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Singh et al.

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(45) **Date of Patent:** **Oct. 31, 2017**

(54) **METHODS AND COMPOSITIONS FOR THE TREATMENT OF BCR-ABL POSITIVE LYMPHOBLASTIC LEUKEMIAS**

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§ 371 (c)(1),

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A61K 45/06 (2006.01)

A61K 31/506 (2006.01)

A61K 31/357 (2006.01)

(52) **U.S. Cl.**

CPC **A61K 31/357** (2013.01); **A61K 31/366** (2013.01); **A61K 31/506** (2013.01); **A61K 45/06** (2013.01)

(58) **Field of Classification Search**

CPC **A61K 31/357**
See application file for complete search history.

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Primary Examiner — Erich A Leeser

(74) *Attorney, Agent, or Firm* — Ballard Spahr LLP

(57) **ABSTRACT**

In one aspect, the invention relates to compositions comprising BCR-ABL tyrosine kinase inhibitors and artemisinin analogs, derivatives thereof, or related compounds, which are useful as in treating Philadelphia chromosome positive leukemias; pharmaceutical compositions comprising the compounds; and methods of treating disorders of uncontrolled cellular proliferation associated with BCR-ABL dysfunction using the compounds and compositions. This abstract is intended as a scanning tool for purposes of searching in the particular art and is not intended to be limiting of the present invention.

23 Claims, 178 Drawing Sheets

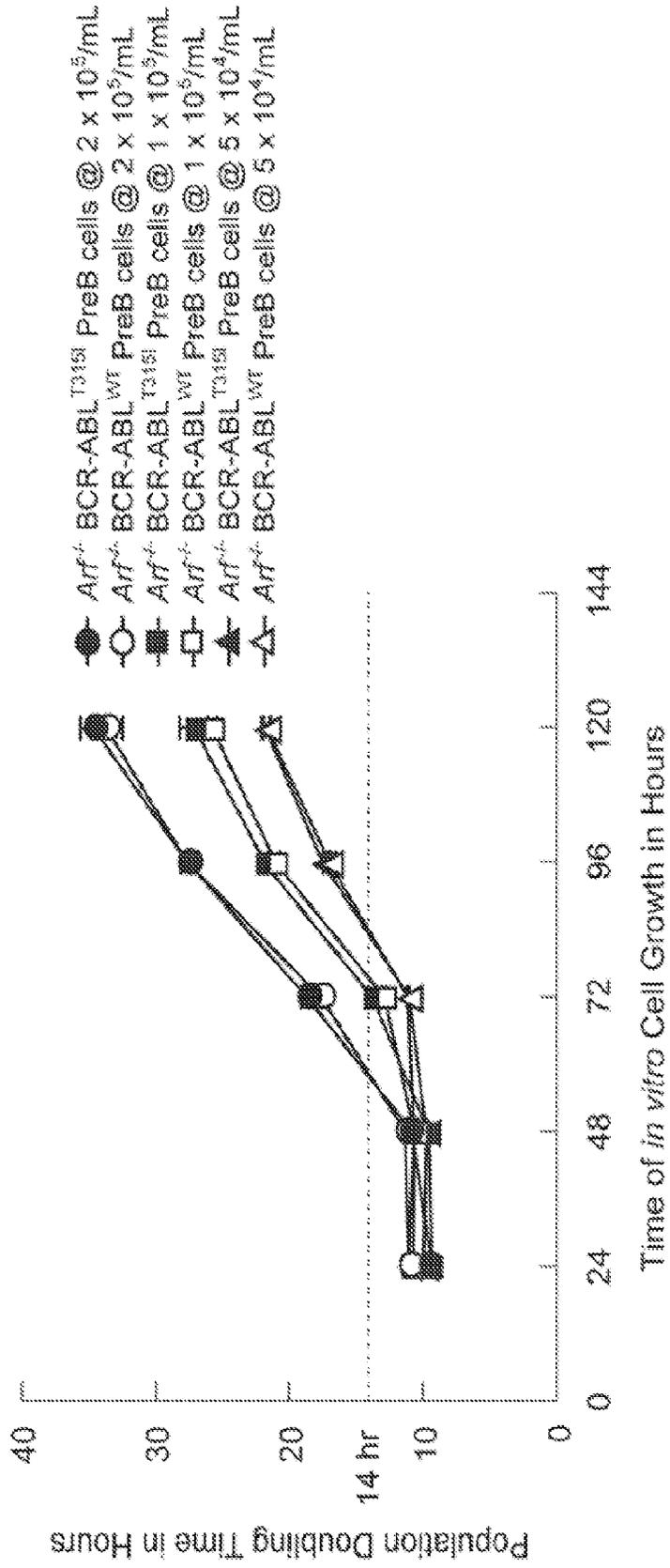
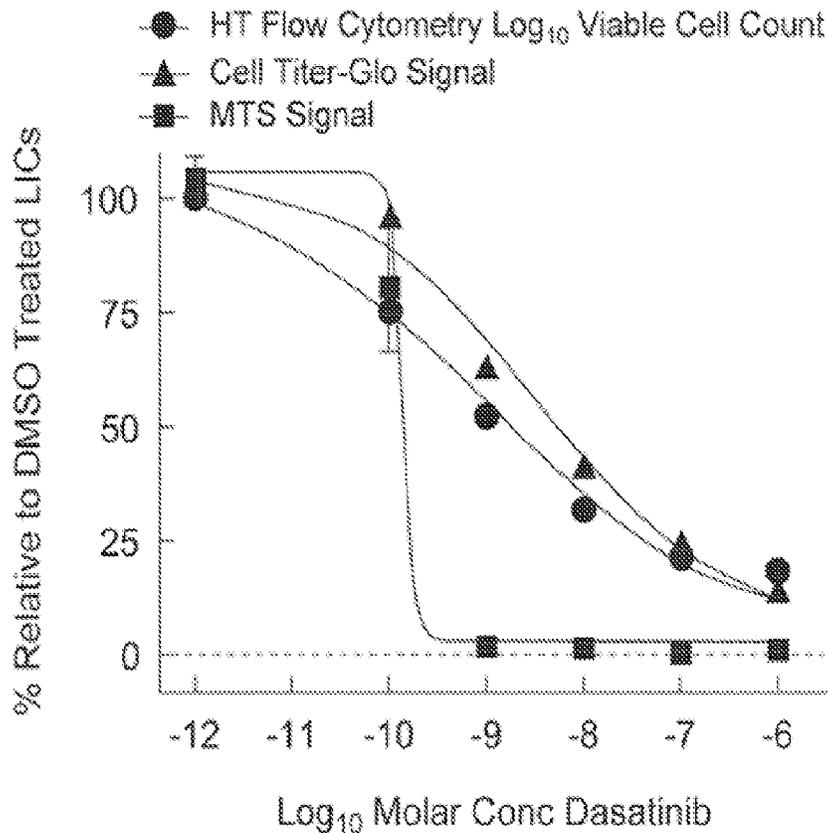


Figure 1



Applications for developed scalable assay

Cell Titer Glo assay output

Uncover clinically-relevant tumor microenvironment imparted drug-resistant phenotypes by varying the soluble cytokines and growth factors during drug challenge

Engineer cytokine mediated drug resistant phenotypes for high throughput drug-screening to design novel treatments

HT Flow cytometry assay output

Uncover clinically-relevant drug-resistant phenotypes by performing drug challenges in the presence of stromal cells, later differentiated from tumor cells by flow cytometry

Address cell-intrinsic drug-resistance through drug-enrichment assays on mixtures of genetically distinct cells marked by fluorescent tags

Figure 2

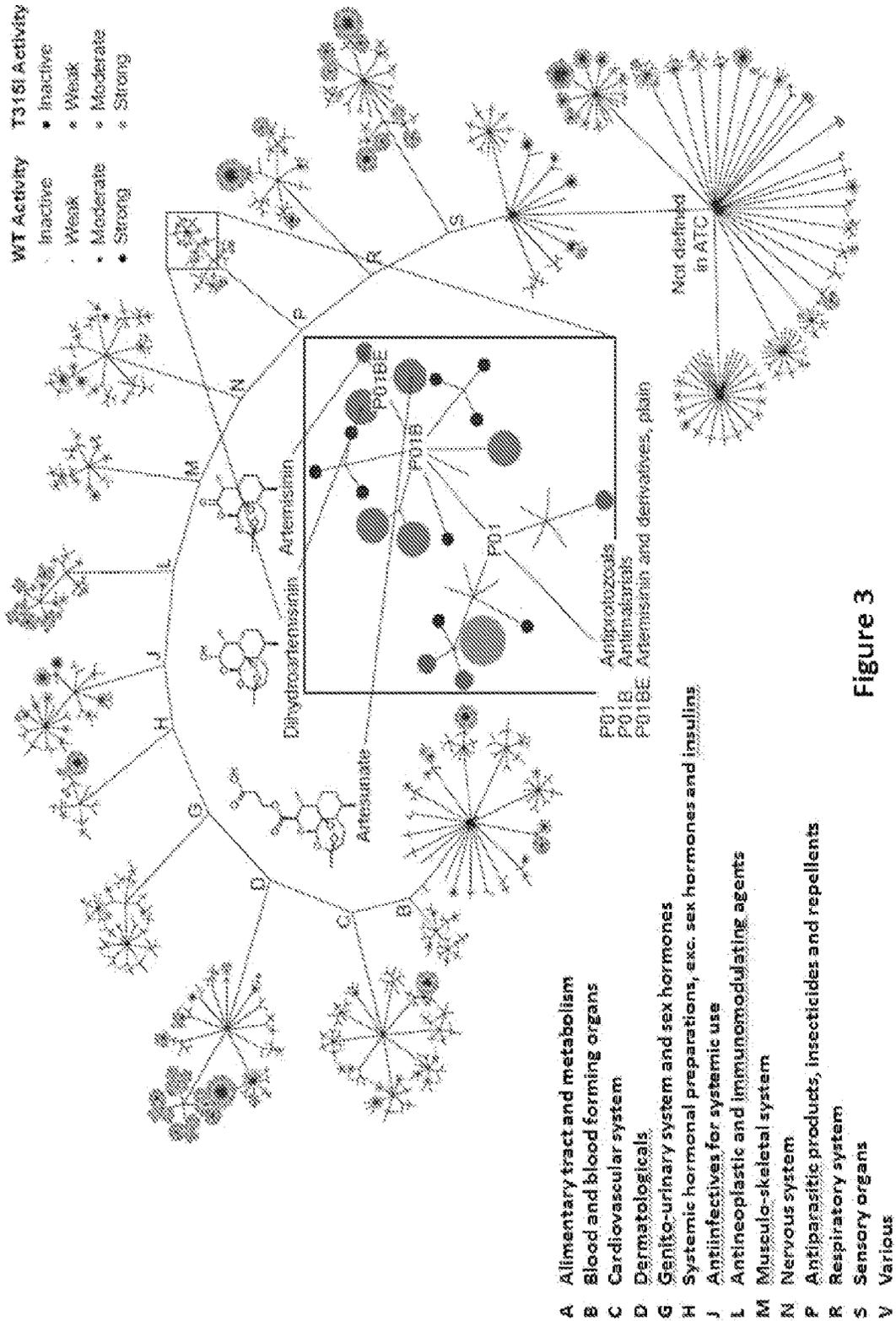


Figure 3

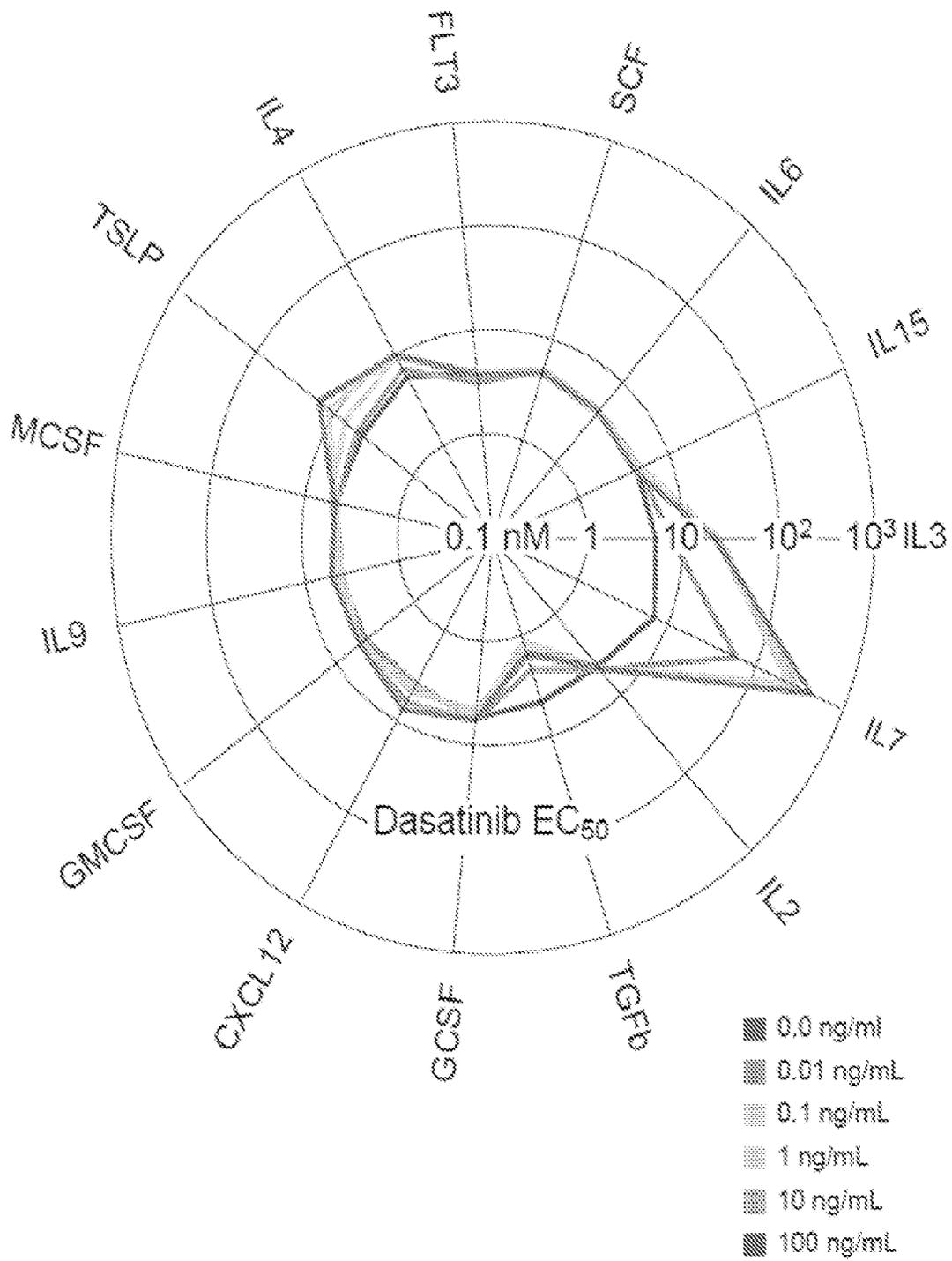


Figure 4

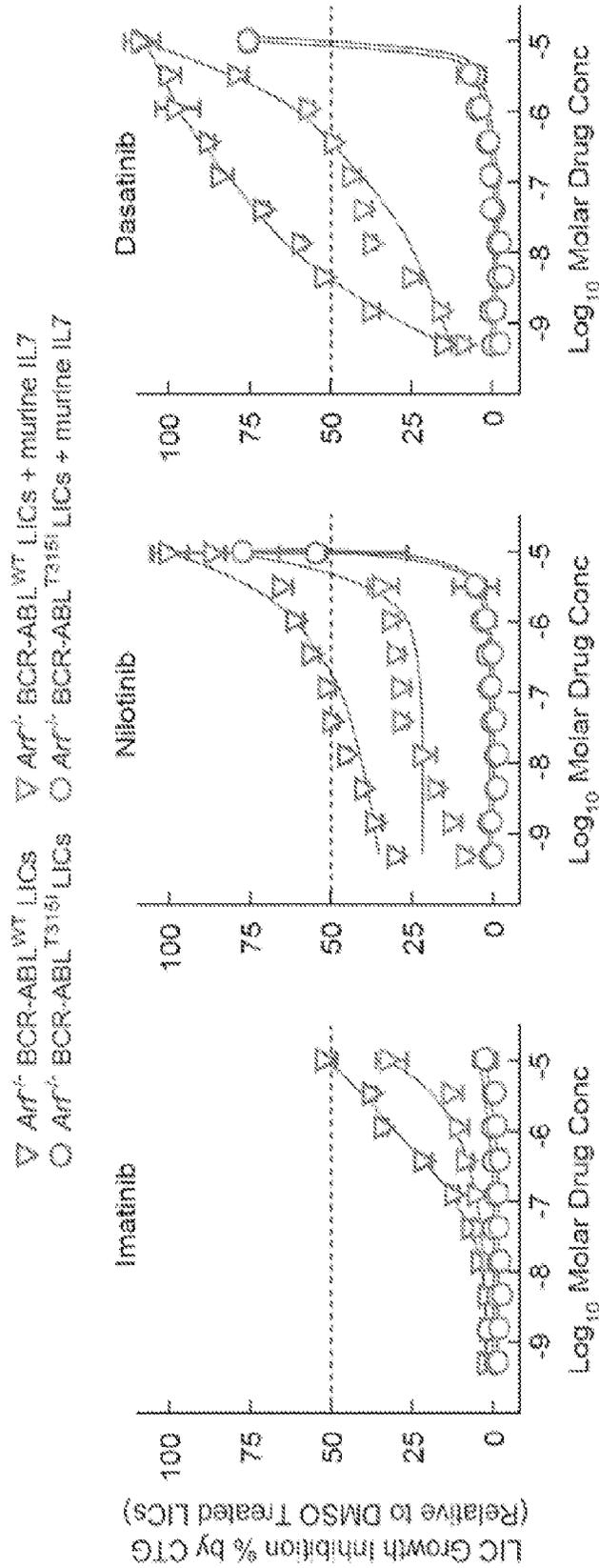


Figure 5

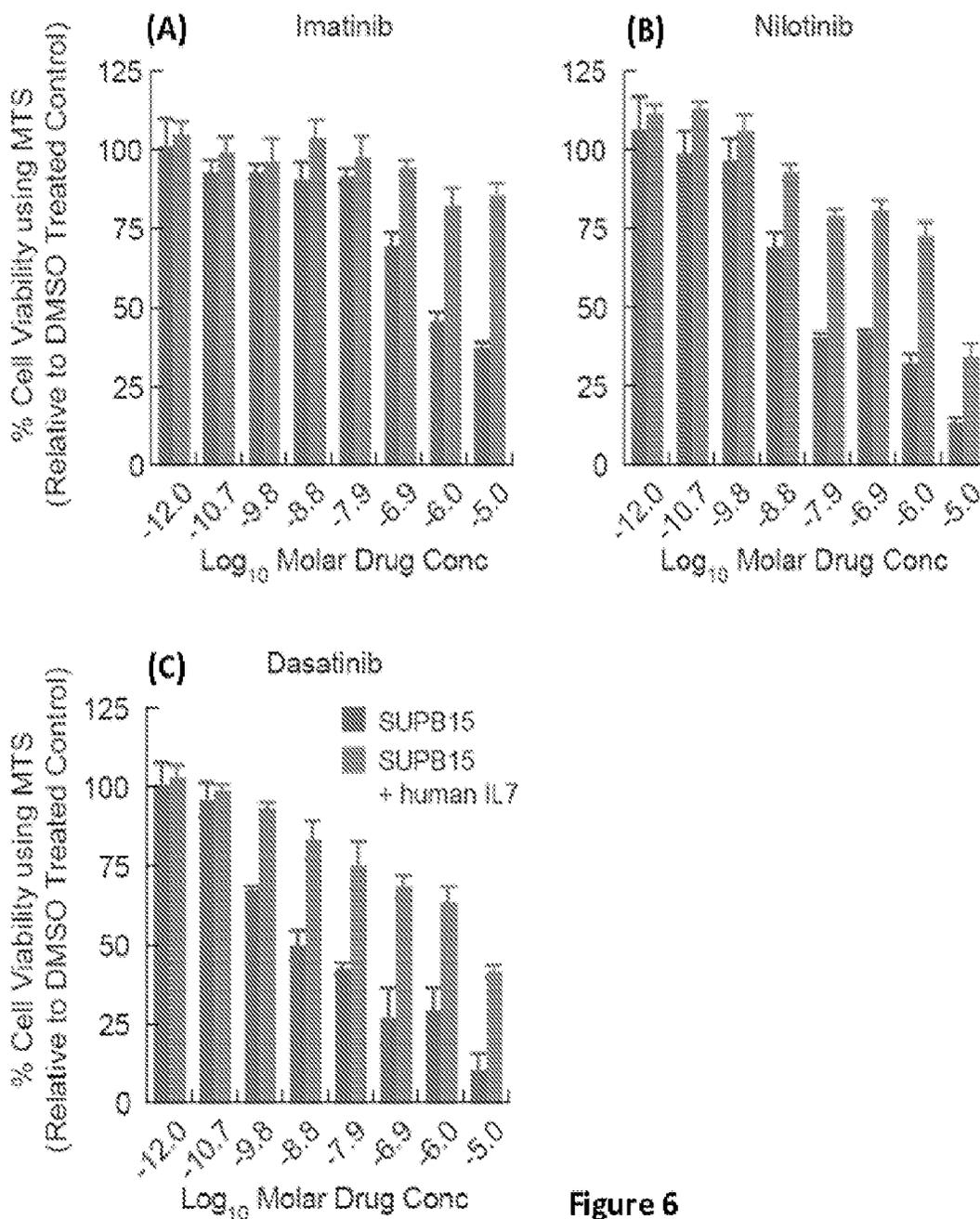


Figure 6

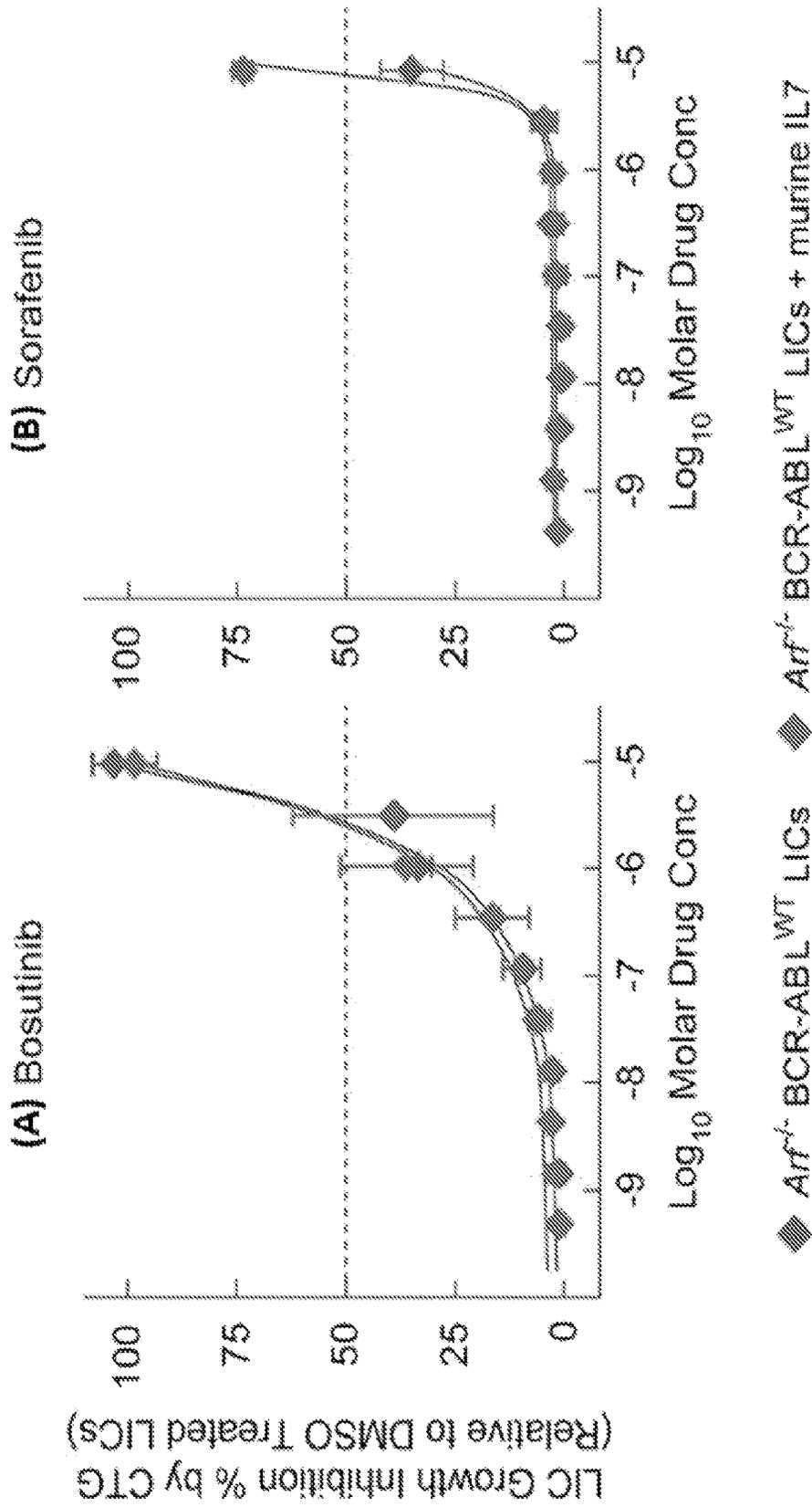


Figure 7

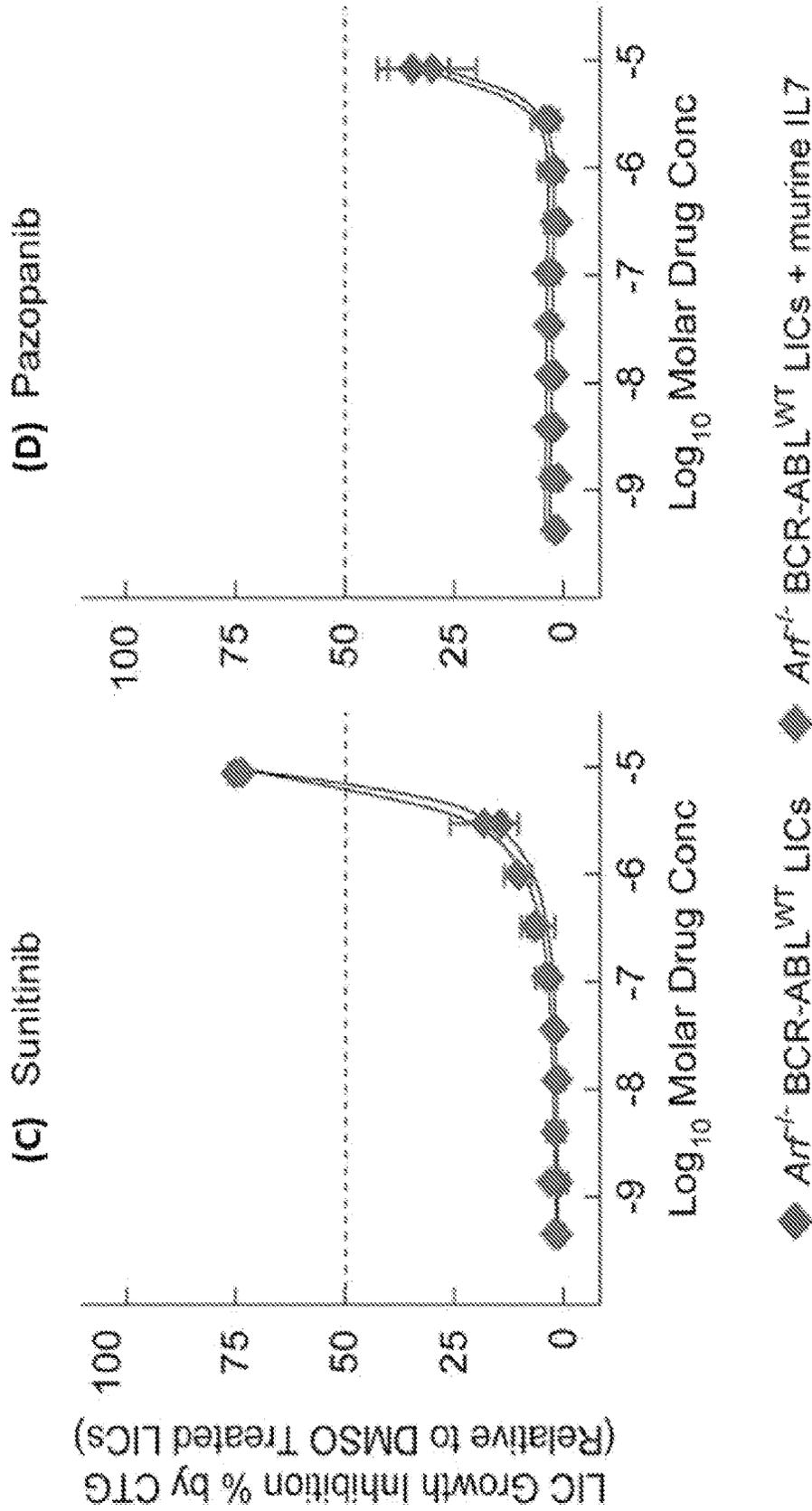


Figure 7, continued

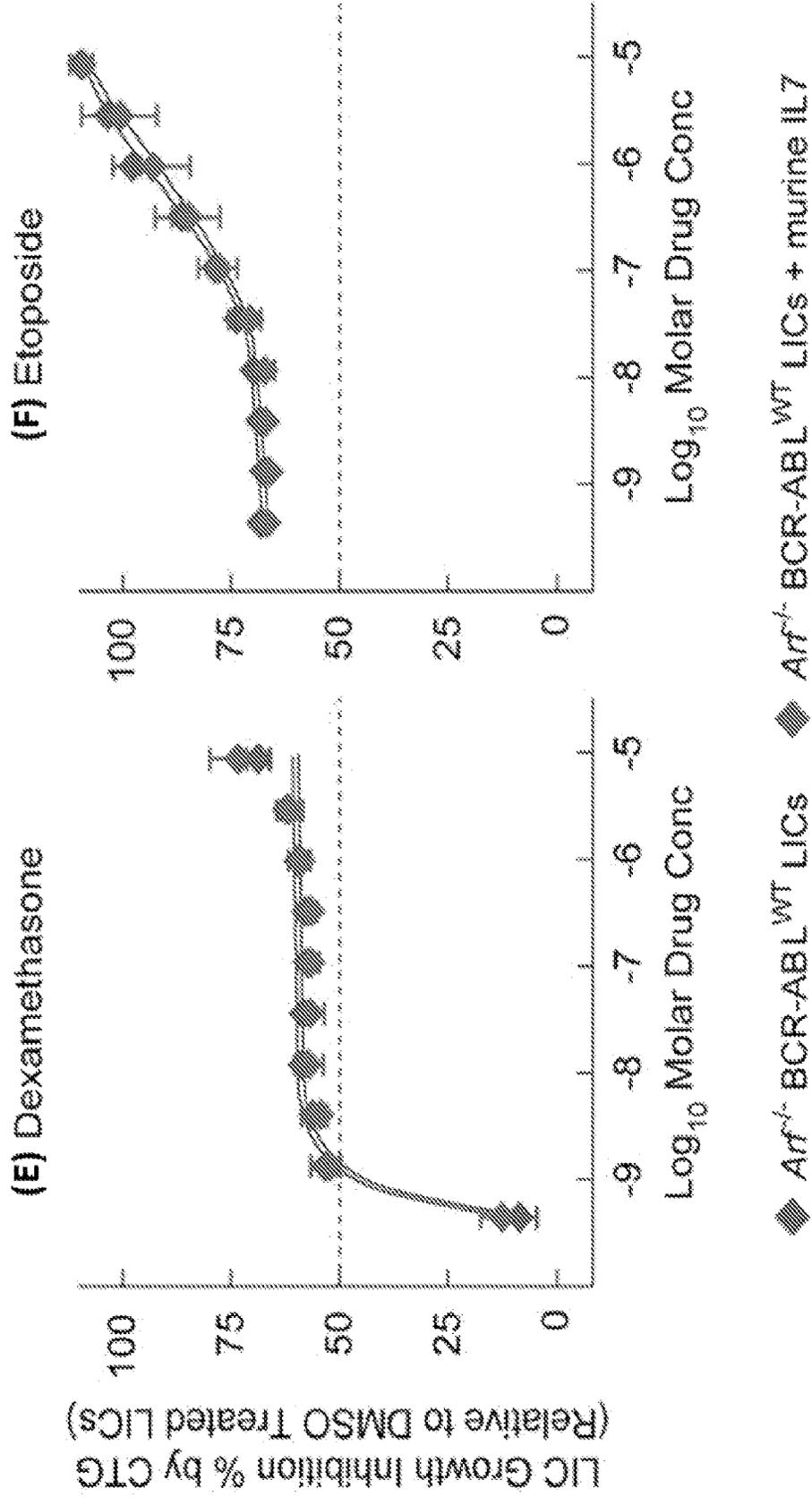


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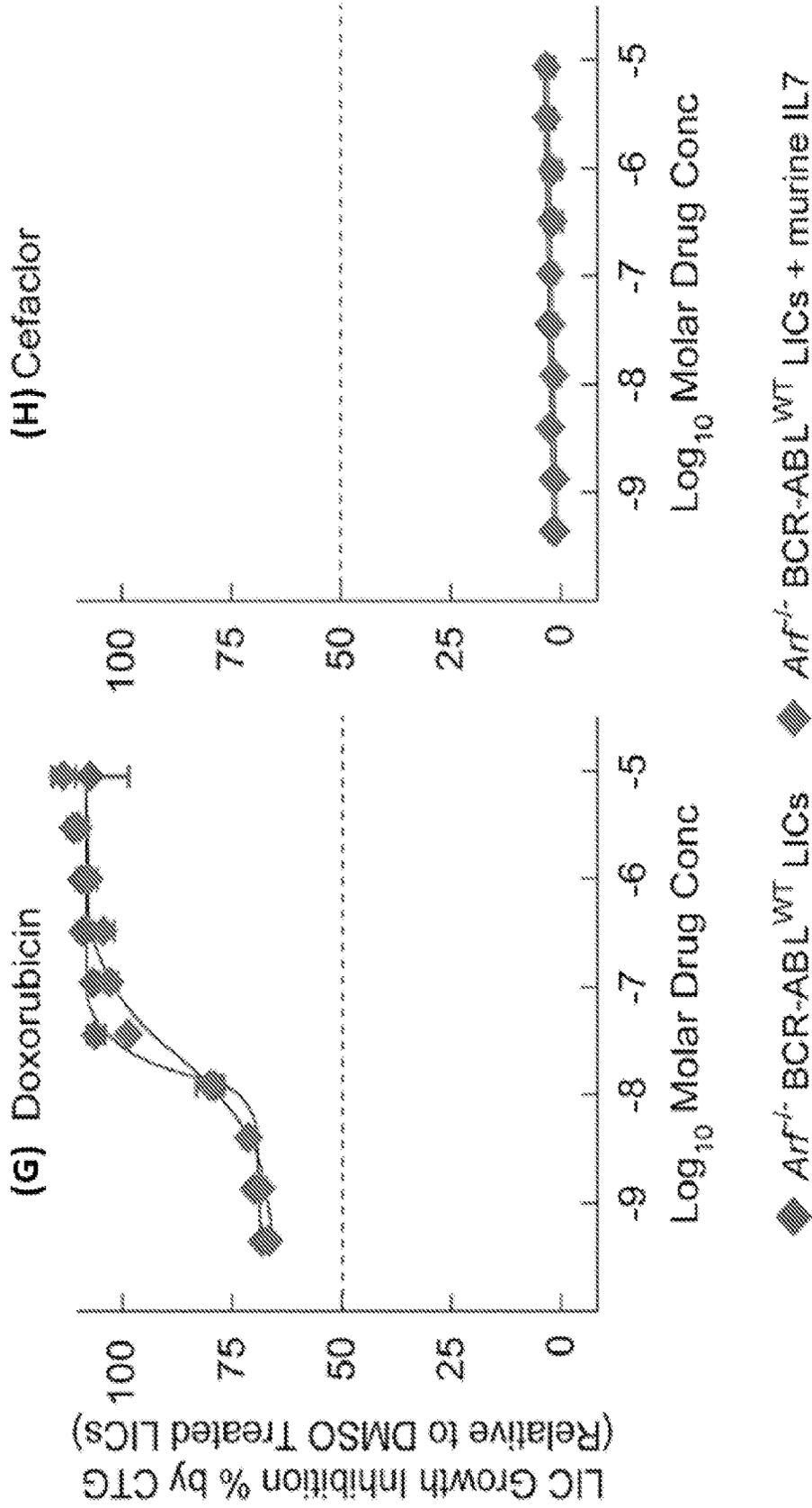


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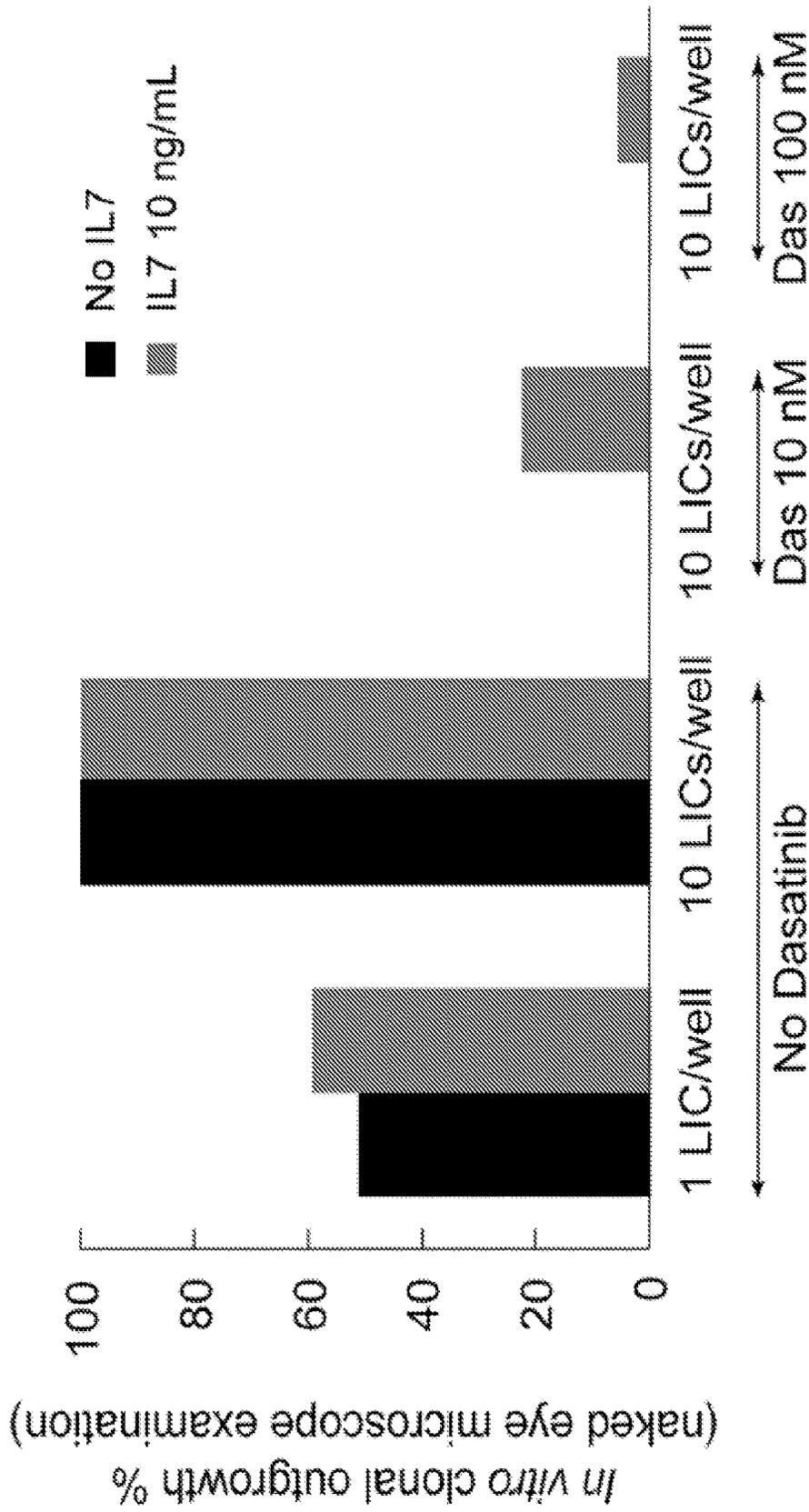


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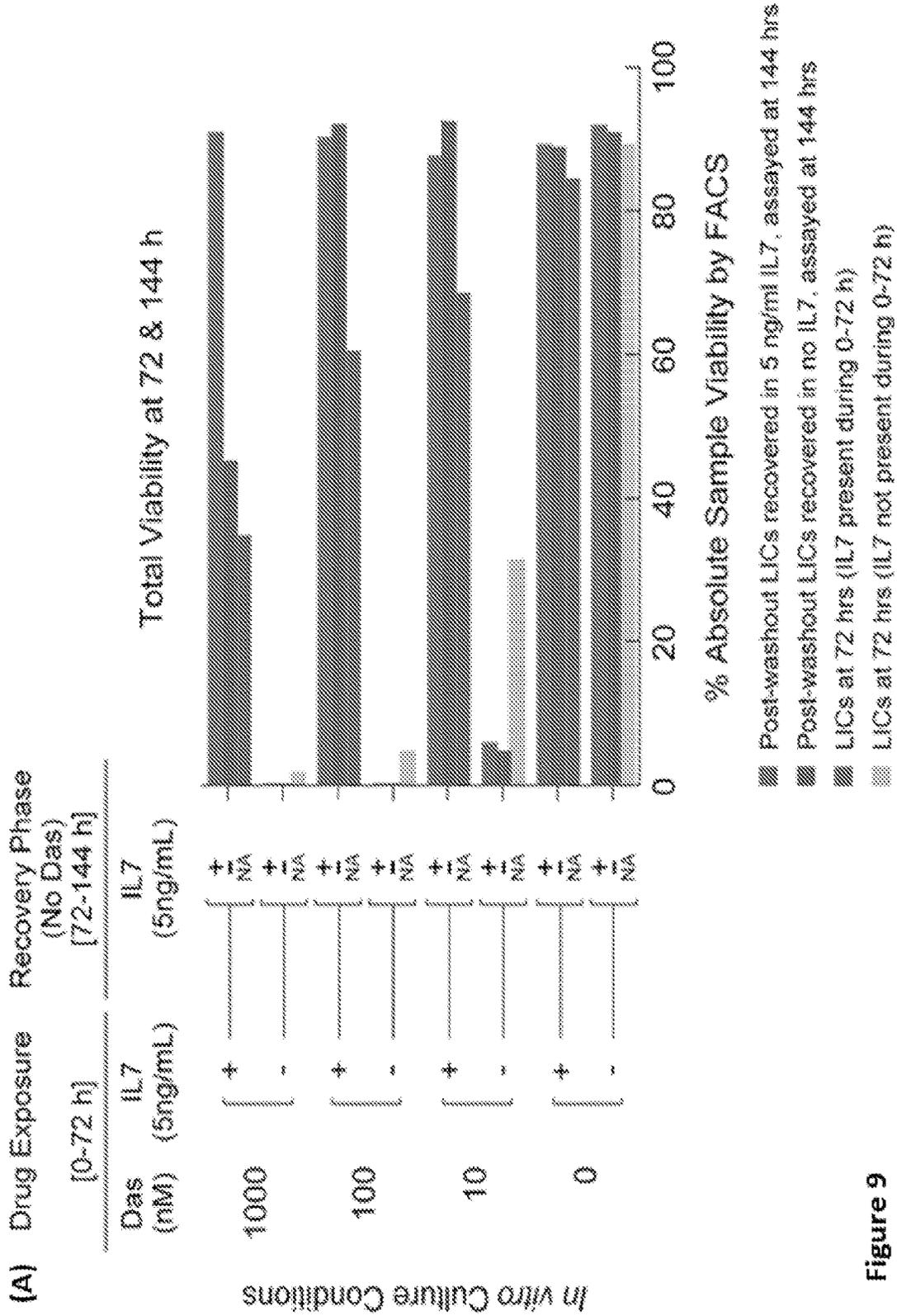


Figure 9

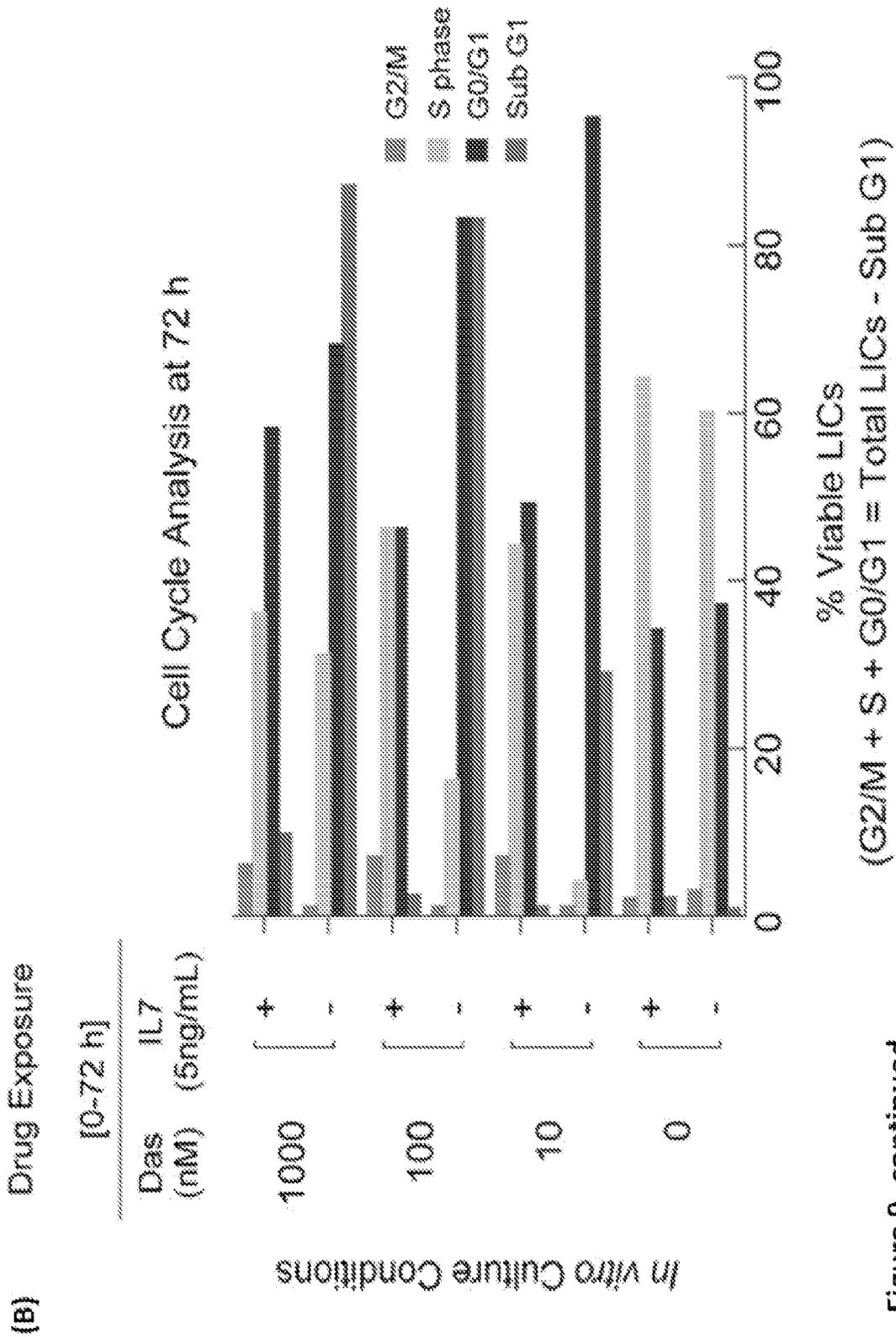


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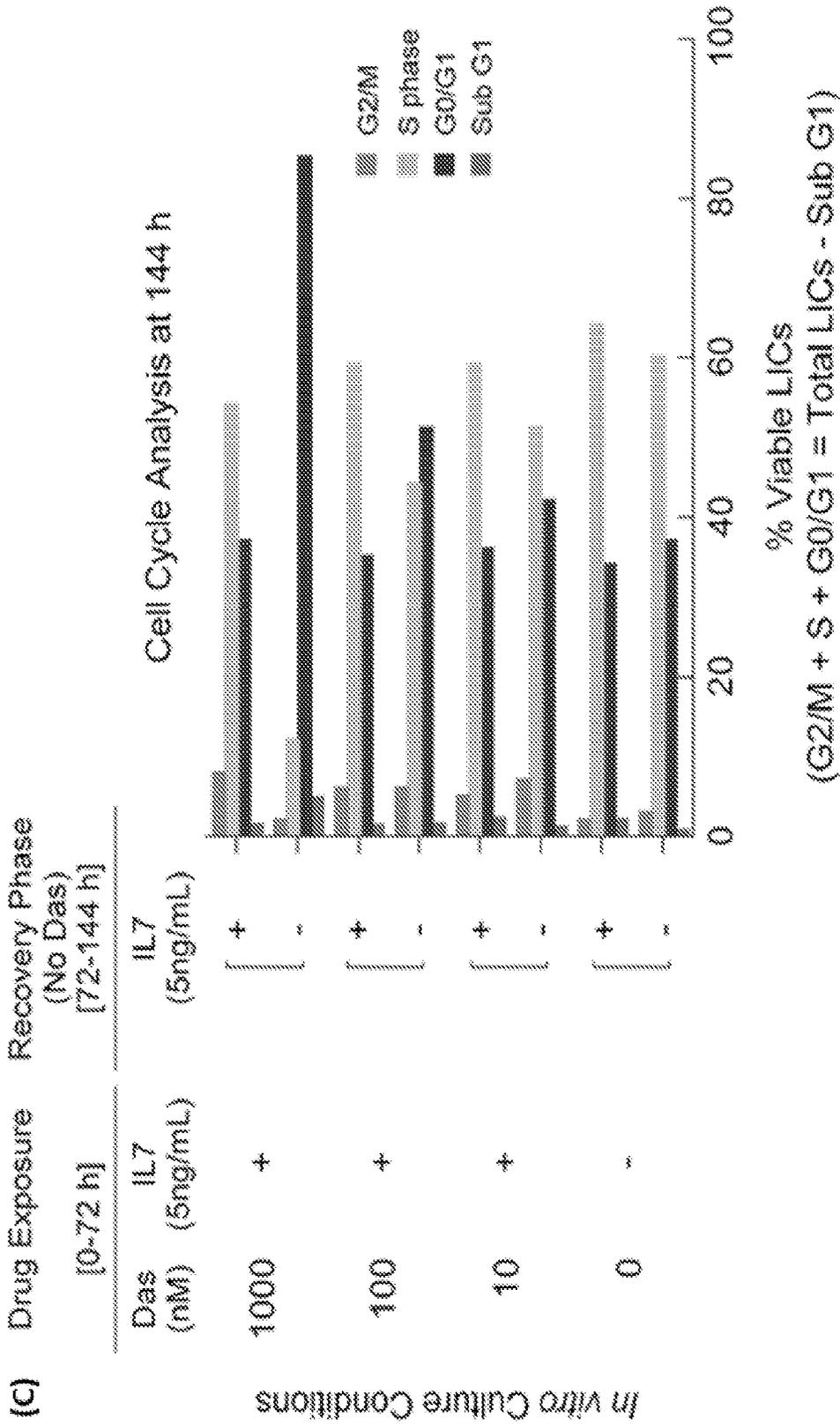


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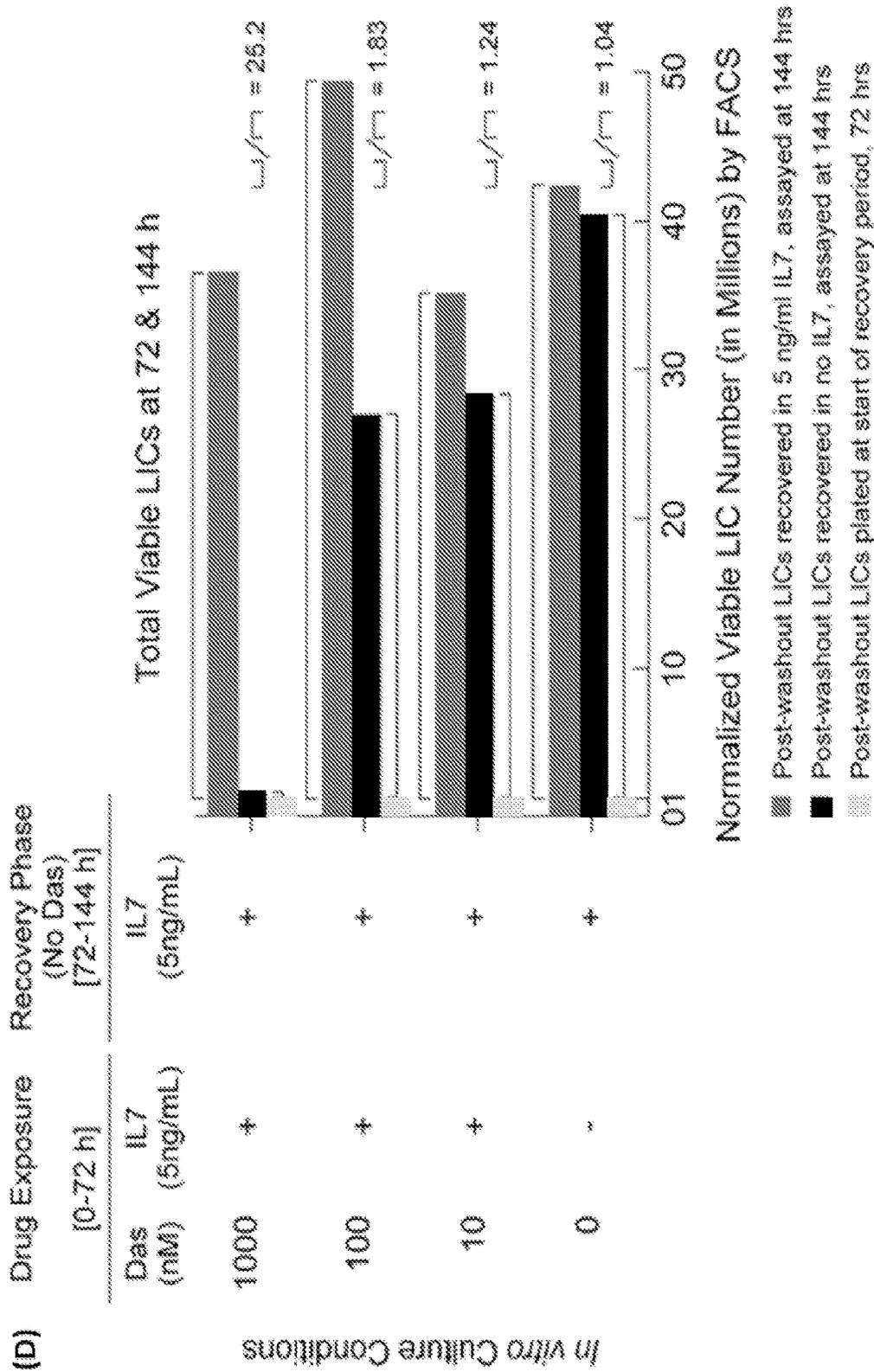


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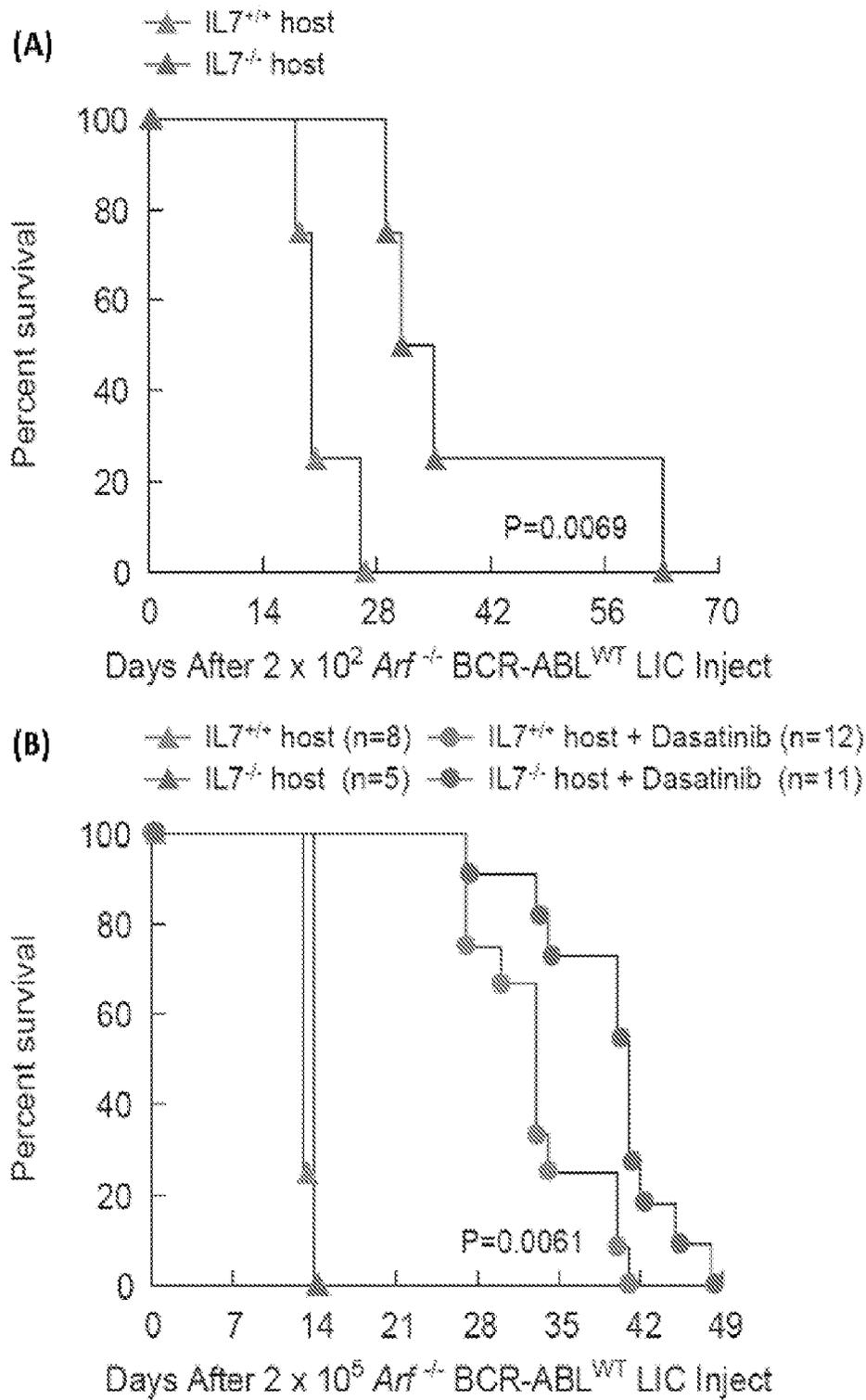


Figure 10

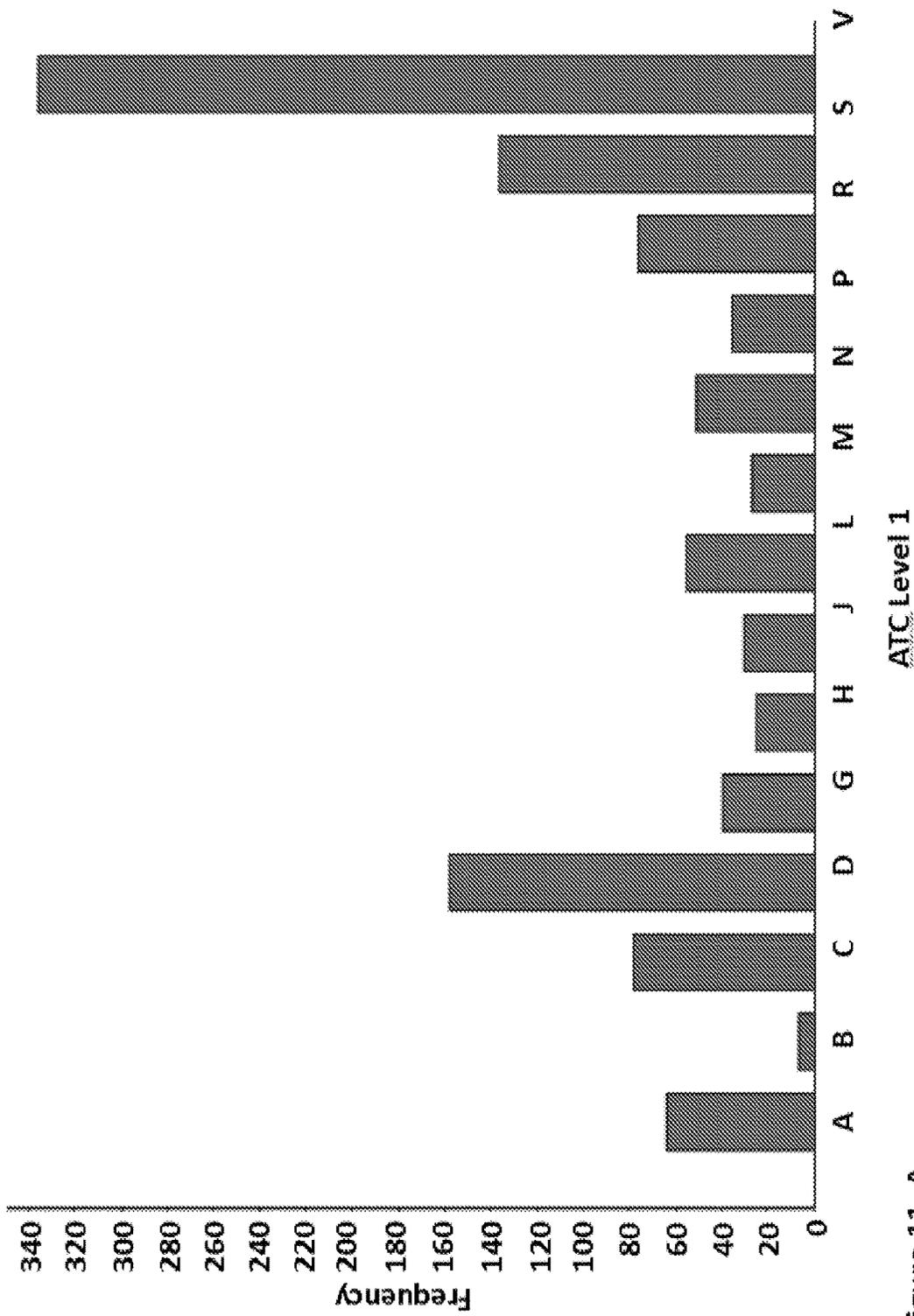


Figure 11, A

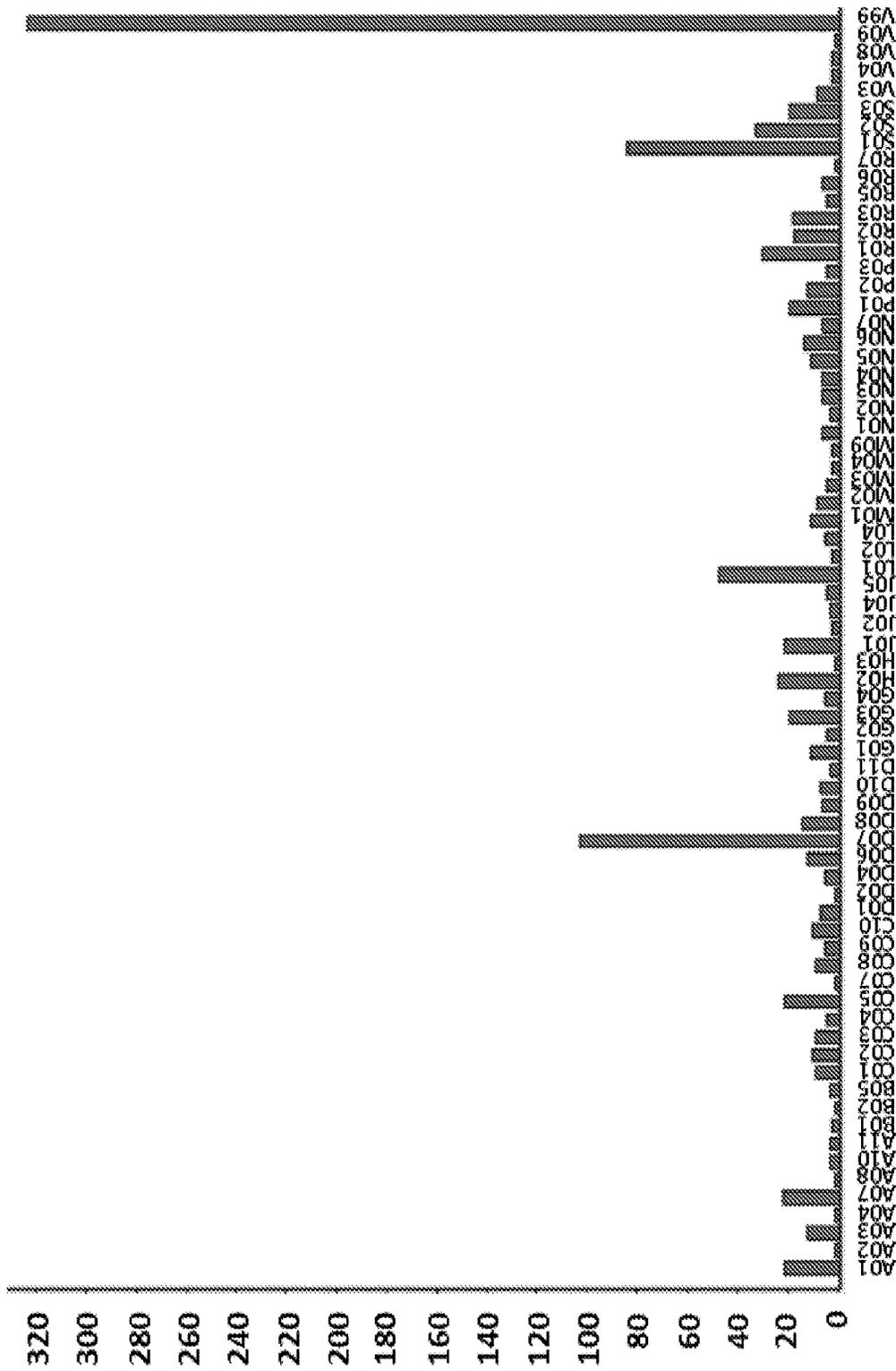
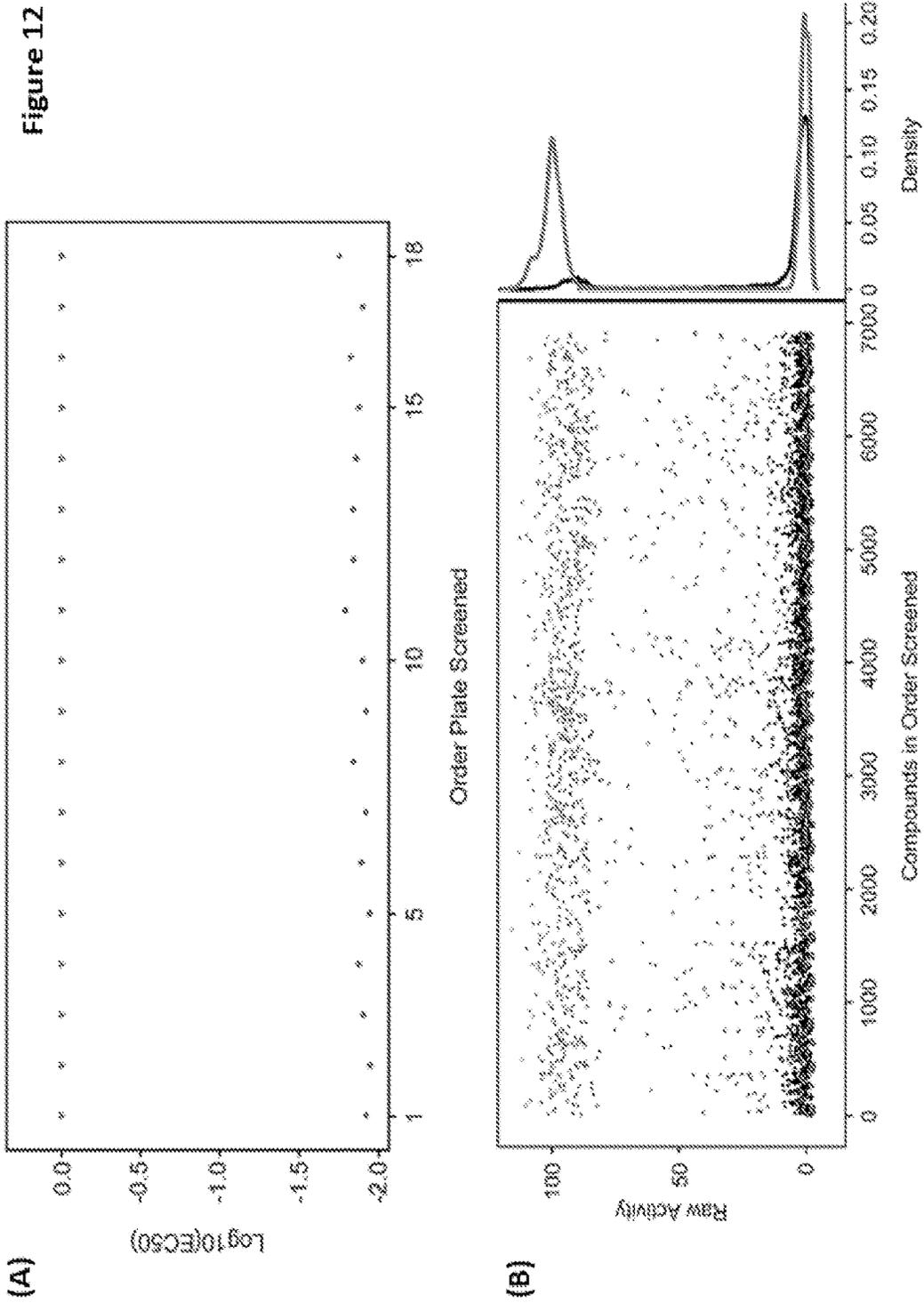


Figure 11, B



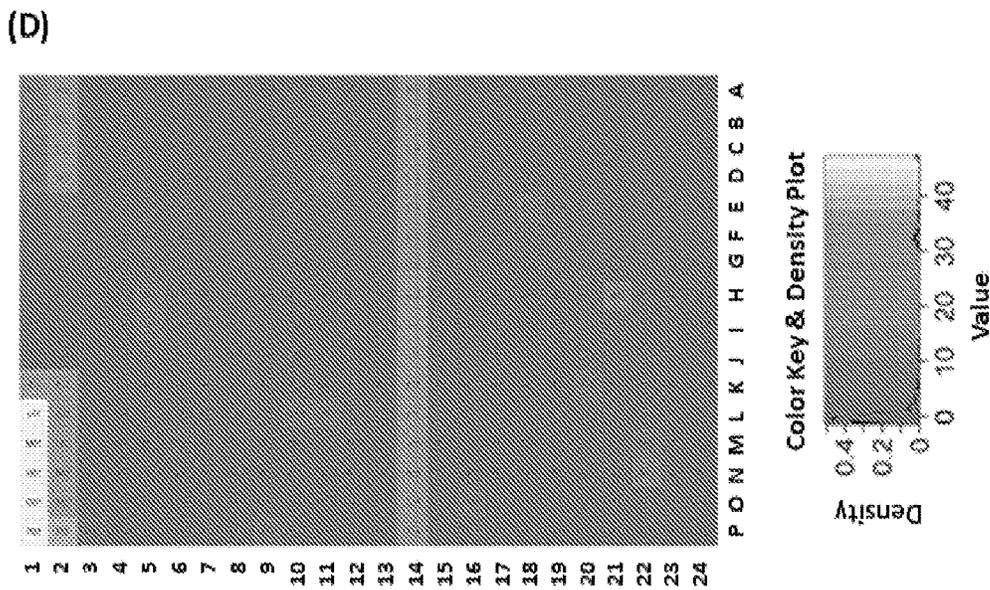
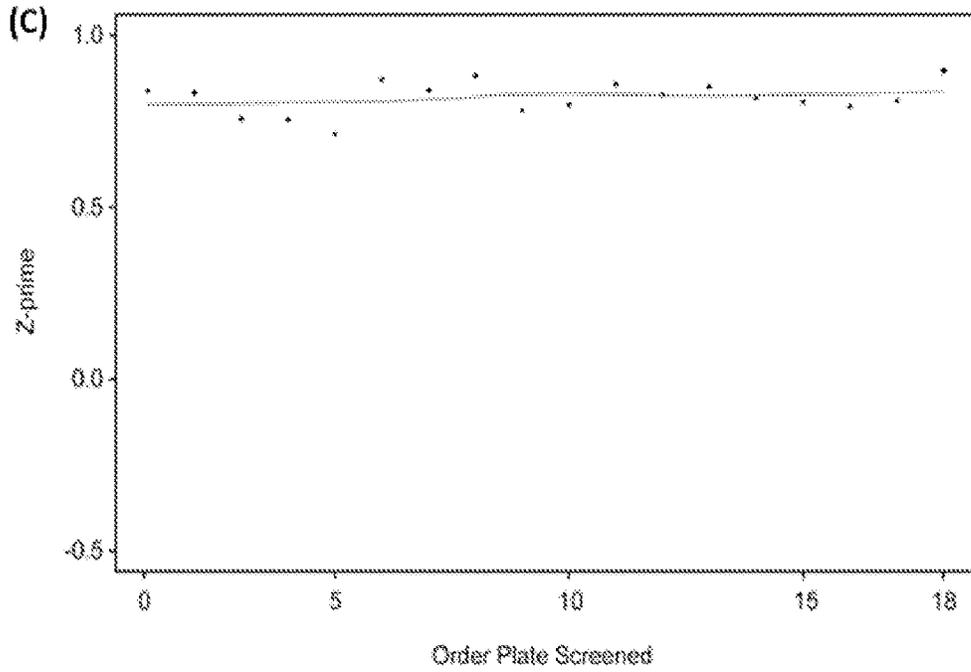
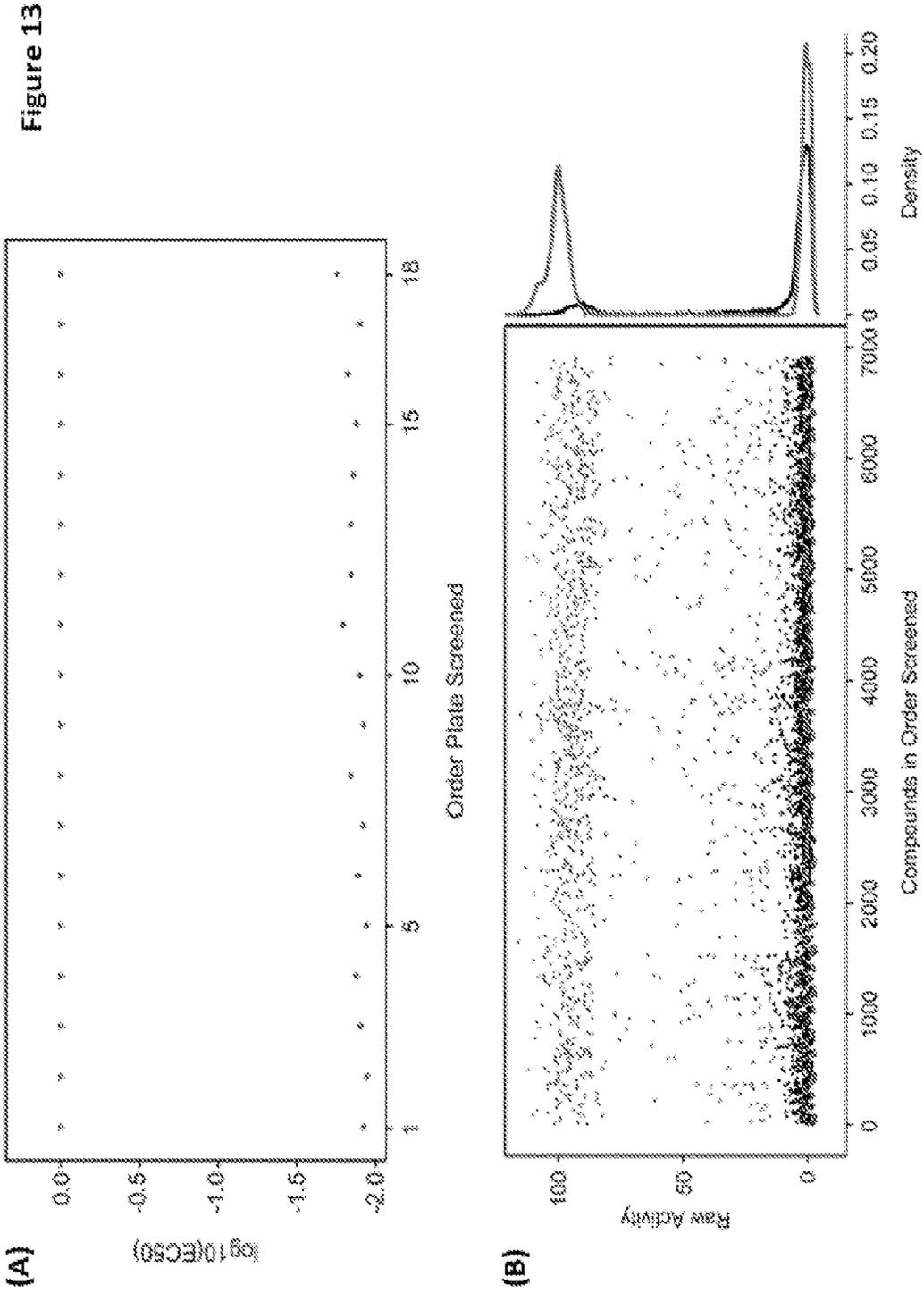


Figure 12, continued



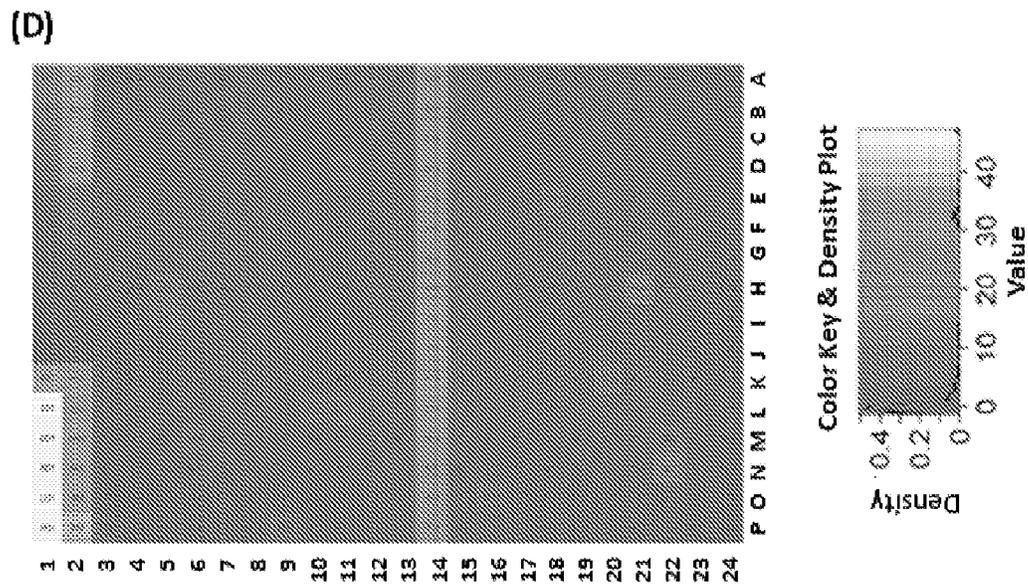
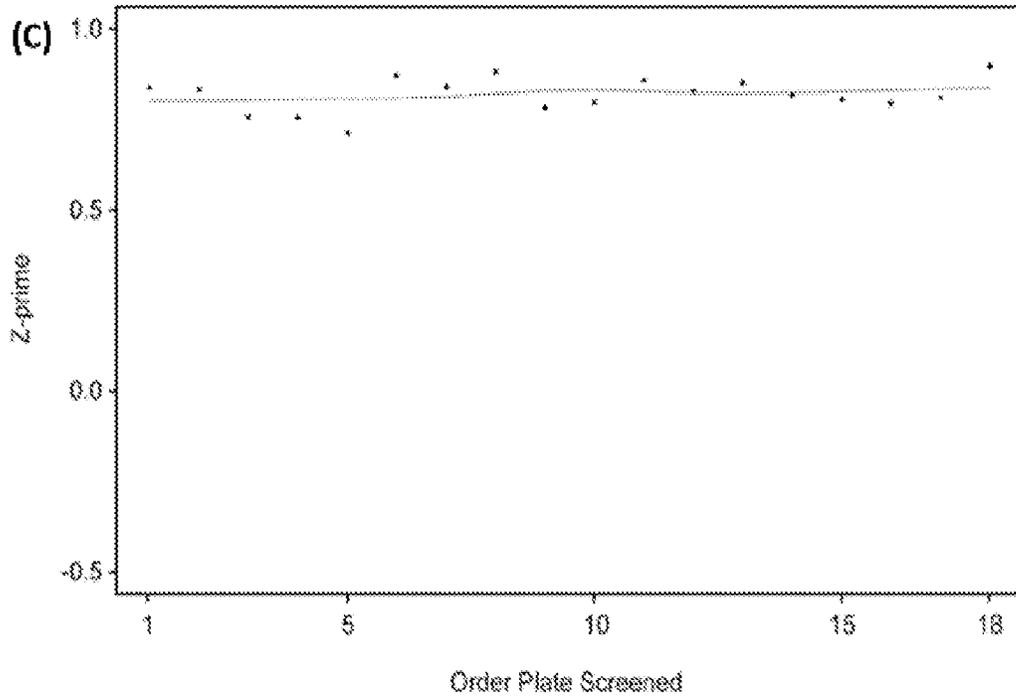


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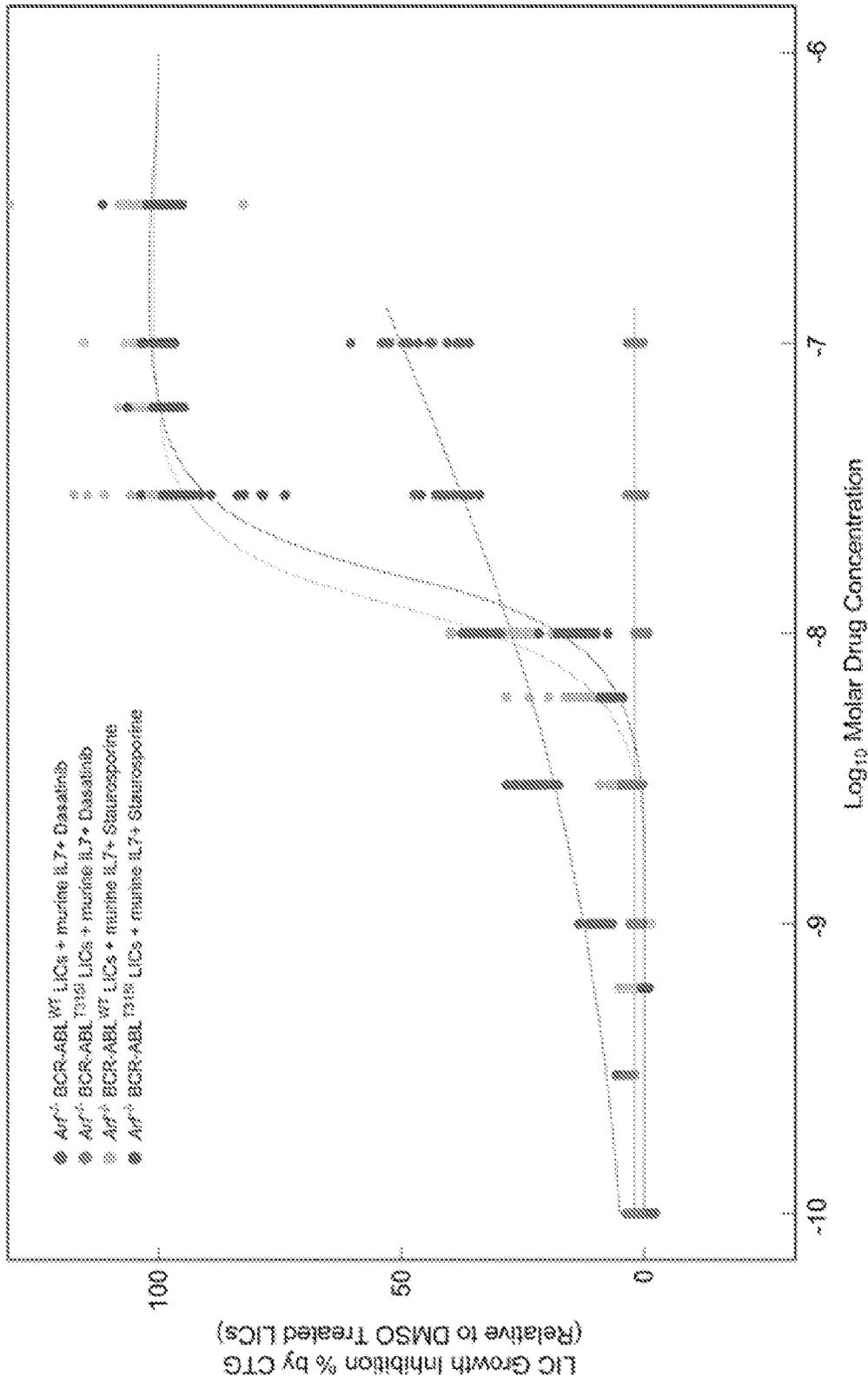
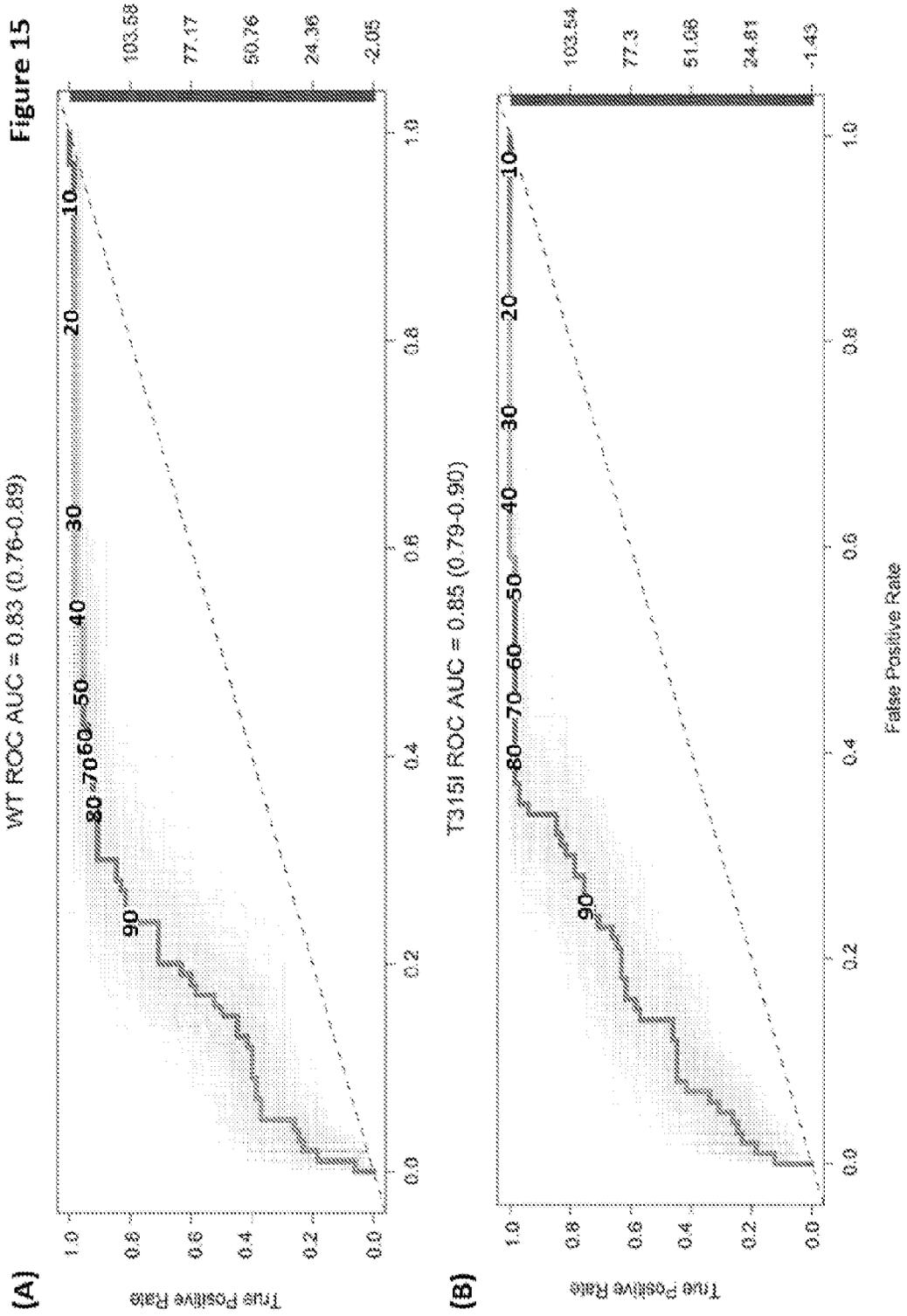


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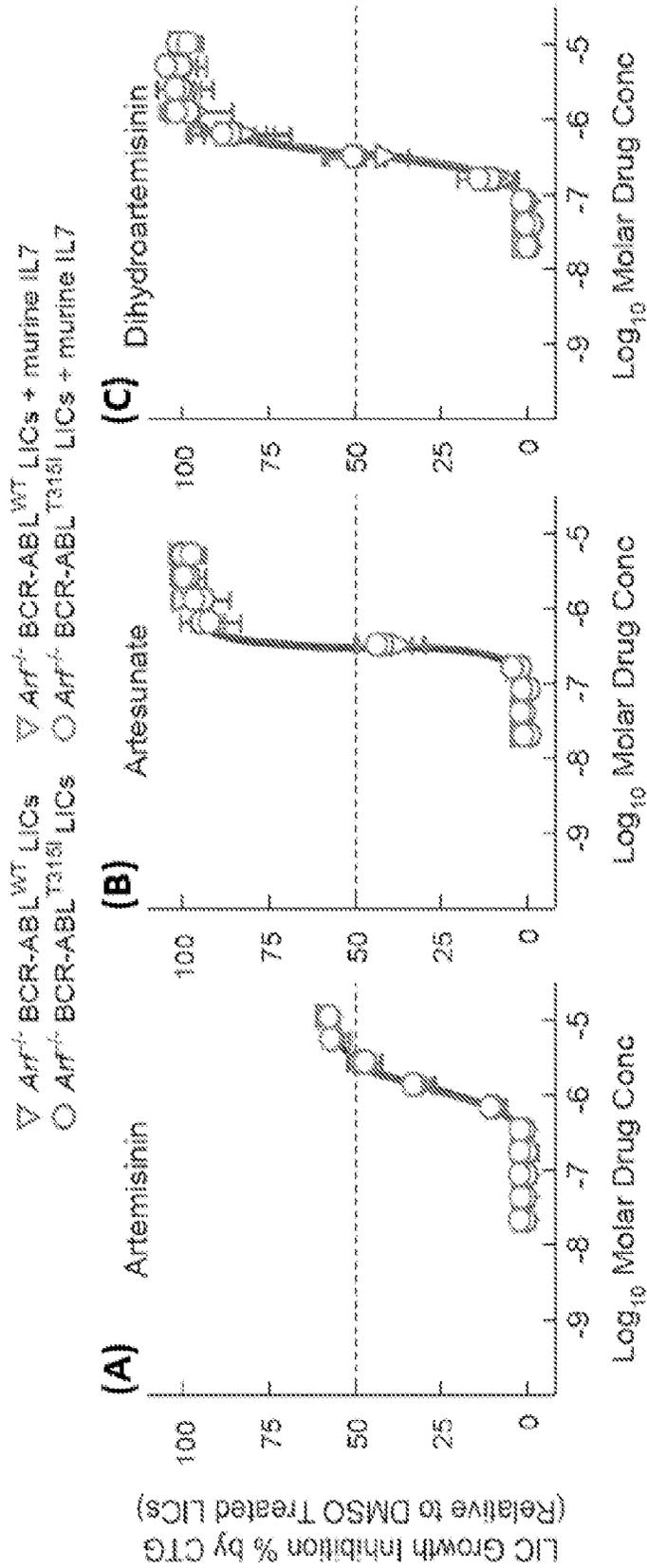


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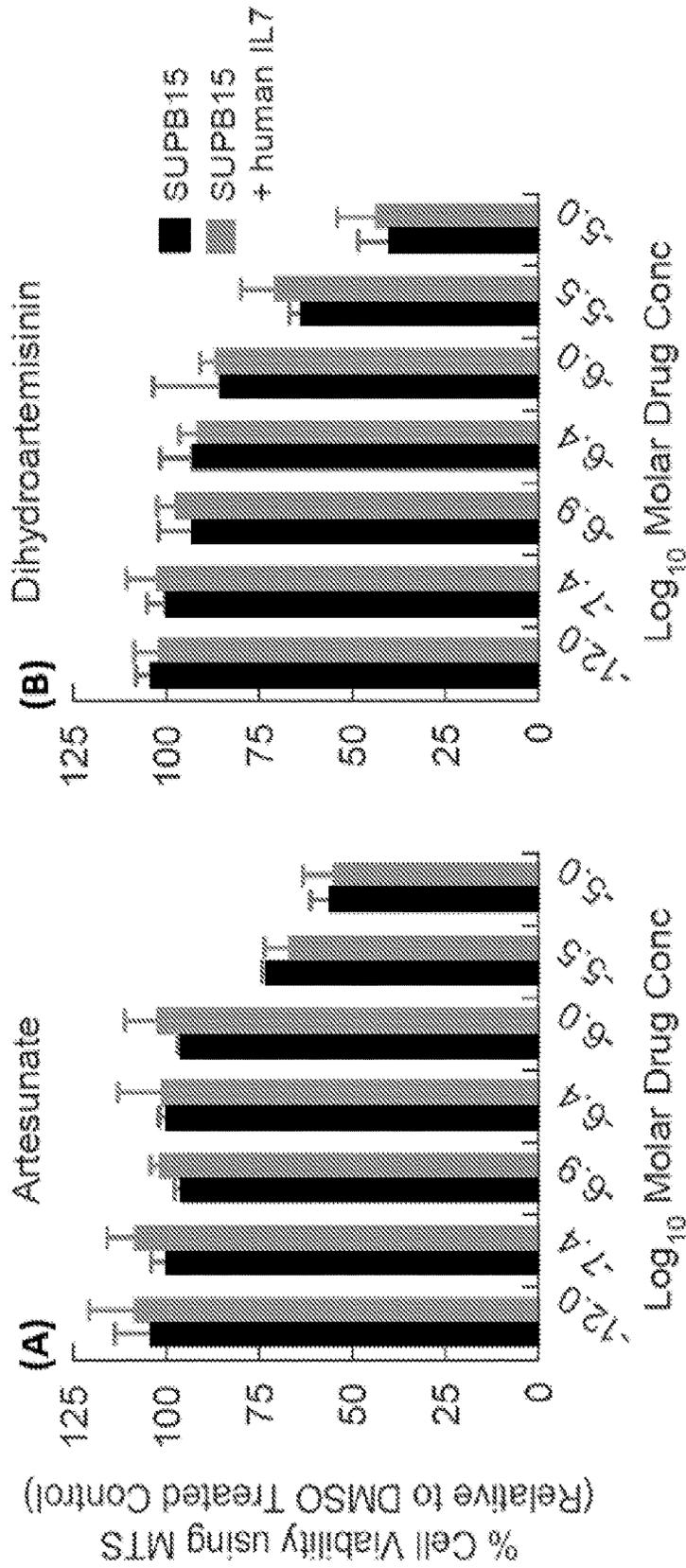


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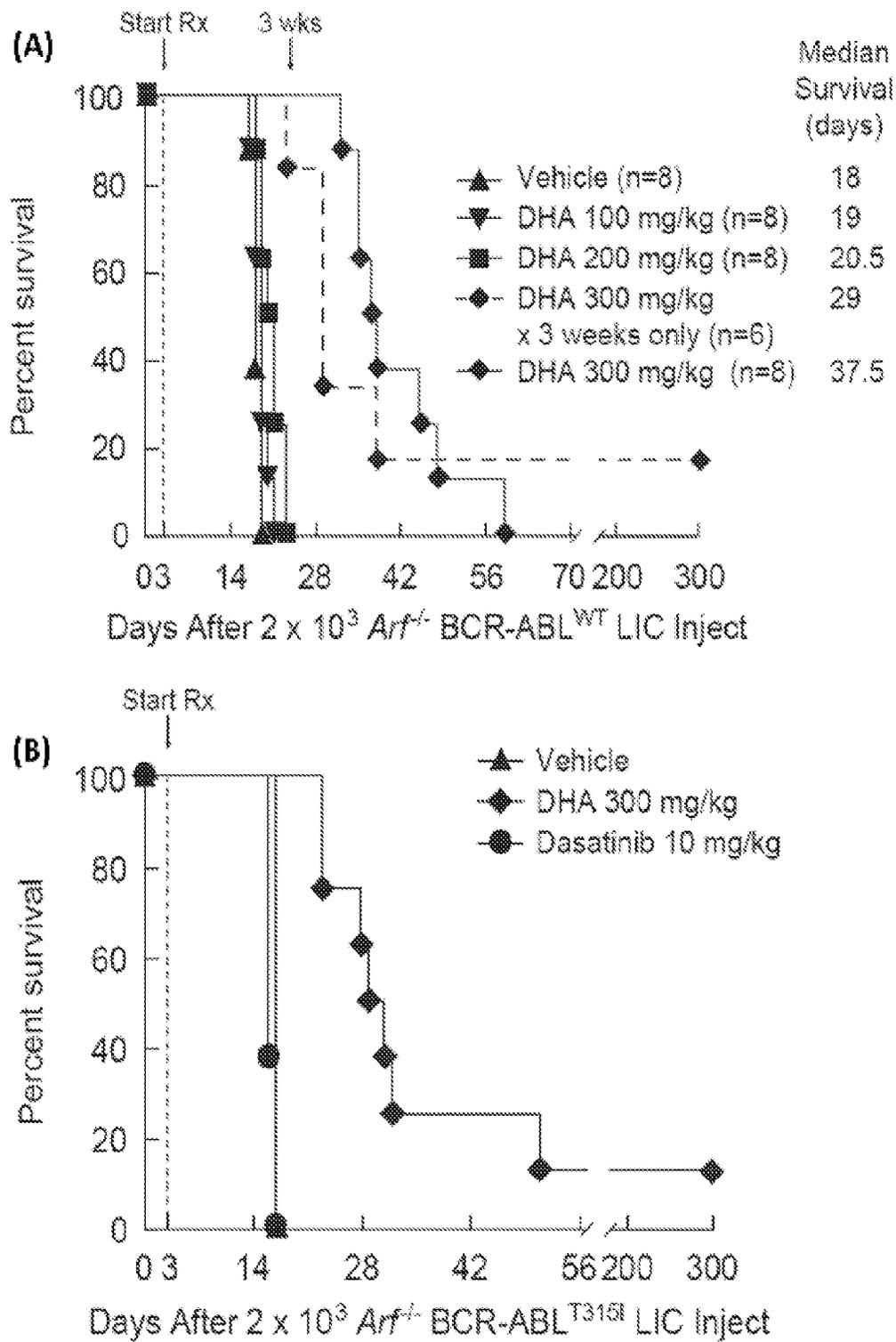


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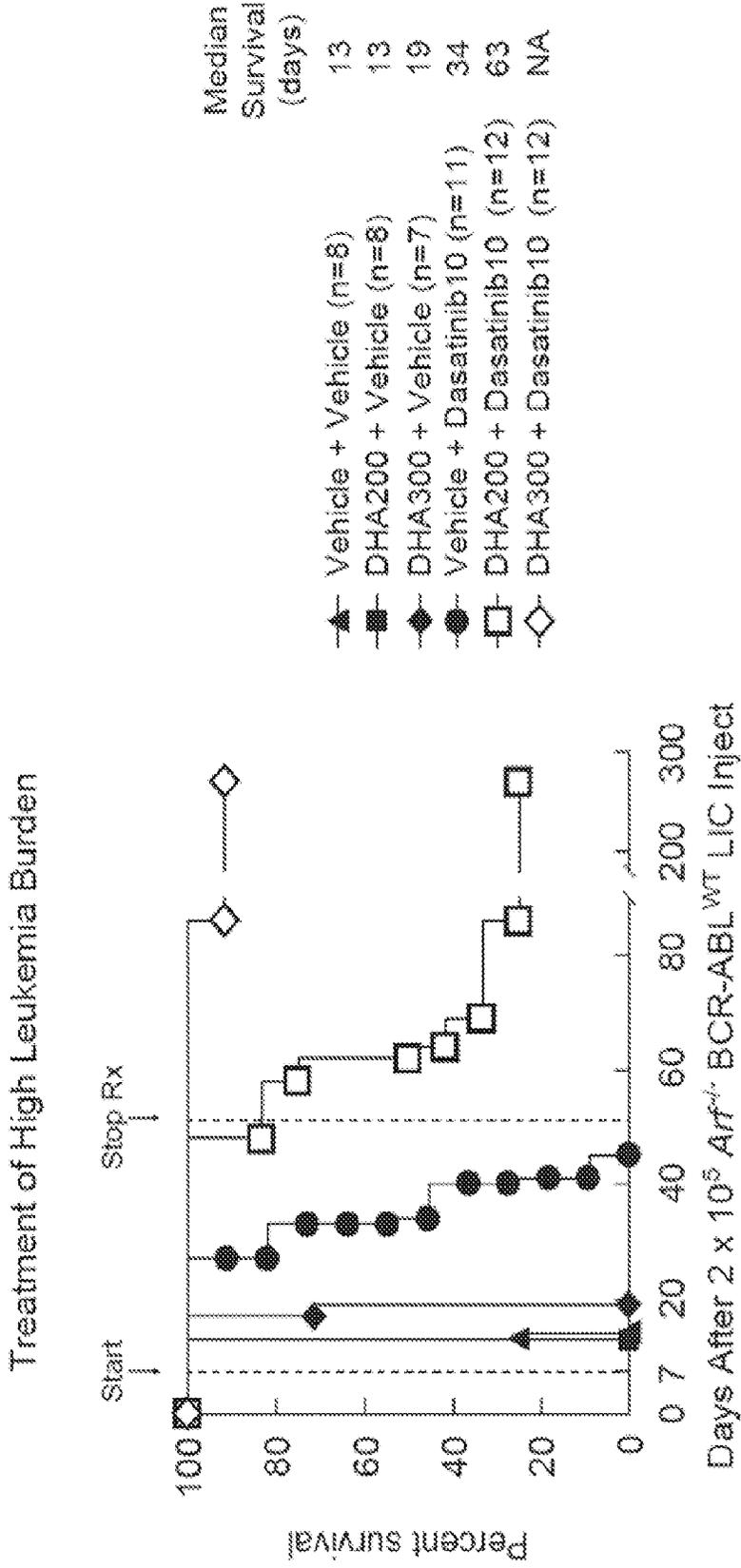


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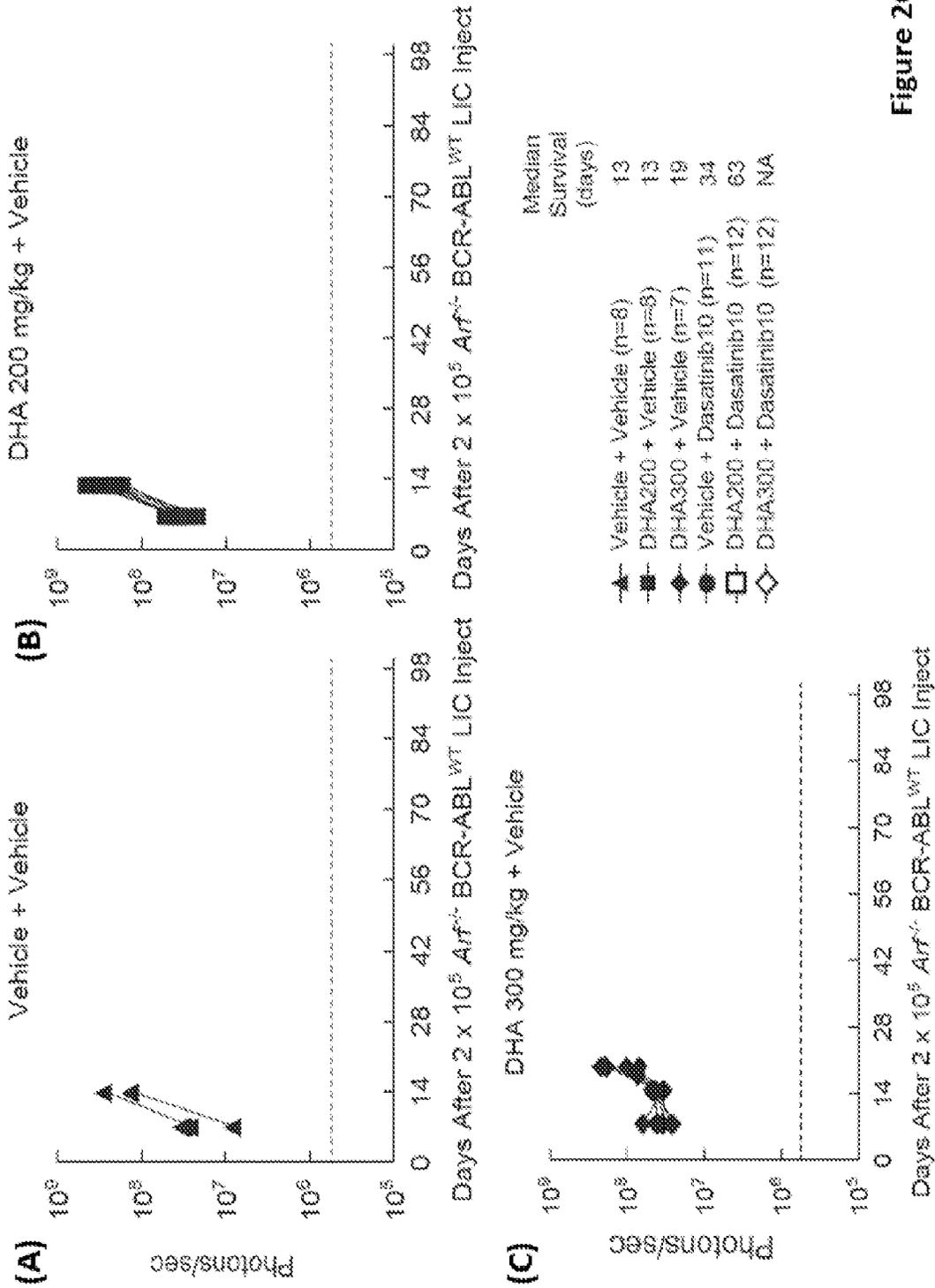


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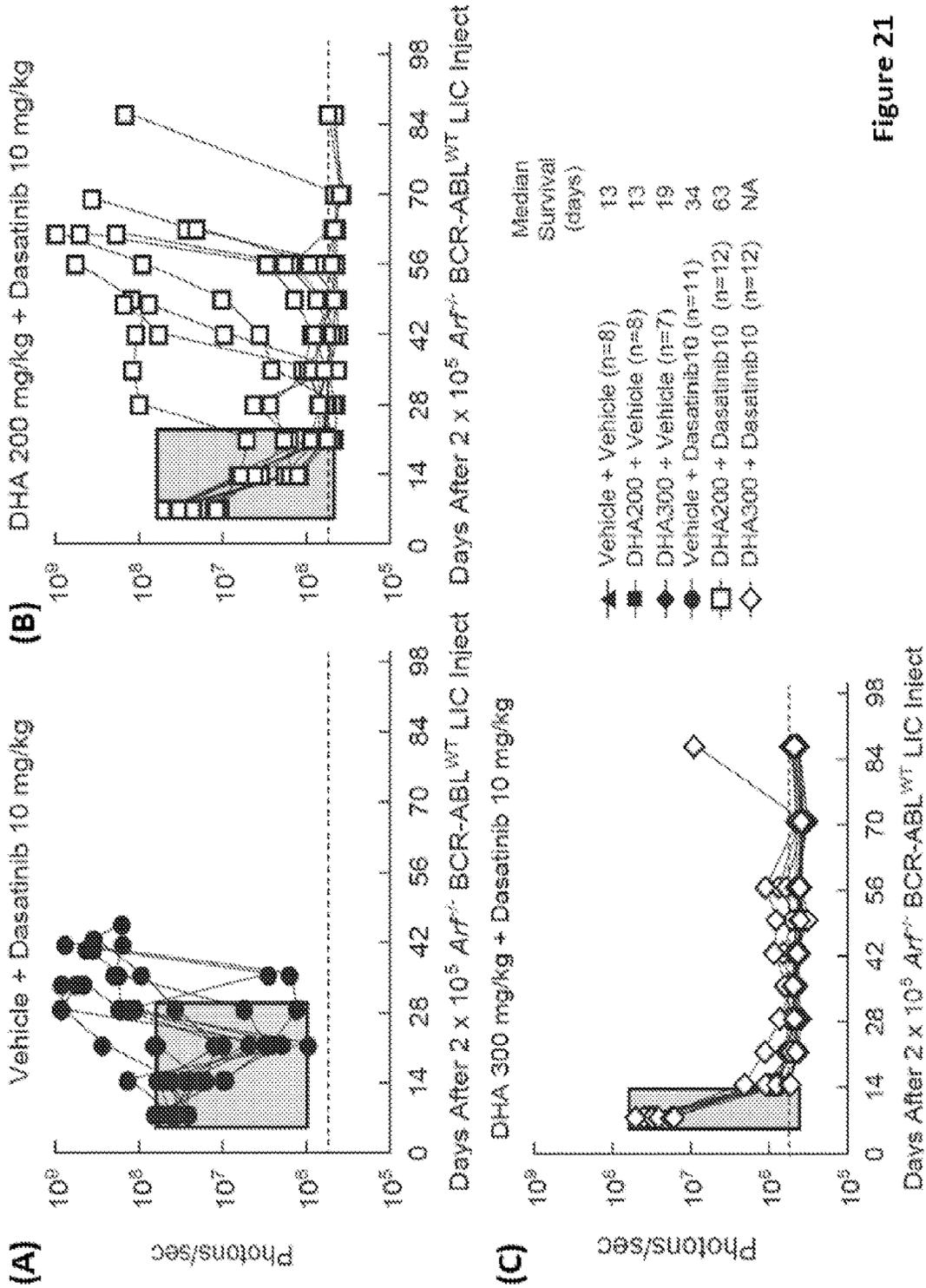


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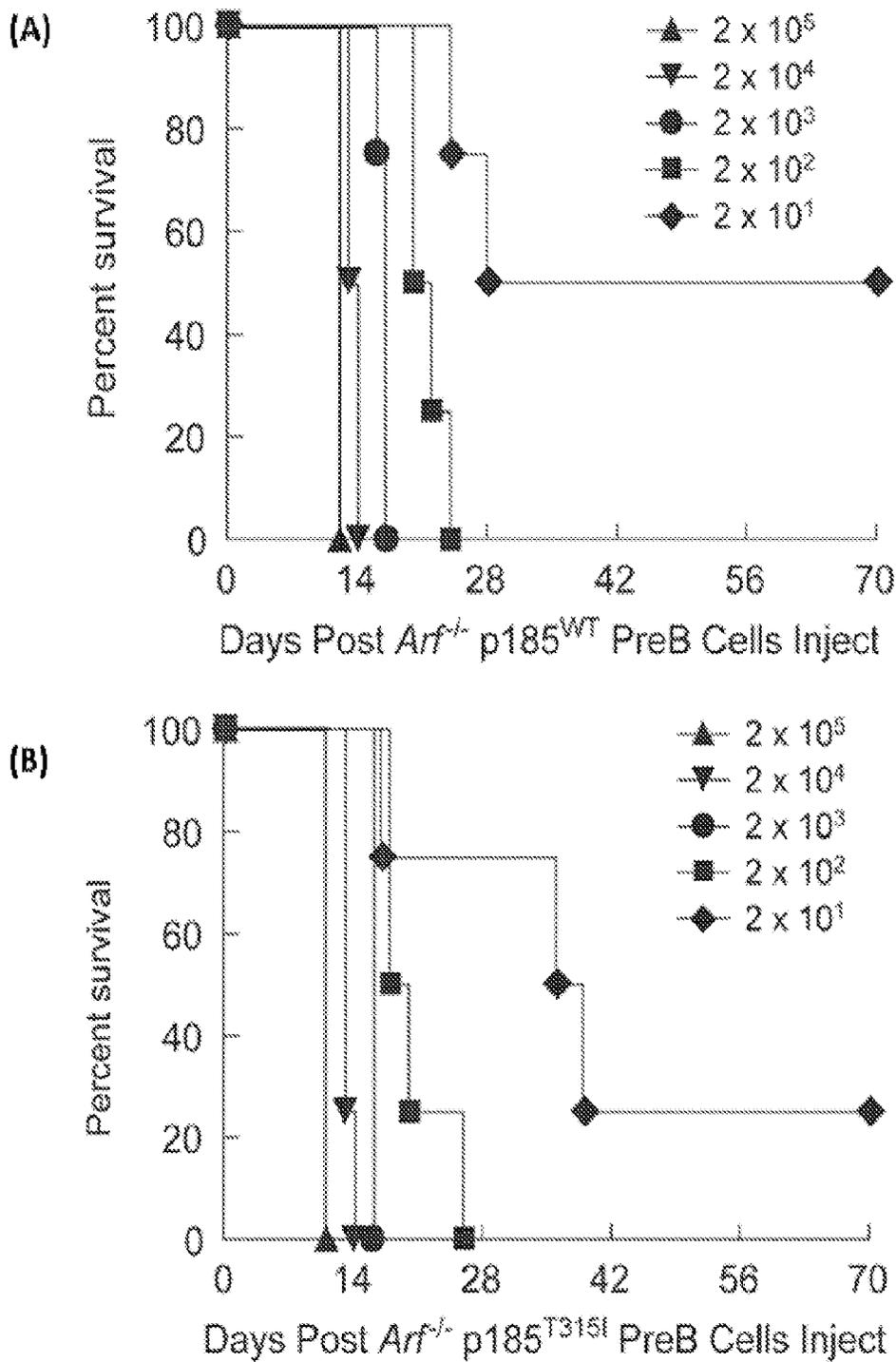


Figure 22

Host Factor	Conc	Hill	EC50	EC50CI	r2
IL3	0.0 ng/ml	0.5391	5.1118	3.8724 - 6.7479	0.987
IL3	0.01 ng/mL	0.4619	7.5159	5.4628 - 10.3405	0.983
IL3	0.1 ng/mL	0.3164	22.1664	12.1764 - 40.3525	0.944
IL3	1 ng/mL	0.3553	23.3197	14.1087 - 38.5443	0.958
IL3	10 ng/mL	0.3911	22.5621	14.9315 - 34.0924	0.971
IL3	100 ng/mL	0.4276	21.5773	15.2841 - 30.4619	0.979
IL15	0.0 ng/ml	0.5374	4.5252	3.4241 - 5.9805	0.987
IL15	0.01 ng/mL	0.5456	4.7956	3.6317 - 6.3325	0.987
IL15	0.1 ng/mL	0.5223	5.1369	3.9508 - 6.6792	0.988
IL15	1 ng/mL	0.5639	4.6853	3.4341 - 6.3924	0.984
IL15	10 ng/mL	0.5474	4.8593	3.7109 - 6.3630	0.987
IL15	100 ng/mL	0.5803	4.2075	3.2656 - 5.4211	0.989
IL6	0.0 ng/ml	0.5269	4.5635	3.2798 - 6.3497	0.982
IL6	0.01 ng/mL	0.5395	4.6483	3.4190 - 6.3197	0.984
IL6	0.1 ng/mL	0.5771	4.2131	3.1209 - 5.6876	0.984
IL6	1 ng/mL	0.5312	4.645	3.4403 - 6.2716	0.984
IL6	10 ng/mL	0.5605	4.494	3.4060 - 5.9295	0.986
IL6	100 ng/mL	0.5772	4.4834	3.4583 - 5.8123	0.988
SCF	0.0 ng/ml	0.5433	5.0496	3.8776 - 6.5759	0.988
SCF	0.01 ng/mL	0.5206	5.1184	3.7436 - 6.9982	0.984
SCF	0.1 ng/mL	0.5289	4.7638	3.5384 - 6.4137	0.985
SCF	1 ng/mL	0.5263	4.9426	3.7637 - 6.4909	0.987
SCF	10 ng/mL	0.5293	4.9611	3.5256 - 6.9812	0.98
SCF	100 ng/mL	0.5473	4.8079	3.7504 - 6.1636	0.989
FLT3	0.0 ng/ml	0.5785	4.0982	2.9655 - 5.6635	0.982
FLT3	0.01 ng/mL	0.5549	3.251	2.3904 - 4.4215	0.984
FLT3	0.1 ng/mL	0.5837	4.0456	3.1306 - 5.2282	0.988
FLT3	1 ng/mL	0.5677	4.1235	2.9621 - 5.7402	0.981
FLT3	10 ng/mL	0.567	3.6648	2.7944 - 4.8065	0.987
FLT3	100 ng/mL	0.6116	3.9157	2.9477 - 5.2015	0.986
IL4	0.0 ng/ml	0.494	6.2811	4.3841 - 8.9990	0.979
IL4	0.01 ng/mL	0.4721	7.6786	5.1536 - 11.4406	0.974
IL4	0.1 ng/mL	0.4582	10.607	7.3974 - 15.2093	0.978
IL4	1 ng/mL	0.4529	11.2471	7.8367 - 16.1418	0.978
IL4	10 ng/mL	0.4687	10.4343	7.1849 - 15.1533	0.977
IL4	100 ng/mL	0.4579	11.1402	7.6311 - 16.2629	0.976

Figure 23

Host Factor	Conc	Hill	EC50	EC50CI	r2
TSLP	0.0 ng/ml	0.5017	4.9482	3.5263 - 6.9434	0.981
TSLP	0.01 ng/mL	0.4805	5.692	3.8453 - 8.4256	0.975
TSLP	0.1 ng/mL	0.5043	8.314	6.0702 - 11.3872	0.983
TSLP	1 ng/mL	0.456	13.35	10.1901 - 17.4896	0.987
TSLP	10 ng/mL	0.4007	18.4296	12.8535 - 26.4247	0.978
TSLP	100 ng/mL	0.4177	17.6412	11.9235 - 26.1008	0.974
MCSF	0.01 ng/mL	0.5375	4.803	3.0670 - 7.5216	0.968
MCSF	0.1 ng/mL	0.5247	5.4838	3.8284 - 7.8550	0.979
MCSF	1 ng/mL	0.5357	4.6983	3.2180 - 6.8595	0.977
MCSF	10 ng/mL	0.517	4.6896	3.2354 - 6.7975	0.978
MCSF	100 ng/mL	0.5489	4.943	3.4050 - 7.1756	0.978
IL9	0.0 ng/ml	0.5582	4.2149	2.9368 - 6.0491	0.979
IL9	0.01 ng/mL	0.5585	4.3679	3.0111 - 6.3359	0.977
IL9	0.1 ng/mL	0.5698	4.0533	2.8653 - 5.7341	0.98
IL9	1 ng/mL	0.538	4.6609	3.1394 - 6.9198	0.975
IL9	10 ng/mL	0.5789	4.4575	2.8883 - 6.8792	0.97
IL9	100 ng/mL	0.5306	5.3572	3.5917 - 7.9905	0.975
GMCSF	0.0 ng/ml	0.4922	4.9682	3.4753 - 7.1024	0.979
GMCSF	0.01 ng/mL	0.5195	4.4331	3.1515 - 6.2359	0.981
GMCSF	0.1 ng/mL	0.4903	5.2002	3.7301 - 7.2496	0.982
GMCSF	1 ng/mL	0.5287	5.0754	3.5354 - 7.2862	0.978
GMCSF	10 ng/mL	0.4985	5.1825	3.6136 - 7.4324	0.979
GMCSF	100 ng/mL	0.5077	5.2664	3.9156 - 7.0832	0.985
CXCL12	0.0 ng/ml	0.5302	4.2517	3.0049 - 6.0157	0.98
CXCL12	0.01 ng/mL	0.5506	4.02	2.8966 - 5.5790	0.982
CXCL12	0.1 ng/mL	0.555	4.3428	3.0724 - 6.1384	0.98
CXCL12	1 ng/mL	0.5543	4.9481	3.5552 - 6.8868	0.982
CXCL12	10 ng/mL	0.5257	6.341	4.6141 - 8.7143	0.983
CXCL12	100 ng/mL	0.5626	7.7776	5.4588 - 11.0814	0.979

Figure 23 (continued)

Host Factor	Conc	Hill	EC50	EC50CI	r2
GCSF	0.0 ng/ml	0.4859	5.3848	3.8070 - 7.6163	0.98
GCSF	0.01 ng/mL	0.4888	5.6829	4.1379 - 7.8048	0.983
GCSF	0.1 ng/mL	0.4995	5.2436	3.5467 - 7.7522	0.975
GCSF	1 ng/mL	0.5238	4.4557	2.9858 - 6.6491	0.974
GCSF	10 ng/mL	0.5082	5.5333	3.8070 - 8.0422	0.977
GCSF	100 ng/mL	0.5071	5.5916	3.8599 - 8.1003	0.978
TGFb	0.0 ng/ml	0.5196	4.4138	3.1588 - 6.1674	0.981
TGFb	0.01 ng/mL	0.8345	2.0792	1.3877 - 3.1152	0.972
TGFb	0.1 ng/mL	1.3386	1.0712	0.6824 - 1.6815	0.943
TGFb	1 ng/mL	1.1768	1.2921	0.8022 - 2.0810	0.949
TGFb	10 ng/mL	1.0645	1.4597	0.8969 - 2.3756	0.954
TGFb	100 ng/mL	1.258	1.4057	0.8535 - 2.3151	0.947
IL2	0.0 ng/ml	0.5186	4.3969	3.0447 - 6.3495	0.978
IL2	0.01 ng/mL	0.4837	4.8218	3.3902 - 6.8578	0.98
IL2	0.1 ng/mL	0.4856	4.531	3.0037 - 6.8346	0.974
IL2	1 ng/mL	0.51	4.4851	3.1998 - 6.2866	0.981
IL2	10 ng/mL	0.5181	4.753	3.2444 - 6.9630	0.977
IL2	100 ng/mL	0.507	4.6062	3.3039 - 6.4219	0.982
IL7	0.0 ng/ml	0.4659	7.0902	5.2763 - 9.5276	0.985
IL7	0.01 ng/mL	0.3318	61.9094	41.1312 - 93.1840	0.971
IL7	0.1 ng/mL	0.3661	251.4246	157.6730 - 400.9203	0.958
IL7	1 ng/mL	0.3761	281.2124	165.0664 - 479.0824	0.947
IL7	10 ng/mL	0.383	286.5185	173.4620 - 473.2615	0.95
IL7	100 ng/mL	0.352	448.189	245.0635 - 819.6787	0.938

Figure 23 (continued)

Reg Number	Molsmiles	Synonym
SJ000000250	<chem>CCCNC[C@H](O)COc1ccccc1C(=O)CCc2ccc2</chem>	PROPAFENONE
SJ000000854	<chem>OC1=C(Oc2cc(O)cc(O)c2C1=O)c3ccc(O)c(O)c3</chem>	QUERCETIN
SJ000113084	<chem>COc1cc2nc(nc(N)c2cc1OC)N3CCN(CC3)C(=O)C4COc5ccccc5O4</chem>	DOXAZOSIN
SJ000126662	<chem>Nc1nc(SCc2ccc(cc2)[N+](=O)[O-])c3ncn([C@@H]4O[C@H](CO)[C@H](O)C4O)c3n1</chem>	NBTGR
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SJ000285194	<chem>NC(Cc1ccc(cc1)N(CCCI)CCCl)C(=O)O</chem>	MELPHALAN
SJ000285195	<chem>Sc1[nH]cnc2ncnc12</chem>	MERCAPTOPURINE
SJ000285196	<chem>CN(Cc1cnc2nc(N)nc(N)c2n1)c3ccc(cc3)C(=O)N[C@@H](CCC(=O)O)C(=O)O</chem>	METHOTREXATE
SJ000285197	<chem>COc1c(C)c2COC(=O)c2c(O)c1C=C(/C)CC(=O)O</chem>	MYCOPHENOLIC ACID
SJ000285200	<chem>NC(=N)c1ccc(OCCCCO)c2ccc(cc2)C(=N)N)cc1</chem>	PENTAMIDINE ISETHIONATE
SJ000285202	<chem>CCN(CC)CCCC(C)Nc1c2ccc(Cl)cc2nc3ccc(OC)cc13</chem>	QUINACRINE
SJ000285203	<chem>COc1cc2OC[C@H]3Oc4c5C[C@@H](Oc5cc4C(=O)[C@H]3c2cc1OC)C(=C)C</chem>	ROTENONE
SJ000285206	<chem>O=C1CC2OCC=C3CN4CC[C@@]56C4C[C@@H]3[C@@H]2C5N1c7ccccc67</chem>	STRYCHNINE
SJ000285207	<chem>CC[Hg]Sc1ccccc1C(=O)O</chem>	THIMEROSAL
SJ000285208	<chem>Nc1nc(S)c2[nH]cnc2n1</chem>	THIOGUANINE
SJ000285210	<chem>OC(=O)CCc1ccc(cc1)N(CCCI)CCCl</chem>	CHLORAMBUCIL
SJ000285212	<chem>COc1ccc(C[C@H](N)C(=O)N[C@@H]2[C@@H](CO)OC([C@@H]2O)n3cnc4c(ncnc34)N(C)C)cc1</chem>	PUROMYCIN

Figure 24

Reg Number	Molsmiles	Synonym
SJ000285215	<chem>CC[C@H]1CN2CCc3cc(OC)c(OC)cc3C2C[C@@H]1CC4NCCc5cc(OC)c(OC)cc45</chem>	EMETINE
SJ000285215	<chem>CC[C@H]1CN2CCc3cc(OC)c(OC)cc3[C@@H]2C[C@@H]1C[C@H]4NCCc5cc(OC)c(OC)cc45</chem>	EMETINE
SJ000285218	<chem>CC12C3CCC(O3)C1(C)C(=O)OC2=O</chem>	CANTHARIDIN
SJ000285219	<chem>C[C@H]1OC(C(O)[C@@H]1O)N2C=C(F)C(=O)NC2=O</chem>	FLUORO-5'-DEOXYURIDINE
SJ000285219	<chem>C[C@H]1O[C@H]([C@H](O)[C@@H]1O)N2C=C(F)C(=O)NC2=O</chem>	FLUORO-5'-DEOXYURIDINE
SJ000285220	<chem>C\C1=C\CC[C@@]2(C)O[C@@H]2[C@H]3OC(=O)C(=C)[C@@H]3CC1</chem>	PARTHENOLIDE
SJ000285221	<chem>Nc1nc(N)c2nc(CNc3ccc(cc3)C(=O)NC(CCC(=O)O)C(=O)O)cnc2n1</chem>	AMINOPTERIN
SJ000285225	<chem>CCCC[C@@H]1[C@@H](OC(=O)CC(C)C)[C@H](C)OC(=O)[C@@H](NC(=O)c2ccc(NC(=O)c2O)[C@@H](C)OC1=O</chem>	ANTIMYCIN A
SJ000285226	<chem>CC1=CN([C@H]2C[C@@H]([N-][N+]#N)[C@@H](CO)O2)C(=O)NC1=O</chem>	ZIDOVUDINE
SJ000285227	<chem>NC1=NC(=O)N(C=N1)[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O</chem>	AZACITIDINE
SJ000285228	<chem>C[C@H]1C[C@H](C)C(=O)[C@@H](C1)[C@H](O)CC2CC(=O)NC(=O)C2</chem>	CYCLOHEXIMIDE
SJ000285229	<chem>NC(COC(=O)[CH-][N+]#N)C(=O)O</chem>	AZASERINE
SJ000285231	<chem>CC(C)CC(=O)OC1C(O[C@@H]2C[C@H]([C@H]3CC[C@@]45CC(CC[C@H]4[C@@]3(C)C2)C(=C)[C@@H]5O)C(=O)O)OC(CO)C(OS(=O)(=O)[O-])C1OS(=O)(=O)[O-]</chem>	ATRACTYLOSIDE
SJ000285232	<chem>COc1cc(cc(OC)c1OC)[C@H]2[C@@H]3[C@H](COC3=O)[C@@H](O)c4cc5OCOc5cc24</chem>	PODOFILOX
SJ000285232	<chem>COc1cc(cc(OC)c1OC)[C@H]2[C@@H]3C(COC3=O)[C@@H](O)c4cc5OCOc5cc24</chem>	PODOFILOX
SJ000285234	<chem>CC[C@H]([C@H]1CC[C@H](C)[C@@H](O1)[C@@H](C)[C@H](O)[C@H](C)C(=O)[C@H](CC)[C@H]2OC3(O[C@@]4(CC[C@](C)(O4)[C@H]5CC[C@](O)(CC)[C@H](C)O5)[C@H](O)C=C3)[C@H](C)C[C@@H]2C)C(=O)O</chem>	SALINOMYCIN
SJ000285235	<chem>COc1cc(cc(OC)c1O)[C@H]2[C@@H]3[C@H](COC3=O)[C@H](O[C@@H]4O[C@@H]5CO[C@@H](C)O[C@H]5[C@H](O)[C@H]4O)c6cc7OCOc7cc26</chem>	ETOPOSIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285238	<chem>COC1=CC=C2C(=CC1=O)[C@H](CCc3cc(OC)c(OC)c(OC)c23)NC(=O)C</chem>	COLCHICINE
SJ000285241	<chem>Cn1cnc(c1Sc2[nH]cnc3ncnc23)[N+](=O)[O-]</chem>	AZATHIOPRINE
SJ000285242	<chem>CC(C)(C)CC(C)(C)c1ccc(OCCOCC[N+](C)(C)Cc2ccccc2)cc1</chem>	BENZETHONIUM CHLORIDE
SJ000285243	<chem>CO[C@@]12[C@@H]3NC3CN1C4=C([C@@H]2COC(=O)N)C(=O)C(=C(C)C4=O)N</chem>	MITOMYCIN
SJ000285244	<chem>CC(C)CC1NC(=O)C(CCCN)NC(=O)C(NC(=O)C2CCCN2C(=O)C(Cc3ccccc3)NC(=O)C(CC(C)C)NC(=O)C(CCCN)NC(=O)C(NC(=O)C4CCCN4C(=O)C(Cc5ccccc5)NC1=O)C(C)C)C(C)C</chem>	GRAMICIDIN
SJ000285246	<chem>C[n+]1c2cc(N)ccc2cc3ccc(N)cc13</chem>	ACRIFLAVINIUM
SJ000285249	<chem>CC(C)C1NC(=O)C(NC(=O)C2=C(N)C(=O)C(=C3Oc4c(C)ccc(C(=O)NC5C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C6CCCC6C(=O)C(NC5=O)C(C)C)c4N=C23)C)C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C7CC7C1=O</chem>	DACTINOMYCIN
SJ000285256	<chem>CC[C@@]1(O)C[C@H](O[C@H]2C[C@@H]([C@H](O)[C@H](C)O2)N(C)C)c3c(O)c4C(=O)c5c(O)cccc5C(=O)c4cc3[C@H]1C(=O)OC</chem>	AKLAVINE HYDROCHLORIDE
SJ000285261	<chem>CN(C)c1ccc(cc1)C(=C2C=CC(=[N+](C)C)C=C2)c3ccc(cc3)N(C)C</chem>	GENTIAN VIOLET
SJ000285262	<chem>C[C@@H]1OC(=O)CC(O)CC(O)CCC(O)C(O)CC(O)C[C@]2(O)C[C@H](O)C(C(C[C@@H](OC3OC(C)C(O)[C@@H](N)C3O)\C=C\C=C\C=C\C=C\C=C\C=C\C=C\C[C@H](C)[C@@H](O)[C@H]1C)O2)C(=O)O</chem>	AMPHOTERICIN B
SJ000285263	<chem>OC(=O)c1ccc(cc1)S(=O)(=O)N(Cl)Cl</chem>	HALAZONE
SJ000285267	<chem>CN(C)C(=S)SSC(=S)N(C)C</chem>	THIRAM
SJ000285270	<chem>S=P(N1CC1)(N2CC2)N3CC3</chem>	THIOTEPA
SJ000285272	<chem>OC[C@H]1OC(C[C@H]1O)N2C=C(F)C(=O)NC2=O</chem>	FLOXURIDINE
SJ000285273	<chem>Oc1c(Cl)cc(Cl)c(Cl)c1Cc2c(O)c(Cl)cc(Cl)c2Cl</chem>	HEXACHLOROPHEN E
SJ000285276	<chem>CCN(CC)CCNc1ccc(CO)c2Sc3ccccc3C(=O)c12</chem>	HYCANTHONE
SJ000285278	<chem>COC(=O)Nc1nc2cc(ccc2[nH]1)C(=O)c3cccs3</chem>	NOCODAZOLE
SJ000285279	<chem>CC[N+](C)(C)c1cccc(O)c1</chem>	EDROPHONIUM
SJ000285285	<chem>CN(C)c1nc(nc(n1)N(C)C)N(C)C</chem>	ALTRETAMINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285292	<chem>N[C@@H]1CONC1=O</chem>	CYCLOSERINE
SJ000285294	<chem>CC(=O)O[Hg]c1cccc1</chem>	PHENYLMERCURIC ACETATE
SJ000285299	<chem>CCC1=CN(C2OCC(O)C2CO)C(=O)NC1=O</chem>	EDOXUDINE
SJ000285307	<chem>CC[C@H](C1OC(CC)(C[C@@H]1C)C2CC[C@](O)(CC)[C@H](C)O2)C(=O)C(C)[C@@H](O)[C@H](C)CCc3ccc(C)c(O)c3C(=O)O</chem>	LASALOCID SODIUM
SJ000285308	<chem>Cc1cc(N)c2ccccc2[n+]1CCCCCCCCC[n+]3c(C)cc(N)c4ccccc34</chem>	DEQUALINIUM CHLORIDE
SJ000285313	<chem>CCCCCCCC\C=C\CCCCCCCCOP(=O)(O)OCC[N+](C)(C)C</chem>	ELAIDYLPHOSPHOC HOLINE
SJ000285315	<chem>CCCCCNC(=O)N1C=C(F)C(=O)NC1=O</chem>	CARMOFUR
SJ000285316	<chem>CCC[C@@H]1C[C@H](N(C)C1)C(=O)N[C@H]([C@@H](C)O)[C@H]2O[C@H](SC)[C@H](O)[C@@H](O)[C@@H]2O</chem>	LINCOMYCIN
SJ000285317	<chem>Oc1cccc2ccnc12</chem>	OXYQUINOLINE
SJ000285318	<chem>CNC(=O)Oc1ccc2N(C)[C@H]3N(C)CC[C@@]3(C)c2c1</chem>	PHYSOSTIGMINE SALICYLATE
SJ000285319	<chem>CCCC(CC)CN=C(N)N=C(N)NCCCCCN C(=NC(=NCC(CC)CCCC)N)N</chem>	ALEXIDINE HYDROCHLORIDE
SJ000285321	<chem>OCCNCCNc1ccc(NCCNCCO)c2C(=O)c3c(O)ccc(O)c3C(=O)c12</chem>	MITOXANTRONE
SJ000285323	<chem>O[Hg]c1c(O)c(Br)cc2C(=C3C=C(Br)C(=O)C=C3O)c12c4ccccc4C(=O)O</chem>	MERBROMIN
SJ000285327	<chem>C[n+]1cc2c3OCOc3ccc2c4ccc5cc6OCOc6cc5c14</chem>	SANGUINARINE SULFATE
SJ000285332	<chem>S=C1CC=CC=[N+]1O[Zn]ON2C=CC=CC2=S</chem>	PYRITHIONE ZINC
SJ000285334	<chem>CO[C@H]1C[C@H](O[C@H]2[C@H](C)[C@@H](O[C@@H]3O[C@H](C)C[C@@H]([C@H]3O)N(C)C)[C@@H](C)C[C@@]4(CO4)C(=O)[C@H](C)[C@@H](O)[C@@H](C)[C@@H](C)OC(=O)[C@@H]2C)O[C@@H](C)[C@@H]1O</chem>	OLEANDOMYCIN PHOSPHATE
SJ000285335	<chem>CC[C@]1(O)CC2CN(Cc3c([nH]c4ccccc34)[C@@](C2)(C(=O)OC)c5cc6c(cc5OC)N(C)[C@H]7[C@](O)([C@H](OC(=O)C)[C@]8(C)C=CCN9CC[C@]67[C@H]89)C(=O)OC)C1</chem>	VINBLASTINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285335	<chem>CCC1(O)CC2CN(CCc3c([nH]c4ccccc34)[C@@](C2)(C(=O)OC)c5cc6c(cc5OC)N(C)C7[C@](O)([C@H](OC(=O)C)[C@]8(CC)C=CCN9CC[C@]67[C@H]89)C(=O)OC)C1</chem>	VINBLASTINE
SJ000285337	<chem>C\C(=C\C(=O)O)\C=C\C(/C)\C=C\C1=C(C)CCCC1(C)C</chem>	ISOTRETINOIN
SJ000285337	<chem>C\C(=C/C=C/C(=C/C(=O)O)/C)\C=C\C1=C(C)CCCC1(C)C</chem>	TRETINOIN
SJ000285338	<chem>Clc1ccc(NC(=N)NC(=N)NCCCCCNC(=N)NC(=N)Nc2ccc(Cl)cc2)cc1</chem>	CHLORHEXIDINE
SJ000285343	<chem>OC(=O)CCC(=O)Nc1ccc(cc1)S(=O)(=O)Nc2nccs2</chem>	SUCCINYLSULFATHIAZOLE
SJ000285358	<chem>C[C@]12CCC(=O)C=C1CC[C@H]3[C@@H]4CC[C@](O)(C(=O)CO)[C@@]4(C)C[C@H](O)[C@H]23</chem>	HYDROCORTISONE
SJ000285363	<chem>CSc1ccc2Sc3ccccc3CC(N4CCN(C)CC4)c2c1</chem>	METITEPINE
SJ000285364	<chem>COc1ccc(cc1)[C@@H]2Sc3ccccc3N(CCN(C)C)C(=O)[C@@H]2OC(=O)C</chem>	DILTIAZEM
SJ000285365	<chem>CC[C@]1(O)OC([C@@H](C)C[C@H]1C)[C@H]2C[C@H](C)C(O2)[C@]3(CC)CC[C@@H](O3)[C@]4(C)CCC5(C[C@H](O)[C@@H](C)[C@H](O5)[C@H](C)[C@@H](OC)[C@H](C)C(=O)O)O4</chem>	MONENSIN SODIUM SALT
SJ000285368	<chem>C[C@]12CC[C@H]3[C@@H](CC[C@]4(O)C[C@@H](O)CC[C@]34C=O)[C@@]1(O)CC[C@@H]2C5=CC(=O)OC5</chem>	STROPHANTHIDIN
SJ000285369	<chem>OC1=CC=Cc2ccc(O)c(O)c2C1=O</chem>	PYROGALLIN
SJ000285373	<chem>CN1C2CCC1CC(C2)OC(=O)C(CO)c3ccccc3</chem>	ATROPINE
SJ000285375	<chem>CC(NC(C)(C)C)C(=O)c1cccc(Cl)c1</chem>	BUPROPION
SJ000285382	<chem>C[C@@H]1CC[C@@]2(OC1)O[C@H]3C[C@H]4[C@@H]5CC[C@H]6C[C@@H](O)CC[C@]6(C)[C@H]5CC(=O)[C@]4(C)[C@H]3[C@@H]2C</chem>	HECOGENIN
SJ000285383	<chem>CN1CCC(=C2c3ccccc3Sc4ccccc24)CC1</chem>	PIMETHIXENE MALEATE
SJ000285387	<chem>CN[C@@H](C)[C@H](O)c1ccccc1</chem>	PSEUDOEPHEDRINE HYDROCHLORIDE
SJ000285396	<chem>NC(Cc1ccc(Cl)cc1)C(=O)O</chem>	CHLOROPHENYLALANINE
SJ000285400	<chem>C[C@H]1CCC[C@]2(C)C[C@H]3OC(=O)C(=C)[C@H]3C=C12</chem>	HELENINE
SJ000285410	<chem>CC[C@@]1(O)C(=O)OCC2=C1C=C3N(Cc4cc5ccccc5nc34)C2=O</chem>	CAMPTOTHECIN

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285413	<chem>CC(=O)OCC(O)CC(=O)CCCCCCCCCCC#C</chem>	AVOCADYNONE ACETATE
SJ000285423	<chem>COC(=O)[C@]1(C)CC[C@]2(C)CC[C@]3(C)C4=CC=C5C(=C(O)C(=O)C=C5[C@]4(C)CC[C@@]3(C)[C@@H]2C1)C</chem>	PRISTIMERIN
SJ000285426	<chem>CSCCC(N)C(=O)NC(CC(C)C)C(=O)NC(Cc1cccc1)C(=O)O</chem>	METHIONYL-LEUCYLPHENYLALANINE ACETATE
SJ000285431	<chem>COC1=CC(C)[C@@H]2C[C@H]3OC(=O)C[C@H]4C(=C(OC)C(=O)C([C@@]34C)[C@@]2(C)C1=O)C</chem>	QUASSIN
SJ000285433	<chem>O=C1CCc2cc(OCCCCc3nnnn3C4CCCC4)cc2N1</chem>	CILOSTAZOL
SJ000285436	<chem>C[C@@H]1CC[C@H]2[C@@H](C)C(=O)O[C@@H]3O[C@@]4(C)CC[C@@H]1[C@@]23OO4</chem>	ARTEMISININ
SJ000285439	<chem>CC(C)CC1NC(=O)C(CCCN)NC(=O)C(NC(=O)C(Cc2ccc(O)cc2)NC(=O)C(CCC(=O)O)NC(=O)C(CC(=O)O)NC(=O)C(Cc3cccc3)NC(=O)C(Cc4cccc4)NC(=O)C5CCCN5C(=O)C(Cc6cccc6)NC1=O)C(C)C</chem>	TYROTHRIN
SJ000285440	<chem>O=C1C=CC(=O)c2cccc12</chem>	1,4-NAPHTHOQUINONE
SJ000285442	<chem>COc1cc(\C=C\C(=CC(=O)\C=C\c2ccc(O)c(O)C)c2)O)ccc1O</chem>	CURCUMIN
SJ000285443	<chem>Oc1ccc(cc1)C(=C2C=CC(=O)C=C2)c3ccc(O)cc3</chem>	ROSOLIC ACID
SJ000285445	<chem>OC(=O)Cc1cc(I)c(Oc2cc(I)c(O)c(I)c2)c(I)c1</chem>	TETRAC
SJ000285450	<chem>Nc1c2ccccc2nc3ccccc13</chem>	9-AMINOACRIDINE
SJ000285451	<chem>COc1ccc2cc3c4cc5OCOc5cc4CC[n+]3cc2c1OC</chem>	BERBERINE CHLORIDE
SJ000285452	<chem>CCCC1O[C@@H]2CC3C4CCC5=CC(=O)C=CC5(C)C4[C@@H](O)CC3(C)[C@@]2(O1)C(=O)CO</chem>	BUDESONIDE
SJ000285452	<chem>CCCC1O[C@@H]2C[C@H]3[C@@H]4CC5=CC(=O)C=C[C@]5(C)[C@H]4[C@@H](O)C[C@]3(C)[C@@]2(O1)C(=O)CO</chem>	BUDESONIDE
SJ000285453	<chem>C[C@]12CCC(=O)C=C1C=C[C@@H]3[C@@H]2CC[C@@]4(C)[C@H]3CC[C@@]4(O)CCC(=O)O</chem>	POTASSIUM CANRENOATE
SJ000285454	<chem>CC(=O)OCC1=C(N2C(SC1)[C@H](NC(=O)CCCC(N)C(=O)O)C2=O)C(=O)O</chem>	CEPHALOSPORIN C SODIUM
SJ000285460	<chem>CCN1C=C(C(=O)O)C(=O)c2cc3OCOc3cc12</chem>	OXOLINIC ACID

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285461	<chem>CCN(CCCOC(=O)c1ccc(OC)c(OC)c1)C(C)C2ccc(OC)cc2</chem>	MEBEVERINE HYDROCHLORIDE
SJ000285462	<chem>CN(C)[C@@H]1[C@@@H]2[C@@@H](O)[C@@H]3C(=C)c4c(Cl)ccc(O)c4C(=C3C(=O)[C@]2(O)C(=C(C(=O)N)C1=O)O)O</chem>	MECLOCYCLINE SULFOSALICYLATE
SJ000285465	<chem>CC12CC3CC(C)(C1)CC(N)(C3)C2</chem>	MEMANTINE
SJ000285466	<chem>NCCCS(=O)(=O)[O-]</chem>	HOMOTAUROINE
SJ000285484	<chem>NCC(O)c1ccc(O)cc1</chem>	OCTOPAMINE HYDROCHLORIDE
SJ000285487	<chem>CN1C(=O)NC(=O)c2c1ncn2C</chem>	THEOBROMINE
SJ000285490	<chem>CC(=CCCC1(C)O)c2c(CC=C(C)C)c3OC45C6CC(C=C4C(=O)c3c(O)c2C=C1)C(O)C5(C\C=C\C)/C(=O)O)OC6(C)C)C</chem>	DIHYDROGAMBOGI C ACID
SJ000285502	<chem>CCCCc1oc2ccccc2c1C(=O)c3cc(D)c(OCCN(CC)CC)c(I)c3</chem>	AMIODARONE
SJ000285504	<chem>CCCNC(C)C(=O)Nc1ccccc1C</chem>	PRILOCAINE
SJ000285506	<chem>CCN(CC)CCOc1ccc2c(c1)C(=O)c3cc(OCCN(CC)CC)ccc23</chem>	TILORONE
SJ000285508	<chem>CC(=O)O[C@H]1C(=O)[C@]2(C)[C@@H](O)C[C@H]3OC[C@@]3(OC(=O)C)C2[C@H](OC(=O)c4ccccc4)[C@]5(O)C[C@H](OC(=O)[C@H](O)[C@@H](NC(=O)c6ccccc6)c7ccccc7)C(=C1C5(C)C)C</chem>	PACLITAXEL
SJ000285512	<chem>CC(=O)OC1C\C(=C\C)C\C(=C\C)CC[C@](C)(O)C2CC1C(=C)C(=O)O2)\C)C</chem>	CRASSIN ACETATE
SJ000285522	<chem>C[C@@H](N)[C@@H](O)c1ccccc1</chem>	EPHEDRINE
SJ000285526	<chem>OC(=O)C1CCCNC1</chem>	NIPECOTIC ACID
SJ000285536	<chem>CC[C@H]1[C@@H](Cc2cncn2C)COC1=O</chem>	PILOCARPINE
SJ000285540	<chem>COc1cc2nc(nc(N)c2cc1OC)N3CCN(CC3)C(=O)c4occcc4</chem>	PRAZOSIN
SJ000285541	<chem>C[C@]12C[C@H](O)[C@H]3[C@@H](CC4=CC(=O)C=C[C@]34C)[C@@H]1CC[C@]2(O)C(=O)CO</chem>	PREDNISOLONE
SJ000285542	<chem>CC(=O)OCC(=O)[C@@]1(O)CCC2C3CCC4=CC(=O)C=CC4(C)C3[C@@H](O)C[C@]12C</chem>	PREDNISOLONE ACETATE
SJ000285543	<chem>C[C@]12CC(=O)C3C(CCC4=CC(=O)C=C[C@]34C)C1CC[C@]2(O)C(=O)CO</chem>	PREDNISONONE
SJ000285544	<chem>COc1cc(NC(C)CCCN)c2nccccc2c1</chem>	PRIMAQUINE
SJ000285547	<chem>CCN(CC)CCNC(=O)c1ccc(N)cc1</chem>	PROCAINAMIDE
SJ000285549	<chem>CN1CCN(CCCN2c3ccccc3Sc4ccc(Cl)cc24)CC1</chem>	PROCHLORPERAZIN E

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285551	<chem>CC(=O)[C@H]1CCC2C3CCC4=CC(=O)CC[C@]4(C)C3CC[C@]12C</chem>	PROGESTERONE
SJ000285554	<chem>CC(=CCc1c(O)c2C(=O)C(=COc2c3C=CC(C)(C)Oc13)c4ccc(O)c(O)c4)C</chem>	POMIFERIN
SJ000285564	<chem>NNCCc1ccccc1</chem>	PHENELZINE
SJ000285569	<chem>C1CNCCN1</chem>	PIPERAZINE
SJ000285572	<chem>COc1ccc2nccc([C@H](O)[C@H]3C[C@@H]4CCN3C[C@@H]4C=C)c2c1</chem>	QUININE SULFATE
SJ000285572	<chem>COc1ccc2nccc([C@H](O)[C@H]3C[C@@H]4CCN3C[C@@H]4C=C)c2c1</chem>	QUININE SULFATE
SJ000285574	<chem>OCc1ccccc1O</chem>	SALICYL ALCOHOL
SJ000285577	<chem>CC(=O)S[C@@H]1CC2=CC(=O)CC[C@]2(C)[C@H]3CC[C@@]4(C)[C@@H](CC[C@@]45CCC(=O)O5)C13</chem>	SPIRONOLACTONE
SJ000285584	<chem>Oc1ccc2C(=O)c3c(O)ccc(O)c3C(=O)c2c1O</chem>	QUINALIZARIN
SJ000285586	<chem>C[C@]12CCC(=O)C[C@@H]1CCC3C2CC[C@@]4(C)C3CCC4=O</chem>	5-ALPHA-ANDROSTAN-3,17-DIONE
SJ000285587	<chem>CC(=CCCC1(C)Oe2c(CC=C(C)C)c3OC45C6CC(C=C4C(=O)c3c(O)c2C=C1)C(=O)C5(C)C=C(C)C(=O)O)OC6(C)C</chem>	GAMBOGIC ACID
SJ000285588	<chem>Oc1ccc(cc1)C2=COc3cc(O)ccc3C2=O</chem>	DAIDZEIN
SJ000285591	<chem>CCCCC1C(=O)N(N(C1=O)c2ccc(O)cc2)c3ccc3</chem>	OXYPHENBUTAZONE
SJ000285592	<chem>CC\C(=C(/c1ccccc1)c2ccc(OCCN(C)C)cc2)\c3ccccc3</chem>	TAMOXIFEN
SJ000285606	<chem>CCCCNc1ccc(cc1)C(=O)OCCN(C)C</chem>	TETRACAINE HYDROCHLORIDE
SJ000285608	<chem>CN(C)S(=O)(=O)c1ccc2Sc3ccccc3\C(=C/CCN4CCN(C)CC4)c2c1</chem>	THIOTHIXENE
SJ000285608	<chem>CN(C)S(=O)(=O)c1ccc2Sc3ccccc3\C(=C\CCN4CCN(C)CC4)c2c1</chem>	THIOTHIXENE
SJ000285610	<chem>CSc1ccc2Sc3ccccc3N(CCC4CCCCN4C)c2c1</chem>	THIORIDAZINE
SJ000285614	<chem>Cc1ccc(cc1)C(=O)c2ccc(CC(=O)O)n2C</chem>	TOLMETIN
SJ000285618	<chem>Cc1cc(CC(=O)O)n(C)c1C(=O)c2ccc(Cl)cc2</chem>	ZOMEPIRAC SODIUM
SJ000285619	<chem>CN1N(C(=O)C(=C1)N)c2ccccc2</chem>	AMINOPHENAZONE
SJ000285625	<chem>COC(=O)[C@@H]1[C@@H](O)CC[C@@H]2CN3CCc4c([nH]c5ccccc45)[C@@H]3C[C@H]12</chem>	YOHIMBINE HYDROCHLORIDE
SJ000285630	<chem>CC(C)Cc1ccc(cc1)[C@H](C)C(=O)O</chem>	IBUPROFEN
SJ000285635	<chem>CC(C)[N+]1(C)[C@@H]2CCC1C[C@@H](C2)OC(=O)C(CO)c3ccccc3</chem>	IPRATROPIUM

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285638	<chem>C[C@H](COc1ccccc1)N[C@H](C)[C@H](O)c2ccc(O)cc2</chem>	ISOXSUPRINE HYDROCHLORIDE
SJ000285643	<chem>Cc1cccc(CN2CCN(CC2)C(c3ccccc3)c4ccc(Cl)cc4)c1</chem>	MECLOZINE
SJ000285646	<chem>C[C@H]1CC2C3CC[C@H](C(=O)C)[C@@]3(C)C[C@H](O)C2[C@@]4(C)CCC(=O)C=C14</chem>	MEDRYSONE
SJ000285651	<chem>Cn1ccnc1S</chem>	THIAMAZOLE
SJ000285652	<chem>COc1ccccc1OCC(O)COC(=O)N</chem>	METHOCARBAMOL
SJ000285655	<chem>C[C@](N)(Cc1ccc(O)c(O)c1)C(=O)O</chem>	METHYLDOPA
SJ000285657	<chem>C[C@H]1CC2C3CC[C@](O)(C(=O)CO)[C@@]3(C)C[C@H](O)C2[C@@]4(C)C=CC(=O)C=C14</chem>	METHYLPREDNISOLONE
SJ000285659	<chem>CN(C)[C@H]1[C@@H]2C[C@@H]3Cc4c(cc(O)c4C(=C3C(=O)[C@]2(O)C(=C(C(=O)N)C1=O)O)N(C)C</chem>	MINOCYCLINE
SJ000285664	<chem>C(C1=NCCN1)c2cccc3ccccc23</chem>	NAPHAZOLINE
SJ000285666	<chem>COC(=C1C(C(=C(C)N=C1C)C(=O)OC)c2ccc2[N+](=O)[O-])O</chem>	NIFEDIPINE
SJ000285667	<chem>[O-][N+](=O)c1oc(\C=NN2CC(=O)NC2=O)cc1</chem>	NITROFURANTOIN
SJ000285668	<chem>COc1ccc2[C@H](OC(=O)c2c1OC)[C@@H]3N(C)CCc4cc5OCOc5c(OC)c34</chem>	NOSCAPINE HYDROCHLORIDE
SJ000285671	<chem>CC(=O)O[C@]1(CCC2C3CCC4=CC(=O)CC[C@@H]4C3CC[C@]12C)C#C</chem>	NORETHISTERONE ACETATE
SJ000285674	<chem>CC[C@]12CC[C@H]3[C@@H](CCC4=CC(=O)CC[C@H]34)[C@@H]1CC[C@@]2(O)C#C</chem>	NORGESTREL
SJ000285678	<chem>Oc1ccc(Cl)cc1</chem>	PARACHLOROPHENOL
SJ000285683	<chem>COc1ccc(Cc2nccc3cc(OC)c(OC)cc23)cc1OC</chem>	PAPAVERINE HYDROCHLORIDE
SJ000285684	<chem>COc1ccc(C(=O)c2ccccc2)c(O)c1</chem>	OXYBENZONE
SJ000285686	<chem>NCC(CC(=O)O)c1ccc(Cl)cc1</chem>	BACLOFEN
SJ000285687	<chem>CC(C[N+](C)(C)C)OC(=O)N</chem>	BETHANECHOL
SJ000285688	<chem>NC(CO)C(=O)NNCc1ccc(O)c(O)c1O</chem>	BENSERAZIDE HYDROCHLORIDE
SJ000285689	<chem>CCOC(=O)c1ccc(N)cc1</chem>	BENZOCAINE
SJ000285692	<chem>C[C@H]1CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]2(C)[C@]1(O)C(=O)CO</chem>	BETAMETHASONE
SJ000285695	<chem>C[N+](C)(C)CCOC(=O)N</chem>	CARBACHOL
SJ000285696	<chem>NC(=O)N1c2ccccc2C=Cc3ccccc13</chem>	CARBAMAZEPINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285704	<chem>CC1=C(N2C(SC1)[C@H](NC(=O)[C@H](N)C3=CCC=CC3)C2=O)C(=O)O</chem>	CEFRADINE
SJ000285710	<chem>CC1=CC(=O)N(O)C(=C1)C2CCCCC2</chem>	CICLOPIROX
SJ000285712	<chem>CCN(CC)CCOc1ccc(cc1)C(=C(/Cl)\c2ccccc2)\c3ccccc3</chem>	CLOMIPHENE
SJ000285713	<chem>Clc1ccccc1C(c2ccccc2)(c3ccccc3)n4ccnc4</chem>	CLOTRIMAZOLE
SJ000285715	<chem>Oc1ccc(Cl)c2ccnc12</chem>	CLOXYQUIN
SJ000285718	<chem>CN(C)N=Nc1[nH]cnc1C(=O)N</chem>	DACARBAZINE
SJ000285725	<chem>CC(=O)N(O)CCCCNC(=O)CCC(=O)N(O)CCCCNC(=O)CCC(=O)N(O)CCCCN</chem>	DEFEROXAMINE
SJ000285727	<chem>CN(C)[C@H]1[C@@H]2C[C@@H]3[C@H](O)c4c(Cl)ccc(O)c4C(=C3C(=O)[C@]2(O)C(=C(C(=O)N)C1=O)O)O</chem>	DEMECLOCYCLINE HYDROCHLORIDE
SJ000285728	<chem>C[C@@H]1CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]2(C)[C@@]1(O)C(=O)COC(=O)C</chem>	DEXAMETHASONE ACETATE
SJ000285729	<chem>C[C@@H]1CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]2(C)[C@@]1(O)C(=O)COP(=O)(O)O</chem>	DEXAMETHASONE
SJ000285740	<chem>CN[C@H]1C(O)C(O)C(CO)OC1OC2[C@H](O)[C@H]3[C@H](O)[C@@H](O)[C@H](N=C(N)N)[C@@H](O)[C@@H]3N=C(N)N)OC(C)[C@]2(O)CO</chem>	DIHYDROSTREPTO MYCIN SULFATE
SJ000285742	<chem>CC1(C)OC(=O)NC1=O</chem>	DIMETHADIONE
SJ000285745	<chem>OCCN(CCO)c1nc(N2CCCCC2)c3nc(nc(N4CCCC4)c3n1)N(CCO)CCO</chem>	DIPYRIDAMOLE
SJ000285747	<chem>CCN(CC)C(=S)SSC(=S)N(CC)CC</chem>	DISULFIRAM
SJ000285748	<chem>NCCc1ccc(O)c(O)c1</chem>	DOPAMINE
SJ000285750	<chem>C[C@@H]1[C@H]2[C@H](O)[C@H]3[C@H](N(C)C)C(=O)C(=C(O)[C@@]3(O)C(=C2C(=O)c4c(O)cccc14)O)C(=O)N</chem>	DOXYCYCLINE
SJ000285752	<chem>CCCCOc1ccc(cc1)C(=O)CCN2CCCCC2</chem>	DYCLONINE
SJ000285761	<chem>CCC(=C)C(=O)c1ccc(OCC(=O)O)c(Cl)c1Cl</chem>	ETACRYNIC ACID
SJ000285764	<chem>CCc1cc(cen1)C(=S)N</chem>	ETHIONAMIDE
SJ000285766	<chem>CC(=O)OCC(=O)[C@@]1(O)CCC2C3CCC4=CC(=O)CC[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]12C</chem>	FLUDROCORTISON E ACETATE
SJ000285767	<chem>C[C@@H]1CC2C3C[C@H](F)C4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]2(C)[C@@]1(O)C(=O)COC(=O)C(C)C</chem>	FLUMETASONE PIVALATE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285768	<chem>CC(=O)OCC(=O)[C@@]12OC(C)(C)O[C@@H]1CC3C4C[C@H](F)C5=CC(=O)C=C[C@]5(C)[C@@]4(F)[C@@H](O)C[C@]23C</chem>	FLUOCINONIDE
SJ000285769	<chem>C[C@H]1CC2C3CC[C@](O)(C(=O)C)[C@@]3(C)C[C@H](O)[C@]2(F)C4(C)C=CC(=O)C=C14</chem>	FLUOROMETHOLONE
SJ000285770	<chem>CC(C(=O)O)c1ccc(c(F)c1)c2ccccc2</chem>	FLURBIPROFEN
SJ000285778	<chem>NC(=N)N\N=C/c1c(Cl)cccc1Cl</chem>	GUANABENZ
SJ000285781	<chem>CCCCCclccc(O)cc1O</chem>	HEXYLRESORCINOL
SJ000285783	<chem>C[N+]1(C)[C@H]2CCC1C[C@@H](C2)OC(=O)C(O)c3ccccc3</chem>	HOMATROPINE
SJ000285786	<chem>CC(=O)OCC(=O)[C@@]1(O)CCC2C3CCC4=CC(=O)CC[C@]4(C)C3[C@@H](O)C[C@]12C</chem>	HYDROCORTISONE ACETATE
SJ000285787	<chem>C[C@]12CCC(=O)C=C1CCC3C4CC[C@](O)(C(=O)COC(=O)CCC(=O)O)[C@@]4(C)C[C@H](O)C23</chem>	HYDROCORTISONE HEMISUCCINATE
SJ000285787	<chem>C[C@]12CCC(=O)C=C1CC[C@H]3[C@@H]4CC[C@](O)(C(=O)COC(=O)CCC(=O)O)[C@@]4(C)C[C@H](O)[C@H]23</chem>	HYDROCORTISONE HEMISUCCINATE
SJ000285790	<chem>CN1CCc2cccc3c2C1Cc4ccc(O)c(O)c34</chem>	APOMORPHINE
SJ000285797	<chem>Nc1ccc(cc1)C(=O)O</chem>	POTASSIUM p-AMINO BENZOATE
SJ000285801	<chem>C1C1=CC2=NC=CC(NC3=CC=C(C(CN(CC)CC)=C3)O)=C2C=C1</chem>	AMODIAQUINE DIHYDROCHLORIDE
SJ000285812	<chem>COc1cc(Cc2enc(N)nc2N)cc(OC)c1OC</chem>	TRIMETHOPRIM
SJ000285814	<chem>CC(C)CC1N2C(=O)[C@](NC(=O)C3CN(C)[C@@H]4Cc5c(Br)[nH]c6cccc(C4=C3)c56)(OC2(O)[C@@H]7CCCN7C1=O)C(C)C</chem>	BROMOCRIPTINE
SJ000285814	<chem>CC(C)C[C@@H]1N2C(=O)[C@](NC(=O)[C@H]3CN(C)[C@@H]4Cc5c(Br)[nH]c6cccc(C4=C3)c56)(O[C@@]2(O)[C@@H]7CCCN7C1=O)C(C)C</chem>	BROMOCRIPTINE
SJ000285818	<chem>CN(C)[C@H]1[C@@H]2[C@@H](O)[C@@H]3C(=C)c4cccc(O)c4C(=C3C(=O)[C@]2(O)C(=C(C(=O)N)C1=O)O</chem>	METACYCLINE HYDROCHLORIDE
SJ000285820	<chem>CCC(=O)OCC(=O)C1(OC(=O)CC)C(C)CC2C3CCC4=CC(=O)C=CC4(C)C3(C1)C(O)CC12C</chem>	BECLOMETHASONE DIPROPIONATE
SJ000285827	<chem>CCOc1ccc(Cc2nccc3cc(OCC)c(OCC)cc23)cc1OCC</chem>	ETHAVERINE HYDROCHLORIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285831	<chem>CCc1cccc2c3CCOC(CC)(CC(=O)O)c3[nH]c12</chem>	ETODOLAC
SJ000285834	<chem>CC(C)OC(=O)C(C)(C)Oc1ccc(cc1)C(=O)c2c cc(Cl)cc2</chem>	FENOFIBRATE
SJ000285835	<chem>COC(=O)Nc1nc2cc(Sc3ccccc3)ccc2[nH]1</chem>	FENBENDAZOLE
SJ000285836	<chem>O=C1NCC2(CCN(CCc3ccccc3)CC2)O1</chem>	FENSPIRIDE HYDROCHLORIDE
SJ000285837	<chem>CC(NCCC(c1ccccc1)c2ccccc2)c3ccccc3</chem>	FENDILINE HYDROCHLORIDE
SJ000285838	<chem>CCN(CC)CCNC(=O)COc1ccc(OC)cc1</chem>	MEFEXAMIDE
SJ000285840	<chem>COC(=O)Nc1nc2cc(ccc2[nH]1)C(=O)c3cccc c3</chem>	MEBENDAZOLE
SJ000285842	<chem>Nc1ccc(cc1)C(=O)NCC(=O)O</chem>	AMINOHIPURIC ACID
SJ000285845	<chem>COC(=C1C(C(=C(C)N=C1C)C(=O)OCCN(C)Cc2ccccc2)c3ccccc3)[N+](=O)[O-])O</chem>	NICARDIPINE
SJ000285849	<chem>CCCCOc1ccc(OCCCN2CCOCC2)cc1</chem>	PRAMOCAINE
SJ000285858	<chem>CN\C=C/[N+](=O)[O-])\NCCSCc1oc(CN(C)C)cc1</chem>	RANITIDINE
SJ000285860	<chem>CCCCCCCCNC(C)C(O)c1ccc(SC(C)C)cc1</chem>	SULOCTIDIL
SJ000285864	<chem>CCCCC1(COC(=O)CCC(=O)O)C(=O)N(N(C 1=O)c2ccccc2)c3ccccc3</chem>	SUXIBUZONE
SJ000285866	<chem>CC(C(=O)O)c1ccc(cc1)C(=O)c2cccs2</chem>	SUPROFEN
SJ000285878	<chem>CC(=O)OC1CCC2C3CCc4cc(O)ccc4C3CCC 12C</chem>	ESTRADIOL ACETATE
SJ000285879	<chem>Clc1ccc(COC(Cn2ccnc2)c3ccc(Cl)cc3Cl)cc1</chem>	ECONAZOLE
SJ000285880	<chem>CC1(C)O[C@@H]2CC3C4C[C@H](F)C5=C C(=O)C=CC5(C)C4C(O)CC3(C)[C@@]2(O 1)C(=O)CO</chem>	FLUNISOLIDE
SJ000285881	<chem>O=C1N([Se]c2ccccc12)c3ccccc3</chem>	EBSELEN
SJ000285882	<chem>CC12CCC3C(CCc4cc(OCc5ccccc5)ccc34)C1 C[C@@H](O)[C@@H]2O</chem>	ESTRIOL BENZYL ETHER
SJ000285885	<chem>CCCOc1cccc1c2nc(O)c3[nH]nnc3n2</chem>	ZAPRINAST
SJ000285887	<chem>Cc1ccc(cc1)S(=O)(=O)NC(=O)NN2CCCC C2</chem>	TOLAZAMIDE
SJ000285888	<chem>CCOC(=O)[C@H](CCc1ccccc1)N[C@@H](C)C(=O)N2CCC[C@H]2C(=O)O</chem>	ENALAPRIL
SJ000285890	<chem>NCCCC[C@H](N[C@@H](CCc1ccccc1)C(= O)O)C(=O)N2CCC[C@H]2C(=O)O</chem>	LISINOPRIL
SJ000285892	<chem>CCCCOc1ccc(CC(=O)NO)cc1</chem>	BUFEXAMAC
SJ000285903	<chem>CCN1C=C(C(=O)O)C(=O)c2cc(F)c(N3CCN C(C)C3)c(F)c12</chem>	LOMEFLOXACIN HYDROCHLORIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285909	<chem>C[n+]1cccc1\C=N\O</chem>	PRALIDOXIME
SJ000285920	<chem>NC\C=C/C(=O)O</chem>	TACA
SJ000285922	<chem>OC(=O)C1=CCNCC1</chem>	ISOGUVACINE HYDROCHLORIDE
SJ000285925	<chem>CC(Cc1ccc(O)c(O)c1)(NN)C(=O)O</chem>	CARBIDOPA
SJ000285935	<chem>OC(C1CCCN1)c2cc(nc3c(cccc23)C(F)(F)F)C(F)(F)F</chem>	MEFLOQUINE
SJ000285936	<chem>CCN(CC)CCOC(=O)C(c1cccc1)c2ccccc2</chem>	ADIPHENINE HYDROCHLORIDE
SJ000285940	<chem>Nc1c(Br)cc(Br)cc1CNC2CCC(O)CC2</chem>	AMBROXOL HYDROCHLORIDE
SJ000285949	<chem>CC(C)COCC(CN(Cc1cccc1)c2ccccc2)N3CCCC3</chem>	BEPRIDIL HYDROCHLORIDE
SJ000285950	<chem>CN(Cc1cc(Br)cc(Br)c1N)C2CCCC2</chem>	BROMHEXINE HYDROCHLORIDE
SJ000285951	<chem>CCN(CC)CCNC(=O)c1cc(Br)c(N)cc1OC</chem>	BROMOPRIDE
SJ000285958	<chem>CC(C)(C)CC(C)(C)c1ccc(O)c(Cc2ccc(Cl)cc2Cl)c1</chem>	CLOFOCTOL
SJ000285959	<chem>CC(=O)NS(=O)(=O)c1ccc(N)cc1</chem>	SULFACETAMIDE SODIUM
SJ000285960	<chem>CN(C)CCC=C1c2ccccc2C=Cc3ccccc13</chem>	CYCLOBENZAPRIN E
SJ000285965	<chem>Clc1ccc(OCC(=O)N2CCN(Cc3ccc4OCOc4c3)CC2)cc1</chem>	FIPEXIDE HYDROCHLORIDE
SJ000285966	<chem>Nc1cccc(c1)C(=C2C=CC(=N)C=C2)c3cccc(N)c3</chem>	PARAROSANILINE PAMOATE
SJ000285967	<chem>C(C(C1CCCC1)C2CCCC2)C3CCCN3</chem>	PERHEXILINE MALEATE
SJ000285971	<chem>CN1N=C(S/C/1=N\C(=O)C)S(=O)(=O)N</chem>	METHAZOLAMIDE
SJ000285972	<chem>Cc1cc(ccc1OCCOCC[N+](C)(C)Cc2ccccc2)C(C)(C)CC(C)(C)C</chem>	METHYLBENZETHO NIUM CHLORIDE
SJ000285973	<chem>C[C@H]1CC2C3CC[C@](O)(C(=O)COC(=O)C)C3(C)C[C@H](O)C2C4(C)C=CC(=O)C=C14</chem>	6-ALPHA- METHYLPREDNISO LONE ACETATE
SJ000285974	<chem>COc1cc(NS(=O)(=O)C)ccc1Cc2c3ccccc3nc4ccccc24</chem>	AMSACRINE
SJ000285978	<chem>CCCC(=O)O[C@@]1(CCC2[C@@H]3CCC4=CC(=O)CC[C@]4(C)C3[C@@H](O)C[C@@]12C)C(=O)CO</chem>	HYDROCORTISONE BUTYRATE
SJ000285980	<chem>CN(CS(=O)(=O)[O-])C1=C(C)N(C)N(C1=O)c2ccccc2</chem>	METAMIZOLE
SJ000285983	<chem>Fc1ccc(cc1)C(=O)C2CCN(CCN3C(=O)Nc4ccccc4C3=O)CC2</chem>	KETANSERIN TARTRATE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000285987	<chem>CCCCOc1ccc2[nH]c(NC(=O)OC)nc2c1</chem>	OXIBENDAZOLE
SJ000285991	<chem>CCCCCCCCCCCC[N+](C)(C)Cc1cccc1</chem>	BENZALKONIUM CHLORIDE
SJ000285996	<chem>CC(C)c1c(C(=O)c2ccccc2)c(c3ccccc3)c(c4cc c(F)cc4)n1CC[C@@H](O)C[C@@H](O)CC (=O)O</chem>	ATORVASTATIN
SJ000285998	<chem>CC(=O)OCC(=O)[C@@]12OC3(CCCC3)O[C@@H]1CC4C5CCC6=CC(=O)C=C[C@]6(C)[C@@]5(F)[C@@H](O)C[C@]24C</chem>	AMCINONIDE
SJ000285999	<chem>CCCCN1CCCC1C(=O)Nc2c(C)cccc2C</chem>	BUPIVACAINE
SJ000286003	<chem>CO[C@@H]1C[C@@H](C[C@H]2CC[C@ H](C)[C@@H](O2)[C@@H](C)C(=O)O)O[C@]3(O[C@@](C)(C[C@H]3C)[C@H]4CC [C@](C)(O4)C5O[C@H](C[C@@H]5C)C6 O[C@@](O)(CO)[C@H](C)C[C@@H]6C)[C@@H]1C</chem>	NIGERICIN SODIUM
SJ000286004	<chem>CC(=O)C1=C(O)C2C3C(Cc4cccc5[nH]cc3c4 5)C(C)(C)N2C1=O</chem>	CYCLOPIAZONIC ACID
SJ000286006	<chem>CCC(=O)OC1([C@@H](C)C[C@H]2[C@@ H]3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]12C)C(=O)CC1</chem>	CLOBETASOL PROPIONATE
SJ000286007	<chem>CC1CCCC(C)NINC(=O)c2ccc(Cl)c(c2)S(=O) (=O)N</chem>	CLOPAMIDE
SJ000286008	<chem>Clc1ccc(cc1)C(OCCN2CCCC2)c3ccccc3</chem>	CLOPERASTINE HYDROCHLORIDE
SJ000286018	<chem>OC(=O)CCCCC1CCSS1</chem>	THIOCTIC ACID
SJ000286024	<chem>OC(Cn1cncn1)(Cn2cncn2)c3ccc(F)cc3F</chem>	FLUCONAZOLE
SJ000286025	<chem>CC[C@H](C)C(=O)O[C@H]1C[C@@H](C) C=C2C=C[C@H](C)[C@H](CC[C@@H]3C [C@@H](O)CC(=O)O3)[C@@H]12</chem>	LOVASTATIN
SJ000286030	<chem>COc1cc(cc(OC)c1O)[C@H]2[C@@H]3C(C OC3=O)C(O[C@@H]4O[C@@H]5CO[C@ H](OC5[C@H](O)[C@H]4O)c6cccs6)c7cc8 OCOc8cc27</chem>	TENIPOSIDE
SJ000286034	<chem>Clc1c(Cl)c(C#N)c(Cl)c(C#N)c1Cl</chem>	CHLOROTHALONIL
SJ000286035	<chem>CC1=C2CCC3C4CCC(=O)[C@@]4(C)CCC 3[C@@]2(C)CCC1=O</chem>	FORMESTANE
SJ000286036	<chem>C[C@@H]1CC(Cl)CC[C@H]1C(=O)OC(C)(C)C</chem>	TRIMEDLURE
SJ000286037	<chem>CC(N)C(=O)OC(C)(C)Cc1ccc(Cl)cc1</chem>	ALAPROCLATE
SJ000286038	<chem>OC[C@H]1OC2[C@@H](OC3=NC(=N)C= CN23)[C@@H]1O</chem>	ANCITABINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286038	<chem>OC[C@H]1O[C@@H]2C(OC3=NC(=N)C=CN23)[C@H]1O</chem>	ANCITABINE
SJ000286039	<chem>Cc1ccc(cc1)S(=O)(=O)NC(=O)NN2CC3CCC3C2</chem>	GLICLAZIDE
SJ000286041	<chem>CC(=O)Nc1c(I)cc(I)c(C(=O)O)c1I</chem>	ACETRIAZOIC ACID
SJ000286044	<chem>O=C1OC(=O)C2C3CCC(O3)C12</chem>	NORCANTHARIDIN
SJ000286046	<chem>CNCC[C@@H](Oc1ccc(cc1)C(F)(F)F)c2ccc cc2</chem>	FLUOXETINE
SJ000286046	<chem>CNCCC(Oc1ccc(cc1)C(F)(F)F)c2ccccc2</chem>	FLUOXETINE
SJ000286052	<chem>OC1=C([C@@H]2CC[C@H](CC2)c3ccc(Cl)cc3)C(=O)C(=O)c4ccccc14</chem>	ATOVAQUONE
SJ000286053	<chem>CC(C)N=C(N)N=C(N)Nc1ccc(Cl)cc1</chem>	PROGUANIL HYDROCHLORIDE
SJ000286056	<chem>NC(=N)NC(=O)c1nc(Cl)c(nc1N)N2CCCCC2</chem>	N,N- HEXAMETHYLENE AMILORIDE
SJ000286057	<chem>CCCCCc1ccc(O)cc1O.Nc2c3ccccc3nc4cccc c24</chem>	ACRISORCIN
SJ000286063	<chem>CCC(C)(C)C(=O)O[C@H]1C[C@@H](C)C=C2C=C[C@H](C)[C@H](CC[C@@H]3C[C@@H](O)CC(=O)O3)[C@@H]12</chem>	SIMVASTATIN
SJ000286065	<chem>COc1ccccc1OCCNCC(O)COc2ccccc3[nH]c4c cccc4c23</chem>	CARVEDILOL
SJ000286075	<chem>CC(C)N(CCC(c1ccccc1)c2cc(C)ccc2O)C(C)C</chem>	TOLTERODINE
SJ000286086	<chem>Cc1cc2N=C3C(=O)NC(=O)N=C3N(C[C@H](O)[C@H](O)[C@H](O)CO)c2cc1C</chem>	RIBOFLAVIN
SJ000286093	<chem>CN[C@H]1CC[C@@H](c2ccc(Cl)c(Cl)c2)c3 cccc13</chem>	SERTRALINE
SJ000286097	<chem>OC(=O)CCc1oc(c2ccccc2)c(n1)c3ccccc3</chem>	OXAPROZIN
SJ000286098	<chem>CCN(C(=O)\C=C\C)c1ccccc1C</chem>	CROTAMITON
SJ000286101	<chem>NC(=NCc1ccccc1)NC(=O)c2nc(Cl)c(N)nc2N</chem>	BENZAMIL HYDROCHLORIDE
SJ000286109	<chem>CN1C2CCC1CC(C2)OC(c3ccccc3)c4ccccc4 N</chem>	AMINO BENZ TROPI NE
SJ000286112	<chem>OC1CCCCC1N2CCC(CC2)c3ccccc3</chem>	VESAMICOL HYDROCHLORIDE
SJ000286113	<chem>COc1ccc(CCN(C)CCCC(C#N)(C(C)C)c2ccc(OC)c(OC)c2)cc1OC</chem>	VERAPAMIL
SJ000286118	<chem>COc1ccc(CCN2CCC(CC2)Nc3nc4ccccc4n3C c5ccc(F)cc5)cc1</chem>	ASTEMIZOLE
SJ000286121	<chem>Clc1ccc2Oc3ccccc3N=C(N4CCNCC4)c2c1</chem>	AMOXAPINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286124	NC1CC1c2ccccc2	TRANLYCYPROMIN E
SJ000286127	C1CCc2nnnn2CC1	PENTETRAZOL
SJ000286128	CC1=C(O)C(=O)C=C2C1=CC=C3[C@@]2(C)CC[C@@]4(C)[C@@H]5C[C@@](C)(CC[C@]5(C)CC[C@]34C)C(=O)O	CELASTROL
SJ000286133	Fe1ccc(cc1)C(N2CCN(C\C=C\c3ccccc3)CC2)c4ccc(F)cc4	FLUNARIZINE HYDROCHLORIDE
SJ000286134	OCCN1CCN(CCCN2c3ccccc3Sc4ccc(cc24)C(F)(F)F)CC1	FLUPHENAZINE
SJ000286142	CC(=O)OCC(=O)[C@@]1(O)[C@@H](CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]12C)OC(=O)C	TRIAMCINOLONE DIACETATE
SJ000286143	NS(=O)(=O)c1cc2c(NC(NS2(=O)=O)C(Cl)Cl)cc1Cl	TRICHLORMETHIAZ IDE
SJ000286144	Nc1nc(N)c2nc(c(N)nc2n1)c3ccccc3	TRIAMTERENE
SJ000286146	OC(=O)c1cc(ccc1O)N=Nc2ccc(cc2)S(=O)(=O)Nc3cccn3	SULFASALAZINE
SJ000286151	Nc1ccc(cc1)S(=O)(=O)Nc2ccc(Cl)nn2	SULFACHLORPYRID AZINE
SJ000286152	OC(=O)c1ccnc1Nc2cccc(c2)C(F)(F)F	NIFLUMIC ACID
SJ000286154	CCCCC(=O)O[C@@]1([C@@H](C)CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)C(O)C[C@]12C)C(=O)CO	BETAMETHASONE VALERATE
SJ000286155	CN1CCCC1CCOC(C)(c2ccccc2)c3ccc(Cl)cc3	CLEMASTINE
SJ000286156	CC12CCC(=O)C=C1CCC3C4CC[C@](O)(C(=O)COP(=O)(O)O)C4(C)C[C@H](O)C23	HYDROCORTISONE SODIUM PHOSPHATE
SJ000286159	CCc1nc(N)nc(N)c1c2ccc(Cl)cc2	PYRIMETHAMINE
SJ000286160	CN(C)c1ccc2c(ccc(C=C\c3cc(C)n(c3C)c4ccc4)[n+]2C)c1	PYRVINIUM PAMOATE
SJ000286162	CCCCCCCCc1ccc(OCCOCCOCCOCCOCCOCCOCCOCCOCCO)cc1	NONOXYNOL-9
SJ000286166	CN[C@@H]1[C@@H](O)C(OC2[C@@H](N)C[C@@H](N)[C@H](O)[C@H]3O[C@H](C(C)O)[C@@H](O)[C@H](O)[C@H]3N)[C@H]2O)OC[C@]1(C)O	GENETICIN
SJ000286172	O=C(CC(=O)c1ccccc1)c2ccccc2	DIBENZOYLMETHA NE
SJ000286174	OC(=O)C1=CN(c2ccc(F)cc2)c3cc(N4CCNC4)c(F)cc3C1=O	SARAFLOXACIN HYDROCHLORIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286175	<chem>NC(=O)c1ccc(N)nc1</chem>	6-AMINONICOTINAMIDE
SJ000286178	<chem>O=C1O[C@@]23C[C@@H](C=CC2=C1)N4CCCC[C@H]34</chem>	SECURININE
SJ000286181	<chem>CCCCCCCCCCCCCCCCOP(=O)(O)OCC[N+](C)(C)C</chem>	MILTEFOSINE
SJ000286185	<chem>CN1CCN(CCCN2c3ccccc3Sc4ccc(cc24)C(F)(F)F)CC1</chem>	TRIFLUOPERAZINE
SJ000286186	<chem>OC(CCN1CCCCC1)(C2CCCC2)c3ccccc3</chem>	TRIHXYPHENIDYL
SJ000286187	<chem>COc1cc(cc(OC)c1O)[C@H]2C3C(COC3=O)[C@H](O)c4cc5OCOc5cc24</chem>	4'-DEMETHYLEPIPODOPHYLLOTOXIN
SJ000286188	<chem>C[C@@H](N)CO</chem>	L-ALANINOL
SJ000286191	<chem>COc1ccc2C[C@H]3N(C)CCc4cc(OC)c(Oc5c6OCOc6cc7CCN(C)[C@@H](Cc8ccc(Oc1c2)cc8)c57)cc34</chem>	CEPHARANTHINE
SJ000286195	<chem>Clc1ccc(CO\N=C(/Cn2ccnc2)c3ccc(Cl)cc3Cl)c(Cl)c1</chem>	OXICONAZOLE
SJ000286199	<chem>COC(=O)N\N=C\c1c[n+](([O-])c2ccccc2[n+])1[O-]</chem>	CARBODOX
SJ000286204	<chem>CC(CN1c2ccccc2Sc3ccccc13)N(C)C</chem>	PROMETHAZINE
SJ000286205	<chem>CC1(C)O[C@@H]2CC3C4CCC5=CC(=O)C=C[C@]5(C)[C@@]4(F)[C@@H](O)C[C@]3(C)[C@@]2(O1)C(=O)CO</chem>	TRIAMCINOLONE ACETONIDE
SJ000286213	<chem>Cc1nccc2c3ccc(O)cc3[nH]c12</chem>	HARMOL HYDROCHLORIDE
SJ000286217	<chem>CS(=O)(=O)c1ccc(cc1)[C@@H](O)[C@@H](CO)NC(=O)C(Cl)Cl</chem>	THIAMPHENICOL
SJ000286225	<chem>C1CN2CC(N=C2S1)c3ccccc3</chem>	LEVAMISOLE
SJ000286229	<chem>CC(=O)OC1C(O)C2C(C)(C)CCC(O)C2(C)C3(O)C(=O)CC(C)(OC13C)C=C</chem>	COLFORSIN
SJ000286231	<chem>NCCCCNCCCN</chem>	SPERMIDINE TRIHYDROCHLORIDE
SJ000286236	<chem>NC(=O)N1c2ccccc2CC(=O)c3ccccc13</chem>	OXCARBAZEPINE
SJ000286243	<chem>CC(C)(O)CC[C@@H](O)[C@](C)(O)C1CC[C@@]2(O)C3=CC(=O)C4C[C@@H](O)[C@@H](O)C[C@]4(C)C3CC[C@]12C</chem>	CRUSTECDYSONE
SJ000286248	<chem>CC(=O)O[C@@H]1C[C@@]2(C)[C@@H](C[C@H]3O[C@@]23[C@@]4(C)C1[C@@]5(C)C=CC(=O)C(C)(C)C5=C(O)C4=O)c6ccoc6</chem>	ANTHOTHECOL

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286251	<chem>CC1(C)C(=O)C=C[C@@]2(C)C3CC[C@@@]4(C)[C@@H](C[C@H]5O[C@@]45[C@@]3(C)C(=O)C(=C12)O)c6cocc6</chem>	CEDRELONE
SJ000286267	<chem>CCC(C)C(O)C(=O)O[C@H]1[C@H](OC=O)C(C(=C)C2(O)C(=O)C[C@@H](c3cocc3)[C@]12C)[C@@]4(C)[C@H](CC(=O)O[C@](C)(COC(=O)C)C4CC(=O)OC)OC(=O)C</chem>	PRIEURIANIN
SJ000286300	<chem>O[C@H]1C=C2CCN3Cc4cc5OCOc5cc4C([C@@H]1O)C23</chem>	LYCORINE HYDROCHLORIDE
SJ000286312	<chem>C[C@@H]1CC[C@@]2(OC1)OC3C(O)C4C5CC[C@H]6C[C@H](O[C@@H]7O[C@H](CO)[C@H](O[C@@H]8O[C@H](CO)[C@@H](O)[C@H](O[C@@H]9OC[C@@H](O)[C@H](O)[C@H]9O)[C@H]8O[C@@H]%10O[C@H](CO)[C@H](O)[C@H](O[C@@H]%11O[C@H](CO)[C@@H](O)[C@H](O)[C@H]%11O)[C@H]10O)[C@H](O)[C@H]7O)[C@H](O)C[C@]6(C)C5CC[C@]4(C)C3[C@@H]2C</chem>	DIGITONIN
SJ000286359	<chem>CN(C)Cc1c(C)[nH]c2ccccc12</chem>	2-METHYL GRAMINE
SJ000286366	<chem>COC(=O)[C@@H]1OC(=O)C2OC23[C@@]1(C)CCC4[C@@]5(C)[C@H](C[C@@H](OC(=O)C)C(C)C)C5C[C@@H](O)[C@@]34C)OC(=O)C</chem>	7-BETA-HYDROXY- 7- DESACETOXYKHIV ORINIC ACID, METHYL ESTER
SJ000286380	<chem>Oc1ccc2C3c4cc(O)c(O)cc4CC3(O)COc2c1</chem>	BRAZILIN
SJ000286381	<chem>COc1cc2OC[C@H]3Oc4c(ccc5oc(cc45)C(C)C)C(=O)[C@H]3c2cc1OC</chem>	ISOROTENONE
SJ000286382	<chem>COC(=O)c1c(C)c2Oc3c(Cl)c(O)c(Cl)c(C)c3C(=O)Oc2c(C)c1O</chem>	LEOIDIN
SJ000286387	<chem>CC(C)(C=C)c1c2Oc3c(O)c(O)ccc3C(=O)c2c(O)c4C=CC(C)(C)Oc14</chem>	MACLUROXANTHONINE
SJ000286389	<chem>OC(=CC(=O)c1ccccc1)c2ccccc2O</chem>	2',BETA- DIHYDROXYCHALCONE
SJ000286393	<chem>OC[C@H]1O[C@@H](Oc2ccc(C(=O)C=C\c3ccccc3)c(O)c2)[C@H](O)[C@@H](O)[C@@H]1O</chem>	2',4'- DIHYDROXYCHALCONE 4'-GLUCOSIDE
SJ000286395	<chem>O=C1CC(Oc2ccccc12)c3ccccc3</chem>	FLAVANONE
SJ000286396	<chem>Oc1ccc(cc1)C(=O)\C=C\c2ccccc2</chem>	4'- HYDROXYCHALCONE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286398	<chem>COC1=CC(=O)C=C(OC)C1=O</chem>	2,6-DIMETHOXYQUINONE
SJ000286406	<chem>COc1ccc2C(=O)C(Cc3ccc(OC)c(O)c3)COc2c1</chem>	DEOXYSAIPPANONE B 7,3'-DIMETHYL ETHER
SJ000286408	<chem>CC(C)C(C)\C=C\C(C)C1CCC2C3=CC=C4C(C(O)CCC4(C)C3CCC12C</chem>	ERGOSTEROL
SJ000286413	<chem>COC1=CC(=O)C(=CC1=O)C(C=C)c2ccc(O)cc2</chem>	DALBERGIONE, 4-METHOXY-4'-HYDROXY-
SJ000286415	<chem>COc1cc2OC[C@H]3Oc4c(CC=C(C)C)c(O)c4C(=O)[C@H]3c2cc1OC</chem>	ROTENONIC ACID
SJ000286419	<chem>COc1cc(C\C=C\C)c2ccccc2)c(OC)cc1O</chem>	VIOLASTYRENE
SJ000286421	<chem>COC1=CC(=O)C(=CC1=O)C(C=C)c2ccccc2</chem>	4-METHOXYDALBERGIONE
SJ000286423	<chem>COc1ccc2C(=O)\C(=C\c3ccc(OC)c(O)c3)\COc2c1</chem>	SAPPANONE A DIMETHYL ETHER
SJ000286424	<chem>COc1cc2OC[C@H]3Oc4c5CCC(C)(C)Oc5cc4C(=O)[C@H]3c2cc1OC</chem>	BETA-DIHYDROROTENONE
SJ000286430	<chem>C=CC(C1=CC(=O)C=CC1=O)c2ccccc2</chem>	DALBERGIONE
SJ000286434	<chem>COc1ccc2C(=O)C(Cc3ccc(OC)c(OC(=O)C)c3)COc2c1</chem>	DEOXYSAIPPANONE B 7,3'-DIMETHYL ETHER ACETATE
SJ000286436	<chem>COc1cc2OC[C@H]3Oc4c5CC(Oc5ccc4C(=O)[C@H]3c2cc1OC)C(C)C</chem>	DIHYDROROTENONE
SJ000286438	<chem>COc1ccc2C(=O)[C@@H]3[C@@H](COc4c4c(OC)c(OC)cc34)Oc2c1</chem>	MUNDOSERONE
SJ000286446	<chem>COc1cc(O)c(C(=O)\C=C\c2ccccc2)c(OC)c1</chem>	FLAVOKAWAIN B
SJ000286448	<chem>CC[C@@]1(O)C[C@H](O[C@H]2C[C@@H]([C@H](O)[C@H](C)O2)N(C)C)c3c(O)c4C(=O)c5c(O)ccc(O)c5C(=O)c4cc3[C@H]1C(=O)OC</chem>	PYRROMYCIN
SJ000286450	<chem>Oc1ccc2C3Oc4cc5OCOc5cc4C3COc2c1</chem>	MAACKIAIN
SJ000286451	<chem>CC(=O)O[C@@H]1C2CC[C@H]3[C@@](C)(O)[C@@H]4C[C@H](O)C(C)(C)[C@@]4(O)[C@H](O)CC13C[C@@]2(C)O</chem>	GRAYANOTOXIN I
SJ000286453	<chem>Cc1cc(O)c(C=O)c2Oc3c(OC(=O)c12)c(C)c(O)c4C(=O)OC(O)c34</chem>	NORSTICTIC ACID
SJ000286455	<chem>O[C@H]1Cc2ccc(O)cc2O[C@@H]1c3ccc(O)c(O)c3</chem>	FISETINIDOL

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286458	<chem>COc1c(CC(=O)c2cc3CC(O)C(C)(C)Oc3cc2O)ccc4OC(C)(C)C=Cc14</chem>	DIHYDROMUNDUL ETONE
SJ000286481	<chem>Clc1cccc(Cl)c1NC2=NCCN2</chem>	CLONIDINE
SJ000286496	<chem>Nc1[nH]cnc2ncnc12</chem>	ADENINE
SJ000286501	<chem>CN1Cc2c3OCOc3ccc2[C@H]4[C@@H](O)Cc5cc6OCOc6cc5[C@@H]14</chem>	CHELIDONINE
SJ000286511	<chem>CC(C)CCCC(C)[C@H]1CCC2C3C[C@@H](O)[C@@]4(O)C[C@@H](O)CC[C@]4(C)C3CC[C@]12C</chem>	CHOLESTAN-3- BETA,5-ALPHA,6- BETA-TRIOL
SJ000286515	<chem>COc1cc(cc(OC)c1OC)[C@H]2[C@H]3[C@H](COC3=O)[C@@H](OC(=O)C)c4cc5OCOc5cc24</chem>	PODOPHYLLOTOXI N ACETATE
SJ000286515	<chem>COc1cc(cc(OC)c1OC)[C@H]2[C@@H]3[C@H](COC3=O)[C@@H](OC(=O)C)c4cc5OCOc5cc24</chem>	PODOPHYLLOTOXI N ACETATE
SJ000286516	<chem>Oc1ccc(Cl)cc1C(=O)Nc2ccc(cc2Cl)[N+](=O)[O-]</chem>	NICOLSAMIDE
SJ000286520	<chem>Oc1ccc(cc1)C2=COc3cc(O)cc(O)c3C2=O</chem>	GENISTEIN
SJ000286522	<chem>COC1=CC(=O)C(=CC1=O)C(C=C)c2ccc(OC)cc2</chem>	4,4'- DIMETHOXYDALBE RGIONE
SJ000286525	<chem>COc1cccc1C2=COc3cc(O)ccc3C2=O</chem>	7-HYDROXY-2'- METHOXYISOFLAV ONE
SJ000286530	<chem>CCOC(=O)c1c(C)cc(O)cc1O</chem>	ORSELLINIC ACID, ETHYL ESTER
SJ000286533	<chem>COc1ccc(cc1)[C@@H](C)C(=O)c2ccc(O)cc2O</chem>	ANGOLENSIN
SJ000286536	<chem>CC(=C)\C=C/1\C=CC(=O)C(=C1)C</chem>	RETUSOQUINONE
SJ000286537	<chem>COc1cc2OCC3Oc4cc5OC(C)(C)C=Cc5c(O)c4C(=O)C3c2cc1OC</chem>	BETA-TOXICAROL
SJ000286548	<chem>COc1cc2cc[n+]3c(C)c4cc(OC)c(OC)cc4cc3c2cc1OC</chem>	CORALYNE CHLORIDE
SJ000286550	<chem>CC(N)COc1c(C)cccc1C</chem>	MEXILETINE
SJ000286552	<chem>CCC(=O)OCC(=O)[C@@]1(OC(=O)CC)[C@@H](C)CC2C3CCC4=CC(=O)C=C[C@]4(C)C3(F)[C@@H](O)C[C@]12C</chem>	BETAMETHASONE 17,21- DIPROPIONATE
SJ000286565	<chem>CC(=CCC1=C(O)C(=O)c2cccc2C1=O)C</chem>	LAPACHOL
SJ000286572	<chem>C[C@]12CCC3C(CCC4=CC(=O)CC[C@]34C)C1CC[C@@H]2O</chem>	TESTOSTERONE
SJ000286576	<chem>OC1OCC=C2OC(=O)C=C12</chem>	PATULIN
SJ000286594	<chem>CC(C)Nc1nc(Cl)nc(NC(C)C)n1</chem>	PROPAZINE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286616	CCCCCCC(C)OC(=O)COc1ccc(Cl)cc1Cl	2,4-DICHLOROPHENOXYACETIC ACID, ISOCTYL ESTER
SJ000286619	CC(C)N(C(=O)CCL)c1ccccc1	PROPACHLOR
SJ000286644	CCCCOC(=O)c1ccccc1C(=O)OCc2ccccc2	BENZYL BUTYLPHOSPHATE
SJ000286645	CCCCCCCCC1ccc(O)cc1	4-NONYLPHENOL
SJ000286646	CCOCN(C(=O)CCL)c1c(C)cccc1CC	ACETOCHLOR
SJ000286648	COc1cc2OCOc2cc1C3=Cc4cc5ccoc5cc4OC3=O	PACHYRRHIZIN
SJ000286657	COc1ccc2c(c1)[nH]c3c(C)nc23	HARMINE
SJ000286658	COc1ccc2cc3c4cc(OC)c(OC)cc4CC[n+]3cc2c1OC	PALMATINE CHLORIDE
SJ000286694	OCC(O)CC(O)CCCCCCCCCCC=C	AVOCADENE
SJ000286708	COc1cc(cc(OC)c1OC)[C@H]2[C@@H]3[C@H](COC3=O)Cc4c(O)c5OCc5cc24	BETA-PELTATIN
SJ000286710	OC[C@H]1O[C@H]([C@H](O)[C@@H]1O)n2cnc3c(NC4occc4)ncnc23	KINETIN RIBOSIDE
SJ000286711	CC(C)c1c(O)c(O)c(C=O)c2c(O)c(c(C)cc12)c3c(C)cc4c(C(C)C)c(O)c(C=O)c4c3O	GOSSYPOL
SJ000286715	C/C=C(/C)/C(=O)OC1[C@H](OC(=O)C)C2(CO)[C@H](O)C[C@]3(C)C(=CCC4C5(C)CC(O)[C@@H]6O[C@@H]([C@@H](O)[C@@H]7O[C@H](CO)[C@@H](O)[C@H](O)[C@H]7O)[C@H](O)[C@H]6O[C@@H]8O[C@H](CO)[C@@H](O)[C@H](O)[C@H]8O)C(=O)O[C@](C)(CO)C5CCC34C)C2CC1(C)C	BETA-ESCIIN
SJ000286728	COc1cc2OC[C@H]3Oc4c5C=CC(C)(C)Oc5cc4C(=O)[C@H]3c2cc1OC	DEGUELIN
SJ000286729	NC(C(O)C(=O)O)C(=O)O	D,L-THREO-3-HYDROXYASPARTIC ACID
SJ000286749	COC1C[C@H]2N3CC(O)C2(C=C1)c4cc5OCOc5cc4C3	CRINAMINE
SJ000286751	CCCCCCCCCCCCCCCC[N+](C)(C)C	CETRIMONIUM BROMIDE
SJ000286753	COc1cc2CC[C@H](NC(=O)C)C3=C(C=CC(=O)C(=C3)O)c2c(OC)c1OC	COLCHICEINE
SJ000286767	COc1ccccc(O)c1O	3-METHOXYCATECHOL

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286769	<chem>OCC(O)CC(O)CCCCCCCCCCC=C.OCC(O)CC(O)CCCCCCCCCCC#C</chem>	AVOCATIN B
SJ000286772	<chem>COc1ccc(cc1)C(=O)\C=C\c2ccccc2</chem>	4'-METHOXYCHALCONE
SJ000286775	<chem>CCC(C)[C@H]1O[C@@]2(C[C@@H]3C[C@@H](C\C=C/C)\[C@@H](OC4C[C@H](OC)C(O[C@H]5C[C@H](OC)[C@@H](O)[C@H](C)O5)[C@H](C)O4)[C@@H](C)C=C\C=6/CO[C@@H]7[C@H](O)C(=C[C@@H](C(=O)O3)[C@]67O)C)O2)C=C[C@@H]1C</chem>	AVERMECTIN B1
SJ000286776	<chem>NCCCCN</chem>	PUTRESCINE DIHYDROCHLORIDE
SJ000286780	<chem>N[C@@H](CCON=C(N)N)C(=O)O</chem>	CANAVANINE
SJ000286781	<chem>C[C@H]1CC[C@]2(NC1)OC3C4CCC5C[C@H](CC[C@]5(C)C4CC[C@]3(C)[C@@H]2C)O[C@H]6O[C@H](CO)[C@H](O[C@H]7O[C@H](CO)[C@@H](O)[C@H](O[C@H]8OC[C@@H](O)[C@H](O)[C@H]8O[C@H]9O[C@H](CO)[C@@H](O)[C@H](O)[C@H]9O)[C@H]7O)[C@H](O)[C@H]6O</chem>	TOMATINE
SJ000286782	<chem>COc1cc(O)cc(OC)c1OC</chem>	ANTIAROL
SJ000286783	<chem>O[C@@H]1O[C@H](COC(=O)CC[N+](=O)[O-])[C@@H](OC(=O)CC[N+](=O)[O-])[C@H](OC(=O)CC[N+](=O)[O-])[C@H]1OC(=O)CC[N+](=O)[O-]</chem>	ENDECAPHYLLIN X
SJ000286797	<chem>C1CCN(CCC1)CCCl</chem>	TRICHLORMETHINE
SJ000286800	<chem>COC1(C)CCC2OC2(C)CCC3C1CC3(C)C</chem>	2-METHOXY-5(6)EPOXY-TETRAHYDROCARYOPHYLENE
SJ000286801	<chem>CC1(C)CC2C1CCC(=O)C(CCC2=C)C3CC(=O)OC3=O</chem>	2-METHYLENE-5-(2,5-DIOXOTETRAHYDROFURAN-3-YL)-6-OXO--10,10-DIMETHYLBICYCLO[7:2:0]UNDECANE
SJ000286802	<chem>OC[C@H]1O[C@@H](Oc2cc(O)c3C(=O)C=C(Oc3c2)c4ccc(O)cc4)[C@H](O)[C@@H](O)[C@@H]1O</chem>	COSMOSIIN

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286804	<chem>CCC(=O)O[C@H]1CC[C@H]2[C@@H]3CCC4=CC(=O)CC[C@]4(C)[C@H]3CC[C@]12C</chem>	TESTOSTERONE PROPIONATE
SJ000286809	<chem>COC1=C(C(=O)O)c2cc3OC(C)(C)C=Cc3c(OC)c12)c4ccc(OC)cc4</chem>	ROBUSTIC ACID METHYL ETHER
SJ000286813	<chem>COc1c(O)cc2C(=CC(=O)O)c2c1OC)c3ccccc3</chem>	KUHLMANNIN
SJ000286816	<chem>COc1c2C=CC(C)(C)Oc2ccc1C3=COc4cc5OC(C)(C)C(O)Cc5cc4C3=O</chem>	MUNDULONE
SJ000286821	<chem>COc1ccc(cc1)C2=CC(=O)c3c(OC)cccc3O2</chem>	5,4'- DIMETHOXYFLAVONE
SJ000286829	<chem>CC(=O)O[C@H]1CC[C@]2(C)[C@H]3CC[C@@]4(C)[C@@H](CCC4=O)[C@@H]3CC=C2C1</chem>	5- DEHYDROEPIANDROSTERONE ACETATE
SJ000286830	<chem>C[C@@]1(CO)[C@H](O)CC[C@@]2(C)[C@H](C\C=C\C3/[C@H](O)COC3=O)C(=C)CC12</chem>	ANDROGRAPHOLIDE
SJ000286847	<chem>COc1cc2OCC3Oc4c5C=CC(C)(C)Oc5cc(O)c4C(=O)C3c2cc1OC</chem>	ALPHA-TOXICAROL
SJ000286853	<chem>CC(=O)OCC(=O)[C@H]1CCC2C3CCC4=CC(=O)CC[C@]4(C)C3CC[C@]12C</chem>	DESOXYCORTICOSTERONE ACETATE
SJ000286865	<chem>COC(=O)c1c(C)c2Oc3c(Cl)c(OC)c(Cl)c(C)c3C(=O)Oc2c(C)c1OC</chem>	LEOIDIN DIMETHYL ETHER
SJ000286868	<chem>CC(=O)OC1CCC(=C)[C@H]2CC(C)(C)[C@@H]2C\C=C\C1/C</chem>	CARYOPHYLLENYL ACETATE
SJ000286877	<chem>COc1ccc2C(=O)[C@@H]3[C@@H](COc4cc(OC)c(OC)cc34)Oc2c1CC=C(C)C</chem>	ROTENONIC ACID, METHYL ETHER
SJ000286884	<chem>CC(C)CCCC(C)CCCC(C)CCCC1(C)CCc2c(C)c(O)c(C)c(C)c2O1</chem>	ALPHA- TOCOPHEROL
SJ000286890	<chem>CC(C)C1=CC(=O)C(=CC1=O)C</chem>	THYMOQUINONE
SJ000286899	<chem>C[C@]12CC[C@@H](O)CC1CC[C@@H]3[C@@H]2CC[C@@]4(C)[C@H]3CCC4=O</chem>	EPIANDROSTERONE
SJ000286902	<chem>C[C@]12C[C@H](O)[C@@]3(F)[C@@H](CCC4=CC(=O)C=C[C@]34C)[C@@H]1C[C@@H](O)[C@]2(O)C(=O)CO</chem>	TRIAMCINOLONE
SJ000286904	<chem>OC(=O)CCC1NCC2CC1CN3CCCCC23</chem>	LUPANYL ACID HYDROCHLORIDE
SJ000286906	<chem>NCCCC(=O)O</chem>	GABA
SJ000286948	<chem>CC1(C)O[C@@H]2CC3C4CCC5=CC(=O)CC5(C)C4(F)C(O)CC3(C)[C@@]2(O1)C(=O)CC1</chem>	HALCINONIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000286950	<chem>CCC1NC(=O)C(C(O)C(C)C)C=C\C(C)N(C)C(=O)C(C(C)C)N(C)C(=O)C(CC(C)C)N(C)C(=O)C(CC(C)C)N(C)C(=O)C(C)NC(=O)C(C)NC(=O)C(CC(C)C)N(C)C(=O)C(NC(=O)C(C(C)C)N(C)C(=O)CN(C)C1=O)C(C)C</chem>	CICLOSPORIN
SJ000286959	<chem>CC(C)CC(=O)c1c(O)c(C)c(O)c2c1oc3c(C(=O)CC(C)C)c(O)c(C)c(O)c23</chem>	RHODOMYRTOXIN
SJ000286960	<chem>Cc1c(O)c(O)cc2c1CC=C3[C@@]2(C)CC[C@@]4(C)C5C[C@@](C)(CC[C@]5(C)CC[C@]34C)C(=O)O</chem>	DIHYDROCELASTR OL
SJ000286962	<chem>Oc1cc(O)c2C(=O)C=C(Oc2c1)c3cc(O)c(O)c(O)c3</chem>	HIERACIN
SJ000286963	<chem>CCC(C)C(=O)c1c(O)c(C)c2oc3c(C)c(O)c(C(=O)C(C)CC)c(O)c3c2c1O</chem>	RHODOMYRTOXIN B
SJ000286965	<chem>CC[C@@]1(O)C(=O)OCC2=C1C=C3N(Cc4cc5cc(O)ccc5nc34)C2=O</chem>	10- HYDROXYCAMTOT HECIN
SJ000286983	<chem>OC[C@H]1OC(C[C@@H]1O)N2C=C(C(=O)NC2=O)C(F)(F)F</chem>	TRIFLURIDINE
SJ000286986	<chem>COC(=O)[C@]1(C)CC[C@]2(C)CC[C@]3(C)C4=CCc5c(C)c(O)c(O)cc5[C@]4(C)CC[C@@]3(C)C2C1</chem>	PRISTIMEROL
SJ000286993	<chem>COC1=CC(=O)C(=C/C1=C\C=C\Cc2ccccc2)O</chem>	OBTUSAQUINONE
SJ000287007	<chem>COc1cc(O)c2C(=O)C=C(Oc2c1)c3ccc(OC)c(c3)c4c(O)cc(O)c5C(=O)C=C(Oc45)c6ccc(O)cc6</chem>	GINKGETIN, POTASSIUM SALT
SJ000287016	<chem>CC1(C)O[C@@H]2CC3C4C[C@H](F)C5=C(C(=O)C=C[C@]5(C)[C@@]4(F)[C@@H](O)C[C@]3(C)[C@@]2(O1)C(=O)CO</chem>	FLUOCINOLONE ACETONIDE
SJ000287020	<chem>CC(C)C1=CC2=CC[C@H]3[C@](C)(CO)CC[C@]3(C)C2CC1</chem>	ABIETANOL
SJ000287054	<chem>Oc1cc(O)c2C[C@@H](OC(=O)c3cc(O)c(O)c(O)c3)[C@H](Oc2c1)c4cc(O)c(O)c(O)c4c5c(O)c(O)c(O)cc5[C@H]6Oc7cc(O)cc(O)c7C[C@H]6OC(=O)c8cc(O)c(O)c(O)c8</chem>	THEASINENSIN
SJ000287055	<chem>CC[C@H](C)C(=O)O[C@H]1CCC=C2C=C[C@H](C)[C@H](CC[C@@H]3C[C@@H](O)CC(=O)O3)[C@@H]12</chem>	COMPACTIN
SJ000287058	<chem>CC(C)CCC[C@@H](C)CCC[C@@H](C)CC\C(=C\CO)\C</chem>	PHYTOL

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287132	<chem>Fc1ccc(cc1)C(=O)CCCN2CCN(CC2)c3ccccc3</chem>	AZAPERONE
SJ000287133	<chem>CC(=O)O[C@@H]1CC(=O)OC(C)(C)C2CC(=O)[C@]3(C)C(CC[C@@]4(C)[C@@H](OC(=O)[C@H]5O[C@@]345)c6ccccc6)[C@@]12C</chem>	NOMILIN
SJ000287134	<chem>Oc1ccc(\C=C\C(=O)OCCc2ccccc2)cc1O</chem>	PHENETHYL CAFFEATE
SJ000287136	<chem>OC(=O)C(Cc1ccc(O)c(O)c1)OC(=O)\C=C\c2ccc(O)c(O)c2</chem>	ROSMARINIC ACID
SJ000287138	<chem>CC1(C)O[C@@H]2CC3C4C[C@H](F)C5=C(C(=O)CC[C@]5(C)C4[C@@H](O)C[C@]3(C)[C@@]2(O1)C(=O)CO</chem>	FLUDROXYCORTID E
SJ000287139	<chem>CS(=O)(=O)CCCCN=C=S</chem>	ERYSOLIN
SJ000287147	<chem>O=C1c2ccccc2C(=O)c3ccccc13</chem>	ANTHRAQUINONE
SJ000287149	<chem>CC[C@@]1(O)C(=O)OCC2=C1C=C3N(Cc4cc5c(CN(C)C)c(O)ccc5nc34)C2=O</chem>	TOPOTECAN
SJ000287150	<chem>OC(=O)c1ccccc1O</chem>	SALICYLIC ACID
SJ000287152	<chem>Nc1nc(O)c2[nH]nnc2n1</chem>	AZAGUANINE-8
SJ000287155	<chem>CC(=O)OCC(=O)[C@@]1(O)CC[C@H]2[C@@H]3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]12C</chem>	ISOFLUPREDONE ACETATE
SJ000287160	<chem>OC[C@H]1O[C@H](C[C@@H]1O)N2C=C(C)C(=O)NC2=O</chem>	IDOXURIDINE
SJ000287177	<chem>CN(C)C\C=C/(c1ccc(Br)cc1)\c2ccnc2</chem>	ZIMELIDINE DIHYDROCHLORID E MONOHYDRATE
SJ000287181	<chem>C[C@H]1CCC2(NC1)O[C@H]3C[C@H]4[C@@H]5CC[C@H]6C[C@H](CC[C@]6(C)[C@H]5CC[C@]4(C)[C@H]3[C@@H]2C)O[C@@H]7O[C@H](CO)[C@H](O[C@@H]8O[C@H](CO)[C@@H](O)[C@H](O[C@@H]9OC[C@@H](O)[C@H](O)[C@H]9O)[C@H]8O[C@@H]%10O[C@H](CO)[C@@H](O)[C@H](O)[C@H]%10O)[C@H](O)[C@H]7O</chem>	TOMATINE
SJ000287182	<chem>CC12NC(Cc3ccccc13)c4ccccc24</chem>	DIZOCILPINE MALEATE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287193	<chem>CC[C@@H](C)[C@H]1O[C@]2(CC[C@@H]1C)C[C@@H]3C[C@@H](C\C=C(/C)\[C@@H](O[C@H]4C[C@H](OC)[C@@H](O[C@H]5C[C@H](OC)[C@@H](O)[C@H](C)O5)[C@H](C)O4)[C@@H](C)\C=C\C=C\6/CO[C@@H]7[C@H](O)C(=C[C@@H](C(=O)O3)[C@]67O)C)O2</chem>	IVERMECTIN
SJ000287195	<chem>CC(C)N1CCN(CC1)c2ccc(OC[C@H]3CO[C@@](Cn4cn4)(O3)c5ccc(Cl)cc5Cl)cc2</chem>	TERCONAZOLE
SJ000287203	<chem>CC(=O)N(CC(O)CO)c1c(I)c(C(=O)NCC(O)CO)c(I)c(C(=O)NCC(O)CO)c1I</chem>	IOHEXOL
SJ000287206	<chem>CC1OC(=O)CC(O)CC(O)CC(O)CCC(O)C(O)CC(=O)CC(O)C(C(O)CC(O)[C@@H]2O[C@H](C)[C@@H](O)[C@H](N)[C@@H]2O)\C=C\C=C\C=C\C=C\C=C\C=C\C=C\C(C)C(O)C1C)C(=O)O</chem>	NYSTATIN
SJ000287209	<chem>CC(C)n1c\C=C\[C@H](O)C[C@H](O)CC(=O)O)c(c2ccc(F)cc2)c3ccccc13</chem>	FLUVASTATIN
SJ000287215	<chem>OC(=O)COC(=O)Cc1ccccc1Nc2c(Cl)cccc2C1</chem>	ACECLOFENAC
SJ000287222	<chem>CCCCC[C@@H]1[C@@H](OC(=O)CC(C)C)[C@H](C)OC(=O)C(NC(=O)c2ccccc(NC=O)c2O)[C@@H](C)OC1=O</chem>	ANTIMYCIN A
SJ000287228	<chem>CCCS1ccc2[nH]c(NC(=O)OC)nc2c1</chem>	ALBENDAZOLE
SJ000287229	<chem>OC(CCCN1CCCC1)(c2ccccc2)c3ccccc3</chem>	DIPHENIDOL
SJ000287231	<chem>CC(=O)OCC(=O)[C@@]1(O)CC[C@H]2[C@@H]3CCC4=CC(=O)CC[C@]4(C)C3(F)C(=O)C[C@]12C</chem>	FLUDROCORTISON E ACETATE
SJ000287238	<chem>CC(C(O)c1ccc(O)cc1)N2CCC(Cc3ccccc3)CC2</chem>	IFENPRODIL TARTRATE
SJ000287239	<chem>CCCCCCC[N+](CC)(CC)CCCCc1ccc(Cl)cc1</chem>	CLOFILUM TOSYLATE
SJ000287245	<chem>OCCN1CCN(CC\C=C/2\c3ccccc3Sc4ccc(cc24)C(F)(F)F)CC1</chem>	FLUPENTIXOL
SJ000287247	<chem>Nc1nc(S)c2nen([C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)c2n1</chem>	THIOGUANOSINE
SJ000287256	<chem>Fc1ccc(cc1)C(OCCN2CCN(CCCc3ccccc3)CC2)c4ccc(F)cc4</chem>	GBR 12909 DIHYDROCHLORID E
SJ000287261	<chem>COc1ccc(C[C@H]2NC[C@H](O)[C@H]2OC(=O)C)cc1</chem>	ANISOMYCIN

Figure 24 (continued)

Reg Number	MolSmiles	Synonym
SJ000287270	<chem>C[C@]12C[C@H](O)[C@H]3[C@@H](CC4=CC(=O)CC[C@]34C)[C@@H]1CC[C@@H]2C(=O)CO</chem>	CORTICOSTERONE
SJ000287281	<chem>CC1=CC(=O)c2ccccc2C1=O</chem>	MENADIONE
SJ000287282	<chem>CCCC[C@H](O)\C=C\[C@H]1[C@H](O)C[C@H](O)[C@@H]1C\C=C/CCCC(=O)O</chem>	DINOPROST TROMETAMOL
SJ000287283	<chem>Oc1nc2ccccc2n1CCCN3CCC(CC3)n4c(O)nc5cc(Cl)ccc45</chem>	DOMPERIDONE MALEATE
SJ000287295	<chem>Cc1nnc(O)nc1O</chem>	AZATHYMININE, 6
SJ000287300	<chem>NC(=N)NCc1cccc(I)c1</chem>	IOBENGUANE SULFATE
SJ000287313	<chem>Oc1ccc(cc1)C(=O)N\N=C\c2oc(cc2)[N+](=O)[O-]</chem>	NIFUROXAZIDE
SJ000287314	<chem>COc1ccccc1N2CCN(CCCCNC(=O)c3ccc4ccc4c3)CC2</chem>	DO 897/99
SJ000287317	<chem>CC(C)[C@@]1(NC(=O)[C@@H]2C[C@H]3[C@@H](Cc4c[nH]c5cccc3c45)N(C)C2)O[C@@]6(O)[C@@H]7CCCN7C(=O)[C@H](Cc8ccccc8)N6C1=O</chem>	DIHYDROERGOCRISTINE MESYLATE
SJ000287320	<chem>C[C@@H]1C[C@H]2[C@@H]3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(Cl)[C@@H](O)C[C@]2(C)[C@@]1(OC(=O)c5occc5)C(=O)CCl</chem>	MOMETASONE
SJ000287329	<chem>COc1cc2CCN3Cc4c(C[C@H]3c2cc1O)ccc(O)C)c4O</chem>	SCOULERINE
SJ000287330	<chem>COc1cc(\C=C\C(=O)N2CCC=CC2=O)cc(OC)c1OC</chem>	PIPERLONGUMINE
SJ000287331	<chem>Cc1c2ccncc2c(C)c3c4ccccc4[nH]c13</chem>	ELLIPTICINE
SJ000287333	<chem>C[C@H]1C[C@H]2[C@@H]3C[C@H](F)C4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]2(C)[C@@]1(OC(=O)C)C(=O)COC(=O)C</chem>	DIFLORASONE DIACETATE
SJ000287335	<chem>COc1ccc2[nH]c3C(=NCCc3c2c1)C</chem>	METHOXY-6-HARMALAN
SJ000287348	<chem>C1CN=C(C1)c2ccncc2</chem>	MYOSMINE
SJ000287350	<chem>NCCC(O)C(=O)N[C@@H]1C[C@H](N)[C@@H](OC2O[C@H](CN)[C@@H](O)[C@H](O)[C@H]2N)[C@H](OC3O[C@H](CO)O)[C@H]3O)[C@H]1O</chem>	BUTIROSIN DISULFATE SALT
SJ000287365	<chem>COc1=C(C#N)C(=O)N(C)C=C1</chem>	RICININE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287368	<chem>CC[N+]1(C)[C@@H]2CC[C@H]1CC(C2)OC(=O)[C@H]3CCC(C(=O)OC4[C@H]5CC[C@@H](C4)[N+]5(C)CC)(c6ccccc6)c7ccccc37</chem>	BETA-BELLADONNINE DICHLOROETHYLATE
SJ000287384	<chem>CC[C@]1(CC[C@@H](O1)[C@]2(C)CC[C@]3(C[C@H](O)[C@@H](C)[C@H](O3)[C@@H](C)[C@@H](OC)[C@H](C)C(=O)O)O2)[C@@H]4O[C@H](C[C@@H]4C)[C@H]5O[C@@](O)(CO)[C@H](C)C[C@@H]5C</chem>	MONENSIN SODIUM SALT
SJ000287393	<chem>CCC(=O)OCC(=O)C1(OC(=O)CC)[C@H](C)C[C@H]2[C@@H]3[C@H](Cl)CC4=CC(=O)C=C[C@]4(C)[C@H]3[C@@H](O)C[C@]12C</chem>	ALCLOMETASONE DIPROPIONATE
SJ000287394	<chem>Cc1oncc1C(=O)Nc2ccc(cc2)C(F)(F)F</chem>	LEFLUNOMIDE
SJ000287395	<chem>O[Hg]c1c(O)c(Br)cc2c1Oc3cc(O)c(Br)cc3C24OC(=O)c5ccccc45</chem>	MERBROMIN
SJ000287397	<chem>CC[N+](C)(CC)CCC[n+]1c(c2ccccc2)c3cc(N)ccc3c4ccc(N)cc14</chem>	PROPIDIUM IODIDE
SJ000287398	<chem>CC1CC(CC(C)(C)N1C)OC(=O)C(O)c2ccccc2</chem>	EUCATROPINE HYDROCHLORIDE
SJ000287400	<chem>COc1ccc2Sc3ccccc3N(C[C@H](C)CN(C)C)c2c1</chem>	LEVOMEPRMAZINE
SJ000287409	<chem>CC(C)(C)NC[C@@H](O)COc1ccc2C(=O)CCc12</chem>	LEVOBUNOLOL
SJ000287413	<chem>Fe1ccc(cc1)[C@@H]2CCNC[C@H]2COc3cc4OCc4c3</chem>	PAROXETINE
SJ000287428	<chem>Oc1c(I)cc(Cl)c2ccnc12</chem>	CLIOQUINOL
SJ000287441	<chem>Oc1ccc(OCc2ccccc2)cc1</chem>	MONOBENZONE
SJ000287448	<chem>CCCCCCCCCCCC[N+](C)(C)CCN(Cc1ccc(OC)cc1)c2ncccn2</chem>	THONZONIUM BROMIDE
SJ000287450	<chem>CNCCCC1c2ccccc2C=Cc3ccccc13</chem>	PROTRIPTYLINE
SJ000287457	<chem>OC(=O)CN(CCN(CC(=O)O)CC(=O)O)CCN(CC(=O)O)CC(=O)O</chem>	PENTETIC ACID
SJ000287461	<chem>CS(=O)(=O)c1ccc(cc1)[C@@H](O)[C@@H](CF)NC(=O)C(Cl)Cl</chem>	FLORFENICOL
SJ000287462	<chem>C[C@]12CC[C@H]3[C@@H](CCC4=CC(=O)CC[C@]34C)[C@@H]1CC[C@@H]2C(=O)CO</chem>	DEOXYCORTICOSTERONE
SJ000287467	<chem>C[N+](C)(C)CCCCCCCC[N+](C)(C)C</chem>	DECAMETHONIUM BROMIDE
SJ000287484	<chem>COc1ccc2c(c1)C(=O)N(Cc3ccc(cc3)S(=O)(=O)NC(=O)NC4CCCC4)C(=O)C2(C)C</chem>	GLIQUIDONE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287488	<chem>CCC(=O)O[C@@]1([C@H](C)C[C@H]2[C@@H]3C[C@H](F)C4=CC(=O)C=C[C@]4(C)[C@@]3(F)[C@@H](O)C[C@]12C)C(=O)SCF</chem>	FLUTICASONE PROPIONATE
SJ000287490	<chem>CN(C)[C@H]1[C@@H]2C[C@H]3C(=C(O)[C@]2(O)C(=C(C(=O)NCNC(CCCCN)C(=O)O)C1=O)O)C(=O)c4c(O)cccc4[C@@]3(C)O</chem>	LYMECYCLINE
SJ000287493	<chem>CC(=O)[C@H]1CC[C@H]2[C@@H]3CC[C@H]4C[C@H](O)CC[C@]4(C)[C@H]3C(=O)C[C@]12C</chem>	ALFAXALONE
SJ000287506	<chem>CCCCC[C@H](O)\C=C\[C@H]1[C@H](O)CC(=O)[C@@H]1CCCCCCC(=O)O</chem>	ALPROSTADIL
SJ000287508	<chem>CCC(=O)[C@@]1(C)[C@H](C)C[C@H]2[C@@H]3CCC4=CC(=O)C=C[C@]4(C)[C@H]3[C@@H](O)C[C@]12C</chem>	RIMEXOLONE
SJ000287523	<chem>CCOC(=O)O[C@@]1(CC[C@H]2[C@@H]3CCC4=CC(=O)C=C[C@]4(C)[C@H]3[C@@H](O)C[C@]12C)C(=O)COC(=O)CC</chem>	PREDNICARBATE
SJ000287543	<chem>CC[N+](C)(CC)CCOC(=O)C1c2cccc2Oc3cccc13</chem>	METHANTHELIN BROMIDE
SJ000287544	<chem>OCN1C(NC(=O)NCNC(=O)NC2N(CO)C(=O)NC2=O)C(=O)NC1=O</chem>	IMIDUREA
SJ000287545	<chem>COC(=O)Nc1nc2cc(SC(C)C)ccc2[nH]1</chem>	METHIAZOLE
SJ000287547	<chem>CN1CC[C@]2(C)C1N(C)c3ccc(O)cc23</chem>	ESEROLINE FUMARATE SALT
SJ000287561	<chem>COC(=O)C1C(=CC=C2c3cc4[nH]c(cc5[nH]c(cc6nc(cc(n3)[C@]12C)c(C)c6CCC(=O)O)C(=C5)CCC(=O)O)c(C=C)c4C)C(=O)OC</chem>	VERTEPORFIN
SJ000287562	<chem>CCC(C)N1CCC2(CC1)N=C3C4=C(O)c5c(O)c(C)c6O[C@](C)(O\C=C\[C@H](OC)[C@@H](C)[C@@H](OC(=O)C)[C@H](C)[C@H](O)[C@H](C)[C@@H](O)[C@@H](C)\C=C\C=C(/C)\C(=O)N4)C(=O)c6c5C3=N2</chem>	RIFABUTIN
SJ000287563	<chem>CCCCc1ccc2[nH]c(NC(=O)OC)nc2c1</chem>	PARBENDAZOLE
SJ000287568	<chem>C[C@@H]1C[C@H]2[C@@H]3C[C@H](F)C4=CC(=O)C=C[C@]4(C)[C@@]3(Cl)[C@@H](O)C[C@]2(C)[C@H]1C(=O)COC(=O)C(C)(C)C</chem>	CLOCORTOLONE PIVALATE
SJ000287585	<chem>CC1=C(C)C(=O)C(=C(C)C1=O)CCCC#CCC#CCO</chem>	AA-861

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287590	<chem>CCN(C(C)C)c1nc(N)c(nc1Cl)C(=O)N=C(N)N</chem>	5-(N-ETHYL-N-ISOPROPYL)AMILORIDE
SJ000287618	<chem>CC(C)(C)c1onc(OCP(=O)(O)O)c1CC(N)C(=O)O</chem>	ATPO
SJ000287619	<chem>CC(=O)NCCc1ccc(O)c(O)c1</chem>	N-ACETYLDOPAMINE MONOHYDRATE
SJ000287632	<chem>Nc1ccc(CCNe2ncnc3c2ncn3C4OC(CO)C(O)C4O)cc1</chem>	N6-2-(4-AMINOPHENYL)ETHYLADENOSINE
SJ000287647	<chem>BrC1ccc(\C=C\CNCCNS(=O)(=O)c2cccc3ncC23)cc1</chem>	H-89
SJ000287648	<chem>N[C@@H](CC=C)C(=O)O</chem>	L-ALLYGLYCINE
SJ000287657	<chem>COc1cc(NS(=O)(=O)C)ccc1Nc2c3ccccc3nc4ccccc24</chem>	AMSACRINE
SJ000287660	<chem>C[C@H]1CC2C3CCC4=CC(=O)C=C[C@]4(C)[C@@]3(Cl)[C@@H](O)C[C@]2(C)[C@@]1(O)C(=O)CO</chem>	BECLOMETHASONE
SJ000287663	<chem>C[C@H]1CCC\C=C\C2C[C@H](O)C[C@@]2(O)\C=C\C(=O)O1</chem>	BREFELDIN A
SJ000287667	<chem>Oc1ccc(cc1)c2nc(c3ccc(F)cc3)c([nH]2)c4ccncc4</chem>	SB 202190
SJ000287668	<chem>OC[C@H]1O[C@H](C[C@@H]1O)N2C=C(\C=C\Br)C(=O)NC2=O</chem>	BRIVUDINE
SJ000287676	<chem>CC(C)(C)c1ccc(cc1)S(=O)(=O)\C=C\C#N</chem>	BAY 11-7085
SJ000287677	<chem>Nc1ncnc2c1nc(Br)n2C3OC4COP(=O)(O)O[C@@H]4C3O</chem>	8-BROMO-CAMP SODIUM
SJ000287680	<chem>CC(C)(C)[C@]1(O)CCN2C[C@H]3c4ccccc4CCc5ccc([C@@H]2C1)c35</chem>	BUTACLAMOL HYDROCHLORIDE
SJ000287682	<chem>Oc1ccc2C[C@H]3N(CC=C)CCc4cccc(c34)c2c1O</chem>	R-N-ALLYLNORAPOMOPHINE HYDROBROMIDE
SJ000287686	<chem>NC(=NC(=O)c1nc(Cl)c(N)nc1N)NCc2ccc(Cl)c(Cl)c2</chem>	3',4'-DICHLOROBENZAMIL
SJ000287690	<chem>Oc1[nH]c2ccccc2c1c3[nH]c4ccccc4c3N=O</chem>	INDIRUBIN-3'-OXIME
SJ000287692	<chem>COC(=O)[C@H](NC(=O)c1cc(nc2ccccc12)c3ccccc3)c4ccccc4</chem>	SB 218795
SJ000287693	<chem>\C(=C/C=C/C(=C/C(=O)Nc1ccc(O)cc1)/C)\C=C\C2=C(C)CCCC2(C)C</chem>	RETINOIC ACID P-HYDROXYANILIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287697	<chem>OCCSC1=C(SCCO)C(=O)c2ccccc2C1=O</chem>	NSC 95397
SJ000287703	<chem>OC[C@H]1O[C@H](C(O)[C@H]1O)n2cnc3c(SCc4ccc(cc4)[N+](=O)[O-])ncnc23</chem>	S-(4-NITROBENZYL)-6-THIOINOSINE
SJ000287705	<chem>CC(C)N(CCC(=O)c1ccc2ccccc2c1)Cc3ccccc3</chem>	ZM 39923 HYDROCHLORIDE
SJ000287706	<chem>COc1ccccc1N2CCN(CCCCN(S(=O)(=O)c3ccc4c(cccc34)N(C)C)CC2</chem>	N-(4-[4-(2-METHOXYPHENYL)-PIPERAZIN-1-YL]-BUTYL-5-(DIMETHYLAMINO)-NAPHTALENE-1-SULFONAMIDE
SJ000287714	<chem>CCCCCCCCC=C/CCCCCCCC(=O)NCCc1ccc(O)c(O)c1</chem>	N-OLEOYL DOPAMINE
SJ000287728	<chem>OC[C@H]1O[C@H](C[C@@H]1O)N2C=C(Br)C(=O)NC2=O</chem>	BROMODEOXYURIDINE
SJ000287730	<chem>CC(C)(NC(=O)CBr)[C@H]1CCC[C@](C)(C1)NCC(O)COc2ccccc2CC=C</chem>	BROMOACETYL ALPRENOLOL MENTHANE
SJ000287734	<chem>COc1cccc(OC)c1OCCNCC2CSc3ccccc3O2</chem>	BENOXANTHIAN HYDROCHLORIDE
SJ000287737	<chem>CN(C)S(=O)(=O)c1cc(ccc1C)[N+](=O)[O-]</chem>	BRL 50481
SJ000287741	<chem>COc1ccc2c(c[n+](C)c3c2ccc4cc5OCOc5cc34)c1OC</chem>	CHELERYTHRINE CHLORIDE
SJ000287744	<chem>Cc1cc(NC(=O)Nc2ccc3c(ccn3C)c2)sn1</chem>	SB 204741
SJ000287749	<chem>N[C@@H](CCl)C(=O)O</chem>	BETA-CHLORO-L-ALANINE HYDROCHLORIDE
SJ000287750	<chem>Clc1ccc(cc1)C(c2ccc(Cl)cc2)[n+]3ccn(CC(O)Cc4ccc(Cl)cc4Cl)c5ccc(Cl)cc5Cl)c3</chem>	CALMIDAZOLIUM
SJ000287752	<chem>OC(=O)c1ccc([Hg]Cl)cc1</chem>	4-CHLOROMERCURIBENZOIC ACID
SJ000287758	<chem>CCn1cnc2c(Nc3ccccc3Cl)c3nc(N[C@@H]4CCCC[C@@H]4N)nc12</chem>	CGP-74514A HYDROCHLORIDE
SJ000287762	<chem>CCN(CCCl)Cc1ccccc1Br</chem>	DSP-4 HYDROCHLORIDE
SJ000287767	<chem>CCc1cccc(c1)N(C)C(=N)Nc2ccccc3ccccc23</chem>	CNS-1102
SJ000287768	<chem>CNc1ccc2oc(C[C@H]3O[C@@]4(CC[C@H]3C)O[C@H]([C@H](C)C(=O)c5ccc[nH]5)[C@H](C)C[C@H]4C)nc2c1C(=O)O</chem>	CALCIMYCIN
SJ000287769	<chem>CC1(C2CCC(O2)C1(C)C(=O)O)C(=O)O</chem>	CANTHARIDIC ACID

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287778	<chem>CN1CCN(CC1)c2nc3cc(ccc3n4cccc24)C(F)(F)F</chem>	CGS-12066A MALEATE
SJ000287799	<chem>I1c2ccccc2c3ccccc13</chem>	DIPHENYLENEIODO NIUM CHLORIDE
SJ000287810	<chem>OC[C@H]1O[C@H]([C@H](O)[C@@H]1O)c2nc3cc(Cl)c(Cl)cc3[nH]2</chem>	D- RIBOFURANOSYLB ENZIMIDAZOLE
SJ000287813	<chem>CNCCc1ccc(O)c(O)c1</chem>	N- METHYLDOPAMINE HYDROCHLORIDE
SJ000287814	<chem>Oc1cc2C(CN(CC=C)CCc2c(Cl)c1O)c3ccccc3</chem>	CHLORO-APB HYDROBROMIDE
SJ000287821	<chem>COC1=C(OC)C(=O)c2ccccc2C1=O</chem>	2,3-DIMETHOXY-1,4- NAPHTHOQUINONE
SJ000287827	<chem>COc1cc(cc(OC)c1O)[C@H]2[C@@H]3[C@H](COC3=O)[C@H](O[C@@H]4O[C@@H]5CO[C@@H](C)O[C@@]5(O)C[C@H]4O)c6cc7OCOc7cc26</chem>	ETOPOSIDE
SJ000287837	<chem>Oc1cc2CCNCC(c3ccccc3)c2cc1O</chem>	SKF-38393 HYDROCHLORIDE
SJ000287841	<chem>ClC1=C(Cl)c2ccccc2C(=O)O1</chem>	3,4- DICHLOROISOCO MARIN
SJ000287864	<chem>Oc1c2ccccc2c3N=Nc4cccc1c34</chem>	SP600125
SJ000287868	<chem>CCCCCCCCCCCCCCCC(=O)NCC(COP(=O)(O)OCC[N+](C)(C)C)OCC</chem>	2-ETHOXY-3- OCTADECANAMIDO -1- PROPYLPHOSPHOC HOLINE
SJ000287873	<chem>CCN1C(=O)C=CC1=O</chem>	N- ETHYLMALEIMIDE
SJ000287875	<chem>OC[C@H]1O[C@H]([C@H](O)[C@@H]1O)n2nc3c(N[C@H]4CC5CCC4C5)ncnc23</chem>	ENBA (S)
SJ000287882	<chem>CN(C)c1cc2c(Nc3ccc4c(cnn4Cc5ccccc5)c3)ncnc2n1</chem>	GW 2947
SJ000287889	<chem>COc1cccc2OC[C@H]3CN(CCCCN4C(=O)Nc5c(sc6ncc(nc56)c7ccccc7)C4=O)C[C@H]3c12</chem>	FIDUXOSIN HYDROCHLORIDE
SJ000287891	<chem>CNC(=O)c1cc2c(c[nH]1)nc3ccccc23</chem>	N-METHYL-BETA- CARBOLINE_3- CARBOXAMIDE

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000287899	CCCCCCCCCCCCCCCC(=O)NCC(COP(=O)(O)OCC[N+](C)(C)C)OCC	2-ETHOXY-3-HEXADECANAMID O-1-PROPYLPHOSPHOC HOLINE
SJ000287901	NC(=N)Nc1ccc2[nH]c3[C@@H]4Oc5c(O)cc6C[C@H]7N(CC8CC8)CC[C@@]4(c56)[C@@]7(O)Cc3c2c1	GUANIDINYLNALTRINDOLE DI-TRIFLUOROACETATE
SJ000287902	C(CN1CCN(CCOC(c2ccccc2)c3ccccc3)CC1)Cc4ccccc4	GBR-12935 DIHYDROCHLORIDE
SJ000287925	C[C@@H]1O[C@H](C[C@H](N)[C@@H]1O)O[C@H]2C[C@@](O)(Cc3c(O)c4C(=O)c5ccccc5C(=O)c4c(O)c23)C(=O)C	IDARUBICIN
SJ000287942	OC(=O)Cc1c[nH]c2ccc(O)cc12	5-HYDROXYINDOLACETIC ACID
SJ000287955	C[C@H](N)CN1CCc2ccc(Br)cc12	VER-3323 HEMIFUMARATE SALT
SJ000287956	CC(C)c1cc(F)cc2CC[C@](CCN(C)CCCc3nc4ccccc4[nH]3)(Cc12)OC(=O)C5CC5	NNC 55-0396
SJ000287970	CN[C@@H]1C[C@@H](c2ccc(Cl)c(Cl)c2)c3ccccc13	INDATRALINE HYDROCHLORIDE
SJ000287972	Nc1nnc(c(N)n1)c2ccc(Cl)c2Cl	LAMOTRIGINE
SJ000287975	Fc1ccc(cc1)C(OCCCc2c[nH]cn2)c3ccc(F)cc3	3-(1H-IMIDAZOL-4-YL)PROPYL DI(P-FLUOROPHENYL)METHYL ETHER HYDROCHLORIDE
SJ000287985	O=C1C=C(Oc2c1cccc2c3ccccc3)N4CCOCC4	LY-294,002 HYDROCHLORIDE
SJ000287990	CC1(C)CCC2=C(O1)c3ccccc3C(=O)C2=O	BETA-LAPACHONE
SJ000287995	Cc1cn[nH]c1	FOMEPIZOLE
SJ000288002	COc1cc2[C@H]3CC[C@]4(C)[C@@H](O)C[C@H]4[C@@H]3CCc2cc1O	2-METHOXYESTRADIOL
SJ000288007	COCC(=O)O[C@]1(CCNC(C)CCCc2nc3ccccc3[nH]2)CCc4cc(F)ccc4[C@@H]1C(C)C	MIBEFRADIL HYDROCHLORIDE
SJ000288017	CC[N+](CC)(CC)COc1ccc(C=C)c2ccccc2)c1	MG 624

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000288020	<chem>Oc1ccc2C[C@@H]3C4CCCC[C@]4(CCN3CC=C)c2c1</chem>	LEVALLORPHAN TARTRATE
SJ000288025	<chem>Cc1nc(N=Nc2ccc(cc2)C(=O)O)c(COP(=O)(O)O)c(C=O)c1O</chem>	MRS 2159
SJ000288026	<chem>COc1cc(CNC(=O)CCCCC(C)C)ccc1O</chem>	DIHYDROCAPSAICIN
SJ000288030	<chem>COc1ccc(NC(=O)c2ccc(cc2)c3ccc(cc3C)c4ncc(C)n4)cc1N5CCN(C)CC5</chem>	GR 127935 HYDROCHLORIDE
SJ000288031	<chem>Clc1ccc(cc1)N2CCN(Cc3c[nH]c4ncccc34)CC2</chem>	L-745,870
SJ000288034	<chem>[O-][N+](=O)c1ccc(Cl)c(c1)C(=O)Nc2ccccc2</chem>	GW9662
SJ000288037	<chem>CC(C)[C@H]1[C@@H]2C[C@@H]3Cc4c(cc(O)c4C(=C3C(=O)[C@]2(O)C(=C(C(=O)N)C1=O)O)O)N(C)C</chem>	MINOCYCLINE
SJ000288041	<chem>[O-]S(=O)(=O)c1cc(c2c(NC(=O)c3cccc(NC(=O)Nc4cccc(c4)C(=O)Nc5ccc(c6cc(cc56)S(=O)(=O)[O-])S(=O)(=O)[O-])S(=O)(=O)[O-])c3)ccc(c2c1)S(=O)(=O)[O-]S(=O)(=O)[O-]</chem>	NF 023
SJ000288052	<chem>OC1C(CC(=O)O)CCc2ccccc12</chem>	NCS-382
SJ000288058	<chem>C[C@@H]1O[C@H](C[N+](C)(C)C)[C@H]1O</chem>	MUSCARINE CHLORIDE
SJ000288059	<chem>Nc1on[n+](c1)N2CCOCC2</chem>	3- MORPHOLINOSYDN ONIMINE HYDROCHLORIDE
SJ000288063	<chem>COc1ccccc1CNCCCCCNCCCCCCCNC CCCCNCc2ccccc2OC</chem>	METHOCTRAMINE TETRAHYDROCHLO RIDE
SJ000288073	<chem>C[C@H](Cc1ccc(O)c(O)c1)[C@@H](C)Cc2ccc(O)c(O)c2</chem>	MASOPROCOL
SJ000288074	<chem>NC(=O)C1=CN(C=CC1)C2OC(COP(=O)(O)OP(=O)(O)OC[C@H]3O[C@H](C(OP(=O)(O)O)[C@H]3O)n4cnc5c(N)nnc45)C(O)C2O</chem>	NADPH TETRASODIUM
SJ000288081	<chem>CCCCCCC=C/CCCCCCCC(=O)O</chem>	OLEIC ACID
SJ000288084	<chem>S=C(Nc1ccccc1)Nc2nccs2</chem>	1-PHENYL-3-(2- THIAZOLYL)-2- THIOUREA
SJ000288092	<chem>Oc1cc(O)cc(\C=C\c2ccc(O)c(O)c2)c1</chem>	PICEATANNOL

Figure 24 (continued)

Reg Number	Molsmiles	Synonym
SJ000288093	<chem>CC(=C)[C@@H]1[C@H]2OC(=O)[C@@H]1[C@]3(O)C[C@H]4O[C@]45C(=O)O[C@H]2[C@]35C.CC(C)(O)[C@@H]6[C@H]7OC(=O)[C@@H]6[C@]8(O)C[C@H]9O[C@]9%10C(=O)O[C@H]7[C@]8%10C</chem>	PICROTOXIN
SJ000288098	<chem>Oc1nc2ccccc2n1CCCN3CCN(CC3)C(c4cccc4)c5ccccc5</chem>	OXATOMIDE
SJ000288099	<chem>[O-][n+]1onc(c2ccccc2)c1C#N</chem>	4-PHENYL-3-FUROXAN CARBONITRILE
SJ000288114	<chem>C[C@H](Cc1ccccc1)Nc2ncnc3c2ncn3[C@@H]4O[C@H](CO)[C@H](O)C4O</chem>	R-N6-(2-PHENYLISOPROPYL)ADENOSINE
SJ000288126	<chem>c1enc2c(c1)ccc3ccnc23</chem>	1,10-PHENANTHROLINE MONOHYDRATE
SJ000288139	<chem>NCC#Cc1ccccc1</chem>	3-PHENYLPROPARGYLAMINE HYDROCHLORIDE
SJ000288140	<chem>COc1cc(OC)c(\C=C/2\C(=O)Nc3ccccc23)c(OC)c1</chem>	IC 261
SJ000288147	<chem>SC(=S)N1CCCC1</chem>	PYRROLIDINE-1-CARBODITHIOIC ACID
SJ000288150	<chem>C[C@]12CCC(=O)C=C1CC[C@@H]3[C@@H]2CC[C@@]4(C)[C@H]3CC[C@]4(O)C(=O)CO</chem>	CORTEXOLONE MALEATE
SJ000288156	<chem>CCCCCCCCCCCCCCCCCNC(=O)OCC(COP(=O)(O)OCC[n+]1ccsc1)OC</chem>	CV-3988
SJ000288159	<chem>NC1CCN(CC1)c2cccc(Cl)n2</chem>	SR 57227A
SJ000288163	<chem>C\N=C/1/SN(C(=N1)c2ccccc2)c3ccccc3</chem>	SCH-202676
SJ000288173	<chem>CC(C)COC(=O)OCN1C(=O)CN(CCN2CC(=O)N(COC(=O)OCC(C)C(=O)C2)CC1=O</chem>	SOBUZOXANE
SJ000288175	<chem>CC(=O)NNC(=O)N1Cc2ccccc2Oc3ccc(Cl)cc13</chem>	SC 19220
SJ000288176	<chem>COc1ccc(CCCOc2cc(CCN3ccnc3)ccc2OC)cc1</chem>	SKF 96365
SJ000288181	<chem>CCCC[N+](C)C2CC(CCN1C3OC23)OC(=O)[C@H](CO)c4ccccc4</chem>	SCOPOLAMINE, N-BUTYL-, BROMIDE
SJ000288182	<chem>Cc1cc(C)c(\C=C/2\C(=O)Nc3ccccc23)[nH]1</chem>	SEMAXANIB

Figure 24 (continued)

Reg Number	Mol smiles	Synonym
SJ000288186	<chem>CCCCCCCCCCCCCCCC(=O)OC(CC(=O)O)C[N+](C)(C)C</chem>	DL-STEAROYL CARNITINE CHLORIDE
SJ000288194	<chem>CCc1cccc1OC[C@@H](O)CN[C@H]2CCc3cccc3C2</chem>	SR 59230A OXALATE
SJ000288209	<chem>CCCCCCCCCCCCCCCCSCC(=O)O</chem>	TETRADECYLTHIO ACETIC ACID
SJ000288210	<chem>Cc1ccc(cc1)S(=O)(=O)N[C@@H](Cc2cccc2)C(=O)CC1</chem>	S-N-(4-CHLORO-3- OXO-1- PHENYLBUTAN-2- YL)-4- METHYLBENZENE SULFONAMIDE
SJ000288211	<chem>Oc1ccc(\C=C(/C#N)\C(=O)NCCCc2cccc2)cc1O</chem>	TYRPHOSTIN AG 555
SJ000288216	<chem>COc1cc2CCN3C(=O)N(C)\C(=N\c4c(C)cc(C)cc4C)\C=C3c2cc1OC</chem>	TREQUINSIN HYDROCHLORIDE
SJ000288219	<chem>Oc1ccc(\C=C(/C#N)\C(=O)NCCCc2cccc2)cc1O</chem>	TYRPHOSTIN AG 698
SJ000288224	<chem>CN1CCC2(CC1)COc3cc4CCN(C(=O)c5ccc(cc5)c6ccc(cc6C)c7noc(C)n7)c4cc23</chem>	SB 224289 HYDROCHLORIDE
SJ000288226	<chem>CC(C)(C)c1cc(\C=C(/C#N)\C(=S)N)cc(c1O)C(C)(C)C</chem>	TYRPHOSTIN AG 879
SJ000288238	<chem>CC(COc1ccc(\C=C\c2cccc2)cc1)[N+](C)(C)C</chem>	N,N,N-TRIMETHYL- 1-(4-TRANS- STILBENOXY)-2- PROPYLAMMONIUM IODIDE
SJ000288244	<chem>CCC1(O)CC2CN(CCC3c([nH]c4cccc34)[C@@](C2)(C(=O)OC)c5ccc6(cc5OC)N(C=O)C7[C@](O)([C@H](OC(=O)C)[C@]8(CC)C=CCN9CC[C@]67[C@H]89)C(=O)OC)C1</chem>	VINCRIStINE
SJ000288246	<chem>COC(=O)C1=C(c2cc(OC)c(OC)c(OC)c2)c3cnc(OCc4nccn4)c3C(=O)N1Cc5ccnc(C)c5</chem>	T-0156
SJ000288249	<chem>Brc1c(NC2=NCCN2)ccc3ncnc13</chem>	BRIMONIDINE
SJ000288262	<chem>C[C@@H](Oc1ccc(Oc2cnc3ccc(Cl)cc3n2)cc1)C(=O)O[Na]</chem>	XK469
SJ000288270	<chem>COC[C@H]1OC(=O)c2coc3C(=O)C4=C([C@@H](C[C@@]5(C)C4CCC5=O)OC(=O)C)[C@]1(C)c23</chem>	WORTMANNIN
SJ000288274	<chem>CC(C)(C)c1cc(C=C(C#N)C#N)cc(c1O)C(C)(C)C</chem>	TYRPHOSTIN A9

Figure 24 (continued)

Reg Number	Mol smiles	Synonym
SJ000288278	<chem>CCCCCCCC(=O)O[C@@H]1[C@@H](OC(=O)\C(=C/C)\C)C(=C2[C@@H]3OC(=O)[C@@](C)(O)[C@@]3(O)[C@H](C[C@](C)(O)C(=O)C)[C@@H]12)OC(=O)CCC)C</chem>	THAPSIGARGIN
SJ000288284	<chem>CCCC\C=C/CC(O)\C=C\c1cccc(CC(O)CCCO)n1</chem>	U-75302
SJ000288304	<chem>CCCCN1C2CCC1CC(C2)OC(c3ccc(F)cc3)c4ccc(F)cc4</chem>	JHW 007 HYDROCHLORIDE
SJ000288306	<chem>CC[n+]1c(\C=C\C=C/2\N(C)c3ccccc3C2(C)C)sc4ccccc14</chem>	AC-93253
SJ000288308	<chem>Nc1ccc(cc1)c2nc3cc(ccc3[nH]2)c4nc5cc(N)ccc5[nH]4</chem>	RO 90-7501
SJ000288312	<chem>Oc1[nH]c2cc(Br)ccc2c1c3[nH]c4ccccc4c3N=O</chem>	BIO
SJ000288313	<chem>COc1ccc(CN=O)c(c1)C(=O)CCNC(=O)C</chem>	AFMK
SJ000288316	<chem>CCN(CCCl)CCOC(=O)C</chem>	ACETYLCHOLINE MUSTARD HYDROCHLORIDE
SJ000288318	<chem>C1COc2c(O1)cccc2N3CCN(CC3)C4Cc5cccc5C4</chem>	S15535
SJ000288320	<chem>COc1ccc2NC(=O)\C(=C/c3c[nH]cn3)\c2c1</chem>	SU 9516
SJ000288325	<chem>NS(=O)(=O)C#Cc1ccccc1</chem>	PIFITHRIN-MU
SJ000288326	<chem>CC(C)Cn1enc2c(N)nc3ccccc3c12</chem>	IMIQUIMOD
SJ000288327	<chem>CCCCCCCCc1ccc(cc1)c2ccc(cc2)C(=O)O</chem>	AC-55649
SJ000288328	<chem>Nc1[nH]enc2nnc(Nc3ccc(F)cc3)c12</chem>	CGP 57380
SJ000518967	<chem>CC1CCC2C(C)C(O)OC3OC4(C)CCC1C23OO4</chem>	DIHYDROARTEMISININ
SJ000518972	<chem>CC1CCC2C(C)C(OC(=O)CCC(=O)O)OC3OC4(C)CCC1C23OO4</chem>	ARTESUNATE

Figure 24 (continued)

Agent	WT EC50	WT EC50CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50CI	T3151 Curve Score	T3151 Act Class
CYTARABINE	0.0639	0.0425 - 0.0961	A113	HIGH	0.0603	0.0355 - 0.1023	A113	HIGH
MELPHALAN	>5	NA	C555	WEAK	3.9408	NA	C555	WEAK
MERCAPTOPURINE	0.0211	0.0013 - 0.3518	A111	HIGH	0.0444	0.0342 - 0.0575	B110	HIGH
METHOTREXATE	0.0225	0.0014 - 0.3699	A111	HIGH	0.0438	0.0316 - 0.0606	A112	HIGH
THIOGUANINE	0.0441	0.0248 - 0.0786	B110	HIGH	0.0202	0.0010 - 0.4084	B110	HIGH
AMENOPTINE	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
AZACITIDINE	1.2936	0.9338 - 1.7920	B311	WEAK	1.2871	0.8082 - 2.0498	B311	WEAK
EIOPOSIDE	0.1369	0.1148 - 0.1632	A212	MED	0.1368	0.1164 - 0.1608	A212	MED
MITOXANTRONE	0.0433	0.0348 - 0.0539	A112	HIGH	0.044	0.0361 - 0.0536	A112	HIGH
HYDROCORTISONE	0.1905	0.1782 - 0.2036	A212	MED	0.19	0.1788 - 0.2020	A212	MED
PREDNISOLONE	0.1573	0.1495 - 0.1654	A212	MED	0.1541	0.1406 - 0.1689	A212	MED
DEXAMETHASONE	<0.1	0.0039 - 4.1318	B110	HIGH	0.0374	0.0102 - 0.1371	B110	HIGH
AMSACRINE	0.0861	0.0767 - 0.0967	A112	HIGH	0.0747	0.0627 - 0.0889	A112	HIGH
IDARUBICIN	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
VINCRIStINE	0.1045	0.0914 - 0.1194	A213	MED	0.1311	0.0021 - 8.2851	A214	MED

Figure 25

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000000250	>5	NA	B241	INACTIVE	>5	NA	D555	INACTIVE
SJ000000854	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000113084	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000126662	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285182	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285183	0.221	0.1535 - 0.3190	A211	MED	0.21	0.1479 - 0.2981	A212	MED
SJ000285185	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285188	0.064	0.0425 - 0.0961	A113	HIGH	0.0603	0.0355 - 0.1023	A113	HIGH
SJ000285190	0.793	0.7229 - 0.8703	A212	MED	0.7231	0.6469 - 0.8083	A212	MED
SJ000285193	2.103	2.0841 - 2.1214	B313	WEAK	2.285	2.2763 - 2.2937	B313	WEAK
SJ000285194	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285194	>5	NA	C555	WEAK	3.9408	NA	C555	WEAK
SJ000285195	0.021	0.0013 - 0.3518	A111	HIGH	0.0444	0.0342 - 0.0575	B110	HIGH
SJ000285196	0.023	0.0014 - 0.3699	A111	HIGH	0.0438	0.0316 - 0.0606	A112	HIGH
SJ000285197	0.15	0.1248 - 0.1800	A212	MED	0.1542	0.1235 - 0.1926	A212	MED
SJ000285200	1.203	0.8162 - 1.7718	B311	WEAK	1.1389	0.8043 - 1.6128	B311	WEAK
SJ000285202	1.834	1.7982 - 1.8703	B313	WEAK	1.7597	1.6984 - 1.8232	A313	WEAK
SJ000285203	<0.1	NA	B110	HIGH	0.0824	0.0695 - 0.0978	A111	HIGH
SJ000285206	>5	NA	NC555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285207	0.404	0.3822 - 0.4278	A213	MED	0.4118	0.3793 - 0.4471	A213	MED
SJ000285208	0.044	0.0248 - 0.0786	B110	HIGH	0.0202	0.0010 - 0.4084	B110	HIGH
SJ000285210	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285212	1.628	1.5516 - 1.7085	A313	WEAK	1.7678	1.7312 - 1.8052	B313	WEAK
SJ000285215	1.048	0.8816 - 1.2467	A313	WEAK	1.0426	0.8815 - 1.2333	A313	WEAK
SJ000285215	0.055	0.0513 - 0.0594	A113	HIGH	0.0527	0.0477 - 0.0583	A113	HIGH
SJ000285218	>5	NA	B332	INACTIVE	>5	NA	C555	INACTIVE
SJ000285219	2.084	2.0004 - 2.1703	B312	WEAK	1.7397	1.5755 - 1.9210	B312	WEAK

Figure 26

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285219	2.939	2.8596 - 3.0208	B312	WEAK	2.8605	2.7902 - 2.9326	B312	WEAK
SJ000285220	>5	NA	C555	WEAK	2.8062	0.5197 - 15.1529	B314	WEAK
SJ000285221	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285225	0.161	0.1521 - 0.1698	A212	MED	0.1603	0.1544 - 0.1665	A213	MED
SJ000285226	>5	NA	B130	INACTIVE	>5	NA	A231	INACTIVE
SJ000285227	1.294	0.9338 - 1.7920	B311	WEAK	1.2871	0.8082 - 2.0498	B311	WEAK
SJ000285228	0.334	0.3149 - 0.3551	A211	MED	0.4033	0.3922 - 0.4148	A211	MED
SJ000285229	1.976	1.9316 - 2.0207	B322	WEAK	1.9622	1.8651 - 2.0644	B322	WEAK
SJ000285231	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285232	0.117	0.1002 - 0.1366	A213	MED	0.1133	0.0999 - 0.1285	A213	MED
SJ000285232	0.062	0.0351 - 0.1092	A114	HIGH	0.0566	0.0444 - 0.0721	A114	HIGH
SJ000285234	0.323	0.2286 - 0.4550	A211	MED	0.3737	0.3442 - 0.4058	A211	MED
SJ000285235	0.137	0.1148 - 0.1632	A212	MED	0.1368	0.1164 - 0.1608	A212	MED
SJ000285238	0.102	0.0880 - 0.1188	A213	MED	0.1214	0.0955 - 0.1542	A214	MED
SJ000285241	0.157	0.1188 - 0.2071	B110	MED	0.1024	0.0737 - 0.1421	A211	MED
SJ000285242	4.469	NA	C555	WEAK	>5	NA	C555	INACTIVE
SJ000285243	0.48	0.4327 - 0.5325	A213	MED	0.4074	0.3682 - 0.4508	A213	MED
SJ000285244	1.512	1.4902 - 1.5347	A313	WEAK	1.7214	1.6838 - 1.7597	A313	WEAK
SJ000285246	0.823	0.6899 - 0.9806	A212	MED	0.9896	0.8088 - 1.2108	A212	MED
SJ000285249	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285256	0.334	0.2737 - 0.4077	A212	MED	0.3286	0.2649 - 0.4076	A212	MED
SJ000285261	0.234	0.1932 - 0.2840	A213	MED	0.2457	0.1708 - 0.3535	A214	MED
SJ000285262	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000285263	>5	NA	D555	INACTIVE	>5	NA	A241	INACTIVE
SJ000285267	0.085	0.0560 - 0.1301	A112	HIGH	0.1561	0.1245 - 0.1956	A212	MED
SJ000285270	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285272	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285273	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285276	4.052	NA	C555	WEAK	3.1302	2.9524 - 3.3187	B312	WEAK
SJ000285278	<1.0	NA	C555	MED	<1.0	NA	C555	MED
SJ000285279	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285285	>5	NA	B141	INACTIVE	>5	NA	B241	INACTIVE
SJ000285292	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000285294	0.074	0.0659 - 0.0830	A113	HIGH	0.0742	0.0666 - 0.0828	A113	HIGH
SJ000285299	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285307	>5	NA	B344	INACTIVE	>5	NA	B334	INACTIVE
SJ000285308	0.546	0.5060 - 0.5886	A213	MED	0.5062	0.4281 - 0.5985	A213	MED
SJ000285313	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285315	1.056	1.0324 - 1.0803	B312	WEAK	0.7384	0.6862 - 0.7946	A212	MED
SJ000285316	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285317	>5	NA	NC555	INACTIVE	3.8254	NA	C555	WEAK
SJ000285318	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285319	1.741	1.6595 - 1.8256	A314	WEAK	2.0096	1.9300 - 2.0925	B314	WEAK
SJ000285321	0.043	0.0348 - 0.0539	A112	HIGH	0.044	0.0361 - 0.0536	A112	HIGH
SJ000285323	>5	NA	B332	INACTIVE	>5	NA	B321	INACTIVE
SJ000285327	1.653	1.6211 - 1.6851	A313	WEAK	1.8204	1.7962 - 1.8449	B313	WEAK
SJ000285332	0.152	0.1256 - 0.1826	A212	MED	0.2075	0.1841 - 0.2338	A212	MED
SJ000285334	>5	NA	C555	INACTIVE	0	NA	C555	INACTIVE
SJ000285335	0.067	0.0196 - 0.2261	A114	HIGH	0.0687	0.0028 - 1.6949	A114	HIGH
SJ000285335	0.139	0.0008 - 22.9222	A214	MED	0.1244	0.0676 - 0.2290	A214	MED
SJ000285337	>5	NA	B342	INACTIVE	>5	NA	D555	INACTIVE
SJ000285337	>5	NA	B140	INACTIVE	>5	NA	A241	INACTIVE
SJ000285338	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285343	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T315I EC50	T315I EC50 CI	T315I Curve Score	T315I Act Class
SJ000285358	0.191	0.1782 - 0.2036	A212	MED	0.19	0.1788 - 0.2020	A212	MED
SJ000285363	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285364	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285365	2.293	1.1080 - 4.7433	B321	WEAK	>5	NA	B334	INACTIVE
SJ000285368	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000285369	>5	NA	C555	WEAK	3.9664	NA	B313	WEAK
SJ000285373	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285375	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285382	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285383	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285387	>5	NA	NC555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285396	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285400	>5	NA	B342	INACTIVE	>5	NA	B344	INACTIVE
SJ000285410	0.03	0.0268 - 0.0342	A113	HIGH	0.0276	0.0238 - 0.0319	B110	HIGH
SJ000285413	0.964	0.8101 - 1.1461	A214	MED	2.5855	NA	C555	WEAK
SJ000285423	0.94	0.8608 - 1.0260	A212	MED	0.9064	0.7444 - 1.1035	A212	MED
SJ000285426	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285431	>5	NA	D555	INACTIVE	>5	NA	NBI42	INACTIVE
SJ000285433	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285436	1.178	1.1246-1.2303	A322	WEAK	1.183	1.1246-1.2445	A322	WEAK
SJ000285439	>5	NA	C555	INACTIVE	>5	NA	B313	INACTIVE
SJ000285440	2.613	2.3056 - 2.9611	B312	WEAK	1.7108	1.0736 - 2.7263	B311	WEAK
SJ000285442	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285443	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285445	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285450	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000285451	1.578	1.1606 - 2.1448	B321	WEAK	4.852	NA	C555	WEAK

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T315I EC50	T315I EC50 CI	T315I Curve Score	T315I Act Class
SJ000285452	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285452	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285453	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285454	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285460	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285461	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285462	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285465	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285466	0.174	0.1186 - 0.2559	A211	MED	0.1286	0.0965 - 0.1716	B110	MED
SJ000285484	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285487	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285490	1.551	1.5019 - 1.6022	A313	WEAK	>5	NA	B333	INACTIVE
SJ000285502	>5	NA	B342	INACTIVE	>5	NA	C555	INACTIVE
SJ000285504	>5	NA	C555	INACTIVE	>5	NA	A241	INACTIVE
SJ000285506	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285508	0.216	0.1969 - 0.2377	A213	MED	0.2332	0.2081 - 0.2613	A213	MED
SJ000285512	3.558	3.5015 - 3.6156	B313	WEAK	4.287	NA	C555	WEAK
SJ000285522	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285526	>5	NA	A241	INACTIVE	>5	NA	B241	INACTIVE
SJ000285536	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285540	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285541	0.157	0.1495 - 0.1654	A212	MED	0.1541	0.1406 - 0.1689	A212	MED
SJ000285542	0.135	0.1233 - 0.1468	A212	MED	0.1274	0.1191 - 0.1363	A212	MED
SJ000285543	>5	NA	A242	INACTIVE	>5	NA	B331	INACTIVE
SJ000285544	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285547	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285549	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285551	>5	NA	C555	INACTIVE	>5	NA	A242	INACTIVE
SJ000285554	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285564	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285569	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285572	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285572	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285574	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285577	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285584	>5	NA	C555	INACTIVE	>5	NA	B141	INACTIVE
SJ000285586	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285587	0.202	0.0239 - 1.7053	A211	MED	0.2793	0.0259 - 3.0073	A211	MED
SJ000285588	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000285591	>5	NA	C555	WEAK	3.2243	2.9841 - 3.4838	B312	WEAK
SJ000285592	>5	NA	C555	INACTIVE	>5	NA	B344	INACTIVE
SJ000285606	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285608	>5	NA	A241	INACTIVE	>5	NA	B341	INACTIVE
SJ000285608	>5	NA	C555	INACTIVE	>5	NA	B341	INACTIVE
SJ000285610	>5	NA	C555	INACTIVE	>5	NA	B344	INACTIVE
SJ000285614	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285618	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285619	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285625	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285630	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285635	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285638	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285643	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285646	0.212	0.1898 - 0.2367	A212	MED	0.1965	0.1746 - 0.2213	A212	MED

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285651	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285652	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285655	>5	NA	B243	INACTIVE	>5	NA	B241	INACTIVE
SJ000285657	0.125	0.1140 - 0.1376	A212	MED	0.125	0.1179 - 0.1324	A212	MED
SJ000285659	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285664	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285666	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285667	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285668	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285671	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000285674	>5	NA	A241	INACTIVE	>5	NA	B241	INACTIVE
SJ000285678	>5	NA	B141	INACTIVE	>5	NA	C555	INACTIVE
SJ000285683	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285684	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285686	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285687	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285688	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285689	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285692	0.04	0.0322 - 0.0495	A112	HIGH	0.0358	0.0302 - 0.0424	A113	HIGH
SJ000285695	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285696	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285704	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285710	1.454	1.3330 - 1.5866	A312	WEAK	1.2069	1.1588 - 1.2569	A313	WEAK
SJ000285712	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285713	>5	NA	C555	INACTIVE	>5	NA	B314	INACTIVE
SJ000285715	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T315I EC50	T315I EC50 CI	T315I Curve Score	T315I Act Class
SJ000285718	2.971	2.5382 - 3.4763	B322	WEAK	>5	NA	B322	INACTIVE
SJ000285725	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285727	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285728	0.035	0.0313 - 0.0390	B110	HIGH	0.0363	0.0314 - 0.0420	A112	HIGH
SJ000285729	<0.1	0.0039 - 4.1318	B110	HIGH	0.0374	0.0102 - 0.1371	B110	HIGH
SJ000285740	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285742	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285745	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285747	0.138	0.1316 - 0.1452	A213	MED	0.1465	0.1407 - 0.1526	A213	MED
SJ000285748	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285750	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000285752	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285761	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285764	4.19	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000285766	0.044	0.0401 - 0.0487	B110	HIGH	0.046	0.0427 - 0.0495	A113	HIGH
SJ000285767	0.021	0.0184 - 0.0249	B110	HIGH	0.0255	0.0228 - 0.0285	A113	HIGH
SJ000285768	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285769	0.041	0.0358 - 0.0459	A112	HIGH	0.0434	0.0403 - 0.0468	A113	HIGH
SJ000285770	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285778	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285781	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285783	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285786	0.131	0.0938 - 0.1821	A212	MED	0.1136	0.0838 - 0.1538	A213	MED
SJ000285787	0.818	0.7921 - 0.8455	A213	MED	0.8671	0.8509 - 0.8837	A213	MED
SJ000285787	0.557	0.5418 - 0.5729	A213	MED	0.5282	0.5051 - 0.5523	A213	MED
SJ000285790	2.509	2.4752 - 2.5439	B313	WEAK	2.9331	2.8664 - 3.0014	B313	WEAK
SJ000285797	>5	NA	A243	INACTIVE	>5	NA	C555	INACTIVE
SJ000285801	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T315I EC50	T315I EC50 CI	T315I Curve Score	T315I Act Class
SJ000285812	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000285814	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285814	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285818	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285820	0.042	0.0213 - 0.0814	A111	HIGH	0.0512	0.0395 - 0.0664	A112	HIGH
SJ000285827	1.568	1.1031 - 2.2285	B311	WEAK	>5	NA	C555	WEAK
SJ000285831	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285834	>5	NA	B341	INACTIVE	>5	NA	D555	INACTIVE
SJ000285835	>5	NA	C555	INACTIVE	>5	NA	B244	INACTIVE
SJ000285836	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285837	>5	NA	B313	INACTIVE	>5	NA	C555	INACTIVE
SJ000285838	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285840	0.919	0.8184 - 1.0322	A214	MED	0.8819	0.8216 - 0.9466	A214	MED
SJ000285842	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285845	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285849	0.444	0.3978 - 0.4944	A212	MED	0.4338	0.3884 - 0.4846	A212	MED
SJ000285858	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285860	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285864	1.213	1.1502 - 1.2785	A313	WEAK	1.3427	1.2789 - 1.4096	A313	WEAK
SJ000285866	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285878	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285879	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285880	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285881	3.105	2.9783 - 3.2377	B312	WEAK	2.3759	2.3476 - 2.4045	B313	WEAK
SJ000285882	>5	NA	A242	INACTIVE	>5	NA	C555	INACTIVE
SJ000285885	>5	NA	NA241	INACTIVE	>5	NA	D555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285887	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285888	>5	NA	C555	WEAK	>5	NA	B313	WEAK
SJ000285890	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285892	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285903	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000285909	>5	NA	A242	INACTIVE	>5	NA	D555	INACTIVE
SJ000285920	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000285922	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285925	>5	NA	B241	INACTIVE	>5	NA	D555	INACTIVE
SJ000285935	>5	NA	C555	INACTIVE	>5	NA	B344	INACTIVE
SJ000285936	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285940	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285949	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285950	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285951	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000285958	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285959	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000285960	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285965	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285966	1.297	0.7065 - 2.3798	A314	WEAK	2.0144	1.9973 - 2.0317	B312	WEAK
SJ000285967	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000285971	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285972	4.208	NA	C555	WEAK	2.4586	2.4189 - 2.4989	B312	WEAK
SJ000285973	0.17	0.1572 - 0.1833	A212	MED	0.1623	0.1542 - 0.1709	A212	MED
SJ000285974	0.086	0.0767 - 0.0967	A112	HIGH	0.0747	0.0627 - 0.0889	A112	HIGH
SJ000285978	0.221	0.1336 - 0.3662	A211	MED	0.1961	0.1048 - 0.3669	A211	MED
SJ000285980	4.293	NA	C555	WEAK	3.3236	3.1759 - 3.4782	B312	WEAK

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000285983	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285987	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285991	1.105	0.7753 - 1.5756	B311	WEAK	0.7808	0.7463 - 0.8169	A212	MED
SJ000285996	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000285998	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000285999	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286003	0.727	0.2263 - 2.3376	A211	MED	0.3626	0.3272 - 0.4017	A211	MED
SJ000286004	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286006	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000286007	1.006	0.8964 - 1.1294	A313	WEAK	0.9628	0.8199 - 1.1308	A212	MED
SJ000286008	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286018	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286024	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286025	>5	NA	C555	INACTIVE	>5	NA	B332	INACTIVE
SJ000286030	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000286034	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000286035	>5	NA	D555	INACTIVE	>5	NA	B341	INACTIVE
SJ000286036	>5	NA	B143	INACTIVE	>5	NA	C555	INACTIVE
SJ000286037	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286038	0.093	0.0858 - 0.1010	A113	HIGH	0.0782	0.0723 - 0.0846	A113	HIGH
SJ000286038	0.051	0.0445 - 0.0581	A113	HIGH	0.0578	0.0515 - 0.0649	A113	HIGH
SJ000286039	0.024	0.0179 - 0.0317	B110	HIGH	0.021	0.0145 - 0.0303	B110	HIGH
SJ000286041	>5	NA	B141	INACTIVE	>5	NA	B341	INACTIVE
SJ000286044	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286046	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286046	>5	NA	C555	INACTIVE	>5	NA	A241	INACTIVE
SJ000286052	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286053	>5	NA	B332	INACTIVE	>5	NA	B321	INACTIVE
SJ000286056	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286057	>5	NA	C555	WEAK	2.4313	2.4033 - 2.4597	B312	WEAK
SJ000286063	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000286065	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286075	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286086	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286093	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286097	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286098	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286101	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286109	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286112	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000286113	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286118	>5	NA	D555	INACTIVE	>5	NA	A344	INACTIVE
SJ000286121	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286124	>5	NA	C555	INACTIVE	>5	NA	B341	INACTIVE
SJ000286127	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286128	0.47	0.3938 - 0.5597	A213	MED	0.4789	0.3911 - 0.5864	A213	MED
SJ000286133	>5	NA	C555	INACTIVE	>5	NA	B343	INACTIVE
SJ000286134	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286142	0.472	0.4465 - 0.4984	A213	MED	0.4944	0.4672 - 0.5231	A212	MED
SJ000286143	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286144	1.232	1.1244 - 1.3489	B312	WEAK	1.1138	0.9772 - 1.2695	B312	WEAK
SJ000286146	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286151	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286152	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000286154	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000286155	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000286156	1.038	0.8985 - 1.1994	A313	WEAK	1.0097	0.8164 - 1.2487	A313	WEAK
SJ000286159	0.289	0.2448 - 0.3404	A212	MED	0.3018	0.2554 - 0.3567	A212	MED
SJ000286160	0.459	0.3777 - 0.5586	A211	MED	0.3036	0.2841 - 0.3245	A213	MED
SJ000286162	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286166	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286172	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286174	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286175	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286178	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286181	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286185	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286186	2.415	2.3733 - 2.4579	B313	WEAK	2.4276	1.7583 - 3.3517	B314	WEAK
SJ000286187	0.943	0.8364 - 1.0635	A213	MED	0.9116	0.8686 - 0.9568	A213	MED
SJ000286188	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286191	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286195	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286199	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE
SJ000286204	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286205	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000286213	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286217	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286225	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286229	>5	NA	A242	INACTIVE	>5	NA	A241	INACTIVE
SJ000286231	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286236	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286243	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286248	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286251	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286267	>5	NA	C555	WEAK	4.6918	NA	C555	WEAK
SJ000286300	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000286312	>5	NA	C555	INACTIVE	>5	NA	B344	INACTIVE
SJ000286359	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286366	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286380	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286381	0.179	0.1603 - 0.2003	A222	MED	0.329	0.0988 - 1.0953	A234	MED
SJ000286382	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286387	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286389	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286393	4.618	NA	C555	WEAK	>5	NA	C555	INACTIVE
SJ000286395	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286396	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286398	2.056	1.9918 - 2.1214	B313	WEAK	2.928	2.8242 - 3.0356	B312	WEAK
SJ000286406	0.953	0.9390 - 0.9676	A213	MED	1.0358	0.9951 - 1.0783	A312	MED
SJ000286408	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286413	>5	NA	C555	WEAK	3.4496	3.4248 - 3.4745	B313	WEAK
SJ000286415	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286419	>5	NA	B241	INACTIVE	>5	NA	D555	INACTIVE
SJ000286421	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286423	2.032	1.9745 - 2.0914	B314	WEAK	2.0036	1.9296 - 2.0805	B314	WEAK
SJ000286424	0.314	0.1913 - 0.5154	A221	MED	0.7253	0.6854 - 0.7675	A212	MED
SJ000286430	>5	NA	C555	WEAK	>5	NA	C555	WEAK

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286434	1.532	1.6097 - 1.6345	B313	WEAK	1.4706	1.3664 - 1.5827	B312	WEAK
SJ000286436	<0.1	NA	B110	HIGH	0.1213	0.1021 - 0.1440	B110	MED
SJ000286438	>5	NA	B321	INACTIVE	>5	NA	C555	INACTIVE
SJ000286446	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286448	0.145	0.1099 - 0.1906	A212	MED	0.1909	0.1448 - 0.2516	A212	MED
SJ000286450	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286451	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286453	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286455	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286458	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286481	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286496	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286501	>5	NA	B314	INACTIVE	>5	NA	C555	INACTIVE
SJ000286511	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286515	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286515	0.065	0.0536 - 0.0783	A113	HIGH	0.0651	0.0561 - 0.0754	A113	HIGH
SJ000286516	>5	NA	C555	INACTIVE	>5	NA	B313	INACTIVE
SJ000286520	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286522	4.001	NA	C555	WEAK	2.834	2.6811 - 2.9956	B312	WEAK
SJ000286525	>5	NA	B141	INACTIVE	>5	NA	C555	INACTIVE
SJ000286530	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286533	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286536	0.707	0.6825 - 0.7325	A212	MED	0.6411	0.6184 - 0.6645	A212	MED
SJ000286537	0.308	0.2752 - 0.3452	A221	MED	0.9009	0.7435 - 1.0917	A222	MED
SJ000286548	2.046	1.9915 - 2.1018	B322	WEAK	2.2948	2.2635 - 2.3267	B312	WEAK
SJ000286550	>5	NA	NB241	INACTIVE	>5	NA	D555	INACTIVE
SJ000286552	0.05	0.0427 - 0.0592	B110	HIGH	0.042	0.0353 - 0.0499	B110	HIGH

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286565	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286572	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286576	0.83	0.7823 - 0.8814	A212	MED	0.7585	0.7253 - 0.7932	A212	MED
SJ000286594	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286616	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286619	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286644	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286645	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286646	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286648	>5	NA	B141	INACTIVE	>5	NA	C555	INACTIVE
SJ000286657	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286658	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286694	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286708	3.054	2.3308 - 4.0015	B313	WEAK	2.6085	2.1808 - 3.1201	B314	WEAK
SJ000286710	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286711	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286715	1.952	1.8621 - 2.0453	B312	WEAK	2.4069	2.3605 - 2.4543	B312	WEAK
SJ000286728	0.217	0.1313 - 0.3584	A211	MED	0.3591	0.3283 - 0.3927	A212	MED
SJ000286729	>5	NA	D555	INACTIVE	>5	NA	B141	INACTIVE
SJ000286749	3.028	2.9392 - 3.1196	B312	WEAK	2.4661	2.4380 - 2.4945	B312	WEAK
SJ000286751	0.295	0.1510 - 0.5765	A212	MED	0.2616	0.1867 - 0.3665	A212	MED
SJ000286753	0.721	0.6923 - 0.7509	A213	MED	0.808	0.7737 - 0.8438	A213	MED
SJ000286767	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286769	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286772	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286775	>5	NA	B314	INACTIVE	>5	NA	C555	INACTIVE
SJ000286776	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286780	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286781	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286782	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286783	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286797	>5	NA	C555	INACTIVE	>5	NA	B314	INACTIVE
SJ000286800	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286801	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286802	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286804	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286809	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286813	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286816	1.182	0.5135 - 2.7190	B311	WEAK	2.1215	1.3636 - 3.3006	B311	WEAK
SJ000286821	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286829	>5	NA	B241	INACTIVE	>5	NA	A241	INACTIVE
SJ000286830	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286847	0.333	0.3014 - 0.3686	A232	WEAK	0.6878	0.5576 - 0.8483	A233	WEAK
SJ000286853	>5	NA	B241	INACTIVE	>5	NA	A242	INACTIVE
SJ000286865	>5	NA	D555	INACTIVE	>5	NA	NA141	INACTIVE
SJ000286868	>5	NA	A241	INACTIVE	>5	NA	D555	INACTIVE
SJ000286877	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286884	>5	NA	B141	INACTIVE	>5	NA	D555	INACTIVE
SJ000286890	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286899	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286902	0.188	0.1689 - 0.2098	A212	MED	0.1934	0.1731 - 0.2160	A212	MED
SJ000286904	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000286906	>5	NA	A242	INACTIVE	>5	NA	D555	INACTIVE
SJ000286948	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000286950	2.787	2.6267 - 2.9574	B312	WEAK	>5	NA	C555	INACTIVE
SJ000286959	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286960	2.057	2.0333 - 2.0817	B313	WEAK	1.9578	1.9446 - 1.9711	B313	WEAK
SJ000286962	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000286963	>5	NA	C555	INACTIVE	>5	NA	B334	INACTIVE
SJ000286965	<0.1	NA	C555	HIGH	<0.1	NA	C555	HIGH
SJ000286983	0.032	0.0238 - 0.0438	B110	HIGH	0.0213	0.0159 - 0.0287	B110	HIGH
SJ000286986	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000286993	1.03	0.8297 - 1.2786	A312	WEAK	1.3651	1.1879 - 1.5686	B312	WEAK
SJ000287007	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287016	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287020	>5	NA	D555	INACTIVE	>5	NA	NB141	INACTIVE
SJ000287054	>5	NA	A241	INACTIVE	>5	NA	D555	INACTIVE
SJ000287055	1.5	1.3631 - 1.6505	B312	WEAK	1.291	0.7246 - 2.3002	A324	WEAK
SJ000287058	>5	NA	B141	INACTIVE	>5	NA	A241	INACTIVE
SJ000287059	0.342	0.3018 - 0.3866	A221	MED	2.4681	1.2594 - 4.8369	B311	WEAK
SJ000287062	>5	NA	C555	WEAK	2.3374	2.3101 - 2.3651	B313	WEAK
SJ000287073	>5	NA	A241	INACTIVE	>5	NA	B244	INACTIVE
SJ000287074	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287076	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287077	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287078	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287087	1.931	1.8976 - 1.9652	B313	WEAK	1.9031	1.8028 - 2.0090	B313	WEAK
SJ000287088	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287090	>5	NA	A233	INACTIVE	1.2339	0.8712 - 1.7477	A324	WEAK
SJ000287092	0.121	0.0807 - 0.1827	A213	MED	0.1039	0.0705 - 0.1531	A212	MED
SJ000287098	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000287101	>5	NA	B341	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287102	0.036	0.0314 - 0.0418	B110	HIGH	0.0365	0.0165 - 0.0806	B110	HIGH
SJ000287131	>5	NA	NB144	INACTIVE	>5	NA	C555	INACTIVE
SJ000287132	>5	NA	A141	INACTIVE	>5	NA	A241	INACTIVE
SJ000287133	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287134	1.403	1.1796 - 1.6684	B312	WEAK	1.2957	1.1132 - 1.5081	B312	WEAK
SJ000287136	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287138	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287139	>5	NA	C555	WEAK	>5	NA	C555	WEAK
SJ000287147	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287149	<1.0	NA	C555	MED	<1.0	NA	C555	MED
SJ000287150	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287152	0.377	0.3328 - 0.4266	A212	MED	0.3899	0.3213 - 0.4731	A212	MED
SJ000287155	0.078	0.0708 - 0.0858	A112	HIGH	0.0669	0.0607 - 0.0738	A113	HIGH
SJ000287160	1.879	1.8381 - 1.9199	B312	WEAK	2.2265	2.1794 - 2.2747	B312	WEAK
SJ000287177	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287181	>5	NA	C555	INACTIVE	>5	NA	A241	INACTIVE
SJ000287182	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287193	>5	NA	B314	INACTIVE	>5	NA	D555	INACTIVE
SJ000287195	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287203	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287206	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287209	1.754	1.6223 - 1.8964	B312	WEAK	2.295	2.1725 - 2.4243	B312	WEAK
SJ000287215	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287222	0.062	0.0510 - 0.0749	A112	HIGH	0.0575	0.0479 - 0.0689	A112	HIGH
SJ000287228	2.055	2.0312 - 2.0791	B312	WEAK	>1.0	0.0010 - 699.2647	A214	WEAK
SJ000287229	>5	NA	B241	INACTIVE	>5	NA	D555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287231	0.091	0.0792 - 0.1044	A112	HIGH	0.0837	0.0727 - 0.0963	A112	HIGH
SJ000287238	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287239	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287245	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287247	0.067	0.0513 - 0.0878	B110	HIGH	0.0582	0.0412 - 0.0823	B110	HIGH
SJ000287256	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287261	0.183	0.1553 - 0.2162	A212	MED	0.1749	0.1482 - 0.2063	A212	MED
SJ000287270	0.407	0.3609 - 0.4595	A212	MED	0.3365	0.2582 - 0.4385	A212	MED
SJ000287281	>5	NA	B343	INACTIVE	>5	NA	C555	INACTIVE
SJ000287282	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287283	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287295	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287300	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000287313	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000287314	1.024	NA	C555	WEAK	>5	NA	D555	INACTIVE
SJ000287317	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287320	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287329	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287330	2.872	2.6847 - 3.0727	B312	WEAK	2.0003	1.9539 - 2.0478	B312	WEAK
SJ000287331	0.218	0.1905 - 0.2501	A212	MED	0.1906	0.1602 - 0.2267	A213	MED
SJ000287333	0.053	0.0458 - 0.0619	A113	HIGH	0.0577	0.0502 - 0.0663	A112	HIGH
SJ000287335	>5	NA	A241	INACTIVE	>5	NA	B241	INACTIVE
SJ000287348	0.081	0.0681 - 0.0956	A112	HIGH	0.0847	0.0705 - 0.1018	A112	HIGH
SJ000287350	>5	NA	B342	INACTIVE	>5	NA	C555	INACTIVE
SJ000287365	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287368	1.096	0.8387 - 1.4317	B311	WEAK	0.5999	0.5365 - 0.6708	A211	MED
SJ000287384	1.037	0.9357 - 1.1498	A322	WEAK	1.4013	1.3316 - 1.4747	B312	WEAK

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287393	0.046	0.0382 - 0.0547	B110	HIGH	0.0452	0.0368 - 0.0554	B110	HIGH
SJ000287394	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287395	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287397	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287398	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287400	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287409	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287413	>5	NA	B343	INACTIVE	>5	NA	C555	INACTIVE
SJ000287428	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287441	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287448	4.723	NA	C555	WEAK	>5	NA	C555	INACTIVE
SJ000287450	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287457	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287461	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287462	>5	NA	B331	INACTIVE	>5	NA	B331	INACTIVE
SJ000287467	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287484	>5	NA	B241	INACTIVE	>5	NA	C555	INACTIVE
SJ000287488	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287490	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287493	>5	NA	C555	INACTIVE	>5	NA	B343	INACTIVE
SJ000287506	>5	NA	B130	INACTIVE	>5	NA	B130	INACTIVE
SJ000287508	0.022	0.0176 - 0.0283	B110	HIGH	0.0249	0.0201 - 0.0308	B110	HIGH
SJ000287523	0.088	0.0770 - 0.1006	B110	HIGH	0.0797	0.0702 - 0.0905	A112	HIGH
SJ000287543	>5	NA	NA141	INACTIVE	>5	NA	D555	INACTIVE
SJ000287544	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000287545	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287547	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287561	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE
SJ000287562	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287563	0.143	0.1270 - 0.1612	A213	MED	0.1397	0.1150 - 0.1698	A213	MED
SJ000287568	0.01	0.0086 - 0.0121	B110	HIGH	0.0069	0.0018 - 0.0267	B110	HIGH
SJ000287585	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287590	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287618	>5	NA	D555	INACTIVE	>5	NA	B341	INACTIVE
SJ000287619	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287632	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287647	>5	NA	B334	INACTIVE	>5	NA	C555	INACTIVE
SJ000287648	>5	NA	A241	INACTIVE	>5	NA	D555	INACTIVE
SJ000287657	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287660	0.066	0.0514 - 0.0847	A112	HIGH	0.0578	0.0446 - 0.0751	A112	HIGH
SJ000287663	2.663	1.6576 - 4.2777	B314	WEAK	2.5982	2.5103 - 2.6892	B314	WEAK
SJ000287667	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287668	>5	NA	C555	INACTIVE	>5	NA	A241	INACTIVE
SJ000287676	1.758	1.6958 - 1.8221	B313	WEAK	1.7042	1.6139 - 1.7996	B322	WEAK
SJ000287677	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287680	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287682	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287686	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287690	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287692	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287693	>5	NA	A344	INACTIVE	>5	NA	B342	INACTIVE
SJ000287697	>5	NA	B130	INACTIVE	>5	NA	C555	INACTIVE
SJ000287703	>5	NA	B343	INACTIVE	>5	NA	B343	INACTIVE
SJ000287705	>5	NA	C555	INACTIVE	>5	NA	B333	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287706	>5	NA	B334	INACTIVE	>5	NA	C555	INACTIVE
SJ000287714	1.078	0.3018 - 3.8488	A314	WEAK	1.692	1.0254 - 2.7920	B311	WEAK
SJ000287728	1.631	1.5355 - 1.7329	B312	WEAK	1.6193	1.4530 - 1.8047	B312	WEAK
SJ000287730	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287734	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287737	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287741	0.467	0.3855 - 0.5661	A213	MED	0.4667	0.3819 - 0.5704	A213	MED
SJ000287744	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287749	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287750	>5	NA	B344	INACTIVE	>5	NA	C555	INACTIVE
SJ000287752	>5	NA	B342	INACTIVE	>5	NA	B341	INACTIVE
SJ000287758	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287762	>5	NA	B141	INACTIVE	>5	NA	B244	INACTIVE
SJ000287767	>5	NA	D555	INACTIVE	>5	NA	B341	INACTIVE
SJ000287768	0.448	0.4035 - 0.4969	A214	MED	0.4379	0.3997 - 0.4798	A213	MED
SJ000287769	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287778	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287799	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287810	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287813	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287814	>5	NA	B314	INACTIVE	>5	NA	C555	INACTIVE
SJ000287821	>5	NA	C555	INACTIVE	>5	NA	B313	INACTIVE
SJ000287827	0.047	0.0338 - 0.0657	B110	HIGH	0.0435	0.0345 - 0.0548	A112	HIGH
SJ000287837	>5	NA	B341	INACTIVE	>5	NA	C555	INACTIVE
SJ000287841	>5	NA	B342	INACTIVE	>5	NA	C555	INACTIVE
SJ000287864	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287868	>5	NA	B332	INACTIVE	2.2448	2.1303 - 2.3655	B314	WEAK
SJ000287873	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287875	>5	NA	NC555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000287882	>5	NA	D555	INACTIVE	>5	NA	NC555	INACTIVE
SJ000287889	>5	NA	B334	INACTIVE	>5	NA	C555	INACTIVE
SJ000287891	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287899	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287901	>5	NA	B342	INACTIVE	>5	NA	B332	INACTIVE
SJ000287902	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287925	<0.1	NA	B110	HIGH	<0.1	NA	B110	HIGH
SJ000287942	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000287955	>5	NA	B244	INACTIVE	>5	NA	A241	INACTIVE
SJ000287956	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287970	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287972	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000287975	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000287985	>5	NA	C555	INACTIVE	>5	NA	B344	INACTIVE
SJ000287990	2.2	2.1724 - 2.2288	B313	WEAK	2.2877	2.2204 - 2.3570	B313	WEAK
SJ000287995	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288002	2.005	1.9724 - 2.0387	B313	WEAK	2.0943	2.0403 - 2.1498	B314	WEAK
SJ000288007	>5	NA	C555	INACTIVE	>5	NA	B241	INACTIVE
SJ000288017	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288020	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288025	>5	NA	B342	INACTIVE	>5	NA	C555	INACTIVE
SJ000288026	>5	NA	NB241	INACTIVE	>5	NA	D555	INACTIVE
SJ000288030	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288031	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288034	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288037	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288041	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288052	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288058	>5	NA	NA141	INACTIVE	>5	NA	D555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000288059	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288063	1.202	1.0820 - 1.3352	B322	WEAK	>5	NA	A342	INACTIVE
SJ000288073	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288074	>5	NA	A241	INACTIVE	>5	NA	C555	INACTIVE
SJ000288081	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288084	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288092	>5	NA	NB144	INACTIVE	>5	NA	D555	INACTIVE
SJ000288093	>5	NA	NB242	INACTIVE	>5	NA	D555	INACTIVE
SJ000288098	>5	NA	C555	INACTIVE	>5	NA	B342	INACTIVE
SJ000288099	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288114	>5	NA	D555	INACTIVE	>5	NA	B241	INACTIVE
SJ000288126	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288139	>5	NA	C555	WEAK	2.2411	2.2103 - 2.2723	B313	WEAK
SJ000288140	>5	NA	C555	INACTIVE	>5	NA	B314	INACTIVE
SJ000288147	1.01	0.6912 - 1.4743	A314	WEAK	0.9875	0.7673 - 1.2708	A214	MED
SJ000288150	>5	NA	B331	INACTIVE	>5	NA	B331	INACTIVE
SJ000288156	>5	NA	C555	INACTIVE	>5	NA	B323	INACTIVE
SJ000288159	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288163	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288173	>5	NA	C555	WEAK	1.4271	1.2596 - 1.6168	B311	WEAK
SJ000288175	>5	NA	NC555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288176	>5	NA	C555	INACTIVE	>5	NA	B333	INACTIVE
SJ000288181	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288182	>5	NA	B241	INACTIVE	>5	NA	A241	INACTIVE
SJ000288186	>5	NA	A141	INACTIVE	>5	NA	C555	INACTIVE
SJ000288194	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288209	>5	NA	D555	INACTIVE	>5	NA	A241	INACTIVE
SJ000288210	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE

Figure 26 (continued)

Reg Number	WT EC50	WT EC50 CI	WT Curve Score	WT Act Class	T3151 EC50	T3151 EC50 CI	T3151 Curve Score	T3151 Act Class
SJ000288211	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288216	>5	NA	B141	INACTIVE	>5	NA	C555	INACTIVE
SJ000288219	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288224	>5	NA	C555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288226	>5	NA	C555	INACTIVE	>5	NA	B242	INACTIVE
SJ000288238	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288244	0.105	0.0914 - 0.1194	A213	MED	0.1311	0.0021 - 8.2851	A214	MED
SJ000288246	>5	NA	NB141	INACTIVE	>5	NA	D555	INACTIVE
SJ000288249	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288262	>5	NA	C555	INACTIVE	4.0527	NA	C555	WEAK
SJ000288270	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288274	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288278	0.015	0.0104 - 0.0214	B110	HIGH	0.0159	0.0113 - 0.0225	B110	HIGH
SJ000288284	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288304	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288306	0.306	0.1694 - 0.5530	A211	MED	0.171	0.0776 - 0.3768	A211	MED
SJ000288308	>5	NA	B341	INACTIVE	>5	NA	B344	INACTIVE
SJ000288312	>5	NA	D555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288313	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288316	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288318	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288320	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000288325	>5	NA	B333	INACTIVE	4.198	4.0769 - 4.3227	B313	WEAK
SJ000288326	>5	NA	A241	INACTIVE	>5	NA	B341	INACTIVE
SJ000288327	>5	NA	D555	INACTIVE	>5	NA	D555	INACTIVE
SJ000288328	>5	NA	C555	INACTIVE	>5	NA	C555	INACTIVE
SJ000518967	0.318	0.2999-0.3357	A212	MED	0.3133	0.2964-0.3311	A212	MED
SJ000518972	0.358	0.3459-0.3639	A212	MED	0.3311	0.3206-0.3428	A212	MED

Figure 26 (continued)

Reg Number	ATC L1	ATC L2
SJ000000250	C Cardiovascular system	C01 Cardiac therapy
SJ000000854	V Various	V99 Unassigned
SJ000113084	C Cardiovascular system	C02 Antihypertensives
SJ000126662	V Various	V99 Unassigned
SJ000285182	V Various	V99 Unassigned
SJ000285183	B Blood and blood forming organs; #D Dermatologicals; #R Respiratory system	B05 Blood substituted and perfusion solutions; #D08 Antiseptics and disinfectants; #D09 Medicated dressings; #R02 Throat preparations
SJ000285185	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285188	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285190	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285193	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285194	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285194	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285195	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285196	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents; #L04 Immunosuppressants
SJ000285197	L Antineoplastic and immunomodulating agents	L04 Immunosuppressants
SJ000285200	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285202	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285203	V Various	V99 Unassigned
SJ000285206	V Various	V99 Unassigned
SJ000285207	D Dermatologicals	D08 Antiseptics and disinfectants
SJ000285208	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285210	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285212	V Various	V99 Unassigned
SJ000285215	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals

Figure 27

Reg Number	ATC L1	ATC L2
SJ000285215	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285218	V Various	V99 Unassigned
SJ000285219	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285219	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285220	V Various	V99 Unassigned
SJ000285221	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285225	V Various	V99 Unassigned
SJ000285226	J Antiinfectives for systemic use	J05 Antivirals for systemic use
SJ000285227	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285228	V Various	V99 Unassigned
SJ000285229	V Various	V99 Unassigned
SJ000285231	V Various	V99 Unassigned
SJ000285232	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000285232	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000285234	V Various	V99 Unassigned
SJ000285235	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285238	M Musculo-skeletal system	M04 Antigout preparations
SJ000285241	L Antineoplastic and immunomodulating agents	L04 Immunosuppressants
SJ000285242	D Dermatologicals; #R Respiratory system	D08 Antiseptics and disinfectants; #R02 Throat preparations
SJ000285243	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285244	R Respiratory system	R02 Throat preparations
SJ000285246	R Respiratory system	R02 Throat preparations
SJ000285249	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285256	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285261	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285262	A Alimentary tract and metabolism; #G Genito-urinary system and sex hormones; #J Antiinfectives for systemic use	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #G01 Gynecological anti-infectives and antiseptics; #J02 Antimycotics for systemic use
SJ000285263	V Various	V99 Unassigned
SJ000285267	P Antiparasitic products, insecticides, and repellents	P03 Ectoparasiticides, including scabicides, insecticides, and repellents
SJ000285270	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285272	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285273	D Dermatologicals	D08 Antiseptics and disinfectants
SJ000285276	V Various	V99 Unassigned
SJ000285278	V Various	V99 Unassigned
SJ000285279	N Nervous system	N07 Other nervous system drugs
SJ000285285	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ0002852920	J Antiinfectives for systemic use	J04 Antimycobacterials
SJ000285294	D Dermatologicals	D09 Medicated dressings
SJ000285299	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000285307	V Various	V99 Unassigned
SJ000285308	D Dermatologicals; #G Genito-urinary system and sex hormones; #R Respiratory system	D08 Antiseptics and disinfectants; #G01 Gynecological anti-infectives and antiseptics; #R02 Throat preparations
SJ000285313	V Various	V99 Unassigned
SJ000285315	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285316	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285317	A Alimentary tract and metabolism; #D Dermatologicals; #G Genito-urinary system and sex hormones; #R Respiratory system	A01 Stomatological preparations; #D08 Antiseptics and disinfectants; #G01 Gynecological anti-infectives and antiseptics; #R02 Throat preparations
SJ000285318	S Sensory organics; #V Various	S01 Ophthalmologicals; #V03 All other therapeutics products

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285319	A Alimentary tract and metabolism; #B Blood and blood forming organs; #D Dermatologicals; #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #B05 Blood substituted and perfusion solutions; #D08 Antiseptics and disinfectants; #D09 Medicated dressings; #R02 Throat preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285321	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285323	V Various	V99 Unassigned
SJ000285327	V Various	V99 Unassigned
SJ000285332	D Dermatologicals	D11 ther dermatological preparations
SJ000285334	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285335	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285335	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285337	D Dermatologicals	D10 Anti-acne preparations
SJ000285337	D Dermatologicals; #L Antineoplastic and immunomodulating agents	D10 Anti-acne preparations; #L01 Antineoplastics agents
SJ000285338	A Alimentary tract and metabolism; #B Blood and blood forming organs; #D Dermatologicals; #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #B05 Blood substituted and perfusion solutions; #D08 Antiseptics and disinfectants; #D09 Medicated dressings; #R02 Throat preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285343	A Alimentary tract and metabolism	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285358	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285363	N Nervous system	N05 Psycholeptics
SJ000285364	C Cardiovascular system	C08 Calcium channel blockers
SJ000285365	V Various	V99 Unassigned
SJ000285368	V Various	V99 Unassigned
SJ000285369	V Various	V99 Unassigned
SJ000285373	A Alimentary tract and metabolism; #S Sensory organics	A03 Drugs for functional gastrointestinal disorders; #S01 Ophthalmologicals
SJ000285375	N Nervous system	N06 Psychoanaleptics
SJ000285382	V Various	V99 Unassigned
SJ000285383	R Respiratory system	R06 Antihistamines for systemic use
SJ000285387	R Respiratory system	R01 Nasal preparations
SJ000285396	V Various	V99 Unassigned
SJ000285400	V Various	V99 Unassigned
SJ000285410	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285413	V Various	V99 Unassigned
SJ000285423	V Various	V99 Unassigned
SJ000285426	V Various	V99 Unassigned
SJ000285431	P Antiparasitic products, insecticides, and repellents	P03 Ectoparasiticides, including scabicides, insecticides, and repellents
SJ000285433	B Blood and blood forming organs	B01 Antithrombotic agents
SJ000285436	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285439	D Dermatologicals; #R Respiratory system; #S Sensory organics	D06 Antibiotics and chemotherapeutics for dermatological use; #R02 Throat preparations; #S01 Ophthalmologicals
SJ000285440	V Various	V99 Unassigned
SJ000285442	V Various	V99 Unassigned
SJ000285443	V Various	V99 Unassigned
SJ000285445	V Various	V99 Unassigned
SJ000285450	D Dermatologicals	D08 Antiseptics and disinfectants
SJ000285451	V Various	V99 Unassigned
SJ000285452	A Alimentary tract and metabolism; #D Dermatologicals; #R Respiratory system	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000285452	A Alimentary tract and metabolism; #D Dermatologicals; #R Respiratory system	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000285453	C Cardiovascular system	C03 Diuretics
SJ000285454	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285460	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285461	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000285462	D Dermatologicals	D10 Anti-acne preparations
SJ000285465	N Nervous system	N06 Psychoanaleptics
SJ000285466	N Nervous system	N03 Antiepileptics
SJ000285484	C Cardiovascular system	C01 Cardiac therapy
SJ000285487	C Cardiovascular system; #R Respiratory system	C03 Diuretics; #R03 Drugs for obstructive airway diseases
SJ000285490	V Various	V99 Unassigned
SJ000285502	C Cardiovascular system	C01 Cardiac therapy
SJ000285504	N Nervous system	N01 Anesthetics
SJ000285506	V Various	V99 Unassigned
SJ000285508	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285512	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285522	A Alimentary tract and metabolism; #C Cardiovascular system; #R Respiratory system; #S Sensory organics	A08 Antiobesity preparation, excluding diet products; #C01 Cardiac therapy; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals
SJ000285526	V Various	V99 Unassigned
SJ000285536	N Nervous system; #S Sensory organics	N07 Other nervous system drugs; #S01 Ophthalmologicals
SJ000285540	C Cardiovascular system	C02 Antihypertensives
SJ000285541	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics; #V Various	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations; #V03 All other therapeutics products
SJ000285542	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics; #V Various	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations; #V03 All other therapeutics products
SJ000285543	A Alimentary tract and metabolism; #H Systemics hormonal preparations (excluding sex hormones and insulins)	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #H02 Corticosteroids for systemic use
SJ000285544	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285547	C Cardiovascular system	C01 Cardiac therapy
SJ000285549	N Nervous system	N05 Psycholeptics

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285551	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285554	V Various	V99 Unassigned
SJ000285564	N Nervous system	N06 Psychoanaleptics
SJ000285569	P Antiparasitic products, insecticides, and repellents	P02 Antihelmintics
SJ000285572	M Musculo-skeletal system; #P Antiparasitic products, insecticides, and repellents	M09 Other drugs for disorders of the musculo-skeletal system; #P01 Antiprotozoals
SJ000285572	M Musculo-skeletal system; #P Antiparasitic products, insecticides, and repellents	M09 Other drugs for disorders of the musculo-skeletal system; #P01 Antiprotozoals
SJ000285574	V Various	V99 Unassigned
SJ000285577	C Cardiovascular system	C03 Diuretics
SJ000285584	V Various	V99 Unassigned
SJ000285586	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285587	V Various	V99 Unassigned
SJ000285588	V Various	V99 Unassigned
SJ000285591	M Musculo-skeletal system; #S Sensory organics	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain; #S01 Ophthalmologicals
SJ000285592	L Antineoplastic and immunomodulating agents	L02 Endocrine therapy
SJ000285606	C Cardiovascular system; #D Dermatologicals; #N Nervous system; #S Sensory organics	C05 Vasoprotectives; #D04 Antipruritics, including antihistamines, anesthetics, etc.; #N01 Anesthetics; #S01 Ophthalmologicals
SJ000285608	N Nervous system	N05 Psycholeptics
SJ000285608	N Nervous system	N05 Psycholeptics
SJ000285610	N Nervous system	N05 Psycholeptics
SJ000285614	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain
SJ000285618	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products
SJ000285619	N Nervous system	N02 Analgesics

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285625	G Genito-urinary system and sex hormones	G04 Urologicals
SJ000285630	C Cardiovascular system; #G Genito-urinary system and sex hormones; #M Musculo-skeletal system	C01 Cardiac therapy; #G02 Other gynecologicals; #M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain
SJ000285635	R Respiratory system	R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000285638	C Cardiovascular system	C04 Peripheral vasodilators
SJ000285643	R Respiratory system	R06 Antihistamines for systemic use
SJ000285646	S Sensory organics	S01 Ophthalmologicals
SJ000285651	H Systemics hormonal preparations (excluding sex hormones and insulins)	H03 Thyroid therapy
SJ000285652	M Musculo-skeletal system	M03 Muscle relaxants
SJ000285655	C Cardiovascular system	C02 Antihypertensives
SJ000285657	D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #S Sensory organics	D07 Corticosteroids, dermatological preparations; #D10 Anti-acne preparations; #H02 Corticosteroids for systemic use; #S01 Ophthalmologicals
SJ000285659	A Alimentary tract and metabolism; #J Antiinfectives for systemic use	A01 Stomatological preparations; #J01 Antibacterials for systemic use
SJ000285664	R Respiratory system; #S Sensory organics	R01 Nasal preparations; #S01 Ophthalmologicals
SJ000285666	C Cardiovascular system	C08 Calcium channel blockers
SJ000285667	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285668	R Respiratory system	R05 Cough and cold preparations
SJ000285671	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285674	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285678	V Various	V99 Unassigned
SJ000285683	A Alimentary tract and metabolism; #G Genito-urinary system and sex hormones	A03 Drugs for functional gastrointestinal disorders; #G04 Urologicals
SJ000285684	V Various	V99 Unassigned
SJ000285686	M Musculo-skeletal system	M03 Muscle relaxants

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285687	N Nervous system	N07 Other nervous system drugs
SJ000285688	V Various	V99 Unassigned
SJ000285689	C Cardiovascular system; #D Dermatologicals; #N Nervous system; #R Respiratory system	C05 Vasoprotectives; #D04 Antipruritics, including antihistamines, anesthetics, etc.; #N01 Anesthetics; #R02 Throat preparations
SJ000285692	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285695	N Nervous system; #S Sensory organics	N07 Other nervous system drugs; #S01 Ophthalmologicals
SJ000285696	N Nervous system	N03 Antiepileptics
SJ000285704	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285710	D Dermatologicals; #G Genito-urinary system and sex hormones	D01 Antifungals for dermatological use; #G01 Gynecological anti-infectives and antiseptics
SJ000285712	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285713	A Alimentary tract and metabolism; #D Dermatologicals; #G Genito-urinary system and sex hormones	A01 Stomatological preparations; #D01 Antifungals for dermatological use; #G01 Gynecological anti-infectives and antiseptics
SJ000285715	V Various	V99 Unassigned
SJ000285718	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285725	V Various	V03 All other therapeutics products
SJ000285727	D Dermatologicals; #J Antiinfectives for systemic use	D06 Antibiotics and chemotherapeutics for dermatological use; #J01 Antibacterials for systemic use

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285728	D Dermatologicals; #R Respiratory system; #S Sensory organics	D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285729	D Dermatologicals; #R Respiratory system; #S Sensory organics	D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285740	S Sensory organics	S01 Ophthalmologicals
SJ000285742	N Nervous system	N03 Antiepileptics
SJ000285745	B Blood and blood forming organs	B01 Antithrombotic agents
SJ000285747	N Nervous system; #P Antiparasitic products, insecticides, and repellents	N07 Other nervous system drugs; #P03 Ectoparasitocides, including scabicides, insecticides, and repellents
SJ000285748	C Cardiovascular system	C01 Cardiac therapy
SJ000285750	A Alimentary tract and metabolism; #J Antiinfectives for systemic use	A01 Stomatological preparations; #J01 Antibacterials for systemic use
SJ000285752	N Nervous system; #R Respiratory system	N01 Anesthetics; #R02 Throat preparations
SJ000285761	C Cardiovascular system	C03 Diuretics
SJ000285764	J Antiinfectives for systemic use	J04 Antimycobacterials
SJ000285766	H Systemics hormonal preparations (excluding sex hormones and insulins); #S Sensory organics	H02 Corticosteroids for systemic use; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285767	D Dermatologicals; #S Sensory organics	D07 Corticosteroids, dermatological preparations; #S02 Otologicals
SJ000285768	C Cardiovascular system; #D Dermatologicals	C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285769	C Cardiovascular system; #D Dermatologicals; #S Sensory organics	C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #D10 Anti-acne preparations; #S01 Ophthalmologicals
SJ000285770	M Musculo-skeletal system; #R Respiratory system; #S Sensory organics	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain; #R02 Throat preparations; #S01 Ophthalmologicals
SJ000285778	C Cardiovascular system	C02 Antihypertensives
SJ000285781	R Respiratory system	R02 Throat preparations
SJ000285783	S Sensory organics	S01 Ophthalmologicals
SJ000285786	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285787	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285787	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000285790	G Genito-urinary system and sex hormones; #N Nervous system	G04 Urologicals; #N04 Anti-parkinson drugs
SJ000285797	D Dermatologicals	D02 Emollients and protectives
SJ000285801	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285812	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285814	G Genito-urinary system and sex hormones; #N Nervous system	G02 Other gynecologicals; #N04 Anti-parkinson drugs
SJ000285814	G Genito-urinary system and sex hormones; #N Nervous system	G02 Other gynecologicals; #N04 Anti-parkinson drugs
SJ000285818	A Alimentary tract and metabolism; #J Antiinfectives for systemic use	A01 Stomatological preparations; #J01 Antibacterials for systemic use
SJ000285820	A Alimentary tract and metabolism; #D Dermatologicals; #R Respiratory system	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000285827	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000285831	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products
SJ000285834	C Cardiovascular system	C10 Lipid modifying agents
SJ000285835	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000285836	R Respiratory system	R03 Drugs for obstructive airway diseases
SJ000285837	C Cardiovascular system	C08 Calcium channel blockers
SJ000285838	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285840	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000285842	V Various	V04 Diagnostic agents
SJ000285845	C Cardiovascular system	C08 Calcium channel blockers
SJ000285849	C Cardiovascular system; #D Dermatologicals	C05 Vasoprotectives; #D04 Antipruritics, including antihistamines, anesthetics, etc.
SJ000285858	A Alimentary tract and metabolism	A02 Drugs for acid related disorders
SJ000285860	C Cardiovascular system	C04 Peripheral vasodilators
SJ000285864	M Musculo-skeletal system	M02 Topical products for joint and muscular pain
SJ000285866	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products
SJ000285878	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285879	D Dermatologicals; #G Genito-urinary system and sex hormones	D01 Antifungals for dermatological use; #G01 Gynecological anti-infectives and antiseptics
SJ000285880	R Respiratory system	R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000285881	V Various	V99 Unassigned
SJ000285882	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000285885	V Various	V99 Unassigned
SJ000285887	A Alimentary tract and metabolism	A10 Drugs used in diabetes
SJ000285888	C Cardiovascular system	C09 Agents acting on the renin-angiotensin system
SJ000285890	C Cardiovascular system	C09 Agents acting on the renin-angiotensin system
SJ000285892	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain
SJ000285903	J Antiinfectives for systemic use; #S Sensory organics	J01 Antibacterials for systemic use; #S01 Ophthalmologicals
SJ000285909	V Various	V03 All other therapeutics products
SJ000285920	V Various	V99 Unassigned
SJ000285922	V Various	V99 Unassigned
SJ000285925	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285935	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000285936	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000285940	R Respiratory system	R05 Cough and cold preparations
SJ000285949	C Cardiovascular system	C08 Calcium channel blockers
SJ000285950	R Respiratory system	R05 Cough and cold preparations
SJ000285951	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000285958	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000285959	S Sensory organics	S01 Ophthalmologicals
SJ000285960	M Musculo-skeletal system	M03 Muscle relaxants
SJ000285965	N Nervous system	N06 Psychoanaleptics
SJ000285966	V Various	V99 Unassigned
SJ000285967	C Cardiovascular system	C08 Calcium channel blockers
SJ000285971	S Sensory organics	S01 Ophthalmologicals
SJ000285972	D Dermatologicals; #R Respiratory system	D08 Antiseptics and disinfectants; #R02 Throat preparations
SJ000285973	D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #S Sensory organics	D07 Corticosteroids, dermatological preparations; #D10 Anti-acne preparations; #H02 Corticosteroids for systemic use; #S01 Ophthalmologicals
SJ000285974	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000285978	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Ophthalmologicals; #S03 Ophthalmological and otological preparations
SJ000285980	N Nervous system	N02 Analgesics
SJ000285983	C Cardiovascular system	C02 Antihypertensives
SJ000285987	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000285991	D Dermatologicals; #R Respiratory system	D08 Antiseptics and disinfectants; #D09 Medicated dressings; #R02 Throat preparations
SJ000285996	C Cardiovascular system	C10 Lipid modifying agents
SJ000285998	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000285999	N Nervous system	N01 Anesthetics
SJ000286003	V Various	V99 Unassigned
SJ000286004	V Various	V99 Unassigned
SJ000286006	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000286007	C Cardiovascular system	C03 Diuretics
SJ000286008	R Respiratory system	R05 Cough and cold preparations
SJ000286018	V Various	V99 Unassigned
SJ000286024	D Dermatologicals; #J Antiinfectives for systemic use	D01 Antifungals for dermatological use; #J02 Antimycotics for systemic use
SJ000286025	C Cardiovascular system	C10 Lipid modifying agents
SJ000286030	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286034	V Various	V99 Unassigned
SJ000286035	L Antineoplastic and immunomodulating agents	L02 Endocrine therapy
SJ000286036	V Various	V99 Unassigned
SJ000286037	N Nervous system	N06 Psychoanaleptics
SJ000286038	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286038	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286039	A Alimentary tract and metabolism	A10 Drugs used in diabetes
SJ000286041	V Various	V08 Contrast media
SJ000286044	V Various	V99 Unassigned
SJ000286046	N Nervous system	N06 Psychoanaleptics
SJ000286046	N Nervous system	N06 Psychoanaleptics
SJ000286052	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000286053	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000286056	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286057	D Dermatologicals; #R Respiratory system	D08 Antiseptics and disinfectants; #R02 Throat preparations
SJ000286063	C Cardiovascular system	C10 Lipid modifying agents
SJ000286065	C Cardiovascular system	C07 Beta blocking agents
SJ000286075	G Genito-urinary system and sex hormones	G04 Urologicals
SJ000286086	A Alimentary tract and metabolism	A11 Vitamins
SJ000286093	N Nervous system	N06 Psychoanaleptics
SJ000286097	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products
SJ000286098	P Antiparasitic products, insecticides, and repellents	P03 Ectoparasiticides, including scabicides, insecticides, and repellents
SJ000286101	V Various	V99 Unassigned
SJ000286109	N Nervous system	N04 Anti-parkinson drugs
SJ000286112	V Various	V99 Unassigned
SJ000286113	C Cardiovascular system	C08 Calcium channel blockers
SJ000286118	R Respiratory system	R06 Antihistamines for systemic use
SJ000286121	N Nervous system	N06 Psychoanaleptics
SJ000286124	N Nervous system	N06 Psychoanaleptics
SJ000286127	R Respiratory system	R07 Other respiratory system products
SJ000286128	V Various	V99 Unassigned
SJ000286133	N Nervous system	N07 Other nervous system drugs
SJ000286134	N Nervous system	N05 Psycholeptics
SJ000286142	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otolologicals
SJ000286143	C Cardiovascular system	C03 Diuretics
SJ000286144	C Cardiovascular system	C03 Diuretics
SJ000286146	A Alimentary tract and metabolism	A07 Antidiarrheals, intestinal anti- inflammatory/anti-infective agents
SJ000286151	G Genito-urinary system and sex hormones	G01 Gynecological anti-infectives and antiseptics

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286152	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain
SJ000286154	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000286155	D Dermatologicals; #R Respiratory system	D04 Antipruritics, including antihistamines, anesthetics, etc.; #R06 Antihistamines for systemic use
SJ000286156	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000286159	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000286160	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000286162	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286166	D Dermatologicals; #J Antiinfectives for systemic use; #S Sensory organics	D06 Antibiotics and chemotherapeutics for dermatological use; #J01 Antibacterials for systemic use; #S01 Ophthalmologicals; #S02 Otolologicals; #S03 Ophthalmological and otological preparations
SJ000286172	D Dermatologicals	D01 Antifungals for dermatological use
SJ000286174	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000286175	V Various	V99 Unassigned
SJ000286178	V Various	V99 Unassigned
SJ000286181	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286185	N Nervous system	N05 Psycholeptics
SJ000286186	N Nervous system	N04 Anti-parkinson drugs
SJ000286187	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000286188	V Various	V99 Unassigned
SJ000286191	V Various	V99 Unassigned
SJ000286195	D Dermatologicals; #G Genito- urinary system and sex hormones	D01 Antifungals for dermatological use; #G01 Gynecological anti- infectives and antiseptics
SJ000286199	V Various	V99 Unassigned
SJ000286204	D Dermatologicals; #R Respiratory system	D04 Antipruritics, including antihistamines, anesthetics, etc.; #R06 Antihistamines for systemic use
SJ000286205	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otolologicals
SJ000286213	V Various	V99 Unassigned
SJ000286217	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000286225	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286229	V Various	V99 Unassigned
SJ000286231	V Various	V99 Unassigned
SJ000286236	N Nervous system	N03 Antiepileptics
SJ000286243	V Various	V99 Unassigned
SJ000286248	V Various	V99 Unassigned
SJ000286251	V Various	V99 Unassigned
SJ000286267	V Various	V99 Unassigned
SJ000286300	V Various	V99 Unassigned
SJ000286312	V Various	V99 Unassigned
SJ000286359	V Various	V99 Unassigned
SJ000286366	V Various	V99 Unassigned
SJ000286380	V Various	V99 Unassigned
SJ000286381	V Various	V99 Unassigned
SJ000286382	V Various	V99 Unassigned
SJ000286387	V Various	V99 Unassigned
SJ000286389	V Various	V99 Unassigned
SJ000286393	V Various	V99 Unassigned
SJ000286395	V Various	V99 Unassigned
SJ000286396	V Various	V99 Unassigned
SJ000286398	V Various	V99 Unassigned
SJ000286406	V Various	V99 Unassigned
SJ000286408	A Alimentary tract and metabolism	A11 Vitamins
SJ000286413	V Various	V99 Unassigned
SJ000286415	V Various	V99 Unassigned
SJ000286419	V Various	V99 Unassigned
SJ000286421	V Various	V99 Unassigned
SJ000286423	V Various	V99 Unassigned
SJ000286424	V Various	V99 Unassigned
SJ000286430	V Various	V99 Unassigned
SJ000286434	V Various	V99 Unassigned
SJ000286436	V Various	V99 Unassigned
SJ000286438	V Various	V99 Unassigned
SJ000286446	V Various	V99 Unassigned
SJ000286448	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286450	V Various	V99 Unassigned
SJ000286451	V Various	V99 Unassigned
SJ000286453	V Various	V99 Unassigned
SJ000286455	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286458	V Various	V99 Unassigned
SJ000286481	C Cardiovascular system; #N Nervous system; #S Sensory organics	C02 Antihypertensives; #N02 Analgesics; #S01 Ophthalmologicals
SJ000286496	V Various	V99 Unassigned
SJ000286501	V Various	V99 Unassigned
SJ000286511	V Various	V99 Unassigned
SJ000286515	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000286515	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000286516	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000286520	V Various	V99 Unassigned
SJ000286522	V Various	V99 Unassigned
SJ000286525	V Various	V99 Unassigned
SJ000286530	V Various	V99 Unassigned
SJ000286533	V Various	V99 Unassigned
SJ000286536	V Various	V99 Unassigned
SJ000286537	V Various	V99 Unassigned
SJ000286548	V Various	V99 Unassigned
SJ000286550	C Cardiovascular system	C01 Cardiac therapy
SJ000286552	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000286565	V Various	V99 Unassigned
SJ000286572	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000286576	V Various	V99 Unassigned
SJ000286594	V Various	V99 Unassigned
SJ000286616	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286619	V Various	V99 Unassigned
SJ000286644	V Various	V99 Unassigned
SJ000286645	V Various	V99 Unassigned
SJ000286646	V Various	V99 Unassigned
SJ000286648	V Various	V99 Unassigned
SJ000286657	V Various	V99 Unassigned
SJ000286658	V Various	V99 Unassigned
SJ000286694	V Various	V99 Unassigned
SJ000286708	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000286710	V Various	V99 Unassigned
SJ000286711	V Various	V99 Unassigned
SJ000286715	V Various	V99 Unassigned
SJ000286728	V Various	V99 Unassigned
SJ000286729	V Various	V99 Unassigned
SJ000286749	V Various	V99 Unassigned
SJ000286751	D Dermatologicals; #R Respiratory system	D08 Antiseptics and disinfectants; #R02 Throat preparations
SJ000286753	M Musculo-skeletal system	M04 Antigout preparations
SJ000286767	V Various	V99 Unassigned
SJ000286769	V Various	V99 Unassigned
SJ000286772	V Various	V99 Unassigned
SJ000286775	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000286776	V Various	V99 Unassigned
SJ000286780	V Various	V99 Unassigned
SJ000286781	V Various	V99 Unassigned
SJ000286782	V Various	V99 Unassigned
SJ000286783	V Various	V99 Unassigned
SJ000286797	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286800	V Various	V99 Unassigned
SJ000286801	V Various	V99 Unassigned
SJ000286802	V Various	V99 Unassigned
SJ000286804	G Genito-urinary system and sex hormones	G03 Sex hormones and modulators of the genital system
SJ000286809	V Various	V99 Unassigned
SJ000286813	V Various	V99 Unassigned
SJ000286816	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000286821	V Various	V99 Unassigned
SJ000286829	V Various	V99 Unassigned
SJ000286830	V Various	V99 Unassigned
SJ000286847	V Various	V99 Unassigned
SJ000286853	H Systemics hormonal preparations (excluding sex hormones and insulins)	H02 Corticosteroids for systemic use
SJ000286865	V Various	V99 Unassigned
SJ000286868	V Various	V99 Unassigned
SJ000286877	V Various	V99 Unassigned
SJ000286884	A Alimentary tract and metabolism	A11 Vitamins
SJ000286890	V Various	V99 Unassigned
SJ000286899	V Various	V99 Unassigned
SJ000286902	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics	A01 Stomatological preparations; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases; #S01 Ophthalmologicals; #S02 Otologicals
SJ000286904	V Various	V99 Unassigned
SJ000286906	N Nervous system	N03 Antiepileptics
SJ000286948	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000286950	L Antineoplastic and immunomodulating agents; #S Sensory organics	L04 Immunosuppressants; #S01 Ophthalmologicals
SJ000286959	V Various	V99 Unassigned
SJ000286960	V Various	V99 Unassigned
SJ000286962	V Various	V99 Unassigned
SJ000286963	V Various	V99 Unassigned
SJ000286965	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000286983	S Sensory organics	S01 Ophthalmologicals
SJ000286986	V Various	V99 Unassigned
SJ000286993	V Various	V99 Unassigned
SJ000287007	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287016	C Cardiovascular system; #D Dermatologicals; #S Sensory organics	C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #S01 Ophthalmologicals; #S02 Otologicals
SJ000287020	V Various	V99 Unassigned
SJ000287054	V Various	V99 Unassigned
SJ000287055	C Cardiovascular system	C10 Lipid modifying agents
SJ000287058	V Various	V99 Unassigned
SJ000287059	V Various	V99 Unassigned
SJ000287062	V Various	V99 Unassigned
SJ000287073	V Various	V99 Unassigned
SJ000287074	V Various	V99 Unassigned
SJ000287076	N Nervous system	N05 Psycholeptics
SJ000287077	V Various	V99 Unassigned
SJ000287078	V Various	V99 Unassigned
SJ000287087	V Various	V99 Unassigned
SJ000287088	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000287090	V Various	V99 Unassigned
SJ000287092	V Various	V99 Unassigned
SJ000287098	V Various	V99 Unassigned
SJ000287101	V Various	V99 Unassigned
SJ000287102	D Dermatologicals; #S Sensory organics	D07 Corticosteroids, dermatological preparations; #S02 Otologicals
SJ000287131	V Various	V99 Unassigned
SJ000287132	N Nervous system	N05 Psycholeptics
SJ000287133	V Various	V99 Unassigned
SJ000287134	V Various	V99 Unassigned
SJ000287136	V Various	V99 Unassigned
SJ000287138	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000287139	V Various	V99 Unassigned
SJ000287147	V Various	V99 Unassigned
SJ000287149	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287150	D Dermatologicals; #S Sensory organics	D01 Antifungals for dermatological use; #S01 Ophthalmologicals
SJ000287152	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287155	A Alimentary tract and metabolism; #C Cardiovascular system; #D Dermatologicals; #H Systemics hormonal preparations (excluding sex hormones and insulins); #R Respiratory system; #S Sensory organics; #V Various	A01 Stomatological preparations; #A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #C05 Vasoprotectives; #D07 Corticosteroids, dermatological preparations; #H02 Corticosteroids for systemic use; #R01 Nasal preparations; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations; #V03 All other therapeutics products
SJ000287160	D Dermatologicals; #J Antiinfectives for systemic use; #S Sensory organics	D06 Antibiotics and chemotherapeutics for dermatological use; #J05 Antivirals for systemic use; #S01 Ophthalmologicals
SJ000287177	N Nervous system	N06 Psychoanaleptics
SJ000287181	V Various	V99 Unassigned
SJ000287182	V Various	V99 Unassigned
SJ000287193	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000287195	G Genito-urinary system and sex hormones	G01 Gynecological anti-infectives and antiseptics
SJ000287203	V Various	V08 Contrast media
SJ000287206	A Alimentary tract and metabolism; #D Dermatologicals; #G Genito-urinary system and sex hormones	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #D01 Antifungals for dermatological use; #G01 Gynecological anti-infectives and antiseptics
SJ000287209	C Cardiovascular system	C10 Lipid modifying agents
SJ000287215	M Musculo-skeletal system	M01 Anti-inflammatory and antirheumatics products; #M02 Topical products for joint and muscular pain
SJ000287222	V Various	V99 Unassigned
SJ000287228	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000287229	A Alimentary tract and metabolism	A04 Antiemetics and antinauseants

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287231	H Systemics hormonal preparations (excluding sex hormones and insulins); #S Sensory organics	H02 Corticosteroids for systemic use; #S01 Ophthalmologicals; #S02 Otologicals; #S03 Ophthalmological and otological preparations
SJ000287238	C Cardiovascular system	C04 Peripheral vasodilators
SJ000287239	V Various	V99 Unassigned
SJ000287245	N Nervous system	N05 Psycholeptics
SJ000287247	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287256	V Various	V99 Unassigned
SJ000287261	V Various	V99 Unassigned
SJ000287270	V Various	V99 Unassigned
SJ000287281	B Blood and blood forming organs	B02 Antihemorrhagics
SJ000287282	G Genito-urinary system and sex hormones	G02 Other gynecologicals
SJ000287283	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000287295	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287300	V Various	V09 Diagnostics radiopharmaceuticals
SJ000287313	A Alimentary tract and metabolism	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents
SJ000287314	V Various	V99 Unassigned
SJ000287317	C Cardiovascular system	C04 Peripheral vasodilators; #N04 Anti-parkinson drugs
SJ000287320	D Dermatologicals; #R Respiratory system	D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000287329	V Various	V99 Unassigned
SJ000287330	V Various	V99 Unassigned
SJ000287331	V Various	V99 Unassigned
SJ000287333	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000287335	V Various	V99 Unassigned
SJ000287348	V Various	V99 Unassigned
SJ000287350	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000287365	V Various	V99 Unassigned
SJ000287368	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287384	V Various	V99 Unassigned
SJ000287393	D Dermatologicals; #S Sensory organics	D07 Corticosteroids, dermatological preparations; #S01 Ophthalmologicals
SJ000287394	L Antineoplastic and immunomodulating agents	L04 Immunosuppressants
SJ000287395	V Various	V99 Unassigned
SJ000287397	V Various	V99 Unassigned
SJ000287398	S Sensory organics	S01 Ophthalmologicals
SJ000287400	N Nervous system	N05 Psycholeptics
SJ000287409	S Sensory organics	S01 Ophthalmologicals
SJ000287413	N Nervous system	N06 Psychoanaleptics
SJ000287428	D Dermatologicals; #G Genito-urinary system and sex hormones; #P Antiparasitic products, insecticides, and repellents; #S Sensory organics	D08 Antiseptics and disinfectants; #D09 Medicated dressings; #G01 Gynecological anti-infectives and antiseptics; #P01 Antiprotozoals; #S02 Otologicals
SJ000287441	D Dermatologicals	D11 ther dermatological preparations
SJ000287448	V Various	V99 Unassigned
SJ000287450	N Nervous system	N06 Psychoanaleptics
SJ000287457	V Various	V99 Unassigned
SJ000287461	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000287462	V Various	V99 Unassigned
SJ000287467	M Musculo-skeletal system	M03 Muscle relaxants
SJ000287484	A Alimentary tract and metabolism	A10 Drugs used in diabetes
SJ000287488	D Dermatologicals; #R Respiratory system	D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000287490	J Antiinfectives for systemic use	J01 Antibacterials for systemic use
SJ000287493	N Nervous system	N01 Anesthetics
SJ000287506	C Cardiovascular system; #G Genito-urinary system and sex hormones	C01 Cardiac therapy; #G04 Urologicals
SJ000287508	H Systemics hormonal preparations (excluding sex hormones and insulins); #S Sensory organics	H02 Corticosteroids for systemic use; #S01 Ophthalmologicals
SJ000287523	D Dermatologicals	D07 Corticosteroids, dermatological preparations

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287543	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000287544	V Various	V99 Unassigned
SJ000287545	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000287547	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000287561	S Sensory organics	S01 Ophthalmologicals
SJ000287562	J Antiinfectives for systemic use	J04 Antimycobacterials
SJ000287563	P Antiparasitic products, insecticides, and repellents	P02 Anthelmintics
SJ000287568	D Dermatologicals	D07 Corticosteroids, dermatological preparations
SJ000287585	V Various	V99 Unassigned
SJ000287590	V Various	V99 Unassigned
SJ000287618	V Various	V99 Unassigned
SJ000287619	V Various	V99 Unassigned
SJ000287632	V Various	V99 Unassigned
SJ000287647	V Various	V99 Unassigned
SJ000287648	V Various	V99 Unassigned
SJ000287657	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287660	A Alimentary tract and metabolism; #D Dermatologicals; #R Respiratory system	A07 Antidiarrheals, intestinal anti-inflammatory/anti-infective agents; #D07 Corticosteroids, dermatological preparations; #R01 Nasal preparations; #R03 Drugs for obstructive airway diseases
SJ000287663	V Various	V99 Unassigned
SJ000287667	V Various	V99 Unassigned
SJ000287668	J Antiinfectives for systemic use	J05 Antivirals for systemic use
SJ000287676	V Various	V99 Unassigned
SJ000287677	V Various	V99 Unassigned
SJ000287680	V Various	V99 Unassigned
SJ000287682	V Various	V99 Unassigned
SJ000287686	V Various	V99 Unassigned
SJ000287690	V Various	V99 Unassigned
SJ000287692	V Various	V99 Unassigned
SJ000287693	V Various	V99 Unassigned
SJ000287697	V Various	V99 Unassigned
SJ000287703	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287705	V Various	V99 Unassigned
SJ000287706	V Various	V99 Unassigned
SJ000287714	V Various	V99 Unassigned
SJ000287728	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287730	V Various	V99 Unassigned
SJ000287734	C Cardiovascular system	C02 Antihypertensives
SJ000287737	V Various	V99 Unassigned
SJ000287741	V Various	V99 Unassigned
SJ000287744	V Various	V99 Unassigned
SJ000287749	V Various	V99 Unassigned
SJ000287750	V Various	V99 Unassigned
SJ000287752	V Various	V99 Unassigned
SJ000287758	V Various	V99 Unassigned
SJ000287762	V Various	V99 Unassigned
SJ000287767	V Various	V99 Unassigned
SJ000287768	V Various	V99 Unassigned
SJ000287769	V Various	V99 Unassigned
SJ000287778	V Various	V99 Unassigned
SJ000287799	V Various	V99 Unassigned
SJ000287810	V Various	V99 Unassigned
SJ000287813	V Various	V99 Unassigned
SJ000287814	V Various	V99 Unassigned
SJ000287821	V Various	V99 Unassigned
SJ000287827	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000287837	V Various	V99 Unassigned
SJ000287841	V Various	V99 Unassigned
SJ000287864	V Various	V99 Unassigned
SJ000287868	V Various	V99 Unassigned
SJ000287873	V Various	V99 Unassigned
SJ000287875	V Various	V99 Unassigned
SJ000287882	V Various	V99 Unassigned
SJ000287889	V Various	V99 Unassigned
SJ000287891	V Various	V99 Unassigned
SJ000287899	V Various	V99 Unassigned
SJ000287901	V Various	V99 Unassigned
SJ000287902	V Various	V99 Unassigned
SJ000287925	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000287942	V Various	V04 Diagnostic agents
SJ000287955	V Various	V99 Unassigned
SJ000287956	V Various	V99 Unassigned
SJ000287970	V Various	V99 Unassigned
SJ000287972	N Nervous system	N03 Antiepileptics
SJ000287975	V Various	V99 Unassigned
SJ000287985	V Various	V99 Unassigned
SJ000287990	V Various	V99 Unassigned
SJ000287995	V Various	V03 All other therapeutics products
SJ000288002	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000288007	C Cardiovascular system	C08 Calcium channel blockers
SJ000288017	V Various	V99 Unassigned
SJ000288020	V Various	V03 All other therapeutics products
SJ000288025	V Various	V99 Unassigned
SJ000288026	V Various	V99 Unassigned
SJ000288030	V Various	V99 Unassigned
SJ000288031	V Various	V99 Unassigned
SJ000288034	V Various	V99 Unassigned
SJ000288037	A Alimentary tract and metabolism; #J Antiinfectives for systemic use	A01 Stomatological preparations; #J01 Antibacterials for systemic use
SJ000288041	V Various	V99 Unassigned
SJ000288052	V Various	V99 Unassigned
SJ000288058	V Various	V99 Unassigned
SJ000288059	V Various	V99 Unassigned
SJ000288063	V Various	V99 Unassigned
SJ000288073	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000288074	V Various	V99 Unassigned
SJ000288081	V Various	V99 Unassigned
SJ000288084	V Various	V99 Unassigned
SJ000288092	V Various	V99 Unassigned
SJ000288093	V Various	V99 Unassigned
SJ000288098	R Respiratory system	R06 Antihistamines for systemic use
SJ000288099	V Various	V99 Unassigned
SJ000288114	V Various	V99 Unassigned
SJ000288126	V Various	V99 Unassigned
SJ000288139	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000288140	V Various	V99 Unassigned
SJ000288147	V Various	V99 Unassigned
SJ000288150	V Various	V99 Unassigned
SJ000288156	V Various	V99 Unassigned
SJ000288159	V Various	V99 Unassigned
SJ000288163	V Various	V99 Unassigned
SJ000288173	V Various	V99 Unassigned
SJ000288175	V Various	V99 Unassigned
SJ000288176	V Various	V99 Unassigned
SJ000288181	A Alimentary tract and metabolism	A03 Drugs for functional gastrointestinal disorders
SJ000288182	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000288186	V Various	V99 Unassigned
SJ000288194	V Various	V99 Unassigned
SJ000288209	V Various	V99 Unassigned
SJ000288210	V Various	V99 Unassigned
SJ000288211	V Various	V99 Unassigned
SJ000288216	V Various	V99 Unassigned
SJ000288219	V Various	V99 Unassigned
SJ000288224	V Various	V99 Unassigned
SJ000288226	V Various	V99 Unassigned
SJ000288238	V Various	V99 Unassigned
SJ000288244	L Antineoplastic and immunomodulating agents	L01 Antineoplastics agents
SJ000288246	V Various	V99 Unassigned
SJ000288249	S Sensory organics	S01 Ophthalmologicals
SJ000288262	V Various	V99 Unassigned
SJ000288270	V Various	V99 Unassigned
SJ000288274	V Various	V99 Unassigned
SJ000288278	V Various	V99 Unassigned
SJ000288284	V Various	V99 Unassigned
SJ000288304	V Various	V99 Unassigned
SJ000288306	V Various	V99 Unassigned
SJ000288308	V Various	V99 Unassigned
SJ000288312	V Various	V99 Unassigned
SJ000288313	V Various	V99 Unassigned
SJ000288316	S Sensory organics	S01 Ophthalmologicals
SJ000288318	V Various	V99 Unassigned
SJ000288320	V Various	V99 Unassigned

Figure 27 (continued)

Reg Number	ATC L1	ATC L2
SJ000288325	V Various	V99 Unassigned
SJ000288326	D Dermatologicals	D06 Antibiotics and chemotherapeutics for dermatological use
SJ000288327	V Various	V99 Unassigned
SJ000288328	V Various	V99 Unassigned
SJ000518967	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals
SJ000518972	P Antiparasitic products, insecticides, and repellents	P01 Antiprotozoals

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000000250	C01B Antiarrhythmics, class I and III	C01BC Antiarrhythmics, class Ic
SJ000000854	V99M Natural products	V99ME Flavone
SJ000113084	C02C Antiadrenergic agents, peripherally acting	C02CA Alpha-adrenoreceptor antagonists
SJ000126662	V99N Neurotransmitter	V99NU Purinergic agonist
SJ000285182	V99N Neurotransmitter	V99NJ GABA antagonist
SJ000285183	B05C Irrigating solutions; #D08A Antiseptics and disinfectants; #D09A Medicated dressings; #R02A Throat preparations	B05CA Antiinfectives; #D08AJ Quaternary ammonium compounds; #D09AA Medicated dressings with antiinfectives; #R02AA Antiseptics
SJ000285185	P01B Antimalarials	P01BA Aminoquinolines
SJ000285188	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285190	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285193	L01A Alkylating agents	L01AA Nitrogen mustard analogues
SJ000285194	L01A Alkylating agents	L01AA Nitrogen mustard analogues
SJ000285194	L01A Alkylating agents	L01AA Nitrogen mustard analogues
SJ000285195	L01B Antimetabolites	L01BB Purine analogues
SJ000285196	L01B Antimetabolites; #L04A Immunosuppressants	L01BA Folic acid analogues; #L04AX Other immunosuppressants
SJ000285197	L04A Immunosuppressants	L04AA Selective immunosuppressants
SJ000285200	P01C Agents against leishmaniasis and trypanosomiasis	P01CX Other agents against leishmaniasis and trypanosomiasis
SJ000285202	P01A Agents against amoebiasis and other protozoal diseases	P01AX Other agents against amoebiasis and other protozoal diseases
SJ000285203	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000285206	V99A Agricultural/Industrial	V99AG Rodenticide
SJ000285207	D08A Antiseptics and disinfectants	D08AK Mercurial products
SJ000285208	L01B Antimetabolites	L01BB Purine analogues
SJ000285210	L01A Alkylating agents	L01AA Nitrogen mustard analogues
SJ000285212	V99W Protein synthesis inhibitors	V99WA Other

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285215	P01A Agents against amoebiasis and other protozoal diseases	P01AX Other agents against amoebiasis and other protozoal diseases
SJ000285215	P01A Agents against amoebiasis and other protozoal diseases	P01AX Other agents against amoebiasis and other protozoal diseases
SJ000285218	V99U Phosphatase	V99UB PPA2/PP1
SJ000285219	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285219	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285220	V99M Natural products	V99ML Terpene
SJ000285221	L01B Antimetabolites	L01BA Folic acid analogues
SJ000285225	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000285226	J05A Direct acting antiviral drugs	J05AF Nucleoside and nucleotide reverse transcriptase inhibitors; #J05AR Antivirals for treatment of HIV infections, combinations
SJ000285227	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285228	V99W Protein synthesis inhibitors	V99WA Other
SJ000285229	V99R Other	V99RA Various
SJ000285231	V99S Oxidative phosphorylation	V99SD Transport inhibitors
SJ000285232	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000285232	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000285234	V99J Ion	V99JE Ionophore
SJ000285235	L01C Plant alkaloids and other natural products	L01CB Podophyllotoxin derivatives
SJ000285238	M04A Antigout preparations	M04AC Preparations with no effect on uric acid metabolism
SJ000285241	L04A Immunosuppressants	L04AX Other immunosuppressants
SJ000285242	D08A Antiseptics and disinfectants; #R02A Throat preparations	D08AJ Quaternary ammonium compounds; #R02AA Antiseptics
SJ000285243	L01D Cytotoxic antibiotics and related substances	L01DC Other cytotoxic antibiotics
SJ000285244	R02A Throat preparations	R02AB Antibiotics
SJ000285246	R02A Throat preparations	R02AA Antiseptics
SJ000285249	L01D Cytotoxic antibiotics and related substances	L01DA Actinomycines

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285256	L01D Cytotoxic antibiotics and related substances	L01DB Anthracyclines and related substances
SJ000285261	V99H Dermatological	V99HA Antiseptic
SJ000285262	A01A Stomatological preparations; #A07A Intestinal anti-infectives; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids; #J02A Antimycotics for systemic use	A01AB Anti-infectives and antiseptics for local oral treatment; #A07AA Antibiotics; #G01AA Antibiotics; #J02AA Antibiotics
SJ000285263	V99A Agricultural/Industrial	V99AA Disinfectant
SJ000285267	P03A Ectoparasitocides, including scabicides	P03AA Sulphur containing products
SJ000285270	L01A Alkylating agents	L01AC Ethylene imines
SJ000285272	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285273	D08A Antiseptics and disinfectants	D08AE Phenol and derivatives
SJ000285276	V99C Antimicrobial	V99CA Antimicrobial
SJ000285278	V99G Cytoskeletal	V99GB Inhibitors microtubule polymerization
SJ000285279	N07A Parasympathomimetics	N07AA Anticholinesterases
SJ000285285	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ0002852920	J04A Drugs for treatment of tuberculosis	J04AB Antibiotics
SJ000285294	D09A Medicated dressings	D09AA Medicated dressings with antiinfectives
SJ000285299	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000285307	V99C Antimicrobial	V99CA Antimicrobial
SJ000285308	D08A Antiseptics and disinfectants; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids; #R02A Throat preparations	D08AH Quinoline derivatives; #G01AC Quinoline derivatives; #R02AA Antiseptics
SJ000285313	V99M Natural products	V99MF Lipid
SJ000285315	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000285316	J01F Macrolides, lincosamides and streptogramins	J01FF Lincosamides

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285317	A01A Stomatological preparations; #D08A Antiseptics and disinfectants; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids; #R02A Throat preparations	A01AB Anti-infectives and antiseptics for local oral treatment; #D08AH Quinoline derivatives; #G01AC Quinoline derivatives; #R02AA Antiseptics
SJ000285318	S01E Antiglaucoma preparations and miotics; #V03A All other therapeutic products	S01EB Parasympathomimetics; #V03AB Antidotes
SJ000285319	A01A Stomatological preparations; #B05C Irrigating solutions; #D08A Antiseptics and disinfectants; #D09A Medicated dressings; #R02A Throat preparations; #S01A Anti-infectives; #S02A Anti-infectives; #S03A Anti-infectives	A01AB Anti-infectives and antiseptics for local oral treatment; #B05CA Antiinfectives; #D08AC Biguanides and amidines; #D09AA Medicated dressings with antiinfectives; #R02AA Antiseptics; #S01AX Other anti-infectives; #S02AA Anti-infectives; #S03AA Anti-infectives
SJ000285321	L01D Cytotoxic antibiotics and related substances	L01DB Anthracyclines and related substances
SJ000285323	V99H Dermatological	V99HA Antiseptic
SJ000285327	V99M Natural products	V99MA Alkaloid
SJ000285332	D11A Other dermatological preparations	D11AX Other dermatologicals
SJ000285334	J01F Macrolides, lincosamides and streptogramins	J01FA Macrolides
SJ000285335	L01C Plant alkaloids and other natural products	L01CA Vinca alkaloids and analogues
SJ000285335	L01C Plant alkaloids and other natural products	L01CA Vinca alkaloids and analogues
SJ000285337	D10A Anti-acne preparations for topical use; #D10B Anti-acne preparations for systemic use	D10AD Retinoids for topical use in acne; #D10BA Retinoids for treatment of acne
SJ000285337	D10A Anti-acne preparations for topical use; #L01X Other antineoplastic agents	D10AD Retinoids for topical use in acne; #L01XX Other antineoplastic agents

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285338	A01A Stomatological preparations; #B05C Irrigating solutions; #D08A Antiseptics and disinfectants; #D09A Medicated dressings; #R02A Throat preparations; #S01A Anti-infectives; #S02A Anti-infectives; #S03A Anti-infectives	A01AB Anti-infectives and antiseptics for local oral treatment; #B05CA Antiinfectives; #D08AC Biguanides and amidines; #D09AA Medicated dressings with antiinfectives; #R02AA Antiseptics; #S01AX Other anti-infectives; #S02AA Anti-infectives; #S03AA Anti-infectives
SJ000285343	A07A Intestinal anti-infectives	A07AB Sulfonamides
SJ000285358	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti-infectives in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000285363	N05A Antipsychotics	N05AH Diazepines, oxazepines, thiazepines and oxepines

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285364	C08D Selective calcium channel blockers with direct cardiac effects	C08DB Benzothiazepine derivatives
SJ000285365	V99J Ion	V99JE Ionophore
SJ000285368	V99M Natural products	V99MJ Steroid
SJ000285369	V99A Agricultural/Industrial	V99AA Disinfectant
SJ000285373	A03B Belladonna and derivatives, plain; #A03C Antispasmodics in combination with psycholeptics; #S01F Mydriatics and cycloplegics	A03BA Belladonna alkaloids, tertiary amines; #A03CB Belladonna and derivatives in combination with psycholeptics; #S01FA Anticholinergics
SJ000285375	N06A Antidepressants	N06AX Other antidepressants
SJ000285382	V99M Natural products	V99MJ Steroid
SJ000285383	R06A Antihistamines for systemic use	R06AX Other antihistamines for systemic use
SJ000285387	R01B Nasal decongestants for systemic use	R01BA Sympathomimetics
SJ000285396	V99N Neurotransmitter	V99NX Serotonin antagonist
SJ000285400	V99C Antimicrobial	V99CA Antimicrobial
SJ000285410	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000285413	V99M Natural products	V99MF Lipid
SJ000285423	V99L Lipase	V99LA Monoacylglycerol lipase
SJ000285426	V99R Other	V99RA Various
SJ000285431	P03A Ectoparasiticides, including scabicides	P03AX Other ectoparasiticides, including scabicides
SJ000285433	B01A Antithrombotic agents	B01AC Platelet aggregation inhibitors excluding heparin
SJ000285436	P01B Antimalarials	P01BE Artemisinin and derivatives, plain
SJ000285439	D06A Antibiotics for topical use; #R02A Throat preparations; #S01A Anti-infectives	D06AX Other antibiotics for topical use; #R02AB Antibiotics; #S01AA Antibiotics
SJ000285440	V99M Natural products	V99MH Quinone
SJ000285442	V99D Antioxidant	V99DA Antioxidant
SJ000285443	V99A Agricultural/Industrial	V99AB Dye
SJ000285445	V99O Nuclear hormone receptor	V99OI TR antagonist
SJ000285450	D08A Antiseptics and disinfectants	D08AA Acridine derivatives
SJ000285451	V99M Natural products	V99MA Alkaloid

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285452	A07E Intestinal anti-inflammatory agents; #D07A Corticosteroids, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	A07EA Corticosteroids acting locally; #D07AC Corticosteroids, potent (group III); #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000285452	A07E Intestinal anti-inflammatory agents; #D07A Corticosteroids, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	A07EA Corticosteroids acting locally; #D07AC Corticosteroids, potent (group III); #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000285453	C03D Potassium-sparing agents	C03DA Aldosterone antagonists
SJ000285454	J01D Other beta-lactam antibacterials	J01DB First-generation cephalosporins
SJ000285460	J01M Quinolone antibacterials	J01MB Other quinolones
SJ000285461	A03A Drugs for functional bowel disorders	A03AA Synthetic anticholinergics, esters with tertiary amino group
SJ000285462	D10A Anti-acne preparations for topical use	D10AF Anti-infectives for treatment of acne
SJ000285465	N06D Anti-dementia drugs	N06DX Other anti-dementia drugs
SJ000285466	N03A Antiepileptics	N03AG Fatty acid derivatives
SJ000285484	C01C Cardiac stimulants excluding cardiac glycosides	C01CA Adrenergic and dopaminergic agents
SJ000285487	C03B Low-ceiling diuretics, excluding thiazides; #R03D Other systemic drugs for obstructive airway diseases	C03BD Xanthine derivatives; #R03DA Xanthines
SJ000285490	V99M Natural products	V99MM Xanthanoid
SJ000285502	C01B Antiarrhythmics, class I and III	C01BD Antiarrhythmics, class III
SJ000285504	N01B Anesthetics, local	N01BB Amides
SJ000285506	V99R Other	V99RA Various
SJ000285508	L01C Plant alkaloids and other natural products	L01CD Taxanes
SJ000285512	V99M Natural products	V99ML Terpene

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285522	A08A Antiobesity preparations, excluding diet products; #C01C Cardiac stimulants excluding cardiac glycosides; #R01A Decongestants and other nasal preparations for topical use; #R03C Adrenergics for systemic use; #S01F Mydriatics and cycloplegics	A08AA Centrally acting antiobesity products; #C01CA Adrenergic and dopaminergic agents; #R01AA Sympathomimetics, plain; #R01AB Sympathomimetics, combinations excluding corticosteroids; #R03CA Alpha- and beta-adrenoreceptor agonists; #S01FB Sympathomimetics excluding antiglaucoma preparations
SJ000285526	V99N Neurotransmitter	V99NK GABA reuptake inhibitor
SJ000285536	N07A Parasympathomimetics; #S01E Antiglaucoma preparations and miotics	N07AX Other parasympathomimetics; #S01EB Parasympathomimetics
SJ000285540	C02C Antiadrenergic agents, peripherally acting; #C02L Antihypertensives and diuretics in combination	C02CA Alpha-adrenoreceptor antagonists; #C02LE Alpha-adrenoreceptor antagonists and diuretics
SJ000285541	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids; #V03A All other therapeutic products	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07CA Corticosteroids, weak, combinations with antibiotics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids; #V03AB Antidotes

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285542	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids; #V03A All other therapeutic products	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07CA Corticosteroids, weak, combinations with antibiotics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids; #V03AB Antidotes
SJ000285543	A07E Intestinal anti-inflammatory agents; #H02A Corticosteroids for systemic use, plain	A07EA Corticosteroids acting locally; #H02AB Glucocorticoids
SJ000285544	P01B Antimalarials	P01BA Aminoquinolines
SJ000285547	C01B Antiarrhythmics, class I and III	C01BA Antiarrhythmics, class Ia
SJ000285549	N05A Antipsychotics	N05AB Phenothiazines with piperazine structure
SJ000285551	G03D Progestogens; #G03F Progestogens and estrogens in combination	G03DA Pregnen-(4) derivatives; #G03FA Progestogens and estrogens, fixed combinations
SJ000285554	V99M Natural products	V99ME Flavone
SJ000285564	N06A Antidepressants	N06AF Monoamine oxidase inhibitors, non-selective
SJ000285569	P02C Antinematodal agents	P02CB Piperazine and derivatives
SJ000285572	M09A Other drugs for disorders of the musculo-skeletal system; #P01B Antimalarials	M09AA Quinine and derivatives; #P01BC Methanolquinolines

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285572	M09A Other drugs for disorders of the musculo-skeletal system; #P01B Antimalarials	M09AA Quinine and derivatives; #P01BC Methanolquinolines
SJ000285574	V99H Dermatological	V99HC Local anesthetic
SJ000285577	C03D Potassium-sparing agents	C03DA Aldosterone antagonists
SJ000285584	V99K Kinase	V99KC CK2 inhibitor
SJ000285586	G03B Androgens	G03BB 5-androstanon-(3) derivatives
SJ000285587	V99M Natural products	V99MM Xanthanoid
SJ000285588	V99M Natural products	V99ME Flavone
SJ000285591	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain; #S01B Anti-inflammatory agents	M01AA Butylpyrazolidines; #M02AA Anti-inflammatory preparations, non-steroids for topical use; #S01BC Anti-inflammatory agents, non-steroids
SJ000285592	L02B Hormone antagonists and related agents	L02BA Anti-estrogens
SJ000285606	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D04A Antipruritics, including antihistamines, anesthetics, etc.; #N01B Anesthetics, local; #S01H Local anesthetics	C05AD Local anesthetics; #D04AB Anesthetics for topical use; #N01BA Esters of aminobenzoic acid; #S01HA Local anesthetics
SJ000285608	N05A Antipsychotics	N05AF Thioxanthene derivative
SJ000285608	N05A Antipsychotics	N05AF Thioxanthene derivative
SJ000285610	N05A Antipsychotics	N05AC Phenothiazines with piperidine structure
SJ000285614	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain	M01AB Acetic acid derivatives and related substances; #M02AA Anti-inflammatory preparations, non-steroids for topical use
SJ000285618	M01A Anti-inflammatory and antirheumatic products, non-steroids	M01AB Acetic acid derivatives and related substances
SJ000285619	N02B Other analgesics and antipyretics	N02BB Pyrazolones
SJ000285625	G04B Other urologicals, including antispasmodics	G04BE Drugs used in erectile dysfunction

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285630	C01E Other cardiac preparations; #G02C Other gynecologicals; #M01A Anti-inflammatory and antirheumatic products, non- steroids; #M02A Topical products for joint and muscular pain	C01EB Other cardiac preparations; #G02CC Anti- inflammatory products for vaginal administration; #M01AE Propionic acid derivatives; #M02AA Anti-inflammatory preparations, non-steroids for topical use
SJ000285635	R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	R01AX Other nasal preparations; #R03BB Anticholinergics
SJ000285638	C04A Peripheral vasodilators	C04AA 2-amino-1-phenylethanol derivatives
SJ000285643	R06A Antihistamines for systemic use	R06AE Piperazine derivatives
SJ000285646	S01B Anti-inflammatory agents	S01BA Corticosteroids, plain
SJ000285651	H03B Antithyroid preparations	H03BB Sulphur-containing imidazole derivatives
SJ000285652	M03B Muscle relaxants, centrally acting agents	M03BA Carbamic acid esters
SJ000285655	C02A Antiadrenergic agents, centrally acting; #C02L Antihypertensives and diuretics in combination	C02AB Methyldopa; #C02LB Methyldopa and diuretics in combination
SJ000285657	D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics; #D10A Anti-acne preparations for topical use; #H02A Corticosteroids for systemic use, plain; #H02B Corticosteroids for systemic use, combinations; #S01E Antiglaucoma preparations and miotics	D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07CA Corticosteroids, weak, combinations with antibiotics; #D10AA Corticosteroids, combinations for treatment of acne; #H02AB Glucocorticoids; #H02BX Corticosteroids for systemic use, combinations; #S01CA Corticosteroids and anti- infectives in combination
SJ000285659	A01A Stomatological preparations; #J01A Tetracyclines	A01AB Anti-infectives and antiseptics for local oral treatment; #J01AA Tetracyclines

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285664	R01A Decongestants and other nasal preparations for topical use; #S01G Decongestants and antiallergics	R01AA Sympathomimetics, plain; #R01AB Sympathomimetics, combinations excluding corticosteroids; #S01GA Sympathomimetics used as decongestants
SJ000285666	C08C Selective calcium channel blockers with mainly vascular effects; #C08G Calcium channel blockers and diuretics	C08CA Dihydropyridine derivatives; #C08GA Calcium channel blockers and diuretics
SJ000285667	J01X Other antibacterials	J01XE Nitrofurans derivatives
SJ000285668	R05D Cough suppressants, excluding combinations with expectorants	R05DA Opium alkaloids and derivatives
SJ000285671	G03A Hormonal contraceptives for systemic use; #G03D Progestogens; #G03F Progestogens and estrogens in combination	G03AA Progestogens and estrogens, fixed combinations; #G03AB Progestogens and estrogens, sequential preparations; #G03AC Progestogens; #G03DC Estren derivatives; #G03FA Progestogens and estrogens, fixed combinations
SJ000285674	G03A Hormonal contraceptives for systemic use; #G03F Progestogens and estrogens in combination	G03AA Progestogens and estrogens, fixed combinations; #G03FA Progestogens and estrogens, fixed combinations; #G03FB Progestogens and estrogens, sequential preparations
SJ000285678	V99H Dermatological	V99HA Antiseptic
SJ000285683	A03A Drugs for functional bowel disorders; #G04B Other urologicals, including antispasmodics	A03AD Papaverine and derivatives; #G04BE Drugs used in erectile dysfunction
SJ000285684	V99H Dermatological	V99HD Sunscreen
SJ000285686	M03B Muscle relaxants, centrally acting agents	M03BX Other centrally acting agents
SJ000285687	N07A Parasympathomimetics	N07AB Choline esters
SJ000285688	V99N Neurotransmitter	V99ND Disrupts Dopamine biosynthesis

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285689	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D04A Antipruritics, including antihistamines, anesthetics, etc.; #N01B Anesthetics, local; #R02A Throat preparations	C05AD Local anesthetics; #D04AB Anesthetics for topical use; #N01BA Esters of aminobenzoic acid; #R02AD Anesthetics, local
SJ000285692	A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids	A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AC Corticosteroids, potent (group III); #D07BC Corticosteroids, potent, combinations with antiseptics; #D07CC Corticosteroids, potent, combinations with antibiotics; #D07XC Corticosteroids, potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids
SJ000285695	N07A Parasympathomimetics; #S01E Antiglaucoma preparations and miotics	N07AB Choline esters; #S01EB Parasympathomimetics
SJ000285696	N03A Antiepileptics	N03AF Carboxamide derivatives
SJ000285704	J01D Other beta-lactam antibacterials	J01DB First-generation cephalosporins
SJ000285710	D01A Antifungals for topical use; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	D01AE Other antifungals for topical use; #G01AX Other anti-infectives and antiseptics
SJ000285712	G03G Gonadotropins and other ovulation stimulants	G03GB Ovulation stimulants, synthetic

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285713	A01A Stomatological preparations; #D01A Antifungals for topical use; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	A01AB Anti-infectives and antiseptics for local oral treatment; #D01AC Imidazole and triazole derivatives; #G01AF Imidazole derivatives
SJ000285715	V99C Antimicrobial	V99CA Antimicrobial
SJ000285718	L01A Alkylating agents	L01AX Other alkylating agents
SJ000285725	V03A All other therapeutic products	V03AC Iron chelating agents
SJ000285727	D06A Antibiotics for topical use; #J01A Tetracyclines	D06AA Tetracycline and derivatives; #J01AA Tetracyclines
SJ000285728	D07C Corticosteroids, combinations with antibiotics; #R01A Decongestants and other nasal preparations for topical use; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02C Corticosteroids and anti- infectives in combination; #S03C Corticosteroids and anti-infectives in combination	D07CB Corticosteroids, moderately potent, combinations with antibiotics; #R01AD Corticosteroids; #S01CA Corticosteroids and anti- infectives in combination; #S02CA Corticosteroids and anti- infectives in combination; #S03CA Corticosteroids and anti- infectives in combination
SJ000285729	D07C Corticosteroids, combinations with antibiotics; #R01A Decongestants and other nasal preparations for topical use; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02C Corticosteroids and anti- infectives in combination; #S03C Corticosteroids and anti-infectives in combination	D07CB Corticosteroids, moderately potent, combinations with antibiotics; #R01AD Corticosteroids; #S01CA Corticosteroids and anti- infectives in combination; #S02CA Corticosteroids and anti- infectives in combination; #S03CA Corticosteroids and anti- infectives in combination
SJ000285740	S01A Anti-infectives	S01AA Antibiotics
SJ000285742	N03A Antiepileptics	N03AC Oxazolidine derivatives
SJ000285745	B01A Antithrombotic agents	B01AC Platelet aggregation inhibitors excluding heparin
SJ000285747	N07B Drugs used in addictive disorders; #P03A Ectoparasitocides, including scabicides	N07BB Drugs used in alcohol dependence; #P03AA Sulphur containing products
SJ000285748	C01C Cardiac stimulants excluding cardiac glycosides	C01CA Adrenergic and dopaminergic agents

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285750	A01A Stomatological preparations; #J01A Tetracyclines	A01AB Anti-infectives and antiseptics for local oral treatment; #J01AA Tetracyclines
SJ000285752	N01B Anesthetics, local; #R02A Throat preparations	N01BX Other local anesthetics; #R02AD Anesthetics, local
SJ000285761	C03C High-ceiling diuretics	C03CC Aryloxyacetic acid derivatives
SJ000285764	J04A Drugs for treatment of tuberculosis	J04AD Thiocarbamide derivatives
SJ000285766	H02A Corticosteroids for systemic use, plain; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	H02AA Mineralocorticoids; #S01CA Corticosteroids and anti-infectives in combination; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000285767	D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #S02C Corticosteroids and anti-infectives in combination	D07AB Corticosteroids, moderately potent (group II); #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07CB Corticosteroids, moderately potent, combinations with antibiotics; #D07XB Corticosteroids, moderately potent, other combinations; #S02CA Corticosteroids and anti-infectives in combination
SJ000285768	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics	C05AA Corticosteroids; #D07AC Corticosteroids, potent (group III); #D07CC Corticosteroids, potent, combinations with antibiotics

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285769	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #D10A Anti-acne preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination	C05AA Corticosteroids; #D07AB Corticosteroids, moderately potent (group II); #D07CB Corticosteroids, moderately potent, combinations with antibiotics; #D07XB Corticosteroids, moderately potent, other combinations; #D10AA Corticosteroids, combinations for treatment of acne; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination
SJ000285770	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain; #R02A Throat preparations; #S01B Anti-inflammatory agents	M01AE Propionic acid derivatives; #M02AA Anti-inflammatory preparations, non-steroids for topical use; #R02AX Other throat preparations; #S01BC Anti-inflammatory agents, non-steroids
SJ000285778	C02C Antiadrenergic agents, peripherally acting	C02CC Guanidine derivatives
SJ000285781	R02A Throat preparations	R02AA Antiseptics
SJ000285783	S01F Mydriatics and cycloplegics	S01FA Anticholinergics

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285786	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti- infectives in combination; #S01CB Corticosteroids/anti- infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti- infectives in combination; #S03CA Corticosteroids and anti- infectives in combination

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285787	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti- infectives in combination; #S01CB Corticosteroids/anti- infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti- infectives in combination; #S03CA Corticosteroids and anti- infectives in combination

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285787	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti-infectives in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000285790	G04B Other urologicals, including antispasmodics; #N04B Dopaminergic agents	G04BE Drugs used in erectile dysfunction; #N04BC Dopamine agonists
SJ000285797	D02B Protectives against UV-radiation	D02BA Protectives against UV-radiation for topical use
SJ000285801	P01B Antimalarials	P01BA Aminoquinolines
SJ000285812	J01E Sulfonamides and trimethoprim	J01EA Trimethoprim and derivatives
SJ000285814	G02C Other gynecologicals; #N04B Dopaminergic agents	G02CB Prolactin inhibitors; #N04BC Dopamine agonists
SJ000285814	G02C Other gynecologicals; #N04B Dopaminergic agents	G02CB Prolactin inhibitors; #N04BC Dopamine agonists

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285818	A01A Stomatological preparations; #J01A Tetracyclines	A01AB Anti-infectives and antiseptics for local oral treatment; #J01AA Tetracyclines
SJ000285820	A07E Intestinal anti-inflammatory agents; #D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	A07EA Corticosteroids acting locally; #D07AC Corticosteroids, potent (group III); #D07CC Corticosteroids, potent, combinations with antibiotics; #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000285827	A03A Drugs for functional bowel disorders	A03AD Papaverine and derivatives
SJ000285831	M01A Anti-inflammatory and antirheumatic products, non-steroids	M01AB Acetic acid derivatives and related substances
SJ000285834	C10A Lipid modifying agents, plain	C10AB Fibrates
SJ000285835	P02C Antinematodal agents	P02CA Benzimidazole derivatives
SJ000285836	R03B Other drugs for obstructive airway diseases, inhalants; #R03D Other systemic drugs for obstructive airway diseases	R03BX Other drugs for obstructive airway diseases, inhalants; #R03DX Other systemic drugs for obstructive airway diseases
SJ000285837	C08E Non-selective calcium channel blockers	C08EA Phenylalkylamine derivatives
SJ000285838	V99N Neurotransmitter	V99NT Other
SJ000285840	P02C Antinematodal agents	P02CA Benzimidazole derivatives
SJ000285842	V04C Other diagnostic agents	V04CH Tests for renal function
SJ000285845	C08C Selective calcium channel blockers with mainly vascular effects	C08CA Dihydropyridine derivatives
SJ000285849	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D04A Antipruritics, including antihistamines, anesthetics, etc.	C05AD Local anesthetics; #D04AB Anesthetics for topical use
SJ000285858	A02B Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)	A02BA H2-receptor antagonists

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285860	C04A Peripheral vasodilators	C04AX Other peripheral vasodilators
SJ000285864	M02A Topical products for joint and muscular pain	M02AA Anti-inflammatory preparations, non-steroids for topical use
SJ000285866	M01A Anti-inflammatory and antirheumatic products, non-steroids	M01AE Propionic acid derivatives
SJ000285878	G03C Estrogens	G03CA Natural and semisynthetic estrogens, plain
SJ000285879	D01A Antifungals for topical use; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	D01AC Imidazole and triazole derivatives; #G01AF Imidazole derivatives
SJ000285880	R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000285881	V99D Antioxidant	V99DA Antioxidant
SJ000285882	G03C Estrogens	G03CA Natural and semisynthetic estrogens, plain; #G03CC Estrogens, combinations with other drugs
SJ000285885	V99V Phosphodiesterase	V99VC Other
SJ000285887	A10B Blood glucose lowering drugs, excluding insulins	A10BB Sulfonamides, urea derivatives
SJ000285888	C09A ACE inhibitors, plain; #C09B ACE inhibitors, combinations	C09AA ACE inhibitors, plain; #C09BB ACE inhibitors and calcium channel blockers
SJ000285890	C09A ACE inhibitors, plain; #C09B ACE inhibitors, combinations	C09AA ACE inhibitors, plain; #C09BA ACE inhibitors and diuretics; #C09BB ACE inhibitors and calcium channel blockers
SJ000285892	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain	M01AB Acetic acid derivatives and related substances; #M02AA Anti-inflammatory preparations, non-steroids for topical use
SJ000285903	J01M Quinolone antibacterials; #S01A Anti-infectives	J01MA Fluoroquinolones; #S01AX Other anti-infectives
SJ000285909	V03A All other therapeutic products	V03AB Antidotes
SJ000285920	V99N Neurotransmitter	V99NI GABA agonist

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285922	V99N Neurotransmitter	V99NI GABA agonist
SJ000285925	V99N Neurotransmitter	V99ND Disrupts Dopamine biosynthesis
SJ000285935	P01B Antimalarials	P01BC Methanolquinolines
SJ000285936	A03A Drugs for functional bowel disorders	A03AA Synthetic anticholinergics, esters with tertiary amino group
SJ000285940	R05C Expectorants, excluding combinations with cough suppressants	R05CB Mucolytics
SJ000285949	C08E Non-selective calcium channel blockers	C08EA Phenylalkylamine derivatives
SJ000285950	R05C Expectorants, excluding combinations with cough suppressants	R05CB Mucolytics
SJ000285951	A03F Propulsives	A03FA Propulsives
SJ000285958	J01X Other antibacterials	J01XX Other antibacterials
SJ000285959	S01A Anti-infectives	S01AB Sulfonamides
SJ000285960	M03B Muscle relaxants, centrally acting agents	M03BX Other centrally acting agents
SJ000285965	N06B Psychostimulants, agents used for ADHD and nootropics	N06BX Other psychostimulants and nootropics
SJ000285966	V99H Dermatological	V99HA Antiseptic
SJ000285967	C08E Non-selective calcium channel blockers	C08EX Other non-selective calcium channel blockers
SJ000285971	S01E Antiglaucoma preparations and miotics	S01EC Carbonic anhydrase inhibitors
SJ000285972	D08A Antiseptics and disinfectants; #R02A Throat preparations	D08AJ Quaternary ammonium compounds; #R02AA Antiseptics
SJ000285973	D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics; #D10A Anti-acne preparations for topical use; #H02A Corticosteroids for systemic use, plain; #H02B Corticosteroids for systemic use, combinations; #S01E Antiglaucoma preparations and miotics	D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07CA Corticosteroids, weak, combinations with antibiotics; #D10AA Corticosteroids, combinations for treatment of acne; #H02AB Glucocorticoids; #H02BX Corticosteroids for systemic use, combinations; #S01CA Corticosteroids and anti-infectives in combination

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285974	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000285978	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti-infectives in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000285980	N02B Other analgesics and antipyretics	N02BB Pyrazolones
SJ000285983	C02K Other antihypertensives	C02KD Serotonin antagonists
SJ000285987	P02C Antinematodal agents	P02CA Benzimidazole derivatives
SJ000285991	D08A Antiseptics and disinfectants; #D09A Medicated dressings; #R02A Throat preparations	D08AJ Quaternary ammonium compounds; #D09AA Medicated dressings with antiinfectives; #R02AA Antiseptics

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000285996	C10A Lipid modifying agents, plain; #C10B Lipid modifying agents, combinations	C10AA HMG CoA reductase inhibitors; #C10BX HMG CoA reductase inhibitors, other combinations
SJ000285998	D07A Corticosteroids, plain	D07AC Corticosteroids, potent (group III)
SJ000285999	N01B Anesthetics, local	N01BB Amides
SJ000286003	V99J Ion	V99JE Ionophore
SJ000286004	V99J Ion	V99JC SERCA inhibitor
SJ000286006	D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics	D07AD Corticosteroids, very potent (group IV); #D07CD Corticosteroids, very potent, combinations with antibiotics
SJ000286007	C03B Low-ceiling diuretics, excluding thiazides	C03BA Sulfonamides, plain; #C03BB Sulfonamides and potassium in combination
SJ000286008	R05D Cough suppressants, excluding combinations with expectorants	R05DB Other cough suppressants
SJ000286018	V99D Antioxidant	V99DA Antioxidant
SJ000286024	D01A Antifungals for topical use; #J02A Antimycotics for systemic use	D01AC Imidazole and triazole derivatives; #J02AC Triazole derivatives
SJ000286025	C10A Lipid modifying agents, plain; #C10B Lipid modifying agents, combinations	C10AA HMG CoA reductase inhibitors; #C10BA HMG CoA reductase inhibitors in combination with other lipid modifying agents
SJ000286030	L01C Plant alkaloids and other natural products	L01CB Podophyllotoxin derivatives
SJ000286034	V99A Agricultural/Industrial	V99AC Fungicide
SJ000286035	L02B Hormone antagonists and related agents	L02BG Enzyme inhibitors
SJ000286036	V99O Nuclear hormone receptor	V99OF RAR-alpha agonist
SJ000286037	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors
SJ000286038	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000286038	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000286039	A10B Blood glucose lowering drugs, excluding insulins	A10BB Sulfonamides, urea derivatives
SJ000286041	V08A X-ray contrast media, iodinated	V08AA Water-soluble, nephrotropic, high osmolar X-ray contrast media

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286044	V99U Phosphatase	V99UB PPA2/PP1
SJ000286046	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors
SJ000286046	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors
SJ000286052	P01A Agents against amoebiasis and other protozoal diseases	P01AX Other agents against amoebiasis and other protozoal diseases
SJ000286053	P01B Antimalarials	P01BB Biguanides
SJ000286056	V99J Ion	V99JH Sodium/Proton antiport inhibitor
SJ000286057	D08A Antiseptics and disinfectants; #R02A Throat preparations	D08AA Acridine derivatives; #R02AA Antiseptics
SJ000286063	C10A Lipid modifying agents, plain; #C10B Lipid modifying agents, combinations	C10AA HMG CoA reductase inhibitors; #C10BA HMG CoA reductase inhibitors in combination with other lipid modifying agents; #C10BX HMG CoA reductase inhibitors, other combinations
SJ000286065	C07A Beta blocking agents	C07AG Alpha and beta blocking agents
SJ000286075	G04B Other urologicals, including antispasmodics	G04BD Urinary antispasmodics
SJ000286086	A11H Other plain vitamin preparations	A11HA Other plain vitamin preparations
SJ000286093	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors
SJ000286097	M01A Anti-inflammatory and antirheumatic products, non-steroids	M01AE Propionic acid derivatives
SJ000286098	P03A Ectoparasiticides, including scabicides	P03AX Other ectoparasiticides, including scabicides
SJ000286101	V99J Ion	V99JG Sodium/calcium exchange inhibitor
SJ000286109	N04A Anticholinergic agents	N04AC Ethers of tropine or tropine derivatives
SJ000286112	V99N Neurotransmitter	V99NB Adrenergic agonist
SJ000286113	C08D Selective calcium channel blockers with direct cardiac effects	C08DA Phenylalkylamine derivatives
SJ000286118	R06A Antihistamines for systemic use	R06AX Other antihistamines for systemic use

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286121	N06A Antidepressants	N06AA Non-selective monoamine reuptake inhibitors
SJ000286124	N06A Antidepressants	N06AF Monoamine oxidase inhibitors, non-selective
SJ000286127	R07A Other respiratory system products	R07AB Respiratory stimulants
SJ000286128	V99D Antioxidant	V99DA Antioxidant
SJ000286133	N07C Antivertigo preparations	N07CA Antivertigo preparations
SJ000286134	N05A Antipsychotics	N05AB Phenothiazines with piperazine structure
SJ000286142	A01A Stomatological preparations; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S02C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #C05AA Corticosteroids; #D07AB Corticosteroids, moderately potent (group II); #D07XB Corticosteroids, moderately potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S02CA Corticosteroids and anti-infectives in combination
SJ000286143	C03A Low-ceiling diuretics, thiazides; #C03E Diuretics and potassium-sparing agents in combination	C03AA Thiazides, plain; #C03EA Low-ceiling diuretics and potassium-sparing agents
SJ000286144	C03D Potassium-sparing agents	C03DB Other potassium-sparing agents
SJ000286146	A07E Intestinal anti-inflammatory agents	A07EC Aminosalicyclic acid and similar agents
SJ000286151	G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	G01AE Sulfonamides
SJ000286152	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain	M01AX Other anti-inflammatory and antirheumatic agents, non-steroids; #M02AA Anti-inflammatory preparations, non-steroids for topical use

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286154	A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids	A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AC Corticosteroids, potent (group III); #D07BC Corticosteroids, potent, combinations with antiseptics; #D07CC Corticosteroids, potent, combinations with antibiotics; #D07XC Corticosteroids, potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids
SJ000286155	D04A Antipruritics, including antihistamines, anesthetics, etc.; #R06A Antihistamines for systemic use	D04AA Antihistamines for topical use; #R06AA Aminoalkyl ethers

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286156	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07AC Corticosteroids, potent (group III); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CA Corticosteroids and anti-infectives in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000286159	P01B Antimalarials	P01BD Diaminopyrimidines
SJ000286160	P02C Antineoplastic agents	P02CX Other antineoplastics
SJ000286162	V99A Agricultural/Industrial	V99AH Surfactant
SJ000286166	D06A Antibiotics for topical use; #J01G Aminoglycoside antibacterials; #S01A Anti-infectives; #S02A Anti-infectives; #S03A Anti-infectives	D06AX Other antibiotics for topical use; #J01GB Other aminoglycosides; #S01AA Antibiotics; #S02AA Anti-infectives; #S03AA Anti-infectives
SJ000286172	D11A Other dermatological preparations	D11AX Other dermatologicals
SJ000286174	J01M Quinolone antibacterials	J01MA Fluoroquinolones
SJ000286175	V99R Other	V99RA Various
SJ000286178	V99N Neurotransmitter	V99NJ GABA antagonist

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286181	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000286185	N05A Antipsychotics	N05AB Phenothiazines with piperazine structure
SJ000286186	N04A Anticholinergic agents	N04AA Tertiary amines
SJ000286187	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000286188	V99F Biochemicals	V99FA Amino acid
SJ000286191	V99M Natural products	V99MA Alkaloid
SJ000286195	D01A Antifungals for topical use; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	D01AC Imidazole and triazole derivatives; #G01AF Imidazole derivatives
SJ000286199	V99A Agricultural/Industrial	V99AE Pesticide
SJ000286204	D04A Antipruritics, including antihistamines, anesthetics, etc.; #R06A Antihistamines for systemic use	D04AA Antihistamines for topical use; #R06AD Phenothiazine derivatives
SJ000286205	A01A Stomatological preparations; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S02C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #C05AA Corticosteroids; #D07AB Corticosteroids, moderately potent (group II); #D07XB Corticosteroids, moderately potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S02CA Corticosteroids and anti-infectives in combination
SJ000286213	V99N Neurotransmitter	V99NO MOA inhibitor
SJ000286217	J01B Amphenicols	J01BA Amphenicols
SJ000286225	P02C Antinematodal agents	P02CE Imidazothiazole derivatives
SJ000286229	V99K Kinase	V99KI PKA activator
SJ000286231	V99N Neurotransmitter	V99NL Glutamine agonist
SJ000286236	N03A Anticpileptics	N03AF Carboxamide derivatives
SJ000286243	V99R Other	V99RA Various
SJ000286248	V99M Natural products	V99MG Other
SJ000286251	V99M Natural products	V99ML Terpene

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286267	V99M Natural products	V99ML Terpene
SJ000286300	V99W Protein synthesis inhibitors	V99WA Other
SJ000286312	V99A Agricultural/Industrial	V99AH Surfactant
SJ000286359	V99M Natural products	V99MA Alkaloid
SJ000286366	V99M Natural products	V99MJ Steroid
SJ000286380	V99A Agricultural/Industrial	V99AB Dye
SJ000286381	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000286382	V99M Natural products	V99MG Other
SJ000286387	V99M Natural products	V99ME Flavone
SJ000286389	V99M Natural products	V99MD Chalcone
SJ000286393	V99M Natural products	V99MD Chalcone
SJ000286395	V99M Natural products	V99ME Flavone
SJ000286396	V99M Natural products	V99MD Chalcone
SJ000286398	V99M Natural products	V99MH Quinone
SJ000286406	V99M Natural products	V99MG Other
SJ000286408	A11C Vitamin A and D, including combinations of the two	A11CC Vitamin D and analogues
SJ000286413	V99M Natural products	V99MH Quinone
SJ000286415	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000286419	V99M Natural products	V99MG Other
SJ000286421	V99M Natural products	V99MH Quinone
SJ000286423	V99M Natural products	V99MG Other
SJ000286424	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000286430	V99M Natural products	V99MH Quinone
SJ000286434	V99M Natural products	V99MG Other
SJ000286436	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000286438	V99M Natural products	V99MG Other
SJ000286446	V99M Natural products	V99MD Chalcone
SJ000286448	L01D Cytotoxic antibiotics and related substances	L01DB Anthracyclines and related substances
SJ000286450	V99M Natural products	V99MG Other
SJ000286451	V99J Ion	V99JF Sodium channel agonist
SJ000286453	V99C Antimicrobial	V99CA Antimicrobial
SJ000286455	V99M Natural products	V99ME Flavone
SJ000286458	V99M Natural products	V99MG Other

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286481	C02A Antiadrenergic agents, centrally acting; #C02L Antihypertensives and diuretics in combination; #N02C Antimigraine preparations; #S01E Antiglaucoma preparations and miotics	C02AC Imidazoline receptor agonists; #C02LC Imidazoline receptor agonists in combination with diuretics; #N02CX Other antimigraine preparations; #S01EA Sympathomimetics in glaucoma therapy
SJ000286496	V99F Biochemicals	V99FC Nucleic acid
SJ000286501	V99M Natural products	V99MA Alkaloid
SJ000286511	V99M Natural products	V99MJ Steroid
SJ000286515	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000286515	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000286516	P02D Anticestodals	P02DA Salicylic acid derivatives
SJ000286520	V99M Natural products	V99ME Flavone
SJ000286522	V99M Natural products	V99MH Quinone
SJ000286525	V99M Natural products	V99ME Flavone
SJ000286530	V99M Natural products	V99MG Other
SJ000286533	V99M Natural products	V99MG Other
SJ000286536	V99M Natural products	V99ML Terpene
SJ000286537	V99M Natural products	V99MG Other
SJ000286548	V99Q Nucleic acid	V99QA DNA intercalator
SJ000286550	C01B Antiarrhythmics, class I and III	C01BB Antiarrhythmics, class Ib

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286552	A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids	A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AC Corticosteroids, potent (group III); #D07BC Corticosteroids, potent, combinations with antiseptics; #D07CC Corticosteroids, potent, combinations with antibiotics; #D07XC Corticosteroids, potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids
SJ000286565	V99M Natural products	V99MH Quinone
SJ000286572	G03B Androgens; #G03E Androgens and female sex hormones in combination	G03BA 3-oxoandrostene-(4) derivatives; #G03EA Androgens and estrogens
SJ000286576	V99R Other	V99RA Various
SJ000286594	V99A Agricultural/Industrial	V99AD Herbicide
SJ000286616	V99A Agricultural/Industrial	V99AD Herbicide
SJ000286619	V99A Agricultural/Industrial	V99AD Herbicide
SJ000286644	V99A Agricultural/Industrial	V99AF Plasticizer
SJ000286645	V99A Agricultural/Industrial	V99AH Surfactant
SJ000286646	V99A Agricultural/Industrial	V99AD Herbicide
SJ000286648	V99M Natural products	V99MG Other
SJ000286657	V99N Neurotransmitter	V99NO MOA inhibitor
SJ000286658	V99M Natural products	V99MA Alkaloid
SJ000286694	V99M Natural products	V99MF Lipid
SJ000286708	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000286710	V99R Other	V99RA Various
SJ000286711	V99M Natural products	V99MG Other
SJ000286715	V99M Natural products	V99MI Saponin
SJ000286728	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286729	V99N Neurotransmitter	V99NL Glutamine agonist
SJ000286749	V99M Natural products	V99MG Other
SJ000286751	D08A Antiseptics and disinfectants; #R02A Throat preparations	D08AJ Quaternary ammonium compounds; #R02AA Antiseptics
SJ000286753	M04A Antigout preparations	M04AC Preparations with no effect on uric acid metabolism
SJ000286767	V99M Natural products	V99MC Catechol
SJ000286769	V99M Natural products	V99MF Lipid
SJ000286772	V99M Natural products	V99MD Chalcone
SJ000286775	P02C Antinematodal agents	P02CF Avermectines
SJ000286776	V99N Neurotransmitter	V99NL Glutamine agonist
SJ000286780	V99F Biochemicals	V99FA Amino acid
SJ000286781	V99C Antimicrobial	V99CA Antimicrobial
SJ000286782	V99M Natural products	V99MG Other
SJ000286783	V99M Natural products	V99MG Other
SJ000286797	L01A Alkylating agents	L01AA Nitrogen mustard analogues
SJ000286800	V99M Natural products	V99ML Terpene
SJ000286801	V99M Natural products	V99ML Terpene
SJ000286802	V99M Natural products	V99ME Flavone
SJ000286804	G03B Androgens; #G03E Androgens and female sex hormones in combination	G03BA 3-oxoandrostene-(4) derivatives; #G03EA Androgens and estrogens
SJ000286809	V99M Natural products	V99MG Other
SJ000286813	V99M Natural products	V99ME Flavone
SJ000286816	V99M Natural products	V99MG Other
SJ000286821	V99M Natural products	V99ME Flavone
SJ000286829	V99F Biochemicals	V99FD Steroid
SJ000286830	V99M Natural products	V99ML Terpene
SJ000286847	V99M Natural products	V99MG Other
SJ000286853	H02A Corticosteroids for systemic use, plain	H02AA Mineralocorticoids
SJ000286865	V99M Natural products	V99MG Other
SJ000286868	V99M Natural products	V99ML Terpene
SJ000286877	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000286884	A11H Other plain vitamin preparations	A11HA Other plain vitamin preparations
SJ000286890	V99M Natural products	V99MH Quinone
SJ000286899	V99F Biochemicals	V99FD Steroid

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000286902	A01A Stomatological preparations; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants; #S01B Anti-inflammatory agents; #S02C Corticosteroids and anti-infectives in combination	A01AC Corticosteroids for local oral treatment; #C05AA Corticosteroids; #D07AB Corticosteroids, moderately potent (group II); #D07XB Corticosteroids, moderately potent, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #R03BA Glucocorticoids; #S01BA Corticosteroids, plain; #S02CA Corticosteroids and anti-infectives in combination
SJ000286904	V99M Natural products	V99MG Other
SJ000286906	N03A Antiepileptics	N03AG Fatty acid derivatives
SJ000286948	D07A Corticosteroids, plain	D07AD Corticosteroids, very potent (group IV)
SJ000286950	L04A Immunosuppressants; #S01X Other ophthalmologicals	L04AD Calcineurin inhibitors; #S01XA Other ophthalmologicals
SJ000286959	V99M Natural products	V99MG Other
SJ000286960	V99D Antioxidant	V99DA Antioxidant
SJ000286962	V99M Natural products	V99ME Flavone
SJ000286963	V99M Natural products	V99MG Other
SJ000286965	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000286983	S01A Anti-infectives	S01AD Antivirals
SJ000286986	V99L Lipase	V99LA Monoacylglycerol lipase
SJ000286993	V99M Natural products	V99MG Other
SJ000287007	V99M Natural products	V99ME Flavone

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287016	C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S02C Corticosteroids and anti-infectives in combination	C05AA Corticosteroids; #D07AC Corticosteroids, potent (group III); #D07BC Corticosteroids, potent, combinations with antiseptics; #D07CC Corticosteroids, potent, combinations with antibiotics; #S01BA Corticosteroids, plain; #S01CA Corticosteroids and anti-infectives in combination; #S02BA Corticosteroids; #S02CA Corticosteroids and anti-infectives in combination
SJ000287020	V99M Natural products	V99ML Terpene
SJ000287054	V99M Natural products	V99MN Polyphenol
SJ000287055	C10A Lipid modifying agents, plain	C10AA HMG CoA reductase inhibitors
SJ000287058	V99M Natural products	V99ML Terpene
SJ000287059	V99D Antioxidant	V99DA Antioxidant
SJ000287062	V99T Peptidase	V99TF Other
SJ000287073	V99M Natural products	V99MK Stilbene
SJ000287074	V99M Natural products	V99MK Stilbene
SJ000287076	N05A Antipsychotics	N05AH Diazepines, oxazepines, thiazepines and oxepines
SJ000287077	V99M Natural products	V99MH Quinone
SJ000287078	V99M Natural products	V99MK Stilbene
SJ000287087	V99T Peptidase	V99TF Other
SJ000287088	J01D Other beta-lactam antibacterials	J01DC Second-generation cephalosporins
SJ000287090	V99C Antimicrobial	V99CA Antimicrobial
SJ000287092	V99S Oxidative phosphorylation	V99SB Phosphorylation inhibitors
SJ000287098	V99M Natural products	V99ME Flavone
SJ000287101	V99M Natural products	V99MG Other

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287102	D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #S02C Corticosteroids and anti-infectives in combination	D07AB Corticosteroids, moderately potent (group II); #D07BB Corticosteroids, moderately potent, combinations with antiseptics; #D07CB Corticosteroids, moderately potent, combinations with antibiotics; #D07XB Corticosteroids, moderately potent, other combinations; #S02CA Corticosteroids and anti- infectives in combination
SJ000287131	V99M Natural products	V99ME Flavone
SJ000287132	N05A Antipsychotics	N05AD Butyrophenone derivatives
SJ000287133	V99M Natural products	V99MG Other
SJ000287134	V99B Anti-inflammatory	V99BA Inhibits NF-kB
SJ000287136	V99D Antioxidant	V99DA Antioxidant
SJ000287138	D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics	D07AC Corticosteroids, potent (group III); #D07CC Corticosteroids, potent, combinations with antibiotics
SJ000287139	V99R Other	V99RA Various
SJ000287147	V99M Natural products	V99MH Quinone
SJ000287149	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000287150	D01A Antifungals for topical use; #S01B Anti-inflammatory agents	D01AE Other antifungals for topical use; #S01BC Anti- inflammatory agents, non- steroids
SJ000287152	L01B Antimetabolites	L01BB Purine analogues

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287155	A01A Stomatological preparations; #A07E Intestinal anti-inflammatory agents; #C05A Agents for treatment of hemorrhoids and anal fissures for topical use; #D07A Corticosteroids, plain; #D07B Corticosteroids, combinations with antiseptics; #D07C Corticosteroids, combinations with antibiotics; #D07X Corticosteroids, other combinations; #H02A Corticosteroids for systemic use, plain; #R01A Decongestants and other nasal preparations for topical use; #S01B Anti-inflammatory agents; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02B Corticosteroids; #S03B Corticosteroids; #V03A All other therapeutic products	A01AC Corticosteroids for local oral treatment; #A07EA Corticosteroids acting locally; #C05AA Corticosteroids; #D07AA Corticosteroids, weak (group I); #D07BA Corticosteroids, weak, combinations with antiseptics; #D07CA Corticosteroids, weak, combinations with antibiotics; #D07XA Corticosteroids, weak, other combinations; #H02AB Glucocorticoids; #R01AD Corticosteroids; #S01BA Corticosteroids, plain; #S01BB Corticosteroids and mydriatics in combination; #S01CB Corticosteroids/anti-infectives/mydriatics in combination; #S02BA Corticosteroids; #S03BA Corticosteroids; #V03AB Antidotes
SJ000287160	D06B Chemotherapeutics for topical use; #J05A Direct acting antiviral drugs; #S01A Anti-infectives	D06BB Antivirals; #J05AB Nucleosides and nucleotides excluding reverse transcriptase inhibitors; #S01AD Antivirals
SJ000287177	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors
SJ000287181	V99C Antimicrobial	V99CA Antimicrobial
SJ000287182	V99N Neurotransmitter	V99NM Glutamine antagonist
SJ000287193	P02C Antinematodal agents	P02CF Avermectines
SJ000287195	G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	G01AG Triazole derivatives
SJ000287203	V08A X-ray contrast media, iodinated	V08AB Water-soluble, nephrotropic, low osmolar X-ray contrast media
SJ000287206	A07A Intestinal anti-infectives; #D01A Antifungals for topical use; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids	A07AA Antibiotics; #D01AA Antibiotics; #G01AA Antibiotics

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287209	C10A Lipid modifying agents, plain	C10AA HMG CoA reductase inhibitors
SJ000287215	M01A Anti-inflammatory and antirheumatic products, non-steroids; #M02A Topical products for joint and muscular pain	M01AB Acetic acid derivatives and related substances; #M02AA Anti-inflammatory preparations, non-steroids for topical use
SJ000287222	V99S Oxidative phosphorylation	V99SA Respiratory chain inhibitors
SJ000287228	P02C Antinematodal agents	P02CA Benzimidazole derivatives
SJ000287229	A04A Antiemetics and antinauseants	A04AD Other antiemetics
SJ000287231	H02A Corticosteroids for systemic use, plain; #S01C Anti-inflammatory agents and anti-infectives in combination; #S02C Corticosteroids and anti-infectives in combination; #S03C Corticosteroids and anti-infectives in combination	H02AA Mineralocorticoids; #S01CA Corticosteroids and anti-infectives in combination; #S02CA Corticosteroids and anti-infectives in combination; #S03CA Corticosteroids and anti-infectives in combination
SJ000287238	C04A Peripheral vasodilators	C04AX Other peripheral vasodilators
SJ000287239	V99J Ion	V99JI Potassium channel inhibitor
SJ000287245	N05A Antipsychotics	N05AF Thioxanthene derivative
SJ000287247	L01B Antimetabolites	L01BB Purine analogues
SJ000287256	V99N Neurotransmitter	V99NG Dopamine reuptake inhibitor
SJ000287261	V99W Protein synthesis inhibitors	V99WA Other
SJ000287270	V99F Biochemicals	V99FD Steroid
SJ000287281	B02B Vitamin K and other hemostatics	B02BA Vitamin K
SJ000287282	G02A Oxytocics	G02AD Prostaglandins
SJ000287283	A03F Propulsives	A03FA Propulsives
SJ000287295	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000287300	V09I Tumour detection	V09IX Other diagnostic radiopharmaceuticals for tumour detection
SJ000287313	A07A Intestinal anti-infectives	A07AX Other intestinal anti-infectives
SJ000287314	V99N Neurotransmitter	V99NE Dopamine agonist

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287317	C04A Peripheral vasodilators; #N04B Dopaminergic agents	C04AE Ergot alkaloids; #N04BC Dopamine agonists
SJ000287320	D07A Corticosteroids, plain; #D07X Corticosteroids, other combinations; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	D07AC Corticosteroids, potent (group III); #D07XC Corticosteroids, potent, other combinations; #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000287329	V99M Natural products	V99MA Alkaloid
SJ000287330	V99M Natural products	V99MG Other
SJ000287331	V99Q Nucleic acid	V99QA DNA intercalator
SJ000287333	D07A Corticosteroids, plain	D07AC Corticosteroids, potent (group III)
SJ000287335	V99N Neurotransmitter	V99NO MOA inhibitor
SJ000287348	V99M Natural products	V99MA Alkaloid
SJ000287350	J01G Aminoglycoside antibacterials	J01GB Other aminoglycosides
SJ000287365	V99M Natural products	V99MA Alkaloid
SJ000287368	V99M Natural products	V99MA Alkaloid
SJ000287384	V99J Ion	V99JE Ionophore
SJ000287393	D07A Corticosteroids, plain; #S01B Anti-inflammatory agents	D07AB Corticosteroids, moderately potent (group II); #S01BA Corticosteroids, plain
SJ000287394	L04A Immunosuppressants	L04AA Selective immunosuppressants
SJ000287395	V99H Dermatological	V99HA Antiseptic
SJ000287397	V99Q Nucleic acid	V99QA DNA intercalator
SJ000287398	S01F Mydriatics and cycloplegics	S01FA Anticholinergics
SJ000287400	N05A Antipsychotics	N05AA Phenothiazines with aliphatic side-chain
SJ000287409	S01E Antiglaucoma preparations and miotics	S01ED Beta blocking agents
SJ000287413	N06A Antidepressants	N06AB Selective serotonin reuptake inhibitors

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287428	D08A Antiseptics and disinfectants; #D09A Medicated dressings; #G01A Antiinfectives and antiseptics, excluding combinations with corticosteroids; #P01A Agents against amoebiasis and other protozoal diseases; #S02A Anti-infectives	D08AH Quinoline derivatives; #D09AA Medicated dressings with antiinfectives; #G01AC Quinoline derivatives; #P01AA Hydroxyquinoline derivatives; #S02AA Anti-infectives
SJ000287441	D11A Other dermatological preparations	D11AX Other dermatologicals
SJ000287448	V99A Agricultural/Industrial	V99AH Surfactant
SJ000287450	N06A Antidepressants	N06AA Non-selective monoamine reuptake inhibitors
SJ000287457	V99J Ion	V99JD Chelator
SJ000287461	J01B Amphenicols	J01BA Amphenicols
SJ000287462	V99F Biochemicals	V99FD Steroid
SJ000287467	M03A Muscle relaxants, peripherally acting agents	M03AB Choline derivatives
SJ000287484	A10B Blood glucose lowering drugs, excluding insulins	A10BB Sulfonamides, urea derivatives
SJ000287488	D07A Corticosteroids, plain; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	D07AC Corticosteroids, potent (group III); #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000287490	J01A Tetracyclines	J01AA Tetracyclines
SJ000287493	N01A Anesthetics, general	N01AX Other general anesthetics
SJ000287506	C01E Other cardiac preparations; #G04B Other urologicals, including antispasmodics	C01EA Prostaglandins; #G04BE Drugs used in erectile dysfunction
SJ000287508	H02A Corticosteroids for systemic use, plain; #S01B Anti-inflammatory agents	H02AB Glucocorticoids; #S01BA Corticosteroids, plain
SJ000287523	D07A Corticosteroids, plain	D07AC Corticosteroids, potent (group III)
SJ000287543	A03A Drugs for functional bowel disorders	A03AB Synthetic anticholinergics, quaternary ammonium compounds
SJ000287544	V99C Antimicrobial	V99CA Antimicrobial
SJ000287545	P02C Antinematodal agents	P02CA Benzimidazole derivatives

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287547	A03D Antispasmodics in combination with analgesics	A03DA Synthetic anticholinergic agents in combination with analgesics
SJ000287561	S01L Ocular vascular disorder agents	S01LA Antineovascularisation agents
SJ000287562	J04A Drugs for treatment of tuberculosis	J04AB Antibiotics
SJ000287563	P02C Antinematodal agents	P02CA Benzimidazole derivatives
SJ000287568	D07A Corticosteroids, plain	D07AB Corticosteroids, moderately potent (group II)
SJ000287585	V99I Eicosanoid	V99IA 5-Lipoxygenase inhibitor
SJ000287590	V99J Ion	V99JH Sodium/Proton antiport inhibitor
SJ000287618	V99N Neurotransmitter	V99NM Glutamine antagonist
SJ000287619	V99N Neurotransmitter	V99ND Disrupts Dopamine biosynthesis
SJ000287632	V99N Neurotransmitter	V99NU Purinergic agonist
SJ000287647	V99K Kinase	V99KJ PKA inhibitor
SJ000287648	V99N Neurotransmitter	V99NH Disrupts GABA biosynthesis
SJ000287657	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000287660	A07E Intestinal anti-inflammatory agents; #D07A Corticosteroids, plain; #D07C Corticosteroids, combinations with antibiotics; #R01A Decongestants and other nasal preparations for topical use; #R03B Other drugs for obstructive airway diseases, inhalants	A07EA Corticosteroids acting locally; #D07AC Corticosteroids, potent (group III); #D07CC Corticosteroids, potent, combinations with antibiotics; #R01AD Corticosteroids; #R03BA Glucocorticoids
SJ000287663	V99W Protein synthesis inhibitors	V99WA Other
SJ000287667	V99K Kinase	V99KG p38MAP inhibitor
SJ000287668	J05A Direct acting antiviral drugs	J05AB Nucleosides and nucleotides excluding reverse transcriptase inhibitors
SJ000287676	V99B Anti-inflammatory	V99BA Inhibits NF-kB
SJ000287677	V99K Kinase	V99KI PKA activator
SJ000287680	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287682	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287686	V99J Ion	V99JG Sodium/calcium exchange inhibitor

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287690	V99K Kinase	V99KB CDK/GSK3 inhibitor
SJ000287692	V99N Neurotransmitter	V99NS NK3 antagonist
SJ000287693	V99O Nuclear hormone receptor	V99OF RAR-alpha agonist
SJ000287697	V99U Phosphatase	V99UA CDC25
SJ000287703	V99Q Nucleic acid	V99QC Nucleotide transport inhibitor
SJ000287705	V99K Kinase	V99KE JNK inhibitor
SJ000287706	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287714	V99J Ion	V99JK VR1 agonist
SJ000287728	L01B Antimetabolites	L01BC Pyrimidine analogues
SJ000287730	V99N Neurotransmitter	V99NC Adrenergic antagonist
SJ000287734	C02C Antiadrenergic agents, peripherally acting	C02CA Alpha-adrenoreceptor antagonists
SJ000287737	V99V Phosphodiesterase	V99VB PD7
SJ000287741	V99K Kinase	V99KK PKC inhibitor
SJ000287744	V99N Neurotransmitter	V99NX Serotonin antagonist
SJ000287749	V99R Other	V99RA Various
SJ000287750	V99R Other	V99RA Various
SJ000287752	V99T Peptidase	V99TF Other
SJ000287758	V99K Kinase	V99KB CDK/GSK3 inhibitor
SJ000287762	V99N Neurotransmitter	V99NC Adrenergic antagonist
SJ000287767	V99N Neurotransmitter	V99NM Glutamine antagonist
SJ000287768	V99J Ion	V99JE Ionophore
SJ000287769	V99U Phosphatase	V99UB PPA2/PP1
SJ000287778	V99N Neurotransmitter	V99NW Serotonin agonist
SJ000287799	V99P Nitric oxide pathway	V99PB NOS inhibitor
SJ000287810	V99Q Nucleic acid	V99QB Inhibits RNA synthesis
SJ000287813	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287814	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287821	V99M Natural products	V99MH Quinone
SJ000287827	L01C Plant alkaloids and other natural products	L01CB Podophyllotoxin derivatives
SJ000287837	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000287841	V99T Peptidase	V99TA Serine
SJ000287864	V99K Kinase	V99KE JNK inhibitor
SJ000287868	V99K Kinase	V99KK PKC inhibitor
SJ000287873	V99R Other	V99RA Various
SJ000287875	V99N Neurotransmitter	V99NU Purinergic agonist
SJ000287882	V99K Kinase	V99KD ERBB inhibitor
SJ000287889	V99N Neurotransmitter	V99NC Adrenergic antagonist

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000287891	V99N Neurotransmitter	V99NJ GABA antagonist
SJ000287899	V99K Kinase	V99KK PKC inhibitor
SJ000287901	V99R Other	V99RA Various
SJ000287902	V99N Neurotransmitter	V99NG Dopamine reuptake inhibitor
SJ000287925	L01D Cytotoxic antibiotics and related substances	L01DB Anthracyclines and related substances
SJ000287942	V04B Urine tests	V04BA Various
SJ000287955	V99N Neurotransmitter	V99NW Serotonin agonist
SJ000287956	V99J Ion	V99JA Calcium channel inhibitor
SJ000287970	V99N Neurotransmitter	V99NP Monoamine uptake inhibitor
SJ000287972	N03A Antiepileptics	N03AX Other antiepileptics
SJ000287975	V99N Neurotransmitter	V99NN Histamine antagonist
SJ000287985	V99K Kinase	V99KH PI3K inhibitor
SJ000287990	V99M Natural products	V99MH Quinone
SJ000287995	V03A All other therapeutic products	V03AB Antidotes
SJ000288002	L01X Other antineoplastic agents	L01XX Other antineoplastic agents
SJ000288007	C08C Selective calcium channel blockers with mainly vascular effects	C08CX Other selective calcium channel blockers with mainly vascular effects
SJ000288017	V99N Neurotransmitter	V99NR Cholinergic antagonist
SJ000288020	V03A All other therapeutic products	V03AB Antidotes
SJ000288025	V99N Neurotransmitter	V99NV Purinergic antagonist
SJ000288026	V99H Dermatological	V99HB Irritant
SJ000288030	V99N Neurotransmitter	V99NX Serotonin antagonist
SJ000288031	V99N Neurotransmitter	V99NE Dopamine agonist
SJ000288034	V99N Neurotransmitter	V99OE PPAR antagonist
SJ000288037	A01A Stomatological preparations; #J01A Tetracyclines	A01AB Anti-infectives and antiseptics for local oral treatment; #J01AA Tetracyclines
SJ000288041	V99N Neurotransmitter	V99NV Purinergic antagonist
SJ000288052	V99N Neurotransmitter	V99NT Other
SJ000288058	V99N Neurotransmitter	V99NQ Cholinergic agonist
SJ000288059	V99P Nitric oxide pathway	V99PA NO donor
SJ000288063	V99N Neurotransmitter	V99NR Cholinergic antagonist
SJ000288073	L01X Other antineoplastic agents	L01XX Other antineoplastic agents

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000288074	V99F Biochemicals	V99FB Cofactor
SJ000288081	V99M Natural products	V99MF Lipid
SJ000288084	V99N Neurotransmitter	V99ND Disrupts Dopamine biosynthesis
SJ000288092	V99M Natural products	V99MK Stilbene
SJ000288093	V99N Neurotransmitter	V99NJ GABA antagonist
SJ000288098	R06A Antihistamines for systemic use	R06AE Piperazine derivatives
SJ000288099	V99P Nitric oxide pathway	V99PA NO donor
SJ000288114	V99N Neurotransmitter	V99NU Purinergic agonist
SJ000288126	V99T Peptidase	V99TE Metalloprotease
SJ000288139	V99N Neurotransmitter	V99ND Disrupts Dopamine biosynthesis
SJ000288140	V99K Kinase	V99KA Casein kinase inhibitor
SJ000288147	V99P Nitric oxide pathway	V99PB NOS inhibitor
SJ000288150	V99F Biochemicals	V99FD Steroid
SJ000288156	V99R Other	V99RA Various
SJ000288159	V99N Neurotransmitter	V99NW Serotonin agonist
SJ000288163	V99R Other	V99RA Various
SJ000288173	V99Q Nucleic acid	V99QD Topoisomerase II inhibitor
SJ000288175	V99I Eicosanoid	V99II Prostanoid antagonist
SJ000288176	V99J Ion	V99JA Calcium channel inhibitor
SJ000288181	A03B Belladonna and derivatives, plain; #A03D Antispasmodics in combination with analgesics	A03BB Belladonna alkaloids, semisynthetic, quaternary ammonium compounds; #A03DB Belladonna and derivatives in combination with analgesics
SJ000288182	L01X Other antineoplastic agents	L01XE Protein kinase inhibitors
SJ000288186	V99K Kinase	V99KK PKC inhibitor
SJ000288194	V99N Neurotransmitter	V99NC Adrenergic antagonist
SJ000288209	V99N Neurotransmitter	V99OD PPAR agonist
SJ000288210	V99B Anti-inflammatory	V99BA Inhibits NF-kB
SJ000288211	V99K Kinase	V99KD ERBB inhibitor
SJ000288216	V99V Phosphodiesterase	V99VC Other
SJ000288219	V99K Kinase	V99KD ERBB inhibitor
SJ000288224	V99N Neurotransmitter	V99NX Serotonin antagonist
SJ000288226	V99K Kinase	V99KN TRKA inhibitor
SJ000288238	V99N Neurotransmitter	V99NR Cholinergic antagonist
SJ000288244	L01C Plant alkaloids and other natural products	L01CA Vinca alkaloids and analogues

Figure 27 (continued)

Reg Number	ATC L3	ATC L4
SJ000288246	V99V Phosphodiesterase	V99VA PD5
SJ000288249	S01E Antiglaucoma preparations and miotics	S01EA Sympathomimetics in glaucoma therapy
SJ000288262	V99Q Nucleic acid	V99QD Topoisomerase II inhibitor
SJ000288270	V99K Kinase	V99KH PI3K inhibitor
SJ000288274	V99K Kinase	V99KO VEGF/PDGF inhibitor
SJ000288278	V99J Ion	V99JB SERCA agonist
SJ000288284	V99I Eicosanoid	V99IB Leukotriene agonist
SJ000288304	V99N Neurotransmitter	V99NG Dopamine reuptake inhibitor
SJ000288306	V99N Neurotransmitter	V99OF RAR-alpha agonist
SJ000288308	V99R Other	V99RA Various
SJ000288312	V99K Kinase	V99KB CDK/GSK3 inhibitor
SJ000288313	V99D Antioxidant	V99DA Antioxidant
SJ000288316	S01E Antiglaucoma preparations and miotics	S01EB Parasympathomimetics
SJ000288318	V99N Neurotransmitter	V99NW Serotonin agonist
SJ000288320	V99K Kinase	V99KB CDK/GSK3 inhibitor
SJ000288325	V99E Apoptosis	V99EA Modulates P53 response
SJ000288326	D06B Chemotherapeutics for topical use	D06BB Antivirals
SJ000288327	V99N Neurotransmitter	V99OG RAR-beta agonist
SJ000288328	V99K Kinase	V99KF MNK1 inhibitor
SJ000518967	P01B Antimalarials	P01BE Artemisinin and derivatives, plain; #P01BF Artemisinin and derivatives, combinations
SJ000518972	P01B Antimalarials	P01BE Artemisinin and derivatives, plain; #P01BF Artemisinin and derivatives, combinations

Figure 27 (continued)

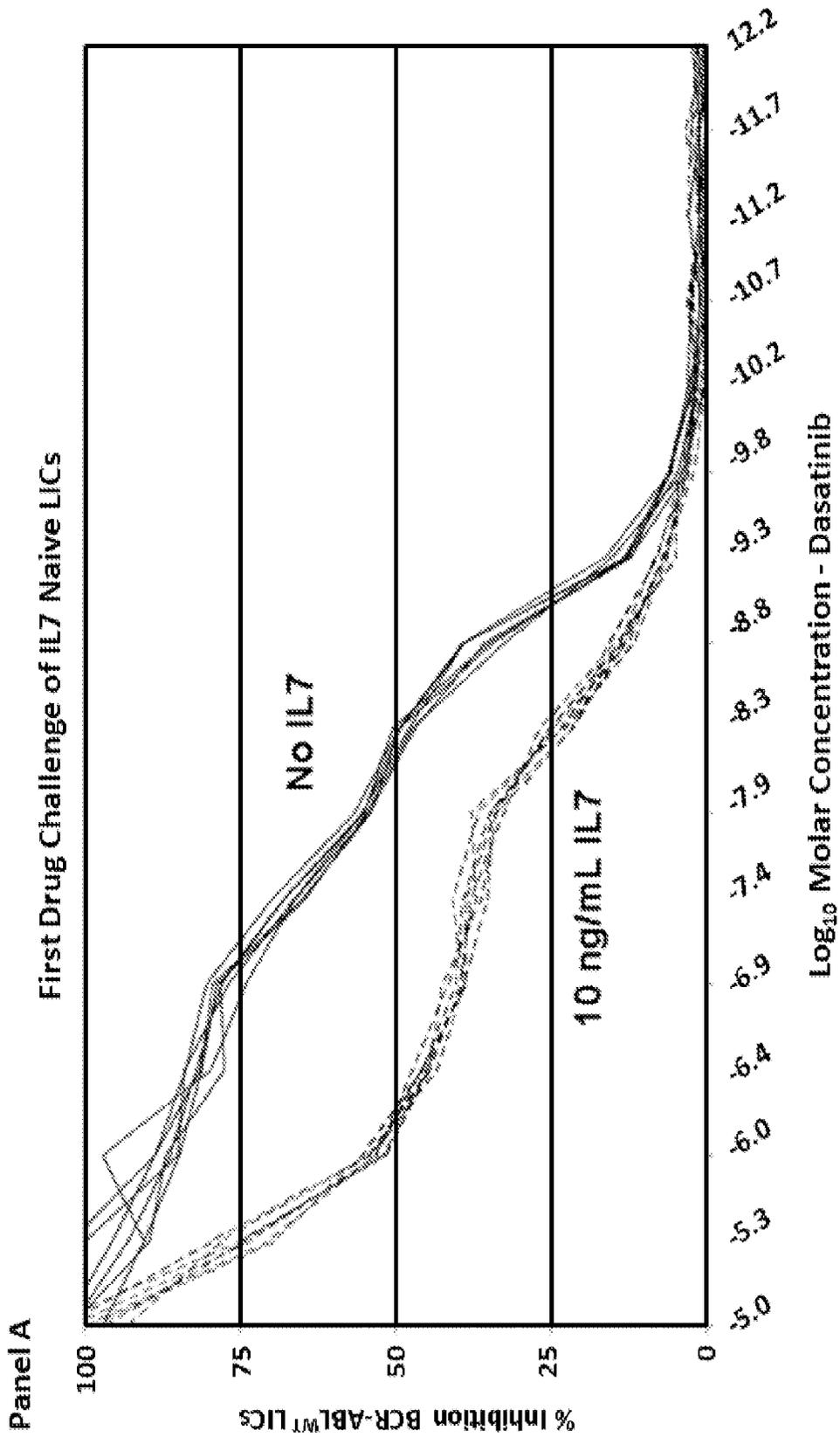


Figure 28

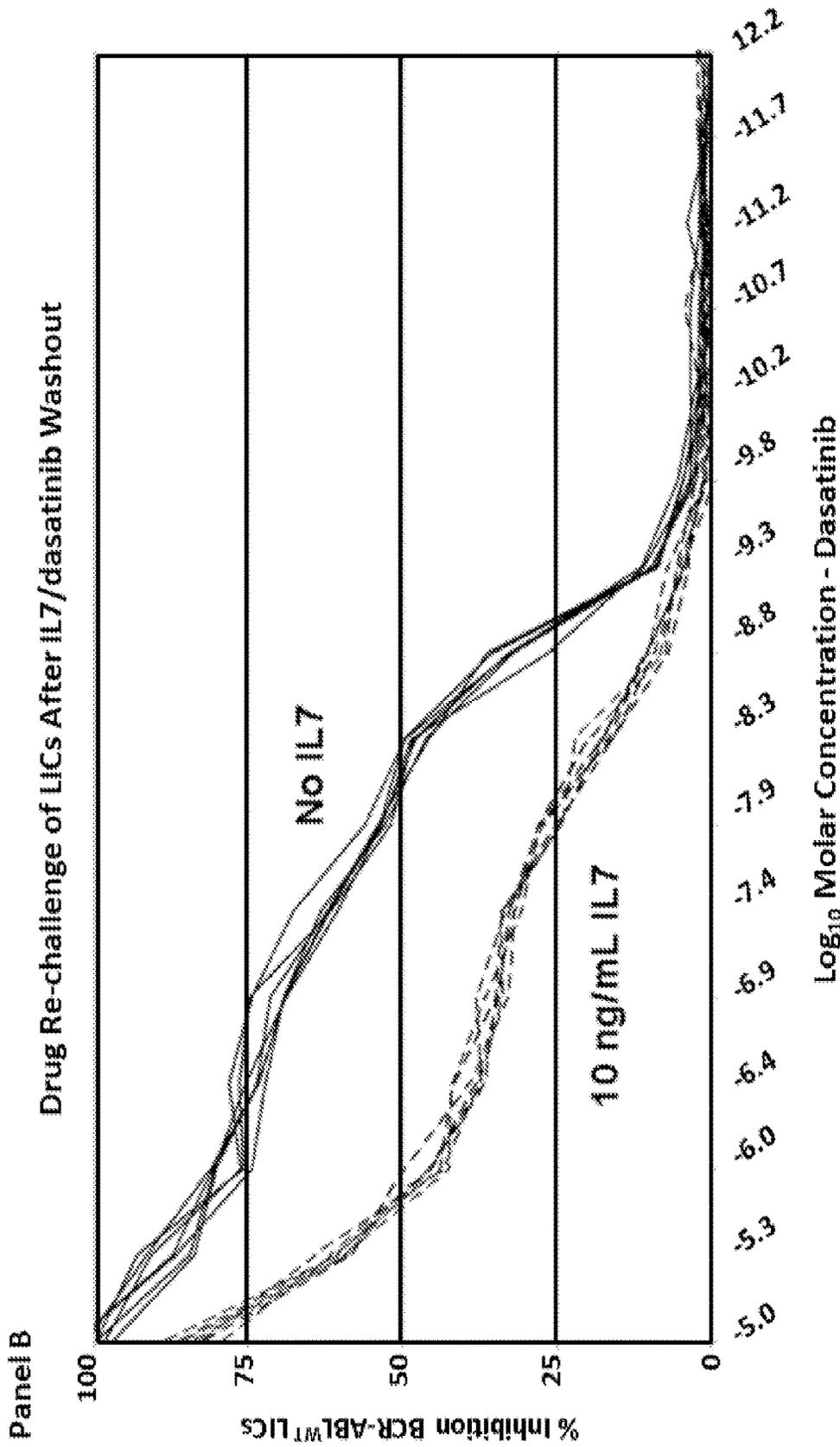


Figure 28, continued

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METHODS AND COMPOSITIONS FOR THE TREATMENT OF BCR-ABL POSITIVE LYMPHOBLASTIC LEUKEMIAS

CROSS-REFERENCE TO RELATED APPLICATIONS

This Application claims the benefit of U.S. Provisional Application No. 61/650,948 filed on May 23, 2012, which is incorporated herein by reference in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

This invention was made in part with government support under grant numbers NIH CA021765 and NIH NS066460 awarded by the National Institute of Health (NIH). The United States government has certain rights in the invention.

BACKGROUND

Hyperproliferative disorders, such as cancer, are associated with the growth of abnormal, or neoplastic cells. In cancer, this uncontrolled cellular proliferation will often result in unregulated growth of malignant tissue and invasion of adjacent or local cells. Eventually, the malignant cells spread, or metastasize, to lymph nodes or remote areas by traveling through the blood or lymphatic system. Moreover, these abnormal cells are often able to proliferate under conditions where a normal cell would not grow.

Although the etiology of cancer has not been clearly defined, numerous mechanisms and processes have been implicated in disease onset and progression, including both environmental and genetic factors. However, cancer pathogenesis ultimately results from DNA mutations that impact cell growth, differentiation, and/or survival.

Cancer encompasses a broad group of medical conditions and syndromes, and can manifest in almost any organ and/or tissue in the body. As a result, there are many types of cancer, for example, bladder, breast, cervical, colon, hematologic, lung, ovarian, pancreatic, prostate, renal cell, and testicular. Moreover, cancer can present in any age, in many forms, and with varying degrees of invasiveness and aggressiveness.

Traditionally, treatments for cancer have involved surgery, radiation and chemotherapy. Depending on the type and location of the cancer, surgery can be an option for certain patients. Surgery is often a radical step and can invariably carry serious risks for the patient. In addition to surgical complications, there always exists the risk the entire cancer cannot be removed. Radiation therapy involves the use of ionizing radiation to kill cancer cells. Although radiation therapy is effective in killing cancer cells, it carries the risk of concurrently damaging non-cancerous cells. Higher and frequent radiation dosing can have long-term risks, such as secondary malignancies and reproductive effects. Chemotherapy involves administering cytotoxic drugs to the patient, often in a regimen involving a combination of such drugs. While chemotherapy is effective in killing cancer cells, it also harms normal cells that divide rapidly, leading to adverse side effects such as myelosuppression. Chemotherapy is often accompanied by additional side effects, such as severe nausea/vomiting and organ specific toxicities, which can force premature discontinuation of treatment.

Most recently, research has focused on identifying specific cellular targets for therapies. Unlike standard chemo-

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therapy, targeted therapies are designed to only interact with specific molecular targets involved in the pathways and processes. These pathways and processes are used by cancer cells to grow, divide, and spread throughout the body. In the body, tyrosine kinases (TKs) are known to phosphorylate specific tyrosyl residues in specific proteins involved in regulating cell proliferation and differentiation. Unregulated activation of such kinases, resulting from genetic abnormalities (e.g. point mutations; translocation and genomic amplification) in the genes that encode these proteins, can result in unregulated cell growth. For example, BCR-ABL tyrosine kinase (BCR-ABL TK) has been known to activate many pro-growth and cell survival mechanisms, which in turn promote cell proliferation and survival, and contribute to BCR-ABL mediated leukemic transformation of bone marrow progenitor cells. Therefore, BCR-ABL TK-specific inhibition has been the focus of significant drug discovery efforts. BCR-ABL TK-specific inhibitors (BCR-ABL TKIs), such as imatinib, can bind and stabilize the inactive conformation, and have been successful in maintaining certain chronic myelogenous leukemias (CML) in remission to a controlled chronic condition.

However, BCR-ABL TKIs have failed to produce a similar long-term response in related leukemias, such as pediatric and adult Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL). While current BCR-ABL-targeted drugs appear to kill Ph+ ALL cells in vitro, these drugs fail to meaningfully maintain low levels of leukemia burden in patients with Ph+ ALL, invariably leading to relapse and poor long-term outcomes. Additionally, such therapy also fails to eradicate persistent disease in patients with either Ph+ ALL or CML. Although additional chemotherapy and/or hematopoietic stem cell transplantation (HSCT) can improve the remission rate for some Ph+ ALL patients, relapses remain common, with an 18- to 24-month survival rate of 64% and an even worse relapse-free survival rate.

Resistance to BCR-ABL TKIs is believed to contribute to the inability to induce adequate clinical responses. A major mechanism of BCR-ABL TKI resistance is thought to relate to mutations that result in the interference of drug binding to the BCR-ABL kinase domain. BCR-ABL mutations confer different levels of resistance, ranging from concentration dependent resistance to complete BCR-ABL TKI resistance. The most clinically significant BCR-ABL kinase domain (KD) mutations are P-loop mutations and the T315I mutation. Significantly, the T315I mutation produces the most common and highest form of resistance of any mutation, resulting in resistance to both imatinib and second generation BCR-ABL TKIs, dasatinib and nilotinib. Nevertheless, differences in clinical responses to BCR-ABL TKIs in patients with Ph+ ALL and CML remain poorly understood, and cannot be exclusively attributed to mutations in the BCR-ABL kinase domain that impair drug binding.

Therefore, defining and countering the factors that underlie the transient response to BCR-ABL TKIs in patients with non-mutated BCR-ABL Ph+ ALL is critical for developing effective therapies that improve long-term survival. Moreover, contemporary medicine advocates co-treatment with agents of complementary mechanisms of action to counteract clinical drug resistance and improve outcomes. Therefore, there remains a need for therapies that are both safe, efficacious and complement targeted therapeutic agents for the treatment of cancer. These needs and other needs are satisfied by the present invention.

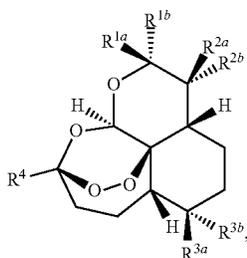
SUMMARY

In accordance with the purpose(s) of the invention, as embodied and broadly described herein, the invention, in

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one aspect, relates to compounds and compositions useful as therapies in disorders of uncontrolled cellular proliferation, pharmaceutical compositions comprising same, and methods of treating BCR-ABL-mediated disorders using same. For example, compounds capable of counteracting or overcoming cytokine-related drug resistance (e.g., dihydroartemisinin (DHA)), in combination with a BCR-ABL tyrosine kinase inhibitor, can be useful in hematologic cancer therapies (e.g., for treating leukemias or lymphomas).

Disclosed herein are pharmaceutical compositions comprising a therapeutically effective amount of a BCR-ABL tyrosine kinase inhibitor; and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:



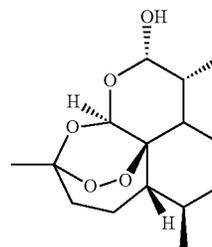
wherein R^{1a} and R^{1b} together are (C=O) or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-\text{NH}_2$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-\text{NH}(\text{C1-C6 alkyl})$, $-\text{N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, $-\text{O}(\text{C1-C8 alkyl})\text{C3-C6 cycloalkyl}$, $-\text{O}(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{OH}$, $-\text{O}(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$, $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$, $-\text{O}(\text{C1-C8 alkyl})\text{-aryl}$, and $-\text{O}\text{-aryl}$; wherein each of aryl, C2-05 heterocycloalkyl, C3-C6 cycloalkyl, and $-\text{O}(\text{C1-C8 alkyl})\text{C3-C6 cycloalkyl}$, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, $-\text{NH}_2$, $-(\text{C}=\text{O})\text{OH}$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-\text{NH}(\text{C1-C6 alkyl})$, $-\text{N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$, $-(\text{C1-C6 alkyl})\text{-NH}(\text{C1-C6 alkyl})$, and $-(\text{C1-C6 alkyl})\text{-N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$; wherein R^{2a} and R^{2b} together are $(\text{C}=\text{CR}^{5a}\text{R}^{5b})$ or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$; wherein each of R^{5a} and R^{5b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl; wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and wherein R^4 is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$; or a pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; and optionally a pharmaceutically acceptable carrier.

Also disclosed herein are methods for the treatment of a Philadelphia chromosome positive leukemia in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof.

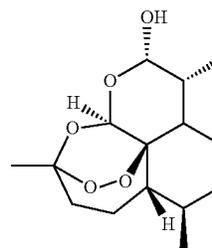
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Also disclosed herein are method for the treatment of a gastrointestinal stromal tumor (GIST) in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof.

Also disclosed herein are methods for the treatment of a Philadelphia chromosome positive leukemia in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor, and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; wherein administering the artemisinin analogue to a patient produces a metabolite in the patient with a structure represented by the formula:



Also disclosed herein are methods for the treatment of a gastrointestinal stromal tumor (GIST) in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor, and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; wherein administering the artemisinin analogue to a patient produces a metabolite in the patient with a structure represented by the formula:



Also disclosed herein are kits comprising a BCR-ABL kinase inhibitor, at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof; and instructions for treatment of a disease of uncontrolled cellular proliferation; and wherein the instructions comprise administration of a BCR-ABL kinase inhibitor and the at least one artemisinin analogue to a patient that has become refractory to treatment with a BCR-ABL kinase inhibitor.

Also disclosed are methods for manufacturing a medicament comprising combining at least one disclosed compound with a pharmaceutically acceptable carrier or diluent, wherein the medicament is used to treat a Philadelphia chromosome positive leukemia.

Also disclosed are uses of a disclosed composition or compound for the treatment of a disease of uncontrolled cellular proliferation in a patient.

While aspects of the present invention can be described and claimed in a particular statutory class, such as the system statutory class, this is for convenience only and one of skill in the art will understand that each aspect of the present invention can be described and claimed in any statutory class. Unless otherwise expressly stated, it is in no way intended that any method or aspect set forth herein be construed as requiring that its steps be performed in a specific order. Accordingly, where a method claim does not specifically state in the claims or descriptions that the steps are to be limited to a specific order, it is no way intended that an order be inferred, in any respect. This holds for any possible non-express basis for interpretation, including matters of logic with respect to arrangement of steps or operational flow, plain meaning derived from grammatical organization or punctuation, or the number or type of aspects described in the specification.

BRIEF DESCRIPTION OF THE FIGURES

The accompanying figures, which are incorporated in and constitute a part of this specification, illustrate several aspects and together with the description serve to explain the principles of the invention.

FIG. 1 shows representative in vitro data pertaining to the growth properties of Arf^{-/-}BCR-ABL+preB cells.

FIG. 2 shows representative data pertaining to development of the high-throughput LIC-based phenotypic assay.

FIG. 3 shows a representative schematic of screen used to identify compounds preventing growth of wild type and BCR-ABL^{MUTANT} Ph+ ALL cells in the presence of IL7.

FIG. 4 shows a representative radar plot pertaining to the effect of 15 hematopoietic cytokines on dasatinib potency (EC₅₀) against Arf^{-/-} BCR-ABL^{WT} LICs.

FIG. 5 shows representative data pertaining to LIC growth inhibition following 72-h treatment with drug or DMSO in the absence (dark gray) or presence (light gray) of 1 ng/mL murine IL7.

FIG. 6 shows representative data pertaining to cell viability of human Ph+ ALL SUPB15 cells following 72-h drug-treatment in absence or presence of 25 ng/mL human IL7.

FIG. 7 shows representative data pertaining to LIC growth inhibition following 72-hr treatment with drug.

FIG. 8 shows representative data pertaining to in vitro leukemia clonal outgrowth following treatment with drug or DMSO.

FIG. 9 shows representative data pertaining to LIC viability following treatment with drug in the presence or absence of IL7.

FIG. 10 shows representative data pertaining to overall survival of host mice receiving Arf^{-/-} BCR-ABL^{WT} LICs injections following treatment with vehicle or drug.

FIG. 11 shows frequency of ATC Level 1 and ATC Level 2 compounds for the 706 compounds submitted to secondary analysis.

FIG. 12 shows representative data pertaining to screening quality metrics for High Throughput (HT) drug screen against BCR-ABL^{WT} LICs.

FIG. 13 shows representative data pertaining to screening quality metrics for High Throughput (HT) drug screen against BCR-ABL^{T315I} LICs.

FIG. 14 shows representative data pertaining to LIC growth inhibition following treatment with drug.

FIG. 15 shows representative data pertaining to the discriminatory power of the phenotypic assay.

FIG. 16 shows representative data pertaining to LIC growth inhibition following 72-hr treatment with artemisinin, artesunate, and dihydroartemisinin.

FIG. 17 shows representative data pertaining to cell viability of human Ph+ ALL SUPB15 cells following 72-h drug-treatment.

FIG. 18 shows representative data pertaining to overall survival of host mice receiving Arf^{-/-} BCR-ABL^{WT} LICs injections following treatment with vehicle or drug.

FIG. 19 shows representative data pertaining to overall survival of host mice receiving Arf^{-/-} BCR-ABL^{WT} LICs injections following treatment with vehicle or drug.

FIG. 20 shows representative data pertaining to overall survival of host mice receiving Arf^{-/-} BCR-ABL^{WT} LICs injections following treatment with vehicle or drug.

FIG. 21 shows representative data pertaining to overall survival of host mice receiving Arf^{-/-} BCR-ABL^{WT} LICs injections following treatment with vehicle or drug.

FIG. 22 shows representative data pertaining to overall survival of nonconditioned immunocompetent C57Bl/6J mice receiving LIC injections.

FIG. 23 shows the data relating to the 15 leukemia microenvironment cytokine assay.

FIG. 24 shows structural information for the 706 compounds screened.

FIG. 25 shows the data relating to the clinically used anti-leukemic agents for dose-response screening experiments.

FIG. 26 shows data relating to the dose-response screen for the 706 compounds screened.

FIG. 27 shows the ATC classification for the 706 compounds screened.

FIG. 28 shows drug challenge of IL7 naïve LICs with dasatinib in the presence and absence of IL7 (Panel A), and rechallenge after washout of IL7 and dasatinib (Panel B).

Additional advantages of the invention will be set forth in part in the description which follows, and in part will be obvious from the description, or can be learned by practice of the invention. The advantages of the invention will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

DESCRIPTION

The present invention can be understood more readily by reference to the following detailed description of the invention and the Examples included therein.

Before the present compounds, compositions, articles, systems, devices, and/or methods are disclosed and described, it is to be understood that they are not limited to specific synthetic methods unless otherwise specified, or to particular reagents unless otherwise specified, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular aspects only and is not intended to be limiting. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, example methods and materials are now described.

While aspects of the present invention can be described and claimed in a particular statutory class, such as the

system statutory class, this is for convenience only and one of skill in the art will understand that each aspect of the present invention can be described and claimed in any statutory class. Unless otherwise expressly stated, it is in no way intended that any method or aspect set forth herein be construed as requiring that its steps be performed in a specific order. Accordingly, where a method claim does not specifically state in the claims or descriptions that the steps are to be limited to a specific order, it is no way intended that an order be inferred, in any respect. This holds for any possible non-express basis for interpretation, including matters of logic with respect to arrangement of steps or operational flow, plain meaning derived from grammatical organization or punctuation, or the number or type of aspects described in the specification.

Throughout this application, various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this pertains. The references disclosed are also individually and specifically incorporated by reference herein for the material contained in them that is discussed in the sentence in which the reference is relied upon. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided herein may be different from the actual publication dates, which can require independent confirmation.

A. Definitions

As used in the specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to “a functional group,” “an alkyl,” or “a residue” includes mixtures of two or more such functional groups, alkyls, or residues, and the like.

Ranges can be expressed herein as from “about” one particular value, and/or to “about” another particular value. When such a range is expressed, another aspect includes from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent “about,” it will be understood that the particular value forms another aspect. It will be further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint. It is also understood that there are a number of values disclosed herein, and that each value is also herein disclosed as “about” that particular value in addition to the value itself. For example, if the value “10” is disclosed, then “about 10” is also disclosed. It is also understood that each unit between two particular units are also disclosed. For example, if 10 and 15 are disclosed, then 11, 12, 13, and 14 are also disclosed.

As used herein, nomenclature for compounds, including organic compounds, can be given using common names, IUPAC, IUBMB, or CAS recommendations for nomenclature. When one or more stereochemical features are present, Cahn-Ingold-Prelog rules for stereochemistry can be employed to designate stereochemical priority, E/Z specification, and the like. One of skill in the art can readily ascertain the structure of a compound if given a name, either by systemic reduction of the compound structure using naming conventions, or by commercially available software, such as CHEMDRAW™ (Cambridgesoft Corporation, U.S.A.).

As used herein, the terms “Philadelphia chromosome” and “Ph” refer to a reciprocal, chromosomal translocation between chromosomes 9 and 22, resulting in the oncogenic BCR-ABL gene fusion, and encodes the BCR-ABL fusion protein. Specifically, this translocation results in a portion of the BCR gene from chromosome 22 (region q11) becoming fused with a portion of the ABL gene from chromosome 9 (region q34), and is designated as t(9;22)(q34;q11) under the International System for Human Cytogenetic Nomenclature (ISCN). Depending on the precise location of the fusion, the molecular weight of the protein can range from 185 to 210 kDa, and the term is inclusive of all variants of this gene. In this context, “Philadelphia chromosome positive” and “Ph+” is understood to represent the presence of this chromosomal defect, resulting in a chimeric BCR-ABL protein and constitutively active BCR-ABL TK activity.

As used herein, the term “BCR-ABL” refers to the fusion oncogene which encodes a chimeric BCR-ABL protein with a constitutively active BCR-ABL tyrosine kinase (TK) activity. In this context, protein tyrosine kinases encoded by the BCR-ABL gene can include, for example BCR-ABL p210 fusion protein (accession number: A1Z199) and BCR-ABL p185 fusion protein (accession number: Q13745). The term BCR-ABL is intended to be inclusive of alternative BCR-ABL gene products and also is inclusive of alternative designations such as BCR-ABL oncogene, BCR-ABL protooncogene, and BCR-ABL oncoprotein used by those skilled in the art.

As used herein, the terms “BCR-ABL tyrosine kinase inhibitor,” “BCR-ABL kinase inhibitor,” “BCR-ABL KI” and “BCR-ABL TKI” refer to any compound or agent that can inhibit BCR-ABL TK activity in an animal, in particular a mammal, for example a human. In this context, an inhibitor is understood to decrease the activity of a BCR-ABL tyrosine kinase compared to the activity in the absence of the exogenously administered compound or agent. The term is intended to include indirectly or directly acting compounds or agents. As used in the art, BCR-ABL TKI generally refers to a class of compounds which are known to inhibit BCR-ABL TK, but may further inhibit alternative signaling pathways, such as for example, Src pathway.

As used herein, the term “BCR-ABL related disorders” refers to disorders or diseases which are associated with or manifest from BCR-ABL-mediated activity, and is intended to be inclusive of mutated forms of BCR-ABL. In this context, disorders associated with BCR-ABL would benefit by direct or indirect BCR-ABL inhibition.

As used herein, the terms “BCR-ABL^{MUTANT},” or “mutant BCR-ABL” refer to a BCR-ABL tyrosine kinase amino acid sequence that differs from wild type BCR-ABL tyrosine kinase or “BCR-ABL^{WT}” by one or more amino acid substitutions, additions or deletions. In this context, an amino acid substitution at position 315 of wild type BCR-ABL with another amino acid would result in a mutant BCR-ABL tyrosine kinase, such as for example T315I, which may be designated as “BCR-ABL^{T315I}”.

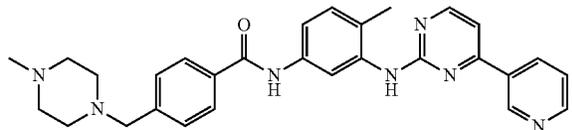
As used herein, the term “KIT” refers to the gene which encodes for the c-KIT protein. The term KIT is intended to be inclusive of alternative KIT transcript variants and gene products and also is inclusive of alternative designations such as “proto oncogene c-KIT,” “tyrosine-protein kinase KIT,” and “CD117” used by those skilled in the art.

As used herein, “cytokine” refers to a signaling molecule used in intercellular communication resulting in alteration of cell function, and encompasses lymphokines, interleukins, and chemokines, such as for example, IL7. In this context, “cytokine signaling” is meant to include cell-extrinsic and

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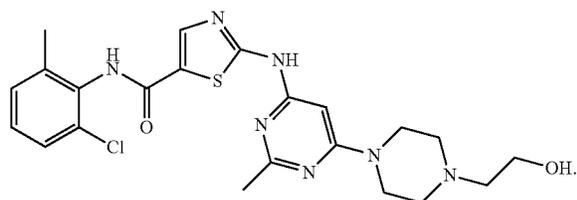
cell-intrinsic activity mediated by extracellular cytokines or by over-expression of a gene product that mimics constitutive cytokine signaling.

The term "imatinib" as used herein refers to a compound having a structure represented by the formula:



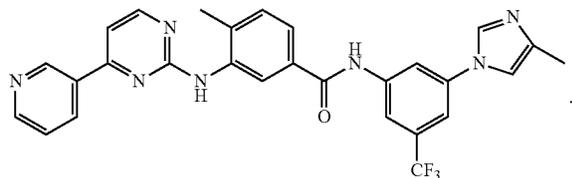
This compound has been described as inhibiting the activity of BCR-ABL, KIT, and the platelet-derived growth factor receptor (PDGFR).

The term "dasatinib" as used herein refers to a compound having a structure represented by the formula:



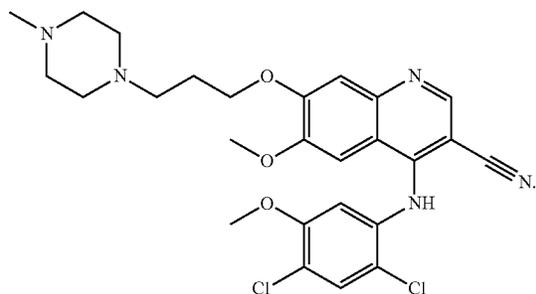
This compound has been described as inhibiting the activity of SRC and SRC-family kinases, BCR-ABL, KIT, PDGFR and ephrin receptor tyrosine kinases.

The term "nilotinib" as used herein refers to a compound having a structure represented by the formula:



This compound has been described as inhibiting the activity BCR-ABL, KIT, and PDGFR. It is also suspected of inhibiting ABL-related kinase ARG and the ephrin receptor EPHB4.

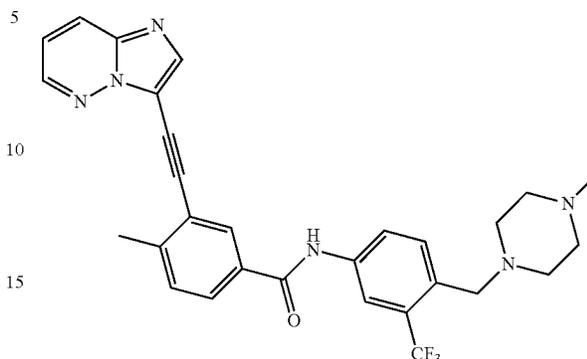
The term "bosutinib" as used herein refers to a compound having a structure represented by the formula:



This compound has been described as inhibiting the activity of BCR-ABL, SRC-family kinases, and STAT5.

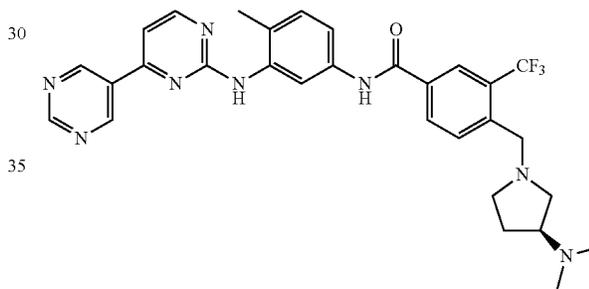
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The term "ponatinib" as used herein refers to a compound having a structure represented by the formula:



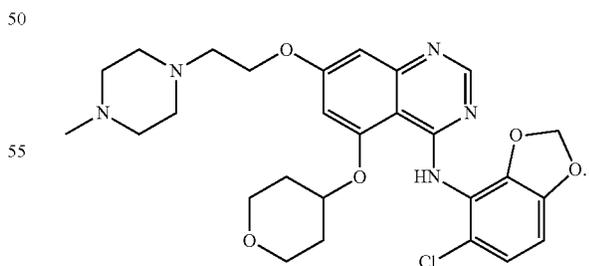
This compound has been described as inhibiting the activity of BCR-ABL, FLT3, vascular endothelial growth factors (VEGFRs), fibroblast growth factors (FGFRs), and angiopoietin (Tie2).

The term "bafetinib" as used herein refers to a compound having a structure represented by the formula:



This compound has been described as inhibiting the activity of BCR-ABL, LYN, PDGFR, and KIT.

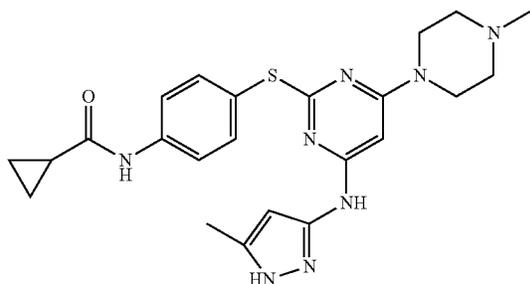
The term "saracatinib" as used herein refers to a compound having a structure represented by the formula:



This compound has been described as inhibiting the activity of BCR-ABL and the SRC-family kinases.

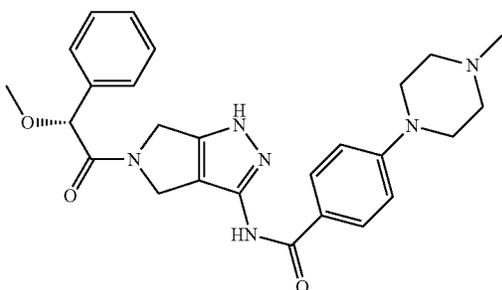
The term "tozasertib" as used herein refers to a compound having a structure represented by the formula:

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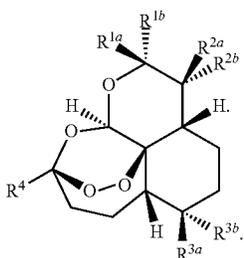
This compound has been described as inhibiting the activity of BCR-ABL, Aurora kinases, FLT3, and JAK2.

The term “danusertib” as used herein refers to a compound having a structure represented by the formula:

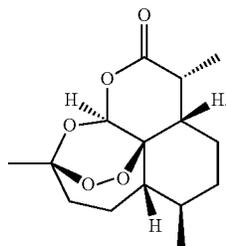


This compound has been described as inhibiting the activity of BCR-ABL and Aurora kinases.

As used herein, the terms “artemisinin analogue,” “artemisinin class,” and “ARTs” can be used interchangeably and refer to a compound structurally related to artemisinin comprising one or more substitutions on artemisinin and generally represented by the formula:

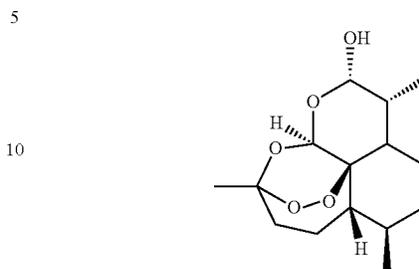


As used herein, the term “artemisinin” refers to a compound having a structure represented by the formula:

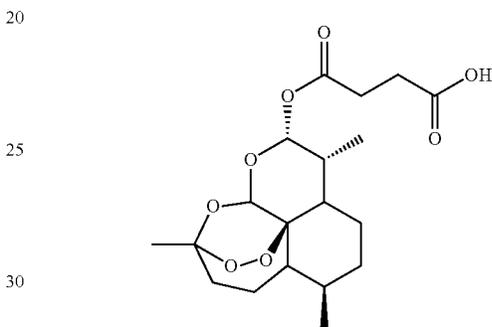


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As used herein, the terms “dihydroartemisinin” or “DHA” refer to a compound having a structure represented by the formula:



As used herein, the term “artesunate” refers to a compound having a structure represented by the formula:



As used herein, the terms “cancer” or “cancerous” refer to a condition or disorder of uncontrolled cellular proliferation. Examples of cancer include, for example, leukemia, lymphoma, blastoma, carcinoma and sarcoma. More specific examples of such cancers include chronic myeloid leukemia, acute lymphoblastic leukemia, Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL), and gastrointestinal stromal tumors (GIST).

As used herein, the terms “optional” or “optionally” means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances where it does not.

As used herein, the term “subject” can be a vertebrate, such as a mammal, a fish, a bird, a reptile, or an amphibian. Thus, the subject of the herein disclosed methods can be a human, non-human primate, horse, pig, rabbit, dog, sheep, goat, cow, cat, guinea pig or rodent. The term does not denote a particular age or sex. Thus, adult and newborn subjects, as well as fetuses, whether male or female, are intended to be covered. In one aspect, the subject is a mammal. A patient refers to a subject afflicted with a disease or disorder. The term “patient” includes human and veterinary subjects. In some aspects of the disclosed methods, the subject has been diagnosed with a need for treatment of a disorder of uncontrolled cellular proliferation associated with a protein kinase dysfunction prior to the administering step. In some aspects of the disclosed method, the subject has been diagnosed with a need for inhibition of a protein kinase prior to the administering step.

As used herein, the term “treatment” refers to the medical management of a patient with the intent to cure, ameliorate, stabilize, or prevent a disease, pathological condition, or disorder. This term includes active treatment, that is, treat-

ment directed specifically toward the improvement of a disease, pathological condition, or disorder, and also includes causal treatment, that is, treatment directed toward removal of the cause of the associated disease, pathological condition, or disorder. In addition, this term includes palliative treatment, that is, treatment designed for the relief of symptoms rather than the curing of the disease, pathological condition, or disorder; preventative treatment, that is, treatment directed to minimizing or partially or completely inhibiting the development of the associated disease, pathological condition, or disorder; and supportive treatment, that is, treatment employed to supplement another specific therapy directed toward the improvement of the associated disease, pathological condition, or disorder; and supportive treatment, that is, treatment employed to supplement another specific therapy directed toward the improvement of the associated disease, pathological condition, or disorder. In various aspects, the term covers any treatment of a subject, including a mammal (e.g., a human), and includes: (i) preventing the disease from occurring in a subject that can be predisposed to the disease but has not yet been diagnosed as having it; (ii) inhibiting the disease, i.e., arresting its development; or (iii) relieving the disease, i.e., causing regression of the disease. In one aspect, the subject is a mammal such as a primate, and, in a further aspect, the subject is a human. The term "subject" also includes domesticated animals (e.g., cats, dogs, etc.), livestock (e.g., cattle, horses, pigs, sheep, goats, etc.), and laboratory animals (e.g., mouse, rabbit, rat, guinea pig, fruit fly, etc.).

As used herein, the term "prevent" or "preventing" refers to precluding, averting, obviating, forestalling, stopping, or hindering something from happening, especially by advance action. It is understood that where reduce, inhibit or prevent are used herein, unless specifically indicated otherwise, the use of the other two words is also expressly disclosed.

As used herein, the term "diagnosed" means having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition that can be diagnosed or treated by the compounds, compositions, or methods disclosed herein. For example, "diagnosed with a disorder of uncontrolled cellular proliferation" means having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition that can be diagnosed or treated by a compound or composition that can inhibit a protein kinase. As a further example, "diagnosed with a need for inhibition of a protein kinase" refers to having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition characterized by a protein kinase dysfunction. Such a diagnosis can be in reference to a disorder, such as a disorder of uncontrolled cellular proliferation, cancer and the like, as discussed herein. For example, the term "diagnosed with a need for inhibition of protein kinase activity" refers to having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition that can be diagnosed or treated by inhibition of protein kinase activity. For example, "diagnosed with a need for treatment of one or more disorders of uncontrolled cellular proliferation associated with a protein kinase dysfunction" means having been subjected to a physical examination by a person of skill, for example, a physician, and found to have one or more disorders of uncontrolled cellular proliferation associated with a protein kinase dysfunction. For example, "diagnosed with a disorder treatable by selective inhibition of BCR-ABL" means having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition that can be

diagnosed or treated by a compound or composition that can inhibit BCR-ABL. As a further example, "diagnosed with a need for selective inhibition of BCR-ABL" refers to having been subjected to a physical examination by a person of skill, for example, a physician, and found to have a condition characterized by BCR-ABL activity. Such a diagnosis can be in reference to a disorder, such as a disease of uncontrolled cellular proliferation, and the like, as discussed herein.

As used herein, the phrase "identified to be in need of treatment for a disorder," or the like, refers to selection of a subject based upon need for treatment of the disorder. For example, a subject can be identified as having a need for treatment of a disorder (e.g., a disorder related to a dysfunction of protein kinase activity or a disorder related to BCR-ABL activity) based upon an earlier diagnosis by a person of skill and thereafter subjected to treatment for the disorder. It is contemplated that the identification can, in one aspect, be performed by a person different from the person making the diagnosis. It is also contemplated, in a further aspect, that the administration can be performed by one who subsequently performed the administration.

As used herein, the terms "administering" and "administration" refer to any method of providing a pharmaceutical preparation to a subject. Such methods are well known to those skilled in the art and include, but are not limited to, oral administration, transdermal administration, administration by inhalation, nasal administration, topical administration, intravaginal administration, ophthalmic administration, intraaural administration, intracerebral administration, rectal administration, sublingual administration, buccal administration, and parenteral administration, including injectable such as intravenous administration, intra-arterial administration, intramuscular administration, and subcutaneous administration. Administration can be continuous or intermittent. In various aspects, a preparation can be administered therapeutically; that is, administered to treat an existing disease or condition. In further various aspects, a preparation can be administered prophylactically; that is, administered for prevention of a disease or condition.

The term "contacting" as used herein refers to bringing a disclosed compound and a cell, target histamine receptor, or other biological entity together in such a manner that the compound can affect the activity of the target (e.g., spliceosome, cell, etc.), either directly; i.e., by interacting with the target itself, or indirectly; i.e., by interacting with another molecule, co-factor, factor, or protein on which the activity of the target is dependent.

As used herein, the terms "effective amount" and "amount effective" refer to an amount that is sufficient to achieve the desired result or to have an effect on an undesired condition. For example, a "therapeutically effective amount" refers to an amount that is sufficient to achieve the desired therapeutic result or to have an effect on undesired symptoms, but is generally insufficient to cause adverse side effects. The specific therapeutically effective dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration; the route of administration; the rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed and like factors well known in the medical arts. For example, it is well within the skill of the art to start doses of a compound at levels lower than those required to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is

achieved. If desired, the effective daily dose can be divided into multiple doses for purposes of administration. Consequently, single dose compositions can contain such amounts or submultiples thereof to make up the daily dose. The dosage can be adjusted by the individual physician in the event of any contraindications. Dosage can vary, and can be administered in one or more dose administrations daily, for one or several days. Guidance can be found in the literature for appropriate dosages for given classes of pharmaceutical products. In further various aspects, a preparation can be administered in a "prophylactically effective amount"; that is, an amount effective for prevention of a disease or condition.

As used herein, "kit" means a collection of at least two components constituting the kit. Together, the components constitute a functional unit for a given purpose. Individual member components may be physically packaged together or separately. For example, a kit comprising an instruction for using the kit may or may not physically include the instruction with other individual member components. Instead, the instruction can be supplied as a separate member component, either in a paper form or an electronic form which may be supplied on computer readable memory device or downloaded from an internet website, or as recorded presentation.

As used herein, "instruction(s)" means documents describing relevant materials or methodologies pertaining to a kit. These materials may include any combination of the following: background information, list of components and their availability information (purchase information, etc.), brief or detailed protocols for using the kit, trouble-shooting, references, technical support, and any other related documents. Instructions can be supplied with the kit or as a separate member component, either as a paper form or an electronic form which may be supplied on computer readable memory device or downloaded from an internet website, or as recorded presentation. Instructions can comprise one or multiple documents, and are meant to include future updates.

As used herein, the terms "therapeutic agent" include any synthetic or naturally occurring biologically active compound or composition of matter which, when administered to an organism (human or nonhuman animal), induces a desired pharmacologic, immunogenic, and/or physiologic effect by local and/or systemic action. The term therefore encompasses those compounds or chemicals traditionally regarded as drugs, vaccines, and biopharmaceuticals including molecules such as proteins, peptides, hormones, nucleic acids, gene constructs and the like. Examples of therapeutic agents are described in well-known literature references such as the Merck Index (14th edition), the Physicians' Desk Reference (64th edition), and The Pharmacological Basis of Therapeutics (12th edition), and they include, without limitation, medicaments; vitamins; mineral supplements; substances used for the treatment, prevention, diagnosis, cure or mitigation of a disease or illness; substances that affect the structure or function of the body, or pro-drugs, which become biologically active or more active after they have been placed in a physiological environment. For example, the term "therapeutic agent" includes compounds or compositions for use in all of the major therapeutic areas including, but not limited to, adjuvants; anti-infectives such as antibiotics and antiviral agents; analgesics and analgesic combinations, anorexics, anti-inflammatory agents, anti-epileptics, local and general anesthetics, hypnotics, sedatives, antipsychotic agents, neuroleptic agents, antidepressants, anxiolytics, antagonists, neuron blocking agents, anticholin-

ergic and cholinomimetic agents, antimuscarinic and muscarinic agents, antiadrenergics, antiarrhythmics, antihypertensive agents, hormones, and nutrients, antiarthritics, antiasthmatic agents, anticonvulsants, antihistamines, antinauseants, antineoplastics, antipruritics, antipyretics; antispasmodics, cardiovascular preparations (including calcium channel blockers, beta-blockers, beta-agonists and antiarrhythmics), antihypertensives, diuretics, vasodilators; central nervous system stimulants; cough and cold preparations; decongestants; diagnostics; hormones; bone growth stimulants and bone resorption inhibitors; immunosuppressives; muscle relaxants; psychostimulants; sedatives; tranquilizers; proteins, peptides, and fragments thereof (whether naturally occurring, chemically synthesized or recombinantly produced); and nucleic acid molecules (polymeric forms of two or more nucleotides, either ribonucleotides (RNA) or deoxyribonucleotides (DNA) including both double- and single-stranded molecules, gene constructs, expression vectors, antisense molecules and the like), small molecules (e.g., doxorubicin) and other biologically active macromolecules such as, for example, proteins and enzymes. The agent may be a biologically active agent used in medical, including veterinary, applications and in agriculture, such as with plants, as well as other areas. The term therapeutic agent also includes without limitation, medicaments; vitamins; mineral supplements; substances used for the treatment, prevention, diagnosis, cure or mitigation of disease or illness; or substances which affect the structure or function of the body; or pro-drugs, which become biologically active or more active after they have been placed in a predetermined physiological environment.

As used herein, "EC₅₀," is intended to refer to the concentration of a substance (e.g., a compound or a drug) that is required for 50% agonism or activation of a biological process, or component of a process, including a protein, subunit, organelle, ribonucleoprotein, etc. In one aspect, an EC₅₀ can refer to the concentration of a substance that is required for 50% agonism or activation in an in vitro assay. In a further aspect, EC₅₀ refers to the concentration of agonist or activator that provokes a response halfway between the baseline and maximum response. For example, an EC₅₀ for compound or agent can be determined in an in vitro or cell-based assay system. Such in vitro assay systems frequently utilize a cell line that either expresses endogenously a target of interest, or has been transfected with a suitable expression vector that directs expression of a target of interest.

As used herein, "IC₅₀," is intended to refer to the concentration of a substance (e.g., a compound or a drug) that is required for 50% inhibition of a biological process, or component of a process, including a protein, subunit, organelle, ribonucleoprotein, etc. For example, an IC₅₀ can refer to the concentration of a substance that is required for 50% inhibition in vivo or the inhibition is measured in vitro, as further defined elsewhere herein. Alternatively, IC₅₀ refers to the half maximal (50%) inhibitory concentration (IC) of a substance. For example, the IC₅₀ for a compound can be determined using murine leukemia initiating cells (LICs) transfected either the wild-type (WT) allele of human p185^{BCR-ABL} or mutant BCR-ABL allele p185^{T315I}.

A residue of a chemical species, as used in the specification and concluding claims, refers to the moiety that is the resulting product of the chemical species in a particular reaction scheme or subsequent formulation or chemical product, regardless of whether the moiety is actually obtained from the chemical species. Thus, an ethylene glycol residue in a polyester refers to one or more

—OCH₂CH₂O— units in the polyester, regardless of whether ethylene glycol was used to prepare the polyester. Similarly, a sebacic acid residue in a polyester refers to one or more —CO(CH₂)₈CO— moieties in the polyester, regardless of whether the residue is obtained by reacting

sebacic acid or an ester thereof to obtain the polyester. As used herein, the term “substituted” is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, and aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described below. The permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this disclosure, the heteroatoms, such as nitrogen, can have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valences of the heteroatoms. This disclosure is not intended to be limited in any manner by the permissible substituents of organic compounds. Also, the terms “substitution” or “substituted with” include the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., a compound that does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc.

The term “aliphatic” refers to a non-aromatic carbon-based moiety. Aliphatic can include both acyclic or cyclic moieties (e.g., alkyl and cycloalkyl) and can include both saturated and unsaturated moieties (e.g., alkyl, alkenyl, and alkenyl).

In defining various terms, “A¹,” “A²,” “A³,” and “A⁴” are used herein as generic symbols to represent various specific substituents. These symbols can be any substituent, not limited to those disclosed herein, and when they are defined to be certain substituents in one instance, they can, in another instance, be defined as some other substituents.

The term “alkyl” as used herein is a branched or unbranched saturated hydrocarbon group of from 1 to 24 carbon atoms, for example from 1 to 12 carbons, from 1 to 8 carbons, from 1 to 6 carbons, or from 1 to 4 carbons, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, s-butyl, t-butyl, n-pentyl, isopentyl, s-pentyl, neopentyl, hexyl, heptyl, octyl, nonyl, decyl, dodecyl, tetradecyl, hexadecyl, eicosyl, tetracosyl, and the like. The alkyl group can be cyclic or acyclic. The alkyl group can be branched or unbranched. The alkyl group can also be substituted or unsubstituted. For example, the alkyl group can be substituted with one or more groups including optionally substituted alkyl, cycloalkyl, alkoxy, amino, ether, halide, hydroxy, nitro, silyl, sulfo-oxo, or thiol, as described herein. A “lower alkyl” group is an alkyl group containing from one to six (e.g., from one to four) carbon atoms.

Throughout the specification “alkyl” is generally used to refer to both unsubstituted alkyl groups and substituted alkyl groups; however, substituted alkyl groups are also specifically referred to herein by identifying the specific substituent(s) on the alkyl group. For example, the term “halogenated alkyl” specifically refers to an alkyl group that is substituted with one or more halide, e.g., fluorine, chlorine, bromine, or iodine. The term “alkoxyalkyl” specifically refers to an alkyl group that is substituted with one or more alkoxy groups, as described below. The term “alkylamino” specifically refers to an alkyl group that is substituted with one or more amino groups, as described below, and the like. When “alkyl” is used in one instance and a specific term

such as “alkylalcohol” is used in another, it is not meant to imply that the term “alkyl” does not also refer to specific terms such as “alkylalcohol” and the like.

This practice is also used for other groups described herein. That is, while a term such as “cycloalkyl” refers to both unsubstituted and substituted cycloalkyl moieties, the substituted moieties can, in addition, be specifically identified herein; for example, a particular substituted cycloalkyl can be referred to as, e.g., an “alkylcycloalkyl.” Similarly, a substituted alkoxy can be specifically referred to as, e.g., a “halogenated alkoxy,” a particular substituted alkenyl can be, e.g., an “alkenylalcohol,” and the like. Again, the practice of using a general term, such as “cycloalkyl,” and a specific term, such as “alkylcycloalkyl,” is not meant to imply that the general term does not also include the specific term.

The term “cycloalkyl” as used herein is a non-aromatic carbon-based ring composed of at least three carbon atoms. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, norbornyl, and the like. The cycloalkyl group can be substituted or unsubstituted. The cycloalkyl group can be substituted with one or more groups including, but not limited to, alkyl, cycloalkyl, alkoxy, amino, ether, halide, hydroxy, nitro, silyl, sulfo-oxo, or thiol as described herein.

The terms “alkoxy” and “alkoxy” as used herein to refer to an alkyl or cycloalkyl group bonded through an ether linkage; that is, an “alkoxy” group can be defined as —OA¹ where A¹ is alkyl or cycloalkyl as defined above. “Alkoxy” also includes polymers of alkoxy groups as just described; that is, an alkoxy can be a polyether such as —OA¹-OA² or —OA¹-(OA²)_a-OA³, where “a” is an integer of from 1 to 200 and A¹, A², and A³ are alkyl and/or cycloalkyl groups.

The term “aryl” as used herein is a group that contains any carbon-based aromatic group including, but not limited to, benzene, naphthalene, phenyl, biphenyl, anthracene, and the like. The aryl group can be substituted or unsubstituted. The aryl group can be substituted with one or more groups including, but not limited to, alkyl, cycloalkyl, alkoxy, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, heteroaryl, aldehyde, amino, carboxylic acid, ester, ether, halide, hydroxy, ketone, azide, nitro, silyl, sulfo-oxo, or thiol as described herein. The term “biaryl” is a specific type of aryl group and is included in the definition of “aryl.” Biaryl refers to two aryl groups that are bound together via a fused ring structure, as in naphthalene, or are attached via one or more carbon-carbon bonds, as in biphenyl.

The term “aldehyde” as used herein is represented by the formula —C(O)H. Throughout this specification “C(O)” is a short hand notation for a carbonyl group, i.e., C=O.

The terms “amine” or “amino” as used herein are represented by the formula NA¹A²A³, where A¹, A², and A³ can be, independently, hydrogen or optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein. A specific example of amino is —NH₂.

The term “alkylamino” as used herein is represented by the formula —NH(-alkyl) where alkyl is a described herein. Representative examples include, but are not limited to, methylamino group, ethylamino group, propylamino group, isopropylamino group, butylamino group, isobutylamino group, (sec-butyl)amino group, (tert-butyl)amino group, pentylamino group, isopentylamino group, (tert-pentyl)amino group, hexylamino group, and the like.

The term “dialkylamino” as used herein is represented by the formula —N(-alkyl)₂ where alkyl is a described herein. Representative examples include, but are not limited to,

dimethylamino group, diethylamino group, dipropylamino group, diisopropylamino group, dibutylamino group, diisobutylamino group, di(sec-butyl)amino group, di(tert-butyl)amino group, dipentylamino group, diisopentylamino group, di(tert-pentyl)amino group, dihexylamino group, N-ethyl-N-methylamino group, N-methyl-N-propylamino group, N-ethyl-N-propylamino group and the like.

The term "carboxylic acid" as used herein is represented by the formula —C(O)OH .

The term "ester" as used herein is represented by the formula —OC(O)A^1 or —C(O)OA^1 , where A^1 can be an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein. The term "polyester" as used herein is represented by the formula $\text{—(A}^1\text{O(O)C—A}^2\text{—C(O)O)}_a\text{—}$ or $\text{—(A}^1\text{O(O)C—A}^2\text{—OC(O))}_a\text{—}$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group described herein and "a" is an integer from 1 to 500. "Polyester" is as the term used to describe a group that is produced by the reaction between a compound having at least two carboxylic acid groups with a compound having at least two hydroxyl groups.

The term "ether" as used herein is represented by the formula $A^1\text{OA}^2$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group described herein. The term "polyether" as used herein is represented by the formula $\text{—(A}^1\text{O—A}^2\text{O)}_a\text{—}$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group described herein and "a" is an integer of 1 to 500. Examples of polyether groups include polyethylene oxide, polypropylene oxide, and polybutylene oxide.

The term "halide" as used herein refers to the halogens fluorine, chlorine, bromine, and iodine.

The term "heteroaryl," as used herein refers to an aromatic group that has at least one heteroatom incorporated within the ring of the aromatic group. Examples of heteroatoms include, but are not limited to, nitrogen, oxygen, sulfur, and phosphorus, where N-oxides, sulfur oxides, and dioxides are permissible heteroatom substitutions. The heteroaryl group can be substituted or unsubstituted. The heteroaryl group can be substituted with one or more groups including, but not limited to, alkyl, cycloalkyl, alkoxy, amino, ether, halide, hydroxy, nitro, silyl, sulfo-oxo, or thiol as described herein. Heteroaryl groups can be monocyclic, or alternatively fused ring systems. Heteroaryl groups include, but are not limited to, furyl, imidazolyl, pyrimidinyl, tetrazolyl, thienyl, pyridinyl, pyrrolyl, N-methylpyrrolyl, quinolinyl, isoquinolinyl, pyrazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, isothiazolyl, pyridazinyl, pyrazinyl, benzofuranyl, benzodioxolyl, benzothiophenyl, indolyl, indazolyl, benzimidazolyl, imidazopyridinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, 1,3-oxazolyl, 1,2,4-oxadiazol-5-yl, 1,2,3-triazolyl, 1,3-thiazol-4-yl, pyridinyl, and pyrimidin-5-yl.

The term "heterocycle," as used herein refers to single and multi-cyclic aromatic or non-aromatic ring systems in which at least one of the ring members is other than carbon. Heterocycle includes pyridine, pyrimidine, furan, thiophene, pyrrole, isoxazole, isothiazole, pyrazole, oxazole, thiazole, imidazole, oxazole, including, 1,2,3-oxadiazole, 1,2,5-oxadiazole and 1,3,4-oxadiazole, thiadiazole, including, 1,2,3-thiadiazole, 1,2,5-thiadiazole, and 1,3,4-thiadiazole, triaz-

ole, including, 1,2,3-triazole, 1,3,4-triazole, tetrazole, including 1,2,3,4-tetrazole and 1,2,4,5-tetrazole, pyridine, pyridazine, pyrimidine, pyrazine, triazine, including 1,2,4-triazine and 1,3,5-triazine, tetrazine, including 1,2,4,5-tetrazine, pyrrolidine, piperidine, piperazine, morpholine, azetidine, tetrahydropyran, tetrahydrofuran, dioxane, and the like.

The term "heterocycloalkyl" as used herein is a non-aromatic carbon-based ring composed of at least two carbon atoms and at least one non-carbon heteroatom. For example, the non-carbon heteroatom can include, but is not limited to, oxygen, nitrogen, sulphur, phosphorus and the like. Examples of heterocycloalkyl groups include, aziridine, oxirane, thiirane, azetidene, oxetane, thietane, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, piperidine, tetrahydro-2H-pyran, tetrahydro-2H-thiopyran, azepane, oxepane, thiopane, azocane, oxocane, thiocane, pyrazolidine, imidazolidine, diazetidine, hexahydropyridazine, piperazine, diazepane, oxazinane, oxazepane, oxazolidine, oxazetidine, and the like. The heterocycloalkyl group can be substituted or unsubstituted. The heterocycloalkyl group can be substituted with one or more groups including, but not limited to, alkyl, cycloalkyl, alkoxy, amino, ether, halide, hydroxy, nitro, silyl, sulfo-oxo, or thiol as described herein.

The term "hydroxyl" as used herein is represented by the formula —OH .

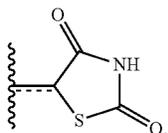
The term "ketone" as used herein is represented by the formula $A^1\text{C(O)A}^2$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein.

The term "sulfo-oxo" as used herein is represented by the formulas —S(O)A^1 , $\text{—S(O)}_2\text{A}^1$, $\text{—OS(O)}_2\text{A}^1$, or $\text{—OS(O)}_2\text{OA}^1$, where A^1 can be hydrogen or an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein. Throughout this specification "S(O)" is a short hand notation for S=O . The term "sulfonyl" is used herein to refer to the sulfo-oxo group represented by the formula $\text{—S(O)}_2\text{A}^1$, where A^1 can be hydrogen or an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein. The term "sulfone" as used herein is represented by the formula $A^1\text{S(O)}_2\text{A}^2$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein. The term "sulfoxide" as used herein is represented by the formula $A^1\text{S(O)A}^2$, where A^1 and A^2 can be, independently, an optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, cycloalkynyl, aryl, or heteroaryl group as described herein.

The term "organic residue" defines a carbon containing residue, i.e., a residue comprising at least one carbon atom, and includes but is not limited to the carbon-containing groups, residues, or radicals defined herein above. Organic residues can contain various heteroatoms, or be bonded to another molecule through a heteroatom, including oxygen, nitrogen, sulfur, phosphorus, or the like. Examples of organic residues include but are not limited alkyl or substituted alkyls, alkoxy or substituted alkoxy, mono or di-substituted amino, amide groups, etc. Organic residues can preferably comprise 1 to 18 carbon atoms, 1 to 15, carbon atoms, 1 to 12 carbon atoms, 1 to 8 carbon atoms, 1 to 6 carbon atoms, or 1 to 4 carbon atoms. In a further aspect, an organic residue can comprise 2 to 18 carbon atoms, 2 to 15, carbon atoms, 2 to 12 carbon atoms, 2 to 8 carbon atoms, 2 to 4 carbon atoms, or 2 to 4 carbon atoms.

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A very close synonym of the term “residue” is the term “radical,” which as used in the specification and concluding claims, refers to a fragment, group, or substructure of a molecule described herein, regardless of how the molecule is prepared. For example, a 2,4-thiazolidinedione radical in a particular compound has the structure

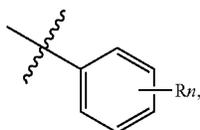


regardless of whether thiazolidinedione is used to prepare the compound. In some embodiments the radical (for example an alkyl) can be further modified (i.e., substituted alkyl) by having bonded thereto one or more “substituent radicals.” The number of atoms in a given radical is not critical to the present invention unless it is indicated to the contrary elsewhere herein.

“Organic radicals,” as the term is defined and used herein, contain one or more carbon atoms. An organic radical can have, for example, 1-26 carbon atoms, 1-18 carbon atoms, 1-12 carbon atoms, 1-8 carbon atoms, 1-6 carbon atoms, or 1-4 carbon atoms. In a further aspect, an organic radical can have 2-26 carbon atoms, 2-18 carbon atoms, 2-12 carbon atoms, 2-8 carbon atoms, 2-6 carbon atoms, or 2-4 carbon atoms. Organic radicals often have hydrogen bound to at least some of the carbon atoms of the organic radical. One example, of an organic radical that comprises no inorganic atoms is a 5,6,7,8-tetrahydro-2-naphthyl radical. In some embodiments, an organic radical can contain 1-10 inorganic heteroatoms bound thereto or therein, including halogens, oxygen, sulfur, nitrogen, phosphorus, and the like. Examples of organic radicals include but are not limited to an alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, mono-substituted amino, di-substituted amino, acyloxy, cyano, carboxy, carboalkoxy, alkylcarboxamide, substituted alkylcarboxamide, dialkylcarboxamide, substituted dialkylcarboxamide, alkylsulfonyl, alkylsulfinyl, thioalkyl, thiohaloalkyl, alkoxy, substituted alkoxy, haloalkyl, haloalkoxy, aryl, substituted aryl, heteroaryl, heterocyclic, or substituted heterocyclic radicals, wherein the terms are defined elsewhere herein. A few non-limiting examples of organic radicals that include heteroatoms include alkoxy radicals, trifluoromethoxy radicals, acetoxy radicals, dimethylamino radicals and the like.

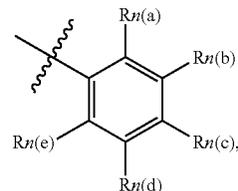
Likewise, amides with an N-hydrogen can exist in an equilibrium of the amide form and the imidic acid form. Unless stated to the contrary, the invention includes all such possible tautomers.

In some aspects, a structure of a compound can be represented by a formula:



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which is understood to be equivalent to a formula:



wherein n is typically an integer. That is, R^n is understood to represent five independent substituents, $R^{n(a)}$, $R^{n(b)}$, $R^{n(c)}$, $R^{n(d)}$, $R^{n(e)}$. By “independent substituents,” it is meant that each R substituent can be independently defined. For example, if in one instance $R^{n(a)}$ is halogen, then $R^{n(b)}$ is not necessarily halogen in that instance.

Certain instances of the above defined terms may occur more than once in the structural formulae, and upon such occurrence each term shall be defined independently of the other.

The term “pharmaceutically acceptable” describes a material that is not biologically or otherwise undesirable, i.e., without causing an unacceptable level of undesirable biological effects or interacting in a deleterious manner.

As used herein, the term “pharmaceutically acceptable carrier” refers to sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol and the like), carboxymethylcellulose and suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials such as lecithin, by the maintenance of the required particle size in the case of dispersions and by the use of surfactants. These compositions can also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms can be ensured by the inclusion of various antibacterial and antifungal agents such as paraben, chlorobutanol, phenol, sorbic acid and the like. It can also be desirable to include isotonic agents such as sugars, sodium chloride and the like. Prolonged absorption of the injectable pharmaceutical form can be brought about by the inclusion of agents, such as aluminum monostearate and gelatin, which delay absorption. Injectable depot forms are made by forming microcapsule matrices of the drug in biodegradable polymers such as polylactide-polyglycolide, poly(orthoesters) and poly(anhydrides). Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions that are compatible with body tissues. The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable media just prior to use. Suitable inert carriers can include sugars such as lactose. Desirably, at least 95% by weight of the particles of the active ingredient have an effective particle size in the range of 0.01 to 10 micrometers.

As used herein, the term “derivative” refers to a compound having a structure derived from the structure of a parent compound (e.g., a compound disclosed herein) and

whose structure is sufficiently similar to those disclosed herein and based upon that similarity, would be expected by one skilled in the art to exhibit the same or similar activities and utilities as the claimed compounds, or to induce, as a precursor, the same or similar activities and utilities as the claimed compounds. Exemplary derivatives include salts, esters, amides, salts of esters or amides, and N-oxides of a parent compound.

The compounds described in the invention can be present as a solvate. In some cases, the solvent used to prepare the solvate is an aqueous solution, and the solvate is then often referred to as a hydrate. The compounds can be present as a hydrate, which can be obtained, for example, by crystallization from a solvent or from aqueous solution. In this connection, one, two, three or any arbitrary number of solvent or water molecules can combine with the compounds according to the invention to form solvates and hydrates. Unless stated to the contrary, the invention includes all such possible solvates.

The term "co-crystal" means a physical association of two or more molecules which owe their stability through non-covalent interaction. One or more components of this molecular complex provide a stable framework in the crystalline lattice. In certain instances, the guest molecules are incorporated in the crystalline lattice as anhydrides or solvates, see e.g. "Crystal Engineering of the Composition of Pharmaceutical Phases. Do Pharmaceutical Co-crystals Represent a New Path to Improved Medicines?" Almarason, O., et. al., The Royal Society of Chemistry, 1889-1896, 2004. Examples of co-crystals include p-toluenesulfonic acid and benzenesulfonic acid.

Compounds described herein can contain one or more double bonds and, thus, potentially give rise to cis/trans (E/Z) isomers, as well as other conformational isomers. Unless stated to the contrary, the invention includes all such possible isomers, as well as mixtures of such isomers.

Unless stated to the contrary, a formula with chemical bonds shown only as solid lines and not as wedges or dashed lines contemplates each possible isomer, e.g., each enantiomer and diastereomer, and a mixture of isomers, such as a racemic or scalemic mixture. Compounds described herein can contain one or more asymmetric centers and, thus, potentially give rise to diastereomers and optical isomers. Unless stated to the contrary, the present invention includes all such possible diastereomers as well as their racemic mixtures, their substantially pure resolved enantiomers, all possible geometric isomers, and pharmaceutically acceptable salts thereof. Mixtures of stereoisomers, as well as isolated specific stereoisomers, are also included. During the course of the synthetic procedures used to prepare such compounds, or in using racemization or epimerization procedures known to those skilled in the art, the products of such procedures can be a mixture of stereoisomers.

Many organic compounds exist in optically active forms having the ability to rotate the plane of plane-polarized light. In describing an optically active compound, the prefixes D and L or R and S are used to denote the absolute configuration of the molecule about its chiral center(s). The prefixes d and l or (+) and (-) are employed to designate the sign of rotation of plane-polarized light by the compound, with (-) or meaning that the compound is levorotatory. A compound prefixed with (+) or d is dextrorotatory. For a given chemical structure, these compounds, called stereoisomers, are identical except that they are non-superimposable mirror images of one another. A specific stereoisomer can also be referred to as an enantiomer, and a mixture of such isomers is often

called an enantiomeric mixture. A 50:50 mixture of enantiomers is referred to as a racemic mixture. Many of the compounds described herein can have one or more chiral centers and therefore can exist in different enantiomeric forms. If desired, a chiral carbon can be designated with an asterisk (*). When bonds to the chiral carbon are depicted as straight lines in the disclosed formulas, it is understood that both the (R) and (S) configurations of the chiral carbon, and hence both enantiomers and mixtures thereof, are embraced within the formula. As is used in the art, when it is desired to specify the absolute configuration about a chiral carbon, one of the bonds to the chiral carbon can be depicted as a wedge (bonds to atoms above the plane) and the other can be depicted as a series or wedge of short parallel lines (bonds to atoms below the plane). The Cahn-Ingold-Prelog system can be used to assign the (R) or (S) configuration to a chiral carbon.

When the disclosed compounds contain one chiral center, the compounds exist in two enantiomeric forms. Unless specifically stated to the contrary, a disclosed compound includes both enantiomers and mixtures of enantiomers, such as the specific 50:50 mixture referred to as a racemic mixture. The enantiomers can be resolved by methods known to those skilled in the art, such as formation of diastereoisomeric salts which may be separated, for example, by crystallization (see, CRC Handbook of Optical Resolutions via Diastereomeric Salt Formation by David Kozma (CRC Press, 2001)); formation of diastereoisomeric derivatives or complexes which may be separated, for example, by crystallization, gas-liquid or liquid chromatography; selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic esterification; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support for example silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where the desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step can liberate the desired enantiomeric form. Alternatively, specific enantiomers can be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer into the other by asymmetric transformation.

Designation of a specific absolute configuration at a chiral carbon in a disclosed compound is understood to mean that the designated enantiomeric form of the compounds can be provided in enantiomeric excess (ee). Enantiomeric excess, as used herein, is the presence of a particular enantiomer at greater than 50%, for example, greater than 60%, greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, greater than 98%, or greater than 99%. In one aspect, the designated enantiomer is substantially free from the other enantiomer. For example, the "R" forms of the compounds can be substantially free from the "S" forms of the compounds and are, thus, in enantiomeric excess of the "S" forms. Conversely, "S" forms of the compounds can be substantially free of "R" forms of the compounds and are, thus, in enantiomeric excess of the "R" forms.

When a disclosed compound has two or more chiral carbons, it can have more than two optical isomers and can exist in diastereoisomeric forms. For example, when there are two chiral carbons, the compound can have up to four optical isomers and two pairs of enantiomers ((S,S)/(R,R) and (R,S)/(S,R)). The pairs of enantiomers (e.g., (S,S)/(R,R)) are mirror image stereoisomers of one another. The stereoisomers that are not mirror-images (e.g., (S,S) and

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(R,S)) are diastereomers. The diastereoisomeric pairs can be separated by methods known to those skilled in the art, for example chromatography or crystallization and the individual enantiomers within each pair may be separated as described above. Unless otherwise specifically excluded, a disclosed compound includes each diastereoisomer of such compounds and mixtures thereof.

Disclosed are the components to be used to prepare the compositions of the invention as well as the compositions themselves to be used within the methods disclosed herein. These and other materials are disclosed herein, and it is understood that when combinations, subsets, interactions, groups, etc. of these materials are disclosed that while specific reference of each various individual and collective combinations and permutation of these compounds cannot be explicitly disclosed, each is specifically contemplated and described herein. For example, if a particular compound is disclosed and discussed and a number of modifications that can be made to a number of molecules including the compounds are discussed, specifically contemplated is each and every combination and permutation of the compound and the modifications that are possible unless specifically indicated to the contrary. Thus, if a class of molecules A, B, and C are disclosed as well as a class of molecules D, E, and F and an example of a combination molecule, A-D is disclosed, then even if each is not individually recited each is individually and collectively contemplated meaning combinations, A-E, A-F, B-D, B-E, B-F, C-D, C-E, and C-F are considered disclosed. Likewise, any subset or combination of these is also disclosed. Thus, for example, the sub-group of A-E, B-F, and C-E would be considered disclosed. This concept applies to all aspects of this application including steps in methods of making and using the compositions of the invention. Thus, if there are a variety of additional steps that can be performed it is understood that each of these additional steps can be performed with any specific embodiment or combination of embodiments of the methods of the invention.

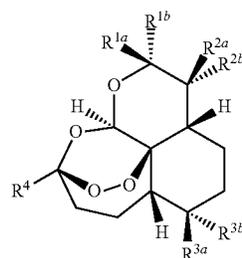
It is understood that the compositions disclosed herein have certain functions. Disclosed herein are certain structural requirements for performing the disclosed functions, and it is understood that there are a variety of structures that can perform the same function that are related to the disclosed structures, and that these structures will typically achieve the same result.

Unless otherwise expressly stated, it is in no way intended that any method set forth herein be construed as requiring that its steps be performed in a specific order. Accordingly, where a method claim does not actually recite an order to be followed by its steps or it is not otherwise specifically stated in the claims or descriptions that the steps are to be limited to a specific order, it is no way intended that an order be inferred, in any respect. This holds for any possible non-express basis for interpretation, including: matters of logic with respect to arrangement of steps or operational flow; plain meaning derived from grammatical organization or punctuation; and the number or type of embodiments described in the specification.

B. Artemisinin Analogues

In various aspects, the invention relates to pharmaceutical compositions comprising a therapeutically effective amount of a BCR-ABL tyrosine kinase inhibitor; and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:

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wherein R^{1a} and R^{1b} together are (C=O) or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-\text{NH}_2$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-\text{NH}(\text{C1-C6 alkyl})$, $-\text{N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, $-\text{O}(\text{C1-C8 alkyl})\text{C3-C6 cycloalkyl}$, $-\text{O}(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{OH}$, $-\text{O}(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$, $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$, $-\text{O}(\text{C1-C8 alkyl})$ -aryl, and $-\text{O}$ -aryl; wherein each of aryl, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, and $-\text{O}(\text{C1-C8 alkyl})$ C3-C6 cycloalkyl, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, $-\text{NH}_2$, $-(\text{C}=\text{O})\text{OH}$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-\text{NH}(\text{C1-C6 alkyl})$, $-\text{N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$, $-(\text{C1-C6 alkyl})-\text{NH}(\text{C1-C6 alkyl})$, and $-(\text{C1-C6 alkyl})-\text{N}(\text{C1-C6 alkyl})(\text{C1-C6 alkyl})$; wherein R^{2a} and R^{2b} together are (C=CR^{5a}R^{5b}) or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$; wherein each of R^{5a} and R^{5b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl; wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and wherein R^4 is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(\text{C1-C8 alkyl})-(\text{C}=\text{O})\text{OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C1-C6 alkyl})-(\text{C}=\text{O})\text{O}(\text{C1-C6 alkyl})$; or a pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; and optionally a pharmaceutically acceptable carrier.

It is understood that the disclosed compounds can be used in connection with the disclosed methods, compositions, kits, and uses.

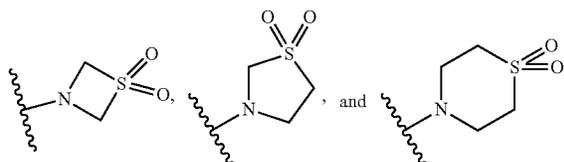
1. R^{1A} and R^{1B} Groups

In one aspect, R^{1a} and R^{1b} together are (C=O). In a further aspect, R^{1a} and R^{1b} are hydrogen. In a yet further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-\text{NH}_2$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl. In a still further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-\text{NH}_2$, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl. In an even further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-\text{NH}_2$, C1-C3 alkyl, C1-C3 alkoxy, C1-C3 monohaloalkyl, and C1-C3 polyhaloalkyl.

In a further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, and C1-C8 alkoxy. In a yet further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, and C1-C6 alkoxy. In a still further aspect, each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, and C1-C3 alkoxy.

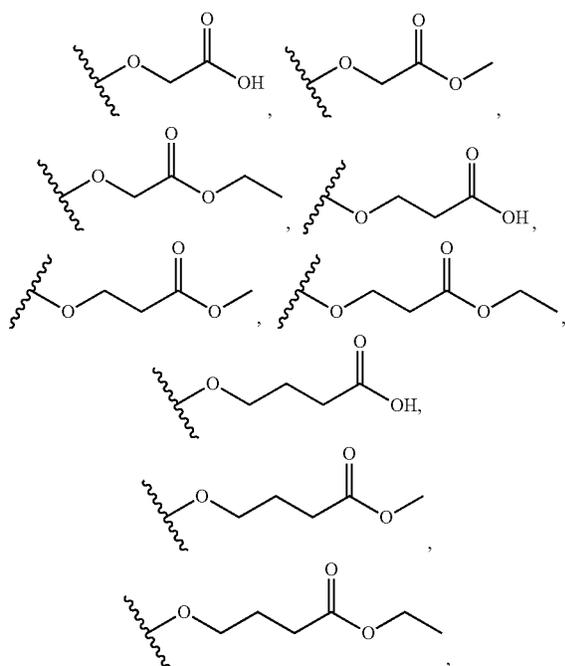
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pyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopentylethyl, and cyclohexylethyl; and wherein R^{1b} , when not hydrogen, is unsubstituted. In yet a further aspect, R^{1b} is hydrogen and R^{1a} is a group selected from the following:



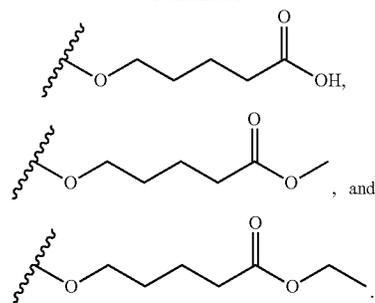
In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a still further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a yet further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$. In an even further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a still further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a yet further aspect, R^{1a} is hydrogen and R^{1b} is selected from $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$.

In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from:

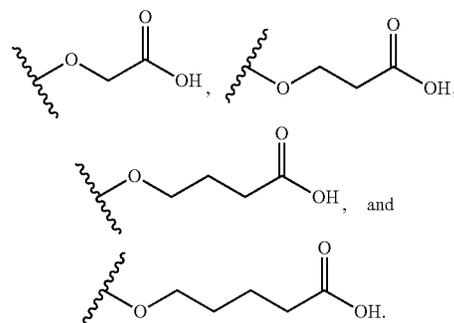


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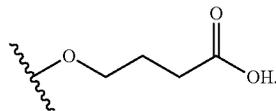
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In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from:



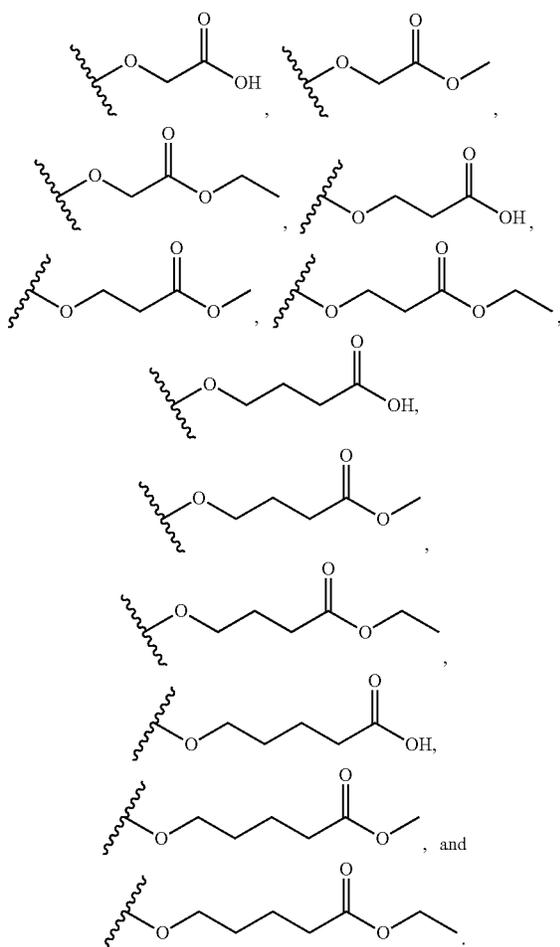
In a further aspect, R^{1a} is hydrogen and R^{1b} is:



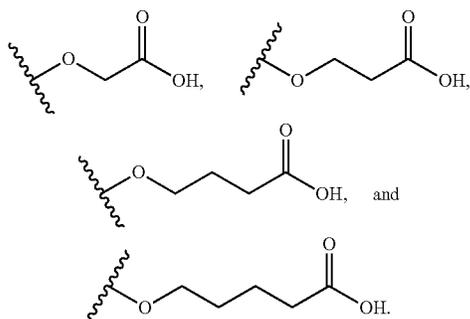
In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a still further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a yet further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C=O})(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$, and $-\text{O}(\text{C=O})(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$. In an even further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a still further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a yet further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)OH}$, and, $-\text{O}(\text{C}1\text{-C}3 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}3 \text{ alkyl})$.

In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from:

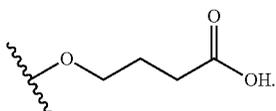
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In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from:



In a further aspect, R^{1b} is hydrogen and R^{1a} is:



In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from —O(C1-C8 alkyl)-aryl, —O-aryl; and aryl; and

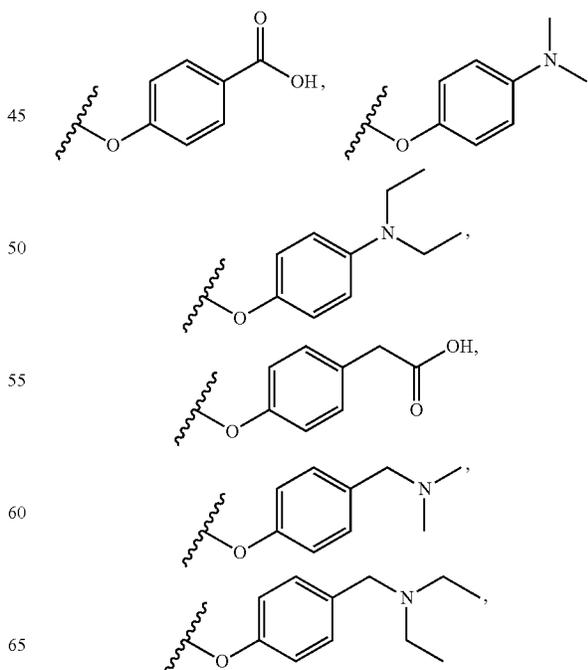
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wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl). In a still further aspect, R^{1a} is hydrogen and R^{1b} is selected from —O(C1-C8 alkyl)-aryl, —O-aryl; and aryl; and wherein R^{1b} is unsubstituted.

In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from —O(C1-C8 alkyl)-aryl, —O-aryl; and aryl; and wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl). In a still further aspect, R^{1b} is hydrogen and R^{1a} is selected from —O(C1-C8 alkyl)-aryl, —O-aryl; and aryl; and wherein R^{1b} is unsubstituted.

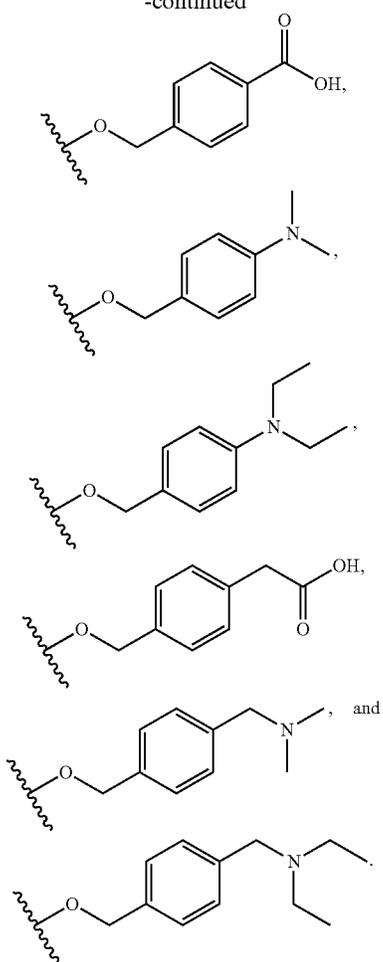
In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from —O(C1-C8 alkyl)-aryl and —O-aryl; and wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl). In a still further aspect, R^{1a} is hydrogen and R^{1b} is selected from —OCH₂-phenyl, —O(CH₂)₂-phenyl, —O(CH₂)₃-phenyl, and —O-aryl; and wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl).

In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from:

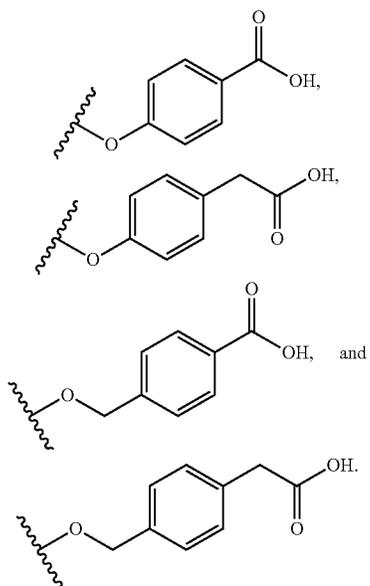


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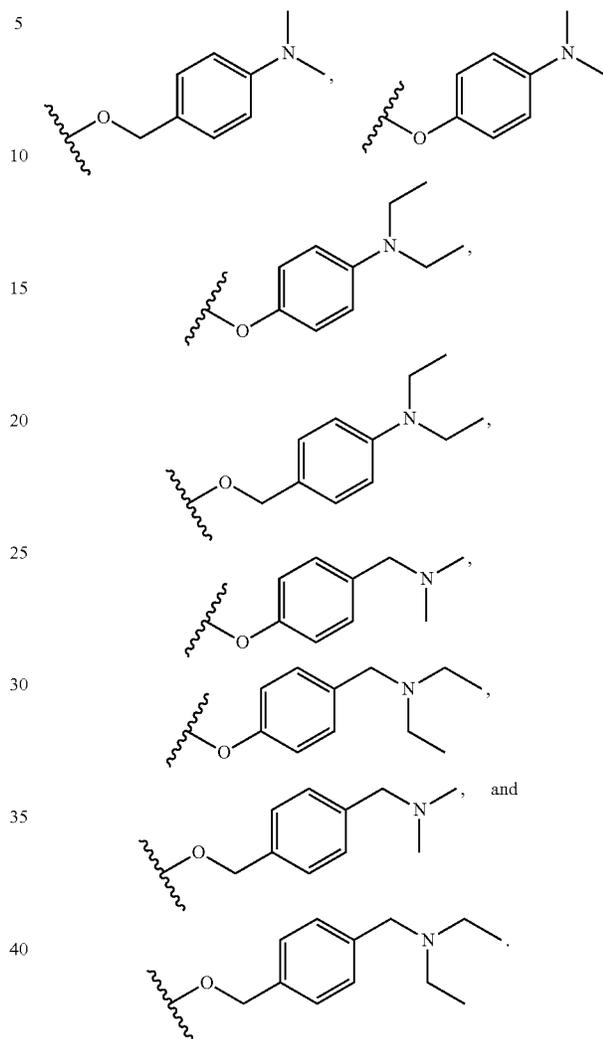


In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from:

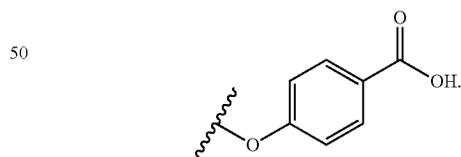


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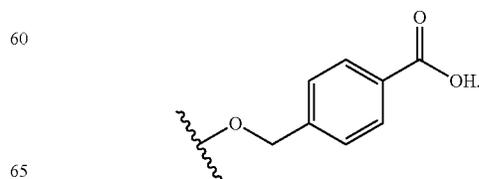
In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from:



In a further aspect, R^{1a} is hydrogen and R^{1b} is:



In a further aspect, R^{1a} is hydrogen and R^{1b} is:

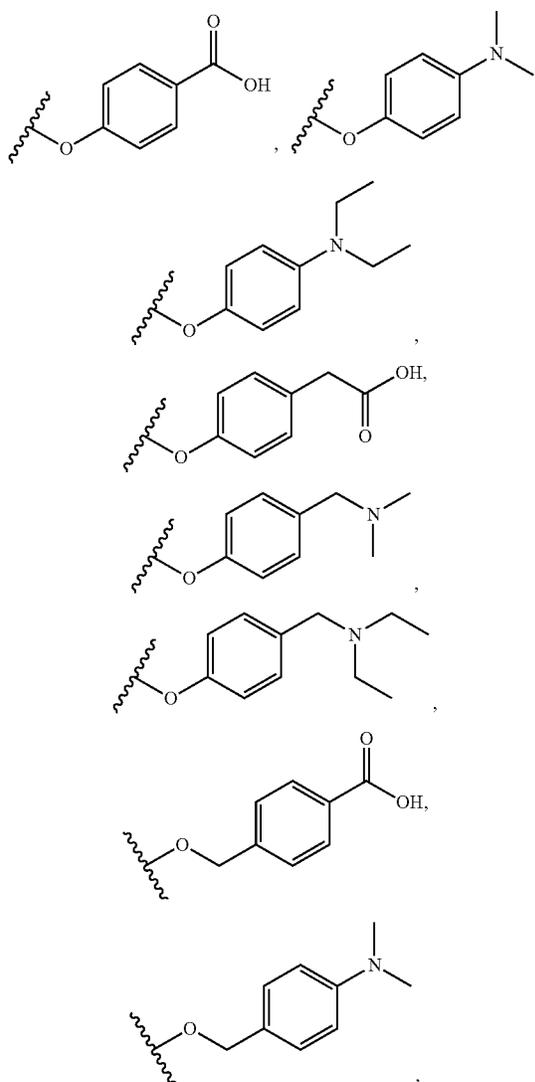


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In a further aspect, R^{1a} is hydrogen and R^{1b} is selected from —O(C1-C8 alkyl)-aryl and —O-aryl; and wherein R^{1b} is unsubstituted.

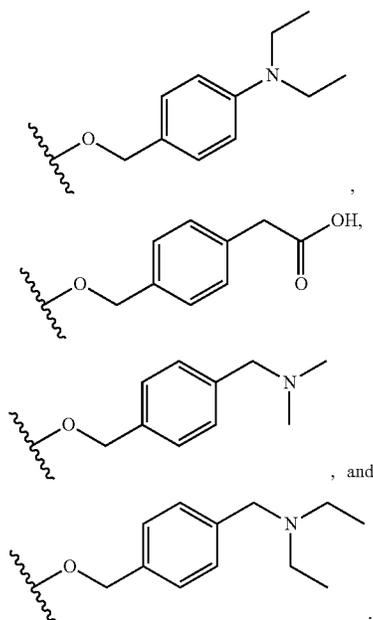
In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from —O(C1-C8 alkyl)-aryl and —O-aryl; and wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl). In a yet further aspect, R^{1b} is hydrogen and R^{1a} is selected from —OCH₂-phenyl, —O(CH₂)₂-phenyl, —O(CH₂)₃-phenyl, and —O-aryl; and wherein R^{1b} is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl).

In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from:

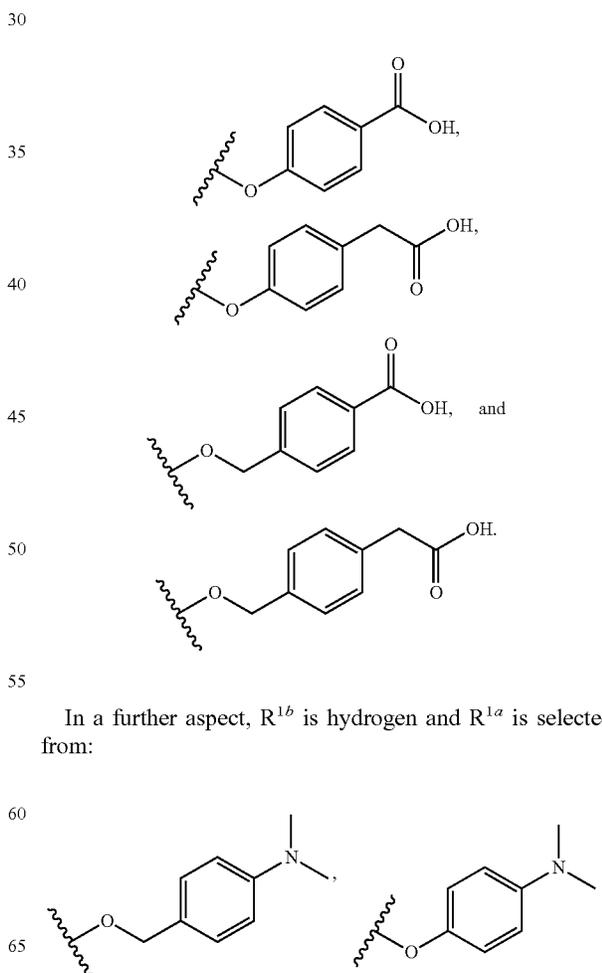


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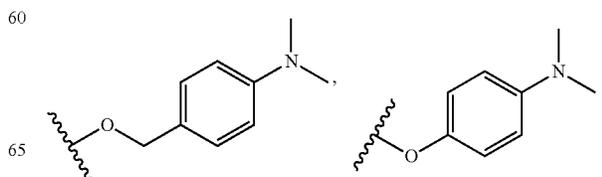
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In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from:

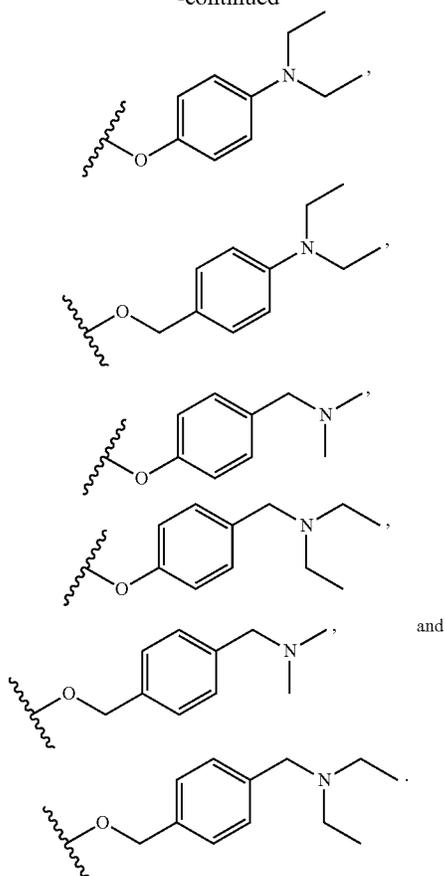


In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from:



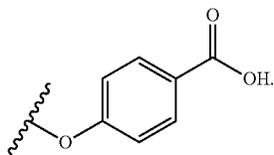
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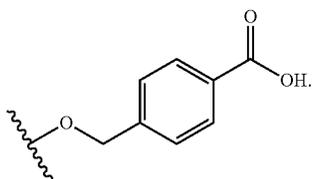


and

In a further aspect, R^{1b} is hydrogen and R^{1a} is:



In a further aspect, R^{1b} is hydrogen and R^{1a} is:



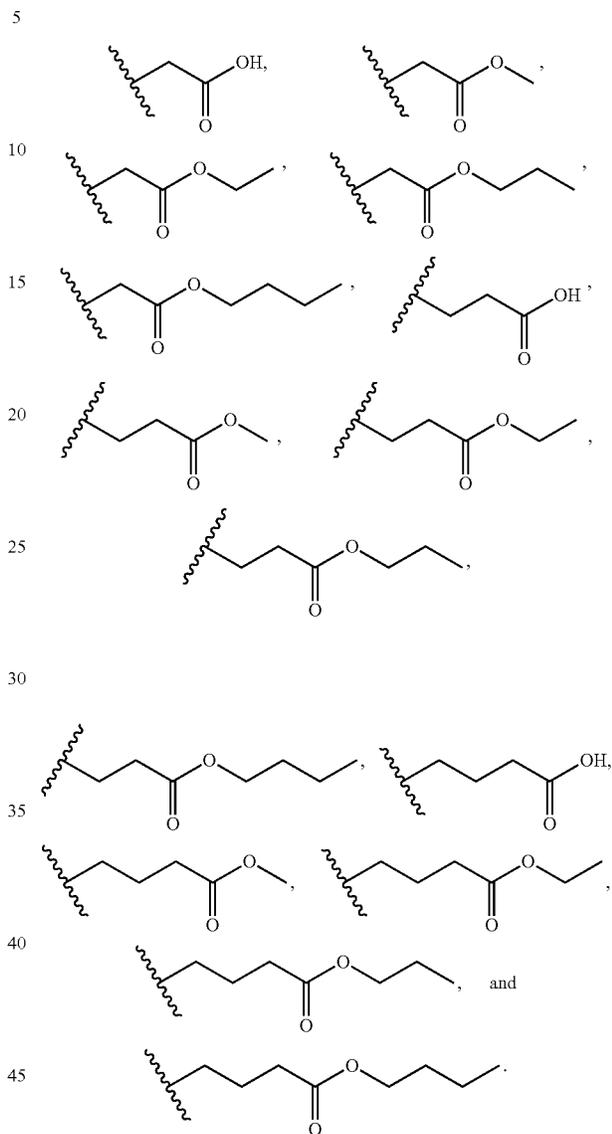
In a further aspect, R^{1b} is hydrogen and R^{1a} is selected from $-\text{O}(\text{C}1\text{-C}8 \text{ alkyl})\text{-aryl}$ and $-\text{O-aryl}$; and wherein R^{1b} is unsubstituted.

2. R^{2A} and R^{2B} Groups

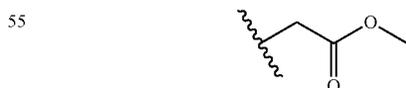
In one aspect, R^{2a} and R^{2b} together are (CH_2) . In a further aspect, each of R^{2a} and R^{2b} is independently selected from hydrogen, $-(\text{C}1\text{-C}8 \text{ alkyl})\text{-(CO)OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C)O}(\text{C}1\text{-C}6 \text{ alkyl})$.

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In a further aspect, each of R^{2a} and R^{2b} is independently selected from hydrogen and a moiety having a structure represented by the formula:



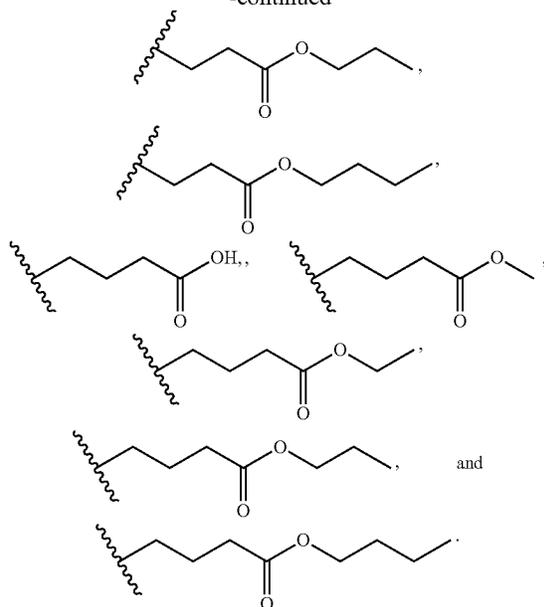
In a further aspect, each of R^{2a} and R^{2b} is independently selected from hydrogen and a moiety having a structure represented by the formula:



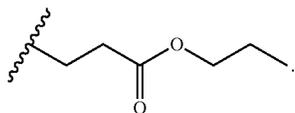
In a further aspect, R^{2a} is hydrogen and R^{2b} is selected from hydrogen, $-(\text{C}1\text{-C}8 \text{ alkyl})\text{-(C=O)OH}$, and $-\text{O}(\text{C}=\text{O})(\text{C}1\text{-C}6 \text{ alkyl})\text{-(C=O)O}(\text{C}1\text{-C}6 \text{ alkyl})$. In a still further aspect, R^{2a} is hydrogen and R^{2b} is selected from hydrogen and a moiety having a structure represented by the formula:

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In a further aspect, R^4 is:



In a further aspect, R^4 is selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl. In a still further aspect, R^4 is selected from hydrogen, C1-C3 alkyl, C1-C3 monohaloalkyl, and C1-C3 polyhaloalkyl. In a yet further aspect, R^4 is selected from hydrogen and C1-C8 alkyl. In an even further aspect, R^4 is selected from hydrogen and C1-C6 alkyl. In a still further aspect, R^4 is selected from hydrogen and C1-C3 alkyl.

In a further aspect, R^4 is selected from hydrogen, methyl, ethyl, propyl, isopropyl, tert-butyl, sec-butyl, isobutyl, neopentyl, isopentyl, tert-pentyl, methylbutyl, dimethylbutyl, methylpentyl, and dimethylpentyl. In a still further aspect, R^4 is selected from hydrogen, methyl, ethyl, propyl, isopropyl, and tert-butyl. In a yet further aspect, R^4 is selected from hydrogen and methyl. In a still further aspect, R^4 is hydrogen. In a yet further aspect, R^4 is methyl.

5. R^{5a} and R^{5b} Groups

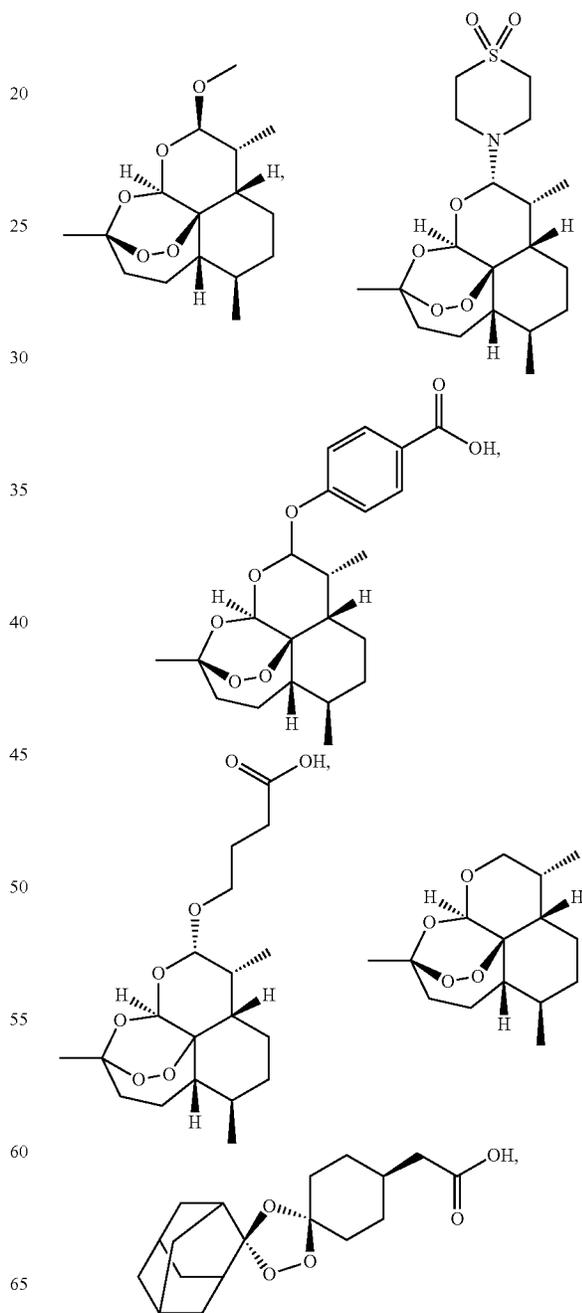
In one aspect, each of R^{5a} and R^{5b} are hydrogen. In a further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl. In a still further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen, C1-C3 alkyl, C1-C3 monohaloalkyl, and C1-C3 polyhaloalkyl. In a yet further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen and C1-C8 alkyl. In an even further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen and C1-C6 alkyl. In a still further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen and C1-C3 alkyl.

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In a further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen, methyl, ethyl, propyl, isopropyl, tert-butyl, sec-butyl, isobutyl, neopentyl, isopentyl, sec-pentyl, tert-pentyl, methylbutyl, dimethylbutyl, methylpentyl, and dimethylpentyl. In a still further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen, methyl, ethyl, propyl, isopropyl, and tert-butyl. In a yet further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen, methyl, ethyl, propyl, and isopropyl. In an even further aspect, each of R^{5a} and R^{5b} is independently selected from hydrogen and methyl.

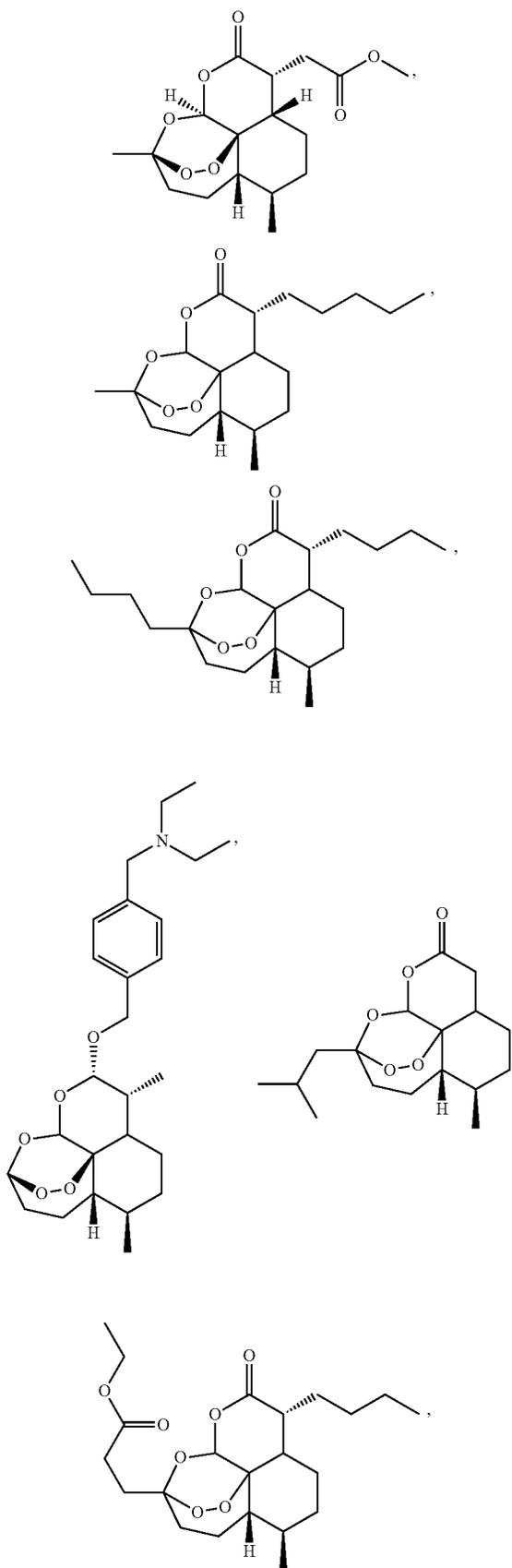
6. Exemplary Artemisinin Analogue Compounds

In one aspect, the invention relates to pharmaceutical compositions comprising a at least one artemisinin analogue selected from:



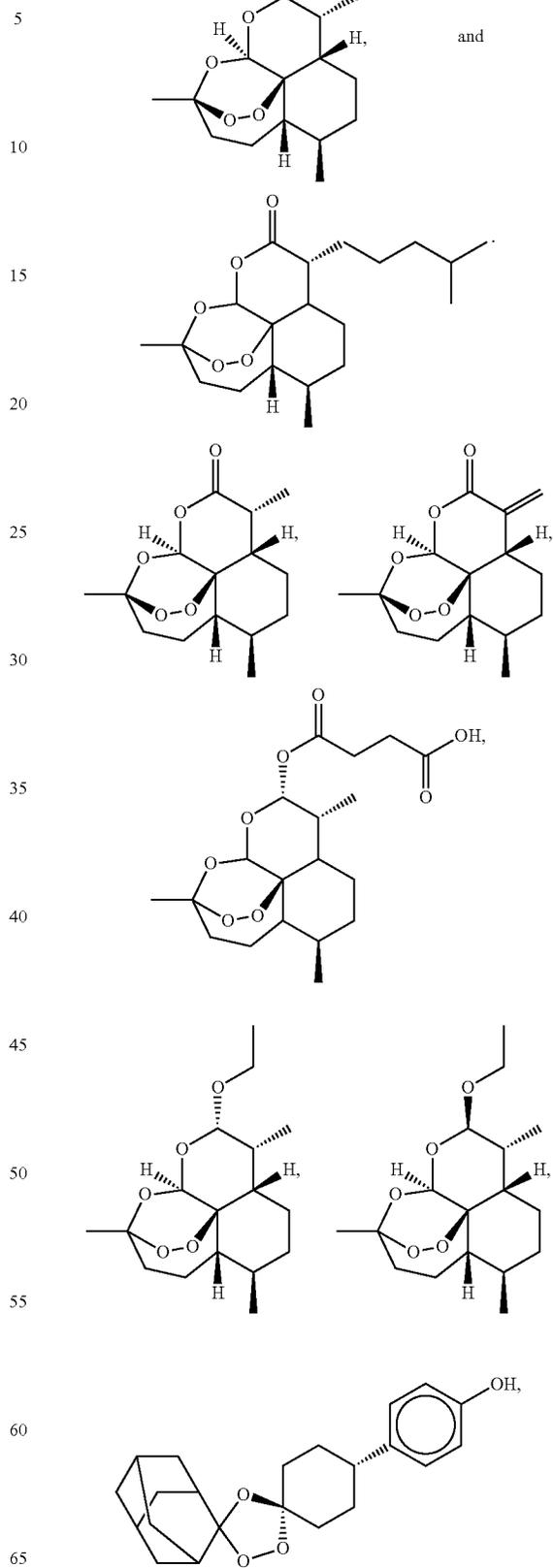
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and

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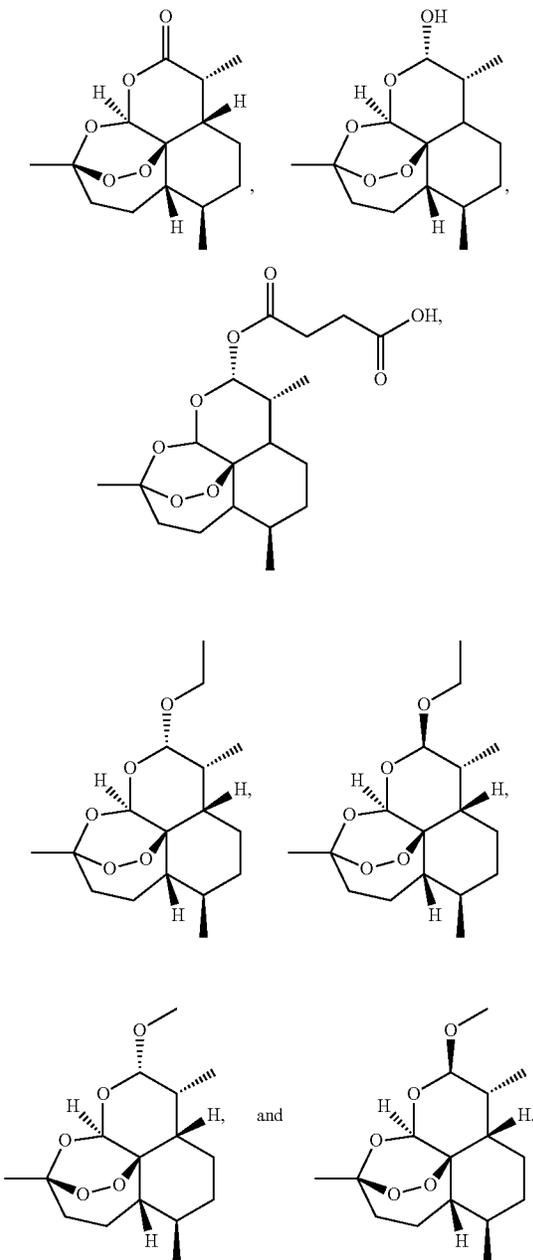
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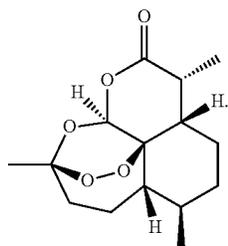
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In one aspect, the artemisinin analogue is selected from:

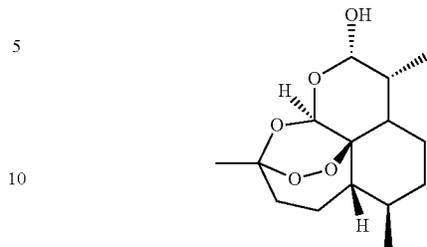


In one aspect, the artemisinin analogue is:

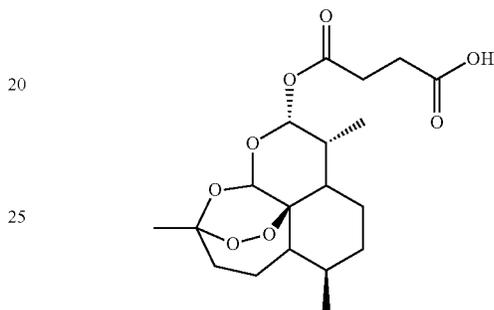


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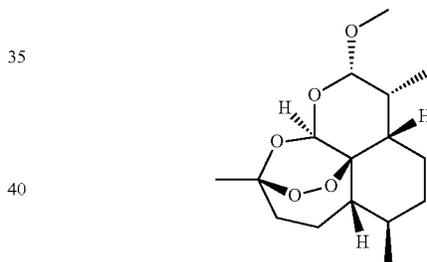
In one aspect, the artemisinin analogue is:



15 In one aspect, the artemisinin analogue is:



30 In one aspect, the artemisinin analogue is:



45 C. BCR-ABL Tyrosine Kinase Inhibitors

In various aspects, the invention relates to compositions comprising a therapeutically effective amount of a BCR-ABL tyrosine kinase inhibitor. In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, and tozasertib.

55 In a further aspect, the BCR-ABL tyrosine kinase inhibitor is imatinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is dasatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is nilotinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is bosutinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is ponatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is bafetinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is saracatinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is tozasertib.

65 In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from a BCR-ABL selective inhibitor, a dual

BCR-ABL and Src-family kinases inhibitor, Aurora kinase inhibitor, Kit inhibitor, ATP competitive inhibitor and non-ATP competitive BCR-ABL inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a selective BCR-ABL inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a dual BCR-ABL and Src-family kinases inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a Aurora kinase inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a KIT inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a ATP competitive BCR-ABL inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a non-ATP competitive BCR-ABL inhibitor.

D. Pharmaceutical Compositions

In one aspect, the invention relates to pharmaceutical compositions comprising the disclosed compounds. That is, a pharmaceutical composition can be provided comprising a therapeutically effective amount of at least one disclosed compound and a pharmaceutically acceptable carrier.

In certain aspects, the disclosed pharmaceutical compositions comprise the disclosed compounds (including pharmaceutically acceptable derivatives (e.g., salt(s)) thereof) as an active ingredient, a pharmaceutically acceptable carrier, and, optionally, other therapeutic ingredients or adjuvants. The compositions include those suitable for oral, rectal, topical, and parenteral (including subcutaneous, intramuscular, and intravenous) administration, although the most suitable route in any given case will depend on the particular host, and nature and severity of the conditions for which the active ingredient is being administered. The pharmaceutical compositions can be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

The disclosed compounds can be administered by oral, parenteral (e.g., intramuscular, intraperitoneal, intravenous, intracerebroventricular, intracisternal injection or infusion, subcutaneous injection, or implant), by inhalation spray, nasal, vaginal, rectal, sublingual, or topical routes of administration and can be formulated, alone or together, in suitable dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles appropriate for each route of administration. In addition to the treatment of warm-blooded animals such as mice, rats, horses, cattle, sheep, dogs, cats, monkeys, etc., the compounds of the invention are effective for use in humans. The term "composition" as used herein is intended to encompass a product comprising specified ingredients in predetermined amounts or proportions, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. This term in relation to pharmaceutical compositions is intended to encompass a product comprising one or more active ingredients, and an optional carrier comprising inert ingredients, as well as any product which results, directly or indirectly, from combination, complexation or aggregation of any two or more of the ingredients, or from dissociation of one or more of the ingredients, or from other types of reactions or interactions of one or more of the ingredients. In general, pharmaceutical compositions are prepared by uniformly and intimately bringing the active ingredient into association with a liquid carrier or a finely divided solid carrier or both, and then, if necessary, shaping the product into the desired formulation. In the pharmaceutical composition the active object compound is included in an amount sufficient to produce the desired effect upon the process or condition of

diseases. Accordingly, the pharmaceutical compositions encompass any composition made by admixing a compound of the present invention and a pharmaceutically acceptable carrier.

As used herein, the term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids. When a disclosed compound is acidic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic bases, including inorganic bases and organic bases. Salts derived from such inorganic bases include aluminum, ammonium, calcium, copper (-ic and -ous), ferric, ferrous, lithium, magnesium, manganese (-ic and -ous), potassium, sodium, zinc and the like salts. Particularly preferred are the ammonium, calcium, magnesium, potassium and sodium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, as well as cyclic amines and substituted amines such as naturally occurring and synthesized substituted amines. Other pharmaceutically acceptable organic non-toxic bases from which salts can be formed include ion exchange resins such as, for example, arginine, betaine, caffeine, choline, N,N'-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

As used herein, the term "pharmaceutically acceptable non-toxic acids," includes inorganic acids, organic acids, and salts prepared therefrom, for example, acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid and the like. Preferred are citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, and tartaric acids.

In practice, the compounds of the invention, or pharmaceutically acceptable derivatives thereof, of this invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier can take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral or parenteral (including intravenous). Thus, the pharmaceutical compositions can be presented as discrete units suitable for oral administration such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient. Further, the compositions can be presented as a powder, as granules, as a solution, as a suspension in an aqueous liquid, as a non-aqueous liquid, as an oil-in-water emulsion or as a water-in-oil liquid emulsion. In addition to the common dosage forms set out above, the compounds of the invention, and/or pharmaceutically acceptable salt(s) thereof, can also be administered by controlled release means and/or delivery devices. The compositions can be prepared by any of the methods of pharmacy. In general, such methods include a step of bringing into association the active ingredient with the carrier that constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the active ingredient with liquid carriers or finely divided solid carriers or both. The product can then be conveniently shaped into the desired presentation.

Thus, the pharmaceutical compositions of this invention can include a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of the compounds of the invention. The compounds of the invention, or pharmaceutically acceptable salts thereof, can also

be included in pharmaceutical compositions in combination with one or more other therapeutically active compounds. The pharmaceutical carrier employed can be, for example, a solid, liquid, or gas. Examples of solid carriers include lactose, terra alba, sucrose, talc, gelatin, agar, pectin, acacia, magnesium stearate, and stearic acid. Examples of liquid carriers are sugar syrup, peanut oil, olive oil, and water. Examples of gaseous carriers include carbon dioxide and nitrogen.

In preparing the compositions for oral dosage form, any convenient pharmaceutical media can be employed. For example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like can be used to form oral liquid preparations such as suspensions, elixirs and solutions; while carriers such as starches, sugars, microcrystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like can be used to form oral solid preparations such as powders, capsules and tablets. Because of their ease of administration, tablets and capsules are the preferred oral dosage units whereby solid pharmaceutical carriers are employed. Optionally, tablets can be coated by standard aqueous or nonaqueous techniques.

A tablet containing the composition of this invention can be prepared by compression or molding, optionally with one or more accessory ingredients or adjuvants. Compressed tablets can be prepared by compressing, in a suitable machine, the active ingredient in a free-flowing form such as powder or granules, optionally mixed with a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets can be made by molding in a suitable machine, a mixture of the powdered compound moistened with an inert liquid diluent.

Pharmaceutical compositions suitable for parenteral administration can be prepared as solutions or suspensions of the active compounds in water. A suitable surfactant can be included such as, for example, hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof in oils. Further, a preservative can be included to prevent the detrimental growth of microorganisms.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions or dispersions. Furthermore, the compositions can be in the form of sterile powders for the extemporaneous preparation of such sterile injectable solutions or dispersions. In all cases, the final injectable form must be sterile and must be effectively fluid for easy syringability. The pharmaceutical compositions must be stable under the conditions of manufacture and storage; thus, preferably should be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol and liquid polyethylene glycol), vegetable oils, and suitable mixtures thereof.

Pharmaceutical compositions can be in a form suitable for topical use such as, for example, an aerosol, cream, ointment, lotion, dusting powder, mouth washes, gargles, and the like. Further, the compositions can be in a form suitable for use in transdermal devices. These formulations can be prepared, utilizing a compound of the invention, or pharmaceutically acceptable salts thereof, via conventional pro-

cessing methods. As an example, a cream or ointment is prepared by mixing hydrophilic material and water, together with about 5 wt % to about 10 wt % of the compound, to produce a cream or ointment having a desired consistency.

Pharmaceutical compositions of this invention can be in a form suitable for rectal administration wherein the carrier is a solid. It is preferable that the mixture forms unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art. The suppositories can be conveniently formed by first admixing the composition with the softened or melted carriers) followed by chilling and shaping in molds.

In addition to the aforementioned carrier ingredients, the pharmaceutical formulations described above can include, as appropriate, one or more additional carrier ingredients such as diluents, buffers, flavoring agents, binders, surface-active agents, thickeners, lubricants, preservatives (including anti-oxidants) and the like. Furthermore, other adjuvants can be included to render the formulation isotonic with the blood of the intended recipient. Compositions containing a compound of the invention, and/or pharmaceutically acceptable salts thereof, can also be prepared in powder or liquid concentrate form.

In the treatment of the disclosed conditions, an appropriate dosage level will generally be about 0.01 to 500 mg per kg patient body weight per day which can be administered in single or multiple doses. Preferably, the dosage level will be about 0.1 to about 250 mg/kg per day; more preferably about 0.5 to about 100 mg/kg per day. A suitable dosage level can be about 0.01 to 250 mg/kg per day, about 0.05 to 100 mg/kg per day, or about 0.1 to 50 mg/kg per day. Within this range the dosage can be 0.05 to 0.5, 0.5 to 5 or 5 to 50 mg/kg per day. For oral administration, the compositions are preferably provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, particularly 1.0, 5.0, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 400, 500, 600, 750, 800, 900, and 1000 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The compounds can be administered on a regimen of 1 to 4 times per day, preferably once or twice per day. This dosage regimen can be adjusted to provide the optimal therapeutic response. It will be understood, however, that the specific dose level and frequency of dosage for any particular patient can be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular condition, and the host undergoing therapy.

The disclosed pharmaceutical compositions can further comprise other therapeutically active compounds, as discussed further herein, which are usually applied in the treatment of the above mentioned pathological conditions.

In a further aspect, a pharmaceutical composition can comprise a therapeutically effective amount of any one or more disclosed compound and a pharmaceutically acceptable carrier. In a further aspect, a pharmaceutical composition can comprise a therapeutically effective amount of one or more product of any disclosed method and a pharmaceutically acceptable carrier. In one aspect, the invention relates to a method for manufacturing a medicament comprising combining at least one disclosed compound or at least one product of a disclosed method with a pharmaceutically acceptable carrier or diluent.

It is understood that the disclosed compositions can be prepared from the disclosed compounds. It is also under-

stood that the disclosed compositions can be employed in the disclosed methods of using.

E. Methods of Using the Compounds and Compositions

BCR-ABL tyrosine kinase (BCR-ABL TK) has been known to activate many pro-growth and cell survival mechanisms, which in turn promote cell proliferation and survival, and contribute to BCR-ABL mediated leukemic transformation of bone marrow progenitor cells. BCR-ABL TK-specific inhibition has previously been established as an effective therapeutic target. BCR-ABL tyrosine kinase shifts between a catalytically active open conformation and an inactive closed one. The structure of BCR-ABL contains two flexible loops, the ATP-binding P-loop (P-loop) and the activation loop (A-loop). These loops have specific arrangements in the inactive conformation of BCR-ABL that stabilize the basal conformation. In the inactive form the A-loop blocks the catalytic site and prevents BCR-ABL activity. BCR-ABL TK-specific inhibitors (BCR-ABL TKIs), such as imatinib, have been observed to bind and stabilize the inactive conformation, and have reduced previously poor chronic myelogenous leukemia (CML) outcomes to a controlled chronic condition. However, BCR-ABL TKIs have failed to produce a similar long-term response in related leukemias, such as pediatric and adult Ph+acute lymphoblastic leukemia (ALL). While current BCR-ABL-inhibition agents appear to kill Ph+ ALL cells in vitro, these drugs fails to meaningfully reduce leukemia burden in patients with Ph+ ALL, invariably leading to relapse and poor long-term outcomes.

Resistance to BCR-ABL TKIs is believed to contribute to the inability to induce adequate clinical responses. A major mechanism of BCR-ABL TKI resistance is thought to relate to mutations that result in the interference of binding to the BCR-ABL kinase domain. BCR-ABL mutations can confer different levels of resistance, ranging from concentration dependent resistance to complete BCR-ABL TKIs resistance. The most clinically significant mutations are P-loop mutations and the T315I mutation. Significantly, the T315I mutation produces the most common and highest form of resistance of any mutation, resulting in resistance to both imatinib and second generation BCR-ABL TKIs, dasatinib and nilotinib. Moreover, differences in clinical responses to BCR-ABL TKIs in patients with Ph+ ALL and CML remain poorly understood. Without wishing to be bound by a particular theory, these differences cannot be exclusively attributed to mutations in the BCR-ABL kinase domain that weaken drug binding.

Previously, a role has been reported for host cytokines of the common gamma chain receptor family in modulating primary imatinib resistance, but many alternative host-derived growth factors have similarly been proposed. Currently, no consensus exists on the relative importance of cytokines that control the cellular responses to BCR-ABL-targeted agents. Interleukin 7 (IL7) is a multifunctional cytokine essential for human T cell and post-fetal B cell development and is a major contributor to the regulation and maintenance of mature T cells. This non-redundant cytokine is constitutively produced by stromal cells in bone marrow, spleen, lymph nodes and thymus, as well as other tissues. IL7-rich niches have been observed to harbor early persistent drug-refractory leukemias in humans and mice. Without wishing to be bound by a particular theory, in these niches, BCR-ABL mutations are believed to be eventually acquired under continuous drug exposures, causing secondary drug

resistance. Moreover, the responsiveness to extrinsic cytokines increases in persistent (drug-refractory) human Ph+ leukemia samples collected from BCR-ABL TKI-treated patients. In keeping with the critical homeostatic role of IL7 in human immune-reconstitution, IL7 levels dramatically vary in inverse proportion to an individual patient's absolute lymphocyte counts (ALC). Without wishing to be bound by a particular theory, contemporary BCR-ABL TKI-combined protocols deploy high-dose corticosteroids, conventional chemotherapy agents, allo-HSCT, and immune-suppressants, all of which induce profound iatrogenic-lymphopenias, and activate the immune IL7-axis thus likely blunting dasatinib efficacy. Moreover, the relatively robust dasatinib survival benefit in human patients with prolonged lymphocytosis may arise from their inherently low levels of IL7, and vice versa. Without wishing to be bound by a particular theory, it is believed that reducing the IL7-related activity through pharmacological intervention in diseases harboring BCR-ABL defects or mutations can have an important therapeutic benefit. Thus, IL7 provides an attractive, BCR-ABL-independent target for therapeutic intervention.

Additionally, human Ph+ ALL patients with increased levels of pSTAT5, a latent transcription factor whose phosphorylation is triggered by IL7, have been reported to respond poorly to imatinib therapy. Without wishing to be bound by a particular theory, c-MYC, a strong proto-oncogene, may play a role in IL7-induced BCR-ABL TKI resistance because expression of c-MYC can be induced by activated STAT5, in turn induced by IL7-JAK signaling. This phenomenon has been implicated in other stroma-induced drug resistance as well as used as an explanation for resistance to imatinib. Moreover, STAT5 activation and c-MYC expression is reportedly necessary to sustain BCR-ABL transformed cells. This extensive family of signaling proteins regulates important cell processes that, when dysregulated, lead to typical tumorigenic phenotype features. Therefore, inhibition at any point along this signaling cascade may provide clinical benefit to patients with pathologies that are driven by overactive signaling in this pathway. Without wishing to be bound by a particular theory, it is believed that inhibition of c-MYC activity, thereby countering the protective effects of IL7, can resolve and rescue the IL7-induced BCR-ABL TKI resistance that is a consequence of these mutations.

1. Treatment Methods

The compounds disclosed herein are useful for treating, preventing, ameliorating, controlling or reducing the risk of a variety of disorders of uncontrolled cellular proliferation. In one aspect, the disorder of uncontrolled cellular proliferation is associated with the BCR-ABL pathway. In a further aspect, the disorder of uncontrolled cellular proliferation is associated with a Philadelphia chromosome positive leukemia. In a further aspect, the BCR-ABL dysfunction is a mutation of the BCR-ABL gene. In one aspect, the disorder of uncontrolled cellular proliferation is associated with a gastrointestinal stromal tumor (GIST).

Examples of disorders of uncontrolled cellular proliferation include cancers such as leukemias, lymphomas, and solid tumors. In one aspect, the cancer can be a cancer selected from cancers of the gastrointestinal tract, hematologic, colon, rectum, liver, omentum, breast, kidney, lymphatic system, stomach, lung, pancreas, liver and skin. In a further aspect, the cancer is selected from leukemia and gastrointestinal stroma tumor.

Examples of disorders associated with BCR-ABL include leukemias, chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and Philadelphia chromosome

positive acute lymphoblastic leukemia (Ph+ALL). It can be appreciated that additional cancers, such as those associated with tyrosine kinase dysfunction, may benefit from using the present invention, including, for example, carcinomas, colon, kidney, liver, lung, pancreas, stomach, thyroid, testis, testicular seminomas, squamous cell carcinoma, and other hematologic tumors.

a. Treatment of a Philadelphia Chromosome Positive Leukemia

In one aspect, the invention relates to a method for the treatment of a Philadelphia chromosome positive leukemia in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is administered prior to administration of the artemisinin analogue. In a yet further aspect, the artemisinin analogue is administered prior to administration of the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered in a second period. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are not the same. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are the same.

In a further aspect, the Philadelphia chromosome positive leukemia after the first treatment period is refractory to treatment by the BCR-ABL tyrosine kinase inhibitor. In a still further aspect, the Philadelphia chromosome positive leukemia during the first treatment period becomes refractory to treatment by the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the Philadelphia chromosome positive leukemia comprises a mutation. In a yet further aspect, the Philadelphia chromosome positive leukemia after the first treatment period comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a still further aspect, the mutation is T315I.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, and tozasertib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is imatinib. In yet a further aspect, the BCR-ABL tyrosine kinase inhibitor is dasatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is nilotinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is bosutinib. In a yet further aspect, the BCR-ABL tyrosine

kinase inhibitor is ponatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is bafetinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is saracatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is tozasertib.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from a BCR-ABL selective inhibitor, a dual BCR-ABL and Src-family kinases inhibitor, Aurora kinase inhibitor, Kit inhibitor, ATP competitive inhibitor and non-ATP competitive BCR-ABL inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a selective BCR-ABL inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a dual BCR-ABL and Src-family kinases inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a Aurora kinase inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a KIT inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a ATP competitive BCR-ABL inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a non-ATP competitive BCR-ABL inhibitor.

In further aspect, the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step. In a still further aspect, the method further comprises the step of identifying a patient in need of treatment of a Philadelphia chromosome positive leukemia.

In a further aspect, the patient has been diagnosed with a Philadelphia chromosome positive leukemia refractory to treatment with a BCR-ABL kinase inhibitor. In a still further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL kinase domain mutation. In a yet further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL mutation. In an even further aspect, the mutation is selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a still further aspect, the mutation is T315I.

In a further aspect, the Philadelphia chromosome positive leukemia is selected from acute lymphoblastic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia.

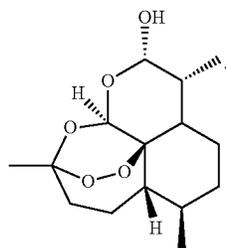
In a further aspect, the Philadelphia chromosome positive leukemia is chronic myelogenous leukemia ("CML"). In a yet further aspect, the chronic myelogenous leukemia is chronic phase CML. In an even further aspect, the chronic myelogenous leukemia is lymphoid blast phase CML. In a still further aspect, the chronic myelogenous leukemia is myeloid blast phase CML. In a yet further aspect, the chronic myelogenous leukemia is accelerated phase CML.

In a further aspect, the Philadelphia chromosome positive leukemia is acute lymphoblastic leukemia. In a still further aspect, the a Philadelphia chromosome positive leukemia is acute myelogenous leukemia.

In one aspect, the invention relates to a method for the treatment of a Philadelphia chromosome positive leukemia in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL tyrosine kinase inhibitor, and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a

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pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; wherein administering the artemisinin analogue to a patient produces a metabolite in the patient with a structure represented by the formula:



In a further aspect, the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is administered prior to administration of the artemisinin analogue. In a yet further aspect, the artemisinin analogue is administered prior to administration of the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered in a second period. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are not the same. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are the same.

In a further aspect, the Philadelphia chromosome positive leukemia after the first treatment period is refractory to treatment by the BCR-ABL tyrosine inhibitor. In a still further aspect, the Philadelphia chromosome positive leukemia during the first treatment period becomes refractory to treatment by the BCR-ABL tyrosine inhibitor.

In a further aspect, the Philadelphia chromosome positive leukemia after the first treatment period comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a still further aspect, the mutation is T315I.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, and tozasertib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is imatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is dasatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is nilotinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is bosutinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is ponatinib. In an even further aspect, the

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BCR-ABL tyrosine kinase inhibitor is bafetinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is saracatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is tozasertib.

5 In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from a BCR-ABL selective inhibitor, a dual BCR-ABL and Src-family kinases inhibitor, Aurora kinase inhibitor, Kit inhibitor, ATP competitive inhibitor and non-ATP competitive BCR-ABL inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a selective BCR-ABL inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a dual BCR-ABL and Src-family kinases inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a Aurora kinase inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a KIT inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a ATP competitive BCR-ABL inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a non-ATP competitive BCR-ABL inhibitor.

In a further aspect, the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step. In a still further aspect, the method further comprises the step of identifying a patient in need of treatment of a Philadelphia chromosome positive leukemia.

In a further aspect, the patient has been diagnosed with a Philadelphia chromosome positive leukemia refractory to treatment with a BCR-ABL kinase inhibitor. In a still further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL kinase domain mutation. In a yet further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL mutation. In an even further aspect, the mutation is selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a still further aspect, the mutation is T315I.

In a further aspect, the Philadelphia chromosome positive leukemia is selected from acute lymphoblastic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia. In a still further aspect, the a Philadelphia chromosome positive leukemia is chronic myelogenous leukemia ("CML"). In a yet further aspect, the chronic myelogenous leukemia is chronic phase CML. In an even further aspect, the chronic myelogenous leukemia is lymphoid blast phase CML. In a still further aspect, the chronic myelogenous leukemia is myeloid blast phase CML. In a yet further aspect, the chronic myelogenous leukemia is accelerated phase CML.

In a further aspect, the Philadelphia chromosome positive leukemia is acute lymphoblastic leukemia. In a still further aspect, the Philadelphia chromosome positive leukemia is acute myelogenous leukemia.

b. Treatment of a Gastrointestinal Stromal Tumor

In one aspect, the present invention relates to methods for the treatment of a gastrointestinal stromal tumor (GIST) in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least

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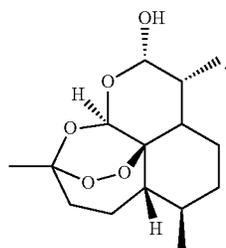
one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is administered prior to administration of the artemisinin analogue. In a yet further aspect, the artemisinin analogue is administered prior to administration of the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered in a second period. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are not the same. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are the same.

In a further aspect, the after the first treatment period is refractory to treatment by the BCR-ABL tyrosine kinase inhibitor. In a still further aspect, the gastrointestinal stromal tumor during the first treatment period becomes refractory to treatment by the BCR-ABL tyrosine kinase inhibitor.

In one aspect, the invention relates to a method for the treatment of a gastrointestinal stromal tumor (GIST) in a patient comprising the step of administering to the patient a therapeutically effective amount of a BCR-ABL tyrosine kinase inhibitor, and a therapeutically effective amount of at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, hydrate, solvate, or polymorph thereof; wherein administering the artemisinin analogue to a patient produces a metabolite in the patient with a structure represented by the formula:



In a further aspect, the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is administered prior to administration of the artemisinin analogue. In a yet further aspect, the artemisinin analogue is administered prior to administration of the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered in a second period. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are not the same. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are the same.

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In a further aspect, the gastrointestinal stromal tumor after the first treatment period is refractory to treatment by the BCR-ABL tyrosine kinase inhibitor. In a still further aspect, the stromal tumor during the first treatment period becomes refractory to treatment by the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the gastrointestinal stromal tumor after the first treatment period comprises a mutation. In a still further aspect, the mutation is a KIT mutation.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, and tozasertib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is imatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is dasatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is nilotinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is bosutinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is ponatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is bafetinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is saracatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is tozasertib.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from a BCR-ABL selective inhibitor, a dual BCR-ABL and Src-family kinases inhibitor, Aurora kinase inhibitor, Kit inhibitor, ATP competitive inhibitor and non-ATP competitive BCR-ABL inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a selective BCR-ABL inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a dual BCR-ABL and Src-family kinases inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a Aurora kinase inhibitor. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is a KIT inhibitor. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is a ATP competitive BCR-ABL inhibitor. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is a non-ATP competitive BCR-ABL inhibitor.

In a further aspect, the patient has been diagnosed with a need for treatment of a gastrointestinal stromal tumor prior to the administering step. In a still further aspect, the method further comprises the step of identifying a patient in need of treatment of a gastrointestinal stromal tumor.

In a further aspect, the patient has been diagnosed with a gastrointestinal stromal tumor refractory to treatment with a BCR-ABL kinase inhibitor. In a still further aspect, the refractory gastrointestinal stromal tumor comprises a mutation. In a yet further aspect, the mutation is a KIT mutation.

2. Manufacture of a Medicament

In one aspect, the invention relates to use of at least one disclosed compound in the manufacture of a medicament for the treatment of an uncontrolled cellular proliferative disorder in a patient. In a further aspect, the use is in the manufacture of a medicament for the treatment of a Philadelphia chromosome positive leukemia. In a further aspect, the use is in the manufacture of a medicament for the treatment of a gastrointestinal stromal cancer.

In a further aspect, the invention relates to a method for the manufacture of a medicament to overcome BCR-ABL tyrosine kinase inhibitor drug resistance in a patient comprising combining a therapeutically effective amount of a disclosed compound or product of a disclosed method with a pharmaceutically acceptable carrier or diluent.

In various aspect, the invention relates methods for the manufacture of a medicament for modulating the activity

IL7 (e.g., treatment of one or more Philadelphia chromosome positive leukemias associated with cytokine-related BCR-ABL tyrosine kinase inhibitor drug resistance) in patients comprising combining one or more disclosed compounds, products, or compositions or a pharmaceutically acceptable salt, solvate, hydrate, or polymorph thereof, with a pharmaceutically acceptable carrier. It is understood that the disclosed methods can be performed with the disclosed compounds, products, and pharmaceutical compositions. It is also understood that the disclosed methods can be employed in connection with the disclosed methods of using.

It is understood that the disclosed methods can be performed with the disclosed compounds, products, and pharmaceutical compositions. It is also understood that the disclosed methods can be employed in connection with the disclosed methods of using.

3. Use of Compounds

It is understood that the disclosed uses can be employed in connection with the disclosed compounds, methods, compositions, and kits.

4. Kits

In one aspect, the invention relates to a kit comprising a BCR-ABL kinase inhibitor, at least one disclosed artemisinin analogue, or a pharmaceutically acceptable salt, solvate, or polymorph thereof; and instructions for treatment of a disease of uncontrolled cellular proliferation; and wherein the instructions comprise administration of a BCR-ABL kinase inhibitor and the at least one artemisinin analogue to a patient that has become refractory to treatment with a BCR-ABL kinase inhibitor.

In a further aspect, the BCR-ABL kinase inhibitor and the at least one disclosed artemisinin analogue are co-formulated. In a still further aspect, the BCR-ABL kinase inhibitor and the at least one disclosed artemisinin analogue are co-packaged.

In a further aspect, the instructions further comprise co-administration of the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue. In a still further aspect, the instructions further comprise administration of the BCR-ABL tyrosine kinase inhibitor prior to administration of the artemisinin analogue. In a yet further aspect, the instructions further comprise administration of the artemisinin analogue prior to administration of the BCR-ABL tyrosine kinase inhibitor.

In a further aspect, the instructions further comprise administration of the BCR-ABL kinase inhibitor and the at least one disclosed artemisinin analogue to a patient with a Philadelphia chromosome positive leukemia.

In a further aspect, the instructions further comprise administration of the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and co-administration of the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue in a second period. In a still further aspect, the instructions further comprise that the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are not the same. In a yet further aspect, the instructions further comprise that the BCR-ABL tyrosine kinase inhibitor administered in a first period and the BCR-ABL tyrosine kinase inhibitor administered in a second period are the same.

In a further aspect, the instructions further comprise administration of the BCR-ABL kinase inhibitor and the at least one disclosed artemisinin analogue to a patient with a Philadelphia chromosome positive leukemia in the first treatment period.

In a further aspect, the instructions further comprise administration to a patient that is refractory to treatment by the BCR-ABL tyrosine kinase inhibitor after the first treatment period. In a still further aspect, the instructions further comprise that the Philadelphia chromosome positive leukemia after the first treatment period comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a yet further aspect, the mutation is T315I.

In a further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, and tozasertib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is imatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is dasatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is nilotinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is bosutinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is ponatinib. In an even further aspect, the BCR-ABL tyrosine kinase inhibitor is bafetinib. In a still further aspect, the BCR-ABL tyrosine kinase inhibitor is saracatinib. In a yet further aspect, the BCR-ABL tyrosine kinase inhibitor is tozasertib.

In a further aspect, the instructions further comprise the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step. In a still further aspect, the instructions further comprise identifying a patient in need of treatment of a Philadelphia chromosome positive leukemia.

In a further aspect, the instructions further comprise the patient has been diagnosed with a Philadelphia chromosome positive leukemia refractory to treatment with a BCR-ABL kinase inhibitor. In a still further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL kinase domain mutation. In a yet further aspect, the refractory Philadelphia chromosome positive leukemia comprises a BCR-ABL mutation. In an even further aspect, the mutation is selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E. In a still further aspect, the mutation is T315I.

In a further aspect, the Philadelphia chromosome positive leukemia is selected from acute lymphoblastic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia. In a still further aspect, the a Philadelphia chromosome positive leukemia is chronic myelogenous leukemia ("CML"). In a yet further aspect, the chronic myelogenous leukemia is chronic phase CML. In an even further

aspect, the chronic myelogenous leukemia is lymphoid blast phase CML. In a still further aspect, the chronic myelogenous leukemia is myeloid blast phase CML. In a yet further aspect, the chronic myelogenous leukemia is accelerated phase CML.

In a further aspect, the Philadelphia chromosome positive leukemia is acute lymphoblastic leukemia. In a still further aspect, the Philadelphia chromosome positive leukemia is acute myelogenous leukemia.

In a further aspect, the instructions further comprise identifying a patient in need of treatment of a gastrointestinal stromal tumor. In a still further aspect, instructions further comprise the patient has been diagnosed with a gastrointestinal stromal tumor refractory to treatment with a BCR-ABL kinase inhibitor. In a yet further aspect, the refractory gastrointestinal stromal tumor comprises a mutation. In an even further aspect, the refractory gastrointestinal stromal tumor comprises a KIT mutation.

The kits can also comprise compounds and/or products co-packaged, co-formulated, and/or co-delivered with other components. For example, a drug manufacturer, a drug reseller, a physician, a compounding shop, or a pharmacist can provide a kit comprising a disclosed compound and/or product and another component for delivery to a patient.

It is contemplated that the disclosed kits can be used in connection with the disclosed methods of making, the disclosed methods of using, and/or the disclosed compositions.

F. Experimental

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how the compounds, compositions, articles, devices and/or methods claimed herein are made and evaluated, and are intended to be purely exemplary and are not intended to limit the disclosure. Efforts have been made to ensure accuracy with respect to numbers (e.g., amounts, temperature, etc.), but some errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, temperature is in ° C. or is at ambient temperature, and pressure is at or near atmospheric.

1. General Methods

a. Production and Culture of Murine Leukemia Initiating Cells (LICs)

Replication-defective mouse stem cell virus (MSCV) retroviral vectors co-expressing either the wild-type (WT) allele of human p185^{BCR-ABL} or mutant BCR-ABL alleles p185^{T315I} or p185^{F317L}, and either green fluorescent protein (GFP) or luciferase, were packaged into replication-incompetent ecotropic virions. Whole bone marrow cell suspensions from Arf^{-/-} young adult mice were infected to produce Arf^{-/-} p185+ pre-B cells. After initial establishment on autologous stromal cell layers over 7 days, transformed pre-B cells were briefly expanded in the absence of a stromal layer for 2 days in liquid culture in basal culture media (BCM10) (RPMI1640 supplemented with 10% Hyclone fetal calf serum, 4 mM glutamine, 100 Units/mL penicillin, 100 µg/mL streptomycin, and 55 µM beta-mercaptoethanol), and cryopreserved. Prior to use in any assays, Arf^{-/-} p185^{WT} and Arf^{-/-} p185^{T315I} pre-B cells (BCR-ABL^{WT} leukemia initiating cells (LICs) and BCR-ABL^{T315I} LICs, respectively) were thawed and allowed to recover in BCM10 for 3 days.

b. In Vivo Adoptive Leukemia Transfer PH+ Model

Mice were housed in an American Association of Laboratory Animal Care (AALAC)-accredited facility and treated on Institutional Animal Care and Use Committee (IACUC)-

approved protocols in accordance with NIH guidelines. Adoptive cell transfers were performed by injecting LICs into tail veins of healthy, non-conditioned, immune-competent 10 to 12-week-old IL7^{-/-} or IL7^{-/-}C57Bl/6J mice (Jackson Labs, Bar Harbor, Me.). Animals were observed daily and sacrificed when moribund (dehydration, ruffled fur, poor mobility, respiratory distress). Survival curves were generated using GraphPad Prism Version 5.0 (La Jolla, Calif.). The Mantel-Cox test was applied to pairwise comparisons of survival data.

c. Development of LIC-Based Screening Assay

Before use in any in vitro assay, LICs had to pass the following quality control parameters: test thawing (benchmark: 95% viability at 24 h); PCR genotyping to confirm Arf^{-/-} status; mycoplasma testing (negative by Takara Bio Mycoplasma PCR assay, Clontech, Madison Wis.); sequence verification of BCR-ABL allele; and in vitro dasatinib potency confirmation.

The maximum dimethyl sulfoxide (DMSO) concentration tolerated by LICs in culture was determined to be 0.2% (by volume) and was maintained at ≤0.1% (by volume) in all subsequent work. LICs were plated in 384-well micro-titer plates at a cellular density of 5×10⁴ per mL (1250 LICs per well in 25 µL BCM10) and confirmed to give exponential growth during first 72 h. FIG. 1 shows the growth properties of Arf^{-/-} p185^{WT} (filled symbols) and Arf^{-/-} p185^{T315I} preB (empty symbols) populations during in vitro cell culture. Both cell types were plated at multiple cell dilutions (n=3 for each condition, time=0 h) in 6-well plates and serially followed daily for 5 days to evaluate absolute viable cell count, total viability, doubling times, and total population doublings, using the Beckman Coulter cell counter (trypan blue staining) and fluorescence-activated cell sorting (FACS) analysis in parallel. Both cell types had identical growth properties. Only the comparison for population doubling time in hours (+/-sd) for 3 relevant plating densities is presented. FACS cell-cycle analysis confirmed that a population doubling time less than 14 h was sufficient to maintain cells in exponential growth (>50% cells in S-phase).

To select assay reagents, three high throughput screening (HTS) relevant cellular assays were evaluated according to manufacturer's instructions. As represented in FIG. 2, BCR-ABL^{WT} LICs plated at 5×10⁴ per mL were challenged with 6 log-fold concentration range of dasatinib or DMSO in 384-well microplates. After a 72 h drug challenge, LIC growth was measured by the 3 cellular readouts: CellTiter-Glo® (CTG) assay (ATP content), MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay (viability), and high-throughput flow cytometry (total viability and viable cell counts by DAPI exclusion). Measured assay readouts at various drug concentrations (x-axis) were normalized to DMSO-treated LICs and graphed (+/-sd) on y-axis. Total viable LIC counts were determined by FACS, reflecting dasatinib-induced phenotypic changes across a 6 log-fold drug-concentration, were closely paralleled by the CTG cellular assay output but not by the commonly used MTS assay.

The luminescent CTG (CellTiter-Glo; Promega Madison, Wis.) assay, which monitors cellular ATP content, was inherently more sensitive than the colorimetric MTS assay, which monitors cellular reductive capacity. The CTG assay accurately detected low number of LICs producing results comparable to those obtained by flow cytometry, and provided ease of use in HTS (no prolonged incubation step required between reagent addition and assay readout). When carried out after 72 h, the CTG assay had a 10,000 fold

dynamic range, low signal variance (Z' =0.9 in semi-automated mode, and Z' =0.8 in fully automated mode), displayed minimal drift or edge effects, and had robust inter-plate and inter-day reproducibility.

d. Forward Cytokine Phenotypic Screen

Lyophilized murine and human recombinant cytokines (R&D Systems, Minneapolis, Minn.) were diluted with 1 mg/mL bovine serum albumin (BSA) in sterile phosphate buffered saline (PBS) to a final concentration 20 µg/mL and stored at 4° C. Anti-leukemia drugs, BCR-ABL-TKIs, and non-BCR-ABL-specific-TKIs (LC labs, Sigma), were solubilized in DMSO to obtain 10 mM stocks concentrations. Subsequent serial titrations were prepared using DMSO in 0.5 mL vials or 384-well drug master plates, and stored at -20° C.

To study the impact of murine cytokines on dasatinib action, LIC stocks containing different concentrations of candidate cytokines were prepared in multi-channel sterile reservoirs and plated into 384-well plates. Drug delivery to cell suspensions was accomplished with a V & P Scientific (San Diego, Calif.) pin. For murine-human comparisons, human SUP-B15 Ph+ ALL cells (DSMZ cell culture collec-

tion, Germany) in McCoy's media containing 20% fetal calf serum and penicillin/streptomycin (Invitrogen, Carlsbad, Calif.), were plated at 12,500 cells in 25 µL per well in black clear-bottom 384-well microtiter plates. Drugs were transferred by pin-transfer. After 72 h incubation at 37° C., 20% (by volume) MTS assay reagent (CellTiter 96 Aqueous One Solution, Promega, Madison, Wis.) was added, microtiter plates were incubated for 75 min at 37° C., and read colorimetrically at 490 nm.

e. High-Throughput (HT) Phenotypic Drug Screening

An IL7 concentration of 0.85 ng/mL was confirmed using cytokine titration assays to confer near-maximal and reproducible resistance against nilotinib and imatinib in BCR-ABL^{WT} LICs. A primary screening of 5600 compounds including FDA approved drugs was then carried out at a fixed dose (10 µM). Active compounds were retested to establish dose-response relationships using a multi-step, 2-fold dilution scheme (Table 1). Multiple control assay plates were set-up during all screening runs to allow for inter-plate and inter-day comparisons at 0, 24, 48, and 72 hrs. Table 1 below shows steps used in the optimized high-throughput screening assay.

TABLE 1

Step	Parameter	Value	Description
1	Plate cells	25 µL	Plate LICs 5×10^4 per mL (25 µL/well) in BCM10 + 0.85 ng/mL IL7 into 384-well opaque bottom white microplates using Wellmate (Matrix)
2	Primary drug screening controls in columns 1-2 and 13-14	25 nL	1A-1I: Nine dasatinib concentrations (100 nM, 30 nM, 10 nM, 3 nM, 1 nM, 0.3 nM, 0.1 nM, 0.03 nM and 0.01 nM)-control for IL7-and BCR-ABL mutation-imparted resistance against BCR-ABL-TKIs 2A-2I: Nine staurosporine concentrations (300 nM, 100 nM, 60 nM, 30 nM, 10 nM, 6 nM, 3 nM, 1 nM, 0.6 nM)-non-BCR-ABL-specific reference control in the presence of IL7
	Secondary drug screening controls in columns 21-24	25 nL	13A-13P, 1J, 2J: DMSO 0.1% (Max Signal OR Negative Control); 14A-14P: staurosporine at 300 nM (Min Signal OR Positive Control); 1K-1P, 2K-2P: 40 µM dasatinib 21A-21P: DMSO 0.1% (Max Signal); 22A-22P, 23K-24P, 24K-24P: staurosporine at 300 nM (Min Signal) 23A-23J: Staurosporine-10 log-fold dilutions (3 µM to 0.3 pM)-non-BCR-ABL-specific reference control in the presence of IL7 24A-24J: Dasatinib: 10 log-fold dilutions (1 µM to 0.1 pM)-control for IL7-and BCR-ABL mutation-imparted BCR-ABL-KI drug-resistance
3	Add test compounds in columns 3-12 and 15-24 in primary; columns 1-20 in secondary screen	25 nL	Primary screening: Single final drug concentration of 10 µM Secondary screening: Triplicate ten half-log serial dilutions (5 µM to 2 nM final concentration) of primary screening hits to determine their half-maximal inhibitory concentrations (IC ₅₀) against LICs 384-well master drug-stock plates prepared at 1000x in DMSO. Drug delivered to assay plates by pin transfer (using V&P Scientific pin tool, 10 H pins), giving a final drug concentration of 1x and 0.1% DMSO in all control and test wells of assay plates
4	Incubation 1	72 h	Liconics incubator, 8% CO ₂ , 37° C. (std. LIC culture conditions)
5	Incubation 2	20 min	Room temp, low light (instructions as per Promega)
6	Add reagent	25 µL	CellTiter-Glo® (Promega) pre-equilibrated to RT before use
7	Incubation 3	25 min	Room temp, low light (per Promega)
8	Assay readout	ATP levels	Envision, Luminescent mode-ATP levels as a measure of LIC number and viable growth in 72 h-Signal measured in RLU

TABLE 1-continued

Step	Parameter	Value	Description
9	Data processing	Pipeline Pilot	% inhibition by test compound = $100 * (\text{Log}_{10}\text{Test Signal} - \text{Log}_{10}\text{Min Signal mean}) / (\text{Log}_{10}\text{Min Signal mean} - \text{Log}_{10}\text{Max Signal mean})$ $Z\text{-prime (Z')} = 1 - [(3 * \text{stdev of Log}_{10} \text{Max Signal} + 3 * \text{stdev of Log}_{10} \text{Min Signal}) / (\text{Log}_{10}\text{Max Signal mean} - \text{Log}_{10}\text{Min Signal mean})]$ Z' is a dimensionless calculation to assess assay quality-for a good assay Z' \geq 0.5, and for a perfect assay Z' = 1

f. In Vivo Preclinical Therapeutic Studies

For in vivo use, dasatinib (LC Labs, Woburn, Mass.) in citric acid (pH 3.1), and DHA (Avachem, San Antonio, Tex.) in 0.5% carboxy-methylcellulose/0.5% Tween 80/0.5% benzyl alcohol, were administered by oral gavage. In toxicity studies, DHA was ranged up to 300 mg/kg as a single or split dose for 5 days/week over a six week time period. Repeated single doses of 300 mg/kg (5 days/week) were determined to induce no significant weight loss, lethargy, seizures or deaths. During therapeutic studies, animal weights were monitored daily to ensure no significant body weight reductions.

g. Bioluminescent Imaging and Evaluation of Cures

Bioluminescent imaging and analysis were performed using a Xenogen IVIS-200 system and Living Image software 3.01 (Caliper Life Sciences, Hopkinton, Mass.). Total bioluminescent flux measurements (photons/second) were quantified over the whole animal body. Recipient mice that remained clinically healthy 12 months after terminating therapy and had no detectable bioluminescent signal in vivo were designated "long-term survivors."

h. Assessment of LIC Viability

Viability of LICs was estimated after counterstaining approximately 5×10^5 LICs (in 0.5 mL volume) with 35 μ L of a propidium iodide (PI) solution (0.25 mg/mL in PBS). The percentage of viable cells was calculated by electronic gating on PI-negative cells on PI versus forward scatter dot plots, with forward scatter signals consistent with LICs, and comparison of this number with total cell number. Data were collected and analyzed on a BD Biosciences LSR II flow cytometer (San Jose, Calif.), using BD Biosciences FACS DiVa software.

i. Assessment of Cell Cycle Percentages

For determination of percentages in cell cycle phases, 5×10^5 LICs were centrifuged, washed once with PBS, recentrifuged, and cell pellets were resuspended in 0.5 mL PI staining solution (0.05 mg/mL PI, 0.1% sodium citrate, 0.1% Triton X100). This process lysed the cells and stained the nuclear DNA with PI. Samples were then treated with DNase-free RNase (0.2 mg/mL in 10 M Tris-HCl/15 mM NaCl, pH 7.5) for 30 min at room temperature, filtered, and analyzed for red fluorescence from a PI-labeled DNA on BD Biosciences FACS Calibur flow cytometer (San Jose, Calif.) by using BD Biosciences CellQuest Pro software. The percentages of cells within each cell cycle phase were computed using the computer program ModFit (Verity Software House, Topsham, Me.).

j. Drug/Cytokine Washout and Cytokine Recovery Studies

For washout studies, BCR-ABL^{WT} LICs were diluted to a density of 1×10^5 LICs/mL in BCM-10 containing no or 5 mg/mL IL7, and treatment with either dasatinib or 0.1% DMSO by volume (non-drug treated controls) was initiated at time 0 h in triplicate 100 mm petri dishes. Daily moni-

toring for expected drug-induced changes was performed by naked-eye microscopy from 0 to 72 h. At the 72 h time point, after harvesting under identical conditions, total LIC density and viability percentage for all samples were determined using Beckman Coulter Vi-cell (trypan blue) in triplicates. Each sample was spun down in 50 mL BD Falcon™ tubes; the supernatant was discarded and LIC pellet resuspended in freshly prepared BCM10 (not containing any cytokine or drug). This washing step was repeated four times to ensure complete removal of the drug and/or cytokine. After the last wash, each pellet was resuspended to 1×10^6 total LICs per mL master stocks. Aliquots from master stocks were taken for (i) flow assessment of viability and cell cycle percentages (as described above) and (ii) manual CTG assay using 25 μ L sample per well in 384-well microplates (in triplicates), as an independent determination for LIC growth. For assessment of extracellular cytokine on recovery of LICs that were previously challenged with dasatinib (0 to 72 h), washed master stocks were diluted to 5×10^5 total LICs per mL in BCM10 with or without 5 ng/mL IL7, plated in 6 well plates (approximately 10 cm²), and incubated at 37° C. from 72 to 144 h for recovery, during which time daily naked-eye microscopic examinations were performed. At 144 h, for each sample total LIC density and viability percentage assessment by Beckman, viability and cell cycle percentages by flow assessment and independent CTG evaluations were performed as described for the 72 h time point. Total viable LICs in a sample were calculated as a product of absolute LIC count determined by Beckman and absolute sample viability determined by FACS analysis.

k. Dasatinib Re-Challenge Studies

Further studies were performed to evaluate the possibility of a genetically drug-resistant subpopulation that could undergo selection with dasatinib/IL7 co-treatment during 0-72 h of dasatinib/cytokine washout studies above. To this aim, BCR-ABL^{WT} LICs were treated with 100 nM dasatinib or 0.1% DMSO in the absence or presence of 5 ng/mL IL7 in 100 mm dishes from 0-72 h, as described above. In addition, a dasatinib challenge (first-time challenge) across 6 log-fold concentration in the presence or absence of 5 ng/mL IL7 was also performed using CTG assay during this time period (0-72 h). At 72 h, dasatinib/IL7 co-treated LICs from 100 mm dishes were washed (as described above) and immediately challenged (second challenge) from 72 to 144 h with six log-fold concentration range of dasatinib in 384-well microplates either in the presence or absence of 5 ng/mL IL7 using CTG assay.

l. Description of Chemical Screening Library

The screening library consisted of 5600 (approximately 3200 unique) approved drugs and chemicals with known biological activity (bioactives). The library was assembled from 3 commercial suppliers: Microsource, Prestwick, and Sigma. The Microsource compounds included the following: (a) the Spectrum collection, which contains 2000 bio-

logically active and structurally diverse compounds, including known drugs, experimental bioactives, and pure natural products; (b) the U.S. Drug Collection, which contains 1040 drugs that have reached clinical trials in the US and have been assigned USAN or US Pharmacopeia status; and (c) the Killer collection, which contains a reference set of 160 synthetic and natural toxic substances (<http://www.msdiscovery.com/index.html>). The Prestwick compounds include 1120 small molecules selected for high chemical and pharmacologic diversity. Ninety percent of the collection is composed of known marketed drugs, and the remainder includes bioactive alkaloids or related substances. Sigma LOPAC1280 (Library of Pharmacologically Active Compounds) collection reflects the most commonly screened targets in the drug discovery community, including marketed drugs, failed development candidates, and "gold standards" that have well-characterized activities (<http://www.sigmaaldrich.com/chemistry/drug-discovery/validation-libraries.html>).

m. Data Processing, Quality Control and Hit Scoring Criteria

All data processing and visualization was performed using custom programs written in the Pipeline Pilot platform (Accelrys, v.7.5) and the R program 6.6. The R drc package was used to fit sigmoidal curves. Receiver operating characteristic (ROC) statistics were computed using the ROCR package.

The quality of the primary drug-screening studies, performed in parallel against BCR-ABL^{WT} and BCR-ABL^{T315I} LICs, was evaluated by multiple methods including, but not limited to, identification of known antileukemic agents, identification of multiple compound replicates intentionally included in the 5600 collection, and Z' and other screening quality metrics. An empirically determined, statistically significant but liberal cut-off of >10% activity was chosen to include agents of relatively lower activity considering the

high-risk nature of Ph+ ALL and the drug-rich nature of the library as well as to allow for a more complete structure-activity relationship and therapeutic class analysis after subsequent potency determination through secondary screening.

The discriminatory power of the phenotypic assay was assessed using receiver operating characteristic (ROC) statistics. A total of 165 compounds were selected to sample the primary assay according to the distribution of observed activities.

n. Cluster Analysis of Hits Using Therapeutic Classes

The therapeutic cluster graph was generated by first assigning each compound an Anatomical Therapeutic Chemical Classification System (ATC). This classification system groups drugs into a five level hierarchy according to therapeutic indication and chemical properties. The first level indicates anatomical main group and consists of one letter; the second level indicates therapeutic main group and consists of two digits; the third level indicates therapeutic or pharmacological subgroup and consists of one letter; the fourth level indicates chemical, therapeutic or pharmacological subgroup and consists of one letter; and the fifth level indicates the chemical substance and consists of two digits. The resulting seven characters constitute an ATC code, and a compound can be assigned multiple ATC codes. ATC codes can be depicted as a network graph by defining a node to represent each level in the ATC code and then connecting nodes according to parent-child relationships (e.g., first-level node A is the parent of second level nodes A01, A02, etc.). Compounds without an ATC code were assigned based on similarity to known agents, or were assigned to custom codes located under the parent V99 (labeled as "Not defined in ATC" in FIG. 3). The resulting network, as shown in FIG. 3, was visualized in Cytoscape® (v 2.8.1) using the yFiles circular layout algorithm.

Descriptions and legends for data presented in the following sections and figures are shown in Table 2 below.

TABLE 2

Figure Data	Description	Legend
Host Factors	The effect of 15 leukemia-microenvironment relevant cytokines on dasatinib potency (EC ₅₀) against Arf-/-BCR-ABLWT LICs	Host Factor: cytokine name Conc: cytokine concentration Hill: hill slope EC ₅₀ : dasatinib EC ₅₀ (nM) EC ₅₀ CI: = EC ₅₀ 95% confidence interval r ² : r-squared of the non-linear regression
Structure	Structural information for 706 compounds	Reg Number: St. Jude registration root number Mol smiles: molecular SMILES Synonym: alternate names for compound
Screen Summary (1)	List of 15 clinically-used conventional anti-leukemic agents validated during dose-response screening experiments	Agent: Name of clinical anti-leukemic agent WT EC50: mouse WT BCR-ABL B-cell EC ₅₀ (mM) WT EC50 CI: WT EC ₅₀ 95% confidence interval WT Act Class: WT activity classification WT Curve Score: grade for quality of WT dose-response curve T315I EC50: mouse T315I BCR-ABL B-cell EC ₅₀ (mM) T315I EC50 CI: T315I EC ₅₀ 95% confidence interval T315I Act Class: T315I activity classification T315I Curve Score: grade for quality of the T315I dose-response curve
Screen Summary (2)	Complete dose-response screening data for 706 compounds	WT EC50: mouse WT BCR-ABL B-cell EC ₅₀ (mM) WT EC50 CI: WT EC ₅₀ 95% confidence interval WT Act Class: WT activity classification WT Curve Score: grade for quality of WT dose-response curve T315I EC50: mouse T315I BCR-ABL B-cell EC ₅₀ (mM)

TABLE 2-continued

Figure Data	Description	Legend
		T315I EC ₅₀ CI: T315I EC ₅₀ 95% confidence interval
		T315I Act Class: T315I activity classification
		T315I Curve Score: grade for quality of the T315I dose-response curve
ATC Classification	Anatomical Therapeutic Chemical (ATC)	ATC L1: ATC 1st level (anatomical main group)
		ATC L2: ATC 2nd level (therapeutic main group)
		ATC L3: ATC 3rd level (therapeutic/pharmacological subgroup)
	Classification for 706 compounds	ATC L4: ATC 4th level (chemical/therapeutic/pharmacological subgroup)

2. Identification of Which Leukemia-Microenvironment Cytokines Induce Drug-Resistance Against BCR-ABL-TKIs

BCR-ABL^{WT} LICs are transformed primary Arf^{-/-} pre-B cells that retain phenotypic and signaling properties essential for suspended leukemic blasts to interact with the surrounding host-environment not typically present in established leukemic cell lines that have been extensively subjected to long term culture. As shown in FIG. 23, fifteen leukemia-microenvironment cytokines were evaluated for their ability to protect murine BCR-ABL^{WT} LICs from dasatinib, the most potent clinical BCR-ABL inhibitor. CTG assay measured LIC populations after 72-h dasatinib exposures in presence of increasing concentrations of indicated cytokines. FIG. 4 shows a radar plot representing the effect of the fifteen hematopoietic cytokines on dasatinib potency against Arf^{-/-} BCR-ABL^{WT} LICs. Each spoke in FIG. 4 represents an individual cytokine and each line graph represents dasatinib proliferation inhibition EC₅₀(nM) at the indicated titration of the parent cytokine. IL7 was observed to provide the strongest protection against dasatinib. In addition, IL3, thymic stromal lymphopoietin (TSLP, IL7-like cytokine), and IL4 appeared to confer some resistance, but with greatly reduced potency. In contrast, TGF-β appeared to enhance dasatinib activity.

As represented in FIG. 5, Arf^{-/-} BCR-ABL^{WT} (triangles) and Art BCR-ABL^{T315I} (circles) LICs were treated with drug or DMSO for 72 hours in the absence (dark gray) or presence (light gray) of 1 ng/mL murine IL7. LIC growth inhibition was measured by CTG assay, normalized to DMSO-treated LICs and fit using nonlinear regression (+/-sd). As represented in FIG. 6, Human Ph+ ALL SUPB15 cells were also treated with drug or DMSO for 72 hours in absence or presence of 25 ng/mL human IL7. IL7 was observed to attenuate the potency of all FDA-approved BCR-ABL-TKIs against murine BCR-ABL^{WT} LICs and the human Ph+ ALL cell line SUP-B15.

As represented in FIG. 7, Arf^{-/-} BCR-ABL^{WT} LICs were treated with drug or DMSO (no drug) for 72 hour in the absence (dark gray) or presence (light gray) of high (10 ng/mL) murine IL7 to evaluate IL7-mediated protection conferred against non-BCR-ABL-specific, multi-targeted drugs (FIG. 7, panels A-D) and conventional cytotoxic anti-leukemic clinical drugs (FIG. 7, panels E-G). The drug cefaclor (FIG. 7, panel H), an antibiotic often used in leukemia clinics, was used as a non anti-leukemic drug control. For each drug concentration, LIC growth was measured by CTG assay and average values were normalized to DMSO-treated LICs and graphed (+/-sd). IL7 was not observed to exhibit the same effect on potency of these tested drugs in BCR-ABL^{WT} LICs. Without wishing to be bound by a particular theory, bosutinib, which has shown activity against BCR-ABL, is believed to counter any IL7-

mediated protection through its ability to inhibit STAT5, which is thought to be necessary to sustain BCR-ABL transformed cells. These results indicate that IL7 appears to play a role in driving a specific cellular response that can provide resistance to BCR-ABL-TKIs.

The specificity was further confirmed using three additional in vitro studies. As represented in FIG. 8, 1 or 10 viable BCR-ABL^{WT} LICs per well, sorted by single-cell flow cytometry into 3 clear-bottom 384-well plates for each condition, were treated (t=0) with DMSO (0.1% by volume) or dasatinib in the absence (dark gray) or presence (light gray) of IL7 (5 ng/mL) to evaluate in vitro leukemia clonal outgrowth. After 8 days of incubation, naked-eye microscopic examination was performed. Wells showing significant positive growth (approximately ≥50 LICs per well) were scored positive and percentage of positive wells for each condition indicated on the x-axis was calculated. These results suggests the presence of IL7 during prolonged dasatinib treatment can rescue the clonal outgrowth capacity of Arf^{-/-} BCR-ABL^{WT} LICs.

To assess protection of BCR-ABL^{WT} LICs by IL7 during dasatinib exposures (0 to 72 h) and in the post-exposure recovery period (72 to 144 h, no dasatinib), drug/cytokine washout and cytokine recovery studies were performed by the methods described above. Cell growth trends by CTG readout corroborated the findings from trypan blue (Beckman) and DAPI staining (FACS). FIG. 9a shows the total sample viabilities (DAPI staining, FACS) at the end of exposure period (light gray=IL7; dark gray=No IL7) and recovery period (black=IL7; gray=No IL7), and depicts IL7 protection during dasatinib exposures. The few LICs surviving dasatinib exposures in the absence of IL7, later deteriorated and died during recovery period, irrespective of IL7, suggesting that BCR-ABL inhibitor exposures can commit BCR-ABL+ cells to death. IL7 was observed to improve recovery of dasatinib/IL7 co-treated LICs at 1000 nM, but not at 100 nM and 10 nM dasatinib concentration, most likely due to over-confluent growth in presence of IL7. FIG. 9b shows cell cycle changes (FACS) at the end of exposure period. Incremental dasatinib doses, presumably resulting in incremental BCR-ABL inhibition, appears to induce cell cycle arrest and apoptosis. Without wishing to be bound by a particular theory, IL7 appears to protect LICs from these changes. FIG. 9c shows the cell cycle analysis at the end of recovery period. FIG. 9d shows conditions showing positive LIC growth during recovery period, normalized for equal number of LICs plated at start of recovery. The ratio of fold LIC-change in the presence (FIG. 9d, face-down bracket) to that in the absence (FIG. 9d, face-up bracket) of IL7 was observed to increase in LICs with higher previous BCR-ABL inhibition from higher dasatinib concentrations during exposure period. Without wishing to be bound by a particular theory, these results suggest transient

pharmacologic BCR-ABL inhibition increases LIC responsiveness to cell-extrinsic IL7.

Additional re-challenge studies were performed to evaluate the possibility of a genetically drug-resistant subpopulation that could undergo selection with dasatinib/IL7 co-treatment during 0-72 hr of the dasatinib/cytokine washout studies described above. At 144 hrs, dasatinib was observed to exhibit a similar potency against LICs in the absence of IL7, irrespective of previous dasatinib exposure. Furthermore, potency of dasatinib appeared to be blunted, to a similar extent, during both the first and second drug challenges only when extracellular IL7 was present (FIG. 28, Panels A and B). These results suggest that removing IL7 can completely reverse its protective effects and restores dasatinib potency. Without wishing to be bound by a particular theory, these findings also suggest that IL7 exposure drives both the location of sequestration and the acquisition of resistance.

3. Physiological Levels of IL7 Confer an Aggressive, Dasatinib-Resistant Phenotype to PL+ ALL In Vivo

The effect of IL7 on leukemia progression and dasatinib responsiveness in vivo was studied in IL7^{+/+} and IL7^{-/-} B16 host-mice. FIG. 10 shows the Kaplan-Meier survival curves showing overall survival in IL7^{+/+} and IL7^{-/-} B16 host-mice receiving day 0 tail vein injection of 2×10² Arf^{-/-} BCR-ABL^{WT} LICs (FIG. 10, panel A, vehicle treated) or 2×10⁵ Arf^{-/-} BCR-ABL^{WT} LICs (FIG. 10, panel B, vehicle or drug treated). Median survival in 2×10² Arf^{-/-} BCR-ABL^{WT} LICs injections ("low burden model") was 20 days in IL7^{+/+} (n=4) versus 33 days in IL7^{-/-} mice (n=4) (P=0.0069). In 2×10⁵ Arf^{-/-} BCR-ABL^{WT} LICs injections ("high burden model"), survivals of vehicle-treated IL7^{+/+} and IL7^{-/-} mice were comparable. Dasatinib treatment caused a median survival of 33 days in IL7^{+/+} (n=12) versus 41 days in IL7^{-/-} (n=11) mice, P=0.0061. The data is an average of 2 independent experiments in which vehicle or dasatinib therapy was initiated on day 7 or 9. IL7^{+/+}, but not IL7^{-/-}, host mice injected with relatively small numbers (200) of BCR-ABL^{WT} LICs ("low burden model") showed decreased survival (FIG. 10, panel A), suggesting that murine Ph+ ALL responds to host-IL7 with accelerated progression. Injecting higher numbers (200,000) of LICs ("high burden model") (FIG. 10, panel B), appears to overcome this trend, suggesting the phenomena is most important during initial establishment and/or expansion of the leukemic cell population. Treatment of animals in the high burden model revealed a shortened survival benefit from dasatinib monotherapy of BCR-ABL^{WT}-driven leukemias. Without wishing to be bound by a particular theory, a single host-cytokine can induce meaningful BCR-ABL-TKI drug resistance in vivo. From a therapeutic perspective, these findings suggest that in vivo responses to dasatinib therapy in Ph+ ALL are modulated by cell-extrinsic IL7, independent of BCR-ABL KD mutations. The IL7-imparted primary protection, coupled with higher disease burdens in Ph+ ALL compared to CML in the clinical setting, can contribute to greater BCR-ABL-TKI refractoriness in Ph+ ALL relative to CML.

4. High-Throughput Screens Against Primary (IL7-Induced) and Acquired (BCR-ABL-Mutation) BCR-ABL-TKI Drug-Resistant Phenotypes

In one aspect, pharmacologic agents could be identified that would overcome IL7-induced BCR-ABL-TKI-resistance. A collection of 3200 mechanistically diverse bioactive agents, including approved oncology and anti-infective drugs, was screened against BCR-ABL^{WT} and BCR-ABL^{T315I} LICs in the presence of IL7 (0.85 ng/mL) at a fixed concentration (10 μM). The quality of the screen and

minimum significant activity (>10% growth inhibition) was confirmed by receiver operating characteristic (ROC) analysis and other statistical metrics. 627 compounds showed statistically significant activity (≥10% growth inhibition). These hits were augmented with available structural analogs and drugs of the same pharmacologic classes to yield 706 active compounds, which are shown in FIG. 24. FIG. 11 shows the frequency of ATC Level 1 and Level 2 codes among the 706 compounds submitted to dose-response analysis. FIG. 27 provides the ATC classifications of the 706 active compounds. As shown in FIG. 26, concentration-response relationships were established for these compounds against BCR-ABL^{WT} and drug-resistant BCR-ABL^{T315I} LICs in the presence of IL7, giving 229 validated hits with reasonable potency. All validated hits were equipotent in inhibiting the growth of BCR-ABL^{WT} and BCR-ABL^{T315I} LICs. As shown in FIG. 25, this set included 15 conventional anti-leukemic drugs, some of which were observed to enhance BCR-ABL-TKI-therapy in vivo, thus appearing to validate the detection of appropriate phenotypic responses. Furthermore, cluster analysis (FIG. 3), demonstrates that this set effectively sampled the space of all existing therapeutic classes. A single compound in FIG. 3 can be represented more than once because of multiple therapeutic indications, as is the case for corticosteroids (highly active clusters in A, C, D, H, R, and S). This appears to further demonstrate that the active compounds come from drugs used to treat many indications.

FIG. 12 shows the quality control used for the primary screen of 5600 agents against BCR-ABL^{WT} LICs performed in the presence of 0.85 ng/mL IL7. FIG. 12a shows the distribution of EC₅₀ of non-BCR-ABL-inhibiting reference compound staurosporine (calculated from wells 2A-2J in FIG. 12d). FIG. 12b shows the scatter plot of percent activity of the test compounds relative to controls. Good separation is seen between negative controls (DMSO-treated, max signal, column 13 in (FIG. 12d)) and positive controls (300 nM staurosporine, min signal, column 14 in (FIG. 12d)). FIG. 12b shows test compounds exhibited statistically significant activity relative to background noise (negative controls and background noise are depicted in grayscale; inactive test compounds are black). Densities for positive, negative, and test compounds are shown on the right. FIG. 12c shows the distribution of Z' values for each plate in the primary screen (Z' values throughout the run-average=0.82, lowest=0.71 and highest=0.9). FIG. 12d shows a heat map comparison of well activity averaged across all plates. Wells 1A-1J and 2A-2J show serial dilutions of dasatinib and staurosporine. In the presence of IL7, an average LIC growth inhibition of approximately 45% was achieved by 100 nM dasatinib (well 1A), the later approaching maximum concentration achieved in human plasma. FIG. 13 shows the quality control used for primary screen of 5600 agents against BCR-ABL^{T315I} LICs performed in the presence of 0.85 ng/mL IL7. FIG. 13a shows distribution of EC₅₀ of non-BCR-ABL-inhibiting reference compound staurosporine (calculated from wells 2A-2J in (FIG. 13d)). FIG. 13b shows a scatterplot of percent activity of the test compounds relative to controls. Good separation is seen between negative controls (DMSO-treated, max signal, column 13 in (FIG. 13d)) and positive controls (300 nM staurosporine, min signal, column 14 in (FIG. 13d)). FIG. 13b shows test compounds exhibited statistically significant activity relative to background noise (negative controls and background noise are depicted in grayscale; inactive test compounds are black). FIG. 13c shows distribution of Z' values for each plate in the primary screen (Z' values

throughout the run—average=0.85, lowest=0.77, and highest=0.92). FIG. 13d shows a heat map comparison of well activity averaged across all plates. Wells 1A-1J and 2A-2J show serial dilutions of dasatinib and staurosporine tested against BCR-ABL^{T315I} LICs. Although 100 nM dasatinib (Well 1A) was totally ineffective, well 2A with the highest staurosporine concentration (300 nM) showed average LIC growth inhibition of approximately 100%.

FIG. 14 shows distributions of independent dose response curves of dasatinib and staurosporine against BCR-ABL^{WT} and BCR-ABL^{T315I} LICs in the presence of 0.85 ng/mL IL7 calculated separately from all assay plates (wells 1A-1J and 2A-2J) of primary drug screening experiments. Both IL7-imparted dasatinib-resistant phenotype in BCR-ABL^{WT} LICs (EC₅₀ in nM: 95% CI=86-116, average>100) and BCR-ABL-mutation-imparted BCR-ABL-TKI-resistant phenotype in BCR-ABL^{T315I} LICs, similar to FIG. 5, were consistently captured across all plates. Low interplate variability in calculated EC₅₀ values was observed for the non-BCR-ABL-targeting reference compound staurosporine (95% CI for EC₅₀ in nM: WT=11-12, T315I=15-16) and the majority of the validated hits. This data suggests that the primary high-throughput drug screening experiments capture BCR-ABL-TKI drug-resistant phenotypes with high accuracy.

FIG. 15 shows Receiver Operating Characteristic (ROC) analysis of BCR-ABL^{WT} and BCR-ABL^{T315I} LIC-based assays. This data indicates that both (a) BCR-ABL^{WT} and (b) BCR-ABL^{T315I} LIC-based assays have similarly high discriminatory power (AUC 0.83 and 0.85, respectively). The ROC curve is plotted as a function of % activity, and is color coded according to the right Y-axis. The ROC curves in gray are calculated from 200 bootstrap simulations. The dashed line corresponds to a random assay (an ideal assay has an AUC of 1.0, whereas a random assay has an AUC of 0.5).

5. In Vitro and In Vivo Anti-PH+ All Activity of Dihydroartemisinin

Validated hits included many compounds with varying mechanisms of action. Initial compound evaluation focused on approved drugs having favorable human pharmacokinetic and toxicity profiles that also had been previously used in pediatric populations. The drug class selected for further study was the artemisinin class of antimalarials (ARTs), which includes artemisinin, artesunate, and dihydroartemisinin (DHA). As shown in FIG. 16, Arf^{-/-} BCR-ABL^{WT} (triangles) and Arf^{-/-} BCR-ABL^{T315I} (circles) LICs were treated with artemisinin, artesunate, dihydroartemisinin, or DMSO for 72 h in the absence (dark gray) or presence (light gray) of 1 ng/mL murine IL7. For each drug concentration, LIC growth (measured by the CTG assay) was normalized to DMSO-treated LICs and fit using nonlinear regression (+/-sd). The ARTs as a class were observed to be equipotent against BCR-ABL^{WT} and BCR-ABL^{T315I} LICs, but the anti-LIC potency of artemisinin was lower than that of artesunate or DHA. As represented in FIG. 17, human Ph+ ALL SUPB15 cells were also treated with artesunate, dihydroartemisinin, or DMSO (no drug) for 72 h in the absence (dark gray) or presence (light gray) of 25 ng/mL human IL7. Viability was measured by the MTS assay. Values were normalized to DMSO-treated cells. DHA and artesunate were also observed to actively kill the human Ph+ ALL cell line SUP-B15 and showed similar anti-Ph+ ALL potency in the presence of IL7.

DHA was selected for further analysis because of its potency, cellular selectivity, oral formulation, favorable pharmacokinetics, known bioavailability in the hematopoietic system, and tolerability in all human age groups. FIG.

18 shows the Kaplan-Meier survival curves showing the overall survival in response to therapy (survival benefit) in IL7^{+/+} B16 host mice receiving day 0 tail vein injections of 2x10³ Arf^{-/-} BCR-ABL^{WT} Luc+ or BCR-ABL^{T315I} LICs.

On day 3, the mice began once daily treatment for 5 days of each week. In mice bearing low burdens of BCR-ABL^{WT}-driven leukemia, treatment was once per day with either vehicle, 100 mg/kg DHA, 200 mg/kg DHA, 300 mg/kg DHA, or 300 mg/kg. In mice bearing low burdens of BCR-ABL^{T315I}-driven leukemia, treatment was either vehicle, 300 mg/kg DHA, or 10 mg/kg dasatinib. DHA monotherapy appears to confer a dose-dependent survival benefit to IL7^{+/+} host mice bearing low-burden BCR-ABL^{WT} leukemia (FIG. 18, panel A). BCR-ABL mutations, which are often selected with dasatinib treatment of mice bearing Arf^{-/-} BCR-ABL^{WT} LICs in this model, were absent in leukemic samples collected from terminally moribund DHA-treated mice. DHA monotherapy was also observed to give a similar response in mice with low-burden BCR-ABL^{T315I} leukemia, which is completely refractory to dasatinib (FIG. 18, panel B). Thus, unlike BCR-ABL-TKIs, DHA appears to act against Ph+ ALL via a BCR-ABL kinase-independent mechanism. Without wishing to be bound by a particular theory, the data suggests the artemisinin family of antimalarial drugs circumvents IL7-induced resistance to dasatinib in Ph+ ALL cells in vitro and Ph+ ALL in IL7^{+/+} host mice.

6. DHA Synergistically Enhances Response to Dasatinib

Because BCR-ABL^{WT} leukemias in IL7-deficient mice were found to be more sensitive to dasatinib and DHA displayed anti-Ph+ ALL activity in IL7^{+/+} host mice, the potential for synergy between the two drugs was evaluated. As represented in FIG. 19, cohorts of IL7^{+/+} immunocompetent mice bearing high burdens of Arf^{-/-} BCR-ABL^{WT}-driven leukemia were treated with dasatinib alone (10 mg/kg), DHA alone (200 or 300 mg/kg) or binary combinations. Continuous monotherapy treatment with dasatinib induced only weak initial responses, and all animals later relapsed with complete mortality within 6 weeks of initiating therapy. As represented in FIG. 20, DHA alone was observed to be completely ineffective (200 mg/kg) or poorly effective (300 mg/kg) in the high-burden leukemia model. However, the combination of DHA and dasatinib, represented in FIG. 21, provided a strong and rapid initial response, and led to significantly increased overall survival in comparison to the treatment with either of the two drugs alone. Of the 12 mice given 200 mg/kg DHA and 10 mg/kg dasatinib, 3 survived long-term. All mice given 300 mg/kg DHA and 10 mg/kg dasatinib (n=12) survived the treatment period. 4 weeks after completion of combination therapy, 1 mouse succumbed to an isolated CNS relapse, which may be related to the poor CNS availability of dasatinib. Remarkably, the 14 surviving mice taken off dasatinib-combined therapy (3/12 at 200 mg/kg and 11/12 at 300 mg/kg DHA) showed no leukemia during the one year follow-up period, the longest period monitored.

In comparison, FIG. 22 shows data obtained in the leukemia stem cell function (LSC) function assay comparing the in vivo leukemia initiating capacity of Arf^{-/-} p185^{WT} (left) and Arf^{-/-} p185^{T315I} preB (right) populations. The Kaplan-Meier curves shown represent the overall survival of nonconditioned immunocompetent C57Bl/6J recipient mice that received serial log-fold dilutions (n=4 per arm) of LIC-number (as indicated in the inset legend) on day 0 in Arf^{-/-} p185^{WT} (FIG. 22, panel A) and Arf^{-/-} p185^{T315I} preB (FIG. 22, panel B) populations. The data show that all animals that remain untreated succumb to full blown leu-

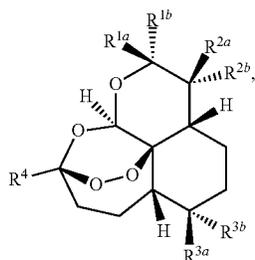
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kemia within 4 weeks of injecting a very low numbers of LICs, suggesting that the drug combination cured the disease. All dasatinib-DHA regimens were well tolerated in leukemic and non-leukemic mice. Without wishing to be bound by a particular theory, the DHA-dasatinib combination appears more efficacious than the clinically-used triple combination between dasatinib, dexamethasone and asparaginase previously assessed in the same model.

It will be apparent to those skilled in the art that various modifications and variations can be made in the present invention without departing from the scope or spirit of the invention. Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.

What is claimed:

1. A method for the treatment of a Philadelphia chromosome positive leukemia comprising the step of administering to a patient having a Philadelphia chromosome leukemia with a mutation in the kinase domain in the BCR-ABL gene a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:



wherein R^{1a} and R^{1b} together are (C=O) or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, —NH₂, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, —O(C1-C8 alkyl) C3-C6 cycloalkyl, —O(C1-C8 alkyl)-(C=O)OH, —O(C=O)(C1-C6 alkyl)-(C=O)OH, —O(C1-C8 alkyl)-(C=O)O(C1-C6 alkyl), —O(C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl), —O(C1-C8 alkyl)-aryl, and —O-aryl;

wherein each of aryl, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, and —O(C1-C8 alkyl)C3-C6 cycloalkyl, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, —NH₂, —(C=O)OH, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —NH(C1-C6 alkyl), —N(C1-C6 alkyl)(C1-C6 alkyl), —(C1-C6 alkyl)-NH(C1-C6 alkyl), and —(C1-C6 alkyl)-N(C1-C6 alkyl)(C1-C6 alkyl);

wherein R^{2a} and R^{2b} together are (C=CR^{5a}R^{5b}) or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —(C1-C8 alkyl)-(C=O)OH, and —O(C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl);

wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl;

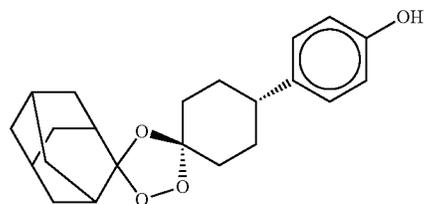
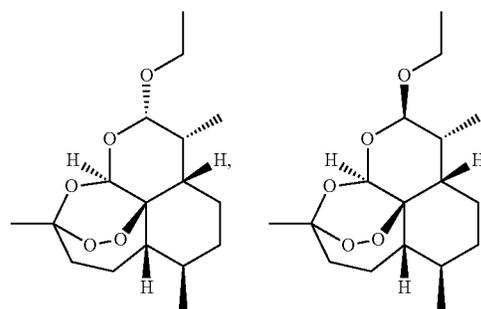
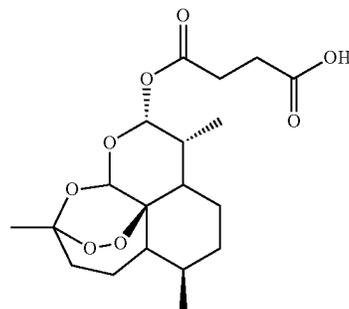
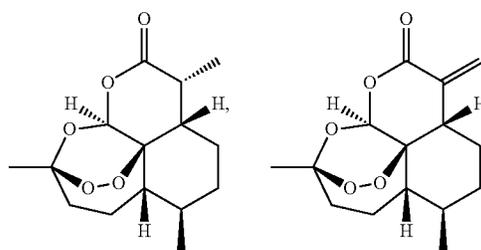
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wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and

wherein R⁴ is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, —(C1-C8 alkyl)-(C=O)OH, and —O(C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl), or a pharmaceutically acceptable salt thereof,

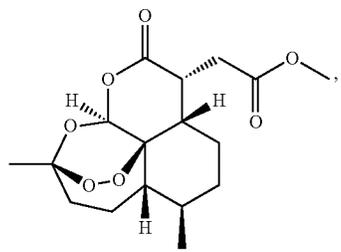
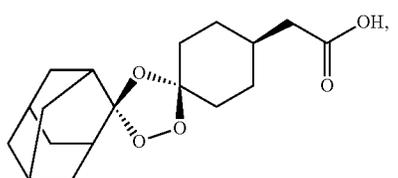
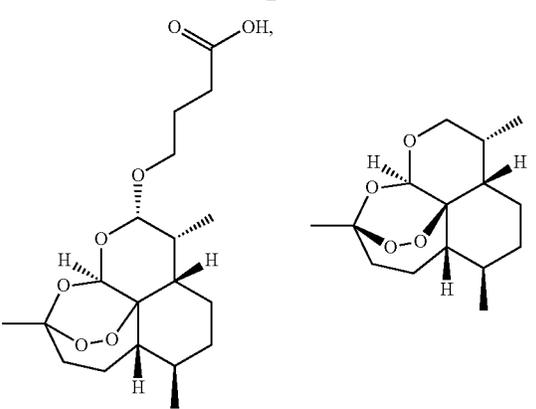
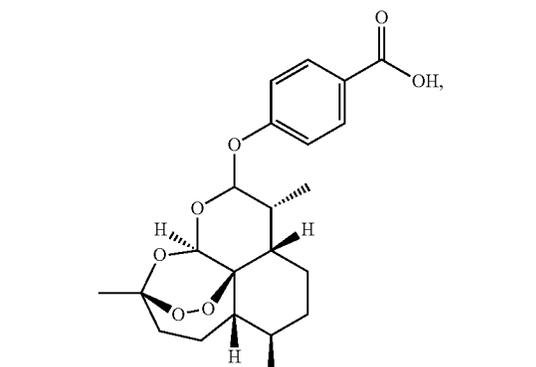
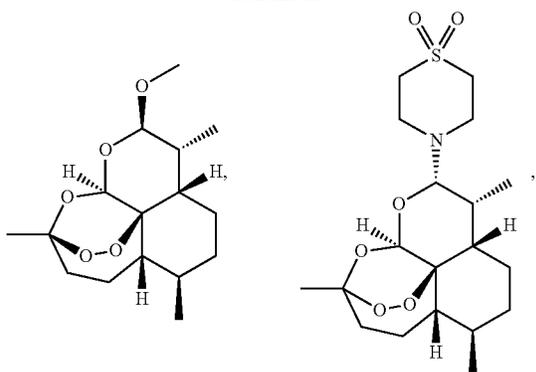
wherein the BCR-ABL tyrosine kinase inhibitor is administered in a first period; and the BCR-ABL tyrosine kinase inhibitor and the artemisinin analogue are co-administered in a second period.

2. The method of claim 1, wherein the artemisinin analogue is selected from:



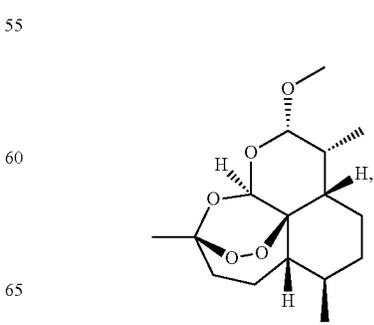
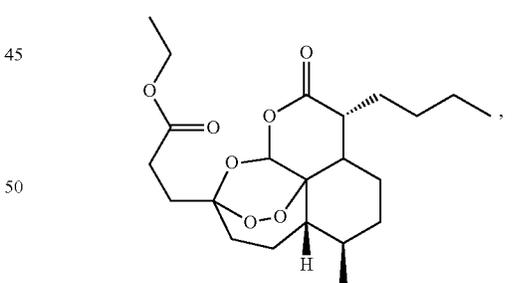
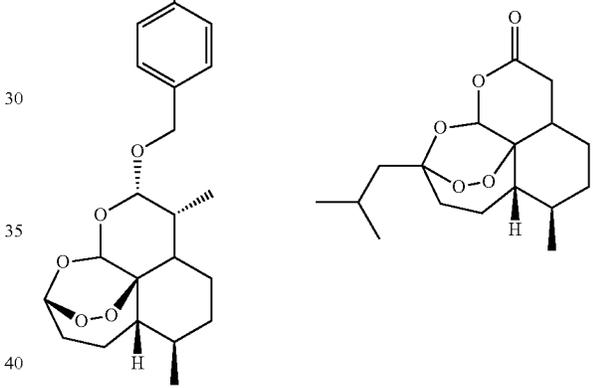
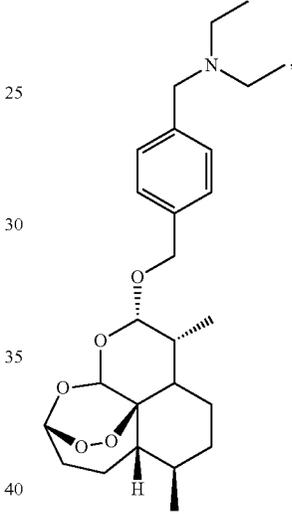
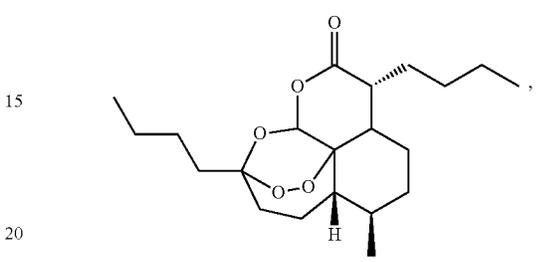
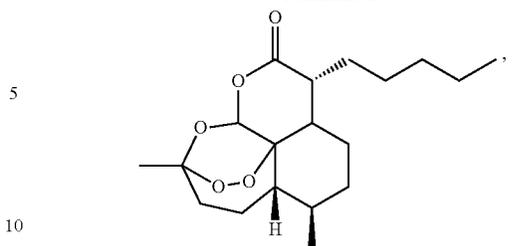
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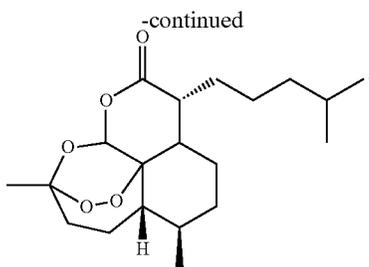
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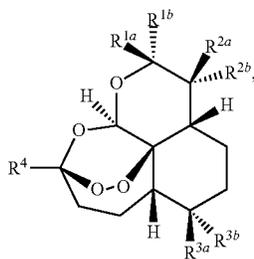
3. The method of claim 1, wherein the Philadelphia chromosome positive leukemia during the first treatment period becomes refractory to treatment by the BCR-ABL tyrosine kinase inhibitor.

4. The method of claim 1, wherein the Philadelphia chromosome positive leukemia mutation comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E.

5. The method of claim 1, wherein the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib.

6. The method of claim 1, wherein the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step.

7. A method for the treatment of a Philadelphia chromosome positive leukemia comprising the step of administering to a patient having a Philadelphia chromosome leukemia with a mutation in the kinase domain in the BCR-ABL gene a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:



wherein R^{1a} and R^{1b} together are $(C=O)$ or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-NH(C1-C6$ alkyl), $-N(C1-C6$ alkyl)(C1-C6 alkyl), C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, $-O(C1-C8$ alkyl)C3-C6 cycloalkyl, $-O(C1-C8$ alkyl)-(C=O)OH, $-O(C=O)(C1-C6$ alkyl)-(C=O)OH, $-O(C1-C8$ alkyl)-(C=O)O(C1-C6 alkyl), $-O(C=O)(C1-C6$ alkyl)-(C=O)O(C1-C6 alkyl), $-O(C1-C8$ alkyl)-aryl, and $-O$ -aryl;

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wherein each of aryl, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, and $-O(C1-C8$ alkyl)C3-C6 cycloalkyl, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, $-NH_2$, $-(C=O)OH$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-NH(C1-C6$ alkyl), $-N(C1-C6$ alkyl)(C1-C6 alkyl), $-(C1-C6$ alkyl)- $NH(C1-C6$ alkyl), and $-(C1-C6$ alkyl)- $N(C1-C6$ alkyl)(C1-C6 alkyl);

wherein R^{2a} and R^{2b} together are $(C=CR^{5a}R^{5b})$ or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8$ alkyl)-(C=O)OH, and $-O(C=O)(C1-C6$ alkyl)-(C=O)O(C1-C6 alkyl);

wherein each of R^{5a} and R^{5b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl;

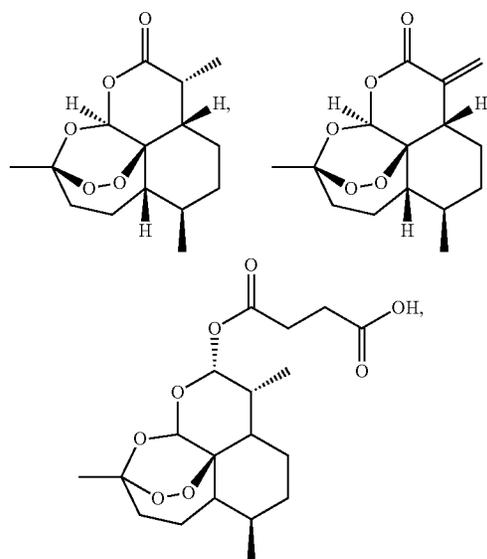
wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and

wherein R^4 is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8$ alkyl)-(C=O)OH, and $-O(C=O)(C1-C6$ alkyl)-(C=O)O(C1-C6 alkyl), or a pharmaceutically acceptable salt thereof,

wherein the Philadelphia chromosome positive leukemia mutation comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E.

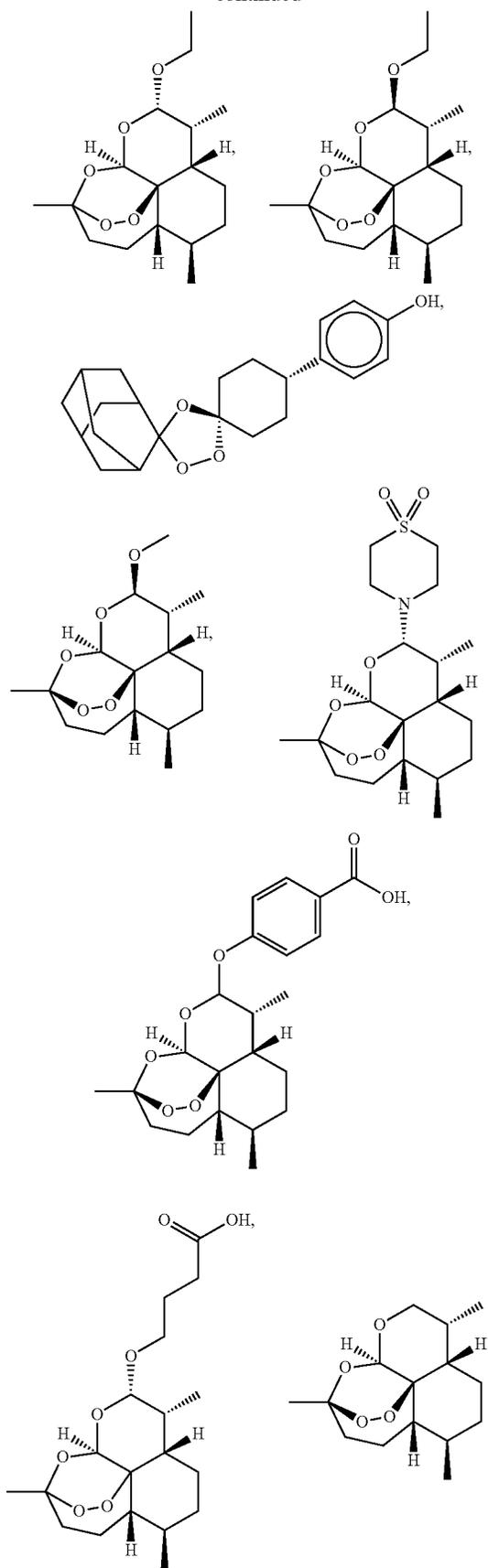
8. The method of claim 7, wherein the mutation is T315I.

9. The method of claim 7, wherein the artemisinin analogue is selected from:



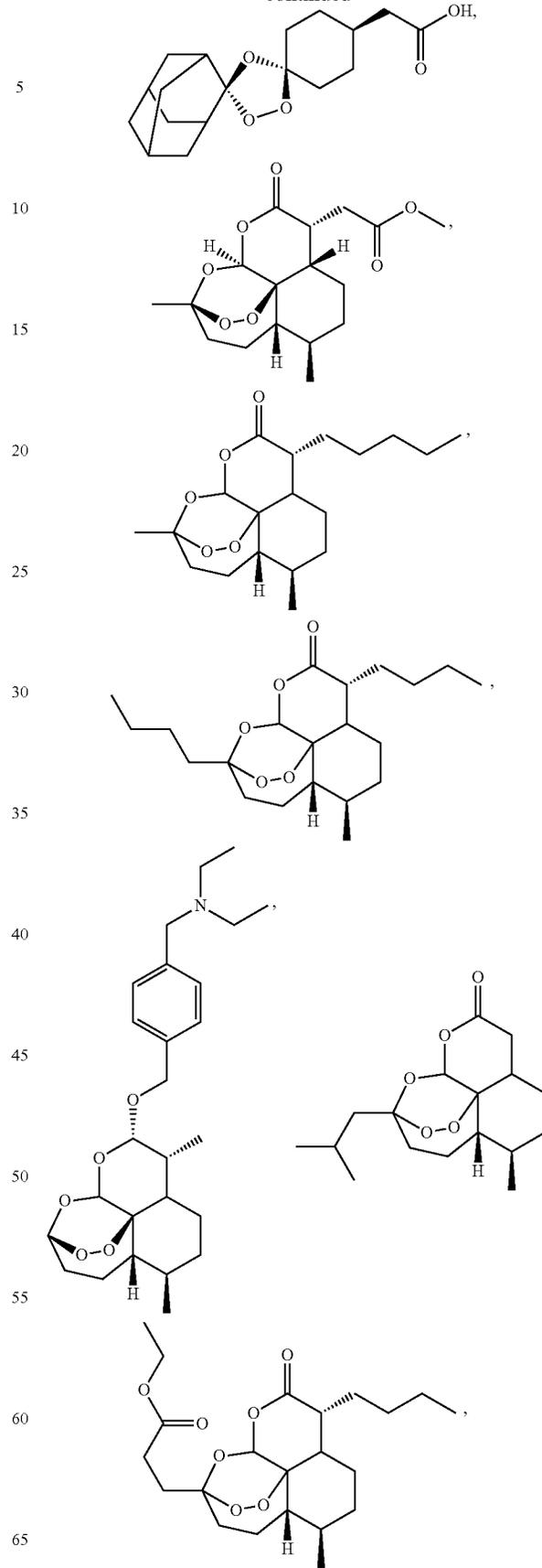
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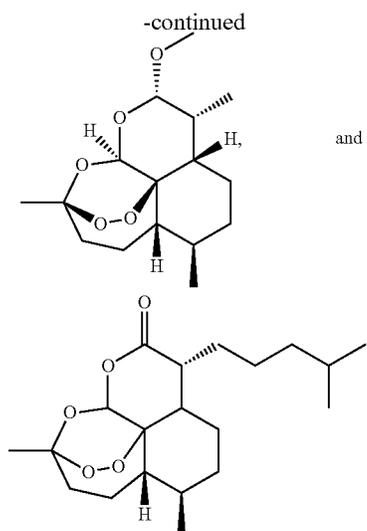


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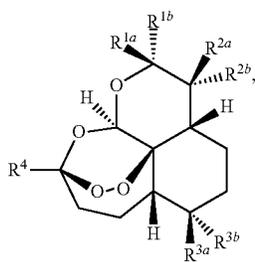
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10. The method of claim 7, wherein the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib.

11. The method of claim 7, wherein the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step.

12. A method for the treatment of a Philadelphia chromosome positive leukemia comprising the step of administering to a patient having a Philadelphia chromosome leukemia with a mutation in the kinase domain in the BCR-ABL gene a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:



wherein R^{1a} and R^{1b} together are $(C=O)$ or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-NH_2$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-NH$ (C1-C6 alkyl), $-N$ (C1-C6 alkyl)(C1-C6 alkyl), C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, $-O$ (C1-C8 alkyl) C3-C6 cycloalkyl, $-O$ (C1-C8 alkyl)-(C=O)OH, $-O$ (C=O)(C1-C6 alkyl)-(C=O)OH, $-O$ (C1-C8 alkyl)-(C=O)O(C1-C6 alkyl), $-O$ (C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl), $-O$ (C1-C8 alkyl)-aryl, and $-O$ -aryl;

wherein each of aryl, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, and $-O$ (C1-C8 alkyl)C3-C6 cycloalkyl, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, $-NH_2$, $-(C=O)OH$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8

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polyhaloalkyl, $-NH$ (C1-C6 alkyl), $-N$ (C1-C6 alkyl)(C1-C6 alkyl), $-(C1-C6 alkyl)-NH$ (C1-C6 alkyl), and $-(C1-C6 alkyl)-N$ (C1-C6 alkyl)(C1-C6 alkyl);

wherein R^{2a} and R^{2b} together are $(C=CR^{5a}R^{5b})$ or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8 alkyl)-(C=O)OH$, and $-O$ (C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl);

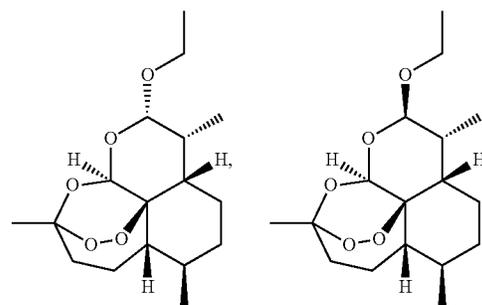
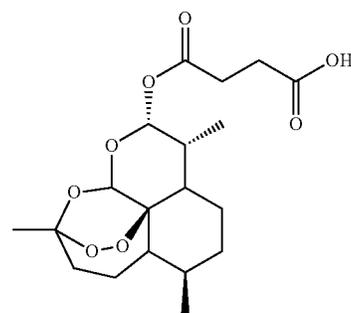
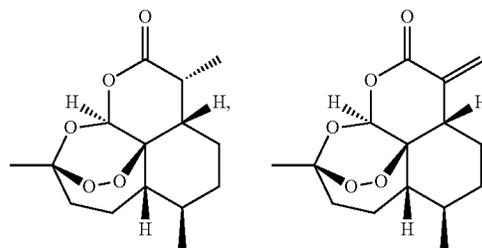
wherein each of R^{5a} and R^{5b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl;

wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and

wherein R^4 is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8 alkyl)-(C=O)OH$, and $-O$ (C=O)(C1-C6 alkyl)-(C=O)O(C1-C6 alkyl), or a pharmaceutically acceptable salt thereof,

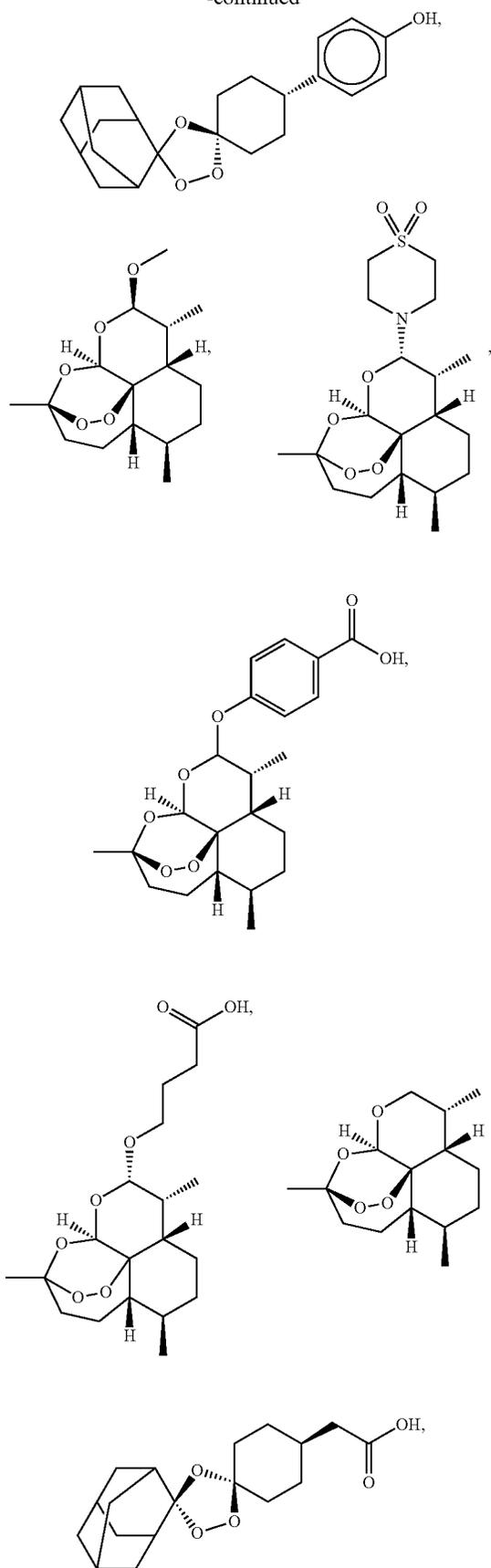
wherein the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib.

13. The method of claim 12, wherein the artemisinin analogue is selected from:



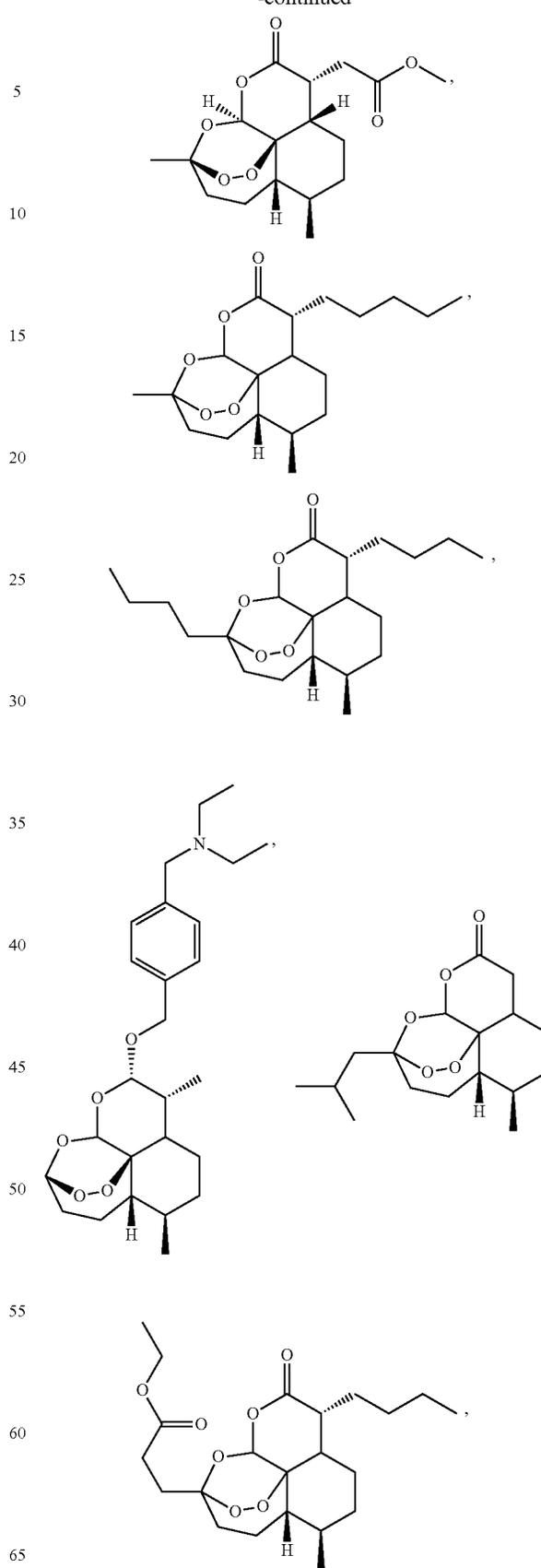
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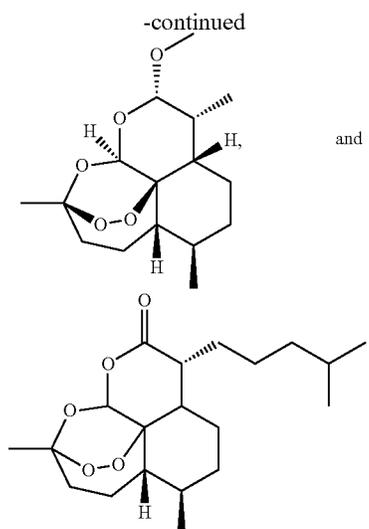


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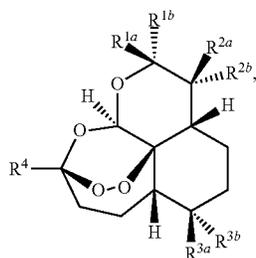
14. The method of claim 12, wherein the Philadelphia chromosome positive leukemia mutation comprises a mutation selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E.

15. The method of claim 12, wherein the BCR-ABL tyrosine kinase inhibitor is imatinib.

16. The method of claim 12, wherein the BCR-ABL tyrosine kinase inhibitor is dasatinib.

17. The method of claim 12, wherein the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step.

18. A method for the treatment of a Philadelphia chromosome positive leukemia comprising the step of administering to a patient having a Philadelphia chromosome leukemia with a mutation in the kinase domain in the BCR-ABL gene a therapeutically effective amount of a BCR-ABL kinase inhibitor and a therapeutically effective amount of at least one artemisinin analogue having a structure represented by a formula:



wherein R^{1a} and R^{1b} together are $(C=O)$ or wherein each of R^{1a} and R^{1b} are independently selected from hydrogen, hydroxyl, $-NH_2$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-NH$

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(C1-C6 alkyl), $-N(C1-C6\text{ alkyl})(C1-C6\text{ alkyl})$, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, $-O(C1-C8\text{ alkyl})$ C3-C6 cycloalkyl, $-O(C1-C8\text{ alkyl})-(C=O)OH$, $-O(C=O)(C1-C6\text{ alkyl})-(C=O)OH$, $-O(C1-C8\text{ alkyl})-(C=O)O(C1-C6\text{ alkyl})$, $-O(C=O)(C1-C6\text{ alkyl})-(C=O)O(C1-C6\text{ alkyl})$, $-O(C1-C8\text{ alkyl})-aryl$, and $-O-aryl$;

wherein each of aryl, C2-C5 heterocycloalkyl, C3-C6 cycloalkyl, and $-O(C1-C8\text{ alkyl})C3-C6\text{ cycloalkyl}$, when present, is substituted with 0-3 groups selected from halogen, hydroxyl, $-NH_2$, $-(C=O)OH$, C1-C8 alkyl, C1-C8 alkoxy, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-NH(C1-C6\text{ alkyl})$, $-N(C1-C6\text{ alkyl})(C1-C6\text{ alkyl})$, $-(C1-C6\text{ alkyl})-NH(C1-C6\text{ alkyl})$, and $-(C1-C6\text{ alkyl})-N(C1-C6\text{ alkyl})(C1-C6\text{ alkyl})$;

wherein R^{2a} and R^{2b} together are $(C=CR^{5a}R^{5b})$ or wherein each of R^{2a} and R^{2b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8\text{ alkyl})-(C=O)OH$, and $-O(C=O)(C1-C6\text{ alkyl})-(C=O)O(C1-C6\text{ alkyl})$;

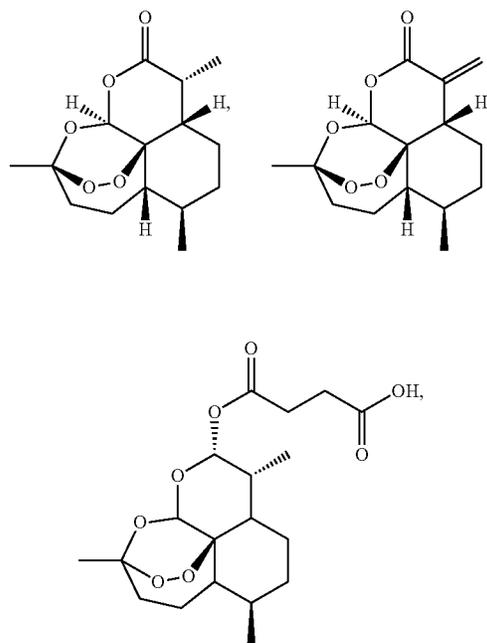
wherein each of R^{5a} and R^{5b} are independently selected from hydrogen, C1-C6 alkyl, C1-C6 monohaloalkyl, and C1-C6 polyhaloalkyl;

wherein each of R^{3a} and R^{3b} are independently selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, and C1-C8 polyhaloalkyl; and

wherein R^4 is selected from hydrogen, C1-C8 alkyl, C1-C8 monohaloalkyl, C1-C8 polyhaloalkyl, $-(C1-C8\text{ alkyl})-(C=O)OH$, and $-O(C=O)(C1-C6\text{ alkyl})-(C=O)O(C1-C6\text{ alkyl})$, or a pharmaceutically acceptable salt thereof,

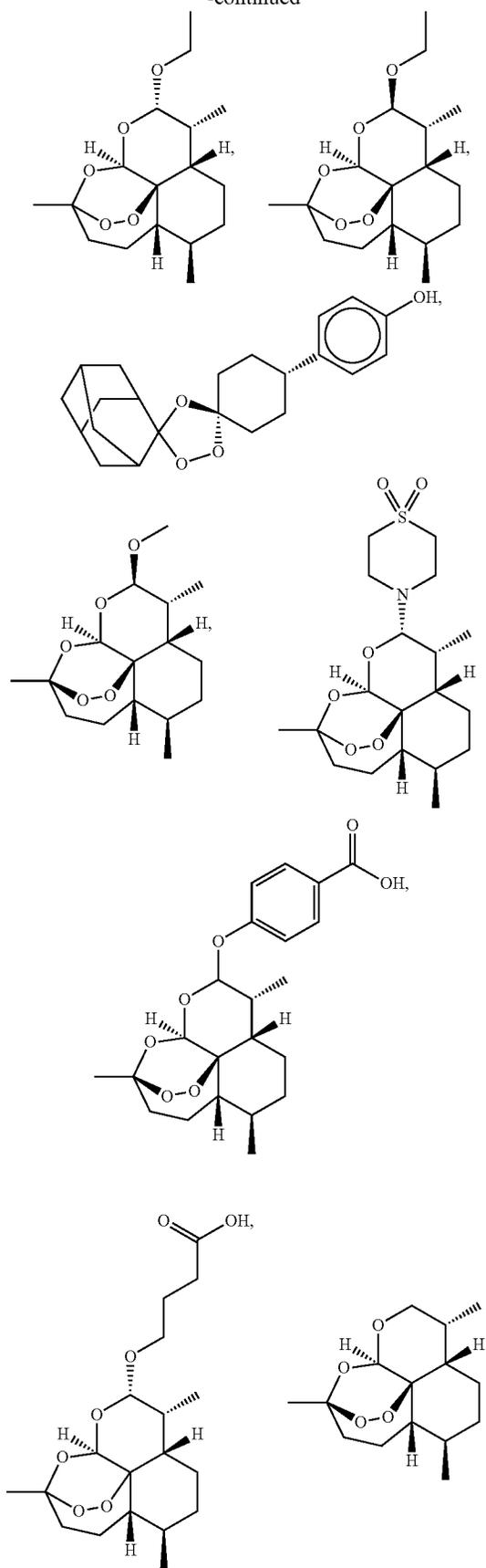
wherein the patient has been diagnosed with a need for treatment of a Philadelphia chromosome positive leukemia prior to the administering step.

19. The method of claim 18, wherein the artemisinin analogue is selected from:



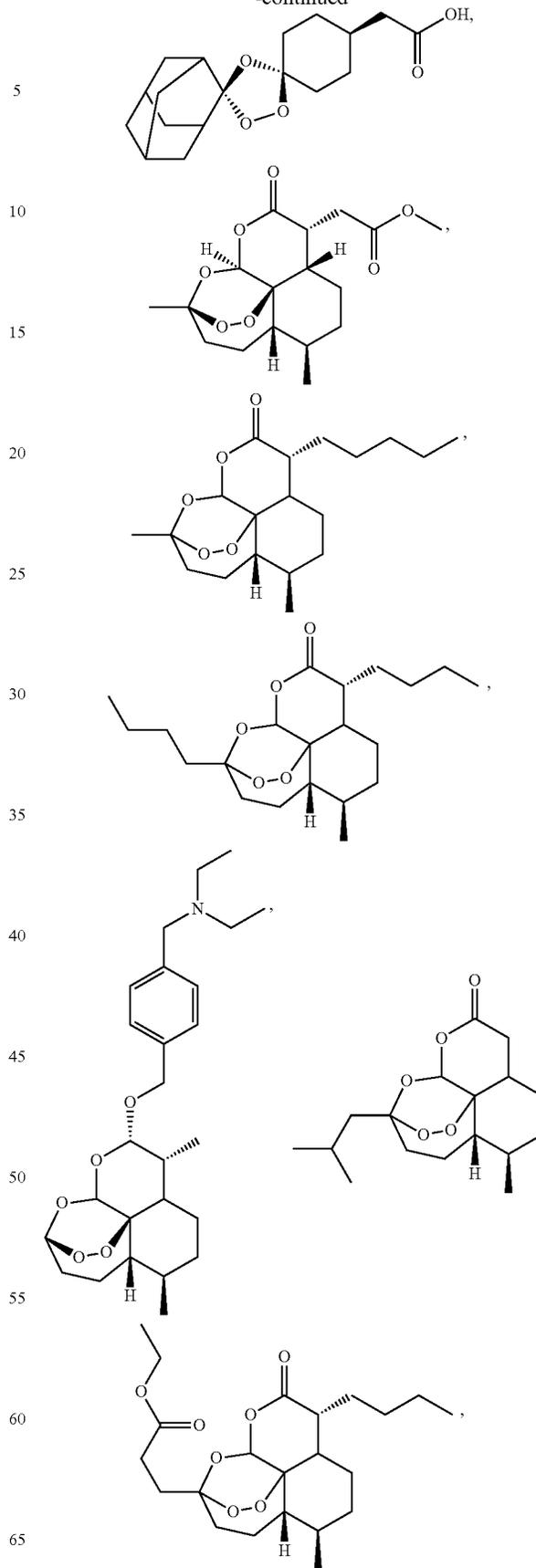
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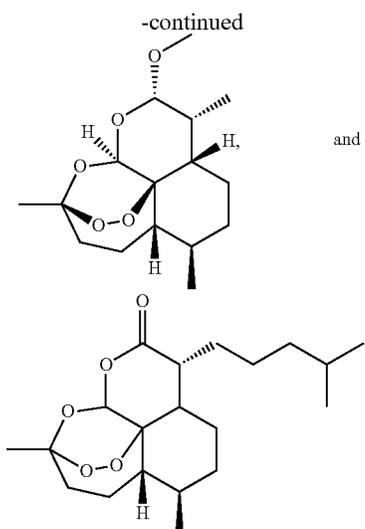


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20. The method of claim 18, wherein the Philadelphia chromosome positive leukemia mutation comprises a muta-

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tion selected from H201L, Y232S, M237V, I242T, M244V, L248V, del248-274, G250E, G250V, Q252H, Y253F, Y253H, E255K, E255V, E258D, L273M, D276G, E279K, E281X, V289I, E292V, L298V, V299L, F311I, F311L, T315I, F317L, Y342H, M351T, E355G, F359C, F359I, F359V, D363Y, L364I, A365V, A366G, V379I, L384M, L387M, M388L, Y393C, H396P, H396R, A397P, S417Y, I418S, I418V, S438C, P441L, E450A, E450G, E450K, E450V, E453K, E453V, E459G, E459K, M472I, P480L, F486S, D504D, G514S, T240T, K247R, F311V, and E499E.

21. The method of claim 18, wherein the BCR-ABL tyrosine kinase inhibitor is selected from imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib and rebastinib.

22. The method of claim 18, further comprising the step of identifying a patient in need of treatment of a Philadelphia chromosome positive leukemia.

23. The method of claim 18, wherein the patient has been diagnosed with a Philadelphia chromosome positive leukemia refractory prior to treatment with a BCR-ABL kinase inhibitor.

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