQ ID NOs:147 和 574)，或其修饰变体或未修饰变体。

[2429] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38168.1(SEQ ID NOs:148 和 575)，或其修饰变体或未修饰变体。

[2430] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38174.1(SEQ ID NOs:149 和 576)，或其修饰变体或未修饰变体。

[2431] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39683.1(SEQ ID NOs:150 和 577)，或其修饰变体或未修饰变体。

[2432] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39689.1(SEQ ID NOs:151 和 578)，或其修饰变体或未修饰变体。

[2433] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39695.1(SEQ ID NOs:152 和 579)，或其修饰变体或未修饰变体。

[2434] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39701.1(SEQ ID NOs:153 和 580)，或其修饰变体或未修饰变体。

[2435] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39707.1(SEQ ID NOs:154 和 581)，或其修饰变体或未修饰变体。

[2436] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39713.1(SEQ ID NOs:155 和 582)，或其修饰变体或未修

饰变体。

[2437] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39719.1(SEQ ID NOs:156 和 583)，或其修饰变体或未修饰变体。

[2438] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39725.1(SEQ ID NOs:157 和 584)，或其修饰变体或未修饰变体。

[2439] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39684.1(SEQ ID NOs:158 和 585)，或其修饰变体或未修饰变体。

[2440] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39690.1(SEQ ID NOs:159 和 586)，或其修饰变体或未修饰变体。

[2441] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39696.1(SEQ ID NOs:160 和 587)，或其修饰变体或未修饰变体。

[2442] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39702.1(SEQ ID NOs:161 和 588)，或其修饰变体或未修饰变体。

[2443] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39708.1(SEQ ID NOs:162 和 589)，或其修饰变体或未修饰变体。

[2444] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39714.1(SEQ ID NOs:163 和 590)，或其修饰变体或未修饰变体。

[2445] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39720.1(SEQ ID NOs:164 和 591)，或其修饰变体或未修饰变体。

[2446] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39726.1(SEQ ID NOs:165 和 592)，或其修饰变体或未修饰变体。

[2447] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39685.1(SEQ ID NOs:166 和 593)，或其修饰变体或未修饰变体。

[2448] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39691.1(SEQ ID NOs:167 和 594)，或其修饰变体或未修饰变体。

[2449] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39697.1(SEQ ID NOs:168 和 595)，或其修饰变体或未修

饰变体。

[2450] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39703.1(SEQ ID NOs:169 和 596)，或其修饰变体或未修饰变体。

[2451] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39709.1(SEQ ID NOs:170 和 597)，或其修饰变体或未修饰变体。

[2452] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39715.1(SEQ ID NOs:171 和 598)，或其修饰变体或未修饰变体。

[2453] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39721.1(SEQ ID NOs:172 和 599)，或其修饰变体或未修饰变体。

[2454] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39727.1(SEQ ID NOs:173 和 600)，或其修饰变体或未修饰变体。

[2455] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39686.1(SEQ ID NOs:174 和 601)，或其修饰变体或未修饰变体。

[2456] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39692.1(SEQ ID NOs:175 和 602)，或其修饰变体或未修饰变体。

[2457] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39698.1(SEQ ID NOs:176 和 603)，或其修饰变体或未修饰变体。

[2458] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39704.1(SEQ ID NOs:177 和 604)，或其修饰变体或未修饰变体。

[2459] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39710.1(SEQ ID NOs:178 和 605)，或其修饰变体或未修饰变体。

[2460] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39716.1(SEQ ID NOs:179 和 606)，或其修饰变体或未修饰变体。

[2461] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39722.1(SEQ ID NOs:180 和 607)，或其修饰变体或未修饰变体。

[2462] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39728.1(SEQ ID NOs:181 和 608)，或其修饰变体或未修

饰变体。

[2463] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39687.1(SEQ ID NOs:182 和 609)，或其修饰变体或未修饰变体。

[2464] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39693.1(SEQ ID NOs:183 和 610)，或其修饰变体或未修饰变体。

[2465] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39699.1(SEQ ID NOs:184 和 611)，或其修饰变体或未修饰变体。

[2466] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39705.1(SEQ ID NOs:185 和 612)，或其修饰变体或未修饰变体。

[2467] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39711.1(SEQ ID NOs:186 和 613)，或其修饰变体或未修饰变体。

[2468] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39717.1(SEQ ID NOs:187 和 614)，或其修饰变体或未修饰变体。

[2469] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39723.1(SEQ ID NOs:188 和 615)，或其修饰变体或未修饰变体。

[2470] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39729.1(SEQ ID NOs:189 和 616)，或其修饰变体或未修饰变体。

[2471] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39688.1(SEQ ID NOs:190 和 617)，或其修饰变体或未修饰变体。

[2472] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39694.1(SEQ ID NOs:191 和 618)，或其修饰变体或未修饰变体。

[2473] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39700.1(SEQ ID NOs:192 和 619)，或其修饰变体或未修饰变体。

[2474] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39706.1(SEQ ID NOs:193 和 620)，或其修饰变体或未修饰变体。

[2475] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39712.1(SEQ ID NOs:194 和 621)，或其修饰变体或未修

饰变体。

[2476] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39718.1(SEQ ID NOs:195 和 622)，或其修饰变体或未修饰变体。

[2477] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39724.1(SEQ ID NOs:196 和 623)，或其修饰变体或未修饰变体。

[2478] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39730.1(SEQ ID NOs:197 和 624)，或其修饰变体或未修饰变体。

[2479] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39736.1(SEQ ID NOs:198 和 625)，或其修饰变体或未修饰变体。

[2480] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39742.1(SEQ ID NOs:199 和 626)，或其修饰变体或未修饰变体。

[2481] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39748.1(SEQ ID NOs:200 和 627)，或其修饰变体或未修饰变体。

[2482] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39754.1(SEQ ID NOs:201 和 628)，或其修饰变体或未修饰变体。

[2483] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39760.1(SEQ ID NOs:202 和 629)，或其修饰变体或未修饰变体。

[2484] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39766.1(SEQ ID NOs:203 和 630)，或其修饰变体或未修饰变体。

[2485] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39772.1(SEQ ID NOs:204 和 631)，或其修饰变体或未修饰变体。

[2486] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39731.1(SEQ ID NOs:205 和 632)，或其修饰变体或未修饰变体。

[2487] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39737.1(SEQ ID NOs:206 和 633)，或其修饰变体或未修饰变体。

[2488] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39743.1(SEQ ID NOs:207 和 634)，或其修饰变体或未修

饰变体。

[2489] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39749.1(SEQ ID NOs:208 和 635)，或其修饰变体或未修饰变体。

[2490] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39755.1(SEQ ID NOs:209 和 636)，或其修饰变体或未修饰变体。

[2491] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39761.1(SEQ ID NOs:210 和 637)，或其修饰变体或未修饰变体。

[2492] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39767.1(SEQ ID NOs:211 和 638)，或其修饰变体或未修饰变体。

[2493] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39773.1(SEQ ID NOs:212 和 639)，或其修饰变体或未修饰变体。

[2494] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39732.1(SEQ ID NOs:213 和 640)，或其修饰变体或未修饰变体。

[2495] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39738.1(SEQ ID NOs:214 和 641)，或其修饰变体或未修饰变体。

[2496] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39744.1(SEQ ID NOs:215 和 642)，或其修饰变体或未修饰变体。

[2497] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39750.1(SEQ ID NOs:216 和 643)，或其修饰变体或未修饰变体。

[2498] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39756.1(SEQ ID NOs:217 和 644)，或其修饰变体或未修饰变体。

[2499] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39762.1(SEQ ID NOs:218 和 645)，或其修饰变体或未修饰变体。

[2500] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39768.1(SEQ ID NOs:219 和 646)，或其修饰变体或未修饰变体。

[2501] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39774.1(SEQ ID NOs:220 和 647)，或其修饰变体或未修

饰变体。

[2502] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39733.1(SEQ ID NOs:221 和 648)，或其修饰变体或未修饰变体。

[2503] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39739.1(SEQ ID NOs:222 和 649)，或其修饰变体或未修饰变体。

[2504] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39745.1(SEQ ID NOs:223 和 650)，或其修饰变体或未修饰变体。

[2505] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39751.1(SEQ ID NOs:224 和 651)，或其修饰变体或未修饰变体。

[2506] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39757.1(SEQ ID NOs:225 和 652)，或其修饰变体或未修饰变体。

[2507] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39763.1(SEQ ID NOs:226 和 653)，或其修饰变体或未修饰变体。

[2508] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39769.1(SEQ ID NOs:227 和 654)，或其修饰变体或未修饰变体。

[2509] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39775.1(SEQ ID NOs:228 和 655)，或其修饰变体或未修饰变体。

[2510] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39734.1(SEQ ID NOs:229 和 656)，或其修饰变体或未修饰变体。

[2511] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39740.1(SEQ ID NOs:230 和 657)，或其修饰变体或未修饰变体。

[2512] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39746.1(SEQ ID NOs:231 和 658)，或其修饰变体或未修饰变体。

[2513] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39752.1(SEQ ID NOs:232 和 659)，或其修饰变体或未修饰变体。

[2514] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39758.1(SEQ ID NOs:233 和 660)，或其修饰变体或未修

饰变体。

[2515] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39764.1(SEQ ID NOs:234 和 661)，或其修饰变体或未修饰变体。

[2516] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39770.1(SEQ ID NOs:235 和 662)，或其修饰变体或未修饰变体。

[2517] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39776.1(SEQ ID NOs:236 和 663)，或其修饰变体或未修饰变体。

[2518] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39735.1(SEQ ID NOs:237 和 664)，或其修饰变体或未修饰变体。

[2519] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39741.1(SEQ ID NOs:238 和 665)，或其修饰变体或未修饰变体。

[2520] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39747.1(SEQ ID NOs:239 和 666)，或其修饰变体或未修饰变体。

[2521] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39753.1(SEQ ID NOs:240 和 667)，或其修饰变体或未修饰变体。

[2522] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39759.1(SEQ ID NOs:241 和 668)，或其修饰变体或未修饰变体。

[2523] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39765.1(SEQ ID NOs:242 和 669)，或其修饰变体或未修饰变体。

[2524] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39771.1(SEQ ID NOs:243 和 670)，或其修饰变体或未修饰变体。

[2525] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39778.1(SEQ ID NOs:244 和 671)，或其修饰变体或未修饰变体。

[2526] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39784.1(SEQ ID NOs:245 和 672)，或其修饰变体或未修饰变体。

[2527] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39790.1(SEQ ID NOs:246 和 673)，或其修饰变体或未修

饰变体。

[2528] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39796.1(SEQ ID NOs:247 和 674)，或其修饰变体或未修饰变体。

[2529] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39802.1(SEQ ID NOs:248 和 675)，或其修饰变体或未修饰变体。

[2530] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39808.1(SEQ ID NOs:249 和 676)，或其修饰变体或未修饰变体。

[2531] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39814.1(SEQ ID NOs:250 和 677)，或其修饰变体或未修饰变体。

[2532] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39820.1(SEQ ID NOs:251 和 678)，或其修饰变体或未修饰变体。

[2533] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39779.1(SEQ ID NOs:252 和 679)，或其修饰变体或未修饰变体。

[2534] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39785.1(SEQ ID NOs:253 和 680)，或其修饰变体或未修饰变体。

[2535] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39791.1(SEQ ID NOs:254 和 681)，或其修饰变体或未修饰变体。

[2536] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39797.1(SEQ ID NOs:255 和 682)，或其修饰变体或未修饰变体。

[2537] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39803.1(SEQ ID NOs:256 和 683)，或其修饰变体或未修饰变体。

[2538] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39809.1(SEQ ID NOs:257 和 684)，或其修饰变体或未修饰变体。

[2539] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39815.1(SEQ ID NOs:258 和 685)，或其修饰变体或未修饰变体。

[2540] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39821.1(SEQ ID NOs:259 和 686)，或其修饰变体或未修

饰变体。

[2541] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39780.1(SEQ ID NOs:260 和 687)，或其修饰变体或未修饰变体。

[2542] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39786.1(SEQ ID NOs:261 和 688)，或其修饰变体或未修饰变体。

[2543] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39792.1(SEQ ID NOs:262 和 689)，或其修饰变体或未修饰变体。

[2544] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39798.1(SEQ ID NOs:263 和 690)，或其修饰变体或未修饰变体。

[2545] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39804.1(SEQ ID NOs:264 和 691)，或其修饰变体或未修饰变体。

[2546] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39810.1(SEQ ID NOs:265 和 692)，或其修饰变体或未修饰变体。

[2547] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39816.1(SEQ ID NOs:266 和 693)，或其修饰变体或未修饰变体。

[2548] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39822.1(SEQ ID NOs:267 和 694)，或其修饰变体或未修饰变体。

[2549] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39781.1(SEQ ID NOs:268 和 695)，或其修饰变体或未修饰变体。

[2550] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39787.1(SEQ ID NOs:269 和 696)，或其修饰变体或未修饰变体。

[2551] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39793.1(SEQ ID NOs:270 和 697)，或其修饰变体或未修饰变体。

[2552] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39799.1(SEQ ID NOs:271 和 698)，或其修饰变体或未修饰变体。

[2553] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39805.1(SEQ ID NOs:272 和 699)，或其修饰变体或未修

饰变体。

[2554] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39811.1(SEQ ID NOs:273 和 700)，或其修饰变体或未修饰变体。

[2555] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39817.1(SEQ ID NOs:274 和 701)，或其修饰变体或未修饰变体。

[2556] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39823.1(SEQ ID NOs:275 和 702)，或其修饰变体或未修饰变体。

[2557] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39782.1(SEQ ID NOs:276 和 703)，或其修饰变体或未修饰变体。

[2558] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39788.1(SEQ ID NOs:277 和 704)，或其修饰变体或未修饰变体。

[2559] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39794.1(SEQ ID NOs:278 和 705)，或其修饰变体或未修饰变体。

[2560] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39800.1(SEQ ID NOs:279 和 706)，或其修饰变体或未修饰变体。

[2561] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39806.1(SEQ ID NOs:280 和 707)，或其修饰变体或未修饰变体。

[2562] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39812.1(SEQ ID NOs:281 和 708)，或其修饰变体或未修饰变体。

[2563] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39818.1(SEQ ID NOs:282 和 709)，或其修饰变体或未修饰变体。

[2564] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39824.1(SEQ ID NOs:283 和 710)，或其修饰变体或未修饰变体。

[2565] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39783.1(SEQ ID NOs:284 和 711)，或其修饰变体或未修饰变体。

[2566] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39789.1(SEQ ID NOs:285 和 712)，或其修饰变体或未修

饰变体。

[2567] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39795.1(SEQ ID NOs:286 和 713)，或其修饰变体或未修饰变体。

[2568] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39801.1(SEQ ID NOs:287 和 714)，或其修饰变体或未修饰变体。

[2569] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39807.1(SEQ ID NOs:288 和 715)，或其修饰变体或未修饰变体。

[2570] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39813.1(SEQ ID NOs:289 和 716)，或其修饰变体或未修饰变体。

[2571] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39819.1(SEQ ID NOs:290 和 717)，或其修饰变体或未修饰变体。

[2572] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39825.1(SEQ ID NOs:291 和 718)，或其修饰变体或未修饰变体。

[2573] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39831.1(SEQ ID NOs:292 和 719)，或其修饰变体或未修饰变体。

[2574] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39837.1(SEQ ID NOs:293 和 720)，或其修饰变体或未修饰变体。

[2575] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39843.1(SEQ ID NOs:294 和 721)，或其修饰变体或未修饰变体。

[2576] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39849.1(SEQ ID NOs:295 和 722)，或其修饰变体或未修饰变体。

[2577] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39855.1(SEQ ID NOs:296 和 723)，或其修饰变体或未修饰变体。

[2578] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39861.1(SEQ ID NOs:297 和 724)，或其修饰变体或未修饰变体。

[2579] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39867.1(SEQ ID NOs:298 和 725)，或其修饰变体或未修

饰变体。

[2580] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39826.1(SEQ ID NOs:299 和 726)，或其修饰变体或未修饰变体。

[2581] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39832.1(SEQ ID NOs:300 和 727)，或其修饰变体或未修饰变体。

[2582] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39838.1(SEQ ID NOs:301 和 728)，或其修饰变体或未修饰变体。

[2583] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39844.1(SEQ ID NOs:302 和 729)，或其修饰变体或未修饰变体。

[2584] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39850.1(SEQ ID NOs:303 和 730)，或其修饰变体或未修饰变体。

[2585] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39856.1(SEQ ID NOs:304 和 731)，或其修饰变体或未修饰变体。

[2586] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39862.1(SEQ ID NOs:305 和 732)，或其修饰变体或未修饰变体。

[2587] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39868.1(SEQ ID NOs:306 和 733)，或其修饰变体或未修饰变体。

[2588] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39827.1(SEQ ID NOs:307 和 734)，或其修饰变体或未修饰变体。

[2589] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39833.1(SEQ ID NOs:308 和 735)，或其修饰变体或未修饰变体。

[2590] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39839.1(SEQ ID NOs:309 和 736)，或其修饰变体或未修饰变体。

[2591] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39845.1(SEQ ID NOs:310 和 737)，或其修饰变体或未修饰变体。

[2592] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39851.1(SEQ ID NOs:311 和 738)，或其修饰变体或未修

饰变体。

[2593] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39857.1(SEQ ID NOs:312 和 739)，或其修饰变体或未修饰变体。

[2594] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39863.1(SEQ ID NOs:313 和 740)，或其修饰变体或未修饰变体。

[2595] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39869.1(SEQ ID NOs:314 和 741)，或其修饰变体或未修饰变体。

[2596] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39828.1(SEQ ID NOs:315 和 742)，或其修饰变体或未修饰变体。

[2597] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39834.1(SEQ ID NOs:316 和 743)，或其修饰变体或未修饰变体。

[2598] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39840.1(SEQ ID NOs:317 和 744)，或其修饰变体或未修饰变体。

[2599] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39846.1(SEQ ID NOs:318 和 745)，或其修饰变体或未修饰变体。

[2600] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39852.1(SEQ ID NOs:319 和 746)，或其修饰变体或未修饰变体。

[2601] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39858.1(SEQ ID NOs:320 和 747)，或其修饰变体或未修饰变体。

[2602] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39864.1(SEQ ID NOs:321 和 748)，或其修饰变体或未修饰变体。

[2603] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39870.1(SEQ ID NOs:322 和 749)，或其修饰变体或未修饰变体。

[2604] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39829.1(SEQ ID NOs:323 和 750)，或其修饰变体或未修饰变体。

[2605] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39835.1(SEQ ID NOs:324 和 751)，或其修饰变体或未修

饰变体。

[2606] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39841.1(SEQ ID NOs:325 和 752)，或其修饰变体或未修饰变体。

[2607] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39853.1(SEQ ID NOs:326 和 753)，或其修饰变体或未修饰变体。

[2608] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39859.1(SEQ ID NOs:327 和 754)，或其修饰变体或未修饰变体。

[2609] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39865.1(SEQ ID NOs:328 和 755)，或其修饰变体或未修饰变体。

[2610] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39871.1(SEQ ID NOs:329 和 756)，或其修饰变体或未修饰变体。

[2611] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39830.1(SEQ ID NOs:330 和 757)，或其修饰变体或未修饰变体。

[2612] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39836.1(SEQ ID NOs:331 和 758)，或其修饰变体或未修饰变体。

[2613] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39842.1(SEQ ID NOs:332 和 759)，或其修饰变体或未修饰变体。

[2614] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39848.1(SEQ ID NOs:333 和 760)，或其修饰变体或未修饰变体。

[2615] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39854.1(SEQ ID NOs:334 和 761)，或其修饰变体或未修饰变体。

[2616] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39860.1(SEQ ID NOs:335 和 762)，或其修饰变体或未修饰变体。

[2617] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39866.1(SEQ ID NOs:336 和 763)，或其修饰变体或未修饰变体。

[2618] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39992.1(SEQ ID NOs:337 和 764)，或其修饰变体或未修

饰变体。

[2619] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39998.1(SEQ ID NOs:338 和 765)，或其修饰变体或未修饰变体。

[2620] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40004.1(SEQ ID NOs:339 和 766)，或其修饰变体或未修饰变体。

[2621] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40010.1(SEQ ID NOs:340 和 767)，或其修饰变体或未修饰变体。

[2622] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40016.1(SEQ ID NOs:341 和 768)，或其修饰变体或未修饰变体。

[2623] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40022.1(SEQ ID NOs:342 和 769)，或其修饰变体或未修饰变体。

[2624] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40028.1(SEQ ID NOs:343 和 770)，或其修饰变体或未修饰变体。

[2625] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40034.1(SEQ ID NOs:344 和 771)，或其修饰变体或未修饰变体。

[2626] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39999.1(SEQ ID NOs:345 和 772)，或其修饰变体或未修饰变体。

[2627] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40005.1(SEQ ID NOs:346 和 773)，或其修饰变体或未修饰变体。

[2628] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40011.1(SEQ ID NOs:347 和 774)，或其修饰变体或未修饰变体。

[2629] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40017.1(SEQ ID NOs:348 和 775)，或其修饰变体或未修饰变体。

[2630] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40029.1(SEQ ID NOs:349 和 776)，或其修饰变体或未修饰变体。

[2631] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40035.1(SEQ ID NOs:350 和 777)，或其修饰变体或未修

饰变体。

[2632] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39994.1(SEQ ID NOs:351 和 778)，或其修饰变体或未修饰变体。

[2633] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40000.1(SEQ ID NOs:352 和 779)，或其修饰变体或未修饰变体。

[2634] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40006.1(SEQ ID NOs:353 和 780)，或其修饰变体或未修饰变体。

[2635] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40012.1(SEQ ID NOs:354 和 781)，或其修饰变体或未修饰变体。

[2636] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40018.1(SEQ ID NOs:355 和 782)，或其修饰变体或未修饰变体。

[2637] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40024.1(SEQ ID NOs:356 和 783)，或其修饰变体或未修饰变体。

[2638] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40030.1(SEQ ID NOs:357 和 784)，或其修饰变体或未修饰变体。

[2639] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40036.1(SEQ ID NOs:358 和 785)，或其修饰变体或未修饰变体。

[2640] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39995.1(SEQ ID NOs:359 和 786)，或其修饰变体或未修饰变体。

[2641] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40001.1(SEQ ID NOs:360 和 787)，或其修饰变体或未修饰变体。

[2642] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40007.1(SEQ ID NOs:361 和 788)，或其修饰变体或未修饰变体。

[2643] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40013.1(SEQ ID NOs:362 和 789)，或其修饰变体或未修饰变体。

[2644] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40019.1(SEQ ID NOs:363 和 790)，或其修饰变体或未修

饰变体。

[2645] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40025.1(SEQ ID NOs:364 和 791)，或其修饰变体或未修饰变体。

[2646] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40031.1(SEQ ID NOs:365 和 792)，或其修饰变体或未修饰变体。

[2647] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40037.1(SEQ ID NOs:366 和 793)，或其修饰变体或未修饰变体。

[2648] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39996.1(SEQ ID NOs:367 和 794)，或其修饰变体或未修饰变体。

[2649] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40002.1(SEQ ID NOs:368 和 795)，或其修饰变体或未修饰变体。

[2650] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40008.1(SEQ ID NOs:369 和 796)，或其修饰变体或未修饰变体。

[2651] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40014.1(SEQ ID NOs:370 和 797)，或其修饰变体或未修饰变体。

[2652] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40020.1(SEQ ID NOs:371 和 798)，或其修饰变体或未修饰变体。

[2653] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40026.1(SEQ ID NOs:372 和 799)，或其修饰变体或未修饰变体。

[2654] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40032.1(SEQ ID NOs:373 和 800)，或其修饰变体或未修饰变体。

[2655] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40038.1(SEQ ID NOs:374 和 801)，或其修饰变体或未修饰变体。

[2656] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39997.1(SEQ ID NOs:375 和 802)，或其修饰变体或未修饰变体。

[2657] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40009.1(SEQ ID NOs:376 和 803)，或其修饰变体或未修

饰变体。

[2658] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40015.1(SEQ ID NOs:377 和 804)，或其修饰变体或未修饰变体。

[2659] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40021.1(SEQ ID NOs:378 和 805)，或其修饰变体或未修饰变体。

[2660] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40027.1(SEQ ID NOs:379 和 806)，或其修饰变体或未修饰变体。

[2661] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40033.1(SEQ ID NOs:380 和 807)，或其修饰变体或未修饰变体。

[2662] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40039.1(SEQ ID NOs:381 和 808)，或其修饰变体或未修饰变体。

[2663] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40045.1(SEQ ID NOs:382 和 809)，或其修饰变体或未修饰变体。

[2664] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40051.1(SEQ ID NOs:383 和 810)，或其修饰变体或未修饰变体。

[2665] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40057.1(SEQ ID NOs:384 和 811)，或其修饰变体或未修饰变体。

[2666] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40063.1(SEQ ID NOs:385 和 812)，或其修饰变体或未修饰变体。

[2667] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40069.1(SEQ ID NOs:386 和 813)，或其修饰变体或未修饰变体。

[2668] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40075.1(SEQ ID NOs:387 和 814)，或其修饰变体或未修饰变体。

[2669] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40081.1(SEQ ID NOs:388 和 815)，或其修饰变体或未修饰变体。

[2670] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40040.1(SEQ ID NOs:389 和 816)，或其修饰变体或未修

饰变体。

[2671] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40046.1(SEQ ID NOs:390 和 817)，或其修饰变体或未修饰变体。

[2672] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40052.1(SEQ ID NOs:391 和 818)，或其修饰变体或未修饰变体。

[2673] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40058.1(SEQ ID NOs:392 和 819)，或其修饰变体或未修饰变体。

[2674] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40064.1(SEQ ID NOs:393 和 820)，或其修饰变体或未修饰变体。

[2675] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40070.1(SEQ ID NOs:394 和 821)，或其修饰变体或未修饰变体。

[2676] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40076.1(SEQ ID NOs:395 和 822)，或其修饰变体或未修饰变体。

[2677] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40082.1(SEQ ID NOs:396 和 823)，或其修饰变体或未修饰变体。

[2678] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40041.1(SEQ ID NOs:397 和 824)，或其修饰变体或未修饰变体。

[2679] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40047.1(SEQ ID NOs:398 和 825)，或其修饰变体或未修饰变体。

[2680] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40053.1(SEQ ID NOs:399 和 826)，或其修饰变体或未修饰变体。

[2681] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40059.1(SEQ ID NOs:400 和 827)，或其修饰变体或未修饰变体。

[2682] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40065.1(SEQ ID NOs:401 和 828)，或其修饰变体或未修饰变体。

[2683] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40071.1(SEQ ID NOs:402 和 829)，或其修饰变体或未修

饰变体。

[2684] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40077.1(SEQ ID NOs:403 和 830)，或其修饰变体或未修饰变体。

[2685] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40083.1(SEQ ID NOs:404 和 831)，或其修饰变体或未修饰变体。

[2686] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40042.1(SEQ ID NOs:405 和 832)，或其修饰变体或未修饰变体。

[2687] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40048.1(SEQ ID NOs:406 和 833)，或其修饰变体或未修饰变体。

[2688] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40054.1(SEQ ID NOs:407 和 834)，或其修饰变体或未修饰变体。

[2689] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40060.1(SEQ ID NOs:408 和 835)，或其修饰变体或未修饰变体。

[2690] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40066.1(SEQ ID NOs:409 和 836)，或其修饰变体或未修饰变体。

[2691] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40072.1(SEQ ID NOs:410 和 837)，或其修饰变体或未修饰变体。

[2692] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40078.1(SEQ ID NOs:411 和 838)，或其修饰变体或未修饰变体。

[2693] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40084.1(SEQ ID NOs:412 和 839)，或其修饰变体或未修饰变体。

[2694] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40043.1(SEQ ID NOs:413 和 840)，或其修饰变体或未修饰变体。

[2695] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40049.1(SEQ ID NOs:414 和 841)，或其修饰变体或未修饰变体。

[2696] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40055.1(SEQ ID NOs:415 和 842)，或其修饰变体或未修

饰变体。

[2697] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40061.1(SEQ ID NOs:416 和 843)，或其修饰变体或未修饰变体。

[2698] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40067.1(SEQ ID NOs:417 和 844)，或其修饰变体或未修饰变体。

[2699] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40073.1(SEQ ID NOs:418 和 845)，或其修饰变体或未修饰变体。

[2700] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40079.1(SEQ ID NOs:419 和 846)，或其修饰变体或未修饰变体。

[2701] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40085.1(SEQ ID NOs:420 和 847)，或其修饰变体或未修饰变体。

[2702] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40044.1(SEQ ID NOs:421 和 848)，或其修饰变体或未修饰变体。

[2703] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40050.1(SEQ ID NOs:422 和 849)，或其修饰变体或未修饰变体。

[2704] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40056.1(SEQ ID NOs:423 和 850)，或其修饰变体或未修饰变体。

[2705] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40062.1(SEQ ID NOs:424 和 851)，或其修饰变体或未修饰变体。

[2706] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40068.1(SEQ ID NOs:425 和 852)，或其修饰变体或未修饰变体。

[2707] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40074.1(SEQ ID NOs:426 和 853)，或其修饰变体或未修饰变体。

[2708] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40080.1(SEQ ID NOs:427 和 854)，或其修饰变体或未修饰变体。

[2709] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39720.1(SEQ ID NOs:1716 和 1754)，或其修饰变体或未

修饰变体。

[2710] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39706.1(SEQ ID NOs:1717 和 1755)，或其修饰变体或未修饰变体。

[2711] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39712.1(SEQ ID NOs:1718 和 1756)，或其修饰变体或未修饰变体。

[2712] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39760.1(SEQ ID NOs:1719 和 1757)，或其修饰变体或未修饰变体。

[2713] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39732.1(SEQ ID NOs:1720 和 1758)，或其修饰变体或未修饰变体。

[2714] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35541.4(SEQ ID NOs:1721 和 1759)，或其修饰变体或未修饰变体。

[2715] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NOs:1722 和 1760)，或其修饰变体或未修饰变体。

[2716] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39741.1，或其修饰变体或未修饰变体。

[2717] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS_322_A22S26(SEQ IDNOs:1723 和 1761)，或其修饰变体或未修饰变体。

[2718] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39778.1(SEQ ID NOs:1724 和 1762)，或其修饰变体或未修饰变体。

[2719] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39790.1(SEQ ID NOs:1725 和 1763)，或其修饰变体或未修饰变体。

[2720] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39822.1(SEQ ID NOs:1726 和 1764)，或其修饰变体或未修饰变体。

[2721] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35609.4(SEQ ID NOs:1727 和 1765)，或其修饰变体或未修饰变体。

[2722] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:1728 和 1766)，或其修饰变体或未修饰变体。

[2723] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39845.1(SEQ ID NOs:1729 和 1767)，或其修饰变体或未修饰变体。

[2724] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39858.1(SEQ ID NOs:1730 和 1768)，或其修饰变体或未修饰变体。

[2725] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39870.1(SEQ ID NOs:1731 和 1769)，或其修饰变体或未修饰变体。

[2726] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:1732 和 1770)，或其修饰变体或未修饰变体。

[2727] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:1733 和 1771)，或其修饰变体或未修饰变体。

[2728] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:1734 和 1772)，或其修饰变体或未修饰变体。

[2729] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:1735 和 1773)，或其修饰变体或未修饰变体。

[2730] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38151.1(SEQ ID NOs:1736 和 1774)，或其修饰变体或未修饰变体。

[2731] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38163.1(SEQ ID NOs:1737 和 1775)，或其修饰变体或未修饰变体。

[2732] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39999.1(SEQ ID NOs:1738 和 1776)，或其修饰变体或未修饰变体。

[2733] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1739 和 1777)，或其修饰变体或未修饰变体。

[2734] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1740 和 1778)，或其修饰变体或未修饰变体。

[2735] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38136.1(SEQ ID NOs:1741 和 1779)，或其修饰变体或未修饰变体。

[2736] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40036.1(SEQ ID NOs:1742 和 1780)，或其修饰变体或未修饰变体。

[2737] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40008.1(SEQ ID NOs:1743 和 1781)，或其修饰变体或未修饰变体。

[2738] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40021.1(SEQ ID NOs:1744 和 1782)，或其修饰变体或未修饰变体。

[2739] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40077.1(SEQ ID NOs:1745 和 1783)，或其修饰变体或未修饰变体。

[2740] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40072.1(SEQ ID NOs:1746 和 1784)，或其修饰变体或未修饰变体。

[2741] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40061.1(SEQ ID NOs:1747 和 1785)，或其修饰变体或未修饰变体。

[2742] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-40068.1(SEQ ID NOs:1748 和 1786)，或其修饰变体或未修饰变体。

[2743] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38131.1(SEQ ID NOs:1749 和 1787)，或其修饰变体或未修饰变体。

[2744] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38167.1(SEQ ID NOs:1750 和 1788)，或其修饰变体或未修饰变体。

[2745] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 1273_A22S26(SEQ IDNOs:1751 和 1789)，或其修饰变体或未修饰变体。

[2746] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 2892_A37S26(SEQ IDNOs:1752 和 1790)，或其修饰变体或未修饰变体。

[2747] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :hs_KRAS 4731_A22S26(SEQ IDNOs:1753 和 1791)，或其修饰变体或未修饰变体。

[2748] 其中第一链和 / 或第二链的序列是本文公开的 RNAi 剂的第一链和 / 或第二链的序列，并且还包含至多约 20 个额外的核苷酸的具体实施方案

[2749] 在一个实施方案中，本公开涉及一种包含任意一种或多种 RNAi 剂的组合物，所述

RNAi 剂包含第一链和第二链，其中第一链和 / 或第二链的序列是来自表 1 至 6 的任何一个的任一种 RNAi 剂或其修饰变体和未修饰变体的第一链和 / 或第二链的序列，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2750] 因此，在多种实施方案中，本公开涉及包含任意一种或多种如下 RNAi 剂的组合物：

[2751] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35523.3(SEQ ID NOs:1 和 428)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2752] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35529.1(SEQ ID NOs:2 和 429)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2753] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35535.4(SEQ ID NOs:3 和 430)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2754] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35541.4(SEQ ID NOs:4 和 431)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2755] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35547.4(SEQ ID NOs:5 和 432)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2756] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35553.4(SEQ ID NOs:6 和 433)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2757] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35559.4(SEQ ID NOs:7 和 434)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2758] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35565.4(SEQ ID NOs:8 和 435)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2759] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35524.4(SEQ ID NOs:9 和 436)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2760] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35530.4(SEQ ID NOs:10 和 437)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2761] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35536.4(SEQ ID NOs:11 和 438)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2762] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35542.4(SEQ ID NOs:12 和 439),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2763] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35548.4(SEQ ID NOs:13 和 440),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2764] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35554.4(SEQ ID NOs:14 和 441),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2765] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35560.2(SEQ ID NOs:15 和 442),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2766] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35566.4(SEQ ID NOs:16 和 443),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2767] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35525.2(SEQ ID NOs:17 和 444),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2768] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35531.4(SEQ ID NOs:18 和 445),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2769] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35537.4(SEQ ID NOs:19 和 446),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2770] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35543.2(SEQ ID NOs:20 和 447),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2771] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35549.4(SEQ ID NOs:21 和 448),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2772] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35555.4(SEQ ID NOs:22 和 449),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2773] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35561.4(SEQ ID NOs:23 和 450),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2774] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35567.4(SEQ ID NOs:24 和 451),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2775] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35526.4(SEQ ID NOs:25 和 452),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2776] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35532.4(SEQ ID NOs:26 和 453),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2777] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35538.4(SEQ ID NOs:27 和 454),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2778] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35544.4(SEQ ID NOs:28 和 455),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2779] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35550.4(SEQ ID NOs:29 和 456),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2780] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35556.4(SEQ ID NOs:30 和 457),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2781] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35562.4(SEQ ID NOs:31 和 458),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2782] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35568.4(SEQ ID NOs:32 和 459),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2783] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35527.4(SEQ ID NOs:33 和 460),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2784] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35533.4(SEQ ID NOs:34 和 461),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2785] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35539.4(SEQ ID NOs:35 和 462),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2786] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35545.4(SEQ ID NOs:36 和 463),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2787] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35551.4(SEQ ID NOs:37 和 464),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2788] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35563.4(SEQ ID NOs:38 和 465),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2789] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35528.4(SEQ ID NOs:39 和 466),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2790] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35540.4(SEQ ID NOs:40 和 467),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2791] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35546.4(SEQ ID NOs:41 和 468),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2792] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35552.4(SEQ ID NOs:42 和 469),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2793] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35558.4(SEQ ID NOs:43 和 470),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2794] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35564.4(SEQ ID NOs:44 和 471),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2795] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35570.4(SEQ ID NOs:45 和 472),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2796] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35571.4(SEQ ID NOs:46 和 473),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2797] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35577.4(SEQ ID NOs:47 和 474),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2798] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35583.4(SEQ ID NOs:48 和 475),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2799] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35589.4(SEQ ID NOs:49 和 476),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2800] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35595.4(SEQ ID NOs:50 和 477),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2801] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35601.4(SEQ ID NOs:51 和 478),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2802] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35607.4(SEQ ID NOs:52 和 479),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2803] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35613.4(SEQ ID NOs:53 和 480),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2804] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35572.4(SEQ ID NOs:54 和 481),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2805] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35578.4(SEQ ID NOs:55 和 482),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2806] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35584.4(SEQ ID NOs:56 和 483),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2807] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35590.4(SEQ ID NOs:57 和 484),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2808] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35596.4(SEQ ID NOs:58 和 485),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2809] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35602.4(SEQ ID NOs:59 和 486),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2810] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35608.4(SEQ ID NOs:60 和 487),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2811] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35614.4(SEQ ID NOs:61 和 488),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2812] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35573.4(SEQ ID NOs:62 和 489),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2813] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35579.4(SEQ ID NOs:63 和 490),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2814] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和/或第二链的序列:AD-35585.4(SEQ ID NOs:64 和 491),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2815] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35591.4(SEQ ID NOs:65 和 492),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2816] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35597.4(SEQ ID NOs:66 和 493),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2817] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35603.4(SEQ ID NOs:67 和 494),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2818] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35609.4(SEQ ID NOs:68 和 495),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2819] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35615.4(SEQ ID NOs:69 和 496),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2820] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35574.4(SEQ ID NOs:70 和 497),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2821] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35580.1(SEQ ID NOs:71 和 498),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2822] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35586.4(SEQ ID NOs:72 和 499),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2823] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35592.4(SEQ ID NOs:73 和 500),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2824] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35598.4(SEQ ID NOs:74 和 501),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2825] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35604.4(SEQ ID NOs:75 和 502),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2826] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂的第一链和/或第二链的序列:AD-35610.4(SEQ ID NOs:76 和 503),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约 20 个额外的核苷酸。

[2827] 包含第一链和第二链的 RNAi 剂,其中第一链和/或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35616.4(SEQ ID NOs:77 和 504),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2828] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35575.4(SEQ ID NOs:78 和 505),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2829] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:79 和 506),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2830] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35587.4(SEQ ID NOs:80 和 507),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2831] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35593.4(SEQ ID NOs:81 和 508),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2832] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35599.4(SEQ ID NOs:82 和 509),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2833] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35605.4(SEQ ID NOs:83 和 510),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2834] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35611.4(SEQ ID NOs:84 和 511),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2835] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35617.4(SEQ ID NOs:85 和 512),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2836] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:86 和 513),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2837] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:87 和 514),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2838] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35667.1(SEQ ID NOs:88 和 515),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2839] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35673.1(SEQ ID NOs:89 和 516),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2840] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和 / 或第二链的序列 :AD-35679.1(SEQ ID NOs:90 和 517),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2841] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35685.1(SEQ ID NOs:91 和 518),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2842] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35691.1(SEQ ID NOs:92 和 519),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2843] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35557.1(SEQ ID NOs:93 和 520),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2844] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35618.1(SEQ ID NOs:94 和 521),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2845] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35569.1(SEQ ID NOs:95 和 522),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2846] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35534.1(SEQ ID NOs:96 和 523),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2847] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35582.1(SEQ ID NOs:97 和 524),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2848] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35594.1(SEQ ID NOs:98 和 525),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2849] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:99 和 526),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2850] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:100 和 527),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2851] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35612.1(SEQ ID NOs:101 和 528),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2852] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38127.1(SEQ ID NOs:102 和 529),或其修饰变体或未修饰变体,其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[2853] 包含第一链和第二链的 RNAi 剂,其中第一链和 / 或第二链的序列是如下 RNAi 剂

的第一链和/或第二链的序列:AD-38133.1(SEQ ID NOs:103和530),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2854] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38139.1(SEQ ID NOs:104和531),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2855] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38145.1(SEQ ID NOs:105和532),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2856] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38151.1(SEQ ID NOs:106和533),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2857] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38157.1(SEQ ID NOs:107和534),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2858] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38163.1(SEQ ID NOs:108和535),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2859] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38169.1(SEQ ID NOs:109和536),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2860] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38128.1(SEQ ID NOs:110和537),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2861] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38134.1(SEQ ID NOs:111和538),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2862] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38140.1(SEQ ID NOs:112和539),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2863] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38146.1(SEQ ID NOs:113和540),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2864] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38152.1(SEQ ID NOs:114和541),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2865] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38158.1(SEQ ID NOs:115和542),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2866] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-38164.1(SEQ ID NOs:116和543),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2867] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38170.1(SEQ ID NOs:117和544),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2868] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38129.1(SEQ ID NOs:118和545),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2869] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38135.1(SEQ ID NOs:119和546),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2870] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38141.1(SEQ ID NOs:120和547),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2871] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38147.1(SEQ ID NOs:121和548),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2872] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38153.1(SEQ ID NOs:122和549),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2873] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38159.1(SEQ ID NOs:123和550),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2874] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38165.1(SEQ ID NOs:124和551),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2875] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38171.1(SEQ ID NOs:125和552),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2876] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38130.1(SEQ ID NOs:126和553),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2877] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38136.1(SEQ ID NOs:127和554),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2878] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38142.1(SEQ ID NOs:128和555),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2879] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-38148.1(SEQ ID NOs:129和556),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2880] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38154.1(SEQ ID NOs:130和557),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2881] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38160.1(SEQ ID NOs:131和558),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2882] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38166.1(SEQ ID NOs:132和559),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2883] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38172.1(SEQ ID NOs:133和560),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2884] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38131.1(SEQ ID NOs:134和561),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2885] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38137.1(SEQ ID NOs:135和562),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2886] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38143.1(SEQ ID NOs:136和563),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2887] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38149.1(SEQ ID NOs:137和564),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2888] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38155.1(SEQ ID NOs:138和565),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2889] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38161.1(SEQ ID NOs:139和566),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2890] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38167.1(SEQ ID NOs:140和567),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2891] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38173.1(SEQ ID NOs:141和568),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2892] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-38132.1(SEQ ID NOs:142和569),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2893] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38138.1(SEQ ID NOs:143和570),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2894] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38144.1(SEQ ID NOs:144和571),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2895] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38150.1(SEQ ID NOs:145和572),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2896] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38156.1(SEQ ID NOs:146和573),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2897] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38162.1(SEQ ID NOs:147和574),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2898] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38168.1(SEQ ID NOs:148和575),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2899] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-38174.1(SEQ ID NOs:149和576),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2900] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39683.1(SEQ ID NOs:150和577),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2901] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39689.1(SEQ ID NOs:151和578),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2902] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39695.1(SEQ ID NOs:152和579),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2903] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39701.1(SEQ ID NOs:153和580),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2904] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39707.1(SEQ ID NOs:154和581),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2905] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39713.1(SEQ ID NOs:155和582),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2906] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39719.1(SEQ ID NOs:156和583),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2907] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39725.1(SEQ ID NOs:157和584),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2908] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39684.1(SEQ ID NOs:158和585),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2909] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39690.1(SEQ ID NOs:159和586),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2910] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39696.1(SEQ ID NOs:160和587),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2911] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39702.1(SEQ ID NOs:161和588),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2912] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39708.1(SEQ ID NOs:162和589),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2913] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39714.1(SEQ ID NOs:163和590),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2914] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39720.1(SEQ ID NOs:164和591),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2915] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39726.1(SEQ ID NOs:165和592),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2916] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39685.1(SEQ ID NOs:166和593),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2917] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39691.1(SEQ ID NOs:167和594),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2918] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39697.1(SEQ ID NOs:168和595),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2919] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39703.1(SEQ ID NOs:169和596),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2920] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39709.1(SEQ ID NOs:170和597),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2921] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39715.1(SEQ ID NOs:171和598),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2922] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39721.1(SEQ ID NOs:172和599),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2923] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39727.1(SEQ ID NOs:173和600),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2924] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39686.1(SEQ ID NOs:174和601),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2925] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39692.1(SEQ ID NOs:175和602),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2926] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39698.1(SEQ ID NOs:176和603),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2927] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39704.1(SEQ ID NOs:177和604),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2928] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39710.1(SEQ ID NOs:178和605),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2929] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39716.1(SEQ ID NOs:179和606),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2930] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39722.1(SEQ ID NOs:180和607),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2931] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39728.1(SEQ ID NOs:181和608),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2932] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39687.1(SEQ ID NOs:182和609),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2933] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39693.1(SEQ ID NOs:183和610),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2934] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39699.1(SEQ ID NOs:184和611),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2935] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39705.1(SEQ ID NOs:185和612),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2936] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39711.1(SEQ ID NOs:186和613),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2937] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39717.1(SEQ ID NOs:187和614),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2938] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39723.1(SEQ ID NOs:188和615),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2939] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39729.1(SEQ ID NOs:189和616),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2940] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39688.1(SEQ ID NOs:190和617),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2941] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39694.1(SEQ ID NOs:191和618),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2942] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39700.1(SEQ ID NOs:192和619),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2943] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39706.1(SEQ ID NOs:193和620),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2944] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39712.1(SEQ ID NOs:194和621),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2945] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39718.1(SEQ ID NOs:195和622),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2946] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39724.1(SEQ ID NOs:196和623),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2947] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39730.1(SEQ ID NOs:197和624),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2948] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39736.1(SEQ ID NOs:198和625),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2949] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39742.1(SEQ ID NOs:199和626),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2950] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39748.1(SEQ ID NOs:200和627),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2951] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39754.1(SEQ ID NOs:201和628),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2952] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39760.1(SEQ ID NOs:202和629),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2953] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39766.1(SEQ ID NOs:203和630),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2954] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39772.1(SEQ ID NOs:204和631),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2955] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39731.1(SEQ ID NOs:205和632),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2956] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39737.1(SEQ ID NOs:206和633),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2957] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39743.1(SEQ ID NOs:207和634),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2958] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39749.1(SEQ ID NOs:208和635),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2959] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39755.1(SEQ ID NOs:209和636),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2960] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39761.1(SEQ ID NOs:210和637),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2961] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39767.1(SEQ ID NOs:211和638),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2962] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39773.1(SEQ ID NOs:212和639),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2963] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39732.1(SEQ ID NOs:213和640),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2964] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39738.1(SEQ ID NOs:214和641),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2965] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39744.1(SEQ ID NOs:215和642),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2966] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39750.1(SEQ ID NOs:216和643),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2967] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39756.1(SEQ ID NOs:217和644),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2968] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39762.1(SEQ ID NOs:218和645),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2969] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39768.1(SEQ ID NOs:219和646),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2970] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39774.1(SEQ ID NOs:220和647),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2971] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39733.1(SEQ ID NOs:221和648),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2972] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39739.1(SEQ ID NOs:222和649),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2973] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39745.1(SEQ ID NOs:223和650),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2974] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39751.1(SEQ ID NOs:224和651),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2975] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39757.1(SEQ ID NOs:225和652),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2976] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39763.1(SEQ ID NOs:226和653),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2977] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39769.1(SEQ ID NOs:227和654),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2978] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39775.1(SEQ ID NOs:228和655),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2979] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39734.1(SEQ ID NOs:229和656),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2980] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39740.1(SEQ ID NOs:230和657),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2981] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39746.1(SEQ ID NOs:231和658),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2982] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39752.1(SEQ ID NOs:232和659),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2983] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39758.1(SEQ ID NOs:233和660),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2984] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39764.1(SEQ ID NOs:234和661),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2985] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39770.1(SEQ ID NOs:235和662),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2986] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39776.1(SEQ ID NOs:236和663),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2987] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39735.1(SEQ ID NOs:237和664),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2988] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39741.1(SEQ ID NOs:238和665),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2989] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39747.1(SEQ ID NOs:239和666),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2990] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39753.1(SEQ ID NOs:240和667),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2991] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39759.1(SEQ ID NOs:241和668),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2992] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39765.1(SEQ ID NOs:242和669),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2993] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39771.1(SEQ ID NOs:243和670),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2994] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39778.1(SEQ ID NOs:244和671),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2995] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39784.1(SEQ ID NOs:245和672),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2996] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39790.1(SEQ ID NOs:246和673),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2997] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39796.1(SEQ ID NOs:247和674),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2998] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39802.1(SEQ ID NOs:248和675),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[2999] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39808.1(SEQ ID NOs:249和676),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3000] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39814.1(SEQ ID NOs:250和677),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3001] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39820.1(SEQ ID NOs:251和678),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3002] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39779.1(SEQ ID NOs:252和679),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3003] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39785.1(SEQ ID NOs:253和680),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3004] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39791.1(SEQ ID NOs:254和681),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3005] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39797.1(SEQ ID NOs:255和682),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3006] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39803.1(SEQ ID NOs:256和683),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3007] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39809.1(SEQ ID NOs:257和684),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3008] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39815.1(SEQ ID NOs:258和685),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3009] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39821.1(SEQ ID NOs:259和686),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3010] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39780.1(SEQ ID NOs:260和687),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3011] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39786.1(SEQ ID NOs:261和688),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3012] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39792.1(SEQ ID NOs:262和689),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3013] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39798.1(SEQ ID NOs:263和690),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3014] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39804.1(SEQ ID NOs:264和691),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3015] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39810.1(SEQ ID NOs:265和692),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3016] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39816.1(SEQ ID NOs:266和693),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3017] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39822.1(SEQ ID NOs:267和694),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3018] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39781.1(SEQ ID NOs:268和695),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3019] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39787.1(SEQ ID NOs:269和696),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3020] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39793.1(SEQ ID NOs:270和697),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3021] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39799.1(SEQ ID NOs:271和698),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3022] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39805.1(SEQ ID NOs:272和699),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3023] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39811.1(SEQ ID NOs:273和700),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3024] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39817.1(SEQ ID NOs:274和701),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3025] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39823.1(SEQ ID NOs:275和702),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3026] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39782.1(SEQ ID NOs:276和703),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3027] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39788.1(SEQ ID NOs:277和704),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3028] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39794.1(SEQ ID NOs:278和705),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3029] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39800.1(SEQ ID NOs:279和706),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3030] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39806.1(SEQ ID NOs:280和707),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3031] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39812.1(SEQ ID NOs:281和708),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3032] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39818.1(SEQ ID NOs:282和709),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3033] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39824.1(SEQ ID NOs:283和710),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3034] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39783.1(SEQ ID NOs:284和711),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3035] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39789.1(SEQ ID NOs:285和712),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3036] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39795.1(SEQ ID NOs:286和713),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3037] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39801.1(SEQ ID NOs:287和714),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3038] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39807.1(SEQ ID NOs:288和715),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3039] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39813.1(SEQ ID NOs:289和716),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3040] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39819.1(SEQ ID NOs:290和717),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3041] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39825.1(SEQ ID NOs:291和718),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3042] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39831.1(SEQ ID NOs:292和719),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3043] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39837.1(SEQ ID NOs:293和720),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3044] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39843.1(SEQ ID NOs:294和721),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3045] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39849.1(SEQ ID NOs:295和722),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3046] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39855.1(SEQ ID NOs:296和723),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3047] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39861.1(SEQ ID NOs:297和724),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3048] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39867.1(SEQ ID NOs:298和725),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3049] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39826.1(SEQ ID NOs:299和726),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3050] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39832.1(SEQ ID NOs:300和727),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3051] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39838.1(SEQ ID NOs:301和728),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3052] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39844.1(SEQ ID NOs:302和729),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3053] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39850.1(SEQ ID NOs:303和730),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3054] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39856.1(SEQ ID NOs:304和731),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3055] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39862.1(SEQ ID NOs:305和732),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3056] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39868.1(SEQ ID NOs:306和733),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3057] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39827.1(SEQ ID NOs:307和734),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3058] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39833.1(SEQ ID NOs:308和735),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3059] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39839.1(SEQ ID NOs:309和736),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3060] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39845.1(SEQ ID NOs:310和737),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3061] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39851.1(SEQ ID NOs:311和738),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3062] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39857.1(SEQ ID NOs:312和739),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3063] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39863.1(SEQ ID NOs:313和740),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3064] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39869.1(SEQ ID NOs:314和741),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3065] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39828.1(SEQ ID NOs:315和742),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3066] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39834.1(SEQ ID NOs:316和743),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3067] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39840.1(SEQ ID NOs:317和744),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3068] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39846.1(SEQ ID NOs:318和745),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3069] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39852.1(SEQ ID NOs:319和746),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3070] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39858.1(SEQ ID NOs:320和747),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3071] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39864.1(SEQ ID NOs:321和748),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3072] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39870.1(SEQ ID NOs:322和749),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3073] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39829.1(SEQ ID NOs:323和750),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3074] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39835.1(SEQ ID NOs:324和751),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3075] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39841.1(SEQ ID NOs:325和752),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3076] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39853.1(SEQ ID NOs:326和753),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3077] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39859.1(SEQ ID NOs:327和754),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3078] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39865.1(SEQ ID NOs:328和755),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3079] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39871.1(SEQ ID NOs:329和756),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3080] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39830.1(SEQ ID NOs:330和757),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3081] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39836.1(SEQ ID NOs:331和758),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3082] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39842.1(SEQ ID NOs:332和759),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3083] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39848.1(SEQ ID NOs:333和760),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3084] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39854.1(SEQ ID NOs:334和761),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3085] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39860.1(SEQ ID NOs:335和762),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3086] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39866.1(SEQ ID NOs:336和763),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3087] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39992.1(SEQ ID NOs:337和764),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3088] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39998.1(SEQ ID NOs:338和765),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3089] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40004.1(SEQ ID NOs:339和766),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3090] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40010.1(SEQ ID NOs:340和767),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3091] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40016.1(SEQ ID NOs:341和768),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3092] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40022.1(SEQ ID NOs:342和769),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3093] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40028.1(SEQ ID NOs:343和770),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3094] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40034.1(SEQ ID NOs:344和771),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3095] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39999.1(SEQ ID NOs:345和772),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3096] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40005.1(SEQ ID NOs:346和773),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3097] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40011.1(SEQ ID NOs:347和774),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3098] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40017.1(SEQ ID NOs:348和775),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3099] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40029.1(SEQ ID NOs:349和776),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3100] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40035.1(SEQ ID NOs:350和777),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3101] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39994.1(SEQ ID NOs:351和778),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3102] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40000.1(SEQ ID NOs:352和779),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3103] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40006.1(SEQ ID NOs:353和780),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3104] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40012.1(SEQ ID NOs:354和781),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3105] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40018.1(SEQ ID NOs:355和782),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3106] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40024.1(SEQ ID NOs:356和783),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3107] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40030.1(SEQ ID NOs:357和784),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3108] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40036.1(SEQ ID NOs:358和785),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3109] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39995.1(SEQ ID NOs:359和786),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3110] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40001.1(SEQ ID NOs:360和787),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3111] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40007.1(SEQ ID NOs:361和788),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3112] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40013.1(SEQ ID NOs:362和789),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3113] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40019.1(SEQ ID NOs:363和790),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3114] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40025.1(SEQ ID NOs:364和791),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3115] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40031.1(SEQ ID NOs:365和792),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3116] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40037.1(SEQ ID NOs:366和793),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3117] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39996.1(SEQ ID NOs:367和794),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3118] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40002.1(SEQ ID NOs:368和795),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3119] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40008.1(SEQ ID NOs:369和796),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3120] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40014.1(SEQ ID NOs:370和797),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3121] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40020.1(SEQ ID NOs:371和798),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3122] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40026.1(SEQ ID NOs:372和799),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3123] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40032.1(SEQ ID NOs:373和800),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3124] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40038.1(SEQ ID NOs:374和801),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3125] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39997.1(SEQ ID NOs:375和802),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3126] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40009.1(SEQ ID NOs:376和803),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3127] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40015.1(SEQ ID NOs:377和804),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3128] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40021.1(SEQ ID NOs:378和805),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3129] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40027.1(SEQ ID NOs:379和806),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3130] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40033.1(SEQ ID NOs:380和807),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3131] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40039.1(SEQ ID NOs:381和808),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3132] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40045.1(SEQ ID NOs:382和809),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3133] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40051.1(SEQ ID NOs:383和810),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3134] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40057.1(SEQ ID NOs:384和811),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3135] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40063.1(SEQ ID NOs:385和812),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3136] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40069.1(SEQ ID NOs:386和813),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3137] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40075.1(SEQ ID NOs:387和814),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3138] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40081.1(SEQ ID NOs:388和815),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3139] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40040.1(SEQ ID NOs:389和816),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3140] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40046.1(SEQ ID NOs:390和817),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3141] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40052.1(SEQ ID NOs:391和818),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3142] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40058.1(SEQ ID NOs:392和819),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3143] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40064.1(SEQ ID NOs:393和820),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3144] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40070.1(SEQ ID NOs:394和821),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3145] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40076.1(SEQ ID NOs:395和822),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3146] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40082.1(SEQ ID NOs:396和823),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3147] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40041.1(SEQ ID NOs:397和824),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3148] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40047.1(SEQ ID NOs:398和825),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3149] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40053.1(SEQ ID NOs:399和826),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3150] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40059.1(SEQ ID NOs:400和827),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3151] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40065.1(SEQ ID NOs:401和828),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3152] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40071.1(SEQ ID NOs:402和829),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3153] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40077.1(SEQ ID NOs:403和830),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3154] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40083.1(SEQ ID NOs:404和831),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3155] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40042.1(SEQ ID NOs:405和832),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3156] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40048.1(SEQ ID NOs:406和833),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3157] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40054.1(SEQ ID NOs:407和834),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3158] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40060.1(SEQ ID NOs:408和835),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3159] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40066.1(SEQ ID NOs:409和836),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3160] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40072.1(SEQ ID NOs:410和837),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3161] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40078.1(SEQ ID NOs:411和838),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3162] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40084.1(SEQ ID NOs:412和839),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3163] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40043.1(SEQ ID NOs:413和840),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3164] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40049.1(SEQ ID NOs:414和841),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3165] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-40055.1(SEQ ID NOs:415和842),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3166] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40061.1(SEQ ID NOs:416和843),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3167] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40067.1(SEQ ID NOs:417和844),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3168] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40073.1(SEQ ID NOs:418和845),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3169] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40079.1(SEQ ID NOs:419和846),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3170] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40085.1(SEQ ID NOs:420和847),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3171] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40044.1(SEQ ID NOs:421和848),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3172] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40050.1(SEQ ID NOs:422和849),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3173] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40056.1(SEQ ID NOs:423和850),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3174] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40062.1(SEQ ID NOs:424和851),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3175] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40068.1(SEQ ID NOs:425和852),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3176] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40074.1(SEQ ID NOs:426和853),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3177] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-40080.1(SEQ ID NOs:427和854),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3178] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:AD-39720.1(SEQ ID NOs:1716和1754),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3179] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39706.1(SEQ ID NOs:1717和1755),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3180] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39712.1(SEQ ID NOs:1718和1756),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3181] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39760.1(SEQ ID NOs:1719和1757),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3182] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39732.1(SEQ ID NOs:1720和1758),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3183] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-35541.4(SEQ ID NOs:1721和1759),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3184] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39735.1或hs_KRAS_321_A22S26(SEQ ID NOs:1722和1760),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3185] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39741.1,或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3186] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:hs_KRAS_322_A22S26(SEQ IDNOs:1723和1761),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3187] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39778.1(SEQ ID NOs:1724和1762),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3188] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39790.1(SEQ ID NOs:1725和1763),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3189] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-39822.1(SEQ ID NOs:1726和1764),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3190] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列:AD-35609.4(SEQ ID NOs:1727和1765),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3191] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35581.4(SEQ ID NOs:1728 和 1766)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3192] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39845.1(SEQ ID NOs:1729 和 1767)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3193] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39858.1(SEQ ID NOs:1730 和 1768)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3194] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39870.1(SEQ ID NOs:1731 和 1769)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3195] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35576.4(SEQ ID NOs:1732 和 1770)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3196] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35588.4(SEQ ID NOs:1733 和 1771)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3197] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35600.1(SEQ ID NOs:1734 和 1772)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3198] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-35606.1(SEQ ID NOs:1735 和 1773)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3199] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38151.1(SEQ ID NOs:1736 和 1774)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3200] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38163.1(SEQ ID NOs:1737 和 1775)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3201] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-39999.1(SEQ ID NOs:1738 和 1776)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3202] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1739 和 1777)，或其修饰变体或未修饰变体，其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[3203] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是如下 RNAi 剂的第一链和 / 或第二链的序列 :AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1740 和

1778)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3204] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-38136.1(SEQ ID NOs:1741和1779)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3205] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40036.1(SEQ ID NOs:1742和1780)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3206] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40008.1(SEQ ID NOs:1743和1781)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3207] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40021.1(SEQ ID NOs:1744和1782)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3208] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40077.1(SEQ ID NOs:1745和1783)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3209] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40072.1(SEQ ID NOs:1746和1784)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3210] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40061.1(SEQ ID NOs:1747和1785)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3211] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-40068.1(SEQ ID NOs:1748和1786)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3212] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-38131.1(SEQ ID NOs:1749和1787)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3213] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：AD-38167.1(SEQ ID NOs:1750和1788)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3214] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：hs_KRAS 1273_A22S26(SEQ IDNOs:1751和1789)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3215] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂的第一链和/或第二链的序列：hs_KRAS 2892_A37S26(SEQ IDNOs:1752和1790)，或其修饰变体或未修饰变体，其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3216] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列是如下RNAi剂

的第一链和/或第二链的序列:hs_KRAS 4731_A22S26(SEQ IDNOs:1753和1791),或其修饰变体或未修饰变体,其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[3217] 在多种实施方案中,本公开包括包含有义链和反义链的RNAi剂,其中反义链包含与本文公开的任一种RNAi剂或其修饰变体或未修饰变体的反义链差异0、1、2或3个核苷酸的至少15个连续核苷酸,其中的反义链还任选地包含0、1、2、3、4、5、6、7、8、9或10个或更多个核苷酸(或其中的任何范围,例如0-1、1-2、1-3、1-4个核苷酸等)。

[3218] 在一个实施方案中,本公开包括文中列出的任意一种或多种RNAi剂。其中第一链和/或第二链的序列是本文公开的RNAi剂的第一链和/或第二链的序列,还包含至多约20个额外的核苷酸的具体实施方案

[3219] 在一个实施方案中,本公开涉及一种包含任意一种或多种RNAi剂的组合物,所述RNAi剂包含第一链和第二链,其中第一链和/或第二链的序列包含来自表1至6的任何一个的任一种RNAi剂或其修饰变体和未修饰变体的第一链和/或第二链的15个连续核苷酸的序列。

[3220] 因此,在多种实施方案中,本公开涉及包含任意一种或多种如下RNAi剂的组合物:

[3221] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35523.3(SEQ ID NOs:1和428),或其修饰变体或未修饰变体。

[3222] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35529.1(SEQ ID NOs:2和429),或其修饰变体或未修饰变体。

[3223] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35535.4(SEQ ID NOs:3和430),或其修饰变体或未修饰变体。

[3224] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35541.4(SEQ ID NOs:4和431),或其修饰变体或未修饰变体。

[3225] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35547.4(SEQ ID NOs:5和432),或其修饰变体或未修饰变体。

[3226] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35553.4(SEQ ID NOs:6和433),或其修饰变体或未修饰变体。

[3227] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35559.4(SEQ ID NOs:7和434),或其修饰变体或未修饰变体。

[3228] 包含第一链和第二链的RNAi剂,其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列:AD-35565.4(SEQ ID NOs:8和435),或其修饰变体或未修饰变体。

[3229] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35524.4(SEQ ID NOs:9 和 436)，或其修饰变体或未修饰变体。

[3230] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35530.4(SEQ ID NOs:10 和 437)，或其修饰变体或未修饰变体。

[3231] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35536.4(SEQ ID NOs:11 和 438)，或其修饰变体或未修饰变体。

[3232] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35542.4(SEQ ID NOs:12 和 439)，或其修饰变体或未修饰变体。

[3233] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35548.4(SEQ ID NOs:13 和 440)，或其修饰变体或未修饰变体。

[3234] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35554.4(SEQ ID NOs:14 和 441)，或其修饰变体或未修饰变体。

[3235] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35560.2(SEQ ID NOs:15 和 442)，或其修饰变体或未修饰变体。

[3236] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35566.4(SEQ ID NOs:16 和 443)，或其修饰变体或未修饰变体。

[3237] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35525.2(SEQ ID NOs:17 和 444)，或其修饰变体或未修饰变体。

[3238] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35531.4(SEQ ID NOs:18 和 445)，或其修饰变体或未修饰变体。

[3239] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35537.4(SEQ ID NOs:19 和 446)，或其修饰变体或未修饰变体。

[3240] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35543.2(SEQ ID NOs:20 和 447)，或其修饰变体或未修饰变体。

[3241] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35549.4(SEQ ID NOs:21 和 448)，或其修饰变体或未修饰变体。

[3242] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35555.4(SEQ ID NOs:22 和 449)，或其修饰变体或未修饰变体。

[3243] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35561.4(SEQ ID NOs:23 和 450)，或其修饰变体或未修饰变体。

[3244] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35567.4(SEQ ID NOs:24 和 451)，或其修饰变体或未修饰变体。

[3245] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35526.4(SEQ ID NOs:25 和 452)，或其修饰变体或未修饰变体。

[3246] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35532.4(SEQ ID NOs:26 和 453)，或其修饰变体或未修饰变体。

[3247] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35538.4(SEQ ID NOs:27 和 454)，或其修饰变体或未修饰变体。

[3248] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35544.4(SEQ ID NOs:28 和 455)，或其修饰变体或未修饰变体。

[3249] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35550.4(SEQ ID NOs:29 和 456)，或其修饰变体或未修饰变体。

[3250] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35556.4(SEQ ID NOs:30 和 457)，或其修饰变体或未修饰变体。

[3251] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35562.4(SEQ ID NOs:31 和 458)，或其修饰变体或未修饰变体。

[3252] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35568.4(SEQ ID NOs:32 和 459)，或其修饰变体或未修饰变体。

[3253] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35527.4(SEQ ID NOs:33 和 460)，或其修饰变体或未修饰变体。

[3254] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35533.4(SEQ ID NOs:34 和 461)，或其修饰变体或未修饰变体。

[3255] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35539.4(SEQ ID NOs:35 和 462)，或其修饰变体或未修饰变体。

[3256] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35545.4(SEQ ID NOs:36 和 463)，或其修饰变体或未修饰变体。

[3257] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35551.4(SEQ ID NOs:37 和 464)，或其修饰变体或未修饰变体。

[3258] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35563.4(SEQ ID NOs:38 和 465)，或其修饰变体或未修饰变体。

[3259] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35528.4(SEQ ID NOs:39 和 466)，或其修饰变体或未修饰变体。

[3260] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35540.4(SEQ ID NOs:40 和 467)，或其修饰变体或未修饰变体。

[3261] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35546.4(SEQ ID NOs:41 和 468)，或其修饰变体或未修饰变体。

[3262] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35552.4(SEQ ID NOs:42 和 469)，或其修饰变体或未修饰变体。

[3263] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35558.4(SEQ ID NOs:43 和 470)，或其修饰变体或未修饰变体。

[3264] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35564.4(SEQ ID NOs:44 和 471)，或其修饰变体或未修饰变体。

[3265] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35570.4(SEQ ID NOs:45 和 472)，或其修饰变体或未修饰变体。

[3266] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35571.4(SEQ ID NOs:46 和 473)，或其修饰变体或未修饰变体。

[3267] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35577.4(SEQ ID NOs:47 和 474)，或其修饰变体或未修饰变体。

[3268] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35583.4(SEQ ID NOs:48 和 475)，或其修饰变体或未修饰变体。

[3269] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35589.4(SEQ ID NOs:49 和 476)，或其修饰变体或未修饰变体。

[3270] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35595.4(SEQ ID NOs:50 和 477)，或其修饰变体或未修饰变体。

[3271] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35601.4(SEQ ID NOs:51 和 478)，或其修饰变体或未修饰变体。

[3272] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35607.4(SEQ ID NOs:52 和 479)，或其修饰变体或未修饰变体。

[3273] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35613.4(SEQ ID NOs:53 和 480)，或其修饰变体或未修饰变体。

[3274] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35572.4(SEQ ID NOs:54 和 481)，或其修饰变体或未修饰变体。

[3275] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35578.4(SEQ ID NOs:55 和 482)，或其修饰变体或未修饰变体。

[3276] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35584.4(SEQ ID NOs:56 和 483)，或其修饰变体或未修饰变体。

[3277] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35590.4(SEQ ID NOs:57 和 484)，或其修饰变体或未修饰变体。

[3278] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35596.4(SEQ ID NOs:58 和 485)，或其修饰变体或未修饰变体。

[3279] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35602.4(SEQ ID NOs:59 和 486)，或其修饰变体或未修饰变体。

[3280] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35608.4(SEQ ID NOs:60 和 487)，或其修饰变体或未修饰变体。

[3281] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35614.4(SEQ ID NOs:61 和 488)，或其修饰变体或未修饰变体。

[3282] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35573.4(SEQ ID NOs:62 和 489)，或其修饰变体或未修饰变体。

[3283] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35579.4(SEQ ID NOs:63 和 490)，或其修饰变体或未修饰变体。

[3284] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35585.4(SEQ ID NOs:64 和 491)，或其修饰变体或未修饰变体。

[3285] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35591.4(SEQ ID NOs:65 和 492)，或其修饰变体或未修饰变体。

[3286] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35597.4(SEQ ID NOs:66 和 493)，或其修饰变体或未修饰变体。

[3287] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35603.4(SEQ ID NOs:67 和 494)，或其修饰变体或未修饰变体。

[3288] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35609.4(SEQ ID NOs:68 和 495)，或其修饰变体或未修饰变体。

[3289] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35615.4(SEQ ID NOs:69 和 496)，或其修饰变体或未修饰变体。

[3290] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35574.4(SEQ ID NOs:70 和 497)，或其修饰变体或未修饰变体。

[3291] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35580.1(SEQ ID NOs:71 和 498)，或其修饰变体或未修饰变体。

[3292] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35586.4(SEQ ID NOs:72 和 499)，或其修饰变体或未修饰变体。

[3293] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35592.4(SEQ ID NOs:73 和 500)，或其修饰变体或未修饰变体。

[3294] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35598.4(SEQ ID NOs:74 和 501)，或其修饰变体或未修饰变体。

[3295] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35604.4(SEQ ID NOs:75 和 502)，或其修饰变体或未修饰变体。

[3296] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35610.4(SEQ ID NOs:76 和 503)，或其修饰变体或未修饰变体。

[3297] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35616.4(SEQ ID NOs:77 和 504)，或其修饰变体或未修饰变体。

[3298] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35575.4(SEQ ID NOs:78 和 505)，或其修饰变体或未修饰变体。

[3299] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35581.4(SEQ ID NOs:79 和 506)，或其修饰变体或未修饰变体。

[3300] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35587.4(SEQ ID NOs:80 和 507)，或其修饰变体或未修饰变体。

[3301] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35593.4(SEQ ID NOs:81 和 508)，或其修饰变体或未修饰变体。

[3302] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35599.4(SEQ ID NOs:82 和 509)，或其修饰变体或未修饰变体。

[3303] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35605.4(SEQ ID NOs:83 和 510)，或其修饰变体或未修饰变体。

[3304] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35611.4(SEQ ID NOs:84 和 511)，或其修饰变体或未修饰变体。

[3305] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35617.4(SEQ ID NOs:85 和 512)，或其修饰变体或未修饰变体。

[3306] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35576.4(SEQ ID NOs:86 和 513)，或其修饰变体或未修饰变体。

[3307] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35588.4(SEQ ID NOs:87 和 514)，或其修饰变体或未修饰变体。

[3308] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35667.1(SEQ ID NOs:88 和 515)，或其修饰变体或未修饰变体。

[3309] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35673.1(SEQ ID NOs:89 和 516)，或其修饰变体或未修饰变体。

[3310] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35679.1(SEQ ID NOs:90 和 517)，或其修饰变体或未修饰变体。

[3311] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35685.1(SEQ ID NOs:91 和 518)，或其修饰变体或未修饰变体。

[3312] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35691.1(SEQ ID NOs:92 和 519)，或其修饰变体或未修饰变体。

[3313] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35557.1(SEQ ID NOs:93 和 520)，或其修饰变体或未修饰变体。

[3314] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35618.1(SEQ ID NOs:94 和 521)，或其修饰变体或未修饰变体。

[3315] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35569.1(SEQ ID NOs:95 和 522)，或其修饰变体或未修饰变体。

[3316] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35534.1(SEQ ID NOs:96 和 523)，或其修饰变体或未修饰变体。

[3317] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35582.1(SEQ ID NOs:97 和 524)，或其修饰变体或未修饰变体。

[3318] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35594.1(SEQ ID NOs:98 和 525)，或其修饰变体或未修饰变体。

[3319] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35600.1(SEQ ID NOs:99 和 526)，或其修饰变体或未修饰变体。

[3320] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35606.1(SEQ ID NOs:100 和 527)，或其修饰变体或未修饰变体。

[3321] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35612.1(SEQ ID NOs:101 和 528)，或其修饰变体或未修饰变体。

[3322] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38127.1(SEQ ID NOs:102 和 529)，或其修饰变体或未修饰变体。

[3323] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38133.1(SEQ ID NOs:103 和 530)，或其修饰变体或未修饰变体。

[3324] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38139.1(SEQ ID NOs:104 和 531)，或其修饰变体或未修饰变体。

[3325] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38145.1(SEQ ID NOs:105 和 532)，或其修饰变体或未修饰变体。

[3326] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38151.1(SEQ ID NOs:106 和 533)，或其修饰变体或未修饰变体。

[3327] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38157.1(SEQ ID NOs:107 和 534)，或其修饰变体或未修饰变体。

[3328] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38163.1(SEQ ID NOs:108 和 535)，或其修饰变体或未修饰变体。

[3329] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38169.1(SEQ ID NOs:109 和 536)，或其修饰变体或未修饰变体。

[3330] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38128.1(SEQ ID NOs:110 和 537)，或其修饰变体或未修饰变体。

[3331] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38134.1(SEQ ID NOs:111 和 538)，或其修饰变体或未修饰变体。

[3332] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38140.1(SEQ ID NOs:112 和 539)，或其修饰变体或未修饰变体。

[3333] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38146.1(SEQ ID NOs:113 和 540)，或其修饰变体或未修饰变体。

[3334] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38152.1(SEQ ID NOs:114 和 541)，或其修饰变体或未修饰变体。

[3335] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38158.1(SEQ ID NOs:115 和 542)，或其修饰变体或未修饰变体。

[3336] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38164.1(SEQ ID NOs:116 和 543)，或其修饰变体或未修饰变体。

[3337] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38170.1(SEQ ID NOs:117 和 544)，或其修饰变体或未修饰变体。

[3338] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38129.1(SEQ ID NOs:118 和 545)，或其修饰变体或未修饰变体。

[3339] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38135.1(SEQ ID NOs:119 和 546)，或其修饰变体或未修饰变体。

[3340] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38141.1(SEQ ID NOs:120 和 547)，或其修饰变体或未修饰变体。

[3341] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38147.1(SEQ ID NOs:121 和 548)，或其修饰变体或未修饰变体。

[3342] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38153.1(SEQ ID NOs:122 和 549)，或其修饰变体或未修饰变体。

[3343] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38159.1(SEQ ID NOs:123 和 550)，或其修饰变体或未修饰变体。

[3344] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38165.1(SEQ ID NOs:124 和 551)，或其修饰变体或未修饰变体。

[3345] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38171.1(SEQ ID NOs:125 和 552)，或其修饰变体或未修饰变体。

[3346] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38130.1(SEQ ID NOs:126 和 553)，或其修饰变体或未修饰变体。

[3347] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38136.1(SEQ ID NOs:127 和 554)，或其修饰变体或未修饰变体。

[3348] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38142.1(SEQ ID NOs:128 和 555)，或其修饰变体或未修饰变体。

[3349] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38148.1(SEQ ID NOs:129 和 556)，或其修饰变体或未修饰变体。

[3350] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38154.1(SEQ ID NOs:130 和 557)，或其修饰变体或未修饰变体。

[3351] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38160.1(SEQ ID NOs:131 和 558)，或其修饰变体或未修饰变体。

[3352] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38166.1(SEQ ID NOs:132 和 559)，或其修饰变体或未修饰变体。

[3353] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38172.1(SEQ ID NOs:133 和 560)，或其修饰变体或未修饰变体。

[3354] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38131.1(SEQ ID NOs:134 和 561)，或其修饰变体或未修饰变体。

[3355] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38137.1(SEQ ID NOs:135 和 562)，或其修饰变体或未修饰变体。

[3356] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38143.1(SEQ ID NOs:136 和 563)，或其修饰变体或未修饰变体。

[3357] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38149.1(SEQ ID NOs:137 和 564)，或其修饰变体或未修饰变体。

[3358] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38155.1(SEQ ID NOs:138 和 565)，或其修饰变体或未修饰变体。

[3359] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38161.1(SEQ ID NOs:139 和 566)，或其修饰变体或未修饰变体。

[3360] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38167.1(SEQ ID NOs:140 和 567)，或其修饰变体或未修饰变体。

[3361] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38173.1(SEQ ID NOs:141 和 568)，或其修饰变体或未修饰变体。

[3362] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38132.1(SEQ ID NOs:142 和 569)，或其修饰变体或未修饰变体。

[3363] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38138.1(SEQ ID NOs:143 和 570)，或其修饰变体或未修饰变体。

[3364] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38144.1(SEQ ID NOs:144 和 571)，或其修饰变体或未修饰变体。

[3365] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38150.1(SEQ ID NOs:145 和 572)，或其修饰变体或未修饰变体。

[3366] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38156.1(SEQ ID NOs:146 和 573)，或其修饰变体或未修饰变体。

[3367] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38162.1(SEQ ID NOs:147 和 574)，或其修饰变体或未修饰变体。

[3368] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38168.1(SEQ ID NOs:148 和 575)，或其修饰变体或未修饰变体。

[3369] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38174.1(SEQ ID NOs:149 和 576)，或其修饰变体或未修饰变体。

[3370] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39683.1(SEQ ID NOs:150 和 577)，或其修饰变体或未修饰变体。

[3371] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39689.1(SEQ ID NOs:151 和 578)，或其修饰变体或未修饰变体。

[3372] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39695.1(SEQ ID NOs:152 和 579)，或其修饰变体或未修饰变体。

[3373] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39701.1(SEQ ID NOs:153 和 580)，或其修饰变体或未修饰变体。

[3374] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39707.1(SEQ ID NOs:154 和 581)，或其修饰变体或未修饰变体。

[3375] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39713.1(SEQ ID NOs:155 和 582)，或其修饰变体或未修饰变体。

[3376] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39719.1(SEQ ID NOs:156 和 583)，或其修饰变体或未修饰变体。

[3377] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39725.1(SEQ ID NOs:157 和 584)，或其修饰变体或未修饰变体。

[3378] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39684.1(SEQ ID NOs:158 和 585)，或其修饰变体或未修饰变体。

[3379] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39690.1(SEQ ID NOs:159 和 586)，或其修饰变体或未修饰变体。

[3380] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39696.1(SEQ ID NOs:160 和 587)，或其修饰变体或未修饰变体。

[3381] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39702.1(SEQ ID NOs:161 和 588)，或其修饰变体或未修饰变体。

[3382] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39708.1(SEQ ID NOs:162 和 589)，或其修饰变体或未修饰变体。

[3383] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39714.1(SEQ ID NOs:163 和 590)，或其修饰变体或未修饰变体。

[3384] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39720.1(SEQ ID NOs:164 和 591)，或其修饰变体或未修饰变体。

[3385] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39726.1(SEQ ID NOs:165 和 592)，或其修饰变体或未修饰变体。

[3386] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39685.1(SEQ ID NOs:166 和 593)，或其修饰变体或未修饰变体。

[3387] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39691.1(SEQ ID NOs:167 和 594)，或其修饰变体或未修饰变体。

[3388] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39697.1(SEQ ID NOs:168 和 595)，或其修饰变体或未修饰变体。

[3389] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39703.1(SEQ ID NOs:169 和 596)，或其修饰变体或未修饰变体。

[3390] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39709.1(SEQ ID NOs:170 和 597)，或其修饰变体或未修饰变体。

[3391] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39715.1(SEQ ID NOs:171 和 598)，或其修饰变体或未修饰变体。

[3392] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39721.1(SEQ ID NOs:172 和 599)，或其修饰变体或未修饰变体。

[3393] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39727.1(SEQ ID NOs:173 和 600)，或其修饰变体或未修饰变体。

[3394] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39686.1(SEQ ID NOs:174 和 601)，或其修饰变体或未修饰变体。

[3395] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39692.1(SEQ ID NOs:175 和 602)，或其修饰变体或未修饰变体。

[3396] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39698.1(SEQ ID NOs:176 和 603)，或其修饰变体或未修饰变体。

[3397] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39704.1(SEQ ID NOs:177 和 604)，或其修饰变体或未修饰变体。

[3398] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39710.1(SEQ ID NOs:178 和 605)，或其修饰变体或未修饰变体。

[3399] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39716.1(SEQ ID NOs:179 和 606)，或其修饰变体或未修饰变体。

[3400] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39722.1(SEQ ID NOs:180 和 607)，或其修饰变体或未修饰变体。

[3401] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39728.1(SEQ ID NOs:181 和 608)，或其修饰变体或未修饰变体。

[3402] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39687.1(SEQ ID NOs:182 和 609)，或其修饰变体或未修饰变体。

[3403] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39693.1(SEQ ID NOs:183 和 610)，或其修饰变体或未修饰变体。

[3404] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39699.1(SEQ ID NOs:184 和 611)，或其修饰变体或未修饰变体。

[3405] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39705.1(SEQ ID NOs:185 和 612)，或其修饰变体或未修饰变体。

[3406] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39711.1(SEQ ID NOs:186 和 613)，或其修饰变体或未修饰变体。

[3407] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39717.1(SEQ ID NOs:187 和 614)，或其修饰变体或未修饰变体。

[3408] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39723.1(SEQ ID NOs:188 和 615)，或其修饰变体或未修饰变体。

[3409] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39729.1(SEQ ID NOs:189 和 616)，或其修饰变体或未修饰变体。

[3410] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39688.1(SEQ ID NOs:190 和 617)，或其修饰变体或未修饰变体。

[3411] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39694.1(SEQ ID NOs:191 和 618)，或其修饰变体或未修饰变体。

[3412] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39700.1(SEQ ID NOs:192 和 619)，或其修饰变体或未修饰变体。

[3413] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39706.1(SEQ ID NOs:193 和 620)，或其修饰变体或未修饰变体。

[3414] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39712.1(SEQ ID NOs:194 和 621)，或其修饰变体或未修饰变体。

[3415] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39718.1(SEQ ID NOs:195 和 622)，或其修饰变体或未修饰变体。

[3416] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39724.1(SEQ ID NOs:196 和 623)，或其修饰变体或未修饰变体。

[3417] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39730.1(SEQ ID NOs:197 和 624)，或其修饰变体或未修饰变体。

[3418] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39736.1(SEQ ID NOs:198 和 625)，或其修饰变体或未修饰变体。

[3419] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39742.1(SEQ ID NOs:199 和 626)，或其修饰变体或未修饰变体。

[3420] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39748.1(SEQ ID NOs:200 和 627)，或其修饰变体或未修饰变体。

[3421] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39754.1(SEQ ID NOs:201 和 628)，或其修饰变体或未修饰变体。

[3422] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39760.1(SEQ ID NOs:202 和 629)，或其修饰变体或未修饰变体。

[3423] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39766.1(SEQ ID NOs:203 和 630)，或其修饰变体或未修饰变体。

[3424] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39772.1(SEQ ID NOs:204 和 631)，或其修饰变体或未修饰变体。

[3425] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39731.1(SEQ ID NOs:205 和 632)，或其修饰变体或未修饰变体。

[3426] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39737.1(SEQ ID NOs:206 和 633)，或其修饰变体或未修饰变体。

[3427] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39743.1(SEQ ID NOs:207 和 634)，或其修饰变体或未修饰变体。

[3428] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39749.1(SEQ ID NOs:208 和 635)，或其修饰变体或未修饰变体。

[3429] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39755.1(SEQ ID NOs:209 和 636)，或其修饰变体或未修饰变体。

[3430] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39761.1(SEQ ID NOs:210 和 637)，或其修饰变体或未修饰变体。

[3431] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39767.1(SEQ ID NOs:211 和 638)，或其修饰变体或未修饰变体。

[3432] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39773.1(SEQ ID NOs:212 和 639)，或其修饰变体或未修饰变体。

[3433] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39732.1(SEQ ID NOs:213 和 640)，或其修饰变体或未修饰变体。

[3434] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39738.1(SEQ ID NOs:214 和 641)，或其修饰变体或未修饰变体。

[3435] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39744.1(SEQ ID NOs:215 和 642)，或其修饰变体或未修饰变体。

[3436] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39750.1(SEQ ID NOs:216 和 643)，或其修饰变体或未修饰变体。

[3437] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39756.1(SEQ ID NOs:217 和 644)，或其修饰变体或未修饰变体。

[3438] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39762.1(SEQ ID NOs:218 和 645)，或其修饰变体或未修饰变体。

[3439] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39768.1(SEQ ID NOs:219 和 646)，或其修饰变体或未修饰变体。

[3440] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39774.1(SEQ ID NOs:220 和 647)，或其修饰变体或未修饰变体。

[3441] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39733.1(SEQ ID NOs:221 和 648)，或其修饰变体或未修饰变体。

[3442] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39739.1(SEQ ID NOs:222 和 649)，或其修饰变体或未修饰变体。

[3443] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39745.1(SEQ ID NOs:223 和 650)，或其修饰变体或未修饰变体。

[3444] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39751.1(SEQ ID NOs:224 和 651)，或其修饰变体或未修饰变体。

[3445] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39757.1(SEQ ID NOs:225 和 652)，或其修饰变体或未修饰变体。

[3446] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39763.1(SEQ ID NOs:226 和 653)，或其修饰变体或未修饰变体。

[3447] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39769.1(SEQ ID NOs:227 和 654)，或其修饰变体或未修饰变体。

[3448] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39775.1(SEQ ID NOs:228 和 655)，或其修饰变体或未修饰变体。

[3449] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39734.1(SEQ ID NOs:229 和 656)，或其修饰变体或未修饰变体。

[3450] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39740.1(SEQ ID NOs:230 和 657)，或其修饰变体或未修饰变体。

[3451] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39746.1(SEQ ID NOs:231 和 658)，或其修饰变体或未修饰变体。

[3452] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39752.1(SEQ ID NOs:232 和 659)，或其修饰变体或未修饰变体。

[3453] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39758.1(SEQ ID NOs:233 和 660)，或其修饰变体或未修饰变体。

[3454] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39764.1(SEQ ID NOs:234 和 661)，或其修饰变体或未修饰变体。

[3455] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39770.1(SEQ ID NOs:235 和 662)，或其修饰变体或未修饰变体。

[3456] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39776.1(SEQ ID NOs:236 和 663)，或其修饰变体或未修饰变体。

[3457] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39735.1(SEQ ID NOs:237 和 664)，或其修饰变体或未修饰变体。

[3458] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39741.1(SEQ ID NOs:238 和 665)，或其修饰变体或未修饰变体。

[3459] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39747.1(SEQ ID NOs:239 和 666)，或其修饰变体或未修饰变体。

[3460] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39753.1(SEQ ID NOs:240 和 667)，或其修饰变体或未修饰变体。

[3461] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39759.1(SEQ ID NOs:241 和 668)，或其修饰变体或未修饰变体。

[3462] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39765.1(SEQ ID NOs:242 和 669)，或其修饰变体或未修饰变体。

[3463] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39771.1(SEQ ID NOs:243 和 670)，或其修饰变体或未修饰变体。

[3464] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39778.1(SEQ ID NOs:244 和 671)，或其修饰变体或未修饰变体。

[3465] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39784.1(SEQ ID NOs:245 和 672)，或其修饰变体或未修饰变体。

[3466] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39790.1(SEQ ID NOs:246 和 673)，或其修饰变体或未修饰变体。

[3467] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39796.1(SEQ ID NOs:247 和 674)，或其修饰变体或未修饰变体。

[3468] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39802.1(SEQ ID NOs:248 和 675)，或其修饰变体或未修饰变体。

[3469] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39808.1(SEQ ID NOs:249 和 676)，或其修饰变体或未修饰变体。

[3470] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39814.1(SEQ ID NOs:250 和 677)，或其修饰变体或未修饰变体。

[3471] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39820.1(SEQ ID NOs:251 和 678)，或其修饰变体或未修饰变体。

[3472] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39779.1(SEQ ID NOs:252 和 679)，或其修饰变体或未修饰变体。

[3473] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39785.1(SEQ ID NOs:253 和 680)，或其修饰变体或未修饰变体。

[3474] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39791.1(SEQ ID NOs:254 和 681)，或其修饰变体或未修饰变体。

[3475] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39797.1(SEQ ID NOs:255 和 682)，或其修饰变体或未修饰变体。

[3476] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39803.1(SEQ ID NOs:256 和 683)，或其修饰变体或未修饰变体。

[3477] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39809.1(SEQ ID NOs:257 和 684)，或其修饰变体或未修饰变体。

[3478] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39815.1(SEQ ID NOs:258 和 685)，或其修饰变体或未修饰变体。

[3479] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39821.1(SEQ ID NOs:259 和 686)，或其修饰变体或未修饰变体。

[3480] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39780.1(SEQ ID NOs:260 和 687)，或其修饰变体或未修饰变体。

[3481] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39786.1(SEQ ID NOs:261 和 688)，或其修饰变体或未修饰变体。

[3482] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39792.1(SEQ ID NOs:262 和 689)，或其修饰变体或未修饰变体。

[3483] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39798.1(SEQ ID NOs:263 和 690)，或其修饰变体或未修饰变体。

[3484] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39804.1(SEQ ID NOs:264 和 691)，或其修饰变体或未修饰变体。

[3485] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39810.1(SEQ ID NOs:265 和 692)，或其修饰变体或未修饰变体。

[3486] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39816.1(SEQ ID NOs:266 和 693)，或其修饰变体或未修饰变体。

[3487] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39822.1(SEQ ID NOs:267 和 694)，或其修饰变体或未修饰变体。

[3488] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39781.1(SEQ ID NOs:268 和 695)，或其修饰变体或未修饰变体。

[3489] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39787.1(SEQ ID NOs:269 和 696)，或其修饰变体或未修饰变体。

[3490] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39793.1(SEQ ID NOs:270 和 697)，或其修饰变体或未修饰变体。

[3491] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39799.1(SEQ ID NOs:271 和 698)，或其修饰变体或未修饰变体。

[3492] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39805.1(SEQ ID NOs:272 和 699)，或其修饰变体或未修饰变体。

[3493] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39811.1(SEQ ID NOs:273 和 700)，或其修饰变体或未修饰变体。

[3494] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39817.1(SEQ ID NOs:274 和 701)，或其修饰变体或未修饰变体。

[3495] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39823.1(SEQ ID NOs:275 和 702)，或其修饰变体或未修饰变体。

[3496] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39782.1(SEQ ID NOs:276 和 703)，或其修饰变体或未修饰变体。

[3497] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39788.1(SEQ ID NOs:277 和 704)，或其修饰变体或未修饰变体。

[3498] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39794.1(SEQ ID NOs:278 和 705)，或其修饰变体或未修饰变体。

[3499] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39800.1(SEQ ID NOs:279 和 706)，或其修饰变体或未修饰变体。

[3500] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39806.1(SEQ ID NOs:280 和 707)，或其修饰变体或未修饰变体。

[3501] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39812.1(SEQ ID NOs:281 和 708)，或其修饰变体或未修饰变体。

[3502] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39818.1(SEQ ID NOs:282 和 709)，或其修饰变体或未修饰变体。

[3503] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39824.1(SEQ ID NOs:283 和 710)，或其修饰变体或未修饰变体。

[3504] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39783.1(SEQ ID NOs:284 和 711)，或其修饰变体或未修饰变体。

[3505] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39789.1(SEQ ID NOs:285 和 712)，或其修饰变体或未修饰变体。

[3506] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39795.1(SEQ ID NOs:286 和 713)，或其修饰变体或未修饰变体。

[3507] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39801.1(SEQ ID NOs:287 和 714)，或其修饰变体或未修饰变体。

[3508] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39807.1(SEQ ID NOs:288 和 715)，或其修饰变体或未修饰变体。

[3509] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39813.1(SEQ ID NOs:289 和 716)，或其修饰变体或未修饰变体。

[3510] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39819.1(SEQ ID NOs:290 和 717)，或其修饰变体或未修饰变体。

[3511] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39825.1(SEQ ID NOs:291 和 718)，或其修饰变体或未修饰变体。

[3512] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39831.1(SEQ ID NOs:292 和 719)，或其修饰变体或未修饰变体。

[3513] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39837.1(SEQ ID NOs:293 和 720)，或其修饰变体或未修饰变体。

[3514] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39843.1(SEQ ID NOs:294 和 721)，或其修饰变体或未修饰变体。

[3515] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39849.1(SEQ ID NOs:295 和 722)，或其修饰变体或未修饰变体。

[3516] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39855.1(SEQ ID NOs:296 和 723)，或其修饰变体或未修饰变体。

[3517] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39861.1(SEQ ID NOs:297 和 724)，或其修饰变体或未修饰变体。

[3518] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39867.1(SEQ ID NOs:298 和 725)，或其修饰变体或未修饰变体。

[3519] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39826.1(SEQ ID NOs:299 和 726)，或其修饰变体或未修饰变体。

[3520] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39832.1(SEQ ID NOs:300 和 727)，或其修饰变体或未修饰变体。

[3521] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39838.1(SEQ ID NOs:301 和 728)，或其修饰变体或未修饰变体。

[3522] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39844.1(SEQ ID NOs:302 和 729)，或其修饰变体或未修饰变体。

[3523] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39850.1(SEQ ID NOs:303 和 730)，或其修饰变体或未修饰变体。

[3524] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39856.1(SEQ ID NOs:304 和 731)，或其修饰变体或未修饰变体。

[3525] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39862.1(SEQ ID NOs:305 和 732)，或其修饰变体或未修饰变体。

[3526] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39868.1(SEQ ID NOs:306 和 733)，或其修饰变体或未修饰变体。

[3527] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39827.1(SEQ ID NOs:307 和 734)，或其修饰变体或未修饰变体。

[3528] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39833.1(SEQ ID NOs:308 和 735)，或其修饰变体或未修饰变体。

[3529] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39839.1(SEQ ID NOs:309 和 736)，或其修饰变体或未修饰变体。

[3530] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39845.1(SEQ ID NOs:310 和 737)，或其修饰变体或未修饰变体。

[3531] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39851.1(SEQ ID NOs:311 和 738)，或其修饰变体或未修饰变体。

[3532] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39857.1(SEQ ID NOs:312 和 739)，或其修饰变体或未修饰变体。

[3533] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39863.1(SEQ ID NOs:313 和 740)，或其修饰变体或未修饰变体。

[3534] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39869.1(SEQ ID NOs:314 和 741)，或其修饰变体或未修饰变体。

[3535] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39828.1(SEQ ID NOs:315 和 742)，或其修饰变体或未修饰变体。

[3536] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39834.1(SEQ ID NOs:316 和 743)，或其修饰变体或未修饰变体。

[3537] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39840.1(SEQ ID NOs:317 和 744)，或其修饰变体或未修饰变体。

[3538] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39846.1(SEQ ID NOs:318 和 745)，或其修饰变体或未修饰变体。

[3539] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39852.1(SEQ ID NOs:319 和 746)，或其修饰变体或未修饰变体。

[3540] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39858.1(SEQ ID NOs:320 和 747)，或其修饰变体或未修饰变体。

[3541] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39864.1(SEQ ID NOs:321 和 748)，或其修饰变体或未修饰变体。

[3542] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39870.1(SEQ ID NOs:322 和 749)，或其修饰变体或未修饰变体。

[3543] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39829.1(SEQ ID NOs:323 和 750)，或其修饰变体或未修饰变体。

[3544] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39835.1(SEQ ID NOs:324 和 751)，或其修饰变体或未修饰变体。

[3545] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39841.1(SEQ ID NOs:325 和 752)，或其修饰变体或未修饰变体。

[3546] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39853.1(SEQ ID NOs:326 和 753)，或其修饰变体或未修饰变体。

[3547] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39859.1(SEQ ID NOs:327 和 754)，或其修饰变体或未修饰变体。

[3548] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39865.1(SEQ ID NOs:328 和 755)，或其修饰变体或未修饰变体。

[3549] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39871.1(SEQ ID NOs:329 和 756)，或其修饰变体或未修饰变体。

[3550] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39830.1(SEQ ID NOs:330 和 757)，或其修饰变体或未修饰变体。

[3551] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39836.1(SEQ ID NOs:331 和 758)，或其修饰变体或未修饰变体。

[3552] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39842.1(SEQ ID NOs:332 和 759)，或其修饰变体或未修饰变体。

[3553] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39848.1(SEQ ID NOs:333 和 760)，或其修饰变体或未修饰变体。

[3554] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39854.1(SEQ ID NOs:334 和 761)，或其修饰变体或未修饰变体。

[3555] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39860.1(SEQ ID NOs:335 和 762)，或其修饰变体或未修饰变体。

[3556] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39866.1(SEQ ID NOs:336 和 763)，或其修饰变体或未修饰变体。

[3557] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39992.1(SEQ ID NOs:337 和 764)，或其修饰变体或未修饰变体。

[3558] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39998.1(SEQ ID NOs:338 和 765)，或其修饰变体或未修饰变体。

[3559] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40004.1(SEQ ID NOs:339 和 766)，或其修饰变体或未修饰变体。

[3560] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40010.1(SEQ ID NOs:340 和 767)，或其修饰变体或未修饰变体。

[3561] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40016.1(SEQ ID NOs:341 和 768)，或其修饰变体或未修饰变体。

[3562] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40022.1(SEQ ID NOs:342 和 769)，或其修饰变体或未修饰变体。

[3563] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40028.1(SEQ ID NOs:343 和 770)，或其修饰变体或未修饰变体。

[3564] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40034.1(SEQ ID NOs:344 和 771)，或其修饰变体或未修饰变体。

[3565] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39999.1(SEQ ID NOs:345 和 772)，或其修饰变体或未修饰变体。

[3566] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40005.1(SEQ ID NOs:346 和 773)，或其修饰变体或未修饰变体。

[3567] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40011.1(SEQ ID NOs:347 和 774)，或其修饰变体或未修饰变体。

[3568] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40017.1(SEQ ID NOs:348 和 775)，或其修饰变体或未修饰变体。

[3569] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40029.1(SEQ ID NOs:349 和 776)，或其修饰变体或未修饰变体。

[3570] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40035.1(SEQ ID NOs:350 和 777)，或其修饰变体或未修饰变体。

[3571] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39994.1(SEQ ID NOs:351 和 778)，或其修饰变体或未修饰变体。

[3572] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40000.1(SEQ ID NOs:352 和 779)，或其修饰变体或未修饰变体。

[3573] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40006.1(SEQ ID NOs:353 和 780)，或其修饰变体或未修饰变体。

[3574] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40012.1(SEQ ID NOs:354 和 781)，或其修饰变体或未修饰变体。

[3575] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40018.1(SEQ ID NOs:355 和 782)，或其修饰变体或未修饰变体。

[3576] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40024.1(SEQ ID NOs:356 和 783)，或其修饰变体或未修饰变体。

[3577] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40030.1(SEQ ID NOs:357 和 784)，或其修饰变体或未修饰变体。

[3578] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40036.1(SEQ ID NOs:358 和 785)，或其修饰变体或未修饰变体。

[3579] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39995.1(SEQ ID NOs:359 和 786)，或其修饰变体或未修饰变体。

[3580] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40001.1(SEQ ID NOs:360 和 787)，或其修饰变体或未修饰变体。

[3581] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40007.1(SEQ ID NOs:361 和 788)，或其修饰变体或未修饰变体。

[3582] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40013.1(SEQ ID NOs:362 和 789)，或其修饰变体或未修饰变体。

[3583] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40019.1(SEQ ID NOs:363 和 790)，或其修饰变体或未修饰变体。

[3584] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40025.1(SEQ ID NOs:364 和 791)，或其修饰变体或未修饰变体。

[3585] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40031.1(SEQ ID NOs:365 和 792)，或其修饰变体或未修饰变体。

[3586] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40037.1(SEQ ID NOs:366 和 793)，或其修饰变体或未修饰变体。

[3587] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39996.1(SEQ ID NOs:367 和 794)，或其修饰变体或未修饰变体。

[3588] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40002.1(SEQ ID NOs:368 和 795)，或其修饰变体或未修饰变体。

[3589] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40008.1(SEQ ID NOs:369 和 796)，或其修饰变体或未修饰变体。

[3590] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40014.1(SEQ ID NOs:370 和 797)，或其修饰变体或未修饰变体。

[3591] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40020.1(SEQ ID NOs:371 和 798)，或其修饰变体或未修饰变体。

[3592] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40026.1(SEQ ID NOs:372 和 799)，或其修饰变体或未修饰变体。

[3593] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40032.1(SEQ ID NOs:373 和 800)，或其修饰变体或未修饰变体。

[3594] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40038.1(SEQ ID NOs:374 和 801)，或其修饰变体或未修饰变体。

[3595] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39997.1(SEQ ID NOs:375 和 802)，或其修饰变体或未修饰变体。

[3596] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40009.1(SEQ ID NOs:376 和 803)，或其修饰变体或未修饰变体。

[3597] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40015.1(SEQ ID NOs:377 和 804)，或其修饰变体或未修饰变体。

[3598] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40021.1(SEQ ID NOs:378 和 805)，或其修饰变体或未修饰变体。

[3599] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40027.1(SEQ ID NOs:379 和 806)，或其修饰变体或未修饰变体。

[3600] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40033.1(SEQ ID NOs:380 和 807)，或其修饰变体或未修饰变体。

[3601] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40039.1(SEQ ID NOs:381 和 808)，或其修饰变体或未修饰变体。

[3602] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40045.1(SEQ ID NOs:382 和 809)，或其修饰变体或未修饰变体。

[3603] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40051.1(SEQ ID NOs:383 和 810)，或其修饰变体或未修饰变体。

[3604] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40057.1(SEQ ID NOs:384 和 811)，或其修饰变体或未修饰变体。

[3605] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40063.1(SEQ ID NOs:385 和 812)，或其修饰变体或未修饰变体。

[3606] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40069.1(SEQ ID NOs:386 和 813)，或其修饰变体或未修饰变体。

[3607] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40075.1(SEQ ID NOs:387 和 814)，或其修饰变体或未修饰变体。

[3608] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40081.1(SEQ ID NOs:388 和 815)，或其修饰变体或未修饰变体。

[3609] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40040.1(SEQ ID NOs:389 和 816)，或其修饰变体或未修饰变体。

[3610] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40046.1(SEQ ID NOs:390 和 817)，或其修饰变体或未修饰变体。

[3611] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40052.1(SEQ ID NOs:391 和 818)，或其修饰变体或未修饰变体。

[3612] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40058.1(SEQ ID NOs:392 和 819)，或其修饰变体或未修饰变体。

[3613] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40064.1(SEQ ID NOs:393 和 820)，或其修饰变体或未修饰变体。

[3614] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40070.1(SEQ ID NOs:394 和 821)，或其修饰变体或未修饰变体。

[3615] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40076.1(SEQ ID NOs:395 和 822)，或其修饰变体或未修饰变体。

[3616] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40082.1(SEQ ID NOs:396 和 823)，或其修饰变体或未修饰变体。

[3617] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40041.1(SEQ ID NOs:397 和 824)，或其修饰变体或未修饰变体。

[3618] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40047.1(SEQ ID NOs:398 和 825)，或其修饰变体或未修饰变体。

[3619] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40053.1(SEQ ID NOs:399 和 826)，或其修饰变体或未修饰变体。

[3620] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40059.1(SEQ ID NOs:400 和 827)，或其修饰变体或未修饰变体。

[3621] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40065.1(SEQ ID NOs:401 和 828)，或其修饰变体或未修饰变体。

[3622] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40071.1(SEQ ID NOs:402 和 829)，或其修饰变体或未修饰变体。

[3623] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40077.1(SEQ ID NOs:403 和 830)，或其修饰变体或未修饰变体。

[3624] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40083.1(SEQ ID NOs:404 和 831)，或其修饰变体或未修饰变体。

[3625] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40042.1(SEQ ID NOs:405 和 832)，或其修饰变体或未修饰变体。

[3626] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40048.1(SEQ ID NOs:406 和 833)，或其修饰变体或未修饰变体。

[3627] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40054.1(SEQ ID NOs:407 和 834)，或其修饰变体或未修饰变体。

[3628] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40060.1(SEQ ID NOs:408 和 835)，或其修饰变体或未修饰变体。

[3629] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40066.1(SEQ ID NOs:409 和 836)，或其修饰变体或未修饰变体。

[3630] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40072.1(SEQ ID NOs:410 和 837)，或其修饰变体或未修饰变体。

[3631] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40078.1(SEQ ID NOs:411 和 838)，或其修饰变体或未修饰变体。

[3632] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40084.1(SEQ ID NOs:412 和 839)，或其修饰变体或未修饰变体。

[3633] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40043.1(SEQ ID NOs:413 和 840)，或其修饰变体或未修饰变体。

[3634] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40049.1(SEQ ID NOs:414 和 841)，或其修饰变体或未修饰变体。

[3635] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40055.1(SEQ ID NOs:415 和 842)，或其修饰变体或未修饰变体。

[3636] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40061.1(SEQ ID NOs:416 和 843)，或其修饰变体或未修饰变体。

[3637] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40067.1(SEQ ID NOs:417 和 844)，或其修饰变体或未修饰变体。

[3638] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40073.1(SEQ ID NOs:418 和 845)，或其修饰变体或未修饰变体。

[3639] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40079.1(SEQ ID NOs:419 和 846)，或其修饰变体或未修饰变体。

[3640] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40085.1(SEQ ID NOs:420 和 847)，或其修饰变体或未修饰变体。

[3641] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40044.1(SEQ ID NOs:421 和 848)，或其修饰变体或未修饰变体。

[3642] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40050.1(SEQ ID NOs:422 和 849)，或其修饰变体或未修饰变体。

[3643] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40056.1(SEQ ID NOs:423 和 850)，或其修饰变体或未修饰变体。

[3644] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40062.1(SEQ ID NOs:424 和 851)，或其修饰变体或未修饰变体。

[3645] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40068.1(SEQ ID NOs:425 和 852)，或其修饰变体或未修饰变体。

[3646] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40074.1(SEQ ID NOs:426 和 853)，或其修饰变体或未修饰变体。

[3647] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40080.1(SEQ ID NOs:427 和 854)，或其修饰变体或未修饰变体。

[3648] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39720.1(SEQ ID NOs:1716 和 1754)，或其修饰变体或未修饰变体。

[3649] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39706.1(SEQ ID NOs:1717 和 1755)，或其修饰变体或未修饰变体。

[3650] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39712.1(SEQ ID NOs:1718 和 1756)，或其修饰变体或未修饰变体。

[3651] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39760.1(SEQ ID NOs:1719 和 1757)，或其修饰变体或未修饰变体。

[3652] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39732.1(SEQ ID NOs:1720 和 1758)，或其修饰变体或未修饰变体。

[3653] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-35541.4(SEQ ID NOs:1721 和 1759)，或其修饰变体或未修饰变体。

[3654] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39735.1 或 hs_KRAS_321_A22S26(SEQ ID NOs:1722 和 1760)，或其修饰变体或未修饰变体。

[3655] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39741.1，或其修饰变体或未修饰变体。

[3656] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :hs_KRAS_322_A22S26(SEQ ID NOs:1723 和 1761)，或其修饰变体或未修饰变体。

[3657] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39778.1(SEQ ID NOs:1724 和 1762)，或其修饰变体或未修饰变体。

[3658] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-39790.1(SEQ ID NOs:1725和1763)，或其修饰变体或未修饰变体。

[3659] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-39822.1(SEQ ID NOs:1726和1764)，或其修饰变体或未修饰变体。

[3660] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35609.4(SEQ ID NOs:1727和1765)，或其修饰变体或未修饰变体。

[3661] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35581.4(SEQ ID NOs:1728和1766)，或其修饰变体或未修饰变体。

[3662] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-39845.1(SEQ ID NOs:1729和1767)，或其修饰变体或未修饰变体。

[3663] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-39858.1(SEQ ID NOs:1730和1768)，或其修饰变体或未修饰变体。

[3664] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-39870.1(SEQ ID NOs:1731和1769)，或其修饰变体或未修饰变体。

[3665] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35576.4(SEQ ID NOs:1732和1770)，或其修饰变体或未修饰变体。

[3666] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35588.4(SEQ ID NOs:1733和1771)，或其修饰变体或未修饰变体。

[3667] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35600.1(SEQ ID NOs:1734和1772)，或其修饰变体或未修饰变体。

[3668] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-35606.1(SEQ ID NOs:1735和1773)，或其修饰变体或未修饰变体。

[3669] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-38151.1(SEQ ID NOs:1736和1774)，或其修饰变体或未修饰变体。

[3670] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列包含来自如下RNAi剂的第一链和/或第二链序列的15个连续核苷酸的序列：AD-38163.1(SEQ ID NOs:1737和1775)，或其修饰变体或未修饰变体。

[3671] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-39999.1(SEQ ID NOs:1738 和 1776)，或其修饰变体或未修饰变体。

[3672] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38159.1 或 hs_KRAS_528_A22S26(SEQ ID NOs:1739 和 1777)，或其修饰变体或未修饰变体。

[3673] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38130.1 或 hs_KRAS_531_A22S26(SEQ ID NOs:1740 和 1778)，或其修饰变体或未修饰变体。

[3674] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38136.1(SEQ ID NOs:1741 和 1779)，或其修饰变体或未修饰变体。

[3675] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40036.1(SEQ ID NOs:1742 和 1780)，或其修饰变体或未修饰变体。

[3676] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40008.1(SEQ ID NOs:1743 和 1781)，或其修饰变体或未修饰变体。

[3677] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40021.1(SEQ ID NOs:1744 和 1782)，或其修饰变体或未修饰变体。

[3678] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40077.1(SEQ ID NOs:1745 和 1783)，或其修饰变体或未修饰变体。

[3679] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40072.1(SEQ ID NOs:1746 和 1784)，或其修饰变体或未修饰变体。

[3680] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40061.1(SEQ ID NOs:1747 和 1785)，或其修饰变体或未修饰变体。

[3681] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-40068.1(SEQ ID NOs:1748 和 1786)，或其修饰变体或未修饰变体。

[3682] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38131.1(SEQ ID NOs:1749 和 1787)，或其修饰变体或未修饰变体。

[3683] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :AD-38167.1(SEQ ID NOs:1750 和 1788)，或其修饰变体或未修饰变体。

[3684] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :hs_KRAS 1273_A22S26(SEQ ID NOs:1751 和 1789)，或其修饰变体或未修饰变体。

[3685] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :hs_KRAS 2892_A37S26(SEQ ID NOs:1752 和 1790)，或其修饰变体或未修饰变体。

[3686] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含来自如下 RNAi 剂的第一链和 / 或第二链序列的 15 个连续核苷酸的序列 :hs_KRAS 4731_A22S26(SEQ ID NOs:1753 和 1791)，或其修饰变体或未修饰变体。

[3687] 在多种实施方案中，本公开包括包含有义链和反义链的 RNAi 剂，其中反义链包含与本文公开的任一种 RNAi 剂或其修饰变体或未修饰变体的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中的反义链还任选地包含 0、1、2、3、4、5、6、7、8、9 或 10 个或更多个核苷酸（或其中的任何范围，例如 0-1、1-2、1-3、1-4 个核苷酸等）。

[3688] 在一个实施方案中，本公开包括文中列出的任意一种或多种 RNAi 剂。针对 KRAS 的 RNAi 剂的重叠群组

[3689] 在多种实施方案中，本公开涉及具有重叠序列的针对 KRAS 的 RNAi 剂群组。因此，本公开涵盖 RNAi 剂群组，其中该群组中的每种 RNAi 剂与相同群组中的各其它 RNAi 剂重叠至少 5、6、7、8、9、10、11、12、13、14、15、16、17、18、19 或更多个核苷酸。特别地，在一个实施方案中，该重叠是至少 12 个核苷酸。

[3690] 本文中所列的某些 RNAi 剂在序列中彼此重叠。表 2 中显示了某些重叠 RNAi 剂群组的汇编，其中群组的每个成员与相同群组的各其它成员重叠至少 12 个核苷酸。显示了有义链的 12 个核苷酸重叠部分和反义链的 12 个核苷酸重叠部分。

[3691] 因此，例如，如表 4 中所示，双链体 AD-39695.1、AD-39689.1、AD-39707.1、AD-39683.1 和 AD-39701.1 的序列均有重叠，其中有义链中的重叠包含序列 CUGAAUAUAAAC(SEQ ID NO:1874)，反义链中的重叠包含序列 GUUUAUAUUCAG(SEQ ID NO:1875)。

[3692] 但是，本公开涵盖享有序列重叠（例如重叠至少 12 个核苷酸）这一共同技术特征的 KRAS RNAi 剂的任何群或亚群或组或亚组。因此，本公开不仅涵盖示例性的组 AD-39695.1、AD-39689.1、AD-39707.1、AD-39683.1 和 AD-39701.1，而且涵盖如下亚组 :AD-39695.1 和 AD-39689.1 ;AD-39695.1 和 AD-39707.1 ;AD-39695.1、AD-39689.1 和 AD-39701.1 ;AD-39689.1、AD-39707.1 和 AD-39701.1 ;AD-39707.1 和 AD-39683.1 ; AD-39707.1、AD-39683.1 和 AD-39701.1 等 ;以及重叠 KRAS RNAi 剂的任何其它组。.

[3693] 因此，表 4 中列出的这些以及其它多个群组的重叠 RNAi 剂享有共同的技术特征，例如，在有义链和反义链中的重叠。

[3694] 以下在表 4 中提供针对 KRAS 的重叠 RNAi 剂的特定群组。

[3695] 因此，本公开涵盖包含共同技术特征的 RNAi 剂的任何组或亚组，其中的共同技术特征是有义链或反义链中的序列的重叠（例如重叠至少 12 个核苷酸）。

[3696] 因此，本公开涵盖包含第一链和第二链的 RNAi 剂，其中第一链包含与表 4 中提供的重叠 RNAi 剂的任何组或亚组或群或亚群的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个

连续核苷酸，和/或第二链包含与表4中提供的重叠RNAi剂的任何组或亚组或群或亚群的第二链差异0、1、2或3个核苷酸的至少15个连续核苷酸。

[3697] 本公开还涵盖包括表4中列出的重叠RNAi剂组的多种实施方案。

[3698] 额外的定义

[3699] 除非另外定义，否则本文所用的技术和科学术语具有与熟悉本公开所属技术领域的专业人员通常所理解的相同含义。

[3700] 除非另外指明，否则没有详细地具体描述的全部方法、步骤、技术和操作可以并且已经按本身已知的方式进行，这对技术人员是显而易见的。例如，再次参考本文中提到的标准手册和一般背景技术并参考其中所引用的其它参考文献。

[3701] 对本公开的权利要求是非限制性的并且在下文提供。

[3702] 虽然已经在本文中详细公开了具体实施方案和权利要求，但是这仅出于说明目的以举例方式进行，并且不意欲限制所附权利要求书的范围或任何相应未来应用的权利要求的主题的范围。具体而言，发明人构思了可以对本公开作出各种替换、改变和修饰而不脱离如权利要求书所定义的本公开的精神和范围。确信选择核酸起始材料、目的克隆或文库类型是知晓本文所述的实施方案的本领域普通技术人员的例行工作。其它方面、优点和修改视为处于以下权利要求的范围内。对之后提交的相应申请中权利要求书范围的重新撰写可能是由于各个国家的专利法的限制并且不应当解读为放弃权利要求的主题。

[3703] 本领域普通技术人员可以构思所描述的针对KRAS的RNAi剂的各种额外制剂和明显变体。以下实施例中描述了针对KRAS的RNAi剂的非限制性例子，所述例子不限制如权利要求书中所述的本公开的范围。

实施例

[3704] 实施例1

[3705] 生物信息学和KRAS RNAi剂(siRNA)序列

[3706] 在如下的表2和表3中提供未修饰和示例性修饰的KRAS RNAi剂的序列。

[3707] 进行KRAS寡核苷酸设计以鉴定靶向于编码KRAS基因的mRNA的siRNA。

[3708] 实验方法

[3709] 生物信息学

[3710] 转录物

[3711] 进行siRNA设计以鉴定靶向于人Kirsten大鼠肉瘤病毒致癌基因(KRAS)的RNAi剂(例如siRNAs)。该设计使用来自NCBI(国家生物技术信息中心)参考序列集合的如下转录物:KRAS-NM_033360.2、NM_004985.3。对于KRAS，不要求与非人灵长类食蟹猴的完美匹配。

[3712] siRNA设计和特异性预测

[3713] 从每个序列预测全部可能的19聚物的预测特异性。然后选择候选19聚物作为匹配编码序列(“CDS”)或非翻译区(“UTR”)。使用FASTA算法，将各基因(KRAS，来自CDS的432个)的候选siRNA用于针对人转录组(定义为人NCBI参考序列集合内部的NM_记录和XM_记录的集合)的综合检索。然后用perl脚本‘parseFasta.pl’来解析比对结果并基于siRNA和任何潜在’脱靶’转录物之间错配的位置和数目产生评分。将脱靶评分加

权以强调 siRNA 的“种子”区域内（距分子 5’ 末端的位置 2-9 中）的差异。通过汇总独立错配评分，向来自 FASTA 检索的每个寡聚物 - 转录物对给予错配评分；将位置 2-9 中的错配计为 2.8，将切割位点位置 10-11 中的错配计为 1.2，并且将区域 12-19 中的错配计为 1.0。通过比较从每种寡聚物的种子衍生的 3 种不同六聚物所衍生的七聚物和八聚物的频率实施额外的脱靶预测。相对于 5’起点距离位置 2-7 的六聚物用来产生 2 种七聚物和 1 种八聚物。通过添加一个 3’A 至六聚物产生‘七聚物 1’；通过添加一个 5’A 至六聚物产生‘七聚物 2’；通过在六聚物的 5’ 末端和 3’ 末端都添加 A 产生‘八聚物’。事先计算人 3’ UTRome（定义为来自其中清晰限定编码区（‘CDS’）末端的 NCBI 参考序列数据库的转录组的子序列）中八聚物和七聚物的频率。使用来自八聚物频率范围的中位值，将八聚物频率对七聚物频率归一化。随后通过计算 [(3X 归一化八聚物计数)+(2X 七聚物 2 计数)+(1X 七聚物 1 计数)] 的总和，计算出“mirSeedScore”。

[3714] 两条 siRNA 链均根据计算的评分分配至一个特异性分类：将高于 3 的评分看做高度特异性，将等于 3 的评分看做特异性并且将 2.2 和 2.8 之间的评分看做中等特异性。借助反义链的特异性进行分选。

[3715] siRNA 序列选择

[3716] 合成了衍生的有义和反义 siRNA 寡聚物并形成双链体。每个基因的双链体总数为：KRAS，432 个。

[3717] KRAS 序列的合成

[3718] 合成：

[3719] 在 MerMade 192 合成仪上以 1 μmol 规模合成 KRAS 序列。合成用于人 KRAS 基因的总共 864 个单链序列 (432 个双链体)。对于全部序列，如下文详述那样实施‘endolight’化学法。

[3720] • 将有义链中的全部嘧啶（胞嘧啶和尿苷）均替换为相应的 2’-O- 甲基碱基 (2’ O- 甲基 C 和 2’ -O- 甲基 U)

[3721] • 在反义链中，将毗邻（指向 5’ 位置）核糖 A 核苷的嘧啶 (C 和 U) 替换为它们相应的 2-O- 甲基核苷

[3722] • 在有义序列和反义序列的 3’ 末端引入双碱基 dTdT 延长。这个双碱基突出端具有磷酸二酯键

[3723] • 序列文件转换成文本文件，以便使其相容于在 MerMade 192 合成软件中加载。

[3724] 利用亚磷酰胺化学法，采用固相支持的寡核苷酸合成法合成 KRAS 序列。

[3725] 上述序列的合成以 1 μm 规模在 96 孔板中进行并且每轮产生 192 个序列。以 0.1M 浓度制备亚磷酰胺 (amidite) 溶液并使用乙基硫代四唑 (0.6M 的乙腈溶液) 作为活化剂。

[3726] 切割和脱保护：

[3727] 在 96 孔平板中，在第一步中使用甲胺的水溶液和乙醇溶液的混合物 (3:1 比例) 并在第二步中使用三乙胺 ^{3}HF，切下合成的序列并使其脱保护。使用丙酮：乙醇混合物沉淀如此获得的粗制序列并将沉淀物重悬于 0.02M 乙酸钠缓冲液中。通过 LC-MS 分析来自每个序列的样品，所得的质量数据证实序列的身份。还通过 IEX 色谱分析所选择的样品集合。

[3728] 纯化和脱盐：

[3729] 在复性步骤前，所有的单链以脱盐水溶液的形式分离。将序列在 AKTA 探索者纯化

系统上使用 Source 15Q 柱纯化。使用柱和设定在 60℃的内嵌缓冲液加热器进行纯化。将对应于全长序列的单峰收集在洗脱剂中并随后通过离子交换色谱分析纯度。

[3730] 使用 AKTA 纯化仪，在 SephadexG25 柱上使纯化的序列脱盐。对脱盐的 KRAS 序列分析浓度和纯度。随后使单链在自动化平台上复性以形成 siRNA 双链体。每种双链体以 10 μM 的浓度在 1x PBS 中制备并通过毛细管凝胶电泳分析纯度。在表 1 和表 3 中提供了各双链体的详细信息。表 2 以及本文中其它表中的一些序列代表列举的 RNAi 剂的 DNA 靶（这些 DNA 靶包含含有 T 的 DNA 序列而不是含有 U 的 RNA 序列）。

[3731] 表 2. 具有未修饰的序列的 KRAS 双链体

[3732]

双链体	有义序列	SEQ ID NO:	反义序列	SEQ ID NO:
AD-35523.3	GGACGAAUAUGAUCCAACA	1	UGUUGGAUCAUAUUCGUCC	428
AD-35529.1	GACGAAUAUGAUCCAACAA	2	UUGUUGGAUCAUAUUCGUC	429
AD-35535.4	ACGAAUAUGAUCCAACAAU	3	AUUGUUGGAUCAUAUUCGU	430
AD-35541.4	CGAAUAUGAUCCAACAAUA	4	UAUUGUUGGAUCAUAUUCG	431
AD-35547.4	GAAUAUGAUCCAACAAUAG	5	CUAUUGUUGGAUCAUAUUC	432
AD-35553.4	AAUAUGAUCCAACAAUAGA	6	UCUAUUGUUGGAUCAUAUU	433
AD-35559.4	AUAUGAUCCAACAAUAGAG	7	CUCUAUUGUUGGAUCAUAU	434
AD-35565.4	UAUGAUCCAACAAUAGAGG	8	CCUCUAUUGUUGGAUCAUA	435
AD-35524.4	AUGAUCCAACAAUAGAGGA	9	UCCUCUAUUGUUGGAUCAU	436
AD-35530.4	UGAUCCAACAAUAGAGGAU	10	AUCCUCUAUUGUUGGAUCA	437

[3733]

AD-35536.4	GAUCCAACAAUAGAGGAUU	11	AAUCCUCUAUUGUUGGAUC	438
AD-35542.4	AUCCAACAAUAGAGGAUUC	12	GAAUCCUCUAUUGUUGGAU	439
AD-35548.4	UCCAACAAUAGAGGAUUCC	13	GGAAUCCUCUAUUGUUGGA	440
AD-35554.4	CCAACAAUAGAGGAUUCCU	14	AGGAAUCCUCUAUUGUUGG	441
AD-35560.2	CAACAAUAGAGGAUUCCUA	15	UAGGAAUCCUCUAUUGUUG	442
AD-35566.4	AACAAUAGAGGAUUCCUAC	16	GUAGGAAUCCUCUAUUGUU	443
AD-35525.2	ACAAUAGAGGAUUCCUACA	17	UGUAGGAAUCCUCUAUUGU	444
AD-35531.4	CAAUAGAGGAUUCCUACAG	18	CUGUAGGAAUCCUCUAUUG	445
AD-35537.4	AAUAGAGGAUUCCUACAGG	19	CCUGUAGGAAUCCUCUAUU	446
AD-35543.2	AUAGAGGAUUCCUACAGGA	20	UCCUGUAGGAAUCCUCUAU	447
AD-35549.4	UAGAGGAUUCCUACAGGAA	21	UUCCUGUAGGAAUCCUCUA	448
AD-35555.4	AGAGGAUUCCUACAGGAAG	22	CUUCCUGUAGGAAUCCUCU	449
AD-35561.4	GAGGAUUCCUACAGGAAGC	23	GCUUCCUGUAGGAAUCCUC	450
AD-35567.4	AGGAUUCCUACAGGAAGCA	24	UGCUUCCUGUAGGAAUCCU	451
AD-35526.4	GGAUUCCUACAGGAAGCAA	25	UUGCUUCCUGUAGGAAUCC	452
AD-35532.4	GAUUCCUACAGGAAGCAAG	26	CUUGCUUCCUGUAGGAAUC	453
AD-35538.4	AUUCCUACAGGAAGCAAGU	27	ACUUGCUUCCUGUAGGAAU	454
AD-35544.4	UUCCUACAGGAAGCAAGUA	28	UACUUGCUUCCUGUAGGAA	455
AD-35550.4	UCCUACAGGAAGCAAGUAG	29	CUACUUGCUUCCUGUAGGA	456
AD-35556.4	CCUACAGGAAGCAAGUAGU	30	ACUACUUGCUUCCUGUAGG	457
AD-35562.4	CUACAGGAAGCAAGUAGUA	31	UACUACUUGCUUCCUGUAG	458
AD-35568.4	UACAGGAAGCAAGUAGUAA	32	UUACUACUUGCUUCCUGUA	459
AD-35527.4	ACAGGAAGCAAGUAGUAAU	33	AUUACUACUUGCUUCCUGU	460
AD-35533.4	CAGGAAGCAAGUAGUAAUU	34	AAUUACUACUUGCUUCCUG	461
AD-35539.4	UUGGAUAUUCUCGACACAG	35	CUGUGUCGAGAAUAUCCAA	462
AD-35545.4	UGGAUAUUCUCGACACAGC	36	GCUGUGUCGAGAAUAUCCA	463
AD-35551.4	GGAUAUUCUCGACACAGCA	37	UGCUGUGUCGAGAAUAUCC	464
AD-35563.4	AUAUUCUCGACACAGCAGG	38	CCUGCUGUGUCGAGAAUAU	465
AD-35528.4	AUUCUCGACACAGCAGGUC	39	GACCUGCUGUGUCGAGAAU	466
AD-35540.4	UCUCGACACAGCAGGUCAA	40	UUGACCUGCUGUGUCGAGA	467
AD-35546.4	CUCGACACAGCAGGUCAAG	41	CUUGACCUGCUGUGUCGAG	468
AD-35552.4	UCGACACAGCAGGUCAAGA	42	UCUUGACCUGCUGUGUCGA	469
AD-35558.4	CGACACAGCAGGUCAAGAG	43	CUCUUGACCUGCUGUGUCG	470
AD-35564.4	GACACAGCAGGUCAAGAGG	44	CCUCUUGACCUGCUGUGUC	471
AD-35570.4	ACACAGCAGGUCAAGAGGA	45	UCCUCUUGACCUGCUGUGU	472
AD-35571.4	CACAGCAGGUCAAGAGGAG	46	CUCCUCUUGACCUGCUGUG	473
AD-35577.4	ACAGCAGGUCAAGAGGAGU	47	ACUCCUCUUGACCUGCUGU	474
AD-35583.4	CAGCAGGUCAAGAGGAGUA	48	UACUCCUCUUGACCUGCUG	475
AD-35589.4	AGCAGGUCAAGAGGAGUAC	49	GUACUCCUCUUGACCUGCU	476
AD-35595.4	GCAGGUCAAGAGGAGUACA	50	UGUACUCCUCUUGACCUGC	477
AD-35601.4	CAGGUCAAGAGGAGUACAG	51	CUGUACUCCUCUUGACCUG	478
AD-35607.4	AGGUCAAGAGGAGUACAGU	52	ACUGUACUCCUCUUGACCU	479
AD-35613.4	GGUCAAGAGGAGUACAGUG	53	CACUGUACUCCUCUUGACC	480
AD-35572.4	CUCAAGACCAGUACAGUCC	54	GCACUGUACUCCUCUUGAC	481

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AD-35578.4	UCAAGAGGAGUACAGUGCA	55	UGCACUGUACUCCUCUUGA	482
AD-35584.4	CAAGAGGAGUACAGUGCAA	56	UUGCACUGUACUCCUCUUG	483
AD-35590.4	AAGAGGAGUACAGUGCAAU	57	AUUGCACUGUACUCCUCUU	484
AD-35596.4	AGAGGAGUACAGUGCAAUG	58	CAUUGCACUGUACUCCUCU	485
AD-35602.4	GAGGAGUACAGUGCAAUGA	59	UCAUUGCACUGUACUCCUC	486
AD-35608.4	AGGAGUACAGUGCAAUGAG	60	CUCAUUGCACUGUACUCCU	487
AD-35614.4	GGAGUACAGUGCAAUGAGG	61	CCUCAUUGCACUGUACUCC	488
AD-35573.4	GAGUACAGUGCAAUGAGGG	62	CCCUCAUUGCACUGUACUC	489
AD-35579.4	GGGGAGGGCUUUCUUUGUG	63	CACAAAGAAAGCCCUCCCC	490
AD-35585.4	GGGAGGGCUUUCUUUGUGU	64	ACACAAAGAAAGCCCUCCC	491
AD-35591.4	GGAGGGCUUUCUUUGUGUA	65	UACACAAAGAAAGCCCUCC	492
AD-35597.4	GAGGGCUUUCUUUGUGUAU	66	AUACACAAAGAAAGCCCUC	493
AD-35603.4	AGGGCUUUCUUUGUGUAUU	67	AAUACACAAAGAAAGCCCU	494
AD-35609.4	GGGCUUUCUUUGUGUAUUU	68	AAAUACACAAAGAAAGCCC	495
AD-35615.4	GGCUUUCUUUGUGUAUUUG	69	CAAAUACACAAAGAAAGCC	496
AD-35574.4	GCUUUCUUUGUGUAUUUGC	70	GCAAAUACACAAAGAAAGC	497
AD-35580.1	CUUUCUUUGUGUAUUUGCC	71	GGCAAAUACACAAAGAAAG	498
AD-35586.4	UUUCUUUGUGUAUUUGCCA	72	UGGCAAAUACACAAAGAAA	499
AD-35592.4	UUCUUUGUGUAUUUGCCAU	73	AUGGCAAAUACACAAAGAA	500
AD-35598.4	UCUUUGUGUAUUUGCCAUA	74	UAUGGCAAAUACACAAAGA	501
AD-35604.4	CUUUGUGUAUUUGCCAUAA	75	UUAUGGCAAAUACACAAAG	502
AD-35610.4	UUUGUGUAUUUGCCAUAAA	76	UUUAUGGCAAAUACACAAA	503
AD-35616.4	UUGUGUAUUUGCCAUAAAU	77	AUUUAUGGCAAAUACACAA	504
AD-35575.4	UGUGUAUUUGCCAUAAAUA	78	UAUUUAUGGCAAAUACACA	505
AD-35581.4	GUGUAUUUGCCAUAAAUAA	79	UUAUUUAUGGCAAAUACAC	506
AD-35587.4	UGUAUUUGCCAUAAAUAAU	80	AUUAUUUAUGGCAAAUACA	507
AD-35593.4	GUAUUUGCCAUAAAUAAUA	81	UAUUAUUUAUGGCAAAUAC	508
AD-35599.4	UAUUUGCCAUAAAUAAUAC	82	GUAUUAUUUAUGGCAAAUA	509
AD-35605.4	AUUUGCCAUAAAUAAUACU	83	AGUAUUAUUUAUGGCAAAU	510
AD-35611.4	UUUGCCAUAAAUAAUACUA	84	UAGUAUUAUUUAUGGCAAA	511
AD-35617.4	UGAAGAUAUUCACCAUUAU	85	AUAAUGGUGAAUAUCUUCA	512
AD-35576.4	GAAGAUAUUCACCAUUAUA	86	UAUAAUGGUGAAUAUCUUC	513
AD-35588.4	AGAUAUUCACCAUUAUAGA	87	UCUAUAAUGGUGAAUAUCU	514
AD-35667.1	AAACAUCAGCAAAGACAAG	88	CUUGUCUUUGCUGAUGUUU	515
AD-35673.1	AACAUCAGCAAAGACAAGA	89	UCUUGUCUUUGCUGAUGUU	516
AD-35679.1	ACAUCAGCAAAGACAAGAC	90	GUCUUGUCUUUGCUGAUGU	517
AD-35685.1	CAUCAGCAAAGACAAGACA	91	UGUCUUGUCUUUGCUGAUG	518
AD-35691.1	AUCAGCAAAGACAAGACAG	92	CUGUCUUGUCUUUGCUGAU	519
AD-35557.1	GAUAUUCUCGACACAGCAG	93	CUGCUGUGUCGAGAAUAUC	520
AD-35618.1	UUCACCAUUAUAGAGAACA	94	UGUUCUCUAUAAUGGUGAA	521
AD-35569.1	UAUUCUCGACACAGCAGGU	95	ACCUGCUGUGUCGAGAAUA	522
AD-35534.1	UUCUCGACACAGCAGGUCA	96	UGACCUGCUGUGUCGAGAA	523
AD-35582.1	AAGAUAUUCACCAUUAUAG	97	CUAUAAUGGUGAAUAUCUU	524
AD-35594.1	CAUAUUCACCAUUAUAGAG	98	CUCUAUAAUGGUGAAUAUC	525

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AD-35600.1	AUAUUCACCAUUAUAGAGA	99	UCUCUAUAAUGGUGAAUAU	526
AD-35606.1	UAUUCACCAUUAUAGAGAA	100	UUCUCUAUAAUGGUGAAUA	527
AD-35612.1	AUUCACCAUUAUAGAGAAC	101	GUUCUCUAUAAUGGUGAAU	528
AD-38127.1	UCACCAUUAUAGAGAACAA	102	UUGUUCUCUAUAAUGGUGA	529
AD-38133.1	CACCAUUAUAGAGAACAAA	103	UUUGUUCUCUAUAAUGGUG	530
AD-38139.1	ACCAUUAUAGAGAACAAAU	104	AUUUGUUCUCUAUAAUGGU	531
AD-38145.1	CCAUUAUAGAGAACAAAUU	105	AAUUUGUUCUCUAUAAUGG	532
AD-38151.1	CAUUAUAGAGAACAAAUUA	106	UAAUUUGUUCUCUAUAAUG	533
AD-38157.1	AUUAUAGAGAACAAAUUAA	107	UUAAUUUGUUCUCUAUAAU	534
AD-38163.1	UUAUAGAGAACAAAUUAAA	108	UUUAAUUUGUUCUCUAUAA	535
AD-38169.1	UAUAGAGAACAAAUUAAAA	109	UUUUAAUUUGUUCUCUAUA	536
AD-38128.1	AUAGAGAACAAAUUAAAAG	110	CUUUUAAUUUGUUCUCUAU	537
AD-38134.1	UAGAGAACAAAUUAAAAGA	111	UCUUUUAAUUUGUUCUCUA	538
AD-38140.1	AGAGAACAAAUUAAAAGAG	112	CUCUUUUAAUUUGUUCUCU	539
AD-38146.1	GAAGAUGUACCUAUGGUCC	113	GGACCAUAGGUACAUCUUC	540
AD-38152.1	AAGAUGUACCUAUGGUCCU	114	AGGACCAUAGGUACAUCUU	541
AD-38158.1	AGAUGUACCUAUGGUCCUA	115	UAGGACCAUAGGUACAUCU	542
AD-38164.1	GAUGUACCUAUGGUCCUAG	116	CUAGGACCAUAGGUACAUC	543
AD-38170.1	AUGUACCUAUGGUCCUAGU	117	ACUAGGACCAUAGGUACAU	544
AD-38129.1	UGUACCUAUGGUCCUAGUA	118	UACUAGGACCAUAGGUACA	545
AD-38135.1	GUACCUAUGGUCCUAGUAG	119	CUACUAGGACCAUAGGUAC	546
AD-38141.1	UACCUAUGGUCCUAGUAGG	120	CCUACUAGGACCAUAGGUA	547
AD-38147.1	ACCUAUGGUCCUAGUAGCA	121	UCCUACUAGGACCAUAGGU	548
AD-38153.1	CCUAUGGUCCUAGUAGGAA	122	UUCCUACUAGGACCAUAGG	549
AD-38159.1	CUAUGGUCCUAGUAGGAAA	123	UUUCCUACUAGGACCAUAG	550
AD-38165.1	UAUGGUCCUAGUAGGAAAU	124	AUUUCCUACUAGGACCAUA	551
AD-38171.1	AUGGUCCUAGUAGGAAAUA	125	UAUUUCCUACUAGGACCAU	552
AD-38130.1	UGGUCCUAGUAGGAAAUAA	126	UUAUUUCCUACUAGGACCA	553
AD-38136.1	GGUCCUAGUAGGAAAUAAA	127	UUUAUUUCCUACUAGGACC	554
AD-38142.1	GUCCUAGUAGGAAAUAAAU	128	AUUUAUUUCCUACUAGGAC	555
AD-38148.1	UCCUAGUAGGAAAUAAAUG	129	CAUUUAUUUCCUACUAGGA	556
AD-38154.1	CCUAGUAGGAAAUAAAUGU	130	ACAUUUAUUUCCUACUAGG	557
AD-38160.1	CUAGUAGGAAAUAAAUGUG	131	CACAUUUAUUUCCUACUAG	558
AD-38166.1	UAGUAGGAAAUAAAUGUGA	132	UCACAUUUAUUUCCUACUA	559
AD-38172.1	AGUAGGAAAUAAAUGUGAU	133	AUCACAUUUAUUUCCUACU	560
AD-38131.1	GGAAUUCCUUUUAUUGAAA	134	UUUCAAUAAAAGGAAUUCC	561
AD-38137.1	GAAUUCCUUUUAUUGAAAC	135	GUUUCAAUAAAAGGAAUUC	562
AD-38143.1	AAUUCCUUUUAUUGAAACA	136	UGUUUCAAUAAAAGGAAUU	563
AD-38149.1	AUUCCUUUUAUUGAAACAU	137	AUGUUUCAAUAAAAGGAAU	564
AD-38155.1	UUCCUUUUAUUGAAACAUC	138	GAUGUUUCAAUAAAAGGAA	565
AD-38161.1	UCCUUUUAUUGAAACAUCA	139	UGAUGUUUCAAUAAAAGGA	566
AD-38167.1	CCUUUUAUUGAAACAUCAG	140	CUGAUGUUUCAAUAAAAGG	567
AD-38173.1	CUUUUAUUGAAACAUCAGC	141	GCUGAUGUUUCAAUAAAAG	568
AD-38132.1	UUUUAUUGAAACAUCAGCA	142	UGCUGAUGUUUCAAUAAAA	569

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AD-38138.1	UUUAUUGAAACAUCAGCAA	143	UUGCUGAUGUUUCAAUAAA	570
AD-38144.1	UUAUUGAAACAUCAGCAAA	144	UUUGCUGAUGUUUCAAUAA	571
AD-38150.1	UAUUGAAACAUCAGCAAAG	145	CUUUGCUGAUGUUUCAAUA	572
AD-38156.1	AUUGAAACAUCAGCAAAGA	146	UCUUUGCUGAUGUUUCAAU	573
AD-38162.1	UUGAAACAUCAGCAAAGAC	147	GUCUUUGCUGAUGUUUCAA	574
AD-38168.1	UGAAACAUCAGCAAAGACA	148	UGUCUUUGCUGAUGUUUCA	575
AD-38174.1	GAAACAUCAGCAAAGACAA	149	UUGUCUUUGCUGAUGUUUC	576
AD-39683.1	AUGACUGAAUAUAAACUUG	150	CAAGUUUAUAUUCAGUCAU	577
AD-39689.1	UGACUGAAUAUAAACUUGU	151	ACAAGUUUAUAUUCAGUCA	578
AD-39695.1	GACUGAAUAUAAACUUGUG	152	CACAAGUUUAUAUUCAGUC	579
AD-39701.1	ACUGAAUAUAAACUUGUGG	153	CCACAAGUUUAUAUUCAGU	580
AD-39707.1	CUGAAUAUAAACUUGUGGU	154	ACCACAAGUUUAUAUUCAG	581
AD-39713.1	UGAAUAUAAACUUGUGGUA	155	UACCACAAGUUUAUAUUCA	582
AD-39719.1	GAAUAUAAACUUGUGGUAG	156	CUACCACAAGUUUAUAUUC	583
AD-39725.1	AAUAUAAACUUGUGGUAGU	157	ACUACCACAAGUUUAUAUU	584
AD-39684.1	AUAUAAACUUGUGGUAGUU	158	AACUACCACAAGUUUAUAU	585
AD-39690.1	UAUAAACUUGUGGUAGUUG	159	CAACUACCACAAGUUUAUA	586
AD-39696.1	AUAAACUUGUGGUAGUUGG	160	CCAACUACCACAAGUUUAU	587
AD-39702.1	UAAACUUGUGGUAGUUGGA	161	UCCAACUACCACAAGUUUA	588
AD-39708.1	AAACUUGUGGUAGUUGGAG	162	CUCCAACUACCACAAGUUU	589
AD-39714.1	AACUUGUGGUAGUUGGAGC	163	GCUCCAACUACCACAAGUU	590
AD-39720.1	ACUUGUGGUAGUUGGAGCU	164	AGCUCCAACUACCACAAGU	591
AD-39726.1	CUUGUGGUAGUUGGAGCUG	165	CAGCUGCAACUACCACAAG	592
AD-39685.1	UUGUGGUAGUUGGAGCUGG	166	CCAGCUCCAACUACCACAA	593
AD-39691.1	UGUGGUAGUUGGAGCUGGU	167	ACCAGCUCCAACUACCACA	594
AD-39697.1	GUGGUAGUUGGAGCUGGUG	168	CACCAGCUGCAACUACCAC	595
AD-39703.1	UGGUAGUUGGAGCUGGUGG	169	CCACCAGCUCCAACUACCA	596
AD-39709.1	GGUAGUUGGAGCUGGUGGC	170	GCCACCAGCUCCAACUACC	597
AD-39715.1	GUAGUUGGAGCUCGUGCCG	171	CGGCACCAGGUCCAACUAC	598
AD-39721.1	UAGUUGGAGCUGGUGGCGU	172	ACGCCACCAGCUCCAACUA	599
AD-39727.1	AGUUGGAGCUGGUGGCGUA	173	UACGCCACCAGCUCCAACU	600
AD-39686.1	GUUGGAGCUGGUGGCGUAG	174	CUACGCCACCAGCUCCAAC	601
AD-39692.1	UUGGAGCUGGUGGCGUAGG	175	CCUACGCCACCAGCUCCAA	602
AD-39698.1	UGGAGCUGGUGGCGUAGGC	176	GCCUACGCCACCAGCUCCA	603
AD-39704.1	GGAGCUGGUGGCGUAGGCA	177	UGCCUACGCCACCAGCUCC	604
AD-39710.1	GAGCUGGUGGCGUAGGCAA	178	UUGCCUACGCCACCAGCUC	605
AD-39716.1	AGCUGGUGGCGUAGGCAAG	179	CUUGCCUACGCCACCAGCU	606
AD-39722.1	GCUGGUGGCGUAGGCAAGA	180	UCUUGCCUACGCCACCAGC	607
AD-39728.1	CUGGUGGCGUAGGCAAGAG	181	CUCUUGCCUACGCCACCAG	608
AD-39687.1	UGGUGGCGUAGGCAAGAGU	182	ACUCUUGCCUACGCCACCA	609
AD-39693.1	GGUGGCGUAGGCAAGAGUG	183	CACUCUUGCCUACGCCACC	610
AD-39699.1	GUGGCGUAGGCAAGAGUGC	184	GCACUCUUGCCUACGCCAC	611
AD-39705.1	UGGCGUAGGCAAGAGUGCC	185	GGCACUCUUGCCUACGCCA	612
AD-39711.1	GGCGUAGGCAAGAGUGCCU	186	AGGCACUCUUGCCUACGCC	613

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AD-39717.1	GCGUAGGCAAGAGUGCCUU	187	AAGGCACUCUUGCCUACGC	614
AD-39723.1	CGUAGGCAAGAGUGCCUUG	188	CAAGGCACUCUUGCCUACG	615
AD-39729.1	GUAGGCAAGAGUGCCUUGA	189	UCAAGGCACUCUUGCCUAC	616
AD-39688.1	UAGGCAAGAGUGCCUUGAC	190	GUCAAGGCACUCUUGCCUA	617
AD-39694.1	AGGCAAGAGUGCCUUGACG	191	CGUCAAGGCACUCUUGCCU	618
AD-39700.1	GGCAAGAGUGCCUUGACGA	192	UCGUCAAGGCACUCUUGCC	619
AD-39706.1	GCAAGAGUGCCUUGACGAU	193	AUCGUCAAGGCACUCUUGC	620
AD-39712.1	CAAGAGUGCCUUGACGAUA	194	UAUCGUCAAGGCACUCUUG	621
AD-39718.1	AAGAGUGCCUUGACGAUAC	195	GUAUCGUCAAGGCACUCUU	622
AD-39724.1	AGAGUGCCUUGACGAUACA	196	UGUAUCGUCAAGGCACUCU	623
AD-39730.1	GAGUGCCUUGACGAUACAG	197	CUGUAUCGUCAAGGCACUC	624
AD-39736.1	AGUGCCUUGACGAUACAGC	198	GCUGUAUCGUCAAGGCACU	625
AD-39742.1	GUGCCUUGACGAUACAGCU	199	AGCUGUAUCGUCAAGGCAC	626
AD-39748.1	UGCCUUGACGAUACAGCUA	200	UAGCUGUAUCGUCAAGGCA	627
AD-39754.1	GCCUUGACGAUACAGCUAA	201	UUAGCUGUAUCGUCAAGGC	628
AD-39760.1	CCUUGACGAUACAGCUAAU	202	AUUAGCUGUAUCGUCAAGC	629
AD-39766.1	CUUGACGAUACAGCUAAUU	203	AAUUAGCUGUAUCGUCAAG	630
AD-39772.1	UUGACGAUACAGCUAAUUC	204	GAAUUAGCUGUAUCGUCAA	631
AD-39731.1	UGACGAUACAGCUAAUUCA	205	UGAAUUAGCUGUAUCGUCA	632
AD-39737.1	GACGAUACAGCUAAUUCAG	206	CUGAAUUAGCUGUAUCGUC	633
AD-39743.1	ACGAUACAGCUAAUUCAGA	207	UCUGAAUUAGCUGUAUCGU	634
AD-39749.1	CGAUACAGCUAAUUCAGAA	208	UUCUGAAUUAGCUGUAUCG	635
AD-39755.1	GAUACAGCUAAUUCAGAAU	209	AUUCUGAAUUAGCUGUAUC	636
AD-39761.1	AUACAGCUAAUUCAGAAUC	210	GAUUCUGAAUUAGCUGUAU	637
AD-39767.1	UACAGCUAAUUCAGAAUCA	211	UGAUUCUGAAUUAGCUGUA	638
AD-39773.1	ACAGCUAAUUCAGAAUCAU	212	AUGAUUCUGAAUUAGCUGU	639
AD-39732.1	CAGCUAAUUCAGAAUCAUU	213	AAUGAUUCUGAAUUAGCUG	640
AD-39738.1	AGCUAAUUCAGAAUCAUUU	214	AAAUGAUUCUGAAUUAGCU	641
AD-39744.1	GCUAAUUCAGAAUCAUUUU	215	AAAAUGAUUCUGAAUUAGC	642
AD-39750.1	CUAAUUCAGAAUCAUUUUG	216	CAAAAUGAUUCUGAAUUAG	643
AD-39756.1	UAAUUCAGAAUCAUUUUGU	217	ACAAAAUGAUUCUGAAUUA	644
AD-39762.1	AAUUCAGAAUCAUUUUGUG	218	CACAAAAUGAUUCUGAAUU	645
AD-39768.1	AUUCAGAAUCAUUUUGUGG	219	CCACAAAAUGAUUCUGAAU	646
AD-39774.1	UUCAGAAUCAUUUUGUGGA	220	UCCACAAAAUGAUUCUGAA	647
AD-39733.1	UCAGAAUCAUUUUGUGGAC	221	GUCCACAAAAUGAUUCUGA	648
AD-39739.1	CAGAAUCAUUUUGUGGACG	222	CGUCCACAAAAUGAUUCUG	649
AD-39745.1	AGAAUCAUUUUGUGGACGA	223	UCGUCCACAAAAUGAUUCU	650
AD-39751.1	GAAUCAUUUUGUGGACGAA	224	UUCGUCCACAAAAUGAUUC	651
AD-39757.1	AAUCAUUUUGUGGACGAAU	225	AUUCGUCCACAAAAUGAUU	652
AD-39763.1	AUCAUUUUGUGGACGAAUA	226	UAUUCGUCCACAAAAUGAU	653
AD-39769.1	UCAUUUUGUGGACGAAUAU	227	AUAUUCGUCCACAAAAUGA	654
AD-39775.1	CAUUUUGUGGACGAAUAUG	228	CAUAUUCGUCCACAAAAUG	655
AD-39734.1	AUUUUGUGGACGAAUAUGA	229	UCAUAUUCGUCCACAAAAU	656
AD-39740.1	UUUUGUCGACGAAUAUGAU	230	AUCAUAUUCGUCCACAAAA	657

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AD-39746.1	UUUGUGGACGAAUAUGAUC	231	GAUCAUAUUCGUCCACAAA	658
AD-39752.1	UUGUGGACGAAUAUGAUCC	232	GGAUCAUAUUCGUCCACAA	659
AD-39758.1	UGUGGACGAAUAUGAUCCA	233	UGGAUCAUAUUCGUCCACA	660
AD-39764.1	GUGGACGAAUAUGAUCCAA	234	UUGGAUCAUAUUCGUCCAC	661
AD-39770.1	UGGACGAAUAUGAUCCAAC	235	GUUGGAUCAUAUUCGUCCA	662
AD-39776.1	AGGAAGCAAGUAGUAAUUG	236	CAAUUACUACUUGCUUCCU	663
AD-39735.1	GGAAGCAAGUAGUAAUUGA	237	UCAAUUACUACUUGCUUCC	664
AD-39741.1	GAAGCAAGUAGUAAUUGAU	238	AUCAAUUACUACUUGCUUC	665
AD-39747.1	AAGCAAGUAGUAAUUGAUG	239	CAUCAAUUACUACUUGCUU	666
AD-39753.1	AGCAAGUAGUAAUUGAUGG	240	CCAUCAAUUACUACUUGCU	667
AD-39759.1	GCAAGUAGUAAUUGAUGGA	241	UCCAUCAAUUACUACUUGC	668
AD-39765.1	CAAGUAGUAAUUGAUGGAG	242	CUCCAUCAAUUACUACUUG	669
AD-39771.1	AAGUAGUAAUUGAUGGAGA	243	UCUCCAUCAAUUACUACUU	670
AD-39778.1	AGUAGUAAUUGAUGGAGAA	244	UUCUCCAUCAAUUACUACU	671
AD-39784.1	GUAGUAAUUGAUGGAGAAA	245	UUUCUCCAUCAAUUACUAC	672
AD-39790.1	UAGUAAUUGAUGGAGAAAC	246	GUUUCUCCAUCAAUUACUA	673
AD-39796.1	AGUAAUUGAUGGAGAAACC	247	GGUUUCUCCAUCAAUUACU	674
AD-39802.1	GUAAUUGAUGGAGAAACCU	248	AGGUUUCUCCAUCAAUUAC	675
AD-39808.1	UAAUUGAUGGAGAAACCUG	249	CAGGUUUCUCCAUCAAUUA	676
AD-39814.1	AAUUGAUGGAGAAACCUGU	250	ACAGGUUUCUCCAUCAAUU	677
AD-39820.1	AUUGAUGGAGAAACCUGUC	251	GACAGGUUUCUCCAUCAAU	678
AD-39779.1	UUGAUGGAGAAACCUGUCU	252	AGACAGGUUUCUCCAUCAA	679
AD-39785.1	UGAUGGAGAAACCUGUCUC	253	GAGACAGGUUUCUCCAUCA	680
AD-39791.1	GAUGGAGAAACCUGUCUCU	254	AGAGACAGGUUUCUCCAUC	681
AD-39797.1	AUGGAGAAACCUGUCUCUU	255	AAGAGACAGGUUUCUCCAU	682
AD-39803.1	UGGAGAAACCUGUCUCUUG	256	CAAGAGACAGGUUUCUCCA	683
AD-39809.1	GGAGAAACCUGUCUCUUGG	257	CCAAGAGACAGGUUUCUCC	684
AD-39815.1	GAGAAACCUGUCUCUUGGA	258	UCCAAGAGACAGGUUUCUC	685
AD-39821.1	AGAAACCUGUCUCUUGGAU	259	AUCCAAGAGACAGGUUUCU	686
AD-39780.1	GAAACCUGUCUCUUGGAUA	260	UAUCCAAGAGACAGGUUUC	687
AD-39786.1	AAACCUGUCUCUUGGAUAU	261	AUAUCCAAGAGACAGGUUU	688
AD-39792.1	AACCUGUCUCUUGGAUAUU	262	AAUAUCCAAGAGACAGGUU	689
AD-39798.1	ACCUGUCUCUUGGAUAUUC	263	GAAUAUCCAAGAGACAGGU	690
AD-39804.1	CCUGUCUCUUGGAUAUUCU	264	AGAAUAUCCAAGAGACAGG	691
AD-39810.1	CUGUCUCUUGGAUAUUCUC	265	GAGAAUAUCCAAGAGACAG	692
AD-39816.1	UGUCUCUUGGAUAUUCUCG	266	CGAGAAUAUCCAAGAGACA	693
AD-39822.1	GUCUCUUGGAUAUUCUCGA	267	UCGAGAAUAUCCAAGAGAC	694
AD-39781.1	UCUCUUGGAUAUUCUCGAC	268	GUCGAGAAUAUCCAAGAGA	695
AD-39787.1	CUCUUGGAUAUUCUCGACA	269	UGUCGAGAAUAUCCAAGAG	696
AD-39793.1	UCUUGGAUAUUCUCGACAC	270	GUGUCGAGAAUAUCCAAGA	697
AD-39799.1	CUUGGAUAUUCUCGACACA	271	UGUGUCGAGAAUAUCCAAG	698
AD-39805.1	AGUACAGUGCAAUGAGGGA	272	UCCCUCAUUGCACUGUACU	699
AD-39811.1	GUACAGUGCAAUGAGGGAC	273	GUCCCUCAUUGCACUGUAC	700
AD-39817.1	UACACUGCAAUGAGGGACC	274	GGUCCCUCAUUGCACUGUA	701

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AD-39823.1	ACAGUGCAAUGAGGGACCA	275	UGGUCCCUCAUUGCACUGU	702
AD-39782.1	CAGUGCAAUGAGGGACCAG	276	CUGGUCCCUCAUUGCACUG	703
AD-39788.1	AGUGCAAUGAGGGACCAGU	277	ACUGGUCCCUCAUUGCACU	704
AD-39794.1	GUGCAAUGAGGGACCAGUA	278	UACUGGUCCCUCAUUGCAC	705
AD-39800.1	UGCAAUGAGGGACCAGUAC	279	GUACUGGUCCCUCAUUGCA	706
AD-39806.1	GCAAUGAGGGACCAGUACA	280	UGUACUGGUCCCUCAUUGC	707
AD-39812.1	CAAUGAGGGACCAGUACAU	281	AUGUACUGGUCCCUCAUUG	708
AD-39818.1	AAUGAGGGACCAGUACAUG	282	CAUGUACUGGUCCCUCAUU	709
AD-39824.1	AUGAGGGACCAGUACAUGA	283	UCAUGUACUGGUCCCUCAU	710
AD-39783.1	UGAGGGACCAGUACAUGAG	284	CUCAUGUACUGGUCCCUCA	711
AD-39789.1	GAGGGACCAGUACAUGAGG	285	CCUCAUGUACUGGUCCCUC	712
AD-39795.1	AGGGACCAGUACAUGAGGA	286	UCCUCAUGUACUGGUCCCU	713
AD-39801.1	GGGACCAGUACAUGAGGAC	287	GUCCUCAUGUACUGGUCCC	714
AD-39807.1	GGACCAGUACAUGAGGACU	288	AGUCCUCAUGUACUGGUCC	715
AD-39813.1	GACCAGUACAUGAGGACUG	289	CAGUCCUCAUGUACUGGUC	716
AD-39819.1	ACCAGUACAUGAGGACUGG	290	CCAGUCCUCAUGUACUGGU	717
AD-39825.1	CCAGUACAUGAGGACUGGG	291	CCCAGUCCUCAUGUACUGG	718
AD-39831.1	CAGUACAUGAGGACUGGGG	292	CCCCAGUCCUCAUGUACUG	719
AD-39837.1	AGUACAUGAGGACUGGGGA	293	UCCCCAGUCCUCAUGUACU	720
AD-39843.1	GUACAUGAGGACUGGGGAG	294	CUCCCCAGUCCUCAUGUAC	721
AD-39849.1	UACAUGAGGACUGGGGAGG	295	CCUCCCCAGUCCUCAUGUA	722
AD-39855.1	ACAUGAGGACUGGGGAGGG	296	CCCUCCCCAGUCCUCAUGU	723
AD-39861.1	CAUGAGGACUGGGGAGGGC	297	GCCCUCCCCAGUCCUCAUG	724
AD-39867.1	AUGAGGACUGGGGAGGGCU	298	AGCCCUCCCCAGUCCUCAU	725
AD-39826.1	UGAGGACUGGGGAGGGCUU	299	AAGCCCUCCCCAGUCCUCA	726
AD-39832.1	GAGGACUGGGGAGGGCUUU	300	AAAGCCCUCCCCAGUCCUC	727
AD-39838.1	AGGACUGGGGAGGGCUUUC	301	GAAAGCCCUCCCCAGUCCU	728
AD-39844.1	GGACUGGGGAGGGCUUUCU	302	AGAAAGCCCUCCCCAGUCC	729
AD-39850.1	GACUGGGGAGGGCUUUCUU	303	AAGAAAGCCCUCCCCAGUC	730
AD-39856.1	ACUGGGGAGGGCUUUCUUU	304	AAAGAAAGCCCUCCCCAGU	731
AD-39862.1	CUGGGGAGGGCUUUCUUUG	305	CAAAGAAAGCCCUCCCCAG	732
AD-39868.1	UGGGGAGGGCUUUCUUUGU	306	ACAAAGAAAGCCCUCCCCA	733
AD-39827.1	UUGCCAUAAAUAAUACUAA	307	UUAGUAUUAUUUAUGGCAA	734
AD-39833.1	UGCCAUAAAUAAUACUAAA	308	UUUAGUAUUAUUUAUGGCA	735
AD-39839.1	GCCAUAAAUAAUACUAAAU	309	AUUUAGUAUUAUUUAUGGC	736
AD-39845.1	CCAUAAAUAAUACUAAAUC	310	GAUUUAGUAUUAUUUAUGG	737
AD-39851.1	CAUAAAUAAUACUAAAUCA	311	UGAUUUAGUAUUAUUUAUG	738
AD-39857.1	AUAAAUAAUACUAAAUCAU	312	AUGAUUUAGUAUUAUUUAU	739
AD-39863.1	UAAAUAAUACUAAAUCAUU	313	AAUGAUUUAGUAUUAUUUA	740
AD-39869.1	AAAUAAUACUAAAUCAUUU	314	AAAUGAUUUAGUAUUAUUU	741
AD-39828.1	AAUAAUACUAAAUCAUUUG	315	CAAAUGAUUUAGUAUUAUU	742
AD-39834.1	AUAAUACUAAAUCAUUUGA	316	UCAAAUGAUUUAGUAUUAU	743
AD-39840.1	UAAUACUAAAUCAUUUGAA	317	UUCAAAUGAUUUAGUAUUA	744
AD-39846.1	AAUACUAAAUCAUUUGAAG	318	CUUCAAAUGAUUUAGUAUU	745

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AD-39852.1	AUACUAAAUCAUUUGAAGA	319	UCUUCAAAUGAUUUAGUAU	746
AD-39858.1	UACUAAAUCAUUUGAAGAU	320	AUCUUCAAAUGAUUUAGUA	747
AD-39864.1	ACUAAAUCAUUUGAAGAUA	321	UAUCUUCAAAUGAUUUAGU	748
AD-39870.1	CUAAAUCAUUUGAAGAUAU	322	AUAUCUUCAAAUGAUUUAG	749
AD-39829.1	UAAAUCAUUUGAAGAUAUU	323	AAUAUCUUCAAAUGAUUUA	750
AD-39835.1	AAAUCAUUUGAAGAUAUUC	324	GAAUAUCUUCAAAUGAUUU	751
AD-39841.1	AAUCAUUUGAAGAUAUUCA	325	UGAAUAUCUUCAAAUGAUU	752
AD-39853.1	UCAUUUGAAGAUAUUCACC	326	GGUGAAUAUCUUCAAAUGA	753
AD-39859.1	CAUUUGAAGAUAUUCACCA	327	UGGUGAAUAUCUUCAAAUG	754
AD-39865.1	AUUUGAAGAUAUUCACCAU	328	AUGGUGAAUAUCUUCAAAU	755
AD-39871.1	UUUGAAGAUAUUCACCAUU	329	AAUGGUGAAUAUCUUCAAA	756
AD-39830.1	UUGAAGAUAUUCACCAUUA	330	UAAUGGUGAAUAUCUUCAA	757
AD-39836.1	GAGAACAAAUUAAAAGAGU	331	ACUCUUUUAAUUUGUUCUC	758
AD-39842.1	AGAACAAAUUAAAAGAGUU	332	AACUCUUUUAAUUUGUUCU	759
AD-39848.1	GAACAAAUUAAAAGAGUUA	333	UAACUCUUUUAAUUUGUUC	760
AD-39854.1	AACAAAUUAAAAGAGUUAA	334	UUAACUCUUUUAAUUUGUU	761
AD-39860.1	ACAAAUUAAAAGAGUUAAG	335	CUUAACUCUUUUAAUUUGU	762
AD-39866.1	CAAAUUAAAAGAGUUAAGG	336	CCUUAACUCUUUUAAUUUG	763
AD-39992.1	AAAUUAAAAGAGUUAAGGA	337	UCCUUAACUCUUUUAAUUU	764
AD-39998.1	AAUUAAAAGAGUUAAGGAC	338	GUCCUUAACUCUUUUAAUU	765
AD-40004.1	AUUAAAAGAGUUAAGGACU	339	AGUCCUUAACUCUUUUAAU	766
AD-40010.1	UUAAAAGAGUUAAGGACUC	340	GAGUCCUUAACUCUUUUAA	767
AD-40016.1	UAAAAGAGUUAAGGACUCU	341	AGAGUCCUUAACUCUUUUA	768
AD-40022.1	AAAAGAGUUAAGGACUCUG	342	CAGAGUCCUUAACUCUUUU	769
AD-40028.1	AAAGAGUUAAGGACUCUGA	343	UCAGAGUCCUUAACUCUUU	770
AD-40034.1	AAGAGUUAAGGACUCUGAA	344	UUCAGAGUCCUUAACUCUU	771
AD-39999.1	GAGUUAAGGACUCUGAAGA	345	UCUUCAGAGUCCUUAACUC	772
AD-40005.1	AGUUAAGGACUCUGAAGAU	346	AUCUUCAGAGUCCUUAACU	773
AD-40011.1	GUUAAGGACUCUGAACAUG	347	CAUGUUCAGAGUCCUUAAC	774
AD-40017.1	UUAAGGACUCUGAAGAUGU	348	ACAUCUUCAGAGUCCUUAA	775
AD-40029.1	AAGGACUCUGAAGAUGUAC	349	GUACAUCUUCAGAGUCCUU	776
AD-40035.1	AGGACUCUGAAGAUGUACC	350	GGUACAUCUUCAGAGUCCU	777
AD-39994.1	GGACUCUGAAGAUGUACCU	351	AGGUACAUCUUCAGAGUCC	778
AD-40000.1	GACUCUGAAGAUGUACCUA	352	UAGGUACAUCUUCAGAGUC	779
AD-40006.1	ACUCUGAAGAUGUACCUAU	353	AUAGGUACAUCUUCAGAGU	780
AD-40012.1	CUCUGAAGAUGUACCUAUG	354	CAUAGGUACAUCUUCAGAG	781
AD-40018.1	UCUGAAGAUGUACCUAUGG	355	CCAUAGGUACAUCUUCAGA	782
AD-40024.1	CUGAAGAUGUACCUAUGGU	356	ACCAUAGGUACAUCUUCAG	783
AD-40030.1	UGAAGAUGUACCUAUGGUC	357	GACCAUAGGUACAUCUUCA	784
AD-40036.1	GUAGGAAAUAAAUGUGAUU	358	AAUCACAUUUAUUUCCUAC	785
AD-39995.1	UAGGAAAUAAAUGUGAUUU	359	AAAUCACAUUUAUUUCCUA	786
AD-40001.1	AGGAAAUAAAUGUGAUUUG	360	CAAAUCACAUUUAUUUCCU	787
AD-40007.1	GGAAAUAAAUGUGAUUUGC	361	GCAAAUCACAUUUAUUUCC	788
AD-40013.1	GAAAUAAAUGUGAUUUGCC	362	GGCAAAUCACAUUUAUUUC	789

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AD-40019.1	AAAUAAAUGUGAUUUGCCU	363	AGGCAAAUCACAUUUAUUU	790
AD-40025.1	AAUAAAUGUGAUUUGCCUU	364	AAGGCAAAUCACAUUUAUU	791
AD-40031.1	AUAAAUGUGAUUUGCCUUC	365	GAAGGCAAAUCACAUUUAU	792
AD-40037.1	UAAAUGUGAUUUGCCUUCU	366	AGAAGGCAAAUCACAUUUA	793
AD-39996.1	AAAUGUGAUUUGCCUUCUA	367	UAGAAGGCAAAUCACAUUU	794
AD-40002.1	AAUGUGAUUUGCCUUCUAG	368	CUAGAAGGCAAAUCACAUU	795
AD-40008.1	AUGUGAUUUGCCUUCUAGA	369	UCUAGAAGGCAAAUCACAU	796
AD-40014.1	UGUGAUUUGCCUUCUAGAA	370	UUCUAGAAGGCAAAUCACA	797
AD-40020.1	GUGAUUUGCCUUCUAGAAC	371	GUUCUAGAAGGCAAAUCAC	798
AD-40026.1	UGAUUUGCCUUCUAGAACA	372	UGUUCUAGAAGGCAAAUCA	799
AD-40032.1	GAUUUGCCUUCUAGAACAG	373	CUGUUCUAGAAGGCAAAUC	800
AD-40038.1	AUUUGCCUUCUAGAACAGU	374	ACUGUUCUAGAAGGCAAAU	801
AD-39997.1	UUUGCCUUCUAGAACAGUA	375	UACUGUUCUAGAAGGCAAA	802
AD-40009.1	UGCCUUCUAGAACAGUAGA	376	UCUACUGUUCUAGAAGGCA	803
AD-40015.1	GCCUUCUAGAACAGUAGAC	377	GUCUACUGUUCUAGAAGGC	804
AD-40021.1	CCUUCUAGAACAGUAGACA	378	UGUCUACUGUUCUAGAAGC	805
AD-40027.1	CUUCUAGAACAGUAGACAC	379	GUGUCUACUGUUCUAGAAG	806
AD-40033.1	UUCUAGAACAGUAGACACA	380	UGUGUCUACUGUUCUAGAA	807
AD-40039.1	UCUAGAACAGUAGACACAA	381	UUGUGUCUACUGUUCUAGA	808
AD-40045.1	CUAGAACAGUAGACACAAA	382	UUUGUGUCUACUGUUCUAG	809
AD-40051.1	UAGAACAGUAGACACAAAA	383	UUUUGUGUCUACUGUUCUA	810
AD-40057.1	AGAACAGUAGACACAAAAC	384	GUUUUGUGUCUACUGUUCU	811
AD-40063.1	GAACAGUAGACACAAAACA	385	UGUUUUGUGUCUACUGUUC	812
AD-40069.1	AACAGUAGACACAAAACAG	386	CUGUUUUGUGUCUACUGUU	813
AD-40075.1	ACAGUAGACACAAAACAGG	387	CCUGUUUUGUGUCUACUGU	814
AD-40081.1	CAGUAGACACAAAACAGGC	388	GCCUGUUUUGUGUCUACUG	815
AD-40040.1	AGUAGACACAAAACAGGCU	389	AGCCUGUUUUGUGUCUACU	816
AD-40046.1	GUAGACACAAAACAGGCUC	390	GAGCCUGUUUUGUGUCUAC	817
AD-40052.1	UAGACACAAAACAGGCUCA	391	UGAGCCUGUUUUGUGUCUA	818
AD-40058.1	AGACACAAAACAGGCUCAG	392	CUGAGCCUGUUUUGUGUCU	819
AD-40064.1	GACACAAAACAGGCUCAGG	393	CCUGAGCCUGUUUUGUGUC	820
AD-40070.1	ACACAAAACAGGCUCAGGA	394	UCCUGAGCCUGUUUUGUGU	821
AD-40076.1	CACAAAACAGGCUCAGGAC	395	GUCCUGAGCCUGUUUUGUG	822
AD-40082.1	ACAAAACAGGCUCAGGACU	396	AGUCCUGAGCCUGUUUUGU	823
AD-40041.1	CAAAACAGGCUCAGGACUU	397	AAGUCCUGAGCCUGUUUUG	824
AD-40047.1	AAAACAGGCUCAGGACUUA	398	UAAGUCCUGAGCCUGUUUU	825
AD-40053.1	AAACAGGCUCAGGACUUAG	399	CUAAGUCCUGAGCCUGUUU	826
AD-40059.1	AACAGGCUCAGGACUUAGC	400	GCUAAGUCCUGAGCCUGUU	827
AD-40065.1	ACAGGCUCAGGACUUAGCA	401	UGCUAAGUCCUGAGCCUGU	828
AD-40071.1	CAGGCUCAGGACUUAGCAA	402	UUGCUAAGUCCUGAGCCUG	829
AD-40077.1	AGGCUCAGGACUUAGCAAG	403	CUUGCUAAGUCCUGAGCCU	830
AD-40083.1	GGCUCAGGACUUAGCAAGA	404	UCUUGCUAAGUCCUGAGCC	831
AD-40042.1	GCUCAGGACUUAGCAAGAA	405	UUCUUGCUAAGUCCUGAGC	832
AD-40048.1	CUCAGGACUUAGCAAGAAG	406	CUUCUUGCUAAGUCCUGAG	833

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AD-40054.1	UCAGGACUUAGCAAGAAGU	407	ACUUCUUGCUAAGUCCUGA	834
AD-40060.1	CAGGACUUAGCAAGAAGUU	408	AACUUCUUGCUAAGUCCUG	835
AD-40066.1	AGGACUUAGCAAGAAGUUA	409	UAACUUCUUGCUAAGUCCU	836
AD-40072.1	GGACUUAGCAAGAAGUUAU	410	AUAACUUCUUGCUAAGUCC	837
AD-40078.1	GACUUAGCAAGAAGUUAUG	411	CAUAACUUCUUGCUAAGUC	838
AD-40084.1	ACUUAGCAAGAAGUUAUGG	412	CCAUAACUUCUUGCUAAGU	839
AD-40043.1	CUUAGCAAGAAGUUAUGGA	413	UCCAUAACUUCUUGCUAAG	840
AD-40049.1	UUAGCAAGAAGUUAUGGAA	414	UUCCAUAACUUCUUGCUAA	841
AD-40055.1	UAGCAAGAAGUUAUGGAAU	415	AUUCCAUAACUUCUUGCUA	842
AD-40061.1	AGCAAGAAGUUAUGGAAUU	416	AAUUCCAUAACUUCUUGCU	843
AD-40067.1	GCAAGAAGUUAUGGAAUUC	417	GAAUUCCAUAACUUCUUGC	844
AD-40073.1	CAAGAAGUUAUGGAAUUCC	418	GGAAUUCCAUAACUUCUUG	845
AD-40079.1	AAGAAGUUAUGGAAUUCCU	419	AGGAAUUCCAUAACUUCUU	846
AD-40085.1	AGAAGUUAUGGAAUUCCUU	420	AAGGAAUUCCAUAACUUCU	847
AD-40044.1	GAAGUUAUGGAAUUCCUUU	421	AAAGGAAUUCCAUAACUUC	848
AD-40050.1	AAGUUAUGGAAUUCCUUUU	422	AAAAGGAAUUCCAUAACUU	849
AD-40056.1	AGUUAUGGAAUUCCUUUUA	423	UAAAAGGAAUUCCAUAACU	850
AD-40062.1	GUUAUGGAAUUCCUUUUAU	424	AUAAAAGGAAUUCCAUAAC	851
AD-40068.1	UUAUGGAAUUCCUUUUAUU	425	AAUAAAAGGAAUUCCAUAA	852
AD-40074.1	UAUGGAAUUCCUUUUAUUG	426	CAAUAAAAGGAAUUCCAUA	853
AD-40080.1	AUGGAAUUCCUUUUAUUGA	427	UCAAUAAAAGGAAUUCCAU	854
AD-39720.1	ACTTGTGGTAGTTGGAGCT	1716	AGCTCCAACTACCACAAGT	1754
AD-39706.1	GCAAGAGTGCCTTGACGAT	1717	ATCGTCAAGGCACTCTTGC	1755
AD-39712.1	CAAGAGTGCCTTGACGATA	1718	TATCGTCAAGGCACTCTTG	1756
AD-39760.1	CCTTGACGATACAGCTAAT	1719	ATTAGCTGTATCGTCAAGG	1757
AD-39732.1	CAGCTAATTCAGAATCATT	1720	AATGATTCTGAATTAGCTG	1758
AD-35541.4	CGAATATGATCCAACAATA	1721	TATTGTTGGATCATATTCG	1759
AD-39735.1 或 hs_KRAS_321_A22S26	GCAAGCAAGTAGTAATTGA	1722	TCAATTACTACTTGCTTCC	1760
AD-39741.1 或 hs_KRAS_322_A22S26	GAAGCAAGTAGTAATTGAT	1723	ATCAATTACTACTTGCTTC	1761
AD-39778.1	AGTAGTAATTGATGGAGAA	1724	TTCTCCATCAATTACTACT	1762
AD-39790.1	TAGTAATTGATGGAGAAAC	1725	GTTTCTCCATCAATTACTA	1763
AD-39822.1	GTCTCTTGGATATTCTCGA	1726	TCGAGAATATCCAAGAGAC	1764
AD-35609.4	GGGCTTTCTTTGTGTATTT	1727	AAATACACAAAGAAAGCCC	1765
AD-35581.4	GTGTATTTGCCATAAATAA	1728	TTATTTATGGCAAATACAC	1766
AD-39845.1	CCATAAATAATACTAAATC	1729	GATTTAGTATTATTTATGG	1767
AD-39858.1	TACTAAATCATTTGAAGAT	1730	ATCTTCAAATGATTTAGTA	1768
AD-39870.1	CTAAATCATTTGAAGATAT	1731	ATATCTTCAAATGATTTAG	1769
AD-35576.4	GAAGATATTCACCATTATA	1732	TATAATGGTGAATATCTTC	1770
AD-35588.4	AGATATTCACCATTATAGA	1733	TCTATAATGGTGAATATCT	1771
AD-35600.1	ATATTCACCATTATAGAGA	1734	TCTCTATAATGGTGAATAT	1772
AD-35606.1	TATTCACCATTATAGAGAA	1735	TTCTCTATAATGGTGAATA	1773

[3743]

AD-38151.1	CATTATAGAGAACAAATTA	1736	TAATTTGTTCTCTATAATG	1774
AD-38163.1	TTATAGAGAACAAATTAAA	1737	TTTAATTTGTTCTCTATAA	1775
AD-39999.1	GAGTTAAGGACTCTGAAGA	1738	TCTTCAGAGTCCTTAACTC	1776
AD-38159.1 或 hs_KRAS_528_A22S26	CTATGGTCCTAGTAGGAAA	1739	TTTCCTACTAGGACCATAG	1777
AD-38130.1 或 hs_KRAS_531_A22S26	TGGTCCTAGTAGGAAATAA	1740	TTATTTCCTACTAGGACCA	1778
AD-38136.1	GGTCCTAGTAGGAAATAAA	1741	TTTATTTCCTACTAGGACC	1779
AD-40036.1	GTAGGAAATAAATGTGATT	1742	AATCACATTTATTTCCTAC	1780
AD-40008.1	ATGTGATTTGCCTTCTAGA	1743	TCTAGAAGGCAAATCACAT	1781
AD-40021.1	CCTTCTAGAACAGTAGACA	1744	TGTCTACTGTTCTAGAAGG	1782
AD-40077.1	AGGCTCAGGACTTAGCAAG	1745	CTTGCTAAGTCCTGAGCCT	1783
AD-40072.1	GGACTTAGCAAGAAGTTAT	1746	ATAACTTCTTGCTAAGTCC	1784
AD-40061.1	AGCAAGAAGTTATGGAATT	1747	AATTCCATAACTTCTTGCT	1785
AD-40068.1	TTATGGAATTCCTTTTATT	1748	AATAAAAGGAATTCCATAA	1786
AD-38131.1	GGAATTCCTTTTATTGAAA	1749	TTTCAATAAAAGGAATTCC	1787
AD-38167.1	CCTTTTATTGAAACATCAG	1750	CTGATGTTTCAATAAAAGG	1788
hs_KRAS_1273_A22S26	CCTGATGAATGTAAAGTTA	1751	TAACTTTACATTCATCAGG	1789
hs_KRAS_2892_A37S26	GGAGAATTTAATAAAGATA	1752	TATCTTTATTAAATTCTCC	1790
hs_KRAS_4731_A22S26	GAATAGTCATAACTAGATT	1753	AATCTAGTTATGACTATTC	1791

[3744] 表 3. 具有修饰的序列的 KRAS 双链体

[3745]

双链体	有义序列	Seq SEQ ID NO:	反义序列	Seq SEQ ID NO:
AD-35523.3	GGAcGAAuAuGAuccAAcAdTdT	855	UGUUGGAUcAuAUUCGUCCdTdT	1282
AD-35529.1	GAcGAAuAuGAuccAAcAAdTdT	856	UUGUUGGAUcAuAUUCGUCdTdT	1283
AD-35535.4	AcGAAuAuGAuccAAcAAudTdT	857	AUUGUUGGAUcAuAUUCGUdTdT	1284
AD-35541.4	cGAAuAuGAuccAAcAAuAdTdT	858	uAUUGUUGGAUcAuAUUCGdTdT	1285
AD-35547.4	GAAuAuGAuccAAcAAuAGdTdT	859	CuAUUGUUGGAUcAuAUUCdTdT	1286
AD-35553.4	AAuAuGAuccAAcAAuAGAdTdT	860	UCuAUUGUUGGAUcAuAUUdTdT	1287
AD-35559.4	AuAuGAuccAAcAAuAGAGdTdT	861	CUCuAUUGUUGGAUcAuAUdTdT	1288
AD-35565.4	uAuGAuccAAcAAuAGAGGdTdT	862	CCUCuAUUGUUGGAUcAuAdTdT	1289
AD-35524.4	AuGAuccAAcAAuAGAGGAdTdT	863	UCCUCuAUUGUUGGAUcAUdTdT	1290
AD-35530.4	uGAuccAAcAAuAGAGGAudTdT	864	AUCCUCuAUUGUUGGAUcAdTdT	1291
AD-35536.4	GAuccAAcAAuAGAGGAuudTdT	865	AAUCCUCuAUUGUUGGAUCdTdT	1292
AD-35542.4	AuccAAcAAuAGAGGAuucdTdT	866	GAAUCCUCuAUUGUUGGAUdTdT	1293
AD-35548.4	uccAAcAAuAGAGGAuuccdTdT	867	GGAAUCCUCuAUUGUUGGAdTdT	1294
AD-35554.4	ccAAcAAuAGAGGAuuccudTdT	868	AGGAAUCCUCuAUUGUUGGdTdT	1295

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AD-35560.2	cAAcAAuAGAGGAuuccuAdTdT	869	uAGGAAUCCUCuAUUGUUGdTdT	1296
AD-35566.4	AAcAAuAGAGGAuuccuAcdTdT	870	GuAGGAAUCCUCuAUUGUUdTdT	1297
AD-35525.2	AcAAuAGAGGAuuccuAcAdTdT	871	UGuAGGAAUCCUCuAUUGUdTdT	1298
AD-35531.4	cAAuAGAGGAuuccuAcAGdTdT	872	CUGuAGGAAUCCUCuAUUGdTdT	1299
AD-35537.4	AAuAGAGGAuuccuAcAGGdTdT	873	CCUGuAGGAAUCCUCuAUUdTdT	1300
AD-35543.2	AuAGAGGAuuccuAcAGGAdTdT	874	UCCUGuAGGAAUCCUCuAUdTdT	1301
AD-35549.4	uAGAGGAuuccuAcAGGAAdTdT	875	UUCCUGuAGGAAUCCUCuAdTdT	1302
AD-35555.4	AGAGGAuuccuAcAGGAAGdTdT	876	CUUCCUGuAGGAAUCCUCUdTdT	1303
AD-35561.4	GAGGAuuccuAcAGGAAGcdTdT	877	GCUUCCUGuAGGAAUCCUCdTdT	1304
AD-35567.4	AGGAuuccuAcAGGAAGcAdTdT	878	UGCUUCCUGuAGGAAUCCUdTdT	1305
AD-35526.4	GGAuuccuAcAGGAAGcAAdTdT	879	UUGCUUCCUGuAGGAAUCCdTdT	1306
AD-35532.4	GAuuccuAcAGGAAGcAAGdTdT	880	CUUGCUUCCUGuAGGAAUCdTdT	1307
AD-35538.4	AuuccuAcAGGAAGcAAGudTdT	881	ACUUGCUUCCUGuAGGAAUdTdT	1308
AD-35544.4	uuccuAcAGGAAGcAAGuAdTdT	882	uACUUGCUUCCUGuAGGAAdTdT	1309
AD-35550.4	uccuAcAGGAAGcAAGuAGdTdT	883	CuACUUGCUUCCUGuAGGAdTdT	1310
AD-35556.4	ccuAcAGGAAGcAAGuAGudTdT	884	ACuACUUGCUUCCUGuAGGdTdT	1311
AD-35562.4	cuAcAGGAAGcAAGuAGuAdTdT	885	uACuACUUGCUUCCUGuAGdTdT	1312
AD-35568.4	uAcAGGAAGcAAGuAGuAAdTdT	886	UuACuACUUGCUUCCUGuAdTdT	1313
AD-35527.4	AcAGGAAGcAAGuAGuAAudTdT	887	AUuACuACUUGCUUCCUGUdTdT	1314
AD-35533.4	cAGGAAGcAAGuAGuAAuudTdT	888	AAUuACuACUUGCUUCCUGdTdT	1315
AD-35539.4	uuGGAuAuucucGAcAcAGdTdT	889	CUGUGUCGAGAAuAUCcAAdTdT	1316
AD-35545.4	uGGAuAuucucGAcAcAGcdTdT	890	GCUGUGUCGAGAAuAUCcAdTdT	1317
AD-35551.4	GGAuAuucucGAcAcAGcAdTdT	891	UGCUGUGUCGAGAAuAUCCdTdT	1318
AD-35563.4	AuAuucucGAcAcAGcAGGdTdT	892	CCUGCUGUGUCGAGAAuAUdTdT	1319
AD-35528.4	AuucucGAcAcAGcAGGucdTdT	893	GACCUGCUGUGUCGAGAAUdTdT	1320
AD-35540.4	ucucGAcAcAGcAGGucAAdTdT	894	UUGACCUGCUGUGUCGAGAdTdT	1321
AD-35546.4	cucGAcAcAGcAGGucAAGdTdT	895	CUUGACCUGCUGUGUCGAGdTdT	1322
AD-35552.4	ucGAcAcAGcAGGucAAGAdTdT	896	UCUUGACCUGCUGUGUCGAdTdT	1323
AD-35558.4	cGAcAcAGcAGGucAAGAGdTdT	897	CUCUUGACCUGCUGUGUCGdTdT	1324
AD-35564.4	GAcAcAGcAGGucAAGAGGdTdT	898	CCUCUUGACCUGCUGUGUCdTdT	1325
AD-35570.4	AcAcAGcAGGucAAGAGGAdTdT	899	UCCUCUUGACCUGCUGUGUdTdT	1326
AD-35571.4	cAcAGcAGGucAAGAGGAGdTdT	900	CUCCUCUUGACCUGCUGUGdTdT	1327
AD-35577.4	AcAGcAGGucAAGAGGAGudTdT	901	ACUCCUCUUGACCUGCUGUdTdT	1328
AD-35583.4	cAGcAGGucAAGAGGAGuAdTdT	902	uACUCCUCUUGACCUGCUGdTdT	1329
AD-35589.4	AGcAGGucAAGAGGAGuAcdTdT	903	GuACUCCUCUUGACCUGCUdTdT	1330
AD-35595.4	GcAGGucAAGAGGAGuAcAdTdT	904	UGuACUCCUCUUGACCUGCdTdT	1331
AD-35601.4	cAGGucAAGAGGAGuAcAGdTdT	905	CUGuACUCCUCUUGACCUGdTdT	1332
AD-35607.4	AGGucAAGAGGAGuAcAGudTdT	906	ACUGuACUCCUCUUGACCUdTdT	1333
AD-35613.4	GGucAAGAGGAGuAcAGuGdTdT	907	cACUGuACUCCUCUUGACCdTdT	1334
AD-35572.4	GucAAGAGGAGuAcAGuGcdTdT	908	GcACUGuACUCCUCUUGACdTdT	1335
AD-35578.4	ucAAGAGGAGuAcAGuGcAdTdT	909	UGcACUGuACUCCUCUUGAdTdT	1336
AD-35584.4	cAAGAGGAGuAcAGuGcAAdTdT	910	UUGcACUGuACUCCUCUUGdTdT	1337
AD-35590.4	AAGAGGAGuAcAGuGcAAudTdT	911	AUUGcACUGuACUCCUCUUdTdT	1338
AD-35596.4	AGAGGAGuAcAGuGcAAuGdTdT	912	cAUUGcACUGuACUCCUCUdTdT	1339

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AD-35602.4	GAGGAGuAcAGuGcAAuGAdTdT	913	UcAUUGcACUGuACUCCUCdTdT	1340
AD-35608.4	AGGAGuAcAGuGcAAuGAGdTdT	914	CUcAUUGcACUGuACUCCUdTdT	1341
AD-35614.4	GGAGuAcAGuGcAAuGAGGdTdT	915	CCUcAUUGcACUGuACUCCdTdT	1342
AD-35573.4	GAGuAcAGuGcAAuGAGGGdTdT	916	CCCUcAUUGcACUGuACUCdTdT	1343
AD-35579.4	GGGGAGGGcuuucuuuGuGdTdT	917	cAcAAAGAAAGCCCUCCCCdTdT	1344
AD-35585.4	GGGAGGGcuuucuuuGuGudTdT	918	AcAcAAAGAAAGCCCUCCCdTdT	1345
AD-35591.4	GGAGGGcuuucuuuGuGuAdTdT	919	uAcAcAAAGAAAGCCCUCCdTdT	1346
AD-35597.4	GAGGGcuuucuuuGuGuAudTdT	920	AuAcAcAAAGAAAGCCCUCdTdT	1347
AD-35603.4	AGGGcuuucuuuGuGuAuudTdT	921	AAuAcAcAAAGAAAGCCCUdTdT	1348
AD-35609.4	GGGcuuucuuuGuGuAuuudTdT	922	AAAuAcAcAAAGAAAGCCCdTdT	1349
AD-35615.4	GGcuuucuuuGuGuAuuuGdTdT	923	cAAAuAcAcAAAGAAAGCCdTdT	1350
AD-35574.4	GcuuucuuuGuGuAuuuGcdTdT	924	GcAAAuAcAcAAAGAAAGCdTdT	1351
AD-35580.1	cuuucuuuGuGuAuuuGccdTdT	925	GGcAAAuAcAcAAAGAAAGdTdT	1352
AD-35586.4	uuucuuuGuGuAuuuGccAdTdT	926	UGGcAAAuAcAcAAAGAAAdTdT	1353
AD-35592.4	uucuuuGuGuAuuuGccAudTdT	927	AUGGcAAAuAcAcAAAGAAdTdT	1354
AD-35598.4	ucuuuGuGuAuuuGccAuAdTdT	928	uAUGGcAAAuAcAcAAAGAdTdT	1355
AD-35604.4	cuuuGuGuAuuuGccAuAAdTdT	929	UuAUGGcAAAuAcAcAAAGdTdT	1356
AD-35610.4	uuuGuGuAuuuGccAuAAAdTdT	930	UUuAUGGcAAAuAcAcAAAdTdT	1357
AD-35616.4	uuGuGuAuuuGccAuAAAUdTdT	931	AUUuAUGGcAAAuAcAcAAdTdT	1358
AD-35575.4	uGuGuAuuuGccAuAAAuAdTdT	932	uAUUuAUGGcAAAuAcAcAdTdT	1359
AD-35581.4	GuGuAuuuGccAuAAAuAAdTdT	933	UuAUUuAUGGcAAAuAcACdTdT	1360
AD-35587.4	uGuAuuuGccAuAAAuAAudTdT	934	AUuAUUuAUGGcAAAuAcAdTdT	1361
AD-35593.4	GuAuuuGccAuAAAuAAuAdTdT	935	uAUuAUUuAUGGcAAAuACdTdT	1362
AD-35599.4	uAuuuGccAuAAAuAAuAcdTdT	936	GuAUuAUUuAUGGcAAAuAdTdT	1363
AD-35605.4	AuuuGccAuAAAuAAuAcudTdT	937	AGuAUuAUUuAUGGcAAAUdTdT	1364
AD-35611.4	uuuGccAuAAAuAAuAcuAdTdT	938	uAGuAUuAUUuAUGGcAAAdTdT	1365
AD-35617.4	uGAAGAuAuucAccAuuAudTdT	939	AuAAUGGUGAAuAUCUUcAdTdT	1366
AD-35576.4	GAAGAuAuucAccAuuAuAdTdT	940	uAuAAUGGUGAAuAUCUUCdTdT	1367
AD-35588.4	AGAuAuucAccAuuAuAGAdTdT	941	UCuAuAAUGGUGAAuAUCUdTdT	1368
AD-35667.1	AAAcAucAGcAAAGAcAAGdTdT	942	CUUGUCUUUGCUGAUGUUUdTdT	1369
AD-35673.1	AAcAucAGcAAAGAcAAGAdTdT	943	UCUUGUCUUUGCUGAUGUUdTdT	1370
AD-35679.1	AcAucAGcAAAGAcAAGAcdTdT	944	GUCUUGUCUUUGCUGAUGUdTdT	1371
AD-35685.1	cAucAGcAAAGAcAAGAcAdTdT	945	UGUCUUGUCUUUGCUGAUGdTdT	1372
AD-35691.1	AucAGcAAAGAcAAGAcAGdTdT	946	CUGUCUUGUCUUUGCUGAUdTdT	1373
AD-35557.1	GAuAuucucGAcAcAGcAGdTdT	947	CUGCUGUGUCGAGAAuAUCdTdT	1374
AD-35618.1	uucAccAuuAuAGAGAAcAdTdT	948	UGUUCUCuAuAAUGGUGAAdTdT	1375
AD-35569.1	uAuucucGAcAcAGcAGGudTdT	949	ACCUGCUGUGUCGAGAAuAdTdT	1376
AD-35534.1	uucucGAcAcAGcAGGucAdTdT	950	UGACCUGCUGUGUCGAGAAdTdT	1377
AD-35582.1	AAGAuAuucAccAuuAuAGdTdT	951	CuAuAAUGGUGAAuAUCUUdTdT	1378
AD-35594.1	GAuAuucAccAuuAuAGAGdTdT	952	CUCuAuAAUGGUGAAuAUCdTdT	1379
AD-35600.1	AuAuucAccAuuAuAGAGAdTdT	953	UCUCuAuAAUGGUGAAuAUdTdT	1380
AD-35606.1	uAuucAccAuuAuAGAGAAdTdT	954	UUCUCuAuAAUGGUGAAuAdTdT	1381
AD-35612.1	AuucAccAuuAuAGAGAAcdTdT	955	GUUCUCuAuAAUGGUGAAUdTdT	1382
AD-38127.1	ucAccAuuAuAGAGAAcAAdTdT	956	UUGUUCUCuAuAAUGGUGAdTdT	1383

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AD-38133.1	cAccAuuAuAGAGAAcAAAdTdT	957	UUUGUUCUCuAuAAUGGUGdTdT	1384
AD-38139.1	AccAuuAuAGAGAAcAAAudTdT	958	AUUUGUUCUCuAuAAUGGUdTdT	1385
AD-38145.1	ccAuuAuAGAGAAcAAAuudTdT	959	AAUUUGUUCUCuAuAAUGGdTdT	1386
AD-38151.1	cAuuAuAGAGAAcAAAuuAdTdT	960	uAAUUUGUUCUCuAuAAUGdTdT	1387
AD-38157.1	AuuAuAGAGAAcAAAuuAAdTdT	961	UuAAUUUGUUCUCuAuAAUdTdT	1388
AD-38163.1	uuAuAGAGAAcAAAuuAAAdTdT	962	UUuAAUUUGUUCUCuAuAAdTdT	1389
AD-38169.1	uAuAGAGAAcAAAuuAAAAdTdT	963	UUUuAAUUUGUUCUCuAuAdTdT	1390
AD-38128.1	AuAGAGAAcAAAuuAAAAGdTdT	964	CUUUuAAUUUGUUCUCuAUdTdT	1391
AD-38134.1	uAGAGAAcAAAuuAAAAGAdTdT	965	UCUUUuAAUUUGUUCUCuAdTdT	1392
AD-38140.1	AGAGAAcAAAuuAAAAGAGdTdT	966	GUCUUUuAAUUUGUUCUCUdTdT	1393
AD-38146.1	GAAGAuGuAccuAuGGuccdTdT	967	GGACcAuAGGuAcAUCUUCdTdT	1394
AD-38152.1	AAGAuGuAccuAuGGuccudTdT	968	AGGACcAuAGGuAcAUCUUdTdT	1395
AD-38158.1	AGAuGuAccuAuGGuccuAdTdT	969	uAGGACcAuAGGuAcAUCUdTdT	1396
AD-38164.1	GAuGuAccuAuGGuccuAGdTdT	970	CuAGGACcAuAGGuAcAUCdTdT	1397
AD-38170.1	AuGuAccuAuGGuccuAGudTdT	971	ACuAGGACcAuAGGuAcAUdTdT	1398
AD-38129.1	uGuAccuAuGGuccuAGuAdTdT	972	uACuAGGACcAuAGGuAcAdTdT	1399
AD-38135.1	GuAccuAuGGuccuAGuAGdTdT	973	CuACuAGGACcAuAGGuACdTdT	1400
AD-38141.1	uAccuAuGGuccuAGuAGGdTdT	974	CCuACuAGGACcAuAGGuAdTdT	1401
AD-38147.1	AccuAuGGuccuAGuAGGAdTdT	975	UCCuACuAGGACcAuAGGUdTdT	1402
AD-38153.1	ccuAuGGuccuAGuAGGAAdTdT	976	UUCCuACuAGGACcAuAGGdTdT	1403
AD-38159.1	cuAuGGuccuAGuAGGAAAdTdT	977	UUUCCuACuAGGACcAuAGdTdT	1404
AD-38165.1	uAuGGuccuAGuAGGAAAudTdT	978	AUUUCCuACuAGGACcAuAdTdT	1405
AD-38171.1	AuGGuccuAGuAGGAAAuAdTdT	979	uAUUUCCuACuAGGACcAUdTdT	1406
AD-38130.1	uGGuccuAGuAGGAAAuAAdTdT	980	UuAUUUCCuACuAGGACcAdTdT	1407
AD-38136.1	GGuccuAGuAGGAAAuAAAdTdT	981	UUuAUUUCCuACuAGGACCdTdT	1408
AD-38142.1	GuccuAGuAGGAAAuAAAudTdT	982	AUUuAUUUCCuACuAGGACdTdT	1409
AD-38148.1	uccuAGuAGGAAAuAAAuGdTdT	983	cAUUuAUUUCCuACuAGGAdTdT	1410
AD-38154.1	ccuAGuAGGAAAuAAAuGudTdT	984	AcAUUuAUUUCCuACuAGGdTdT	1411
AD-38160.1	cuAGuAGGAAAuAAAuGuGdTdT	985	cAcAUUuAUUUCCuACuAGdTdT	1412
AD-38166.1	uAGuAGGAAAuAAAuGuGAdTdT	986	UcAcAUUuAUUUCCuACuAdTdT	1413
AD-38172.1	AGuAGGAAAuAAAuGuGAudTdT	987	AUcAcAUUuAUUUCCuACUdTdT	1414
AD-38131.1	GGAAuuccuuuuAuuGAAAdTdT	988	UUUcAAuAAAAGGAAUUCCdTdT	1415
AD-38137.1	GAAuuccuuuuAuuGAAAcdTdT	989	GUUUcAAuAAAAGGAAUUCdTdT	1416
AD-38143.1	AAuuccuuuuAuuGAAAcAdTdT	990	UGUUUcAAuAAAAGGAAUUdTdT	1417
AD-38149.1	AuuccuuuuAuuGAAAcAudTdT	991	AUGUUUcAAuAAAAGGAAUdTdT	1418
AD-38155.1	uuccuuuuAuuGAAAcAucdTdT	992	GAUGUUUcAAuAAAAGGAAdTdT	1419
AD-38161.1	uccuuuuAuuGAAAcAucAdTdT	993	UGAUGUUUcAAuAAAAGGAdTdT	1420
AD-38167.1	ccuuuuAuuGAAAcAucAGdTdT	994	CUGAUGUUUcAAuAAAAGGdTdT	1421
AD-38173.1	cuuuuAuuGAAAcAucAGcdTdT	995	GCUGAUGUUUcAAuAAAAGdTdT	1422
AD-38132.1	uuuuAuuGAAAcAucAGcAdTdT	996	UGCUGAUGUUUcAAuAAAAdTdT	1423
AD-38138.1	uuuAuuGAAAcAucAGcAAdTdT	997	UUGCUGAUGUUUcAAuAAAdTdT	1424
AD-38144.1	uuAuuGAAAcAucAGcAAAdTdT	998	UUUGCUGAUGUUUcAAuAAdTdT	1425
AD-38150.1	uAuuGAAAcAucAGcAAAGdTdT	999	CUUUGCUGAUGUUUcAAuAdTdT	1426
AD-38156.1	AuuGAAAcAucAGcAAAGAdTdT	1000	UCUUUGCUGAUGUUUcAAUdTdT	1427

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AD-38162.1	uuGAAAcAucAGcAAAGAcdTdT	1001	GUCUUUGCUGAUGUUUcAAdTdT	1428
AD-38168.1	uGAAAcAucAGcAAAGAcAdTdT	1002	UGUCUUUGCUGAUGUUUcAdTdT	1429
AD-38174.1	GAAAcAucAGcAAAGAcAAdTdT	1003	UUGUCUUUGCUGAUGUUUCdTdT	1430
AD-39683.1	AuGAcuGAAuAuAAAcuuGdTdT	1004	cAAGUUuAuAUUcAGUcAUdTdT	1431
AD-39689.1	uGAcuGAAuAuAAAcuuGudTdT	1005	AcAAGUUuAuAUUcAGUcAdTdT	1432
AD-39695.1	GAcuGAAuAuAAAcuuGuGdTdT	1006	cAcAAGUUuAuAUUcAGUCdTdT	1433
AD-39701.1	AcuGAAuAuAAAcuuGuGGdTdT	1007	CcAcAAGUUuAuAUUcAGUdTdT	1434
AD-39707.1	cuGAAuAuAAAcuuGuGGudTdT	1008	ACcAcAAGUUuAuAUUcAGdTdT	1435
AD-39713.1	uGAAuAuAAAcuuGuGGuAdTdT	1009	uACcAcAAGUUuAuAUUcAdTdT	1436
AD-39719.1	GAAuAuAAAcuuGuGGuAGdTdT	1010	CuACcAcAAGUUuAuAUUCdTdT	1437
AD-39725.1	AAuAuAAAcuuGuGGuAGudTdT	1011	ACuACcAcAAGUUuAuAUUdTdT	1438
AD-39684.1	AuAuAAAcuuGuGGuAGuudTdT	1012	AACuACcAcAAGUUuAuAUdTdT	1439
AD-39690.1	uAuAAAcuuGuGGuAGuuGdTdT	1013	cAACuACcAcAAGUUuAuAdTdT	1440
AD-39696.1	AuAAAcuuGuGGuAGuuGGdTdT	1014	CcAACuACcAcAAGUUuAUdTdT	1441
AD-39702.1	uAAAcuuGuGGuAGuuGGAdTdT	1015	UCcAACuACcAcAAGUUuAdTdT	1442
AD-39708.1	AAAcuuGuGGuAGuuGGAGdTdT	1016	CUCcAACuACcAcAAGUUUdTdT	1443
AD-39714.1	AAcuuGuGGuAGuuGGAGcdTdT	1017	GCUCcAACuACcAcAAGUUdTdT	1444
AD-39720.1	AcuuGuGGuAGuuGGAGcudTdT	1018	AGCUCcAACuACcAcAAGUdTdT	1445
AD-39726.1	cuuGuGGuAGuuGGAGcuGdTdT	1019	cAGCUCcAACuACcAcAAGdTdT	1446
AD-39685.1	uuGuGGuAGuuGGAGcuGGdTdT	1020	CcAGCUCcAACuACcAcAAdTdT	1447
AD-39691.1	uGuGGuAGuuGGAGcuGGudTdT	1021	ACcAGCUCcAACuACcAcAdTdT	1448
AD-39697.1	GuGGuAGuuGGAGcuGGuGdTdT	1022	cACcAGCUCcAACuACcACdTdT	1449
AD-39703.1	uGGuAGuuGGAGcuGGuGGdTdT	1023	CcACcAGCUCcAACuACcAdTdT	1450
AD-39709.1	GGuAGuuGGAGcuGGuGGcdTdT	1024	GCcACcAGCUCcAACuACCdTdT	1451
AD-39715.1	GuAGuuGGAGcuGGuGGcGdTdT	1025	CGCcACcAGCUCcAACuACdTdT	1452
AD-39721.1	uAGuuGGAGcuGGuGGcGudTdT	1026	ACGCcACcAGCUCcAACuAdTdT	1453
AD-39727.1	AGuuGGAGcuGGuGGcGuAdTdT	1027	uACGCcACcAGCUCcAACUdTdT	1454
AD-39686.1	GuuGGAGcuGGuGGcGuAGdTdT	1028	CuACGCcACcAGCUCcAACdTdT	1455
AD-39692.1	uuGGAGcuGGuGGcGuAGGdTdT	1029	CCuACGCcACcAGCUCcAAdTdT	1456
AD-39698.1	uGGAGcuGGuGGcGuAGGcdTdT	1030	GCCuACGCcACcAGCUCcAdTdT	1457
AD-39704.1	GGAGcuGGuGGcGuAGGcAdTdT	1031	UGCCuACGCcACcAGCUCCdTdT	1458
AD-39710.1	GAGcuGGuGGcGuAGGcAAdTdT	1032	UUGCCuACGCcACcAGCUCdTdT	1459
AD-39716.1	AGcuGGuGGcGuAGGcAAGdTdT	1033	CUUGCCuACGCcACcAGCUdTdT	1460
AD-39722.1	GcuGGuGGcGuAGGcAAGAdTdT	1034	UCUUGCCuACGCcACcAGCdTdT	1461
AD-39728.1	cuGGuGGcGuAGGcAAGAGdTdT	1035	CUCUUGCCuACGCcACcAGdTdT	1462
AD-39687.1	uGGuGGcGuAGGcAAGAGudTdT	1036	ACUCUUGCCuACGCcACcAdTdT	1463
AD-39693.1	GGuGGcGuAGGcAAGAGuGdTdT	1037	cACUCUUGCCuACGCcACCdTdT	1464
AD-39699.1	GuGGcGuAGGcAAGAGuGcdTdT	1038	GcACUCUUGCCuACGCcACdTdT	1465
AD-39705.1	uGGcGuAGGcAAGAGuGccdTdT	1039	GGcACUCUUGCCuACGCcAdTdT	1466
AD-39711.1	GGcGuAGGcAAGAGuGccudTdT	1040	AGGcACUCUUGCCuACGCCdTdT	1467
AD-39717.1	GcGuAGGcAAGAGuGccuudTdT	1041	AAGGcACUCUUGCCuACGCdTdT	1468
AD-39723.1	cGuAGGcAAGAGuGccuuGdTdT	1042	cAAGGcACUCUUGCCuACGdTdT	1469
AD-39729.1	GuAGGcAAGAGuGccuuGAdTdT	1043	UcAAGGcACUCUUGCCuACdTdT	1470
AD-39688.1	uAGGcAAGAGuGccuuGAcdTdT	1044	GUcAAGGcACUCUUGCCuAdTdT	1471

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AD-39694.1	AGGcAAGAGuGccuuGAcGdTdT	1045	CGUcAAGGcACUCUUGCCUdTdT	1472
AD-39700.1	GGcAAGAGuGccuuGAcGAdTdT	1046	UCGUcAAGGcACUCUUGCCdTdT	1473
AD-39706.1	GcAAGAGuGccuuGAcGAudTdT	1047	AUCGUcAAGGcACUCUUGCdTdT	1474
AD-39712.1	cAAGAGuGccuuGAcGAuAdTdT	1048	uAUCGUcAAGGcACUCUUGdTdT	1475
AD-39718.1	AAGAGuGccuuGAcGAuAcdTdT	1049	GuAUCGUcAAGGcACUCUUdTdT	1476
AD-39724.1	AGAGuGccuuGAcGAuAcAdTdT	1050	UGuAUCGUcAAGGcACUCUdTdT	1477
AD-39730.1	GAGuGccuuGAcGAuAcAGdTdT	1051	CUGuAUCGUcAAGGcACUCdTdT	1478
AD-39736.1	AGuGccuuGAcGAuAcAGcdTdT	1052	GCUGuAUCGUcAAGGcACUdTdT	1479
AD-39742.1	GuGccuuGAcGAuAcAGcudTdT	1053	AGCUGuAUCGUcAAGGcACdTdT	1480
AD-39748.1	uGccuuGAcGAuAcAGcuAdTdT	1054	uAGCUGuAUCGUcAAGGcAdTdT	1481
AD-39754.1	GccuuGAcGAuAcAGcuAAdTdT	1055	UuAGCUGuAUCGUcAAGGCdTdT	1482
AD-39760.1	ccuuGAcGAuAcAGcuAAudTdT	1056	AUuAGCUGuAUCGUcAAGGdTdT	1483
AD-39766.1	cuuGAcGAuAcAGcuAAuudTdT	1057	AAUuAGCUGuAUCGUcAAGdTdT	1484
AD-39772.1	uuGAcGAuAcAGcuAAuucdTdT	1058	GAAUuAGCUGuAUCGUcAAdTdT	1485
AD-39731.1	uGAcGAuAcAGcuAAuucAdTdT	1059	UGAAUuAGCUGuAUCGUcAdTdT	1486
AD-39737.1	GAcGAuAcAGcuAAuucAGdTdT	1060	CUGAAUuAGCUGuAUCGUCdTdT	1487
AD-39743.1	AcGAuAcAGcuAAuucAGAdTdT	1061	UCUGAAUuAGCUGuAUCGUdTdT	1488
AD-39749.1	cGAuAcAGcuAAuucAGAAdTdT	1062	UUCUGAAUuAGCUGuAUCGdTdT	1489
AD-39755.1	GAuAcAGcuAAuucAGAAudTdT	1063	AUUCUGAAUuAGCUGuAUCdTdT	1490
AD-39761.1	AuAcAGcuAAuucAGAAucdTdT	1064	GAUUCUGAAUuAGCUGuAUdTdT	1491
AD-39767.1	uAcAGcuAAuucAGAAucAdTdT	1065	UGAUUCUGAAUuAGCUGuAdTdT	1492
AD-39773.1	AcAGcuAAuucAGAAucAudTdT	1066	AUGAUUCUGAAUuAGCUGUdTdT	1493
AD-39732.1	cAGcuAAuucAGAAucAuudTdT	1067	AAUGAUUCUGAAUuAGCUGdTdT	1494
AD-39738.1	AGcuAAuucAGAAucAuuudTdT	1068	AAAUGAUUCUGAAUuAGCUdTdT	1495
AD-39744.1	GcuAAuucAGAAucAuuuudTdT	1069	AAAAUGAUUCUGAAUuAGCdTdT	1496
AD-39750.1	cuAAuucAGAAucAuuuuGdTdT	1070	cAAAAUGAUUCUGAAUuAGdTdT	1497
AD-39756.1	uAAuucAGAAucAuuuuGudTdT	1071	AcAAAAUGAUUCUGAAUuAdTdT	1498
AD-39762.1	AAuucAGAAucAuuuuGuGdTdT	1072	cAcAAAAUGAUUCUGAAUUdTdT	1499
AD-39768.1	AuucAGAAucAuuuuGuGGdTdT	1073	CcAcAAAAUGAUUCUGAAUdTdT	1500
AD-39774.1	uucAGAAucAuuuuGuGGAdTdT	1074	UCcAcAAAAUGAUUCUGAAdTdT	1501
AD-39733.1	ucAGAAucAuuuuGuGGAcdTdT	1075	GUCcAcAAAAUGAUUCUGAdTdT	1502
AD-39739.1	cAGAAucAuuuuGuGGAcGdTdT	1076	CGUCcAcAAAAUGAUUCUGdTdT	1503
AD-39745.1	AGAAucAuuuuGuGGAcGAdTdT	1077	UCGUCcAcAAAAUGAUUCUdTdT	1504
AD-39751.1	GAAucAuuuuGuGGAcGAAdTdT	1078	UUCGUCcAcAAAAUGAUUCdTdT	1505
AD-39757.1	AAucAuuuuGuGGAcGAAudTdT	1079	AUUCGUCcAcAAAAUGAUUdTdT	1506
AD-39763.1	AucAuuuuGuGGAcGAAuAdTdT	1080	uAUUCGUCcAcAAAAUGAUdTdT	1507
AD-39769.1	ucAuuuuGuGGAcGAAuAudTdT	1081	AuAUUCGUCcAcAAAAUGAdTdT	1508
AD-39775.1	cAuuuuGuGGAcGAAuAuGdTdT	1082	cAuAUUCGUCcAcAAAAUGdTdT	1509
AD-39734.1	AuuuuGuGGAcGAAuAuGAdTdT	1083	UcAuAUUCGUCcAcAAAAUdTdT	1510
AD-39740.1	uuuuGuGGAcGAAuAuGAudTdT	1084	AUcAuAUUCGUCcAcAAAAdTdT	1511
AD-39746.1	uuuGuGGAcGAAuAuGAucdTdT	1085	GAUcAuAUUCGUCcAcAAAdTdT	1512
AD-39752.1	uuGuGGAcGAAuAuGAuccdTdT	1086	GGAUcAuAUUCGUCcAcAAdTdT	1513
AD-39758.1	uGuGGAcGAAuAuGAuccAdTdT	1087	UGGAUcAuAUUCGUCcAcAdTdT	1514
AD-39764.1	GuGGAcGAAuAuGAuccAAdTdT	1088	UUGGAUcAuAUUCGUCcACdTdT	1515

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AD-39770.1	uGGAcGAAuAuGAuccAAcdTdT	1089	GUUGGAUcAuAUUCGUCcAdTdT	1516
AD-39776.1	AGGAAGcAAGuAGuAAuuGdTdT	1090	cAAUuACuACUUGCUUCCUdTdT	1517
AD-39735.1	GGAAGcAAGuAGuAAuuGAdTdT	1091	UcAAUuACuACUUGCUUCCdTdT	1518
AD-39741.1	GAAGcAAGuAGuAAuuGAudTdT	1092	AUcAAUuACuACUUGCUUCdTdT	1519
AD-39747.1	AAGcAAGuAGuAAuuGAuGdTdT	1093	cAUcAAUuACuACUUGCUUdTdT	1520
AD-39753.1	AGcAAGuAGuAAuuGAuGGdTdT	1094	CcAUcAAUuACuACUUGCUdTdT	1521
AD-39759.1	GcAAGuAGuAAuuGAuGGAdTdT	1095	UCcAUcAAUuACuACUUGCdTdT	1522
AD-39765.1	cAAGuAGuAAuuGAuGGAGdTdT	1096	CUCcAUcAAUuACuACUUGdTdT	1523
AD-39771.1	AAGuAGuAAuuGAuGGAGAdTdT	1097	UCUCcAUcAAUuACuACUUdTdT	1524
AD-39778.1	AGuAGuAAuuGAuGGAGAAdTdT	1098	UUCUCcAUcAAUuACuACUdTdT	1525
AD-39784.1	GuAGuAAuuGAuGGAGAAAdTdT	1099	UUUCUCcAUcAAUuACuACdTdT	1526
AD-39790.1	uAGuAAuuGAuGGAGAAAcdTdT	1100	GUUUCUCcAUcAAUuACuAdTdT	1527
AD-39796.1	AGuAAuuGAuGGAGAAAccdTdT	1101	GGUUUCUCcAUcAAUuACUdTdT	1528
AD-39802.1	GuAAuuGAuGGAGAAAccudTdT	1102	AGGUUUCUCcAUcAAUuACdTdT	1529
AD-39808.1	uAAuuGAuGGAGAAAccuGdTdT	1103	cAGGUUUCUCcAUcAAUuAdTdT	1530
AD-39814.1	AAuuGAuGGAGAAAccuGudTdT	1104	AcAGGUUUCUCcAUcAAUUdTdT	1531
AD-39820.1	AuuGAuGGAGAAAccuGucdTdT	1105	GAcAGGUUUCUCcAUcAAUdTdT	1532
AD-39779.1	uuGAuGGAGAAAccuGucudTdT	1106	AGAcAGGUUUCUCcAUcAAdTdT	1533
AD-39785.1	uGAuGGAGAAAccuGucucdTdT	1107	GAGAcAGGUUUCUCcAUcAdTdT	1534
AD-39791.1	GAuGGAGAAAccuGucucudTdT	1108	AGAGAcAGGUUUCUCcAUCdTdT	1535
AD-39797.1	AuGGAGAAAccuGucucuudTdT	1109	AAGAGAcAGGUUUCUCcAUdTdT	1536
AD-39803.1	uGGAGAAAccuGucucuuGdTdT	1110	cAAGAGAcAGGUUUCUCcAdTdT	1537
AD-39809.1	GGAGAAAccuGucucuuGGdTdT	1111	CcAAGAGAcAGGUUUCUCCdTdT	1538
AD-39815.1	GAGAAAccuGucucuuGGAdTdT	1112	UCcAAGAGAcAGGUUUCUCdTdT	1539
AD-39821.1	AGAAAccuGucucuuGGAudTdT	1113	AUCcAAGAGAcAGGUUUCUdTdT	1540
AD-39780.1	GAAAccuGucucuuGGAuAdTdT	1114	uAUCcAAGAGAcAGGUUUCdTdT	1541
AD-39786.1	AAAccuGucucuuGGAuAudTdT	1115	AuAUCcAAGAGAcAGGUUUdTdT	1542
AD-39792.1	AAccuGucucuuGGAuAuudTdT	1116	AAuAUCcAAGAGAcAGGUUdTdT	1543
AD-39798.1	AccuGucucuuGGAuAuucdTdT	1117	GAAuAUCcAAGAGAcAGGUdTdT	1544
AD-39804.1	ccuGucucuuGGAuAuucudTdT	1118	AGAAuAUCcAAGAGAcAGGdTdT	1545
AD-39810.1	cuGucucuuGGAuAuucuGdTdT	1119	GAGAAuAUCcAAGAGAcAGdTdT	1546
AD-39816.1	uGucucuuGGAuAuucuGdTdT	1120	CGAGAAuAUCcAAGAGAcAdTdT	1547
AD-39822.1	GucucuuGGAuAuucucGAdTdT	1121	UCGAGAAuAUCcAAGAGACdTdT	1548
AD-39781.1	ucucuuGGAuAuucucGAcdTdT	1122	GUCGAGAAuAUCcAAGAGAdTdT	1549
AD-39787.1	cucuuGGAuAuucucGAcAdTdT	1123	UGUCGAGAAuAUCcAAGAGdTdT	1550
AD-39793.1	ucuuGGAuAuucucGAcAcdTdT	1124	GUGUCGAGAAuAUCcAAGAdTdT	1551
AD-39799.1	cuuGGAuAuucucGAcAcAdTdT	1125	UGUGUCGAGAAuAUCcAAGdTdT	1552
AD-39805.1	AGuAcAGuGcAAuGAGGGAdTdT	1126	UCCCUcAUUGcACUGuACUdTdT	1553
AD-39811.1	GuAcAGuGcAAuGAGGGAcdTdT	1127	GUCCCUcAUUGcACUGuACdTdT	1554
AD-39817.1	uAcAGuGcAAuGAGGGAccdTdT	1128	GGUCCCUcAUUGcACUGuAdTdT	1555
AD-39823.1	AcAGuGcAAuGAGGGAccAdTdT	1129	UGGUCCCUcAUUGcACUGUdTdT	1556
AD-39782.1	cAGuGcAAuGAGGGAccAGdTdT	1130	CUGGUCCCUcAUUGcACUGdTdT	1557
AD-39788.1	AGuGcAAuGAGGGAccAGudTdT	1131	ACUGGUCCCUcAUUGcACUdTdT	1558
AD-39794.1	GuGcAAuGAGGGAccAGuAdTdT	1132	uACUGGUCCCUcAUUGcACdTdT	1559

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AD-39800.1	uGcAAuGAGGGAccAGuAcdTdT	1133	GuACUGGUCCCUcAUUGcAdTdT	1560
AD-39806.1	GcAAuGAGGGAccAGuAcAdTdT	1134	UGuACUGGUCCCUcAUUGCdTdT	1561
AD-39812.1	cAAuGAGGGAccAGuAcAudTdT	1135	AUGuACUGGUCCCUcAUUGdTdT	1562
AD-39818.1	AAuGAGGGAccAGuAcAuGdTdT	1136	cAUGuACUGGUCCCUcAUUdTdT	1563
AD-39824.1	AuGAGGGAccAGuAcAuGAdTdT	1137	UcAUGuACUGGUCCCUcAUdTdT	1564
AD-39783.1	uGAGGGAccAGuAcAuGAGdTdT	1138	CUcAUGuACUGGUCCCUcAdTdT	1565
AD-39789.1	GAGGGAccAGuAcAuGAGGdTdT	1139	CCUcAUGuACUGGUCCCUCdTdT	1566
AD-39795.1	AGGGAccAGuAcAuGAGGAdTdT	1140	UCCUcAUGuACUGGUCCCUdTdT	1567
AD-39801.1	GGGAccAGuAcAuGAGGAcdTdT	1141	GUCCUcAUGuACUGGUCCCdTdT	1568
AD-39807.1	GGAccAGuAcAuGAGGAcudTdT	1142	AGUCCUcAUGuACUGGUCCdTdT	1569
AD-39813.1	GAccAGuAcAuGAGGAcuGdTdT	1143	cAGUCCUcAUGuACUGGUCdTdT	1570
AD-39819.1	AccAGuAcAuGAGGAcuGGdTdT	1144	CcAGUCCUcAUGuACUGGUdTdT	1571
AD-39825.1	ccAGuAcAuGAGGAcuGGGdTdT	1145	CCcAGUCCUcAUGuACUGGdTdT	1572
AD-39831.1	cAGuAcAuGAGGAcuGGGGdTdT	1146	CCCcAGUCCUcAUGuACUGdTdT	1573
AD-39837.1	AGuAcAuGAGGAcuGGGGAdTdT	1147	UCCCcAGUCCUcAUGuACUdTdT	1574
AD-39843.1	GuAcAuGAGGAcuGGGGAGdTdT	1148	CUCCCcAGUCCUcAUGuACdTdT	1575
AD-39849.1	uAcAuGAGGAcuGGGGAGGdTdT	1149	CCUCCCcAGUCCUcAUGuAdTdT	1576
AD-39855.1	AcAuGAGGAcuGGGGAGGGdTdT	1150	CCCUCCCcAGUCCUcAUGUdTdT	1577
AD-39861.1	cAuGAGGAcuGGGGAGGGcdTdT	1151	GCCCUCCCcAGUCCUcAUGdTdT	1578
AD-39867.1	AuGAGGAcuGGGGAGGGcudTdT	1152	AGCCCUCCCcAGUCCUcAUdTdT	1579
AD-39826.1	uGAGGAcuGGGGAGGGcuudTdT	1153	AAGCCCUCCCcAGUCCUcAdTdT	1580
AD-39832.1	GAGGAcuGGGGAGGGcuuudTdT	1154	AAAGCCCUCCCcAGUCCUCdTdT	1581
AD-39838.1	AGGAcuGGGGAGGGcuuucdTdT	1155	GAAAGCCCUCCCcAGUCCUdTdT	1582
AD-39844.1	GGAcuGGGGAGGGcuuucudTdT	1156	AGAAAGCCCUCCCcAGUCCdTdT	1583
AD-39850.1	GAcuGGGGAGGGcuuucuudTdT	1157	AAGAAAGCCCUCCCcAGUCdTdT	1584
AD-39856.1	AcuGGGGAGGGcuuucuuudTdT	1158	AAAGAAAGCCCUCCCcAGUdTdT	1585
AD-39862.1	cuGGGGAGGGcuuucuuuGdTdT	1159	cAAAGAAAGCCCUCCCcAGdTdT	1586
AD-39868.1	uGGGGAGGGcuuucuuuGudTdT	1160	AcAAAGAAAGCCCUCCCcAdTdT	1587
AD-39827.1	uuGccAuAAAuAAuAcuAAdTdT	1161	UuAGuAUuAUUuAUGGcAAdTdT	1588
AD-39833.1	uGccAuAAAuAAuAcuAAAdTdT	1162	UUuAGuAUuAUUuAUGGcAdTdT	1589
AD-39839.1	GccAuAAAuAAuAcuAAAudTdT	1163	AUUuAGuAUuAUUuAUGGCdTdT	1590
AD-39845.1	ccAuAAAuAAuAcuAAAucdTdT	1164	GAUUuAGuAUuAUUuAUGGdTdT	1591
AD-39851.1	cAuAAAuAAuAcuAAAucAdTdT	1165	UGAUUuAGuAUuAUUuAUGdTdT	1592
AD-39857.1	AuAAAuAAuAcuAAAucAudTdT	1166	AUGAUUuAGuAUuAUUuAUdTdT	1593
AD-39863.1	uAAAuAAuAcuAAAucAuudTdT	1167	AAUGAUUuAGuAUuAUUuAdTdT	1594
AD-39869.1	AAAuAAuAcuAAAucAuuudTdT	1168	AAAUGAUUuAGuAUuAUUUdTdT	1595
AD-39828.1	AAuAAuAcuAAAucAuuuGdTdT	1169	cAAAUGAUUuAGuAUuAUUdTdT	1596
AD-39834.1	AuAAuAcuAAAucAuuuGAdTdT	1170	UcAAAUGAUUuAGuAUuAUdTdT	1597
AD-39840.1	uAAuAcuAAAucAuuuGAAdTdT	1171	UUcAAAUGAUUuAGuAUuAdTdT	1598
AD-39846.1	AAuAcuAAAucAuuuGAAGdTdT	1172	CUUcAAAUGAUUuAGuAUUdTdT	1599
AD-39852.1	AuAcuAAAucAuuuGAAGAdTdT	1173	UCUUcAAAUGAUUuAGuAUdTdT	1600
AD-39858.1	uAcuAAAucAuuuGAAGAudTdT	1174	AUCUUcAAAUGAUUuAGuAdTdT	1601
AD-39864.1	AcuAAAucAuuuGAAGAuAdTdT	1175	uAUCUUcAAAUGAUUuAGUdTdT	1602
AD-39870.1	cuAAAucAuuuGAAGAuAudTdT	1176	AuAUCUUcAAAUGAUUuAGdTdT	1603

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AD-39829.1	uAAAucAuuuGAAGAuAuudTdT	1177	AAuAUCUUcAAAUGAUUuAdTdT	1604
AD-39835.1	AAAucAuuuGAAGAuAuucdTdT	1178	GAAuAUCUUcAAAUGAUUUdTdT	1605
AD-39841.1	AAucAuuuGAAGAuAuucAdTdT	1179	UGAAuAUCUUcAAAUGAUUdTdT	1606
AD-39853.1	ucAuuuGAAGAuAuucAccdTdT	1180	GGUGAAuAUCUUcAAAUGAdTdT	1607
AD-39859.1	cAuuuGAAGAuAuucAccAdTdT	1181	UGGUGAAuAUCUUcAAAUGdTdT	1608
AD-39865.1	AuuuGAAGAuAuucAccAudTdT	1182	AUGGUGAAuAUCUUcAAAUdTdT	1609
AD-39871.1	uuuGAAGAuAuucAccAuudTdT	1183	AAUGGUGAAuAUCUUcAAAdTdT	1610
AD-39830.1	uuGAAGAuAuucAccAuuAdTdT	1184	uAAUGGUGAAuAUCUUcAAdTdT	1611
AD-39836.1	GAGAAcAAAuuAAAAGAGudTdT	1185	ACUCUUUuAAUUUGUUCUCdTdT	1612
AD-39842.1	AGAAcAAAuuAAAAGAGuudTdT	1186	AACUCUUUuAAUUUGUUCUdTdT	1613
AD-39848.1	GAAcAAAuuAAAAGAGuuAdTdT	1187	uAACUCUUUuAAUUUGUUCdTdT	1614
AD-39854.1	AAcAAAuuAAAAGAGuuAAdTdT	1188	UuAACUCUUUuAAUUUGUUdTdT	1615
AD-39860.1	AcAAAuuAAAAGAGuuAAGdTdT	1189	CUuAACUCUUUuAAUUUGUdTdT	1616
AD-39866.1	cAAAuuAAAAGAGuuAAGGdTdT	1190	CCUuAACUCUUUuAAUUUGdTdT	1617
AD-39992.1	AAAuuAAAAGAGuuAAGGAdTdT	1191	UCCUuAACUCUUUuAAUUUdTdT	1618
AD-39998.1	AAuuAAAAGAGuuAAGGAcdTdT	1192	GUCCUuAACUCUUUuAAUUdTdT	1619
AD-40004.1	AuuAAAAGAGuuAAGGAcudTdT	1193	AGUCCUuAACUCUUUuAAUdTdT	1620
AD-40010.1	uuAAAAGAGuuAAGGAcucdTdT	1194	GAGUCCUuAACUCUUUuAAdTdT	1621
AD-40016.1	uAAAAGAGuuAAGGAcucudTdT	1195	AGAGUCCUuAACUCUUUuAdTdT	1622
AD-40022.1	AAAAGAGuuAAGGAcucuGdTdT	1196	cAGAGUCCUuAACUCUUUUdTdT	1623
AD-40028.1	AAAGAGuuAAGGAcucuGAdTdT	1197	UcAGAGUCCUuAACUCUUUdTdT	1624
AD-40034.1	AAGAGuuAAGGAcucuGAAdTdT	1198	UUcAGAGUCCUuAACUCUUdTdT	1625
AD-39999.1	GAGuuAAGGAcucuGAAGAdTdT	1199	UCUUcAGAGUCCUuAACUCdTdT	1626
AD-40005.1	AGuuAAGGAcucuGAAGAudTdT	1200	AUCUUcAGAGUCCUuAACUdTdT	1627
AD-40011.1	GuuAAGGAcucuGAAGAuGdTdT	1201	cAUCUUcAGAGUCCUuAACdTdT	1628
AD-40017.1	uuAAGGAcucuGAAGAuGudTdT	1202	AcAUCUUcAGAGUCCUuAAdTdT	1629
AD-40029.1	AAGGAcucuGAAGAuGuAcdTdT	1203	GuAcAUCUUcAGAGUCCUUdTdT	1630
AD-40035.1	AGGAcucuGAAGAuGuAccdTdT	1204	GGuAcAUCUUcAGAGUCCUdTdT	1631
AD-39994.1	GGAcucuGAAGAuGuAccudTdT	1205	AGGuAcAUCUUcAGAGUCCdTdT	1632
AD-40000.1	GAcucuGAAGAuGuAccuAdTdT	1206	uAGGuAcAUCUUcAGAGUCdTdT	1633
AD-40006.1	AcucuGAAGAuGuAccuAudTdT	1207	AuAGGuAcAUCUUcAGAGUdTdT	1634
AD-40012.1	cucuGAAGAuGuAccuAuGdTdT	1208	cAuAGGuAcAUCUUcAGAGdTdT	1635
AD-40018.1	ucuGAAGAuGuAccuAuGGdTdT	1209	CcAuAGGuAcAUCUUcAGAdTdT	1636
AD-40024.1	cuGAAGAuGuAccuAuGGudTdT	1210	ACcAuAGGuAcAUCUUcAGdTdT	1637
AD-40030.1	uGAAGAuGuAccuAuGGucdTdT	1211	GACcAuAGGuAcAUCUUcAdTdT	1638
AD-40036.1	GuAGGAAAuAAAuGuGAuudTdT	1212	AAUcAcAUUuAUUUCCuACdTdT	1639
AD-39995.1	uAGGAAAuAAAuGuGAuuudTdT	1213	AAAUcAcAUUuAUUUCCuAdTdT	1640
AD-40001.1	AGGAAAuAAAuGuGAuuuGdTdT	1214	cAAAUcAcAUUuAUUUCCUdTdT	1641
AD-40007.1	GGAAAuAAAuGuGAuuuGcdTdT	1215	GcAAAUcAcAUUuAUUUCCdTdT	1642
AD-40013.1	GAAAuAAAuGuGAuuuGccdTdT	1216	GGcAAAUcAcAUUuAUUUCdTdT	1643
AD-40019.1	AAAuAAAuGuGAuuuGccudTdT	1217	AGGcAAAUcAcAUUuAUUUdTdT	1644
AD-40025.1	AAuAAAuGuGAuuuGccuudTdT	1218	AAGGcAAAUcAcAUUuAUUdTdT	1645
AD-40031.1	AuAAAuGuGAuuuGccuucdTdT	1219	GAAGGcAAAUcAcAUUuAUdTdT	1646
AD-40037.1	uAAAuGuGAuuuGccuucudTdT	1220	AGAAGGcAAAUcAcAUUuAdTdT	1647

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AD-39996.1	AAAuGuGAuuuGccuucuAdTdT	1221	uAGAAGGcAAAUcAcAUUUdTdT	1648
AD-40002.1	AAuGuGAuuuGccuucuAGdTdT	1222	CuAGAAGGcAAAUcAcAUUdTdT	1649
AD-40008.1	AuGuGAuuuGccuucuAGAdTdT	1223	UCuAGAAGGcAAAUcAcAUdTdT	1650
AD-40014.1	uGuGAuuuGccuucuAGAAdTdT	1224	UUCuAGAAGGcAAAUcAcAdTdT	1651
AD-40020.1	GuGAuuuGccuucuAGAAcdTdT	1225	GUUCuAGAAGGcAAAUcACdTdT	1652
AD-40026.1	uGAuuuGccuucuAGAAcAdTdT	1226	UGUUCuAGAAGGcAAAUcAdTdT	1653
AD-40032.1	GAuuuGccuucuAGAAcAGdTdT	1227	CUGUUCuAGAAGGcAAAUCdTdT	1654
AD-40038.1	AuuuGccuucuAGAAcAGudTdT	1228	ACUGUUCuAGAAGGcAAAUdTdT	1655
AD-39997.1	uuuGccuucuAGAAcAGuAdTdT	1229	uACUGUUCuAGAAGGcAAAdTdT	1656
AD-40009.1	uGccuucuAGAAcAGuAGAdTdT	1230	UCuACUGUUCuAGAAGGcAdTdT	1657
AD-40015.1	GccuucuAGAAcAGuAGAcdTdT	1231	GUCuACUGUUCuAGAAGGCdTdT	1658
AD-40021.1	ccuucuAGAAcAGuAGAcAdTdT	1232	UGUCuACUGUUCuAGAAGGdTdT	1659
AD-40027.1	cuucuAGAAcAGuAGAcAcdTdT	1233	GUGUCuACUGUUCuAGAAGdTdT	1660
AD-40033.1	uucuAGAAcAGuAGAcAcAdTdT	1234	UGUGUCuACUGUUCuAGAAdTdT	1661
AD-40039.1	ucuAGAAcAGuAGAcAcAAdTdT	1235	UUGUGUCuACUGUUCuAGAdTdT	1662
AD-40045.1	cuAGAAcAGuAGAcAcAAAdTdT	1236	UUUGUGUCuACUGUUCuAGdTdT	1663
AD-40051.1	uAGAAcAGuAGAcAcAAAAdTdT	1237	UUUUGUGUCuACUGUUCuAdTdT	1664
AD-40057.1	AGAAcAGuAGAcAcAAAAcdTdT	1238	GUUUUGUGUCuACUGUUCUdTdT	1665
AD-40063.1	GAAcAGuAGAcAcAAAAcAdTdT	1239	UGUUUUGUGUCuACUGUUCdTdT	1666
AD-40069.1	AAcAGuAGAcAcAAAAcAGdTdT	1240	CUGUUUUGUGUCuACUGUUdTdT	1667
AD-40075.1	AcAGuAGAcAcAAAAcAGGdTdT	1241	CCUGUUUUGUGUCuACUGUdTdT	1668
AD-40081.1	cAGuAGAcAcAAAAcAGGcdTdT	1242	GCCUGUUUUGUGUCuACUGdTdT	1669
AD-40040.1	AGuAGAcAcAAAAcAGGcudTdT	1243	AGCCUGUUUUGUGUCuACUdTdT	1670
AD-40046.1	GuAGAcAcAAAAcAGGcucdTdT	1244	GAGCCUGUUUUGUGUCuACdTdT	1671
AD-40052.1	uAGAcAcAAAAcAGGcucAdTdT	1245	UGAGCCUGUUUUGUGUCuAdTdT	1672
AD-40058.1	AGAcAcAAAAcAGGcucAGdTdT	1246	CUGAGCCUGUUUUGUGUCUdTdT	1673
AD-40064.1	GAcAcAAAAcAGGcucAGGdTdT	1247	CCUGAGCCUGUUUUGUGUCdTdT	1674
AD-40070.1	AcAcAAAAcAGGcucAGGAdTdT	1248	UCCUGAGCCUGUUUUGUGUdTdT	1675
AD-40076.1	cAcAAAAcAGGcucAGGAcdTdT	1249	GUCCUGAGCCUGUUUUGUGdTdT	1676
AD-40082.1	AcAAAAcAGGcucAGGAcudTdT	1250	AGUCCUGAGCCUGUUUUGUdTdT	1677
AD-40041.1	cAAAAcAGGcucAGGAcuudTdT	1251	AAGUCCUGAGCCUGUUUUGdTdT	1678
AD-40047.1	AAAAcAGGcucAGGAcuuAdTdT	1252	uAAGUCCUGAGCCUGUUUUdTdT	1679
AD-40053.1	AAAcAGGcucAGGAcuuAGdTdT	1253	CuAAGUCCUGAGCCUGUUUdTdT	1680
AD-40059.1	AAcAGGcucAGGAcuuAGcdTdT	1254	GCuAAGUCCUGAGCCUGUUdTdT	1681
AD-40065.1	AcAGGcucAGGAcuuAGcAdTdT	1255	UGCuAAGUCCUGAGCCUGUdTdT	1682
AD-40071.1	cAGGcucAGGAcuuAGcAAdTdT	1256	UUGCuAAGUCCUGAGCCUGdTdT	1683
AD-40077.1	AGGcucAGGAcuuAGcAAGdTdT	1257	CUUGCuAAGUCCUGAGCCUdTdT	1684
AD-40083.1	GGcucAGGAcuuAGcAAGAdTdT	1258	UCUUGCuAAGUCCUGAGCCdTdT	1685
AD-40042.1	GcucAGGAcuuAGcAAGAAdTdT	1259	UUCUUGCuAAGUCCUGAGCdTdT	1686
AD-40048.1	cucAGGAcuuAGcAAGAAGdTdT	1260	CUUCUUGCuAAGUCCUGAGdTdT	1687
AD-40054.1	ucAGGAcuuAGcAAGAAGudTdT	1261	ACUUCUUGCuAAGUCCUGAdTdT	1688
AD-40060.1	cAGGAcuuAGcAAGAAGuudTdT	1262	AACUUCUUGCuAAGUCCUGdTdT	1689
AD-40066.1	AGGAcuuAGcAAGAAGuuAdTdT	1263	uAACUUCUUGCuAAGUCCUdTdT	1690
AD-40072.1	GGAcuuAGcAAGAAGuuAudTdT	1264	AuAACUUCUUGCuAAGUCCdTdT	1691

[3755]

AD-40078.1	GAcuuAGcAAGAAGuuAuGdTdT	1265	cAuAACUUCUUGCuAAGUCdTdT	1692
AD-40084.1	AcuuAGcAAGAAGuuAuGGdTdT	1266	CcAuAACUUCUUGCuAAGUdTdT	1693
AD-40043.1	cuuAGcAAGAAGuuAuGGAdTdT	1267	UCcAuAACUUCUUGCuAAGdTdT	1694
AD-40049.1	uuAGcAAGAAGuuAuGGAAdTdT	1268	UUCcAuAACUUCUUGCuAAdTdT	1695
AD-40055.1	uAGcAAGAAGuuAuGGAAudTdT	1269	AUUCcAuAACUUCUUGCuAdTdT	1696
AD-40061.1	AGcAAGAAGuuAuGGAAuudTdT	1270	AAUUCcAuAACUUCUUGCUdTdT	1697
AD-40067.1	GcAAGAAGuuAuGGAAuucdTdT	1271	GAAUUCcAuAACUUCUUGCdTdT	1698
AD-40073.1	cAAGAAGuuAuGGAAuuccdTdT	1272	GGAAUUCcAuAACUUCUUGdTdT	1699
AD-40079.1	AAGAAGuuAuGGAAuuccudTdT	1273	AGGAAUUCcAuAACUUCUUdTdT	1700
AD-40085.1	AGAAGuuAuGGAAuuccuudTdT	1274	AAGGAAUUCcAuAACUUCUdTdT	1701
AD-40044.1	GAAGuuAuGGAAuuccuuudTdT	1275	AAAGGAAUUCcAuAACUUCdTdT	1702
AD-40050.1	AAGuuAuGGAAuuccuuuudTdT	1276	AAAAGGAAUUCcAuAACUUdTdT	1703
AD-40056.1	AGuuAuGGAAuuccuuuuAdTdT	1277	uAAAAGGAAUUCcAuAACUdTdT	1704
AD-40062.1	GuuAuGGAAuuccuuuuAudTdT	1278	AuAAAAGGAAUUCcAuAACdTdT	1705
AD-40068.1	uuAuGGAAuuccuuuuAuudTdT	1279	AAuAAAAGGAAUUCcAuAAdTdT	1706
AD-40074.1	uAuGGAAuuccuuuuAuuGdTdT	1280	cAAuAAAAGGAAUUCcAuAdTdT	1707
AD-40080.1	AuGGAAuuccuuuuAuuGAdTdT	1281	UcAAuAAAAGGAAUUCcAUdTdT	1708
AD-39720.1	ActtGtGGtAGttGGAGcttt	1792	AGCTCcAACtACcAcAAGTtt	1830
AD-39706.1	GcAAGAGtGccttGAcGAttt	1793	ATCGTcAAGGcACTCTTGCtt	1831
AD-39712.1	cAAGAGtGccttGAcGAtAtt	1794	tATCGTcAAGGcACTCTTGtt	1832
AD-39760.1	ccttGAcGAtAcAGctAAttt	1795	ATtAGCTGtATCGTcAAGGtt	1833
AD-39732.1	cAGctAAttcAGAAtcAtttt	1796	AATGATTCTGAATTAGCTGtt	1834
AD-35541.4	cGAAtAtGAtccAAcAAtAtt	1797	tATTGTTGGATcAtATTCGtt	1835
AD-39735.1 或 hs_KRAS 321_A22S26	GGAAGcAAGtAGtAAttGAuu	1798	TcAATTACtACTTGCTTCCuu	1836
AD-39741.1 或 hs_KRAS 322_A22S26	GAAGcAAGtAGtAAttGAtuu	1799	ATcAATTACtACTTGCTTCuu	1837
AD-39778.1	AGtAGtAAttGAtGGAGAAtt	1800	TTCTCcATcAATTACtACTTt	1838
AD-39790.1	tAGtAAttGAtGGAGAAActt	1801	GTTTCTCcATcAATTACtAtt	1839
AD-39822.1	GtctcttGGAtAttctcGAtt	1802	TCGAGAAtATCcAAGAGACtt	1840
AD-35609.4	GGGctttctttGtGtAttttt	1803	AAAtAcAcAAAGAAAGCCCtt	1841
AD-35581.4	GtGtAtttGccAtAAAtAAtt	1804	TtATTtATGGcAAAtAcACtt	1842
AD-39845.1	ccAtAAAtAAtActAAAtctt	1805	GATTtAGtATtATTtATGGtt	1843
AD-39858.1	tActAAAtcAtttGAAGAttt	1806	ATCTTcAAATGATTtAGtAtt	1844
AD-39870.1	ctAAAtcAtttGAAGAtAtuu	1807	AtATCTTcAAATGATTtAGuu	1845
AD-35576.4	GAAGAtAttcAccAttAtAtt	1808	tAtAATGGTGAAtATCTTCtt	1846
AD-35588.4	AGAtAttcAccAttAtAGAtt	1809	TCtAtAATGGTGAAtATCTTt	1847
AD-35600.1	AtAttcAccAttAtAGAGAtt	1810	TCTCtAtAATGGTGAAtATtt	1848
AD-35606.1	tAttcAccAttAtAGAGAAtt	1811	TTCTCtAtAATGGTGAAtAtt	1849
AD-38151.1	cAttAtAGAGAAcAAAttAtt	1812	tAATTTGTTCTCtAtAATGtt	1850
AD-38163.1	ttAtAGAGAAcAAAttAAAtt	1813	TTtAATTTGTTCTCtAtAAtt	1851
AD-39999.1	GAGttAAGGActctGAAGAtt	1814	TCTTcAGAGTCCTtAACTCtt	1852

[3756]

AD-38159.1 或 hs_KRAS 528_A22S26	ctAtGGtcctAGtAGGAAAuu	1815	TTTCCtACtAGGACcAtAGuu	1853
AD-38130.1 或 hs_KRAS 531_A22S26	tGGtcctAGtAGGAAAtAAuu	1816	TtATTTCCtACtAGGACcAuu	1854
AD-38136.1	GGtcctAGtAGGAAAtAAAtt	1817	TTtATTTCCtACtAGGACCtt	1855
AD-40036.1	GtAGGAAAtAAAtGtGAtttt	1818	AATcAcATTtATTTCCtACtt	1856
AD-40008.1	AtGtGAtttGccttctAGAtt	1819	TCtAGAAGGcAAATcAcATtt	1857
AD-40021.1	ccttctAGAAcAGtAGAcAtt	1820	TGTCtACTGTTCtAGAAGGtt	1858
AD-40077.1	AGGctcAGGActtAGcAAGtt	1821	CTTGCtAAGTCCTGAGCCTtt	1859
AD-40072.1	GGActtAGcAAGAAGttAttt	1822	AtAACTTCTTGCtAAGTCCtt	1860
AD-40061.1	AGcAAGAAGttAtGGAAtttt	1823	AATTCcAtAACTTCTTGCTtt	1861
AD-40068.1	ttAtGGAAttccttttAtttt	1824	AAtAAAAGGAATTCcAtAAtt	1862
AD-38131.1	GGAAttccttttAttGAAAtt	1825	TTTcAAtAAAAGGAATTCCtt	1863
AD-38167.1	cctttttAttGAAAcAtcAGtt	1826	CTGATGTTTcAAtAAAAGGtt	1864
hs_KRAS 1273_A22S26	cctGAtGAAtGtAAAGttAuu	1827	tAACTTTtAcATTcATcAGGuu	1865
hs_KRAS 2892_A37S26	GGAGAAtttAAtAAAGAtAuu	1828	TATCTTtATTtAAATTCTCCuu	1866
hs_KRAS 4731_A22S26	GAAtAGtcAtAActAGAttuu	1829	AATCtAGTtATGACtATTCuu	1867

[3757] 本领域技术人员很容易设想对 RNAi 剂序列的修饰。构想了这些序列的示例性和非限制性修饰并同样列于表 3 中。应注意到，许多序列的末端为 dTdT。其为已知可保护 siRNA 免遭核酸酶（如血清或肠液中的那些核酸酶）降解的 TT 末端突出端的变体。dTdT 或 TT 末端突出端是任选的；它们可被各种类型的 3’末端帽结构代替，条件是 3’末端帽结构能够介导核酸酶抗性并使 siRNA 具有活性。

[3758] 将一些修饰置于据预测对核酸内切酶敏感的位点处。某些修饰被设计为用于消除对 siRNA 的免疫反应并同时保留活性。通常，对有义链的修饰较重，对反义链的修饰较轻。某些修饰具有一种以上的目的。

[3759] 表 1 至 3 中的序列由如下这些缩写代表：

[3760] 表 1A. 缩写

[3761]

缩写	核苷酸
A	腺苷 -5’ - 磷酸
C	胞苷 -5’ - 磷酸
G	鸟苷 -5’ - 磷酸
dT	2’ - 脱氧胸苷 -5’ - 磷酸
U	尿苷 -5’ - 磷酸

C	2'-O- 甲基胞苷 -5'- 磷酸
U	2'-O- 甲基尿苷 -5'- 磷酸
sdT	2'- 脱氧胸苷 5'- 硫代磷酸酯

[3762] siRNA 序列选择

[3763] 按照本文中的描述合成有义和反义的人 SCNNB1- 衍生的 siRNA 寡聚物（针对 KRAS 的 RNAi 剂）。将有义寡聚物和其相应的反义寡聚物复性成双链体。

[3764] 实施例 2

[3765] KRAS RNAi 剂的重叠群组

[3766] 本公开还涉及具有重叠序列的针对 KRAS 的 RNAi 剂群组。因此，本公开涵盖 RNAi 剂群组，其中该群组中的每种 RNAi 剂与相同群组中的各其它 RNAi 重叠至少 5、6、7、8、9、10、11、12、13、14、15、16、17、18、19 或更多个核苷酸。特别是，在一个实施方案中，该重叠是至少 12 个核苷酸。

[3767] 本文中所列的某些 RNAi 剂在序列中彼此重叠。表 4 中显示了某些重叠 RNAi 剂群组的汇编，其中群组的每个成员与相同群组的各其它成员重叠至少 12 个核苷酸。显示了有义链的 12 个核苷酸重叠部分和反义链的 12 个核苷酸重叠部分。

[3768] 因此，例如，如表 4 中所示，双链体 AD-39695.1、AD-39689.1、AD-39707.1、AD-39683.1 和 AD-39701.1 的序列均有重叠，其中有义链中的重叠包含序列 CUGAAUAUAAAC(SEQ ID NO:1874)，反义链中的重叠包含序列 GUUUAUAUUCAG(SEQ ID NO:1875)。

[3769] 但是，本公开涵盖享有序列重叠（例如重叠至少 12 个核苷酸）这一共同技术特征的 KRAS RNAi 剂的任何群或亚群或组或亚组。因此，本公开不仅涵盖示例性的组 AD-39695.1、AD-39689.1、AD-39707.1、AD-39683.1 和 AD-39701.1，而且涵盖如下亚组 :AD-39695.1 和 AD-39689.1 ;AD-39695.1 和 AD-39707.1 ;AD-39695.1、AD-39689.1 和 AD-39701.1 ;AD-39689.1、AD-39707.1 和 AD-39701.1 ;AD-39707.1 和 AD-39683.1 ;AD-39707.1、AD-39683.1 和 AD-39701.1 等 ;以及重叠 KRAS RNAi 剂的任何其它组。

[3770] 表 4.KRAS RNAi 剂的重叠群组

[3771]

有义链重叠	SEQ ID NO:	反义链重叠	SEQ ID NO:	针对 KRAS 的重叠 RNAi 剂
UGACUGAAUAUA	1868	UAUAUUCAGUCA	1869	AD-39689.1,AD-39683.1
GACUGAAUAUAA	1870	UUAUAUUCAGUC	1871	AD-39695.1,AD-39689.1,AD-39683.1
ACUGAAUAUAAA	1872	UUUAUAUUCAGU	1873	AD-39695.1,AD-39689.1,AD-39683.1,AD-39701.1
CUGAAUAUAAAC	1874	GUUUAUAUUCAG	1875	AD-39695.1,AD-39689.1,AD-39707.1,AD-39683.1,AD-39701.1
UGAAUAUAAACU	1876	AGUUUAUAUUCA	1877	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1
GAAUAUAAACUU	1878	AAGUUUAUAUUC	1879	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1,AD-39719.1
AAUAUAAACUUG	1880	CAAGUUUAUAUU	1881	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39683.1,AD-39701.1,AD-39725.1,AD-39719.1
AUAUAAACUUGU	1882	ACAAGUUUAUAU	1883	AD-39695.1,AD-39689.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1
UAUAAACUUGUG	1884	CACAAGUUUAUA	1885	AD-39690.1,AD-39695.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1
AUAAACUUGUGG	1886	CCACAAGUUUAU	1887	AD-39690.1,AD-39713.1,AD-39707.1,AD-39701.1,AD-39725.1,AD-39719.1,AD-39684.1,AD-39696.1
UAAACUUGUGGU	1888	ACCACAAGUUUA	1889	AD-39690.1,AD-39713.1,AD-39707.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39696.1

[3772]

AAACUUGUGGUA	1890	UACCACAAGUUU	1891	AD-39690.1,AD-39713.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39696.1,AD-39708.1
AACUUGUGGUAG	1892	CUACCACAAGUU	1893	AD-39690.1,AD-39725.1,AD-39702.1,AD-39719.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1
ACUUGUGGUAGU	1894	ACUACCACAAGU	1895	AD-39690.1,AD-39725.1,AD-39702.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1
CUUGUGGUAGUU	1896	AACUACCACAAG	1897	AD-39690.1,AD-39702.1,AD-39684.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1
UUGUCGUAGUUG	1898	CAACUACCACAA	1899	AD-39690.1,AD-39702.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
UGUGGUAGUUGG	1900	CCAACUACCACA	1901	AD-39691.1,AD-39702.1,AD-39714.1,AD-39696.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
GUGGUAGUUGGA	1902	UCCAACUACCAC	1903	AD-39691.1,AD-39697.1,AD-39702.1,AD-39714.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
UGGUAGUUGGAG	1904	CUCCAACUACCA	1905	AD-39703.1,AD-39691.1,AD-39697.1,AD-39714.1,AD-39708.1,AD-39720.1,AD-39726.1,AD-39685.1
GGUAGUUGGAGC	1906	GCUCCAACUACC	1907	AD-39703.1,AD-39691.1,AD-39697.1,AD-39714.1,AD-39709.1,AD-39720.1,AD-39726.1,AD-39685.1
GUAGUUGGAGCU	1908	AGCUCCAACUAC	1909	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39720.1,AD-39726.1,AD-39685.1
UAGUUGGAGCUG	1910	CAGCUCCAACUA	1911	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39726.1,AD-39685.1
AGUUGGAGCUCG	1912	CGAGCUCCAACU	1913	AD-39703.1,AD-39691.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1,AD-39685.1
GUUGGAGCUGGU	1914	ACCAGCUCCAAC	1915	AD-39703.1,AD-39691.1,AD-39686.1,AD-39697.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1
UUGGAGCUGGUG	1916	CACCAGCUCCAA	1917	AD-39703.1,AD-39686.1,AD-39697.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39721.1,AD-39727.1
UGGAGCUGGUGG	1918	CCACCAGCUCCA	1919	AD-39703.1,AD-39686.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39698.1,AD-39721.1,AD-39727.1
GGAGCUGGUGGC	1920	GCCACCAGCUCC	1921	AD-39686.1,AD-39692.1,AD-39715.1,AD-39709.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
GAGCUGGUGGCG	1922	CGCCACCAGCUC	1923	AD-39710.1,AD-39686.1,AD-39692.1,AD-39715.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
AGCUGGUGGCGU	1924	ACGCCACCAGCU	1925	AD-39710.1,AD-39686.1,AD-39692.1,AD-39716.1,AD-39698.1,AD-39721.1,AD-39704.1,AD-39727.1
GCUGGUGGCGUA	1926	UACGCCACCAGC	1927	AD-39710.1,AD-39686.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39698.1,AD-39704.1,AD-39727.1
CUGGUGGCGUAG	1928	CUACGCCACCAG	1929	AD-39710.1,AD-39686.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1
UGGUGGCGUAGG	1930	CCUACGCCACCA	1931	AD-39710.1,AD-39687.1,AD-39692.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1
GGUGGCGUAGGC	1932	GCCUACGCCACC	1933	AD-39693.1,AD-39710.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39698.1,AD-39704.1

[3773]

GUGGCGUAGGCA	1934	UGCCUACGCCAC	1935	AD-39693.1,AD-39710.1,AD-39699.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39728.1,AD-39704.1
UGGCGUAGGCAA	1936	UUGCCUACGCCA	1937	AD-39693.1,AD-39710.1,AD-39699.1,AD-39687.1,AD-39722.1,AD-39716.1,AD-39705.1,AD-39728.1
GCCGUAGCCAAG	1938	CUUGCCUACGCC	1939	AD-39693.1,AD-39699.1,AD-39687.1,AD-39711.1,AD-39722.1,AD-39716.1,AD-39705.1,AD-39728.1
GCGUAGGCAAGA	1940	UCUUGCCUACGC	1941	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-39722.1,AD-39705.1,AD-39728.1
CGUACGCAACAG	1942	CUCUUGCCUACG	1943	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-39705.1,AD-39728.1,AD-39723.1
GUAGGCAAGAGU	1944	ACUCUUGCCUAC	1945	AD-39693.1,AD-39699.1,AD-39687.1,AD-39717.1,AD-39711.1,AD-39729.1,AD-39705.1,AD-39723.1
UAGGCAAGAGUG	1946	CACUCUUGCCUA	1947	AD-39693.1,AD-39699.1,AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39723.1
AGGCAAGAGUGC	1948	GCACUCUUGCCU	1949	AD-39699.1,AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39694.1,AD-39723.1
GGCAAGAGUGCC	1950	GGCACUCUUGCC	1951	AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39705.1,AD-39694.1,AD-39700.1,AD-39723.1
GCAAGAGUGCCU	1952	AGGCACUCUUGC	1953	AD-39717.1,AD-39711.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
CAAGAGUGCCUU	1954	AAGGCACUCUUG	1955	AD-39712.1,AD-39717.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
AAGACUCCCUUG	1956	CAACCCACUCUU	1957	AD-39718.1,AD-39712.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39723.1
AGAGUGCCUUGA	1958	UCAAGGCACUCU	1959	AD-39718.1,AD-39712.1,AD-39724.1,AD-39688.1,AD-39729.1,AD-39706.1,AD-39694.1,AD-39700.1
GAGUGCCUUGAC	1960	GUCAAGGCACUC	1961	AD-39718.1,AD-39712.1,AD-39724.1,AD-39688.1,AD-39706.1,AD-39694.1,AD-39700.1,AD-39730.1
AGUGCCUUGACG	1962	CGUCAAGGCACU	1963	AD-39718.1,AD-39712.1,AD-39724.1,AD-39706.1,AD-39694.1,AD-39736.1,AD-39700.1,AD-39730.1
GUGCCUUGACGA	1964	UCGUCAAGGCAC	1965	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39706.1,AD-39736.1,AD-39700.1,AD-39730.1
UGCCUUGACGAU	1966	AUCGUCAAGGCA	1967	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39706.1,AD-39736.1,AD-39748.1,AD-39730.1
GCCUUGACGAUA	1968	UAUCGUCAAGGC	1969	AD-39718.1,AD-39712.1,AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39730.1
CCUUGACGAUAC	1970	GUAUCGUCAAGG	1971	AD-39718.1,AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1
CUUGACGAUACA	1972	UGUAUCGUCAAG	1973	AD-39724.1,AD-39742.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1,AD-39766.1
UUGACGAUACAG	1974	CUGUAUCGUCAA	1975	AD-39742.1,AD-39772.1,AD-39754.1,AD-39736.1,AD-39748.1,AD-39760.1,AD-39730.1,AD-39766.1
UGACGAUACAGC	1976	GCUGUAUCGUCA	1977	AD-39742.1,AD-39772.1,AD-39754.1,AD-39736.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1

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GACGAUACAGCU	1978	AGCUGJAUCGUC	1979	AD-39737.1,AD-39742.1,AD-39772.1,AD-39754.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1
ACGAUACAGCUA	1980	UAGCUGUAUCGU	1981	AD-39737.1,AD-39772.1,AD-39754.1,AD-39743.1,AD-39731.1,AD-39748.1,AD-39760.1,AD-39766.1
CGAUACAGCUAA	1982	UUAGCJGUAUCG	1983	AD-39737.1,AD-39772.1,AD-39754.1,AD-39743.1,AD-39731.1,AD-39760.1,AD-39749.1,AD-39766.1
GAUACAGCUAAU	1984	AUUAGCUGUAUC	1985	AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39760.1,AD-39749.1,AD-39755.1,AD-39766.1
AUACAGCUAAUU	1986	AAUUAGCUGUAU	1987	AD-39761.1,AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39749.1,AD-39755.1,AD-39766.1
UACAGCUAAUUC	1988	GAAUUAGCUGUA	1989	AD-39767.1,AD-39761.1,AD-39737.1,AD-39772.1,AD-39743.1,AD-39731.1,AD-39749.1,AD-39755.1
ACAGCUAAUUCA	1990	UGAAUUAGCUGU	1991	AD-39767.1,AD-39761.1,AD-39737.1,AD-39743.1,AD-39731.1,AD-39773.1,AD-39749.1,AD-39755.1
CAGCUAAUUCAG	1992	CUGAAJUAGCUG	1993	AD-39767.1,AD-39761.1,AD-39737.1,AD-39732.1,AD-39743.1,AD-39773.1,AD-39749.1,AD-39755.1
AGCUAAUUCAGA	1994	UCUGAAUUAGCU	1995	AD-39767.1,AD-39761.1,AD-39732.1,AD-39743.1,AD-39738.1,AD-39773.1,AD-39749.1,AD-39755.1
GCUAAUUCAGAA	1996	UUCUGAAUUAGC	1997	AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39738.1,AD-39773.1,AD-39749.1,AD-39755.1
CUAAUUCAGAAU	1998	AUUCUGAAUUAG	1999	AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1,AD-39755.1
UAAUUCACAAUC	2000	GAUUCJGAAUUA	2001	AD-39756.1,AD-39767.1,AD-39761.1,AD-39744.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1
AAUUCAGAAUCA	2002	UGAUUCUGAAUU	2003	AD-39756.1,AD-39767.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39750.1,AD-39738.1,AD-39773.1
AUUCAGAAUCAU	2004	AUGAUUCUGAAU	2005	AD-39756.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39768.1,AD-39750.1,AD-39738.1,AD-39773.1
UUCAGAAUCAUU	2006	AAUGAJUCUGAA	2007	AD-39756.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39732.1,AD-39768.1,AD-39750.1,AD-39738.1
UCAGAAUCAUUU	2008	AAAUGAUUCUGA	2009	AD-39756.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1,AD-39738.1
CAGAAUCAUUUU	2010	AAAAUGAUUCUG	2011	AD-39756.1,AD-39739.1,AD-39774.1,AD-39744.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1
AGAAUCAUUUUG	2012	CAAAAUGAUUCU	2013	AD-39745.1,AD-39756.1,AD-39739.1,AD-39774.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39750.1
GAAUCAUUUUGU	2014	ACAAAAUCAUUC	2015	AD-39745.1,AD-39756.1,AD-39739.1,AD-39774.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39751.1
AAUCAUUUUGUG	2016	CACAAAAUGAUU	2017	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39762.1,AD-39733.1,AD-39768.1,AD-39751.1
AUCAUUUUGUGG	2018	CCACAAAAUGAU	2019	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39733.1,AD-39768.1,AD-39751.1,AD-39763.1
UCAUUUUGUGGA	2020	UCCACAAAAUGA	2021	AD-39745.1,AD-39739.1,AD-39774.1,AD-39757.1,AD-39733.1,AD-39751.1,AD-39769.1,AD-39763.1

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CAUUUUGUGGAC	2022	GUCCACAAAAUG	2023	AD-39745.1,AD-39739.1,AD-39775.1,AD-39757.1,AD-39733.1,AD-39751.1,AD-39769.1,AD-39763.1
AUUUUGUGGACG	2024	CGUCCACAAAAU	2025	AD-39745.1,AD-39739.1,AD-39775.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39763.1,AD-39734.1
UUUUGUGGACGA	2026	UCGUCCACAAAA	2027	AD-39745.1,AD-39775.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UUUGUGGACGAA	2028	UUCGUCCACAAA	2029	AD-39775.1,AD-39746.1,AD-39757.1,AD-39751.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UUGUCCACGAAU	2030	AUUCGUCCACAA	2031	AD-39752.1,AD-39775.1,AD-39746.1,AD-39757.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
UGUGGACGAAUA	2032	UAUUCGUCCACA	2033	AD-39752.1,AD-39775.1,AD-39746.1,AD-39758.1,AD-39769.1,AD-39740.1,AD-39763.1,AD-39734.1
GUGGACGAAUAU	2034	AUAUUCGUCCAC	2035	AD-39752.1,AD-39775.1,AD-39764.1,AD-39746.1,AD-39758.1,AD-39769.1,AD-39740.1,AD-39734.1
UGGACGAAUAUG	2036	CAUAUUCGUCCA	2037	AD-39752.1,AD-39775.1,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1,AD-39734.1
GGACGAAUAUGA	2038	UCAUAUUCGUCC	2039	AD-39752.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1,AD-39734.1
GACGAAUAUGAU	2040	AUCAUAUUCGUC	2041	AD-39752.1,AD-35529.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-39770.1,AD-39758.1,AD-39740.1
ACGAAUAUGAUC	2042	GAUCAUAUUCGU	2043	AD-39752.1,AD-35529.1,AD-35523.3,AD-39764.1,AD-39746.1,AD-35535.4,AD-39770.1,AD-39758.1
CGAAUAUCAUCC	2044	GGAUCAUAUUCG	2045	AD-39752.1,AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-39758.1
GAAUAUGAUCCA	2046	UGGAUCAUAUUC	2047	AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-39758.1,AD-35547.4
AAUAUGAUCCAA	2048	UUGGAUCAUAUU	2049	AD-35529.1,AD-35523.3,AD-35541.4,AD-39764.1,AD-35535.4,AD-39770.1,AD-35553.4,AD-35547.4
AUAUGAUCCAAC	2050	GUUGGAUCAUAU	2051	AD-35529.1,AD-35523.3,AD-35541.4,AD-35559.4,AD-35535.4,AD-39770.1,AD-35553.4,AD-35547.4
UAUGAUCCAACA	2052	UGUUGGAUCAUA	2053	AD-35529.1,AD-35523.3,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4
AUGAUCCAACAA	2054	UUGUUGGAUCAU	2055	AD-35529.1,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4,AD-35524.4
UGAUCCAACAAU	2056	AUUGUUGGAUCA	2057	AD-35530.4,AD-35541.4,AD-35565.4,AD-35559.4,AD-35535.4,AD-35553.4,AD-35547.4,AD-35524.4
GAUCCAACAAUA	2058	UAUUGUUGGAUC	2059	AD-35530.4,AD-35541.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35536.4,AD-35547.4,AD-35524.4
AUCCAACAAUAG	2060	CUAUUGUUGGAU	2061	AD-35530.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35542.4,AD-35536.4,AD-35547.4,AD-35524.4
UCCAACAAUAGA	2062	UCUAUUGUUGGA	2063	AD-35530.4,AD-35565.4,AD-35559.4,AD-35553.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35524.4
CCAACAAUAGAG	2064	CUCUAUUGUUGG	2065	AD-35554.4,AD-35530.4,AD-35565.4,AD-35559.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35524.4

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CAACAAUAGAGG	2066	CCUCUAUUGUUG	2067	AD-35554.4,AD-35530.4,AD-35565.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2,AD-35524.4
AACAAJAGAGGA	2068	UCCUCUAUUGUJ	2069	AD-35554.4,AD-35530.4,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2,AD-35524.4
ACAAUAGAGGAU	2070	AUCCUCUAUUGJ	2071	AD-35554.4,AD-35530.4,AD-35525.2,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35560.2
CAAUAGAGGAUU	2072	AAUCCUCUAUUG	2073	AD-35554.4,AD-35525.2,AD-35566.4,AD-35548.4,AD-35542.4,AD-35536.4,AD-35531.4,AD-35560.2
AAUAGAGGAUUC	2074	GAAUCCUCUAUJ	2075	AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35548.4,AD-35542.4,AD-35531.4,AD-35560.2
AUAGAGGAUUCC	2076	GGAAUCCUCUAJ	2077	AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35548.4,AD-35531.4,AD-35560.2,AD-35543.2
UAGAGGAUUCCU	2078	AGGAAUCCUCUA	2079	AD-35549.4,AD-35554.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35560.2,AD-35543.2
AGAGGAUUCCUA	2080	UAGGAAUCCUCJ	2081	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35560.2,AD-35543.2
GAGGAJUCCUAC	2082	GUAGGAAUCCUC	2083	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35566.4,AD-35531.4,AD-35561.4,AD-35543.2
AGGAUJCCUACA	2084	UGUAGGAAUCCJ	2085	AD-35549.4,AD-35555.4,AD-35525.2,AD-35537.4,AD-35531.4,AD-35561.4,AD-35543.2,AD-35567.4
GGAUUCCUACAG	2086	CUGUAGGAAUCC	2087	AD-35549.4,AD-35555.4,AD-35526.4,AD-35537.4,AD-35531.4,AD-35561.4,AD-35543.2,AD-35567.4
GAUUCCUACAGG	2088	CCUGUAGGAAUC	2089	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35537.4,AD-35561.4,AD-35543.2,AD-35567.4
AUUCCUACAGGA	2090	UCCUGUAGGAAJ	2091	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35538.4,AD-35561.4,AD-35543.2,AD-35567.4
UUCCUACAGGAA	2092	UUCCUGUAGGAA	2093	AD-35549.4,AD-35555.4,AD-35532.4,AD-35526.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
UCCUACAGGAAG	2094	CUUCCUGUAGGA	2095	AD-35555.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
CCUACAGGAAGC	2096	GCUUCCUGUAGG	2097	AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35561.4,AD-35567.4
CUACAGGAAGCA	2098	UGCUUCCUGUAG	2099	AD-35562.4,AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35538.4,AD-35544.4,AD-35567.4
UACAGGAAGCAA	2100	UUGCUUCCUGUA	2101	AD-35562.4,AD-35556.4,AD-35532.4,AD-35526.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4
ACAGGAAGCAAG	2102	CUUGCUUCCUGJ	2103	AD-35562.4,AD-35556.4,AD-35532.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4,AD-35527.4
CAGGAAGCAAGU	2104	ACUUGCUUCCUG	2105	AD-35562.4,AD-35556.4,AD-35550.4,AD-35568.4,AD-35538.4,AD-35544.4,AD-35533.4,AD-35527.4
AGGAAGCAAGUA	2106	UACUUGCUUCCJ	2107	AD-35562.4,AD-35556.4,AD-35550.4,AD-39776.1,AD-35568.4,AD-35544.4,AD-35533.4,AD-35527.4
GGAAGCAAGUAG	2108	CUACUUGCUUCC	2109	AD-35562.4,AD-39735.1,AD-35556.4,AD-35550.4,AD-39776.1,AD-35568.4,AD-35533.4,AD-35527.4

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GAAGCAAGUAGU	2110	ACUACUUGCUUC	2111	AD-35562.4,AD-39735.1,AD-35556.4,AD-39776.1,AD-35568.4,AD-35533.4,AD-35527.4,AD-39741.1
AAGCAAGUAGUA	2112	UACUACUUGCUU	2113	AD-35562.4,AD-39735.1,AD-39776.1,AD-35568.4,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
AGCAAGUAGUAA	2114	UUACUACUUGCU	2115	AD-39735.1,AD-39753.1,AD-39776.1,AD-35568.4,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
GCAAGUAGUAAU	2116	AUUACUACUUGC	2117	AD-39735.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-35533.4,AD-35527.4,AD-39741.1
CAAGUAGUAAUU	2118	AAUUACUACUUG	2119	AD-39735.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-35533.4,AD-39765.1,AD-39741.1
AAGUAGUAAUUG	2120	CAAUUACUACUU	2121	AD-39735.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39776.1,AD-39747.1,AD-39765.1,AD-39741.1
AGUAGUAAUUGA	2122	UCAAUUACUACU	2123	AD-39735.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39747.1,AD-39765.1,AD-39741.1
GUAGUAAUUGAU	2124	AUCAAUUACUAC	2125	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39747.1,AD-39765.1,AD-39741.1
UAGUAAUUGAUG	2126	CAUCAAUUACUA	2127	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39747.1,AD-39765.1,AD-39790.1
AGUAAUUGAUGG	2128	CCAUCAAUUACU	2129	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39753.1,AD-39796.1,AD-39765.1,AD-39790.1
GUAAUUGAUGGA	2130	UCCAUCAAUUAC	2131	AD-39784.1,AD-39778.1,AD-39771.1,AD-39759.1,AD-39796.1,AD-39765.1,AD-39802.1,AD-39790.1
UAAUUGAUGGAG	2132	CUCCAUCAAUUA	2133	AD-39784.1,AD-39778.1,AD-39808.1,AD-39771.1,AD-39796.1,AD-39765.1,AD-39802.1,AD-39790.1
AAUUGAUGGAGA	2134	UCUCCAUCAAUU	2135	AD-39784.1,AD-39814.1,AD-39778.1,AD-39808.1,AD-39771.1,AD-39796.1,AD-39802.1,AD-39790.1
AUUGAUGGAGAA	2136	UUCUCCAUCAAU	2137	AD-39784.1,AD-39814.1,AD-39778.1,AD-39808.1,AD-39820.1,AD-39796.1,AD-39802.1,AD-39790.1
UUGAUGGAGAAA	2138	UUUCUCCAUCAA	2139	AD-39784.1,AD-39814.1,AD-39808.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1,AD-39790.1
UGAUGGAGAAAC	2140	GUUUCUCCAUCA	2141	AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1,AD-39790.1
GAUGGAGAAACC	2142	GGUUUCUCCAUC	2143	AD-39791.1,AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39796.1,AD-39802.1
AUGGAGAAACCU	2144	AGGUUUCUCCAU	2145	AD-39791.1,AD-39814.1,AD-39808.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39797.1,AD-39802.1
UGGACAAACCUC	2146	CAGGUUUCUCCA	2147	AD-39791.1,AD-39814.1,AD-39808.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39779.1,AD-39797.1
GGAGAAACCUGU	2148	ACAGGUUUCUCC	2149	AD-39791.1,AD-39814.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39809.1,AD-39779.1,AD-39797.1
GAGAAACCUGUC	2150	GACAGGUUUCUC	2151	AD-39815.1,AD-39791.1,AD-39803.1,AD-39785.1,AD-39820.1,AD-39809.1,AD-39779.1,AD-39797.1
AGAAACCUGUCU	2152	AGACAGGUUUCU	2153	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39785.1,AD-39809.1,AD-39779.1,AD-39797.1

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GAAACCUGUCUC	2154	GAGACAGGUUUC	2155	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39785.1,AD-39809.1,AD-39780.1,AD-39797.1
AAACCUGUCUCU	2156	AGAGACAGGUUU	2157	AD-39815.1,AD-39791.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39780.1,AD-39797.1,AD-39786.1
AACCUGUCUCUU	2158	AAGAGACAGGUU	2159	AD-39815.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39780.1,AD-39797.1,AD-39786.1
ACCUGUCUCUUG	2160	CAAGAGACAGGU	2161	AD-39815.1,AD-39803.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39780.1,AD-39798.1,AD-39786.1
CCUGUCUCUUCG	2162	CCAAGAGACAGG	2163	AD-39815.1,AD-39821.1,AD-39809.1,AD-39792.1,AD-39804.1,AD-39780.1,AD-39798.1,AD-39786.1
CUGUCUCUUGGA	2164	UCCAAGAGACAG	2165	AD-39815.1,AD-39821.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39798.1,AD-39786.1
UGUCUCUUGGAU	2166	AUCCAAGAGACA	2167	AD-39816.1,AD-39821.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39798.1,AD-39786.1
GUCUCUUGGAUA	2168	UAUCCAAGAGAC	2169	AD-39816.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39780.1,AD-39822.1,AD-39798.1,AD-39786.1
UCUCUUGGAUAU	2170	AUAUCCAAGAGA	2171	AD-39816.1,AD-39792.1,AD-39804.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1,AD-39786.1
CUCUUGGAUAUU	2172	AAUAUCCAAGAG	2173	AD-39816.1,AD-39792.1,AD-39804.1,AD-39787.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1
UCUUGGAUAUUC	2174	GAAUAUCCAAGA	2175	AD-39816.1,AD-39793.1,AD-39804.1,AD-39787.1,AD-39810.1,AD-39781.1,AD-39822.1,AD-39798.1
CUUGCAUAUUCU	2176	ACAAUAUCCAAG	2177	AD-39799.1,AD-39816.1,AD-39793.1,AD-39804.1,AD-39787.1,AD-39781.1,AD-39822.1
UUGGAUAUUCUC	2178	GAGAAUAUCCAA	2179	AD-39799.1,AD-39816.1,AD-39793.1,AD-39787.1,AD-35539.4,AD-39810.1,AD-39781.1,AD-39822.1
UGGAUAUUCUCG	2180	CGAGAAUAUCCA	2181	AD-39799.1,AD-39816.1,AD-39793.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1,AD-39822.1
GGAUAUUCUCGA	2182	UCGAGAAUAUCC	2183	AD-39799.1,AD-35551.4,AD-39793.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1,AD-39822.1
GAUAUUCUCGAC	2184	GUCGAGAAUAUC	2185	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-39781.1
AUAUUCUCGACA	2186	UGUCGAGAAUAU	2187	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-39787.1,AD-35539.4,AD-35545.4,AD-35563.4
UAUUCUCGACAC	2188	GUGUCGAGAAUA	2189	AD-39799.1,AD-35551.4,AD-39793.1,AD-35557.1,AD-35539.4,AD-35545.4,AD-35569.1,AD-35563.4
AUUCUCGACACA	2190	UGUGUCGAGAAU	2191	AD-39799.1,AD-35528.4,AD-35551.4,AD-35557.1,AD-35539.4,AD-35545.4,AD-35569.1,AD-35563.4
UUCUCGACACAG	2192	CUGUGUCGAGAA	2193	AD-35528.4,AD-35551.4,AD-35557.1,AD-35539.4,AD-35534.1,AD-35545.4,AD-35569.1,AD-35563.4
UCUCGACACAGC	2194	GCUGUGUCGAGA	2195	AD-35528.4,AD-35551.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35545.4,AD-35569.1,AD-35563.4
CUCGACACAGCA	2196	UGCUGUGUCGAG	2197	AD-35528.4,AD-35551.4,AD-35546.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4

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UCGACACAGCAG	2198	CUGCUGUGUCGA	2199	AD-35552.4,AD-35528.4,AD-35546.4,AD-35557.1,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4
CGACACAGCAGG	2200	CCUGCUGUGUCG	2201	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35534.1,AD-35569.1,AD-35563.4
GACACAGCAGGU	2202	ACCUGCUGUGUC	2203	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35534.1,AD-35564.4,AD-35569.1
ACACAGCAGGUC	2204	GACCUGCUGUGU	2205	AD-35552.4,AD-35528.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35534.1,AD-35564.4
CACAGCAGGUCA	2206	UGACCUGCUGUG	2207	AD-35552.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35534.1,AD-35564.4,AD-35571.4
ACAGCAGGUCAA	2208	UUGACCUGCUGU	2209	AD-35577.4,AD-35552.4,AD-35558.4,AD-35546.4,AD-35540.4,AD-35570.4,AD-35564.4,AD-35571.4
CAGCAGGUCAAG	2210	CUUGACCUGCUG	2211	AD-35577.4,AD-35552.4,AD-35558.4,AD-35546.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35571.4
AGCAGGUCAAGA	2212	UCUUGACCUGCU	2213	AD-35577.4,AD-35552.4,AD-35558.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35589.4,AD-35571.4
GCAGGUCAAGAG	2214	CUCUUGACCUGC	2215	AD-35577.4,AD-35595.4,AD-35558.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35589.4,AD-35571.4
CAGGUCAAGAGG	2216	CCUCUUGACCUG	2217	AD-35577.4,AD-35595.4,AD-35583.4,AD-35570.4,AD-35564.4,AD-35589.4,AD-35571.4,AD-35601.4
AGGUCAAGAGGA	2218	UCCUCUUGACCU	2219	AD-35577.4,AD-35595.4,AD-35583.4,AD-35570.4,AD-35589.4,AD-35607.4,AD-35571.4,AD-35601.4
GGUCAAGAGGAG	2220	CUCCUCUUGACC	2221	AD-35577.4,AD-35595.4,AD-35583.4,AD-35589.4,AD-35607.4,AD-35571.4,AD-35613.4,AD-35601.4
GUCAAGAGGAGU	2222	ACUCCUCUUGAC	2223	AD-35577.4,AD-35595.4,AD-35583.4,AD-35572.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
UCAAGAGGAGUA	2224	UACUCCUCUUGA	2225	AD-35595.4,AD-35583.4,AD-35578.4,AD-35572.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
CAAGAGGAGUAC	2226	GUACUCCUCUUG	2227	AD-35595.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35589.4,AD-35607.4,AD-35613.4,AD-35601.4
AAGAGGAGUACA	2228	UGUACUCCUCUU	2229	AD-35590.4,AD-35595.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35607.4,AD-35613.4,AD-35601.4
AGAGGAGUACAG	2230	CUGUACUCCUCU	2231	AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35584.4,AD-35607.4,AD-35613.4,AD-35601.4
GAGGAGUACAGU	2232	ACUGUACUCCUC	2233	AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35602.4,AD-35584.4,AD-35607.4,AD-35613.4
AGGAGUACAGUG	2234	CACUGUACUCCU	2235	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35602.4,AD-35584.4,AD-35613.4
GGAGUACAGUGC	2236	GCACUGUACUCC	2237	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35572.4,AD-35614.4,AD-35602.4,AD-35584.4
GAGUACAGUGCA	2238	UGCACUGUACUC	2239	AD-35608.4,AD-35596.4,AD-35590.4,AD-35578.4,AD-35614.4,AD-35602.4,AD-35584.4,AD-35573.4
AGUACAGUGCAA	2240	UUGCACUGUACU	2241	AD-39805.1,AD-35608.4,AD-35596.4,AD-35590.4,AD-35614.4,AD-35602.4,AD-35584.4,AD-35573.4

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GUACAGUGCAAU	2242	AUUGCACUGUAC	2243	AD-39805.1,AD-35608.4,AD-35596.4,AD-35590.4,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
UACAGUGCAAUG	2244	CAUUGCACUGUA	2245	AD-39805.1,AD-35608.4,AD-35596.4,AD-39817.1,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
ACAGUGCAAUGA	2246	UCAUUGCACUGU	2247	AD-39805.1,AD-35608.4,AD-39823.1,AD-39817.1,AD-39811.1,AD-35614.4,AD-35602.4,AD-35573.4
CAGUGCAAUGAG	2248	CUCAUUGCACUG	2249	AD-39805.1,AD-35608.4,AD-39823.1,AD-39817.1,AD-39811.1,AD-35614.4,AD-35573.4,AD-39782.1
AGUCCAAUCACC	2250	CCUCAUUGCACU	2251	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-35614.4,AD-35573.4,AD-39782.1
GUGCAAUGAGGG	2252	CCCUCAUUGCAC	2253	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-35573.4,AD-39782.1,AD-39794.1
UGCAAUGAGGGA	2254	UCCCUCAUUGCA	2255	AD-39805.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-39782.1,AD-39794.1,AD-39800.1
GCAAUGAGGGAC	2256	GUCCCUCAUUGC	2257	AD-39806.1,AD-39823.1,AD-39817.1,AD-39788.1,AD-39811.1,AD-39782.1,AD-39794.1,AD-39800.1
CAAUGAGGGACC	2258	GGUCCCUCAUUG	2259	AD-39806.1,AD-39823.1,AD-39812.1,AD-39817.1,AD-39788.1,AD-39782.1,AD-39794.1,AD-39800.1
AAUGAGGGACCA	2260	UGGUCCCUCAUU	2261	AD-39806.1,AD-39823.1,AD-39812.1,AD-39788.1,AD-39782.1,AD-39794.1,AD-39818.1,AD-39800.1
AUGAGGGACCAG	2262	CUGGUCCCUCAU	2263	AD-39806.1,AD-39812.1,AD-39788.1,AD-39824.1,AD-39782.1,AD-39794.1,AD-39818.1,AD-39800.1
UCAGCGACCACU	2264	ACUGCGCCCUCA	2265	AD-39806.1,AD-39812.1,AD-39788.1,AD-39824.1,AD-39783.1,AD-39794.1,AD-39818.1,AD-39800.1
GAGGGACCAGUA	2266	UACUGGUCCCUC	2267	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39783.1,AD-39794.1,AD-39818.1,AD-39800.1
AGGGACCAGUAC	2268	GUACUGGUCCCU	2269	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39818.1,AD-39800.1
GGGACCAGUACA	2270	UGUACUGGUCCC	2271	AD-39789.1,AD-39806.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39818.1
GGACCAGUACAU	2272	AUGUACUGGUCC	2273	AD-39789.1,AD-39807.1,AD-39812.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39818.1
GACCAGUACAUG	2274	CAUGUACUGGUC	2275	AD-39789.1,AD-39807.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39818.1
ACCAGUACAUGA	2276	UCAUGUACUGGU	2277	AD-39789.1,AD-39807.1,AD-39824.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39819.1
CCAGUACAUCAC	2278	CUCAUGUACUGG	2279	AD-39789.1,AD-39807.1,AD-39795.1,AD-39783.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39819.1
CAGUACAUGAGG	2280	CCUCAUGUACUG	2281	AD-39789.1,AD-39807.1,AD-39795.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1
AGUACAUGAGGA	2282	UCCUCAUGUACU	2283	AD-39807.1,AD-39837.1,AD-39795.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1
GUACAUGAGGAC	2284	GUCCUCAUGUAC	2285	AD-39807.1,AD-39837.1,AD-39843.1,AD-39801.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39819.1

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UACAUGAGGACU	2286	AGUCCUCAUGUA	2287	AD-39807.1,AD-39837.1,AD-39843.1,AD-39813.1,AD-39825.1,AD-39831.1,AD-39849.1,AD-39819.1
ACAUGAGGACUG	2288	CAGUCCUCAUGU	2289	AD-39837.1,AD-39843.1,AD-39813.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39849.1,AD-39819.1
CAUGAGGACUGC	2290	CCAGUCCUCAUG	2291	AD-39861.1,AD-39837.1,AD-39843.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39849.1,AD-39819.1
AUGAGGACUGGG	2292	CCCAGUCCUCAU	2293	AD-39861.1,AD-39837.1,AD-39843.1,AD-39825.1,AD-39855.1,AD-39831.1,AD-39867.1,AD-39849.1
UGAGCACUGCCG	2294	CCCCAGUCCUCA	2295	AD-39861.1,AD-39837.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39831.1,AD-39867.1,AD-39849.1
GAGGACUGGGGA	2296	UCCCCAGUCCUC	2297	AD-39861.1,AD-39832.1,AD-39837.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1
AGGACUGGGGAG	2298	CUCCCCAGUCCU	2299	AD-39861.1,AD-39832.1,AD-39843.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1,AD-39838.1
GGACUGGGGAGG	2300	CCUCCCCAGUCC	2301	AD-39844.1,AD-39861.1,AD-39832.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39849.1,AD-39838.1
GACUGGGGAGGG	2302	CCCUCCCCAGUC	2303	AD-39850.1,AD-39844.1,AD-39861.1,AD-39832.1,AD-39826.1,AD-39855.1,AD-39867.1,AD-39838.1
ACUGGGGAGGGC	2304	GCCCUCCCCAGU	2305	AD-39850.1,AD-39844.1,AD-39861.1,AD-39832.1,AD-39856.1,AD-39826.1,AD-39867.1,AD-39838.1
CUGGGGAGGGCU	2306	AGCCCUCCCCAG	2307	AD-39850.1,AD-39844.1,AD-39862.1,AD-39832.1,AD-39856.1,AD-39826.1,AD-39867.1,AD-39838.1
UCGGCAGCGCUU	2308	AACCCCUCCCCA	2309	AD-39850.1,AD-39844.1,AD-39868.1,AD-39862.1,AD-39832.1,AD-39856.1,AD-39826.1,AD-39838.1
GGGGAGGGCUUU	2310	AAAGCCCUCCCC	2311	AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39832.1,AD-39856.1,AD-39838.1
GGGAGGGCUUUC	2312	GAAAGCCCUCCC	2313	AD-35585.4,AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39856.1,AD-39838.1
GGAGGGCUUUCU	2314	AGAAAGCCCUCC	2315	AD-35585.4,AD-39850.1,AD-39844.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-39856.1,AD-35591.4
GAGGGCUUUCUU	2316	AAGAAAGCCCUC	2317	AD-35585.4,AD-39850.1,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-39856.1,AD-35591.4
AGGGCUUUCUUU	2318	AAAGAAAGCCCU	2319	AD-35585.4,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-39856.1,AD-35591.4,AD-35603.4
GGGCUUUCUUUG	2320	CAAAGAAAGCCC	2321	AD-35585.4,AD-39868.1,AD-35579.4,AD-39862.1,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4
GGCUUUCUUUCU	2322	ACAAAGAAAGCC	2323	AD-35585.4,AD-39868.1,AD-35579.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4
GCUUUCUUUGUG	2324	CACAAAGAAAGC	2325	AD-35585.4,AD-35579.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35574.4
CUUUCUUUGUGU	2326	ACACAAAGAAAG	2327	AD-35585.4,AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35580.1,AD-35574.4
UUUCUUUGUGUA	2328	UACACAAAGAAA	2329	AD-35615.4,AD-35597.4,AD-35609.4,AD-35591.4,AD-35603.4,AD-35586.4,AD-35580.1,AD-35574.4

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UUCUUUGUGUAU	2330	AUACACAAAGAA	2331	AD-35615.4,AD-35597.4,AD-35609.4,AD-35592.4,AD-35603.4,AD-35586.4,AD-35580.1,AD-35574.4
UCUUUGUGUAUU	2332	AAUACACAAAGA	2333	AD-35615.4,AD-35609.4,AD-35592.4,AD-35603.4,AD-35586.4,AD-35598.4,AD-35580.1,AD-35574.4
CUUUGUGUAUUU	2334	AAAUACACAAAG	2335	AD-35604.4,AD-35615.4,AD-35609.4,AD-35592.4,AD-35586.4,AD-35598.4,AD-35580.1,AD-35574.4
UUUGUGUAUUUG	2336	CAAAUACACAAA	2337	AD-35604.4,AD-35615.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35580.1,AD-35574.4
UUCUCUAUUUCC	2338	GCAAAUACACAA	2339	AD-35604.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35580.1,AD-35574.4
UGUGUAUUUGCC	2340	GGCAAAUACACA	2341	AD-35604.4,AD-35575.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35580.1
GUGUAUUUGCCA	2342	UGGCAAAUACAC	2343	AD-35604.4,AD-35575.4,AD-35581.4,AD-35592.4,AD-35586.4,AD-35610.4,AD-35598.4,AD-35616.4
UGUAUUUGCCAU	2344	AUGGCAAAUACA	2345	AD-35604.4,AD-35575.4,AD-35581.4,AD-35592.4,AD-35587.4,AD-35610.4,AD-35598.4,AD-35616.4
GUAUUUGCCAUA	2346	UAUGGCAAAUAC	2347	AD-35604.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35598.4,AD-35616.4,AD-35593.4
UAUUUGCCAUAA	2348	UUAUGGCAAAUA	2349	AD-35604.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35616.4,AD-35593.4,AD-35599.4
AUUUGCCAUAAA	2350	UUUAUGGCAAAU	2351	AD-35575.4,AD-35581.4,AD-35587.4,AD-35610.4,AD-35605.4,AD-35616.4,AD-35593.4,AD-35599.4
UUUGCCAUAAAU	2352	AUUUAUGGCAAA	2353	AD-35611.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35605.4,AD-35616.4,AD-35593.4,AD-35599.4
UUGCCAUAAAUA	2354	UAUUUAUGGCAA	2355	AD-35611.4,AD-35575.4,AD-35581.4,AD-35587.4,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
UGCCAUAAAUAA	2356	UUAUUUAUGGCA	2357	AD-35611.4,AD-35581.4,AD-35587.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
GCCAUAAAUAAU	2358	AUUAUUUAUGGC	2359	AD-39839.1,AD-35611.4,AD-35587.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4
CCAUAAAUAAUA	2360	UAUUAUUUAUGG	2361	AD-39839.1,AD-35611.4,AD-39833.1,AD-35605.4,AD-35593.4,AD-39827.1,AD-35599.4,AD-39845.1
CAUAAAUAAUAC	2362	GUAUUAUUUAUG	2363	AD-39839.1,AD-35611.4,AD-39833.1,AD-35605.4,AD-39851.1,AD-39827.1,AD-35599.4,AD-39845.1
AUAAAUAAUACU	2364	AGUAUUAUUUAU	2365	AD-39839.1,AD-35611.4,AD-39857.1,AD-39833.1,AD-35605.4,AD-39851.1,AD-39827.1,AD-39845.1
UAAAUAAUACUA	2366	UACUAUUAUUUA	2367	AD-39839.1,AD-35611.4,AD-39857.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39827.1,AD-39845.1
AAAUAAUACUAA	2368	UUAGUAUUAUUU	2369	AD-39839.1,AD-39857.1,AD-39869.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39827.1,AD-39845.1
AAUAAUACUAAA	2370	UUUAGUAUUAUU	2371	AD-39828.1,AD-39839.1,AD-39857.1,AD-39869.1,AD-39833.1,AD-39851.1,AD-39863.1,AD-39845.1
AUAAUACUAAAU	2372	AUUUAGUAUUAU	2373	AD-39828.1,AD-39839.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39851.1,AD-39863.1,AD-39845.1

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UAAUACUAAAUC	2374	GAUUUAGUAUUA	2375	AD-39828.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39851.1,AD-39863.1,AD-39845.1
AAUACUAAAUCA	2376	UGAUUUAGUAUU	2377	AD-39828.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39851.1,AD-39863.1,AD-39846.1
AUACUAAAUCAU	2378	AUGAUUUAGUAU	2379	AD-39828.1,AD-39852.1,AD-39857.1,AD-39834.1,AD-39869.1,AD-39840.1,AD-39863.1,AD-39846.1
UACUAAAUCAUU	2380	AAUGAUUUAGUA	2381	AD-39828.1,AD-39852.1,AD-39834.1,AD-39858.1,AD-39869.1,AD-39840.1,AD-39863.1,AD-39846.1
ACUAAAUCAUUU	2382	AAAUCAUUUAGU	2383	AD-39828.1,AD-39852.1,AD-39834.1,AD-39858.1,AD-39869.1,AD-39840.1,AD-39864.1,AD-39846.1
CUAAAUCAUUUG	2384	CAAAUGAUUUAG	2385	AD-39828.1,AD-39852.1,AD-39870.1,AD-39834.1,AD-39858.1,AD-39840.1,AD-39864.1,AD-39846.1
UAAAUCAUUUGA	2386	UCAAAUGAUUUA	2387	AD-39852.1,AD-39870.1,AD-39829.1,AD-39834.1,AD-39858.1,AD-39840.1,AD-39864.1,AD-39846.1
AAAUCAUUUGAA	2388	UUCAAAUGAUUU	2389	AD-39852.1,AD-39870.1,AD-39829.1,AD-39858.1,AD-39840.1,AD-39835.1,AD-39864.1,AD-39846.1
AAUCAUUUGAAG	2390	CUUCAAAUGAUU	2391	AD-39852.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-39864.1,AD-39846.1
AUCAUUUGAAGA	2392	UCUUCAAAUGAU	2393	AD-39852.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-39864.1
UCAUUUGAAGAU	2394	AUCUUCAAAUGA	2395	AD-39870.1,AD-39841.1,AD-39829.1,AD-39858.1,AD-39835.1,AD-39864.1,AD-39853.1
CAUUUGAACAUA	2396	UAUCUUCAAAUG	2397	AD-39870.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39864.1,AD-39853.1
AUUUGAAGAUAU	2398	AUAUCUUCAAAU	2399	AD-39865.1,AD-39870.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39853.1
UUUGAAGAUAUU	2400	AAUAUCUUCAAA	2401	AD-39871.1,AD-39865.1,AD-39841.1,AD-39829.1,AD-39835.1,AD-39859.1,AD-39853.1
UUGAAGAUAUUC	2402	GAAUAUCUUCAA	2403	AD-39871.1,AD-39865.1,AD-39841.1,AD-39830.1,AD-39835.1,AD-39859.1,AD-39853.1
UGAAGAUAUUCA	2404	UGAAUAUCUUCA	2405	AD-39871.1,AD-39865.1,AD-39841.1,AD-39830.1,AD-35617.4,AD-39859.1,AD-39853.1
GAAGAUAUUCAC	2406	GUGAAUAUCUUC	2407	AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-39853.1
AAGAUAUUCACC	2408	GGUGAAUAUCUU	2409	AD-35582.1,AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-39853.1
AGAUAUUCACCA	2410	UGGUGAAUAUCU	2411	AD-35582.1,AD-39871.1,AD-39865.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-39859.1,AD-35588.4
GAUAUUCACCAU	2412	AUGGUGAAUAUC	2413	AD-35582.1,AD-39871.1,AD-39865.1,AD-35594.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4
AUAUUCACCAUU	2414	AAUGGUGAAUAU	2415	AD-35582.1,AD-39871.1,AD-35594.1,AD-35600.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4
UAUUCACCAUUA	2416	UAAUGGUGAAUA	2417	AD-35582.1,AD-35606.1,AD-35594.1,AD-35600.1,AD-39830.1,AD-35617.4,AD-35576.4,AD-35588.4

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AUUCACCAUUAU	2418	AUAAUGGUGAAU	2419	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35617.4,AD-35576.4,AD-35588.4
UUCACCAUUAUA	2420	UAUAAUGGUGAA	2421	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35576.4,AD-35618.1,AD-35588.4
UCACCAUUAUAG	2422	CUAUAAUGGUGA	2423	AD-35582.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35618.1,AD-35588.4,AD-38127.1
CACCAUUAUAGA	2424	UCUAUAAUGGUG	2425	AD-38133.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-35618.1,AD-35588.4,AD-38127.1
ACCAUUAUAGAG	2426	CUCUAUAAUGGU	2427	AD-38133.1,AD-35606.1,AD-35594.1,AD-35612.1,AD-35600.1,AD-38139.1,AD-35618.1,AD-38127.1
CCAUUAUAGAGA	2428	UCUCUAUAAUGG	2429	AD-38133.1,AD-35606.1,AD-35612.1,AD-35600.1,AD-38145.1,AD-38139.1,AD-35618.1,AD-38127.1
CAUUAUAGAGAA	2430	UUCUCUAUAAUG	2431	AD-38133.1,AD-35606.1,AD-35612.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-35618.1,AD-38127.1
AUUAUAGAGAAC	2432	GUUCUCUAUAAU	2433	AD-38133.1,AD-35612.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-35618.1,AD-38127.1
UUAUAGAGAACA	2434	UGUUCUCUAUAA	2435	AD-38133.1,AD-38163.1,AD-38145.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-35618.1,AD-38127.1
UAUAGAGAACAA	2436	UUGUUCUCUAUA	2437	AD-38133.1,AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38127.1
AUAGAGAACAAA	2438	UUUGUUCUCUAU	2439	AD-38133.1,AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38128.1
UAGAGAACAAAU	2440	AUUUGUUCUCUA	2441	AD-38163.1,AD-38145.1,AD-38169.1,AD-38139.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-38134.1
AGAGAACAAAUU	2442	AAUUUGUUCUCU	2443	AD-38163.1,AD-38145.1,AD-38140.1,AD-38169.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-38134.1
GAGAACAAAUUA	2444	UAAUUUGUUCUC	2445	AD-38163.1,AD-38140.1,AD-38169.1,AD-38151.1,AD-38157.1,AD-38128.1,AD-39836.1,AD-38134.1
AGAACAAAUUAA	2446	UUAAUUUGUUCU	2447	AD-38163.1,AD-38140.1,AD-38169.1,AD-38157.1,AD-38128.1,AD-39842.1,AD-39836.1,AD-38134.1
GAACAAAUUAAA	2448	UUUAAUUUGUUC	2449	AD-38163.1,AD-38140.1,AD-38169.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
AACAAAUUAAAA	2450	UUUUAAUUUGUU	2451	AD-38140.1,AD-38169.1,AD-39854.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
ACAAAUUAAAAG	2452	CUUUUAAUUUGU	2453	AD-39860.1,AD-38140.1,AD-39854.1,AD-38128.1,AD-39842.1,AD-39848.1,AD-39836.1,AD-38134.1
CAAAUUAAAAGA	2454	UCUUUUAAUUUG	2455	AD-39860.1,AD-38140.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1,AD-38134.1
AAAUUAAAAGAG	2456	CUCUUUUAAUUU	2457	AD-39992.1,AD-39860.1,AD-38140.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1
AAUUAAAAGAGU	2458	ACUCUUUUAAUU	2459	AD-39992.1,AD-39860.1,AD-39998.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1,AD-39836.1
AUUAAAAGAGUU	2460	AACUCUUUUAAU	2461	AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-39842.1,AD-39848.1,AD-39866.1

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UUAAAAGAGUUA	2462	UAACUCUUUUAA	2463	AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-40010.1,AD-39848.1,AD-39866.1
UAAAAGAGUUAA	2464	UUAACUCUUUUA	2465	AD-40016.1,AD-39992.1,AD-39860.1,AD-40004.1,AD-39998.1,AD-39854.1,AD-40010.1,AD-39866.1
AAAAGAGUUAAG	2466	CUUAACUCUUUU	2467	AD-40016.1,AD-39992.1,AD-39860.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1,AD-39866.1
AAAGAGUUAAGG	2468	CCUUAACUCUUU	2469	AD-40016.1,AD-40028.1,AD-39992.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1,AD-39866.1
AAGAGUUAAGGA	2470	UCCUUAACUCUU	2471	AD-40016.1,AD-40028.1,AD-40034.1,AD-39992.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1
AGAGUUAAGGAC	2472	GUCCUUAACUCU	2473	AD-40016.1,AD-40028.1,AD-40034.1,AD-40022.1,AD-40004.1,AD-39998.1,AD-40010.1
GAGUUAAGGACU	2474	AGUCCUUAACUC	2475	AD-40016.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40004.1,AD-40010.1
AGUUAAGGACUC	2476	GAGUCCUUAACU	2477	AD-40016.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1,AD-40010.1
GUUAAGGACUCU	2478	AGAGUCCUUAAC	2479	AD-40016.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1
UUAAGGACUCUG	2480	CAGAGUCCUUAA	2481	AD-40017.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40022.1,AD-40005.1
UAAGGACUCUGA	2482	UCAGAGUCCUUA	2483	AD-40017.1,AD-40011.1,AD-40028.1,AD-40034.1,AD-39999.1,AD-40005.1
AAGGACUCUGAA	2484	UUCAGAGUCCUU	2485	AD-40017.1,AD-40029.1,AD-40011.1,AD-40034.1,AD-39999.1,AD-40005.1
AGGACUCUGAAG	2486	CUUCAGAGUCCU	2487	AD-40017.1,AD-40029.1,AD-40011.1,AD-39999.1,AD-40005.1,AD-40035.1
GGACUCUGAAGA	2488	UCUUCAGAGUCC	2489	AD-40017.1,AD-40029.1,AD-40011.1,AD-39994.1,AD-39999.1,AD-40005.1,AD-40035.1
GACUCUGAAGAU	2490	AUCUUCAGAGUC	2491	AD-40017.1,AD-40029.1,AD-40011.1,AD-40000.1,AD-39994.1,AD-40005.1,AD-40035.1
ACUCUGAAGAUG	2492	CAUCUUCAGAGU	2493	AD-40017.1,AD-40029.1,AD-40011.1,AD-40000.1,AD-39994.1,AD-40006.1,AD-40035.1
CUCUGAAGAUGU	2494	ACAUCUUCAGAG	2495	AD-40017.1,AD-40029.1,AD-40000.1,AD-39994.1,AD-40012.1,AD-40006.1,AD-40035.1
UCUGAAGAUGUA	2496	UACAUCUUCAGA	2497	AD-40029.1,AD-40000.1,AD-39994.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
CUGAAGAUGUAC	2498	GUACAUCUUCAG	2499	AD-40029.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
UGAAGAUGUACC	2500	GGUACAUCUUCA	2501	AD-40030.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-40035.1,AD-40018.1
GAAGAUGUACCU	2502	AGGUACAUCUUC	2503	AD-40030.1,AD-40000.1,AD-39994.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38146.1,AD-40018.1
AAGAUGUACCUA	2504	UAGGUACAUCUU	2505	AD-40030.1,AD-40000.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38146.1,AD-40018.1,AD-38152.1
AGAUGUACCUAU	2506	AUAGGUACAUCU	2507	AD-40030.1,AD-40024.1,AD-40012.1,AD-40006.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1

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GAUGUACCUAUG	2508	CAUAGGUACAUC	2509	AD-40030.1,AD-40024.1,AD-40012.1,AD-38164.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1
AUGUACCUAUGG	2510	CCAUAGGUACAU	2511	AD-40030.1,AD-40024.1,AD-38164.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-40018.1,AD-38152.1
UGUACCUAUGGU	2512	ACCAUAGGUACA	2513	AD-40030.1,AD-40024.1,AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38152.1
GUACCUAUGGUC	2514	GACCAUAGGUAC	2515	AD-40030.1,AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38152.1,AD-38135.1
UACCUAUCCUCC	2516	CCACCAUAGCUA	2517	AD-38164.1,AD-38129.1,AD-38170.1,AD-38158.1,AD-38146.1,AD-38141.1,AD-38152.1,AD-38135.1
ACCUAUGGUCCU	2518	AGGACCAUAGGU	2519	AD-38164.1,AD-38129.1,AD-38170.1,AD-38147.1,AD-38158.1,AD-38141.1,AD-38152.1,AD-38135.1
CCUAUGGUCCUA	2520	UAGGACCAUAGG	2521	AD-38164.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38158.1,AD-38141.1,AD-38135.1
CUAUGGUCCUAG	2522	CUAGGACCAUAG	2523	AD-38164.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38141.1,AD-38135.1
UAUGGUCCUAGU	2524	ACUAGGACCAUA	2525	AD-38165.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38170.1,AD-38147.1,AD-38141.1,AD-38135.1
AUGGUCCUAGUA	2526	UACUAGGACCAU	2527	AD-38165.1,AD-38171.1,AD-38159.1,AD-38129.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38135.1
UGGUCCUAGUAG	2528	CUACUAGGACCA	2529	AD-38165.1,AD-38171.1,AD-38159.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38130.1,AD-38135.1
CCUCCUACUAGC	2530	CCUACUAGGACC	2531	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38153.1,AD-38147.1,AD-38141.1,AD-38130.1
GUCCUAGUAGGA	2532	UCCUACUAGGAC	2533	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38153.1,AD-38147.1,AD-38142.1,AD-38130.1
UCCUAGUAGGAA	2534	UUCCUACUAGGA	2535	AD-38165.1,AD-38171.1,AD-38159.1,AD-38136.1,AD-38148.1,AD-38153.1,AD-38142.1,AD-38130.1
CCUAGUAGGAAA	2536	UUUCCUACUAGG	2537	AD-38165.1,AD-38171.1,AD-38154.1,AD-38159.1,AD-38136.1,AD-38148.1,AD-38142.1,AD-38130.1
CUAGUAGGAAAU	2538	AUUUCCUACUAG	2539	AD-38165.1,AD-38171.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38160.1,AD-38142.1,AD-38130.1
UAGUAGGAAAUA	2540	UAUUUCCUACUA	2541	AD-38171.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38166.1,AD-38160.1,AD-38142.1,AD-38130.1
AGUAGGAAAUAA	2542	UUAUUUCCUACU	2543	AD-38154.1,AD-38136.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1,AD-38130.1
GUAGCAAAUAAA	2544	UUUAUUUCCUAC	2545	AD-40036.1,AD-38154.1,AD-38136.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1
UAGGAAAUAAAU	2546	AUUUAUUUCCUA	2547	AD-39995.1,AD-40036.1,AD-38154.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-38142.1
AGGAAAUAAAUG	2548	CAUUUAUUUCCU	2549	AD-39995.1,AD-40036.1,AD-38154.1,AD-40001.1,AD-38148.1,AD-38172.1,AD-38166.1,AD-38160.1
GGAAAUAAAUGU	2550	ACAUUUAUUUCC	2551	AD-39995.1,AD-40036.1,AD-38154.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-40007.1

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GAAAUAAAUGUG	2552	CACAUJUAUUUC	2553	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-38160.1,AD-40007.1
AAAUAAAUGUGA	2554	UCACAJUUAUUU	2555	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-38172.1,AD-38166.1,AD-40007.1,AD-40019.1
AAUAAAUGUGAU	2556	AUCACAUUUAUU	2557	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-40025.1,AD-38172.1,AD-40007.1,AD-40019.1
AUAAAUGUGAUU	2558	AAUCACAUUUAU	2559	AD-39995.1,AD-40036.1,AD-40013.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-40019.1
UAAAUGUGAUUU	2560	AAAUCACAUUUA	2561	AD-39995.1,AD-40013.1,AD-40037.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-40019.1
AAAUGUGAUUUG	2562	CAAAUCACAUUU	2563	AD-40013.1,AD-40037.1,AD-40001.1,AD-40025.1,AD-40031.1,AD-40007.1,AD-39996.1,AD-40019.1
AAUGUGAUUUGC	2564	GCAAAJCACAUU	2565	AD-40013.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40007.1,AD-39996.1,AD-40019.1
AUGUGAUUUGCC	2566	GGCAAAUCACAU	2567	AD-40008.1,AD-40013.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-39996.1,AD-40019.1
UGUGAUUUGCCU	2568	AGGCAAAUCACA	2569	AD-40008.1,AD-40037.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1,AD-40019.1
GUGAUUUGCCUU	2570	AAGGCAAAUCAC	2571	AD-40008.1,AD-40037.1,AD-40020.1,AD-40025.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1
UGAUUUGCCUUC	2572	GAAGGCAAAUCA	2573	AD-40026.1,AD-40008.1,AD-40037.1,AD-40020.1,AD-40031.1,AD-40002.1,AD-40014.1,AD-39996.1
GAUUUCCCUUCU	2574	ACAAGGCAAAUC	2575	AD-40026.1,AD-40008.1,AD-40032.1,AD-40037.1,AD-40020.1,AD-40002.1,AD-40014.1,AD-39996.1
AUUUGCCUUCUA	2576	UAGAAGGCAAAU	2577	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-40002.1,AD-40014.1,AD-39996.1
UUUGCCUUCUAG	2578	CUAGAAGGCAAA	2579	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-40002.1,AD-39997.1,AD-40014.1
UUGCCUUCUAGA	2580	UCUAGAAGGCAA	2581	AD-40038.1,AD-40026.1,AD-40008.1,AD-40032.1,AD-40020.1,AD-39997.1,AD-40014.1
UGCCUUCUAGAA	2582	UUCUAGAAGGCA	2583	AD-40038.1,AD-40026.1,AD-40032.1,AD-40020.1,AD-40009.1,AD-39997.1,AD-40014.1
GCCUUCUAGAAC	2584	GUUCUAGAAGGC	2585	AD-40038.1,AD-40026.1,AD-40015.1,AD-40032.1,AD-40020.1,AD-40009.1,AD-39997.1
CCUUCUAGAACA	2586	UGUUCUAGAAGG	2587	AD-40038.1,AD-40026.1,AD-40015.1,AD-40021.1,AD-40032.1,AD-40009.1,AD-39997.1
CUUCUAGAACAG	2588	CUGUUCUAGAAG	2589	AD-40038.1,AD-40027.1,AD-40015.1,AD-40021.1,AD-40032.1,AD-40009.1,AD-39997.1
UUCUAGAACAGU	2590	ACUGUJCUAGAA	2591	AD-40038.1,AD-40027.1,AD-40015.1,AD-40021.1,AD-40009.1,AD-40033.1,AD-39997.1
UCUAGAACAGUA	2592	UACUGJUCUAGA	2593	AD-40027.1,AD-40015.1,AD-40021.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-39997.1
CUAGAACAGUAG	2594	CUACUGUUCUAG	2595	AD-40027.1,AD-40015.1,AD-40021.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-40045.1

[3788]

UAGAACAGUAGA	2596	UCUACUGUUCUA	2597	AD-40027.1,AD-40015.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40009.1,AD-40033.1,AD-40045.1
AGAACAGUAGAC	2598	GUCUACUGUUCU	2599	AD-40027.1,AD-40057.1,AD-40015.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40033.1,AD-40045.1
GAACAGUAGACA	2600	UGUCUACUGUUC	2601	AD-40027.1,AD-40057.1,AD-40021.1,AD-40051.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1
AACAGUAGACAC	2602	GUGUCUACUGUU	2603	AD-40027.1,AD-40057.1,AD-40051.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1,AD-40069.1
ACACUACACACA	2604	UGUGUCUACUGU	2605	AD-40057.1,AD-40051.1,AD-40075.1,AD-40039.1,AD-40063.1,AD-40033.1,AD-40045.1,AD-40069.1
CAGUAGACACAA	2606	UUGUGUCUACUG	2607	AD-40057.1,AD-40051.1,AD-40075.1,AD-40039.1,AD-40081.1,AD-40063.1,AD-40045.1,AD-40069.1
AGUAGACACAAA	2608	UUUGUGUCUACU	2609	AD-40057.1,AD-40051.1,AD-40075.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40045.1,AD-40069.1
GUAGACACAAAA	2610	UUUUGUGUCUAC	2611	AD-40057.1,AD-40051.1,AD-40075.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
UAGACACAAAAC	2612	GUUUUGUGUCUA	2613	AD-40057.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
AGACACAAAACA	2614	UGUUUUGUGUCU	2615	AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40063.1,AD-40069.1
GACACAAAACAG	2616	CUGUUUUGUGUC	2617	AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40064.1,AD-40069.1
ACACAAAACAGC	2618	CCUGUUUUCUGU	2619	AD-40070.1,AD-40058.1,AD-40075.1,AD-40052.1,AD-40046.1,AD-40040.1,AD-40081.1,AD-40064.1
CACAAAACAGGC	2620	GCCUGUUUUGUG	2621	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40040.1,AD-40081.1,AD-40064.1
ACAAAACAGGCU	2622	AGCCUGUUUUGU	2623	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40040.1,AD-40082.1,AD-40064.1
CAAAACAGGCUC	2624	GAGCCUGUUUUG	2625	AD-40070.1,AD-40058.1,AD-40052.1,AD-40046.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40064.1
AAAACAGGCUCA	2626	UGAGCCUGUUUU	2627	AD-40070.1,AD-40058.1,AD-40052.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40064.1,AD-40047.1
AAACAGGCUCAG	2628	CUGAGCCUGUUU	2629	AD-40070.1,AD-40058.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40064.1,AD-40047.1
AACAGGCUCAGG	2630	CCUGAGCCUGUU	2631	AD-40059.1,AD-40070.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40064.1,AD-40047.1
ACAGCCUCAGGA	2632	UCCUGAGCCUGU	2633	AD-40059.1,AD-40070.1,AD-40065.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40053.1,AD-40047.1
CAGGCUCAGGAC	2634	GUCCUGAGCCUG	2635	AD-40059.1,AD-40065.1,AD-40076.1,AD-40041.1,AD-40082.1,AD-40071.1,AD-40053.1,AD-40047.1
AGGCUCAGGACU	2636	AGUCCUGAGCCU	2637	AD-40059.1,AD-40065.1,AD-40041.1,AD-40082.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40047.1
GGCUCAGGACUU	2638	AAGUCCUGAGCC	2639	AD-40059.1,AD-40065.1,AD-40041.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1,AD-40047.1

[3789]

GCUCAGGACUUA	2640	UAAGUCCUGAGC	2641	AD-40059.1,AD-40065.1,AD-40042.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1,AD-40047.1
CUCAGGACUUAG	2642	CUAAGUCCUGAG	2643	AD-40059.1,AD-40065.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40053.1,AD-40083.1
UCAGGACUUAGC	2644	GCUAAGUCCUGA	2645	AD-40059.1,AD-40065.1,AD-40054.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
CAGGACUUAGCA	2646	UGCUAAGUCCUG	2647	AD-40065.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
AGGACUUAGCAA	2648	UUGCUAAGUCCU	2649	AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40077.1,AD-40071.1,AD-40083.1
GGACUUAGCAAG	2650	CUUGCUAAGUCC	2651	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40077.1,AD-40083.1
GACUUAGCAAGA	2652	UCUUGCUAAGUC	2653	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40078.1,AD-40083.1
ACUUAGCAAGAA	2654	UUCUUGCUAAGU	2655	AD-40072.1,AD-40054.1,AD-40060.1,AD-40042.1,AD-40066.1,AD-40048.1,AD-40084.1,AD-40078.1
CUUAGCAAGAAG	2656	CUUCUUGCUAAG	2657	AD-40072.1,AD-40054.1,AD-40060.1,AD-40066.1,AD-40043.1,AD-40048.1,AD-40084.1,AD-40078.1
UUAGCAAGAAGU	2658	ACUUCUUGCUAA	2659	AD-40072.1,AD-40054.1,AD-40060.1,AD-40066.1,AD-40043.1,AD-40084.1,AD-40049.1,AD-40078.1
UAGCAAGAAGUU	2660	AACUUCUUGCUA	2661	AD-40072.1,AD-40060.1,AD-40066.1,AD-40055.1,AD-40043.1,AD-40084.1,AD-40049.1,AD-40078.1
AGCAAGAAGUUA	2662	UAACUUCUUGCU	2663	AD-40072.1,AD-40066.1,AD-40055.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40049.1,AD-40078.1
GCAAGAAGUUAU	2664	AUAACUUCUUGC	2665	AD-40072.1,AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40049.1,AD-40078.1
CAAGAAGUUAUG	2666	CAUAACUUCUUG	2667	AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40073.1,AD-40049.1,AD-40078.1
AAGAAGUUAUGG	2668	CCAUAACUUCUU	2669	AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40084.1,AD-40073.1,AD-40079.1,AD-40049.1
AGAAGUUAUGGA	2670	UCCAUAACUUCU	2671	AD-40085.1,AD-40055.1,AD-40067.1,AD-40043.1,AD-40061.1,AD-40073.1,AD-40079.1,AD-40049.1
GAAGUUAUGGAA	2672	UUCCAUAACUUC	2673	AD-40085.1,AD-40044.1,AD-40055.1,AD-40067.1,AD-40061.1,AD-40073.1,AD-40079.1,AD-40049.1
AAGUUAUGGAAU	2674	AUUCCAUAACUU	2675	AD-40085.1,AD-40044.1,AD-40055.1,AD-40067.1,AD-40061.1,AD-40050.1,AD-40073.1,AD-40079.1
AGUUAUGGAAUU	2676	AAUUCCAUAACU	2677	AD-40085.1,AD-40044.1,AD-40067.1,AD-40056.1,AD-40061.1,AD-40050.1,AD-40073.1,AD-40079.1
GUUAUGGAAUUC	2678	GAAUUCCAUAAC	2679	AD-40062.1,AD-40085.1,AD-40044.1,AD-40067.1,AD-40056.1,AD-40050.1,AD-40073.1,AD-40079.1
UUAUGGAAUUCC	2680	GGAAUUCCAUAA	2681	AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1,AD-40073.1,AD-40079.1
UAUGGAAUUCCU	2682	AGGAAUUCCAUA	2683	AD-40074.1,AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1,AD-40079.1

[3790]

AUGGAAUUCCUU	2684	AAGGAAUUCCAU	2685	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40085.1,AD-40044.1,AD-40056.1,AD-40050.1
UGGAAUUCCUUU	2686	AAAGGAAUUCCA	2687	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40044.1,AD-40056.1,AD-40050.1
GGAAUUCCUUUU	2688	AAAAGGAAUUCC	2689	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-40056.1,AD-40050.1,AD-38131.1
GAAUUCCUUUUA	2690	UAAAAGGAAUUC	2691	AD-40080.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-38137.1,AD-40056.1,AD-38131.1
AAUUCCUUUUAU	2692	AUAAAAGGAAUU	2693	AD-40080.1,AD-38143.1,AD-40074.1,AD-40068.1,AD-40062.1,AD-38137.1,AD-38131.1
AUUCCUUUUAUU	2694	AAUAAAAGGAAU	2695	AD-40080.1,AD-38149.1,AD-38143.1,AD-40074.1,AD-40068.1,AD-38137.1,AD-38131.1
UUCCUUUUAUUG	2696	CAAUAAAAGGAA	2697	AD-40080.1,AD-38149.1,AD-38143.1,AD-40074.1,AD-38137.1,AD-38155.1,AD-38131.1
UCCUUUUAUUGA	2698	UCAAUAAAAGGA	2699	AD-40080.1,AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38155.1,AD-38131.1
CCUUUUAUUGAA	2700	UUCAAUAAAAGG	2701	AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38167.1,AD-38155.1,AD-38131.1
CUUUUAUUGAAA	2702	UUUCAAUAAAAG	2703	AD-38149.1,AD-38143.1,AD-38137.1,AD-38161.1,AD-38173.1,AD-38167.1,AD-38155.1,AD-38131.1
UUUUAUUGAAAC	2704	GUUUCAAUAAAA	2705	AD-38149.1,AD-38143.1,AD-38132.1,AD-38137.1,AD-38161.1,AD-38173.1,AD-38167.1,AD-38155.1
UUUAUUCAAACA	2706	UGUUUCAAUAAA	2707	AD-38149.1,AD-38143.1,AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1
UUAUUGAAACAU	2708	AUGUUUCAAUAA	2709	AD-38149.1,AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1,AD-38144.1
UAUUGAAACAUC	2710	GAUGUUUCAAUA	2711	AD-38132.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38155.1,AD-38150.1,AD-38144.1
AUUGAAACAUCA	2712	UGAUGUUUCAAU	2713	AD-38132.1,AD-38156.1,AD-38161.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38150.1,AD-38144.1
UUGAAACAUCAG	2714	CUGAUGUUUCAA	2715	AD-38132.1,AD-38162.1,AD-38156.1,AD-38173.1,AD-38138.1,AD-38167.1,AD-38150.1,AD-38144.1
UGAAACAUCAGC	2716	GCUGAUGUUUCA	2717	AD-38132.1,AD-38162.1,AD-38156.1,AD-38168.1,AD-38173.1,AD-38138.1,AD-38150.1,AD-38144.1
GAAACAUCAGCA	2718	UGCUGAUGUUUC	2719	AD-38174.1,AD-38132.1,AD-38162.1,AD-38156.1,AD-38168.1,AD-38138.1,AD-38150.1,AD-38144.1
AAACAUCAGCAA	2720	UUGCUGAUCUUU	2721	AD-38174.1,AD-38162.1,AD-35667.1,AD-38156.1,AD-38168.1,AD-38138.1,AD-38150.1,AD-38144.1
AACAUCAGCAAA	2722	UUUGCUGAUGUU	2723	AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-38156.1,AD-38168.1,AD-38150.1,AD-38144.1
ACAUCAGCAAAG	2724	CUUUGCUGAUGU	2725	AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38156.1,AD-38168.1,AD-38150.1
CAUCAGCAAAGA	2726	UCUUUGCUGAUG	2727	AD-35685.1,AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38156.1,AD-38168.1

[3791]

AUCAGCAAAGAC	2728	GUCUUUGCUGAU	2729	AD-35685.1,AD-38174.1,AD-35673.1,AD-38162.1,AD-35667.1,AD-35679.1,AD-38168.1,AD-35691.1
UCAGCAAAGACA	2730	UGUCUUUGCUGA	2731	AD-35685.1,AD-38174.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-38168.1,AD-35691.1
CAGCAAAGACAA	2732	UUGUCUUUGCUG	2733	AD-35685.1,AD-38174.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-35691.1
AGCAAAGACAAG	2734	CUUGUCUUUGCU	2735	AD-35685.1,AD-35673.1,AD-35667.1,AD-35679.1,AD-35691.1
GCAAAGACAAGA	2736	UCUUGUCUUUGC	2737	AD-35685.1,AD-35673.1,AD-35679.1,AD-35691.1
CAAAGACAAGAC	2738	GUCUUGUCUUUG	2739	AD-35685.1,AD-35679.1,AD-35691.1
AAAGACAAGACA	2740	UGUCUUGUCUUU	2741	AD-35685.1,AD-35691.1

[3792] 指明了在 NM_000336.2 中的位置（“Pos”）。给出了有义链和反义链中重叠的 12 个示例性核苷酸；在许多情况下，重叠实际上要更长。

[3793] 实施例 3

[3794] KRAS RNAi 剂的效力

[3795] 测试 KRAS RNAi 剂的效力，结果如下表 5 和表 6 所示。

[3796] 体外筛选：

[3797] 细胞培养物和转染：

[3798] 将 RKO 细胞（ATCC，马纳萨斯，VA）在 37℃在 5% CO_2 气氛下，在补充有 10% FBS、链霉素和谷氨酰胺（ATCC）的 McCoy’s 培养基（ATCC）中培育至接近汇合，之后，通过胰蛋白酶消化法从平板释放。通过将每孔 5μl siRNA 双链体连同每孔 14.8μl Opti-MEM 外加 0.2μl 脂质转染胺（lipofectamine）RNAiMax（Invitrogen，Carlsbad，CA. 目录号 13778-150）一起添加至 96 孔板中并在室温温育 15 分钟，实施转染。然后将 80μl 不含抗生素，含有约 $2x10^4$ 个 RKO 细胞的完全生长培养基添加至 siRNA 混合物中。在 RNA 纯化之前，将细胞温育 24 小时。单剂量实验以 10nM、在一些情况下以 0.1nM 的双链体终浓度进行并且剂量反应实验以 10、1、0.5、0.1、0.05、0.01、0.005、0.001、0.0005、0.0001、0.00005、0.00001nM 双链体终浓度进行。

[3799] 使用 DYNABEADS mRNA 分离试剂盒（Invitrogen，产品号：610-12）分离总 RNA：

[3800] 收获细胞并使其在 150μl 裂解/结合溶液中裂解，随后使用 Eppendorf 热混合仪以 850 转/分钟混合 5 分钟（混合速度在整个过程中始终相同）。将 10 微升磁珠和 80μl 裂解/结合缓冲液混合物添加至圆底板中并混合 1 分钟。使用磁力支座捕获磁珠并且在不扰动磁珠的情况下除去上清液。在移除上清液后，将裂解的细胞加入到剩余的磁珠中并混合 5 分钟。在移除上清液后，将磁珠用 150μl 洗涤缓冲液 A 洗涤 2 次并混合 1 分钟。再次捕获磁珠并移除上清液。随后将磁珠用 150μl 洗涤缓冲液 B 洗涤，捕获并移除上清液。然后再将磁珠用 150μl 洗脱缓冲液洗涤，捕获并移除上清液。使磁珠干燥 2 分钟。干燥后，加入 50μl 洗脱缓冲液并在 70℃混合 5 分钟。将磁珠捕获在磁铁上 5 分钟。移除 40μl 上清液并加入到另一个 96 孔板中。

[3801] 使用 ABI 高容量 cDNA 逆转录试剂盒（Applied Biosystems，Foster City，CA，目录号 4368813）合成 cDNA：

[3802] 按每个反应添加主混合物：2μl 10X 缓冲液，0.8μl 25XdNTP，2μl 随机引物，1μl 逆转录酶，1μl RNA 酶抑制剂和 3.2μl H_2O 至 10μl 总 RNA。使用 Bio-Rad C-1000

或S-1000热循环仪(Hercules,CA)通过以下步骤产生cDNA:25℃ 10分钟,37℃ 120分钟,85℃ 5秒,4℃保持。

[3803] 实时PCR:

[3804] 在MicroAmp Optical 96孔平板(Applied Biosystems目录号#4326659)中,将2μl cDNA添加至每孔含有1μl 18S TaqMan探针(Applied Biosystems目录号#4319413E)、1ul KRAS TaqMan探针(Applied Biosystems目录号HS00180035_m1,HS00932330_m1或HS00610483)和10μl TaqMan通用PCR主混合物(Applied Biosystems目录号#4324018)的主混合物中。在ABI 7900HT实时PCR系统(Applied Biosystems)中使用ΔΔCt(RQ)测定法进行实时PCR。除非在总结表中另外指出,否则在两次独立转染中测试每种双链体并且重复分析每次转染。

[3805] 将实时数据利用ΔΔCt方法分析并针对采用用10nM AD-1955转染的细胞进行的测定法归一化以计算相对倍数变化。

[3806] 表5.KRAS RNAi剂,0.1和10nM KD,24小时

[3807] SD=标准偏差,AVG=平均值

[3808]

	10nM KRAS		.1nM KRAS		10nM	.1nM	10nM	.1nM
双链 ID	bio1	bio2	bio1	bio2	SD	SD	AVG	AVG
AD-35613.4	0.332	0.542	1.814	1.365	0.1484	0.3177	0.437	1.589
AD-35572.4	0.403	0.666	1.850	1.571	0.1859	0.1975	0.535	1.711
AD-35578.4	0.194	0.905	0.622	0.485	0.5030	0.0965	0.550	0.554
AD-35584.4	0.171	0.239	0.953	0.654	0.0480	0.2115	0.205	0.803
AD-35590.4	0.167	0.296	0.988	0.832	0.0919	0.1105	0.231	0.910
AD-35596.4	0.782	0.837	1.540	1.263	0.0392	0.1962	0.809	1.402
AD-35602.4	1.013	0.915	1.264	0.934	0.0694	0.2334	0.964	1.099
AD-35608.4	0.818	0.631	1.120	1.093	0.1321	0.0191	0.725	1.106
AD-35614.4	0.898	1.025	1.929	1.195	0.0898	0.5194	0.961	1.562
AD-35573.4	0.920	0.809	1.412	0.957	0.0785	0.3219	0.865	1.185
AD-35579.4	0.794	0.946	1.694	1.244	0.1072	0.3189	0.870	1.469
AD-35585.4	0.861	0.738	3.016	2.552	0.0870	0.3281	0.800	2.784
AD-35591.4	0.458	0.325	1.238	1.073	0.0938	0.1162	0.392	1.156
AD-35597.4	0.948	0.897	1.523	0.864	0.0358	0.4657	0.922	1.194
AD-35603.4	0.401	0.405	0.817	0.618	0.0025	0.1402	0.403	0.718
AD-35609.4	0.168	0.165	0.503	0.320	0.0022	0.1295	0.167	0.411
AD-35615.4	0.555	0.620	1.397	0.818	0.0460	0.4099	0.587	1.108
AD-35574.4	0.762	0.650	1.009	0.643	0.0790	0.2590	0.706	0.826
AD-35580.1	0.436	0.398	1.334	0.768	0.0275	0.4003	0.417	1.051
AD-35586.4	0.242	0.266	0.908	0.577	0.0175	0.2337	0.254	0.743
AD-35592.4	0.212	0.166	0.600	0.504	0.0324	0.0685	0.189	0.552
AD-35598.4	0.828	0.893	1.318	1.147	0.0461	0.1205	0.861	1.232
AD-35604.4	0.070	0.179	0.594	0.496	0.0770	0.0692	0.124	0.545
AD-35610.4	0.415	0.633	1.068	0.887	0.1537	0.1275	0.524	0.977
AD-35616.4	0.159	0.342	0.300	0.213	0.1288	0.0610	0.251	0.256
AD-35575.4	0.470	0.689	0.789	0.749	0.1547	0.0284	0.579	0.769
AD-35581.4	0.137	0.288	0.220	0.196	0.1064	0.0170	0.212	0.208
AD-35587.4	0.637	0.670	1.059	0.975	0.0231	0.0591	0.653	1.017
AD-35593.4	0.200	0.463	0.724	0.489	0.1859	0.1661	0.332	0.607

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AD-35599.4	0.685	1.281	1.273	0.952	0.4217	0.2266	0.983	1.113
AD-35605.4	0.564	0.798	1.423	0.897	0.1649	0.3718	0.681	1.160
AD-35611.4	0.644	0.844	1.189	0.922	0.1418	0.1887	0.744	1.055
AD-35617.4	0.219	0.213	0.594	0.625	0.0047	0.0220	0.216	0.609
AD-35576.4	0.451	0.365	1.167	0.928	0.0604	0.1693	0.408	1.047
AD-35588.4	0.185	0.290	0.442	0.323	0.0736	0.0841	0.237	0.383
AD-35667.1	0.497	0.623	1.030	0.857	0.0897	0.1228	0.560	0.943
AD-35673.1	0.367	0.405	0.771	0.693	0.0268	0.0547	0.386	0.732
AD-35679.1	0.217	0.330	0.329	0.293	0.0798	0.0258	0.274	0.311
AD-35685.1	0.310	0.255	0.345	0.339	0.0390	0.0045	0.283	0.342
AD-35691.1	0.258	0.257	0.955	0.535	0.0005	0.2968	0.258	0.745
AD-35557.1	0.843	0.624	1.056	0.947	0.1547	0.0766	0.734	1.002
AD-35618.1	0.447	0.425	0.611	0.439	0.0157	0.1218	0.436	0.525
AD-35569.1	0.319	0.404	0.805	0.715	0.0605	0.0636	0.362	0.760
AD-35534.1	0.578	0.582	0.877	0.944	0.0028	0.0475	0.580	0.910
AD-35582.1	0.518	0.974	0.982	0.977	0.3223	0.0035	0.746	0.980
AD-35594.1	0.441	0.317	0.884	0.679	0.0877	0.1451	0.379	0.782
AD-35600.1	0.207	0.394	0.309	0.233	0.1322	0.0539	0.301	0.271
AD-35606.1	0.285	0.177	0.384	0.346	0.0770	0.0272	0.231	0.365
AD-35612.1	1.070	0.947	1.027	0.827	0.0870	0.1415	1.009	0.927
AD-38127.1	0.217	0.162	0.594	0.491	0.0388	0.0728	0.189	0.542
AD-38128.1	0.157	0.146	0.521	0.366	0.0072	0.1095	0.151	0.443
AD-38164.1	1.112	1.993	1.213	0.982	0.6224	0.1633	1.553	1.097
AD-38165.1	0.619	0.731	1.002	0.837	0.0790	0.1173	0.675	0.920
AD-38160.1	1.159	1.129	1.300	0.920	0.0216	0.2685	1.144	1.110
AD-38161.1	0.144	0.125	0.355	0.319	0.0130	0.0256	0.134	0.337
AD-38133.1	0.164	0.142	0.574	0.590	0.0154	0.0113	0.153	0.582
AD-38170.1	0.147	0.191	0.734	0.487	0.0311	0.1744	0.169	0.611
AD-38171.1	0.858	1.067	1.408	1.101	0.1480	0.2168	0.962	1.254
AD-38166.1	0.319	0.486	0.846	0.848	0.1184	0.0016	0.402	0.847
AD-38167.1	0.119	0.182	0.740	0.546	0.0440	0.1368	0.150	0.643
AD-38139.1	0.148	0.085	0.259	0.198	0.0445	0.0433	0.116	0.229
AD-38134.1	0.117	0.190	0.248	0.380	0.0514	0.0936	0.154	0.314
AD-38129.1	0.776	0.860	1.038	1.089	0.0596	0.0356	0.818	1.064
AD-38130.1	0.528	0.820	0.900	0.846	0.2064	0.0386	0.674	0.873
AD-38172.1	0.076	0.094	0.289	0.247	0.0127	0.0298	0.085	0.268
AD-38145.1	0.150	0.128	0.440	0.371	0.0154	0.0488	0.139	0.406
AD-38135.1	0.959	1.429	0.965	0.900	0.3321	0.0459	1.194	0.932
AD-38131.1	0.135	0.173	0.414	0.279	0.0267	0.0955	0.154	0.347
AD-38173.1	0.609	0.988	1.132	1.373	0.2681	0.1707	0.798	1.253
AD-38151.1	0.211	0.181	0.378	0.554	0.0218	0.1246	0.196	0.466
AD-38140.1	0.652	0.794	1.087	1.045	0.1004	0.0298	0.723	1.066
AD-38141.1	0.450	0.512	1.002	0.840	0.0433	0.1147	0.481	0.921

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AD-38136.1	0.053	0.096	0.150	0.121	0.0301	0.0199	0.074	0.136
AD-38137.1	0.283	0.259	0.677	0.580	0.0169	0.0687	0.271	0.628
AD-38132.1	0.256	0.333	0.669	0.726	0.0543	0.0404	0.294	0.697
AD-38157.1	0.760	0.543	0.768	0.900	0.1536	0.0937	0.651	0.834
AD-38146.1	0.249	0.240	0.617	0.584	0.0065	0.0237	0.245	0.600
AD-38147.1	0.271	0.361	0.858	0.909	0.0638	0.0365	0.316	0.883
AD-38142.1	0.389	0.634	0.971	0.712	0.1732	0.1831	0.512	0.841
AD-38143.1	0.378	0.657	0.920	0.808	0.1966	0.0791	0.518	0.864
AD-38163.1	0.088	0.083	0.143	0.172	0.0036	0.0206	0.085	0.158
AD-38152.1	0.755	0.580	1.057	0.897	0.1238	0.1134	0.667	0.977
AD-38153.1	0.727	0.781	0.855	1.006	0.0380	0.1067	0.754	0.930
AD-38148.1	0.553	0.522	0.784	0.831	0.0215	0.0333	0.537	0.807
AD-38149.1	0.269	0.295	0.607	0.641	0.0186	0.0242	0.282	0.624
AD-38138.1	0.330	0.417	0.402	0.448	0.0615	0.0321	0.373	0.425
AD-38169.1	0.380	0.248	0.626	0.540	0.0929	0.0607	0.314	0.583
AD-38158.1	0.699	0.611	0.800	1.250	0.0619	0.3184	0.655	1.025
AD-38159.1	0.161	0.122	0.210	0.227	0.0274	0.0123	0.142	0.219
AD-38154.1	0.212	0.172	0.628	0.507	0.0286	0.0858	0.192	0.567
AD-38155.1	0.198	0.215	0.331	0.309	0.0122	0.0153	0.207	0.320
AD-39683.1	0.471	0.536	1.135	0.812	0.0461	0.2283	0.504	0.973
AD-39689.1	0.630	0.627	1.148	0.979	0.0025	0.1194	0.629	1.064
AD-39695.1	0.659	0.557	1.222	1.022	0.0723	0.1414	0.608	1.122
AD-39701.1	1.218	1.231	0.704	0.724	0.0092	0.0141	1.225	0.714
AD-39707.1	0.384	0.160	1.387	1.087	0.1584	0.2121	0.272	1.237
AD-39713.1	1.157	0.481	1.128	1.228	0.4778	0.0707	0.819	1.178
AD-39719.1	0.885	0.631	1.178	1.189	0.1791	0.0073	0.758	1.183
AD-39725.1	1.105	1.074	1.203	1.751	0.0222	0.3878	1.089	1.477
AD-39684.1	0.321	0.186	0.954	1.222	0.0952	0.1895	0.253	1.088
AD-39690.1	0.825	0.828	0.832	0.852	0.0019	0.0139	0.826	0.842
AD-39696.1	1.071	0.996	1.087	0.883	0.0532	0.1443	1.034	0.985
AD-39702.1	0.360	0.334	1.050	1.285	0.0179	0.1660	0.347	1.167
AD-39708.1	0.757	0.969	1.049	1.091	0.1494	0.0299	0.863	1.070
AD-39714.1	0.953	1.056	0.779	0.639	0.0731	0.0995	1.004	0.709
AD-39720.1	0.210	0.182	0.404	0.691	0.0199	0.2030	0.196	0.548
AD-39726.1	0.774	0.968	0.921	1.068	0.1372	0.1037	0.871	0.995
AD-39685.1	1.022	1.358	1.053	0.997	0.2378	0.0399	1.190	1.025
AD-39691.1	0.494	0.380	0.913	0.967	0.0806	0.0379	0.437	0.940
AD-39697.1	0.892	1.333	0.937	1.344	0.3125	0.2883	1.113	1.140
AD-39703.1	1.071	1.141	0.983	0.864	0.0497	0.0842	1.106	0.924
AD-39709.1	0.905	1.086	0.944	1.079	0.1284	0.0953	0.995	1.011
AD-39715.1	0.347	0.385	1.398	1.013	0.0265	0.2722	0.366	1.205
AD-39721.1	0.911	0.781	1.128	1.119	0.0918	0.0066	0.846	1.123
AD-39727.1	0.267	0.271	0.911	1.038	0.0028	0.0894	0.269	0.975

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AD-39686.1	0.897	0.490	0.781	0.633	0.2877	0.1044	0.694	0.707
AD-39692.1	0.936	0.879	0.814	0.802	0.0403	0.0083	0.908	0.808
AD-39698.1	1.257	1.375	0.829	0.876	0.0834	0.0333	1.316	0.853
AD-39704.1	1.211	1.189	0.909	0.735	0.0155	0.1234	1.200	0.822
AD-39710.1	1.389	1.136	0.881	0.862	0.1789	0.0130	1.263	0.871
AD-39716.1	0.787	0.943	0.991	0.963	0.1099	0.0199	0.865	0.977
AD-39722.1	1.147	1.049	0.872	0.716	0.0688	0.1108	1.098	0.794
AD-39728.1	0.846	0.974	0.891	0.928	0.0902	0.0264	0.910	0.909
AD-39683.1	0.374	0.307	0.996	0.982	0.0469	0.0098	0.341	0.989
AD-39687.1	1.015	0.775	1.035	1.642	0.1695	0.4296	0.895	1.338
AD-39689.1	0.340	0.328	0.769	0.762	0.0090	0.0047	0.334	0.765
AD-39693.1	1.262	0.832	0.855	0.967	0.3040	0.0791	1.047	0.911
AD-39699.1	1.173	1.113	1.113	1.307	0.0423	0.1375	1.143	1.210
AD-39705.1	0.622	0.582	0.730	0.807	0.0282	0.0542	0.602	0.768
AD-39711.1	1.996	0.864	0.720	0.829	0.8006	0.0770	1.430	0.774
AD-39717.1	0.551	0.523	1.136	1.064	0.0197	0.0511	0.537	1.100
AD-39723.1	1.179	0.695	0.877	0.873	0.3428	0.0025	0.937	0.875
AD-39729.1	1.083	0.864	0.898	0.873	0.1547	0.0178	0.973	0.885
AD-39688.1	0.341	0.492	0.700	0.782	0.1064	0.0577	0.416	0.741
AD-39694.1	0.230	0.327	0.923	1.087	0.0685	0.1164	0.279	1.005
AD-39700.1	0.529	0.760	0.600	0.671	0.1631	0.0497	0.645	0.635
AD-39706.1	0.180	0.217	0.447	0.522	0.0263	0.0528	0.198	0.484
AD-39712.1	0.330	0.394	0.798	0.777	0.0452	0.0147	0.362	0.787
AD-39718.1	0.672	0.798	0.688	0.724	0.0889	0.0255	0.735	0.706
AD-39724.1	0.599	1.136	0.643	0.680	0.3804	0.0261	0.868	0.661
AD-39730.1	0.996	1.459	0.848	0.784	0.3271	0.0448	1.228	0.816
AD-39736.1	1.085	1.121	0.733	0.883	0.0254	0.1064	1.103	0.808
AD-39742.1	0.518	0.561	0.651	0.703	0.0308	0.0374	0.539	0.677
AD-39748.1	0.445	0.609	0.772	0.788	0.1163	0.0113	0.527	0.780
AD-39754.1	0.549	0.823	0.691	0.894	0.1942	0.1438	0.686	0.793
AD-39760.1	0.233	0.210	0.417	0.747	0.0158	0.2332	0.221	0.582
AD-39766.1	0.700	0.882	0.849	0.836	0.1291	0.0095	0.791	0.843
AD-39772.1	0.323	0.379	0.797	0.870	0.0393	0.0519	0.351	0.833
AD-39731.1	0.804	0.222	0.452	0.417	0.4116	0.0251	0.513	0.434
AD-39737.1	0.450	0.347	0.737	0.768	0.0726	0.0219	0.399	0.753
AD-39743.1	0.375	0.533	0.794	0.852	0.1112	0.0415	0.454	0.823
AD-39695.1	0.610	0.492	0.831	0.821	0.0836	0.0070	0.551	0.826
AD-39749.1	0.292	0.121	0.545	0.695	0.1205	0.1059	0.206	0.620
AD-39755.1	0.226	0.275	0.874	1.170	0.0350	0.2093	0.251	1.022
AD-39761.1	0.821	0.841	0.942	1.101	0.0141	0.1124	0.831	1.022
AD-39767.1	0.360	0.374	0.730	0.711	0.0097	0.0134	0.367	0.720
AD-39773.1	0.223	0.236	0.802	1.159	0.0096	0.2520	0.229	0.980
AD-39732.1	0.446	0.662	1.593	1.181	0.1532	0.2914	0.554	1.387

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AD-39738.1	0.257	0.147	1.369	1.482	0.0776	0.0801	0.202	1.426
AD-39744.1	0.259	0.200	1.097	0.871	0.0414	0.1592	0.230	0.984
AD-39750.1	0.182	0.302	0.642	0.782	0.0853	0.0988	0.242	0.712
AD-39756.1	0.568	0.548	0.808	0.993	0.0144	0.1308	0.558	0.900
AD-39762.1	0.684	0.916	0.783	0.929	0.1641	0.1031	0.800	0.856
AD-39768.1	0.929	1.239	1.000	1.033	0.2194	0.0239	1.084	1.016
AD-39774.1	0.391	0.447	1.087	1.087	0.0399	0.0003	0.419	1.087
AD-39733.1	0.605	0.569	1.020	1.212	0.0251	0.1355	0.587	1.116
AD-39739.1	0.950	1.271	0.959	1.030	0.2265	0.0501	1.111	0.994
AD-39701.1	0.798	1.193	1.221	1.018	0.2794	0.1437	0.996	1.120
AD-39745.1	0.257	0.212	1.116	1.226	0.0317	0.0779	0.234	1.171
AD-39751.1	0.260	0.248	1.037	2.286	0.0085	0.8828	0.254	1.662
AD-39757.1	0.319	0.566	1.098	0.949	0.1753	0.1053	0.443	1.023
AD-39763.1	0.235	0.300	0.667	0.531	0.0463	0.0961	0.267	0.599
AD-39769.1	0.637	0.531	0.526	0.826	0.0749	0.2120	0.584	0.676
AD-39775.1	0.472	0.526	0.760	1.002	0.0382	0.1711	0.499	0.881
AD-39734.1	0.915	0.920	0.751	0.837	0.0035	0.0606	0.917	0.794
AD-39740.1	0.323	0.302	0.406	0.632	0.0145	0.1593	0.312	0.519
AD-39746.1	0.553	0.702	0.949	1.145	0.1058	0.1382	0.627	1.047
AD-39752.1	0.440	0.577	0.855	0.860	0.0965	0.0030	0.509	0.857
AD-39758.1	1.129	1.095	0.952	0.830	0.0238	0.0863	1.112	0.891
AD-39764.1	1.125	0.898	1.205	1.405	0.1606	0.1409	1.011	1.305
AD-39770.1	0.647	0.314	0.672	0.461	0.2356	0.1486	0.480	0.566
AD-39776.1	1.013	0.970	1.035	0.739	0.0304	0.2092	0.992	0.887
AD-39735.1	0.284	0.201	0.613	0.976	0.0588	0.2564	0.242	0.794
AD-39741.1	0.177	0.188	0.526	0.806	0.0074	0.1977	0.182	0.666
AD-39747.1	1.047	0.926	1.247	1.483	0.0854	0.1666	0.986	1.365
AD-39753.1	1.082	0.823	1.034	1.662	0.1833	0.4437	0.953	1.348
AD-39759.1	0.327	0.292	0.638	0.412	0.0252	0.1600	0.309	0.525
AD-39765.1	1.099	0.596	1.270	1.027	0.3554	0.1714	0.847	1.148
AD-39771.1	0.238	0.334	0.801	0.460	0.0679	0.2407	0.286	0.631
AD-39778.1	0.217	0.250	0.502	0.354	0.0235	0.1042	0.233	0.428
AD-39784.1	0.698	0.598	1.036	0.944	0.0708	0.0655	0.648	0.990
AD-39790.1	0.150	0.260	0.614	0.787	0.0777	0.1221	0.205	0.700
AD-39796.1	0.635	0.610	0.731	0.846	0.0178	0.0813	0.622	0.788
AD-39802.1	0.349	0.150	0.898	0.970	0.1408	0.0509	0.249	0.934
AD-39808.1	0.734	0.972	1.079	0.955	0.1680	0.0881	0.853	1.017
AD-39814.1	1.070	1.294	0.979	0.968	0.1588	0.0074	1.182	0.974
AD-39820.1	0.381	0.209	0.786	0.687	0.1218	0.0701	0.295	0.737
AD-39779.1	0.744	0.889	1.038	0.942	0.1020	0.0683	0.817	0.990
AD-39785.1	0.182	0.218	0.509	0.506	0.0255	0.0022	0.200	0.507
AD-39791.1	0.214	0.308	0.556	0.519	0.0667	0.0260	0.261	0.537
AD-39797.1	0.341	0.326	0.788	0.543	0.0100	0.1730	0.333	0.665

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AD-39803.1	0.229	0.210	0.808	0.648	0.0135	0.1133	0.220	0.728
AD-39809.1	0.624	0.829	1.060	1.031	0.1450	0.0211	0.727	1.046
AD-39815.1	0.441	0.449	0.862	0.852	0.0057	0.0072	0.445	0.857
AD-39821.1	0.582	0.592	0.722	0.608	0.0071	0.0806	0.587	0.665
AD-39780.1	0.748	0.784	0.973	0.976	0.0252	0.0025	0.766	0.974
AD-39786.1	0.376	0.455	0.466	0.640	0.0557	0.1226	0.416	0.553
AD-39792.1	1.195	1.019	0.908	1.168	0.1249	0.1835	1.107	1.038
AD-39798.1	0.429	0.342	0.933	0.936	0.0615	0.0020	0.386	0.934
AD-39804.1	0.551	0.588	0.942	0.959	0.0259	0.0119	0.570	0.950
AD-39810.1	0.605	0.532	0.989	0.956	0.0518	0.0236	0.568	0.972
AD-39764.1	1.112	1.027	0.961	0.746	0.0602	0.1522	1.070	0.854
AD-39816.1	0.805	0.645	1.014	0.839	0.1130	0.1236	0.725	0.927
AD-39770.1	0.420	0.371	0.858	0.887	0.0345	0.0201	0.396	0.873
AD-39822.1	0.288	0.313	0.589	0.494	0.0178	0.0671	0.301	0.542
AD-39781.1	0.276	0.379	0.404	0.305	0.0725	0.0701	0.328	0.354
AD-39787.1	0.982	1.065	0.675	0.803	0.0584	0.0909	1.024	0.739
AD-39793.1	0.165	0.291	0.487	0.488	0.0893	0.0007	0.228	0.487
AD-39799.1	0.444	0.540	0.686	0.746	0.0675	0.0423	0.492	0.716
AD-39805.1	0.295	0.250	0.474	0.421	0.0320	0.0371	0.273	0.448
AD-39811.1	0.646	0.792	0.892	0.882	0.1030	0.0070	0.719	0.887
AD-39817.1	0.583	0.824	0.848	0.846	0.1708	0.0012	0.703	0.847
AD-39823.1	1.229	1.075	1.080	0.859	0.1083	0.1564	1.152	0.970
AD-39782.1	0.605	0.757	1.162	0.883	0.1076	0.1972	0.681	1.022
AD-39788.1	0.257	0.289	0.665	0.534	0.0227	0.0926	0.273	0.599
AD-39794.1	0.667	0.699	1.196	1.102	0.0229	0.0668	0.683	1.149
AD-39800.1	0.888	0.734	1.201	0.908	0.1092	0.2072	0.811	1.054
AD-39806.1	0.505	0.637	0.630	0.849	0.0935	0.1549	0.571	0.739
AD-39812.1	0.281	0.390	0.521	0.597	0.0771	0.0538	0.335	0.559
AD-39818.1	0.999	1.049	0.789	0.936	0.0347	0.1044	1.024	0.863
AD-39824.1	1.086	1.053	1.370	1.034	0.0235	0.2377	1.070	1.202
AD-39783.1	0.460	0.731	0.736	0.822	0.1916	0.0609	0.595	0.779
AD-39789.1	0.859	1.454	1.139	1.308	0.4213	0.1195	1.157	1.224
AD-39795.1	1.165	0.901	1.015	0.916	0.1866	0.0698	1.033	0.965
AD-39801.1	1.222	1.191	1.098	0.843	0.0216	0.1801	1.207	0.971
AD-39807.1	0.776	0.807	1.007	1.002	0.0215	0.0036	0.791	1.004
AD-39813.1	0.923	1.206	1.008	0.901	0.1998	0.0753	1.065	0.955
AD-39819.1	0.952	1.021	1.024	0.916	0.0484	0.0765	0.986	0.970
AD-39825.1	0.648	0.864	1.028	0.981	0.1529	0.0336	0.756	1.004
AD-39776.1	0.795	1.019	0.891	1.046	0.1581	0.1094	0.907	0.969
AD-39831.1	0.648	0.601	1.018	1.034	0.0334	0.0119	0.624	1.026
AD-39837.1	0.799	0.984	0.969	0.903	0.1308	0.0463	0.891	0.936
AD-39843.1	0.325	0.385	0.695	0.572	0.0427	0.0866	0.355	0.634
AD-39849.1	0.702	1.075	0.903	0.969	0.2638	0.0469	0.889	0.936

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AD-39855.1	0.309	0.490	1.202	0.800	0.1280	0.2840	0.399	1.001
AD-39861.1	0.762	1.162	1.020	1.000	0.2825	0.0141	0.962	1.010
AD-39867.1	0.873	1.162	1.219	0.918	0.2040	0.2126	1.017	1.069
AD-39826.1	1.358	1.043	1.148	0.961	0.2226	0.1320	1.201	1.055
AD-39832.1	0.792	1.337	1.214	0.873	0.3849	0.2413	1.065	1.043
AD-39838.1	0.429	0.270	0.793	0.530	0.1128	0.1859	0.349	0.661
AD-39844.1	0.572	0.789	0.833	0.692	0.1536	0.0997	0.680	0.762
AD-39850.1	0.535	0.231	0.505	0.529	0.2152	0.0169	0.383	0.517
AD-39856.1	0.323	0.377	0.835	0.784	0.0384	0.0359	0.350	0.810
AD-39862.1	0.405	0.429	0.835	0.615	0.0167	0.1552	0.417	0.725
AD-39868.1	0.386	0.484	0.683	0.643	0.0697	0.0284	0.435	0.663
AD-39735.1	0.168	0.255	0.439	0.294	0.0616	0.1026	0.211	0.366
AD-39827.1	0.202	0.313	0.616	0.413	0.0787	0.1432	0.258	0.515
AD-39833.1	0.190	0.492	1.007	1.026	0.2134	0.0135	0.341	1.017
AD-39839.1	0.790	1.002	1.227	1.327	0.1503	0.0708	0.896	1.277
AD-39845.1	0.192	0.213	0.391	0.218	0.0147	0.1220	0.202	0.304
AD-39851.1	0.779	0.493	1.243	0.929	0.2022	0.2220	0.636	1.086
AD-39857.1	0.602	1.444	0.992	0.692	0.5960	0.2120	1.023	0.842
AD-39863.1	0.482	0.135	0.906	0.632	0.2449	0.1937	0.308	0.769
AD-39869.1	0.357	0.025	0.799	0.558	0.2347	0.1708	0.191	0.678
AD-39828.1	1.185	1.085	1.176	0.952	0.0707	0.1585	1.135	1.064
AD-39834.1	1.140	1.273	1.315	1.075	0.0938	0.1698	1.207	1.195
AD-39840.1	0.251	0.541	0.766	0.591	0.2050	0.1239	0.396	0.679
AD-39846.1	0.635	0.646	1.044	0.984	0.0077	0.0425	0.641	1.014
AD-39852.1	0.434	0.555	0.707	0.719	0.0857	0.0085	0.494	0.713
AD-39858.1	0.169	0.192	0.363	0.268	0.0160	0.0670	0.180	0.316
AD-39864.1	1.612	1.161	0.825	0.919	0.3189	0.0665	1.387	0.872
AD-39870.1	0.321	0.186	0.072	0.170	0.0952	0.0695	0.253	0.121
AD-39829.1	0.283	0.133	0.353	0.266	0.1060	0.0611	0.208	0.310
AD-39835.1	1.265	0.792	0.460	0.641	0.3343	0.1277	1.029	0.551
AD-39841.1	0.345	0.267	0.416	0.369	0.0552	0.0335	0.306	0.392
AD-39853.1	0.257	0.268	0.640	0.527	0.0081	0.0799	0.262	0.584
AD-39859.1	0.316	0.290	0.773	0.886	0.0182	0.0801	0.303	0.830
AD-39865.1	0.228	0.216	0.456	0.424	0.0084	0.0231	0.222	0.440
AD-39871.1	0.218	0.338	0.502	0.571	0.0849	0.0489	0.278	0.537
AD-39830.1	0.284	0.293	0.770	0.716	0.0063	0.0379	0.289	0.743
AD-39836.1	0.267	0.232	0.615	0.580	0.0249	0.0254	0.250	0.598
AD-39842.1	0.242	0.259	0.707	0.654	0.0121	0.0373	0.250	0.681
AD-39848.1	0.515	0.591	1.071	1.012	0.0536	0.0416	0.553	1.042
AD-39854.1	0.853	1.128	1.035	1.059	0.1943	0.0169	0.991	1.047
AD-39860.1	0.969	1.119	0.965	0.833	0.1058	0.0936	1.044	0.899
AD-39866.1	0.247	0.395	0.733	0.834	0.1045	0.0711	0.321	0.784
AD-39992.1	0.507	0.837	0.985	0.990	0.2334	0.0032	0.672	0.988

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AD-39998.1	0.384	0.549	0.745	0.676	0.1167	0.0486	0.466	0.711
AD-40004.1	0.509	0.664	1.090	1.042	0.1096	0.0340	0.587	1.066
AD-40010.1	0.212	0.245	0.954	0.885	0.0232	0.0487	0.228	0.919
AD-40016.1	0.261	0.514	0.731	1.050	0.1790	0.2254	0.387	0.891
AD-40022.1	0.784	1.221	0.955	0.939	0.3089	0.0112	1.003	0.947
AD-40028.1	0.907	1.194	1.062	0.976	0.2026	0.0608	1.050	1.019
AD-40034.1	0.367	0.483	0.902	0.718	0.0819	0.1298	0.425	0.810
AD-39999.1	0.227	0.339	0.910	0.837	0.0789	0.0511	0.283	0.873
AD-40005.1	0.219	0.202	0.419	0.421	0.0121	0.0012	0.211	0.420
AD-40011.1	0.470	0.529	0.731	0.637	0.0413	0.0663	0.499	0.684
AD-40017.1	0.209	0.402	0.873	0.806	0.1364	0.0475	0.306	0.839
AD-40029.1	0.793	0.821	0.904	0.834	0.0199	0.0496	0.807	0.869
AD-39846.1	0.591	0.468	0.690	0.823	0.0867	0.0942	0.529	0.757
AD-40035.1	0.872	1.166	1.079	1.090	0.2083	0.0081	1.019	1.085
AD-39852.1	0.439	0.346	0.784	0.995	0.0659	0.1492	0.393	0.890
AD-39994.1	0.396	0.517	0.936	1.097	0.0854	0.1137	0.457	1.016
AD-40000.1	0.574	0.734	1.100	1.100	0.1133	0.0004	0.654	1.100
AD-40006.1	0.402	0.389	0.831	0.800	0.0094	0.0223	0.395	0.815
AD-40012.1	0.211	0.435	0.704	0.929	0.1588	0.1593	0.323	0.816
AD-40018.1	0.692	1.163	0.808	0.933	0.3325	0.0883	0.928	0.871
AD-40024.1	0.182	0.428	0.772	0.716	0.1739	0.0399	0.305	0.744
AD-40030.1	0.437	0.651	0.825	0.874	0.1516	0.0344	0.544	0.849
AD-40036.1	0.092	0.216	0.452	0.532	0.0876	0.0567	0.154	0.492
AD-39995.1	0.290	0.686	0.918	0.618	0.2803	0.2122	0.488	0.768
AD-40001.1	0.672	0.758	0.709	1.090	0.0607	0.2698	0.715	0.899
AD-40007.1	0.785	0.477	0.780	0.928	0.2177	0.1048	0.631	0.854
AD-40013.1	0.503	0.901	0.782	1.056	0.2814	0.1936	0.702	0.919
AD-40019.1	0.264	0.125	0.615	0.731	0.0979	0.0818	0.194	0.673
AD-40025.1	0.864	1.208	0.968	1.047	0.2430	0.0562	1.036	1.007
AD-40031.1	0.268	0.286	0.995	0.805	0.0124	0.1344	0.277	0.900
AD-40037.1	0.579	0.647	0.689	1.211	0.0484	0.3693	0.613	0.950
AD-39996.1	0.338	0.400	0.618	0.680	0.0438	0.0442	0.369	0.649
AD-40002.1	0.993	0.812	0.746	0.851	0.1281	0.0747	0.903	0.798
AD-40008.1	0.227	0.154	0.309	0.434	0.0516	0.0879	0.190	0.372
AD-40014.1	0.612	0.631	0.702	0.613	0.0136	0.0630	0.622	0.658
AD-40020.1	0.386	0.409	0.962	1.008	0.0164	0.0324	0.398	0.985
AD-40026.1	0.229	0.130	0.370	0.498	0.0702	0.0901	0.180	0.434
AD-40032.1	0.421	0.454	0.979	0.954	0.0232	0.0176	0.437	0.966
AD-40038.1	0.491	0.674	0.851	1.008	0.1291	0.1106	0.582	0.930
AD-39997.1	0.644	0.860	0.749	0.878	0.1531	0.0917	0.752	0.814
AD-39858.1	0.146	0.293	0.681	0.569	0.1043	0.0792	0.219	0.625
AD-40009.1	0.191	0.382	0.912	1.055	0.1351	0.1012	0.287	0.984
AD-40015.1	0.897	0.856	0.778	1.065	0.0292	0.2034	0.876	0.922

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AD-40021.1	0.225	0.282	0.850	0.658	0.0401	0.1358	0.254	0.754
AD-40027.1	0.466	1.083	0.916	0.854	0.4358	0.0437	0.774	0.885
AD-40033.1	0.278	0.311	0.426	0.588	0.0230	0.1150	0.295	0.507
AD-40039.1	0.257	0.447	0.666	0.739	0.1348	0.0511	0.352	0.703
AD-40045.1	0.263	0.147	0.526	0.945	0.0821	0.2962	0.205	0.735
AD-40051.1	0.162	0.126	0.665	0.837	0.0255	0.1209	0.144	0.751
AD-40057.1	0.150	0.176	0.641	0.791	0.0178	0.1066	0.163	0.716
AD-40063.1	0.220	0.287	0.650	0.977	0.0468	0.2311	0.253	0.813
AD-40069.1	0.431	0.559	0.729	0.922	0.0907	0.1363	0.495	0.825
AD-40075.1	0.399	0.613	0.834	0.972	0.1511	0.0971	0.506	0.903
AD-40081.1	0.287	0.351	0.499	0.612	0.0453	0.0795	0.319	0.556
AD-40040.1	0.861	0.850	0.888	1.077	0.0077	0.1337	0.856	0.983
AD-40046.1	0.386	0.397	0.607	0.634	0.0083	0.0191	0.392	0.621
AD-39864.1	0.930	0.933	0.810	1.018	0.0022	0.1468	0.931	0.914
AD-40052.1	0.272	0.216	0.526	0.852	0.0396	0.2299	0.244	0.689
AD-40058.1	0.398	0.305	0.928	1.079	0.0655	0.1071	0.351	1.003
AD-40064.1	0.460	0.208	0.909	1.083	0.1777	0.1230	0.334	0.996
AD-40070.1	0.116	0.454	0.447	0.885	0.2390	0.3095	0.285	0.666
AD-40076.1	0.396	1.498	0.634	1.054	0.7792	0.2969	0.947	0.844
AD-40082.1	0.584	0.553	0.760	1.053	0.0218	0.2073	0.569	0.906
AD-40041.1	0.196	0.241	0.862	0.978	0.0322	0.0819	0.218	0.920
AD-40047.1	0.289	0.214	0.699	1.096	0.0535	0.2806	0.251	0.897
AD-40053.1	0.973	1.094	0.717	1.079	0.0854	0.2560	1.033	0.898
AD-40059.1	1.064	0.985	0.720	1.088	0.0562	0.2601	1.025	0.904
AD-40065.1	0.855	0.863	0.589	1.020	0.0057	0.3048	0.859	0.805
AD-40071.1	0.242	0.346	0.846	0.826	0.0739	0.0142	0.294	0.836
AD-40077.1	0.249	0.187	0.649	0.738	0.0437	0.0633	0.218	0.693
AD-40083.1	0.286	0.339	0.807	1.130	0.0373	0.2279	0.312	0.968
AD-40042.1	0.549	0.288	1.205	1.288	0.1845	0.0587	0.418	1.246
AD-40048.1	0.413	0.345	0.713	0.940	0.0483	0.1610	0.379	0.826
AD-40054.1	0.278	0.258	0.685	0.825	0.0146	0.0989	0.268	0.755
AD-40060.1	0.288	0.230	0.781	0.811	0.0410	0.0217	0.259	0.796
AD-40066.1	0.779	0.829	0.950	1.284	0.0357	0.2361	0.804	1.117
AD-40072.1	0.273	0.169	0.579	0.963	0.0738	0.2716	0.221	0.771
AD-40078.1	0.747	0.841	1.177	1.410	0.0666	0.1645	0.794	1.294
AD-40084.1	1.064	0.972	0.944	1.036	0.0647	0.0651	1.018	0.990
AD-40043.1	0.340	0.313	0.804	0.795	0.0190	0.0065	0.327	0.800
AD-40049.1	0.179	0.159	0.339	0.312	0.0141	0.0191	0.169	0.326
AD-40055.1	0.243	0.248	0.811	0.817	0.0034	0.0044	0.245	0.814
AD-40061.1	0.153	0.229	0.357	0.519	0.0537	0.1146	0.191	0.438
AD-40067.1	0.260	0.141	0.715	0.692	0.0837	0.0156	0.201	0.703
AD-40073.1	0.241	0.156	0.833	0.858	0.0597	0.0180	0.199	0.846
AD-40079.1	0.236	0.236	0.694	0.991	0.0002	0.2099	0.236	0.842

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AD-40085.1	0.188	0.210	0.558	0.519	0.0155	0.0276	0.199	0.539
AD-40044.1	0.229	0.126	0.342	0.506	0.0728	0.1157	0.178	0.424
AD-40050.1	1.016	0.566	0.933	1.088	0.3183	0.1097	0.791	1.011
AD-40056.1	0.274	0.244	0.801	1.155	0.0215	0.2506	0.259	0.978
AD-40062.1	0.536	0.653	0.900	1.143	0.0822	0.1719	0.595	1.022
AD-40068.1	0.175	0.131	0.218	0.438	0.0313	0.1551	0.153	0.328
AD-40074.1	0.366	0.462	0.911	0.734	0.0674	0.1256	0.414	0.823
AD-40080.1	0.273	0.296	0.844	0.932	0.0166	0.0623	0.284	0.888
AD-40071.1	0.341	0.214	0.691	0.912	0.0902	0.1562	0.277	0.801
AD-40077.1	0.192	0.180	0.483	0.404	0.0083	0.0563	0.186	0.444
AD-40083.1	0.145	0.238	0.514	0.872	0.0657	0.2536	0.192	0.693
AD-40042.1	0.403	0.288	0.626	0.747	0.0814	0.0856	0.346	0.686
AD-35523.3	0.228	0.350	1.165	1.104	0.0862	0.0434	0.289	1.135
AD-35529.1	0.367	0.368	1.099	0.831	0.0004	0.1893	0.368	0.965
AD-35535.4	0.466	0.362	0.563	0.600	0.0735	0.0264	0.414	0.582
AD-35541.4	0.585	0.358	1.003	0.713	0.1606	0.2052	0.472	0.858
AD-35547.4	0.491	0.546	0.732	0.626	0.0393	0.0753	0.518	0.679
AD-35553.4	0.785	0.690	1.043	0.744	0.0677	0.2115	0.738	0.893
AD-35559.4	0.387	0.437	0.779	0.776	0.0357	0.0021	0.412	0.778
AD-35565.4	0.549	0.568	0.930	1.163	0.0132	0.1647	0.559	1.046
AD-35524.4	0.358	0.399	0.997	0.915	0.0289	0.0576	0.379	0.956
AD-35530.4	0.212	0.406	1.129	0.981	0.1374	0.1046	0.309	1.055
AD-35536.4	0.463	0.272	1.028	1.131	0.1352	0.0727	0.368	1.080
AD-35542.4	0.573	0.537	0.804	0.919	0.0255	0.0808	0.555	0.861
AD-35548.4	0.944	0.574	0.886	0.728	0.2619	0.1113	0.759	0.807
AD-35554.4	0.490	0.393	1.021	0.679	0.0682	0.2416	0.442	0.850
AD-35560.2	1.199	0.386	0.796	0.610	0.5748	0.1310	0.793	0.703
AD-35566.4	1.082	0.981	0.747	0.840	0.0714	0.0652	1.031	0.794
AD-35525.2	0.645	0.767	0.956	0.627	0.0864	0.2323	0.706	0.792
AD-35531.4	0.425	0.328	0.755	0.776	0.0683	0.0144	0.376	0.765
AD-35537.4	0.824	0.823	0.710	0.628	0.0004	0.0578	0.824	0.669
AD-35543.2	0.232	0.367	0.980	0.845	0.0954	0.0949	0.300	0.912
AD-35549.4	1.492	0.378	1.057	0.665	0.7877	0.2769	0.935	0.861
AD-35555.4	0.382	0.460	1.133	1.096	0.0554	0.0260	0.421	1.115
AD-35561.4	1.037	0.685	1.036	0.854	0.2488	0.1285	0.861	0.945
AD-35567.4	1.437	0.698	1.098	0.909	0.5222	0.1337	1.068	1.004
AD-35526.4	1.354	0.995	0.597	0.754	0.2540	0.1111	1.174	0.675
AD-35532.4	0.645	0.312	1.117	0.944	0.2357	0.1222	0.479	1.031
AD-35535.4	0.694	0.362	0.856	1.093	0.2353	0.1672	0.528	0.974
AD-35538.4	0.280	0.358	1.121	0.733	0.0551	0.2744	0.319	0.927
AD-35544.4	1.562	0.806	0.895	1.104	0.5351	0.1477	1.184	1.000
AD-35550.4	0.988	0.683	0.745	1.159	0.2155	0.2926	0.836	0.952
AD-35556.4	0.597	0.298	1.087	0.890	0.2119	0.1388	0.448	0.989

[3818]

AD-35562.4	0.412	0.652	0.796	0.857	0.1700	0.0436	0.532	0.826
AD-35568.4	0.324	0.544	0.986	1.171	0.1556	0.1304	0.434	1.079
AD-35527.4	0.218	0.272	1.079	1.097	0.0380	0.0122	0.245	1.088
AD-35533.4	0.488	0.226	1.236	1.089	0.1848	0.1038	0.357	1.162
AD-35539.4	0.821	0.660	1.065	1.155	0.1140	0.0637	0.740	1.110
AD-35545.4	1.206	0.787	0.990	1.097	0.2968	0.0755	0.997	1.043
AD-35551.4	0.860	0.404	1.011	1.078	0.3220	0.0473	0.632	1.044
AD-35563.4	1.183	0.977	0.908	1.277	0.1461	0.2606	1.080	1.092
AD-35528.4	0.955	0.770	1.094	0.757	0.1309	0.2387	0.863	0.926
AD-35540.4	0.560	0.541	1.061	1.052	0.0132	0.0065	0.550	1.056
AD-35546.4	0.716	0.605	1.121	0.996	0.0789	0.0886	0.660	1.058
AD-35541.4	0.847	0.358	1.046	1.002	0.3458	0.0314	0.603	1.024
AD-35552.4	0.468	0.529	1.057	1.002	0.0431	0.0391	0.499	1.029
AD-35558.4	0.424	0.342	1.241	1.045	0.0578	0.1385	0.383	1.143
AD-35564.4	0.485	0.438	0.980	0.968	0.0329	0.0085	0.461	0.974
AD-35570.4	0.579	0.413	0.839	1.108	0.1175	0.1900	0.496	0.973
AD-35571.4	0.476	0.348	0.818	0.951	0.0907	0.0943	0.412	0.885
AD-35577.4	0.300	0.393	0.844	0.882	0.0660	0.0267	0.347	0.863
AD-35583.4	1.305	0.679	0.970	1.085	0.4424	0.0813	0.992	1.027
AD-35589.4	1.799	1.425	1.223	1.155	0.2646	0.0480	1.612	1.189
AD-35595.4	0.504	0.417	0.976	1.013	0.0619	0.0261	0.461	0.995
AD-35601.4	0.834	0.338	1.076	0.938	0.3513	0.0973	0.586	1.007
AD-35607.4	0.597	0.419	1.000	1.074	0.1256	0.0523	0.508	1.037

[3819] 表 6. IC_{50}数据 :KRAS 倍数变化值

[3820] SD ＝标准偏差 , Avg ＝平均值

[3821]

双链体	IC50_bio1	IC50_bio2	AvgIC50	SD
AD - 39731.1	0.020	0.003	0.012	0.0122
AD - 39706.1	0.004	0.000	0.002	0.0028
AD - 39720.1	0.012	0.002	0.007	0.0070
AD - 39741.1	0.002	0.000	0.001	0.0015
AD - 39738.1	0.002	0.001	0.002	0.0008
AD - 39870.1	0.159	0.069	0.114	0.0636
AD - 39845.1	0.056	0.015	0.036	0.0294
AD - 39829.1	0.133	0.027	0.080	0.0750

AD - 39778.1	0.135	0.040	0.088	0.0670
AD - 39865.1	0.179	0.038	0.109	0.0996
AD - 39793.1	0.003	0.078	0.041	0.0526
AD - 39785.1	0.004	0.014	0.009	0.0068
AD - 40068.1	0.010	0.002	0.006	0.0052
AD - 40008.1	0.041	0.011	0.026	0.0217

[3822]

AD - 40026.1	0.014	0.009	0.012	0.0036
AD - 40061.1	0.014	0.004	0.009	0.0068
AD - 40036.1	0.040	0.013	0.027	0.0196
AD - 40057.1	0.030	0.111	0.071	0.0577
AD - 35581.4	0.017	0.027	0.022	0.0071
AD - 35616.4	0.032	0.044	0.038	0.0091
AD - 35588.4	0.036	0.060	0.048	0.0164
AD - 35604.4	0.088	0.373	0.231	0.2015
AD - 35592.4	0.086	0.266	0.176	0.1270
AD - 35685.1	0.036	0.019	0.027	0.0120
AD - 38159.1	0.093	0.096	0.095	0.0027
AD - 38139.1	0.092	0.354	0.223	0.1849
AD - 38172.1	0.130	0.180	0.155	0.0352
AD - 38134.1	0.120	0.199	0.159	0.0557
AD - 38161.1	0.109	0.173	0.141	0.0448
AD - 38131.1	0.134	0.374	0.254	0.1699
AD - 38128.1	0.014	0.070	0.042	0.0394

AD - 38151.1	0.093	0.315	0.204	0.1571
AD - 38127.1	0.064	0.089	0.077	0.0177
AD - 38154.1	0.041	0.284	0.163	0.1721
AD - 38133.1	0.036	0.203	0.120	0.1182
AD - 38170.1	0.140	0.332	0.236	0.1352
AD - 38167.1	0.247	0.262	0.255	0.0104
AD - 39735.1	0.060	0.034	0.047	0.0186
AD - 39858.1	0.040	0.037	0.039	0.0016
AD - 39781.1	0.009	0.016	0.013	0.0043
AD - 39841.1	0.420	0.242	0.331	0.1255
AD - 39805.1	0.057	0.073	0.065	0.0114
AD - 39869.1	0.182	0.142	0.162	0.0281
AD - 39790.1	0.143	0.059	0.101	0.0595
AD - 40044.1	0.019	0.057	0.038	0.0265
AD - 40049.1	0.017	0.039	0.028	0.0154
AD - 40005.1	0.013	0.066	0.039	0.0372
AD - 40077.1	0.049	0.241	0.145	0.1358
AD - 40085.1	0.039	0.488	0.264	0.3173
AD - 40019.1	0.103	0.340	0.222	0.1677
AD - 40083.1	0.108	0.426	0.267	0.2253
AD - 35609.4	0.055	0.055	0.055	0.0001
AD - 35679.1	0.113	0.209	0.161	0.0673
AD - 35600.1	0.046	0.027	0.037	0.0134
AD - 35606.1	0.045	0.043	0.044	0.0018

AD - 38136.1	0.035	0.043	0.039	0.0061
AD - 38163.1	0.019	0.016	0.018	0.0017

[3823]

AD - 38155.1	0.236	0.220	0.228	0.0118
AD - 38145.1	0.111	0.230	0.171	0.0842
AD - 38138.1	0.260	0.675	0.468	0.2933

[3824] Bio1：生物复制物 1 和 2；相对于对照的残余 mRNA 水平。

[3825] 表 6.1. 特定 KRAS siRNA 的效力

[3826] 在 RKO 细胞中体外测定各种 KRAS siRNA 的效力。结果提供在下表 6.1 中。提供的数据为 10nM（第 2 栏）和 0.1nM（第 3 栏）下的残留基因活性。例如，对于 AD-39720.1，10nM 下的残留基因活性为 0.2 或 20%（表明 80%基因敲减），0.1nM 下的残留基因活性为 0.55 或 55%（45%基因敲减）。还提供了在 MiaPaca 2 细胞中的敲减 IC_{50}值（nM）。

[3827]

K-RAS siRNA	10nM RKO	0.1nM RKO	敲减 IC_{50}MiaPaca 2
AD-35600.1	0.3	0.27	0.0934
AD-35609.4	0.17	0.41	0.037049
AD-38136.1	0.07	0.14	0.0346
AD-38159.1	0.14	0.22	0.01861
AD-38163.1	0.09	0.16	0.0383
AD-39720.1	0.2	0.55	0.005496
AD-39735.1	0.21	0.37	0.0473
AD-39741.1	0.18	0.67	0.0394
AD-39760.1			0.0806
AD-39778.1	0.23	0.43	0.040545
AD-39822.1			1.3242
AD-39845.1	0.2	0.3	0.020622
AD-39870.1	0.25	0.12	0.026542

AD-40008.1	0.19	0.37	0.033536
AD-40021.1			0.1217
AD-40061.1	0.19	0.44	0.009348
AD-40068.1	0.15	0.33	0.009477
AD-40072.1			0.2838

[3828] 表 6.2. 特定 KRAS siRNA 的效力

[3829] 下表 6.2 提供了与特定 KRAS siRNA 的活性有关的额外数据。提供了通用靶序列。在 MiaPaca2 细胞中体外测定增殖，所述细胞为 KRAS 突变型，因此是 K-RAS 依赖型的。利用 0 至 10nM 的测试浓度研究 IC_{50}。提供了 IC_{50}数据。例如，在第一行，siRNA AD-39822.1 的 IC_{50}为 1.3242nM。

[3830] 在 BXPC3 和 NCIH28 细胞中测定了增殖，这两种细胞均是 KRAS 野生型的，因此是 KRAS 非依赖型的。利用 0 至 10nM 的测试浓度研究 IC_{50}。在这些研究中，>10nM 的 IC_{50}表明 KRAS siRNAs 的效力对 KRAS 是特异性的（很少或基本没有脱靶效应）。

[3831]

AlnyID	别名	引导链 19 聚物通用	SEQ ID NO:	增殖 BXPC3	增殖 NCIH28	IC50 MiaPaca 2
AD-35600.1	NA	TCTCTATAATGGTGAATAT	2742	>10	>10	0.0934
AD-35609.4	NA	AAATACACAAAGAAAGCCC	2743	>10	>10	0.037049395
AD-38136.1	NA	TTTATTTCCTACTAGGACC	2744	>10	>10	0.0346
AD-38159.1	hs KRAS 528 A22S26	TTTCCTACTAGGACCATAG	2745	>10	>10	0.01861
AD-38163.1	NA	TTTAATTTGTTCTCTATAA	2746	>10	>10	0.0383
AD-39720.1	NA	AGCTCCAACTACCACAAGT	2747	>10	>10	0.005495521
AD-39735.1	hs KRAS 321 A22S26	TCAATTACTACTTGCTTCC	2748	>10	>10	0.0473
AD-39741.1	hs KRAS 322 A22S26	ATCAATTACTACTTGCTTC	2749	>10	>10	0.0394
AD-39760.1	NA	ATTAGCTGTATCGTCAAGG	2750	>10	>10	0.0806
AD-39778.1	NA	TTCTCCATCAATTACTACT	2751	>10	>10	0.040544532
AD-39822.1	NA	TCGAGAATATCCAAGAGAC	2752	>10	>10	1.3242
AD-39845.1	NA	GATTTAGTATTATTTATGG	2753	>10	>10	0.020622331
AD-39870.1	NA	ATATCTTCAAATGATTTAG	2754	>10	>10	0.026542015
AD-40008.1	NA	TCTAGAAGGCAAATCACAT	2755	>10	>10	0.033536261
AD-40021.1	NA	TGTCTACTGTTCTAGAAGG	2756	>10	>10	0.1217
AD-40061.1	NA	AATTCCATAACTTCTTGCT	2757	>10	>10	0.00934829

[3832]

AD-40068.1	NA	AATAAAAGGAATTCCATAA	2758	>10	>10	0.009476662
AD-40072.1	NA	ATAACTTCTTGCTAAGTCC	2759	>10	>10	0.2838

[3833] 等同物

[3834] 实施方案 1 的组合物是包含了含有有义链和反义链的 RNAi 剂的组合物，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[3835] 实施方案 1 的组合物，其中组合物还包含针对 KRAS 的第二 RNAi 剂。

[3836] 实施方案 1 的组合物，其中反义链具有 30 个或更少的核苷酸长度。

[3837] 实施方案 1 的组合物，其中有义链和反义链形成具有 15 至 30 个核苷酸对长度的双链体区。

[3838] 实施方案 1 的组合物，其中反义链和有义链独立地是 19 至 23 个核苷酸长度。

[3839] 实施方案 1 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增

加的稳定性的修饰。

[3840] 实施方案 1 的组合物，其中 RNAi 剂包含至少一条修饰的主链和 / 或至少一个 2' 修饰的核苷酸。

[3841] 实施方案 1 的组合物，其中 RNAi 剂包含 ：

[3842] a) 至少一个 5' - 尿苷 - 腺嘌呤 -3' (5' -ua-3') 二核苷酸，其中尿苷是 2' - 修饰的核苷酸 ；和 / 或

[3843] b) 至少一个 5' - 尿苷 - 鸟嘌呤 -3' (5' -ug-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸 ；和 / 或

[3844] c) 至少一个 5' - 胞苷 - 腺嘌呤 -3' (5' -ca-3') 二核苷酸，其中 5' - 胞苷是 2' - 修饰的核苷酸 ；和 / 或

[3845] d) 至少一个 5' - 尿苷 - 尿苷 -3' (5' -uu-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸。

[3846] 实施方案 1 的组合物，其中 RNAi 剂包含选自以下的 2' - 修饰 ：2' - 脱氧、2' - 脱氧 -2' - 氟、2' -O- 甲基、2' -O- 甲氧基乙基 (2' -O-MOE)、2' -O- 氨基丙基 (2' -O-AP)、2' -O- 二甲基氨基乙基 (2' -O-DMAOE)、2' -O- 二甲氨基丙基 (2' -O-DMAP)、2' -O- 二甲基氨基乙氧基乙基 (2' -O-DMAEOE) 和 2' -O-N- 甲基乙酰氨基 (2' -O-NMA)。

[3847] 实施方案 1 的组合物，其中 RNAi 剂包含平末端。

[3848] 实施方案 1 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸的突出端。

[3849] 实施方案 1 的组合物，其中 RNAi 剂在 RNAi 剂的反义链的 3' 末端处包含突出端。

[3850] 实施方案 1 的组合物，其中 RNAi 剂连接至选自以下的一种或多种物质 ：一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[3851] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 60％。

[3852] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 70％。

[3853] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 80％。

[3854] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 90％。

[3855] 实施方案 1 的组合物，其中 RNAi 剂具有不高于约 0.1nM 的 EC_{50}。

[3856] 实施方案 1 的组合物，其中 RNAi 剂具有不高于约 0.01nM 的 EC_{50}。

[3857] 实施方案 1 的组合物，其中 RNAi 剂具有不高于约 0.001nM 的 EC_{50}。

[3858] 实施方案 2 的组合物，其包含含有第一链和第二链的 RNAi 剂，其中第一链和第二链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的第一链和第二链分别差异 0、1、2 或 3

个核苷酸的至少 15 个连续核苷酸。

[3859] 实施方案 2 的组合物，其中组合物包含针对 KRAS 的第二 RNAi 剂。

[3860] 实施方案 2 的组合物，其中第二链具有 30 个或更少的核苷酸长度。

[3861] 实施方案 2 的组合物，其中第一链和第二链形成具有 15 至 30 个核苷酸对长度的双链体区。

[3862] 实施方案 2 的组合物，其中第一链和第二链独立地是 19 至 23 个核苷酸长度。

[3863] 实施方案 2 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[3864] 实施方案 2 的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2' - 修饰的核苷酸。

[3865] 实施方案 2 的组合物，其中 RNAi 剂包含 :

[3866] 至少一个 5' - 尿苷 - 腺嘌呤 -3' (5' -ua-3') 二核苷酸，其中尿苷是 2' - 修饰的核苷酸 ;和 / 或至少一个 5' - 尿苷 - 鸟嘌呤 -3' (5' -ug-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸 ;

[3867] 和 / 或至少一个 5' - 胞苷 - 腺嘌呤 -3' (5' -ca-3') 二核苷酸，其中 5' - 胞苷是 2' - 修饰的核苷酸 ;

[3868] 和 / 或至少一个 5' - 尿苷 - 尿苷 -3' (5' -uu-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸。

[3869] 实施方案 2 的组合物，其中 RNAi 剂包含选自以下的一个或多个 2' - 修饰 :

[3870] 2' - 脱氧、2' - 脱氧 -2' - 氟、2' -O- 甲基、2' -O- 甲氧基乙基 (2' -O-MOE)、2' -O- 氨基丙基 (2' -O-AP)、2' -O- 二甲基氨基乙基 (2' -O-DMAOE)、2' -O- 二甲氨基丙基 (2' -O-DMAP)、2' -O- 二甲基氨基乙氧基乙基 (2' -O-DMAEOE) 和 2' -O-N- 甲基乙酰氨基 (2' -O-NMA)。

[3871] 实施方案 2 的组合物，其中 RNAi 剂包含平末端。

[3872] 实施方案 2 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸的突出端。

[3873] 实施方案 2 的组合物，其中 RNAi 剂在反义链的 3' 末端处包含突出端。

[3874] 实施方案 2 的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自 :一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁兰多糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[3875] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 60％。

[3876] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 70％。

[3877] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 80％。

[3878] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 的浓度在 RKO 细胞中体外抑制 KRAS 的表达至少约 90％。

[3879] 实施方案 2 的组合物，其中 RNAi 剂具有不高于约 0.1nM 的 EC_{50}。

[3880] 实施方案 2 的组合物，其中 RNAi 剂具有不高于约 0.01nM 的 EC_{50}。

[3881] 实施方案 2 的组合物，其中 RNAi 剂具有不高于约 0.001nM 的 EC_{50}。

[3882] 实施方案 3 的方法是一种治疗个体中 KRAS 相关疾病的方法，包括向所述个体施用治疗有效量的包含 RNAi 剂的组合物的步骤，所述 RNAi 剂含有有义链和反义链，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[3883] 实施方案 3 的方法，其中 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征。

[3884] 实施方案 3 的方法，其中 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征。

[3885] 实施方案 3 的方法，其中该方法还包括施用针对增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的额外治疗的步骤。

[3886] 实施方案 3 的方法，其中该方法还包括施用针对增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的额外治疗的步骤，其中的增殖性疾病包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌。

[3887] 实施方案 3 的方法，其中的组合物包含针对 KRAS 的第二 RNAi 剂。

[3888] 实施方案 3 的方法，其中该方法还包括施用针对 KRAS 的额外 RNAi 剂的步骤。

[3889] 实施方案 3 的方法，还包括施用额外的治疗。

[3890] 实施方案 3 的方法，其中额外的治疗是组合物。

[3891] 实施方案 3 的方法，其中额外的治疗是一种方法。

[3892] 实施方案 3 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[3893] 实施方案 4 的方法，所述方法包括抑制个体中 KRAS 的表达，其包括向所述个体施用治疗有效量的包含 RNAi 剂的组合物的步骤，所述 RNAi 剂含有有义链和反义链，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[3894] 实施方案 4 的方法，其中的个体罹患或易患 KRAS 相关疾病。

[3895] 实施方案 4 的方法，其中 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征。

[3896] 实施方案 4 的方法，其中 KRAS 相关疾病是增殖性疾病。

[3897] 实施方案 4 的方法，其中 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征，其中的增殖性疾病包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌。

[3898] 实施方案 4 的方法，还包括施用额外的治疗。

[3899] 实施方案 4 的方法，其中额外的治疗是组合物。

[3900] 实施方案 4 的方法，其中额外的治疗是方法。

[3901] 实施方案 4 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[3902] 实施方案 5 的组合物，所述组合物包含一种用于 RNAi 制剂中的药物，所述 RNAi 制剂包含含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 KRAS 特异性的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[3903] 位于药学有效的制剂中的以上的任何组合物。

[3904] 根据实施方案 5 的组合物，用于治疗个体中 KRAS 相关疾病的方法中，所述方法包括向所述个体施用治疗有效量的根据实施方案 1 的组合物的步骤。

[3905] 根据实施方案 5 的组合物用于制造治疗 KRAS 相关疾病的药物的用途。

[3906] 根据实施方案 5 的组合物用于制造治疗增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征的药物的用途，其中的增殖性疾病包括但不限于固体或液体癌、腺癌、结肠直肠癌、晚期和 / 或转移的结肠直肠癌、结肠癌、肺癌、非小细胞肺癌和肺腺癌、急性髓细胞性肺癌、膀胱癌、脑癌、乳癌、宫颈癌、子宫内膜癌、胃癌、头颈癌、肾癌、白血病、骨髓增生异常综合症、髓系白血病、肝癌、黑素瘤、卵巢癌、胰腺癌、前列腺癌、睾丸癌、甲状腺癌。

[3907] 根据实施方案 5 的用途，其中的 KRAS 相关疾病是增殖性疾病、心面皮肤 (CFC) 综合征或努南综合征。

[3908] 实施方案 1 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[3909] 实施方案 1 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[3910] 除非另外定义，否则本文所用的技术和科学术语具有与熟悉本公开所属技术领域的专业人员通常所理解的相同含义。

[3911] 除非另外指明，否则没有详细地具体描述的全部方法、步骤、技术和操作可以并且已经按本身已知的方式进行，这对技术人员是显而易见的。例如，再次参考本文中提到的标准手册和一般背景技术并参考其中所引用的其它参考文献。除非另外指明，否则本文引用的每份参考文献均全文引入作为参考。

[3912] 权利要求是非限制性的并且在下文提供。

[3913] 虽然已经在本文中详细公开了具体实施方案和权利要求，但是这仅出于说明目的以举例方式进行，并且不意欲限制所附权利要求书的范围或任何相应未来应用的权利要求的主题的范围。具体而言，发明人构思了可以对本公开作出各种替换、改变和修饰而不脱离如权利要求书所定义的本公开的精神和范围。确信选择核酸起始材料、目的克隆或文库类型是知晓本文所述的实施方案的本领域普通技术人员的例行工作。其它方面、优点和修改视为处于以下权利要求的范围内。本领域技术人员采用常规实验即可识别或确定本文所述的本发明具体实施方案的许多等同物。此类等同物意在由以下权利要求书涵盖。对之后提交的相应申请中权利要求书范围的重新撰写可能是由于各个国家的专利法的限制并且不应当解读为放弃权利要求的主题。

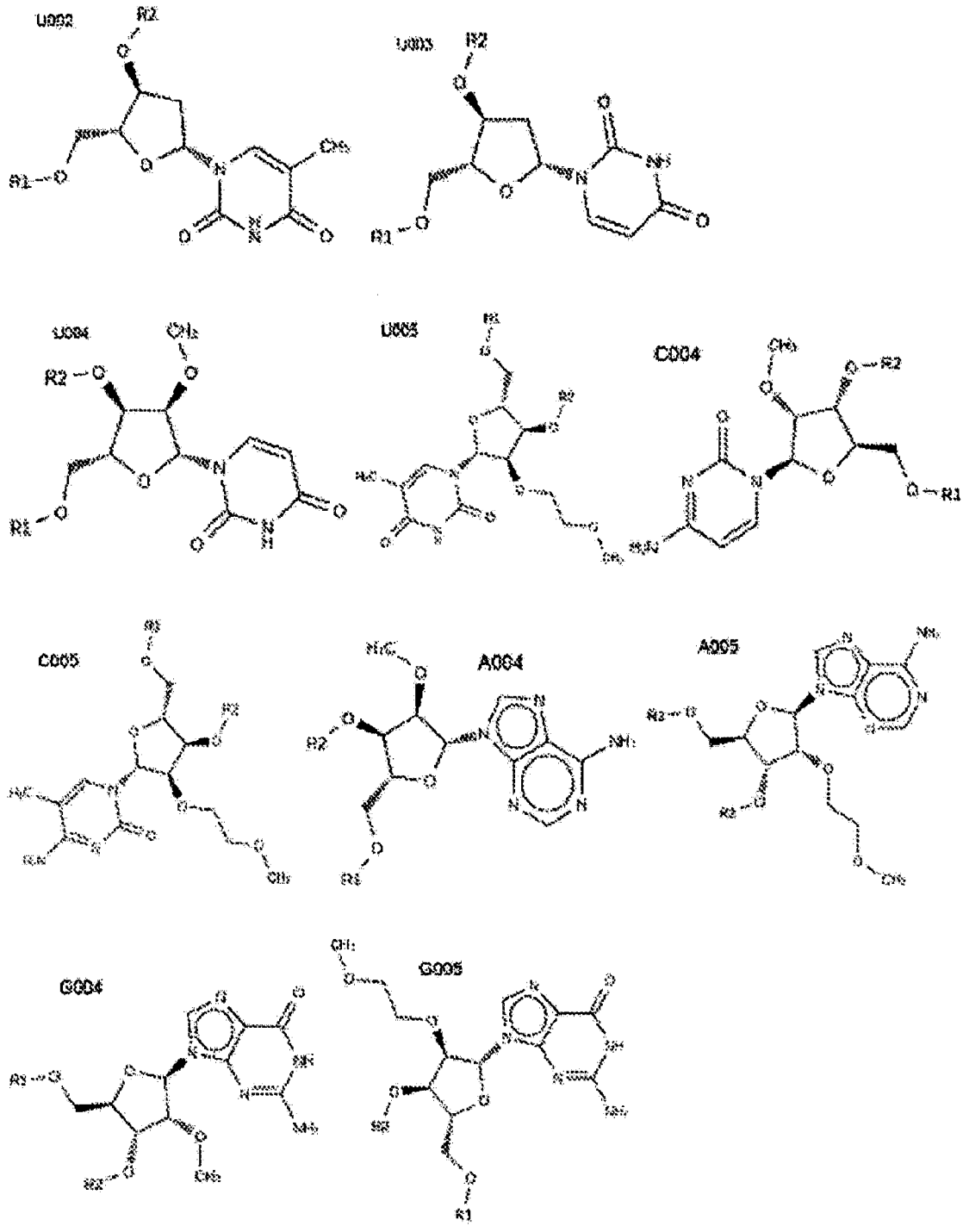


图 1

Abstract

The present disclosure relates to RNAi agents useful in methods of treating KRAS-related diseases such as a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to KRAS.