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(71) Applicant: **DICERNA PHARMACEUTICALS, INC.** [US/US]; 75 Hayden Avenue, Lexington, Massachusetts 02421 (US).

(72) Inventors: **BROWN, Bob Dale**; c/o Dicerna Pharmaceuticals, Inc., 75 Hayden Avenue, Lexington, Massachusetts 02421 (US). **DUDEK, Henryk T.**; c/o Dicerna Pharmaceuticals, Inc., 75 Hayden Avenue, Lexington, Massachusetts 02421 (US). **CHEONG, Seongmoon**; c/o Dicerna Pharmaceuticals, Inc., 75 Hayden Avenue, Lexington, Massachusetts 02421 (US). **SPIEGELMAN, Nicole Alexis**; c/o Dicerna Pharmaceuticals, Inc., 75 Hayden Avenue, Lexington, Massachusetts 02421 (US).

(74) Agent: **REID, Andrea L.C.** et al.; c/o Dechert LLP, One International Place, 40th Floor, 100 Oliver Street, Boston, Massachusetts 02110-2605 (US).

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(54) Title: COMPOSITIONS AND METHODS FOR MODULATING *SCAP* ACTIVITY

(57) Abstract: Oligonucleotides and compositions including the same are disclosed that modulate (*e.g.*, inhibit, limit or reduce) sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity. Methods of making and using the oligonucleotides also are disclosed, particularly uses relating to treating diseases, disorders, and/or conditions associated with *SCAP* activity such as nonalcoholic fatty liver disease (NAFLD), (NASH), dyslipidemia, atherosclerotic cardiovascular disease (ASCVD), and/or other *SCAP*-associated conditions, diseases, and/or disorders.

COMPOSITIONS AND METHODS FOR MODULATING *SCAP* ACTIVITY

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] The present application claims priority under 35 U.S.C. § 119(e) from U.S. Provisional Application No. 63/363,091, filed April 15, 2022, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[002] The disclosure relates generally to biology and medicine, and more particularly it relates to oligonucleotides and compositions including the same for modulating (*e.g.*, inhibiting or reducing) sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, as well as their use for treating conditions, diseases and/or disorders associated with *SCAP*.

BACKGROUND

[003] SCAP is a cholesterol-binding endoplasmic reticulum (ER) membrane protein encoded by *SCAP* that binds and transports SREBP transcription factors from the ER to the Golgi apparatus for processing. Once processed in the Golgi apparatus, SREBP transcription factors migrate to the nucleus where they participate in regulating genes involved in lipid homeostasis. SREBP1a, SREBP1c and SREBP2 are regulated by the SREBP cleavage-activating protein (SCAP) encoded by the *SCAP* gene. SREBP1c is the most abundant SREBP in the liver and its regulation is important for maintaining lipid homeostasis. Specifically, SREBPs affect lipid homeostasis by modulating genes involved in lipid biosynthesis as well as modulating genes involved in lipid clearance (*e.g.*, low-density lipoprotein receptor (LDLR) and proprotein convertase subtilisin/kexin type (PCSK9)). SCAP also plays a role in NLR family pyrin domain containing 3 (NLRP3) inflammasome activation.

[004] Human *SCAP* is ubiquitously expressed throughout the body, but protein expression is highest in the bone marrow, brain, endocrine tissue, gastrointestinal tract, liver, lymphoid tissue, muscle tissue, pancreas, reproductive organs, and respiratory tract. The role SCAP plays in regulating the transcription of genes involved in lipid homeostasis make it a promising therapeutic target to attenuate NASH progression at various stages.

[005] Despite the existence of some therapeutics toward *SCAP*, there is a need for additional therapeutics for inhibiting or reducing *SCAP* activity for treating liver disease, especially NAFLD and non-alcoholic steatohepatitis (NASH).

BRIEF SUMMARY

[006] To address this need, the disclosure describes compositions for and methods of treating a disease, disorder and/or condition related to *SCAP* activity. The disclosure is based, in part, on discovering and developing double-stranded (ds) oligonucleotides (*e.g.*, RNAi oligonucleotides) for selectively modulating (*e.g.*, inhibiting and/or reducing) *SCAP* activity in, for example, the liver. Accordingly, target sequences within *SCAP* are identified, and RNAi oligonucleotides that bind to these target sequences and inhibit SCAP mRNA expression are generated. As shown herein, some oligonucleotides inhibit at least human and non-human primate (NHP) (*i.e.*, double-common), while others inhibit mouse, human and NHP (*i.e.*, triple-common) *SCAP* activity in the liver. Without being bound by theory, the RNAi oligonucleotides herein are useful for treating a disease, disorder and/or condition associated with *SCAP* activity (*e.g.*, liver diseases such as, for example, NAFLD, NASH, dyslipidemia, and/or atherosclerotic cardiovascular disease (ASCVD)).

[007] Accordingly, the disclosure describes RNAi oligonucleotides for reducing or inhibiting *SCAP* activity that include a sense strand (also known as a passenger strand) and/or an antisense strand (also known as a guide strand), where the sense strand has a sequence as set forth in Table 3, and where the antisense strand has a sequence as set forth in Table 3.

[008] In some embodiments, the sense strand has a sequence as set forth in Table 3 (*e.g.*, any one of the odd numbers of SEQ ID NOs: 9 to 392), especially any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333, and 361.

[009] In some embodiments, the antisense strand has a sequence as set forth in Table 3 (*e.g.*, any one of the even numbers of SEQ ID NOs: 9 to 392), especially any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334, and 362.

[0010] Alternatively, the disclosure describes RNAi oligonucleotides for reducing or inhibiting *SCAP* activity that include a sense strand and/or an antisense strand, where the sense strand has a sequence as set forth in Table 4, and where the antisense strand has a sequence as set forth in Table 4.

[0011] In some embodiments, the sense strand has a sequence as set forth in Table 4 (*e.g.*, any one of the odd numbers of SEQ ID NOs: 393 to 776), especially any one of SEQ ID NOs: 523, 531, 605, 657, 705, 717, and 745.

[0012] In some embodiments, the antisense strand has a sequence as set forth in Table 4 (*e.g.*, any one of the even numbers of SEQ ID NOs: 393 to 776), especially any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746.

[0013] Alternatively, RNAi oligonucleotides are described for reducing or inhibiting *SCAP* activity that include a sense strand and an antisense strand, where the sense and antisense strands form a duplex region, and where the antisense strand has a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783.

[0014] In any of the embodiments above, the sense strand is from about 15 nucleotides to about 50 nucleotides in length. In some embodiments, the sense strand is from about 20 nucleotides to about 40 nucleotides in length. In some embodiments, the sense strand is 36 nucleotides in length.

[0015] In any of the embodiments above, the antisense strand is from about 15 nucleotides to about 30 nucleotides in length. In some embodiments, the antisense strand is from about 20 nucleotides to about 25 nucleotides. In some embodiments, the antisense strand is 22 nucleotides in length.

[0016] In any of the embodiments above, the duplex region is from about 19 nucleotides in length to about 21 nucleotides in length. In certain embodiment, the duplex region is 20 nucleotides in length.

[0017] In any of the embodiments above, the region of complementarity is at least 15 contiguous nucleotides in length. In some embodiments, the region of complementarity is from about 19 contiguous nucleotides in length to about 21 contiguous nucleotides in length. In other embodiments, the region of complementarity is 19 contiguous nucleotides in length or 21 contiguous nucleotides in length.

[0018] In any of the embodiments above, the RNAi oligonucleotides include on the sense strand a 3' end a stem-loop set forth as: S1-L-S2, where a first stem portion (S1) is complementary to a second stem portion (S2), and where L is a loop between S1 and S2 of about 3 to about 5 nucleotides in length.

[0019] In any of the embodiments above, the antisense strand, the sense strand, or both have an overhang sequence. In some embodiments, the antisense strand includes a 3' overhang of 1

or more nucleotides in length. In other embodiments, the 3' overhang sequence is 2 nucleotides in length such as, for example, GG.

[0020] Oligonucleotides also are described that include an antisense strand and a sense strand for reducing or inhibiting *SCAP* activity, where the antisense strand can be from about 21 nucleotides to about 27 nucleotides in length and has a region of complementarity to SCAP mRNA, wherein the sense strand includes a stem-loop at its 3' end set forth as: S1-L-S2, wherein S1 is complementary to S2, wherein L forms a loop between S1 and S2 from about 3 nucleotides to about 5 nucleotides in length, and wherein the antisense strand and the sense strand form a duplex structure of at least about 19 nucleotides in length but are not covalently linked.

[0021] In some embodiments, the loop L is a triloop (triL) or a tetraloop (tetraL). In some embodiments, L is a tetraL of 4 nucleotides in length. In certain embodiments, L is a tetraL having a sequence of 5'-GAAA-3'.

[0022] In some embodiments, S1 and S2 are 1-10 nucleotides in length and have the same length. In other embodiments, S1 and S2 are 1 nucleotide, 2 nucleotides, 3 nucleotides, 4 nucleotides, 5 nucleotides, 6 nucleotides, 7 nucleotides, 8 nucleotides, 9 nucleotides, or 10 nucleotides in length. In other embodiments, S1 and S2 are 6 nucleotides in length. In certain embodiments, the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784).

[0023] In some embodiments, the sense strand is 25 nucleotides in length and the antisense strand is 27 nucleotides in length. In other embodiments, the sense strand is 36 nucleotides in length and the antisense strand is 22 nucleotides in length.

[0024] In the embodiments above, the duplex region includes a 3' overhang sequence on the antisense strand. In some embodiments, the 3' overhang sequence on the antisense strand is 2 nucleotides in length.

[0025] In any of the embodiments above, at least one nucleotide in an oligonucleotide is a modified nucleotide. In some embodiments, all nucleotides in the oligonucleotide are modified except for nucleotides in the stem-loop (*i.e.*, S1-L-S2). In other embodiments, all nucleotides in the oligonucleotide are modified except for nucleotides in the L.

[0026] In some embodiments, the modified nucleotide includes a 2'-modification such as, for example, 2'-aminoethyl (EA), 2'-fluoro (2'-F), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE) and 2'-deoxy-2'-fluoro-β-arabinonucleic acid (2'-FANA). In certain embodiments, all nucleotides in an oligonucleotide include a 2'-modification such as, for example, 2'-F or 2'-

OMe. In some embodiments, about 18% to about 23%, or 18%, 19%, 20%, 21%, 22%, or 23% of the nucleotides of the sense strand comprise a 2'-F modification. In other embodiments, about 38% to about 43%, or 38%, 39%, 40%, 41%, 42%, or 43% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, about 25% to about 35%, or 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the antisense strand comprise a 2'-F modification. In some embodiments, about 25% to about 35%, or 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the oligonucleotide comprise a 2'-F modification. In some embodiments, about 35% to about 45%, or 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44%, or 45% of the nucleotides of the oligonucleotide comprise a 2'-F modification.

[0027] In any of the embodiments above, at least one nucleotide in an oligonucleotide includes a modified internucleotide linkage. In some embodiments, the modified internucleotide linkage is a phosphorothioate (PS) linkage.

[0028] In any of the embodiments above, a 4'-carbon of a sugar of a 5'-nucleotide of the antisense strand includes a phosphate analog such as, for example, an oxymethylphosphonate, vinylphosphonate or malonylphosphonate. Alternatively, or optionally, the phosphate analog is a 4'-phosphate analog including 5'-methoxyphosphonate-4'-oxy.

[0029] In any of the embodiments above, at least one nucleotide of an oligonucleotide is conjugated to one or more targeting ligands such as, for example, an amino sugar, carbohydrate, cholesterol, lipid, or polypeptide. In some embodiments, the targeting ligand is a N-acetylgalactosamine (GalNAc) moiety. In other embodiments, the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety, or a tetravalent GalNAc moiety.

[0030] In some embodiments, the targeting ligands are conjugated to one or more nucleotides of L of the stem loop. In certain embodiments, up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

[0031] In certain embodiments, one or more nucleotides at positions 8, 9, 10, or 11 of the sense strand are modified with a 2'-F. In other embodiments, the sugar moiety at each nucleotide at positions 1 to 7, 12 to 27 and 31 to 36 in the sense strand is modified with a 2'-OMe. In certain embodiments, nucleotides at positions 8 to 11 of the sense strand are modified with a 2'-F, and positions 1 to 7, 12 to 27 and 31 to 36 are modified with a 2'-OMe.

[0032] In certain other embodiments, one or more nucleotides at positions 2 to 5, 7, 10 and 14 of the antisense strand are modified with 2'-F, and one or more nucleotides at positions 1, 6, 8-

9, 11-13 and 15-22 modified with a 2'-OMe. In other embodiments, the antisense strand includes a 2'-F-modified nucleotide at positions 2 to 5, 7, 10 and 14, and a 2'-OMe-modified nucleotide at positions 1, 6, 8 to 9, 11 to 13 and 15 to 22.

[0033] In certain embodiments, the oligonucleotides have a modification pattern as shown in FIG. 1.

[0034] In any of the embodiments above, the oligonucleotide is a RNAi oligonucleotide. In some embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence as set forth in Table 3, especially any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333, and 361. In certain embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence as set forth in Table 4, especially any one of SEQ ID NOs: 523, 531, 605, 657, 705, 717, and 745. In some embodiments, the RNAi oligonucleotide includes an antisense strand having a nucleotide sequence as set for the in Table 3, especially any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334, and 362. In certain embodiments, the RNAi oligonucleotide includes an antisense strand having a nucleotide sequence as set forth in Table 4, especially any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746.

[0035] In certain embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence of any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333, and 361, and an antisense strand having a nucleotide sequence of any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334, and 362.

[0036] In certain other embodiments, the sense strand and the antisense strand of the RNAi oligonucleotide, respectively, are selected from:

(a) SEQ ID NOs: 139 and 140,

(b) SEQ ID NOs: 147 and 148,

(c) SEQ ID NOs: 221 and 222,

(d) SEQ ID NOs :273 and 274,

(e) SEQ ID NOs: 321 and 322,

(f) SEQ ID NOs: 333 and 334, and

(g) SEQ ID NOs: 361 and 362.

[0037] In certain embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence of any one of SEQ ID NOs: 147 and 333, and an antisense strand having a nucleotide sequence of any one of SEQ ID NOs: 148 and 334 respectively.

[0038] In certain embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence of any one of SEQ ID NOs: 523, 531, 605, 657, 705, 717, and 745, and an

antisense strand having a nucleotide sequence of any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746 respectively.

[0039] In certain other embodiments, the sense strand and the antisense strand of the RNAi oligonucleotide, respectively, are selected from:

(a') SEQ ID NOs: 523 and 524,

(b') SEQ ID NOs :531 and 532,

(c') SEQ ID NOs: 605 and 606,

(d') SEQ ID NOs: 657 and 658,

(e') SEQ ID NOs: 705 and 706,

(f') SEQ ID NOs: 717 and 718, and

(g') SEQ ID NOs: 745 and 746.

[0040] In certain embodiments, the RNAi oligonucleotide includes a sense strand having a nucleotide sequence of any one of SEQ ID NOs: 531 and 717, and an antisense strand having a nucleotide sequence of any one of SEQ ID NOs: 532 and 718 respectively.

[0041] RNAi oligonucleotides also are described for inhibiting or reducing *SCAP* activity that include a sense strand and an antisense strand, where the sense strand and the antisense strand form a duplex region, where all nucleotides of the sense strand and the antisense strand include a modification of a base, a sugar and/or an internucleotide linkage, where the antisense strand includes a region of complementarity to a SCAP mRNA target sequence of one of SEQ ID NOs: 777 to 783, and where the region of complementarity is at least about 15 contiguous nucleotides in length.

[0042] In other aspects, pharmaceutical compositions are described that include at least one oligonucleotide herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, delivery agent or excipient. In some embodiments, the pharmaceutical compositions include an additional therapeutic agent such as, for example, a lipid-lowering agent, an antidiabetic agent, or anti-obesity agent.

[0043] In other aspects, methods are described for reducing *SCAP* activity in a cell, a population of cells, a tissue, an organ, or an individual that include at least a step of administering/contacting the cell, the population of cells, the tissue, the organ, or the individual with an oligonucleotide herein or a pharmaceutical composition herein. In some embodiments, reducing *SCAP* activity includes reducing an amount or level of SCAP mRNA, an amount or level of SCAP protein, SCAP activity or a combination thereof in the cell, the population of cells, the tissue, the organ, or the individual. In some embodiments, the cell, the cell population,

the tissue, the organ, or the individual has a disease, disorder, or condition associated with *SCAP* activity. In certain embodiments, the disease, disorder, or condition associated with *SCAP* activity is NAFLD, NASH, dyslipidemia, and/or ASCVD.

[0044] In other aspects, methods are described for treating an individual having or suspected of having a disease, disorder, or condition associated with *SCAP* activity. The methods include at least a step of administering to an individual in need thereof an effective amount of an oligonucleotide herein or a pharmaceutical composition herein. In some embodiments, the disease, disorder, or condition associated with *SCAP* activity is NAFLD, NASH, dyslipidemia, and/or ASCVD. In some embodiments, the oligonucleotide or pharmaceutical composition is administered daily, weekly, monthly, quarterly, yearly *via* subcutaneous (SQ) administration, especially monthly or quarterly.

[0045] In some embodiments, the individual has alcoholic hepatitis (AH), alcoholic liver disease (ALD), cholangiocarcinoma (CCA), cirrhosis, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), liver steatosis, NAFLD, NASH, primary sclerosing cholangitis (PSC), hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, diabetes, and/or obesity, and/or ASCVD.

[0046] In any of the embodiments above, the methods may comprise additional steps such as measuring or obtaining genotype information, SCAP mRNA, SCAP protein levels, SCAP activity, the individual's weight and/or blood glucose and/or cholesterol and/or TG, and then comparing such obtained values to one or more baseline values or previously obtained values to assess the effectiveness of contacting or administering.

[0047] In any of the embodiments above, the methods include administering the RNAi oligonucleotide or pharmaceutical composition simultaneously, separately, or sequentially with a second composition or a second therapeutic agent. In some embodiments, the second composition or a second therapeutic agent is a SCAP antibody or fragment thereof, a lipid-lowering agent, an anti-diabetic agent or anti-obesity agent. In some embodiments, the second composition or second therapeutic agent is administered with a frequency same as the RNAi oligonucleotide (*i.e.*, every other day, twice a week, or even weekly). In other embodiments, the second composition or second therapeutic agent is administered with a frequency distinct from the RNAi oligonucleotide. Likewise, in other embodiments, the second composition or second therapeutic agent is administered *via* the same route as the RNAi oligonucleotide (*e.g.*, SQ). In still other embodiments, the second composition or second therapeutic agent is administered *via* a route that differs from the RNAi oligonucleotide).

[0048] In other aspects, uses are described for the RNAi oligonucleotides herein for treating a disease, disorder, or condition associated with *SCAP* activity, which optionally are administered simultaneously, separately, or sequentially (*i.e.*, in combination) with a second composition or second therapeutic agent.

[0049] In other aspects, uses are described for the RNAi oligonucleotides herein in manufacturing a medicament for treating a disease, disorder, or condition associated with *SCAP* activity, where the medicament optionally further includes a second composition or second therapeutic agent.

[0050] In other aspects, kits are described that include at least one oligonucleotide herein, an optional pharmaceutically acceptable carrier, and a package insert having instructions for administering the same to an individual having a disease, disorder, or condition associated with *SCAP* activity.

[0051] An advantage of the oligonucleotides and compositions herein is that suppressed *SCAP* activity exerts a beneficial effect on the entire spectrum of NAFLD, NASH, dyslipidemia and/or ASCVD.

BRIEF DESCRIPTION OF THE DRAWINGS

[0052] The advantages, effects, features, and objects other than those set forth above will become more readily apparent when consideration is given to the detailed description below. Such detailed description refers to the following drawing(s), where:

[0053] FIG. 1 discloses a schematic depicting the structure and chemical modification pattern for a generic GalNAc-conjugated SCAP oligonucleotides (modification pattern M1).

DETAILED DESCRIPTION

[0054] *Overview*

[0055] NAFLD and NASH are serious public health burdens as they are chronic liver disorders that begin with hepatic TG accumulation (steatosis) and progress to hepatic inflammation and fibrosis, cirrhosis and even liver cancer. SCAP is a transcription regulator that has been shown to be associated with NAFLD and NASH. Here, targeted silencing of SCAP mRNA *via* RNAi can prevent processing of active SREBP and downstream transcriptional changes in regulating *de novo* lipogenesis and TG accumulation within the liver.

[0056] RNAi is a process of introducing exogeneous RNA into a cell leading to specific degradation of the mRNA encoding the targeted protein with a resultant decrease in target gene expression.

[0057] In humans, SCAP is 1279 amino acids in length with a predicted molecular weight of 140 kD. Exemplary nucleic acid sequences for *SCAP* can be found in NCBI Ref. Seq. No. NM_012235 (isoform 1) and NM_001320044 (isoform 2) (human); NM_001001144 and NM_001103162 (mouse); NM_001100966 (rat); and XM_001100342 (primate). Other exemplary nucleic acid sequences for *SCAP* include NCBI Ref. Seqs Nos. XM_017005918 (human variant X1), XM_011533501 (human variant X2), XM_005264967 (human variant X3), XM_005264968 (human variant X4), XM_011533502 (human variant X5), XM_005264971 (human variant X6), XM_017005921 (human variant X7), XM_006512083 (mouse variant X1), XM_006512084 (mouse variant X2), XM_006512085 (mouse variant X3), XM_006243922 (rat variant X1), XM_017595596 (rat variant X2), XM_006243923 (rat variant X3), XM_006243924 (rat variant X5), XM_006243925 (rat variant X5), XM_017595597 (rat variant X6), XM_005546961 (primate variant X1), XM_015445807 (primate variant X2), XM_005546962 (primate variant X3), XM_005546963 (primate variant X4), and XM_015445808 (primate variant X5). One of skill in the art, however, understands that additional examples of SCAP mRNA sequences are readily available using publicly available databases such as, for example, GenBank and UniProt.

[0058] *Abbreviations and Definitions*

[0059] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of skill in the art to which the disclosure pertains. Although any methods and materials similar to or equivalent to those described herein can be used in the practice or testing of the RNAi oligonucleotides herein, pharmaceutical compositions including the same and methods of making and using such RNAi oligonucleotides, the preferred methods and materials are described herein.

[0060] Moreover, reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one element is present, unless the context clearly requires that there be one and only one element. The indefinite article "a" or "an" thus usually means "at least one."

[0061] Furthermore, use of "including," as well as other forms, such as "include," "includes" and "included" is not limiting.

[0062] Certain definitions used herein are defined as follows:

[0063] As used herein, "about" means within a statistically meaningful range of a value or values such as, for example, a stated concentration, length, molecular weight, pH, sequence similarity, time frame, temperature, volume, *etc.* Such a value or range can be within an order of magnitude typically within 20%, more typically within 10%, and even more typically within 5% of a given value or range. The allowable variation encompassed by "about" will depend upon the particular system under study, and can be readily appreciated by one of skill in the art.

[0064] As used herein, "administer," "administering," "administration" and the like refers to providing a substance (*e.g.*, an oligonucleotide herein or a composition herein) to an individual in a manner that is pharmacologically useful (*e.g.*, to treat a disease, disorder, or condition in the individual).

[0065] As used herein, "antisense strand" means an oligonucleotide herein that is complimentary to a region of a target sequence. Likewise, and as used herein, "sense strand" means an oligonucleotide herein that is complimentary to a region of an antisense strand.

[0066] As used herein, "asialoglycoprotein receptor" or "ASGPR" means a bipartite C-type lectin formed by a major 48 kDa subunit (ASGPR-1) and minor 40 kDa subunit (ASGPR-2). ASGPR is primarily expressed on the sinusoidal surface of hepatocyte cells and has a major role in binding, internalizing and subsequent clearing of circulating glycoproteins that contain terminal galactose or GalNAc residues (asialoglycoproteins).

[0067] As used herein, "attenuate," "attenuating," "attenuation" and the like refers to reducing or effectively halting. As a non-limiting example, one or more of the treatments herein may reduce or effectively halt the onset or progression of AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD, NASH and PSC, as well as related diseases, disorders, and conditions in an individual such as, for example, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity. This attenuation may be exemplified by, for example, a decrease in one or more aspects (*e.g.*, symptoms, tissue characteristics, and cellular, inflammatory, or immunological activity, *etc.*) of AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD, NASH and PSC, as well as related diseases, disorders, and conditions in an individual such as, for example, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity; no detectable progression (worsening) of one or more aspects of AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD,

NASH and PSC, as well as related diseases, disorders, and conditions in an individual such as, for example hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity; or no detectable aspects of AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD, NASH and PSC, as well as related diseases, disorders, and conditions in an individual such as, for example, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity in an individual when they might otherwise be expected.

[0068] As used herein, "complementary" means a structural relationship between two nucleotides (*e.g.*, on two opposing nucleic acids or on opposing regions of a single nucleic acid strand) that permits the two nucleotides to form base pairs with one another. For example, a purine nucleotide of one nucleic acid that is complementary to a pyrimidine nucleotide of an opposing nucleic acid may base pair together by forming hydrogen bonds with one another. Complementary nucleotides can base pair in the Watson-Crick manner or in any other manner that allows for the formation of stable duplexes. Likewise, two nucleic acids may have regions of multiple nucleotides that are complementary with each other to form regions of complementarity, as described herein.

[0069] As used herein, "contact," "contacting" and the like means directly or indirectly introducing or delivering an oligonucleotide such as a RNAi oligonucleotide into, for example, a cell by facilitating or effecting uptake or absorption into the cell.

[0070] As used herein, "deoxyribonucleotide" means a nucleotide having a hydrogen in place of a hydroxyl at the 2' position of its pentose sugar when compared with a ribonucleotide. A modified deoxyribonucleotide has one or more modifications or substitutions of atoms other than at the 2' position, including modifications or substitutions in or of the nucleobase, sugar, or phosphate group.

[0071] As used herein, "double-stranded oligonucleotide" or "ds oligonucleotide" means an oligonucleotide that is substantially in a duplex form. The complementary base-pairing of duplex region(s) of a ds oligonucleotide can be formed between antiparallel sequences of nucleotides of covalently separate nucleic acid strands. Likewise, complementary base-pairing of duplex region(s) of a ds oligonucleotide can be formed between antiparallel sequences of nucleotides of nucleic acid strands that are covalently linked. Moreover, complementary base-pairing of duplex region(s) of a ds oligonucleotide can be formed from single nucleic acid strand that is folded (*e.g., via* a hairpin) to provide complementary antiparallel sequences of nucleotides that base pair together. A ds oligonucleotide can include two covalently separate

nucleic acid strands that are fully duplexed with one another. However, a ds oligonucleotide can include two covalently separate nucleic acid strands that are partially duplexed (*e.g.*, having overhangs at one or both ends). A ds oligonucleotide can include an antiparallel sequence of nucleotides that are partially complementary, and thus, may have one or more mismatches, which may include internal mismatches or end mismatches.

[0072] As used herein, "duplex," in reference to nucleic acids (*e.g.*, oligonucleotides), means a structure formed through complementary base pairing of two antiparallel sequences of nucleotides.

[0073] As used herein, "excipient" means a non-therapeutic agent that may be included in a composition herein, for example, to provide or contribute to a desired consistency or stabilizing effect.

[0074] As used herein, "hepatocyte" or "hepatocytes" means cells of the parenchymal tissues of the liver. These cells make up about 70%-85% of the liver's mass and manufacture serum albumin, fibrinogen (FBN) and the prothrombin group of clotting factors (except for Factors 3 and 4). Markers for hepatocyte lineage cells include, but are not limited to, transthyretin (Ttr), glutamine synthetase (Glul), hepatocyte nuclear factor 1a (Hnf1a) and hepatocyte nuclear factor 4a (Hnf4a). Markers for mature hepatocytes may include, but are not limited to, cytochrome P450 (Cyp3a11), fumarylacetoacetate hydrolase (Fah), glucose 6-phosphate (G6p), albumin (Alb) and OC2-2F8. *See*, *e.g.*, Huch *et al.* (2013) *Nature* 494:247-250.

[0075] As used herein, a "hepatotoxic agent" means a chemical compound, virus or other substance that is itself toxic to the liver or can be processed to form a metabolite that is toxic to the liver. Hepatotoxic agents may include, but are not limited to, carbon tetrachloride (CCl_4), acetaminophen (paracetamol), vinyl chloride, arsenic, chloroform, and nonsteroidal anti-inflammatory drugs (such as aspirin and phenylbutazone).

[0076] As used herein, "individual" means any mammal, including cats, dogs, mice, rats, and primates, especially humans. Moreover, "subject" or "patient" may be used interchangeably with "individual."

[0077] As used herein, "labile linker" means a linker that can be cleaved (*e.g.*, by acidic pH). Likewise, "fairly stable linker" means a linker that cannot be cleaved.

[0078] As used herein, "liver inflammation" or "hepatitis" means a physical condition in which the liver becomes swollen, dysfunctional and/or painful, especially because of injury or infection, as may be caused by exposure to a hepatotoxic agent. Symptoms may include

jaundice, fatigue, weakness, nausea, vomiting, appetite reduction, and weight loss. Liver inflammation, if left untreated, may progress to fibrosis, cirrhosis, liver failure or liver cancer.

[0079] As used herein, "liver fibrosis," "hepatic fibrosis" or "fibrosis of the liver" refers to an excessive accumulation in the liver of extracellular matrix proteins, which could include collagens (I, III, and IV), FBN, undulin, elastin, laminin, hyaluronan, and proteoglycans resulting from inflammation and liver cell death. Liver fibrosis, if left untreated, may progress to cirrhosis, liver failure, or liver cancer.

[0080] As used herein, "loop" means an unpaired region of a nucleic acid (*e.g.*, oligonucleotide) that is flanked by two antiparallel regions of the nucleic acid that are sufficiently complementary to one another, such that under appropriate hybridization conditions (*e.g.*, in a phosphate buffer, in a cells), the two antiparallel regions, which flank the unpaired region, hybridize to form a duplex (referred to as a "stem").

[0081] As used herein, "modified internucleotide linkage" means an internucleotide linkage having one or more chemical modifications when compared with a reference internucleotide linkage having a phosphodiester bond. A modified nucleotide can be a non-naturally occurring linkage. Typically, a modified internucleotide linkage confers one or more desirable properties to a nucleic acid in which the modified internucleotide linkage is present. For example, a modified nucleotide may improve thermal stability, resistance to degradation, nuclease resistance, solubility, bioavailability, bioactivity, reduced immunogenicity, *etc.*

[0082] As used herein, "modified nucleotide" refers to a nucleotide having one or more chemical modifications when compared with a corresponding reference nucleotide selected from: adenine ribonucleotide, guanine ribonucleotide, cytosine ribonucleotide, uracil ribonucleotide, adenine deoxyribonucleotide, guanine deoxyribonucleotide, cytosine deoxyribonucleotide and thymidine deoxyribonucleotide. A modified nucleotide can be a non-naturally occurring nucleotide. A modified nucleotide can have, for example, one or more chemical modifications in its sugar, nucleobase and/or phosphate group. Additionally or alternatively, a modified nucleotide can have one or more chemical moieties conjugated to a corresponding reference nucleotide. Typically, a modified nucleotide confers one or more desirable properties to a nucleic acid in which the modified nucleotide is present. For example, a modified nucleotide may improve thermal stability, resistance to degradation, nuclease resistance, solubility, bioavailability, bioactivity, reduced immunogenicity, *etc.*

[0083] As used herein, "nicked tetraloop structure" mean a structure of a RNAi oligonucleotide that is characterized by separate sense and antisense strands, in which the sense strand has a

region of complementarity with the antisense strand, and in which at least one of the strands, generally the sense strand, has a tetraloop configured to stabilize an adjacent stem region formed within the at least one strand.

[0084] As used herein, "nucleoside" means a nucleobase-sugar combination, where the nucleobase portion is normally a heterocyclic base. The two most common classes of such heterocyclic bases are purines and pyrimidines. The sugar is normally a pentose sugar such as a ribose or a deoxyribose (*e.g.*, 2'-deoxyribose).

[0085] As used herein, "nucleotide" means an organic molecule having a nucleoside (a nucleobase such as, for example, adenine, cytosine, guanine, thymine, or uracil; and a pentose sugar such as, *e.g.*, ribose or 2'-deoxyribose) and a phosphate group, which can serve as a monomeric unit of nucleic acid polymers such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

[0086] As used herein, "oligonucleotide" means a short nucleic acid molecule (*e.g.*, less than about 100 nucleotides in length). An oligonucleotide may be single-stranded (ss) or ds. An oligonucleotide may or may not have duplex regions. As a set of non-limiting examples, an oligonucleotide may be, but is not limited to, a small interfering RNA (siRNA), microRNA (miRNA), short hairpin RNA (shRNA), Dicer substrate interfering RNA (DsiRNA), antisense oligonucleotide (ASO), short siRNA or ss siRNA. Typically, a ds oligonucleotide is a RNAi oligonucleotide.

[0087] As used herein, "overhang" means a terminal non-base pairing nucleotide(s) resulting from one strand or region extending beyond the terminus of a complementary strand with which the one strand or region forms a duplex. An overhang may include one or more unpaired nucleotides extending from a duplex region at the 5' terminus or 3' terminus of a ds oligonucleotide. The overhang can be a 3' or 5' overhang on the antisense strand or sense strand of a ds oligonucleotide.

[0088] As used herein, "phosphate analog" means a chemical moiety that mimics the electrostatic and/or steric properties of a phosphate group. In some embodiments, a phosphate analog is positioned at the 5' terminal nucleotide of an oligonucleotide in place of a 5'-phosphate, which is often susceptible to enzymatic removal. A 5' phosphate analog can include a phosphatase-resistant linkage. Examples of phosphate analogs include, but are not limited to, 5' phosphonates, such as 5' methylenephosphonate (5'-MP) and 5'-(E)-vinylphosphonate (5'-VP). An oligonucleotide can have a phosphate analog at a 4'-carbon position of the sugar (referred to as a "4'-phosphate analog") at a 5'-terminal nucleotide. An example of a 4'-

phosphate analog is oxymethylphosphonate, in which the oxygen atom of the oxymethyl group is bound to the sugar moiety (*e.g.*, at its 4'-carbon) or analog thereof. *See*, *e.g.*, Intl. Patent Application Publication No. WO 2018/045317. Other modifications have been developed for the 5′ end of oligonucleotides (*see*, *e.g.*, Intl. Patent Application No. WO 2011/133871; US Patent No. 8,927,513; and Prakash *et al.* (2015) *Nucleic Acids Res.* 43:2993-3011).

[0089] As used herein, or "SCAP-associated condition," "SCAP-associated disease" or "SCAP-associated disorder" means such a disease, disorder, or condition having increased SCAP activity and/or the presence of, for example, a SCAP polymorphism. Exemplary SCAP-associated conditions, diseases or disorders include, but are not limited to, AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD, NASH and PSC, as well as related diseases, disorders, and conditions in an individual such as, for example hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity.

[0090] As used herein, "reduced expression" or "reduced activity," and with respect to a gene (*e.g.*, *SCAP*), means a decrease in the amount or level of RNA transcript (*e.g.*, SCAP mRNA) or protein (*e.g.*, SCAP protein) encoded by the gene and/or a decrease in the amount or level of activity of the gene or protein in a cell, a population of cells, a sample or a subject, when compared to an appropriate reference (*e.g.*, a reference cell, population of cells, sample or individual). For example, the act of contacting a cell with an oligonucleotide herein (*e.g.*, an oligonucleotide having an antisense strand having a nucleotide sequence that is complementary to a nucleotide sequence including SCAP mRNA) may result in a decrease in the amount or level of mRNA, protein and/or activity (*e.g.*, *via* degradation of SCAP mRNA by the RNAi pathway) when compared to a cell that is not treated with the ds oligonucleotide. Similarly, and as used herein, "reducing expression" or "reducing activity" means an act that results in reduced expression of a gene (*e.g.*, *SCAP*). Specifically, and as used herein, "reduction of *SCAP* expression" or "reduction of *SCAP* activity" means a decrease in the amount or level of *SCAP* activity such as, for example, SCAP mRNA and/or SCAP protein and/or SCAP activity in a cell, a population of cells, a sample or a subject when compared to an appropriate reference (*e.g.*, a reference cell, population of cells, tissue or individual).

[0091] As used herein, "region of complementarity" means a sequence of nucleotides of a nucleic acid (*e.g.*, a ds oligonucleotide) that is sufficiently complementary to an antiparallel sequence of nucleotides to permit hybridization between the two sequences of nucleotides under appropriate hybridization conditions (*e.g.*, in a phosphate buffer, in a cell, *etc.*). An

oligonucleotide herein includes a targeting sequence having a region of complementary to a mRNA target sequence.

[0092] As used herein, "ribonucleotide" means a nucleotide having a ribose as its pentose sugar, which contains a hydroxyl group at its 2' position. A modified ribonucleotide is a ribonucleotide having one or more modifications or substitutions of atoms other than at the 2' position, including modifications or substitutions in or of the nucleobase, sugar, or phosphate group.

[0093] As used herein, "iRNA," "iRNA agent," "RNAi," "RNAi agent" and "RNA interference agent" means an agent such as, for example, a RNAi oligonucleotide, which contains RNA and which mediates the targeted cleavage of an RNA transcript *via* a RNA-induced silencing complex (RISC) pathway to direct sequence-specific degradation of mRNA *via* RNA interference. The agent thus modulates, inhibits or reduces gene expression in a cell.

[0094] As used herein, "RNAi oligonucleotide" refers to either (a) a ds oligonucleotide having a sense strand and antisense strand, in which the antisense strand or part of the antisense strand is used by the Argonaute 2 (Ago2) endonuclease in the cleavage of a target mRNA or (b) a ss oligonucleotide having a single antisense strand, where that antisense strand (or part of that antisense strand) is used by the Ago2 endonuclease in the cleavage of a target mRNA.

[0095] As used herein, "strand" refers to a single, contiguous sequence of nucleotides linked together through internucleotide linkages (*e.g.*, phosphodiester linkages or phosphorothioate linkages). A strand can have two free ends (*e.g.*, a 5' end and a 3' end).

[0096] As used herein, "synthetic" refers to a nucleic acid or other molecule that is artificially synthesized (*e.g.*, using a machine such as, for example, a solid-state nucleic acid synthesizer) or that is otherwise not derived from a natural source (*e.g.*, a cell or organism) that normally produces the nucleic acid or other molecule.

[0097] As used herein, "targeting ligand" means a molecule (*e.g.*, an amino sugar, carbohydrate, cholesterol, lipid, or polypeptide) that selectively binds to a cognate molecule (*e.g.*, a receptor) of a tissue or cell of interest and that is conjugatable to another substance for targeting another substance to the tissue or cell of interest. For example, a targeting ligand may be conjugated to an oligonucleotide herein for purposes of targeting the oligonucleotide to a specific tissue or cell of interest. A targeting ligand can selectively bind to a cell surface receptor. Accordingly, a targeting ligand, when conjugated to an oligonucleotide, facilitates delivery of the oligonucleotide into a particular cell through selective binding to a receptor expressed on the surface of the cell and endosomal internalization by the cell of the complex

comprising the oligonucleotide, targeting ligand and receptor. Moreover, a targeting ligand can be conjugated to an oligonucleotide *via* a linker that is cleaved following or during cellular internalization such that the oligonucleotide is released from the targeting ligand in the cell.

[0098] As used herein, "tetraloop" or "teraL" means a loop that increases stability of an adjacent duplex formed by hybridization of flanking sequences of nucleotides. The increase in stability is detectable as an increase in melting temperature (T_m) of an adjacent stem duplex that is higher than the T_m of the adjacent stem duplex expected, on average, from a set of loops of comparable length consisting of randomly selected sequences of nucleotides. For example, a tetraL can confer a T_m of at least about 50°C, at least about 55°C, at least about 56°C, at least about 58°C, at least about 60°C, at least about 65°C, or at least about 75°C in 10 mM $NaHPO_4$ to a hairpin comprising a duplex of at least 2 base pairs (bp) in length. A tetraL also may stabilize a bp in an adjacent stem duplex by stacking interactions. Additionally, interactions among the nucleotides in a tetraloop include, but are not limited to, non-Watson-Crick base pairing, stacking interactions, hydrogen bonding, and contact interactions (Cheong *et al.* (1990) NATURE 346:680-82; Heus & Pardi (1991) SCIENCE 253:191-94). Here, a tetraL can include or can have about 3 to about 6 nucleotides, and typically is about 4 to about 5 nucleotides. A tetraL therefore can have 3, 4, 5, or 6 nucleotides, which may or may not be modified (*e.g.*, which may or may not be conjugated to a targeting moiety), especially 4 nucleotides. Any nucleotide may be used in the tetraL, and standard IUPAC-IUB symbols for such nucleotides may be used as described in Cornish-Bowden (1985) NUCLEIC ACIDS RES. 13:3021-30. For example, the letter "N" may be used to mean that any base may be in that position, the letter "R" may be used to show that A (adenine) or G (guanine) may be in that position, and "B" may be used to show that C (cytosine), G (guanine), or T (thymine) may be in that position. Examples of tetraL include the UNCG family of tetraloops (*e.g.*, UUCG), the GNRA family of tetraloops (*e.g.*, GAAA) and the CUUG tetraloop (Woese *et al.* (1990) PROC. NATL. ACAD. SCI. USA 87:8467-71; Antao *et al.* (1991) NUCLEIC ACIDS RES. 19:5901-05). Examples of DNA tetraloops include the d(GNNA) family of tetraloops (*e.g.*, d(GTTA)), the d(GNRA) family of tetraloops, the d(GNAB) family of tetraloops, the d(CNNG) family of tetraloops, and the d(TNCG) family of tetraloops (*e.g.*, d(TTCG)). *See*, *e.g.*, Nakano *et al.* (2002) BIOCHEM. 41:4281-92; and Shinji *et al.* (2000) NIPPON KAGAKKAI KOEN YOKOSHU 78:731. Here, the tetraL can be within a nicked tetraL structure.

[0099] As used herein, "treat" or "treating" means an act of providing care to an individual in need thereof, for example, by administering a therapeutic agent (*e.g.*, an oligonucleotide herein)

to the individual for purposes of improving the health and/or well-being of the individual with respect to an existing a disease, disorder, or condition, or to prevent or decrease the likelihood of the occurrence of a disease, disorder, or condition. Treating also can involve reducing the frequency or severity of at least one sign, symptom or contributing factor of a disease, disorder, or condition experienced by the individual.

[00100] *Compositions*

[00101] Oligonucleotide Inhibitors of *SCAP* Activity

[00102] I. SCAP Target Sequences: The oligonucleotides herein (*e.g.*, an antisense strand of a ds oligonucleotide such as a RNAi oligonucleotide) are targeted to a target sequence within SCAP mRNA. For example, an oligonucleotide, or a portion, fragment, or strand thereof binds or anneals to a target sequence within a SCAP mRNA, thereby inhibiting *SCAP* activity. In some embodiments, the oligonucleotide is targeted to a SCAP target sequence for inhibiting *SCAP* activity *in vivo*. In some embodiments, the amount or extent of inhibition of *SCAP* activity by an oligonucleotide targeted to a SCAP target sequence correlates with the potency of the oligonucleotide. In some embodiments, the amount or extent of inhibition of *SCAP* activity by an oligonucleotide targeted to a SCAP target sequence correlates with the amount or extent of therapeutic benefit in an individual having or suspected of having a disease, disorder, or condition associated with *SCAP* activity treated with the oligonucleotide.

[00103] Through examining and analyzing the nucleotide sequence of SCAP mRNAs, including mRNAs of multiple different species (*e.g.*, human, mouse and/or monkey; *see*, *e.g.*, Example 2) and because of *in vitro* and *in vivo* testing (*see*, *e.g.*, Examples 3 and 4), it is shown herein that certain nucleotide sequences of SCAP mRNA are more amenable than others to oligonucleotide-based inhibition of *SCAP* activity and are thus useful as target sequences for the oligonucleotides herein. In some embodiments, a sense strand of an oligonucleotide herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide; *e.g.*, in Table 3) includes a SCAP target sequence. In some instances, a portion or region of the sense strand of RNAi oligonucleotdie herein (*e.g.*, in Table 3) includes a SCAP target sequence. In some embodiments, a SCAP target sequence comprises, or consists of, a sequence of any one of SEQ ID NOs: 777 to 783 or any one of the odd numbers of SEQ ID NOs: 785 to 1168 (especially any one of SEQ ID NOs: 915, 923, 997, 1049, 1097, 1109, and 1137).

[00104] II. SCAP mRNA Targeting Sequences: In some embodiments, the oligonucleotide herein (*e.g.*, an antisense strand of a ds oligonucleotide such as a RNAi oligonucleotide) has a region of complementarity to SCAP mRNA (*e.g.*, within a target sequence of SCAP mRNA) for targeting SCAP mRNA in cells and inhibiting *SCAP* activity. In some embodiments, the oligonucleotide comprises a SCAP targeting sequence (*e.g.*, an antisense strand of a ds oligonucleotide) having a region of complementarity that binds or anneals to a SCAP mRNA target sequence by complementary (Watson-Crick) base pairing. The targeting sequence or region of complementarity is of a suitable length and base content to enable binding or annealing of the oligonucleotide (or a strand thereof) to a SCAP mRNA for inhibiting its expression. In some embodiments, the targeting sequence or region of complementarity is at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, at least about 25, at least about 26, at least about 27, at least about 28, at least about 29, or at least about 30 nucleotides in length. Alternatively, the targeting sequence or region of complementarity is about 12 to about 30 (*e.g.*, 12 to 30, 12 to 22, 15 to 25, 17 to 21, 18 to 27, 19 to 27, or 15 to 30) nucleotides in length. Alternatively, the targeting sequence or region of complementarity is about 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 18 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 19 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 20 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 21 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 22 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 23 nucleotides in length. In certain embodiments, the targeting sequence or region of complementarity is 24 nucleotides in length.

[00105] In some embodiments, the oligonucleotide herein comprises a targeting sequence or a region of complementarity (*e.g.*, an antisense strand of a ds oligonucleotide) that is fully complementary to a SCAP mRNA targeting sequence. In some embodiments, the targeting sequence or region of complementarity is partially complementary to a SCAP mRNA targeting sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a sequence of any one of SEQ ID NOs: 777 to 783. In some embodiments, the oligonucleotide comprises a targeting sequence or region of

complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 777 to 783.

[00106] Alternatively, in some embodiments, the oligonucleotide herein comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a SCAP mRNA, where the contiguous sequence of nucleotides is about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 28, 12 to 26, 12 to 24, 12 to 20, 12 to 18, 12 to 16, 14 to 22, 16 to 20, 18 to 20, or 18 to 19 nucleotides in length). In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a SCAP mRNA, where the contiguous sequence of nucleotides is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a SCAP mRNA, where the contiguous sequence of nucleotides is 19 nucleotides in length. In some embodiments, the oligonucleotides comprise a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a SCAP mRNA, where the contiguous sequence of nucleotides is 20 nucleotides in length. In other embodiments, the oligonucleotides comprise a targeting sequence or a region of complementarity that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 777 to 783, optionally where the contiguous sequence of nucleotides is 19 nucleotides in length.

[00107] With regard to the targeting sequence or region of complementarity of the oligonucleotides herein, it is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 777 to 783 and spans the entire length of an antisense strand. In some embodiments, the region of complementarity of the oligonucleotide is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 777 to 783 and spans a portion of the entire length of an antisense strand. In some additional embodiments, the oligonucleotide includes a region of complementarity (*e.g.*, on an antisense strand of a ds oligonucleotide) that is at least partially (*e.g.*, fully) complementary to a contiguous stretch of nucleotides spanning nucleotides 1-20, 1-19, 1-18, *etc.* of a sequence as set forth in any one of SEQ ID NOs: 777 to 783.

[00108] Alternatively, the oligonucleotide comprises a targeting sequence or region of complementarity having one or more base pair (bp) mismatches with the corresponding SCAP mRNA target sequence. In some embodiments, the targeting sequence or region of

complementarity is up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding SCAP target sequence, provided that the ability of the targeting sequence or region of complementarity to bind or anneal to a SCAP mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide to reduce or inhibit *SCAP* activity is maintained. Stated differently, the targeting sequence or region of complementarity is no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding SCAP target sequence provided that the ability of the targeting sequence or region of complementarity to bind or anneal to a SCAP mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide to reduce or inhibit *SCAP* activity is maintained. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 1 mismatch with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 2 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity having 3 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 4 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 5 mismatches with the corresponding target sequence. In other embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity more than one mismatch (*e.g.*, 2, 3, 4, 5 or more mismatches) with the corresponding target sequence, where at least 2 (*e.g.*, all) of the mismatches are positioned consecutively (*e.g.*, 2, 3, 4, 5 or more mismatches in a row), or where the mismatches are interspersed in any position throughout the targeting sequence or region of complementarity. In other embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity more than one mismatch (*e.g.*, 2, 3, 4, 5 or more mismatches) with the corresponding target sequence, where at least 2 (*e.g.*, all) of the mismatches are positioned consecutively (*e.g.*, 2, 3, 4, 5 or more mismatches in a row), or where at least one or more non-mismatched bp is located between the mismatches, or a combination thereof.

[00109] III. Types of Oligonucleotides: A variety of oligonucleotide types and/or structures are useful for targeting SCAP mRNA including, but not limited to, RNAi oligonucleotides, ASOs, miRNAs, *etc.* Any of the oligonucleotide types described herein or elsewhere are

contemplated for use as a framework to incorporate a targeting sequence herein for the purposes of inhibiting *SCAP* activity. In some embodiments, the oligonucleotide herein inhibits *SCAP* activity by engaging with RNAi pathways upstream or downstream of Dicer involvement. For example, RNAi oligonucleotides have been developed with each strand having sizes of about 19-25 nucleotides with at least one 3' overhang of 1 to 5 nucleotides (*see*, *e.g.*, US Patent No. 8,372,968). Longer oligonucleotides also have been developed that are processed by Dicer to generate active RNAi products (*see*, *e.g.*, US Patent No. 8,883,996). Further work produced extended ds oligonucleotides where at least one end of at least one strand is extended beyond a duplex targeting region, including structures where one of the strands includes a thermodynamically stabilizing tetraL (*see*, *e.g.*, US Patent Nos. 8,513,207 and 8,927,705, as well as Intl. Patent Application Publication No. WO 2010/033225). Such structures include ss extensions (on one or both sides of the molecule) as well as ds extensions.

[00110] The oligonucleotides herein engage with the RNAi pathway downstream of the involvement of Dicer (*e.g.*, Dicer cleavage). In some embodiments, the oligonucleotide has an overhang (*e.g.*, of 1, 2, or 3 nucleotides in length) in the 3' end of the sense strand. In some embodiments, the oligonucleotide (*e.g.*, siRNA) includes a 21-nucleotide antisense strand that is antisense to a target mRNA (*e.g.*, SCAP mRNA) and a complementary sense strand, in which both strands anneal to form a 19-bp duplex and 2 nucleotide overhangs at either or both 3' ends. Longer oligonucleotide designs also are contemplated, including oligonucleotides having an antisense strand of 23 nucleotides and a sense strand of 21 nucleotides, where there is a blunt end on the right side of the molecule (3' end of sense strand/5' end of antisense strand) and a two nucleotide 3' antisense strand overhang on the left side of the molecule (5' end of the sense strand/3' end of the antisense strand). In such molecules, there is a 21 bp duplex region. *See*, *e.g.*, US Patent Nos. 9,012,138; 9,012,621 and 9,193,753.

[00111] The oligonucleotide herein comprises sense and antisense strands that are both in the range of about 17 to about 26 (*e.g.*, 17 to 26, 20 to 25, or 21-23) nucleotides in length. In some embodiments, the oligonucleotide comprises a sense and antisense strand that are both in the range of about 19 to about 22 nucleotides in length. In some embodiments, the sense and antisense strands are of equal length. In some embodiments, the oligonucleotide comprises sense and antisense strands, such that there is a 3' overhang on either the sense strand or the antisense strand, or both the sense and antisense strand. In some embodiments, for an oligonucleotide having sense and antisense strands that are both in the range of about 21 to about 23 nucleotides in length, a 3' overhang on the sense, antisense or both sense and antisense

strands is 1 or 2 nucleotides in length. In some embodiments, the oligonucleotide comprises an antisense strand of 22 nucleotides and a sense strand of 20 nucleotides, where there is a blunt end on the right side of the molecule (3' end of sense strand/5' end of antisense strand) and a 2 nucleotide 3' antisense strand overhang on the left side of the molecule (5' end of the sense strand/3' end of the antisense strand). In such molecules, there is a 20-bp duplex region.

[00112] Other oligonucleotide designs for use herein include: 16-mer siRNAs (*see*, *e.g.*, "NUCLEIC ACIDS IN CHEMISTRY & BIOLOGY," Blackburn (ed.), Royal Society of Chemistry, 2006), shRNAs (*e.g.*, having 19 bp or shorter stems; *see*, *e.g.*, Moore *et al.* (2010) METHODS MOL. BIOL. 629:141-58), blunt siRNAs (*e.g.*, of 19 bps in length; *see*, *e.g.*, Kraynack & Baker (2006) *RNA* 12:163-76), asymmetrical siRNAs (aiRNA; *see*, *e.g.*, Sun *et al.* (2008) NAT. BIOTECHNOL. 26:1379-82), asymmetric shorter-duplex siRNA (*see*, *e.g.*, Chang *et al.* (2009) MOL. THER. 17:725-32), fork siRNAs (*see*, *e.g.*, Hohjoh (2004) FEBS LETT. 557:193-98), ss siRNAs (*see*, *e.g.*, Elsner (2012) NAT. BIOTECHNOL. 30:1063), dumbbell-shaped circular siRNAs (*see*, *e.g.*, Abe *et al.* (2007) J. AM. CHEM. SOC. 129:15108-09), and small internally segmented interfering RNA (sisiRNA; *see, e.g.*, Bramsen *et al.* (2007) NUCLEIC ACIDS RES. 35:5886-97). Further non-limiting examples of oligonucleotide structures that may be used herein to reduce or inhibit *SCAP* activity are miRNA, shRNA, and short siRNA (*see*, *e.g.*, Hamilton *et al.* (2002) EMBO J. 21:4671-79; *see also*, US Patent No. 7,659,389).

[00113] Alternatively, the oligonucleotide herein is ss. Such structures include, but are not limited to, ss RNAi molecules. Recent efforts have demonstrated the activity of ss RNAi molecules (*see*, *e.g.*, Matsui *et al.* (2016) MOL. THER. 24:946-55). In some embodiments, the oligonucleotide is an ASOs. An ASO is a ss oligonucleotide that has a nucleobase sequence that, when written or depicted in the 5' to 3' direction, includes a reverse complement of a targeted segment of a particular nucleic acid and is suitably modified (*e.g.*, as a gapmer) to induce RNaseH-mediated cleavage of its target RNA in cells or (*e.g.*, as a mixmer) so as to inhibit translation of the target mRNA in cells. ASOs for use herein are modified in any suitable manner known in the art including, for example, as shown in US Patent No. 9,567,587 (including, for example, length, sugar moieties of the nucleobase (pyrimidine, purine), and alterations of the heterocyclic portion of the nucleobase). Further, ASOs have been used for decades to reduce expression of specific target genes (*see*, *e.g.*, Bennett *et al.* (2017) ANNU. REV. PHARMACOL. 57:81-105).

[00114] IV. ds RNAi Oligonucleotides: ds RNAi oligonucleotides for targeting SCAP mRNA and inhibiting *SCAP* activity (*e.g.*, *via* the RNAi pathway) comprise a sense strand and an antisense strand. In some embodiments, the sense strand and antisense strand are separate strands and are not covalently linked. In some embodiments, the sense strand and antisense strand are covalently linked.

[00115] In some embodiments, the sense strand comprises a first region (R1) and a second region (R2), where R2 comprises a first subregion (S1), a triL or a L, and a second subregion (S2), where triL or L is located between S1 and S2, and where S1 and S2 form a second duplex (D2). D2 has various lengths. In some embodiments, D2 is about 1 to about 6 bp in length. In other embodiments, D2 is 2-6, 3-6, 4-6, 5-6, 1-5, 2-5, 3-5 or 4-5 bp in length. In other embodiments, D2 is 1, 2, 3, 4, 5 or 6 bp in length. In certain embodiments, D2 is 6 bp in length.

[00116] In some embodiments, R1 of the sense strand and the antisense strand forms a first duplex (D1). In some embodiments, D1 is at least about 15 (*e.g.*, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20 or at least 21) nucleotides in length. In other embodiments, D1 is about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 15 to 22, 18 to 22, 18 to 25, 18 to 27, 18 to 30 or 21 to 30 nucleotides in length). In other embodiments, D1 is at least 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 20, at least 25 or at least 30 nucleotides in length). In other embodiments, D1 is 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 nucleotides in length. In certain embodiments, D1 is 20 nucleotides in length. In some embodiments, D1 does not span the entire length of the sense strand and/or antisense strand. In other embodiments, D1 spans the entire length of either the sense strand or antisense strand or both. In certain embodiments, D1 spans the entire length of both the sense strand and the antisense strand.

[00117] In certain embodiments, the disclosure describes RNAi oligonucleotides for reducing or inhibiting *SCAP* activity that include a sense strand comprising, or alternatively consisting of, a sequence as set forth in Table 3 (*e.g.*, any one of the odd numbers of SEQ ID NOs: 9 to 392), especially SEQ ID NOs: 139, 147, 221, 273, 321, 333, and 361.

[00118] In certain embodiments, the disclosure describes RNAi oligonucleotides for reducing or inhibiting *SCAP* activity that include an antisense strand comprising, or alternatively consisting of, a sequence as set forth in Table 3 (*e.g.*, any one of the even numbers of SEQ ID NOs: 9 to 392), especially SEQ ID NOs: 140, 148, 222, 274, 322, 334, and 362.

[00119] In certain other embodiments, the RNAi oligonucleotide includes a sense strand comprising, or alternatively consisting of, a nucleotide sequence of any one of SEQ ID NOs:

139, 147, 221, 273, 321, 333 and 361, and an antisense strand comprising, or alternatively consisting of, a nucleotide sequence of any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334 and 362.

[00120] In certain embodiments, the sense strand and the antisense strand of a RNAi oligonucleotide, respectively, are selected from:

(a) SEQ ID NOs: 139 and 140,

(b) SEQ ID NOs: 147 and 148,

(c) SEQ ID NOs: 221 and 222,

(d) SEQ ID NOs: 273 and 274,

(e) SEQ ID NOs: 321 and 322,

(f) SEQ ID NOs: 333 and 334, and

(g) SEQ ID NOs: 361 and 362.

[00121] In certain additional embodiments, the RNAi oligonucleotide includes a sense strand comprising, or alternatively consisting of, a nucleotide sequence of SEQ ID NO: 147 or 333, and an antisense strand comprising, or alternatively consisting of, a nucleotide sequence of SEQ ID NO: 148 or 334. Alternatively, the sense strand is SEQ ID NO: 147 and the antisense strand is SEQ ID NO: 148. Alternatively, the sense strand is SEQ ID NO: 333 and the antisense strand is SEQ ID NO: 334.

[00122] In some embodiments, the RNAi oligonucleotide includes a sense strand comprising, or alternatively consisting of, a nucleotide sequence as set forth in Table 4 (*e.g.*, any one of the odd numbers of SEQ ID NOs: 393 to 776), especially SEQ ID NOs: 523, 531, 605, 657, 705, 717, and 745.

[00123] In certain embodiments, the RNAi oligonucleotide includes an antisense strand comprising, or alternatively consisting of, a nucleotide sequence as set forth in Table 4 (*e.g.*, any one of the even numbers of SEQ ID NOs: 393 to 776), especially SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746.

[00124] In certain other embodiments, the RNAi oligonucleotide includes a sense strand comprising, or alternatively consisting of, a nucleotide sequence of any one of SEQ ID NOs: 523, 531, 605, 657, 705, 717 and 745, and an antisense strand comprising, or alternatively consisting of, a nucleotide sequence of any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718 and 746.

[00125] In certain embodiments, the sense strand, and the antisense strand of the RNAi oligonucleotide, respectively, are selected from:

(a') SEQ ID NOs: 523 and 524,

(b') SEQ ID NOs: 531 and 532,

(c') SEQ ID NOs: 605 and 606,

(d') SEQ ID NOs: 657 and 658,

(e') SEQ ID NOs: 705 and 706,

(f') SEQ ID NOs: 717 and 718, and

(g') SEQ ID NOs: 745 and 746.

[00126] In certain additional embodiments, the RNAi oligonucleotide includes a sense strand comprising, or alternatively consisting of, a nucleotide sequence of SEQ ID NO: 531 or 717, and an antisense strand comprising, or alternatively consisting of, a nucleotide sequence of SEQ ID NO: 532 or 718. Alternatively, the sense strand is SEQ ID NO: 531 and the antisense strand is SEQ ID NO: 532. Alternatively, the sense strand is SEQ ID NO: 717 and the antisense strand is SEQ ID NO: 718.

[00127] One of skill in the art appreciates that in some embodiments, the sequences presented in the Sequence Listing are referred to in describing the structure of an oligonucleotide (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) or other nucleic acid. In such embodiments, the actual oligonucleotide or other nucleic acid has one or more alternative nucleotides (*e.g.*, an RNA counterpart of a DNA nucleotide or a DNA counterpart of an RNA nucleotide) and/or one or more modified nucleotides and/or one or more modified internucleotide linkages and/or one or more other modification when compared with the specified sequence while retaining essentially same or similar complementary properties as the specified sequence.

[00128] In some embodiments, an oligonucleotide herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) includes a 25-nucleotide sense strand and a 27-nucleotide antisense strand that when acted upon by a Dicer enzyme results in an antisense strand that is incorporated into the mature RISC. In other embodiments, the sense strand of the ds oligonucleotide is longer than 25 nucleotides (*e.g.*, 26, 27, 28, 29, or 30 nucleotides). In other embodiments, the sense strand of the ds oligonucleotide is longer than 27 nucleotides (*e.g.*, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides).

[00129] In some embodiments, the oligonucleotide has one 5' end that is thermodynamically less stable when compared to the other 5' end. In some embodiments, the oligonucleotide is asymmetric and includes a blunt end at the 3' end of a sense strand and a 3' overhang at the 3' end of an antisense strand. In some embodiments, the 3' overhang on the antisense strand is about 1 to about 8 nucleotides in length (*e.g.*, 1, 2, 3, 4, 5, 6, 7, or 8 nucleotides in length).

Typically, a ds oligonucleotide for RNAi has a two-nucleotide overhang on the 3' end of the antisense strand. However, other overhangs are possible. In some embodiments, an overhang is a 3' overhang having a length of between about 1 to about 6 nucleotides, optionally 1 to 5, 1 to 4, 1 to 3, 1 to 2, 2 to 6, 2 to 5, 2 to 4, 2 to 3, 3 to 6, 3 to 5, 3 to 4, 4 to 6, 4 to 5, 5 to 6 nucleotides, or 1, 2, 3, 4, 5, or 6 nucleotides. However, in other embodiments, the overhang is a 5' overhang comprising a length of between about 1 to about 6 nucleotides, optionally 1 to 5, 1 to 4, 1 to 3, 1 to 2, 2 to 6, 2 to 5, 2 to 4, 2 to 3, 3 to 6, 3 to 5, 3 to 4, 4 to 6, 4 to 5, 5 to 6 nucleotides, or 1, 2, 3, 4, 5, or 6 nucleotides.

[00130] In some embodiments, 2 terminal nucleotides on the 3' end of an antisense strand are modified. In some embodiments, the 2 terminal nucleotides on the 3' end of the antisense strand are complementary with the target mRNA (*e.g.*, SCAP mRNA). In other embodiments, the 2 terminal nucleotides on the 3' end of the antisense strand are not complementary with the target mRNA. In some embodiments, the 2 terminal nucleotides on the 3′ end of the antisense strand of an oligonucleotide herein are unpaired. In some embodiments, 2 terminal nucleotides on each 3' end of an oligonucleotide in the nicked tetraL structure are GG. Typically, one or both of the 2 terminal GG nucleotides on each 3' end of a ds oligonucleotide are not complementary with the target mRNA.

[00131] In some embodiments, there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between the sense and antisense strand. If there is more than one mismatch between the sense and antisense strand, they may be positioned consecutively (*e.g.*, 2, 3, or more in a row), or interspersed throughout the region of complementarity. In some embodiments, the 3' end of the sense strand contains one or more mismatches. In certain embodiments, two mismatches are incorporated at the 3' end of the sense strand. In some embodiments, base mismatches, or destabilization of segments at the 3' end of the sense strand of the oligonucleotide improves or increases the potency of the ds oligonucleotide.

[00132] In some embodiments, there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between a sense and antisense strand comprising an oligonucleotide herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide). If there is more than one mismatch between a sense and antisense strand, they may be positioned consecutively (*e.g.*, 2, 3 or more in a row), or interspersed throughout the region of complementarity. In some embodiments, the 3' end of the sense strand comprises one or more mismatches. In some embodiments, two (2) mismatches are incorporated at the 3' end of the sense strand. In some embodiments, base mismatches, or destabilization of segments at the 3' end of the sense strand of an oligonucleotide herein

improves or increases the potency of the oligonucleotide. In some embodiments, the sense and antisense strands of an oligonucleotide herein comprise nucleotides sequences selected from Table 3, optionally from the group consisting of:

(a) SEQ ID NOs: 139 and 140,

(b) SEQ ID NOs: 147 and 148,

(c) SEQ ID NOs: 221 and 222,

(d) SEQ ID NOs: 273 and 274,

(e) SEQ ID NOs: 321 and 322,

(f) SEQ ID NOs: 333 and 334, and

(g) SEQ ID NOs: 361 and 362,

wherein there is one or more (*e.g.*, 1, 2, 3, 4 or 5) mismatch(s) between the sense and antisense strands.

[00133] A. Sense Strands: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) include a sense strand sequence including a sequence as set forth in the sense strands of Table 3 or Table 4. In some embodiments, the oligonucleotide includes a sense strand that having at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in in any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333 and 361, or a sense strand having a nucleotide sequence of any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334 and 362.

[00134] Further, the oligonucleotide can include a sense strand of up to about 50 nucleotides in length (*e.g.*, up to 50, up to 40, up to 36, up to 30, up to 27, up to 25, up to 21, up to 19, up to 17, or up to 12 nucleotides in length). In some embodiments, the oligonucleotide can have a sense strand of at least about 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 19, at least 21, at least 25, at least 27, at least 30, at least 36, or at least 38 nucleotides in length). Alternatively, the oligonucleotide can have a sense strand in a range of about 12 to about 40 (*e.g.*, 12 to 40, 12 to 36, 12 to 32, 12 to 28, 15 to 40, 15 to 36, 15 to 32, 15 to 28, 17 to 21, 17 to 25, 19 to 27, 19 to 30, 20 to 40, 22 to 40, 25 to 40, or 32 to 40) nucleotides in length. In certain embodiments, the oligonucleotide can have a sense strand of 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides in length.

[00135] In some embodiments, the sense strand comprises a stem-loop structure at its 3' end. In other embodiments, the sense strand comprises a stem-loop structure at its 5' end. In some embodiments, the stem-loop is formed by intrastrand base pairing. In additional embodiments, the stem is a duplex of about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 bp in length. In some embodiments, the stem of the stem-loop comprises a duplex of 2 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 3 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 4 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 5 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 6 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 7 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 8 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 9 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 10 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 11 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 12 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 13 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 14 nucleotides in length.

[00136] In some embodiments, the stem-loop provides the oligonucleotide protection against degradation (*e.g.*, enzymatic degradation) and facilitates or improves targeting and/or delivery to a target cell, tissue, or organ (*e.g.*, the liver), or both. For example, the L of the stem-loop provides nucleotides having one or more modifications that facilitate, improve, or increase targeting to a target mRNA (*e.g.*, a SCAP mRNA), inhibiting of target gene expression (*e.g.*, *SCAP* activity), and/or delivering to a target cell, tissue, or organ (*e.g.*, the liver), or both. In some embodiments, the stem-loop itself or modification(s) to the stem-loop do not substantially affect the inherent gene expression inhibition activity of the oligonucleotide, but facilitates, improves, or increases stability (*e.g.*, provides protection against degradation) and/or delivery of the oligonucleotide to a target cell, tissue, or organ (*e.g.*, the liver). In certain embodiments, the oligonucleotide comprises a sense strand including (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which L forms a ss loop between S1 and S2 of up to about 10 nucleotides in length (*e.g.*, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in length). In some embodiments, L is 3 nucleotides in length (referred to herein as "triloop" or "triL"). In some embodiments, L is 4 nucleotides in length (referred to herein as "tetraloop" or

"tetraL"). In some embodiments, L is 5 nucleotides in length. In some embodiments, L is 6 nucleotides in length. In some embodiments, L is 7 nucleotides in length. In some embodiments, L is 8 nucleotides in length. In some embodiments, L is 9 nucleotides in length. In some embodiments, L is 10 nucleotides in length. In certain embodiments, L is 4 nucleotides in length. FIG. 1 depicts a non-limiting example of such an oligonucleotide. In some embodiments L of the stem-loop having the structure S1-L-S2 as described above is a tetraL (*e.g.*, within a nicked tetraL structure). In some embodiments, the tetraL comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, delivery ligands and combinations thereof. In certain embodiments, the tetraL comprises the sequence 5'-GAAA-3'. In other certain embodiments, the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784).

[00137] In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of the odd numbers of SEQ ID NOs: 785-1168, especially any one of SEQ ID NOs: 915, 923, 997, 1049, 1097, 1109, and 1137, and the oligonucleotide comprises a sense strand comprising (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which L forms a single-stranded loop between S1 and S2 of up to about 10 nucleotides in length (*e.g.*, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in length). In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of the odd numbers of SEQ ID NOs: 785-1168, especially any one of SEQ ID NOs: 915, 923, 997, 1049, 1097, 1109, and 1137, and the oligonucleotide comprises a sense strand comprising (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which L forms a single-stranded loop between S1 and S2 of 4 nucleotides in length.

[00138] In some embodiments, L of a stem-loop having the structure S1-L-S2 as described herein is a triL. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of the odd numbers of SEQ ID NOs: 785-1168, especially any one of SEQ ID NOs: 915, 923, 997, 1049, 1097, 1109, and 1137 and a triL. In some embodiments, the triL comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof.

[00139] In some embodiments, L of a stem-loop having the structure S1-L-S2 as described above is a tetraL. In some embodiments, the oligonucleotide comprises a targeting sequence or

a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of the odd numbers of SEQ ID NOs: 785-1168, especially any one of SEQ ID NOs: 915, 923, 997, 1049, 1097, 1109, and 1137 and a tetraL. In some embodiments, the tetraL comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof.

[00140] B. Antisense Strands: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) include an antisense strand including a sequence as set forth in the antisense strands of Table 3 (unmodified) or Table 4 (modified). In some embodiments, the oligonucleotide includes an antisense strand having at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333, and 361, or an antisense strand having a nucleotide sequence of any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334, and 362.

[00141] Further, the oligonucleotide can include an antisense strand of up to about 50 nucleotides in length (*e.g.*, up to 50, up to 40, up to 35, up to 30, up to 27, up to 25, up to 21, up to 19, up to 17 or up to 12 nucleotides in length). In some embodiments, an oligonucleotide comprises an antisense strand of at least about 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 19, at least 21, at least 22, at least 25, at least 27, at least 30, at least 35 or at least 38 nucleotides in length). In some embodiments, an oligonucleotide comprises an antisense strand in a range of about 12 to about 40 (*e.g.*, 12 to 40, 12 to 36, 12 to 32, 12 to 28, 15 to 40, 15 to 36, 15 to 32, 15 to 28, 17 to 22, 17 to 25, 19 to 27, 19 to 30, 20 to 40, 22 to 40, 25 to 40 or 32 to 40) nucleotides in length. In some embodiments, an oligonucleotide comprises antisense strand of 15 to 30 nucleotides in length. In some embodiments, an antisense strand of any one of the oligonucleotides disclosed herein is of 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 nucleotides in length. In some embodiments, an oligonucleotide comprises an antisense strand of 22 nucleotides in length.

[00142] In some embodiments, the oligonucleotide comprises an antisense strand comprising or consisting of a sequence as set forth in Table 3 (*e.g.*, any one of the even numbers of SEQ ID NOs: 9 to 392). In some embodiments, an oligonucleotide herein comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22 or at least 23) contiguous

nucleotides of a sequence as set forth in Table 3 (*e.g.*, any one of the even numbers of SEQ ID NOs: 9 to 392). In some embodiments, an oligonucleotide disclosed herein for targeting *SCAP* comprises an antisense strand comprising or consisting of a sequence as set forth as set forth in Table 3 (*e.g.*, any one of the even numbers of SEQ ID NOs: 9 to 392), especially any one of SEQ ID NOs: 140, 148, 222, 274 ,322, 334, and 362. In some embodiments, an oligonucleotide herein comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22 or at least 23) contiguous nucleotides of a sequence as set forth in Table 4 (*e.g.*, any one of the even numbers of SEQ ID NOs: 393 to 776. In some embodiments, an oligonucleotide disclosed herein for targeting *SCAP* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746. In some embodiments, an oligonucleotide herein comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22 or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: SEQ ID NOs: 524, 532, 606, 658, 706, 718, and 746.

[00143] C. Duplex Length: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) include a duplex formed between the sense strand and the antisense strand, which is at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21) nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 12 to 22, 15 to 25, 18 to 30, 18 to 22, 18 to 25, 18 to 27, 18 to 30, 19 to 30, or 21 to 30 nucleotides in length). In some embodiments, the duplex formed between the sense strand and the antisense strand is 12, 13, 14, 15, 16, 17, 18, 19, 29, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 12 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 13 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 14 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 15 nucleotides in length. In some embodiments the duplex formed between the sense strand and the antisense strand is 16 nucleotides in length. In some embodiments, the duplex formed

between the sense strand and the antisense strand is 17 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 18 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 19 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 20 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 21 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 22 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 23 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 24 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 25 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 26 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 27 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 28 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 29 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand is 30 nucleotides in length. In some embodiments, the duplex formed between the sense strand and the antisense strand does not span the entire length of the sense strand and/or antisense strand. In some embodiments, the duplex formed between the sense strand and the antisense strand spans the entire length of either the sense strand or the antisense strand. In some embodiments, the duplex formed between the sense strand and the antisense strand spans the entire length of both the sense strand and the antisense strand.

[00144] D. Oligonucleotide Termini: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) comprises a sense strand and an antisense strand, where a terminus of either or both strands comprise a blunt end. In some embodiments, the oligonucleotide comprises sense and antisense strands that are separate strands that form an asymmetric duplex region having an overhang at a 3' terminus of the antisense strand. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, where a terminus of either or both strands comprise an overhang comprising one or more nucleotides. In some embodiments, the one or more nucleotides comprising the overhang are unpaired

nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the 3' terminus of the sense strand and the 5' terminus of the antisense strand comprise a blunt end. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the 5' terminus of the sense strand and the 3' terminus of the antisense strand comprise a blunt end.

[00145] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the 3' terminus of either or both strands comprise a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein both the sense strand and the antisense strand comprises a 3' overhang comprising one or more nucleotides.

[00146] In some embodiments, the 3' overhang is about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length). In some embodiments, the 3' overhang is about 1 to 19, 1 to 18, 1 to 17, 1 to 16, 1 to 15, 1 to 14, 1 to 13, 1 to 12, 1 to 11, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, or 1 to 2 nucleotides in length. In some embodiments, the 3' overhang is 1 nucleotide in length. In some embodiments, the 3' overhang is 2 nucleotides in length. In some embodiments, the 3' overhang is 3 nucleotides in length. In some embodiments, the 3' overhang is 4 nucleotides in length. In some embodiments, the 3' overhang is 5 nucleotides in length. In some embodiments, the 3' overhang is 6 nucleotides in length. In some embodiments, the 3' overhang is 7 nucleotides in length. In some embodiments, the 3' overhang is 8 nucleotides in length. In some embodiments, the 3' overhang is 9 nucleotides in length. In some embodiments, the 3' overhang is 10 nucleotides in length. In some embodiments, the 3' overhang is 11 nucleotides in length. In some embodiments, the 3' overhang is 12 nucleotides in length. In some embodiments, the 3' overhang is 13 nucleotides in length. In some embodiments, the 3' overhang is 14 nucleotides in length. In some embodiments, the 3' overhang is 15 nucleotides in length. In some embodiments, the 3' overhang is 16 nucleotides in length. In some embodiments, the 3' overhang is 17 nucleotides in length. In some embodiments, the 3' overhang is 18 nucleotides in length. In some embodiments, the 3' overhang is 19 nucleotides in length. In some embodiments, the 3' overhang is 20 nucleotides in length.

[00147] In certain embodiments, the oligonucleotide comprises a sense strand and an antisense strand, where the antisense strand comprises a 3' overhang.

[00148] V. Oligonucleotide Modifications: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) include at least one modification. The oligonucleotide may be modified in various ways to improve or control specificity, stability, delivery, bioavailability, resistance from nuclease degradation, immunogenicity, base-pairing properties, RNA distribution and cellular uptake and other features relevant to therapeutic or research use.

[00149] In some embodiments, the modification is a modified sugar. In some embodiments, the modification is a 5'-terminal phosphate group. In some embodiments, the modification is a modified internucleotide linkage. In some embodiments, the modification is a modified base. In some embodiments, the oligonucleotide comprises any one of the modifications described herein or any combination thereof. For example, in some embodiments, the oligonucleotide comprises at least one modified sugar, a 5'-terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base. In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotide sequences selected from Table 3, optionally the group consisting of:

(a) SEQ ID NOs: 139 and 140,
(b) SEQ ID NOs: 147 and 148,
(c) SEQ ID NOs: 221 and 222,
(d) SEQ ID NOs: 273 and 274,
(e) SEQ ID NOs: 321 and 322,
(f) SEQ ID NOs: 333 and 334, and
(g) SEQ ID NOs: 361 and 362,

wherein the oligonucleotide comprises at least one modified sugar, a 5'-terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base.

[00150] In other embodiments, the oligonucleotide comprises a sense strand and an antisense strand having a modification pattern according to:

Sense Strand: 5'-mX-S-mX-mX-mX-mX-mX-mX-fX-fX-fX-fX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-[ademX-GalNAc]-[ademX-GalNAc]-[ademX-GalNAc]-mX-mX-mX-mX-mX-mX-3' hybridized to:

[00151] Antisense Strand: 5'-[MePhosphonate-4O-mX]-S-fX-S-fX-S-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-mX-mX-mX-mX-mX-S-mX-S-mX-3', wherein mX = 2'-OMe-modified nucleotide, fX = 2'-F-modified nucleotide, -S- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 4'-O-monomethylphosphonate-2'-O-methyl-modified nucleotide, and ademX-GalNAc = GalNAc attached to a nucleotide, and wherein the sense stand and the antisense strand comprise nucleotide sequences selected from Table 3, optionally from the group consisting of:

(a) SEQ ID NOs:139 and 140,

(b) SEQ ID NOs:147 and 148,

(c) SEQ ID NOs:221 and 222,

(d) SEQ ID NOs:273 and 274,

(e) SEQ ID NOs:321 and 322,

(f) SEQ ID NOs:333 and 334, and

(g) SEQ ID NOs:361 and 362.

[00152] A. Sugar Modifications: A modified sugar (also referred to herein as a sugar analog) includes a modified deoxyribose or ribose moiety in which, for example, one or more modifications occur at the 2', 3', 4', and/or 5' carbon position of the sugar. A modified sugar also includes non-natural, alternative, carbon structures such as those present in locked nucleic acids ("LNA"; *see, e.g.*, Koshkin *et al.* (1998) TETRAHEDRON 54:3607-30), unlocked nucleic acids ("UNA"; *see, e.g.*, Snead *et al.* (2013) MOL. THER-NUC. ACIDS 2:e103) and bridged nucleic acids ("BNA"; *see, e.g.*, Imanishi & Obika (2002) CHEM. COMMUN. 16:1653-59).

[00153] In some embodiments, the nucleotide modification in the sugar is a 2'-modification such as, for example, 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, 2'-F, 2'-aminoethyl (EA), 2'-OMe, 2'-MOE, 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), or 2'-FANA. In certain embodiments, the modification is 2'-F, 2'-OMe, or 2'-MOE. In other embodiments, the modification in the sugar is a modification of the sugar ring, which includes modification of one or more carbons of the sugar ring. For example, the modification in the sugar is a 2'-oxygen of the sugar linked to a 1'-carbon or 4'-carbon of the sugar, or a 2'-oxygen linked to the 1'-carbon or 4'-carbon *via* an ethylene or methylene bridge. In other embodiments, the modification is an acyclic sugar that lacks a 2'-carbon to 3'-carbon bond. In other embodiments, the modification is a thiol group such as, for example, in the 4' position of the sugar.

[00154] The oligonucleotides herein include at least 1 modified nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, or more). In some embodiments, the sense strand comprises at least 1 modified nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, or more). In some embodiments, the antisense strand comprises at least 1 modified nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, or more).

[00155] In certain embodiments, all nucleotides of the sense strand except the tetraL are modified. Likewise, all nucleotides of the antisense strand are modified. In some embodiments, all the nucleotides of the oligonucleotide (*i.e.*, paired nucleotides of the sense strand and the antisense strand) are modified. As above, and in some embodiments, the modified nucleotide is a 2'-modification (*e.g.*, a 2'-F, 2'-OMe, 2'-MOE, and/or 2'-FANA. In certain embodiments, the modified nucleotide is a 2'-modification such as, for example, a 2'-F or a 2'-OMe.

[00156] In some embodiments, the oligonucleotide comprises a sense strand with about 10-15%, 10%, 11%, 12%, 13%, 14%, or 15% of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, the oligonucleotide comprises a sense strand with about 18-23% (*e.g.*, 18%, 19%, 20%, 21%, 22%, or 23%) of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, the oligonucleotide comprises a sense strand with about 38-43% (*e.g.*, 38%, 39%, 40%, 41%, 42%, or 43%) of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, about 11% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, about 22% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, about 40% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, the oligonucleotide comprises an antisense strand with about 25% to about 35% (*e.g.*, 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35%) of the nucleotides of the antisense strand comprising a 2'-F modification. In some embodiments, about 32% of the nucleotides of the antisense strand comprise a 2'-F modification. In some embodiments, the oligonucleotide has about 15% to about 25% (*e.g.*, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, or 25%) of its nucleotides comprising a 2'-F modification. In some embodiments, the oligonucleotide has about 35-45% (*e.g.*, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44% or 45%) of its nucleotides comprising a 2'-F modification. In some embodiments, about 19% of the nucleotides in the oligonucleotide comprise a 2'-F modification. In some embodiments, about 29% of the nucleotides in the oligonucleotide

comprise a 2'-F modification. In some embodiments, about 40% of the nucleotides in the oligonucleotide comprise a 2'-F modification.

[00157] Moreover, the oligonucleotides herein can have different modification patterns. In some embodiments, the modified oligonucleotide comprise a sense strand sequence having a modification pattern as set forth in Table 4 (as well as FIG. 1) and an antisense strand having a modification pattern as set forth in Table 4. In some embodiments, one or more of positions 8, 9, 10, or 11 of the sense strand are modified with a 2'-F. In other embodiments, the sugar moiety at each nucleotide at positions 1 to 7, 12 to 27 and 31 to 36 in the sense strand is modified with a 2'-OMe. In certain embodiments, positions 8 to 11 of the sense strand are modified with a 2'-F and positions 1 to 7, 12 to 27 and 31 to 36 are modified with a 2'-OMe.

[00158] In certain additional embodiments, a sense strand comprising a 2'-F modified nucleotide at positions 8-11, a 2'-OMe modified nucleotide at positions 1 to 7, 12 to 27 and 31 to 36, a GalNAc-conjugated nucleotide at position 28, 29 and 30, and a phosphorothioate linkage between positions 1 and 2.

[00159] In some embodiments, the antisense strand comprises one or more nucleotides at positions 2-5, 7, 10 and 14 modified with 2'-F, and one or more nucleotides at positions 1, 6, 8 to 9, 11 to 13 and 15 to 22 modified with a 2'-OMe. Certain embodiments disclose an oligonucleotide with an antisense strand comprising a 2'-F-modified nucleotide at positions 2 to 5, 7, 10 and 14, and a 2'-OMe-modified nucleotide at positions 1, 6, 8 to 9, 11 to 13 and 15 to 22.

[00160] In certain embodiments, the antisense strand comprises a 2'-F modified nucleotide at positions 2 to 5, 7, 10 and 14, a 2'-OMe at positions 1, 6, 8 to 9, 11 to 13 and 15 to 22, a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 3 and 4, positions 20 and 21, and positions 21 and 22.

[00161] B. 5'-Terminal Phosphates: 5'-terminal phosphate groups can be used to enhance the interaction of the oligonucleotides herein with Ago2. However, oligonucleotides having a 5'-phosphate group may be susceptible to degradation *via* phosphatases or other enzymes, which can limit their bioavailability *in vivo*. In some embodiments, the oligonucleotides herein (*e.g.*, a ds oligonucleotide) comprise analogs of 5' phosphates that are resistant to such degradation. Examples of such phosphate analogs include, but are not limited to, oxymethyl phosphonate, vinyl phosphonate, malonyl phosphonate, or a combination thereof. In certain embodiments

the 3' end of a strand of the oligonucleotides is attached to a chemical moiety that mimics the electrostatic and steric properties of a natural 5'-phosphate group ("phosphate mimic").

[00162] Alternatively, or additionally, the oligonucleotides herein have a phosphate analog at a 4'-carbon position of the sugar (referred to as a "4'-phosphate analog"). *See, e.g.*, Intl. Patent Application Publication No. WO 2018/045317. In some embodiments, the oligonucleotides herein include a 4'-phosphate analog at a 5'-terminal nucleotide. In some embodiments, the phosphate analog is an oxymethyl phosphonate, in which the oxygen atom of the oxymethyl group is bound to the sugar moiety (*e.g.*, at its 4'-carbon) or analog thereof. In other embodiments, the 4'-phosphate analog is a thiomethylphosphonate or an aminomethylphosphonate, in which the sulfur atom of the thiomethyl group or the nitrogen atom of the amino methyl group is bound to the 4'-carbon of the sugar moiety or analog thereof. In certain embodiments, the 4'-phosphate analog is an oxymethylphosphonate, which is represented by the formula $–O–CH_2–PO(OH)_2$ or $–O–CH_2–PO(OR)_2$, in which R is independently selected from H, CH_3, an alkyl group, CH_2CH_2CN, $CH_2OCOC(CH_3)_3$, $CH_2OCH_2CH_2Si(CH_3)_3$, or a protecting group. In certain embodiments, the alkyl group is CH_2CH_3. In certain other embodiments, R is independently selected from H, CH_3, or CH_2CH_3.

[00163] C. Modified Internucleotide Linkages: In addition to the above modifications, the oligonucleotides herein (*e.g.*, a ds oligonucleotide) comprise a modified internucleotide linkage. In some embodiments, phosphate modifications or substitutions result in oligonucleotides that comprise at least about 1 (*e.g.*, at least 1, at least 2, at least 3, or at least 5) modified internucleotide linkages. In some embodiments, the oligonucleotides herein (*e.g.*, a ds oligonucleotide) comprise about 1 to about 10 (*e.g.*, 1 to 10, 2 to 8, 4 to 6, 3 to 10, 5 to 10, 1 to 5, 1 to 3, or 1 to 2) modified internucleotide linkages. In other embodiments, the oligonucleotides comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified internucleotide linkages.

[00164] Examples of modified internucleotide linkages include, but are not limited, to, a phosphorodithioate linkage, a phosphorothioate linkage, a phosphotriester linkage, a thionoalkylphosphonate linkage, a thionalkylphosphotriester linkage, a phosphoramidite linkage, a phosphonate linkage, or a boranophosphate linkage. In some embodiments, at least one modified internucleotide linkage of any one of the oligonucleotides as disclosed herein is a phosphorothioate linkage.

[00165] In some embodiments, the oligonucleotides herein include a phosphorothioate linkage between one or more of positions 1 and 2 of the sense strand, positions 1 and 2 of the antisense

strand, positions 2 and 3 of the antisense strand, positions 3 and 4 of the antisense strand, positions 20 and 21 of the antisense strand, and positions 21 and 22 of the antisense strand. In other embodiments, the oligonucleotides comprise a phosphorothioate linkage between each of positions 1 and 2 of the sense strand, positions 1 and 2 of the antisense strand, positions 2 and 3 of the antisense strand, positions 3 and 4 of the antisense strand positions 20 and 21 of the antisense strand, and positions 21 and 22 of the antisense strand.

[00166] In certain embodiments, an oligonucleotide herein includes:

a sense strand having a 2'-F modified nucleotide at positions 8 to 11, a 2'-OMe modified nucleotide at positions 1 to 7, 12 to 27 and 31 to 36, a GalNAc-conjugated nucleotide at position 28, 29 and 30, and a phosphorothioate linkage between positions 1 and 2;

an antisense strand having a 2'-F modified nucleotide at positions 2 to 5, 7, 10 and 14, a 2'-OMe at positions 1, 6, 8 to 9, 11 to 13 and 15 to 22, a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 3 and 4, positions 20 and 21, and positions 21 and 22, and a 5'-terminal nucleotide at position 1 comprising a 4'-phosphate analog, optionally wherein the 5'-terminal nucleotide comprises 4-O-monomethylphosphonate-2'-O-methyl uridine [MePhosphonate-4O-mU]; where positions 1 to 20 of the antisense strand form a duplex region with positions 1 to 20 of the sense strand, where positions 21 to 36 of the sense strand form a stem-loop, where positions 27 to 30 form the loop of the stem-loop, optionally where positions 27 to 30 comprise a tetraL, where positions 21 and 22 of the antisense strand comprise an overhang, and where the sense strand and antisense strands are selected from Table 3, optionally from the group consisting of:

(a) SEQ ID NOs: 139 and 140,

(b) SEQ ID NOs: 147 and 148,

(c) SEQ ID NOs: 221 and 222,

(d) SEQ ID NOs: 273 and 274,

(e) SEQ ID NOs: 321 and 322,

(f) SEQ ID NOs: 333 and 334, and

(g) SEQ ID NOs: 361 and 362.

[00167] In certain other embodiments, the modified sense strand and antisense strands are selected from Table 4, optionally from the group consisting of:

(a') SEQ ID NOs: 523 and 524,

(b') SEQ ID NOs: 531 and 532,

(c') SEQ ID NOs:605 and 606,

(d') SEQ ID NOs: 657 and 658,

(e') SEQ ID NOs: 705 and 706,

(f') SEQ ID NOs: 717 and 718, and

(g') SEQ ID NOs: 745 and 746.

[00168] D. Base Modifications: In addition to the above modifications, the oligonucleotides herein (*e.g.*, a ds oligonucleotide) also comprise one or more modified nucleobases. In some embodiments, modified nucleobases (also referred to herein as base analogs) are linked at the 1' position of a nucleotide sugar moiety. In some embodiments, the modified nucleobase is a nitrogenous base. In other embodiments, the modified nucleobase does not contain nitrogen atom. *See*, *e.g.*, US Patent Application Publication No. 2008/0274462. In certain other embodiments, the modified nucleotide is a universal base. However, in certain embodiments, the modified nucleotide does not contain a nucleobase (abasic).

[00169] With regard to universal bases, they comprise a heterocyclic moiety located at the 1' position of a nucleotide sugar moiety in a modified nucleotide, or the equivalent position in a nucleotide sugar moiety substitution, that, when present in a duplex, is positioned opposite more than one type of base without substantially altering structure of the duplex. Moreover, and compared to a reference ss nucleic acid (*e.g.*, oligonucleotide) that is fully complementary to a target nucleic acid, a ss nucleic acid having a universal base forms a duplex with the target nucleic acid that has a lower T_m than a duplex formed with the complementary nucleic acid. However, when compared to a reference ss nucleic acid in which the universal base has been replaced with a base to generate a single mismatch, the ss nucleic acid having the universal base forms a duplex with the target nucleic acid that has a higher T_m than a duplex formed with the nucleic acid having the mismatched base.

[00170] Exemplary universal-binding nucleotides include, but are not limited to, inosine, 1-β-D-ribofuranosyl-5-nitroindole and/or 1-β-D-ribofuranosyl-3-nitropyrrole (*see*, *e.g.*, US Patent Application Publication No. 2007/0254362; Van Aerschot *et al.* (1995) NUCLEIC ACIDS RES. 23:4363-70; Loakes *et al.* (1995) NUCLEIC ACIDS RES. 23:2361-66; and Loakes & Brown (1994) NUCLEIC ACIDS RES. 22:4039-403).

[00171] E. Reversible Modifications: While certain modifications can be made to protect the oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) from the *in vivo* environment before reaching target cells, they also can be made to reduce the potency or

activity of the oligonucleotides once they reach the cytosol of the target cell. Reversible modifications therefore can be made such that the oligonucleotide retains desirable properties outside of the cell, which are then removed upon entering the cytosolic environment of the cell. Reversible modification can be removed, for example, by the action of an intracellular enzyme or by the chemical conditions inside of a cell (*e.g.*, through reduction by intracellular glutathione).

[00172] In some embodiments, a reversibly modified nucleotide comprises a glutathione-sensitive moiety. Typically, oligonucleotides are chemically modified with cyclic disulfide moieties to mask the negative charge created by the internucleotide diphosphate linkages and to improve cellular uptake and nuclease resistance. *See*, US Patent Application Publication No. 2011/0294869, Intl. Patent Application Publication Nos. WO 2014/088920 and WO 2015/188197, and Meade *et al.* (2014) NAT. BIOTECHNOL. 32:1256-63. This reversible modification of the internucleotide diphosphate linkages is designed to be cleaved intracellularly by the reducing environment of the cytosol (*e.g.*, glutathione). Earlier examples include neutralizing phosphotriester modifications that are reported to be cleavable inside cells (*see*, *e.g.*, Dellinger *et al.* (2003) J. AM. CHEM. SOC. 125:940-50).

[00173] Some reversible modifications protect the oligonucleotide during *in vivo* administration (*e.g.*, transit through the blood and/or lysosomal/endosomal compartments of a cell) where the oligonucleotide will be exposed to nucleases and other harsh environmental conditions (*e.g.*, pH). When released into the cytosol of a cell where the levels of glutathione are higher compared to extracellular space, the modification is reversed, and the result is cleaved oligonucleotide. Using reversible, glutathione-sensitive moieties, it is possible to introduce sterically larger chemical groups into the oligonucleotide when compared to the options available using irreversible chemical modifications. This is because these larger chemical groups will be removed in the cytosol and, therefore, should not interfere with the biological activity of the oligonucleotide inside the cytosol of a cell. As a result, these larger chemical groups can be engineered to confer various advantages to the oligonucleotide, such as nuclease resistance, lipophilicity, charge, thermal stability, specificity, and reduced immunogenicity. In some embodiments, the structure of the glutathione-sensitive moiety can be engineered to modify the kinetics of its release.

[00174] In some embodiments, the glutathione-sensitive moiety is attached to the sugar of a nucleotide. In certain embodiments, the glutathione-sensitive moiety is attached to the 2'-carbon of the sugar of a modified nucleotide. Additionally, or alternatively, the glutathione-

sensitive moiety is attached to the 5'-carbon of a sugar, particularly when the modified nucleotide is the 5'-terminal nucleotide of the oligonucleotide. Additionally, or alternatively, the glutathione-sensitive moiety is attached to the 3'-carbon of sugar, particularly when the modified nucleotide is the 3'-terminal nucleotide of the oligonucleotide. In some embodiments, the glutathione-sensitive moiety includes a sulfonyl group (*see, e.g.*, Intl. Patent Application Publication No. WO 2018/039364).

[00175] VI. Targeting Ligands: It is desirable to target the oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) to one or more cells or one or more organs. Such a strategy can help to avoid undesirable effects in other organs or to avoid undue loss of the oligonucleotide to cells, tissue, or organs that would not benefit therefrom. Accordingly, the oligonucleotide can be modified to facilitate targeting and/or delivering to a tissue, cell, or organ (*e.g.*, to facilitate delivering the oligonucleotides to the liver). In some embodiments, the oligonucleotide is modified to facilitate its delivery to the hepatocytes of the liver. In some embodiments, the oligonucleotide comprises at least one nucleotide (*e.g.*, 1, 2, 3, 4, 5, 6, or more nucleotides) conjugated to one or more targeting ligand(s).

[00176] Exemplary targeting ligands include, but are not limited to, a carbohydrate, amino sugar, cholesterol, peptide, polypeptide, protein, or part of a protein (*e.g.*, an antibody or antibody fragment), or lipid. In some embodiments, the targeting ligand is an aptamer. For example, the targeting ligand is an Arg-Gly-Asp (RGD) peptide for targeting tumor vasculature or glioma cells, Cys-Arg-Glu-Lys-Ala (CREKA) peptide for targeting tumor vasculature or stoma, transferrin, lactoferrin, or an aptamer for targeting transferrin receptors expressed on central nervous system (CNS) vasculature, or an anti-epidermal growth factor receptor (EGFR) antibody for targeting EGFR on glioma cells. In certain embodiments, the targeting ligand is one or more GalNAc moieties.

[00177] In some embodiments, 1 or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of the oligonucleotides each can be conjugated to a separate targeting ligand. In some embodiments, 2 to 4 nucleotides of the oligonucleotide each are conjugated to a separate targeting ligand. In other embodiments, targeting ligands can be conjugated to 2 to 4 nucleotides at either ends of the sense strand or antisense strand (*e.g.*, targeting ligands are conjugated to a 2 to 4 nucleotide overhang or extension on the 5' or 3' end of the sense strand or antisense strand) such that the targeting ligands resemble bristles of a toothbrush, and the oligonucleotide resembles a toothbrush. For example, the oligonucleotide comprises a stem-loop at either the 5' or 3' end of

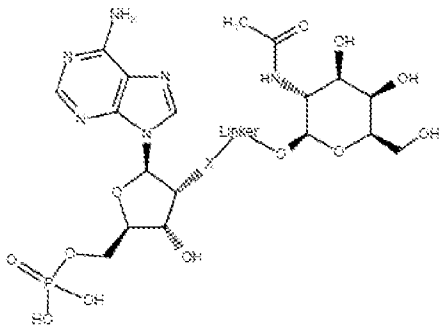
the sense strand and 1, 2, 3, or 4 nucleotides of the L of the stem-loop may be individually conjugated to a targeting ligand. In some embodiments, the oligonucleotide comprises a stem-loop at the 3' end of the sense strand, where the L of the stem-loop includes a triL or a tetraL, and where the 3 or 4 nucleotides of the triL or tetraL, respectfully, are individually conjugated to a targeting ligand.

[00178] GalNAc is a high affinity ligand for the ASGPR, which is primarily expressed on the sinusoidal surface of hepatocyte cells and has a major role in binding, internalizing, and subsequent clearing circulating glycoproteins that contain terminal galactose or GalNAc residues (asialoglycoproteins). Conjugation (either indirect or direct) of GalNAc moieties to the oligonucleotides herein are used to target them to the ASGPR expressed on cells. In some embodiments, the oligonucleotides are conjugated to at least one or more GalNAc moieties, where the GalNAc moieties target the oligonucleotides to an ASGPR expressed on human liver cells (*e.g.*, human hepatocytes).

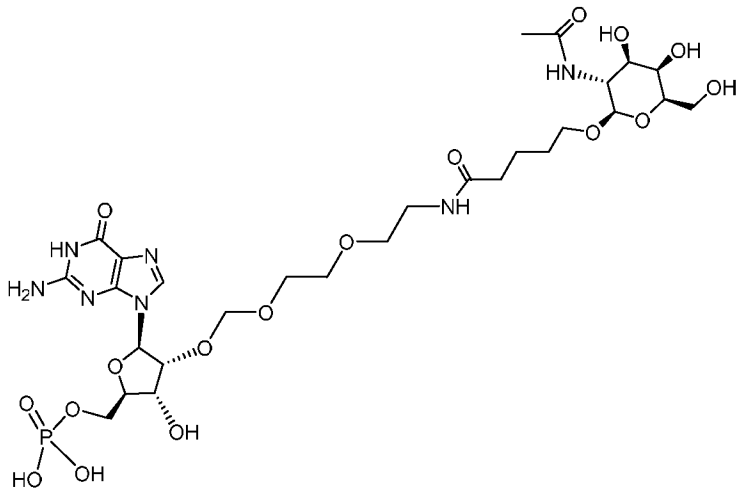
[00179] The oligonucleotides are conjugated directly or indirectly to a monovalent GalNAc. In some embodiments, the oligonucleotides are conjugated directly or indirectly to more than 1 monovalent GalNAc (*i.e.*, is conjugated to 2, 3, or 4 monovalent GalNAc moieties, and is typically conjugated to 3 or 4 monovalent GalNAc moieties). In some embodiments, the oligonucleotides are conjugated to one or more bivalent GalNAc, trivalent GalNAc, or tetravalent GalNAc moieties.

[00180] In some embodiments, 1 or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of the oligonucleotides each can be conjugated to a GalNAc moiety. In some embodiments, 2 to 4 nucleotides of a L each are conjugated to a separate GalNAc. In other embodiments, 1 to 3 nucleotides of a triL each are conjugated to a separate GalNAc. In some embodiments, the targeting ligands are conjugated to 2 to 4 nucleotides at either end of the sense or antisense strand (*e.g.*, ligands are conjugated to a 2 to 4 nucleotide overhang or extension on the 5' or 3' end of the sense or antisense strand) such that the GalNAc moieties resemble bristles of a toothbrush, and the oligonucleotide resembles a toothbrush. In some embodiments, the GalNAc moieties are conjugated to a nucleotide of the sense strand. For example, 4 GalNAc moieties are conjugated to nucleotides in the L of the sense strand, where each GalNAc moiety is conjugated to 1 nucleotide. In certain embodiments, 3 GalNAc moieties are conjugated to nucleotides in the L of the sense strand, where each GalNAc moiety is conjugated to 1 nucleotide.

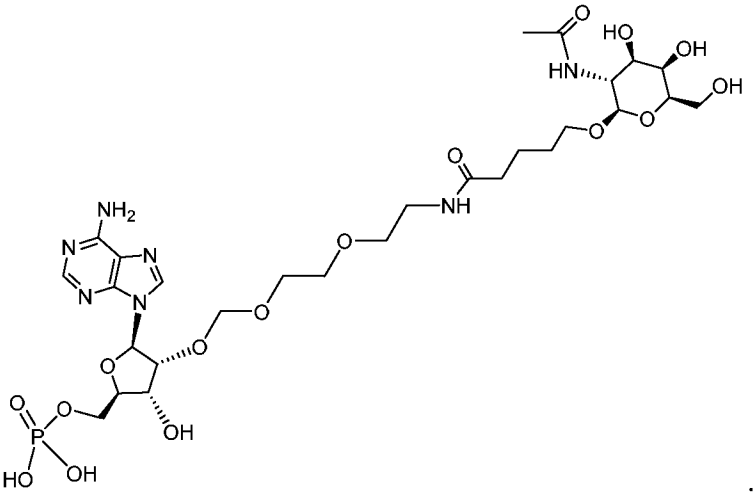
[00181] In some embodiments, the oligonucleotides herein comprise a GalNAc attached to any one or more nucleotides of a triL or tetraL via any linker described herein, as depicted below (X = heteroatom):



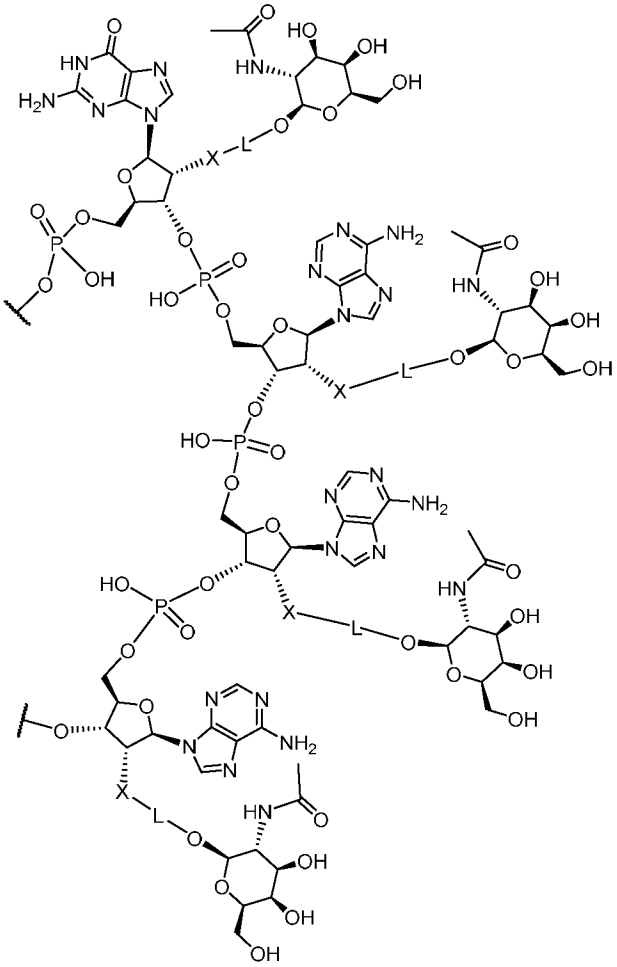
[00182] In certain embodiments, the oligonucleotides herein comprise a monovalent GalNAc attached to a guanine nucleotide referred to as 2'-aminodiethoxymethanol-Guanine-GalNAc or [ademG-GalNAc], as depicted below:



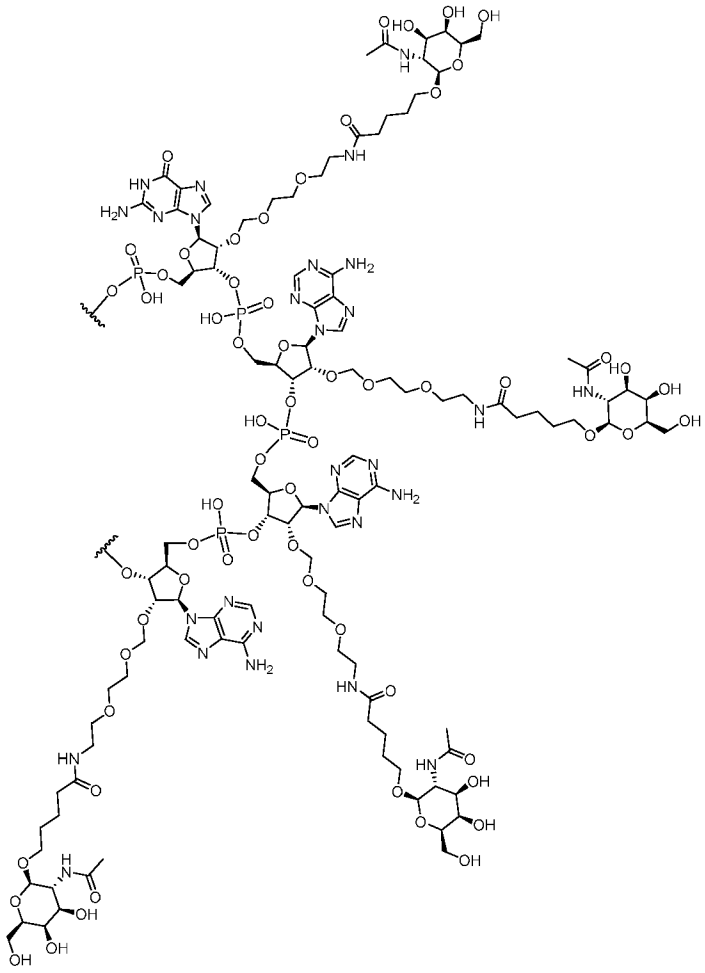
[00183] In certain embodiments, the oligonucleotides herein comprise a monovalent GalNAc attached to an adenine nucleotide, referred to as 2'-aminodiethoxymethanol-Adenine-GalNAc or [ademA-GalNAc], as depicted below:



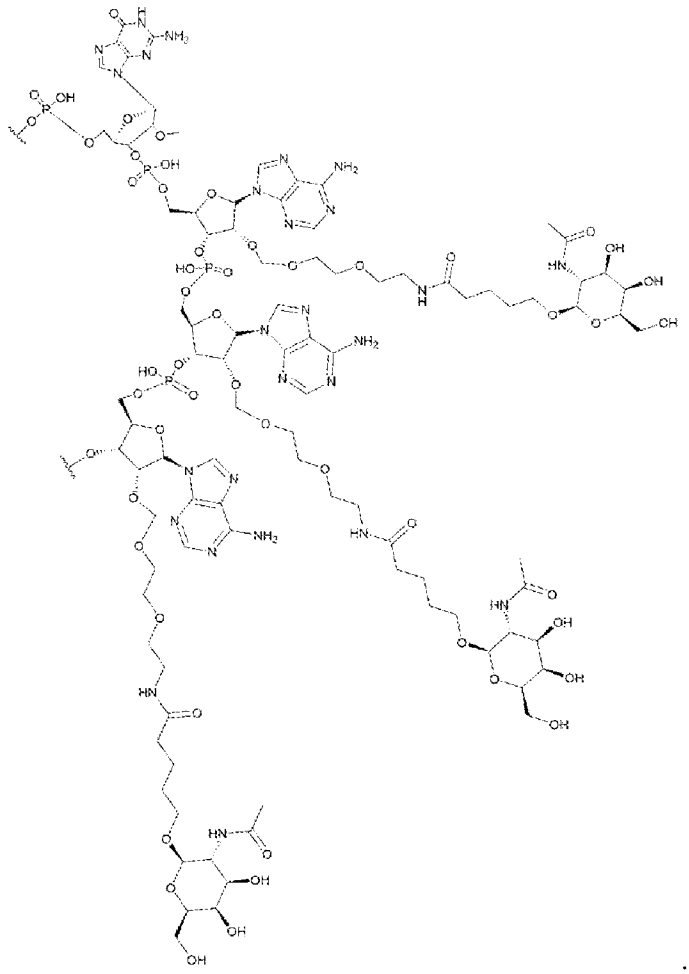
[00184] An example of such conjugation is shown below for a tetraL having from 5' to 3', the nucleotide sequence GAAA (L = linker, X = heteroatom), where stem attachment points are shown. Such a tetraL is present, for example, at positions 27-30 of the sense strand listed in Tables 3 and 4, and as shown in FIG. 1. In the chemical formula,  is used to describe an attachment point to the oligonucleotide strand:



[00185] Appropriate methods or chemistry (*e.g.*, click chemistry) are used to link a targeting ligand to a nucleotide. One way of conjugating the targeting ligand to a nucleotide is by using a click linker. In some embodiments, an acetal-based linker is used to conjugate the targeting ligand to a nucleotide of any one of the oligonucleotides herein. Acetal-based linkers are disclosed, for example, in Intl. Patent Application Publication No. WO 2016/100401. In some embodiments, the linker is a labile linker. However, in other embodiments, the linker is stable. An example is shown below for a teraL having from 5' to 3', the nucleotides GAAA, in which GalNAc moieties are attached to nucleotides of the loop using an acetal linker. Such a loop is present, for example, at positions 27-30 of the any one of the sense strands listed in Tables 3 or 4. In the chemical formula,  is an attachment point to the oligonucleotide strand:



, or



[00186] In some embodiments, a duplex extension (*e.g.*, of up to 3, 4, 5, or 6 bp in length) is provided between the targeting ligand (*e.g.*, a GalNAc moiety), and the oligonucleotide. In other embodiments, the oligonucleotide does not have a GalNAc conjugated thereto.

[00187] Formulations and Pharmaceutical Compositions

[00188] The oligonucleotides herein (*e.g.*, a ds oligonucleotide), or a pharmaceutically acceptable salt thereof (*e.g.*, trifluroacetate salts, acetate salts or hydrochloride salts), are incorporated into a formulation or pharmaceutical composition. Various formulations have been developed to facilitate oligonucleotide use. For example, oligonucleotides can be delivered to an individual or a cellular environment using a formulation that minimizes degradation, facilitates delivery and/or uptake, or provides another beneficial property to the oligonucleotides in the formulation. In some embodiments, the oligonucleotides are formulated

in buffer solutions such as phosphate buffered saline solutions, liposomes, micellar structures, and capsids.

[00189] To improve *in vivo* compatibility and effectiveness, the oligonucleotides may be reacted with any of a number of inorganic and organic acids/bases to form pharmaceutically acceptable acid/base addition salts. Pharmaceutically acceptable salts and common methodologies for preparing them are well known in the art (*see*, *e.g.*, Stahl *et al.*, "Handbook of Pharmaceutical Salts: Properties, Selection and Use," 2nd Revised Edition (Wiley-VCH, 2011)). Pharmaceutically acceptable salts for use herein include sodium, trifluoroacetate, hydrochloride and acetate salts.

[00190] Formulations of oligonucleotides herein with cationic lipids are used to facilitate transfection of the oligonucleotides into cells. For example, cationic lipids, such as lipofectin, cationic glycerol derivatives, and polycationic molecules (*e.g.*, polylysine) can be used. Suitable lipids include Oligofectamine (ThermoFisher Technologies), Lipofectamine (Life Technologies), NC388 (Ribozyme Pharmaceuticals, Inc.), or FuGene 6 (Roche), all of which are used according to the manufacturer's instructions.

[00191] Accordingly, in some embodiments, the formulations herein comprise a liposome, a lipid, a lipid complex, a microsphere, a microparticle, a nanosphere, or a nanoparticle (such as a lipid nanoparticle) or may be otherwise formulated for administration to the cells, tissues, organs, or body of an individual in need thereof (*see*, *e.g.*, Remington, "The Science and Practice of Pharmacy" (L.V. Allen Jr., ed., 22nd Edition, Pharmaceutical Press, 2013).

[00192] In some embodiments, the formulations herein further comprise an excipient, which can confer to a composition improved stability, improved absorption, improved solubility and/or therapeutic enhancement of the active ingredient. In some embodiments, the excipient is a buffering agent (*e.g.*, sodium citrate, sodium phosphate, a tris base, or sodium hydroxide) or a vehicle (*e.g.*, a buffered solution, petrolatum, dimethyl sulfoxide, or mineral oil). In some embodiments, the oligonucleotides herein are lyophilized for extending shelf-life and then made into a solution before use (*e.g.*, administration to an individual). Accordingly, the excipient in a pharmaceutical composition including one or more of the oligonucleotides is a lyoprotectant (*e.g.*, mannitol, lactose, polyethylene glycol, or polyvinylpyrrolidone) or a collapse temperature modifier (*e.g.*, dextran, Ficoll™, or gelatin).

[00193] Pharmaceutical compositions are formulated to be compatible with its intended route of administration. Routes of administration include, but are not limited to, parenteral (*e.g.*,

intravenous, intramuscular, intraperitoneal, intradermal, and subcutaneous), oral (*e.g.*, inhalation), transdermal (*e.g.*, topical), transmucosal, and rectal administration.

[00194] Pharmaceutical compositions suitable for injectable use comprise sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include, but are not limited to, physiological saline, bacteriostatic water, Cremophor EL™ (BASF) or phosphate buffered saline (PBS). The carrier is a solvent or dispersion medium containing, for example, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, liquid polyethylene glycol, and the like), as well as suitable mixtures thereof. In many embodiments, it will be preferable to comprise in the compositions with isotonic agents such as, for example, sugars, polyalcohols such as mannitol, sorbitol and/or sodium chloride. Sterile injectable solutions are prepared by incorporating the oligonucleotides herein in a required amount in a selected solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization.

[00195] Moreover, the pharmaceutical compositions comprise at least about 0.1% of a therapeutic agent (*e.g.*, one or more of the oligonucleotides herein) or more, although the percentage of the therapeutic agent may be between about 1% to about 80% or more of the weight or volume of the total composition. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one of skill in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

[00196] Even though several examples are directed toward liver-targeted delivery of at least one of the oligonucleotides herein, targeting of other tissues also is contemplated.

[00197] Kits

[00198] The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) can be incorporated into a kit comprising one or more of the oligonucleotides herein, and instructions for use. In some embodiments, the kit comprises one or more of the oligonucleotides, and a package insert containing instructions for use of the kit and/or any component thereof. In other embodiments, the kit comprises a suitable container, one or more of the oligonucleotides, one or more controls, and various buffers, reagents, enzymes, and other standard ingredients as are known in the art.

[00199] In some embodiments, the container can be at least one vial, well, test tube, flask, bottle, syringe, or other container means, into which the one or more oligonucleotides are placed, and in some embodiments, suitably aliquoted. In other embodiments, where an additional component is provided, the kit contains additional containers into which this component is placed. The kit also comprises a means for containing the one or more oligonucleotides and any other reagent in close confinement for commercial sale. Such containers include injection or blow-molded plastic containers into which the desired vials are retained. Containers and/or kits comprise labeling with instructions for use and/or warnings.

[00200] In some embodiments, the kit comprises one or more oligonucleotides herein, and a pharmaceutically acceptable carrier, or a pharmaceutical composition comprising one or more of the oligonucleotides and instructions for treating or delaying progression of a disease, disorder, or condition associated with *SCAP* activity in an individual in need thereof.

[00201] *Methods*

[00202] Methods of Making

[00203] The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) are made using methods and/or techniques known to one of skill in the art such as, for example, conventional nucleic acid solid-phase synthesis. The polynucleotides of the oligonucleotides are assembled on a suitable nucleic acid synthesizer utilizing standard nucleotide or nucleoside precursors (*e.g.*, phosphoramidites). Automated nucleic acid synthesizers, including DNA/RNA synthesizers, are commercially available from, for example, Applied Biosystems (Foster City, CA), BioAutomation (Irving, TX), and GE Healthcare Life Sciences (Pittsburgh, PA).

[00204] As one of skill in the art understands, other methods and/or techniques of synthesizing oligonucleotides may be used. Additionally, the various synthetic steps are performed in an alternate sequence or order to give the desired compounds. Other synthetic chemistry transformations, protecting groups (*e.g.*, for hydroxyl, amino, *etc.* present on the bases), and protecting group methodologies (protection and deprotection) useful in synthesizing the oligonucleotides are known in the art and are described in, for example, Larock, "Comprehensive Organic Transformations," VCH Publishers (1989); Greene & Wuts, PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, 2nd Ed., John Wiley & Sons (1991); Fieser & Fieser, FIESER AND FIESER'S REAGENTS FOR ORGANIC SYNTHESIS, John Wiley & Sons (1994);

and Paquette, ed., ENCYCLOPEDIA OF REAGENTS FOR ORGANIC SYNTHESIS, John Wiley & Sons (1995).

[00205] Methods of Using

[00206] I. Methods of Reducing *SCAP* Activity in Cells, Tissue, Organs, and Organisms:

[00207] The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as RNAi oligonucleotides) are used to reduce SCAP mRNA, SCAP protein and/or SCAP activity in cells, tissues, organs, or individuals. The methods comprise the steps described herein, and these may be, but not necessarily, carried out in the sequence as described. Other sequences, however, also are conceivable. Moreover, individual, or multiple steps are carried out either in parallel and/or overlapping in time and/or individually or in multiply repeated steps. Furthermore, the methods comprise additional, unspecified steps.

[00208] The methods comprise contacting or delivering to a cell, population of cells, tissues, organs, or individuals an effective amount any of the oligonucleotides herein for reducing *SCAP* expression. In some embodiments, reduced *SCAP* activity is determined by measuring a reduction in the amount or level of SCAP mRNA, SCAP protein, and/or SCAP activity in a cell.

[00209] With regard to an appropriate cell type, the cell type is any cell that expresses mRNA (*e.g.*, hepatocytes, macrophages, monocyte-derived cells, prostate cancer cells, cells of the brain, endocrine tissue, bone marrow, lymph nodes, lung, gall bladder, liver, duodenum, small intestine, pancreas, kidney, gastrointestinal tract, bladder, adipose and soft tissue, and skin). In some embodiments, the cell is a primary cell obtained from an individual. In some embodiments, the primary cell has undergone a limited number of passages such that the cell substantially maintains is natural phenotypic properties. In some embodiments, the cell is an *ex vivo*, *in vivo*, or *in vitro* cell (*i.e.*, such that one or more of the oligonucleotides herein can be delivered to the cell in culture or to an organism in which the cell resides).

[00210] In some embodiments, the oligonucleotides herein are delivered to a cell or population of cells using a nucleic acid delivery method known in the art including, but not limited to, injecting a solution containing the oligonucleotides, bombarding by particles covered by the oligonucleotides, exposing the cell or population of cells to a solution containing the oligonucleotides, or electroporating cell membranes in the presence of the oligonucleotides. Other methods known in the art for delivering oligonucleotides to cells are used such as, for

example, lipid-mediated carrier transport, chemical-mediated transport, and cationic liposome transfection such as calcium phosphate, and others.

[00211] Reduced *SCAP* activity is determined by an assay or technique that evaluates one or more molecules, properties or characteristics of a cell or population of cells associated with *SCAP* gene expression (*e.g.*, using a *SCAP* expression biomarker) or by an assay or technique that evaluates molecules that are directly indicative of *SCAP* activity in a cell or population of cells (*e.g.*, SCAP mRNA, SCAP protein and/or SCAP activity). In some embodiments, the extent to which the oligonucleotides reduce *SCAP* activity are evaluated by comparing *SCAP* activity in a cell or population of cells contacted with the oligonucleotides to a control cell or population of cells (*e.g.*, a cell or population of cells not contacted with the oligonucleotides or contacted with a control oligonucleotide). In some embodiments, a control amount or level of *SCAP* activity in a control cell or population of cells is predetermined, such that the control amount or level need not be measured in every instance the assay or technique is performed. The predetermined level or value takes a variety of forms including, but not limited to, a single cut-off value, such as a median or mean.

[00212] Contacting or delivering the oligonucleotides herein to a cell or a population of cells result in reduced *SCAP* activity. In some embodiments, reduced *SCAP* activity is relative to a control amount or level of *SCAP* activity in the cell or the population of cells not contacted with the oligonucleotides or contacted with a control oligonucleotide. In some embodiments, reduced *SCAP* activity is about 1% or lower, about 5% or lower, about 10% or lower, about 15% or lower, about 20% or lower, about 25% or lower, about 30% or lower, about 35% or lower, about 40% or lower, about 45% or lower, about 50% or lower, about 55% or lower, about 60% or lower, about 70% or lower, about 80% or lower, or about 90% or lower relative to a control amount or level of *SCAP* activity. In some embodiments, the control amount or level of *SCAP* activity is an amount or level of SCAP mRNA, SCAP protein and/or SCAP activity in the cell or the population of cells that has not been contacted with oligonucleotides herein. In some embodiments, the effect of delivery of the oligonucleotides to the cell or the population of cells according to a method herein is assessed after any finite period or amount of time (*e.g.*, minutes, hours, days, weeks, and/or months). For example, *SCAP* activity is determined in the cell or the population of cells at least about 4 hours, about 8 hours, about 12 hours, about 18 hours, or about 24 hours. Alternatively, *SCAP* activity is determined in the cell or the population of cells at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 11 days,

about 12 days, about 13 days, about 14 days, about 21 days, about 28 days, about 35 days, about 42 days, about 49 days, about 56 days, about 63 days, about 70 days, about 77 days, or about 84 days or more after contacting or delivering the oligonucleotides to the cell or population of cells. In other embodiments, *SCAP* activity is determined in the cell or the population of cells at least about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, or about 6 months or more after contacting or delivering the oligonucleotides to the cell or the population of cells.

[00213] In some embodiments, the oligonucleotides herein are delivered in the form of a transgene that is engineered to express in a cell one or more of the oligonucleotides or strands (*e.g.*, sense and antisense strands). For example, the oligonucleotides are delivered using a transgene engineered to express any oligonucleotide herein. Transgenes may be delivered using viral vectors (*e.g.*, adenovirus, retrovirus, vaccinia virus, poxvirus, adeno-associated virus, or herpes simplex virus) or non-viral vectors (*e.g.*, plasmids or synthetic mRNAs). In some embodiments, the transgenes are injected directly to an individual.

[00214] II. Methods of Treatment:

[00215] Methods of treating an individual having, suspected of having, or at risk of developing a disease, disorder, or condition associated with *SCAP* activity comprise administering at least one or more of the oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) to the individual. Additionally, methods of treating or attenuating an onset or progression of a disease, disorder, or condition associated with *SCAP* activity in an individual comprise using one or more of the oligonucleotides herein. Furthermore, methods of achieving one or more therapeutic benefits in an individual having a disease, disorder, or condition associated with *SCAP* activity comprise providing one or more of the oligonucleotides herein. In some embodiments, the individual can be treated by administering a therapeutically effective amount of any one or more of the oligonucleotides herein. In some embodiments, the treatment comprises reducing *SCAP* activity. In some embodiments, the individual is treated therapeutically. In some embodiments, the individual is treated prophylactically. In all of these embodiments, the oligonucleotide of interest is selected from Table 3 or 4.

[00216] In some embodiments, the one or more oligonucleotides, or a pharmaceutical composition including the same, is administered to the individual having a disease, disorder, or condition associated with *SCAP* activity such that SCAP activity is reduced in the individual, thereby treating the individual. In some embodiments, an amount or level of SCAP mRNA is

reduced in the individual. In other embodiments, an amount or level of SCAP protein is reduced in the individual. In still other embodiments, an amount or level of SCAP activity is reduced in the individual. In yet other embodiments, an amount or level of liver TG (*e.g.*, one or more TG(s) or total TGs in liver) and/or cholesterol is reduced in the individual, especially in the liver. In still other embodiments, an amount or level of liver inflammation can be reduced. In still other embodiments, an amount of level of liver fibrosis is reduced. In still other embodiments, an amount or level of plasma aspartate aminotransferase (AST), plasma alanine aminotransferase (ALT), plasma Cytokeratin 18 (CK-18), or even plasma N-terminal type III collagen propeptide (Pro-C3) is reduced. In any of the above disclosed embodiments, the oligonucleotides comprise a sense strand having a nucleotide sequence of any one of SEQ ID NOs:532, 531, 605, 657, 705, 717 and 745, and an antisense strand having a nucleotide sequence of any one of SEQ ID NOs:524, 532, 606, 658, 706, 718 and 746.

[00217] In some embodiments, *SCAP* activity is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to *SCAP* activity prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In other embodiments, *SCAP* activity is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to *SCAP* activity in an individual (*e.g.*, a reference or control individual) not receiving the one or more oligonucleotides or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment.

[00218] In certain embodiments, an amount or level of SCAP mRNA is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP mRNA prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In some embodiments, the amount or level of SCAP mRNA is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP mRNA in an individual (*e.g.*, a reference or control individual) not administered the one or more oligonucleotides or

pharmaceutical composition or administered a control oligonucleotide, pharmaceutical composition, or treatment.

[00219] In certain embodiments, an amount or level of SCAP protein is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP protein prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In other embodiments, an amount or level of SCAP protein is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP protein in an individual (*e.g.*, a reference or control individual) not administered the one or more oligonucleotides or pharmaceutical composition or administered a control oligonucleotide, pharmaceutical composition or treatment.

[00220] In certain embodiments, an amount or level of SCAP activity is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP activity prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In some embodiments, the amount or level of SCAP activity is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of SCAP activity in an individual (*e.g.*, a reference or control individual) not administered the one or more oligonucleotides or pharmaceutical composition or administered a control oligonucleotide, pharmaceutical composition or treatment.

[00221] In certain embodiments, an amount or level of TG, especially liver TG, can be reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of TG prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In some embodiments, the amount or level of TG is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about

70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of TG in an individual (*e.g.*, a reference or control individual) not administered the one or more oligonucleotides or pharmaceutical composition or administered a control oligonucleotide, pharmaceutical composition or treatment.

[00222] In certain embodiments, an amount or level of cholesterol, especially liver cholesterol, can be reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of cholesterol prior to administering the one or more oligonucleotides or pharmaceutical composition thereof. In some embodiments, the amount or level of cholesterol is reduced in the individual by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of cholesterol in an individual (*e.g.*, a reference or control individual) not administered the one or more oligonucleotides or pharmaceutical composition or administered a control oligonucleotide, pharmaceutical composition or treatment.

[00223] Here, *SCAP* activity, the amount or level of SCAP mRNA, SCAP protein, SCAP activity, liver TG, liver cholesterol, or any combination thereof, is reduced in a cell (*e.g.*, a hepatocyte), a population or a group of cells (*e.g.*, an organoid), a tissue (*e.g.*, liver tissue), a sample (*e.g.*, a liver biopsy sample), an organ (*e.g.*, liver), blood or a fraction thereof (*e.g.*, plasma), or any other biological material obtained or isolated from the individual. In some embodiments, *SCAP* activity, the amount or level of SCAP mRNA, SCAP protein, SCAP activity, TG, cholesterol, or any combination thereof, is reduced in more than one type of cell (*e.g.*, a hepatocyte and one or more other type(s) of cell), more than one groups of cells, more than one type of tissue (*e.g.*, liver tissue and one or more other type(s) of tissue), more than one type of sample (*e.g.*, a liver biopsy sample and one or more other type(s) of biopsy sample), more than one organ (*e.g.*, liver and one or more other organ(s)), more than one fraction of blood (*e.g.*, plasma and one or more other blood fraction(s)) obtained or isolated from the individual.

[00224] Examples of a disease, disorder, or condition associated with *SCAP* activity include, but are not limited to, AH, ALD, CCA, cirrhosis, hepatic fibrosis, hepatic inflammation, HCC, liver steatosis, NAFLD, NASH and PSC, as well as related diseases, disorders, and conditions

in an individual such as, for example, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, ASCVD, diabetes and/or obesity, or a combination thereof.

[00225] Because of their high specificity, the oligonucleotides herein specifically target mRNAs of target genes of cells, tissues, or organs (*e.g.*, liver). In preventing disease, the target gene is the one that is required for initiation or maintenance of the disease or that has been identified as being associated with a higher risk of contracting the disease. In treating disease, one or more of the oligonucleotides herein are brought into contact with the cells, tissue or organ exhibiting or responsible for mediating the disease. For example, an oligonucleotide substantially complimentary to all or part of a wild-type (*i.e.*, native) or mutated gene associated with a disease, disorder, or condition associated with *SCAP* activity is brought into contact with or introduced into a cell or tissue type of interest such as a hepatocyte or other liver cell.

[00226] In some embodiments, the target gene is from any mammal, such as a human. Any gene may be silenced according to the methods herein. Moreover, the methods herein typically involve administering to an individual a therapeutically effective amount of one or more oligonucleotides herein, that is, an amount capable of producing a desirable therapeutic result. The therapeutically acceptable amount is an amount that therapeutically treats a disease or disorder or condition. The appropriate dosage for any one individual will depend on certain factors, including the individual's size, body surface area, age, the composition to be administered, the active ingredient(s) in the composition, time and route of administration, general health, and other therapeutic agents being administered concurrently.

[00227] In the methods, the individual is administered any one of the oligonucleotides or compositions herein either enterally (*e.g.*, orally, by gastric feeding tube, by duodenal feeding tube, *via* gastrostomy, or rectally), parenterally (*e.g.*, subcutaneous injection, intravenous injection or infusion, intra-arterial injection or infusion, intraosseous infusion, intramuscular injection, intracerebral injection, intracerebroventricular injection, or intrathecal), topically (*e.g.*, epicutaneous, inhalational, *via* eye drops, or through a mucous membrane), or by direct injection into a target organ (*e.g.*, the liver of an individual). Typically, the oligonucleotides or compositions are administered intravenously or subcutaneously.

[00228] As a non-limiting set of examples, the oligonucleotides or compositions herein typically are administered quarterly (once every three months), bi-monthly (once every two months), monthly or weekly. For example, the oligonucleotides or compositions are administered every week or at intervals of two, or three weeks. In certain embodiments, the

oligonucleotides, or compositions are administered daily. In some embodiments, an individual is administered one or more loading doses of the oligonucleotides or compositions followed by one or more maintenance doses of the oligonucleotides or compositions.

[00229] In some embodiments, the individual is a human, a NHP, or other mammal. In other embodiments, the individual is a domesticated animal such as a dog or a cats; livestock such as a horse, cattle, pig, sheep, goat, or chicken; and animals such as a mouse, rat, guinea pig or hamster.

[00230] III. Medical Uses: The oligonucleotides herein (*e.g.*, a ds oligonucleotide such as a RNAi oligonucleotide) can be used, or adapted for use, to treat an individual (*e.g.*, a human having a disease, disorder, or condition associated with *SCAP* activity) that would benefit from reducing *SCAP* activity. In some embodiments, the oligonucleotides are provided for use, or adapted for use, to treat an individual having a disease, disorder, or condition associated with *SCAP* activity. Also, the oligonucleotides are provided for use, or adaptable for use, in the manufacture of a medicament or pharmaceutical composition for treating a disease, disorder, or condition associated with *SCAP* activity. In other embodiments, the oligonucleotides are provided for use, or adaptable for use, in targeting SCAP mRNA and reducing SCAP activity (*e.g.*, *via* the RNAi pathway). In other embodiments, the oligonucleotides are provided for use, or adaptable for use, in targeting SCAP mRNA and reducing an amount or level of SCAP mRNA, SCAP protein, and/or SCAP activity (*i.e.*, reducing *SCAP* activity).

[00231] In some embodiments, the methods comprise selecting an individual for treatment based upon the individual having a marker (*e.g.*, a biomarker) for a disease, disorder, or condition associated with *SCAP* activity, or someone predisposed to the same, such as, but not limited to, SCAP mRNA, SCAP protein, SCAP activity, or a combination thereof. Likewise, and as detailed below, the methods also comprise additional steps such as, for example, measuring or obtaining a baseline value for a marker of *SCAP* activity (*e.g.*, SCAP protein or other biomarker) and then comparing such obtained value to one or more other baseline values or values obtained after the individual is administered one or more of the oligonucleotides to assess the effectiveness of treatment.

EXAMPLES

[00232] The following non-limiting examples are offered for purposes of illustration, not limitation.

[00233] SYNTHESIS OF OLIGONUCLEOTIDES

[00234] Example 1: Preparing ds RNAi Oligonucleotides

[00235] *Oligonucleotide synthesizing and purifying:* ds RNAi oligonucleotides in the Examples are chemically synthesized using methods described herein. Generally, ds RNAi oligonucleotides are synthesized using solid phase oligonucleotide synthesis methods as described for 19-23mer siRNAs (*see, e.g.*, Scaringe *et al.* (1990) NUCLEIC ACIDS RES. 18:5433-41 and Usman *et al.* (1987) J. AM. CHEM. SOC. 109:7845-45; *see also*, US Patent Nos. 5,804,683; 5,831,071; 5,998,203; 6,008,400; 6,111,086; 6,117,657; 6,353,098; 6,362,323; 6,437,117 and 6,469,158).

[00236] Individual RNA strands are synthesized and HPLC purified according to standard methods (Integrated DNA Technologies). For example, RNA oligonucleotides are synthesized using solid phase phosphoramidite chemistry, deprotected, and desalted on NAP-5 columns (Amersham Pharmacia Biotech; Piscataway, NJ) using standard techniques (Damha & Olgivie (1993) METHODS MOL. BIOL. 20:81-114; Wincott *et al.* (1995) NUCLEIC ACIDS RES. 23:2677-84). The oligomers are purified using ion-exchange high performance liquid chromatography (IE-HPLC) on an Amersham Source 15Q column (1.0 cm×25 cm; Amersham Pharmacia Biotech) using a 15 min step-linear gradient. The gradient varies from 90:10 Buffers A:B to 52:48 Buffers A:B, where Buffer A is 100 mM Tris pH 8.5 and Buffer B is 100 mM Tris pH 8.5, 1 M NaCl. Samples are monitored at 260 nm and peaks corresponding to the full-length oligonucleotide species are collected, pooled, desalted on NAP-5 columns, and lyophilized.

[00237] The purity of each oligomer is determined by capillary electrophoresis (CE) on a Beckman PACE 5000 (Beckman Coulter, Inc.). The CE capillaries have a 100 μm inner diameter and contain ssDNA 100R Gel (Beckman-Coulter). Typically, about 0.6 nmole of oligonucleotide is injected into a capillary, is run in an electric field of 444 V/cm and is detected by UV absorbance at 260 nm. Denaturing Tris-Borate-7 M-urea running buffer is purchased from Beckman-Coulter. Oligoribonucleotides are obtained that are at least 90% pure as assessed by CE for use in experiments described below. Compound identity is verified by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectroscopy on a Voyager DE™ Biospectometry Work Station (Applied Biosystems) following the manufacturer's recommended protocol. Relative molecular masses of all oligomers are obtained, often within 0.2% of expected molecular mass.

[00238] *Preparing duplexes:* ss RNA oligomers are resuspended (*e.g.*, at 100 μM concentration) in duplex buffer having 100 mM potassium acetate, 30 mM HEPES, pH 7.5. Complementary sense and antisense strands are mixed in equal molar amounts to yield a final solution of, for example, 50 μM duplex. Samples are heated to 100°C for 5 min in RNA buffer (IDT) and are allowed to cool to room temperature before use. The ds RNA oligonucleotides are stored at -20°C. ss RNA oligomers are stored lyophilized or in nuclease-free water at -80°C.

[00239] *IN VITRO* FUNCTION

[00240] Example 2: RNAi Oligonucleotide Modulation of *SCAP* Activity *In Vitro* – DsiRNA-Based Compounds

[00241] *SCAP target sequence identifying:* To identify RNAi oligonucleotide inhibitors of *SCAP* expression, a computer-based algorithm is used to computationally generate SCAP target sequences suitable for assaying *SCAP* expression inhibition by the RNAi pathway. The algorithm provides RNAi oligonucleotide antisense strand sequences that are complementary to suitable *SCAP* target sequences of human SCAP mRNA (*e.g.*, SEQ ID NO:1). Some of the antisense strand sequences identified by the algorithm also are complementary to the corresponding *SCAP* target sequence of mouse and NHP SCAP mRNA (*e.g.*, SEQ ID NOs: 3 and 7, respectively). From this, 192 ds RNAi oligonucleotides (formatted as DsiRNA oligonucleotides) are generated, each with a unique antisense strand having a region of complementarity to a *SCAP* target sequence identified by the algorithm.

[00242] *In vitro cell-based assays:* The ability of each of the 192 DsiRNAs to inhibit *SCAP* expression is determined *via in vitro* cell-based assays. Further, and as shown herein, the nucleotide sequences for the sense strand and antisense strand of the DsiRNAs have a distinct pattern of modified nucleotides and phosphorothioate linkages. Briefly, Huh7 cells stably expressing *SCAP* are transfected with each of the DsiRNAs (1.0 nM) in separate wells of a multi-well cell culture plate. Cells are maintained for 24 hr following transfection, and then levels of remaining SCAP mRNA from the transfected cells are determined using TAQMAN®-based qPCR assays. Two qPCR assays, a 3' assay and a 5' assay, are used to determine mRNA levels as measured by HEX probes (*e.g.*, Hs HPRT-517-591and Hs SFRS9-569-712).

[00243] The results of the Huh7 cell-based assay with the 192 DsiRNAs are shown in Table 1, where the 192 DsiRNAs have antisense strands that are complementary to human, mouse and NHP SCAP mRNA ("triple-common") or that are complementary to human and NHP SCAP mRNA ("double-common"). Transfection of DsiRNA that results in less than or equal to 30%

SCAP mRNA remaining in the cells when compared to negative controls is considered a candidate *SCAP* expression inhibitor (referred to herein as a "hit").

[00244] Table 1: Triple-Common and Double-Common DsiRNA SCAP mRNA Knockdown in Huh7 Cells, 1.0 nM 24 hr-5'and -3' Assays % mRNA Remaining (normalized to Hs HPRT-517 (HEX) and Hs SFRS9-569 (HEX) vs mock control).

	HPRT-517 (HEX)		SFRS9-569 (HEX)		Average	
DsiRNA Oligo	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM
1*	107.4	21.4	106.0	23.5	106.7	1.0
2*	68.9	10.1	52.8	6.2	60.9	11.4
3*	46.4	5.0	39.5	4.7	42.9	4.9
4*	93.2	8.5	72.0	9.6	82.6	15.0
5*	89.3	14.2	69.2	15.6	79.2	14.2
6*	115.4	17.5	115.4	8.0	115.4	0.0
7*	80.3	6.4	76.4	5.8	78.4	2.8
8*	131.0	17.9	126.5	9.7	128.8	3.2
9*	46.8	12.7	42.3	11.1	44.6	3.2
10*	55.4	6.7	53.2	5.4	54.3	1.6
11*	150.4	10.7	125.7	9.2	138.1	17.5
12*	124.7	34.5	122.0	31.5	123.4	1.9
13*	47.8	9.7	47.8	6.0	47.8	0.0
14*	118.5	61.1	132.8	62.8	125.6	10.1
15*	126.7	13.6	125.4	12.5	126.0	0.9
16*	87.3	15.4	91.4	15.7	89.3	2.9
17*	107.4	13.6	105.4	11.8	106.4	1.4
18*	132.1	8.8	133.6	12.2	132.8	1.1
19*	121.1	24.3	109.8	23.5	115.4	8.0
20*	30.5	6.2	36.1	8.3	33.3	3.9
21*	34.4	5.0	42.4	4.4	38.4	5.7
22*	59.7	7.7	67.7	6.8	63.7	5.6
23*	106.6	10.5	111.8	9.8	109.2	3.7
24*	10.5	3.5	9.1	4.4	9.8	1.0
25*	246.5	29.4	152.6	23.9	199.6	66.4
26*	52.0	4.5	41.1	4.5	46.5	7.7
27*	222.2	49.6	175.3	31.2	198.8	33.2
28*	207.2	57.5	156.9	39.5	182.0	35.6
29*	102.7	7.3	96.0	4.8	99.4	4.7
30*	62.1	7.1	70.3	12.4	66.2	5.8
31*	157.0	25.1	121.6	19.7	139.3	25.0
32*	129.3	59.1	131.1	36.6	130.2	1.3
33*	28.1	4.4	24.0	3.4	26.1	2.9
34*	152.3	77.3	166.5	76.4	159.4	10.0
35*	129.4	21.7	124.1	16.7	126.7	3.8
36*	90.1	17.6	89.9	16.3	90.0	0.1
37*	111.7	40.0	111.5	30.2	111.6	0.2

38*	66.9	11.5	73.6	12.5	70.2	4.7
39*	122.1	24.4	123.0	24.7	122.6	0.6
40*	100.7	11.1	93.5	15.4	97.1	5.1
41*	54.0	6.9	54.0	7.9	54.0	0.0
42*	29.3	12.8	39.4	14.5	34.3	7.1
43*	21.0	6.1	18.2	5.5	19.6	1.9
44*	25.5	5.1	29.8	6.3	27.6	3.0
45*	81.3	39.1	89.7	47.4	85.5	6.0
46*	73.8	23.5	83.3	25.4	78.5	6.7
47*	89.6	31.0	96.1	37.1	92.9	4.6
48*	86.4	34.3	87.6	37.9	87.0	0.8
49	40.9	7.0	33.8	5.5	37.3	5.0
50	131.1	15.2	102.5	12.7	116.8	20.2
51	62.6	28.3	52.6	24.2	57.6	7.1
52	44.0	4.8	45.3	5.4	44.6	0.9
53	46.5	9.0	50.6	9.9	48.6	2.9
54	57.5	5.0	58.5	4.8	58.0	0.7
55	58.7	7.7	63.2	10.2	61.0	3.2
56	74.2	14.3	60.2	13.8	67.2	9.9
57	28.8	4.3	24.5	3.0	26.6	3.0
58	87.5	9.6	82.0	8.8	84.7	3.9
59	117.5	28.7	123.7	27.6	120.6	4.4
60	59.3	12.1	51.5	9.5	55.4	5.5
61	40.5	11.0	39.4	8.6	39.9	0.8
62	56.0	26.9	64.0	29.2	60.0	5.7
63	41.1	6.3	43.3	6.7	42.2	1.5
64	29.9	6.3	39.1	7.3	34.5	6.5
65	29.4	5.2	28.1	4.6	28.8	0.9
66	29.3	5.6	27.8	5.5	28.6	1.1
67	41.6	24.9	41.7	22.6	41.6	0.1
68	59.5	8.6	60.2	7.3	59.8	0.5
69	33.4	6.7	37.9	7.3	35.7	3.2
70	16.0	3.9	17.1	4.3	16.6	0.8
71	111.7	22.9	105.5	21.7	108.6	4.4
72	88.8	48.5	45.9	30.6	67.4	30.3
73	34.4	7.9	37.9	8.5	36.2	2.5
74	129.9	11.4	113.4	11.4	121.6	11.6
75	64.9	7.7	65.3	6.7	65.1	0.3
76	187.1	75.1	--	--	187.1	75.1
77	218.5	65.1	--	--	218.5	65.1
78	98.7	7.9	98.8	6.7	98.8	0.1
79	31.8	15.2	62.2	18.1	47.0	21.6
80	161.4	27.9	149.7	26.5	155.6	8.3
81	68.5	5.4	65.2	3.9	66.9	2.4
82	71.5	4.9	70.0	5.0	70.8	1.0
83	111.5	8.3	103.3	6.8	107.4	5.8
84	76.0	4.1	73.1	3.6	74.5	2.1

85	93.6	9.8	94.7	11.5	94.1	0.7
86	78.3	11.1	83.3	12.0	80.8	3.5
87	100.8	13.4	95.3	12.6	98.1	3.9
88	114.1	42.1	167.9	40.7	141.0	38.0
89	35.2	3.6	39.7	4.6	37.4	3.2
90	62.8	7.7	59.1	6.1	61.0	2.6
91	95.4	9.1	76.2	6.8	85.8	13.6
92	149.2	11.9	111.5	12.5	130.4	26.7
93	61.1	7.4	54.1	7.5	57.6	5.0
94	78.7	7.0	82.0	7.2	80.4	2.3
95	67.0	10.3	62.0	9.6	64.5	3.5
96	51.1	5.2	52.1	4.2	51.6	0.7
97	103.5	16.2	97.9	20.3	100.7	3.9
98	83.0	7.7	81.6	6.1	82.3	1.0
99	103.2	12.4	98.9	11.6	101.0	3.0
100	90.9	22.9	116.3	28.3	103.6	18.0
101	44.4	12.9	35.9	9.7	40.1	6.0
102	70.1	7.3	78.0	9.6	74.0	5.5
103	41.6	10.9	35.8	11.0	38.7	4.1
104	25.2	7.6	29.7	9.3	27.5	3.2
105	31.5	4.7	33.1	4.8	32.3	1.1
106	20.4	4.3	23.5	4.6	21.9	2.2
107	20.4	1.5	21.8	2.4	21.1	1.0
108	28.4	6.6	30.6	5.2	29.5	1.5
109	40.1	3.3	42.2	3.7	41.1	1.5
110	34.9	3.7	35.7	3.8	35.3	0.5
111	89.0	5.5	85.6	6.0	87.3	2.4
112	54.3	5.4	54.5	7.7	54.4	0.2
113	30.5	2.0	32.6	2.1	31.6	1.5
114	51.3	3.3	64.5	4.2	57.9	9.3
115	33.9	2.4	36.5	2.6	35.2	1.8
116	86.1	6.6	94.7	7.1	90.4	6.1
117	29.5	3.8	35.5	2.4	32.5	4.2
118	74.0	8.6	81.1	6.3	77.6	5.1
119	33.3	2.7	37.5	3.2	35.4	3.0
120	19.3	2.2	20.1	3.0	19.7	0.6
121	42.7	8.0	39.7	5.4	41.2	2.1
122	78.4	14.0	70.7	12.2	74.5	5.5
123	34.1	3.6	32.2	4.4	33.1	1.3
124	59.9	7.0	66.0	6.9	62.9	4.3
125	64.1	7.9	59.2	7.2	61.6	3.4
126	127.6	23.1	148.6	19.6	138.1	14.9
127	152.4	26.3	139.9	20.1	146.1	8.8
128	209.1	65.6	150.9	44.7	180.0	41.2
129	91.9	9.2	78.7	7.3	85.3	9.3
130	91.0	17.5	88.2	20.2	89.6	2.0
131	54.3	5.3	52.7	3.6	53.5	1.1

132	68.1	6.5	59.3	4.5	63.7	6.2
133	36.1	5.5	33.3	4.2	34.7	2.0
134	83.3	17.0	73.3	17.0	78.3	7.1
135	68.8	4.9	64.7	4.2	66.8	2.9
136	43.4	8.7	48.5	9.2	45.9	3.6
137	61.4	7.4	59.2	5.0	60.3	1.6
138	54.5	6.1	60.9	5.6	57.7	4.6
139	87.3	5.7	83.2	6.4	85.2	2.9
140	89.9	5.4	90.7	6.0	90.3	0.6
141	57.1	4.7	55.2	3.4	56.2	1.3
142	53.8	5.0	56.3	7.2	55.1	1.8
143	81.6	8.7	77.9	9.2	79.7	2.6
144	23.6	4.2	22.9	3.1	23.3	0.5
145	51.5	16.2	37.3	11.8	44.4	10.1
146	79.5	14.9	66.8	19.5	73.2	9.0
147	143.6	14.6	109.5	14.5	126.6	24.1
148	119.3	64.0	74.8	47.1	97.0	31.4
149	117.9	48.3	65.1	23.6	91.5	37.3
150	224.2	88.9	112.2	58.1	168.2	79.2
151	284.8	174.5	162.4	86.4	223.6	86.6
152	82.4	35.3	76.6	39.1	79.5	4.1
153	54.4	7.8	45.0	9.0	49.7	6.7
154	112.6	20.0	102.3	14.6	107.4	7.3
155	115.3	17.1	88.6	10.9	102.0	18.9
156	53.1	6.1	42.5	4.3	47.8	7.5
157	36.7	5.4	32.7	3.4	34.7	2.9
158	42.9	11.3	41.7	9.6	42.3	0.9
159	33.2	5.0	34.0	3.6	33.6	0.6
160	113.5	11.4	102.3	9.4	107.9	7.9
161	69.4	10.0	70.5	8.1	69.9	0.8
162	58.2	6.6	51.1	6.3	54.6	5.1
163	21.3	3.8	14.8	4.0	18.0	4.6
164	23.1	4.0	17.7	2.9	20.4	3.8
165	13.5	1.7	9.7	1.7	11.6	2.7
166	29.2	4.6	28.4	4.2	28.8	0.6
167	83.1	7.6	84.0	7.6	83.5	0.6
168	85.7	25.3	91.5	26.7	88.6	4.1
169	122.6	8.8	91.3	13.8	106.9	22.2
170	134.4	11.8	95.4	8.0	114.9	27.6
171	74.5	8.0	52.5	9.2	63.5	15.6
172	194.8	20.1	158.8	18.1	176.8	25.5
173	168.6	16.7	162.7	18.0	165.7	4.2
174	37.0	6.5	47.8	9.7	42.4	7.6
175	60.3	40.8	46.6	44.7	53.4	9.7
176	19.5	2.7	21.0	2.9	20.3	1.1
177	28.7	2.2	23.3	2.4	26.0	3.8
178	38.1	3.4	35.8	4.1	36.9	1.7

179	61.3	5.4	55.3	3.4	58.3	4.2
180	152.9	13.8	118.6	10.4	135.8	24.3
181	68.4	7.8	69.5	8.1	68.9	0.8
182	57.6	6.2	58.9	5.8	58.2	0.9
183	127.1	9.9	126.5	10.5	126.8	0.4
184	102.8	11.1	107.8	11.5	105.3	3.6
185	106.6	9.0	94.7	8.2	100.7	8.4
186	54.5	28.0	49.0	25.2	51.8	3.9
187	112.8	9.1	85.6	11.3	99.2	19.2
188	70.6	6.3	72.5	7.3	71.6	1.4
189	50.2	4.5	50.0	5.1	50.1	0.1
190	115.9	9.8	130.3	9.9	123.1	10.2
191	102.7	13.1	103.6	6.4	103.2	0.6
192	83.3	18.9	74.9	19.8	79.1	5.9

NOTE: * denotes triple-common.

[00245] Additionally, primary human hepatocytes, such as 3D spheroids, are transfected with each of the DsiRNAs (100 nM) in separate wells of a multi-well cell culture plate. Cells are maintained for 7 days following transfection, and then levels of remaining SCAP mRNA from the transfected cells are determined using TAQMAN®-based qPCR assays. Two qPCR assays, a 3' assay and a 5' assay, are used to determine mRNA levels as measured by HEX probes (*e.g.*, Hs HPRT-517-591and Hs SFRS9-569-712).

[00246] The results of the human hepatocyte 3D spheroid-based assay with the DsiRNAs are shown in Table 2. As above, transfection of a DsiRNA that results in less than or equal to 30% SCAP mRNA remaining in the cells when compared to negative controls is considered a candidate *SCAP* expression inhibitor (referred to herein as a "hit").

[00247] Table 2: Triple-Common and Double-Common DsiRNA SCAP mRNA Knockdown in 3D Human Spheroids, 100 nM 7 days-5'and -3' Assays % mRNA Remaining (normalized to Hs HPRT-517 (HEX) and Hs SFRS9-569 (HEX) vs mock control).

	HPRT-517 (HEX)		SFRS9-569 (HEX)		Average	
DsiRNA Oligo	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM
1*	67.3	11.5	66.3	12.0	66.8	0.7
2*	26.3	12.1	17.7	7.8	22.0	6.1
3*	43.5	4.7	48.0	5.6	45.7	3.2
4*	64.2	12.4	55.8	13.6	60.0	6.0
5*	73.5	10.2	86.3	11.0	79.9	9.0
6*	59.8	10.1	94.1	11.3	77.0	24.3
7*	43.9	7.8	60.8	11.1	52.3	11.9
8*	94.4	26.7	110.7	19.3	102.6	11.5
9*	32.7	5.0	53.7	10.3	43.2	14.8

10*	44.1	3.3	61.7	5.1	52.9	12.4
11*	77.1	21.9	97.5	18.5	87.3	14.4
12*	64.3	54.4	72.5	53.6	68.4	5.8
13*	6.4	1.9	36.3	6.9	21.4	21.1
14*	80.4	16.1	104.2	17.8	92.3	16.8
15*	87.1	10.4	111.2	12.5	99.2	17.0
16*	91.3	19.6	106.5	23.2	98.9	10.8
17*	64.3	6.3	101.3	14.1	82.8	26.2
18*	99.0	18.7	101.6	28.4	100.3	1.8
19*	75.7	11.1	90.1	16.0	82.9	10.2
20*	35.2	7.4	45.6	12.1	40.4	7.3
21*	32.7	7.0	35.0	11.0	33.9	1.6
22*	49.3	4.8	61.6	5.2	55.4	8.7
23*	76.2	16.4	86.0	20.5	81.1	6.9
24*	22.7	4.6	38.0	7.1	30.4	10.8
25*	110.6	19.0	103.6	19.7	107.1	4.9
26*	57.2	16.0	67.9	16.1	62.6	7.6
27*	66.4	11.2	78.6	11.9	72.5	8.6
28*	100.0	22.1	134.8	21.6	117.4	24.6
29*	53.2	13.3	58.1	13.8	55.6	3.5
30*	42.7	10.6	66.5	15.3	54.6	16.8
31*	46.2	5.8	89.9	12.6	68.0	31.0
32*	59.9	12.1	73.3	11.8	66.6	9.5
33*	29.4	5.5	38.5	7.4	33.9	6.4
34*	92.3	19.3	127.0	18.3	109.7	24.6
35*	95.5	25.6	120.3	27.5	107.9	17.5
36*	69.9	20.9	102.1	33.2	86.0	22.8
37*	57.1	20.6	82.3	22.0	69.7	17.8
38*	53.7	12.9	70.4	14.8	62.1	11.8
39*	87.5	19.1	107.1	26.1	97.3	13.8
40*	67.7	16.2	93.7	26.9	80.7	18.4
41*	78.5	16.1	94.7	14.0	86.6	11.5
42*	43.0	5.8	39.2	5.7	41.1	2.7
43*	25.8	4.7	29.7	5.4	27.7	2.8
44*	55.4	7.6	72.2	8.6	63.8	11.9
45*	78.0	7.7	101.9	7.2	89.9	16.9
46*	53.4	38.0	118.6	56.2	86.0	46.1
47*	69.1	10.8	87.4	13.8	78.2	12.9
48*	155.7	107.9	73.6	57.4	114.7	58.0
49	57.1	9.2	62.7	11.9	59.9	3.9
50	61.2	6.3	76.6	7.7	68.9	10.9
51	37.8	6.3	38.1	7.6	38.0	0.2
52	32.6	5.7	35.9	8.4	34.2	2.3
53	50.4	3.8	60.5	6.5	55.4	7.1
54	41.8	9.4	51.4	12.0	46.6	6.8
55	58.5	8.0	57.5	11.4	58.0	0.7
56	82.7	14.0	86.3	17.9	84.5	2.5

57	59.9	5.9	64.3	5.5	62.1	3.1
58	90.3	11.2	87.7	10.9	89.0	1.9
59	78.7	8.1	83.8	7.3	81.3	3.6
60	40.2	8.8	35.7	8.0	37.9	3.2
61	46.5	8.6	49.6	8.7	48.1	2.2
62	33.4	6.5	38.3	7.2	35.9	3.5
63	30.7	5.0	41.2	6.5	36.0	7.4
64	60.0	11.9	48.1	9.6	54.1	8.4
65	39.0	5.5	39.0	6.1	39.0	0.1
66	30.3	3.4	25.6	3.6	28.0	3.3
67	14.2	3.6	17.0	3.7	15.6	1.9
68	33.4	5.2	28.6	5.2	31.0	3.4
69	27.9	1.9	32.7	4.3	30.3	3.4
70	11.0	1.2	12.4	1.7	11.7	1.0
71	74.5	6.9	87.7	7.5	81.1	9.3
72	88.7	7.1	83.0	7.8	85.8	4.1
73	41.3	12.4	46.3	5.4	43.8	3.5
74	77.9	28.7	99.8	29.7	88.9	15.4
75	45.8	20.7	86.2	21.2	66.0	28.6
76	81.9	13.4	86.9	15.8	84.4	3.5
77	94.3	14.9	105.8	13.8	100.0	8.2
78	73.6	10.1	84.8	12.6	79.2	7.9
79	41.2	8.6	47.3	9.2	44.2	4.3
80	68.6	6.7	91.5	8.5	80.0	16.2
81	60.5	5.8	67.7	10.2	64.1	5.1
82	49.4	21.3	49.5	12.3	49.5	0.1
83	65.4	7.3	85.3	10.4	75.4	14.1
84	66.2	10.2	60.9	11.2	63.5	3.8
85	67.7	4.9	78.3	6.6	73.0	7.5
86	58.2	7.3	71.3	9.5	64.7	9.3
87	66.2	4.9	79.2	8.8	72.7	9.2
88	82.1	11.0	94.1	15.9	88.1	8.5
89	83.4	56.0	48.4	20.8	65.9	24.8
90	67.7	9.7	67.3	9.1	67.5	0.3
91	56.9	23.8	55.5	22.0	56.2	1.0
92	83.5	8.7	84.2	9.2	83.9	0.4
93	49.2	4.3	45.6	5.4	47.4	2.5
94	62.6	6.2	79.6	9.5	71.1	12.1
95	43.8	9.1	48.4	10.3	46.1	3.2
96	47.6	6.8	48.7	6.1	48.1	0.7
97	127.0	110.9	66.2	54.3	96.6	43.0
98	56.9	5.5	68.5	5.4	62.7	8.2
99	83.0	6.1	84.6	9.6	83.8	1.1
100	72.1	25.4	137.4	41.3	104.7	46.2
101	39.0	6.9	48.5	9.0	43.8	6.7
102	55.8	6.4	74.0	10.7	64.9	12.9
103	21.6	10.5	41.7	15.9	31.6	14.2

104	12.6	7.3	15.9	11.4	14.2	2.3
105	17.6	3.1	60.0	6.8	38.8	30.0
106	3.3	0.6	13.9	5.1	8.6	7.5
107	6.4	1.5	22.9	5.2	14.7	11.7
108	17.7	2.9	44.6	8.3	31.1	19.1
109	15.8	10.0	57.0	30.9	36.4	29.2
110	12.1	1.4	49.2	5.2	30.6	26.2
111	27.8	6.9	50.5	12.1	39.2	16.1
112	28.8	15.5	64.5	27.3	46.7	25.2
113	20.7	3.0	40.6	5.4	30.6	14.1
114	37.7	17.1	71.2	22.6	54.4	23.7
115	17.5	6.2	30.2	11.8	23.9	9.0
116	63.9	9.2	86.9	11.8	75.4	16.3
117	30.5	2.9	39.4	4.1	34.9	6.3
118	43.9	10.9	61.8	14.2	52.9	12.7
119	44.0	5.2	57.4	8.7	50.7	9.5
120	38.1	12.1	55.8	15.3	46.9	12.5
121	59.4	29.3	86.1	35.7	72.8	18.9
122	62.6	12.2	81.9	13.3	72.3	13.7
123	55.7	19.8	85.2	30.5	70.5	20.8
124	35.2	8.0	80.9	21.6	58.1	32.4
125	57.3	8.2	71.1	7.1	64.2	9.7
126	86.3	21.0	88.9	25.2	87.6	1.8
127	83.4	15.4	106.5	22.9	94.9	16.3
128	119.6	61.8	78.2	59.0	98.9	29.3
129	88.0	14.9	94.3	16.8	91.2	4.4
130	94.3	68.0	83.8	54.1	89.1	7.5
131	50.2	17.0	66.4	14.8	58.3	11.5
132	50.9	5.1	47.6	4.6	49.3	2.4
133	33.1	18.1	45.3	13.4	39.2	8.6
134	38.7	21.1	61.9	25.4	50.3	16.4
135	--	--	52.6	31.5	52.6	31.5
136	34.2	10.0	37.6	10.1	35.9	2.4
137	92.8	24.3	92.7	21.9	92.8	0.1
138	49.7	14.6	48.9	11.4	49.3	0.6
139	74.2	11.0	86.8	11.9	80.5	8.9
140	91.6	25.4	92.3	27.1	91.9	0.5
141	61.9	7.5	64.1	8.2	63.0	1.6
142	60.3	10.8	72.7	17.4	66.5	8.8
143	136.6	56.4	55.2	41.9	95.9	57.6
144	121.2	42.0	59.0	29.7	90.1	44.0
145	83.5	10.9	87.6	12.3	85.5	2.9
146	73.6	7.3	67.9	4.9	70.7	4.0
147	104.3	16.4	77.3	8.5	90.8	19.1
148	84.2	12.7	81.0	10.8	82.6	2.3
149	53.4	9.7	58.5	11.8	55.9	3.6
150	77.3	25.8	69.8	23.9	73.5	5.4

151	108.2	43.9	120.3	39.8	114.3	8.5
152	66.5	12.1	56.5	11.2	61.5	7.1
153	43.3	6.4	57.9	11.6	50.6	10.4
154	78.7	8.2	78.4	9.0	78.5	0.2
155	86.6	8.1	69.9	7.7	78.3	11.8
156	36.0	4.9	40.7	4.3	38.3	3.3
157	39.6	3.7	31.2	3.2	35.4	5.9
158	25.2	11.5	26.4	11.8	25.8	0.8
159	24.6	7.4	22.5	6.1	23.6	1.5
160	101.4	17.4	86.1	16.5	93.7	10.8
161	90.3	12.2	65.3	16.3	77.8	17.7
162	74.4	11.1	66.2	12.6	70.3	5.8
163	19.5	2.8	10.2	2.2	14.8	6.6
164	23.3	2.6	18.1	3.6	20.7	3.6
165	16.7	7.7	10.4	4.2	13.6	4.5
166	27.2	4.2	23.2	2.7	25.2	2.8
167	87.0	10.1	77.9	8.7	82.5	6.4
168	116.7	39.9	89.4	27.8	103.1	19.3
169	100.9	7.7	87.6	5.3	94.2	9.4
170	95.2	22.4	83.3	18.1	89.3	8.4
171	47.4	10.3	42.2	9.8	44.8	3.7
172	63.3	14.3	43.2	10.7	53.2	14.2
173	55.6	10.5	48.9	8.3	52.2	4.7
174	45.5	6.5	38.9	7.5	42.2	4.6
175	45.5	15.1	33.2	13.4	39.4	8.7
176	30.7	7.3	30.2	6.2	30.4	0.3
177	46.4	7.4	45.0	5.9	45.7	1.0
178	38.9	4.9	41.3	5.2	40.1	1.7
179	63.6	12.7	49.6	14.6	56.6	9.9
180	80.4	9.9	72.2	8.1	76.3	5.8
181	68.2	7.5	50.7	7.1	59.4	12.4
182	37.9	22.9	53.0	24.5	45.5	10.7
183	93.8	20.0	89.0	17.9	91.4	3.4
184	95.3	21.4	132.1	24.0	113.7	26.0
185	77.4	5.5	79.3	9.4	78.3	1.4
186	55.1	3.5	39.1	4.1	47.1	11.4
187	69.3	37.6	78.8	30.9	74.0	6.7
188	81.2	15.0	66.2	14.1	73.7	10.6
189	57.2	15.8	58.6	12.4	57.9	1.0
190	69.4	29.6	70.6	28.9	70.0	0.9
191	77.3	8.0	62.2	7.6	69.7	10.7
192	79.9	42.5	67.8	28.7	73.9	8.5

NOTE: * denotes triple-common.

[00248] These results show that DsiRNAs designed to target human SCAP mRNA can inhibit *SCAP* activity in cells (as determined by a reduced amount of SCAP mRNA in DsiRNA-

transfected cells) and that the nucleotide sequences including the DsiRNA hits are useful for generating RNAi oligonucleotides to inhibit *SCAP* activity. Further, these results demonstrate that multiple SCAP target sequences are suitable for the RNAi-mediated inhibition of *SCAP* activity.

[00249] Example 3: RNAi Oligonucleotide Inhibition of *SCAP* Activity *In Vitro* – GalXC™-Based Compounds

[00250] The DsiRNAs screened in Example 2 are selected for evaluation *in vitro* as GalXC™-based compounds. Briefly, the nucleotide sequences of the DsiRNAs are used to generate corresponding ds RNAi oligonucleotides including a nicked tetraloop GalNAc-conjugated structure (referred to herein as "GalXC™-SCAP oligonucleotides") having a 36-mer sense strand and a 22-mer antisense strand. Further, the nucleotide sequences for the sense strand and antisense strand of the GalXC™-SCAP oligonucleotides have a distinct pattern of modified nucleotides and phosphorothioate linkages (*see, e.g.*, FIG. 1 for a schematic of the generic structure and chemical modification patterns of the GalXC™-SCAP oligonucleotides). The three adenosine nucleotides of the tetraloop each are conjugated to a GalNAc moiety (CAS#: 14131-60-3).

[00251] Table 3: GalXC™-SCAP Oligonucleotides (unmodified).

GalXC-SCAP Oligo	Sense Strand (passenger; 36-mer)	SEQ ID NO:	Antisense Strand (guide; 22-mer)	SEQ ID NO:
1	UGUUUGCCUACAUCUACUUAGCAGCCGAAAGGCUGC	9	UAAGUAGAUGUAGGCAAACAGG	10
2	GUUUGCCUACAUCUACUUCAGCAGCCGAAAGGCUGC	11	UGAAGUAGAUGUAGGCAAACGG	12
3	UUUGCCUACAUCUACUUCUAGCAGCCGAAAGGCUGC	13	UAGAAGUAGAUGUAGGCAAAGG	14
4	GCCUACAUCUACUUCUCCAAGCAGCCGAAAGGCUGC	15	UUGGAGAAGUAGAUGUAGGCGG	16
5	AAGAUCGACAUGGUCAAGUAGCAGCCGAAAGGCUGC	17	UACUUGACCAUGUCGAUCUUGG	18
6	AGAUCGACAUGGUCAAGUCAGCAGCCGAAAGGCUGC	19	UGACUUGACCAUGUCGAUCUGG	20

7	AUCGACAUGGUCAAGUCCAAGCAGCCGAAAGGCUGC	21	UUGGACUUGACCAUGUCGAUGG	22
8	GUGUUGGUGCUCACCAAGUAGCAGCCGAAAGGCUGC	23	UACUUGGUGAGCACCAACACGG	24
9	UGUUGGUGCUCACCAAGUCAGCAGCCGAAAGGCUGC	25	UGACUUGGUGAGCACCAACAGG	26
10	GAGAGCUGGUCCAUCAUGAAGCAGCCGAAAGGCUGC	27	UUCAUGAUGGACCAGCUCUCGG	28
11	AGAGCUGGUCCAUCAUGAAAGCAGCCGAAAGGCUGC	29	UUUCAUGAUGGACCAGCUCUGG	30
12	GAGCUGGUCCAUCAUGAAGAGCAGCCGAAAGGCUGC	31	UCUUCAUGAUGGACCAGCUCGG	32
13	AGCUGGUCCAUCAUGAAGAAGCAGCCGAAAGGCUGC	33	UUCUUCAUGAUGGACCAGCUGG	34
14	GCUGGUCCAUCAUGAAGAAAGCAGCCGAAAGGCUGC	35	UUUCUUCAUGAUGGACCAGCGG	36
15	CUGGUCCAUCAUGAAGAACAGCAGCCGAAAGGCUGC	37	UGUUCUUCAUGAUGGACCAGGG	38
16	CCGUUGUCUGGAUUGGCAUAGCAGCCGAAAGGCUGC	39	UAUGCCAAUCCAGACAACGGGG	40
17	UUGUCUGGAUUGGCAUCCUAGCAGCCGAAAGGCUGC	41	UAGGAUGCCAAUCCAGACAAGG	42
18	UGUCUGGAUUGGCAUCCUGAGCAGCCGAAAGGCUGC	43	UCAGGAUGCCAAUCCAGACAGG	44
19	GUCUGGAUUGGCAUCCUGGAGCAGCCGAAAGGCUGC	45	UCCAGGAUGCCAAUCCAGACGG	46
20	CUGGAUUGGCAUCCUGGUAAGCAGCCGAAAGGCUGC	47	UUACCAGGAUGCCAAUCCAGGG	48
21	UGGAUUGGCAUCCUGGUAUAGCAGCCGAAAGGCUGC	49	UAUACCAGGAUGCCAAUCCAGG	50
22	GGAUUGGCAUCCUGGUAUAAGCAGCCGAAAGGCUGC	51	UUAUACCAGGAUGCCAAUCCGG	52

23	GAUUGGCAUCCUGGUAUACAGCAGCCGAAAGGCUGC	53	UGUAUACCAGGAUGCCAAUCGG	54
24	AUUGGCAUCCUGGUAUACAAGCAGCCGAAAGGCUGC	55	UUGUAUACCAGGAUGCCAAUGG	56
25	CUCCAUCUUCCCACCUGAUAGCAGCCGAAAGGCUGC	57	UAUCAGGUGGGAAGAUGGAGGG	58
26	CAUCUGCCUGUGGGAUGUAAGCAGCCGAAAGGCUGC	59	UUACAUCCCACAGGCAGAUGGG	60
27	UCUGCCUGUGGGAUGUACUAGCAGCCGAAAGGCUGC	61	UAGUACAUCCCACAGGCAGAGG	62
28	GUGGUGCAAGCUUGGGUGUAGCAGCCGAAAGGCUGC	63	UACACCCAAGCUUGCACCACGG	64
29	UGGUGCAAGCUUGGGUGUCAGCAGCCGAAAGGCUGC	65	UGACACCCAAGCUUGCACCAGG	66
30	GGUGCAAGCUUGGGUGUCAAGCAGCCGAAAGGCUGC	67	UUGACACCCAAGCUUGCACCGG	68
31	GUGCAAGCUUGGGUGUCAUAGCAGCCGAAAGGCUGC	69	UAUGACACCCAAGCUUGCACGG	70
32	GCAAGCUUGGGUGUCAUCUAGCAGCCGAAAGGCUGC	71	UAGAUGACACCCAAGCUUGCGG	72
33	CAAGCUUGGGUGUCAUCUCAGCAGCCGAAAGGCUGC	73	UGAGAUGACACCCAAGCUUGGG	74
34	AAGCUUGGGUGUCAUCUCAAGCAGCCGAAAGGCUGC	75	UUGAGAUGACACCCAAGCUUGG	76
35	AGCUUGGGUGUCAUCUCAGAGCAGCCGAAAGGCUGC	77	UCUGAGAUGACACCCAAGCUGG	78
36	GCUUGGGUGUCAUCUCAGAAGCAGCCGAAAGGCUGC	79	UUCUGAGAUGACACCCAAGCGG	80
37	GUGUCUCCUUUUGGGACCUAGCAGCCGAAAGGCUGC	81	UAGGUCCCAAAAGGAGACACGG	82
38	UGUCUCCUUUUGGGACCUAAGCAGCCGAAAGGCUGC	83	UUAGGUCCCAAAAGGAGACAGG	84

39	GGGGACCUGUUACAGACAGAGCAGCCGAAAGGCUGC	85	UCUGUCUGUAACAGGUCCCCGG	86
40	GGGACCUGUUACAGACAGUAGCAGCCGAAAGGCUGC	87	UACUGUCUGUAACAGGUCCCGG	88
41	GGACCUGUUACAGACAGUCAGCAGCCGAAAGGCUGC	89	UGACUGUCUGUAACAGGUCCGG	90
42	GACCUGUUACAGACAGUCUAGCAGCCGAAAGGCUGC	91	UAGACUGUCUGUAACAGGUCGG	92
43	ACCUGUUACAGACAGUCUAAGCAGCCGAAAGGCUGC	93	UUAGACUGUCUGUAACAGGUGG	94
44	UGCCAUUGUCUGCAACUUUAGCAGCCGAAAGGCUGC	95	UAAAGUUGCAGACAAUGGCAGG	96
45	GCCAUUGUCUGCAACUUUGAGCAGCCGAAAGGCUGC	97	UCAAAGUUGCAGACAAUGGCGG	98
46	CCAUUGUCUGCAACUUUGGAGCAGCCGAAAGGCUGC	99	UCCAAAGUUGCAGACAAUGGGG	100
47	AUUGUCUGCAACUUUGGCAAGCAGCCGAAAGGCUGC	101	UUGCCAAAGUUGCAGACAAUGG	102
48	UCUGCAACUUUGGCAGUGAAGCAGCCGAAAGGCUGC	103	UUCACUGCCAAAGUUGCAGAGG	104
49	CUACCCACUGCUGAAACUCAGCAGCCGAAAGGCUGC	105	UGAGUUUCAGCAGUGGGUAGGG	106
50	GCCAGGAACAGGACCUGUGAGCAGCCGAAAGGCUGC	107	UCACAGGUCCUGUUCCUGGCGG	108
51	GAACAGGACCUGUGGAAUUAGCAGCCGAAAGGCUGC	109	UAAUUCCACAGGUCCUGUUCGG	110
52	ACAGGACCUGUGGAAUUCAAGCAGCCGAAAGGCUGC	111	UUGAAUUCCACAGGUCCUGUGG	112
53	UGGAAUUCACCACCCCUGUAGCAGCCGAAAGGCUGC	113	UACAGGGGUGGUGAAUUCCAGG	114
54	CUUGUGACCACCUACAUCAAGCAGCCGAAAGGCUGC	115	UUGAUGUAGGUGGUCACAAGGG	116

55	UUGUGACCACCUACAUCAUAGCAGCCGAAAGGCUGC	117	UAUGAUGUAGGUGGUCACAAGG	118
56	UGUGACCACCUACAUCAUCAGCAGCCGAAAGGCUGC	119	UGAUGAUGUAGGUGGUCACAGG	120
57	GUGACCACCUACAUCAUCUAGCAGCCGAAAGGCUGC	121	UAGAUGAUGUAGGUGGUCACGG	122
58	UGACCACCUACAUCAUCUUAGCAGCCGAAAGGCUGC	123	UAAGAUGAUGUAGGUGGUCAGG	124
59	GACCACCUACAUCAUCUUGAGCAGCCGAAAGGCUGC	125	UCAAGAUGAUGUAGGUGGUCGG	126
60	ACCACCUACAUCAUCUUGUAGCAGCCGAAAGGCUGC	127	UACAAGAUGAUGUAGGUGGUGG	128
61	CCACCUACAUCAUCUUGUUAGCAGCCGAAAGGCUGC	129	UAACAAGAUGAUGUAGGUGGGG	130
62	CACCUACAUCAUCUUGUUUAGCAGCCGAAAGGCUGC	131	UAAACAAGAUGAUGUAGGUGGG	132
63	ACCUACAUCAUCUUGUUUGAGCAGCCGAAAGGCUGC	133	UCAAACAAGAUGAUGUAGGUGG	134
64	CCUACAUCAUCUUGUUUGCAGCAGCCGAAAGGCUGC	135	UGCAAACAAGAUGAUGUAGGGG	136
65	CUACAUCAUCUUGUUUGCCAGCAGCCGAAAGGCUGC	137	UGGCAAACAAGAUGAUGUAGGG	138
66	ACAUCAUCUUGUUUGCCUAAGCAGCCGAAAGGCUGC	139	UUAGGCAAACAAGAUGAUGUGG	140
67	AUCAUCUUGUUUGCCUACAAGCAGCCGAAAGGCUGC	141	UUGUAGGCAAACAAGAUGAUGG	142
68	UCAUCUUGUUUGCCUACAUAGCAGCCGAAAGGCUGC	143	UAUGUAGGCAAACAAGAUGAGG	144
69	AUCUUGUUUGCCUACAUCUAGCAGCCGAAAGGCUGC	145	UAGAUGUAGGCAAACAAGAUGG	146
70	UCUUGUUUGCCUACAUCUAAGCAGCCGAAAGGCUGC	147	UUAGAUGUAGGCAAACAAGAGG	148

71	UUUCCCCUACCUUG UGGUGAGCAGCCGA AAGGCUGC	149	UCACCACAAGGUAGGG GAAAGG	150
72	UUCCCCUACCUUGU GGUGGAGCAGCCGA AAGGCUGC	151	UCCACCACAAGGUAGG GGAAGG	152
73	CCCUACCUUGUGGU GGUUAAGCAGCCGA AAGGCUGC	153	UUAACCACCACAAGGU AGGGGG	154
74	CUACCUUGUGGUGG UUAUUAGCAGCCGA AAGGCUGC	155	UAAUAACCACCACAAG GUAGGG	156
75	UACCUUGUGGUGGU UAUUGAGCAGCCGA AAGGCUGC	157	UCAAUAACCACCACAA GGUAGG	158
76	ACCUUGUGGUGGUU AUUGGAGCAGCCGA AAGGCUGC	159	UCCAAUAACCACCACA AGGUGG	160
77	CCUUGUGGUGGUUA UUGGGAGCAGCCGA AAGGCUGC	161	UCCCAAUAACCACCACA AGGGG	162
78	CUUGUGGUGGUUA UUGGGUAGCAGCCG AAAGGCUGC	163	UACCCAAUAACCACCAC AAGGG	164
79	UUGUGGUGGUUAU UGGGUUAGCAGCCG AAAGGCUGC	165	UAACCCAAUAACCACC ACAAGG	166
80	UGUGGUGGUUAUU GGGUUAAGCAGCCG AAAGGCUGC	167	UUAACCCAAUAACCAC CACAGG	168
81	GUGGUGGUUAUUG GGUUAGAGCAGCCG AAAGGCUGC	169	UCUAACCCAAUAACCA CCACGG	170
82	UGGUGGUUAUUGG GUUAGAAGCAGCCG AAAGGCUGC	171	UUCUAACCCAAUAACC ACCAGG	172
83	GGUGGUUAUUGGG UUAGAGAGCAGCCG AAAGGCUGC	173	UCUCUAACCCAAUAAC CACCGG	174
84	GUGGUUAUUGGGU UAGAGAAGCAGCCG AAAGGCUGC	175	UUCUCUAACCCAAUAA CCACGG	176
85	UGGUUAUUGGGUU AGAGAAAGCAGCCG AAAGGCUGC	177	UUUCUCUAACCCAAUA ACCAGG	178
86	GGUUAUUGGGUUA GAGAAUAGCAGCCG AAAGGCUGC	179	UAUUCUCUAACCCAAU AACCGG	180

87	GUUAUUGGGUUAG AGAAUGAGCAGCCG AAAGGCUGC	181	UCAUUCUCUAACCCAA UAACGG	182
88	UUAUUGGGUUAGA GAAUGUAGCAGCCG AAAGGCUGC	183	UACAUUCUCUAACCCA AUAAGG	184
89	AUUGGGUUAGAGA AUGUGUAGCAGCCG AAAGGCUGC	185	UACACAUUCUCUAACC CAAUGG	186
90	UUGGGUUAGAGAA UGUGUUAGCAGCCG AAAGGCUGC	187	UAACACAUUCUCUAAC CCAAGG	188
91	GGUUAGAGAAUGU GUUGGUAGCAGCCG AAAGGCUGC	189	UACCAACACAUUCUCU AACCGG	190
92	GUUAGAGAAUGUG UUGGUGAGCAGCCG AAAGGCUGC	191	UCACCAACACAUUCUC UAACGG	192
93	UUAGAGAAUGUGU UGGUGCAGCAGCCG AAAGGCUGC	193	UGCACCAACACAUUCU CUAAGG	194
94	UAGAGAAUGUGUU GGUGCUAGCAGCCG AAAGGCUGC	195	UAGCACCAACACAUUC UCUAGG	196
95	AGAGAAUGUGUUG GUGCUCAGCAGCCG AAAGGCUGC	197	UGAGCACCAACACAUU CUCUGG	198
96	GAGAAUGUGUUGG UGCUCAAGCAGCCG AAAGGCUGC	199	UUGAGCACCAACACAU UCUCGG	200
97	AGAAUGUGUUGGU GCUCACAGCAGCCG AAAGGCUGC	201	UGUGAGCACCAACACA UUCUGG	202
98	AAUGUGUUGGUGC UCACCAAGCAGCCG AAAGGCUGC	203	UUGGUGAGCACCAACA CAUUGG	204
99	AUGUGUUGGUGCUC ACCAAAGCAGCCGA AAGGCUGC	205	UUUGGUGAGCACCAAC ACAUGG	206
100	UGUGUUGGUGCUCA CCAAGAGCAGCCGA AAGGCUGC	207	UCUUGGUGAGCACCAA CACAGG	208
101	UGGUCCAUCAUGAA GAACAAGCAGCCGA AAGGCUGC	209	UUGUUCUUCAUGAUGG ACCAGG	210
102	GGUCCAUCAUGAAG AACAUAGCAGCCGA AAGGCUGC	211	UAUGUUCUUCAUGAUG GACCGG	212

103	CUGACUUCUUCCUU CAGAUAGCAGCCGA AAGGCUGC	213	UAUCUGAAGGAAGAAG UCAGGG	214
104	ACUUCUUCCUUCAG AUGCUAGCAGCCGA AAGGCUGC	215	UAGCAUCUGAAGGAAG AAGUGG	216
105	UCCUUCAGAUGCUG UUUUUAGCAGCCGA AAGGCUGC	217	UAAAAACAGCAUCUGA AGGAGG	218
106	CCUUCAGAUGCUGU UUUUCAGCAGCCGA AAGGCUGC	219	UGAAAAACAGCAUCUG AAGGGG	220
107	CUUCAGAUGCUGUU UUUCAAGCAGCCGA AAGGCUGC	221	UUGAAAAACAGCAUCU GAAGGG	222
108	UUCAGAUGCUGUUU UUCACAGCAGCCGA AAGGCUGC	223	UGUGAAAAACAGCAUC UGAAGG	224
109	CAGAUGCUGUUUUU CACCAAGCAGCCGA AAGGCUGC	225	UUGGUGAAAAACAGCA UCUGGG	226
110	AGAUGCUGUUUUUC ACCACAGCAGCCGA AAGGCUGC	227	UGUGGUGAAAAACAGC AUCUGG	228
111	GAUGCUGUUUUUCA CCACUAGCAGCCGA AAGGCUGC	229	UAGUGGUGAAAAACAG CAUCGG	230
112	AUGCUGUUUUUCAC CACUGAGCAGCCGA AAGGCUGC	231	UCAGUGGUGAAAAACA GCAUGG	232
113	UGCUGUUUUUCACC ACUGUAGCAGCCGA AAGGCUGC	233	UACAGUGGUGAAAAAC AGCAGG	234
114	GCUGUUUUUCACCA CUGUCAGCAGCCGA AAGGCUGC	235	UGACAGUGGUGAAAAA CAGCGG	236
115	UGUUUUUCACCACU GUCCUAGCAGCCGA AAGGCUGC	237	UAGGACAGUGGUGAAA AACAGG	238
116	GUUUUUCACCACUG UCCUGAGCAGCCGA AAGGCUGC	239	UCAGGACAGUGGUGAA AAACGG	240
117	UUUUUCACCACUGU CCUGUAGCAGCCGA AAGGCUGC	241	UACAGGACAGUGGUGA AAAAGG	242
118	UUUUCACCACUGUC CUGUCAGCAGCCGA AAGGCUGC	243	UGACAGGACAGUGGUG AAAAGG	244

119	UUCACCACUGUCCU GUCCAAGCAGCCGA AAGGCUGC	245	UUGGACAGGACAGUGG UGAAGG	246
120	CACCACUGUCCUGU CCAUUAGCAGCCGA AAGGCUGC	247	UAAUGGACAGGACAGU GGUGGG	248
121	ACCACUGUCCUGUC CAUUGAGCAGCCGA AAGGCUGC	249	UCAAUGGACAGGACAG UGGUGG	250
122	CCACUGUCCUGUCC AUUGAAGCAGCCGA AAGGCUGC	251	UUCAAUGGACAGGACA GUGGGG	252
123	CACUGUCCUGUCCA UUGACAGCAGCCGA AAGGCUGC	253	UGUCAAUGGACAGGAC AGUGGG	254
124	ACUGUCCUGUCCAU UGACAAGCAGCCGA AAGGCUGC	255	UUGUCAAUGGACAGGA CAGUGG	256
125	CUAAGCUACCUGAG AACCAAGCAGCCGA AAGGCUGC	257	UUGGUUCUCAGGUAGC UUAGGG	258
126	GAGGUCCAGCAGAG GUUGUAGCAGCCGA AAGGCUGC	259	UACAACCUCUGCUGGA CCUCGG	260
127	GCAGAGGUUGUCCA UGACAAGCAGCCGA AAGGCUGC	261	UUGUCAUGGACAACCU CUGCGG	262
128	CAGAGGUUGUCCAU GACAGAGCAGCCGA AAGGCUGC	263	UCUGUCAUGGACAACC UCUGGG	264
129	GAGGAUGAGGAAC UUUGGAAGCAGCCG AAAGGCUGC	265	UUCCAAAGUUCCUCAU CCUCGG	266
130	GAACUUUGGAGGA AAUUGUAGCAGCCG AAAGGCUGC	267	UACAAUUUCCUCCAAA GUUCGG	268
131	GACGCUCUUCAGCU AUUACAGCAGCCGA AAGGCUGC	269	UGUAAUAGCUGAAGAG CGUCGG	270
132	ACGCUCUUCAGCUA UUACAAGCAGCCGA AAGGCUGC	271	UUGUAAUAGCUGAAGA GCGUGG	272
133	CGCUCUUCAGCUAU UACAAAGCAGCCGA AAGGCUGC	273	UUUGUAAUAGCUGAAG AGCGGG	274
134	GCUCUUCAGCUAUU ACAACAGCAGCCGA AAGGCUGC	275	UGUUGUAAUAGCUGAA GAGCGG	276

135	CUCUUCAGCUAUUACAACAAGCAGCCGAAAGGCUGC	277	UUGUUGUAAUAGCUGAAGAGGG	278
136	UCUUCAGCUAUUACAACAUAGCAGCCGAAAGGCUGC	279	UAUGUUGUAAUAGCUGAAGAGG	280
137	CUUCAGCUAUUACAACAUCAGCAGCCGAAAGGCUGC	281	UGAUGUUGUAAUAGCUGAAGGG	282
138	UUCAGCUAUUACAACAUCAAGCAGCCGAAAGGCUGC	283	UUGAUGUUGUAAUAGCUGAAGG	284
139	CCAGCCUGACCUCACCCUGCAGCAGCCGAAAGGCUGC	285	UGCAGGUGAGGUCAGGCUGGGG	286
140	CAGCCUGACCUCACCUGCUAGCAGCCGAAAGGCUGC	287	UAGCAGGUGAGGUCAGGCUGGG	288
141	AGCCUGACCUCACCUGCUUAGCAGCCGAAAGGCUGC	289	UAAGCAGGUGAGGUCAGGCUGG	290
142	GCCUGACCUCACCUGCUUAAGCAGCCGAAAGGCUGC	291	UUAAGCAGGUGAGGUCAGGCGG	292
143	CCUGACCUCACCUGCUUAAAGCAGCCGAAAGGCUGC	293	UUUAAGCAGGUGAGGUCAGGGG	294
144	CUGACCUCACCUGCUUAAUAGCAGCCGAAAGGCUGC	295	UAUUAAGCAGGUGAGGUCAGGG	296
145	UGACCUCACCUGCUUAAUUAGCAGCCGAAAGGCUGC	297	UAAUUAAGCAGGUGAGGUCAGG	298
146	GACCUCACCUGCUUAAUUGAGCAGCCGAAAGGCUGC	299	UCAAUUAAGCAGGUGAGGUCGG	300
147	ACCUCACCUGCUUAAUUGAAGCAGCCGAAAGGCUGC	301	UUCAAUUAAGCAGGUGAGGUGG	302
148	CCUCACCUGCUUAAUUGACAGCAGCCGAAAGGCUGC	303	UGUCAAUUAAGCAGGUGAGGGG	304
149	CUCACCUGCUUAAUUGACAAGCAGCCGAAAGGCUGC	305	UUGUCAAUUAAGCAGGUGAGGG	306
150	UCACCUGCUUAAUUGACACAGCAGCCGAAAGGCUGC	307	UGUGUCAAUUAAGCAGGUGAGG	308

151	CACCUGCUUAAUUG ACACCAGCAGCCGA AAGGCUGC	309	UGGUGUCAAUUAAGCA GGUGGG	310
152	ACCUGCUUAAUUGA CACCAAGCAGCCGA AAGGCUGC	311	UUGGUGUCAAUUAAGC AGGUGG	312
153	CCUGCUUAAUUGAC ACCAAAGCAGCCGA AAGGCUGC	313	UUUGGUGUCAAUUAAG CAGGGG	314
154	CUGCUUAAUUGACA CCAACAGCAGCCGA AAGGCUGC	315	UGUUGGUGUCAAUUAA GCAGGG	316
155	UGCUUAAUUGACAC CAACUAGCAGCCGA AAGGCUGC	317	UAGUUGGUGUCAAUUA AGCAGG	318
156	GCUUAAUUGACACC AACUUAGCAGCCGA AAGGCUGC	319	UAAGUUGGUGUCAAUU AAGCGG	320
157	CUUAAUUGACACCA ACUUUAGCAGCCGA AAGGCUGC	321	UAAAGUUGGUGUCAAU UAAGGG	322
158	UUAAUUGACACCAA CUUUUAGCAGCCGA AAGGCUGC	323	UAAAAGUUGGUGUCAA UUAAGG	324
159	UAAUUGACACCAAC UUUUCAGCAGCCGA AAGGCUGC	325	UGAAAAGUUGGUGUCA AUUAGG	326
160	AUUGAAGGGGUGC UGUGCUAGCAGCCG AAAGGCUGC	327	UAGCACAGCACCCCUUC AAUGG	328
161	CUUGGACAAAAGGA UUGUGAGCAGCCGA AAGGCUGC	329	UCACAAUCCUUUUGUC CAAGGG	330
162	UUGGACAAAAGGA UUGUGGAGCAGCCG AAAGGCUGC	331	UCCACAAUCCUUUUGU CCAAGG	332
163	UCAACGGUUCCCUU GAUUUAGCAGCCGA AAGGCUGC	333	UAAAUCAAGGGAACCG UUGAGG	334
164	CAACGGUUCCCUUG AUUUCAGCAGCCGA AAGGCUGC	335	UGAAAUCAAGGGAACC GUUGGG	336
165	AACGGUUCCCUUGA UUUCUAGCAGCCGA AAGGCUGC	337	UAGAAAUCAAGGGAAC CGUUGG	338
166	ACGGUUCCCUUGAU UUCUUAGCAGCCGA AAGGCUGC	339	UAAGAAAUCAAGGGAA CCGUGG	340

167	GUACAUUGACCAGA CCAUGAGCAGCCGA AAGGCUGC	341	UCAUGGUCUGGUCAAU GUACGG	342
168	ACCUGUACCACCUC CUGUGAGCAGCCGA AAGGCUGC	343	UCACAGGAGGUGGUAC AGGUGG	344
169	CCUGUACCACCUCC UGUGUAGCAGCCGA AAGGCUGC	345	UACACAGGAGGUGGUA CAGGGG	346
170	GUACCACCUCCUGU GUCAUAGCAGCCGA AAGGCUGC	347	UAUGACACAGGAGGUG GUACGG	348
171	GCACAGGCAUCAAG UUCUAAGCAGCCGA AAGGCUGC	349	UUAGAACUUGAUGCCU GUGCGG	350
172	ACAGGCAUCAAGUU CUACUAGCAGCCGA AAGGCUGC	351	UAGUAGAACUUGAUGC CUGUGG	352
173	CAGGCAUCAAGUUC UACUCAGCAGCCGA AAGGCUGC	353	UGAGUAGAACUUGAUG CCUGGG	354
174	AGGCAUCAAGUUCU ACUCCAGCAGCCGA AAGGCUGC	355	UGGAGUAGAACUUGAU GCCUGG	356
175	GGCAUCAAGUUCUA CUCCAAGCAGCCGA AAGGCUGC	357	UUGGAGUAGAACUUGA UGCCGG	358
176	GCAUCAAGUUCUAC UCCAUAGCAGCCGA AAGGCUGC	359	UAUGGAGUAGAACUUG AUGCGG	360
177	CAUCAAGUUCUACU CCAUUAGCAGCCGA AAGGCUGC	361	UAAUGGAGUAGAACUU GAUGGG	362
178	AUCAAGUUCUACUC CAUUCAGCAGCCGA AAGGCUGC	363	UGAAUGGAGUAGAACU UGAUGG	364
179	UCAAGUUCUACUCC AUUCAAGCAGCCGA AAGGCUGC	365	UUGAAUGGAGUAGAAC UUGAGG	366
180	CAAGUUCUACUCCA UUCAGAGCAGCCGA AAGGCUGC	367	UCUGAAUGGAGUAGAA CUUGGG	368
181	AAGUUCUACUCCAU UCAGCAGCAGCCGA AAGGCUGC	369	UGCUGAAUGGAGUAGA ACUUGG	370
182	AGUUCUACUCCAUU CAGCAAGCAGCCGA AAGGCUGC	371	UUGCUGAAUGGAGUAG AACUGG	372

183	GUUCUACUCCAUUCAGCAGAGCAGCCGAAAGGCUGC	373	UCUGCUGAAUGGAGUAGAACGG	374
184	GUGUCAUCUCAGACAACCUAGCAGCCGAAAGGCUGC	375	UAGGUUGUCUGAGAUGACACGG	376
185	CAUCUCAGACAACCUGCUGAGCAGCCGAAAGGCUGC	377	UCAGCAGGUUGUCUGAGAUGGG	378
186	UCAGACAACCUGCUGGUGAAGCAGCCGAAAGGCUGC	379	UUCACCAGCAGGUUGUCUGAGG	380
187	CGGGGACCUGUUACAGACAAGCAGCCGAAAGGCUGC	381	UUGUCUGUAACAGGUCCCCGGG	382
188	GACAACGCUGCCAUUGUCUAGCAGCCGAAAGGCUGC	383	UAGACAAUGGCAGCGUUGUCGG	384
189	GCUGCCUCCUGACUGUAAUAGCAGCCGAAAGGCUGC	385	UAUUACAGUCAGGAGGCAGCGG	386
190	CUGCCUCCUGACUGUAAUAAGCAGCCGAAAGGCUGC	387	UUAUUACAGUCAGGAGGCAGGG	388
191	UAAUAUUAAACUUUUUUAAAGCAGCCGAAAGGCUGC	389	UUUAAAAAAGUUUAAUAUUAGG	390
192	AAUAUUAAACUUUUUUAAAGCAGCCGAAAGGCUGC	391	UUUUAAAAAAGUUUAAUAUUGG	392

[00252] Table 4: GalXC™-SCAP Oligonucleotides (modified).

GalXC-SCAP Oligo	Sense Strand (passenger; 36-mer)	SEQ ID NO:	Antisense Strand (guide; 22-mer)	SEQ ID NO:
1	[mUs][mG][mU][mU][mU][mG][mC][fC][fU][fA][fC][mA][mU][mC][mU][mA][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	393	[MePhosphonate-4O-mUs][fAs][fAs][fG][fU][mA][fG][mA][mU][fG][mU][mA][mG][fG][mC][mA][mA][mA][mC][mAs][mGs][mG]	394
2	[mGs][mU][mU][mU][mG][mC][mC][fU][fA][fC][fA][mU][mC][mU][	395	[MePhosphonate-4O-mUs][fGs][fAs][fA][fG][mU][fA][mG][mA][fU][mG][m	396

	mA][mC][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		U][mA][fG][mG][mC][mA][mA][mA][mCs][mGs][mG]	
3	[mUs][mU][mU][mG][mC][mC][mU][fA][fC][fA][fU][mC][mU][mA][mC][mU][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	397	[MePhosphonate-4O-mUs][fAs][fGs][fA][fA][mG][fU][mA][mG][fA][mU][mG][mU][fA][mG][mG][mC][mA][mA][mAs][mGs][mG]	398
4	[mGs][mC][mC][mU][mA][mC][mA][fU][fC][fU][fA][mC][mU][mU][mC][mU][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	399	[MePhosphonate-4O-mUs][fUs][fGs][fG][fA][mG][fA][mA][mG][fU][mA][mG][mA][fU][mG][mU][mA][mG][mG][mCs][mGs][mG]	400
5	[mAs][mA][mG][mA][mU][mC][mG][fA][fC][fA][fU][mG][mG][mU][mC][mA][mA][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	401	[MePhosphonate-4O-mUs][fAs][fCs][fU][fU][mG][fA][mC][mC][fA][mU][mG][mU][fC][mG][mA][mU][mC][mU][mUs][mGs][mG]	402
6	[mAs][mG][mA][mU][mC][mG][mA][fC][fA][fU][fG][mG][mU][mC][mA][mA][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	403	[MePhosphonate-4O-mUs][fGs][fAs][fC][fU][mU][fG][mA][mC][fC][mA][mU][mG][fU][mC][mG][mA][mU][mC][mUs][mGs][mG]	404
7	[mAs][mU][mC][mG][mA][mC][mA][fU][fG][	405	[MePhosphonate-4O-mUs][fUs][fGs][fG][fA][mC	406

	fG][fU][mC][mA][mA][mG][mU][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		][fU][mU][mG][fA][mC][mC][mA][fU][mG][mU][mC][mG][mA][mUs][mGs][mG]	
8	[mGs][mU][mG][mU][mU][mG][mG][fU][fG][fC][fU][mC][mA][mC][mC][mA][mA][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	407	[MePhosphonate-4O-mUs][fAs][fCs][fU][fU][mG][fG][mU][mG][fA][mG][mC][mA][fC][mC][mA][mA][mC][mA][mCs][mGs][mG]	408
9	[mUs][mG][mU][mU][mG][mG][mU][fG][fC][fU][fC][mA][mC][mC][mA][mA][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	409	[MePhosphonate-4O-mUs][fGs][fAs][fC][fU][mU][fG][mG][mU][fG][mA][mG][mC][fA][mC][mC][mA][mA][mC][mAs][mGs][mG]	410
10	[mGs][mA][mG][mA][mG][mC][mU][fG][fG][fU][fC][mC][mA][mU][mC][mA][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	411	[MePhosphonate-4O-mUs][fUs][fCs][fA][fU][mG][fA][mU][mG][fG][mA][mC][mC][fA][mG][mC][mU][mC][mU][mCs][mGs][mG]	412
11	[mAs][mG][mA][mG][mC][mU][mG][fG][fU][fC][fC][mA][mU][mC][mA][mU][mG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	413	[MePhosphonate-4O-mUs][fUs][fUs][fC][fA][mU][fG][mA][mU][fG][mG][mA][mC][fC][mA][mG][mC][mU][mC][mUs][mGs][mG]	414

12	[mGs][mA][mG][mC][mU][mG][mG][fU][fC][fC][fA][mU][mC][mA][mU][mG][mA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	415	[MePhosphonate-4O-mUs][fCs][fUs][fU][fC][mA][fU][mG][mA][fU][mG][mG][mA][fC][mC][mA][mG][mC][mU][mCs][mGs][mG]	416
13	[mAs][mG][mC][mU][mG][mG][mU][fC][fC][fA][fU][mC][mA][mU][mG][mA][mA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	417	[MePhosphonate-4O-mUs][fUs][fCs][fU][fU][mC][fA][mU][mG][fA][mU][mG][mG][fA][mC][mC][mA][mG][mC][mUs][mGs][mG]	418
14	[mGs][mC][mU][mG][mG][mU][mC][fC][fA][fU][fC][mA][mU][mG][mA][mA][mG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	419	[MePhosphonate-4O-mUs][fUs][fUs][fC][fU][mU][fC][mA][mU][fG][mA][mU][mG][fG][mA][mC][mC][mA][mG][mCs][mGs][mG]	420
15	[mCs][mU][mG][mG][mU][mC][mC][fA][fU][fC][fA][mU][mG][mA][mA][mG][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	421	[MePhosphonate-4O-mUs][fGs][fUs][fU][fC][mU][fU][mC][mA][fU][mG][mA][mU][fG][mG][mA][mC][mC][mA][mGs][mGs][mG]	422
16	[mCs][mC][mG][mU][mU][mG][mU][fC][fU][fG][fG][mA][mU][mU][mG][mG][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	423	[MePhosphonate-4O-mUs][fAs][fUs][fG][fC][mC][fA][mA][mU][fC][mC][mA][mG][fA][mC][mA][mA][mC][mG][mGs][mGs][mG]	424

	GalNAc][mG][mG][mC][mU][mG][mC]			
17	[mUs][mU][mG][mU][mC][mU][mG][fG][fA][fU][fU][mG][mG][mC][mA][mU][mC][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	425	[MePhosphonate-4O-mUs][fAs][fGs][fG][fA][mU][fG][mC][mC][fA][mA][mU][mC][fC][mA][mG][mA][mC][mA][mAs][mGs][mG]	426
18	[mUs][mG][mU][mC][mU][mG][mG][fA][fU][fU][fG][mG][mC][mA][mU][mC][mC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	427	[MePhosphonate-4O-mUs][fCs][fAs][fG][fG][mA][fU][mG][mC][fC][mA][mA][mU][fC][mC][mA][mG][mA][mC][mAs][mGs][mG]	428
19	[mGs][mU][mC][mU][mG][mG][mA][fU][fU][fG][fG][mC][mA][mU][mC][mC][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	429	[MePhosphonate-4O-mUs][fCs][fCs][fA][fG][mG][fA][mU][mG][fC][mC][mA][mA][fU][mC][mC][mA][mG][mA][mCs][mGs][mG]	430
20	[mCs][mU][mG][mG][mA][mU][mU][fG][fG][fC][fA][mU][mC][mC][mU][mG][mG][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	431	[MePhosphonate-4O-mUs][fUs][fAs][fC][fC][mA][fG][mG][mA][fU][mG][mC][mC][fA][mA][mU][mC][mC][mA][mGs][mGs][mG]	432
21	[mUs][mG][mG][mA][mU][mU][mG][fG][fC][fA][fU][mC][mC][mU][mG][mG][mU][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-	433	[MePhosphonate-4O-mUs][fAs][fUs][fA][fC][mC][fA][mG][mG][fA][mU][mG][mC][fC][mA][mA][mU][mC][mC][mAs][mGs][mG]	434

	GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
22	[mGs][mG][mA][mU][mU][mG][mG][fC][fA][fU][fC][mC][mU][mG][mG][mU][mA][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	435	[MePhosphonate-4O-mUs][fUs][fAs][fU][fA][mC][fC][mA][mG][fG][mA][mU][mG][fC][mC][mA][mA][mU][mC][mCs][mGs][mG]	436
23	[mGs][mA][mU][mU][mG][mG][mC][fA][fU][fC][fC][mU][mG][mG][mU][mA][mU][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	437	[MePhosphonate-4O-mUs][fGs][fUs][fA][fU][mA][fC][mC][mA][fG][mG][mA][mU][fG][mC][mC][mA][mA][mU][mCs][mGs][mG]	438
24	[mAs][mU][mU][mG][mG][mC][mA][fU][fC][fC][fU][mG][mG][mU][mA][mU][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	439	[MePhosphonate-4O-mUs][fUs][fGs][fU][fA][mU][fA][mC][mC][fA][mG][mG][mA][fU][mG][mC][mC][mA][mA][mUs][mGs][mG]	440
25	[mCs][mU][mC][mC][mA][mU][mC][fU][fU][fC][fC][mC][mA][mC][mC][mU][mG][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	441	[MePhosphonate-4O-mUs][fAs][fUs][fC][fA][mG][fG][mU][mG][fG][mG][mA][mA][fG][mA][mU][mG][mG][mA][mGs][mGs][mG]	442
26	[mCs][mA][mU][mC][mU][mG][mC][fC][fU][fG][fU][mG][mG][mG][mA][mU][mG][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ade	443	[MePhosphonate-4O-mUs][fUs][fAs][fC][fA][mU][fC][mC][mC][fA][mC][mA][mG][fG][mC][mA][mG][mA][mU][mGs][mGs][mG]	444

	mA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
27	[mUs][mC][mU][mG][mC][mC][mU][fG][fU][fG][fG][mG][mA][mU][mG][mU][mA][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	445	[MePhosphonate-4O-mUs][fAs][fGs][fU][fA][mC][fA][mU][mC][fC][mC][mA][mC][fA][mG][mG][mC][mA][mG][mAs][mGs][mG]	446
28	[mGs][mU][mG][mG][mU][mG][mC][fA][fA][fG][fC][mU][mU][mG][mG][mG][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	447	[MePhosphonate-4O-mUs][fAs][fCs][fA][fC][mC][fC][mA][mA][fG][mC][mU][mU][fG][mC][mA][mC][mC][mA][mCs][mGs][mG]	448
29	[mUs][mG][mG][mU][mG][mC][mA][fA][fG][fC][fU][mU][mG][mG][mG][mU][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	449	[MePhosphonate-4O-mUs][fGs][fAs][fC][fA][mC][fC][mC][mA][fA][mG][mC][mU][fU][mG][mC][mA][mC][mC][mAs][mGs][mG]	450
30	[mGs][mG][mU][mG][mC][mA][mA][fG][fC][fU][fU][mG][mG][mG][mU][mG][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	451	[MePhosphonate-4O-mUs][fUs][fGs][fA][fC][mA][fC][mC][mC][fA][mA][mG][mC][fU][mU][mG][mC][mA][mC][mCs][mGs][mG]	452
31	[mGs][mU][mG][mC][mA][mA][mG][fC][fU][fU][fG][mG][mG][mU][mG][mU][mC][mA][mU][mA][mG][mC][mA][	453	[MePhosphonate-4O-mUs][fAs][fUs][fG][fA][mC][fA][mC][mC][fC][mA][mA][mG][fC][mU][mU][mG][mC][mA][mCs][mGs][mG]	454

	mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
32	[mGs][mC][mA][mA][mG][mC][mU][fU][fG][fG][fG][mU][mG][mU][mC][mA][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	455	[MePhosphonate-4O-mUs][fAs][fGs][fA][fU][mG][fA][mC][mA][fC][mC][mC][mA][fA][mG][mC][mU][mU][mG][mCs][mGs][mG]	456
33	[mCs][mA][mA][mG][mC][mU][mU][fG][fG][fG][fU][mG][mU][mC][mA][mU][mC][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	457	[MePhosphonate-4O-mUs][fGs][fAs][fG][fA][mU][fG][mA][mC][fA][mC][mC][mC][fA][mA][mG][mC][mU][mU][mGs][mGs][mG]	458
34	[mAs][mA][mG][mC][mU][mU][mG][fG][fG][fU][fG][mU][mC][mA][mU][mC][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	459	[MePhosphonate-4O-mUs][fUs][fGs][fA][fG][mA][fU][mG][mA][fC][mA][mC][mC][fC][mA][mA][mG][mC][mU][mUs][mGs][mG]	460
35	[mAs][mG][mC][mU][mU][mG][mG][fG][fU][fG][fU][mC][mA][mU][mC][mU][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	461	[MePhosphonate-4O-mUs][fCs][fUs][fG][fA][mG][fA][mU][mG][fA][mC][mA][mC][fC][mC][mA][mA][mG][mC][mUs][mGs][mG]	462
36	[mGs][mC][mU][mU][mG][mG][mG][fU][fG][fU][fC][mA][mU][mC][mU][mC][mA][mG][m	463	[MePhosphonate-4O-mUs][fUs][fCs][fU][fG][mA][fG][mA][mU][fG][mA][m	464

	A][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		C][mA][fC][mC][mC][mA][mA][mG][mCs][mGs][mG]	
37	[mGs][mU][mG][mU][mC][mU][mC][fC][fU][fU][fU][mU][mG][mG][mG][mA][mC][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	465	[MePhosphonate-4O-mUs][fAs][fGs][fG][fU][mC][fC][mC][mA][fA][mA][mA][mG][fG][mA][mG][mA][mC][mA][mCs][mGs][mG]	466
38	[mUs][mG][mU][mC][mU][mC][mC][fU][fU][fU][fU][mG][mG][mG][mA][mC][mC][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	467	[MePhosphonate-4O-mUs][fUs][fAs][fG][fG][mU][fC][mC][mC][fA][mA][mA][mA][fG][mG][mA][mG][mA][mC][mAs][mGs][mG]	468
39	[mGs][mG][mG][mG][mA][mC][mC][fU][fG][fU][fU][mA][mC][mA][mG][mA][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	469	[MePhosphonate-4O-mUs][fCs][fUs][fG][fU][mC][fU][mG][mU][fA][mA][mC][mA][fG][mG][mU][mC][mC][mC][mCs][mGs][mG]	470
40	[mGs][mG][mG][mA][mC][mC][mU][fG][fU][fU][fA][mC][mA][mG][mA][mC][mA][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	471	[MePhosphonate-4O-mUs][fAs][fCs][fU][fG][mU][fC][mU][mG][fU][mA][mA][mC][fA][mG][mG][mU][mC][mC][mCs][mGs][mG]	472
41	[mGs][mG][mA][mC][mC][mU][mG][fU][fU][fA][fC][mA][mG][mA][	473	[MePhosphonate-4O-mUs][fGs][fAs][fC][fU][mG][fU][mC][mU][fG][mU][m	474

	mC][mA][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		A][mA][fC][mA][mG][mG][mU][mC][mCs][mGs][mG]	
42	[mGs][mA][mC][mC][mU][mG][mU][fU][fA][fC][fA][mG][mA][mC][mA][mG][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	475	[MePhosphonate-4O-mUs][fAs][fGs][fA][fC][mU][fG][mU][mC][fU][mG][mU][mA][fA][mC][mA][mG][mG][mU][mCs][mGs][mG]	476
43	[mAs][mC][mC][mU][mG][mU][mU][fA][fC][fA][fG][mA][mC][mA][mG][mU][mC][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	477	[MePhosphonate-4O-mUs][fUs][fAs][fG][fA][mC][fU][mG][mU][fC][mU][mG][mU][fA][mA][mC][mA][mG][mG][mUs][mGs][mG]	478
44	[mUs][mG][mC][mC][mA][mU][mU][fG][fU][fC][fU][mG][mC][mA][mA][mC][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	479	[MePhosphonate-4O-mUs][fAs][fAs][fA][fG][mU][fU][mG][mC][fA][mG][mA][mC][fA][mA][mU][mG][mG][mC][mAs][mGs][mG]	480
45	[mGs][mC][mC][mA][mU][mU][mG][fU][fC][fU][fG][mC][mA][mA][mC][mU][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	481	[MePhosphonate-4O-mUs][fCs][fAs][fA][fA][mG][fU][mU][mG][fC][mA][mG][mA][fC][mA][mA][mU][mG][mG][mCs][mGs][mG]	482
46	[mCs][mC][mA][mU][mU][mG][mU][fC][fU][	483	[MePhosphonate-4O-mUs][fCs][fCs][fA][fA][mA	484

	fG][fC][mA][mA][mC][mU][mU][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		][fG][mU][mU][fG][mC][mA][mG][fA][mC][mA][mA][mU][mG][mGs][mGs][mG]	
47	[mAs][mU][mU][mG][mU][mC][mU][fG][fC][fA][fA][mC][mU][mU][mU][mG][mG][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	485	[MePhosphonate-4O-mUs][fUs][fGs][fC][fC][mA][fA][mA][mG][fU][mU][mG][mC][fA][mG][mA][mC][mA][mA][mUs][mGs][mG]	486
48	[mUs][mC][mU][mG][mC][mA][mA][fC][fU][fU][fU][mG][mG][mC][mA][mG][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	487	[MePhosphonate-4O-mUs][fUs][fCs][fA][fC][mU][fG][mC][mC][fA][mA][mA][mG][fU][mU][mG][mC][mA][mG][mAs][mGs][mG]	488
49	[mCs][mU][mA][mC][mC][mC][mA][fC][fU][fG][fC][mU][mG][mA][mA][mA][mC][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	489	[MePhosphonate-4O-mUs][fGs][fAs][fG][fU][mU][fU][mC][mA][fG][mC][mA][mG][fU][mG][mG][mG][mU][mA][mGs][mGs][mG]	490
50	[mGs][mC][mC][mA][mG][mG][mA][fA][fC][fA][fG][mG][mA][mC][mC][mC][mU][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	491	[MePhosphonate-4O-mUs][fCs][fAs][fC][fA][mG][fG][mU][mC][fC][mU][mG][mU][fU][mC][mC][mU][mG][mG][mCs][mGs][mG]	492

51	[mGs][mA][mA][mC][mA][mG][mG][fA][fC][fC][fU][mG][mU][mG][mG][mA][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	493	[MePhosphonate-4O-mUs][fAs][fAs][fU][fU][mC][fC][mA][mC][fA][mG][mG][mU][fC][mC][mU][mG][mU][mU][mCs][mGs][mG]	494
52	[mAs][mC][mA][mG][mG][mA][mC][fC][fU][fG][fU][mG][mG][mA][mA][mU][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	495	[MePhosphonate-4O-mUs][fUs][fGs][fA][fA][mU][fU][mC][mC][fA][mC][mA][mG][fG][mU][mC][mC][mU][mG][mUs][mGs][mG]	496
53	[mUs][mG][mG][mA][mA][mU][mU][fC][fA][fC][fC][mA][mC][mC][mC][mC][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	497	[MePhosphonate-4O-mUs][fAs][fCs][fA][fG][mG][fG][mG][mU][fG][mG][mU][mG][fA][mA][mU][mU][mC][mC][mAs][mGs][mG]	498
54	[mCs][mU][mU][mG][mU][mG][mA][fC][fC][fA][fC][mC][mU][mA][mC][mA][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	499	[MePhosphonate-4O-mUs][fUs][fGs][fA][fU][mG][fU][mA][mG][fG][mU][mG][mG][fU][mC][mA][mC][mA][mA][mGs][mGs][mG]	500
55	[mUs][mU][mG][mU][mG][mA][mC][fC][fA][fC][fC][mU][mA][mC][mA][mU][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	501	[MePhosphonate-4O-mUs][fAs][fUs][fG][fA][mU][fG][mU][mA][fG][mG][mU][mG][fG][mU][mC][mA][mC][mA][mAs][mGs][mG]	502

	GalNAc][mG][mG][mC][mU][mG][mC]			
56	[mUs][mG][mU][mG][mA][mC][mC][fA][fC][fC][fU][mA][mC][mA][mU][mC][mA][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	503	[MePhosphonate-4O-mUs][fGs][fAs][fU][fG][mA][fU][mG][mU][fA][mG][mG][mU][fG][mG][mU][mC][mA][mC][mAs][mGs][mG]	504
57	[mGs][mU][mG][mA][mC][mC][mA][fC][fC][fU][fA][mC][mA][mU][mC][mA][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	505	[MePhosphonate-4O-mUs][fAs][fGs][fA][fU][mG][fA][mU][mG][fU][mA][mG][mG][fU][mG][mG][mU][mC][mA][mCs][mGs][mG]	506
58	[mUs][mG][mA][mC][mC][mA][mC][fC][fU][fA][fC][mA][mU][mC][mA][mU][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	507	[MePhosphonate-4O-mUs][fAs][fAs][fG][fA][mU][fG][mA][mU][fG][mU][mA][mG][fG][mU][mG][mG][mU][mC][mAs][mGs][mG]	508
59	[mGs][mA][mC][mC][mA][mC][mC][fU][fA][fC][fA][mU][mC][mA][mU][mC][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	509	[MePhosphonate-4O-mUs][fCs][fAs][fA][fG][mA][fU][mG][mA][fU][mG][mU][mA][fG][mG][mU][mG][mG][mU][mCs][mGs][mG]	510
60	[mAs][mC][mC][mA][mC][mC][mU][fA][fC][fA][fU][mC][mA][mU][mC][mU][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-	511	[MePhosphonate-4O-mUs][fAs][fCs][fA][fA][mG][fA][mU][mG][fA][mU][mG][mU][fA][mG][mG][mU][mG][mG][mUs][mGs][mG]	512

	GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
61	[mCs][mC][mA][mC][mC][mU][mA][fC][fA][fU][fC][mA][mU][mC][mU][mU][mG][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	513	[MePhosphonate-4O-mUs][fAs][fAs][fC][fA][mA][fG][mA][mU][fG][mA][mU][mG][fU][mA][mG][mG][mU][mG][mGs][mGs][mG]	514
62	[mCs][mA][mC][mC][mU][mA][mC][fA][fU][fC][fA][mU][mC][mU][mU][mG][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	515	[MePhosphonate-4O-mUs][fAs][fAs][fA][fC][mA][fA][mG][mA][fU][mG][mA][mU][fG][mU][mA][mG][mG][mU][mGs][mGs][mG]	516
63	[mAs][mC][mC][mU][mA][mC][mA][fU][fC][fA][fU][mC][mU][mU][mG][mU][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	517	[MePhosphonate-4O-mUs][fCs][fAs][fA][fA][mC][fA][mA][mG][fA][mU][mG][mA][fU][mG][mU][mA][mG][mG][mUs][mGs][mG]	518
64	[mCs][mC][mU][mA][mC][mA][mU][fC][fA][fU][fC][mU][mU][mG][mU][mU][mU][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	519	[MePhosphonate-4O-mUs][fGs][fCs][fA][fA][mA][fC][mA][mA][fG][mA][mU][mG][fA][mU][mG][mU][mA][mG][mGs][mGs][mG]	520
65	[mCs][mU][mA][mC][mA][mU][mC][fA][fU][fC][fU][mU][mG][mU][mU][mU][mG][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ade	521	[MePhosphonate-4O-mUs][fGs][fGs][fC][fA][mA][fA][mC][mA][fA][mG][mA][mU][fG][mA][mU][mG][mU][mA][mGs][mGs][mG]	522

	mA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
66	[mAs][mC][mA][mU][mC][mA][mU][fC][fU][fU][fG][mU][mU][mU][mG][mC][mC][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	523	[MePhosphonate-4O-mUs][fUs][fAs][fG][fG][mC][fA][mA][mA][fC][mA][mA][mG][fA][mU][mG][mA][mU][mG][mUs][mGs][mG]	524
67	[mAs][mU][mC][mA][mU][mC][mU][fU][fG][fU][fU][mU][mG][mC][mC][mU][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	525	[MePhosphonate-4O-mUs][fUs][fGs][fU][fA][mG][fG][mC][mA][fA][mA][mC][mA][fA][mG][mA][mU][mG][mA][mUs][mGs][mG]	526
68	[mUs][mC][mA][mU][mC][mU][mU][fG][fU][fU][fU][mG][mC][mC][mU][mA][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	527	[MePhosphonate-4O-mUs][fAs][fUs][fG][fU][mA][fG][mG][mC][fA][mA][mA][mC][fA][mA][mG][mA][mU][mG][mAs][mGs][mG]	528
69	[mAs][mU][mC][mU][mU][mG][mU][fU][fU][fG][fC][mC][mU][mA][mC][mA][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	529	[MePhosphonate-4O-mUs][fAs][fGs][fA][fU][mG][fU][mA][mG][fG][mC][mA][mA][fA][mC][mA][mA][mG][mA][mUs][mGs][mG]	530
70	[mUs][mC][mU][mU][mG][mU][mU][fU][fG][fC][fC][mU][mA][mC][mA][mU][mC][mU][mU][mA][mA][mG][mC][mA][	531	[MePhosphonate-4O-mUs][fUs][fAs][fG][fA][mU][fG][mU][mA][fG][mG][mC][mA][fA][mA][mC][mA][mA][mG][mAs][mGs][mG]	532

	mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
71	[mUs][mU][mU][mC][mC][mC][mC][fU][fA][fC][fC][mU][mU][mG][mU][mG][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	533	[MePhosphonate-4O-mUs][fCs][fAs][fC][fC][mA][fC][mA][mA][fG][mG][mU][mA][fG][mG][mG][mG][mA][mA][mAs][mGs][mG]	534
72	[mUs][mU][mC][mC][mC][mC][mU][fA][fC][fC][fU][mU][mG][mU][mG][mG][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	535	[MePhosphonate-4O-mUs][fCs][fCs][fA][fC][mC][fA][mC][mA][fA][mG][mG][mU][fA][mG][mG][mG][mG][mA][mAs][mGs][mG]	536
73	[mCs][mC][mC][mU][mA][mC][mC][fU][fU][fG][fU][mG][mG][mU][mG][mG][mU][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	537	[MePhosphonate-4O-mUs][fUs][fAs][fA][fC][mC][fA][mC][mC][fA][mC][mA][mA][fG][mG][mU][mA][mG][mG][mGs][mGs][mG]	538
74	[mCs][mU][mA][mC][mC][mU][mU][fG][fU][fG][fG][mU][mG][mG][mU][mU][mU][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	539	[MePhosphonate-4O-mUs][fAs][fAs][fU][fA][mA][fC][mC][mA][fC][mC][mA][mC][fA][mA][mG][mG][mU][mA][mGs][mGs][mG]	540
75	[mUs][mA][mC][mC][mU][mU][mG][fU][fG][fG][fU][mG][mG][mU][mU][mA][mU][mU][m	541	[MePhosphonate-4O-mUs][fCs][fAs][fA][fU][mA][fA][mC][mC][fA][mC][m	542

	G][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		C][mA][fC][mA][mA][mG][mG][mU][mAs][mGs][mG]	
76	[mAs][mC][mC][mU][mU][mG][mU][fG][fG][fU][fG][mG][mU][mU][mA][mU][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	543	[MePhosphonate-4O-mUs][fCs][fCs][fA][fA][mU][fA][mA][mC][fC][mA][mC][mC][fA][mC][mA][mA][mG][mG][mUs][mGs][mG]	544
77	[mCs][mC][mU][mU][mG][mU][mG][fG][fU][fG][fG][mU][mU][mA][mU][mU][mG][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	545	[MePhosphonate-4O-mUs][fCs][fCs][fC][fA][mA][fU][mA][mA][fC][mC][mA][mC][fC][mA][mC][mA][mA][mG][mGs][mGs][mG]	546
78	[mCs][mU][mU][mG][mU][mG][mG][fU][fG][fG][fU][mU][mA][mU][mU][mG][mG][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	547	[MePhosphonate-4O-mUs][fAs][fCs][fC][fC][mA][fA][mU][mA][fA][mC][mC][mA][fC][mC][mA][mC][mA][mA][mGs][mGs][mG]	548
79	[mUs][mU][mG][mU][mG][mG][mU][fG][fG][fU][fU][mA][mU][mU][mG][mG][mG][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	549	[MePhosphonate-4O-mUs][fAs][fAs][fC][fC][mC][fA][mA][mU][fA][mA][mC][mC][fA][mC][mC][mA][mC][mA][mAs][mGs][mG]	550
80	[mUs][mG][mU][mG][mG][mU][mG][fG][fU][fU][fA][mU][mU][mG][	551	[MePhosphonate-4O-mUs][fUs][fAs][fA][fC][mC][fC][mA][mA][fU][mA][m	552

	mG][mG][mU][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		A][mC][fC][mA][mC][mC][mA][mC][mAs][mGs][mG]	
81	[mGs][mU][mG][mG][mU][mG][mG][fU][fU][fA][fU][mU][mG][mG][mG][mU][mU][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	553	[MePhosphonate-4O-mUs][fCs][fUs][fA][fA][mC][fC][mC][mA][fA][mU][mA][mA][fC][mC][mA][mC][mC][mA][mCs][mGs][mG]	554
82	[mUs][mG][mG][mU][mG][mG][mU][fU][fA][fU][fU][mG][mG][mG][mU][mU][mA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	555	[MePhosphonate-4O-mUs][fUs][fCs][fU][fA][mA][fC][mC][mC][fA][mA][mU][mA][fA][mC][mC][mA][mC][mC][mAs][mGs][mG]	556
83	[mGs][mG][mU][mG][mG][mU][mU][fA][fU][fU][fG][mG][mG][mU][mU][mA][mG][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	557	[MePhosphonate-4O-mUs][fCs][fUs][fC][fU][mA][fA][mC][mC][fC][mA][mA][mU][fA][mA][mC][mC][mA][mC][mCs][mGs][mG]	558
84	[mGs][mU][mG][mG][mU][mU][mA][fU][fU][fG][fG][mG][mU][mU][mA][mG][mA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	559	[MePhosphonate-4O-mUs][fUs][fCs][fU][fC][mU][fA][mA][mC][fC][mC][mA][mA][fU][mA][mA][mC][mC][mA][mCs][mGs][mG]	560
85	[mUs][mG][mG][mU][mU][mA][mU][fU][fG][	561	[MePhosphonate-4O-mUs][fUs][fUs][fC][fU][mC	562

	fG][fG][mU][mU][mA][mG][mA][mG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		][fU][mA][mA][fC][mC][mC][mA][fA][mU][mA][mA][mC][mC][mAs][mGs][mG]	
86	[mGs][mG][mU][mU][mA][mU][mU][fG][fG][fG][fU][mU][mA][mG][mA][mG][mA][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	563	[MePhosphonate-4O-mUs][fAs][fUs][fU][fC][mU][fC][mU][mA][fA][mC][mC][mC][fA][mA][mU][mA][mA][mC][mCs][mGs][mG]	564
87	[mGs][mU][mU][mA][mU][mU][mG][fG][fG][fU][fU][mA][mG][mA][mG][mA][mA][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	565	[MePhosphonate-4O-mUs][fCs][fAs][fU][fU][mC][fU][mC][mU][fA][mA][mC][mC][fC][mA][mA][mU][mA][mA][mCs][mGs][mG]	566
88	[mUs][mU][mA][mU][mU][mG][mG][fG][fU][fU][fA][mG][mA][mG][mA][mA][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	567	[MePhosphonate-4O-mUs][fAs][fCs][fA][fU][mU][fC][mU][mC][fU][mA][mA][mC][fC][mC][mA][mA][mU][mA][mAs][mGs][mG]	568
89	[mAs][mU][mU][mG][mG][mG][mU][fU][fA][fG][fA][mG][mA][mA][mU][mG][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	569	[MePhosphonate-4O-mUs][fAs][fCs][fA][fC][mA][fU][mU][mC][fU][mC][mU][mA][fA][mC][mC][mC][mA][mA][mUs][mGs][mG]	570

90	[mUs][mU][mG][mG][mG][mU][mU][fA][fG][fA][fG][mA][mA][mU][mG][mU][mG][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	571	[MePhosphonate-4O-mUs][fAs][fAs][fC][fA][mC][fA][mU][mU][fC][mU][mC][mU][fA][mA][mC][mC][mC][mA][mAs][mGs][mG]	572
91	[mGs][mG][mU][mU][mA][mG][mA][fG][fA][fA][fU][mG][mU][mG][mU][mU][mG][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	573	[MePhosphonate-4O-mUs][fAs][fCs][fC][fA][mA][fC][mA][mC][fA][mU][mU][mC][fU][mC][mU][mA][mA][mC][mCs][mGs][mG]	574
92	[mGs][mU][mU][mA][mG][mA][mG][fA][fA][fU][fG][mU][mG][mU][mU][mG][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	575	[MePhosphonate-4O-mUs][fCs][fAs][fC][fC][mA][fA][mC][mA][fC][mA][mU][mU][fC][mU][mC][mU][mA][mA][mCs][mGs][mG]	576
93	[mUs][mU][mA][mG][mA][mG][mA][fA][fU][fG][fU][mG][mU][mU][mG][mG][mU][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	577	[MePhosphonate-4O-mUs][fGs][fCs][fA][fC][mC][fA][mA][mC][fA][mC][mA][mU][fU][mC][mU][mC][mU][mA][mAs][mGs][mG]	578
94	[mUs][mA][mG][mA][mG][mA][mA][fU][fG][fU][fG][mU][mU][mG][mG][mU][mG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	579	[MePhosphonate-4O-mUs][fAs][fGs][fC][fA][mC][fC][mA][mA][fC][mA][mC][mA][fU][mU][mC][mU][mC][mU][mAs][mGs][mG]	580

	GalNAc][mG][mG][mC][mU][mG][mC]			
95	[mAs][mG][mA][mG][mA][mA][mU][fG][fU][fG][fU][mU][mG][mG][mU][mG][mC][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	581	[MePhosphonate-4O-mUs][fGs][fAs][fG][fC][mA][fC][mC][mA][fA][mC][mA][mC][fA][mU][mU][mC][mU][mC][mUs][mGs][mG]	582
96	[mGs][mA][mG][mA][mA][mU][mG][fU][fG][fU][fU][mG][mG][mU][mG][mC][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	583	[MePhosphonate-4O-mUs][fUs][fGs][fA][fG][mC][fA][mC][mC][fA][mA][mC][mA][fC][mA][mU][mU][mC][mU][mCs][mGs][mG]	584
97	[mAs][mG][mA][mA][mU][mG][mU][fG][fU][fU][fG][mG][mU][mG][mC][mU][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	585	[MePhosphonate-4O-mUs][fGs][fUs][fG][fA][mG][fC][mA][mC][fC][mA][mA][mC][fA][mC][mA][mU][mU][mC][mUs][mGs][mG]	586
98	[mAs][mA][mU][mG][mU][mG][mU][fU][fG][fG][fU][mG][mC][mU][mC][mA][mC][mC][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	587	[MePhosphonate-4O-mUs][fUs][fGs][fG][fU][mG][fA][mG][mC][fA][mC][mC][mA][fA][mC][mA][mC][mA][mU][mUs][mGs][mG]	588
99	[mAs][mU][mG][mU][mG][mU][mU][fG][fG][fU][fG][mC][mU][mC][mA][mC][mC][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-	589	[MePhosphonate-4O-mUs][fUs][fUs][fG][fG][mU][fG][mA][mG][fC][mA][mC][mC][fA][mA][mC][mA][mC][mA][mUs][mGs][mG]	590

	GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
100	[mUs][mG][mU][mG][mU][mU][mG][fG][fU][fG][fC][mU][mC][mA][mC][mC][mA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	591	[MePhosphonate-4O-mUs][fCs][fUs][fU][fG][mG][fU][mG][mA][fG][mC][mA][mC][fC][mA][mA][mC][mA][mC][mAs][mGs][mG]	592
101	[mUs][mG][mG][mU][mC][mC][mA][fU][fC][fA][fU][mG][mA][mA][mG][mA][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	593	[MePhosphonate-4O-mUs][fUs][fGs][fU][fU][mC][fU][mU][mC][fA][mU][mG][mA][fU][mG][mG][mA][mC][mC][mAs][mGs][mG]	594
102	[mGs][mG][mU][mC][mC][mA][mU][fC][fA][fU][fG][mA][mA][mG][mA][mA][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	595	[MePhosphonate-4O-mUs][fAs][fUs][fG][fU][mU][fC][mU][mU][fC][mA][mU][mG][fA][mU][mG][mG][mA][mC][mCs][mGs][mG]	596
103	[mCs][mU][mG][mA][mC][mU][mU][fC][fU][fU][fC][mC][mU][mU][mC][mA][mG][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	597	[MePhosphonate-4O-mUs][fAs][fUs][fC][fU][mG][fA][mA][mG][fG][mA][mA][mG][fA][mA][mG][mU][mC][mA][mGs][mGs][mG]	598
104	[mAs][mC][mU][mU][mC][mU][mU][fC][fC][fU][fU][mC][mA][mG][mA][mU][mG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ade	599	[MePhosphonate-4O-mUs][fAs][fGs][fC][fA][mU][fC][mU][mG][fA][mA][mG][mG][fA][mA][mG][mA][mA][mG][mUs][mGs][mG]	600

	mA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
105	[mUs][mC][mC][mU][mU][mC][mA][fG][fA][fU][fG][mC][mU][mG][mU][mU][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	601	[MePhosphonate-4O-mUs][fAs][fAs][fA][fA][mA][fC][mA][mG][fC][mA][mU][mC][fU][mG][mA][mA][mG][mG][mAs][mGs][mG]	602
106	[mCs][mC][mU][mU][mC][mA][mG][fA][fU][fG][fC][mU][mG][mU][mU][mU][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	603	[MePhosphonate-4O-mUs][fGs][fAs][fA][fA][mA][fA][mC][mA][fG][mC][mA][mU][fC][mU][mG][mA][mA][mG][mGs][mGs][mG]	604
107	[mCs][mU][mU][mC][mA][mG][mA][fU][fG][fC][fU][mG][mU][mU][mU][mU][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	605	[MePhosphonate-4O-mUs][fUs][fGs][fA][fA][mA][fA][mA][mC][fA][mG][mC][mA][fU][mC][mU][mG][mA][mA][mGs][mGs][mG]	606
108	[mUs][mU][mC][mA][mG][mA][mU][fG][fC][fU][fG][mU][mU][mU][mU][mU][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	607	[MePhosphonate-4O-mUs][fGs][fUs][fG][fA][mA][fA][mA][mA][fC][mA][mG][mC][fA][mU][mC][mU][mG][mA][mAs][mGs][mG]	608
109	[mCs][mA][mG][mA][mU][mG][mC][fU][fG][fU][fU][mU][mU][mU][mC][mA][mC][mC][mA][mA][mG][mC][mA][	609	[MePhosphonate-4O-mUs][fUs][fGs][fG][fU][mG][fA][mA][mA][fA][mA][mC][mA][fG][mC][mA][mU][mC][mU][mGs][mGs][mG]	610

	mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
110	[mAs][mG][mA][mU][mG][mC][mU][fG][fU][fU][fU][mU][mU][mC][mA][mC][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	611	[MePhosphonate-4O-mUs][fGs][fUs][fG][fG][mU][fG][mA][mA][fA][mA][mA][mC][fA][mG][mC][mA][mU][mC][mUs][mGs][mG]	612
111	[mGs][mA][mU][mG][mC][mU][mG][fU][fU][fU][fU][mU][mC][mA][mC][mC][mA][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	613	[MePhosphonate-4O-mUs][fAs][fGs][fU][fG][mG][fU][mG][mA][fA][mA][mA][mA][fC][mA][mG][mC][mA][mU][mCs][mGs][mG]	614
112	[mAs][mU][mG][mC][mU][mG][mU][fU][fU][fU][fU][mC][mA][mC][mC][mA][mC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	615	[MePhosphonate-4O-mUs][fCs][fAs][fG][fU][mG][fG][mU][mG][fA][mA][mA][mA][fA][mC][mA][mG][mC][mA][mUs][mGs][mG]	616
113	[mUs][mG][mC][mU][mG][mU][mU][fU][fU][fU][fC][mA][mC][mC][mA][mC][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	617	[MePhosphonate-4O-mUs][fAs][fCs][fA][fG][mU][fG][mG][mU][fG][mA][mA][mA][fA][mA][mC][mA][mG][mC][mAs][mGs][mG]	618
114	[mGs][mC][mU][mG][mU][mU][mU][fU][fU][fC][fA][mC][mC][mA][mC][mU][mG][mU][m	619	[MePhosphonate-4O-mUs][fGs][fAs][fC][fA][mG][fU][mG][mG][fU][mG][m	620

	C][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		A][mA][fA][mA][mA][mC][mA][mG][mCs][mGs][mG]	
115	[mUs][mG][mU][mU][mU][mU][mU][fC][fA][fC][fC][mA][mC][mU][mG][mU][mC][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	621	[MePhosphonate-4O-mUs][fAs][fGs][fG][fA][mC][fA][mG][mU][fG][mG][mU][mG][fA][mA][mA][mA][mA][mC][mAs][mGs][mG]	622
116	[mGs][mU][mU][mU][mU][mU][mU][mC][fA][fC][fC][fA][mC][mU][mG][mU][mC][mC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	623	[MePhosphonate-4O-mUs][fCs][fAs][fG][fG][mA][fC][mA][mG][fU][mG][mG][mU][fG][mA][mA][mA][mA][mA][mCs][mGs][mG]	624
117	[mUs][mU][mU][mU][mU][mC][mA][fC][fC][fA][fC][mU][mG][mU][mC][mC][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	625	[MePhosphonate-4O-mUs][fAs][fCs][fA][fG][mG][fA][mC][mA][fG][mU][mG][mG][fU][mG][mA][mA][mA][mA][mAs][mGs][mG]	626
118	[mUs][mU][mU][mU][mC][mA][mC][fC][fA][fC][fU][mG][mU][mC][mC][mU][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	627	[MePhosphonate-4O-mUs][fGs][fAs][fC][fA][mG][fG][mA][mC][fA][mG][mU][mG][fG][mU][mG][mA][mA][mA][mA][mAs][mGs][mG]	628
119	[mUs][mU][mC][mA][mC][mC][mA][fC][fU][fG][fU][mC][mC][mU][	629	[MePhosphonate-4O-mUs][fUs][fGs][fG][fA][mC][fA][mG][mG][fA][mC][m	630

	mG][mU][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		A][mG][fU][mG][mG][mU][mG][mA][mAs][mGs][mG]	
120	[mCs][mA][mC][mC][mA][mC][mU][fG][fU][fC][fC][mU][mG][mU][mC][mC][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	631	[MePhosphonate-4O-mUs][fAs][fAs][fU][fG][mG][fA][mC][mA][fG][mG][mA][mC][fA][mG][mU][mG][mG][mU][mGs][mGs][mG]	632
121	[mAs][mC][mC][mA][mC][mU][mG][fU][fC][fC][fU][mG][mU][mC][mC][mA][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	633	[MePhosphonate-4O-mUs][fCs][fAs][fA][fU][mG][fG][mA][mC][fA][mG][mG][mA][fC][mA][mG][mU][mG][mG][mUs][mGs][mG]	634
122	[mCs][mC][mA][mC][mU][mG][mU][fC][fC][fU][fG][mU][mC][mC][mA][mU][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	635	[MePhosphonate-4O-mUs][fUs][fCs][fA][fA][mU][fG][mG][mA][fC][mA][mG][mG][fA][mC][mA][mG][mU][mG][mGs][mGs][mG]	636
123	[mCs][mA][mC][mU][mG][mU][mC][fC][fU][fG][fU][mC][mC][mA][mU][mU][mG][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	637	[MePhosphonate-4O-mUs][fGs][fUs][fC][fA][mA][fU][mG][mG][fA][mC][mA][mG][fG][mA][mC][mA][mG][mU][mGs][mGs][mG]	638
124	[mAs][mC][mU][mG][mU][mC][mC][fU][fG][	639	[MePhosphonate-4O-mUs][fUs][fGs][fU][fC][mA	640

	fU][fC][mC][mA][mU][mU][mG][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		][fA][mU][mG][fG][mA][mC][mA][fG][mG][mA][mC][mA][mG][mUs][mGs][mG]	
125	[mCs][mU][mA][mA][mG][mC][mU][fA][fC][fC][fU][mG][mA][mG][mA][mA][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	641	[MePhosphonate-4O-mUs][fUs][fGs][fG][fU][mU][fC][mU][mC][fA][mG][mG][mU][fA][mG][mC][mU][mU][mA][mGs][mGs][mG]	642
126	[mGs][mA][mG][mG][mU][mC][mC][fA][fG][fC][fA][mG][mA][mG][mG][mU][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	643	[MePhosphonate-4O-mUs][fAs][fCs][fA][fA][mC][fC][mU][mC][fU][mG][mC][mU][fG][mG][mA][mC][mC][mU][mCs][mGs][mG]	644
127	[mGs][mC][mA][mG][mA][mG][mG][fU][fU][fG][fU][mC][mC][mA][mU][mG][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	645	[MePhosphonate-4O-mUs][fUs][fGs][fU][fC][mA][fU][mG][mG][fA][mC][mA][mA][fC][mC][mU][mC][mU][mG][mCs][mGs][mG]	646
128	[mCs][mA][mG][mA][mG][mG][mU][fU][fG][fU][fC][mC][mA][mU][mG][mA][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	647	[MePhosphonate-4O-mUs][fCs][fUs][fG][fU][mC][fA][mU][mG][fG][mA][mC][mA][fA][mC][mC][mU][mC][mU][mGs][mGs][mG]	648

129	[mGs][mA][mG][mG][mA][mU][mG][fA][fG][fG][fA][mA][mC][mU][mU][mU][mG][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	649	[MePhosphonate-4O-mUs][fUs][fCs][fC][fA][mA][fA][mG][mU][fU][mC][mC][mU][fC][mA][mU][mC][mC][mU][mCs][mGs][mG]	650
130	[mGs][mA][mA][mC][mU][mU][mU][fG][fG][fA][fG][mG][mA][mA][mA][mU][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	651	[MePhosphonate-4O-mUs][fAs][fCs][fA][fA][mU][fU][mU][mC][fC][mU][mC][mC][fA][mA][mA][mG][mU][mU][mCs][mGs][mG]	652
131	[mGs][mA][mC][mG][mC][mU][mC][fU][fU][fC][fA][mG][mC][mU][mA][mU][mU][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	653	[MePhosphonate-4O-mUs][fGs][fUs][fA][fA][mU][fA][mG][mC][fU][mG][mA][mA][fG][mA][mG][mC][mG][mU][mCs][mGs][mG]	654
132	[mAs][mC][mG][mC][mU][mC][mU][fU][fC][fA][fG][mC][mU][mA][mU][mU][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	655	[MePhosphonate-4O-mUs][fUs][fGs][fU][fA][mA][fU][mA][mG][fC][mU][mG][mA][fA][mG][mA][mG][mC][mG][mUs][mGs][mG]	656
133	[mCs][mG][mC][mU][mC][mU][mU][fC][fA][fG][fC][mU][mA][mU][mU][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	657	[MePhosphonate-4O-mUs][fUs][fUs][fG][fU][mA][fA][mU][mA][fG][mC][mU][mG][fA][mA][mG][mA][mG][mC][mGs][mGs][mG]	658

	GalNAc][mG][mG][mC][mU][mG][mC]			
134	[mGs][mC][mU][mC][mU][mU][mC][fA][fG][fC][fU][mA][mU][mU][mA][mC][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	659	[MePhosphonate-4O-mUs][fGs][fUs][fU][fG][mU][fA][mA][mU][fA][mG][mC][mU][fG][mA][mA][mG][mA][mG][mCs][mGs][mG]	660
135	[mCs][mU][mC][mU][mU][mC][mA][fG][fC][fU][fA][mU][mU][mA][mC][mA][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	661	[MePhosphonate-4O-mUs][fUs][fGs][fU][fU][mG][fU][mA][mA][fU][mA][mG][mC][fU][mG][mA][mA][mG][mA][mGs][mGs][mG]	662
136	[mUs][mC][mU][mU][mC][mA][mG][fC][fU][fA][fU][mU][mA][mC][mA][mA][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	663	[MePhosphonate-4O-mUs][fAs][fUs][fG][fU][mU][fG][mU][mA][fA][mU][mA][mG][fC][mU][mG][mA][mA][mG][mAs][mGs][mG]	664
137	[mCs][mU][mU][mC][mA][mG][mC][fU][fA][fU][fU][mA][mC][mA][mA][mC][mA][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	665	[MePhosphonate-4O-mUs][fGs][fAs][fU][fG][mU][fU][mG][mU][fA][mA][mU][mA][fG][mC][mU][mG][mA][mA][mGs][mGs][mG]	666
138	[mUs][mU][mC][mA][mG][mC][mU][fA][fU][fU][fA][mC][mA][mA][mC][mA][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-	667	[MePhosphonate-4O-mUs][fUs][fGs][fA][fU][mG][fU][mU][mG][fU][mA][mA][mU][fA][mG][mC][mU][mG][mA][mAs][mGs][mG]	668

	GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
139	[mCs][mC][mA][mG][mC][mC][mU][fG][fA][fC][fC][mU][mC][mA][mC][mC][mU][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	669	[MePhosphonate-4O-mUs][fGs][fCs][fA][fG][mG][fU][mG][mA][fG][mG][mU][mC][fA][mG][mG][mC][mU][mG][mGs][mGs][mG]	670
140	[mCs][mA][mG][mC][mC][mU][mG][fA][fC][fC][fU][mC][mA][mC][mC][mU][mG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	671	[MePhosphonate-4O-mUs][fAs][fGs][fC][fA][mG][fG][mU][mG][fA][mG][mG][mU][fC][mA][mG][mG][mC][mU][mGs][mGs][mG]	672
141	[mAs][mG][mC][mC][mU][mG][mA][fC][fC][fU][fC][mA][mC][mC][mU][mG][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	673	[MePhosphonate-4O-mUs][fAs][fAs][fG][fC][mA][fG][mG][mU][fG][mA][mG][mG][fU][mC][mA][mG][mG][mC][mUs][mGs][mG]	674
142	[mGs][mC][mC][mU][mG][mA][mC][fC][fU][fC][fA][mC][mC][mU][mG][mC][mU][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	675	[MePhosphonate-4O-mUs][fUs][fAs][fA][fG][mC][fA][mG][mG][fU][mG][mA][mG][fG][mU][mC][mA][mG][mG][mCs][mGs][mG]	676
143	[mCs][mC][mU][mG][mA][mC][mC][fU][fC][fA][fC][mC][mU][mG][mC][mU][mU][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ade	677	[MePhosphonate-4O-mUs][fUs][fUs][fA][fA][mG][fC][mA][mG][fG][mU][mG][mA][fG][mG][mU][mC][mA][mG][mGs][mGs][mG]	678

	mA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
144	[mCs][mU][mG][mA][mC][mC][mU][fC][fA][fC][fC][mU][mG][mC][mU][mU][mA][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	679	[MePhosphonate-4O-mUs][fAs][fUs][fU][fA][mA][fG][mC][mA][fG][mG][mU][mG][fA][mG][mG][mU][mC][mA][mGs][mGs][mG]	680
145	[mUs][mG][mA][mC][mC][mU][mC][fA][fC][fC][fU][mG][mC][mU][mU][mA][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	681	[MePhosphonate-4O-mUs][fAs][fAs][fU][fU][mA][fA][mG][mC][fA][mG][mG][mU][fG][mA][mG][mG][mU][mC][mAs][mGs][mG]	682
146	[mGs][mA][mC][mC][mU][mC][mA][fC][fC][fU][fG][mC][mU][mU][mA][mA][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	683	[MePhosphonate-4O-mUs][fCs][fAs][fA][fU][mU][fA][mA][mG][fC][mA][mG][mG][fU][mG][mA][mG][mG][mU][mCs][mGs][mG]	684
147	[mAs][mC][mC][mU][mC][mA][mC][fC][fU][fG][fC][mU][mU][mA][mA][mU][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	685	[MePhosphonate-4O-mUs][fUs][fCs][fA][fA][mU][fU][mA][mA][fG][mC][mA][mG][fG][mU][mG][mA][mG][mG][mUs][mGs][mG]	686
148	[mCs][mC][mU][mC][mA][mC][mC][fU][fG][fC][fU][mU][mA][mA][mU][mU][mG][mA][mC][mA][mG][mC][mA][	687	[MePhosphonate-4O-mUs][fGs][fUs][fC][fA][mA][fU][mU][mA][fA][mG][mC][mA][fG][mG][mU][mG][mA][mG][mGs][mGs][mG]	688

	mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
149	[mCs][mU][mC][mA][mC][mC][mU][fG][fC][fU][fU][mA][mA][mU][mU][mG][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	689	[MePhosphonate-4O-mUs][fUs][fGs][fU][fC][mA][fA][mU][mU][fA][mA][mG][mC][fA][mG][mG][mU][mG][mA][mGs][mGs][mG]	690
150	[mUs][mC][mA][mC][mC][mU][mG][fC][fU][fU][fA][mA][mU][mU][mG][mA][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	691	[MePhosphonate-4O-mUs][fGs][fUs][fG][fU][mC][fA][mA][mU][fU][mA][mA][mG][fC][mA][mG][mG][mU][mG][mAs][mGs][mG]	692
151	[mCs][mA][mC][mC][mU][mG][mC][fU][fU][fA][fA][mU][mU][mG][mA][mC][mA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	693	[MePhosphonate-4O-mUs][fGs][fGs][fU][fG][mU][fC][mA][mA][fU][mU][mA][mA][fG][mC][mA][mG][mG][mU][mGs][mGs][mG]	694
152	[mAs][mC][mC][mU][mG][mC][mU][fU][fA][fA][fU][mU][mG][mA][mC][mA][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	695	[MePhosphonate-4O-mUs][fUs][fGs][fG][fU][mG][fU][mC][mA][fA][mU][mU][mA][fA][mG][mC][mA][mG][mG][mUs][mGs][mG]	696
153	[mCs][mC][mU][mG][mC][mU][mU][fA][fA][fU][fU][mG][mA][mC][mA][mC][mC][mA][m	697	[MePhosphonate-4O-mUs][fUs][fUs][fG][fG][mU][fG][mU][mC][fA][mA][m	698

	A][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		U][mU][fA][mA][mG][mC][mA][mG][mGs][mGs][mG]	
154	[mCs][mU][mG][mC][mU][mU][mA][fA][fU][fU][fG][mA][mC][mA][mC][mC][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	699	[MePhosphonate-4O-mUs][fGs][fUs][fU][fG][mG][fU][mG][mU][fC][mA][mA][mU][fU][mA][mA][mG][mC][mA][mGs][mGs][mG]	700
155	[mUs][mG][mC][mU][mU][mA][mA][fU][fU][fG][fA][mC][mA][mC][mC][mA][mA][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	701	[MePhosphonate-4O-mUs][fAs][fGs][fU][fU][mG][fG][mU][mG][fU][mC][mA][mA][fU][mU][mA][mA][mG][mC][mAs][mGs][mG]	702
156	[mGs][mC][mU][mU][mA][mA][mU][fU][fG][fA][fC][mA][mC][mC][mA][mA][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	703	[MePhosphonate-4O-mUs][fAs][fAs][fG][fU][mU][fG][mG][mU][fG][mU][mC][mA][fA][mU][mU][mA][mA][mG][mCs][mGs][mG]	704
157	[mCs][mU][mU][mA][mA][mU][mU][fG][fA][fC][fA][mC][mC][mA][mA][mC][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	705	[MePhosphonate-4O-mUs][fAs][fAs][fA][fG][mU][fU][mG][mG][fU][mG][mU][mC][fA][mA][mU][mU][mA][mA][mGs][mGs][mG]	706
158	[mUs][mU][mA][mA][mU][mU][mG][fA][fC][fA][fC][mC][mA][mA][	707	[MePhosphonate-4O-mUs][fAs][fAs][fA][fA][mG][fU][mU][mG][fG][mU][m	708

	mC][mU][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		G][mU][fC][mA][mA][mU][mU][mA][mAs][mGs][mG]	
159	[mUs][mA][mA][mU][mU][mG][mA][fC][fA][fC][fC][mA][mA][mC][mU][mU][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	709	[MePhosphonate-4O-mUs][fGs][fAs][fA][fA][mA][fG][mU][mU][fG][mG][mU][mG][fU][mC][mA][mA][mU][mU][mAs][mGs][mG]	710
160	[mAs][mU][mU][mG][mA][mA][mG][fG][fG][fG][fU][mG][mC][mU][mG][mU][mG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	711	[MePhosphonate-4O-mUs][fAs][fGs][fC][fA][mC][fA][mG][mC][fA][mC][mC][mC][fC][mU][mU][mC][mA][mA][mUs][mGs][mG]	712
161	[mCs][mU][mU][mG][mG][mA][mC][fA][fA][fA][fA][mG][mG][mA][mU][mU][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	713	[MePhosphonate-4O-mUs][fCs][fAs][fC][fA][mA][fU][mC][mC][fU][mU][mU][mU][fG][mU][mC][mC][mA][mA][mGs][mGs][mG]	714
162	[mUs][mU][mG][mG][mA][mC][mA][fA][fA][fA][fG][mG][mA][mU][mU][mG][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	715	[MePhosphonate-4O-mUs][fCs][fCs][fA][fC][mA][fA][mU][mC][fC][mU][mU][mU][fU][mG][mU][mC][mC][mA][mAs][mGs][mG]	716
163	[mUs][mC][mA][mA][mC][mG][mG][fU][fU][	717	[MePhosphonate-4O-mUs][fAs][fAs][fA][fU][mC	718

	fC][fC][mC][mU][mU][mG][mA][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		][fA][mA][mG][fG][mG][mA][mA][fC][mC][mG][mU][mU][mG][mAs][mGs][mG]	
164	[mCs][mA][mA][mC][mG][mG][mU][fU][fC][fC][fC][mU][mU][mG][mA][mU][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	719	[MePhosphonate-4O-mUs][fGs][fAs][fA][fA][mU][fC][mA][mA][fG][mG][mG][mA][fA][mC][mC][mG][mU][mU][mGs][mGs][mG]	720
165	[mAs][mA][mC][mG][mG][mU][mU][fC][fC][fC][fU][mU][mG][mA][mU][mU][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	721	[MePhosphonate-4O-mUs][fAs][fGs][fA][fA][mA][fU][mC][mA][fA][mG][mG][mG][fA][mA][mC][mC][mG][mU][mUs][mGs][mG]	722
166	[mAs][mC][mG][mG][mU][mU][mC][fC][fC][fU][fU][mG][mA][mU][mU][mU][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	723	[MePhosphonate-4O-mUs][fAs][fAs][fG][fA][mA][fA][mU][mC][fA][mA][mG][mG][fG][mA][mA][mC][mC][mG][mUs][mGs][mG]	724
167	[mGs][mU][mA][mC][mA][mU][mU][fG][fA][fC][fC][mA][mG][mA][mC][mC][mA][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	725	[MePhosphonate-4O-mUs][fCs][fAs][fU][fG][mG][fU][mC][mU][fG][mG][mU][mC][fA][mA][mU][mG][mU][mA][mCs][mGs][mG]	726

168	[mAs][mC][mC][mU][mG][mU][mA][fC][fC][fA][fC][mC][mU][mC][mC][mU][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	727	[MePhosphonate-4O-mUs][fCs][fAs][fC][fA][mG][fG][mA][mG][fG][mU][mG][mG][fU][mA][mC][mA][mG][mG][mUs][mGs][mG]	728
169	[mCs][mC][mU][mG][mU][mA][mC][fC][fA][fC][fC][mU][mC][mC][mU][mG][mU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	729	[MePhosphonate-4O-mUs][fAs][fCs][fA][fC][mA][fG][mG][mA][fG][mG][mU][mG][fG][mU][mA][mC][mA][mG][mGs][mGs][mG]	730
170	[mGs][mU][mA][mC][mC][mA][mC][fC][fU][fC][fC][mU][mG][mU][mG][mU][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	731	[MePhosphonate-4O-mUs][fAs][fUs][fG][fA][mC][fA][mC][mA][fG][mG][mA][mG][fG][mU][mG][mG][mU][mA][mCs][mGs][mG]	732
171	[mGs][mC][mA][mC][mA][mG][mG][fC][fA][fU][fC][mA][mA][mG][mU][mU][mC][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	733	[MePhosphonate-4O-mUs][fUs][fAs][fG][fA][mA][fC][mU][mU][fG][mA][mU][mG][fC][mC][mU][mG][mU][mG][mCs][mGs][mG]	734
172	[mAs][mC][mA][mG][mG][mC][mA][fU][fC][fA][fA][mG][mU][mU][mC][mU][mA][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	735	[MePhosphonate-4O-mUs][fAs][fGs][fU][fA][mG][fA][mA][mC][fU][mU][mG][mA][fU][mG][mC][mC][mU][mG][mUs][mGs][mG]	736

	GalNAc][mG][mG][mC][mU][mG][mC]			
173	[mCs][mA][mG][mG][mC][mA][mU][fC][fA][fA][fG][mU][mU][mC][mU][mA][mC][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	737	[MePhosphonate-4O-mUs][fGs][fAs][fG][fU][mA][fG][mA][mA][fC][mU][mU][mG][fA][mU][mG][mC][mC][mU][mGs][mGs][mG]	738
174	[mAs][mG][mG][mC][mA][mU][mC][fA][fA][fG][fU][mU][mC][mU][mA][mC][mU][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	739	[MePhosphonate-4O-mUs][fGs][fGs][fA][fG][mU][fA][mG][mA][fA][mC][mU][mU][fG][mA][mU][mG][mC][mC][mUs][mGs][mG]	740
175	[mGs][mG][mC][mA][mU][mC][mA][fA][fG][fU][fU][mC][mU][mA][mC][mU][mC][mC][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	741	[MePhosphonate-4O-mUs][fUs][fGs][fG][fA][mG][fU][mA][mG][fA][mA][mC][mU][fU][mG][mA][mU][mG][mC][mCs][mGs][mG]	742
176	[mGs][mC][mA][mU][mC][mA][mA][fG][fU][fU][fC][mU][mA][mC][mU][mC][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	743	[MePhosphonate-4O-mUs][fAs][fUs][fG][fG][mA][fG][mU][mA][fG][mA][mA][mC][fU][mU][mG][mA][mU][mG][mCs][mGs][mG]	744
177	[mCs][mA][mU][mC][mA][mA][mG][fU][fU][fC][fU][mA][mC][mU][mC][mC][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-	745	[MePhosphonate-4O-mUs][fAs][fAs][fU][fG][mG][fA][mG][mU][fA][mG][mA][mA][fC][mU][mU][mG][mA][mU][mGs][mGs][mG]	746

	GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
178	[mAs][mU][mC][mA][mA][mG][mU][fU][fC][fU][fA][mC][mU][mC][mC][mA][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	747	[MePhosphonate-4O-mUs][fGs][fAs][fA][fU][mG][fG][mA][mG][fU][mA][mG][mA][fA][mC][mU][mU][mG][mA][mUs][mGs][mG]	748
179	[mUs][mC][mA][mA][mG][mU][mU][fC][fU][fA][fC][mU][mC][mC][mA][mU][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	749	[MePhosphonate-4O-mUs][fUs][fGs][fA][fA][mU][fG][mG][mA][fG][mU][mA][mG][fA][mA][mC][mU][mU][mG][mAs][mGs][mG]	750
180	[mCs][mA][mA][mG][mU][mU][mC][fU][fA][fC][fU][mC][mC][mA][mU][mU][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	751	[MePhosphonate-4O-mUs][fCs][fUs][fG][fA][mA][fU][mG][mG][fA][mG][mU][mA][fG][mA][mA][mC][mU][mU][mGs][mGs][mG]	752
181	[mAs][mA][mG][mU][mU][mC][mU][fA][fC][fU][fC][mC][mA][mU][mU][mC][mA][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	753	[MePhosphonate-4O-mUs][fGs][fCs][fU][fG][mA][fA][mU][mG][fG][mA][mG][mU][fA][mG][mA][mA][mC][mU][mUs][mGs][mG]	754
182	[mAs][mG][mU][mU][mC][mU][mA][fC][fU][fC][fC][mA][mU][mU][mC][mA][mG][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ade	755	[MePhosphonate-4O-mUs][fUs][fGs][fC][fU][mG][fA][mA][mU][fG][mG][mA][mG][fU][mA][mG][mA][mA][mC][mUs][mGs][mG]	756

	mA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
183	[mGs][mU][mU][mC][mU][mA][mC][fU][fC][fC][fA][mU][mU][mC][mA][mG][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	757	[MePhosphonate-4O-mUs][fCs][fUs][fG][fC][mU][fG][mA][mA][fU][mG][mG][mA][fG][mU][mA][mG][mA][mA][mCs][mGs][mG]	758
184	[mGs][mU][mG][mU][mC][mA][mU][fC][fU][fC][fA][mG][mA][mC][mA][mA][mC][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	759	[MePhosphonate-4O-mUs][fAs][fGs][fG][fU][mU][fG][mU][mC][fU][mG][mA][mG][fA][mU][mG][mA][mC][mA][mCs][mGs][mG]	760
185	[mCs][mA][mU][mC][mU][mC][mA][fG][fA][fC][fA][mA][mC][mC][mU][mG][mC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	761	[MePhosphonate-4O-mUs][fCs][fAs][fG][fC][mA][fG][mG][mU][fU][mG][mU][mC][fU][mG][mA][mG][mA][mU][mGs][mGs][mG]	762
186	[mUs][mC][mA][mG][mA][mC][mA][fA][fC][fC][fU][mG][mC][mU][mG][mG][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	763	[MePhosphonate-4O-mUs][fUs][fCs][fA][fC][mC][fA][mG][mC][fA][mG][mG][mU][fU][mG][mU][mC][mU][mG][mAs][mGs][mG]	764
187	[mCs][mG][mG][mG][mG][mA][mC][fC][fU][fG][fU][mU][mA][mC][mA][mG][mA][mC][mA][mA][mG][mC][mA][	765	[MePhosphonate-4O-mUs][fUs][fGs][fU][fC][mU][fG][mU][mA][fA][mC][mA][mG][fG][mU][mC][mC][mC][mC][mGs][mGs][mG]	766

	mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]			
188	[mGs][mA][mC][mA][mA][mC][mG][fC][fU][fG][fC][mC][mA][mU][mU][mG][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	767	[MePhosphonate-4O-mUs][fAs][fGs][fA][fC][mA][fA][mU][mG][fG][mC][mA][mG][fC][mG][mU][mU][mG][mU][mCs][mGs][mG]	768
189	[mGs][mC][mU][mG][mC][mC][mU][fC][fC][fU][fG][mA][mC][mU][mG][mU][mA][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	769	[MePhosphonate-4O-mUs][fAs][fUs][fU][fA][mC][fA][mG][mU][fC][mA][mG][mG][fA][mG][mG][mC][mA][mG][mCs][mGs][mG]	770
190	[mCs][mU][mG][mC][mC][mU][mC][fC][fU][fG][fA][mC][mU][mG][mU][mA][mA][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	771	[MePhosphonate-4O-mUs][fUs][fAs][fU][fU][mA][fC][mA][mG][fU][mC][mA][mG][fG][mA][mG][mG][mC][mA][mGs][mGs][mG]	772
191	[mUs][mA][mA][mU][mA][mU][mU][fA][fA][fA][fC][mU][mU][mU][mU][mU][mU][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	773	[MePhosphonate-4O-mUs][fUs][fUs][fA][fA][mA][fA][mA][mA][fG][mU][mU][mU][fA][mA][mU][mA][mU][mU][mAs][mGs][mG]	774
192	[mAs][mA][mU][mA][mU][mU][mA][fA][fA][fC][fU][mU][mU][mU][mU][mU][mA][mA][m	775	[MePhosphonate-4O-mUs][fUs][fUs][fU][fA][mA][fA][mA][mA][fA][mG][m	776

	A][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]		U][mU][fU][mA][mA][mU][mA][mU][mUs][mGs][mG]	

[00253] The human hepatocyte 3D spheroid-based assay described in Example 2 is repeated with the GalXC™-SCAP oligonucleotides of Table 4, the results of which are shown in Table 5.

[00254] Table 5: GalXC™-SCAP Oligonucleotide SCAP mRNA Knockdown in 3D Human Spheroids; administered at 100 nM for 7 Days;-5' and -3' Assays % mRNA Remaining (normalized to Hs HPRT-517 (HEX) and Hs SFRS9-569 (HEX) vs mock control).

GalXC™ -SCAP	HPRT-517 (HEX)		SFRS9-569 (HEX)		Average	
	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM	% mRNA Remaining	% SEM
1	67.3	11.5	66.3	12.0	66.8	0.7
2	26.3	12.1	17.7	7.8	22.0	6.1
3	43.5	4.7	48.0	5.6	45.7	3.2
4	64.2	12.4	55.8	13.6	60.0	6.0
5	73.5	10.2	86.3	11.0	79.9	9.0
6	59.8	10.1	94.1	11.3	77.0	24.3
7	43.9	7.8	60.8	11.1	52.3	11.9
8	94.4	26.7	110.7	19.3	102.6	11.5
9	32.7	5.0	53.7	10.3	43.2	14.8
10	44.1	3.3	61.7	5.1	52.9	12.4
11	77.1	21.9	97.5	18.5	87.3	14.4
12	64.3	54.4	72.5	53.6	68.4	5.8
13	6.4	1.9	36.3	6.9	21.4	21.1
14	80.4	16.1	104.2	17.8	92.3	16.8
15	87.1	10.4	111.2	12.5	99.2	17.0
16	91.3	19.6	106.5	23.2	98.9	10.8
17	64.3	6.3	101.3	14.1	82.8	26.2
18	99.0	18.7	101.6	28.4	100.3	1.8
19	75.7	11.1	90.1	16.0	82.9	10.2
20	35.2	7.4	45.6	12.1	40.4	7.3
21	32.7	7.0	35.0	11.0	33.9	1.6
22	49.3	4.8	61.6	5.2	55.4	8.7
23	76.2	16.4	86.0	20.5	81.1	6.9
24	22.7	4.6	38.0	7.1	30.4	10.8
25	110.6	19.0	103.6	19.7	107.1	4.9
26	57.2	16.0	67.9	16.1	62.6	7.6
27	66.4	11.2	78.6	11.9	72.5	8.6
28	100.0	22.1	134.8	21.6	117.4	24.6
29	53.2	13.3	58.1	13.8	55.6	3.5

30	42.7	10.6	66.5	15.3	54.6	16.8
31	46.2	5.8	89.9	12.6	68.0	31.0
32	59.9	12.1	73.3	11.8	66.6	9.5
33	29.4	5.5	38.5	7.4	33.9	6.4
34	92.3	19.3	127.0	18.3	109.7	24.6
35	95.5	25.6	120.3	27.5	107.9	17.5
36	69.9	20.9	102.1	33.2	86.0	22.8
37	57.1	20.6	82.3	22.0	69.7	17.8
38	53.7	12.9	70.4	14.8	62.1	11.8
39	87.5	19.1	107.1	26.1	97.3	13.8
40	67.7	16.2	93.7	26.9	80.7	18.4
41	78.5	16.1	94.7	14.0	86.6	11.5
42	43.0	5.8	39.2	5.7	41.1	2.7
43	25.8	4.7	29.7	5.4	27.7	2.8
44	55.4	7.6	72.2	8.6	63.8	11.9
45	78.0	7.7	101.9	7.2	89.9	16.9
46	53.4	38.0	118.6	56.2	86.0	46.1
47	69.1	10.8	87.4	13.8	78.2	12.9
48	155.7	107.9	73.6	57.4	114.7	58.0
49	57.1	9.2	62.7	11.9	59.9	3.9
50	61.2	6.3	76.6	7.7	68.9	10.9
51	37.8	6.3	38.1	7.6	38.0	0.2
52	32.6	5.7	35.9	8.4	34.2	2.3
53	50.4	3.8	60.5	6.5	55.4	7.1
54	41.8	9.4	51.4	12.0	46.6	6.8
55	58.5	8.0	57.5	11.4	58.0	0.7
56	82.7	14.0	86.3	17.9	84.5	2.5
57	59.9	5.9	64.3	5.5	62.1	3.1
58	90.3	11.2	87.7	10.9	89.0	1.9
59	78.7	8.1	83.8	7.3	81.3	3.6
60	40.2	8.8	35.7	8.0	37.9	3.2
61	46.5	8.6	49.6	8.7	48.1	2.2
62	33.4	6.5	38.3	7.2	35.9	3.5
63	30.7	5.0	41.2	6.5	36.0	7.4
64	60.0	11.9	48.1	9.6	54.1	8.4
65	39.0	5.5	39.0	6.1	39.0	0.1
66	30.3	3.4	25.6	3.6	28.0	3.3
67	14.2	3.6	17.0	3.7	15.6	1.9
68	33.4	5.2	28.6	5.2	31.0	3.4
69	27.9	1.9	32.7	4.3	30.3	3.4
70	11.0	1.2	12.4	1.7	11.7	1.0
71	74.5	6.9	87.7	7.5	81.1	9.3
72	88.7	7.1	83.0	7.8	85.8	4.1
73	41.3	12.4	46.3	5.4	43.8	3.5
74	77.9	28.7	99.8	29.7	88.9	15.4
75	45.8	20.7	86.2	21.2	66.0	28.6
76	81.9	13.4	86.9	15.8	84.4	3.5

77	94.3	14.9	105.8	13.8	100.0	8.2
78	73.6	10.1	84.8	12.6	79.2	7.9
79	41.2	8.6	47.3	9.2	44.2	4.3
80	68.6	6.7	91.5	8.5	80.0	16.2
81	60.5	5.8	67.7	10.2	64.1	5.1
82	49.4	21.3	49.5	12.3	49.5	0.1
83	65.4	7.3	85.3	10.4	75.4	14.1
84	66.2	10.2	60.9	11.2	63.5	3.8
85	67.7	4.9	78.3	6.6	73.0	7.5
86	58.2	7.3	71.3	9.5	64.7	9.3
87	66.2	4.9	79.2	8.8	72.7	9.2
88	82.1	11.0	94.1	15.9	88.1	8.5
89	83.4	56.0	48.4	20.8	65.9	24.8
90	67.7	9.7	67.3	9.1	67.5	0.3
91	56.9	23.8	55.5	22.0	56.2	1.0
92	83.5	8.7	84.2	9.2	83.9	0.4
93	49.2	4.3	45.6	5.4	47.4	2.5
94	62.6	6.2	79.6	9.5	71.1	12.1
95	43.8	9.1	48.4	10.3	46.1	3.2
96	47.6	6.8	48.7	6.1	48.1	0.7
97	127.0	110.9	66.2	54.3	96.6	43.0
98	56.9	5.5	68.5	5.4	62.7	8.2
99	83.0	6.1	84.6	9.6	83.8	1.1
100	72.1	25.4	137.4	41.3	104.7	46.2
101	39.0	6.9	48.5	9.0	43.8	6.7
102	55.8	6.4	74.0	10.7	64.9	12.9
103	21.6	10.5	41.7	15.9	31.6	14.2
104	12.6	7.3	15.9	11.4	14.2	2.3
105	17.6	3.1	60.0	6.8	38.8	30.0
106	3.3	0.6	13.9	5.1	8.6	7.5
107	6.4	1.5	22.9	5.2	14.7	11.7
108	17.7	2.9	44.6	8.3	31.1	19.1
109	15.8	10.0	57.0	30.9	36.4	29.2
110	12.1	1.4	49.2	5.2	30.6	26.2
111	27.8	6.9	50.5	12.1	39.2	16.1
112	28.8	15.5	64.5	27.3	46.7	25.2
113	20.7	3.0	40.6	5.4	30.6	14.1
114	37.7	17.1	71.2	22.6	54.4	23.7
115	17.5	6.2	30.2	11.8	23.9	9.0
116	63.9	9.2	86.9	11.8	75.4	16.3
117	30.5	2.9	39.4	4.1	34.9	6.3
118	43.9	10.9	61.8	14.2	52.9	12.7
119	44.0	5.2	57.4	8.7	50.7	9.5
120	38.1	12.1	55.8	15.3	46.9	12.5
121	59.4	29.3	86.1	35.7	72.8	18.9
122	62.6	12.2	81.9	13.3	72.3	13.7
123	55.7	19.8	85.2	30.5	70.5	20.8

124	35.2	8.0	80.9	21.6	58.1	32.4
125	57.3	8.2	71.1	7.1	64.2	9.7
126	86.3	21.0	88.9	25.2	87.6	1.8
127	83.4	15.4	106.5	22.9	94.9	16.3
128	119.6	61.8	78.2	59.0	98.9	29.3
129	88.0	14.9	94.3	16.8	91.2	4.4
130	94.3	68.0	83.8	54.1	89.1	7.5
131	50.2	17.0	66.4	14.8	58.3	11.5
132	50.9	5.1	47.6	4.6	49.3	2.4
133	33.1	18.1	45.3	13.4	39.2	8.6
134	38.7	21.1	61.9	25.4	50.3	16.4
135	--	--	52.6	31.5	52.6	32.5
136	34.2	10.0	37.6	10.1	35.9	2.4
137	92.8	24.3	92.7	21.9	92.8	0.1
138	49.7	14.6	48.9	11.4	49.3	0.6
139	74.2	11.0	86.8	11.9	80.5	8.9
140	91.6	25.4	92.3	27.1	91.9	0.5
141	61.9	7.5	64.1	8.2	63.0	1.6
142	60.3	10.8	72.7	17.4	66.5	8.8
143	136.6	56.4	55.2	41.9	95.9	57.6
144	121.2	42.0	59.0	29.7	90.1	44.0
145	83.5	10.9	87.6	12.3	85.5	2.9
146	73.6	7.3	67.9	4.9	70.7	4.0
147	104.3	16.4	77.3	8.5	90.8	19.1
148	84.2	12.7	81.0	10.8	82.6	2.3
149	53.4	9.7	58.5	11.8	55.9	3.6
150	77.3	25.8	69.8	23.9	73.5	5.4
151	108.2	43.9	120.3	39.8	114.3	8.5
152	66.5	12.1	56.5	11.2	61.5	7.1
153	43.3	6.4	57.9	11.6	50.6	10.4
154	78.7	8.2	78.4	9.0	78.5	0.2
155	86.6	8.1	69.9	7.7	78.3	11.8
156	36.0	4.9	40.7	4.3	38.3	3.3
157	39.6	3.7	31.2	3.2	35.4	5.9
158	25.2	11.5	26.4	11.8	25.8	0.8
159	24.6	7.4	22.5	6.1	23.6	1.5
160	101.4	17.4	86.1	16.5	93.7	10.8
161	90.3	12.2	65.3	16.3	77.8	17.7
162	74.4	11.1	66.2	12.6	70.3	5.8
163	19.5	2.8	10.2	2.2	14.8	6.6
164	23.3	2.6	18.1	3.6	20.7	3.6
165	16.7	7.7	10.4	4.2	13.6	4.5
166	27.2	4.2	23.2	2.7	25.2	2.8
167	87.0	10.1	77.9	8.7	82.5	6.4
168	116.7	39.9	89.4	27.8	103.1	19.3
169	100.9	7.7	87.6	5.3	94.2	9.4
170	95.2	22.4	83.3	18.1	89.3	8.4

171	47.4	10.3	42.2	9.8	44.8	3.7
172	63.3	14.3	43.2	10.7	53.2	14.2
173	55.6	10.5	48.9	8.3	52.2	4.7
174	45.5	6.5	38.9	7.5	42.2	4.6
175	45.5	15.1	33.2	13.4	39.4	8.7
176	30.7	7.3	30.2	6.2	30.4	0.3
177	46.4	7.4	45.0	5.9	45.7	1.0
178	38.9	4.9	41.3	5.2	40.1	1.7
179	63.6	12.7	49.6	14.6	56.6	9.9
180	80.4	9.9	72.2	8.1	76.3	5.8
181	68.2	7.5	50.7	7.1	59.4	12.4
182	37.9	22.9	53.0	24.5	45.5	10.7
183	93.8	20.0	89.0	17.9	91.4	3.4
184	95.3	21.4	132.1	24.0	113.7	26.0
185	77.4	5.5	79.3	9.4	78.3	1.4
186	55.1	3.5	39.1	4.1	47.1	11.4
187	69.3	37.6	78.8	30.9	74.0	6.7
188	81.2	15.0	66.2	14.1	73.7	10.6
189	57.2	15.8	58.6	12.4	57.9	1.0
190	69.4	29.6	70.6	28.9	70.0	0.9
191	77.3	8.0	62.2	7.6	69.7	10.7
192	79.9	42.5	67.8	28.7	73.9	8.5

[00255] *IN VIVO* FUNCTION

[00256] Example 4: RNAi Oligonucleotide Modulation of *SCAP* Activity *In Vivo* – GalXC™-Based Compounds

[00257] *Mouse studies*: The GalXC™-SCAP oligonucleotides, as listed in Tables 3 (unmodified) and 4 (modified), are evaluated in hydrodynamic injection (HDI) mouse model. In the HDI studies, mice are engineered to transiently express human SCAP mRNA in hepatocytes. A GalXC™-SCAP oligonucleotide control (GalXC™-SCAP oligonucleotide no. 42; *see*, SEQ ID NOs: 475 and 476) is used as a benchmark control. Briefly, 6-8-week-old female CD-1 mice are treated SQ with a GalXC-™SCAP oligonucleotide at a dose level of 2 mg/kg. Three days later (72 hr.), the mice are HDI with a DNA plasmid encoding the full human *SCAP* gene under control of a ubiquitous cytomegalovirus (CMV) promoter sequence. One day after introduction of the plasmid, liver samples are collected. Total RNA derived from these mice are subjected to qRT-PCR analysis for SCAP mRNA, relative to mice treated only with an identical volume of PBS. The values are normalized for transfection efficiency using the NeoR gene included on the plasmid.

[00258] As shown in Tables 6 to 8, a number of GalXC™-SCAP oligonucleotides tested inhibited *SCAP* activity, as determined by a reduced amount of SCAP mRNA in liver samples

from oligonucleotide-treated mice relative to mice treated with PBS. The mean % of remaining SCAP mRNA in liver samples of mice treated with the GalXC™-SCAP oligonucleotide control relative to mice treated with PBS. Tables 6 to 8 show that a number of the GalXC™-SCAP oligonucleotides tested inhibit *SCAP* activity to a greater extent than the GalXC™-SCAP oligonucleotide control.

[00259] Table 6: *In Vivo* Activity of GalXC™-SCAP Oligonucleotides in Mice (single-dose, SQ, 2 mg/kg; 96-hr harvest; HDI of hSCAP plasmid in mice).

GalXC™-SCAP Oligo	Animal						
	1	2	3	4	5	Average	SEM
PBS	70.0	125.3	145.2	59.4	--	100.0	20.9
20	120.7	88.7	89.0	90.6	67.1	91.2	8.6
27	47.7	58.4	52.6	45.9	63.5	53.6	3.3
33	--	95.8	--	71.8	72.5	80.0	7.9
42	67.8	70.5	50.7	79.1	26.7	58.9	9.3
43	62.4	46.8	50.2	72.9	90.0	64.5	7.9
44	50.6	108.5	40.0	42.0	79.5	64.1	13.2
57	54.0	--	--	89.2	41.1	61.4	14.4
65	76.6	98.3	39.1	105.1	168.8	97.6	21.2
66	35.7	30.8	26.1	37.5	55.1	37.0	4.9
70	--	12.6	30.8	11.2	5.83*	18.2	6.3
104	53.7	45.8	73.7	54.0	48.3	55.1	4.9
105	23.7	101.6	50.3	62.9	100.6	67.8	15.0
106	59.6	29.8	28.4	53.5	30.5	40.4	6.7
107	30.3	12.4	43.0	13.1	22.1	24.2	5.7
108	35.5	71.6	46.4	54.2	48.1	51.1	5.9
113	50.5	55.2	85.0	38.8	42.9	54.5	8.1
117	58.7	82.1	63.0	46.9	51.6	60.4	6.1
120	54.1	--	43.7	55.7	90.5	61.0	10.2

[00260] Table 7: *In Vivo* Activity of GalXC™-SCAP Oligonucleotides in Mice (single-dose, SQ, 2 mg/kg; 96-hr harvest; HDI of hSCAP plasmid in mice).

GalXC™-SCAP Oligo	Animal						
	1	2	3	4	5	Average	SEM
PBS	105.9	122.9	90.2	105.6	75.4	100.0	8.0
2	32.8	67.0	37.1	57.0	55.7	49.9	6.5
13	44.4	38.9	66.1	77.2	56.4	56.6	7.0
67	36.9	--	32.1	41.5	43.5	38.5	2.5
69	56.5	51.9	50.1	60.5	51.3	54.0	1.9
108	45.7	88.3	80.2	56.6	134.9	81.1	15.5
110	65.7	50.3	24.3	30.4	48.3	43.8	7.4
115	15.0	45.4	--	45.3	32.7	34.6	7.2
133	17.0	21.9	31.6	52.8	25.6	29.8	6.2

144	66.5	93.9	28.0	88.0	32.1	61.7	13.7
157	21.4	22.9	72.8	14.1	43.3	34.9	10.6
159	24.6	45.3	58.0	30.4	34.9	38.6	5.9
163	9.0	40.3	48.8	20.8	24.0	28.6	7.1
164	34.7	68.5	81.0	61.8	55.0	60.2	7.7
165	48.5	32.3	49.2	44.6	39.2	42.8	3.2
166	31.8	29.4	55.4	66.0	70.0	50.5	8.5
176	31.3	32.1	31.6	60.5	30.9	37.3	5.8
177	26.7	22.8	19.7	17.9	15.3	20.5	2.0

[00261] Table 8: *In Vivo* Activity of GalXC™-SCAP Oligonucleotides in Mice (single-dose, SQ, 2 mg/kg; 96-hr harvest; HDI of hSCAP plasmid in mice).

GalXC™-SCAP Oligo	Animal						
	1	2	3	4	5	Average	SEM
PBS	121.8	102.2	82.8	57.4	135.8	100.0	13.9
66	45.5	33.4	36.9	55.5	38.9	42.0	3.9
70	20.0	27.6	42.6	24.4	45.3	32.0	5.1
107	26.3	12.3	18.7	10.5	18.5	17.3	2.8
151	132.9	67.9	83.6	98.1	126.3	101.8	12.4
152	61.4	70.6	100.5	76.0	66.1	74.9	6.8
153	89.8	68.2	54.4	128.9	69.7	82.2	13.0
154	117.0	114.8	124.6	39.4	167.8	112.7	20.7
155	109.6	128.6	61.2	120.9	62.1	96.5	14.5
156	66.2	46.3	58.4	86.0	81.5	67.7	7.3
157	41.6	39.6	34.5	54.1	36.0	41.2	3.5

[00262] The tables above show that the *in vivo* HDI results are consistent with the *in vitro* data in the Huh7 cells and 3D human spheroids of Example 3.

[00263] Based on the results above, 7 GalXC™-SCAP oligonucleotides are selected for a dose-response study in the HDI mouse model, the results of which are shown in Table 9.

[00264] Table 9: Dose-Response of GalXC™-SCAP Oligonucleotides in Mice (GalXC™ multiple-dose, 0.3-3.0 mg/kg, 96-hr harvest; HDI of hSCAP plasmid in mice).

		Dose (mg/kg)	Animal					Avg	SEM
			1	2	3	4	5		
GalXC™-SCAP Oligo	Study 1								
	PBS	--	113.3	106.6	93.6	119.7	66.8	100.0	9.4
		--	82.1	85.1	46.0	57.5	36.7	61.5	9.6
		--	60.6	27.9	36.1	35.4	--	53.3	14.4
	70	0.3	18.8	5.3	10.0	18.3	12.4	13.0	2.6
		1.0	62.5	67.9	43.5	--	--	58.0	7.4
		3.0	20.4	29.4	22.4	29.9	26.9	25.8	1.9
	107	0.3	8.6	9.8	16.4	9.3	6.1	10.0	1.7
		1.0	106.3	101.1	121.0	70.0	61.4	92.0	11.3

		3.0	1.1	47.7	36.2	69.0	57.7	42.3	11.7
	133	0.3	19.7	16.6	20.1	23.3	18.6	19.6	1.1
		1.0	75.7	39.3	44.1	79.7	71.3	62.0	8.4
		3.0	32.7	19.6	44.6	33.4	62.2	38.5	7.1
	177	0.3	15.1	15.7	8.2	27.4	32.7	19.8	4.5
		1.0	113.3	106.6	93.6	119.7	66.8	100.0	9.4
		3.0	82.1	85.1	46.0	57.5	36.7	61.5	9.6
	Study 2								
	PBS	--	60.6	83.1	141.2	40.6	174.4	100.0	25.1
		--	65.1	36.4	70.9	100.7	81.7	71.0	10.6
		--	46.5	40.4	33.5	18.8	59.2	39.7	6.7
	66	0.3	17.8	9.0	30.6	29.2	24.3	22.2	4.0
		1.0	66.9	32.9	48.7	54.1	51.6	50.8	5.5
		3.0	21.2	78.9	42.3	65.8	40.7	49.8	10.2
	157	0.3	7.4	18.7	14.9	20.2	14.6	15.2	2.2
		1.0	101.5	59.7	53.6	110.9	117.5	88.6	13.3
		3.0	21.2	27.4	39.6	45.2	48.3	36.3	5.2
	163	0.3	31.1	13.7	26.3	20.2	47.2	27.7	5.7
		1.0	60.6	83.1	141.2	40.6	174.4	100.0	25.1
		3.0	65.1	36.4	70.9	100.7	81.7	71.0	10.6

[00265] The GalXC™-SCAP oligonucleotides show a dose-dependent reduction of human SCAP mRNA expression. The GalXC™-SCAP oligonucleotides have an ED_{50} between 0.4-0.8 mg/kg against exogenously expressed human SCAP mRNA.

[00266] *Primate (NHP) studies*: Based on the mouse results above, 6 GalXC™-SCAP oligonucleotides are selected for evaluation of their ability to inhibit *SCAP* activity in NHPs (*e.g.*, rhesus macaques; *Macaca mulatta*) for a single-dose (2 or 6 mg/kg), 84-day study. Here, the NHPs are grouped so that their mean body weights (about 5.4 kg) are comparable between the control and experimental groups. Each cohort contains 6 individuals (3 male and 3 female individuals). The GalXC™-SCAP oligonucleotides are administered SQ on Study Day 0. Blood samples are collected at 2 pre-dose time points (*i.e.*, Days -21 and 0) and then weekly after dosing for a liver enzyme panel and lipid profile. Ultrasound-guided core needle liver biopsies are collected on Study Days -21, 28, 56, and 83. At each time point, total RNA derived from the liver biopsy samples is individualed to qRT-PCR analysis to measure SCAP mRNA in oligonucleotide-treated monkeys relative to monkeys treated with a comparable volume of PBS. To normalize the data, the measurements are made relative to the geometric mean of two reference genes, PPIB and 18S rRNA. As shown in Table 10, treating NHPs with the GalXC™-

SCAP oligonucleotides inhibits *SCAP* activity in the liver, as determined by a reduced amount of SCAP mRNA in liver samples from oligonucleotide-treated NHPs relative to NHPs treated with PBS. For all time points evaluated, GalXC™-SCAP oligonucleotides inhibit *SCAP* activity to a greater extent than the benchmark PBS and time-matched controls.

[00267] Table 10: SCAP mRNA Knockdown by Select GalXC™-SCAP Oligonucleotides in NHP Liver (at Day 28 vs. Pre-Dose and Time-Matched PBS).

		Dose (mg/kg)	Animal						Avg	SEM
			1	2	3	4	5	6		
GalXC™-SCAP Oligo	PBS	--	158.8	91.4	79.9	91.3	91.4	87.3	100.0	11.9
	66	6.0	41.4	63.2	38.5	67.1	39.1	55.0	50.7	5.2
	70	6.0	36.6	29.7	33.6	23.9	26.2	27.4	29.6	1.9
	107	2.0	44.0	62.1	50.0	52.4	42.0	72.5	53.8	4.7
	107	6.0	43.8	50.2	56.4	27.9	37.6	12.0	38.0	6.6
	157	6.0	55.7	55.0	39.5	41.9	19.3	42.0	42.2	5.4
	163	6.0	24.6	29.1	32.9	26.6	45.6	37.3	32.7	3.2
	177	6.0	42.7	49.2	33.7	38.3	23.6	50.4	39.7	4.1

[00268] Table 11: SCAP mRNA Knockdown by Select GalXC™-SCAP Oligonucleotides in NHP Liver (at Day 56 vs. Pre-Dose and Time-Matched PBS).

		Dose (mg/kg)	Animal						Avg	SEM
			1	2	3	4	5	6		
GalXC™-SCAP Oligo	PBS	--	186.6	67.8	97.7	89.3	62.0	96.6	100.0	18.4
	66	6.0	58.6	76.4	57.2	42.2	40.8	71.0	57.7	5.9
	70	6.0	43.5	28.1	23.5	37.5	39.9	30.1	33.8	3.1
	107	2.0	40.6	69.1	48.9	74.2	39.7	77.2	58.3	7.0
	107	6.0	37.4	72.7	68.1	29.9	68.3	42.8	53.2	7.6
	157	6.0	54.8	88.6	50.3	30.0	47.8	57.7	54.9	7.8
	163	6.0	36.1	42.9	36.0	29.1	74.3	36.3	42.5	6.6
	177	6.0	56.7	55.5	37.4	42.5	38.9	52.1	47.2	3.5

[00269] Table 12: SCAP mRNA Knockdown by Select GalXC™-SCAP Oligonucleotides in NHP Liver (at Day 84 vs. Pre-Dose and Time-Matched PBS).

		Dose (mg/kg)	Animal						Avg	SEM
			1	2	3	4	5	6		
GalXC™-SCAP Oligo	PBS	--	126.5	101.8	106.6	136.9	32.2	96.1	100.0	15.0
	66	6.0	62.4	82.5	125.0	79.5	88.2	57.5	82.5	9.8
	70	6.0	48.1	44.4	71.9	75.0	109.1	58.6	67.9	9.7
	107	2.0	110.6	97.2	109.1	86.0	136.8	87.4	104.5	7.7
	107	6.0	75.2	90.7	165.7	49.7	125.3	60.5	94.5	17.9
	157	6.0	36.2	88.4	95.2	79.8	83.4	104.1	81.2	9.7
	163	6.0	39.7	72.3	40.3	14.8	81.1	89.2	56.2	11.8

	177	6.0	42.1	80.8	103.4	96.5	94.5	106.1	87.2	9.7

[00270] An about 70% reduction of SCAP mRNA is achieved after a single 6 mg/kg dose of GalXC™-SCAP oligonucleotide nos. 70 and 163, an about 60% reduction of SCAP mRNA is achieved after a single 6 mg/kg dose of GalXC-SCAP oligonucleotide nos. 107, 157 and 177, and an about 50% reduction of SCAP mRNA is achieved after a single 6 mg/kg dose of GalXC™-SCAP oligonucleotide no. 66. Moreover, a dose response is observed following the 2 mg/kg and 6 mg/kg dose of GalXC™-SCAP oligonucleotide no. 107, where the ED_{50} is about 2 mg/kg. Likewise, a sustained reduction of liver SCAP mRNA expression is observed 56 days post a single 6.0 mg/kg dose of the GalXC™-SCAP oligonucleotides. An about 50% reduction of SCAP mRNA is observed 84 days after a single dose of GalXC™-SCAP oligonucleotide nos.70 and 163.

[00271] Taken together, these results show that GalXC™-SCAP oligonucleotides designed to target human and NHP SCAP mRNA inhibit *SCAP* activity *in vivo* (as determined by the reduction of the amount of SCAP mRNA in treated animals).

SEQUENCES

[00272] The following nucleic and/or amino acid sequences are referred to in the disclosure and are provided below for reference.

[00273] SEQ ID NO:1 – wild-type human *SCAP* (4254 bp; NCBI Ref. Seq. No. NM_012235.4)

gggcacccggcggccaggagagagagggagggcgccacgcaccggactgcgggccgagagcgcgcacgccgcgctccgccc
ctgctgccgccccgtcgccgccgccgccgccgcagcttgggaggtgctgccaccacaggtacctgcacatgttgttctttgtca
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[00279] SEQ ID NO:7 – wild-type non-human primate *SCAP* (4135 bp; NCBI Ref. Seq. No. XM_001100342)

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[00280] SEQ ID NO:8 – wild-type non-human primate *SCAP* (1229 aa; NCBI Ref. Seq. No. XP_001100342.2)

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[00281] SEQ ID NOS:9-392 – GalXC™-SCAP Oligonucleotides (unmodified)

GalXC-SCAP Oligo	Sense Strand (passenger; 36-mer)	SEQ ID NO:	Antisense Strand (guide; 22-mer)	SEQ ID NO:
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2	GUUUGCCUACAUCUACUUCAGCAGCCGAAAGGCUGC	11	UGAAGUAGAUGUAGGCAAACGG	12
3	UUUGCCUACAUCUACUUCUAGCAGCCGAAAGGCUGC	13	UAGAAGUAGAUGUAGGCAAAGG	14
4	GCCUACAUCUACUUCUCCAAGCAGCCGAAAGGCUGC	15	UUGGAGAAGUAGAUGUAGGCGG	16
5	AAGAUCGACAUGGUCAAGUAGCAGCCGAAAGGCUGC	17	UACUUGACCAUGUCGAUCUUGG	18
6	AGAUCGACAUGGUCAAGUCAGCAGCCGAAAGGCUGC	19	UGACUUGACCAUGUCGAUCUGG	20
7	AUCGACAUGGUCAAGUCCAAGCAGCCGAAAGGCUGC	21	UUGGACUUGACCAUGUCGAUGG	22
8	GUGUUGGUGCUCACCAAGUAGCAGCCGAAAGGCUGC	23	UACUUGGUGAGCACCAACACGG	24
9	UGUUGGUGCUCACCAAGUCAGCAGCCGAAAGGCUGC	25	UGACUUGGUGAGCACCAACAGG	26
10	GAGAGCUGGUCCAUCAUGAAGCAGCCGAAAGGCUGC	27	UUCAUGAUGGACCAGCUCUCGG	28
11	AGAGCUGGUCCAUCAUGAAAGCAGCCGAAAGGCUGC	29	UUUCAUGAUGGACCAGCUCUGG	30
12	GAGCUGGUCCAUCAUGAAGAGCAGCCGAAAGGCUGC	31	UCUUCAUGAUGGACCAGCUCGG	32
13	AGCUGGUCCAUCAUGAAGAAGCAGCCGAAAGGCUGC	33	UUCUUCAUGAUGGACCAGCUGG	34
14	GCUGGUCCAUCAUGAAGAAAGCAGCCGAAAGGCUGC	35	UUUCUUCAUGAUGGACCAGCGG	36

15	CUGGUCCAUCAUGAAGAACAGCAGCCGAAAGGCUGC	37	UGUUCUUCAUGAUGGACCAGGG	38
16	CCGUUGUCUGGAUUGGCAUAGCAGCCGAAAGGCUGC	39	UAUGCCAAUCCAGACAACGGGG	40
17	UUGUCUGGAUUGGCAUCCUAGCAGCCGAAAGGCUGC	41	UAGGAUGCCAAUCCAGACAAGG	42
18	UGUCUGGAUUGGCAUCCUGAGCAGCCGAAAGGCUGC	43	UCAGGAUGCCAAUCCAGACAGG	44
19	GUCUGGAUUGGCAUCCUGGAGCAGCCGAAAGGCUGC	45	UCCAGGAUGCCAAUCCAGACGG	46
20	CUGGAUUGGCAUCCUGGUAAGCAGCCGAAAGGCUGC	47	UUACCAGGAUGCCAAUCCAGGG	48
21	UGGAUUGGCAUCCUGGUAUAGCAGCCGAAAGGCUGC	49	UAUACCAGGAUGCCAAUCCAGG	50
22	GGAUUGGCAUCCUGGUAUAAGCAGCCGAAAGGCUGC	51	UUAUACCAGGAUGCCAAUCCGG	52
23	GAUUGGCAUCCUGGUAUACAGCAGCCGAAAGGCUGC	53	UGUAUACCAGGAUGCCAAUCGG	54
24	AUUGGCAUCCUGGUAUACAAGCAGCCGAAAGGCUGC	55	UUGUAUACCAGGAUGCCAAUGG	56
25	CUCCAUCUUCCCACCUGAUAGCAGCCGAAAGGCUGC	57	UAUCAGGUGGGAAGAUGGAGGG	58
26	CAUCUGCCUGUGGGAUGUAAGCAGCCGAAAGGCUGC	59	UUACAUCCCACAGGCAGAUGGG	60
27	UCUGCCUGUGGGAUGUACUAGCAGCCGAAAGGCUGC	61	UAGUACAUCCCACAGGCAGAGG	62
28	GUGGUGCAAGCUUGGGUGUAGCAGCCGAAAGGCUGC	63	UACACCCAAGCUUGCACCACGG	64
29	UGGUGCAAGCUUGGGUGUCAGCAGCCGAAAGGCUGC	65	UGACACCCAAGCUUGCACCAGG	66
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31	GUGCAAGCUUGGGU GUCAUAGCAGCCGA AAGGCUGC	69	UAUGACACCCAAGCUU GCACGG	70
32	GCAAGCUUGGGUGU CAUCUAGCAGCCGA AAGGCUGC	71	UAGAUGACACCCAAGC UUGCGG	72
33	CAAGCUUGGGUGUC AUCUCAGCAGCCGA AAGGCUGC	73	UGAGAUGACACCCAAG CUUGGG	74
34	AAGCUUGGGUGUCA UCUCAAGCAGCCGA AAGGCUGC	75	UUGAGAUGACACCCAA GCUUGG	76
35	AGCUUGGGUGUCAU CUCAGAGCAGCCGA AAGGCUGC	77	UCUGAGAUGACACCCA AGCUGG	78
36	GCUUGGGUGUCAUC UCAGAAGCAGCCGA AAGGCUGC	79	UUCUGAGAUGACACCC AAGCGG	80
37	GUGUCUCCUUUUGG GACCUAGCAGCCGA AAGGCUGC	81	UAGGUCCCAAAAGGAG ACACGG	82
38	UGUCUCCUUUUGGG ACCUAAGCAGCCGA AAGGCUGC	83	UUAGGUCCCAAAAGGA GACAGG	84
39	GGGGACCUGUUACA GACAGAGCAGCCGA AAGGCUGC	85	UCUGUCUGUAACAGGU CCCCGG	86
40	GGGACCUGUUACAG ACAGUAGCAGCCGA AAGGCUGC	87	UACUGUCUGUAACAGG UCCCGG	88
41	GGACCUGUUACAGA CAGUCAGCAGCCGA AAGGCUGC	89	UGACUGUCUGUAACAG GUCCGG	90
42	GACCUGUUACAGAC AGUCUAGCAGCCGA AAGGCUGC	91	UAGACUGUCUGUAACA GGUCGG	92
43	ACCUGUUACAGACA GUCUAAGCAGCCGA AAGGCUGC	93	UUAGACUGUCUGUAAC AGGUGG	94
44	UGCCAUUGUCUGCA ACUUUAGCAGCCGA AAGGCUGC	95	UAAAGUUGCAGACAAU GGCAGG	96
45	GCCAUUGUCUGCAA CUUUGAGCAGCCGA AAGGCUGC	97	UCAAAGUUGCAGACAA UGGCGG	98
46	CCAUUGUCUGCAAC UUUGGAGCAGCCGA AAGGCUGC	99	UCCAAAGUUGCAGACA AUGGGG	100

47	AUUGUCUGCAACUUUGGCAAGCAGCCGAAAGGCUGC	101	UUGCCAAAGUUGCAGACAAUGG	102
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49	CUACCCACUGCUGAAACUCAGCAGCCGAAAGGCUGC	105	UGAGUUUCAGCAGUGGGUAGGG	106
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51	GAACAGGACCUGUGGAAUUAGCAGCCGAAAGGCUGC	109	UAAUUCCACAGGUCCUGUUCGG	110
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53	UGGAAUUCACCACCCCUGUAGCAGCCGAAAGGCUGC	113	UACAGGGGUGGUGAAUUCCAGG	114
54	CUUGUGACCACCUACAUCAAGCAGCCGAAAGGCUGC	115	UUGAUGUAGGUGGUCACAAGGG	116
55	UUGUGACCACCUACAUCAUAGCAGCCGAAAGGCUGC	117	UAUGAUGUAGGUGGUCACAAGG	118
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61	CCACCUACAUCAUCUUGUUAGCAGCCGAAAGGCUGC	129	UAACAAGAUGAUGUAGGUGGGGG	130
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63	ACCUACAUCAUCUU GUUUGAGCAGCCGA AAGGCUGC	133	UCAAACAAGAUGAUGU AGGUGG	134
64	CCUACAUCAUCUUG UUUGCAGCAGCCGA AAGGCUGC	135	UGCAAACAAGAUGAUG UAGGGG	136
65	CUACAUCAUCUUGU UUGCCAGCAGCCGA AAGGCUGC	137	UGGCAAACAAGAUGAU GUAGGG	138
66	ACAUCAUCUUGUUU GCCUAAGCAGCCGA AAGGCUGC	139	UUAGGCAAACAAGAUG AUGUGG	140
67	AUCAUCUUGUUUGC CUACAAGCAGCCGA AAGGCUGC	141	UUGUAGGCAAACAAGA UGAUGG	142
68	UCAUCUUGUUUGCC UACAUAGCAGCCGA AAGGCUGC	143	UAUGUAGGCAAACAAG AUGAGG	144
69	AUCUUGUUUGCCUA CAUCUAGCAGCCGA AAGGCUGC	145	UAGAUGUAGGCAAACA AGAUGG	146
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74	CUACCUUGUGGUGG UUAUUAGCAGCCGA AAGGCUGC	155	UAAUAACCACCACAAG GUAGGG	156
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76	ACCUUGUGGUGGUU AUUGGAGCAGCCGA AAGGCUGC	159	UCCAAUAACCACCACA AGGUGG	160
77	CCUUGUGGUGGUUA UUGGGAGCAGCCGA AAGGCUGC	161	UCCCAAUAACCACCACA AGGGG	162
78	CUUGUGGUGGUUA UUGGGUAGCAGCCG AAAGGCUGC	163	UACCCAAUAACCACCAC AAGGG	164

79	UUGUGGUGGUUAU UGGGUUAGCAGCCG AAAGGCUGC	165	UAACCCAAUAACCACC ACAAGG	166
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94	UAGAGAAUGUGUU GGUGCUAGCAGCCG AAAGGCUGC	195	UAGCACCAACACAUUC UCUAGG	196

95	AGAGAAUGUGUUG GUGCUCAGCAGCCG AAAGGCUGC	197	UGAGCACCAACACAUU CUCUGG	198
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97	AGAAUGUGUUGGU GCUCACAGCAGCCG AAAGGCUGC	201	UGUGAGCACCAACACA UUCUGG	202
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103	CUGACUUCUUCCUU CAGAUAGCAGCCGA AAGGCUGC	213	UAUCUGAAGGAAGAAG UCAGGG	214
104	ACUUCUUCCUUCAG AUGCUAGCAGCCGA AAGGCUGC	215	UAGCAUCUGAAGGAAG AAGUGG	216
105	UCCUUCAGAUGCUG UUUUUAGCAGCCGA AAGGCUGC	217	UAAAAACAGCAUCUGA AGGAGG	218
106	CCUUCAGAUGCUGU UUUUCAGCAGCCGA AAGGCUGC	219	UGAAAAACAGCAUCUG AAGGGG	220
107	CUUCAGAUGCUGUU UUUCAAGCAGCCGA AAGGCUGC	221	UUGAAAAACAGCAUCU GAAGGG	222
108	UUCAGAUGCUGUUU UUCACAGCAGCCGA AAGGCUGC	223	UGUGAAAAACAGCAUC UGAAGG	224
109	CAGAUGCUGUUUUU CACCAAGCAGCCGA AAGGCUGC	225	UUGGUGAAAAACAGCA UCUGGG	226
110	AGAUGCUGUUUUUC ACCACAGCAGCCGA AAGGCUGC	227	UGUGGUGAAAAACAGC AUCUGG	228

111	GAUGCUGUUUUUCACCACUAGCAGCCGAAAGGCUGC	229	UAGUGGUGAAAAACAGCAUCGG	230
112	AUGCUGUUUUUCACCACUGAGCAGCCGAAAGGCUGC	231	UCAGUGGUGAAAAACAGCAUGG	232
113	UGCUGUUUUUCACCACUGUAGCAGCCGAAAGGCUGC	233	UACAGUGGUGAAAAACAGCAGG	234
114	GCUGUUUUUCACCACUGUCAGCAGCCGAAAGGCUGC	235	UGACAGUGGUGAAAAACAGCGG	236
115	UGUUUUUCACCACUGUCCUAGCAGCCGAAAGGCUGC	237	UAGGACAGUGGUGAAAAACAGG	238
116	GUUUUUCACCACUGUCCUGAGCAGCCGAAAGGCUGC	239	UCAGGACAGUGGUGAAAAACGG	240
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119	UUCACCACUGUCCUGUCCAAGCAGCCGAAAGGCUGC	245	UUGGACAGGACAGUGGUGAAGG	246
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121	ACCACUGUCCUGUCCAUUGAGCAGCCGAAAGGCUGC	249	UCAAUGGACAGGACAGUGGUGG	250
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124	ACUGUCCUGUCCAUUGACAAGCAGCCGAAAGGCUGC	255	UUGUCAAUGGACAGGACAGUGG	256
125	CUAAGCUACCUGAGAACCAAGCAGCCGAAAGGCUGC	257	UUGGUUCUCAGGUAGCUUAGGG	258
126	GAGGUCCAGCAGAGGUUGUAGCAGCCGAAAGGCUGC	259	UACAACCUCUGCUGGACCUCGG	260

127	GCAGAGGUUGUCCAUGACAAGCAGCCGAAAGGCUGC	261	UUGUCAUGGACAACCUCUGCGG	262
128	CAGAGGUUGUCCAUGACAGAGCAGCCGAAAGGCUGC	263	UCUGUCAUGGACAACCUCUGGG	264
129	GAGGAUGAGGAACUUUGGAAGCAGCCGAAAGGCUGC	265	UUCCAAAGUUCCUCAUCCUCGG	266
130	GAACUUUGGAGGAAAUUGUAGCAGCCGAAAGGCUGC	267	UACAAUUUCCUCCAAAGUUCGG	268
131	GACGCUCUUCAGCUAUUACAGCAGCCGAAAGGCUGC	269	UGUAAUAGCUGAAGAGCGUCGG	270
132	ACGCUCUUCAGCUAUUACAAGCAGCCGAAAGGCUGC	271	UUGUAAUAGCUGAAGAGCGUGG	272
133	CGCUCUUCAGCUAUUACAAAGCAGCCGAAAGGCUGC	273	UUUGUAAUAGCUGAAGAGCGGG	274
134	GCUCUUCAGCUAUUACAACAGCAGCCGAAAGGCUGC	275	UGUUGUAAUAGCUGAAGAGCGG	276
135	CUCUUCAGCUAUUACAACAAGCAGCCGAAAGGCUGC	277	UUGUUGUAAUAGCUGAAGAGGG	278
136	UCUUCAGCUAUUACAACAUAGCAGCCGAAAGGCUGC	279	UAUGUUGUAAUAGCUGAAGAGG	280
137	CUUCAGCUAUUACAACAUCAGCAGCCGAAAGGCUGC	281	UGAUGUUGUAAUAGCUGAAGGG	282
138	UUCAGCUAUUACAACAUCAAGCAGCCGAAAGGCUGC	283	UUGAUGUUGUAAUAGCUGAAGG	284
139	CCAGCCUGACCUCACCUGCAGCAGCCGAAAGGCUGC	285	UGCAGGUGAGGUCAGGCUGGGG	286
140	CAGCCUGACCUCACCUGCUAGCAGCCGAAAGGCUGC	287	UAGCAGGUGAGGUCAGGCUGGG	288
141	AGCCUGACCUCACCUGCUUAGCAGCCGAAAGGCUGC	289	UAAGCAGGUGAGGUCAGGCUGG	290
142	GCCUGACCUCACCUGCUUAAGCAGCCGAAAGGCUGC	291	UUAAGCAGGUGAGGUCAGGCGG	292

143	CCUGACCUCACCUG CUUAAAGCAGCCGA AAGGCUGC	293	UUUAAGCAGGUGAGGU CAGGGG	294
144	CUGACCUCACCUGC UUAAUAGCAGCCGA AAGGCUGC	295	UAUUAAGCAGGUGAGG UCAGGG	296
145	UGACCUCACCUGCU UAAUUAGCAGCCGA AAGGCUGC	297	UAAUUAAGCAGGUGAG GUCAGG	298
146	GACCUCACCUGCUU AAUUGAGCAGCCGA AAGGCUGC	299	UCAAUUAAGCAGGUGA GGUCGG	300
147	ACCUCACCUGCUUA AUUGAAGCAGCCGA AAGGCUGC	301	UUCAAUUAAGCAGGUG AGGUGG	302
148	CCUCACCUGCUUAA UUGACAGCAGCCGA AAGGCUGC	303	UGUCAAUUAAGCAGGU GAGGGG	304
149	CUCACCUGCUUAAU UGACAAGCAGCCGA AAGGCUGC	305	UUGUCAAUUAAGCAGG UGAGGG	306
150	UCACCUGCUUAAUU GACACAGCAGCCGA AAGGCUGC	307	UGUGUCAAUUAAGCAG GUGAGG	308
151	CACCUGCUUAAUUG ACACCAGCAGCCGA AAGGCUGC	309	UGGUGUCAAUUAAGCA GGUGGG	310
152	ACCUGCUUAAUUGA CACCAAGCAGCCGA AAGGCUGC	311	UUGGUGUCAAUUAAGC AGGUGG	312
153	CCUGCUUAAUUGAC ACCAAAGCAGCCGA AAGGCUGC	313	UUUGGUGUCAAUUAAG CAGGGG	314
154	CUGCUUAAUUGACA CCAACAGCAGCCGA AAGGCUGC	315	UGUUGGUGUCAAUUAA GCAGGG	316
155	UGCUUAAUUGACAC CAACUAGCAGCCGA AAGGCUGC	317	UAGUUGGUGUCAAUUA AGCAGG	318
156	GCUUAAUUGACACC AACUUAGCAGCCGA AAGGCUGC	319	UAAGUUGGUGUCAAUU AAGCGG	320
157	CUUAAUUGACACCA ACUUUAGCAGCCGA AAGGCUGC	321	UAAAGUUGGUGUCAAU UAAGGG	322
158	UUAAUUGACACCAA CUUUUAGCAGCCGA AAGGCUGC	323	UAAAAGUUGGUGUCAA UUAAGG	324

159	UAAUUGACACCAACUUUUCAGCAGCCGAAAGGCUGC	325	UGAAAAGUUGGUGUCAAUUAGG	326
160	AUUGAAGGGGUGCUGUGCUAGCAGCCGAAAGGCUGC	327	UAGCACAGCACCCCUUCAAUGG	328
161	CUUGGACAAAAGGAUUGUGAGCAGCCGAAAGGCUGC	329	UCACAAUCCUUUUGUCCAAGGG	330
162	UUGGACAAAAGGAUUGUGGAGCAGCCGAAAGGCUGC	331	UCCACAAUCCUUUUGUCCAAGG	332
163	UCAACGGUUCCCUUGAUUUAGCAGCCGAAAGGCUGC	333	UAAAUCAAGGGAACCGUUGAGG	334
164	CAACGGUUCCCUUGAUUUCAGCAGCCGAAAGGCUGC	335	UGAAAUCAAGGGAACCGUUGGG	336
165	AACGGUUCCCUUGAUUUCUAGCAGCCGAAAGGCUGC	337	UAGAAAUCAAGGGAACCGUUGG	338
166	ACGGUUCCCUUGAUUUCUUAGCAGCCGAAAGGCUGC	339	UAAGAAAUCAAGGGAACCGUGG	340
167	GUACAUUGACCAGACCAUGAGCAGCCGAAAGGCUGC	341	UCAUGGUCUGGUCAAUGUACGG	342
168	ACCUGUACCACCUCCUGUGAGCAGCCGAAAGGCUGC	343	UCACAGGAGGUGGUACAGGUGG	344
169	CCUGUACCACCUCCUGUGUAGCAGCCGAAAGGCUGC	345	UACACAGGAGGUGGUACAGGGG	346
170	GUACCACCUCCUGUGUCAUAGCAGCCGAAAGGCUGC	347	UAUGACACAGGAGGUGGUACGG	348
171	GCACAGGCAUCAAGUUCUAAGCAGCCGAAAGGCUGC	349	UUAGAACUUGAUGCCUGUGCGG	350
172	ACAGGCAUCAAGUUCUACUAGCAGCCGAAAGGCUGC	351	UAGUAGAACUUGAUGCCUGUGG	352
173	CAGGCAUCAAGUUCUACUCAGCAGCCGAAAGGCUGC	353	UGAGUAGAACUUGAUGCCUGGG	354
174	AGGCAUCAAGUUCUACUCCAGCAGCCGAAAGGCUGC	355	UGGAGUAGAACUUGAUGCCUGG	356

175	GGCAUCAAGUUCUACUCCAAGCAGCCGAAAGGCUGC	357	UUGGAGUAGAACUUGAUGCCGG	358
176	GCAUCAAGUUCUACUCCAUAGCAGCCGAAAGGCUGC	359	UAUGGAGUAGAACUUGAUGCGG	360
177	CAUCAAGUUCUACUCCAUUAGCAGCCGAAAGGCUGC	361	UAAUGGAGUAGAACUUGAUGGG	362
178	AUCAAGUUCUACUCCAUUCAGCAGCCGAAAGGCUGC	363	UGAAUGGAGUAGAACUUGAUGG	364
179	UCAAGUUCUACUCCAUUCAAGCAGCCGAAAGGCUGC	365	UUGAAUGGAGUAGAACUUGAGG	366
180	CAAGUUCUACUCCAUUCAGAGCAGCCGAAAGGCUGC	367	UCUGAAUGGAGUAGAACUUGGG	368
181	AAGUUCUACUCCAUUCAGCAGCAGCCGAAAGGCUGC	369	UGCUGAAUGGAGUAGAACUUGG	370
182	AGUUCUACUCCAUUCAGCAAGCAGCCGAAAGGCUGC	371	UUGCUGAAUGGAGUAGAACUGG	372
183	GUUCUACUCCAUUCAGCAGAGCAGCCGAAAGGCUGC	373	UCUGCUGAAUGGAGUAGAACGG	374
184	GUGUCAUCUCAGACAACCUAGCAGCCGAAAGGCUGC	375	UAGGUUGUCUGAGAUGACACGG	376
185	CAUCUCAGACAACCUGCUGAGCAGCCGAAAGGCUGC	377	UCAGCAGGUUGUCUGAGAUGGG	378
186	UCAGACAACCUGCUGGUGAAGCAGCCGAAAGGCUGC	379	UUCACCAGCAGGUUGUCUGAGG	380
187	CGGGGACCUGUUACAGACAAGCAGCCGAAAGGCUGC	381	UUGUCUGUAACAGGUCCCCGGG	382
188	GACAACGCUGCCAUUGUCUAGCAGCCGAAAGGCUGC	383	UAGACAAUGGCAGCGUUGUCGG	384
189	GCUGCCUCCUGACUGUAAUAGCAGCCGAAAGGCUGC	385	UAUUACAGUCAGGAGGCAGCGG	386
190	CUGCCUCCUGACUGUAAUAAGCAGCCGAAAGGCUGC	387	UUAUUACAGUCAGGAGGCAGGG	388

191	UAAUAUUAAACUU UUUUAAAGCAGCCG AAAGGCUGC	389	UUUAAAAAAGUUUAAU AUUAGG	390
192	AAUAUUAAACUUU UUUAAAAGCAGCCG AAAGGCUGC	391	UUUUAAAAAAGUUUAA UAUUGG	392

[00282] SEQ ID NOs:393-776 – GalXC™-SCAP Oligonucleotides (modified)

GalXC-SCAP Oligo	Sense Strand (passenger; 36-mer)	SEQ ID NO:	Antisense Strand (guide; 22-mer)	SEQ ID NO:
1	mU*mGmUmUmUmGmC/i2FC//i2FU//i2FA//i2FC/mAmUmCmUmAmCmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	393	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FG//i2FU/mA/i2FG/mAmU/i2FG/mUmAmG/i2FG/mCmAmAmAmCmA*mG*mG	394
2	mG*mUmUmUmGmCmC/i2FU//i2FA//i2FC//i2FA/mUmCmUmAmCmUmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	395	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FA//i2FG/mU/i2FA/mGmA/i2FU/mGmUmA/i2FG/mGmCmAmAmAmC*mG*mG	396
3	mU*mUmUmGmCmCmU/i2FA//i2FC//i2FA//i2FU/mCmUmAmCmUmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	397	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FA/mG/i2FU/mAmG/i2FA/mUmGmU/i2FA/mGmGmCmAmAmA*mG*mG	398
4	mG*mCmCmUmAmCmA/i2FU//i2FC//i2FU//i2FA/mCmUmUmCmUmCmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	399	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FG//i2FA/mG/i2FA/mAmG/i2FU/mAmGmA/i2FU/mGmUmAmGmGmC*mG*mG	400

5	mA*mAmGmAmUmC mG/i2FA//i2FC//i2FA//i 2FU/mGmGmUmCmA mAmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	401	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FU//i 2FU/mG/i2FA/mCmC/i2FA/ mUmGmU/i2FC/mGmAmU mCmUmU*mG*mG	402
6	mA*mGmAmUmCmG mA/i2FC//i2FA//i2FU//i 2FG/mGmUmCmAmA mGmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	403	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FC//i 2FU/mU/i2FG/mAmC/i2FC/ mAmUmG/i2FU/mCmGmA mUmCmU*mG*mG	404
7	mA*mUmCmGmAmC mA/i2FU//i2FG//i2FG//i 2FU/mCmAmAmGmU mCmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	405	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FG//i 2FA/mC/i2FU/mUmG/i2FA/ mCmCmA/i2FU/mGmUmC mGmAmU*mG*mG	406
8	mG*mUmGmUmUmG mG/i2FU//i2FG//i2FC//i 2FU/mCmAmCmCmA mAmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	407	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FU//i 2FU/mG/i2FG/mUmG/i2FA/ mGmCmA/i2FC/mCmAmA mCmAmC*mG*mG	408
9	mU*mGmUmUmGmG mU/i2FG//i2FC//i2FU//i 2FC/mAmCmCmAmA mGmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	409	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FC//i 2FU/mU/i2FG/mGmU/i2FG/ mAmGmC/i2FA/mCmCmA mAmCmA*mG*mG	410
10	mG*mAmGmAmGmC mU/i2FG//i2FG//i2FU//i 2FC/mCmAmUmCmA mUmGmAmAmGmCm	411	[MePhosphonate-4O- mUs]/i2FU/*/i2FC/*/i2FA//i 2FU/mG/i2FA/mUmG/i2FG/	412

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mAmCmC/i2FA/mGmCmUmCmUmC*mG*mG	
11	mA*mGmAmGmCmUmG/i2FG//i2FU//i2FC//i2FC/mAmUmCmAmUmGmAmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	413	[MePhosphonate-4O-mUs]/i2FU/*/i2FU/*/i2FC//i2FA/mU/i2FG/mAmU/i2FG/mGmAmC/i2FC/mAmGmCmUmCmU*mG*mG	414
12	mG*mAmGmCmUmGmG/i2FU//i2FC//i2FC//i2FA/mUmCmAmUmGmAmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	415	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FU//i2FC/mA/i2FU/mGmA/i2FU/mGmGmA/i2FC/mCmAmGmCmUmC*mG*mG	416
13	mA*mGmCmUmGmGmU/i2FC//i2FC//i2FA//i2FU/mCmAmUmGmAmAmAmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	417	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FU//i2FU/mC/i2FA/mUmG/i2FA/mUmGmG/i2FA/mCmCmAmGmCmU*mG*mG	418
14	mG*mCmUmGmGmUmC/i2FC//i2FA//i2FU//i2FC/mAmUmGmAmAmGmAmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	419	[MePhosphonate-4O-mUs]/i2FU/*/i2FU/*/i2FC//i2FU/mU/i2FC/mAmU/i2FG/mAmUmG/i2FG/mAmCmCmAmGmC*mG*mG	420
15	mC*mUmGmGmUmCmC/i2FA//i2FU//i2FC//i2FA/mUmGmAmAmGmAmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	421	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FU//i2FC/mU/i2FU/mCmA/i2FU/mGmAmU/i2FG/mGmAmCmCmAmG*mG*mG	422

	GalNAc]mGmGmCmU mGmC			
16	mC*mCmGmUmUmG mU/i2FC//i2FU//i2FG//i 2FG/mAmUmUmGmG mCmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	423	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FG//i 2FC/mC/i2FA/mAmU/i2FC/ mCmAmG/i2FA/mCmAmA mCmGmG*mG*mG	424
17	mU*mUmGmUmCmU mG/i2FG//i2FA//i2FU//i 2FU/mGmGmCmAmU mCmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	425	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FG//i 2FA/mU/i2FG/mCmC/i2FA/ mAmUmC/i2FC/mAmGmA mCmAmA*mG*mG	426
18	mU*mGmUmCmUmG mG/i2FA//i2FU//i2FU//i 2FG/mGmCmAmUmC mCmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	427	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FG//i 2FG/mA/i2FU/mGmC/i2FC/ mAmAmU/i2FC/mCmAmG mAmCmA*mG*mG	428
19	mG*mUmCmUmGmG mA/i2FU//i2FU//i2FG//i 2FG/mCmAmUmCmC mUmGmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	429	[MePhosphonate-4O- mUs]/i2FC/*/i2FC/*/i2FA//i 2FG/mG/i2FA/mUmG/i2FC/ mCmAmA/i2FU/mCmCmA mGmAmC*mG*mG	430
20	mC*mUmGmGmAmU mU/i2FG//i2FG//i2FC//i 2FA/mUmCmCmUmG mGmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	431	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FC//i 2FC/mA/i2FG/mGmA/i2FU/ mGmCmC/i2FA/mAmUmC mCmAmG*mG*mG	432
21	mU*mGmGmAmUmU mG/i2FG//i2FC//i2FA//i	433	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FA//i	434

	2FU/mCmCmUmGmG mUmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC		2FC/mC/i2FA/mGmG/i2FA/ mUmGmC/i2FC/mAmAmU mCmCmA*mG*mG	
22	mG*mGmAmUmUmG mG/i2FC//i2FA//i2FU//i 2FC/mCmUmGmGmU mAmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	435	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FU//i 2FA/mC/i2FC/mAmG/i2FG/ mAmUmG/i2FC/mCmAmA mUmCmC*mG*mG	436
23	mG*mAmUmUmGmG mC/i2FA//i2FU//i2FC//i 2FC/mUmGmGmUmA mUmAmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	437	[MePhosphonate-4O- mUs]/i2FG/*/i2FU/*/i2FA//i 2FU/mA/i2FC/mCmA/i2FG/ mGmAmU/i2FG/mCmCmA mAmUmC*mG*mG	438
24	mA*mUmUmGmGmC mA/i2FU//i2FC//i2FC//i 2FU/mGmGmUmAmU mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	439	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FU//i 2FA/mU/i2FA/mCmC/i2FA/ mGmGmA/i2FU/mGmCmC mAmAmU*mG*mG	440
25	mC*mUmCmCmAmU mC/i2FU//i2FU//i2FC//i 2FC/mCmAmCmCmU mGmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	441	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FC//i 2FA/mG/i2FG/mUmG/i2FG/ mGmAmA/i2FG/mAmUmG mGmAmG*mG*mG	442
26	mC*mAmUmCmUmG mC/i2FC//i2FU//i2FG//i 2FU/mGmGmGmAmU mGmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-	443	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FC//i 2FA/mU/i2FC/mCmC/i2FA/ mCmAmG/i2FG/mCmAmG mAmUmG*mG*mG	444

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
27	mU*mCmUmGmCmCmU/i2FG//i2FU//i2FG//i2FG/mGmAmUmGmUmAmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	445	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FU//i2FA/mC/i2FA/mUmC/i2FC/mCmAmC/i2FA/mGmGmCmAmGmA*mG*mG	446
28	mG*mUmGmGmUmGmC/i2FA//i2FA//i2FG//i2FC/mUmUmGmGmUmGmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	447	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FA//i2FC/mC/i2FC/mAmA/i2FG/mCmUmU/i2FG/mCmAmCmCmAmC*mG*mG	448
29	mU*mGmGmUmGmCmA/i2FA//i2FG//i2FC//i2FU/mUmGmGmGmUmGmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	449	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FC//i2FA/mC/i2FC/mCmA/i2FA/mGmCmU/i2FU/mGmCmAmCmCmA*mG*mG	450
30	mG*mGmUmGmCmAmA/i2FG//i2FC//i2FU//i2FU/mGmGmGmUmGmUmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	451	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i2FC/mA/i2FC/mCmC/i2FA/mAmGmC/i2FU/mUmGmCmAmCmC*mG*mG	452
31	mG*mUmGmCmAmAmG/i2FC//i2FU//i2FU//i2FG/mGmGmUmGmUmCmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	453	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FG//i2FA/mC/i2FA/mCmC/i2FC/mAmAmG/i2FC/mUmUmGmCmAmC*mG*mG	454

32	mG*mCmAmAmGmCmU/i2FU//i2FG//i2FG//i2FG/mUmGmUmCmAmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	455	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FU/mG/i2FA/mCmA/i2FC/mCmCmA/i2FA/mGmCmUmUmGmC*mG*mG	456
33	mC*mAmAmGmCmUmU/i2FG//i2FG//i2FG//i2FU/mGmUmCmAmUmCmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	457	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FG//i2FA/mU/i2FG/mAmC/i2FA/mCmCmC/i2FA/mAmGmCmUmUmG*mG*mG	458
34	mA*mAmGmCmUmUmG/i2FG//i2FG//i2FU//i2FG/mUmCmAmUmCmUmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	459	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i2FG/mA/i2FU/mGmA/i2FC/mAmCmC/i2FC/mAmAmGmCmUmU*mG*mG	460
35	mA*mGmCmUmUmGmG/i2FG//i2FU//i2FG//i2FU/mCmAmUmCmUmCmAmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	461	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FG//i2FA/mG/i2FA/mUmG/i2FA/mCmAmC/i2FC/mCmAmAmGmCmU*mG*mG	462
36	mG*mCmUmUmGmGmG/i2FU//i2FG//i2FU//i2FC/mAmUmCmUmCmAmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	463	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FU//i2FG/mA/i2FG/mAmU/i2FG/mAmCmA/i2FC/mCmCmAmAmGmC*mG*mG	464
37	mG*mUmGmUmCmUmC/i2FC//i2FU//i2FU//i2FU/mUmGmGmGmAmCmCmUmAmGmCm	465	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FG//i2FU/mC/i2FC/mCmA/i2FA/	466

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mAmAmG/i2FG/mAmGmAmCmAmC*mG*mG	
38	mU*mGmUmCmUmCmC/i2FU//i2FU//i2FU//i2FU/mGmGmGmAmCmCmUmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	467	[MePhosphonate-4O-mUs]/i2FU/*/i2FA/*/i2FG//i2FG/mU/i2FC/mCmC/i2FA/mAmAmA/i2FG/mGmAmGmAmCmA*mG*mG	468
39	mG*mGmGmGmAmCmC/i2FU//i2FG//i2FU//i2FU/mAmCmAmGmAmCmAmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	469	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FG//i2FU/mC/i2FU/mGmU/i2FA/mAmCmA/i2FG/mGmUmCmCmCmC*mG*mG	470
40	mG*mGmGmAmCmCmU/i2FG//i2FU//i2FU//i2FA/mCmAmGmAmCmAmGmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	471	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FU//i2FG/mU/i2FC/mUmG/i2FU/mAmAmC/i2FA/mGmGmUmCmCmC*mG*mG	472
41	mG*mGmAmCmCmUmG/i2FU//i2FU//i2FA//i2FC/mAmGmAmCmAmGmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	473	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FC//i2FU/mG/i2FU/mCmU/i2FG/mUmAmA/i2FC/mAmGmGmUmCmC*mG*mG	474
42	mG*mAmCmCmUmGmU/i2FU//i2FA//i2FC//i2FA/mGmAmCmAmGmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	475	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FC/mU/i2FG/mUmC/i2FU/mGmUmA/i2FA/mCmAmGmGmUmC*mG*mG	476

	GalNAc]mGmGmCmU mGmC			
43	mA*mCmCmUmGmU mU/i2FA//i2FC//i2FA//i 2FG/mAmCmAmGmU mCmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	477	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FG//i 2FA/mC/i2FU/mGmU/i2FC/ mUmGmU/i2FA/mAmCmA mGmGmU*mG*mG	478
44	mU*mGmCmCmAmU mU/i2FG//i2FU//i2FC//i 2FU/mGmCmAmAmC mUmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	479	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FA//i 2FG/mU/i2FU/mGmC/i2FA/ mGmAmC/i2FA/mAmUmG mGmCmA*mG*mG	480
45	mG*mCmCmAmUmU mG/i2FU//i2FC//i2FU//i 2FG/mCmAmAmCmU mUmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	481	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FA//i 2FA/mG/i2FU/mUmG/i2FC/ mAmGmA/i2FC/mAmAmU mGmGmC*mG*mG	482
46	mC*mCmAmUmUmG mU/i2FC//i2FU//i2FG//i 2FC/mAmAmCmUmU mUmGmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	483	[MePhosphonate-4O- mUs]/i2FC/*/i2FC/*/i2FA//i 2FA/mA/i2FG/mUmU/i2FG/ mCmAmG/i2FA/mCmAmA mUmGmG*mG*mG	484
47	mA*mUmUmGmUmC mU/i2FG//i2FC//i2FA//i 2FA/mCmUmUmUmG mGmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	485	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FC//i 2FC/mA/i2FA/mAmG/i2FU/ mUmGmC/i2FA/mGmAmC mAmAmU*mG*mG	486
48	mU*mCmUmGmCmA mA/i2FC//i2FU//i2FU//i	487	[MePhosphonate-4O- mUs]/i2FU/*/i2FC/*/i2FA//i	488

	2FU/mGmGmCmAmG mUmGmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC		2FC/mU/i2FG/mCmC/i2FA/ mAmAmG/i2FU/mUmGmC mAmGmA*mG*mG	
49	mC*mUmAmCmCmC mA/i2FC//i2FU//i2FG//i 2FC/mUmGmAmAmA mCmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	489	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FG//i 2FU/mU/i2FU/mCmA/i2FG/ mCmAmG/i2FU/mGmGmG mUmAmG*mG*mG	490
50	mG*mCmCmAmGmG mA/i2FA//i2FC//i2FA//i 2FG/mGmAmCmCmU mGmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	491	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FC//i 2FA/mG/i2FG/mUmC/i2FC/ mUmGmU/i2FU/mCmCmU mGmGmC*mG*mG	492
51	mG*mAmAmCmAmG mG/i2FA//i2FC//i2FC//i 2FU/mGmUmGmGmA mAmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	493	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FU//i 2FU/mC/i2FC/mAmC/i2FA/ mGmGmU/i2FC/mCmUmG mUmUmC*mG*mG	494
52	mA*mCmAmGmGmA mC/i2FC//i2FU//i2FG//i 2FU/mGmGmAmAmU mUmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	495	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FA//i 2FA/mU/i2FU/mCmC/i2FA/ mCmAmG/i2FG/mUmCmC mUmGmU*mG*mG	496
53	mU*mGmGmAmAmU mU/i2FC//i2FA//i2FC//i 2FC/mAmCmCmCmC mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-	497	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FA//i 2FG/mG/i2FG/mGmU/i2FG/ mGmUmG/i2FA/mAmUmU mCmCmA*mG*mG	498

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
54	mC*mUmUmGmUmGmA/i2FC//i2FC//i2FA//i2FC/mCmUmAmCmAmUmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	499	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i2FU/mG/i2FU/mAmG/i2FG/mUmGmG/i2FU/mCmAmCmAmAmG*mG*mG	500
55	mU*mUmGmUmGmAmC/i2FC//i2FA//i2FC//i2FC/mUmAmCmAmUmCmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	501	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FG//i2FA/mU/i2FG/mUmA/i2FG/mGmUmG/i2FG/mUmCmAmCmAmA*mG*mG	502
56	mU*mGmUmGmAmCmC/i2FA//i2FC//i2FC//i2FU/mAmCmAmUmCmAmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	503	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FU//i2FG/mA/i2FU/mGmU/i2FA/mGmGmU/i2FG/mGmUmCmAmCmA*mG*mG	504
57	mG*mUmGmAmCmCmA/i2FC//i2FC//i2FU//i2FA/mCmAmUmCmAmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	505	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FU/mG/i2FA/mUmG/i2FU/mAmGmG/i2FU/mGmGmUmCmAmC*mG*mG	506
58	mU*mGmAmCmCmAmC/i2FC//i2FU//i2FA//i2FC/mAmUmCmAmUmCmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	507	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FG//i2FA/mU/i2FG/mAmU/i2FG/mUmAmG/i2FG/mUmGmGmUmCmA*mG*mG	508

59	mG*mAmCmCmAmC mC/i2FU//i2FA//i2FC//i 2FA/mUmCmAmUmC mUmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	509	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FA//i 2FG/mA/i2FU/mGmA/i2FU/ mGmUmA/i2FG/mGmUmG mGmUmC*mG*mG	510
60	mA*mCmCmAmCmC mU/i2FA//i2FC//i2FA//i 2FU/mCmAmUmCmU mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	511	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FA//i 2FA/mG/i2FA/mUmG/i2FA/ mUmGmU/i2FA/mGmGmU mGmGmU*mG*mG	512
61	mC*mCmAmCmCmU mA/i2FC//i2FA//i2FU//i 2FC/mAmUmCmUmU mGmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	513	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FC//i 2FA/mA/i2FG/mAmU/i2FG/ mAmUmG/i2FU/mAmGmG mUmGmG*mG*mG	514
62	mC*mAmCmCmUmA mC/i2FA//i2FU//i2FC//i 2FA/mUmCmUmUmG mUmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	515	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FA//i 2FC/mA/i2FA/mGmA/i2FU/ mGmAmU/i2FG/mUmAmG mGmUmG*mG*mG	516
63	mA*mCmCmUmAmC mA/i2FU//i2FC//i2FA//i 2FU/mCmUmUmGmU mUmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	517	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FA//i 2FA/mC/i2FA/mAmG/i2FA/ mUmGmA/i2FU/mGmUmA mGmGmU*mG*mG	518
64	mC*mCmUmAmCmA mU/i2FC//i2FA//i2FU//i 2FC/mUmUmGmUmU mUmGmCmAmGmCm	519	[MePhosphonate-4O-mUs]/i2FG/*/i2FC/*/i2FA//i 2FA/mA/i2FC/mAmA/i2FG/	520

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mAmUmG/i2FA/mUmGmUmAmGmG*mG*mG	
65	mC*mUmAmCmAmUmC/i2FA//i2FU//i2FC//i2FU/mUmGmUmUmUmGmCmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	521	[MePhosphonate-4O-mUs]/i2FG/*/i2FG/*/i2FC//i2FA/mA/i2FA/mCmA/i2FA/mGmAmU/i2FG/mAmUmGmUmAmG*mG*mG	522
66	mA*mCmAmUmCmAmU/i2FC//i2FU//i2FU//i2FG/mUmUmUmGmCmCmUmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	523	[MePhosphonate-4O-mUs]/i2FU/*/i2FA/*/i2FG//i2FG/mC/i2FA/mAmA/i2FC/mAmAmG/i2FA/mUmGmAmUmGmU*mG*mG	524
67	mA*mUmCmAmUmCmU/i2FU//i2FG//i2FU//i2FU/mUmGmCmCmUmAmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	525	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FU//i2FA/mG/i2FG/mCmA/i2FA/mAmCmA/i2FA/mGmAmUmGmAmU*mG*mG	526
68	mU*mCmAmUmCmUmU/i2FG//i2FU//i2FU//i2FU/mGmCmCmUmAmCmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	527	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FG//i2FU/mA/i2FG/mGmC/i2FA/mAmAmC/i2FA/mAmGmAmUmGmA*mG*mG	528
69	mA*mUmCmUmUmGmU/i2FU//i2FU//i2FG//i2FC/mCmUmAmCmAmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	529	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FU/mG/i2FU/mAmG/i2FG/mCmAmA/i2FA/mCmAmAmGmAmU*mG*mG	530

	GalNAc]mGmGmCmU mGmC			
70	mU*mCmUmUmGmU mU/i2FU//i2FG//i2FC//i 2FC/mUmAmCmAmU mCmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	531	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FG//i 2FA/mU/i2FG/mUmA/i2FG/ mGmCmA/i2FA/mAmCmA mAmGmA*mG*mG	532
71	mU*mUmUmCmCmC mC/i2FU//i2FA//i2FC//i 2FC/mUmUmGmUmG mGmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	533	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FC//i 2FC/mA/i2FC/mAmA/i2FG/ mGmUmA/i2FG/mGmGmG mAmAmA*mG*mG	534
72	mU*mUmCmCmCmC mU/i2FA//i2FC//i2FC//i 2FU/mUmGmUmGmG mUmGmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	535	[MePhosphonate-4O- mUs]/i2FC/*/i2FC/*/i2FA//i 2FC/mC/i2FA/mCmA/i2FA/ mGmGmU/i2FA/mGmGmG mGmAmA*mG*mG	536
73	mC*mCmCmUmAmC mC/i2FU//i2FU//i2FG//i 2FU/mGmGmUmGmG mUmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	537	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FA//i 2FC/mC/i2FA/mCmC/i2FA/ mCmAmA/i2FG/mGmUmA mGmGmG*mG*mG	538
74	mC*mUmAmCmCmU mU/i2FG//i2FU//i2FG//i 2FG/mUmGmGmUmU mAmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	539	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FU//i 2FA/mA/i2FC/mCmA/i2FC/ mCmAmC/i2FA/mAmGmG mUmAmG*mG*mG	540
75	mU*mAmCmCmUmU mG/i2FU//i2FG//i2FG//i	541	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FA//i	542

	2FU/mGmGmUmUmAmUmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		2FU/mA/i2FA/mCmC/i2FA/mCmCmA/i2FC/mAmAmGmGmUmA*mG*mG	
76	mA*mCmCmUmUmGmU/i2FG//i2FG//i2FU//i2FG/mGmUmUmAmUmUmGmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	543	[MePhosphonate-4O-mUs]/i2FC/*/i2FC/*/i2FA//i2FA/mU/i2FA/mAmC/i2FC/mAmCmC/i2FA/mCmAmAmGmGmU*mG*mG	544
77	mC*mCmUmUmGmUmG/i2FG//i2FU//i2FG//i2FG/mUmUmAmUmUmGmGmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	545	[MePhosphonate-4O-mUs]/i2FC/*/i2FC/*/i2FC//i2FA/mA/i2FU/mAmA/i2FC/mCmAmC/i2FC/mAmCmAmAmGmG*mG*mG	546
78	mC*mUmUmGmUmGmG/i2FU//i2FG//i2FG//i2FU/mUmAmUmUmGmGmGmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	547	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FC//i2FC/mA/i2FA/mUmA/i2FA/mCmCmA/i2FC/mCmAmCmAmAmG*mG*mG	548
79	mU*mUmGmUmGmGmU/i2FG//i2FG//i2FU//i2FU/mAmUmUmGmGmGmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	549	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FC//i2FC/mC/i2FA/mAmU/i2FA/mAmCmC/i2FA/mCmCmAmCmAmA*mG*mG	550
80	mU*mGmUmGmGmUmG/i2FG//i2FU//i2FU//i2FA/mUmUmGmGmGmUmUmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-	551	[MePhosphonate-4O-mUs]/i2FU/*/i2FA/*/i2FA//i2FC/mC/i2FC/mAmA/i2FU/mAmAmC/i2FC/mAmCmCmAmCmA*mG*mG	552

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
81	mG*mUmGmGmUmGmG/i2FU//i2FU//i2FA//i2FU/mUmGmGmGmUmUmAmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	553	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FA//i2FA/mC/i2FC/mCmA/i2FA/mUmAmA/i2FC/mCmAmCmCmAmC*mG*mG	554
82	mU*mGmGmUmGmGmU/i2FU//i2FA//i2FU//i2FU/mGmGmGmUmUmAmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	555	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FU//i2FA/mA/i2FC/mCmC/i2FA/mAmUmA/i2FA/mCmCmAmCmCmA*mG*mG	556
83	mG*mGmUmGmGmUmU/i2FA//i2FU//i2FU//i2FG/mGmGmUmUmAmGmAmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	557	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FC//i2FU/mA/i2FA/mCmC/i2FC/mAmAmU/i2FA/mAmCmCmAmCmC*mG*mG	558
84	mG*mUmGmGmUmUmA/i2FU//i2FU//i2FG//i2FG/mGmUmUmAmGmAmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	559	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FU//i2FC/mU/i2FA/mAmC/i2FC/mCmAmA/i2FU/mAmAmCmCmAmC*mG*mG	560
85	mU*mGmGmUmUmAmU/i2FU//i2FG//i2FG//i2FG/mUmUmAmGmAmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	561	[MePhosphonate-4O-mUs]/i2FU/*/i2FU/*/i2FC//i2FU/mC/i2FU/mAmA/i2FC/mCmCmA/i2FA/mUmAmAmCmCmA*mG*mG	562

86	mG*mGmUmUmAmU mU/i2FG//i2FG//i2FG//i 2FU/mUmAmGmAmG mAmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	563	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FU//i 2FC/mU/i2FC/mUmA/i2FA/ mCmCmC/i2FA/mAmUmA mAmCmC*mG*mG	564
87	mG*mUmUmAmUmU mG/i2FG//i2FG//i2FU//i 2FU/mAmGmAmGmA mAmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	565	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FU//i 2FU/mC/i2FU/mCmU/i2FA/ mAmCmC/i2FC/mAmAmU mAmAmC*mG*mG	566
88	mU*mUmAmUmUmG mG/i2FG//i2FU//i2FU//i 2FA/mGmAmGmAmA mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	567	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FA//i 2FU/mU/i2FC/mUmC/i2FU/ mAmAmC/i2FC/mCmAmA mUmAmA*mG*mG	568
89	mA*mUmUmGmGmG mU/i2FU//i2FA//i2FG//i 2FA/mGmAmAmUmG mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	569	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FA//i 2FC/mA/i2FU/mUmC/i2FU/ mCmUmA/i2FA/mCmCmC mAmAmU*mG*mG	570
90	mU*mUmGmGmGmU mU/i2FA//i2FG//i2FA//i 2FG/mAmAmUmGmU mGmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	571	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FC//i 2FA/mC/i2FA/mUmU/i2FC/ mUmCmU/i2FA/mAmCmC mCmAmA*mG*mG	572
91	mG*mGmUmUmAmG mA/i2FG//i2FA//i2FA//i 2FU/mGmUmGmUmU mGmGmUmAmGmCm	573	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FC//i 2FA/mA/i2FC/mAmC/i2FA/	574

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mUmUmC/i2FU/mCmUmAmAmCmC*mG*mG	
92	mG*mUmUmAmGmAmG/i2FA//i2FA//i2FU//i2FG/mUmGmUmUmGmGmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	575	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FC//i2FC/mA/i2FA/mCmA/i2FC/mAmUmU/i2FC/mUmCmUmAmAmC*mG*mG	576
93	mU*mUmAmGmAmGmA/i2FA//i2FU//i2FG//i2FU/mGmUmUmGmGmUmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	577	[MePhosphonate-4O-mUs]/i2FG/*/i2FC/*/i2FA//i2FC/mC/i2FA/mAmC/i2FA/mCmAmU/i2FU/mCmUmCmUmAmA*mG*mG	578
94	mU*mAmGmAmGmAmA/i2FU//i2FG//i2FU//i2FG/mUmUmGmGmUmGmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	579	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FC//i2FA/mC/i2FC/mAmA/i2FC/mAmCmA/i2FU/mUmCmUmCmUmA*mG*mG	580
95	mA*mGmAmGmAmAmU/i2FG//i2FU//i2FG//i2FU/mUmGmGmUmGmCmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	581	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FG//i2FC/mA/i2FC/mCmA/i2FA/mCmAmC/i2FA/mUmUmCmUmCmU*mG*mG	582
96	mG*mAmGmAmAmUmG/i2FU//i2FG//i2FU//i2FU/mGmGmUmGmCmUmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	583	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i2FG/mC/i2FA/mCmC/i2FA/mAmCmA/i2FC/mAmUmUmCmUmC*mG*mG	584

	GalNAc]mGmGmCmU mGmC			
97	mA*mGmAmAmUmG mU/i2FG//i2FU//i2FU//i 2FG/mGmUmGmCmU mCmAmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	585	[MePhosphonate-4O- mUs]/i2FG/*/i2FU/*/i2FG//i 2FA/mG/i2FC/mAmC/i2FC/ mAmAmC/i2FA/mCmAmU mUmCmU*mG*mG	586
98	mA*mAmUmGmUmG mU/i2FU//i2FG//i2FG//i 2FU/mGmCmUmCmA mCmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	587	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FG//i 2FU/mG/i2FA/mGmC/i2FA/ mCmCmA/i2FA/mCmAmC mAmUmU*mG*mG	588
99	mA*mUmGmUmGmU mU/i2FG//i2FG//i2FU//i 2FG/mCmUmCmAmC mCmAmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	589	[MePhosphonate-4O- mUs]/i2FU/*/i2FU/*/i2FG//i 2FG/mU/i2FG/mAmG/i2FC/ mAmCmC/i2FA/mAmCmA mCmAmU*mG*mG	590
100	mU*mGmUmGmUmU mG/i2FG//i2FU//i2FG//i 2FC/mUmCmAmCmC mAmAmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	591	[MePhosphonate-4O- mUs]/i2FC/*/i2FU/*/i2FU//i 2FG/mG/i2FU/mGmA/i2FG/ mCmAmC/i2FC/mAmAmC mAmCmA*mG*mG	592
101	mU*mGmGmUmCmC mA/i2FU//i2FC//i2FA//i 2FU/mGmAmAmGmA mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	593	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FU//i 2FU/mC/i2FU/mUmC/i2FA/ mUmGmA/i2FU/mGmGmA mCmCmA*mG*mG	594
102	mG*mGmUmCmCmA mU/i2FC//i2FA//i2FU//i	595	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FG//i	596

	2FG/mAmAmGmAmA mCmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC		2FU/mU/i2FC/mUmU/i2FC/ mAmUmG/i2FA/mUmGmG mAmCmC*mG*mG	
103	mC*mUmGmAmCmU mU/i2FC//i2FU//i2FU//i 2FC/mCmUmUmCmA mGmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	597	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FC//i 2FU/mG/i2FA/mAmG/i2FG/ mAmAmG/i2FA/mAmGmU mCmAmG*mG*mG	598
104	mA*mCmUmUmCmU mU/i2FC//i2FC//i2FU//i 2FU/mCmAmGmAmU mGmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	599	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FC//i 2FA/mU/i2FC/mUmG/i2FA/ mAmGmG/i2FA/mAmGmA mAmGmU*mG*mG	600
105	mU*mCmCmUmUmC mA/i2FG//i2FA//i2FU//i 2FG/mCmUmGmUmU mUmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	601	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FA//i 2FA/mA/i2FC/mAmG/i2FC/ mAmUmC/i2FU/mGmAmA mGmGmA*mG*mG	602
106	mC*mCmUmUmCmA mG/i2FA//i2FU//i2FG//i 2FC/mUmGmUmUmU mUmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	603	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FA//i 2FA/mA/i2FA/mCmA/i2FG/ mCmAmU/i2FC/mUmGmA mAmGmG*mG*mG	604
107	mC*mUmUmCmAmG mA/i2FU//i2FG//i2FC//i 2FU/mGmUmUmUmU mUmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-	605	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FA//i 2FA/mA/i2FA/mAmC/i2FA/ mGmCmA/i2FU/mCmUmG mAmAmG*mG*mG	606

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
108	mU*mUmCmAmGmAmU/i2FG//i2FC//i2FU//i2FG/mUmUmUmUmCmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	607	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FG//i2FA/mA/i2FA/mAmA/i2FC/mAmGmC/i2FA/mUmCmUmGmAmA*mG*mG	608
109	mC*mAmGmAmUmGmC/i2FU//i2FG//i2FU//i2FU/mUmUmUmCmAmCmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	609	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FG//i2FU/mG/i2FA/mAmA/i2FA/mAmCmA/i2FG/mCmAmUmCmUmG*mG*mG	610
110	mA*mGmAmUmGmCmU/i2FG//i2FU//i2FU//i2FU/mUmUmCmAmCmCmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	611	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FG//i2FG/mU/i2FG/mAmA/i2FA/mAmAmC/i2FA/mGmCmAmUmCmU*mG*mG	612
111	mG*mAmUmGmCmUmG/i2FU//i2FU//i2FU//i2FU/mUmCmAmCmCmAmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	613	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FU//i2FG/mG/i2FU/mGmA/i2FA/mAmAmA/i2FC/mAmGmCmAmUmC*mG*mG	614
112	mA*mUmGmCmUmGmU/i2FU//i2FU//i2FU//i2FU/mCmAmCmCmAmCmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	615	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FG//i2FU/mG/i2FG/mUmG/i2FA/mAmAmA/i2FA/mCmAmGmCmAmU*mG*mG	616

113	mU*mGmCmUmGmU mU/i2FU//i2FU//i2FU//i 2FC/mAmCmCmAmC mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	617	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FA//i 2FG/mU/i2FG/mGmU/i2FG/ mAmAmA/i2FA/mAmCmA mGmCmA*mG*mG	618
114	mG*mCmUmGmUmU mU/i2FU//i2FU//i2FC//i 2FA/mCmCmAmCmU mGmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	619	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FC//i 2FA/mG/i2FU/mGmG/i2FU/ mGmAmA/i2FA/mAmAmC mAmGmC*mG*mG	620
115	mU*mGmUmUmUmU mU/i2FC//i2FA//i2FC//i 2FC/mAmCmUmGmU mCmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	621	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FG//i 2FA/mC/i2FA/mGmU/i2FG/ mGmUmG/i2FA/mAmAmA mAmCmA*mG*mG	622
116	mG*mUmUmUmUmU mC/i2FA//i2FC//i2FC//i 2FA/mCmUmGmUmC mCmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	623	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FG//i 2FG/mA/i2FC/mAmG/i2FU/ mGmGmU/i2FG/mAmAmA mAmAmC*mG*mG	624
117	mU*mUmUmUmUmC mA/i2FC//i2FC//i2FA//i 2FC/mUmGmUmCmC mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	625	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FA//i 2FG/mG/i2FA/mCmA/i2FG/ mUmGmG/i2FU/mGmAmA mAmAmA*mG*mG	626
118	mU*mUmUmUmCmA mC/i2FC//i2FA//i2FC//i 2FU/mGmUmCmCmU mGmUmCmAmGmCm	627	[MePhosphonate-4O- mUs]/i2FG/*/i2FA/*/i2FC//i 2FA/mG/i2FG/mAmC/i2FA/	628

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mGmUmG/i2FG/mUmGmAmAmAmA*mG*mG	
119	mU*mUmCmAmCmCmA/i2FC//i2FU//i2FG//i2FU/mCmCmUmGmUmCmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	629	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FG//i2FA/mC/i2FA/mGmG/i2FA/mCmAmG/i2FU/mGmGmUmGmAmA*mG*mG	630
120	mC*mAmCmCmAmCmU/i2FG//i2FU//i2FC//i2FC/mUmGmUmCmCmAmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	631	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FU//i2FG/mG/i2FA/mCmA/i2FG/mGmAmC/i2FA/mGmUmGmGmUmG*mG*mG	632
121	mA*mCmCmAmCmUmG/i2FU//i2FC//i2FC//i2FU/mGmUmCmCmAmUmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	633	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FA//i2FU/mG/i2FG/mAmC/i2FA/mGmGmA/i2FC/mAmGmUmGmGmU*mG*mG	634
122	mC*mCmAmCmUmGmU/i2FC//i2FC//i2FU//i2FG/mUmCmCmAmUmUmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	635	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FA//i2FA/mU/i2FG/mGmA/i2FC/mAmGmG/i2FA/mCmAmGmUmGmG*mG*mG	636
123	mC*mAmCmUmGmUmC/i2FC//i2FU//i2FG//i2FU/mCmCmAmUmUmGmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	637	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FC//i2FA/mA/i2FU/mGmG/i2FA/mCmAmG/i2FG/mAmCmAmGmUmG*mG*mG	638

	GalNAc]mGmGmCmU mGmC			
124	mA*mCmUmGmUmC mC/i2FU//i2FG//i2FU//i 2FC/mCmAmUmUmG mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	639	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FU//i 2FC/mA/i2FA/mUmG/i2FG/ mAmCmA/i2FG/mGmAmC mAmGmU*mG*mG	640
125	mC*mUmAmAmGmC mU/i2FA//i2FC//i2FC//i 2FU/mGmAmGmAmA mCmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	641	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FG//i 2FU/mU/i2FC/mUmC/i2FA/ mGmGmU/i2FA/mGmCmU mUmAmG*mG*mG	642
126	mG*mAmGmGmUmC mC/i2FA//i2FG//i2FC//i 2FA/mGmAmGmGmU mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	643	[MePhosphonate-4O-mUs]/i2FA/*/i2FC/*/i2FA//i 2FA/mC/i2FC/mUmC/i2FU/ mGmCmU/i2FG/mGmAmC mCmUmC*mG*mG	644
127	mG*mCmAmGmAmG mG/i2FU//i2FU//i2FG//i 2FU/mCmCmAmUmG mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	645	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FU//i 2FC/mA/i2FU/mGmG/i2FA/ mCmAmA/i2FC/mCmUmC mUmGmC*mG*mG	646
128	mC*mAmGmAmGmG mU/i2FU//i2FG//i2FU//i 2FC/mCmAmUmGmA mCmAmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	647	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FG//i 2FU/mC/i2FA/mUmG/i2FG/ mAmCmA/i2FA/mCmCmU mCmUmG*mG*mG	648
129	mG*mAmGmGmAmU mG/i2FA//i2FG//i2FG//i	649	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FC//i	650

	2FA/mAmCmUmUmU mGmGmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC		2FA/mA/i2FA/mGmU/i2FU/ mCmCmU/i2FC/mAmUmC mCmUmC*mG*mG	
130	mG*mAmAmCmUmU mU/i2FG//i2FG//i2FA//i 2FG/mGmAmAmAmU mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	651	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FA//i 2FA/mU/i2FU/mUmC/i2FC/ mUmCmC/i2FA/mAmAmG mUmUmC*mG*mG	652
131	mG*mAmCmGmCmU mC/i2FU//i2FU//i2FC//i 2FA/mGmCmUmAmU mUmAmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	653	[MePhosphonate-4O- mUs]/i2FG/*/i2FU/*/i2FA//i 2FA/mU/i2FA/mGmC/i2FU/ mGmAmA/i2FG/mAmGmC mGmUmC*mG*mG	654
132	mA*mCmGmCmUmC mU/i2FU//i2FC//i2FA//i 2FG/mCmUmAmUmU mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	655	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FU//i 2FA/mA/i2FU/mAmG/i2FC/ mUmGmA/i2FA/mGmAmG mCmGmU*mG*mG	656
133	mC*mGmCmUmCmU mU/i2FC//i2FA//i2FG//i 2FC/mUmAmUmUmA mCmAmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	657	[MePhosphonate-4O- mUs]/i2FU/*/i2FU/*/i2FG//i 2FU/mA/i2FA/mUmA/i2FG/ mCmUmG/i2FA/mAmGmA mGmCmG*mG*mG	658
134	mG*mCmUmCmUmU mC/i2FA//i2FG//i2FC//i 2FU/mAmUmUmAmC mAmAmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-	659	[MePhosphonate-4O- mUs]/i2FG/*/i2FU/*/i2FU//i 2FG/mU/i2FA/mAmU/i2FA/ mGmCmU/i2FG/mAmAmG mAmGmC*mG*mG	660

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
135	mC*mUmCmUmUmCmA/i2FG//i2FC//i2FU//i2FA/mUmUmAmCmAmAmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	661	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FU//i2FU/mG/i2FU/mAmA/i2FU/mAmGmC/i2FU/mGmAmAmGmAmG*mG*mG	662
136	mU*mCmUmUmCmAmG/i2FC//i2FU//i2FA//i2FU/mUmAmCmAmAmCmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	663	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FG//i2FU/mU/i2FG/mUmA/i2FA/mUmAmG/i2FC/mUmGmAmAmGmA*mG*mG	664
137	mC*mUmUmCmAmGmC/i2FU//i2FA//i2FU//i2FU/mAmCmAmAmCmAmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	665	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FU//i2FG/mU/i2FU/mGmU/i2FA/mAmUmA/i2FG/mCmUmGmAmAmG*mG*mG	666
138	mU*mUmCmAmGmCmU/i2FA//i2FU//i2FU//i2FA/mCmAmAmCmAmUmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	667	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i2FU/mG/i2FU/mUmG/i2FU/mAmAmU/i2FA/mGmCmUmGmAmA*mG*mG	668
139	mC*mCmAmGmCmCmU/i2FG//i2FA//i2FC//i2FC/mUmCmAmCmCmUmGmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	669	[MePhosphonate-4O-mUs]/i2FG/*/i2FC/*/i2FA//i2FG/mG/i2FU/mGmA/i2FG/mGmUmC/i2FA/mGmGmCmUmGmG*mG*mG	670

140	mC*mAmGmCmCmU mG/i2FA//i2FC//i2FC//i 2FU/mCmAmCmCmU mGmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	671	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FC//i 2FA/mG/i2FG/mUmG/i2FA/ mGmGmU/i2FC/mAmGmG mCmUmG*mG*mG	672
141	mA*mGmCmCmUmG mA/i2FC//i2FC//i2FU//i 2FC/mAmCmCmUmG mCmUmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	673	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FG//i 2FC/mA/i2FG/mGmU/i2FG/ mAmGmG/i2FU/mCmAmG mGmCmU*mG*mG	674
142	mG*mCmCmUmGmA mC/i2FC//i2FU//i2FC//i 2FA/mCmCmUmGmC mUmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	675	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FA//i 2FG/mC/i2FA/mGmG/i2FU/ mGmAmG/i2FG/mUmCmA mGmGmC*mG*mG	676
143	mC*mCmUmGmAmC mC/i2FU//i2FC//i2FA//i 2FC/mCmUmGmCmU mUmAmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	677	[MePhosphonate-4O- mUs]/i2FU/*/i2FU/*/i2FA//i 2FA/mG/i2FC/mAmG/i2FG/ mUmGmA/i2FG/mGmUmC mAmGmG*mG*mG	678
144	mC*mUmGmAmCmC mU/i2FC//i2FA//i2FC//i 2FC/mUmGmCmUmU mAmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	679	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FU//i 2FA/mA/i2FG/mCmA/i2FG/ mGmUmG/i2FA/mGmGmU mCmAmG*mG*mG	680
145	mU*mGmAmCmCmU mC/i2FA//i2FC//i2FC//i 2FU/mGmCmUmUmA mAmUmUmAmGmCm	681	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FU//i 2FU/mA/i2FA/mGmC/i2FA/	682

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mGmGmU/i2FG/mAmGmGmUmCmA*mG*mG	
146	mG*mAmCmCmUmCmA/i2FC//i2FC//i2FU//i2FG/mCmUmUmAmAmUmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	683	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FA//i2FU/mU/i2FA/mAmG/i2FC/mAmGmG/i2FU/mGmAmGmGmUmC*mG*mG	684
147	mA*mCmCmUmCmAmC/i2FC//i2FU//i2FG//i2FC/mUmUmAmAmUmUmGmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	685	[MePhosphonate-4O-mUs]/i2FU/*/i2FC/*/i2FA//i2FA/mU/i2FU/mAmA/i2FG/mCmAmG/i2FG/mUmGmAmGmGmU*mG*mG	686
148	mC*mCmUmCmAmCmC/i2FU//i2FG//i2FC//i2FU/mUmAmAmUmUmGmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	687	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FC//i2FA/mA/i2FU/mUmA/i2FA/mGmCmA/i2FG/mGmUmGmAmGmG*mG*mG	688
149	mC*mUmCmAmCmCmU/i2FG//i2FC//i2FU//i2FU/mAmAmUmUmGmAmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	689	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FU//i2FC/mA/i2FA/mUmU/i2FA/mAmGmC/i2FA/mGmGmUmGmAmG*mG*mG	690
150	mU*mCmAmCmCmUmG/i2FC//i2FU//i2FU//i2FA/mAmUmUmGmAmCmAmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	691	[MePhosphonate-4O-mUs]/i2FG/*/i2FU/*/i2FG//i2FU/mC/i2FA/mAmU/i2FU/mAmAmG/i2FC/mAmGmGmUmGmA*mG*mG	692

	GalNAc]mGmGmCmU mGmC			
151	mC*mAmCmCmUmG mC/i2FU//i2FU//i2FA//i 2FA/mUmUmGmAmC mAmCmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	693	[MePhosphonate-4O- mUs]/i2FG/*/i2FG/*/i2FU//i 2FG/mU/i2FC/mAmA/i2FU/ mUmAmA/i2FG/mCmAmG mGmUmG*mG*mG	694
152	mA*mCmCmUmGmC mU/i2FU//i2FA//i2FA//i 2FU/mUmGmAmCmA mCmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	695	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FG//i 2FU/mG/i2FU/mCmA/i2FA/ mUmUmA/i2FA/mGmCmA mGmGmU*mG*mG	696
153	mC*mCmUmGmCmU mU/i2FA//i2FA//i2FU//i 2FU/mGmAmCmAmC mCmAmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	697	[MePhosphonate-4O- mUs]/i2FU/*/i2FU/*/i2FG//i 2FG/mU/i2FG/mUmC/i2FA/ mAmUmU/i2FA/mAmGmC mAmGmG*mG*mG	698
154	mC*mUmGmCmUmU mA/i2FA//i2FU//i2FU//i 2FG/mAmCmAmCmC mAmAmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	699	[MePhosphonate-4O- mUs]/i2FG/*/i2FU/*/i2FU//i 2FG/mG/i2FU/mGmU/i2FC/ mAmAmU/i2FU/mAmAmG mCmAmG*mG*mG	700
155	mU*mGmCmUmUmA mA/i2FU//i2FU//i2FG//i 2FA/mCmAmCmCmA mAmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	701	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FU//i 2FU/mG/i2FG/mUmG/i2FU/ mCmAmA/i2FU/mUmAmA mGmCmA*mG*mG	702
156	mG*mCmUmUmAmA mU/i2FU//i2FG//i2FA//i	703	[MePhosphonate-4O- mUs]/i2FA/*/i2FA/*/i2FG//i	704

	2FC/mAmCmCmAmAmCmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		2FU/mU/i2FG/mGmU/i2FG/mUmCmA/i2FA/mUmUmAmAmGmC*mG*mG	
157	mC*mUmUmAmAmUmU/i2FG//i2FA//i2FC//i2FA/mCmCmAmAmCmUmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	705	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FA//i2FG/mU/i2FU/mGmG/i2FU/mGmUmC/i2FA/mAmUmUmAmAmG*mG*mG	706
158	mU*mUmAmAmUmUmG/i2FA//i2FC//i2FA//i2FC/mCmAmAmCmUmUmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	707	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FA//i2FA/mG/i2FU/mUmG/i2FG/mUmGmU/i2FC/mAmAmUmUmAmA*mG*mG	708
159	mU*mAmAmUmUmGmA/i2FC//i2FA//i2FC//i2FC/mAmAmCmUmUmUmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	709	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FA//i2FA/mA/i2FG/mUmU/i2FG/mGmUmG/i2FU/mCmAmAmUmUmA*mG*mG	710
160	mA*mUmUmGmAmAmG/i2FG//i2FG//i2FG//i2FU/mGmCmUmGmUmGmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	711	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FC//i2FA/mC/i2FA/mGmC/i2FA/mCmCmC/i2FC/mUmUmCmAmAmU*mG*mG	712
161	mC*mUmUmGmGmAmC/i2FA//i2FA//i2FA//i2FA/mGmGmAmUmUmGmUmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-	713	[MePhosphonate-4O-mUs]/i2FC/*/i2FA/*/i2FC//i2FA/mA/i2FU/mCmC/i2FU/mUmUmU/i2FG/mUmCmCmAmAmG*mG*mG	714

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
162	mU*mUmGmGmAmCmA/i2FA//i2FA//i2FA//i2FG/mGmAmUmUmGmUmGmGmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	715	[MePhosphonate-4O-mUs]/i2FC/*/i2FC/*/i2FA//i2FC/mA/i2FA/mUmC/i2FC/mUmUmU/i2FU/mGmUmCmCmAmA*mG*mG	716
163	mU*mCmAmAmCmGmG/i2FU//i2FU//i2FC//i2FC/mCmUmUmGmAmUmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	717	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FA//i2FU/mC/i2FA/mAmG/i2FG/mGmAmA/i2FC/mCmGmUmUmGmA*mG*mG	718
164	mC*mAmAmCmGmGmU/i2FU//i2FC//i2FC//i2FC/mUmUmGmAmUmUmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	719	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FA//i2FA/mU/i2FC/mAmA/i2FG/mGmGmA/i2FA/mCmCmGmUmUmG*mG*mG	720
165	mA*mAmCmGmGmUmU/i2FC//i2FC//i2FC//i2FU/mUmGmAmUmUmUmCmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	721	[MePhosphonate-4O-mUs]/i2FA/*/i2FG/*/i2FA//i2FA/mA/i2FU/mCmA/i2FA/mGmGmG/i2FA/mAmCmCmGmUmU*mG*mG	722
166	mA*mCmGmGmUmUmC/i2FC//i2FC//i2FU//i2FU/mGmAmUmUmUmCmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	723	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FG//i2FA/mA/i2FA/mUmC/i2FA/mAmGmG/i2FG/mAmAmCmCmGmU*mG*mG	724

167	mG*mUmAmCmAmU mU/i2FG//i2FA//i2FC//i 2FC/mAmGmAmCmC mAmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	725	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FU//i 2FG/mG/i2FU/mCmU/i2FG/ mGmUmC/i2FA/mAmUmG mUmAmC*mG*mG	726
168	mA*mCmCmUmGmU mA/i2FC//i2FC//i2FA//i 2FC/mCmUmCmCmU mGmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	727	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FC//i 2FA/mG/i2FG/mAmG/i2FG/ mUmGmG/i2FU/mAmCmA mGmGmU*mG*mG	728
169	mC*mCmUmGmUmA mC/i2FC//i2FA//i2FC//i 2FC/mUmCmCmUmG mUmGmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	729	[MePhosphonate-4O- mUs]/i2FA/*/i2FC/*/i2FA//i 2FC/mA/i2FG/mGmA/i2FG/ mGmUmG/i2FG/mUmAmC mAmGmG*mG*mG	730
170	mG*mUmAmCmCmA mC/i2FC//i2FU//i2FC//i 2FC/mUmGmUmGmU mCmAmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	731	[MePhosphonate-4O- mUs]/i2FA/*/i2FU/*/i2FG//i 2FA/mC/i2FA/mCmA/i2FG/ mGmAmG/i2FG/mUmGmG mUmAmC*mG*mG	732
171	mG*mCmAmCmAmG mG/i2FC//i2FA//i2FU//i 2FC/mAmAmGmUmU mCmUmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	733	[MePhosphonate-4O- mUs]/i2FU/*/i2FA/*/i2FG//i 2FA/mA/i2FC/mUmU/i2FG/ mAmUmG/i2FC/mCmUmG mUmGmC*mG*mG	734
172	mA*mCmAmGmGmC mA/i2FU//i2FC//i2FA//i 2FA/mGmUmUmCmU mAmCmUmAmGmCm	735	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FU//i 2FA/mG/i2FA/mAmC/i2FU/	736

	AmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC		mUmGmA/i2FU/mGmCmCmUmGmU*mG*mG	
173	mC*mAmGmGmCmAmU/i2FC//i2FA//i2FA//i2FG/mUmUmCmUmAmCmUmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	737	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FG//i2FU/mA/i2FG/mAmA/i2FC/mUmUmG/i2FA/mUmGmCmCmUmG*mG*mG	738
174	mA*mGmGmCmAmUmC/i2FA//i2FA//i2FG//i2FU/mUmCmUmAmCmUmCmCmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	739	[MePhosphonate-4O-mUs]/i2FG/*/i2FG/*/i2FA//i2FG/mU/i2FA/mGmA/i2FA/mCmUmU/i2FG/mAmUmGmCmCmU*mG*mG	740
175	mG*mGmCmAmUmCmA/i2FA//i2FG//i2FU//i2FU/mCmUmAmCmUmCmCmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	741	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FG//i2FA/mG/i2FU/mAmG/i2FA/mAmCmU/i2FU/mGmAmUmGmCmC*mG*mG	742
176	mG*mCmAmUmCmAmA/i2FG//i2FU//i2FU//i2FC/mUmAmCmUmCmCmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	743	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FG//i2FG/mA/i2FG/mUmA/i2FG/mAmAmC/i2FU/mUmGmAmUmGmC*mG*mG	744
177	mC*mAmUmCmAmAmG/i2FU//i2FU//i2FC//i2FU/mAmCmUmCmCmAmUmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-	745	[MePhosphonate-4O-mUs]/i2FA/*/i2FA/*/i2FU//i2FG/mG/i2FA/mGmU/i2FA/mGmAmA/i2FC/mUmUmGmAmUmG*mG*mG	746

	GalNAc]mGmGmCmU mGmC			
178	mA*mUmCmAmAmG mU/i2FU//i2FC//i2FU//i 2FA/mCmUmCmCmA mUmUmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	747	[MePhosphonate-4O-mUs]/i2FG/*/i2FA/*/i2FA//i 2FU/mG/i2FG/mAmG/i2FU/ mAmGmA/i2FA/mCmUmU mGmAmU*mG*mG	748
179	mU*mCmAmAmGmU mU/i2FC//i2FU//i2FA//i 2FC/mUmCmCmAmU mUmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	749	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FA//i 2FA/mU/i2FG/mGmA/i2FG/ mUmAmG/i2FA/mAmCmU mUmGmA*mG*mG	750
180	mC*mAmAmGmUmU mC/i2FU//i2FA//i2FC//i 2FU/mCmCmAmUmU mCmAmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	751	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FG//i 2FA/mA/i2FU/mGmG/i2FA/ mGmUmA/i2FG/mAmAmC mUmUmG*mG*mG	752
181	mA*mAmGmUmUmC mU/i2FA//i2FC//i2FU//i 2FC/mCmAmUmUmC mAmGmCmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	753	[MePhosphonate-4O-mUs]/i2FG/*/i2FC/*/i2FU//i 2FG/mA/i2FA/mUmG/i2FG/ mAmGmU/i2FA/mGmAmA mCmUmU*mG*mG	754
182	mA*mGmUmUmCmU mA/i2FC//i2FU//i2FC//i 2FC/mAmUmUmCmA mGmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmU mGmC	755	[MePhosphonate-4O-mUs]/i2FU/*/i2FG/*/i2FC//i 2FU/mG/i2FA/mAmU/i2FG/ mGmAmG/i2FU/mAmGmA mAmCmU*mG*mG	756
183	mG*mUmUmCmUmA mC/i2FU//i2FC//i2FC//i	757	[MePhosphonate-4O-mUs]/i2FC/*/i2FU/*/i2FG//i	758

	2FA/mUmUmCmAmG mCmAmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC		2FC/mU/i2FG/mAmA/i2FU/ mGmGmA/i2FG/mUmAmG mAmAmC*mG*mG	
184	mG*mUmGmUmCmA mU/i2FC//i2FU//i2FC//i 2FA/mGmAmCmAmA mCmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	759	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FG//i 2FU/mU/i2FG/mUmC/i2FU/ mGmAmG/i2FA/mUmGmA mCmAmC*mG*mG	760
185	mC*mAmUmCmUmC mA/i2FG//i2FA//i2FC//i 2FA/mAmCmCmUmG mCmUmGmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	761	[MePhosphonate-4O- mUs]/i2FC/*/i2FA/*/i2FG//i 2FC/mA/i2FG/mGmU/i2FU/ mGmUmC/i2FU/mGmAmG mAmUmG*mG*mG	762
186	mU*mCmAmGmAmC mA/i2FA//i2FC//i2FC//i 2FU/mGmCmUmGmG mUmGmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	763	[MePhosphonate-4O- mUs]/i2FU/*/i2FC/*/i2FA//i 2FC/mC/i2FA/mGmC/i2FA/ mGmGmU/i2FU/mGmUmC mUmGmA*mG*mG	764
187	mC*mGmGmGmGmA mC/i2FC//i2FU//i2FG//i 2FU/mUmAmCmAmG mAmCmAmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA- GalNAc][ademA- GalNAc]mGmGmCmU mGmC	765	[MePhosphonate-4O- mUs]/i2FU/*/i2FG/*/i2FU//i 2FC/mU/i2FG/mUmA/i2FA/ mCmAmG/i2FG/mUmCmC mCmCmG*mG*mG	766
188	mG*mAmCmAmAmC mG/i2FC//i2FU//i2FG//i 2FC/mCmAmUmUmG mUmCmUmAmGmCm AmGmCmCmG[ademA -GalNAc][ademA-	767	[MePhosphonate-4O- mUs]/i2FA/*/i2FG/*/i2FA//i 2FC/mA/i2FA/mUmG/i2FG/ mCmAmG/i2FC/mGmUmU mGmUmC*mG*mG	768

	GalNAc][ademA-GalNAc]mGmGmCmUmGmC			
189	mG*mCmUmGmCmCmU/i2FC//i2FC//i2FU//i2FG/mAmCmUmGmUmAmAmUmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	769	[MePhosphonate-4O-mUs]/i2FA/*/i2FU/*/i2FU//i2FA/mC/i2FA/mGmU/i2FC/mAmGmG/i2FA/mGmGmCmAmGmC*mG*mG	770
190	mC*mUmGmCmCmUmC/i2FC//i2FU//i2FG//i2FA/mCmUmGmUmAmAmUmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	771	[MePhosphonate-4O-mUs]/i2FU/*/i2FA/*/i2FU//i2FU/mA/i2FC/mAmG/i2FU/mCmAmG/i2FG/mAmGmGmCmAmG*mG*mG	772
191	mU*mAmAmUmAmUmU/i2FA//i2FA//i2FA//i2FC/mUmUmUmUmUmAmAmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	773	[MePhosphonate-4O-mUs]/i2FU/*/i2FU/*/i2FA//i2FA/mA/i2FA/mAmA/i2FG/mUmUmU/i2FA/mAmUmAmUmUmA*mG*mG	774
192	mA*mAmUmAmUmUmA/i2FA//i2FA//i2FC//i2FU/mUmUmUmUmUmAmAmAmAmGmCmAmGmCmCmG[ademA-GalNAc][ademA-GalNAc][ademA-GalNAc]mGmGmCmUmGmC	775	[MePhosphonate-4O-mUs]/i2FU/*/i2FU/*/i2FU//i2FA/mA/i2FA/mAmA/i2FA/mGmUmU/i2FU/mAmAmUmAmUmU*mG*mG	776

[00283] SEQ ID NO: 777 – Target Sequence 1

ACATCATCTTGTTTGCCTA

[00284] SEQ ID NO:778 – Target Sequence 2

TCTTGTTTGCCTACATCTA

[00285] SEQ ID NO:779 – Target Sequence 3

CTTCAGATGCTGTTTTTCA

[00286] SEQ ID NO:780 – Target Sequence 4

CGCTCTTCAGCTATTACAA

[00287] SEQ ID NO:781 – Target Sequence 5

CTTAATTGACACCAACTTT

[00288] SEQ ID NO:782 – Target Sequence 6

TCAACGGTTCCCTTGATTT

[00289] SEQ ID NO:783 – Target Sequence 7

CATCAAGTTCTACTCCATT

[00290] SEQ ID NO:784 – Artificial Sequence

GCAGCCGAAAGGCUGC

[00291] SEQ ID NOs:785-1168 –SCAP Oligonucleotides

SCAP Oligo	Sense Strand (passenger; 19-mer)	SEQ ID NO:	Antisense Strand (guide; 19-mer)	SEQ ID NO:
1	UGUUUGCCUACAUCUACUU	785	AAGUAGAUGUAGGCAAACA	786
2	GUUUGCCUACAUCUACUUC	787	GAAGUAGAUGUAGGCAAAC	788
3	UUUGCCUACAUCUACUUCU	789	AGAAGUAGAUGUAGGCAAA	790
4	GCCUACAUCUACUUCUCCA	791	UGGAGAAGUAGAUGUAGGC	792
5	AAGAUCGACAUGGUCAAGU	793	ACUUGACCAUGUCGAUCUU	794
6	AGAUCGACAUGGUCAAGUC	795	GACUUGACCAUGUCGAUCU	796
7	AUCGACAUGGUCAAGUCCA	797	UGGACUUGACCAUGUCGAU	798
8	GUGUUGGUGCUCACCAAGU	799	ACUUGGUGAGCACCAACAC	800
9	UGUUGGUGCUCACCAAGUC	801	GACUUGGUGAGCACCAACA	802

10	GAGAGCUGGUCCAUCAUGA	803	UCAUGAUGGACCAGCUCUC	804
11	AGAGCUGGUCCAUCAUGAA	805	UUCAUGAUGGACCAGCUCU	806
12	GAGCUGGUCCAUCAUGAAG	807	CUUCAUGAUGGACCAGCUC	808
13	AGCUGGUCCAUCAUGAAGA	809	UCUUCAUGAUGGACCAGCU	810
14	GCUGGUCCAUCAUGAAGAA	811	UUCUUCAUGAUGGACCAGC	812
15	CUGGUCCAUCAUGAAGAAC	813	GUUCUUCAUGAUGGACCAG	814
16	CCGUUGUCUGGAUUGGCAU	815	AUGCCAAUCCAGACAACGG	816
17	UUGUCUGGAUUGGCAUCCU	817	AGGAUGCCAAUCCAGACAA	818
18	UGUCUGGAUUGGCAUCCUG	819	CAGGAUGCCAAUCCAGACA	820
19	GUCUGGAUUGGCAUCCUGG	821	CCAGGAUGCCAAUCCAGAC	822
20	CUGGAUUGGCAUCCUGGUA	823	UACCAGGAUGCCAAUCCAG	824
21	UGGAUUGGCAUCCUGGUAU	825	AUACCAGGAUGCCAAUCCA	826
22	GGAUUGGCAUCCUGGUAUA	827	UAUACCAGGAUGCCAAUCC	828
23	GAUUGGCAUCCUGGUAUAC	829	GUAUACCAGGAUGCCAAUC	830
24	AUUGGCAUCCUGGUAUACA	831	UGUAUACCAGGAUGCCAAU	832
25	CUCCAUCUUCCCACCUGAU	833	AUCAGGUGGGAAGAUGGAG	834
26	CAUCUGCCUGUGGGAUGUA	835	UACAUCCCACAGGCAGAUG	836
27	UCUGCCUGUGGGAUGUACU	837	AGUACAUCCCACAGGCAGA	838
28	GUGGUGCAAGCUUGGGUGU	839	ACACCCAAGCUUGCACCAC	840
29	UGGUGCAAGCUUGGGUGUC	841	GACACCCAAGCUUGCACCA	842
30	GGUGCAAGCUUGGGUGUCA	843	UGACACCCAAGCUUGCACC	844
31	GUGCAAGCUUGGGUGUCAU	845	AUGACACCCAAGCUUGCAC	846
32	GCAAGCUUGGGUGUCAUCU	847	AGAUGACACCCAAGCUUGC	848
33	CAAGCUUGGGUGUCAUCUC	849	GAGAUGACACCCAAGCUUG	850

34	AAGCUUGGGUGUCAUCUCA	851	UGAGAUGACACCCAAGCUU	852
35	AGCUUGGGUGUCAUCUCAG	853	CUGAGAUGACACCCAAGCU	854
36	GCUUGGGUGUCAUCUCAGA	855	UCUGAGAUGACACCCAAGC	856
37	GUGUCUCCUUUUGGGACCU	857	AGGUCCCAAAAGGAGACAC	858
38	UGUCUCCUUUUGGGACCUA	859	UAGGUCCCAAAAGGAGACA	860
39	GGGGACCUGUUACAGACAG	861	CUGUCUGUAACAGGUCCCC	862
40	GGGACCUGUUACAGACAGU	863	ACUGUCUGUAACAGGUCCC	864
41	GGACCUGUUACAGACAGUC	865	GACUGUCUGUAACAGGUCC	866
42	GACCUGUUACAGACAGUCU	867	AGACUGUCUGUAACAGGUC	868
43	ACCUGUUACAGACAGUCUA	869	UAGACUGUCUGUAACAGGU	870
44	UGCCAUUGUCUGCAACUUU	871	AAAGUUGCAGACAAUGGCA	872
45	GCCAUUGUCUGCAACUUUG	873	CAAAGUUGCAGACAAUGGC	874
46	CCAUUGUCUGCAACUUUGG	875	CCAAAGUUGCAGACAAUGG	876
47	AUUGUCUGCAACUUUGGCA	877	UGCCAAAGUUGCAGACAAU	878
48	UCUGCAACUUUGGCAGUGA	879	UCACUGCCAAAGUUGCAGA	880
49	CUACCCACUGCUGAAACUC	881	GAGUUUCAGCAGUGGGUAG	882
50	GCCAGGAACAGGACCUGUG	883	CACAGGUCCUGUUCCUGGC	884
51	GAACAGGACCUGUGGAAUU	885	AAUUCCACAGGUCCUGUUC	886
52	ACAGGACCUGUGGAAUUCA	887	UGAAUUCCACAGGUCCUGU	888
53	UGGAAUUCACCACCCCUGU	889	ACAGGGGUGGUGAAUUCCA	890
54	CUUGUGACCACCUACAUCA	891	UGAUGUAGGUGGUCACAAG	892
55	UUGUGACCACCUACAUCAU	893	AUGAUGUAGGUGGUCACAA	894
56	UGUGACCACCUACAUCAUC	895	GAUGAUGUAGGUGGUCACA	896
57	GUGACCACCUACAUCAUCU	897	AGAUGAUGUAGGUGGUCAC	898

58	UGACCACCUACAUCAUCUU	899	AAGAUGAUGUAGGUGGUCA	900
59	GACCACCUACAUCAUCUUG	901	CAAGAUGAUGUAGGUGGUC	902
60	ACCACCUACAUCAUCUUGU	903	ACAAGAUGAUGUAGGUGGU	904
61	CCACCUACAUCAUCUUGUU	905	AACAAGAUGAUGUAGGUGG	906
62	CACCUACAUCAUCUUGUUU	907	AAACAAGAUGAUGUAGGUG	908
63	ACCUACAUCAUCUUGUUUG	909	CAAACAAGAUGAUGUAGGU	910
64	CCUACAUCAUCUUGUUUGC	911	GCAAACAAGAUGAUGUAGG	912
65	CUACAUCAUCUUGUUUGCC	913	GGCAAACAAGAUGAUGUAG	914
66	ACAUCAUCUUGUUUGCCUA	915	UAGGCAAACAAGAUGAUGU	916
67	AUCAUCUUGUUUGCCUACA	917	UGUAGGCAAACAAGAUGAU	918
68	UCAUCUUGUUUGCCUACAU	919	AUGUAGGCAAACAAGAUGA	920
69	AUCUUGUUUGCCUACAUCU	921	AGAUGUAGGCAAACAAGAU	922
70	UCUUGUUUGCCUACAUCUA	923	UAGAUGUAGGCAAACAAGA	924
71	UUUCCCCUACCUUGUGGUG	925	CACCACAAGGUAGGGGAAA	926
72	UUCCCCUACCUUGUGGUGG	927	CCACCACAAGGUAGGGGAA	928
73	CCCUACCUUGUGGUGGUUA	929	UAACCACCACAAGGUAGGG	930
74	CUACCUUGUGGUGGUUAUU	931	AAUAACCACCACAAGGUAG	932
75	UACCUUGUGGUGGUUAUUG	933	CAAUAACCACCACAAGGUA	934
76	ACCUUGUGGUGGUUAUUGG	935	CCAAUAACCACCACAAGGU	936
77	CCUUGUGGUGGUUAUUGGG	937	CCCAAUAACCACCACAAGG	938
78	CUUGUGGUGGUUAUUGGGU	939	ACCCAAUAACCACCACAAG	940
79	UUGUGGUGGUUAUUGGGUU	941	AACCCAAUAACCACCACAA	942
80	UGUGGUGGUUAUUGGGUUA	943	UAACCCAAUAACCACCACA	944
81	GUGGUGGUUAUUGGGUUAG	945	CUAACCCAAUAACCACCAC	946

82	UGGUGGUUAUUGGGUUAGA	947	UCUAACCCAAUAACCACCA	948
83	GGUGGUUAUUGGGUUAGAG	949	CUCUAACCCAAUAACCACC	950
84	GUGGUUAUUGGGUUAGAGA	951	UCUCUAACCCAAUAACCAC	952
85	UGGUUAUUGGGUUAGAGAA	953	UUCUCUAACCCAAUAACCA	954
86	GGUUAUUGGGUUAGAGAAU	955	AUUCUCUAACCCAAUAACC	956
87	GUUAUUGGGUUAGAGAAUG	957	CAUUCUCUAACCCAAUAAC	958
88	UUAUUGGGUUAGAGAAUGU	959	ACAUUCUCUAACCCAAUAA	960
89	AUUGGGUUAGAGAAUGUGU	961	ACACAUUCUCUAACCCAAU	962
90	UUGGGUUAGAGAAUGUGUU	963	AACACAUUCUCUAACCCAA	964
91	GGUUAGAGAAUGUGUUGGU	965	ACCAACACAUUCUCUAACC	966
92	GUUAGAGAAUGUGUUGGUG	967	CACCAACACAUUCUCUAAC	968
93	UUAGAGAAUGUGUUGGUGC	969	GCACCAACACAUUCUCUAA	970
94	UAGAGAAUGUGUUGGUGCU	971	AGCACCAACACAUUCUCUA	972
95	AGAGAAUGUGUUGGUGCUC	973	GAGCACCAACACAUUCUCU	974
96	GAGAAUGUGUUGGUGCUCA	975	UGAGCACCAACACAUUCUC	976
97	AGAAUGUGUUGGUGCUCAC	977	GUGAGCACCAACACAUUCU	978
98	AAUGUGUUGGUGCUCACCA	979	UGGUGAGCACCAACACAUU	980
99	AUGUGUUGGUGCUCACCAA	981	UUGGUGAGCACCAACACAU	982
100	UGUGUUGGUGCUCACCAAG	983	CUUGGUGAGCACCAACACA	984
101	UGGUCCAUCAUGAAGAACA	985	UGUUCUUCAUGAUGGACCA	986
102	GGUCCAUCAUGAAGAACAU	987	AUGUUCUUCAUGAUGGACC	988
103	CUGACUUCUUCCUUCAGAU	989	AUCUGAAGGAAGAAGUCAG	990
104	ACUUCUUCCUUCAGAUGCU	991	AGCAUCUGAAGGAAGAAGU	992
105	UCCUUCAGAUGCUGUUUUU	993	AAAAACAGCAUCUGAAGGA	994

106	CCUUCAGAUGCUGUUUUUC	995	GAAAAACAGCAUCUGAAGG	996
107	CUUCAGAUGCUGUUUUUCA	997	UGAAAAACAGCAUCUGAAG	998
108	UUCAGAUGCUGUUUUUCAC	999	GUGAAAAACAGCAUCUGAA	1000
109	CAGAUGCUGUUUUUCACCA	1001	UGGUGAAAAACAGCAUCUG	1002
110	AGAUGCUGUUUUUCACCAC	1003	GUGGUGAAAAACAGCAUCU	1004
111	GAUGCUGUUUUUCACCACU	1005	AGUGGUGAAAAACAGCAUC	1006
112	AUGCUGUUUUUCACCACUG	1007	CAGUGGUGAAAAACAGCAU	1008
113	UGCUGUUUUUCACCACUGU	1009	ACAGUGGUGAAAAACAGCA	1010
114	GCUGUUUUUCACCACUGUC	1011	GACAGUGGUGAAAAACAGC	1012
115	UGUUUUUCACCACUGUCCU	1013	AGGACAGUGGUGAAAAACA	1014
116	GUUUUUCACCACUGUCCUG	1015	CAGGACAGUGGUGAAAAAC	1016
117	UUUUUCACCACUGUCCUGU	1017	ACAGGACAGUGGUGAAAAA	1018
118	UUUUCACCACUGUCCUGUC	1019	GACAGGACAGUGGUGAAAA	1020
119	UUCACCACUGUCCUGUCCA	1021	UGGACAGGACAGUGGUGAA	1022
120	CACCACUGUCCUGUCCAUU	1023	AAUGGACAGGACAGUGGUG	1024
121	ACCACUGUCCUGUCCAUUG	1025	CAAUGGACAGGACAGUGGU	1026
122	CCACUGUCCUGUCCAUUGA	1027	UCAAUGGACAGGACAGUGG	1028
123	CACUGUCCUGUCCAUUGAC	1029	GUCAAUGGACAGGACAGUG	1030
124	ACUGUCCUGUCCAUUGACA	1031	UGUCAAUGGACAGGACAGU	1032
125	CUAAGCUACCUGAGAACCA	1033	UGGUUCUCAGGUAGCUUAG	1034
126	GAGGUCCAGCAGAGGUUGU	1035	ACAACCUCUGCUGGACCUC	1036
127	GCAGAGGUUGUCCAUGACA	1037	UGUCAUGGACAACCUCUGC	1038
128	CAGAGGUUGUCCAUGACAG	1039	CUGUCAUGGACAACCUCUG	1040
129	GAGGAUGAGGAACUUUGGA	1041	UCCAAAGUUCCUCAUCCUC	1042

130	GAACUUUGGAGGAAAUUGU	1043	ACAAUUUCCUCCAAAGUUC	1044
131	GACGCUCUUCAGCUAUUAC	1045	GUAAUAGCUGAAGAGCGUC	1046
132	ACGCUCUUCAGCUAUUACA	1047	UGUAAUAGCUGAAGAGCGU	1048
133	CGCUCUUCAGCUAUUACAA	1049	UUGUAAUAGCUGAAGAGCG	1050
134	GCUCUUCAGCUAUUACAAC	1051	GUUGUAAUAGCUGAAGAGC	1052
135	CUCUUCAGCUAUUACAACA	1053	UGUUGUAAUAGCUGAAGAG	1054
136	UCUUCAGCUAUUACAACAU	1055	AUGUUGUAAUAGCUGAAGA	1056
137	CUUCAGCUAUUACAACAUC	1057	GAUGUUGUAAUAGCUGAAG	1058
138	UUCAGCUAUUACAACAUCA	1059	UGAUGUUGUAAUAGCUGAA	1060
139	CCAGCCUGACCUCACCUGC	1061	GCAGGUGAGGUCAGGCUGG	1062
140	CAGCCUGACCUCACCUGCU	1063	AGCAGGUGAGGUCAGGCUG	1064
141	AGCCUGACCUCACCUGCUU	1065	AAGCAGGUGAGGUCAGGCU	1066
142	GCCUGACCUCACCUGCUUA	1067	UAAGCAGGUGAGGUCAGGC	1068
143	CCUGACCUCACCUGCUUAA	1069	UUAAGCAGGUGAGGUCAGG	1070
144	CUGACCUCACCUGCUUAAU	1071	AUUAAGCAGGUGAGGUCAG	1072
145	UGACCUCACCUGCUUAAUU	1073	AAUUAAGCAGGUGAGGUCA	1074
146	GACCUCACCUGCUUAAUUG	1075	CAAUUAAGCAGGUGAGGUC	1076
147	ACCUCACCUGCUUAAUUGA	1077	UCAAUUAAGCAGGUGAGGU	1078
148	CCUCACCUGCUUAAUUGAC	1079	GUCAAUUAAGCAGGUGAGG	1080
149	CUCACCUGCUUAAUUGACA	1081	UGUCAAUUAAGCAGGUGAG	1082
150	UCACCUGCUUAAUUGACAC	1083	GUGUCAAUUAAGCAGGUGA	1084
151	CACCUGCUUAAUUGACACC	1085	GGUGUCAAUUAAGCAGGUG	1086
152	ACCUGCUUAAUUGACACCA	1087	UGGUGUCAAUUAAGCAGGU	1088
153	CCUGCUUAAUUGACACCAA	1089	UUGGUGUCAAUUAAGCAGG	1090

154	CUGCUUAAUUGACACCAAC	1091	GUUGGUGUCAAUUAAGCAG	1092
155	UGCUUAAUUGACACCAACU	1093	AGUUGGUGUCAAUUAAGCA	1094
156	GCUUAAUUGACACCAACUU	1095	AAGUUGGUGUCAAUUAAGC	1096
157	CUUAAUUGACACCAACUUU	1097	AAAGUUGGUGUCAAUUAAG	1098
158	UUAAUUGACACCAACUUUU	1099	AAAAGUUGGUGUCAAUUAA	1100
159	UAAUUGACACCAACUUUUC	1101	GAAAAGUUGGUGUCAAUUA	1102
160	AUUGAAGGGGUGCUGUGCU	1103	AGCACAGCACCCCUUCAAU	1104
161	CUUGGACAAAAGGAUUGUG	1105	CACAAUCCUUUUGUCCAAG	1106
162	UUGGACAAAAGGAUUGUGG	1107	CCACAAUCCUUUUGUCCAA	1108
163	UCAACGGUUCCCUUGAUUU	1109	AAAUCAAGGGAACCGUUGA	1110
164	CAACGGUUCCCUUGAUUUC	1111	GAAAUCAAGGGAACCGUUG	1112
165	AACGGUUCCCUUGAUUUCU	1113	AGAAAUCAAGGGAACCGUU	1114
166	ACGGUUCCCUUGAUUUCUU	1115	AAGAAAUCAAGGGAACCGU	1116
167	GUACAUUGACCAGACCAUG	1117	CAUGGUCUGGUCAAUGUAC	1118
168	ACCUGUACCACCUCCUGUG	1119	CACAGGAGGUGGUACAGGU	1120
169	CCUGUACCACCUCCUGUGU	1121	ACACAGGAGGUGGUACAGG	1122
170	GUACCACCUCCUGUGUCAU	1123	AUGACACAGGAGGUGGUAC	1124
171	GCACAGGCAUCAAGUUCUA	1125	UAGAACUUGAUGCCUGUGC	1126
172	ACAGGCAUCAAGUUCUACU	1127	AGUAGAACUUGAUGCCUGU	1128
173	CAGGCAUCAAGUUCUACUC	1129	GAGUAGAACUUGAUGCCUG	1130
174	AGGCAUCAAGUUCUACUCC	1131	GGAGUAGAACUUGAUGCCU	1132
175	GGCAUCAAGUUCUACUCCA	1133	UGGAGUAGAACUUGAUGCC	1134
176	GCAUCAAGUUCUACUCCAU	1135	AUGGAGUAGAACUUGAUGC	1136
177	CAUCAAGUUCUACUCCAUU	1137	AAUGGAGUAGAACUUGAUG	1138

178	AUCAAGUUCUACUCCAUUC	1139	GAAUGGAGUAGAACUUGAU	1140
179	UCAAGUUCUACUCCAUUCA	1141	UGAAUGGAGUAGAACUUGA	1142
180	CAAGUUCUACUCCAUUCAG	1143	CUGAAUGGAGUAGAACUUG	1144
181	AAGUUCUACUCCAUUCAGC	1145	GCUGAAUGGAGUAGAACUU	1146
182	AGUUCUACUCCAUUCAGCA	1147	UGCUGAAUGGAGUAGAACU	1148
183	GUUCUACUCCAUUCAGCAG	1149	CUGCUGAAUGGAGUAGAAC	1150
184	GUGUCAUCUCAGACAACCU	1151	AGGUUGUCUGAGAUGACAC	1152
185	CAUCUCAGACAACCUGCUG	1153	CAGCAGGUUGUCUGAGAUG	1154
186	UCAGACAACCUGCUGGUGA	1155	UCACCAGCAGGUUGUCUGA	1156
187	CGGGGACCUGUUACAGACA	1157	UGUCUGUAACAGGUCCCCG	1158
188	GACAACGCUGCCAUUGUCU	1159	AGACAAUGGCAGCGUUGUC	1160
189	GCUGCCUCCUGACUGUAAU	1161	AUUACAGUCAGGAGGCAGC	1162
190	CUGCCUCCUGACUGUAAUA	1163	UAUUACAGUCAGGAGGCAG	1164
191	UAAUAUUAAACUUUUUUAA	1165	UUAAAAAAGUUUAAUAUUA	1166
192	AAUAUUAAACUUUUUUAAA	1167	UUUAAAAAAGUUUAAUAUU	1168

CLAIMS

The invention claimed is:

1. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

2. The RNAi oligonucleotide of Claim 1, wherein the sense strand is 15 to 50 nucleotides in length.

3. The RNAi oligonucleotide of Claims 1 or 2, wherein the sense strand is 18 to 36 nucleotides in length.

4. The RNAi oligonucleotide of any one of Claims 1 to 3, wherein the antisense strand is 15 to 30 nucleotides in length.

5. The RNAi oligonucleotide of any one of Claims 1 to 4, wherein the antisense strand is 22 nucleotides in length, and where in the antisense strand and the sense strand form a duplex region of at least 19 nucleotides in length, optionally at least 20 nucleotides in length.

6. The RNAi oligonucleotide of any one of Claims 1 to 5, wherein the region of complementarity is at least 19 contiguous nucleotides in length, optionally at least 20 nucleotides in length.

7. The RNAi oligonucleotide of any one of Claims 1 to 6, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length.

8. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense

strand of 15 to 50 nucleotides in length and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

9. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 15 to 50 nucleotides in length and an antisense strand of 15 to 30 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

10. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 15 to 50 nucleotides in length and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to an SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

11. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

12. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense

strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

13. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

14. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

15. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand of 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region of at least 19 nucleotides in length, optionally 20 nucleotides in length, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777

to 783, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

16. The RNAi oligonucleotide of any one of Claims 7 and 13 to 15, wherein L is a triloop or a tetraloop.

17. The RNAi oligonucleotide of Claim 16, wherein L is a tetraloop.

18. The RNAi oligonucleotide of Claim 17, wherein the tetraloop comprises a sequence of 5'-GAAA-3'.

19. The RNAi oligonucleotide of any one of Claims 13 to 18, wherein S1 and S2 are 1-10 nucleotides in length and have the same length.

20. The RNAi oligonucleotide of Claim 19, wherein S1 and S2 are 1 nucleotide, 2 nucleotides, 3 nucleotides, 4 nucleotides, 5 nucleotides, 6 nucleotides, 7 nucleotides, 8 nucleotides, 9 nucleotides, or 10 nucleotides in length.

21. The RNAi oligonucleotide of Claim 20, wherein S1 and S2 are 6 nucleotides in length.

22. The RNAi oligonucleotide of any one of Claims 13 to 21, wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784).

23. The RNAi oligonucleotide of any one of Claims 1 to 22, wherein the antisense strand comprises a 3' overhang sequence of 1 or more nucleotides in length.

24. The RNAi oligonucleotide of Claim 23, wherein the 3' overhang sequence is 2 nucleotides in length, and optionally wherein the 3' overhang sequence is GG.

25. The RNAi oligonucleotide of any one of the preceding claims comprising at least 1 modified nucleotide.

26. The RNAi oligonucleotide of any one of Claims 13 to 25, wherein all nucleotides of the oligonucleotide are modified except the nucleotides in the loop of the stem-loop.

27. The RNAi oligonucleotide of Claim 25 or 26, wherein the modified nucleotide comprises a 2'-modification.

28. The RNAi oligonucleotide of Claim 27, wherein the 2'-modification is a modification selected from the group consisting of 2'-aminoethyl, 2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl, and 2'-deoxy-2'-fluoro-β-d-arabinonucleic acid.

29. The RNAi oligonucleotide of any one of Claims 25 to 28, wherein all nucleotides comprising the RNAi oligonucleotide are modified, and optionally wherein the modification is a 2'-modification selected from the group consisting of 2'-fluoro and 2'-O-methyl.

30. The RNAi oligonucleotide of Claim 29, wherein one or more nucleotides at positions 8, 9, 10, or 11 of the sense strand are modified with 2'-fluoro.

31. The RNAi oligonucleotide of Claim 29 or 30, wherein one or more nucleotides at positions 2, 3, 4, 5, 7, 10, or 14 of the antisense strand are modified with 2'-fluoro.

32. The RNAi oligonucleotide of any one of Claims 29 to 31, wherein one or more nucleotides at positions 1, 2, 3, 4, 5, 6, 7, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 31, 32, 33, 34, 35, or 36 of the sense strand are modified with 2'-O-methyl.

33. The RNAi oligonucleotide of any one of Claims 29 to 32, wherein one or more nucleotides at positions 1, 6, 8, 9, 11, 12, 13, 15, 16, 17, 18, 19, 20, 21, or 22 of the antisense strand are modified with 2'-O-methyl.

34. The RNAi oligonucleotide of any one of the preceding claims comprising at least one modified internucleotide linkage.

35. The RNAi oligonucleotide of Claim 34, wherein the at least one modified internucleotide linkage is a phosphorothioate linkage.

36. The RNAi oligonucleotide of Claim 35, wherein the internucleotide linkage of nucleotides at positions 1 and 2 of the sense strand are modified with the phosphorothioate linkage.

37. The RNAi oligonucleotide of Claim 35 or 36, wherein the internucleotide linkage of one or more nucleotides at positions 1 and 2, 2 and 3, 3 and 4, 20 and 21, or 21 and 22 of the antisense strand are modified with the phosphorothioate linkage.

38. The RNAi oligonucleotide of any one of Claims 1 to 24, wherein the RNAi oligonucleotide has a modification pattern as shown in FIG. 1.

39. The RNAi oligonucleotide of any one of the preceding claims, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog.

40. The RNAi oligonucleotide of Claim 39, wherein the phosphate analog is oxymethylphosphonate, vinyl phosphonate or malonylphosphonate, and optionally wherein the phosphate analog is a 4'-phosphate analog comprising 5'-methoxyphosphonate-4'-oxy.

41. The RNAi oligonucleotide of any one of the preceding claims, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands.

42. The RNAi oligonucleotide of Claim 41, wherein each targeting ligand comprises a carbohydrate, amino sugar, cholesterol, polypeptide, or lipid.

43. The RNAi oligonucleotide of Claim 42, wherein each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety.

44. The RNAi oligonucleotide of Claim 43, wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety, or a tetravalent GalNAc moiety.

45. The RNAi oligonucleotide of any one of Claims 16 to 40, wherein up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

46. The RNAi oligonucleotide of any one of the preceding claims, wherein the sense strand comprises a nucleotide sequence of any one of the odd numbers of SEQ ID NOs: 9 to 392.

47. The RNAi oligonucleotide of any one of the preceding claims, wherein the antisense strand comprises a nucleotide sequence of any one of the even numbers of SEQ ID NOs:9 to 392.

48. The RNAi oligonucleotide of any one of the preceding claims, wherein the sense strand and the antisense strands comprise nucleotide sequences selected from the group consisting of:

(a) SEQ ID NOs: 139 and 140, respectively;
(b) SEQ ID NOs: 147 and 148, respectively;
(c) SEQ ID NOs: 221 and 222, respectively;
(d) SEQ ID NOs: 273 and 274, respectively;
(e) SEQ ID NOs: 321 and 322, respectively;
(f) SEQ ID NOs: 333 and 334, respectively; and
(g) SEQ ID NOs: 361 and 362 respectively.

49. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 139 and wherein the antisense strand comprises SEQ ID NO: 140.

50. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 147 and wherein the antisense strand comprises SEQ ID NO: 148.

51. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 221 and wherein the antisense strand comprises SEQ ID NO: 222.

52. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 273 and wherein the antisense strand comprises SEQ ID NO: 274.

53. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 321 and wherein the antisense strand comprises SEQ ID NO: 322.

54. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 333 and wherein the antisense strand comprises SEQ ID NO: 334.

55. The RNAi oligonucleotide of Claim 48, wherein the sense strand comprises SEQ ID NO: 361 and wherein the antisense strand comprises SEQ ID NO: 362.

56. The RNAi oligonucleotide of Claim 48, wherein the sense strand and the antisense strands comprise nucleotide sequences selected from the group consisting of:

(a') SEQ ID NOs: 523 and 524, respectively;
(b') SEQ ID NOs: 531 and 532, respectively;
(c') SEQ ID NOs: 605 and 606, respectively;
(d') SEQ ID NOs: 657 and 658, respectively;
(e') SEQ ID NOs: 705 and 706, respectively;
(f') SEQ ID NOs: 717 and 718, respectively; and
(g') SEQ ID NOs: 745 and 746 respectively.

57. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 523 and the antisense strand is SEQ ID NO: 524.

58. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 531 and the antisense strand is SEQ ID NO: 532.

59. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 605 and the antisense strand is SEQ ID NO: 606.

60. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 657 and the antisense strand is SEQ ID NO: 658.

61. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 705 and the antisense strand is SEQ ID NO: 706.

62. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 717 and the antisense strand is SEQ ID NO: 718.

63. The RNAi oligonucleotide of Claim 56, wherein the sense strand is SEQ ID NO: 745 and the antisense strand is SEQ ID NO: 746.

64. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

65. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs:777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

66. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 19 contiguous nucleotides in length.

67. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and the antisense strand are modified, wherein the antisense strand and the sense strand comprise 1 or more 2'-fluoro and 2'-O-methyl modified nucleotides and at least one phosphorothioate linkage, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

68. The RNAi oligonucleotide of any one of Claims 64 to 67, wherein the sense strand comprises of any one of SEQ ID NOs: 139, 147, 221, 273, 321, 333 and 361; or wherein the sense strand comprises of any one of SEQ ID NOs: 523, 531, 605, 657, 705, 717 and 745.

69. The RNAi oligonucleotide of any one of Claims 64 to 68, wherein the antisense strand comprises of any one of SEQ ID NOs: 140, 148, 222, 274, 322, 334 and 362; or wherein the antisense strand comprises of any one of SEQ ID NOs: 524, 532, 606, 658, 706, 718 and 746.

70. The RNAi oligonucleotide of any one of Claims 64 to 67, wherein the sense strand and antisense strands are selected from the group consisting of:

(a) SEQ ID NOs:139 and 140, respectively;
(b) SEQ ID NOs:147 and 148, respectively;
(c) SEQ ID NOs:221 and 222, respectively;
(d) SEQ ID NOs:273 and 274, respectively;
(e) SEQ ID NOs:321 and 322, respectively;
(f) SEQ ID NOs:333 and 334, respectively; and
(g) SEQ ID NOs:361 and 362 respectively; or
(a') SEQ ID NOs:523 and 524, respectively;
(b') SEQ ID NOs:531 and 532, respectively;
(c') SEQ ID NOs:605 and 606, respectively;
(d') SEQ ID NOs:657 and 658, respectively;
(e') SEQ ID NOs:705 and 706, respectively;

(f') SEQ ID NOs:717 and 718, respectively; and

(g') SEQ ID NOs:745 and 746 respectively.

71 The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 139 and the antisense strand comprises SEQ ID NO: 140.

72. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 147 and the antisense strand comprises SEQ ID NO: 148.

73. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 221 and the antisense strand comprises SEQ ID NO: 222.

74. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 273 and the antisense strand comprises SEQ ID NO: 274.

75. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 321 and the antisense strand comprises SEQ ID NO: 322.

76. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO: 333 and the antisense strand comprises SEQ ID NO: 334.

77. The RNAi oligonucleotide of Claim 70, wherein the sense strand comprises SEQ ID NO:361 and the antisense strand comprises SEQ ID NO:362.

78. The RNAi oligonucleotide of any one of Claims 71 to 77, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands.

79. The RNAi oligonucleotide of Claim 78, wherein each targeting ligand is a carbohydrate, amino sugar, cholesterol, polypeptide, or lipid.

80. The RNAi oligonucleotide of Claim 79, wherein each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety.

81. The RNAi oligonucleotide of Claim 80, wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety, or a tetravalent GalNAc moiety.

82. The RNAi oligonucleotide of Claim 81, wherein a sequence of 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784) in the sense strand forms a stem-loop structure, and wherein the AAA nucleotides in a sequence of 5'-GAAA-3' in the loop are each conjugated to a monovalent GalNAc moiety.

83 The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 523 and the antisense strand is SEQ ID NO: 524.

84. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 531 and the antisense strand is SEQ ID NO: 532.

85. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 605 and the antisense strand is SEQ ID NO: 606.

86. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 657 and the antisense strand is SEQ ID NO: 658.

87. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 705 and the antisense strand is SEQ ID NO: 706.

88. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 717 and the antisense strand is SEQ ID NO: 718.

89. The RNAi oligonucleotide of Claim 70, wherein the sense strand is SEQ ID NO: 745 and the antisense strand is SEQ ID NO: 746.

90. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex

region, and wherein the sense strand and the antisense strand consist of sequences selected from the group consisting of:

(a') SEQ ID NOs:523 and 524, respectively;

(b') SEQ ID NOs:531 and 532, respectively;

(c') SEQ ID NOs: 605 and 606, respectively;

(d') SEQ ID NOs: 657 and 658, respectively;

(e') SEQ ID NOs: 705 and 706, respectively;

(f') SEQ ID NOs:717 and 718, respectively; and

(g') SEQ ID NOs: 745 and 746 respectively.

91. The RNAi oligonucleotide of Claim 90, wherein a sequence of 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784) in the sense strand forms a stem-loop structure, and wherein the AAA nucleotides in a sequence of 5'-GAAA-3' in the loop are each conjugated to a monovalent GalNAc moiety.

92. A pharmaceutical composition comprising:

the RNAi oligonucleotide of any one of Claims 1 to 91, or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier, delivery agent or excipient.

93. A method of delivering an oligonucleotide to an individual, the method comprising the step of:

administering the pharmaceutical composition of Claim 92 to the individual.

94. A method of treating an individual having a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the method comprising the step of:

administering to the individual a therapeutically effective amount of the RNAi oligonucleotide of any one of Claims 1 to 91, or the pharmaceutical composition of Claim 92, thereby treating the individual.

95. A method of reducing sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity in a cell, a population of cells or an individual, the method comprising the step of:

contacting the cell or the population of cells with the RNAi oligonucleotide of any one of Claims 1 to 91 or the pharmaceutical composition of Claim 92; or

administering to the individual the RNAi oligonucleotide of any one of Claims 1 to 91 or the pharmaceutical composition of Claim 92.

96. The method of Claim 95, wherein reducing *SCAP* activity comprises reducing an amount or level of SCAP mRNA, an amount or level of SCAP protein, SCAP activity or a combination thereof.

97. The method of Claim 94 or 95, wherein the individual has a disease, disorder, or condition associated with *SCAP* activity.

98. The method of Claim 97, wherein the disease, disorder or condition associated with *SCAP* activity is acute coronary diseases (ACD), atherosclerotic cardiovascular disease (ASCVD), alcoholic hepatitis (AH), alcoholic liver disease (ALD), cardiometabolic disease, cholangiocarcinoma (CCA), cirrhosis, coronary heart diseases (CHD), diabetes, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), hyperlipidemia, hypertriglyceridemia, high non-HDL cholesterol, insulin resistance, liver steatosis, metabolic syndromes (MetS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), obesity, or primary sclerosing cholangitis (PSC).

99. The method of any one of Claims 94 to 98, wherein the RNAi oligonucleotide or the pharmaceutical composition is administered in combination with a second composition or therapeutic agent.

100. A method of treating an individual having a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the method comprising the step of:

administering to the individual a therapeutically effective amount of a RNAi oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand

and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a SCAP mRNA target sequence of any one of SEQ ID NOs: 777 to 783, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

101. A method of treating an individual having a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the method comprising the step of:

administering to the individual a therapeutically effective amount of a RNAi oligonucleotide comprising a sense strand and an antisense strand selected from a row set forth in Table 3 or Table 4, or a pharmaceutical composition thereof.

102. A method of treating an individual having a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the method comprising the step of:

administering to the individual a therapeutically effective amount of a RNAi oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand comprise nucleotide sequences selected from the group consisting of:

(a) SEQ ID NOs: 139 and 140, respectively;
(b) SEQ ID NOs: 147 and 148, respectively;
(c) SEQ ID NOs: 221 and 222, respectively;
(d) SEQ ID NOs: 273 and 274, respectively;
(e) SEQ ID NOs: 321 and 322, respectively;
(f) SEQ ID NOs: 333 and 334, respectively; and
(g) SEQ ID NOs: 361 and 362 respectively; or
(a') SEQ ID NOs: 523 and 524, respectively;
(b') SEQ ID NOs: 531 and 532, respectively;
(c') SEQ ID NOs: 605 and 606, respectively;
(d') SEQ ID NOs: 657 and 658, respectively;
(e') SEQ ID NOs: 705 and 706, respectively;
(f') SEQ ID NOs: 717 and 718, respectively; and
(g') SEQ ID NOs: 745 and 746 respectively.

103. The method of Claim 102, wherein the sense strand is SEQ ID NO: 523 and the antisense strand is SEQ ID NO: 524.

104. The method of Claim 102, wherein the sense strand is SEQ ID NO: 531 and the antisense strand is SEQ ID NO: 532.

105. The method of Claim 102, wherein the sense strand is SEQ ID NO: 605 and the antisense strand is SEQ ID NO: 606.

106. The method of Claim 102, wherein the sense strand is SEQ ID NO: 657 and the antisense strand is SEQ ID NO: 658.

107. The method of Claim 102, wherein the sense strand is SEQ ID NO: 705 and the antisense strand is SEQ ID NO: 706.

108. The method of Claim 105, wherein the sense strand is SEQ ID NO: 717 and the antisense strand is SEQ ID NO: 718.

109. The method of Claim 75, wherein the sense strand is SEQ ID NO: 745 and the antisense strand is SEQ ID NO: 746.

110. The method of any one of Claims 100 to 109, wherein the disease, disorder or condition associated with *SCAP* activity is selected from the group consisting of acute coronary diseases (ACD), atherosclerotic cardiovascular disease (ASCVD), alcoholic hepatitis (AH), alcoholic liver disease (ALD), cardiometabolic disease, cholangiocarcinoma (CCA), cirrhosis, coronary heart diseases (CHD), diabetes, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), hyperlipidemia, hypertriglyceridemia, high non-HDL cholesterol, insulin resistance, liver steatosis, metabolic syndromes (MetS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), obesity, or primary sclerosing cholangitis (PSC).

111. Use of the RNAi oligonucleotide of any one of Claims 1 to 91, or the pharmaceutical composition of Claim 92, in the manufacture of a medicament for the treatment of a disease,

disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, optionally for the treatment of acute coronary diseases (ACD), atherosclerotic cardiovascular disease (ASCVD), alcoholic hepatitis (AH), alcoholic liver disease (ALD), cardiometabolic disease, cholangiocarcinoma (CCA), cirrhosis, coronary heart diseases (CHD), diabetes, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), hyperlipidemia, hypertriglyceridemia, high non-HDL cholesterol, insulin resistance, liver steatosis, metabolic syndromes (MetS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), obesity, or primary sclerosing cholangitis (PSC).

112. The RNAi oligonucleotide of any one of Claims 1 to 91, or the pharmaceutical composition of Claim 92, for use, or adaptable for use, in the treatment of a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, optionally for the treatment of acute coronary diseases (ACD), atherosclerotic cardiovascular disease (ASCVD), alcoholic hepatitis (AH), alcoholic liver disease (ALD), cardiometabolic disease, cholangiocarcinoma (CCA), cirrhosis, coronary heart diseases (CHD), diabetes, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), hyperlipidemia, hypertriglyceridemia, high non-HDL cholesterol, insulin resistance, liver steatosis, metabolic syndromes (MetS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), obesity, or primary sclerosing cholangitis (PSC).

113. A kit comprising the RNAi oligonucleotide of any one of Claims 1 to 91, an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration to an individual having a disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity.

114. The use of Claim 111, the RNAi oligonucleotide or pharmaceutical composition for use, or adaptable for use, of Claim 112, or the kit of Claim 113, wherein the disease, disorder, or condition associated with sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity is acute coronary diseases (ACD), atherosclerotic cardiovascular disease (ASCVD), alcoholic hepatitis (AH), alcoholic liver disease (ALD), cardiometabolic disease, cholangiocarcinoma (CCA), cirrhosis, coronary heart diseases

(CHD), diabetes, hepatic fibrosis, hepatic inflammation, hepatocellular carcinoma (HCC), hyperlipidemia, hypertriglyceridemia, high non-HDL cholesterol, insulin resistance, liver steatosis, metabolic syndromes (MetS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), obesity, or primary sclerosing cholangitis (PSC).

115. A RNAi oligonucleotide for modulating sterol regulatory element-binding protein (SREBP) cleavage-activating protein (*SCAP*) activity, the oligonucleotide having a sense strand and an antisense strand that are optionally modified, wherein the sense strand and the antisense strand form a duplex region, wherein the sense strand and the antisense strand are a pair selected from the group consisting of:

(a) SEQ ID NOs: 139 and 140, respectively;

(b) SEQ ID NOs: 147 and 148, respectively;

(c) SEQ ID NOs: 221 and 222, respectively;

(d) SEQ ID NOs: 273 and 274, respectively;

(e) SEQ ID NOs: 321 and 322, respectively;

(f) SEQ ID NOs: 333 and 334, respectively; and

(g) SEQ ID NOs: 361 and 362, respectively,

wherein a sequence of 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 784) in the sense strand forms a stem-loop structure, and wherein the AAA nucleotides in a sequence of 5'-GAAA-3' in the loop are each conjugated to a monovalent GalNAc moiety.

116. The RNAi oligonucleotide of Claim 115, wherein the sense strand and the antisense strand are optionally modified and are a pair selected from the group consisting of:

(a') SEQ ID NOs: 523 and 524, respectively;

(b') SEQ ID NOs: 531 and 532, respectively;

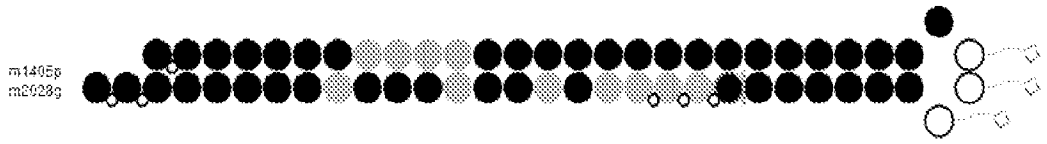
(c') SEQ ID NOs: 605 and 606, respectively;

(d') SEQ ID NOs: 657 and 658, respectively;

(e') SEQ ID NOs: 705 and 706, respectively;

(f') SEQ ID NOs: 717 and 718, respectively; and

(g') SEQ ID NOs: 745 and 746, respectively.



Modification Pattern 1: M1 (SM1405/ASM2028 pattern)

Key:

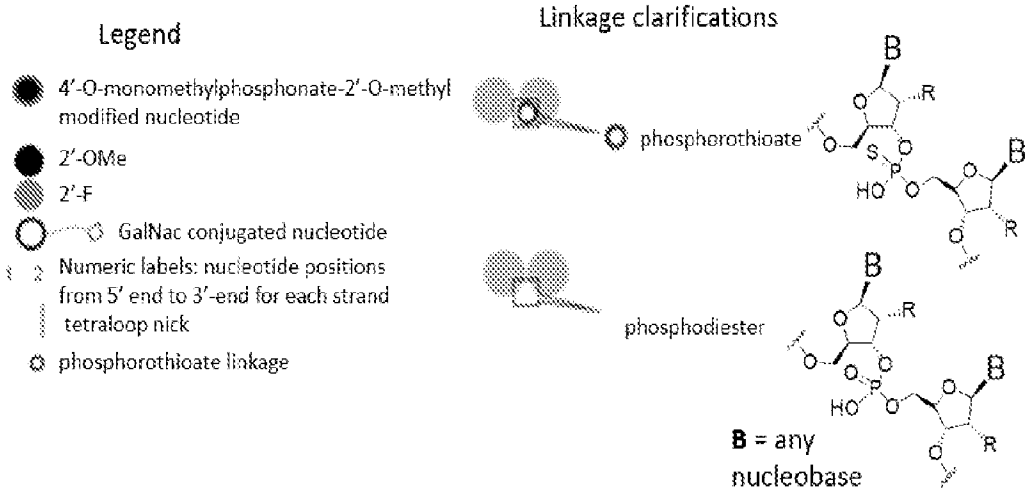


FIG. 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2023/018657

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/113 A61K31/713 A61K47/54
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, Sequence Search, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2017/100542 A1 (ALNYLAM PHARMACEUTICALS INC [US]) 15 June 2017 (2017-06-15) example 1; tables 1-4; sequences 67-75, 193-198 claims 1-120 the whole document ----- -/--	1-50, 56-58, 64-72, 78-84, 90-104, 110-116

[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
3 August 2023	02/10/2023

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

2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2020/243702 A2 (AMGEN INC [US]) 3 December 2020 (2020-12-03) claims 1-39; example 1; table 2 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	WO 2021/146488 A1 (DICERNA PHARMACEUTICALS INC [US]) 22 July 2021 (2021-07-22) figure 4; example 10 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	WO 2021/188795 A1 (DICERNA PHARMACEUTICALS INC [US]) 23 September 2021 (2021-09-23) the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	WO 2022/032288 A1 (DICERNA PHARMACEUTICALS INC [US]) 10 February 2022 (2022-02-10) figure 10 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	WO 2022/077024 A1 (DICERNA PHARMACEUTICALS INC [US]) 14 April 2022 (2022-04-14) figure 1; table A the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	WO 2020/123083 A1 (DICERNA PHARMACEUTICALS INC [US]) 18 June 2020 (2020-06-18) claims 1-29; figures 1, 2, 6 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116

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2

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2023/018657

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Anon: "Taking RNAi under the skin Starring: GalXC", , 1 November 2016 (2016-11-01), XP055868965, Retrieved from the Internet: URL:https://media.nature.com/original/magazine-assets/d43747-020-00189-y/d43747-020-00189-y.pdf [retrieved on 2021-12-03] the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	SETTEN RYAN L ET AL: "The current state and future directions of RNAi-based therapeutics", NATURE REVIEWS DRUG DISCOVERY, NATURE PUBLISHING GROUP, GB, vol. 18, no. 6, 7 March 2019 (2019-03-07), pages 421-446, XP036796447, ISSN: 1474-1776, DOI: 10.1038/S41573-019-0017-4 [retrieved on 2019-03-07] figure 3 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116
A	HU BO ET AL: "Therapeutic siRNA: state of the art", SIGNAL TRANSDUCTION AND TARGETED THERAPY, vol. 5, no. 1, 1 December 2020 (2020-12-01), XP055801687, DOI: 10.1038/s41392-020-0207-x figure 3 the whole document	1-50, 56-58, 64-72, 78-84, 90-104, 110-116

2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2023/018657

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed.

   b. ☒ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

      ☒ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/018657

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.:

49, 50, 57, 58, 71, 72, 83, 84, 103, 104(completely); 1-48, 56, 64-70 78-82, 90-102, 110-116(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: 49, 50, 57, 58, 71, 72, 83, 84, 103, 104(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity of at least 15 contiguous nucleotides to the sequence of SEQ ID NO: 777 or 778, encompassing the antisense strands listed in table 3 and having a sequence of SEQ ID NO: 10, 12, 134, 136, 138, 140, 142, 144, 146 or 148 and the respective modified strands listed in table 4; implementations of said RNAi oligonucleotide(s)

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2. claims: 51, 59, 73, 85, 105(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity to the sequence of SEQ ID NO: 779; implementations of said RNAi oligonucleotide(s)

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3. claims: 52, 60, 74, 86, 106(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity to the sequence of SEQ ID NO: 780; implementations of said RNAi oligonucleotide(s)

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4. claims: 53, 61, 75, 87, 107(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity to the sequence of SEQ ID NO: 781; implementations of said RNAi oligonucleotide(s)

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5. claims: 54, 62, 76, 88, 108(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity to the sequence of SEQ ID NO: 782; implementations of said RNAi oligonucleotide(s)

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6. claims: 55, 63, 77, 89, 109(completely); 1-48, 56, 64-70, 78-82, 90-102, 110-116(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

RNAi oligonucleotide(s) targeting SCAP wherein the antisense strand has a region of complementarity to the sequence of SEQ ID NO: 783; implementations of said RNAi oligonucleotide(s)

7-183. claims: 1-47, 92-101, 110-114(all partially)

RNAi oligonucleotide(s) targeting SCAP wherein the sense strand and/or the antisense strand has a sequence listed in table 3 or 4, not being covered by inventions 1) to 6); implementations of said RNAi oligonucleotide(s)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2023/018657

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Information on patent family members

International application No
PCT/US2023/018657

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