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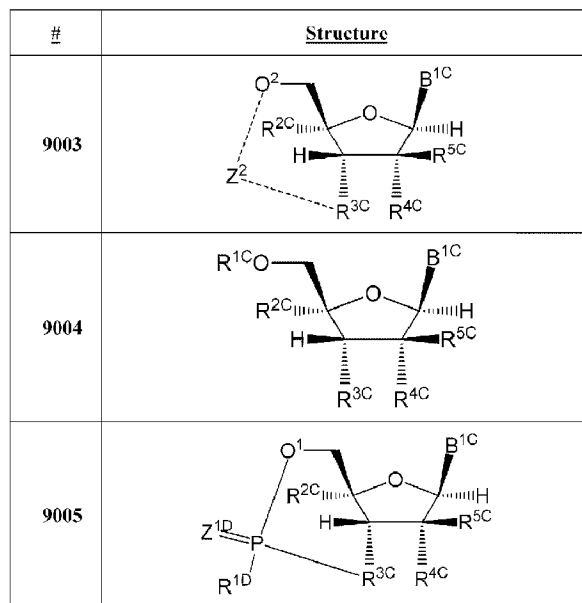
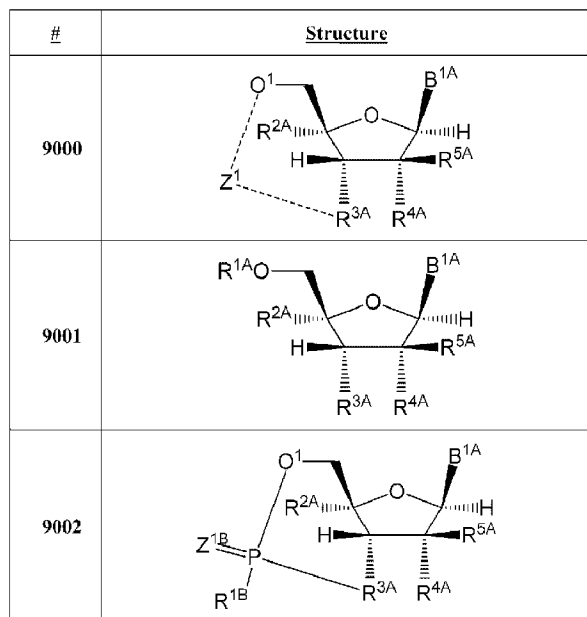
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(54) Titre : NUCLEOSIDES SUBSTITUES, NUCLEOTIDES SUBSTITUES ET ANALOGUES DE CEUX-CI

(54) Title: SUBSTITUTED NUCLEOSIDES, NUCLEOTIDES AND ANALOGS THEREOF

Compounds of Formula (I)



(57) Abrégé/Abstract:

Disclosed herein are nucleosides, nucleotides and nucleotide analogs, methods of synthesizing the same and methods of treating diseases and/or conditions such as a Picornavirus and/or Flaviviridae infection with one or more nucleosides, nucleotides and



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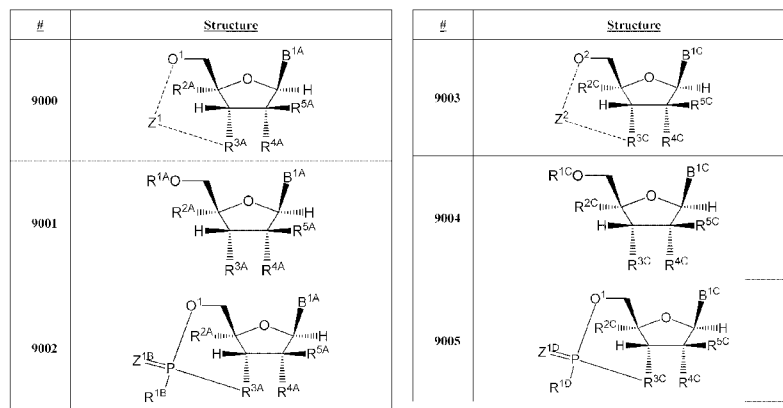
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- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
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(54) Title: SUBSTITUTED NUCLEOSIDES, NUCLEOTIDES AND ANALOGS THEREOF

Figure 9: Compounds of Formula (I)



(57) Abstract: Disclosed herein are nucleosides, nucleotides and nucleotide analogs, methods of synthesizing the same and methods of treating diseases and/or conditions such as a Picornavirus and/or Flaviviridae infection with one or more nucleosides, nucleotides and nucleotide analogs.

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JUMBO APPLICATIONS/PATENTS

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THIS IS VOLUME 1 OF 2
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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

[0001] SUBSTITUTED NUCLEOSIDES, NUCLEOTIDES AND ANALOGS THEREOF

BACKGROUND

Field

[0002] The present application relates to the fields of chemistry, biochemistry and medicine. More particularly, disclosed herein are nucleosides, nucleotides and nucleotide analogs, pharmaceutical compositions that include one or more nucleosides, nucleotides and/or nucleotide analogs and methods of synthesizing the same. Also disclosed herein are methods of treating diseases and/or conditions with a nucleoside, a nucleotide and/or a nucleotide analog, alone or in combination therapy with one or more other agents.

Description

[0003] Nucleoside analogs are a class of compounds that have been shown to exert antiviral and anticancer activity both in vitro and in vivo, and thus, have been the subject of widespread research for the treatment of viral infections. Nucleoside analogs are usually therapeutically inactive compounds that are converted by host or viral enzymes to their respective active anti-metabolites, which, in turn, may inhibit polymerases involved in viral or cell proliferation. The activation occurs by a variety of mechanisms, such as the addition of one or more phosphate groups and, or in combination with, other metabolic processes.

SUMMARY

[0004] Some embodiments disclosed herein relate to a compound of Formula (I), or a pharmaceutically acceptable salt thereof. Other embodiments disclosed herein relate to a compound of Formula (II), or a pharmaceutically acceptable salt thereof.

[0005] Some embodiments disclosed herein relate to a method of ameliorating and/or treating a picornavirus infection that can include administering to a subject identified as suffering from the picornavirus infection an effective amount of one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. Other embodiments described herein relate to using one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in the manufacture of a medicament for ameliorating and/or treating a picornavirus infection. Still other embodiments described herein relate to one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, that can be used for ameliorating and/or treating a picornavirus infection.

[0006] Some embodiments disclosed herein relate to a method of ameliorating and/or treating a picornavirus infection that can include contacting a cell infected with the picornavirus with an effective amount of one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof. Other embodiments described herein relate to using one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt thereof) in the manufacture of a medicament for ameliorating and/or treating a picornavirus infection that can include contacting a cell infected with the picornavirus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof, that can be used for ameliorating and/or treating a picornavirus infection by contacting a cell infected with the picornavirus with an effective amount of said compound(s).

[0007] Some embodiments disclosed herein relate to a method of inhibiting replication of a picornavirus that can include contacting a cell infected with the picornavirus

with an effective amount of one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof. Other embodiments described herein relate to using one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt thereof) in the manufacture of a medicament for inhibiting replication of a picornavirus that can include contacting a cell infected with the picornavirus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof, that can be used for inhibiting replication of a picornavirus by contacting a cell infected with the picornavirus with an effective amount of said compound(s). In some embodiments, the picornavirus can be selected from a rhinovirus, hepatitis A virus, a coxsackie virus and an enterovirus.

[0008] Some embodiments disclosed herein relate to a method of ameliorating and/or treating a *Flaviviridae* viral infection that can include administering to a subject identified as suffering from the *Flaviviridae* viral infection an effective amount of one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. Other embodiments described herein relate to using one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in the manufacture of a medicament for ameliorating and/or treating a *Flaviviridae* viral infection. Still other embodiments described herein relate to one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes one or more compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, that can be used for ameliorating and/or treating a *Flaviviridae* viral infection.

[0009] Some embodiments disclosed herein relate to a method of ameliorating and/or treating a *Flaviviridae* viral infection that can include contacting a cell infected with

the *Flaviviridae* virus with an effective amount of one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof. Other embodiments described herein relate to using one or more compounds described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for ameliorating and/or treating a *Flaviviridae* viral infection that can include contacting a cell infected with the *Flaviviridae* virus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof, that can be used for ameliorating and/or treating a *Flaviviridae* viral infection by contacting a cell infected with the *Flaviviridae* virus with an effective amount of said compound(s).

[0010] Some embodiments disclosed herein relate to a method of inhibiting replication of a *Flaviviridae* virus that can include contacting a cell infected with the *Flaviviridae* virus with an effective amount of one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof. Other embodiments described herein relate to using one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt thereof) in the manufacture of a medicament for inhibiting replication of a *Flaviviridae* virus that can include contacting a cell infected with the *Flaviviridae* virus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein, or a pharmaceutically acceptable salt thereof, that can be used for inhibiting replication of a *Flaviviridae* virus by contacting a cell infected with the *Flaviviridae* virus with an effective amount of said compound(s). In some embodiments, the *Flaviviridae* virus

can be selected from hepatitis C virus, West Nile virus, yellow fever virus, dengue virus and an encephalitis virus from within the *Flaviviridae* virus family.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0011] Figure 1 shows example HCV protease inhibitors.
- [0012] Figure 2 shows example nucleoside HCV polymerase inhibitors.
- [0013] Figure 3 shows example non-nucleoside HCV polymerase inhibitors.
- [0014] Figure 4 shows example NS5A inhibitors.
- [0015] Figure 5 shows example other antivirals.
- [0016] Figure 6 shows example compounds of Formula (CC) and alpha-thiotriphosphates thereof, wherein R^{CC1} , R^{CC2} , R^{CC3a} , R^{CC3b} , R^{CC4} , R^{CC5} , R^{CC6} , R^{CC7} , R^{CC8} , R^{CC9} and B^{CC1} are defined herein.
- [0017] Figure 7 shows example compounds of Formula (AA), wherein R^{1AA} , R^{2AA} , R^{3AA} , R^{4AA} , R^{5AA} and B^{1AA} are defined herein.
- [0018] Figure 8 shows example compounds of Formula (BB), wherein R^{BB1} , R^{BB2} , R^{BB3} , R^{BB4} , R^{BB5} , R^{BB6} , R^{BB7} , R^{BB8} , X^{BB} and B^{BB1} are defined herein.
- [0019] Figure 9 shows example compounds of Formula (I), wherein Z^1 , O^1 , R^{1A} , R^{2A} , R^{3A} , R^{4A} , R^{5A} , B^{1A} , Z^{1B} , R^{1B} , Z^2 , O^2 , R^{1C} , R^{2C} , R^{3C} , R^{4C} , R^{5C} , B^{1C} , Z^{1D} and R^{1D} are defined herein.

DETAILED DESCRIPTION

[0020] The viruses within the *Picornaviridae* family are non-enveloped, positive sense, single-stranded, spherical RNA viruses with an icosahedral capsid. Picornavirus genomes are approximately 7-8 kilobases long and have an IRES (Internal Ribosomal Entry Site). These viruses are polyadenylated at the 3' end, and has a VPg protein at the 5' end in place of a cap. Genera within the *Picornaviridae* family include Aphthovirus, Aquamavirus, Avihepatovirus, Cardiovirus, Cosavirus, Dicipivirus, Enterovirus, Erbovirus, Hepatovirus, Kobuvirus, Megrivirus, Parechovirus, Rhinovirus, Salivirus, Sapelovirus, Senecavirus, Teschovirus and Tremovirus.

[0021] Enteroviruses are transmitted through the fecal-oral route and/or via aerosols of respiratory droplets, and are highly communicable. The genus of Enterovirus

includes several species, including: enterovirus A, enterovirus B, enterovirus C, enterovirus D, enterovirus E, enterovirus F, enterovirus G, enterovirus H, enterovirus J, rhinovirus A, rhinovirus B and rhinovirus C. Within a species of the aforementioned enteroviruses are the following serotypes: polioviruses, rhinoviruses, coxsackieviruses, echoviruses and enterovirus.

[0022] Rhinoviruses are the cause of the common cold. Rhinoviruses are named because of their transmission through the respiratory route and replication in the nose. A person can be infected with numerous rhinoviruses over their lifetime because immunity develops for each serotype. Thus, each serotype can cause a new infection.

[0023] A hepatitis A infection is the result of an infection with a Hepatitis A virus. Hepatovirus is transmitted through the fecal-oral route. Transmission can occur via person-to-person by ingestion of contaminated food or water, or through direct contact with an infectious person.

[0024] Parechovirus include human parechovirus 1 (echovirus 22), human parechovirus 2 (echovirus 23), human parechovirus 3, human parechovirus 4, human parechovirus 5 and human parechovirus 6.

[0025] The viruses with the *Flaviviridae* family are enveloped, positive sense, single-stranded, spherical RNA viruses with an icosahedral shaped capsid. These viruses are polyadenylated at the 5' end but lack a 3' polyadenylate tail. Genera within the *Flaviviridae* family include: Flavivirus, Pestivirus and Hepacivirus. *Flaviviridae* viruses are predominantly arthropod-borne, and are often transmitted via mosquitos and ticks.

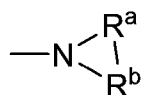
[0026] Flaviviruses include several encephalitis viruses (for example, Japanese Encephalitis virus (JEV), St. Louis encephalitis virus (SLEV) and tick-borne encephalitis virus (TBEV)), dengue virus 1-4 (DENV), West Nile virus (WNV) and yellow fever virus (YFV). Viruses within the Pestivirus genus include bovine viral diarrhea 1, bovine viral diarrhea 2, and classic swine fever virus.

Definitions

[0027] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art. In the

event that there are a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

[0028] As used herein, any "R" group(s) such as, without limitation, R¹, R², R³, R⁴, R^{5A}, R^{5B}, R^{6A}, R^{6B}, R^{6C}, R^{6D}, R^{6E}, R^{6F}, R^{6G}, R^{6H}, R^{7A}, R^{7B}, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R^{A1}, R^{A2}, R^{A3} and R^{A4} represent substituents that can be attached to the indicated atom. An R group may be substituted or unsubstituted. If two "R" groups are described as being "taken together" the R groups and the atoms they are attached to can form a cycloalkyl, cycloalkenyl, aryl, heteroaryl or heterocycle. For example, without limitation, if R^a and R^b of an NR^aR^b group are indicated to be "taken together," it means that they are covalently bonded to one another to form a ring:



In addition, if two "R" groups are described as being "taken together" with the atom(s) to which they are attached to form a ring as an alternative, the R groups are not limited to the variables or substituents defined previously.

[0029] Whenever a group is described as being "optionally substituted" that group may be unsubstituted or substituted with one or more of the indicated substituents. Likewise, when a group is described as being "unsubstituted or substituted" if substituted, the substituent(s) may be selected from one or more of the indicated substituents. If no substituents are indicated, it is meant that the indicated "optionally substituted" or "substituted" group may be substituted with one or more group(s) individually and independently selected from alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl), (heterocyclyl)alkyl, hydroxy, alkoxy, acyl, cyano, halogen, thiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, azido, silyl, sulfenyl, sulfinyl, sulfonyl, haloalkyl, haloalkoxy, trihalomethanesulfonyl, trihalomethanesulfonamido, an amino, a mono-substituted amino group and a di-substituted amino group.

[0030] As used herein, "C_a to C_b" in which "a" and "b" are integers refer to the number of carbon atoms in an alkyl, alkenyl or alkynyl group, or the number of carbon atoms in the ring of a cycloalkyl, cycloalkenyl, aryl, heteroaryl or heterocyclyl group. That is, the

alkyl, alkenyl, alkynyl, ring of the cycloalkyl, ring of the cycloalkenyl, ring of the aryl, ring of the heteroaryl or ring of the heterocyclyl can contain from “a” to “b”, inclusive, carbon atoms. Thus, for example, a “C₁ to C₄ alkyl” group refers to all alkyl groups having from 1 to 4 carbons, that is, CH₃-, CH₃CH₂-, CH₃CH₂CH₂-, (CH₃)₂CH-, CH₃CH₂CH₂CH₂-, CH₃CH₂CH(CH₃)- and (CH₃)₃C-. If no “a” and “b” are designated with regard to an alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, aryl, heteroaryl or heterocyclyl group, the broadest range described in these definitions is to be assumed.

[0031] As used herein, “alkyl” refers to a straight or branched hydrocarbon chain that comprises a fully saturated (no double or triple bonds) hydrocarbon group. The alkyl group may have 1 to 20 carbon atoms (whenever it appears herein, a numerical range such as “1 to 20” refers to each integer in the given range; *e.g.*, “1 to 20 carbon atoms” means that the alkyl group may consist of 1 carbon atom, 2 carbon atoms, 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the present definition also covers the occurrence of the term “alkyl” where no numerical range is designated). The alkyl group may also be a medium size alkyl having 1 to 10 carbon atoms. The alkyl group could also be a lower alkyl having 1 to 6 carbon atoms. The alkyl group of the compounds may be designated as “C₁-C₄ alkyl” or similar designations. By way of example only, “C₁-C₄ alkyl” indicates that there are one to four carbon atoms in the alkyl chain, *i.e.*, the alkyl chain is selected from methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl and t-butyl. Typical alkyl groups include, but are in no way limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tertiary butyl, pentyl and hexyl. The alkyl group may be substituted or unsubstituted.

[0032] As used herein, “alkenyl” refers to an alkyl group that contains in the straight or branched hydrocarbon chain one or more double bonds. Examples of alkenyl groups include allenyl, vinylmethyl and ethenyl. An alkenyl group may be unsubstituted or substituted.

[0033] As used herein, “alkynyl” refers to an alkyl group that contains in the straight or branched hydrocarbon chain one or more triple bonds. Examples of alkynyls include ethynyl and propynyl. An alkynyl group may be unsubstituted or substituted.

[0034] As used herein, “cycloalkyl” refers to a completely saturated (no double or triple bonds) mono- or multi- cyclic hydrocarbon ring system. When composed of two or more rings, the rings may be joined together in a fused fashion. Cycloalkyl groups can

contain 3 to 10 atoms in the ring(s) or 3 to 8 atoms in the ring(s). A cycloalkyl group may be unsubstituted or substituted. Typical cycloalkyl groups include, but are in no way limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

[0035] As used herein, “cycloalkenyl” refers to a mono- or multi- cyclic hydrocarbon ring system that contains one or more double bonds in at least one ring; although, if there is more than one, the double bonds cannot form a fully delocalized pi-electron system throughout all the rings (otherwise the group would be “aryl,” as defined herein). When composed of two or more rings, the rings may be connected together in a fused fashion. A cycloalkenyl can contain 3 to 10 atoms in the ring(s) or 3 to 8 atoms in the ring(s). A cycloalkenyl group may be unsubstituted or substituted.

[0036] As used herein, “aryl” refers to a carbocyclic (all carbon) monocyclic or polycyclic aromatic ring system (including fused ring systems where two carbocyclic rings share a chemical bond) that has a fully delocalized pi-electron system throughout all the rings. The number of carbon atoms in an aryl group can vary. For example, the aryl group can be a C₆-C₁₄ aryl group, a C₆-C₁₀ aryl group, or a C₆ aryl group. Examples of aryl groups include, but are not limited to, benzene, naphthalene and azulene. An aryl group may be substituted or unsubstituted.

[0037] As used herein, “heteroaryl” refers to a monocyclic, bicyclic and tricyclic aromatic ring system (a ring system with fully delocalized pi-electron system) that contain(s) one or more heteroatoms (for example, 1 to 5 heteroatoms), that is, an element other than carbon, including but not limited to, nitrogen, oxygen and sulfur. The number of atoms in the ring(s) of a heteroaryl group can vary. For example, the heteroaryl group can contain 4 to 14 atoms in the ring(s), 5 to 10 atoms in the ring(s) or 5 to 6 atoms in the ring(s). Furthermore, the term “heteroaryl” includes fused ring systems where two rings, such as at least one aryl ring and at least one heteroaryl ring, or at least two heteroaryl rings, share at least one chemical bond. Examples of heteroaryl rings include, but are not limited to, furan, furazan, thiophene, benzothiophene, phthalazine, pyrrole, oxazole, benzoxazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, thiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, benzothiazole, imidazole, benzimidazole, indole, indazole, pyrazole, benzopyrazole, isoxazole, benzoisoxazole, isothiazole, triazole, benzotriazole, thiadiazole, tetrazole, pyridine, pyridazine, pyrimidine,

pyrazine, purine, pteridine, quinoline, isoquinoline, quinazoline, quinoxaline, cinnoline and triazine. A heteroaryl group may be substituted or unsubstituted.

[0038] As used herein, “heterocyclyl” or “heteroalicyclyl” refers to three-, four-, five-, six-, seven-, eight-, nine-, ten-, up to 18-membered monocyclic, bicyclic and tricyclic ring system wherein carbon atoms together with from 1 to 5 heteroatoms constitute said ring system. A heterocycle may optionally contain one or more unsaturated bonds situated in such a way, however, that a fully delocalized pi-electron system does not occur throughout all the rings. The heteroatom(s) is an element other than carbon including, but not limited to, oxygen, sulfur and nitrogen. A heterocycle may further contain one or more carbonyl or thiocarbonyl functionalities, so as to make the definition include oxo-systems and thio-systems such as lactams, lactones, cyclic imides, cyclic thioimides and cyclic carbamates. When composed of two or more rings, the rings may be joined together in a fused fashion. Additionally, any nitrogens in a heterocyclyl or a heteroalicyclyl may be quaternized. Heterocyclyl or heteroalicyclic groups may be unsubstituted or substituted. Examples of such “heterocyclyl” or “heteroalicyclyl” groups include but are not limited to, 1,3-dioxin, 1,3-dioxane, 1,4-dioxane, 1,2-dioxolane, 1,3-dioxolane, 1,4-dioxolane, 1,3-oxathiane, 1,4-oxathiin, 1,3-oxathiolane, 1,3-dithiole, 1,3-dithiolane, 1,4-oxathiane, tetrahydro-1,4-thiazine, 2H-1,2-oxazine, maleimide, succinimide, barbituric acid, thiobarbituric acid, dioxopiperazine, hydantoin, dihydrouracil, trioxane, hexahydro-1,3,5-triazine, imidazoline, imidazolidine, isoxazoline, isoxazolidine, oxazoline, oxazolidine, oxazolidinone, thiazoline, thiazolidine, morpholine, oxirane, piperidine *N*-Oxide, piperidine, piperazine, pyrrolidine, pyrrolidone, pyrrolidione, 4-piperidone, pyrazoline, pyrazolidine, 2-oxopyrrolidine, tetrahydropyran, 4H-pyran, tetrahydrothiopyran, thiamorpholine, thiamorpholine sulfoxide, thiamorpholine sulfone and their benzo-fused analogs (e.g., benzimidazolidinone, tetrahydroquinoline and 3,4-methylenedioxyphenyl).

[0039] As used herein, “aralkyl” and “aryl(alkyl)” refer to an aryl group connected, as a substituent, via a lower alkylene group. The lower alkylene and aryl group of an aryl(alkyl) may be substituted or unsubstituted. Examples include but are not limited to benzyl, 2-phenyl(alkyl), 3-phenyl(alkyl), and naphthyl(alkyl).

[0040] As used herein, “heteroaralkyl” and “heteroaryl(alkyl)” refer to a heteroaryl group connected, as a substituent, via a lower alkylene group. The lower alkylene

and heteroaryl group of heteroaryl(alkyl) may be substituted or unsubstituted. Examples include but are not limited to 2-thienyl(alkyl), 3-thienyl(alkyl), furyl(alkyl), thienyl(alkyl), pyrrolyl(alkyl), pyridyl(alkyl), isoxazolyl(alkyl), imidazolyl(alkyl), and their benzo-fused analogs.

[0041] A “(heteroalicycyl)alkyl” and “(heterocycyl)alkyl” refer to a heterocyclic or a heteroalicyclic group connected, as a substituent, via a lower alkylene group. The lower alkylene and heterocycyl of a heterocycyl(alkyl) may be substituted or unsubstituted. Examples include but are not limited tetrahydro-2H-pyran-4-yl(methyl), piperidin-4-yl(ethyl), piperidin-4-yl(propyl), tetrahydro-2H-thiopyran-4-yl(methyl) and 1,3-thiazinan-4-yl(methyl).

[0042] “Lower alkylene groups” are straight-chained $-CH_2-$ tethering groups, forming bonds to connect molecular fragments via their terminal carbon atoms. Examples include but are not limited to methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), propylene ($-CH_2CH_2CH_2-$) and butylene ($-CH_2CH_2CH_2CH_2-$). A lower alkylene group can be substituted by replacing one or more hydrogen of the lower alkylene group with a substituent(s) listed under the definition of “substituted.”

[0043] As used herein, “alkoxy” refers to the formula $-OR$ wherein R is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocycyl, aralkyl, heteroaryl(alkyl) or heterocycyl(alkyl) is defined herein. A non-limiting list of alkoxy are methoxy, ethoxy, n-propoxy, 1-methylethoxy (isopropoxy), n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy, phenoxy and benzoxy. An alkoxy may be substituted or unsubstituted.

[0044] As used herein, “acyl” refers to a hydrogen an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heteroalicycyl, aralkyl, heteroaryl(alkyl) or heterocycyl(alkyl) connected, as substituents, via a carbonyl group. Examples include formyl, acetyl, propanoyl, benzoyl, and acryl. An acyl may be substituted or unsubstituted.

[0045] As used herein, “hydroxyalkyl” refers to an alkyl group in which one or more of the hydrogen atoms are replaced by a hydroxy group. Exemplary hydroxyalkyl groups include but are not limited to, 2-hydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl and 2,2-dihydroxyethyl. A hydroxyalkyl may be substituted or unsubstituted.

[0046] As used herein, “haloalkyl” refers to an alkyl group in which one or more of the hydrogen atoms are replaced by a halogen (e.g., mono-haloalkyl, di-haloalkyl and tri-haloalkyl). Such groups include but are not limited to, chloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 1-chloro-2-fluoromethyl and 2-fluoroisobutyl. A haloalkyl may be substituted or unsubstituted.

[0047] As used herein, “haloalkoxy” refers to a O-alkyl group in which one or more of the hydrogen atoms are replaced by a halogen (e.g., mono-haloalkoxy, di-haloalkoxy and tri- haloalkoxy). Such groups include but are not limited to, chloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, 1-chloro-2-fluoromethoxy and 2-fluoroisobutoxy. A haloalkoxy may be substituted or unsubstituted.

[0048] A “sulfenyl” group refers to an “-SR” group in which R can be hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). A sulfenyl may be substituted or unsubstituted.

[0049] A “sulfinyl” group refers to an “-S(=O)-R” group in which R can be the same as defined with respect to sulfenyl. A sulfinyl may be substituted or unsubstituted.

[0050] A “sulfonyl” group refers to an “SO₂R” group in which R can be the same as defined with respect to sulfenyl. A sulfonyl may be substituted or unsubstituted.

[0051] An “O-carboxy” group refers to a “RC(=O)O-” group in which R can be hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl), as defined herein. An O-carboxy may be substituted or unsubstituted.

[0052] The terms “ester” and “C-carboxy” refer to a “-C(=O)OR” group in which R can be the same as defined with respect to O-carboxy. An ester and C-carboxy may be substituted or unsubstituted.

[0053] A “thiocarbonyl” group refers to a “-C(=S)R” group in which R can be the same as defined with respect to O-carboxy. A thiocarbonyl may be substituted or unsubstituted.

[0054] A “trihalomethanesulfonyl” group refers to an “X₃CSO₂-” group wherein each X is a halogen.

[0055] A “trihalomethanesulfonamido” group refers to an “X₃CS(O)₂N(R_A)-” group wherein each X is a halogen, and R_A is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl,

cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl).

- [0056] The term “amino” as used herein refers to a -NH_2 group.
- [0057] As used herein, the term “hydroxy” refers to a -OH group.
- [0058] A “cyano” group refers to a “ -CN ” group.
- [0059] The term “azido” as used herein refers to a -N_3 group.
- [0060] An “isocyanato” group refers to a “ -NCO ” group.
- [0061] A “thiocyanato” group refers to a “ -CNS ” group.
- [0062] An “isothiocyanato” group refers to an “ -NCS ” group.
- [0063] A “mercapto” group refers to an “ -SH ” group.
- [0064] A “carbonyl” group refers to a C=O group.
- [0065] An “S-sulfonamido” group refers to a “ $\text{-SO}_2\text{N(R}_A\text{R}_B)$ ” group in which R_A and R_B can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An S-sulfonamido may be substituted or unsubstituted.
- [0066] An “N-sulfonamido” group refers to a “ $\text{RSO}_2\text{N(R}_A\text{)-}$ ” group in which R and R_A can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-sulfonamido may be substituted or unsubstituted.
- [0067] An “O-carbamyl” group refers to a “ $\text{-OC(=O)N(R}_A\text{R}_B)$ ” group in which R_A and R_B can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An O-carbamyl may be substituted or unsubstituted.
- [0068] An “N-carbamyl” group refers to an “ $\text{ROC(=O)N(R}_A\text{)-}$ ” group in which R and R_A can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-carbamyl may be substituted or unsubstituted.
- [0069] An “O-thiocarbamyl” group refers to a “ $\text{-OC(=S)-N(R}_A\text{R}_B)$ ” group in which R_A and R_B can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An O-thiocarbamyl may be substituted or unsubstituted.

[0070] An “N-thiocarbamyl” group refers to an “ $\text{ROC(=S)N(R}_A\text{)-}$ ” group in which R and R_A can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-thiocarbamyl may be substituted or unsubstituted.

[0071] A “C-amido” group refers to a “ $\text{-C(=O)N(R}_A\text{R}_B\text{)-}$ ” group in which R_A and R_B can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). A C-amido may be substituted or unsubstituted.

[0072] An “N-amido” group refers to a “ $\text{RC(=O)N(R}_A\text{)-}$ ” group in which R and R_A can be independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-amido may be substituted or unsubstituted.

[0073] The term “halogen atom” or “halogen” as used herein, means any one of the radio-stable atoms of column 7 of the Periodic Table of the Elements, such as, fluorine, chlorine, bromine and iodine.

[0074] Where the numbers of substituents is not specified (e.g. haloalkyl), there may be one or more substituents present. For example “haloalkyl” may include one or more of the same or different halogens. As another example, “ $\text{C}_1\text{-C}_3$ alkoxyphenyl” may include one or more of the same or different alkoxy groups containing one, two or three atoms.

[0075] As used herein, the abbreviations for any protective groups, amino acids and other compounds, are, unless indicated otherwise, in accord with their common usage, recognized abbreviations, or the IUPAC-IUB Commission on Biochemical Nomenclature (See, Biochem. 11:942-944 (1972)).

[0076] The term “nucleoside” is used herein in its ordinary sense as understood by those skilled in the art, and refers to a compound composed of an optionally substituted pentose moiety or modified pentose moiety attached to a heterocyclic base or tautomer thereof, such as attached via the 9-position of a purine-base or the 1-position of a pyrimidine-base. Examples include, but are not limited to, a ribonucleoside comprising a ribose moiety and a deoxyribonucleoside comprising a deoxyribose moiety. A modified pentose moiety is a pentose moiety in which an oxygen atom has been replaced with a carbon and/or a carbon has been replaced with a sulfur or an oxygen atom. A “nucleoside” is a monomer that can

have a substituted base and/or sugar moiety. Additionally, a nucleoside can be incorporated into larger DNA and/or RNA polymers and oligomers. In some instances, the nucleoside can be a nucleoside analog drug.

[0077] The term “nucleotide” is used herein in its ordinary sense as understood by those skilled in the art, and refers to a nucleoside having a phosphate ester bound to the pentose moiety, for example, at the 5'-position.

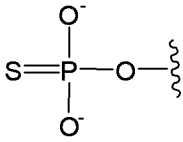
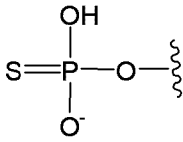
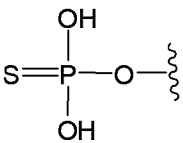
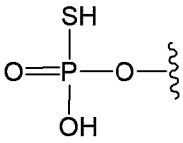
[0078] As used herein, the term “heterocyclic base” refers to an optionally substituted nitrogen-containing heterocyclyl that can be attached to an optionally substituted pentose moiety or modified pentose moiety. In some embodiments, the heterocyclic base can be selected from an optionally substituted purine-base, an optionally substituted pyrimidine-base and an optionally substituted triazole-base (for example, a 1,2,4-triazole). The term “purine-base” is used herein in its ordinary sense as understood by those skilled in the art, and includes its tautomers. Similarly, the term “pyrimidine-base” is used herein in its ordinary sense as understood by those skilled in the art, and includes its tautomers. A non-limiting list of optionally substituted purine-bases includes purine, adenine, guanine, hypoxanthine, xanthine, alloxanthine, 7-alkylguanine (e.g. 7-methylguanine), theobromine, caffeine, uric acid and isoguanine. Examples of pyrimidine-bases include, but are not limited to, cytosine, thymine, uracil, 5,6-dihydrouracil and 5-alkylcytosine (e.g., 5-methylcytosine). An example of an optionally substituted triazole-base is 1,2,4-triazole-3-carboxamide. Other non-limiting examples of heterocyclic bases include diaminopurine, 8-oxo-N⁶-alkyladenine (e.g., 8-oxo-N⁶-methyladenine), 7-deazaxanthine, 7-deazaguanine, 7-deazaadenine, N⁴,N⁴-ethanocytosin, N⁶,N⁶-ethano-2,6-diaminopurine, 5-halouracil (e.g., 5-fluorouracil and 5-bromouracil), pseudoisocytosine, isocytosine, isoguanine, and other heterocyclic bases described in U.S. Patent Nos. 5,432,272 and 7,125,855. In some embodiments, a heterocyclic base can be optionally substituted with an amine or an enol protecting group(s).

[0079] The term “-N-linked amino acid” refers to an amino acid that is attached to the indicated moiety via a main-chain amino or mono-substituted amino group. When the amino acid is attached in an -N-linked amino acid, one of the hydrogens that is part of the main-chain amino or mono-substituted amino group is not present and the amino acid is attached via the nitrogen. N-linked amino acids can be substituted or unsubstituted.

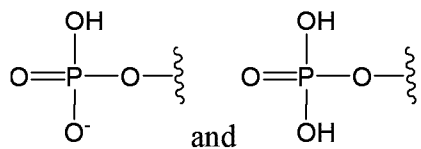
[0080] The term “–N–linked amino acid ester derivative” refers to an amino acid in which a main-chain carboxylic acid group has been converted to an ester group. In some embodiments, the ester group has a formula selected from alkyl-O-C(=O)-, cycloalkyl-O-C(=O)-, aryl-O-C(=O)- and aryl(alkyl)-O-C(=O)-. A non-limiting list of ester groups include substituted and unsubstituted versions of the following: methyl-O-C(=O)-, ethyl-O-C(=O)-, n-propyl-O-C(=O)-, isopropyl-O-C(=O)-, n-butyl-O-C(=O)-, isobutyl-O-C(=O)-, tert-butyl-O-C(=O)-, neopentyl-O-C(=O)-, cyclopropyl-O-C(=O)-, cyclobutyl-O-C(=O)-, cyclopentyl-O-C(=O)-, cyclohexyl-O-C(=O)-, phenyl-O-C(=O)-, benzyl-O-C(=O)- and naphthyl-O-C(=O)-. N-linked amino acid ester derivatives can be substituted or unsubstituted.

[0081] The term “–O–linked amino acid” refers to an amino acid that is attached to the indicated moiety via the hydroxy from its main-chain carboxylic acid group. When the amino acid is attached in an –O–linked amino acid, the hydrogen that is part of the hydroxy from its main-chain carboxylic acid group is not present and the amino acid is attached via the oxygen. O-linked amino acids can be substituted or unsubstituted.

[0082] As used herein, the term “amino acid” refers to any amino acid (both standard and non-standard amino acids), including, but not limited to, α -amino acids, β -amino acids, γ -amino acids and δ -amino acids. Examples of suitable amino acids include, but are not limited to, alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. Additional examples of suitable amino acids include, but are not limited to, ornithine, hypusine, 2-aminoisobutyric acid, dehydroalanine, gamma-aminobutyric acid, citrulline, beta-alanine, alpha-ethyl-glycine, alpha-propyl-glycine and norleucine.

[0083] The terms “phosphorothioate” and “phosphothioate” refer to a compound of the general formula , its protonated forms (for example,  and ) and its tautomers (such as ).

[0084] As used herein, the term “phosphate” is used in its ordinary sense as understood by those skilled in the art, and includes its protonated forms (for example,



). As used herein, the terms “monophosphate,” “diphosphate,” and “triphosphate” are used in their ordinary sense as understood by those skilled in the art, and include protonated forms.

[0085] The terms “protecting group” and “protecting groups” as used herein refer to any atom or group of atoms that is added to a molecule in order to prevent existing groups in the molecule from undergoing unwanted chemical reactions. Examples of protecting group moieties are described in T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3. Ed. John Wiley & Sons, 1999, and in J.F.W. McOmie, *Protective Groups in Organic Chemistry* Plenum Press, 1973, for the limited purpose of disclosing suitable protecting groups. The protecting group moiety may be chosen in such a way, that they are stable to certain reaction conditions and readily removed at a convenient stage using methodology known from the art. A non-limiting list of protecting groups include benzyl; substituted benzyl; alkylcarbonyls and alkoxycarbonyls (e.g., t-butoxycarbonyl (BOC), acetyl, or isobutyryl); arylalkylcarbonyls and arylalkoxycarbonyls (e.g., benzyloxycarbonyl); substituted methyl ether (e.g. methoxymethyl ether); substituted ethyl ether; a substituted benzyl ether; tetrahydropyranyl ether; silyls (e.g., trimethylsilyl, triethylsilyl, triisopropylsilyl, t-butyl dimethylsilyl, tri-*iso*-propylsilyloxymethyl, [2-(trimethylsilyl)ethoxy]methyl or t-butyl diphenylsilyl); esters (e.g. benzoate ester); carbonates (e.g. methoxymethyl carbonate); sulfonates (e.g. tosylate or mesylate); acyclic ketal (e.g. dimethyl acetal); cyclic ketals (e.g., 1,3-dioxane, 1,3-dioxolanes and those described herein); acyclic acetal; cyclic acetal (e.g., those described herein); acyclic hemiacetal; cyclic hemiacetal; cyclic dithioketals (e.g., 1,3-dithiane or 1,3-dithiolane); orthoesters (e.g., those described herein) and triarylmethyl groups (e.g., trityl; monomethoxytrityl (MMTr); 4,4'-dimethoxytrityl (DMTr); 4,4',4''-trimethoxytrityl (TMTr); and those described herein).

[0086] The term “pharmaceutically acceptable salt” refers to a salt of a compound that does not cause significant irritation to an organism to which it is administered and does not abrogate the biological activity and properties of the compound. In some embodiments,

the salt is an acid addition salt of the compound. Pharmaceutical salts can be obtained by reacting a compound with inorganic acids such as hydrohalic acid (e.g., hydrochloric acid or hydrobromic acid), sulfuric acid, nitric acid and phosphoric acid. Pharmaceutical salts can also be obtained by reacting a compound with an organic acid such as aliphatic or aromatic carboxylic or sulfonic acids, for example formic, acetic, succinic, lactic, malic, tartaric, citric, ascorbic, nicotinic, methanesulfonic, ethanesulfonic, p-toluenesulfonic, salicylic or naphthalenesulfonic acid. Pharmaceutical salts can also be obtained by reacting a compound with a base to form a salt such as an ammonium salt, an alkali metal salt, such as a sodium or a potassium salt, an alkaline earth metal salt, such as a calcium or a magnesium salt, a salt of organic bases such as dicyclohexylamine, N-methyl-D-glucamine, tris(hydroxymethyl)methylamine, C₁-C₇ alkylamine, cyclohexylamine, triethanolamine, ethylenediamine, and salts with amino acids such as arginine and lysine.

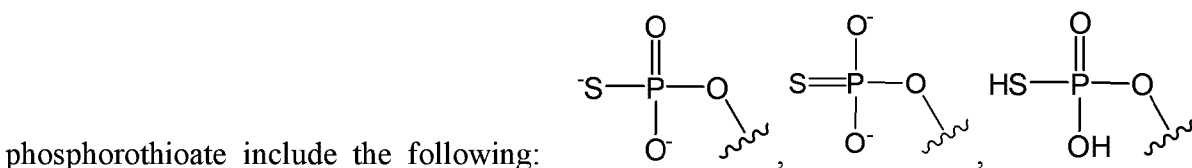
[0087] Terms and phrases used in this application, and variations thereof, especially in the appended claims, unless otherwise expressly stated, should be construed as open ended as opposed to limiting. As examples of the foregoing, the term 'including' should be read to mean 'including, without limitation,' 'including but not limited to,' or the like; the term 'comprising' as used herein is synonymous with 'including,' 'containing,' or 'characterized by,' and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps; the term 'having' should be interpreted as 'having at least;' the term 'includes' should be interpreted as 'includes but is not limited to;' the term 'example' is used to provide exemplary instances of the item in discussion, not an exhaustive or limiting list thereof; and use of terms like 'preferably,' 'preferred,' 'desired,' or 'desirable,' and words of similar meaning should not be understood as implying that certain features are critical, essential, or even important to the structure or function, but instead as merely intended to highlight alternative or additional features that may or may not be utilized in a particular embodiment. In addition, the term "comprising" is to be interpreted synonymously with the phrases "having at least" or "including at least". When used in the context of a process, the term "comprising" means that the process includes at least the recited steps, but may include additional steps. When used in the context of a compound, composition or device, the term "comprising" means that the compound, composition or device includes at least the recited features or components, but may also include additional features or

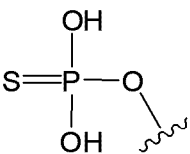
components. Likewise, a group of items linked with the conjunction ‘and’ should not be read as requiring that each and every one of those items be present in the grouping, but rather should be read as ‘and/or’ unless expressly stated otherwise. Similarly, a group of items linked with the conjunction ‘or’ should not be read as requiring mutual exclusivity among that group, but rather should be read as ‘and/or’ unless expressly stated otherwise.

[0088] With respect to the use of substantially any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations may be expressly set forth herein for sake of clarity. The indefinite article “a” or “an” does not exclude a plurality. A single processor or other unit may fulfill the functions of several items recited in the claims. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

[0089] It is understood that, in any compound described herein having one or more chiral centers, if an absolute stereochemistry is not expressly indicated, then each center may independently be of R-configuration or S-configuration or a mixture thereof. Thus, the compounds provided herein may be enantiomerically pure, enantiomerically enriched, racemic mixture, diastereomerically pure, diastereomerically enriched, or a stereoisomeric mixture. In addition it is understood that, in any compound described herein having one or more double bond(s) generating geometrical isomers that can be defined as E or Z, each double bond may independently be E or Z a mixture thereof.

[0090] Likewise, it is understood that, in any compound described, all tautomeric forms are also intended to be included. For example all tautomers of a phosphate and a phosphorothioate groups are intended to be included. Examples of tautomers of a



and  . Furthermore, all tautomers of heterocyclic bases known in the art are intended to be included, including tautomers of natural and non-natural purine-bases and pyrimidine-bases.

[0091] It is to be understood that where compounds disclosed herein have unfilled valencies, then the valencies are to be filled with hydrogens or isotopes thereof, e.g., hydrogen-1 (protium) and hydrogen-2 (deuterium).

[0092] It is understood that the compounds described herein can be labeled isotopically. Substitution with isotopes such as deuterium may afford certain therapeutic advantages resulting from greater metabolic stability, such as, for example, increased *in vivo* half-life or reduced dosage requirements. Each chemical element as represented in a compound structure may include any isotope of said element. For example, in a compound structure a hydrogen atom may be explicitly disclosed or understood to be present in the compound. At any position of the compound that a hydrogen atom may be present, the hydrogen atom can be any isotope of hydrogen, including but not limited to hydrogen-1 (protium) and hydrogen-2 (deuterium). Thus, reference herein to a compound encompasses all potential isotopic forms unless the context clearly dictates otherwise.

[0093] It is understood that the methods and combinations described herein include crystalline forms (also known as polymorphs, which include the different crystal packing arrangements of the same elemental composition of a compound), amorphous phases, salts, solvates and hydrates. In some embodiments, the compounds described herein exist in solvated forms with pharmaceutically acceptable solvents such as water, ethanol, or the like. In other embodiments, the compounds described herein exist in unsolvated form. Solvates contain either stoichiometric or non-stoichiometric amounts of a solvent, and may be formed during the process of crystallization with pharmaceutically acceptable solvents such as water, ethanol, or the like. Hydrates are formed when the solvent is water, or alcoholates are formed when the solvent is alcohol. In addition, the compounds provided herein can exist in unsolvated as well as solvated forms. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the compounds and methods provided herein.

[0094] Where a range of values is provided, it is understood that the upper and lower limit, and each intervening value between the upper and lower limit of the range is encompassed within the embodiments.

Methods of Use

[0095] Some embodiments disclosed herein relate to a method of treating and/or ameliorating a Picornavirus infection that can include administering to a subject infected with the Picornavirus an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments disclosed herein relate to a method of treating and/or ameliorating a Picornavirus infection that can include administering to a subject identified as suffering from the viral infection an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing).

[0096] Some embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for ameliorating and/or treating a Picornavirus infection that can include administering to a subject infected with the Picornavirus an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Still other embodiments described herein relate to one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing) that can be used for ameliorating and/or treating a Picornavirus infection by administering to a subject infected with the Picornavirus an effective amount of one or more compounds described herein.

[0097] Some embodiments disclosed herein relate to methods of ameliorating and/or treating a Picornavirus infection that can include contacting a cell infected with the virus with an effective amount of one or more compounds described herein (such as a

compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for ameliorating and/or treating a Picornavirus infection that can include contacting a cell infected with the virus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), that can be used for ameliorating and/or treating a Picornavirus infection by contacting a cell infected with the virus with an effective amount of said compound(s).

[0098] Some embodiments disclosed herein relate to methods of inhibiting replication of a Picornavirus that can include contacting a cell infected with the virus with an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for inhibiting replication of a Picornavirus that can include contacting a cell infected with the virus with an effective amount of said compound(s). Still other embodiments described herein relate to a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), that can be used for inhibiting replication of a Picornavirus by contacting a cell infected with the virus with an effective amount of said compound(s). In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can inhibit a RNA dependent RNA polymerase of a picornavirus, and thus, inhibit the replication of RNA. In some embodiments, a polymerase of a picornavirus can be inhibited by contacting a cell infected

with the picornavirus with a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing).

[0099] In some embodiments, the picornavirus can be selected from an Aphthovirus, an Enterovirus, a Rhinovirus, a Hepatovirus and a Parechovirus. Within the Enterovirus genus, there are several species of Enteroviruses including enterovirus A, enterovirus B, enterovirus C, enterovirus D, enterovirus E, enterovirus F, enterovirus G, enterovirus H, enterovirus J. Each Enterovirus species includes several serotypes. Examples of Enterovirus serotypes include the following: poliovirus 1, poliovirus 2, poliovirus 3, echovirus 1, echovirus 2, echovirus 3, echovirus 4, echovirus 5, echovirus 6, echovirus 7, echovirus 9, echovirus 11, echovirus 12, echovirus 13, echovirus 14, echovirus 15, echovirus 16, echovirus 17, echovirus 18, echovirus 19, echovirus 20, echovirus 21, echovirus 24, echovirus 25, echovirus 26, echovirus 27, echovirus 29, echovirus 30, echovirus 31, echovirus 32, echovirus 33, enterovirus 68, enterovirus 69, enterovirus 70, enterovirus 71 and varicella human encephalomyelitis virus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat an Enterovirus infection. For example, by administering an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, to a subject infected with the Enterovirus and/or by contacting a cell infected with the Enterovirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of an Enterovirus. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be effective against an Enterovirus, and thereby ameliorate one or more symptoms of an Enterovirus infection. In some embodiments, the Enterovirus can be Enterovirus A. In other embodiments, the Enterovirus can be Enterovirus B. In still other embodiments, the Enterovirus can be Enterovirus C. In yet still other embodiments, the Enterovirus can be Enterovirus D. In other embodiments, the Enterovirus can be Enterovirus E. In still other embodiments, the Enterovirus can be Enterovirus F. In yet still other embodiments, the Enterovirus can be Enterovirus G. In some embodiments, the Enterovirus can be Enterovirus H. In other embodiments, the Enterovirus can be Enterovirus J.

[0100] Coxsackieviruses are divided into group A and group B. Group A coxsackieviruses were noted to cause flaccid paralysis, while group B coxsackieviruses were noted to cause spastic paralysis. Over 20 serotypes of group A (CV-A1, CV-A2, CV-A3, CV-A4, CV-A5, CV-A6, CV-A7, CV-A8, CV-A9, CV-A10, CV-A11, CV-A12, CV-A13, CV-A14, CV-A15, CV-A16, CV-A17, CV-A18, CV-A19, CV-A20, CV-A21, CV-A22 and CV-A23) and 6 serotypes of group B (CV-B1, CV-B2, CV-B3, CV-B4, CV-B5 and CV-B6) are recognized. No specific treatment for coxsackievirus infections is currently approved. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat a coxsackievirus infection. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a coxsackievirus. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be effective against a coxsackievirus as demonstrated by the amelioration of one or more symptoms of a coxsackievirus infection. In some embodiments, a coxsackievirus infection can be ameliorated, treated and/or inhibited by administering an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, to a subject infected with the coxsackievirus and/or by contacting a cell infected with the coxsackievirus. In some embodiments, the coxsackievirus can be a coxsackievirus A. In other embodiments, the coxsackievirus can be a coxsackievirus B. In some embodiments, a compound described herein (one or more a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat hand, food and mouth disease caused by a coxsackie A virus.

[0101] Additional species within the Enterovirus genus includes rhinovirus A, rhinovirus B and rhinovirus C. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat a rhinovirus infection. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a rhinovirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can be effective against

multiple serotypes of a rhinovirus. For example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be used to ameliorate and/or treat 2, 5, 10, 20, 40, 60, 80 or more serotypes of a rhinovirus. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be effective against rhinovirus, and thereby ameliorating one or more symptoms of a rhinovirus infection. In some embodiments, a rhinovirus infection can be ameliorated, treated and/or inhibited by administering an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, to a subject infected with the rhinovirus and/or by contacting a cell infected with the rhinovirus. In some embodiments, the coxsackievirus can be a coxsackievirus A. In some embodiments, the rhinovirus can be rhinovirus A. In other embodiments, the rhinovirus can be rhinovirus B. In still other embodiments, the rhinovirus can be rhinovirus C.

[0102] Another species of Enterovirus is Hepatovirus. Hepatitis A is a serotype of Hepatovirus. Several human genotypes of Hepatitis A are known, IA, IB, IIA, IIB, IIIA and IIIB. Genotype I is the most common. To date, there is no specific therapy for treating a hepatitis A infection. Rather, treatment is supportive in nature. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat a Hepatovirus infection, such as a hepatitis A virus infection. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a Hepatovirus (for example, a hepatitis A virus). In some embodiment, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can treat and/or ameliorate a genotype I of hepatitis A. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, is effective against more than one genotype of hepatitis A, for example, 2, 3, 4, 5 or 6 genotypes of hepatitis A. In some embodiments, a Hepatovirus infection can be ameliorated, treated and/or inhibited by administering an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, to a subject infected with the Hepatovirus and/or by contacting a cell infected with the Hepatovirus.

[0103] Parechovirus is another species of Enterovirus. Serotypes of Parechovirus includes human parechovirus 1 (echovirus 22), human parechovirus 2 (echovirus 23), human

parechovirus 3, human parechovirus 4, human parechovirus 5 and human parechovirus 6. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat a parechovirus infection. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a parechovirus. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, is effective against more than one serotype of a parechovirus. In some embodiments, a parechovirus infection can be ameliorated, treated and/or inhibited by administering an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, to a subject infected with the parechovirus and/or by contacting a cell infected with the parechovirus.

[0104] Other genera of Picornavirus include the following: Aquamavirus, Avihepatovirus, Cardiovirus, Cosavirus, Dicipivirus, Erbovirus, Kobuvirus, Megrivirus, Salivirus, Sapelovirus, Senecavirus, Teschovirus and Tremovirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate and/or treat a picornavirus infection caused by a virus selected from Aquamavirus, Avihepatovirus, Cardiovirus, Cosavirus, Dicipivirus, Erbovirus, Kobuvirus, Megrivirus, Salivirus, Sapelovirus, Senecavirus, Teschovirus and Tremovirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a picornavirus selected from Aquamavirus, Avihepatovirus, Cardiovirus, Cosavirus, Dicipivirus, Erbovirus, Kobuvirus, Megrivirus, Salivirus, Sapelovirus, Senecavirus, Teschovirus and Tremovirus. A compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can ameliorate, treat and/or inhibit a virus selected from Aquamavirus, Avihepatovirus, Cardiovirus, Cosavirus, Dicipivirus, Erbovirus, Kobuvirus, Megrivirus, Salivirus, Sapelovirus, Senecavirus, Teschovirus and Tremovirus by administering an effective amount of a compound described herein to a subject infected by the virus and/or by contacting a cell infected with the virus with an effective amount of a compound described herein.

[0105] In some embodiments, an effective amount of a compound of Formulae (I) and/(II), or a pharmaceutical acceptable salt of the foregoing, or a pharmaceutical composition that includes an effective amount of one or more compounds of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be effective to treat more than one genera of Picornavirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can be used to ameliorate and/or treat more than one species of a Picornavirus. As an example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be used to ameliorate and/or treat 2, 3, 4, 5, or more species of an Enterovirus. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can be effective to treat multiple serotypes of a Picornavirus described herein. For example, a compound described herein (one or more a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can be effective to treat 2, 5, 10, 15 or more serotypes of a coxsackie virus.

[0106] Some embodiments disclosed herein relate to a method of treating and/or ameliorating a *Flaviviridae* virus infection that can include administering to a subject infected with the *Flaviviridae* an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments disclosed herein relate to a method of treating and/or ameliorating a *Flaviviridae* virus infection that can include administering to a subject an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Some embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for ameliorating and/or treating a *Flaviviridae* virus infection that can include administering an effective amount of one or

more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Still other embodiments described herein relate to one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing) that can be used for ameliorating and/or treating a *Flaviviridae* virus infection by administering to a subject an effective amount of one or more compounds described herein.

[0107] Some embodiments disclosed herein relate to methods of ameliorating and/or treating a *Flaviviridae* virus infection that can include contacting a cell infected with the virus with an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for ameliorating and/or treating a *Flaviviridae* virus infection that can include contacting a cell infected with the virus with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), that can be used for ameliorating and/or treating a *Flaviviridae* virus infection by contacting a cell infected with the virus with an effective amount of said compound(s).

[0108] Some embodiments disclosed herein relate to methods of inhibiting replication of a *Flaviviridae* virus that can include contacting a cell infected with the virus with an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for inhibiting replication of a *Flaviviridae* virus that can include contacting a cell infected with the virus

with an effective amount of said compound(s). Still other embodiments described herein relate to a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), that can be used for inhibiting replication of a *Flaviviridae* virus by contacting a cell infected with the virus with an effective amount of said compound(s). In some embodiments, a polymerase of a *Flaviviridae* virus can be inhibited by contacting a cell infected with the *Flaviviridae* virus with a compound described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), and thereby, inhibit the replication of RNA.

[0109] HCV is an enveloped positive strand RNA virus in the Flaviviridae family. There are various nonstructural proteins of HCV, such as NS2, NS3, NS4, NS4A, NS4B, NS5A and NS5B. NS5B is believed to be an RNA-dependent RNA polymerase involved in the replication of HCV RNA.

[0110] Some embodiments disclosed herein relate to methods of ameliorating and/or treating a HCV infection that can include contacting a cell infected with HCV with an effective amount of one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), or a pharmaceutical composition that includes one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Other embodiments described herein relate to using one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), in the manufacture of a medicament for ameliorating and/or treating a HCV infection that can include contacting a cell infected with HCV with an effective amount of said compound(s). Still other embodiments described herein relate to one or more compounds described herein (such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), that can be used for ameliorating and/or treating a HCV infection by contacting a cell infected with HCV with an effective amount of said compound(s).

[0111] Some embodiments described herein relate to a method of inhibiting NS5B polymerase activity that can include contacting a cell infected with hepatitis C virus with an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. Some embodiments described herein relate to a method of

inhibiting NS5B polymerase activity that can include administering to a subject infected with hepatitis C virus an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can inhibit a RNA dependent RNA polymerase, and thus, inhibit the replication of HCV RNA. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can inhibit a HCV polymerase (for example, NS5B polymerase).

[0112] Some embodiments described herein relate to a method of treating a condition selected from liver fibrosis, liver cirrhosis and liver cancer in a subject suffering from one or more of the aforementioned liver conditions that can include administering to the subject an effective amount of a compound or a pharmaceutical composition described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing), wherein the liver condition is caused by a HCV infection. Some embodiments described herein relate to a method of increasing liver function in a subject having a HCV infection that can include administering to the subject an effective amount of a compound or a pharmaceutical composition described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). Also contemplated is a method for reducing or eliminating further virus-caused liver damage in a subject having an HCV infection by administering to the subject an effective amount of a compound or a pharmaceutical composition described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing). In some embodiments, this method can include slowing or halting the progression of liver disease. In other embodiments, the course of the disease can be reversed, and stasis or improvement in liver function is contemplated. In some embodiments, liver fibrosis, liver cirrhosis and/or liver cancer can be treated; liver function can be increased; virus-caused liver damage can be reduced or eliminated; progression of liver disease can be slowed or halted; the course of the liver disease can be reversed and/or liver function can be improved or maintained by contacting a cell infected with hepatitis C virus with an effective amount of a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing.)

[0113] There are a variety of genotypes of HCV, and a variety of subtypes within each genotype. For example, at present it is known that there are eleven (numbered 1 through 11) main genotypes of HCV, although others have classified the genotypes as 6 main genotypes. Each of these genotypes is further subdivided into subtypes (1a-1c; 2a-2c; 3a-3b; 4a-4e; 5a; 6a; 7a- 7b; 8a-8b; 9a; 10a; and 11a). In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, or a pharmaceutical composition that includes an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be effective to treat at least one genotype of HCV. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing) can be effective to treat all 11 genotypes of HCV. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing) can be effective to treat 3 or more, 5 or more, 7 or more, or 9 or more genotypes of HCV. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, can be more effective against a larger number of HCV genotypes than the standard of care. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be more effective against a particular HCV genotype than the standard of care (such as genotype 1, 2, 3, 4, 5 and/or 6).

[0114] Various indicators for determining the effectiveness of a method for treating a HCV infection are known to those skilled in the art. Examples of suitable indicators include, but are not limited to, a reduction in viral load, a reduction in viral replication, a reduction in time to seroconversion (virus undetectable in patient serum), an increase in the rate of sustained viral response to therapy, a reduction of morbidity or mortality in clinical outcomes, a reduction in the rate of liver function decrease; stasis in liver function; improvement in liver function; reduction in one or more markers of liver dysfunction, including alanine transaminase, aspartate transaminase, total bilirubin, conjugated bilirubin, gamma glutamyl transpeptidase and/or other indicator of disease response. Similarly, successful therapy with an effective amount of a compound or a pharmaceutical composition described herein (for example, a compound of Formulae (I)

and/or (II), or a pharmaceutically acceptable salt of the foregoing) can reduce the incidence of liver cancer in HCV infected subjects.

[0115] In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, is an amount that is effective to reduce HCV viral titers to undetectable levels, for example, to about 100 to about 500, to about 50 to about 100, to about 10 to about 50, or to about 15 to about 25 international units/mL serum. In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, is an amount that is effective to reduce HCV viral load compared to the HCV viral load before administration of the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. For example, wherein the HCV viral load is measured before administration of the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and again after completion of the treatment regime with the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing (for example, 1 month after completion). In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be an amount that is effective to reduce HCV viral load to lower than about 25 international units/mL serum. In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, is an amount that is effective to achieve a reduction in HCV viral titer in the serum of the subject in the range of about 1.5-log to about a 2.5-log reduction, about a 3-log to about a 4-log reduction, or a greater than about 5-log reduction compared to the viral load before administration of the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. For example, the HCV viral load can be measured before administration of the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and again after completion of the treatment regime with the compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing (for example, 1 month after completion).

[0116] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in at least a 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, 75, 100-fold or more reduction in the replication of the hepatitis C virus relative

to pre-treatment levels in a subject, as determined after completion of the treatment regime (for example 1 month after completion). In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in a reduction of the replication of the hepatitis C virus relative to pre-treatment levels in the range of about 2 to about 5 fold, about 10 to about 20 fold, about 15 to about 40 fold, or about 50 to about 100 fold. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in a reduction of the hepatitis C virus replication in the range of 1 to 1.5 log, 1.5 log to 2 log, 2 log to 2.5 log, 2.5 to 3 log, 3 log to 3.5 log or 3.5 to 4 log more reduction of the hepatitis C virus replication compared to the reduction of the hepatitis C virus reduction achieved by pegylated interferon in combination with ribavirin, administered according to the standard of care, or may achieve the same reduction as that standard of care therapy in a shorter period of time, for example, in one month, two months, or three months, as compared to the reduction achieved after six months of standard of care therapy with ribavirin and pegylated interferon.

[0117] In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, is an amount that is effective to achieve a sustained viral response, for example, non-detectable or substantially non-detectable HCV RNA (e.g., less than about 500, less than about 200, less than about 100, less than about 25, or less than about 15 international units per milliliter serum) is found in the subject's serum for a period of at least about one month, at least about two months, at least about three months, at least about four months, at least about five months, or at least about six months following cessation of therapy.

[0118] In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can reduce a level of a marker of liver fibrosis by at least about 10%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, or at least about 80%, or more, compared to the level of the marker in an untreated subject, or to a placebo-treated subject. Methods of measuring serum markers are known to those skilled in the art and include immunological-based methods, e.g., enzyme-linked immunosorbent assays (ELISA), radioimmunoassays, and the like, using antibody specific

for a given serum marker. A non-limiting list of examples of markers includes measuring the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and total bilirubin (TBIL) using known methods. In general, an ALT level of less than about 45 IU/L (international units/liter), an AST in the range of 10-34 IU/L, ALP in the range of 44-147 IU/L, GGT in the range of 0-51 IU/L, TBIL in the range of 0.3-1.9 mg/dL is considered normal. In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be an amount effective to reduce ALT, AST, ALP, GGT and/or TBIL levels to with what is considered a normal level.

[0119] Subjects who are clinically diagnosed with HCV infection include “naïve” subjects (e.g., subjects not previously treated for HCV, particularly those who have not previously received IFN-alpha-based and/or ribavirin-based therapy) and individuals who have failed prior treatment for HCV (“treatment failure” subjects). Treatment failure subjects include “non-responders” (i.e., subjects in whom the HCV titer was not significantly or sufficiently reduced by a previous treatment for HCV (≤ 0.5 log IU/mL), for example, a previous IFN-alpha monotherapy, a previous IFN-alpha and ribavirin combination therapy, or a previous pegylated IFN-alpha and ribavirin combination therapy); and “relapsers” (i.e., subjects who were previously treated for HCV, for example, who received a previous IFN-alpha monotherapy, a previous IFN-alpha and ribavirin combination therapy, or a previous pegylated IFN-alpha and ribavirin combination therapy, whose HCV titer decreased, and subsequently increased).

[0120] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a treatment failure subject suffering from HCV. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a non-responder subject suffering from HCV. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a relapsed subject suffering from HCV.

[0121] After a period of time, infectious agents can develop resistance to one or more therapeutic agents. The term “resistance” as used herein refers to a viral strain displaying a delayed, lessened and/or null response to a therapeutic agent(s). For example,

after treatment with an antiviral agent, the viral load of a subject infected with a resistant virus may be reduced to a lesser degree compared to the amount in viral load reduction exhibited by a subject infected with a non-resistant strain. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a subject infected with an HCV strain that is resistant to one or more different anti-HCV agents (for example, an agent used in a conventional standard of care). In some embodiments, development of resistant HCV strains is delayed when a subject is treated with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, compared to the development of HCV strains resistant to other HCV drugs (such as an agent used in a conventional standard of care).

[0122] In some embodiments, an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a subject for whom other anti-HCV medications are contraindicated. For example, administration of pegylated interferon alpha in combination with ribavirin is contraindicated in subjects with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia) and other subjects at risk from the hematologic side effects of current therapy. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be provided to a subject that is hypersensitive to interferon and/or ribavirin.

[0123] Some subjects being treated for HCV experience a viral load rebound. The term "viral load rebound" as used herein refers to a sustained ≥ 0.5 log IU/mL increase of viral load above nadir before the end of treatment, where nadir is a ≥ 0.5 log IU/mL decrease from baseline. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered to a subject experiencing viral load rebound, or can prevent such viral load rebound when used to treat the subject.

[0124] The standard of care for treating HCV has been associated with several side effects (adverse events). In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can decrease the number and/or severity of side effects that can be observed in HCV patients being treated with ribavirin and pegylated interferon according to the standard of care. Examples of side effects include, but are not limited to fever, malaise, tachycardia, chills, headache, arthralgias, myalgias, fatigue,

apathy, loss of appetite, nausea, vomiting, cognitive changes, asthenia, drowsiness, lack of initiative, irritability, confusion, depression, severe depression, suicidal ideation, anemia, low white blood cell counts, and thinning of hair. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be provided to a subject that discontinued a HCV therapy because of one or more adverse effects or side effects associated with one or more other HCV agents (for example, an agent used in a conventional standard of care).

[0125] In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can be ameliorate and/or treat a Flavivirus infection. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can inhibit replication of a Flavivirus.

[0126] In some embodiments, the Flavivirus can be a West Nile virus. A West Nile infection can lead to West Nile fever or severe West Nile disease (also called West Nile encephalitis or meningitis or West Nile poliomyelitis). Symptoms of West Nile fever include fever, headache, tiredness, body aches, nausea, vomiting, a skin rash (on the trunk of the body) and swollen lymph glands. Symptoms of West Nile disease include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness and paralysis. Current treatment for a West Nile virus infection is supportive, and no vaccination is currently available for humans.

[0127] In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can treat and/or ameliorate a dengue virus, such as DENV-1, DENV-2, DENV-3 and DENV-4. A dengue virus infection can cause dengue hemorrhagic fever and/or dengue shock syndrome. In some embodiments, a compound described herein (for example, a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing) can treat and/or ameliorate dengue hemorrhagic fever and/or dengue shock syndrome. According to the World Health Organization (WHO), global incidence of dengue has grown dramatically in recent decades. To date, there is no treatment for a dengue virus infection. Further, recovery from an infection of one serotype of dengue virus provides only partial and temporary immunity against the other serotypes. Subsequent infection(s) with another

serotypes increases the likelihood of developing severe dengue (previously known as dengue hemorrhagic fever). A dengue infection is suspected with a high fever (approx. 104 °F) accompanied by one or more of the following symptoms: severe headache, pain behind the eyes, muscle and joint pain, nausea, vomiting, swollen glands and rash.

[0128] Yellow fever is an acute viral hemorrhagic disease. As provided by the WHO, up to 50% of severely affected persons without treatment die from yellow fever. An estimated 200,000 cases of yellow fever, causing 30,000 deaths, worldwide occur each year. As with other Flaviviruses, there is no cure or specific treatment for yellow fever, and treatment with ribavirin and interferons are insufficient. In some embodiments, the Flavivirus can be yellow fever virus. Symptoms of a yellow fever infection include fever, muscle pain with prominent backache, headache, shivers, loss of appetite, nausea, vomiting, jaundice and bleeding (for example from the mouth, nose, eyes and/or stomach).

[0129] In yet still other embodiments, the Flavivirus can be an encephalitis virus from within the Flavivirus genus. Examples of encephalitis viruses include, but are not limited to, Japanese encephalitis virus, St. Louis encephalitis virus and tick borne encephalitis. Viral encephalitis causes inflammation of the brain and/or meninges. Symptoms include high fever, headache, sensitivity to light, stiff neck and back, vomiting, confusion, seizures, paralysis and coma. There is no specific treatment for an encephalitis infection, such as Japanese encephalitis, St. Louis encephalitis and tick borne encephalitis.

[0130] Various indicators for determining the effectiveness of a method for treating an Picornavirus and/or *Flaviviridae* viral infection are known to those skilled in the art. Example of suitable indicators include, but are not limited to, a reduction in viral load, a reduction in viral replication, a reduction in time to seroconversion (virus undetectable in patient serum), a reduction of morbidity or mortality in clinical outcomes, and/or other indicator(s) of disease response. Further indicators include one or more overall quality of life health indicators, such as reduced illness duration, reduced illness severity, reduced time to return to normal health and normal activity, and reduced time to alleviation of one or more symptoms. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in the reduction, alleviation or positive indication of one or more of the aforementioned indicators compared to a subject who is receiving the standard of care (for HCV) or an untreated subject (picornavirus, and

other *Flaviviridae* infections besides HCV). Effects/symptoms of a Picornavirus infection are described herein, and include, but are not limited to, fever, blisters, rash, meningitis, conjunctivitis, acute hemorrhagic conjunctivitis (AHC), sore throat, nasal congestion, runny nose, sneezing, coughing, loss of appetite, muscle aches, headache, fatigue, nausea, jaundice, encephalitis, herpangina, myocarditis, pericarditis, meningitis, Bornholm disease, myalgia, nasal congestion, muscle weakness, loss of appetite, fever, vomiting, abdominal pain, abdominal discomfort, dark urine and muscle pain. Effects/symptoms of a *Flaviviridae* virus infection are also described herein.

[0131] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in a reduction in the length and/or severity of one or more symptoms associated with a Picornavirus or a *Flaviviridae* virus infection compared to a subject who is receiving the standard of care (for HCV) or an untreated subject (picornavirus, and other *Flaviviridae* infection besides HCV). Table 1 provides some embodiments of the percentage improvements obtained using a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, as compared to the standard of care (for HCV) or an untreated subject (picornavirus, and other *Flaviviridae* infection besides HCV). Examples include the following: in some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, results in a percentage of non-responders that is 10% less than the percentage of non-responders receiving the standard of care for HCV; in some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, results in a duration of illness that is in the range of about 10% to about 30% less than compared to the duration of illness experienced by a subject who is untreated for a yellow fever viral infection; and in some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, results in a severity of a symptom (such as one of those described herein) that is 25% less than compared to the severity of the same symptom experienced by a subject who is untreated for a dengue virus infection. Methods of quantifying the severity of a side effect and/or symptom are known to those skilled in the art.

Table 1

Percentage of non-responders	Percentage of relapsers	Percentage of resistance	Percentage of viral load rebound	Number of side effects	Severity of side effect(s)
10% less	10% less	10% less	10% less	10% less	10% less
25% less	25% less	25% less	25% less	25% less	25% less
40% less	40% less	40% less	40% less	40% less	40% less
50% less	50% less	50% less	50% less	50% less	50% less
60% less	60% less	60% less	60% less	60% less	60% less
70% less	70% less	70% less	70% less	70% less	70% less
80% less	80% less	80% less	80% less	80% less	80% less
90% less	90% less	90% less	90% less	90% less	90% less
about 10% to about 30% less	about 10% to about 30% less	about 10% to about 30% less	about 10% to about 30% less	about 10% to about 30% less	about 10% to about 30% less
about 20% to about 50% less	about 20% to about 50% less	about 20% to about 50% less	about 20% to about 50% less	about 20% to about 50% less	about 20% to about 50% less
about 30% to about 70% less	about 30% to about 70% less	about 30% to about 70% less	about 30% to about 70% less	about 30% to about 70% less	about 30% to about 70% less
about 20% to about 80% less	about 20% to about 80% less	about 20% to about 80% less	about 20% to about 80% less	about 20% to about 80% less	about 20% to about 80% less
Duration of illness	Duration of illness	Duration of illness	Severity of symptom(s)	Severity of symptom(s)	Severity of symptom(s)
10% less	60% less	about 10% to about 30% less	10% less	60% less	about 10% to about 30% less
25% less	70% less	about 20% to about 50% less	25% less	70% less	about 20% to about 50% less
40% less	80% less	about 30% to about 70% less	40% less	80% less	about 30% to about 70% less
50% less	90% less	about 20% to about 80% less	50% less	90% less	about 20% to about 80% less

[0132] In some embodiments, the compound can be a compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, wherein R^{1A} is hydrogen. In other embodiments, the compound can be a compound of Formulae (I) and/or (II), wherein compound of Formulae (I) and/or (II) is a mono, di, or triphosphate, or a pharmaceutically

acceptable salt of the foregoing. In still other embodiments, the compound can be a compound of Formulae (I) and/or (II), wherein compound of Formulae (I) and/or (II) is a thiomonophosphate, alpha-thiodiphosphate, or alpha-thiotriphosphate, or a pharmaceutically acceptable salt of the foregoing. In some embodiments, the compound of Formulae (I) and/or (II), or a pharmaceutical acceptable salt of the foregoing, that can be used to ameliorate and/or treat a Picornavirus infection and/or inhibit replication of a Picornavirus can be any of the embodiments provided in any of the embodiments described in paragraphs [0173]-[0291].

[0133] As used herein, a “subject” refers to an animal that is the object of treatment, observation or experiment. “Animal” includes cold- and warm-blooded vertebrates and invertebrates such as fish, shellfish, reptiles and, in particular, mammals. “Mammal” includes, without limitation, mice, rats, rabbits, guinea pigs, dogs, cats, sheep, goats, cows, horses, primates, such as monkeys, chimpanzees, and apes, and, in particular, humans. In some embodiments, the subject is human.

[0134] As used herein, the terms “treating,” “treatment,” “therapeutic,” or “therapy” do not necessarily mean total cure or abolition of the disease or condition. Any alleviation of any undesired signs or symptoms of a disease or condition, to any extent can be considered treatment and/or therapy. Furthermore, treatment may include acts that may worsen the patient's overall feeling of well-being or appearance.

[0135] The terms “therapeutically effective amount” and “effective amount” are used to indicate an amount of an active compound, or pharmaceutical agent, that elicits the biological or medicinal response indicated. For example, an effective amount of compound can be the amount needed to prevent, alleviate or ameliorate symptoms of disease or prolong the survival of the subject being treated. This response may occur in a tissue, system, animal or human and includes alleviation of the signs or symptoms of the disease being treated. Determination of an effective amount is well within the capability of those skilled in the art, in view of the disclosure provided herein. The effective amount of the compounds disclosed herein required as a dose will depend on the route of administration, the type of animal, including human, being treated, and the physical characteristics of the specific animal under consideration. The dose can be tailored to achieve a desired effect, but will depend on such

factors as weight, diet, concurrent medication and other factors which those skilled in the medical arts will recognize.

[0136] As will be readily apparent to one skilled in the art, the useful *in vivo* dosage to be administered and the particular mode of administration will vary depending upon the age, weight, the severity of the affliction, and mammalian species treated, the particular compounds employed, and the specific use for which these compounds are employed. The determination of effective dosage levels, that is the dosage levels necessary to achieve the desired result, can be accomplished by one skilled in the art using routine methods, for example, human clinical trials and *in vitro* studies.

[0137] The dosage may range broadly, depending upon the desired effects and the therapeutic indication. Alternatively dosages may be based and calculated upon the surface area of the patient, as understood by those of skill in the art. Although the exact dosage will be determined on a drug-by-drug basis, in most cases, some generalizations regarding the dosage can be made. The daily dosage regimen for an adult human patient may be, for example, an oral dose of between 0.01 mg and 3000 mg of each active ingredient, preferably between 1 mg and 700 mg, e.g. 5 to 200 mg. The dosage may be a single one or a series of two or more given in the course of one or more days, as is needed by the subject. In some embodiments, the compounds will be administered for a period of continuous therapy, for example for a week or more, or for months or years. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered less frequently compared to the frequency of administration of an agent within the standard of care. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered one time per day. For example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered one time per day to a subject suffering from a HCV infection. In some embodiments, the total time of the treatment regime with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be less compared to the total time of the treatment regime with the standard of care.

[0138] In instances where human dosages for compounds have been established for at least some condition, those same dosages may be used, or dosages that are between about 0.1% and 500%, more preferably between about 25% and 250% of the established

human dosage. Where no human dosage is established, as will be the case for newly-discovered pharmaceutical compositions, a suitable human dosage can be inferred from ED₅₀ or ID₅₀ values, or other appropriate values derived from *in vitro* or *in vivo* studies, as qualified by toxicity studies and efficacy studies in animals.

[0139] In cases of administration of a pharmaceutically acceptable salt, dosages may be calculated as the free base. As will be understood by those of skill in the art, in certain situations it may be necessary to administer the compounds disclosed herein in amounts that exceed, or even far exceed, the above-stated, preferred dosage range in order to effectively and aggressively treat particularly aggressive diseases or infections.

[0140] Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the modulating effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations. Dosage intervals can also be determined using MEC value. Compositions should be administered using a regimen which maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

[0141] It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity or organ dysfunctions. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administered dose in the management of the disorder of interest will vary with the severity of the condition to be treated and to the route of administration. The severity of the condition may, for example, be evaluated, in part, by standard prognostic evaluation methods. Further, the dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that discussed above may be used in veterinary medicine.

[0142] Compounds disclosed herein can be evaluated for efficacy and toxicity using known methods. For example, the toxicology of a particular compound, or of a subset

of the compounds, sharing certain chemical moieties, may be established by determining *in vitro* toxicity towards a cell line, such as a mammalian, and preferably human, cell line. The results of such studies are often predictive of toxicity in animals, such as mammals, or more specifically, humans. Alternatively, the toxicity of particular compounds in an animal model, such as mice, rats, rabbits, or monkeys, may be determined using known methods. The efficacy of a particular compound may be established using several recognized methods, such as *in vitro* methods, animal models, or human clinical trials. When selecting a model to determine efficacy, the skilled artisan can be guided by the state of the art to choose an appropriate model, dose, route of administration and/or regime.

[0143] As described herein, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have a moiety(ies) that neutralize the charge of the phosphate or thiophosphate. By neutralizing the charge on the phosphate or thiophosphate, penetration of the cell membrane may be facilitated as a result of the increased lipophilicity of the compound. Once absorbed and taken inside the cell, the groups attached to the phosphorus can be easily removed by esterases, proteases and/or other enzymes. In some embodiments, the groups attached to the phosphorus can be removed by simple hydrolysis. Inside the cell, the phosphate thus released may then be metabolized by cellular enzymes to the diphosphate or the active triphosphate. Likewise, the thio-phosphate may be metabolized to the alpha-thiodiphosphate or the alpha-thiotriphosphate. Furthermore, in some embodiments, varying the substituents on a compound described herein, such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can help maintain the efficacy of such the compound by reducing undesirable effects, such as isomerization.

[0144] In some embodiments, the phosphorylation of a thio-monophosphate of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be stereoselective. For example, a thio-monophosphate of a compound of Formulae (I) and/or (II) can be phosphorylated to give an alpha-thiodiphosphate and/or an alpha-thiotriphosphate compound that can be enriched in the (*R*) or (*S*) diastereomer with respect to the 5'-O-phosphorous atom. For example, one of the (*R*) and (*S*) configuration with respect to the 5'-O-phosphorous atom of the alpha-thiodiphosphate and/or the alpha-thiotriphosphate compound can be present in an amount > 50%, ≥ 75%, ≥ 90%, ≥ 95% or ≥ 99% compared to

the amount of the other of the (*R*) or (*S*) configuration with respect to the 5'-O-phosphorous atom. In some embodiments, phosphorylation of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in the formation of a compound that has the (*R*)-configuration at the 5'-O-phosphorous atom. In some embodiments, phosphorylation of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can result in formation of a compound that has the (*S*)-configuration at the 5'-O-phosphorous atom.

[0145] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can act as a chain terminator of RNA synthesis. For example, compounds of Formulae (I) and/or (II) can contain a moiety at the 2'-carbon position such that once the compound is incorporated into an RNA chain, no further elongation is observed to occur. For example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can contain a non-hydrogen 2'-carbon modification such as an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl or an optionally substituted C₂₋₆ alkynyl.

[0146] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have increased metabolic and/or plasma stability. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be more resistant to hydrolysis and/or more resistant to enzymatic transformations. For example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have increased metabolic stability, increased plasma stability, can be more resistant to hydrolysis and/or can be more resistant to enzymatic transformations compared to a compound that is identical in structure but for having O¹ as OH, R^A, R^{2A}, R^{5A}, R^{a1} and R^{a2} are each hydrogen and R^{3A} and R^{4A} are each OH. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have improved properties. A non-limiting list of example properties include, but are not limited to, increased biological half-life, increased bioavailability, increase potency, a sustained in vivo response, increased dosing intervals, decreased dosing amounts, decreased cytotoxicity, reduction in required amounts for treating disease conditions, reduction in viral load, reduction in time to seroconversion (i.e., the virus becomes undetectable in patient serum), increased sustained

viral response, a reduction of morbidity or mortality in clinical outcomes, increased subject compliance, decreased liver conditions (such as liver fibrosis, liver cirrhosis and/or liver cancer), and compatibility with other medications. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have a biological half-life of greater than 24 hours. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have a biological half-life greater than a compound that is identical in structure but for having O¹ as OH, R^A, R^{2A}, R^{5A}, R^{a1} and R^{a2} are each hydrogen and R^{3A} and R^{4A} are each OH. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can have more potent antiviral activity compared to a compound that is identical in structure but for having O¹ as OH, R^A, R^{2A}, R^{5A}, R^{a1} and R^{a2} are each hydrogen and R^{3A} and R^{4A} are each OH.

[0147] Additionally, in some embodiments, the presence of a moiety(ies) that neutralizes the charge of the phosphate or thiophosphate can increase the stability of the compound by inhibiting its degradation. Also, in some embodiments, the presence of a moiety(ies) that neutralizes the charge of the phosphate or thiophosphate can make the compound more resistant to cleavage *in vivo* and provide sustained, extended efficacy. In some embodiments, a moiety(ies) that neutralizes the charge of the phosphate or thiophosphate can facilitate the penetration of the cell membrane by a compound of Formulae (I) and/or (II) by making the compound more lipophilic. In some embodiments, a moiety(ies) that neutralizes the charge of the phosphate or thiophosphate can have improved oral bioavailability, improved aqueous stability and/or reduced risk of byproduct-related toxicity. In some embodiments, for comparison purposes, a compound of Formulae (I) and/or (II) can be compared to a compound that is identical in structure but for having O¹ as OH, R^A, R^{2A}, R^{5A}, R^{a1} and R^{a2} are each hydrogen and R^{3A} and R^{4A} are each OH.

Combination Therapies

[0148] In some embodiments, the compounds disclosed herein, such as a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound described herein, or a pharmaceutically acceptable salt thereof, can be used in combination with one or more

additional agent(s) for treating, ameliorating and/or inhibiting a Picornavirus and/or *Flaviviridae* viral infection.

[0149] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered with one or more additional agent(s) together in a single pharmaceutical composition. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered with one or more additional agent(s) as two or more separate pharmaceutical compositions. For example, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered in one pharmaceutical composition, and at least one of the additional agents can be administered in a second pharmaceutical composition. If there are at least two additional agents, one or more of the additional agents can be in a first pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and at least one of the other additional agent(s) can be in a second pharmaceutical composition.

[0150] The dosing amount(s) and dosing schedule(s) when using a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and one or more additional agents are within the knowledge of those skilled in the art. For example, when performing a conventional standard of care therapy using art-recognized dosing amounts and dosing schedules, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered in addition to that therapy, or in place of one of the agents of a combination therapy, using effective amounts and dosing protocols as described herein.

[0151] The order of administration of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, with one or more additional agent(s) can vary. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered prior to all additional agents. In other embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered prior to at least one additional agent. In still other

embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered concomitantly with one or more additional agent(s). In yet still other embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered subsequent to the administration of at least one additional agent. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be administered subsequent to the administration of all additional agents.

[0152] In some embodiments, the combination of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more additional agent(s) can result in an additive effect. In some embodiments, the combination of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, used in combination with one or more additional agent(s) can result in a synergistic effect. In some embodiments, the combination of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, used in combination with one or more additional agent(s) can result in a strongly synergistic effect. In some embodiments, the combination of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more additional agent(s) is not antagonistic.

[0153] As used herein, the term “antagonistic” means that the activity of the combination of compounds is less compared to the sum of the activities of the compounds in combination when the activity of each compound is determined individually (i.e. as a single compound). As used herein, the term “synergistic effect” means that the activity of the combination of compounds is greater than the sum of the individual activities of the compounds in the combination when the activity of each compound is determined individually. As used herein, the term “additive effect” means that the activity of the combination of compounds is about equal to the sum of the individual activities of the compound in the combination when the activity of each compound is determined individually.

[0154] A potential advantage of utilizing a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more additional agent(s) may be a reduction in the required amount(s) of one or more additional

agent(s) that is effective in treating a disease condition disclosed herein (for example, picornavirus and/or *Flaviviridae* virus infection), as compared to the amount required to achieve same therapeutic result when one or more additional agent(s) are administered without a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing. For example, for treating HCV, the amount of a compound in Figures 1-9 (including a pharmaceutically acceptable salt thereof), can be less compared to the amount of the compound in Figures 1-9 (including a pharmaceutically acceptable salt thereof), needed to achieve the same viral load reduction when administered as a monotherapy. Another potential advantage of utilizing a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more additional agent(s) is that the use of two or more compounds having different mechanism of actions can create a higher barrier to the development of resistant viral strains compared to the barrier when a compound is administered as monotherapy.

[0155] Additional advantages of utilizing a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more additional agent(s) may include little to no cross resistance between a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and one or more additional agent(s) thereof; different routes for elimination of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and one or more additional agent(s); little to no overlapping toxicities between a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and one or more additional agent(s); little to no significant effects on cytochrome P450; little to no pharmacokinetic interactions between a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, and one or more additional agent(s); greater percentage of subjects achieving a sustained viral response compared to when a compound is administered as monotherapy and/or a decrease in treatment time to achieve a sustained viral response compared to when a compound is administered as monotherapy.

[0156] For treating of a picornavirus and/or a *Flaviviridae* virus infection other than HCV, examples of additional agents that can be used in combination with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a

pharmaceutically acceptable salt of the foregoing, include, but are not limited to, ribavirin and an interferon (including those described herein).

[0157] For the treatment of HCV, examples of additional agents that can be used in combination with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, include, but are not limited to, agents currently used in a conventional standard of care for treating HCV, HCV protease inhibitors, HCV polymerase inhibitors, NS5A inhibitors, other antiviral compounds, compounds of Formula (AA), (including pharmaceutically acceptable salts and pharmaceutical compositions that can include a compound of Formula (AA), or a pharmaceutically acceptable salt thereof), compounds of Formula (BB) (including pharmaceutically acceptable salts and pharmaceutical compositions that can include a compound of Formula (BB), or a pharmaceutically acceptable salt thereof), compounds of Formula (CC) (including pharmaceutically acceptable salts and pharmaceutical compositions that can include a compound of Formula (CC), or a pharmaceutically acceptable salt thereof), and/or combinations thereof. In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used with one, two, three or more additional agents described herein. A non-limiting list of examples of combinations of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, is provided in Tables A, B, C, D and E.

[0158] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with an agent(s) currently used in a conventional standard of care therapy. For example, for the treatment of HCV, a compound disclosed herein can be used in combination with Pegylated interferon-alpha-2a (brand name PEGASYS®) and ribavirin, Pegylated interferon-alpha-2b (brand name PEG-INTRON®) and ribavirin, Pegylated interferon-alpha-2a, Pegylated interferon-alpha-2b, or ribavirin.

[0159] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be substituted for an agent currently used in a conventional standard of care therapy. For example, for the treatment of HCV, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in place of ribavirin.

[0160] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with an interferon, such as a pegylated interferon. Examples of suitable interferons include, but are not limited to, Pegylated interferon-alpha-2a (brand name PEGASYS®), Pegylated interferon-alpha-2b (brand name PEG-INTRON®), interferon alfacon-1 (brand name INFERGEN®), pegylated interferon lambda and/or a combination thereof.

[0161] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a HCV protease inhibitor. A non-limiting list of example HCV protease inhibitors include the following: VX-950 (TELAPREVIR®), MK-5172, ABT-450, BILN-2061, BI-201335, BMS-650032, SCH 503034 (BOCEPREVIR®), GS-9256, GS-9451, IDX-320, ACH-1625, ACH-2684, TMC-435, ITMN-191 (DANOPREVIR®) and/or a combination thereof. Additional HCV protease inhibitors suitable for use in combination with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, include VP-19744, PSI-879, VCH-759/VX-759, HCV-371, IDX-375, GL-60667, JTK-109, PSI-6130, R1479, R-1626, R-7182, MK-0608, INX-8014, INX-8018, A-848837, A-837093, BILB-1941, VCH-916, VCH-716, GSK-71185, GSK-625433, XTL-2125 and those disclosed in PCT Publication No. WO 2012/142085, for the limited purpose of its

disclosure of HCV protease inhibitors, HCV polymerase inhibitors and NS5A inhibitors. A non-limiting list of example HCV protease inhibitors includes the compounds numbered 1001-1016 in Figure 1.

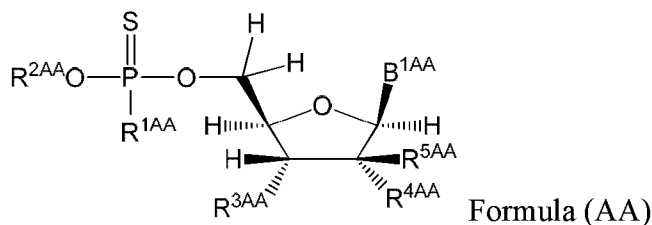
[0162] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a HCV polymerase inhibitor. In some embodiments, the HCV polymerase inhibitor can be a nucleoside inhibitor. In other embodiments, the HCV polymerase inhibitor can be a non-nucleoside inhibitor. Examples of suitable nucleoside inhibitors include, but are not limited to, RG7128, PSI-7851, PSI-7977, INX-189, PSI-352938, PSI-661, 4'-azidouridine (including known prodrugs of 4'-azidouridine), GS-6620, IDX-184, and TMC649128 and/or combinations thereof. A non-limiting list of example nucleoside inhibitors includes compounds numbered 2001-2012 in Figure 2. Examples of suitable non-nucleoside inhibitors include, but are not limited to, ABT-333, ANA-598, VX-222, HCV-796, BI-207127, GS-9190, PF-00868554 (FILIBUVIR®), VX-497 and/or combinations thereof. A non-limiting list of example non-nucleoside inhibitors includes the compounds numbered 3001-3014 in Figure 3. Further HCV polymerase inhibitors suitable for use in combination with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, include VX-500, VX-813, VBY-376, TMC-435350, EZ-058, EZ-063, GS-9132, ACH-1095, IDX-136, IDX-316, ITMN-8356, ITMN-8347, ITMN-8096, ITMN-7587, VX-985, and those disclosed in PCT Publication No. WO 2012/142085.

[0163] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a NS5A inhibitor. Examples of NS5A inhibitors include BMS-790052, PPI-461, ACH-2928, GS-5885, BMS-824393 and/or combinations thereof. A non-limiting list of example NS5A inhibitors includes the compounds numbered 4001-4012 in Figure 4. Additional NS5A inhibitors suitable for use in combination with a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing,

or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, include A-832, PPI-1301 and those disclosed in PCT Publication No. WO 2012/142085.

[0164] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with other antiviral compounds. Examples of other antiviral compounds include, but are not limited to, Debio-025, a MIR-122 inhibitor (for example, Miravirsen (SPC3649)), cyclosporin A and/or combinations thereof. A non-limiting list of example other antiviral compounds includes the compounds numbered 5001-5011 in Figure 5.

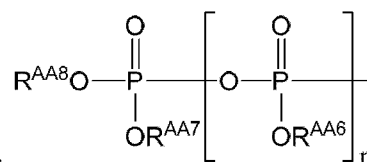
[0165] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a compound of Formula (AA), or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition that includes a compound of Formula (AA), or a pharmaceutically acceptable salt thereof (see, U.S. Publication No. 2013/0164261 A1, filed December 20, 2012):



wherein: B^{AA1} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; R^{AA1} can be selected from O⁻, OH, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{AA2} can be absent or selected from hydrogen, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and

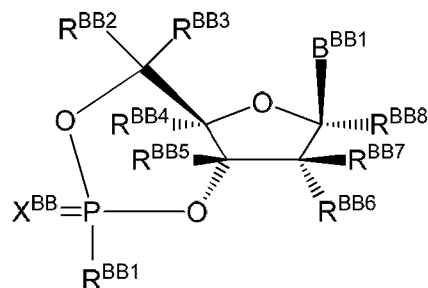


hydrogen, and n^{AA} can be 0 or 1; provided that when R^{AA1} is O or OH, then R^{AA2} is absent,



hydrogen or R^{AA3} can be selected from hydrogen, halogen, -OR^{AA9} and -OC(=O)R^{AA10}; R^{AA4} can be selected from halogen, -OR^{AA11} and -OC(=O)R^{AA12}; or R^{AA3} and R^{AA4} can be both an oxygen atom which are linked together by a carbonyl group; R^{AA5} can be selected from an optionally substituted C₂₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl, an optionally substituted C₂₋₆ alkynyl and an optionally substituted C₃₋₆ cycloalkyl; or R^{AA4} and R^{AA5} together can form -(C₁₋₆ alkyl)-O- or -O-(C₁₋₆ alkyl)-; R^{AA9} and R^{AA11} can be independently hydrogen or an optionally substituted C₁₋₆ alkyl; and R^{AA10} and R^{AA12} can be independently an optionally substituted C₁₋₆ alkyl or an optionally substituted C₃₋₆ cycloalkyl. A non-limiting list of examples of compounds of Formula (AA) includes the compounds numbered 7000-7027 in Figure 7.

[0166] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a compound of Formula (BB), or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition that includes a compound of Formula (BB), or a pharmaceutically acceptable salt thereof (see, U.S. Publication No. 2012/0165286, published June 28, 2012):



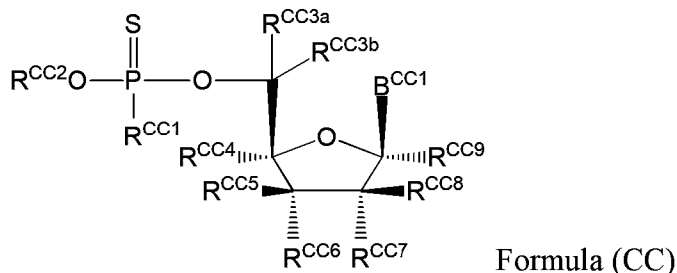
Formula (BB)

wherein B^{BB1} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; X^{BB} can be O (oxygen) or S (sulfur); R^{BB1} can be selected from $-Z^{BB}-R^{BB9}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; Z^{BB} can be selected from O (oxygen), S (sulfur) and N(R^{BB10}); R^{BB2} and R^{BB3} can be independently selected from

hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl, an optionally substituted C₂₋₆ alkynyl, an optionally substituted C₁₋₆ haloalkyl and an optionally substituted aryl(C₁₋₆ alkyl); or R^{BB2} and R^{BB3} can be taken together to form a group selected from an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl, an optionally substituted C₃₋₆ aryl and an optionally substituted C₃₋₆ heteroaryl; R^{BB4} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl, an optionally substituted C₂₋₆ alkynyl and an optionally substituted allenyl; R^{BB5} can be hydrogen or an optionally substituted C₁₋₆ alkyl; R^{BB6} can be selected from hydrogen, halogen, azido, amino, cyano, an optionally substituted C₁₋₆ alkyl, -OR^{BB11} and -OC(=O)R^{BB12}; R^{BB7} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C₁₋₆ alkyl, -OR^{BB13} and -OC(=O)R^{BB14}; R^{BB8} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C₁₋₆ alkyl, -OR^{BB15} and -OC(=O)R^{BB16}; R^{BB9} can be selected from an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted aryl(C₁₋₆alkyl), an optionally substituted heteroaryl(C₁₋₆alkyl) and an optionally substituted heterocyclyl(C₁₋₆alkyl); R^{BB10} can be selected from hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted aryl(C₁₋₆alkyl), an optionally substituted heteroaryl(C₁₋₆alkyl) and an optionally substituted heterocyclyl(C₁₋₆alkyl); R^{BB11}, R^{BB13} and R^{BB15} can be independently hydrogen or an optionally substituted C₁₋₆ alkyl; and R^{BB12}, R^{BB14} and R^{BB16} can be independently an optionally substituted C₁₋₆ alkyl or an optionally substituted C₃₋₆ cycloalkyl. In some embodiments, at least one of R^{BB2} and R^{BB3} is not hydrogen. A non-limiting list of example compounds of Formula (BB) includes the compound numbered 8000-8016 in Figure 8.

[0167] In some embodiments, a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, can be used in combination with a compound of Formula (CC), or a

pharmaceutically acceptable salt thereof, or a pharmaceutical composition that includes a compound of Formula (CC), or a pharmaceutically acceptable salt thereof (see, U.S. Publication No. 2012/0071434, published March 22, 2012):



wherein B^{CC1} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; R^{CC1} can be selected from O^- , OH, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{CC2} can be selected from an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocycl

and $R^{CC21}O-P(=O)(OR^{CC20})-O-P(=O)(OR^{CC19})-O-$ $\left[O-P(=O)(OR^{CC19})-O- \right]_{n^{CC}}$, wherein R^{CC19} , R^{CC20} and R^{CC21} can be independently absent or hydrogen, and n^{CC} can be 0 or 1; provided that when R^{CC1} is O^- or OH, then R^{CC2}

is $R^{CC21}O-P(=O)(OR^{CC20})-O-P(=O)(OR^{CC19})-O-$ $\left[O-P(=O)(OR^{CC19})-O- \right]_{n^{CC}}$; R^{CC3a} and R^{CC3b} can be independently selected from hydrogen, deuterium, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl, an optionally substituted C_{2-6} alkynyl, an optionally substituted C_{1-6} haloalkyl and aryl(C_{1-6} alkyl); or R^{CC3a} and R^{CC3b} can be taken together to form an optionally substituted C_{3-6} cycloalkyl; R^{CC4} can be selected from hydrogen, azido, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl; R^{CC5} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C_{1-6} alkyl, $-OR^{CC10}$ and $-OC(=O)R^{CC11}$; R^{CC6} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C_{1-6} alkyl, $-OR^{CC12}$ and $-OC(=O)R^{CC13}$; R^{CC7} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C_{1-6} alkyl, $-OR^{CC14}$ and $-OC(=O)R^{CC15}$; or R^{CC6} and R^{CC7} can be both oxygen atoms and linked together by a carbonyl group; R^{CC8} can be selected from hydrogen, halogen, azido, cyano, an optionally substituted C_{1-6} alkyl, -

OR^{CC16} and -OC(=O)R^{CC17}; R^{CC9} can be selected from hydrogen, azido, cyano, an optionally substituted C₁₋₆ alkyl and -OR^{CC18}; R^{CC10}, R^{CC12}, R^{CC14}, R^{CC16} and R^{CC18} can be independently selected from hydrogen and an optionally substituted C₁₋₆ alkyl; and R^{CC11}, R^{CC13}, R^{CC15} and R^{CC17} can be independently selected from an optionally substituted C₁₋₆ alkyl and an optionally substituted C₃₋₆ cycloalkyl. In some embodiments, when R^{CC3a}, R^{CC3b}, R^{CC4}, R^{CC5}, R^{CC7}, R^{CC8} and R^{CC9} are all hydrogen, then R^{CC6} is not azido. In some

embodiments, R^{CC2} cannot be
$$\text{R}^{\text{CC21}}\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{OR}^{\text{CC20}} \end{array}\right)-\left[\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{OR}^{\text{CC19}} \end{array}\right)\right]_{\text{n}^{\text{CC}}}$$
 when R^{CC3a} is hydrogen, R^{CC3b} is hydrogen, R^{CC4} is H, R^{CC5} is OH or H, R^{CC6} is hydrogen, OH, or -OC(=O)CH₃, R^{CC7} is hydrogen, OH, OCH₃ or -OC(=O)CH₃, R^{CC8} is hydrogen, OH or OCH₃, R^{CC9} is H and B^{CC1} is an optionally substituted adenine, an optionally substituted guanine, an optionally substituted uracil or an optionally substituted hypoxanthine. In some embodiments, R^{CC2}

cannot be
$$\text{R}^{\text{CC21}}\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{OR}^{\text{CC20}} \end{array}\right)-\left[\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{OR}^{\text{CC19}} \end{array}\right)\right]_{\text{n}^{\text{CC}}}$$
. A non-limiting list of examples of compounds of Formula (CC) includes the compounds numbered 6000-6078 in Figure 6.

[0168] Some embodiments described herein relate to a method of ameliorating or treating a Picornavirus and/or a *Flaviviridae* viral infection that can include contacting a cell infected with the virus with an effective amount of a compound of Formulae (I) and/or (II),

or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds. Some embodiments described herein relate to a method of ameliorating or treating a HCV infection that can include contacting a cell infected with the HCV infection with an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds.

[0169] Some embodiments described herein relate to a method of ameliorating or treating a Picornavirus and/or a *Flaviviridae* viral infection that can include administering to a subject suffering from the viral infection an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds. Some embodiments described herein relate to a method of ameliorating or treating a HCV infection that can include administering to a subject suffering from the HCV infection an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds.

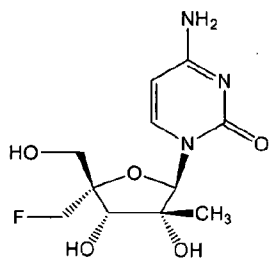
[0170] Some embodiments described herein relate to a method of inhibiting the replication of a Picornavirus and/or a *Flaviviridae* virus that can include contacting a cell infected with the virus with an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of

any of the aforementioned compounds. Some embodiments described herein relate to a method of inhibiting the replication of a hepatitis C virus that can include contacting a cell infected with the hepatitis C virus with an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds.

[0171] Some embodiments described herein relate to a method of inhibiting the replication of a Picornavirus and/or a *Flaviviridae* virus that can include administering to a subject infected with the virus an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds. Some embodiments described herein relate to a method of inhibiting the replication of a hepatitis C virus that can include administering to a subject infected with the hepatitis C virus an effective amount of a compound of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, in combination with one or more agents selected from an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB), a compound of Formula (CC), or a pharmaceutically acceptable salt of any of the aforementioned compounds.

[0172] A non-limiting list of example combination of compounds of Formulae (I) and/or (II), or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition that includes a compound described herein, with one or more additional agent(s) are provided in Tables A, B, C, D and E. Each numbered X and Y compound in Tables A, B, C, D and E has a corresponding name and/or structure provided in Figures 1-9. The numbered compounds in Tables A, B, C, D and E includes pharmaceutically acceptable salts of the compounds and pharmaceutical compositions containing the compounds or a pharmaceutically acceptable salt thereof. For example, 1001 includes the compound corresponding to 1001, pharmaceutically acceptable salts thereof, and pharmaceutical

compositions that include compound 1001 and/or a pharmaceutically acceptable salt thereof. The combinations exemplified in Tables A, B, C, D and E are designated by the formula X:Y, which represents a combination of a compound X with a compound Y. For example, the combination designated as 1001:9044 in Table A represents a combination of compound 1001 with compound 9044, including pharmaceutically acceptable salts of compound 1001 and/or 9044, and pharmaceutical compositions including compound 1001 and 9044 (including pharmaceutical compositions that include pharmaceutically acceptable salts of compound 1001 and/or compound 9044). Thus, the combination designated as 1001:9044 in Table A represents the combination of Telaprevir (compound 1001, as shown in Figure 1)



and (compound 9044, as shown in Figure 9), including pharmaceutically acceptable salts of compound 1001 and/or 9044, and pharmaceutical compositions including compound 1001 and 9044 (including pharmaceutical compositions that include pharmaceutically acceptable salts of compound 1001 and/or compound 9044). Each of the combinations provided in Tables A, B, C, D and E can be used with one, two, three or more additional agents described herein. In some embodiments described herein, the combination of agents can be used to treat, ameliorate and/or inhibit a virus and/or a viral infection, wherein the virus can be Picornavirus and/or *Flaviviridae* virus and the viral infection can be a Picornavirus viral infection and/or *Flaviviridae* virus.

Table A: Example combinations of a compound X with a compound Y.

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9006	1001 : 9007	1001 : 9008	1001 : 9018	1001 : 9020	1001 : 9021
1002 : 9006	1002 : 9007	1002 : 9008	1002 : 9018	1002 : 9020	1002 : 9021
1003 : 9006	1003 : 9007	1003 : 9008	1003 : 9018	1003 : 9020	1003 : 9021
1004 : 9006	1004 : 9007	1004 : 9008	1004 : 9018	1004 : 9020	1004 : 9021
1005 : 9006	1005 : 9007	1005 : 9008	1005 : 9018	1005 : 9020	1005 : 9021
1006 : 9006	1006 : 9007	1006 : 9008	1006 : 9018	1006 : 9020	1006 : 9021
1007 : 9006	1007 : 9007	1007 : 9008	1007 : 9018	1007 : 9020	1007 : 9021
1008 : 9006	1008 : 9007	1008 : 9008	1008 : 9018	1008 : 9020	1008 : 9021
1009 : 9006	1009 : 9007	1009 : 9008	1009 : 9018	1009 : 9020	1009 : 9021
1010 : 9006	1010 : 9007	1010 : 9008	1010 : 9018	1010 : 9020	1010 : 9021
1011 : 9006	1011 : 9007	1011 : 9008	1011 : 9018	1011 : 9020	1011 : 9021
1012 : 9006	1012 : 9007	1012 : 9008	1012 : 9018	1012 : 9020	1012 : 9021
1013 : 9006	1013 : 9007	1013 : 9008	1013 : 9018	1013 : 9020	1013 : 9021
1014 : 9006	1014 : 9007	1014 : 9008	1014 : 9018	1014 : 9020	1014 : 9021
1015 : 9006	1015 : 9007	1015 : 9008	1015 : 9018	1015 : 9020	1015 : 9021
1016 : 9006	1016 : 9007	1016 : 9008	1016 : 9018	1016 : 9020	1016 : 9021
2001 : 9006	2001 : 9007	2001 : 9008	2001 : 9018	2001 : 9020	2001 : 9021
2002 : 9006	2002 : 9007	2002 : 9008	2002 : 9018	2002 : 9020	2002 : 9021
2003 : 9006	2003 : 9007	2003 : 9008	2003 : 9018	2003 : 9020	2003 : 9021
2004 : 9006	2004 : 9007	2004 : 9008	2004 : 9018	2004 : 9020	2004 : 9021
2005 : 9006	2005 : 9007	2005 : 9008	2005 : 9018	2005 : 9020	2005 : 9021
2006 : 9006	2006 : 9007	2006 : 9008	2006 : 9018	2006 : 9020	2006 : 9021
2007 : 9006	2007 : 9007	2007 : 9008	2007 : 9018	2007 : 9020	2007 : 9021
2008 : 9006	2008 : 9007	2008 : 9008	2008 : 9018	2008 : 9020	2008 : 9021
2009 : 9006	2009 : 9007	2009 : 9008	2009 : 9018	2009 : 9020	2009 : 9021
2010 : 9006	2010 : 9007	2010 : 9008	2010 : 9018	2010 : 9020	2010 : 9021
2011 : 9006	2011 : 9007	2011 : 9008	2011 : 9018	2011 : 9020	2011 : 9021
2012 : 9006	2012 : 9007	2012 : 9008	2012 : 9018	2012 : 9020	2012 : 9021

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9025	1001 : 9026	1001 : 9036	1001 : 9038	1001 : 9039	1001 : 9040
1002 : 9025	1002 : 9026	1002 : 9036	1002 : 9038	1002 : 9039	1002 : 9040
1003 : 9025	1003 : 9026	1003 : 9036	1003 : 9038	1003 : 9039	1003 : 9040
1004 : 9025	1004 : 9026	1004 : 9036	1004 : 9038	1004 : 9039	1004 : 9040
1005 : 9025	1005 : 9026	1005 : 9036	1005 : 9038	1005 : 9039	1005 : 9040
1006 : 9025	1006 : 9026	1006 : 9036	1006 : 9038	1006 : 9039	1006 : 9040
1007 : 9025	1007 : 9026	1007 : 9036	1007 : 9038	1007 : 9039	1007 : 9040
1008 : 9025	1008 : 9026	1008 : 9036	1008 : 9038	1008 : 9039	1008 : 9040
1009 : 9025	1009 : 9026	1009 : 9036	1009 : 9038	1009 : 9039	1009 : 9040
1010 : 9025	1010 : 9026	1010 : 9036	1010 : 9038	1010 : 9039	1010 : 9040
1011 : 9025	1011 : 9026	1011 : 9036	1011 : 9038	1011 : 9039	1011 : 9040
1012 : 9025	1012 : 9026	1012 : 9036	1012 : 9038	1012 : 9039	1012 : 9040
1013 : 9025	1013 : 9026	1013 : 9036	1013 : 9038	1013 : 9039	1013 : 9040
1014 : 9025	1014 : 9026	1014 : 9036	1014 : 9038	1014 : 9039	1014 : 9040
1015 : 9025	1015 : 9026	1015 : 9036	1015 : 9038	1015 : 9039	1015 : 9040
1016 : 9025	1016 : 9026	1016 : 9036	1016 : 9038	1016 : 9039	1016 : 9040
2001 : 9025	2001 : 9026	2001 : 9036	2001 : 9038	2001 : 9039	2001 : 9040
2002 : 9025	2002 : 9026	2002 : 9036	2002 : 9038	2002 : 9039	2002 : 9040
2003 : 9025	2003 : 9026	2003 : 9036	2003 : 9038	2003 : 9039	2003 : 9040
2004 : 9025	2004 : 9026	2004 : 9036	2004 : 9038	2004 : 9039	2004 : 9040
2005 : 9025	2005 : 9026	2005 : 9036	2005 : 9038	2005 : 9039	2005 : 9040
2006 : 9025	2006 : 9026	2006 : 9036	2006 : 9038	2006 : 9039	2006 : 9040
2007 : 9025	2007 : 9026	2007 : 9036	2007 : 9038	2007 : 9039	2007 : 9040
2008 : 9025	2008 : 9026	2008 : 9036	2008 : 9038	2008 : 9039	2008 : 9040
2009 : 9025	2009 : 9026	2009 : 9036	2009 : 9038	2009 : 9039	2009 : 9040
2010 : 9025	2010 : 9026	2010 : 9036	2010 : 9038	2010 : 9039	2010 : 9040
2011 : 9025	2011 : 9026	2011 : 9036	2011 : 9038	2011 : 9039	2011 : 9040
2012 : 9025	2012 : 9026	2012 : 9036	2012 : 9038	2012 : 9039	2012 : 9040

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9041	1001 : 9042	1001 : 9043	1001 : 9044	1001 : 9045	1001 : 9047
1002 : 9041	1002 : 9042	1002 : 9043	1002 : 9044	1002 : 9045	1002 : 9047
1003 : 9041	1003 : 9042	1003 : 9043	1003 : 9044	1003 : 9045	1003 : 9047
1004 : 9041	1004 : 9042	1004 : 9043	1004 : 9044	1004 : 9045	1004 : 9047
1005 : 9041	1005 : 9042	1005 : 9043	1005 : 9044	1005 : 9045	1005 : 9047
1006 : 9041	1006 : 9042	1006 : 9043	1006 : 9044	1006 : 9045	1006 : 9047
1007 : 9041	1007 : 9042	1007 : 9043	1007 : 9044	1007 : 9045	1007 : 9047
1008 : 9041	1008 : 9042	1008 : 9043	1008 : 9044	1008 : 9045	1008 : 9047
1009 : 9041	1009 : 9042	1009 : 9043	1009 : 9044	1009 : 9045	1009 : 9047
1010 : 9041	1010 : 9042	1010 : 9043	1010 : 9044	1010 : 9045	1010 : 9047
1011 : 9041	1011 : 9042	1011 : 9043	1011 : 9044	1011 : 9045	1011 : 9047
1012 : 9041	1012 : 9042	1012 : 9043	1012 : 9044	1012 : 9045	1012 : 9047
1013 : 9041	1013 : 9042	1013 : 9043	1013 : 9044	1013 : 9045	1013 : 9047
1014 : 9041	1014 : 9042	1014 : 9043	1014 : 9044	1014 : 9045	1014 : 9047
1015 : 9041	1015 : 9042	1015 : 9043	1015 : 9044	1015 : 9045	1015 : 9047
1016 : 9041	1016 : 9042	1016 : 9043	1016 : 9044	1016 : 9045	1016 : 9047
2001 : 9041	2001 : 9042	2001 : 9043	2001 : 9044	2001 : 9045	2001 : 9047
2002 : 9041	2002 : 9042	2002 : 9043	2002 : 9044	2002 : 9045	2002 : 9047
2003 : 9041	2003 : 9042	2003 : 9043	2003 : 9044	2003 : 9045	2003 : 9047
2004 : 9041	2004 : 9042	2004 : 9043	2004 : 9044	2004 : 9045	2004 : 9047
2005 : 9041	2005 : 9042	2005 : 9043	2005 : 9044	2005 : 9045	2005 : 9047
2006 : 9041	2006 : 9042	2006 : 9043	2006 : 9044	2006 : 9045	2006 : 9047
2007 : 9041	2007 : 9042	2007 : 9043	2007 : 9044	2007 : 9045	2007 : 9047
2008 : 9041	2008 : 9042	2008 : 9043	2008 : 9044	2008 : 9045	2008 : 9047
2009 : 9041	2009 : 9042	2009 : 9043	2009 : 9044	2009 : 9045	2009 : 9047
2010 : 9041	2010 : 9042	2010 : 9043	2010 : 9044	2010 : 9045	2010 : 9047
2011 : 9041	2011 : 9042	2011 : 9043	2011 : 9044	2011 : 9045	2011 : 9047
2012 : 9041	2012 : 9042	2012 : 9043	2012 : 9044	2012 : 9045	2012 : 9047

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9048	1001 : 9049	1001 : 9051	1001 : 9052	1001 : 9053	1001 : 9054
1002 : 9048	1002 : 9049	1002 : 9051	1002 : 9052	1002 : 9053	1002 : 9054
1003 : 9048	1003 : 9049	1003 : 9051	1003 : 9052	1003 : 9053	1003 : 9054
1004 : 9048	1004 : 9049	1004 : 9051	1004 : 9052	1004 : 9053	1004 : 9054
1005 : 9048	1005 : 9049	1005 : 9051	1005 : 9052	1005 : 9053	1005 : 9054
1006 : 9048	1006 : 9049	1006 : 9051	1006 : 9052	1006 : 9053	1006 : 9054
1007 : 9048	1007 : 9049	1007 : 9051	1007 : 9052	1007 : 9053	1007 : 9054
1008 : 9048	1008 : 9049	1008 : 9051	1008 : 9052	1008 : 9053	1008 : 9054
1009 : 9048	1009 : 9049	1009 : 9051	1009 : 9052	1009 : 9053	1009 : 9054
1010 : 9048	1010 : 9049	1010 : 9051	1010 : 9052	1010 : 9053	1010 : 9054
1011 : 9048	1011 : 9049	1011 : 9051	1011 : 9052	1011 : 9053	1011 : 9054
1012 : 9048	1012 : 9049	1012 : 9051	1012 : 9052	1012 : 9053	1012 : 9054
1013 : 9048	1013 : 9049	1013 : 9051	1013 : 9052	1013 : 9053	1013 : 9054
1014 : 9048	1014 : 9049	1014 : 9051	1014 : 9052	1014 : 9053	1014 : 9054
1015 : 9048	1015 : 9049	1015 : 9051	1015 : 9052	1015 : 9053	1015 : 9054
1016 : 9048	1016 : 9049	1016 : 9051	1016 : 9052	1016 : 9053	1016 : 9054
2001 : 9048	2001 : 9049	2001 : 9051	2001 : 9052	2001 : 9053	2001 : 9054
2002 : 9048	2002 : 9049	2002 : 9051	2002 : 9052	2002 : 9053	2002 : 9054
2003 : 9048	2003 : 9049	2003 : 9051	2003 : 9052	2003 : 9053	2003 : 9054
2004 : 9048	2004 : 9049	2004 : 9051	2004 : 9052	2004 : 9053	2004 : 9054
2005 : 9048	2005 : 9049	2005 : 9051	2005 : 9052	2005 : 9053	2005 : 9054
2006 : 9048	2006 : 9049	2006 : 9051	2006 : 9052	2006 : 9053	2006 : 9054
2007 : 9048	2007 : 9049	2007 : 9051	2007 : 9052	2007 : 9053	2007 : 9054
2008 : 9048	2008 : 9049	2008 : 9051	2008 : 9052	2008 : 9053	2008 : 9054
2009 : 9048	2009 : 9049	2009 : 9051	2009 : 9052	2009 : 9053	2009 : 9054
2010 : 9048	2010 : 9049	2010 : 9051	2010 : 9052	2010 : 9053	2010 : 9054
2011 : 9048	2011 : 9049	2011 : 9051	2011 : 9052	2011 : 9053	2011 : 9054
2012 : 9048	2012 : 9049	2012 : 9051	2012 : 9052	2012 : 9053	2012 : 9054

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9055	1001 : 9056	1001 : 9058	1001 : 9060	1001 : 9061	1001 : 9062
1002 : 9055	1002 : 9056	1002 : 9058	1002 : 9060	1002 : 9061	1002 : 9062
1003 : 9055	1003 : 9056	1003 : 9058	1003 : 9060	1003 : 9061	1003 : 9062
1004 : 9055	1004 : 9056	1004 : 9058	1004 : 9060	1004 : 9061	1004 : 9062
1005 : 9055	1005 : 9056	1005 : 9058	1005 : 9060	1005 : 9061	1005 : 9062
1006 : 9055	1006 : 9056	1006 : 9058	1006 : 9060	1006 : 9061	1006 : 9062
1007 : 9055	1007 : 9056	1007 : 9058	1007 : 9060	1007 : 9061	1007 : 9062
1008 : 9055	1008 : 9056	1008 : 9058	1008 : 9060	1008 : 9061	1008 : 9062
1009 : 9055	1009 : 9056	1009 : 9058	1009 : 9060	1009 : 9061	1009 : 9062
1010 : 9055	1010 : 9056	1010 : 9058	1010 : 9060	1010 : 9061	1010 : 9062
1011 : 9055	1011 : 9056	1011 : 9058	1011 : 9060	1011 : 9061	1011 : 9062
1012 : 9055	1012 : 9056	1012 : 9058	1012 : 9060	1012 : 9061	1012 : 9062
1013 : 9055	1013 : 9056	1013 : 9058	1013 : 9060	1013 : 9061	1013 : 9062
1014 : 9055	1014 : 9056	1014 : 9058	1014 : 9060	1014 : 9061	1014 : 9062
1015 : 9055	1015 : 9056	1015 : 9058	1015 : 9060	1015 : 9061	1015 : 9062
1016 : 9055	1016 : 9056	1016 : 9058	1016 : 9060	1016 : 9061	1016 : 9062
2001 : 9055	2001 : 9056	2001 : 9058	2001 : 9060	2001 : 9061	2001 : 9062
2002 : 9055	2002 : 9056	2002 : 9058	2002 : 9060	2002 : 9061	2002 : 9062
2003 : 9055	2003 : 9056	2003 : 9058	2003 : 9060	2003 : 9061	2003 : 9062
2004 : 9055	2004 : 9056	2004 : 9058	2004 : 9060	2004 : 9061	2004 : 9062
2005 : 9055	2005 : 9056	2005 : 9058	2005 : 9060	2005 : 9061	2005 : 9062
2006 : 9055	2006 : 9056	2006 : 9058	2006 : 9060	2006 : 9061	2006 : 9062
2007 : 9055	2007 : 9056	2007 : 9058	2007 : 9060	2007 : 9061	2007 : 9062
2008 : 9055	2008 : 9056	2008 : 9058	2008 : 9060	2008 : 9061	2008 : 9062
2009 : 9055	2009 : 9056	2009 : 9058	2009 : 9060	2009 : 9061	2009 : 9062
2010 : 9055	2010 : 9056	2010 : 9058	2010 : 9060	2010 : 9061	2010 : 9062
2011 : 9055	2011 : 9056	2011 : 9058	2011 : 9060	2011 : 9061	2011 : 9062
2012 : 9055	2012 : 9056	2012 : 9058	2012 : 9060	2012 : 9061	2012 : 9062

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9063	1001 : 9064	1001 : 9065	1001 : 9066	1001 : 9067	1001 : 9068
1002 : 9063	1002 : 9064	1002 : 9065	1002 : 9066	1002 : 9067	1002 : 9068
1003 : 9063	1003 : 9064	1003 : 9065	1003 : 9066	1003 : 9067	1003 : 9068
1004 : 9063	1004 : 9064	1004 : 9065	1004 : 9066	1004 : 9067	1004 : 9068
1005 : 9063	1005 : 9064	1005 : 9065	1005 : 9066	1005 : 9067	1005 : 9068
1006 : 9063	1006 : 9064	1006 : 9065	1006 : 9066	1006 : 9067	1006 : 9068
1007 : 9063	1007 : 9064	1007 : 9065	1007 : 9066	1007 : 9067	1007 : 9068
1008 : 9063	1008 : 9064	1008 : 9065	1008 : 9066	1008 : 9067	1008 : 9068
1009 : 9063	1009 : 9064	1009 : 9065	1009 : 9066	1009 : 9067	1009 : 9068
1010 : 9063	1010 : 9064	1010 : 9065	1010 : 9066	1010 : 9067	1010 : 9068
1011 : 9063	1011 : 9064	1011 : 9065	1011 : 9066	1011 : 9067	1011 : 9068
1012 : 9063	1012 : 9064	1012 : 9065	1012 : 9066	1012 : 9067	1012 : 9068
1013 : 9063	1013 : 9064	1013 : 9065	1013 : 9066	1013 : 9067	1013 : 9068
1014 : 9063	1014 : 9064	1014 : 9065	1014 : 9066	1014 : 9067	1014 : 9068
1015 : 9063	1015 : 9064	1015 : 9065	1015 : 9066	1015 : 9067	1015 : 9068
1016 : 9063	1016 : 9064	1016 : 9065	1016 : 9066	1016 : 9067	1016 : 9068
2001 : 9063	2001 : 9064	2001 : 9065	2001 : 9066	2001 : 9067	2001 : 9068
2002 : 9063	2002 : 9064	2002 : 9065	2002 : 9066	2002 : 9067	2002 : 9068
2003 : 9063	2003 : 9064	2003 : 9065	2003 : 9066	2003 : 9067	2003 : 9068
2004 : 9063	2004 : 9064	2004 : 9065	2004 : 9066	2004 : 9067	2004 : 9068
2005 : 9063	2005 : 9064	2005 : 9065	2005 : 9066	2005 : 9067	2005 : 9068
2006 : 9063	2006 : 9064	2006 : 9065	2006 : 9066	2006 : 9067	2006 : 9068
2007 : 9063	2007 : 9064	2007 : 9065	2007 : 9066	2007 : 9067	2007 : 9068
2008 : 9063	2008 : 9064	2008 : 9065	2008 : 9066	2008 : 9067	2008 : 9068
2009 : 9063	2009 : 9064	2009 : 9065	2009 : 9066	2009 : 9067	2009 : 9068
2010 : 9063	2010 : 9064	2010 : 9065	2010 : 9066	2010 : 9067	2010 : 9068
2011 : 9063	2011 : 9064	2011 : 9065	2011 : 9066	2011 : 9067	2011 : 9068
2012 : 9063	2012 : 9064	2012 : 9065	2012 : 9066	2012 : 9067	2012 : 9068

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9069	1001 : 9070	1001 : 9071	1001 : 9072	1001 : 9073	1001 : 9074
1002 : 9069	1002 : 9070	1002 : 9071	1002 : 9072	1002 : 9073	1002 : 9074
1003 : 9069	1003 : 9070	1003 : 9071	1003 : 9072	1003 : 9073	1003 : 9074
1004 : 9069	1004 : 9070	1004 : 9071	1004 : 9072	1004 : 9073	1004 : 9074
1005 : 9069	1005 : 9070	1005 : 9071	1005 : 9072	1005 : 9073	1005 : 9074
1006 : 9069	1006 : 9070	1006 : 9071	1006 : 9072	1006 : 9073	1006 : 9074
1007 : 9069	1007 : 9070	1007 : 9071	1007 : 9072	1007 : 9073	1007 : 9074
1008 : 9069	1008 : 9070	1008 : 9071	1008 : 9072	1008 : 9073	1008 : 9074
1009 : 9069	1009 : 9070	1009 : 9071	1009 : 9072	1009 : 9073	1009 : 9074
1010 : 9069	1010 : 9070	1010 : 9071	1010 : 9072	1010 : 9073	1010 : 9074
1011 : 9069	1011 : 9070	1011 : 9071	1011 : 9072	1011 : 9073	1011 : 9074
1012 : 9069	1012 : 9070	1012 : 9071	1012 : 9072	1012 : 9073	1012 : 9074
1013 : 9069	1013 : 9070	1013 : 9071	1013 : 9072	1013 : 9073	1013 : 9074
1014 : 9069	1014 : 9070	1014 : 9071	1014 : 9072	1014 : 9073	1014 : 9074
1015 : 9069	1015 : 9070	1015 : 9071	1015 : 9072	1015 : 9073	1015 : 9074
1016 : 9069	1016 : 9070	1016 : 9071	1016 : 9072	1016 : 9073	1016 : 9074
2001 : 9069	2001 : 9070	2001 : 9071	2001 : 9072	2001 : 9073	2001 : 9074
2002 : 9069	2002 : 9070	2002 : 9071	2002 : 9072	2002 : 9073	2002 : 9074
2003 : 9069	2003 : 9070	2003 : 9071	2003 : 9072	2003 : 9073	2003 : 9074
2004 : 9069	2004 : 9070	2004 : 9071	2004 : 9072	2004 : 9073	2004 : 9074
2005 : 9069	2005 : 9070	2005 : 9071	2005 : 9072	2005 : 9073	2005 : 9074
2006 : 9069	2006 : 9070	2006 : 9071	2006 : 9072	2006 : 9073	2006 : 9074
2007 : 9069	2007 : 9070	2007 : 9071	2007 : 9072	2007 : 9073	2007 : 9074
2008 : 9069	2008 : 9070	2008 : 9071	2008 : 9072	2008 : 9073	2008 : 9074
2009 : 9069	2009 : 9070	2009 : 9071	2009 : 9072	2009 : 9073	2009 : 9074
2010 : 9069	2010 : 9070	2010 : 9071	2010 : 9072	2010 : 9073	2010 : 9074
2011 : 9069	2011 : 9070	2011 : 9071	2011 : 9072	2011 : 9073	2011 : 9074
2012 : 9069	2012 : 9070	2012 : 9071	2012 : 9072	2012 : 9073	2012 : 9074

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
1001:9075	1001:9076	1001:9077	1001:9078	1001:9079	1001:9080
1002:9075	1002:9076	1002:9077	1002:9078	1002:9079	1002:9080
1003:9075	1003:9076	1003:9077	1003:9078	1003:9079	1003:9080
1004:9075	1004:9076	1004:9077	1004:9078	1004:9079	1004:9080
1005:9075	1005:9076	1005:9077	1005:9078	1005:9079	1005:9080
1006:9075	1006:9076	1006:9077	1006:9078	1006:9079	1006:9080
1007:9075	1007:9076	1007:9077	1007:9078	1007:9079	1007:9080
1008:9075	1008:9076	1008:9077	1008:9078	1008:9079	1008:9080
1009:9075	1009:9076	1009:9077	1009:9078	1009:9079	1009:9080
1010:9075	1010:9076	1010:9077	1010:9078	1010:9079	1010:9080
1011:9075	1011:9076	1011:9077	1011:9078	1011:9079	1011:9080
1012:9075	1012:9076	1012:9077	1012:9078	1012:9079	1012:9080
1013:9075	1013:9076	1013:9077	1013:9078	1013:9079	1013:9080
1014:9075	1014:9076	1014:9077	1014:9078	1014:9079	1014:9080
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2007 : 9264	2007 : 9265	2007 : 9266	2007 : 9267	2007 : 9268	2007 : 9269
2008 : 9264	2008 : 9265	2008 : 9266	2008 : 9267	2008 : 9268	2008 : 9269
2009 : 9264	2009 : 9265	2009 : 9266	2009 : 9267	2009 : 9268	2009 : 9269
2010 : 9264	2010 : 9265	2010 : 9266	2010 : 9267	2010 : 9268	2010 : 9269
2011 : 9264	2011 : 9265	2011 : 9266	2011 : 9267	2011 : 9268	2011 : 9269
2012 : 9264	2012 : 9265	2012 : 9266	2012 : 9267	2012 : 9268	2012 : 9269

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9270	1001 : 9271	1001 : 9272	1001 : 9273	1001 : 9274	1001 : 9275
1002 : 9270	1002 : 9271	1002 : 9272	1002 : 9273	1002 : 9274	1002 : 9275
1003 : 9270	1003 : 9271	1003 : 9272	1003 : 9273	1003 : 9274	1003 : 9275
1004 : 9270	1004 : 9271	1004 : 9272	1004 : 9273	1004 : 9274	1004 : 9275
1005 : 9270	1005 : 9271	1005 : 9272	1005 : 9273	1005 : 9274	1005 : 9275
1006 : 9270	1006 : 9271	1006 : 9272	1006 : 9273	1006 : 9274	1006 : 9275
1007 : 9270	1007 : 9271	1007 : 9272	1007 : 9273	1007 : 9274	1007 : 9275
1008 : 9270	1008 : 9271	1008 : 9272	1008 : 9273	1008 : 9274	1008 : 9275
1009 : 9270	1009 : 9271	1009 : 9272	1009 : 9273	1009 : 9274	1009 : 9275
1010 : 9270	1010 : 9271	1010 : 9272	1010 : 9273	1010 : 9274	1010 : 9275
1011 : 9270	1011 : 9271	1011 : 9272	1011 : 9273	1011 : 9274	1011 : 9275
1012 : 9270	1012 : 9271	1012 : 9272	1012 : 9273	1012 : 9274	1012 : 9275
1013 : 9270	1013 : 9271	1013 : 9272	1013 : 9273	1013 : 9274	1013 : 9275
1014 : 9270	1014 : 9271	1014 : 9272	1014 : 9273	1014 : 9274	1014 : 9275
1015 : 9270	1015 : 9271	1015 : 9272	1015 : 9273	1015 : 9274	1015 : 9275
1016 : 9270	1016 : 9271	1016 : 9272	1016 : 9273	1016 : 9274	1016 : 9275
2001 : 9270	2001 : 9271	2001 : 9272	2001 : 9273	2001 : 9274	2001 : 9275
2002 : 9270	2002 : 9271	2002 : 9272	2002 : 9273	2002 : 9274	2002 : 9275
2003 : 9270	2003 : 9271	2003 : 9272	2003 : 9273	2003 : 9274	2003 : 9275
2004 : 9270	2004 : 9271	2004 : 9272	2004 : 9273	2004 : 9274	2004 : 9275
2005 : 9270	2005 : 9271	2005 : 9272	2005 : 9273	2005 : 9274	2005 : 9275
2006 : 9270	2006 : 9271	2006 : 9272	2006 : 9273	2006 : 9274	2006 : 9275
2007 : 9270	2007 : 9271	2007 : 9272	2007 : 9273	2007 : 9274	2007 : 9275
2008 : 9270	2008 : 9271	2008 : 9272	2008 : 9273	2008 : 9274	2008 : 9275
2009 : 9270	2009 : 9271	2009 : 9272	2009 : 9273	2009 : 9274	2009 : 9275
2010 : 9270	2010 : 9271	2010 : 9272	2010 : 9273	2010 : 9274	2010 : 9275
2011 : 9270	2011 : 9271	2011 : 9272	2011 : 9273	2011 : 9274	2011 : 9275
2012 : 9270	2012 : 9271	2012 : 9272	2012 : 9273	2012 : 9274	2012 : 9275

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9276	1001 : 9277	1001 : 9278	1001 : 9279	1001 : 9280	1001 : 9281
1002 : 9276	1002 : 9277	1002 : 9278	1002 : 9279	1002 : 9280	1002 : 9281
1003 : 9276	1003 : 9277	1003 : 9278	1003 : 9279	1003 : 9280	1003 : 9281
1004 : 9276	1004 : 9277	1004 : 9278	1004 : 9279	1004 : 9280	1004 : 9281
1005 : 9276	1005 : 9277	1005 : 9278	1005 : 9279	1005 : 9280	1005 : 9281
1006 : 9276	1006 : 9277	1006 : 9278	1006 : 9279	1006 : 9280	1006 : 9281
1007 : 9276	1007 : 9277	1007 : 9278	1007 : 9279	1007 : 9280	1007 : 9281
1008 : 9276	1008 : 9277	1008 : 9278	1008 : 9279	1008 : 9280	1008 : 9281
1009 : 9276	1009 : 9277	1009 : 9278	1009 : 9279	1009 : 9280	1009 : 9281
1010 : 9276	1010 : 9277	1010 : 9278	1010 : 9279	1010 : 9280	1010 : 9281
1011 : 9276	1011 : 9277	1011 : 9278	1011 : 9279	1011 : 9280	1011 : 9281
1012 : 9276	1012 : 9277	1012 : 9278	1012 : 9279	1012 : 9280	1012 : 9281
1013 : 9276	1013 : 9277	1013 : 9278	1013 : 9279	1013 : 9280	1013 : 9281
1014 : 9276	1014 : 9277	1014 : 9278	1014 : 9279	1014 : 9280	1014 : 9281
1015 : 9276	1015 : 9277	1015 : 9278	1015 : 9279	1015 : 9280	1015 : 9281
1016 : 9276	1016 : 9277	1016 : 9278	1016 : 9279	1016 : 9280	1016 : 9281
2001 : 9276	2001 : 9277	2001 : 9278	2001 : 9279	2001 : 9280	2001 : 9281
2002 : 9276	2002 : 9277	2002 : 9278	2002 : 9279	2002 : 9280	2002 : 9281
2003 : 9276	2003 : 9277	2003 : 9278	2003 : 9279	2003 : 9280	2003 : 9281
2004 : 9276	2004 : 9277	2004 : 9278	2004 : 9279	2004 : 9280	2004 : 9281
2005 : 9276	2005 : 9277	2005 : 9278	2005 : 9279	2005 : 9280	2005 : 9281
2006 : 9276	2006 : 9277	2006 : 9278	2006 : 9279	2006 : 9280	2006 : 9281
2007 : 9276	2007 : 9277	2007 : 9278	2007 : 9279	2007 : 9280	2007 : 9281
2008 : 9276	2008 : 9277	2008 : 9278	2008 : 9279	2008 : 9280	2008 : 9281
2009 : 9276	2009 : 9277	2009 : 9278	2009 : 9279	2009 : 9280	2009 : 9281
2010 : 9276	2010 : 9277	2010 : 9278	2010 : 9279	2010 : 9280	2010 : 9281
2011 : 9276	2011 : 9277	2011 : 9278	2011 : 9279	2011 : 9280	2011 : 9281
2012 : 9276	2012 : 9277	2012 : 9278	2012 : 9279	2012 : 9280	2012 : 9281

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9282	1001 : 9283	1001 : 9284	1001 : 9285	1001 : 9286	1001 : 9287
1002 : 9282	1002 : 9283	1002 : 9284	1002 : 9285	1002 : 9286	1002 : 9287
1003 : 9282	1003 : 9283	1003 : 9284	1003 : 9285	1003 : 9286	1003 : 9287
1004 : 9282	1004 : 9283	1004 : 9284	1004 : 9285	1004 : 9286	1004 : 9287
1005 : 9282	1005 : 9283	1005 : 9284	1005 : 9285	1005 : 9286	1005 : 9287
1006 : 9282	1006 : 9283	1006 : 9284	1006 : 9285	1006 : 9286	1006 : 9287
1007 : 9282	1007 : 9283	1007 : 9284	1007 : 9285	1007 : 9286	1007 : 9287
1008 : 9282	1008 : 9283	1008 : 9284	1008 : 9285	1008 : 9286	1008 : 9287
1009 : 9282	1009 : 9283	1009 : 9284	1009 : 9285	1009 : 9286	1009 : 9287
1010 : 9282	1010 : 9283	1010 : 9284	1010 : 9285	1010 : 9286	1010 : 9287
1011 : 9282	1011 : 9283	1011 : 9284	1011 : 9285	1011 : 9286	1011 : 9287
1012 : 9282	1012 : 9283	1012 : 9284	1012 : 9285	1012 : 9286	1012 : 9287
1013 : 9282	1013 : 9283	1013 : 9284	1013 : 9285	1013 : 9286	1013 : 9287
1014 : 9282	1014 : 9283	1014 : 9284	1014 : 9285	1014 : 9286	1014 : 9287
1015 : 9282	1015 : 9283	1015 : 9284	1015 : 9285	1015 : 9286	1015 : 9287
1016 : 9282	1016 : 9283	1016 : 9284	1016 : 9285	1016 : 9286	1016 : 9287
2001 : 9282	2001 : 9283	2001 : 9284	2001 : 9285	2001 : 9286	2001 : 9287
2002 : 9282	2002 : 9283	2002 : 9284	2002 : 9285	2002 : 9286	2002 : 9287
2003 : 9282	2003 : 9283	2003 : 9284	2003 : 9285	2003 : 9286	2003 : 9287
2004 : 9282	2004 : 9283	2004 : 9284	2004 : 9285	2004 : 9286	2004 : 9287
2005 : 9282	2005 : 9283	2005 : 9284	2005 : 9285	2005 : 9286	2005 : 9287
2006 : 9282	2006 : 9283	2006 : 9284	2006 : 9285	2006 : 9286	2006 : 9287
2007 : 9282	2007 : 9283	2007 : 9284	2007 : 9285	2007 : 9286	2007 : 9287
2008 : 9282	2008 : 9283	2008 : 9284	2008 : 9285	2008 : 9286	2008 : 9287
2009 : 9282	2009 : 9283	2009 : 9284	2009 : 9285	2009 : 9286	2009 : 9287
2010 : 9282	2010 : 9283	2010 : 9284	2010 : 9285	2010 : 9286	2010 : 9287
2011 : 9282	2011 : 9283	2011 : 9284	2011 : 9285	2011 : 9286	2011 : 9287
2012 : 9282	2012 : 9283	2012 : 9284	2012 : 9285	2012 : 9286	2012 : 9287

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9288	1001 : 9289	1001 : 9290	1001 : 9291	1001 : 9292	1001 : 9293
1002 : 9288	1002 : 9289	1002 : 9290	1002 : 9291	1002 : 9292	1002 : 9293
1003 : 9288	1003 : 9289	1003 : 9290	1003 : 9291	1003 : 9292	1003 : 9293
1004 : 9288	1004 : 9289	1004 : 9290	1004 : 9291	1004 : 9292	1004 : 9293
1005 : 9288	1005 : 9289	1005 : 9290	1005 : 9291	1005 : 9292	1005 : 9293
1006 : 9288	1006 : 9289	1006 : 9290	1006 : 9291	1006 : 9292	1006 : 9293
1007 : 9288	1007 : 9289	1007 : 9290	1007 : 9291	1007 : 9292	1007 : 9293
1008 : 9288	1008 : 9289	1008 : 9290	1008 : 9291	1008 : 9292	1008 : 9293
1009 : 9288	1009 : 9289	1009 : 9290	1009 : 9291	1009 : 9292	1009 : 9293
1010 : 9288	1010 : 9289	1010 : 9290	1010 : 9291	1010 : 9292	1010 : 9293
1011 : 9288	1011 : 9289	1011 : 9290	1011 : 9291	1011 : 9292	1011 : 9293
1012 : 9288	1012 : 9289	1012 : 9290	1012 : 9291	1012 : 9292	1012 : 9293
1013 : 9288	1013 : 9289	1013 : 9290	1013 : 9291	1013 : 9292	1013 : 9293
1014 : 9288	1014 : 9289	1014 : 9290	1014 : 9291	1014 : 9292	1014 : 9293
1015 : 9288	1015 : 9289	1015 : 9290	1015 : 9291	1015 : 9292	1015 : 9293
1016 : 9288	1016 : 9289	1016 : 9290	1016 : 9291	1016 : 9292	1016 : 9293
2001 : 9288	2001 : 9289	2001 : 9290	2001 : 9291	2001 : 9292	2001 : 9293
2002 : 9288	2002 : 9289	2002 : 9290	2002 : 9291	2002 : 9292	2002 : 9293
2003 : 9288	2003 : 9289	2003 : 9290	2003 : 9291	2003 : 9292	2003 : 9293
2004 : 9288	2004 : 9289	2004 : 9290	2004 : 9291	2004 : 9292	2004 : 9293
2005 : 9288	2005 : 9289	2005 : 9290	2005 : 9291	2005 : 9292	2005 : 9293
2006 : 9288	2006 : 9289	2006 : 9290	2006 : 9291	2006 : 9292	2006 : 9293
2007 : 9288	2007 : 9289	2007 : 9290	2007 : 9291	2007 : 9292	2007 : 9293
2008 : 9288	2008 : 9289	2008 : 9290	2008 : 9291	2008 : 9292	2008 : 9293
2009 : 9288	2009 : 9289	2009 : 9290	2009 : 9291	2009 : 9292	2009 : 9293
2010 : 9288	2010 : 9289	2010 : 9290	2010 : 9291	2010 : 9292	2010 : 9293
2011 : 9288	2011 : 9289	2011 : 9290	2011 : 9291	2011 : 9292	2011 : 9293
2012 : 9288	2012 : 9289	2012 : 9290	2012 : 9291	2012 : 9292	2012 : 9293

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9294	1001 : 9295	1001 : 9296	1001 : 9297	1001 : 9298	1001 : 9299
1002 : 9294	1002 : 9295	1002 : 9296	1002 : 9297	1002 : 9298	1002 : 9299
1003 : 9294	1003 : 9295	1003 : 9296	1003 : 9297	1003 : 9298	1003 : 9299
1004 : 9294	1004 : 9295	1004 : 9296	1004 : 9297	1004 : 9298	1004 : 9299
1005 : 9294	1005 : 9295	1005 : 9296	1005 : 9297	1005 : 9298	1005 : 9299
1006 : 9294	1006 : 9295	1006 : 9296	1006 : 9297	1006 : 9298	1006 : 9299
1007 : 9294	1007 : 9295	1007 : 9296	1007 : 9297	1007 : 9298	1007 : 9299
1008 : 9294	1008 : 9295	1008 : 9296	1008 : 9297	1008 : 9298	1008 : 9299
1009 : 9294	1009 : 9295	1009 : 9296	1009 : 9297	1009 : 9298	1009 : 9299
1010 : 9294	1010 : 9295	1010 : 9296	1010 : 9297	1010 : 9298	1010 : 9299
1011 : 9294	1011 : 9295	1011 : 9296	1011 : 9297	1011 : 9298	1011 : 9299
1012 : 9294	1012 : 9295	1012 : 9296	1012 : 9297	1012 : 9298	1012 : 9299
1013 : 9294	1013 : 9295	1013 : 9296	1013 : 9297	1013 : 9298	1013 : 9299
1014 : 9294	1014 : 9295	1014 : 9296	1014 : 9297	1014 : 9298	1014 : 9299
1015 : 9294	1015 : 9295	1015 : 9296	1015 : 9297	1015 : 9298	1015 : 9299
1016 : 9294	1016 : 9295	1016 : 9296	1016 : 9297	1016 : 9298	1016 : 9299
2001 : 9294	2001 : 9295	2001 : 9296	2001 : 9297	2001 : 9298	2001 : 9299
2002 : 9294	2002 : 9295	2002 : 9296	2002 : 9297	2002 : 9298	2002 : 9299
2003 : 9294	2003 : 9295	2003 : 9296	2003 : 9297	2003 : 9298	2003 : 9299
2004 : 9294	2004 : 9295	2004 : 9296	2004 : 9297	2004 : 9298	2004 : 9299
2005 : 9294	2005 : 9295	2005 : 9296	2005 : 9297	2005 : 9298	2005 : 9299
2006 : 9294	2006 : 9295	2006 : 9296	2006 : 9297	2006 : 9298	2006 : 9299
2007 : 9294	2007 : 9295	2007 : 9296	2007 : 9297	2007 : 9298	2007 : 9299
2008 : 9294	2008 : 9295	2008 : 9296	2008 : 9297	2008 : 9298	2008 : 9299
2009 : 9294	2009 : 9295	2009 : 9296	2009 : 9297	2009 : 9298	2009 : 9299
2010 : 9294	2010 : 9295	2010 : 9296	2010 : 9297	2010 : 9298	2010 : 9299
2011 : 9294	2011 : 9295	2011 : 9296	2011 : 9297	2011 : 9298	2011 : 9299
2012 : 9294	2012 : 9295	2012 : 9296	2012 : 9297	2012 : 9298	2012 : 9299

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
1001 : 9300	1001 : 9301	1001 : 9302	1001 : 9303	1001 : 9304	1001 : 9305
1002 : 9300	1002 : 9301	1002 : 9302	1002 : 9303	1002 : 9304	1002 : 9305
1003 : 9300	1003 : 9301	1003 : 9302	1003 : 9303	1003 : 9304	1003 : 9305
1004 : 9300	1004 : 9301	1004 : 9302	1004 : 9303	1004 : 9304	1004 : 9305
1005 : 9300	1005 : 9301	1005 : 9302	1005 : 9303	1005 : 9304	1005 : 9305
1006 : 9300	1006 : 9301	1006 : 9302	1006 : 9303	1006 : 9304	1006 : 9305
1007 : 9300	1007 : 9301	1007 : 9302	1007 : 9303	1007 : 9304	1007 : 9305
1008 : 9300	1008 : 9301	1008 : 9302	1008 : 9303	1008 : 9304	1008 : 9305
1009 : 9300	1009 : 9301	1009 : 9302	1009 : 9303	1009 : 9304	1009 : 9305
1010 : 9300	1010 : 9301	1010 : 9302	1010 : 9303	1010 : 9304	1010 : 9305
1011 : 9300	1011 : 9301	1011 : 9302	1011 : 9303	1011 : 9304	1011 : 9305
1012 : 9300	1012 : 9301	1012 : 9302	1012 : 9303	1012 : 9304	1012 : 9305
1013 : 9300	1013 : 9301	1013 : 9302	1013 : 9303	1013 : 9304	1013 : 9305
1014 : 9300	1014 : 9301	1014 : 9302	1014 : 9303	1014 : 9304	1014 : 9305
1015 : 9300	1015 : 9301	1015 : 9302	1015 : 9303	1015 : 9304	1015 : 9305
1016 : 9300	1016 : 9301	1016 : 9302	1016 : 9303	1016 : 9304	1016 : 9305
2001 : 9300	2001 : 9301	2001 : 9302	2001 : 9303	2001 : 9304	2001 : 9305
2002 : 9300	2002 : 9301	2002 : 9302	2002 : 9303	2002 : 9304	2002 : 9305
2003 : 9300	2003 : 9301	2003 : 9302	2003 : 9303	2003 : 9304	2003 : 9305
2004 : 9300	2004 : 9301	2004 : 9302	2004 : 9303	2004 : 9304	2004 : 9305
2005 : 9300	2005 : 9301	2005 : 9302	2005 : 9303	2005 : 9304	2005 : 9305
2006 : 9300	2006 : 9301	2006 : 9302	2006 : 9303	2006 : 9304	2006 : 9305
2007 : 9300	2007 : 9301	2007 : 9302	2007 : 9303	2007 : 9304	2007 : 9305
2008 : 9300	2008 : 9301	2008 : 9302	2008 : 9303	2008 : 9304	2008 : 9305
2009 : 9300	2009 : 9301	2009 : 9302	2009 : 9303	2009 : 9304	2009 : 9305
2010 : 9300	2010 : 9301	2010 : 9302	2010 : 9303	2010 : 9304	2010 : 9305
2011 : 9300	2011 : 9301	2011 : 9302	2011 : 9303	2011 : 9304	2011 : 9305
2012 : 9300	2012 : 9301	2012 : 9302	2012 : 9303	2012 : 9304	2012 : 9305

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
1001:9306	1001:9307	1001:9308	1001:9309	1001:9310	
1002:9306	1002:9307	1002:9308	1002:9309	1002:9310	
1003:9306	1003:9307	1003:9308	1003:9309	1003:9310	
1004:9306	1004:9307	1004:9308	1004:9309	1004:9310	
1005:9306	1005:9307	1005:9308	1005:9309	1005:9310	
1006:9306	1006:9307	1006:9308	1006:9309	1006:9310	
1007:9306	1007:9307	1007:9308	1007:9309	1007:9310	
1008:9306	1008:9307	1008:9308	1008:9309	1008:9310	
1009:9306	1009:9307	1009:9308	1009:9309	1009:9310	
1010:9306	1010:9307	1010:9308	1010:9309	1010:9310	
1011:9306	1011:9307	1011:9308	1011:9309	1011:9310	
1012:9306	1012:9307	1012:9308	1012:9309	1012:9310	
1013:9306	1013:9307	1013:9308	1013:9309	1013:9310	
1014:9306	1014:9307	1014:9308	1014:9309	1014:9310	
1015:9306	1015:9307	1015:9308	1015:9309	1015:9310	
1016:9306	1016:9307	1016:9308	1016:9309	1016:9310	
2001:9306	2001:9307	2001:9308	2001:9309	2001:9310	
2002:9306	2002:9307	2002:9308	2002:9309	2002:9310	
2003:9306	2003:9307	2003:9308	2003:9309	2003:9310	
2004:9306	2004:9307	2004:9308	2004:9309	2004:9310	
2005:9306	2005:9307	2005:9308	2005:9309	2005:9310	
2006:9306	2006:9307	2006:9308	2006:9309	2006:9310	
2007:9306	2007:9307	2007:9308	2007:9309	2007:9310	
2008:9306	2008:9307	2008:9308	2008:9309	2008:9310	
2009:9306	2009:9307	2009:9308	2009:9309	2009:9310	
2010:9306	2010:9307	2010:9308	2010:9309	2010:9310	
2011:9306	2011:9307	2011:9308	2011:9309	2011:9310	
2012:9306	2012:9307	2012:9308	2012:9309	2012:9310	

Table B: Example combinations of a compound X with a compound Y.

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
3002 : 9006	3002 : 9007	3002 : 9008	3002 : 9018	3002 : 9020	3002 : 9021
3003 : 9006	3003 : 9007	3003 : 9008	3003 : 9018	3003 : 9020	3003 : 9021
3004 : 9006	3004 : 9007	3004 : 9008	3004 : 9018	3004 : 9020	3004 : 9021
3005 : 9006	3005 : 9007	3005 : 9008	3005 : 9018	3005 : 9020	3005 : 9021
3006 : 9006	3006 : 9007	3006 : 9008	3006 : 9018	3006 : 9020	3006 : 9021
3007 : 9006	3007 : 9007	3007 : 9008	3007 : 9018	3007 : 9020	3007 : 9021
3008 : 9006	3008 : 9007	3008 : 9008	3008 : 9018	3008 : 9020	3008 : 9021
3009 : 9006	3009 : 9007	3009 : 9008	3009 : 9018	3009 : 9020	3009 : 9021
3010 : 9006	3010 : 9007	3010 : 9008	3010 : 9018	3010 : 9020	3010 : 9021
3011 : 9006	3011 : 9007	3011 : 9008	3011 : 9018	3011 : 9020	3011 : 9021
3012 : 9006	3012 : 9007	3012 : 9008	3012 : 9018	3012 : 9020	3012 : 9021
3013 : 9006	3013 : 9007	3013 : 9008	3013 : 9018	3013 : 9020	3013 : 9021
3014 : 9006	3014 : 9007	3014 : 9008	3014 : 9018	3014 : 9020	3014 : 9021
4001 : 9006	4001 : 9007	4001 : 9008	4001 : 9018	4001 : 9020	4001 : 9021
4002 : 9006	4002 : 9007	4002 : 9008	4002 : 9018	4002 : 9020	4002 : 9021
4003 : 9006	4003 : 9007	4003 : 9008	4003 : 9018	4003 : 9020	4003 : 9021
4004 : 9006	4004 : 9007	4004 : 9008	4004 : 9018	4004 : 9020	4004 : 9021
4005 : 9006	4005 : 9007	4005 : 9008	4005 : 9018	4005 : 9020	4005 : 9021
4006 : 9006	4006 : 9007	4006 : 9008	4006 : 9018	4006 : 9020	4006 : 9021
4007 : 9006	4007 : 9007	4007 : 9008	4007 : 9018	4007 : 9020	4007 : 9021
4008 : 9006	4008 : 9007	4008 : 9008	4008 : 9018	4008 : 9020	4008 : 9021
4009 : 9006	4009 : 9007	4009 : 9008	4009 : 9018	4009 : 9020	4009 : 9021
4010 : 9006	4010 : 9007	4010 : 9008	4010 : 9018	4010 : 9020	4010 : 9021
4011 : 9006	4011 : 9007	4011 : 9008	4011 : 9018	4011 : 9020	4011 : 9021
4012 : 9006	4012 : 9007	4012 : 9008	4012 : 9018	4012 : 9020	4012 : 9021
5001 : 9006	5001 : 9007	5001 : 9008	5001 : 9018	5001 : 9020	5001 : 9021
5002 : 9006	5002 : 9007	5002 : 9008	5002 : 9018	5002 : 9020	5002 : 9021
5003 : 9006	5003 : 9007	5003 : 9008	5003 : 9018	5003 : 9020	5003 : 9021
5004 : 9006	5004 : 9007	5004 : 9008	5004 : 9018	5004 : 9020	5004 : 9021
5005 : 9006	5005 : 9007	5005 : 9008	5005 : 9018	5005 : 9020	5005 : 9021
5006 : 9006	5006 : 9007	5006 : 9008	5006 : 9018	5006 : 9020	5006 : 9021
5007 : 9006	5007 : 9007	5007 : 9008	5007 : 9018	5007 : 9020	5007 : 9021
5008 : 9006	5008 : 9007	5008 : 9008	5008 : 9018	5008 : 9020	5008 : 9021
5009 : 9006	5009 : 9007	5009 : 9008	5009 : 9018	5009 : 9020	5009 : 9021
5010 : 9006	5010 : 9007	5010 : 9008	5010 : 9018	5010 : 9020	5010 : 9021
5011 : 9006	5011 : 9007	5011 : 9008	5011 : 9018	5011 : 9020	5011 : 9021

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
3002:9025	3002:9026	3002:9036	3002:9038	3002:9039	3002:9040
3003:9025	3003:9026	3003:9036	3003:9038	3003:9039	3003:9040
3004:9025	3004:9026	3004:9036	3004:9038	3004:9039	3004:9040
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5010 : 9300	5010 : 9301	5010 : 9302	5010 : 9303	5010 : 9304	5010 : 9305
5011 : 9300	5011 : 9301	5011 : 9302	5011 : 9303	5011 : 9304	5011 : 9305

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
3002:9306	3002:9307	3002:9308	3002:9309	3002:9310	--
3003:9306	3003:9307	3003:9308	3003:9309	3003:9310	
3004:9306	3004:9307	3004:9308	3004:9309	3004:9310	
3005:9306	3005:9307	3005:9308	3005:9309	3005:9310	
3006:9306	3006:9307	3006:9308	3006:9309	3006:9310	
3007:9306	3007:9307	3007:9308	3007:9309	3007:9310	
3008:9306	3008:9307	3008:9308	3008:9309	3008:9310	
3009:9306	3009:9307	3009:9308	3009:9309	3009:9310	
3010:9306	3010:9307	3010:9308	3010:9309	3010:9310	
3011:9306	3011:9307	3011:9308	3011:9309	3011:9310	
3012:9306	3012:9307	3012:9308	3012:9309	3012:9310	
3013:9306	3013:9307	3013:9308	3013:9309	3013:9310	
3014:9306	3014:9307	3014:9308	3014:9309	3014:9310	
4001:9306	4001:9307	4001:9308	4001:9309	4001:9310	
4002:9306	4002:9307	4002:9308	4002:9309	4002:9310	
4003:9306	4003:9307	4003:9308	4003:9309	4003:9310	
4004:9306	4004:9307	4004:9308	4004:9309	4004:9310	
4005:9306	4005:9307	4005:9308	4005:9309	4005:9310	
4006:9306	4006:9307	4006:9308	4006:9309	4006:9310	
4007:9306	4007:9307	4007:9308	4007:9309	4007:9310	
4008:9306	4008:9307	4008:9308	4008:9309	4008:9310	
4009:9306	4009:9307	4009:9308	4009:9309	4009:9310	
4010:9306	4010:9307	4010:9308	4010:9309	4010:9310	
4011:9306	4011:9307	4011:9308	4011:9309	4011:9310	
4012:9306	4012:9307	4012:9308	4012:9309	4012:9310	
5001:9306	5001:9307	5001:9308	5001:9309	5001:9310	
5002:9306	5002:9307	5002:9308	5002:9309	5002:9310	
5003:9306	5003:9307	5003:9308	5003:9309	5003:9310	
5004:9306	5004:9307	5004:9308	5004:9309	5004:9310	
5005:9306	5005:9307	5005:9308	5005:9309	5005:9310	
5006:9306	5006:9307	5006:9308	5006:9309	5006:9310	
5007:9306	5007:9307	5007:9308	5007:9309	5007:9310	
5008:9306	5008:9307	5008:9308	5008:9309	5008:9310	
5009:9306	5009:9307	5009:9308	5009:9309	5009:9310	
5010:9306	5010:9307	5010:9308	5010:9309	5010:9310	
5011:9306	5011:9307	5011:9308	5011:9309	5011:9310	

Table C: Example combinations of a compound X with a compound Y.

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
9006 : 7000	9007 : 7000	9008 : 7000	9018 : 7000	9020 : 7000	9021 : 7000
9006 : 7001	9007 : 7001	9008 : 7001	9018 : 7001	9020 : 7001	9021 : 7001
9006 : 7002	9007 : 7002	9008 : 7002	9018 : 7002	9020 : 7002	9021 : 7002
9006 : 7003	9007 : 7003	9008 : 7003	9018 : 7003	9020 : 7003	9021 : 7003
9006 : 7004	9007 : 7004	9008 : 7004	9018 : 7004	9020 : 7004	9021 : 7004
9006 : 7005	9007 : 7005	9008 : 7005	9018 : 7005	9020 : 7005	9021 : 7005
9006 : 7006	9007 : 7006	9008 : 7006	9018 : 7006	9020 : 7006	9021 : 7006
9006 : 7007	9007 : 7007	9008 : 7007	9018 : 7007	9020 : 7007	9021 : 7007
9006 : 7008	9007 : 7008	9008 : 7008	9018 : 7008	9020 : 7008	9021 : 7008
9006 : 7009	9007 : 7009	9008 : 7009	9018 : 7009	9020 : 7009	9021 : 7009
9006 : 7010	9007 : 7010	9008 : 7010	9018 : 7010	9020 : 7010	9021 : 7010
9006 : 7011	9007 : 7011	9008 : 7011	9018 : 7011	9020 : 7011	9021 : 7011
9006 : 7012	9007 : 7012	9008 : 7012	9018 : 7012	9020 : 7012	9021 : 7012
9006 : 7013	9007 : 7013	9008 : 7013	9018 : 7013	9020 : 7013	9021 : 7013
9006 : 7014	9007 : 7014	9008 : 7014	9018 : 7014	9020 : 7014	9021 : 7014
9006 : 7015	9007 : 7015	9008 : 7015	9018 : 7015	9020 : 7015	9021 : 7015
9006 : 7016	9007 : 7016	9008 : 7016	9018 : 7016	9020 : 7016	9021 : 7016
9006 : 7017	9007 : 7017	9008 : 7017	9018 : 7017	9020 : 7017	9021 : 7017
9006 : 7018	9007 : 7018	9008 : 7018	9018 : 7018	9020 : 7018	9021 : 7018
9006 : 7019	9007 : 7019	9008 : 7019	9018 : 7019	9020 : 7019	9021 : 7019
9006 : 7020	9007 : 7020	9008 : 7020	9018 : 7020	9020 : 7020	9021 : 7020
9006 : 7021	9007 : 7021	9008 : 7021	9018 : 7021	9020 : 7021	9021 : 7021
9006 : 7022	9007 : 7022	9008 : 7022	9018 : 7022	9020 : 7022	9021 : 7022
9006 : 7023	9007 : 7023	9008 : 7023	9018 : 7023	9020 : 7023	9021 : 7023
9006 : 7024	9007 : 7024	9008 : 7024	9018 : 7024	9020 : 7024	9021 : 7024
9006 : 7025	9007 : 7025	9008 : 7025	9018 : 7025	9020 : 7025	9021 : 7025
9006 : 7026	9007 : 7026	9008 : 7026	9018 : 7026	9020 : 7026	9021 : 7026
9006 : 7027	9007 : 7027	9008 : 7027	9018 : 7027	9020 : 7027	9021 : 7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9025:7000	9026:7000	9036:7000	9038:7000	9039:7000	9040:7000
9025:7001	9026:7001	9036:7001	9038:7001	9039:7001	9040:7001
9025:7002	9026:7002	9036:7002	9038:7002	9039:7002	9040:7002
9025:7003	9026:7003	9036:7003	9038:7003	9039:7003	9040:7003
9025:7004	9026:7004	9036:7004	9038:7004	9039:7004	9040:7004
9025:7005	9026:7005	9036:7005	9038:7005	9039:7005	9040:7005
9025:7006	9026:7006	9036:7006	9038:7006	9039:7006	9040:7006
9025:7007	9026:7007	9036:7007	9038:7007	9039:7007	9040:7007
9025:7008	9026:7008	9036:7008	9038:7008	9039:7008	9040:7008
9025:7009	9026:7009	9036:7009	9038:7009	9039:7009	9040:7009
9025:7010	9026:7010	9036:7010	9038:7010	9039:7010	9040:7010
9025:7011	9026:7011	9036:7011	9038:7011	9039:7011	9040:7011
9025:7012	9026:7012	9036:7012	9038:7012	9039:7012	9040:7012
9025:7013	9026:7013	9036:7013	9038:7013	9039:7013	9040:7013
9025:7014	9026:7014	9036:7014	9038:7014	9039:7014	9040:7014
9025:7015	9026:7015	9036:7015	9038:7015	9039:7015	9040:7015
9025:7016	9026:7016	9036:7016	9038:7016	9039:7016	9040:7016
9025:7017	9026:7017	9036:7017	9038:7017	9039:7017	9040:7017
9025:7018	9026:7018	9036:7018	9038:7018	9039:7018	9040:7018
9025:7019	9026:7019	9036:7019	9038:7019	9039:7019	9040:7019
9025:7020	9026:7020	9036:7020	9038:7020	9039:7020	9040:7020
9025:7021	9026:7021	9036:7021	9038:7021	9039:7021	9040:7021
9025:7022	9026:7022	9036:7022	9038:7022	9039:7022	9040:7022
9025:7023	9026:7023	9036:7023	9038:7023	9039:7023	9040:7023
9025:7024	9026:7024	9036:7024	9038:7024	9039:7024	9040:7024
9025:7025	9026:7025	9036:7025	9038:7025	9039:7025	9040:7025
9025:7026	9026:7026	9036:7026	9038:7026	9039:7026	9040:7026
9025:7027	9026:7027	9036:7027	9038:7027	9039:7027	9040:7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9041:7000	9042:7000	9043:7000	9044:7000	9045:7000	9047:7000
9041:7001	9042:7001	9043:7001	9044:7001	9045:7001	9047:7001
9041:7002	9042:7002	9043:7002	9044:7002	9045:7002	9047:7002
9041:7003	9042:7003	9043:7003	9044:7003	9045:7003	9047:7003
9041:7004	9042:7004	9043:7004	9044:7004	9045:7004	9047:7004
9041:7005	9042:7005	9043:7005	9044:7005	9045:7005	9047:7005
9041:7006	9042:7006	9043:7006	9044:7006	9045:7006	9047:7006
9041:7007	9042:7007	9043:7007	9044:7007	9045:7007	9047:7007
9041:7008	9042:7008	9043:7008	9044:7008	9045:7008	9047:7008
9041:7009	9042:7009	9043:7009	9044:7009	9045:7009	9047:7009
9041:7010	9042:7010	9043:7010	9044:7010	9045:7010	9047:7010
9041:7011	9042:7011	9043:7011	9044:7011	9045:7011	9047:7011
9041:7012	9042:7012	9043:7012	9044:7012	9045:7012	9047:7012
9041:7013	9042:7013	9043:7013	9044:7013	9045:7013	9047:7013
9041:7014	9042:7014	9043:7014	9044:7014	9045:7014	9047:7014
9041:7015	9042:7015	9043:7015	9044:7015	9045:7015	9047:7015
9041:7016	9042:7016	9043:7016	9044:7016	9045:7016	9047:7016
9041:7017	9042:7017	9043:7017	9044:7017	9045:7017	9047:7017
9041:7018	9042:7018	9043:7018	9044:7018	9045:7018	9047:7018
9041:7019	9042:7019	9043:7019	9044:7019	9045:7019	9047:7019
9041:7020	9042:7020	9043:7020	9044:7020	9045:7020	9047:7020
9041:7021	9042:7021	9043:7021	9044:7021	9045:7021	9047:7021
9041:7022	9042:7022	9043:7022	9044:7022	9045:7022	9047:7022
9041:7023	9042:7023	9043:7023	9044:7023	9045:7023	9047:7023
9041:7024	9042:7024	9043:7024	9044:7024	9045:7024	9047:7024
9041:7025	9042:7025	9043:7025	9044:7025	9045:7025	9047:7025
9041:7026	9042:7026	9043:7026	9044:7026	9045:7026	9047:7026
9041:7027	9042:7027	9043:7027	9044:7027	9045:7027	9047:7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9048:7000	9049:7000	9051:7000	9052:7000	9053:7000	9054:7000
9048:7001	9049:7001	9051:7001	9052:7001	9053:7001	9054:7001
9048:7002	9049:7002	9051:7002	9052:7002	9053:7002	9054:7002
9048:7003	9049:7003	9051:7003	9052:7003	9053:7003	9054:7003
9048:7004	9049:7004	9051:7004	9052:7004	9053:7004	9054:7004
9048:7005	9049:7005	9051:7005	9052:7005	9053:7005	9054:7005
9048:7006	9049:7006	9051:7006	9052:7006	9053:7006	9054:7006
9048:7007	9049:7007	9051:7007	9052:7007	9053:7007	9054:7007
9048:7008	9049:7008	9051:7008	9052:7008	9053:7008	9054:7008
9048:7009	9049:7009	9051:7009	9052:7009	9053:7009	9054:7009
9048:7010	9049:7010	9051:7010	9052:7010	9053:7010	9054:7010
9048:7011	9049:7011	9051:7011	9052:7011	9053:7011	9054:7011
9048:7012	9049:7012	9051:7012	9052:7012	9053:7012	9054:7012
9048:7013	9049:7013	9051:7013	9052:7013	9053:7013	9054:7013
9048:7014	9049:7014	9051:7014	9052:7014	9053:7014	9054:7014
9048:7015	9049:7015	9051:7015	9052:7015	9053:7015	9054:7015
9048:7016	9049:7016	9051:7016	9052:7016	9053:7016	9054:7016
9048:7017	9049:7017	9051:7017	9052:7017	9053:7017	9054:7017
9048:7018	9049:7018	9051:7018	9052:7018	9053:7018	9054:7018
9048:7019	9049:7019	9051:7019	9052:7019	9053:7019	9054:7019
9048:7020	9049:7020	9051:7020	9052:7020	9053:7020	9054:7020
9048:7021	9049:7021	9051:7021	9052:7021	9053:7021	9054:7021
9048:7022	9049:7022	9051:7022	9052:7022	9053:7022	9054:7022
9048:7023	9049:7023	9051:7023	9052:7023	9053:7023	9054:7023
9048:7024	9049:7024	9051:7024	9052:7024	9053:7024	9054:7024
9048:7025	9049:7025	9051:7025	9052:7025	9053:7025	9054:7025
9048:7026	9049:7026	9051:7026	9052:7026	9053:7026	9054:7026
9048:7027	9049:7027	9051:7027	9052:7027	9053:7027	9054:7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9055:7000	9056:7000	9058:7000	9060:7000	9061:7000	9062:7000
9055:7001	9056:7001	9058:7001	9060:7001	9061:7001	9062:7001
9055:7002	9056:7002	9058:7002	9060:7002	9061:7002	9062:7002
9055:7003	9056:7003	9058:7003	9060:7003	9061:7003	9062:7003
9055:7004	9056:7004	9058:7004	9060:7004	9061:7004	9062:7004
9055:7005	9056:7005	9058:7005	9060:7005	9061:7005	9062:7005
9055:7006	9056:7006	9058:7006	9060:7006	9061:7006	9062:7006
9055:7007	9056:7007	9058:7007	9060:7007	9061:7007	9062:7007
9055:7008	9056:7008	9058:7008	9060:7008	9061:7008	9062:7008
9055:7009	9056:7009	9058:7009	9060:7009	9061:7009	9062:7009
9055:7010	9056:7010	9058:7010	9060:7010	9061:7010	9062:7010
9055:7011	9056:7011	9058:7011	9060:7011	9061:7011	9062:7011
9055:7012	9056:7012	9058:7012	9060:7012	9061:7012	9062:7012
9055:7013	9056:7013	9058:7013	9060:7013	9061:7013	9062:7013
9055:7014	9056:7014	9058:7014	9060:7014	9061:7014	9062:7014
9055:7015	9056:7015	9058:7015	9060:7015	9061:7015	9062:7015
9055:7016	9056:7016	9058:7016	9060:7016	9061:7016	9062:7016
9055:7017	9056:7017	9058:7017	9060:7017	9061:7017	9062:7017
9055:7018	9056:7018	9058:7018	9060:7018	9061:7018	9062:7018
9055:7019	9056:7019	9058:7019	9060:7019	9061:7019	9062:7019
9055:7020	9056:7020	9058:7020	9060:7020	9061:7020	9062:7020
9055:7021	9056:7021	9058:7021	9060:7021	9061:7021	9062:7021
9055:7022	9056:7022	9058:7022	9060:7022	9061:7022	9062:7022
9055:7023	9056:7023	9058:7023	9060:7023	9061:7023	9062:7023
9055:7024	9056:7024	9058:7024	9060:7024	9061:7024	9062:7024
9055:7025	9056:7025	9058:7025	9060:7025	9061:7025	9062:7025
9055:7026	9056:7026	9058:7026	9060:7026	9061:7026	9062:7026
9055:7027	9056:7027	9058:7027	9060:7027	9061:7027	9062:7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9063 : 7000	9064 : 7000	9065 : 7000	9066 : 7000	9067 : 7000	9068 : 7000
9063 : 7001	9064 : 7001	9065 : 7001	9066 : 7001	9067 : 7001	9068 : 7001
9063 : 7002	9064 : 7002	9065 : 7002	9066 : 7002	9067 : 7002	9068 : 7002
9063 : 7003	9064 : 7003	9065 : 7003	9066 : 7003	9067 : 7003	9068 : 7003
9063 : 7004	9064 : 7004	9065 : 7004	9066 : 7004	9067 : 7004	9068 : 7004
9063 : 7005	9064 : 7005	9065 : 7005	9066 : 7005	9067 : 7005	9068 : 7005
9063 : 7006	9064 : 7006	9065 : 7006	9066 : 7006	9067 : 7006	9068 : 7006
9063 : 7007	9064 : 7007	9065 : 7007	9066 : 7007	9067 : 7007	9068 : 7007
9063 : 7008	9064 : 7008	9065 : 7008	9066 : 7008	9067 : 7008	9068 : 7008
9063 : 7009	9064 : 7009	9065 : 7009	9066 : 7009	9067 : 7009	9068 : 7009
9063 : 7010	9064 : 7010	9065 : 7010	9066 : 7010	9067 : 7010	9068 : 7010
9063 : 7011	9064 : 7011	9065 : 7011	9066 : 7011	9067 : 7011	9068 : 7011
9063 : 7012	9064 : 7012	9065 : 7012	9066 : 7012	9067 : 7012	9068 : 7012
9063 : 7013	9064 : 7013	9065 : 7013	9066 : 7013	9067 : 7013	9068 : 7013
9063 : 7014	9064 : 7014	9065 : 7014	9066 : 7014	9067 : 7014	9068 : 7014
9063 : 7015	9064 : 7015	9065 : 7015	9066 : 7015	9067 : 7015	9068 : 7015
9063 : 7016	9064 : 7016	9065 : 7016	9066 : 7016	9067 : 7016	9068 : 7016
9063 : 7017	9064 : 7017	9065 : 7017	9066 : 7017	9067 : 7017	9068 : 7017
9063 : 7018	9064 : 7018	9065 : 7018	9066 : 7018	9067 : 7018	9068 : 7018
9063 : 7019	9064 : 7019	9065 : 7019	9066 : 7019	9067 : 7019	9068 : 7019
9063 : 7020	9064 : 7020	9065 : 7020	9066 : 7020	9067 : 7020	9068 : 7020
9063 : 7021	9064 : 7021	9065 : 7021	9066 : 7021	9067 : 7021	9068 : 7021
9063 : 7022	9064 : 7022	9065 : 7022	9066 : 7022	9067 : 7022	9068 : 7022
9063 : 7023	9064 : 7023	9065 : 7023	9066 : 7023	9067 : 7023	9068 : 7023
9063 : 7024	9064 : 7024	9065 : 7024	9066 : 7024	9067 : 7024	9068 : 7024
9063 : 7025	9064 : 7025	9065 : 7025	9066 : 7025	9067 : 7025	9068 : 7025
9063 : 7026	9064 : 7026	9065 : 7026	9066 : 7026	9067 : 7026	9068 : 7026
9063 : 7027	9064 : 7027	9065 : 7027	9066 : 7027	9067 : 7027	9068 : 7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9069 : 7000	9070 : 7000	9071 : 7000	9072 : 7000	9073 : 7000	9074 : 7000
9069 : 7001	9070 : 7001	9071 : 7001	9072 : 7001	9073 : 7001	9074 : 7001
9069 : 7002	9070 : 7002	9071 : 7002	9072 : 7002	9073 : 7002	9074 : 7002
9069 : 7003	9070 : 7003	9071 : 7003	9072 : 7003	9073 : 7003	9074 : 7003
9069 : 7004	9070 : 7004	9071 : 7004	9072 : 7004	9073 : 7004	9074 : 7004
9069 : 7005	9070 : 7005	9071 : 7005	9072 : 7005	9073 : 7005	9074 : 7005
9069 : 7006	9070 : 7006	9071 : 7006	9072 : 7006	9073 : 7006	9074 : 7006
9069 : 7007	9070 : 7007	9071 : 7007	9072 : 7007	9073 : 7007	9074 : 7007
9069 : 7008	9070 : 7008	9071 : 7008	9072 : 7008	9073 : 7008	9074 : 7008
9069 : 7009	9070 : 7009	9071 : 7009	9072 : 7009	9073 : 7009	9074 : 7009
9069 : 7010	9070 : 7010	9071 : 7010	9072 : 7010	9073 : 7010	9074 : 7010
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9294 : 7009	9295 : 7009	9296 : 7009	9297 : 7009	9298 : 7009	9299 : 7009
9294 : 7010	9295 : 7010	9296 : 7010	9297 : 7010	9298 : 7010	9299 : 7010
9294 : 7011	9295 : 7011	9296 : 7011	9297 : 7011	9298 : 7011	9299 : 7011
9294 : 7012	9295 : 7012	9296 : 7012	9297 : 7012	9298 : 7012	9299 : 7012
9294 : 7013	9295 : 7013	9296 : 7013	9297 : 7013	9298 : 7013	9299 : 7013
9294 : 7014	9295 : 7014	9296 : 7014	9297 : 7014	9298 : 7014	9299 : 7014
9294 : 7015	9295 : 7015	9296 : 7015	9297 : 7015	9298 : 7015	9299 : 7015
9294 : 7016	9295 : 7016	9296 : 7016	9297 : 7016	9298 : 7016	9299 : 7016
9294 : 7017	9295 : 7017	9296 : 7017	9297 : 7017	9298 : 7017	9299 : 7017
9294 : 7018	9295 : 7018	9296 : 7018	9297 : 7018	9298 : 7018	9299 : 7018
9294 : 7019	9295 : 7019	9296 : 7019	9297 : 7019	9298 : 7019	9299 : 7019
9294 : 7020	9295 : 7020	9296 : 7020	9297 : 7020	9298 : 7020	9299 : 7020
9294 : 7021	9295 : 7021	9296 : 7021	9297 : 7021	9298 : 7021	9299 : 7021
9294 : 7022	9295 : 7022	9296 : 7022	9297 : 7022	9298 : 7022	9299 : 7022
9294 : 7023	9295 : 7023	9296 : 7023	9297 : 7023	9298 : 7023	9299 : 7023
9294 : 7024	9295 : 7024	9296 : 7024	9297 : 7024	9298 : 7024	9299 : 7024
9294 : 7025	9295 : 7025	9296 : 7025	9297 : 7025	9298 : 7025	9299 : 7025
9294 : 7026	9295 : 7026	9296 : 7026	9297 : 7026	9298 : 7026	9299 : 7026
9294 : 7027	9295 : 7027	9296 : 7027	9297 : 7027	9298 : 7027	9299 : 7027

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
9300 : 7000	9301 : 7000	9302 : 7000	9303 : 7000	9304 : 7000	9305 : 7000
9300 : 7001	9301 : 7001	9302 : 7001	9303 : 7001	9304 : 7001	9305 : 7001
9300 : 7002	9301 : 7002	9302 : 7002	9303 : 7002	9304 : 7002	9305 : 7002
9300 : 7003	9301 : 7003	9302 : 7003	9303 : 7003	9304 : 7003	9305 : 7003
9300 : 7004	9301 : 7004	9302 : 7004	9303 : 7004	9304 : 7004	9305 : 7004
9300 : 7005	9301 : 7005	9302 : 7005	9303 : 7005	9304 : 7005	9305 : 7005
9300 : 7006	9301 : 7006	9302 : 7006	9303 : 7006	9304 : 7006	9305 : 7006
9300 : 7007	9301 : 7007	9302 : 7007	9303 : 7007	9304 : 7007	9305 : 7007
9300 : 7008	9301 : 7008	9302 : 7008	9303 : 7008	9304 : 7008	9305 : 7008
9300 : 7009	9301 : 7009	9302 : 7009	9303 : 7009	9304 : 7009	9305 : 7009
9300 : 7010	9301 : 7010	9302 : 7010	9303 : 7010	9304 : 7010	9305 : 7010
9300 : 7011	9301 : 7011	9302 : 7011	9303 : 7011	9304 : 7011	9305 : 7011
9300 : 7012	9301 : 7012	9302 : 7012	9303 : 7012	9304 : 7012	9305 : 7012
9300 : 7013	9301 : 7013	9302 : 7013	9303 : 7013	9304 : 7013	9305 : 7013
9300 : 7014	9301 : 7014	9302 : 7014	9303 : 7014	9304 : 7014	9305 : 7014
9300 : 7015	9301 : 7015	9302 : 7015	9303 : 7015	9304 : 7015	9305 : 7015
9300 : 7016	9301 : 7016	9302 : 7016	9303 : 7016	9304 : 7016	9305 : 7016
9300 : 7017	9301 : 7017	9302 : 7017	9303 : 7017	9304 : 7017	9305 : 7017
9300 : 7018	9301 : 7018	9302 : 7018	9303 : 7018	9304 : 7018	9305 : 7018
9300 : 7019	9301 : 7019	9302 : 7019	9303 : 7019	9304 : 7019	9305 : 7019
9300 : 7020	9301 : 7020	9302 : 7020	9303 : 7020	9304 : 7020	9305 : 7020
9300 : 7021	9301 : 7021	9302 : 7021	9303 : 7021	9304 : 7021	9305 : 7021
9300 : 7022	9301 : 7022	9302 : 7022	9303 : 7022	9304 : 7022	9305 : 7022
9300 : 7023	9301 : 7023	9302 : 7023	9303 : 7023	9304 : 7023	9305 : 7023
9300 : 7024	9301 : 7024	9302 : 7024	9303 : 7024	9304 : 7024	9305 : 7024
9300 : 7025	9301 : 7025	9302 : 7025	9303 : 7025	9304 : 7025	9305 : 7025
9300 : 7026	9301 : 7026	9302 : 7026	9303 : 7026	9304 : 7026	9305 : 7026
9300 : 7027	9301 : 7027	9302 : 7027	9303 : 7027	9304 : 7027	9305 : 7027

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
9306:7000	9307:7000	9308:7000	9309:7000	9310:7000	
9306:7001	9307:7001	9308:7001	9309:7001	9310:7001	
9306:7002	9307:7002	9308:7002	9309:7002	9310:7002	
9306:7003	9307:7003	9308:7003	9309:7003	9310:7003	
9306:7004	9307:7004	9308:7004	9309:7004	9310:7004	
9306:7005	9307:7005	9308:7005	9309:7005	9310:7005	
9306:7006	9307:7006	9308:7006	9309:7006	9310:7006	
9306:7007	9307:7007	9308:7007	9309:7007	9310:7007	
9306:7008	9307:7008	9308:7008	9309:7008	9310:7008	
9306:7009	9307:7009	9308:7009	9309:7009	9310:7009	
9306:7010	9307:7010	9308:7010	9309:7010	9310:7010	
9306:7011	9307:7011	9308:7011	9309:7011	9310:7011	
9306:7012	9307:7012	9308:7012	9309:7012	9310:7012	
9306:7013	9307:7013	9308:7013	9309:7013	9310:7013	
9306:7014	9307:7014	9308:7014	9309:7014	9310:7014	--
9306:7015	9307:7015	9308:7015	9309:7015	9310:7015	
9306:7016	9307:7016	9308:7016	9309:7016	9310:7016	
9306:7017	9307:7017	9308:7017	9309:7017	9310:7017	
9306:7018	9307:7018	9308:7018	9309:7018	9310:7018	
9306:7019	9307:7019	9308:7019	9309:7019	9310:7019	
9306:7020	9307:7020	9308:7020	9309:7020	9310:7020	
9306:7021	9307:7021	9308:7021	9309:7021	9310:7021	
9306:7022	9307:7022	9308:7022	9309:7022	9310:7022	
9306:7023	9307:7023	9308:7023	9309:7023	9310:7023	
9306:7024	9307:7024	9308:7024	9309:7024	9310:7024	
9306:7025	9307:7025	9308:7025	9309:7025	9310:7025	
9306:7026	9307:7026	9308:7026	9309:7026	9310:7026	
9306:7027	9307:7027	9308:7027	9309:7027	9310:7027	

Table D: Example combinations of a compound X with a compound Y.

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
6000 : 9006	6040 : 9006	6000 : 9007	6040 : 9007	6000 : 9008	6040 : 9008
6001 : 9006	6041 : 9006	6001 : 9007	6041 : 9007	6001 : 9008	6041 : 9008
6002 : 9006	6042 : 9006	6002 : 9007	6042 : 9007	6002 : 9008	6042 : 9008
6003 : 9006	6043 : 9006	6003 : 9007	6043 : 9007	6003 : 9008	6043 : 9008
6004 : 9006	6044 : 9006	6004 : 9007	6044 : 9007	6004 : 9008	6044 : 9008
6005 : 9006	6045 : 9006	6005 : 9007	6045 : 9007	6005 : 9008	6045 : 9008
6006 : 9006	6046 : 9006	6006 : 9007	6046 : 9007	6006 : 9008	6046 : 9008
6007 : 9006	6047 : 9006	6007 : 9007	6047 : 9007	6007 : 9008	6047 : 9008
6008 : 9006	6048 : 9006	6008 : 9007	6048 : 9007	6008 : 9008	6048 : 9008
6009 : 9006	6049 : 9006	6009 : 9007	6049 : 9007	6009 : 9008	6049 : 9008
6010 : 9006	6050 : 9006	6010 : 9007	6050 : 9007	6010 : 9008	6050 : 9008
6011 : 9006	6051 : 9006	6011 : 9007	6051 : 9007	6011 : 9008	6051 : 9008
6012 : 9006	6052 : 9006	6012 : 9007	6052 : 9007	6012 : 9008	6052 : 9008
6013 : 9006	6053 : 9006	6013 : 9007	6053 : 9007	6013 : 9008	6053 : 9008
6014 : 9006	6054 : 9006	6014 : 9007	6054 : 9007	6014 : 9008	6054 : 9008
6015 : 9006	6055 : 9006	6015 : 9007	6055 : 9007	6015 : 9008	6055 : 9008
6016 : 9006	6056 : 9006	6016 : 9007	6056 : 9007	6016 : 9008	6056 : 9008
6017 : 9006	6057 : 9006	6017 : 9007	6057 : 9007	6017 : 9008	6057 : 9008
6018 : 9006	6058 : 9006	6018 : 9007	6058 : 9007	6018 : 9008	6058 : 9008
6019 : 9006	6059 : 9006	6019 : 9007	6059 : 9007	6019 : 9008	6059 : 9008
6020 : 9006	6060 : 9006	6020 : 9007	6060 : 9007	6020 : 9008	6060 : 9008
6021 : 9006	6061 : 9006	6021 : 9007	6061 : 9007	6021 : 9008	6061 : 9008
6022 : 9006	6062 : 9006	6022 : 9007	6062 : 9007	6022 : 9008	6062 : 9008
6023 : 9006	6063 : 9006	6023 : 9007	6063 : 9007	6023 : 9008	6063 : 9008
6024 : 9006	6064 : 9006	6024 : 9007	6064 : 9007	6024 : 9008	6064 : 9008
6025 : 9006	6065 : 9006	6025 : 9007	6065 : 9007	6025 : 9008	6065 : 9008
6026 : 9006	6066 : 9006	6026 : 9007	6066 : 9007	6026 : 9008	6066 : 9008
6027 : 9006	6067 : 9006	6027 : 9007	6067 : 9007	6027 : 9008	6067 : 9008
6028 : 9006	6068 : 9006	6028 : 9007	6068 : 9007	6028 : 9008	6068 : 9008
6029 : 9006	6069 : 9006	6029 : 9007	6069 : 9007	6029 : 9008	6069 : 9008
6030 : 9006	6070 : 9006	6030 : 9007	6070 : 9007	6030 : 9008	6070 : 9008
6031 : 9006	6071 : 9006	6031 : 9007	6071 : 9007	6031 : 9008	6071 : 9008
6032 : 9006	6072 : 9006	6032 : 9007	6072 : 9007	6032 : 9008	6072 : 9008
6033 : 9006	6073 : 9006	6033 : 9007	6073 : 9007	6033 : 9008	6073 : 9008
6034 : 9006	6074 : 9006	6034 : 9007	6074 : 9007	6034 : 9008	6074 : 9008
6035 : 9006	6075 : 9006	6035 : 9007	6075 : 9007	6035 : 9008	6075 : 9008
6036 : 9006	6076 : 9006	6036 : 9007	6076 : 9007	6036 : 9008	6076 : 9008
6037 : 9006	6077 : 9006	6037 : 9007	6077 : 9007	6037 : 9008	6077 : 9008
6038 : 9006	6078 : 9006	6038 : 9007	6078 : 9007	6038 : 9008	6078 : 9008
6039 : 9006		6039 : 9007		6039 : 9008	

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
6000:9018	6040:9018	6000:9020	6040:9020	6000:9021	6040:9021
6001:9018	6041:9018	6001:9020	6041:9020	6001:9021	6041:9021
6002:9018	6042:9018	6002:9020	6042:9020	6002:9021	6042:9021
6003:9018	6043:9018	6003:9020	6043:9020	6003:9021	6043:9021
6004:9018	6044:9018	6004:9020	6044:9020	6004:9021	6044:9021
6005:9018	6045:9018	6005:9020	6045:9020	6005:9021	6045:9021
6006:9018	6046:9018	6006:9020	6046:9020	6006:9021	6046:9021
6007:9018	6047:9018	6007:9020	6047:9020	6007:9021	6047:9021
6008:9018	6048:9018	6008:9020	6048:9020	6008:9021	6048:9021
6009:9018	6049:9018	6009:9020	6049:9020	6009:9021	6049:9021
6010:9018	6050:9018	6010:9020	6050:9020	6010:9021	6050:9021
6011:9018	6051:9018	6011:9020	6051:9020	6011:9021	6051:9021
6012:9018	6052:9018	6012:9020	6052:9020	6012:9021	6052:9021
6013:9018	6053:9018	6013:9020	6053:9020	6013:9021	6053:9021
6014:9018	6054:9018	6014:9020	6054:9020	6014:9021	6054:9021
6015:9018	6055:9018	6015:9020	6055:9020	6015:9021	6055:9021
6016:9018	6056:9018	6016:9020	6056:9020	6016:9021	6056:9021
6017:9018	6057:9018	6017:9020	6057:9020	6017:9021	6057:9021
6018:9018	6058:9018	6018:9020	6058:9020	6018:9021	6058:9021
6019:9018	6059:9018	6019:9020	6059:9020	6019:9021	6059:9021
6020:9018	6060:9018	6020:9020	6060:9020	6020:9021	6060:9021
6021:9018	6061:9018	6021:9020	6061:9020	6021:9021	6061:9021
6022:9018	6062:9018	6022:9020	6062:9020	6022:9021	6062:9021
6023:9018	6063:9018	6023:9020	6063:9020	6023:9021	6063:9021
6024:9018	6064:9018	6024:9020	6064:9020	6024:9021	6064:9021
6025:9018	6065:9018	6025:9020	6065:9020	6025:9021	6065:9021
6026:9018	6066:9018	6026:9020	6066:9020	6026:9021	6066:9021
6027:9018	6067:9018	6027:9020	6067:9020	6027:9021	6067:9021
6028:9018	6068:9018	6028:9020	6068:9020	6028:9021	6068:9021
6029:9018	6069:9018	6029:9020	6069:9020	6029:9021	6069:9021
6030:9018	6070:9018	6030:9020	6070:9020	6030:9021	6070:9021
6031:9018	6071:9018	6031:9020	6071:9020	6031:9021	6071:9021
6032:9018	6072:9018	6032:9020	6072:9020	6032:9021	6072:9021
6033:9018	6073:9018	6033:9020	6073:9020	6033:9021	6073:9021
6034:9018	6074:9018	6034:9020	6074:9020	6034:9021	6074:9021
6035:9018	6075:9018	6035:9020	6075:9020	6035:9021	6075:9021
6036:9018	6076:9018	6036:9020	6076:9020	6036:9021	6076:9021
6037:9018	6077:9018	6037:9020	6077:9020	6037:9021	6077:9021
6038:9018	6078:9018	6038:9020	6078:9020	6038:9021	6078:9021
6039:9018		6039:9020		6039:9021	

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
6000 : 9025	6040 : 9025	6000 : 9026	6040 : 9026	6000 : 9036	6040 : 9036
6001 : 9025	6041 : 9025	6001 : 9026	6041 : 9026	6001 : 9036	6041 : 9036
6002 : 9025	6042 : 9025	6002 : 9026	6042 : 9026	6002 : 9036	6042 : 9036
6003 : 9025	6043 : 9025	6003 : 9026	6043 : 9026	6003 : 9036	6043 : 9036
6004 : 9025	6044 : 9025	6004 : 9026	6044 : 9026	6004 : 9036	6044 : 9036
6005 : 9025	6045 : 9025	6005 : 9026	6045 : 9026	6005 : 9036	6045 : 9036
6006 : 9025	6046 : 9025	6006 : 9026	6046 : 9026	6006 : 9036	6046 : 9036
6007 : 9025	6047 : 9025	6007 : 9026	6047 : 9026	6007 : 9036	6047 : 9036
6008 : 9025	6048 : 9025	6008 : 9026	6048 : 9026	6008 : 9036	6048 : 9036
6009 : 9025	6049 : 9025	6009 : 9026	6049 : 9026	6009 : 9036	6049 : 9036
6010 : 9025	6050 : 9025	6010 : 9026	6050 : 9026	6010 : 9036	6050 : 9036
6011 : 9025	6051 : 9025	6011 : 9026	6051 : 9026	6011 : 9036	6051 : 9036
6012 : 9025	6052 : 9025	6012 : 9026	6052 : 9026	6012 : 9036	6052 : 9036
6013 : 9025	6053 : 9025	6013 : 9026	6053 : 9026	6013 : 9036	6053 : 9036
6014 : 9025	6054 : 9025	6014 : 9026	6054 : 9026	6014 : 9036	6054 : 9036
6015 : 9025	6055 : 9025	6015 : 9026	6055 : 9026	6015 : 9036	6055 : 9036
6016 : 9025	6056 : 9025	6016 : 9026	6056 : 9026	6016 : 9036	6056 : 9036
6017 : 9025	6057 : 9025	6017 : 9026	6057 : 9026	6017 : 9036	6057 : 9036
6018 : 9025	6058 : 9025	6018 : 9026	6058 : 9026	6018 : 9036	6058 : 9036
6019 : 9025	6059 : 9025	6019 : 9026	6059 : 9026	6019 : 9036	6059 : 9036
6020 : 9025	6060 : 9025	6020 : 9026	6060 : 9026	6020 : 9036	6060 : 9036
6021 : 9025	6061 : 9025	6021 : 9026	6061 : 9026	6021 : 9036	6061 : 9036
6022 : 9025	6062 : 9025	6022 : 9026	6062 : 9026	6022 : 9036	6062 : 9036
6023 : 9025	6063 : 9025	6023 : 9026	6063 : 9026	6023 : 9036	6063 : 9036
6024 : 9025	6064 : 9025	6024 : 9026	6064 : 9026	6024 : 9036	6064 : 9036
6025 : 9025	6065 : 9025	6025 : 9026	6065 : 9026	6025 : 9036	6065 : 9036
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6029 : 9025	6069 : 9025	6029 : 9026	6069 : 9026	6029 : 9036	6069 : 9036
6030 : 9025	6070 : 9025	6030 : 9026	6070 : 9026	6030 : 9036	6070 : 9036
6031 : 9025	6071 : 9025	6031 : 9026	6071 : 9026	6031 : 9036	6071 : 9036
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6033 : 9025	6073 : 9025	6033 : 9026	6073 : 9026	6033 : 9036	6073 : 9036
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6036 : 9025	6076 : 9025	6036 : 9026	6076 : 9026	6036 : 9036	6076 : 9036
6037 : 9025	6077 : 9025	6037 : 9026	6077 : 9026	6037 : 9036	6077 : 9036
6038 : 9025	6078 : 9025	6038 : 9026	6078 : 9026	6038 : 9036	6078 : 9036
6039 : 9025		6039 : 9026		6039 : 9036	

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
6000:9038	6040:9038	6000:9039	6040:9039	6000:9040	6040:9040
6001:9038	6041:9038	6001:9039	6041:9039	6001:9040	6041:9040
6002:9038	6042:9038	6002:9039	6042:9039	6002:9040	6042:9040
6003:9038	6043:9038	6003:9039	6043:9039	6003:9040	6043:9040
6004:9038	6044:9038	6004:9039	6044:9039	6004:9040	6044:9040
6005:9038	6045:9038	6005:9039	6045:9039	6005:9040	6045:9040
6006:9038	6046:9038	6006:9039	6046:9039	6006:9040	6046:9040
6007:9038	6047:9038	6007:9039	6047:9039	6007:9040	6047:9040
6008:9038	6048:9038	6008:9039	6048:9039	6008:9040	6048:9040
6009:9038	6049:9038	6009:9039	6049:9039	6009:9040	6049:9040
6010:9038	6050:9038	6010:9039	6050:9039	6010:9040	6050:9040
6011:9038	6051:9038	6011:9039	6051:9039	6011:9040	6051:9040
6012:9038	6052:9038	6012:9039	6052:9039	6012:9040	6052:9040
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6018:9038	6058:9038	6018:9039	6058:9039	6018:9040	6058:9040
6019:9038	6059:9038	6019:9039	6059:9039	6019:9040	6059:9040
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6022:9307	6062:9307	6022:9308	6062:9308	6022:9309	6062:9309
6023:9307	6063:9307	6023:9308	6063:9308	6023:9309	6063:9309
6024:9307	6064:9307	6024:9308	6064:9308	6024:9309	6064:9309
6025:9307	6065:9307	6025:9308	6065:9308	6025:9309	6065:9309
6026:9307	6066:9307	6026:9308	6066:9308	6026:9309	6066:9309
6027:9307	6067:9307	6027:9308	6067:9308	6027:9309	6067:9309
6028:9307	6068:9307	6028:9308	6068:9308	6028:9309	6068:9309
6029:9307	6069:9307	6029:9308	6069:9308	6029:9309	6069:9309
6030:9307	6070:9307	6030:9308	6070:9308	6030:9309	6070:9309
6031:9307	6071:9307	6031:9308	6071:9308	6031:9309	6071:9309
6032:9307	6072:9307	6032:9308	6072:9308	6032:9309	6072:9309
6033:9307	6073:9307	6033:9308	6073:9308	6033:9309	6073:9309
6034:9307	6074:9307	6034:9308	6074:9308	6034:9309	6074:9309
6035:9307	6075:9307	6035:9308	6075:9308	6035:9309	6075:9309
6036:9307	6076:9307	6036:9308	6076:9308	6036:9309	6076:9309
6037:9307	6077:9307	6037:9308	6077:9308	6037:9309	6077:9309
6038:9307	6078:9307	6038:9308	6078:9308	6038:9309	6078:9309
6039:9307		6039:9308		6039:9309	

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
6000:9310	6040:9310				
6001:9310	6041:9310				
6002:9310	6042:9310				
6003:9310	6043:9310				
6004:9310	6044:9310				
6005:9310	6045:9310				
6006:9310	6046:9310				
6007:9310	6047:9310				
6008:9310	6048:9310				
6009:9310	6049:9310				
6010:9310	6050:9310				
6011:9310	6051:9310				
6012:9310	6052:9310				
6013:9310	6053:9310				
6014:9310	6054:9310				
6015:9310	6055:9310				
6016:9310	6056:9310				
6017:9310	6057:9310				
6018:9310	6058:9310				
6019:9310	6059:9310				
6020:9310	6060:9310	--	--	--	--
6021:9310	6061:9310				
6022:9310	6062:9310				
6023:9310	6063:9310				
6024:9310	6064:9310				
6025:9310	6065:9310				
6026:9310	6066:9310				
6027:9310	6067:9310				
6028:9310	6068:9310				
6029:9310	6069:9310				
6030:9310	6070:9310				
6031:9310	6071:9310				
6032:9310	6072:9310				
6033:9310	6073:9310				
6034:9310	6074:9310				
6035:9310	6075:9310				
6036:9310	6076:9310				
6037:9310	6077:9310				
6038:9310	6078:9310				
6039:9310					

Table E: Example combinations of a compound X with a compound Y.

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
8000 : 9006	8000 : 9007	8000 : 9008	8000 : 9018	8000 : 9020	8000 : 9021
8001 : 9006	8001 : 9007	8001 : 9008	8001 : 9018	8001 : 9020	8001 : 9021
8002 : 9006	8002 : 9007	8002 : 9008	8002 : 9018	8002 : 9020	8002 : 9021
8003 : 9006	8003 : 9007	8003 : 9008	8003 : 9018	8003 : 9020	8003 : 9021
8004 : 9006	8004 : 9007	8004 : 9008	8004 : 9018	8004 : 9020	8004 : 9021
8005 : 9006	8005 : 9007	8005 : 9008	8005 : 9018	8005 : 9020	8005 : 9021
8006 : 9006	8006 : 9007	8006 : 9008	8006 : 9018	8006 : 9020	8006 : 9021
8007 : 9006	8007 : 9007	8007 : 9008	8007 : 9018	8007 : 9020	8007 : 9021
8008 : 9006	8008 : 9007	8008 : 9008	8008 : 9018	8008 : 9020	8008 : 9021
8009 : 9006	8009 : 9007	8009 : 9008	8009 : 9018	8009 : 9020	8009 : 9021
8010 : 9006	8010 : 9007	8010 : 9008	8010 : 9018	8010 : 9020	8010 : 9021
8011 : 9006	8011 : 9007	8011 : 9008	8011 : 9018	8011 : 9020	8011 : 9021
8012 : 9006	8012 : 9007	8012 : 9008	8012 : 9018	8012 : 9020	8012 : 9021
8013 : 9006	8013 : 9007	8013 : 9008	8013 : 9018	8013 : 9020	8013 : 9021
8014 : 9006	8014 : 9007	8014 : 9008	8014 : 9018	8014 : 9020	8014 : 9021
8015 : 9006	8015 : 9007	8015 : 9008	8015 : 9018	8015 : 9020	8015 : 9021
8016 : 9006	8016 : 9007	8016 : 9008	8016 : 9018	8016 : 9020	8016 : 9021
8000 : 9025	8000 : 9026	8000 : 9036	8000 : 9038	8000 : 9039	8000 : 9040
8001 : 9025	8001 : 9026	8001 : 9036	8001 : 9038	8001 : 9039	8001 : 9040
8002 : 9025	8002 : 9026	8002 : 9036	8002 : 9038	8002 : 9039	8002 : 9040
8003 : 9025	8003 : 9026	8003 : 9036	8003 : 9038	8003 : 9039	8003 : 9040
8004 : 9025	8004 : 9026	8004 : 9036	8004 : 9038	8004 : 9039	8004 : 9040
8005 : 9025	8005 : 9026	8005 : 9036	8005 : 9038	8005 : 9039	8005 : 9040
8006 : 9025	8006 : 9026	8006 : 9036	8006 : 9038	8006 : 9039	8006 : 9040
8007 : 9025	8007 : 9026	8007 : 9036	8007 : 9038	8007 : 9039	8007 : 9040
8008 : 9025	8008 : 9026	8008 : 9036	8008 : 9038	8008 : 9039	8008 : 9040
8009 : 9025	8009 : 9026	8009 : 9036	8009 : 9038	8009 : 9039	8009 : 9040
8010 : 9025	8010 : 9026	8010 : 9036	8010 : 9038	8010 : 9039	8010 : 9040
8011 : 9025	8011 : 9026	8011 : 9036	8011 : 9038	8011 : 9039	8011 : 9040
8012 : 9025	8012 : 9026	8012 : 9036	8012 : 9038	8012 : 9039	8012 : 9040
8013 : 9025	8013 : 9026	8013 : 9036	8013 : 9038	8013 : 9039	8013 : 9040
8014 : 9025	8014 : 9026	8014 : 9036	8014 : 9038	8014 : 9039	8014 : 9040
8015 : 9025	8015 : 9026	8015 : 9036	8015 : 9038	8015 : 9039	8015 : 9040
8016 : 9025	8016 : 9026	8016 : 9036	8016 : 9038	8016 : 9039	8016 : 9040

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
8000 : 9041	8000 : 9042	8000 : 9043	8000 : 9044	8000 : 9045	8000 : 9047
8001 : 9041	8001 : 9042	8001 : 9043	8001 : 9044	8001 : 9045	8001 : 9047
8002 : 9041	8002 : 9042	8002 : 9043	8002 : 9044	8002 : 9045	8002 : 9047
8003 : 9041	8003 : 9042	8003 : 9043	8003 : 9044	8003 : 9045	8003 : 9047
8004 : 9041	8004 : 9042	8004 : 9043	8004 : 9044	8004 : 9045	8004 : 9047
8005 : 9041	8005 : 9042	8005 : 9043	8005 : 9044	8005 : 9045	8005 : 9047
8006 : 9041	8006 : 9042	8006 : 9043	8006 : 9044	8006 : 9045	8006 : 9047
8007 : 9041	8007 : 9042	8007 : 9043	8007 : 9044	8007 : 9045	8007 : 9047
8008 : 9041	8008 : 9042	8008 : 9043	8008 : 9044	8008 : 9045	8008 : 9047
8009 : 9041	8009 : 9042	8009 : 9043	8009 : 9044	8009 : 9045	8009 : 9047
8010 : 9041	8010 : 9042	8010 : 9043	8010 : 9044	8010 : 9045	8010 : 9047
8011 : 9041	8011 : 9042	8011 : 9043	8011 : 9044	8011 : 9045	8011 : 9047
8012 : 9041	8012 : 9042	8012 : 9043	8012 : 9044	8012 : 9045	8012 : 9047
8013 : 9041	8013 : 9042	8013 : 9043	8013 : 9044	8013 : 9045	8013 : 9047
8014 : 9041	8014 : 9042	8014 : 9043	8014 : 9044	8014 : 9045	8014 : 9047
8015 : 9041	8015 : 9042	8015 : 9043	8015 : 9044	8015 : 9045	8015 : 9047
8016 : 9041	8016 : 9042	8016 : 9043	8016 : 9044	8016 : 9045	8016 : 9047
8000 : 9048	8000 : 9049	8000 : 9051	8000 : 9052	8000 : 9053	8000 : 9054
8001 : 9048	8001 : 9049	8001 : 9051	8001 : 9052	8001 : 9053	8001 : 9054
8002 : 9048	8002 : 9049	8002 : 9051	8002 : 9052	8002 : 9053	8002 : 9054
8003 : 9048	8003 : 9049	8003 : 9051	8003 : 9052	8003 : 9053	8003 : 9054
8004 : 9048	8004 : 9049	8004 : 9051	8004 : 9052	8004 : 9053	8004 : 9054
8005 : 9048	8005 : 9049	8005 : 9051	8005 : 9052	8005 : 9053	8005 : 9054
8006 : 9048	8006 : 9049	8006 : 9051	8006 : 9052	8006 : 9053	8006 : 9054
8007 : 9048	8007 : 9049	8007 : 9051	8007 : 9052	8007 : 9053	8007 : 9054
8008 : 9048	8008 : 9049	8008 : 9051	8008 : 9052	8008 : 9053	8008 : 9054
8009 : 9048	8009 : 9049	8009 : 9051	8009 : 9052	8009 : 9053	8009 : 9054
8010 : 9048	8010 : 9049	8010 : 9051	8010 : 9052	8010 : 9053	8010 : 9054
8011 : 9048	8011 : 9049	8011 : 9051	8011 : 9052	8011 : 9053	8011 : 9054
8012 : 9048	8012 : 9049	8012 : 9051	8012 : 9052	8012 : 9053	8012 : 9054
8013 : 9048	8013 : 9049	8013 : 9051	8013 : 9052	8013 : 9053	8013 : 9054
8014 : 9048	8014 : 9049	8014 : 9051	8014 : 9052	8014 : 9053	8014 : 9054
8015 : 9048	8015 : 9049	8015 : 9051	8015 : 9052	8015 : 9053	8015 : 9054
8016 : 9048	8016 : 9049	8016 : 9051	8016 : 9052	8016 : 9053	8016 : 9054

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
8000:9055	8000:9056	8000:9058	8000:9060	8000:9061	8000:9062
8001:9055	8001:9056	8001:9058	8001:9060	8001:9061	8001:9062
8002:9055	8002:9056	8002:9058	8002:9060	8002:9061	8002:9062
8003:9055	8003:9056	8003:9058	8003:9060	8003:9061	8003:9062
8004:9055	8004:9056	8004:9058	8004:9060	8004:9061	8004:9062
8005:9055	8005:9056	8005:9058	8005:9060	8005:9061	8005:9062
8006:9055	8006:9056	8006:9058	8006:9060	8006:9061	8006:9062
8007:9055	8007:9056	8007:9058	8007:9060	8007:9061	8007:9062
8008:9055	8008:9056	8008:9058	8008:9060	8008:9061	8008:9062
8009:9055	8009:9056	8009:9058	8009:9060	8009:9061	8009:9062
8010:9055	8010:9056	8010:9058	8010:9060	8010:9061	8010:9062
8011:9055	8011:9056	8011:9058	8011:9060	8011:9061	8011:9062
8012:9055	8012:9056	8012:9058	8012:9060	8012:9061	8012:9062
8013:9055	8013:9056	8013:9058	8013:9060	8013:9061	8013:9062
8014:9055	8014:9056	8014:9058	8014:9060	8014:9061	8014:9062
8015:9055	8015:9056	8015:9058	8015:9060	8015:9061	8015:9062
8016:9055	8016:9056	8016:9058	8016:9060	8016:9061	8016:9062
8000:9063	8000:9064	8000:9065	8000:9066	8000:9067	8000:9068
8001:9063	8001:9064	8001:9065	8001:9066	8001:9067	8001:9068
8002:9063	8002:9064	8002:9065	8002:9066	8002:9067	8002:9068
8003:9063	8003:9064	8003:9065	8003:9066	8003:9067	8003:9068
8004:9063	8004:9064	8004:9065	8004:9066	8004:9067	8004:9068
8005:9063	8005:9064	8005:9065	8005:9066	8005:9067	8005:9068
8006:9063	8006:9064	8006:9065	8006:9066	8006:9067	8006:9068
8007:9063	8007:9064	8007:9065	8007:9066	8007:9067	8007:9068
8008:9063	8008:9064	8008:9065	8008:9066	8008:9067	8008:9068
8009:9063	8009:9064	8009:9065	8009:9066	8009:9067	8009:9068
8010:9063	8010:9064	8010:9065	8010:9066	8010:9067	8010:9068
8011:9063	8011:9064	8011:9065	8011:9066	8011:9067	8011:9068
8012:9063	8012:9064	8012:9065	8012:9066	8012:9067	8012:9068
8013:9063	8013:9064	8013:9065	8013:9066	8013:9067	8013:9068
8014:9063	8014:9064	8014:9065	8014:9066	8014:9067	8014:9068
8015:9063	8015:9064	8015:9065	8015:9066	8015:9067	8015:9068
8016:9063	8016:9064	8016:9065	8016:9066	8016:9067	8016:9068

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
8000 : 9069	8000 : 9070	8000 : 9071	8000 : 9072	8000 : 9073	8000 : 9074
8001 : 9069	8001 : 9070	8001 : 9071	8001 : 9072	8001 : 9073	8001 : 9074
8002 : 9069	8002 : 9070	8002 : 9071	8002 : 9072	8002 : 9073	8002 : 9074
8003 : 9069	8003 : 9070	8003 : 9071	8003 : 9072	8003 : 9073	8003 : 9074
8004 : 9069	8004 : 9070	8004 : 9071	8004 : 9072	8004 : 9073	8004 : 9074
8005 : 9069	8005 : 9070	8005 : 9071	8005 : 9072	8005 : 9073	8005 : 9074
8006 : 9069	8006 : 9070	8006 : 9071	8006 : 9072	8006 : 9073	8006 : 9074
8007 : 9069	8007 : 9070	8007 : 9071	8007 : 9072	8007 : 9073	8007 : 9074
8008 : 9069	8008 : 9070	8008 : 9071	8008 : 9072	8008 : 9073	8008 : 9074
8009 : 9069	8009 : 9070	8009 : 9071	8009 : 9072	8009 : 9073	8009 : 9074
8010 : 9069	8010 : 9070	8010 : 9071	8010 : 9072	8010 : 9073	8010 : 9074
8011 : 9069	8011 : 9070	8011 : 9071	8011 : 9072	8011 : 9073	8011 : 9074
8012 : 9069	8012 : 9070	8012 : 9071	8012 : 9072	8012 : 9073	8012 : 9074
8013 : 9069	8013 : 9070	8013 : 9071	8013 : 9072	8013 : 9073	8013 : 9074
8014 : 9069	8014 : 9070	8014 : 9071	8014 : 9072	8014 : 9073	8014 : 9074
8015 : 9069	8015 : 9070	8015 : 9071	8015 : 9072	8015 : 9073	8015 : 9074
8016 : 9069	8016 : 9070	8016 : 9071	8016 : 9072	8016 : 9073	8016 : 9074
8000 : 9075	8000 : 9076	8000 : 9077	8000 : 9078	8000 : 9079	8000 : 9080
8001 : 9075	8001 : 9076	8001 : 9077	8001 : 9078	8001 : 9079	8001 : 9080
8002 : 9075	8002 : 9076	8002 : 9077	8002 : 9078	8002 : 9079	8002 : 9080
8003 : 9075	8003 : 9076	8003 : 9077	8003 : 9078	8003 : 9079	8003 : 9080
8004 : 9075	8004 : 9076	8004 : 9077	8004 : 9078	8004 : 9079	8004 : 9080
8005 : 9075	8005 : 9076	8005 : 9077	8005 : 9078	8005 : 9079	8005 : 9080
8006 : 9075	8006 : 9076	8006 : 9077	8006 : 9078	8006 : 9079	8006 : 9080
8007 : 9075	8007 : 9076	8007 : 9077	8007 : 9078	8007 : 9079	8007 : 9080
8008 : 9075	8008 : 9076	8008 : 9077	8008 : 9078	8008 : 9079	8008 : 9080
8009 : 9075	8009 : 9076	8009 : 9077	8009 : 9078	8009 : 9079	8009 : 9080
8010 : 9075	8010 : 9076	8010 : 9077	8010 : 9078	8010 : 9079	8010 : 9080
8011 : 9075	8011 : 9076	8011 : 9077	8011 : 9078	8011 : 9079	8011 : 9080
8012 : 9075	8012 : 9076	8012 : 9077	8012 : 9078	8012 : 9079	8012 : 9080
8013 : 9075	8013 : 9076	8013 : 9077	8013 : 9078	8013 : 9079	8013 : 9080
8014 : 9075	8014 : 9076	8014 : 9077	8014 : 9078	8014 : 9079	8014 : 9080
8015 : 9075	8015 : 9076	8015 : 9077	8015 : 9078	8015 : 9079	8015 : 9080
8016 : 9075	8016 : 9076	8016 : 9077	8016 : 9078	8016 : 9079	8016 : 9080

X : Y	X : Y	X : Y	X : Y	X : Y	X : Y
8000 : 9081	8000 : 9082	8000 : 9083	8000 : 9084	8000 : 9085	8000 : 9086
8001 : 9081	8001 : 9082	8001 : 9083	8001 : 9084	8001 : 9085	8001 : 9086
8002 : 9081	8002 : 9082	8002 : 9083	8002 : 9084	8002 : 9085	8002 : 9086
8003 : 9081	8003 : 9082	8003 : 9083	8003 : 9084	8003 : 9085	8003 : 9086
8004 : 9081	8004 : 9082	8004 : 9083	8004 : 9084	8004 : 9085	8004 : 9086
8005 : 9081	8005 : 9082	8005 : 9083	8005 : 9084	8005 : 9085	8005 : 9086
8006 : 9081	8006 : 9082	8006 : 9083	8006 : 9084	8006 : 9085	8006 : 9086
8007 : 9081	8007 : 9082	8007 : 9083	8007 : 9084	8007 : 9085	8007 : 9086
8008 : 9081	8008 : 9082	8008 : 9083	8008 : 9084	8008 : 9085	8008 : 9086
8009 : 9081	8009 : 9082	8009 : 9083	8009 : 9084	8009 : 9085	8009 : 9086
8010 : 9081	8010 : 9082	8010 : 9083	8010 : 9084	8010 : 9085	8010 : 9086
8011 : 9081	8011 : 9082	8011 : 9083	8011 : 9084	8011 : 9085	8011 : 9086
8012 : 9081	8012 : 9082	8012 : 9083	8012 : 9084	8012 : 9085	8012 : 9086
8013 : 9081	8013 : 9082	8013 : 9083	8013 : 9084	8013 : 9085	8013 : 9086
8014 : 9081	8014 : 9082	8014 : 9083	8014 : 9084	8014 : 9085	8014 : 9086
8015 : 9081	8015 : 9082	8015 : 9083	8015 : 9084	8015 : 9085	8015 : 9086
8016 : 9081	8016 : 9082	8016 : 9083	8016 : 9084	8016 : 9085	8016 : 9086
8000 : 9088	8000 : 9089	8000 : 9094	8000 : 9095	8000 : 9096	8000 : 9097
8001 : 9088	8001 : 9089	8001 : 9094	8001 : 9095	8001 : 9096	8001 : 9097
8002 : 9088	8002 : 9089	8002 : 9094	8002 : 9095	8002 : 9096	8002 : 9097
8003 : 9088	8003 : 9089	8003 : 9094	8003 : 9095	8003 : 9096	8003 : 9097
8004 : 9088	8004 : 9089	8004 : 9094	8004 : 9095	8004 : 9096	8004 : 9097
8005 : 9088	8005 : 9089	8005 : 9094	8005 : 9095	8005 : 9096	8005 : 9097
8006 : 9088	8006 : 9089	8006 : 9094	8006 : 9095	8006 : 9096	8006 : 9097
8007 : 9088	8007 : 9089	8007 : 9094	8007 : 9095	8007 : 9096	8007 : 9097
8008 : 9088	8008 : 9089	8008 : 9094	8008 : 9095	8008 : 9096	8008 : 9097
8009 : 9088	8009 : 9089	8009 : 9094	8009 : 9095	8009 : 9096	8009 : 9097
8010 : 9088	8010 : 9089	8010 : 9094	8010 : 9095	8010 : 9096	8010 : 9097
8011 : 9088	8011 : 9089	8011 : 9094	8011 : 9095	8011 : 9096	8011 : 9097
8012 : 9088	8012 : 9089	8012 : 9094	8012 : 9095	8012 : 9096	8012 : 9097
8013 : 9088	8013 : 9089	8013 : 9094	8013 : 9095	8013 : 9096	8013 : 9097
8014 : 9088	8014 : 9089	8014 : 9094	8014 : 9095	8014 : 9096	8014 : 9097
8015 : 9088	8015 : 9089	8015 : 9094	8015 : 9095	8015 : 9096	8015 : 9097
8016 : 9088	8016 : 9089	8016 : 9094	8016 : 9095	8016 : 9096	8016 : 9097

X:Y	X:Y	X:Y	X:Y	X:Y	X:Y
8000:9098	8000:9099	8000:9100	8000:9101	8000:9102	8000:9103
8001:9098	8001:9099	8001:9100	8001:9101	8001:9102	8001:9103
8002:9098	8002:9099	8002:9100	8002:9101	8002:9102	8002:9103
8003:9098	8003:9099	8003:9100	8003:9101	8003:9102	8003:9103
8004:9098	8004:9099	8004:9100	8004:9101	8004:9102	8004:9103
8005:9098	8005:9099	8005:9100	8005:9101	8005:9102	8005:9103
8006:9098	8006:9099	8006:9100	8006:9101	8006:9102	8006:9103
8007:9098	8007:9099	8007:9100	8007:9101	8007:9102	8007:9103
8008:9098	8008:9099	8008:9100	8008:9101	8008:9102	8008:9103
8009:9098	8009:9099	8009:9100	8009:9101	8009:9102	8009:9103
8010:9098	8010:9099	8010:9100	8010:9101	8010:9102	8010:9103
8011:9098	8011:9099	8011:9100	8011:9101	8011:9102	8011:9103
8012:9098	8012:9099	8012:9100	8012:9101	8012:9102	8012:9103
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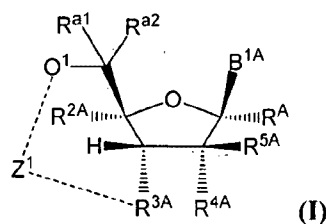
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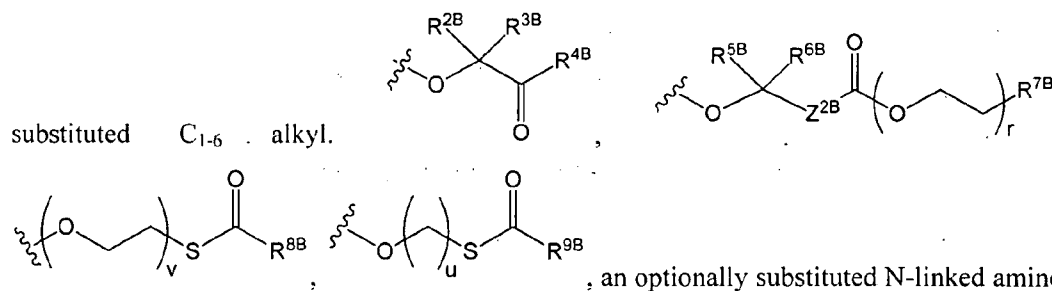
Compounds

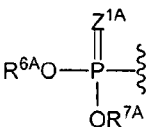
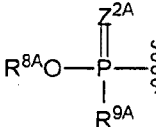
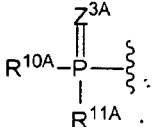
[0173] Some embodiments disclosed herein relate to a method and/or use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof:

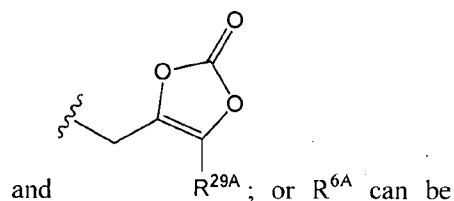
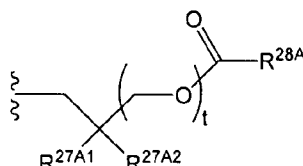
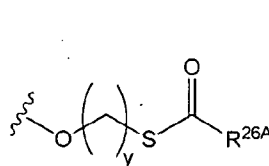
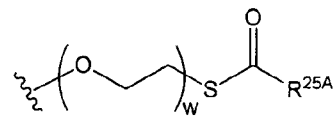
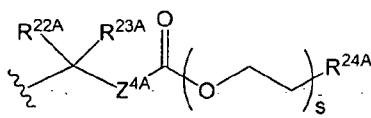
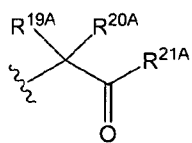


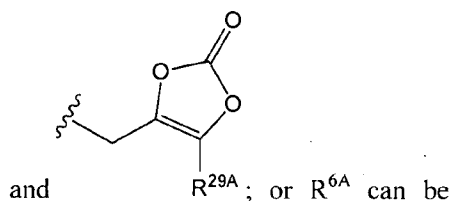
wherein: B^{1A} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; ----- can be absent or a single bond, provided that both ----- are absent or both ----- are a single bond; when ----- are both absent, then Z^1 can be absent, O^1 can be OR^{1A} , R^{3A} can be selected from H, halo, OH, $-OC(=O)R^{''A}$ and an optionally substituted O-linked amino acid, R^{4A} can be selected from H, OH, halo, N_3 , $-OC(=O)R^{''B}$, an optionally substituted O-linked amino acid and $NR^{''B1}R^{''B2}$, or R^{3A} and R^{4A} can be both an oxygen atom connected via a carbonyl to form a 5-membered

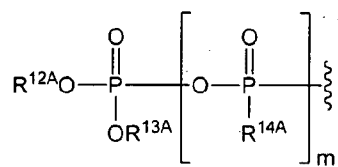
ring; when ----- are each a single bond, then Z^1 can be R^{1B} , O^1 can be O, R^{3A} can be O; R^{4A} can be selected from H, OH, halo, N_3 , $-OC(=O)R^{''B}$, an optionally substituted O-linked amino acid and $NR^{''B1}R^{''B2}$; and R^{1B} can be selected from O, OH, an -O-optionally



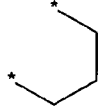
amino acid, ,  and ; R^2A can be hydrogen, halo, an unsubstituted C₁₋₄ alkyl, an unsubstituted C₂₋₄ alkenyl, an unsubstituted C₂₋₄ alkynyl, -CHF₂, -(CH₂)₁₋₆ halogen, -(CH₂)₁₋₆N₃, -(CH₂)₁₋₆NH₂ or -CN; R^{5A} can be selected from H, halo, OH, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl and an optionally substituted C₂₋₆ alkynyl; R^{6A}, R^{7A} and R^{8A} can be independently selected from absent, hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl(C₁₋₆ alkyl), an optionally substituted *(CR^{15A}R^{16A})_p-O-C₁₋₂₄ alkyl, an optionally substituted *(CR^{17A}R^{18A})_q-O-C₁₋₂₄ alkenyl,

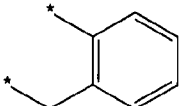


and ; or R^{6A} can be

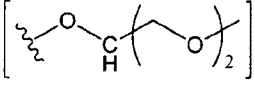


and R^{7A} can be absent or hydrogen; or R^{6A} and R^{7A} can be

taken together to form a moiety selected from an optionally substituted  and an

optionally substituted , wherein the oxygens connected to R^{6A} and R^{7A}, the phosphorus and the moiety form a six-membered to ten-membered ring system; R^{9A} can be independently selected from an optionally substituted C₁₋₂₄ alkyl, an optionally substituted

C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl, NR^{30A}R^{31A}, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{10A} and R^{11A} can be independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative; R^{12A} and R^{13A} can be independently absent or hydrogen; R^{14A} can be O-, OH or methyl; each R^{15A}, each R^{16A}, each R^{17A} and each R^{18A} can be independently hydrogen, an optionally substituted C₁₋₂₄ alkyl or an alkoxy; R^{19A}, R^{20A}, R^{22A}, R^{23A}, R^{2B}, R^{3B}, R^{5B} and R^{6B} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl and an optionally substituted aryl; R^{21A} and R^{4B} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted aryl, an optionally substituted -O-C₁₋₂₄ alkyl, an optionally substituted -O-aryl, an optionally substituted -O-heteroaryl and an optionally substituted -O-monocyclic heterocyclyl; R^{24A} and R^{7B} can be independently selected from of hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted aryl, an optionally substituted -O-C₁₋₂₄ alkyl, an optionally substituted -O-aryl, an optionally substituted -O-heteroaryl, an

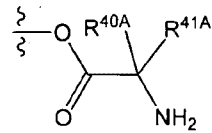
optionally substituted -O-monocyclic heterocyclyl and ; R^{25A}, R^{26A}, R^{29A}, R^{8B} and R^{9B} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl and an optionally substituted aryl; R^{27A1} and R^{27A2} can be independently selected from -C≡N, an optionally substituted C₂₋₈ organylcarbonyl, an optionally substituted C₂₋₈ alkoxycarbonyl and an optionally substituted C₂₋₈ organylaminocarbonyl; R^{28A} can be selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl and an optionally substituted C₃₋₆ cycloalkenyl; R^{30A} and R^{31A} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl and an optionally substituted aryl(C₁₋₄ alkyl); R^{3A} and each R^{3B} can be independently an optionally substituted C₁₋₂₄ alkyl; each R^{3B1} and each R^{3B2} can be independently hydrogen or an optionally substituted C₁₋₆ alkyl; m, v and w can be independently 0 or 1; p and q can be independently 1, 2 or 3; r and s can be independently 0,

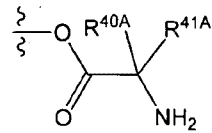
1, 2 or 3; t can be 1 or 2; u and y can be independently 3, 4 or 5; and Z^{1A} , Z^{2A} , Z^{3A} , Z^{4A} , Z^{1B} and Z^{2B} can be independently oxygen (O) or sulfur (S).

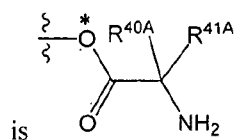
[0174] A compound of Formula (I) can be a nucleoside, a nucleotide (including a monophosphate, a diphosphate, a triphosphate, thiomonophosphate, alpha-thiodiphosphate and/or alpha-thiotriphosphate) or a nucleotide prodrug. In some embodiments, ----- can be both absent, Z^1 can be absent, O^1 can be OR^{1A} , R^{3A} can be selected from H, halo, OH, $-OC(=O)R^{3A}$ and an optionally substituted O-linked amino acid, R^{4A} can be selected from OH, halo, $-OC(=O)R^{3B}$ and an optionally substituted O-linked amino acid, or R^{3A} and R^{4A} can be both an oxygen atom connected via a carbonyl to form a 5-membered ring.

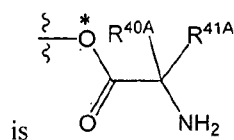
[0175] Various substituents can be attached to the 5'-position of Formula (I) when both ----- are absent. In some embodiments, R^{1A} can be hydrogen. In some embodiments, R^{1A} can be an optionally substituted acyl. For example, R^{1A} can be $-C(=O)R^{39A}$, wherein R^{39A} can be selected from an optionally substituted C_{1-12} alkyl, an optionally substituted C_{2-12} alkenyl, an optionally substituted C_{2-12} alkynyl, an optionally substituted C_{3-8} cycloalkyl, an optionally substituted C_{3-8} cycloalkenyl, an optionally substituted C_{6-10} aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl(C_{1-6} alkyl) and an optionally substituted heterocyclyl(C_{1-6} alkyl). In some embodiments, R^{39A} can be a substituted C_{1-12} alkyl. In other embodiments, R^{39A} can be an unsubstituted C_{1-12} alkyl. In some embodiments, R^{1A} can be $-C(=O)$ -unsubstituted C_{1-4} alkyl. In some embodiments, both R^{a1} and R^{a2} can be hydrogen. In other embodiments, R^{a1} can be hydrogen and R^{a2} can be deuterium. In still other embodiments, both R^{a1} and R^{a2} can be deuterium.

[0176] In still other embodiments, R^{1A} can be an optionally substituted O-linked amino acid. Examples of suitable O-linked amino acids include alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. Additional examples of suitable amino acids include, but are not limited to, ornithine, hypusine, 2-aminoisobutyric acid, dehydroalanine, gamma-aminobutyric acid, citrulline, beta-alanine, alpha-ethyl-glycine, alpha-propyl-glycine and norleucine. In some

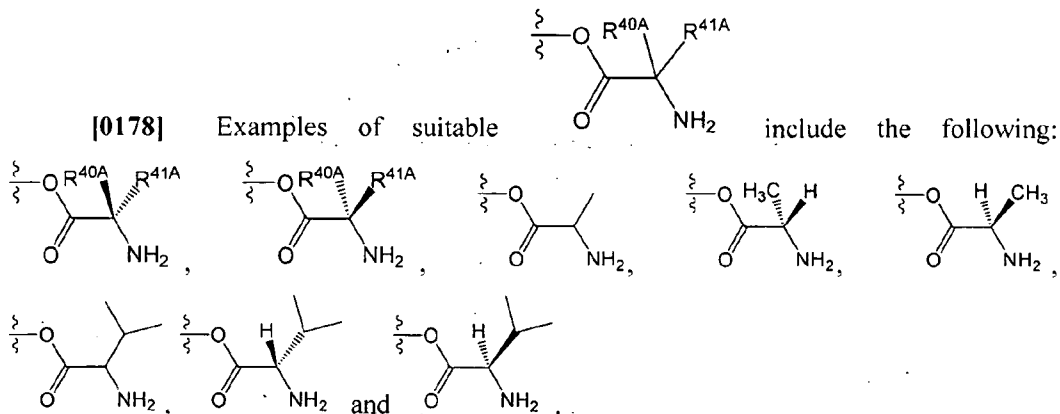


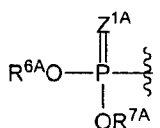
embodiments, the O-linked amino acid can have the structure , wherein R^{40A} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_6 aryl, an optionally substituted C_{10} aryl and an optionally substituted aryl(C_{1-6} alkyl); and R^{41A} can be hydrogen or an optionally substituted C_{1-4} alkyl; or R^{40A} and R^{41A} can be taken together to form an optionally substituted C_{3-6} cycloalkyl. Those skilled in the art understand that when R^{1A} is an optionally substituted O-linked amino acid, the oxygen of $R^{1A}O-$ of Formula (I) is part of the optionally substituted O-linked amino acid. For example, when R^{1A}

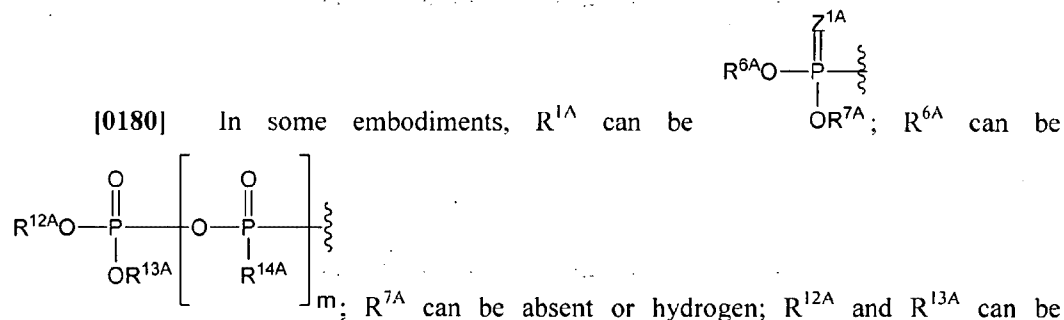


is , the oxygen indicated with "*" is the oxygen of $R^{1A}O-$ of Formula (I).

[0177] When R^{40A} is substituted, R^{40A} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{40A} can be an unsubstituted C_{1-6} alkyl, such as those described herein. In some embodiments, R^{40A} can be hydrogen. In other embodiments, R^{40A} can be methyl. In some embodiments, R^{41A} can be hydrogen. In other embodiments, R^{41A} can be an optionally substituted C_{1-4} alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{41A} can be methyl. Depending on the groups that are selected for R^{40A} and R^{41A} , the carbon to which R^{40A} and R^{41A} are attached may be a chiral center. In some embodiment, the carbon to which R^{40A} and R^{41A} are attached may be a (*R*)-chiral center. In other embodiments, the carbon to which R^{40A} and R^{41A} are attached may be a (*S*)-chiral center.

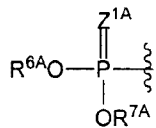


[0179] In some embodiments, R^{1A} can be . In some embodiments, R^{6A} and R^{7A} can be both hydrogen. In other embodiments, R^{6A} and R^{7A} can be both absent. In still other embodiments, at least one R^{6A} and R^{7A} can be absent. In yet still other embodiments, at least one R^{6A} and R^{7A} can be hydrogen. Those skilled in the art understand that when R^{6A} and/or R^{7A} are absent, the associated oxygen(s) will have a negative charge. For example, when R^{6A} is absent, the oxygen associated with R^{6A} will have a negative charge. In some embodiments, Z^{1A} can be O (oxygen). In other embodiments, Z^{1A} can be S (sulfur). In some embodiments, R^{1A} can be a monophosphate. In other embodiments, R^{1A} can be a monothiophosphate.



independently absent or hydrogen; R^{14A} can be O^- , OH or methyl; and m can be 0 or 1. In some embodiments, m can be 0, and R^{7A} , R^{12A} and R^{13A} can be independently absent or hydrogen. In other embodiments, m can be 1, and R^{7A} , R^{12A} and R^{13A} can be independently absent or hydrogen; and R^{14A} can be O^- , OH or methyl. In some embodiments, m can be 1,

and R^{7A} , R^{12A} and R^{13A} can be independently absent or hydrogen; and R^{14A} can be O^- or OH . In other embodiments, m can be 1, and R^{7A} , R^{12A} and R^{13A} can be independently absent or hydrogen; and R^{14A} can be methyl. Those skilled in the art understand that when m is 0, R^{6A} can be a diphosphate, when Z^{1A} is oxygen, or an alpha-thiodiphosphate, when Z^{1A} is sulfur. Likewise, those skilled in the art understand that when m is 1, R^{6A} can be a triphosphate, when Z^{1A} is oxygen, or an alpha-thiotriphosphate, when Z^{1A} is sulfur.

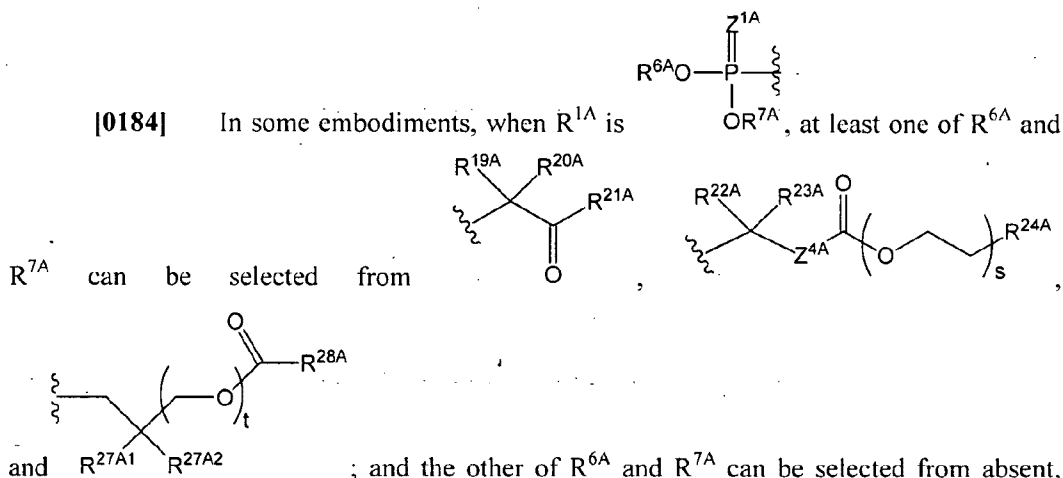


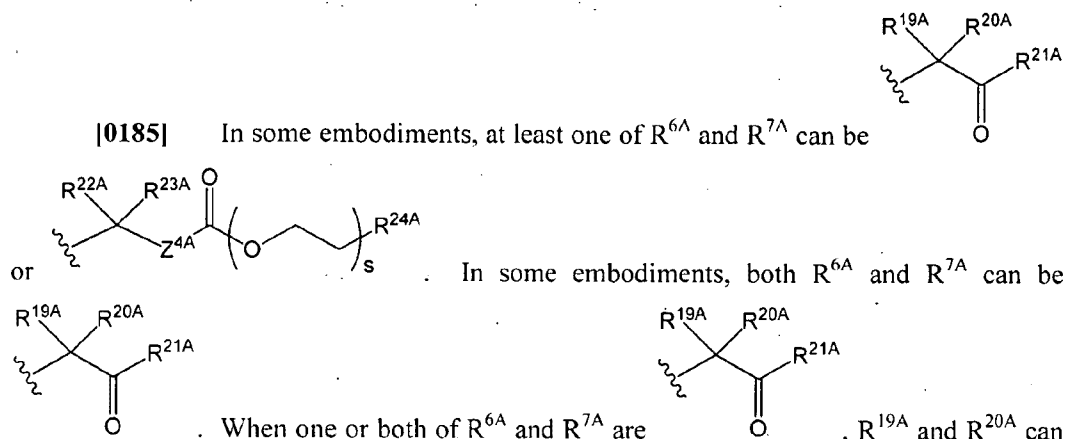
[0181] In some embodiments, when R^{1A} is $R^{6A}O-P(OR^{7A})(Z^{1A})$, one of R^{6A} and R^{7A} can be hydrogen, and the other of R^{6A} and R^{7A} can be selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted aryl(C_{1-6} alkyl). In some embodiments, one of R^{6A} and R^{7A} can be hydrogen, and the other of R^{6A} and R^{7A} can be an optionally substituted C_{1-24} alkyl. In other embodiments, both R^{6A} and R^{7A} can be independently selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted aryl(C_{1-6} alkyl). In some embodiments, both R^{6A} and R^{7A} can be an optionally substituted C_{1-24} alkyl. In other embodiments, both R^{6A} and R^{7A} can be an optionally substituted C_{2-24} alkenyl. In some embodiments, R^{6A} and R^{7A} can be independently an optionally substituted group selected from the following: myristoleyl, myristyl, palmitoleyl, palmityl, sapienyl, oleyl, elaidyl, vaccenyl, linoleyl, α -linolenyl, arachidonyl, eicosapentaenyl, erucyl, docosahexaenyl, caprylyl, capryl, lauryl, stearyl, arachidyl, behenyl, lignoceryl and cerotyl.

[0182] In some embodiments, at least one of R^{6A} and R^{7A} can be $*(CR^{15A}R^{16A})_p-O-C_{1-24}$ alkyl. In other embodiments, R^{6A} and R^{7A} can be both $*(CR^{15A}R^{16A})_p-O-C_{1-24}$ alkyl. In some embodiments, each R^{15A} and each R^{16A} can be hydrogen. In other embodiments, at least one of R^{15A} and R^{16A} can be an optionally substituted C_{1-24} alkyl. In other embodiments, at least one of R^{15A} and R^{16A} can be an alkoxy (for example, benzyloxy).

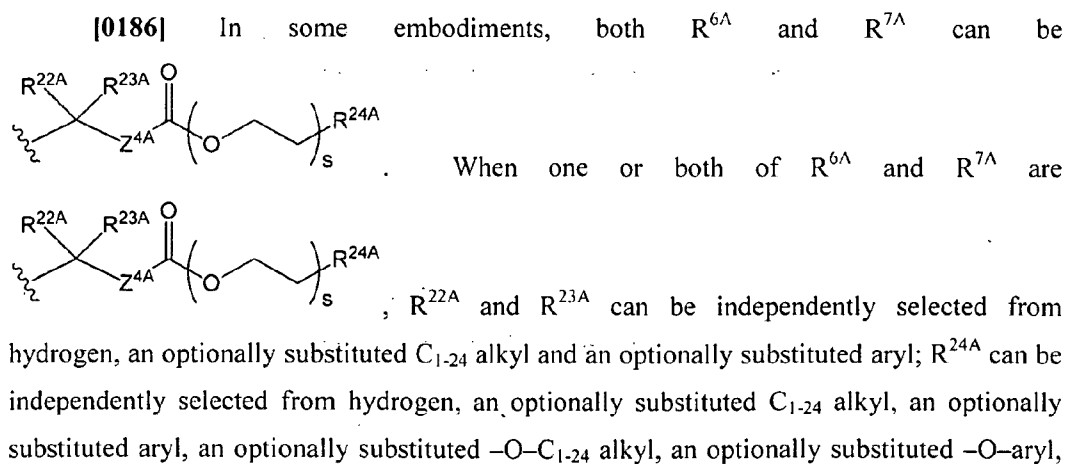
In some embodiments, p can be 1. In other embodiments, p can be 2. In still other embodiments, p can be 3.

[0183] In some embodiments, at least one of R^{6A} and R^{7A} can be $*(CR^{17A}R^{18A})_q-O-C_{2-24}$ alkenyl. In other embodiments, R^{6A} and R^{7A} can be both $*(CR^{17A}R^{18A})_q-O-C_{2-24}$ alkenyl. In some embodiments, each R^{17A} and each R^{18A} can be hydrogen. In other embodiments, at least one of R^{17A} and R^{18A} can be an optionally substituted C_{1-24} alkyl. In some embodiments, q can be 1. In other embodiments, q can be 2. In still other embodiments, q can be 3. When at least one of R^{6A} and R^{7A} is $*(CR^{15A}R^{16A})_p-O-C_{1-24}$ alkyl or $*(CR^{17A}R^{18A})_q-O-C_{2-24}$ alkenyl, the C_{1-24} alkyl can be selected from caprylyl, capryl, lauryl, myristyl, palmityl, stearyl, arachidyl, behenyl, lignoceryl, and cerotyl, and the C_{2-24} alkenyl can be selected from myristoleyl, palmitoleyl, sapienyl, oleyl, elaidyl, vaccenyl, linoleyl, α -linolenyl, arachidonyl, eicosapentaenyl, erucyl and docosahexaenyl.

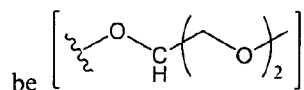




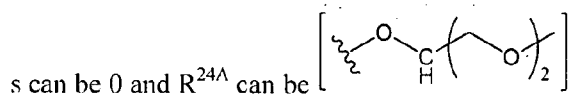
, R^{19A} and R^{20A} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; and R^{21A} can be selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl and an optionally substituted $-O$ -monocyclic heterocyclyl. In some embodiments, R^{19A} and R^{20A} can be hydrogen. In other embodiments, at least one of R^{19A} and R^{20A} can be an optionally substituted C_{1-24} alkyl or an optionally substituted aryl. In some embodiments, R^{21A} can be an optionally substituted C_{1-24} alkyl. In some embodiments, R^{21A} can be an unsubstituted C_{1-4} alkyl. In other embodiments, R^{21A} can be an optionally substituted aryl. In still other embodiments, R^{21A} can be an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl or an optionally substituted $-O$ -monocyclic heterocyclyl. In some embodiments, R^{21A} can be an unsubstituted $-O-C_{1-4}$ alkyl.



an optionally substituted -O-heteroaryl and an optionally substituted -O-monocyclic heterocyclyl; s can be 0, 1, 2 or 3; and Z^{4A} can be independently O (oxygen) or S (sulfur). In some embodiments, R^{22A} and R^{23A} can be hydrogen. In other embodiments, at least one of R^{22A} and R^{23A} can be an optionally substituted C_{1-24} alkyl or an optionally substituted aryl. In some embodiments, R^{24A} can be an optionally substituted C_{1-24} alkyl. In some embodiments, R^{24A} can be an unsubstituted C_{1-4} alkyl. In other embodiments, R^{24A} can be an optionally substituted aryl. In still other embodiments, R^{24A} can be an optionally substituted -O- C_{1-24} alkyl, an optionally substituted -O-aryl, an optionally substituted -O-heteroaryl or an optionally substituted -O-monocyclic heterocyclyl. In yet still other embodiments, R^{24A} can

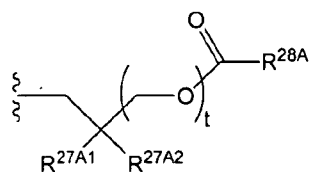


In some embodiments, R^{24A} can be an unsubstituted -O- C_{1-4} alkyl. In some embodiments, Z^{4A} can be O (oxygen). In other embodiments, Z^{4A} can be S (sulfur). In some embodiments, s can be 0. In other embodiments, s can be 1. In still other embodiments, s can be 2. In yet still other embodiments, s can be 3. In some embodiments,

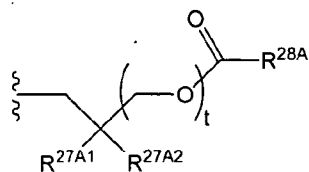


In some embodiments, one or both of R^{6A} and R^{7A} can be isopropoxyloxycarbonyloxymethyl (POC). In some embodiments, R^{6A} and R^{7A} can be both a isopropoxyloxycarbonyloxymethyl (POC) group, and form a bis(isopropoxyloxycarbonyloxymethyl) (bis(POC)) prodrug. In other embodiments, one or both of R^{6A} and R^{7A} can be pivaloyloxymethyl (POM). In some embodiments, R^{6A} and R^{7A} can be both a pivaloyloxymethyl (POM) group, and form a bis(pivaloyloxymethyl) (bis(POM)) prodrug.

[0187] In some embodiments, both R^{6A} and R^{7A} can be



When one or both of R^{6A} and R^{7A} are



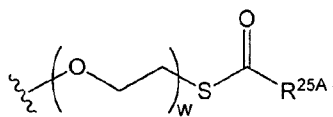
, R^{27A1} and R^{27A2} can be independently -C≡N or an optionally

substituted substituent selected from C₂₋₈ organylcarbonyl, C₂₋₈ alkoxy carbonyl and C₂₋₈ organylaminocarbonyl; R^{28A} can be selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl and an optionally substituted C₃₋₆ cycloalkenyl; and t can be 1 or 2. In some embodiments, R^{27A1} can be -C≡N and R^{27A2} can be an optionally substituted C₂₋₈ alkoxy carbonyl, such as -C(=O)OCH₃. In other embodiments, R^{27A1} can be -C≡N and R^{27A2} can be an optionally substituted C₂₋₈ organylaminocarbonyl, for example, -C(=O)NHCH₂CH₃ and -C(=O)NHCH₂CH₂phenyl. In some embodiments, both R^{27A1} and R^{27A2} can be an optionally substituted C₂₋₈ organylcarbonyl, such as -C(=O)CH₃. In some embodiments, both R^{27A1} and R^{27A2} can be an optionally substituted C₁₋₈ alkoxy carbonyl, for example, -C(=O)OCH₂CH₃ and -C(=O)OCH₃. In some embodiments, including those described in this paragraph, R^{28A} can be an optionally substituted C₁₋₄ alkyl. In some embodiment, R^{28A} can be methyl or tert-butyl. In some embodiments, t can be 1. In other embodiments, t can be 2.

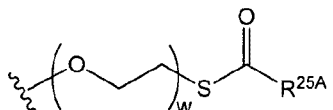
[0188] In some embodiments, R^{6A} and R^{7A} can be both an optionally substituted aryl. In some embodiments, at least one of R^{6A} and R^{7A} can be an optionally substituted aryl. For example, both R^{6A} and R^{7A} can be an optionally substituted phenyl or an optionally substituted naphthyl. When substituted, the substituted aryl can be substituted with 1, 2, 3 or more than 3 substituents. When more the two substituents are present, the substituents can be the same or different. In some embodiments, when at least one of R^{6A} and R^{7A} is a substituted phenyl, the substituted phenyl can be a para-, ortho- or meta-substituted phenyl.

[0189] In some embodiments, R^{6A} and R^{7A} can be both an optionally substituted aryl(C₁₋₆ alkyl). In some embodiments, at least one of R^{6A} and R^{7A} can be an optionally substituted aryl(C₁₋₆ alkyl). For example, both R^{6A} and R^{7A} can be an optionally substituted benzyl. When substituted, the substituted benzyl group can be substituted with 1, 2, 3 or more than 3 substituents. When more the two substituents are present, the substituents can be the same or different. In some embodiments, the aryl group of the aryl(C₁₋₆ alkyl) can be a para-, ortho- or meta-substituted phenyl.

[0190] In some embodiments, R^{6A} and R^{7A} can be both

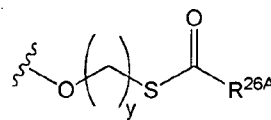


In some embodiments, at least one of R^{6A} and R^{7A} can be

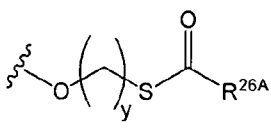


In some embodiments, R^{25A} can be hydrogen. In other embodiments, R^{25A} can be an optionally substituted C_{1-24} alkyl. In still other embodiments, R^{25A} can be an optionally substituted aryl (for example, an optionally substituted phenyl). In some embodiments, R^{25A} can be a C_{1-6} alkyl, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, pentyl (branched and straight-chained), and hexyl (branched and straight-chained). In some embodiments, w can be 0. In other embodiments, w can be 1. In some embodiments, R^{6A} and R^{7A} can be both a S-acylthioethyl (SATE) group and form a SATE ester prodrug.

[0191] In some embodiments, R^{6A} and R^{7A} can be both

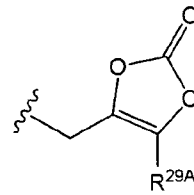


In some embodiments, at least one of R^{6A} and R^{7A} can be



In some embodiments, R^{26A} can be hydrogen. In other embodiments, R^{26A} can be an optionally substituted C_{1-24} alkyl. In still other embodiments, R^{26A} can be an optionally substituted aryl, for example, an optionally substituted phenyl. In some embodiments, R^{26A} can be an optionally substituted C_{1-6} alkyl. In some embodiments, R^{26A} can be an unsubstituted C_{1-6} alkyl. In some embodiments, y can be 3. In other embodiments, y can be 4. In still other embodiments, y can be 5.

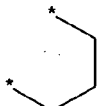
[0192] In some embodiments, R^{6A} and R^{7A} can be both

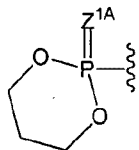


R^{29A} . In

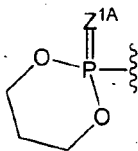
some embodiments, at least one of R^{6A} and R^{7A} can be some embodiments, R^{29A} can be hydrogen. In other embodiments, R^{29A} can be an optionally substituted C_{1-24} alkyl. In some embodiments, R^{29A} can be a C_{1-4} alkyl, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl and t-butyl. In still other embodiments, R^{29A} can be an optionally substituted aryl, such as an optionally substituted phenyl or an optionally substituted naphthyl. In some embodiments, R^{6A} and R^{7A} can be both a dioxolenone group and form a dioxolenone prodrug.

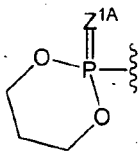
[0193] In some embodiments, R^{6A} and R^{7A} can be taken together to form an

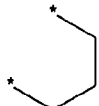
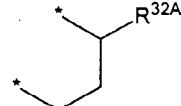
optionally substituted . For example, R^{1A} can be an optionally substituted



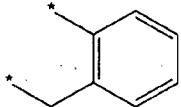
. When substituted, the ring can be substituted 1, 2, 3 or 3 or more times. When substituted with multiple substituents, the substituents can be the same or different. In some

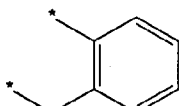
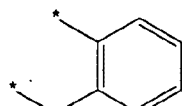
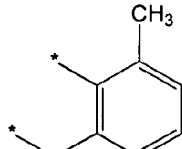
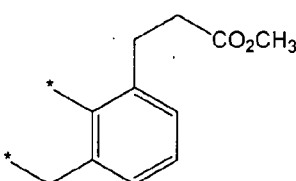
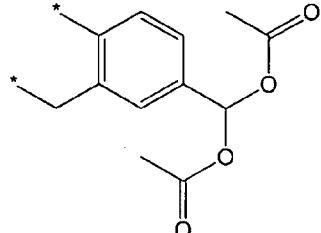


embodiments, when R^{1A} is , the ring can be substituted with an optionally substituted aryl group and/or an optionally substituted heteroaryl. An example of a suitable heteroaryl is pyridinyl. In some embodiments, R^{6A} and R^{7A} can be taken together to form an

optionally substituted  such as , wherein R^{32A} can be an optionally substituted aryl, an optionally substituted heteroaryl or an optionally substituted heterocyclyl. In some embodiments, R^{6A} and R^{7A} can form a cyclic 1-aryl-1,3-propanyl ester (HepDirect) prodrug moiety.

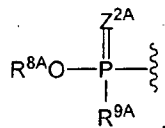
[0194] In some embodiments, R^{6A} and R^{7A} can be taken together to form an

optionally substituted , wherein the oxygens connected to R^{6A} and R^{7A}, the phosphorus and the moiety form a six-membered to ten-membered ring system. Example of

an optionally substituted  include , ,  and . In some embodiments, R^{6A} and R^{7A} can form a cyclosaligenyl (cycloSal) prodrug.

[0195] In some embodiments, R^{6A} and R^{7A} can be the same. In some embodiments, R^{6A} and R^{7A} can be different.

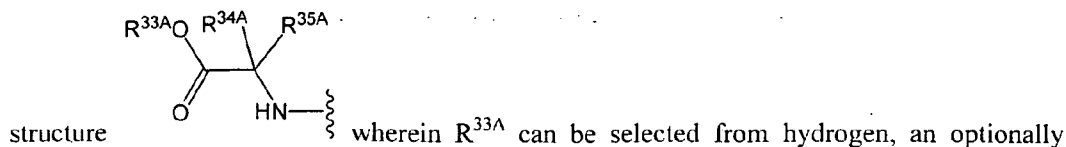
[0196] In some embodiments, Z^{1A} can be oxygen. In other embodiments, Z^{1A} can be sulfur.

[0197] In some embodiments, R^{1A} can be . In some embodiments, R^{8A} can be selected from absent, hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl and an optionally substituted C₃₋₆ cycloalkenyl; and R^{9A} can be independently

selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl and an optionally substituted C_{3-6} cycloalkenyl.

[0198] In some embodiments, R^{8A} can be hydrogen, and R^{9A} can be an optionally substituted C_{1-6} alkyl. Examples of suitable C_{1-6} alkyls include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, pentyl (branched and straight-chained), and hexyl (branched and straight-chained). In other embodiments, R^{8A} can be hydrogen, and R^{9A} can be $NR^{30A}R^{31A}$, wherein R^{30A} and R^{31A} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl and an optionally substituted aryl(C_{1-4} alkyl). In some embodiments, one of R^{30A} and R^{31A} can be hydrogen and the other of R^{30A} and R^{31A} can be an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl, an optionally substituted C_{2-6} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl and an optionally substituted benzyl.

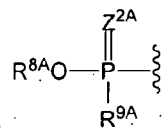
[0199] In some embodiments, R^{8A} can be absent or hydrogen; and R^{9A} can be an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative. In other embodiments, R^{8A} can be an optionally substituted aryl; and R^{9A} can be an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative. In still other embodiments, R^{8A} can be an optionally substituted heteroaryl; and R^{9A} can be an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative. In some embodiments, R^{9A} can be selected from alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine and ester derivatives thereof. Examples of an optionally substituted N-linked amino acid ester derivatives include optionally substituted versions of the following: N-alanine isopropyl ester, N-alanine cyclohexyl ester, N-alanine neopentyl ester, N-valine isopropyl ester and N-leucine isopropyl ester. In some embodiments, R^{9A} can have the

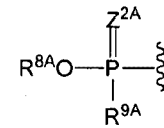


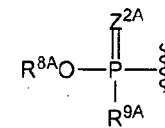
substituted C₁₋₆ alkyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted aryl, an optionally substituted aryl(C₁₋₆ alkyl) and an optionally substituted haloalkyl; R^{34A} can be selected from hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₁₋₆ haloalkyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₆ aryl, an optionally substituted C₁₀ aryl and an optionally substituted aryl(C₁₋₆ alkyl); and R^{35A} can be hydrogen or an optionally substituted C₁₋₄ alkyl; or R^{34A} and R^{35A} can be taken together to form an optionally substituted C₃₋₆ cycloalkyl.

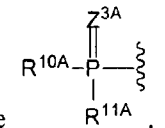
[0200] When R^{34A} is substituted, R^{34A} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{34A} can be an unsubstituted C₁₋₆ alkyl, such as those described herein. In some embodiments, R^{34A} can be hydrogen. In other embodiments, R^{34A} can be methyl. In some embodiments, R^{33A} can be an optionally substituted C₁₋₆ alkyl. Examples of optionally substituted C₁₋₆ alkyls include optionally substituted variants of the following: methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, pentyl (branched and straight-chained), and hexyl (branched and straight-chained). In some embodiments, R^{33A} can be methyl or isopropyl. In some embodiments, R^{33A} can be ethyl or neopentyl. In other embodiments, R^{33A} can be an optionally substituted C₃₋₆ cycloalkyl. Examples of optionally substituted C₃₋₆ cycloalkyl include optionally substituted variants of the following: cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. In some embodiments, R^{33A} can be an optionally substituted cyclohexyl. In still other embodiments, R^{33A} can be an optionally substituted aryl, such as phenyl and naphthyl. In yet still other embodiments, R^{33A} can be an optionally substituted aryl(C₁₋₆ alkyl). In some embodiments, R^{33A} can be an optionally substituted benzyl. In some embodiments, R^{33A} can be an optionally substituted C₁₋₆ haloalkyl, for example, CF₃. In some embodiments, R^{35A} can be hydrogen. In other embodiments, R^{35A} can be an optionally substituted C₁₋₄ alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{35A} can be methyl. In some embodiments, R^{34A} and R^{35A} can be taken together to form an optionally substituted C₃₋₆ cycloalkyl. Examples of optionally substituted C₃₋₆ cycloalkyl include optionally substituted variants of the following: cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Depending on the groups that are selected for R^{34A} and R^{35A}, the carbon to which R^{34A} and R^{35A} are attached may be a chiral

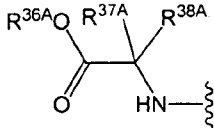
center. In some embodiment, the carbon to which R^{34A} and R^{35A} are attached may be a (*R*)-chiral center. In other embodiments, the carbon to which R^{34A} and R^{35A} are attached may be a (*S*)-chiral center.

[0201] In some embodiments, when R^{1A} is , Z^{2A} can be O (oxygen).

In other embodiments, when R^{1A} is , Z^{2A} can be S (sulfur). In some

embodiments, when R^{1A} is , a compound of Formula (I) can be a phosphoramidate prodrug, such as an aryl phosphoramidate prodrug.

[0202] In some embodiments, R^{1A} can be . In some embodiments, R^{10A} and R^{11A} can be both an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative. In some embodiments, R^{10A} and R^{11A} can be independently selected from alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine and ester derivatives thereof. In some embodiments, R^{10A} and R^{11A} can be an optionally substituted version of the following: N-alanine isopropyl ester, N-alanine cyclohexyl ester, N-alanine neopentyl ester, N-valine isopropyl ester and N-leucine isopropyl ester. In some embodiments, R^{10A} and R^{11A} can

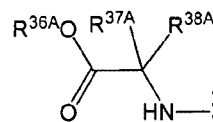
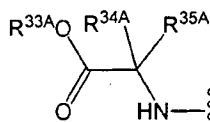
independently have the structure  wherein R^{36A} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-6} alkyl) and an optionally substituted haloalkyl; R^{37A} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an

optionally substituted C₆ aryl, an optionally substituted C₁₀ aryl and an optionally substituted aryl(C₁₋₆ alkyl); and R^{38A} can be hydrogen or an optionally substituted C₁₋₄ alkyl; or R^{37A} and R^{38A} can be taken together to form an optionally substituted C₃₋₆ cycloalkyl.

[0203] When R^{37A} is substituted, R^{37A} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{37A} can be an unsubstituted C₁₋₆ alkyl, such as those described herein. In some embodiments, R^{37A} can be hydrogen. In other embodiments, R^{37A} can be methyl. In some embodiments, R^{36A} can be an optionally substituted C₁₋₆ alkyl. Examples of optionally substituted C₁₋₆ alkyls include optionally substituted variants of the following: methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, pentyl (branched and straight-chained), and hexyl (branched and straight-chained). In some embodiments, R^{36A} can be methyl or isopropyl. In some embodiments, R^{36A} can be ethyl or neopentyl. In other embodiments, R^{36A} can be an optionally substituted C₃₋₆ cycloalkyl. Examples of optionally substituted C₃₋₆ cycloalkyl include optionally substituted variants of the following: cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. In some embodiments, R^{36A} can be an optionally substituted cyclohexyl. In still other embodiments, R^{36A} can be an optionally substituted aryl, such as phenyl and naphthyl. In yet still other embodiments, R^{36A} can be an optionally substituted aryl(C₁₋₆ alkyl). In some embodiments, R^{36A} can be an optionally substituted benzyl. In some embodiments, R^{36A} can be an optionally substituted C₁₋₆ haloalkyl, for example, CF₃. In some embodiments, R^{38A} can be hydrogen. In other embodiments, R^{38A} can be an optionally substituted C₁₋₄ alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{38A} can be methyl. In some embodiments, R^{37A} and R^{38A} can be taken together to form an optionally substituted C₃₋₆ cycloalkyl. Examples of optionally substituted C₃₋₆ cycloalkyl include optionally substituted variants of the following: cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Depending on the groups that are selected for R^{37A} and R^{38A}, the carbon to which R^{37A} and R^{38A} are attached may be a chiral center. In some embodiment, the carbon to which R^{37A} and R^{38A} are attached may be a (*R*)-chiral center. In other embodiments, the carbon to which R^{37A} and R^{38A} are attached may be a (*S*)-chiral center.

[0204]

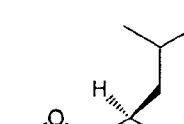
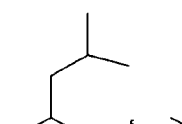
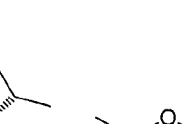
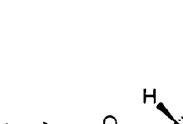
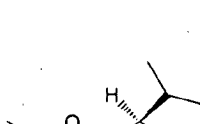
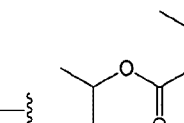
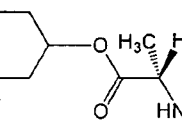
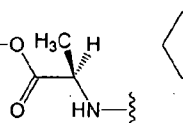
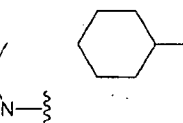
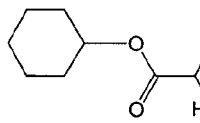
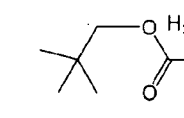
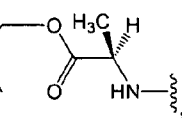
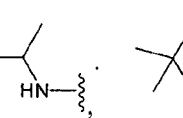
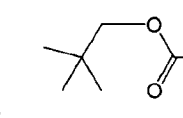
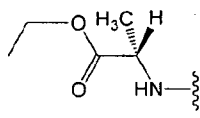
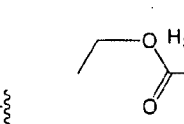
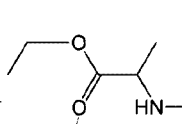
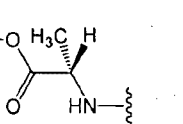
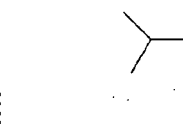
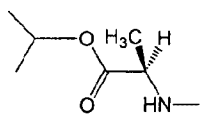
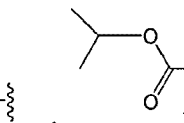
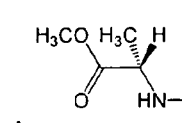
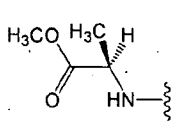
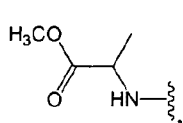
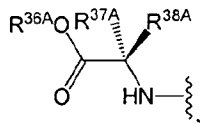
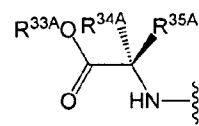
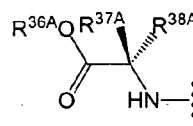
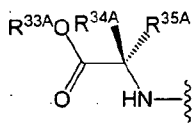
Examples of suitable



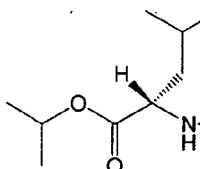
and

groups

include the following:



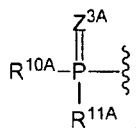
and



[0205]

In some embodiments, R^{10A} and R^{11A} can be the same. In some embodiments, R^{10A} and R^{11A} can be different.

[0206] In some embodiments, Z^{3A} can be O (oxygen). In other embodiments, Z^{3A}

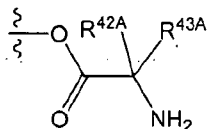
can be S (sulfur). In some embodiments, when R^{1A} is , a compound of Formula (I) can be a phosphonic diamide prodrug.

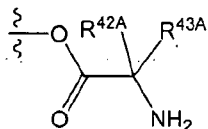
[0207] Various substituents can be present at the 4'-position of the pentose ring. In some embodiments, R^{2A} can be an unsubstituted C_{1-4} alkyl. Unsubstituted C_{1-4} alkyls include methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl and tert-butyl. In other embodiments, R^{2A} can be an unsubstituted C_{2-4} alkenyl, such as ethenyl, propenyl and butenyl. In still other embodiments, R^{2A} can be an unsubstituted C_{2-4} alkynyl, for example, ethynyl, propynyl and butynyl. In yet still other embodiments, R^{2A} can be a haloalkyl. Examples of a haloalkyls are $-(CH_2)_{1-6}$ halogen and $-CHF_2$. In some embodiments, the haloalkyl can be $-(CH_2)_{1-6}F$ or $-(CH_2)_{1-6}Cl$. In some embodiments, the haloalkyl can be fluoromethyl. In other embodiments, R^{2A} can be $-CHF_2$. In yet still other embodiments, R^{2A} can be a C_{1-6} azidoalkyl. For example, R^{2A} can be an azidomethyl, azidoethyl, azidopropyl, azidobutyl, azidopentyl or azidohexyl. In some embodiments, R^{2A} can be a C_{1-6} aminoalkyl. For example, R^{2A} can be an aminomethyl, aminoethyl, aminopropyl, aminobutyl, aminopentyl or aminohexyl. In other embodiments, R^{2A} can be halo. For example, R^{2A} can be fluoro (F) or chloro (Cl). In still other embodiments, R^{2A} can be hydrogen. In yet still other embodiments, R^{2A} can be $-CN$. In some embodiments, R^{2A} can be selected from halogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl, an optionally substituted C_{2-6} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted $-O-C_{1-6}$ alkyl, an optionally substituted $-O-C_{3-6}$ alkenyl, an optionally substituted $-O-C_{3-6}$ alkynyl and cyano.

[0208] A variety of substituents can also be present at the 2'-position of the pentose ring. In some embodiments, R^{4A} can be OH. In other embodiments, R^{4A} can be $-OC(=O)R^{''B}$, wherein $R^{''B}$ can be an optionally substituted C_{1-24} alkyl. In some embodiments, R^{4A} can be $-OC(=O)R^{''B}$, wherein $R^{''B}$ can be an unsubstituted C_{1-4} alkyl. In still other embodiments, R^{4A} can be halo. In some embodiments, R^{4A} can be F. In other embodiments, R^{4A} can be Cl. In some embodiments, R^{4A} can be N_3 . In some embodiments, R^{4A} can be $NR^{''B1}R^{''B2}$. For example, R^{4A} can be NH_2 . Other examples can be a mono-

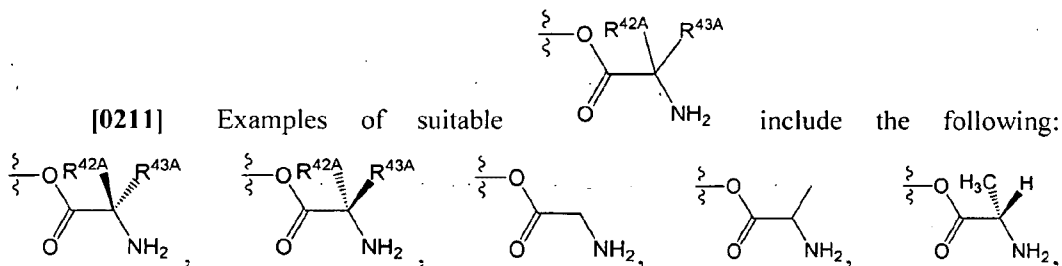
substituted C₁₋₆ alkyl-amine or a di-substituted C₁₋₆ alkyl-amine. In other embodiments, R^{4A} can be hydrogen (H).

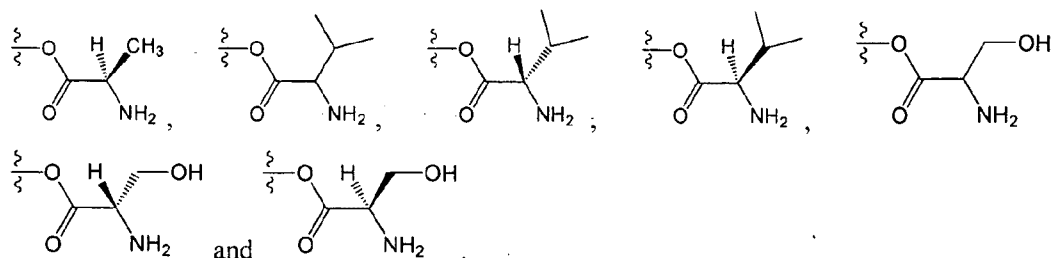
[0209] In still other embodiments, R^{4A} can be an optionally substituted O-linked amino acid, such as a O-linked alpha-amino acid. In some embodiments, the O-linked amino



acid can have the structure , wherein R^{42A} can be selected from hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₁₋₆ haloalkyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₆ aryl, an optionally substituted C₁₀ aryl and an optionally substituted aryl(C₁₋₆ alkyl); and R^{43A} can be hydrogen or an optionally substituted C₁₋₄ alkyl; or R^{42A} and R^{43A} can be taken together to form an optionally substituted C₃₋₆ cycloalkyl.

[0210] When R^{42A} is substituted, R^{42A} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{42A} can be an unsubstituted C₁₋₆ alkyl, such as those described herein. In some embodiments, R^{42A} can be hydrogen. In other embodiments, R^{42A} can be methyl. In some embodiments, R^{43A} can be hydrogen. In other embodiments, R^{43A} can be an optionally substituted C₁₋₄ alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{43A} can be methyl. Depending on the groups that are selected for R^{42A} and R^{43A}, the carbon to which R^{42A} and R^{43A} are attached may be a chiral center. In some embodiment, the carbon to which R^{42A} and R^{43A} are attached may be a (R)-chiral center. In other embodiments, the carbon to which R^{42A} and R^{43A} are attached may be a (S)-chiral center.

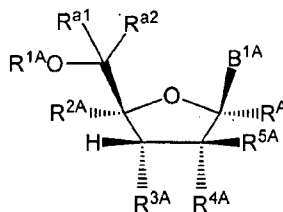




[0212] In some embodiments, R^{5A} can be H. In other embodiments, R^{5A} can be halo, including F and Cl. In still other embodiments, R^{5A} can be an optionally substituted C_{1-6} alkyl. For example, R^{5A} can be a substituted or unsubstituted version of the following: methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, tert-butyl, pentyl (branched or straight) and hexyl (branched or straight). In some embodiments, R^{5A} can be a halo-substituted C_{1-6} alkyl, such as $-CH_2F$. In yet still other embodiments, R^{5A} can be an optionally substituted C_{2-6} alkenyl. In some embodiments, R^{5A} can be an optionally substituted C_{2-6} alkynyl. For example, R^{5A} can be ethynyl. In some embodiments, R^{5A} can be hydroxy (OH).

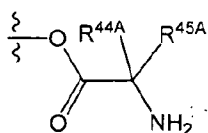
[0213] A variety of substituents can be present at the 1'-position of the pentose ring. In some embodiments, R^A can be hydrogen. In some embodiments, R^A can be deuterium. In still other embodiments, R^A can be an unsubstituted C_{1-3} alkyl (such as methyl, ethyl, n-propyl and iso-propyl). In yet still other embodiments, R^A can be an unsubstituted C_{2-4} alkenyl (for example, ethenyl, propenyl (branched or straight) and butenyl (branched or straight)). In some embodiments, R^A can be an unsubstituted C_{2-3} alkynyl (such as ethynyl and propynyl (branched or straight)). In other embodiments, R^A can be an unsubstituted cyano.

[0214] In some embodiments, ----- can be both absent such that a compound of



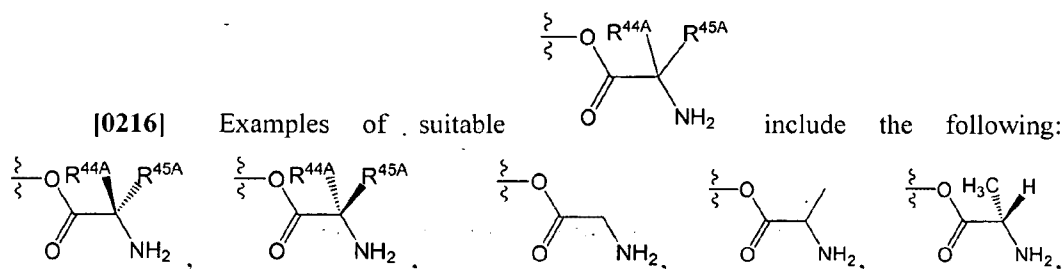
Formula (I) has the structure: . When ----- are both absent, the 3'-position can have various groups present. In some embodiments, R^{3A} can be H. In other embodiments, R^{3A} can be halo. For example, R^{3A} can be fluoro (F) or chloro (Cl). In still other embodiments, R^{3A} can be OH. In some embodiments, R^{3A} can be $-OC(=O)R^{3A}$, wherein R^{3A} can be an optionally substituted C_{1-24} alkyl. In some embodiments, R^{3A} can be

$-\text{OC}(=\text{O})\text{R}^{3\text{A}}$, wherein $\text{R}^{3\text{A}}$ can be an unsubstituted C_{1-4} alkyl. In other embodiments, $\text{R}^{3\text{A}}$ can be an optionally substituted O-linked amino acid, such as an optionally substituted O-linked alpha-amino acid. The optionally substituted O-linked amino acid can have the



structure: $\text{O}-\text{C}(=\text{O})-\text{C}(\text{NH}_2)(\text{R}^{44\text{A}})(\text{R}^{45\text{A}})$, wherein $\text{R}^{44\text{A}}$ can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_6 aryl, an optionally substituted C_{10} aryl and an optionally substituted aryl(C_{1-6} alkyl); and $\text{R}^{45\text{A}}$ can be hydrogen or an optionally substituted C_{1-4} alkyl; or $\text{R}^{44\text{A}}$ and $\text{R}^{45\text{A}}$ can be taken together to form an optionally substituted C_{3-6} cycloalkyl.

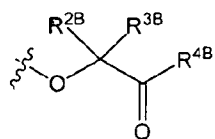
[0215] When $\text{R}^{44\text{A}}$ is substituted, $\text{R}^{44\text{A}}$ can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, $\text{R}^{44\text{A}}$ can be an unsubstituted C_{1-6} alkyl, such as those described herein. In some embodiments, $\text{R}^{44\text{A}}$ can be hydrogen. In other embodiments, $\text{R}^{44\text{A}}$ can be methyl. In some embodiments, $\text{R}^{45\text{A}}$ can be hydrogen. In other embodiments, $\text{R}^{45\text{A}}$ can be an optionally substituted C_{1-4} alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, $\text{R}^{45\text{A}}$ can be methyl. Depending on the groups that are selected for $\text{R}^{44\text{A}}$ and $\text{R}^{45\text{A}}$, the carbon to which $\text{R}^{44\text{A}}$ and $\text{R}^{45\text{A}}$ are attached may be a chiral center. In some embodiment, the carbon to which $\text{R}^{44\text{A}}$ and $\text{R}^{45\text{A}}$ are attached may be a (*R*)-chiral center. In other embodiments, the carbon to which $\text{R}^{44\text{A}}$ and $\text{R}^{45\text{A}}$ are attached may be a (*S*)-chiral center.



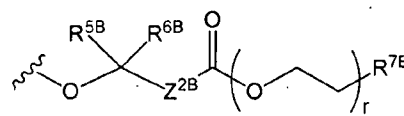


bond, R^{1B} can be an $-O$ -optionally substituted C_{1-6} alkyl. For example, R^{1B} can be an $-O$ -unsubstituted C_{1-6} alkyl.

[0220] In some embodiments, when ----- are each a single bond, R^{1B} can be

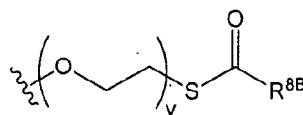


In other embodiments, R^{1B} can be



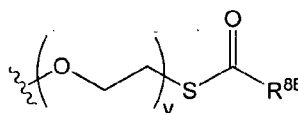
For example, R^{1B} can be a isopropoxyloxycarbonyloxymethoxy or pivaloyloxymethoxy

group. In still some embodiments, R^{1B} can be



A S-acylthioethyl

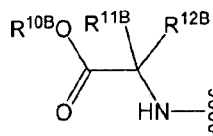
(SATE) group is an example of a



group. In yet still other

embodiments, R^{1B} can be an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative, such as an optionally substituted N-linked alpha-amino acid or an optionally substituted N-linked alpha-amino acid ester derivative.

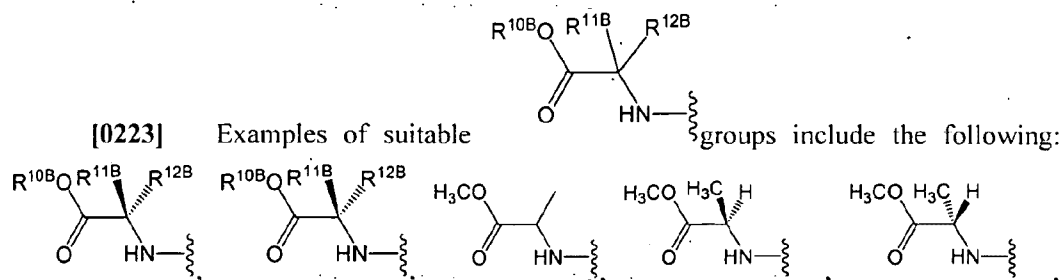
[0221] Examples of an optionally substituted N-linked amino acids and an optionally substituted N-linked amino acid ester derivatives are described herein. In some embodiments, R^{1B} can be selected from alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine and ester derivatives thereof. In some embodiments, R^{1B} can be an optionally substituted version of the following: N-alanine isopropyl ester, N-alanine cyclohexyl ester, N-alanine neopentyl ester, N-valine isopropyl ester and N-leucine isopropyl ester. In some embodiments, R^{1B} can have the structure

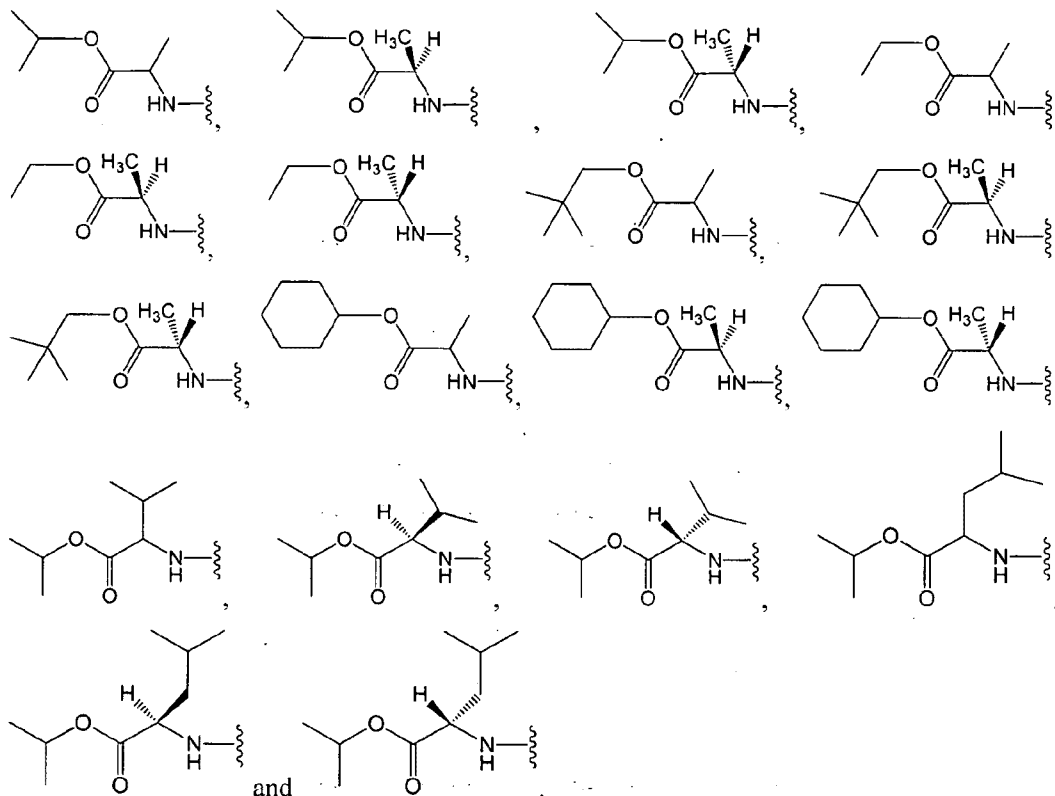


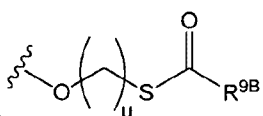
wherein R^{10B} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-6} alkyl) and an optionally substituted haloalkyl; R^{11B} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_6 aryl, an optionally

substituted C_{10} aryl and an optionally substituted aryl(C_{1-6} alkyl); and R^{12B} can be hydrogen or an optionally substituted C_{1-4} alkyl; or R^{11B} and R^{12B} can be taken together to form an optionally substituted C_{3-6} cycloalkyl.

[0222] As described herein, R^{11B} can be substituted. Examples of substituents include one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{11B} can be an unsubstituted C_{1-6} alkyl, such as those described herein. In some embodiments, R^{11B} can be hydrogen. In other embodiments, R^{11B} can be methyl. In some embodiments, R^{10B} can be an optionally substituted C_{1-6} alkyl. In some embodiments, R^{10B} can be methyl, ethyl, isopropyl or neopentyl. In other embodiments, R^{10B} can be an optionally substituted C_{3-6} cycloalkyl. Examples of optionally substituted C_{3-6} cycloalkyl include optionally substituted variants of the following: cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. In some embodiments, R^{10B} can be an optionally substituted cyclohexyl. In still other embodiments, R^{10B} can be an optionally substituted aryl, such as phenyl and naphthyl. In yet still other embodiments, R^{10B} can be an optionally substituted aryl(C_{1-6} alkyl), for example, an optionally substituted benzyl. In some embodiments, R^{10B} can be an optionally substituted C_{1-6} haloalkyl, for example, CF_3 . In some embodiments, R^{12B} can be hydrogen. In other embodiments, R^{12B} can be an optionally substituted C_{1-4} alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{12B} can be methyl. In some embodiments, R^{11B} and R^{12B} can be taken together to form an optionally substituted C_{3-6} cycloalkyl. Depending on the groups that are selected for R^{11B} and R^{12B} , the carbon to which R^{11B} and R^{12B} are attached may be a chiral center. In some embodiment, the carbon to which R^{11B} and R^{12B} are attached may be a (*R*)-chiral center. In other embodiments, the carbon to which R^{11B} and R^{12B} are attached may be a (*S*)-chiral center.



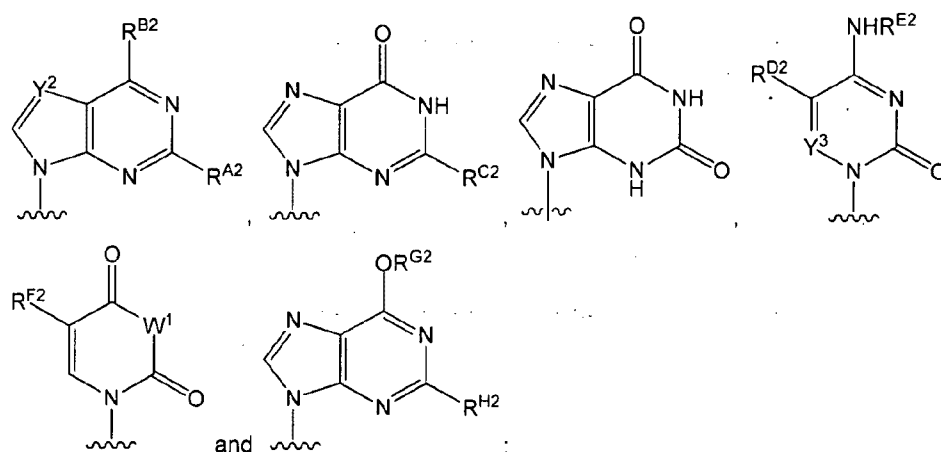


[0224] In some embodiments, R^{1B} can be . In some embodiments, R^{9B} can be hydrogen. In other embodiments, R^{9B} can be an optionally substituted C_{1-24} alkyl. In still other embodiments, R^{9B} can be an optionally substituted aryl, for example, an optionally substituted phenyl. In some embodiments, R^{9B} can be an optionally substituted C_{1-6} alkyl. In some embodiments, R^{9B} can be an unsubstituted C_{1-6} alkyl. In some embodiments, u can be 3. In other embodiments, u can be 4. In still other embodiments, u can be 5.

[0225] In some embodiments, Z^{1B} can be oxygen (O). In other embodiments, Z^{1B} can be S (sulfur).

[0226] Various optionally substituted heterocyclic bases can be attached to the pentose ring. In some embodiments, one or more of the amine and/or amino groups of the optionally substituted heterocyclic base may be protected with a suitable protecting group.

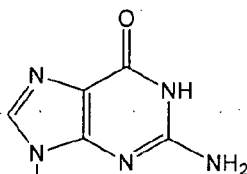
For example, an amino group may be protected by transforming the amine and/or amino group to an amide or a carbamate. In some embodiments, an optionally substituted heterocyclic base or an optionally substituted heterocyclic base can include a group that improves the solubility of the compound (for example, $-(CH_2)_{1-2}-O-P(=O)(OW^{1A})_2$). In some embodiments, an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with one or more protected amino groups can have one of the following structures:



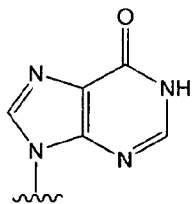
wherein: R^{A2} can be selected from hydrogen, halogen and NHR^{J2} , wherein R^{J2} can be selected from hydrogen, $-C(=O)R^{K2}$ and $-C(=O)OR^{L2}$; R^{B2} can be halogen or NHR^{W2} , wherein R^{W2} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl, an optionally substituted C_{3-8} cycloalkyl, $-C(=O)R^{M2}$ and $-C(=O)OR^{N2}$; R^{C2} can be hydrogen or NHR^{O2} , wherein R^{O2} can be selected from hydrogen, $-C(=O)R^{P2}$ and $-C(=O)OR^{Q2}$; R^{D2} can be selected from hydrogen, deuterium, halogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl; R^{E2} can be selected from hydrogen, hydroxy, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{3-8} cycloalkyl, $-C(=O)R^{R2}$ and $-C(=O)OR^{S2}$; R^{F2} can be selected from hydrogen, halogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl; Y^2 and Y^3 can be independently N (nitrogen) or CR^{I2} , wherein R^{I2} can be selected from hydrogen, halogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl; W^1 can be NH , $-NCH_2-OC(=O)CH(NH_2)-CH(CH_3)_2$ or $-(CH_2)_{1-2}-$

O-P(=O)(OW^{1A})₂, wherein W^{1A} can be selected from absent hydrogen and an optionally substituted C₁₋₆ alkyl; R^{G2} can be an optionally substituted C₁₋₆ alkyl; R^{H2} can be hydrogen or NHR^{I2}, wherein R^{I2} can be independently selected from hydrogen, -C(=O)R^{U2} and -C(=O)OR^{V2}; and R^{K2}, R^{L2}, R^{M2}, R^{N2}, R^{P2}, R^{Q2}, R^{R2}, R^{S2}, R^{U2} and R^{V2} can be independently selected from hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkenyl, C₆₋₁₀ aryl, heteroaryl, heterocyclyl, aryl(C₁₋₆ alkyl), heteroaryl(C₁₋₆ alkyl) and heterocyclyl(C₁₋₆ alkyl). In some embodiments, the structures shown above can be modified by replacing one or more hydrogens with substituents selected from the list of substituents provided for the definition of "substituted." Those skilled in the art understand that when W^{1A} is absent, the oxygen atom will have an associated negative charge. In some embodiments, the substituent on the base can result in the formation of a salt of a compound of Formula (I).

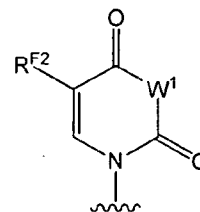
[0227] In some embodiments, B^{1A} can be an optionally substituted purine base. In other embodiments, B^{1A} can be an optionally substituted pyrimidine base. In some



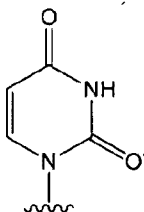
embodiments, B^{1A} can be . In other embodiments, B^{1A} can be



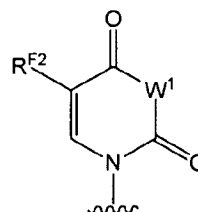
In still other embodiments, B^{1A} can be



, such as

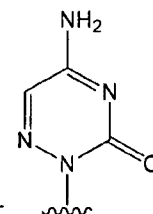
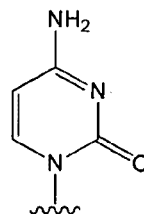
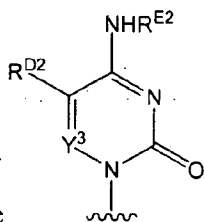


In yet still other embodiments, B^{1A} can be

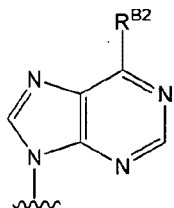


, wherein W¹ can

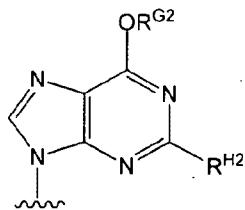
be -NCH₂-OC(=O)CH(NH₂)-CH(CH₃)₂ or -(CH₂)₁₋₂-O-P(=O)(OW^{1A})₂. In some



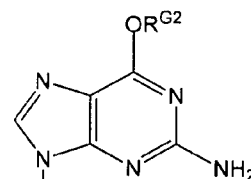
embodiments, B^{1A} can be , for example, or . In other embodiments, R^{D2} can be hydrogen. In still other embodiments, B^{1A} can be



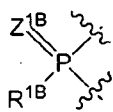
. In some embodiments, R^{B2} can be NH_2 . In other embodiments, R^{B2} can be NHR^{W2} , wherein R^{W2} can be $-C(=O)R^{M2}$ or $-C(=O)OR^{N2}$. In still other embodiments, B^{1A}



can be . In some embodiments, B^{1A} can be

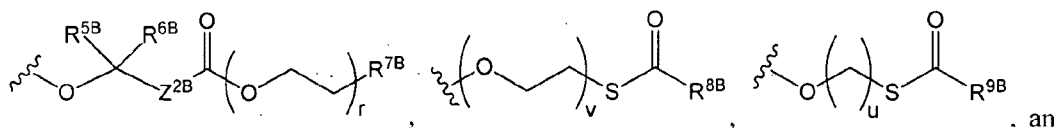
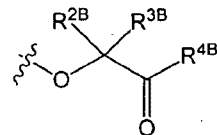


[0228] In some embodiments, a compound of Formula (I), or a pharmaceutically acceptable salt thereof, can be used to ameliorate or treat a viral infection, wherein: B^{1A} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; ----- can be absent or a single bond, provided that both ----- are absent or both ----- are a single bond; when ----- are both absent, then Z^1 can be absent, O^1 can be OR^{1A} , R^{3A} can be selected from H, halo, OH, $-OC(=O)R^{3A}$ and an optionally substituted O-linked amino acid, R^{4A} can be selected from OH, halo, $-OC(=O)R^{4A}$ and an optionally substituted O-linked amino acid, or R^{3A} and R^{4A} can be both an oxygen atom connected via a carbonyl to form a 5-membered ring; when ----- are each a single

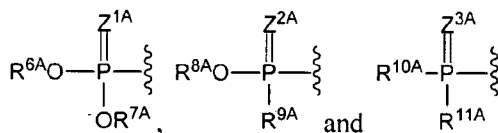


bond, then Z^1 can be R^{1B} , O^1 can be O, R^{3A} can be O; R^{4A} can be selected from OH, halo, $-OC(=O)R^{4A}$ and an optionally substituted O-linked amino acid; and R^{1B} can be

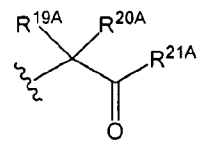
selected from O⁻, OH, an -O-optionally substituted C₁₋₆ alkyl.



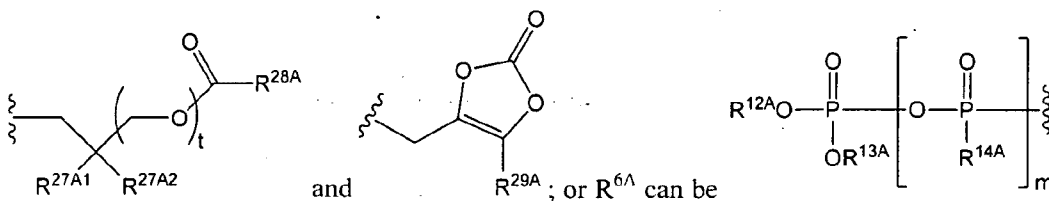
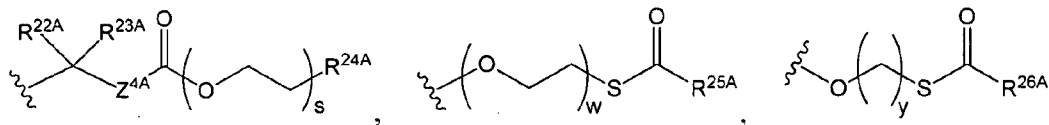
optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{1A} can be selected from hydrogen, an optionally substituted acyl, an



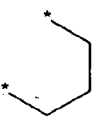
optionally substituted O-linked amino acid, optionally substituted halo, an unsubstituted C₁₋₄ alkyl, an unsubstituted C₂₋₄ alkenyl, -(CH₂)₁₋₆ halogen or -(CH₂)₁₋₆N₃; R^{5A} can be selected from H, halo, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl and an optionally substituted C₂₋₆ alkynyl; R^{6A}, R^{7A} and R^{8A} can be independently selected from absent, hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl(C₁₋₆ alkyl), an optionally substituted $^{*-(CR^{15A}R^{16A})_p-O-C_{1-24}}$ alkyl, an optionally

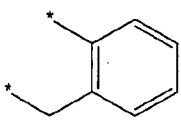


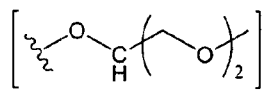
substituted $^{*-(CR^{17A}R^{18A})_q-O-C_{1-24}}$ alkenyl,



and R^{7A} can be absent or hydrogen; or R^{6A} and R^{7A} can be taken together to form a moiety

selected from an optionally substituted  and an optionally substituted

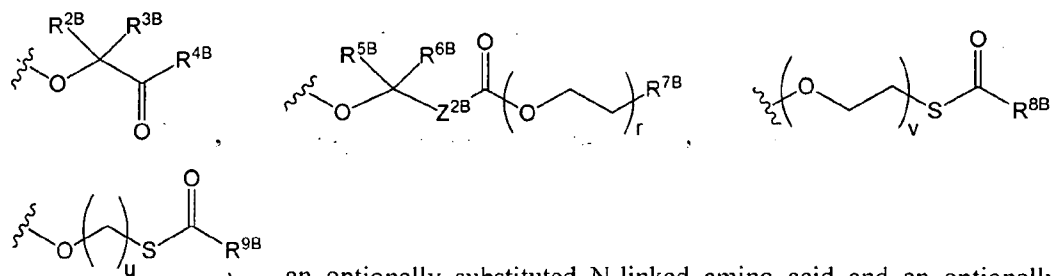
, wherein the oxygens connected to R^{6A} and R^{7A} , the phosphorus and the moiety form a six-membered to ten-membered ring system; R^{9A} can be independently selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{10A} and R^{11A} can be independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative; R^{12A} and R^{13A} can be independently absent or hydrogen; R^{14A} can be absent, hydrogen or methyl; each R^{15A} , each R^{16A} , each R^{17A} and each R^{18A} can be independently hydrogen, an optionally substituted C_{1-24} alkyl or an alkoxy; R^{19A} , R^{20A} , R^{22A} , R^{23A} , R^{21B} , R^{31B} , R^{51B} and R^{61B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{21A} and R^{41B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl and an optionally substituted $-O$ -monocyclic heterocyclyl; R^{24A} and R^{7B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl, an

optionally substituted $-O$ -monocyclic heterocyclyl and ; R^{25A} , R^{26A} , R^{29A} , R^{8B} and R^{9B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{27A1} and R^{27A2} can be independently selected from $-C\equiv N$, an optionally substituted C_{2-8} organylcarbonyl, an optionally substituted C_{2-8} alkoxy carbonyl and an optionally substituted C_{2-8} organylaminocarbonyl; R^{28A} is selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl and an

optionally substituted C₃₋₆ cycloalkenyl; R^{30A} and R^{31A} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl and an optionally substituted C₃₋₆ cycloalkenyl; R^{3A} and R^{3B} can be independently an optionally substituted C₁₋₂₄ alkyl; m, v and w can be 0 or 1; p and q can be independently 1, 2 or 3; r and s can be independently 0, 1, 2 or 3; t is 1 or 2; u and y can be independently 3, 4 or 5; and Z^{1A}, Z^{2A}, Z^{3A}, Z^{4A}, Z^{1B} and Z^{2B} can be independently O or S; wherein the viral infection can be caused by a virus selected from a Picornaviridae virus and a *Flaviviridae* virus; and provided that when the *Flaviviridae* virus is hepatitis C virus, then the compound of Formula (I), or a pharmaceutically acceptable salt thereof, cannot be selected from a compound in paragraphs [0292] and [0295], or a pharmaceutically acceptable salt of the foregoing.

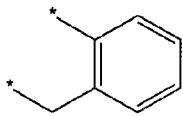
[0229] In some embodiments, a compound of Formula (I), or a pharmaceutically acceptable salt thereof, can be used to ameliorate or treat a viral infection, wherein: B^{1A} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; ----- can be absent or a single bond, provided that both ----- are absent or both ----- are a single bond; when ----- are both absent, then Z¹ can be absent, O¹ can be OR^{1A}, R^{3A} can be selected from H, halo, OH, -OC(=O)R^{3A} and an optionally substituted O-linked amino acid, R^{4A} can be selected from OH, halo, N₃, -OC(=O)R^{4A}, an optionally substituted O-linked amino acid and NR^{3B1}R^{3B2}, or R^{3A} and R^{4A} can be both an oxygen atom connected via a carbonyl to form a 5-membered ring; when -----

-- are each a single bond, then Z¹ can be R^{1B}, O¹ can be O, R^{3A} can be O; R^{4A} can be selected from OH, halo, N₃, -OC(=O)R^{4A}, an optionally substituted O-linked amino acid and NR^{3B1}R^{3B2}; and R^{1B} can be selected from O⁻, OH, an -O-optionally substituted C₁₋₆ alkyl.

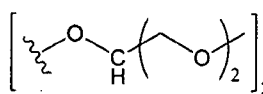


$$\begin{array}{c} \text{Z}^{1\text{A}} \\ \parallel \\ \text{R}^{6\text{A}}\text{O}-\text{P}-\text{OR}^{7\text{A}} \\ | \\ \text{OR}^{7\text{A}} \end{array}$$
$$\begin{array}{ccc} \text{R}^8\text{A}-\text{O}-\text{P} & & \text{R}^{10}\text{A}-\text{P} \\ \text{Z}^{2\text{A}} & & \text{Z}^{3\text{A}} \\ \text{R}^9\text{A} & \text{and} & \text{R}^{11}\text{A} \end{array}$$
$$\begin{array}{c} \text{R}^{19\text{A}} \quad \text{R}^{20\text{A}} \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{C}=\text{O} \quad \text{R}^{21\text{A}} \end{array}$$
$$\begin{array}{c} \text{R}^{22\text{A}} \quad \text{R}^{23\text{A}} \\ \diagdown \quad \diagup \\ \text{---} \text{C} \text{---} \text{Z}^{4\text{A}} \text{---} \text{C}(=\text{O}) \text{---} (\text{O} \text{---} \text{CH}_2 \text{---} \text{CH}_2 \text{---})_s \text{---} \text{R}^{24\text{A}} \\ \diagup \\ \text{wavy line} \end{array}$$
$$\sim \left(\text{O} - \text{CH}_2 - \text{CH}_2 \right)_w \text{S} - \text{C}(=\text{O}) - \text{R}^{25A}$$
*OCC(S(=O)(=O)C(R26A))
$$\begin{array}{c} \text{O} \\ || \\ \text{---} \text{C} \text{---} \text{R}^{28\text{A}} \\ | \\ (\text{---CH}_2\text{---O})_t \\ | \\ \text{---CH}_2\text{---} \\ / \quad \backslash \\ \text{R}^{27\text{A}1} \quad \text{R}^{27\text{A}2} \end{array}$$
$$\text{R}^{12\text{A}}\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{OR}^{13\text{A}} \end{array}\right)-\left[\text{O}-\text{P}\left(\begin{array}{c} \text{O} \\ \parallel \\ \text{R}^{14\text{A}} \end{array}\right)\right]_m$$

selected from an optionally substituted  and an optionally substituted

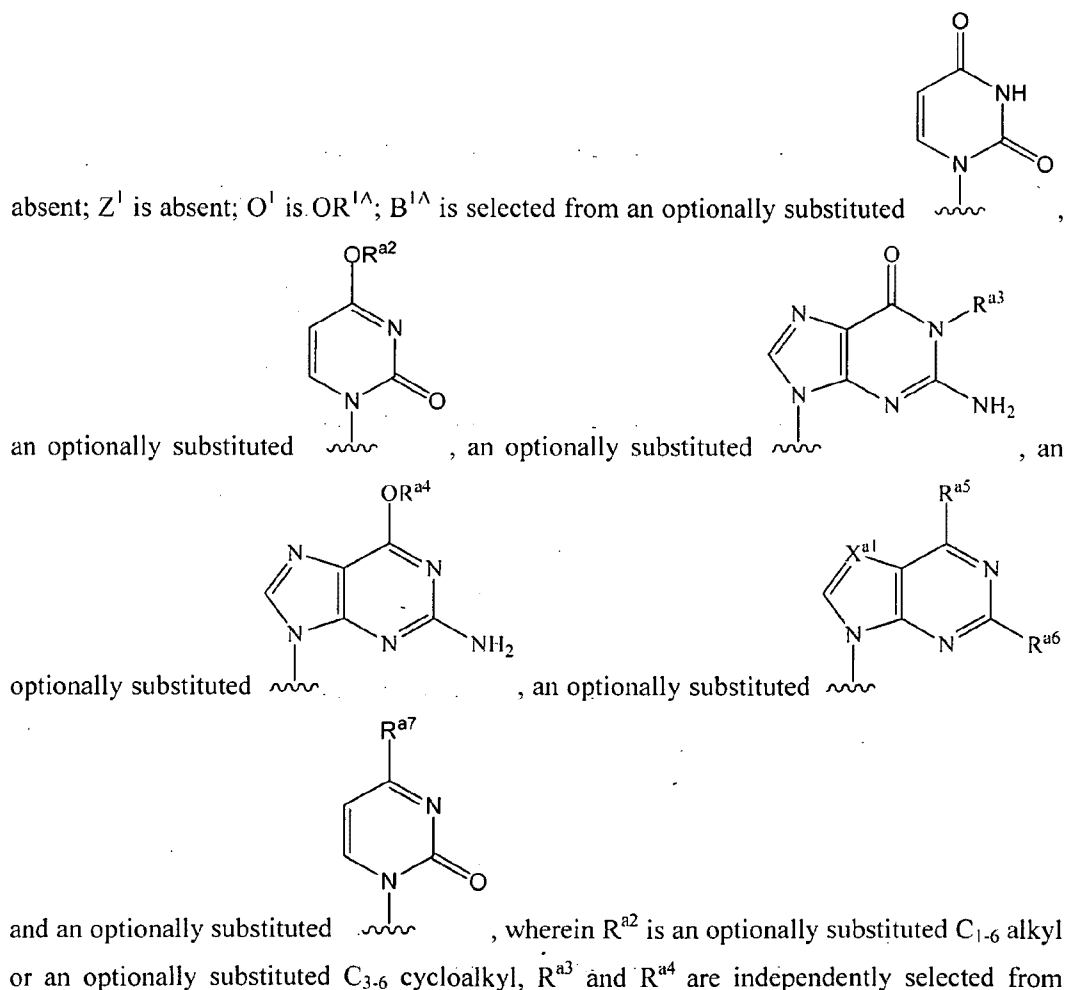


, wherein the oxygens connected to R^{6A} and R^{7A} , the phosphorus and the moiety form a six-membered to ten-membered ring system; R^{9A} can be independently selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{10A} and R^{11A} can be independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative; R^{12A} and R^{13A} can be independently absent or hydrogen; R^{14A} can be O^- , OH or methyl; each R^{15A} , each R^{16A} , each R^{17A} and each R^{18A} can be independently hydrogen, an optionally substituted C_{1-24} alkyl or an alkoxy; R^{19A} , R^{20A} , R^{22A} , R^{23A} , R^{23B} , R^{3B} , R^{5B} and R^{6B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{21A} and R^{4B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl and an optionally substituted $-O$ -monocyclic heterocyclyl; R^{24A} and R^{7B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted $-O$ -aryl, an optionally substituted $-O$ -heteroaryl, an optionally substituted $-O$ -

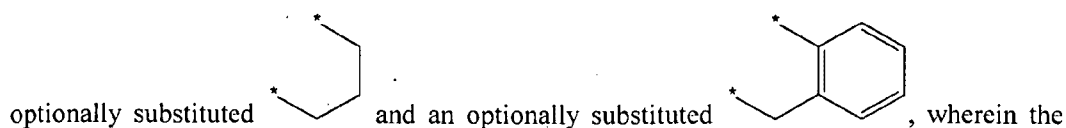
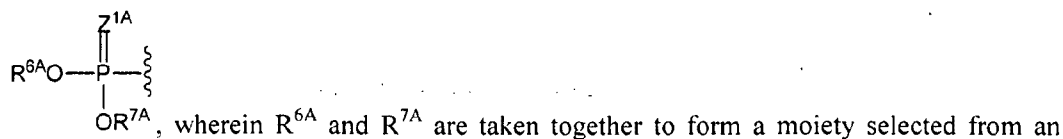
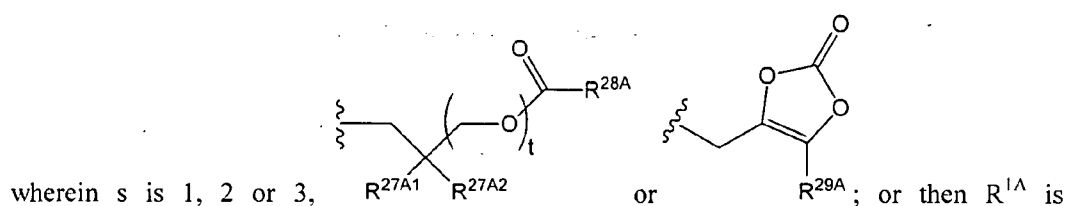
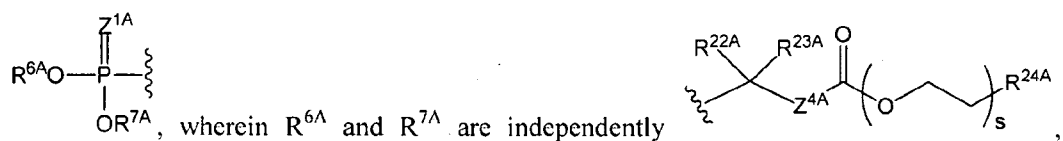
monocyclic heterocyclyl and ; R^{25A} , R^{26A} , R^{29A} , R^{8B} and R^{9B} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{27A1} and R^{27A2} can be independently selected from $-C\equiv N$, an optionally substituted C_{2-8} organylcarbonyl, an optionally substituted C_{2-8} alkoxycarbonyl and an optionally substituted C_{2-8} organylaminocarbonyl; R^{28A} can be selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl and an optionally substituted C_{3-6} cycloalkenyl; R^{30A} and R^{31A} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl and an optionally

substituted C_{3-6} cycloalkenyl; R^{A} and R^{B} can be independently an optionally substituted C_{1-24} alkyl; R^{B1} and R^{B2} can be independently hydrogen and an optionally substituted C_{1-6} alkyl; m , v and w can be 0 or 1; p and q can be independently 1, 2 or 3; r and s can be independently 0, 1, 2 or 3; t can be 1 or 2; u and y can be independently 3, 4 or 5; and Z^{1A} , Z^{2A} , Z^{3A} , Z^{4A} , Z^{1B} and Z^{2B} can be independently O or S; wherein the viral infection is caused by a virus selected from a Picornaviridae virus and a *Flaviviridae* virus; and provided that when the *Flaviviridae* virus is hepatitis C virus, then the compound of Formula (I), or a pharmaceutically acceptable salt thereof, cannot be selected from a compound in paragraphs [0292], [0293], [0294] and [0296], or a pharmaceutically acceptable salt of the foregoing.

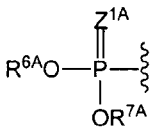
[0230] In some embodiments, when R^{2A} is halo (such as fluoro); ----- are both

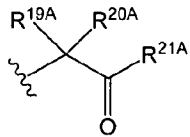


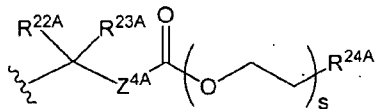
hydrogen, an unsubstituted C₁₋₆ alkyl, an unsubstituted C₃₋₆ alkenyl, an unsubstituted C₃₋₆ alkynyl and an unsubstituted C₃₋₆ cycloalkyl, R^{a5} is NHR^{a8}, and R^{a6} is hydrogen, halogen or NHR^{a9}; R^{a7} is NHR^{a10}; R^{a8} is selected from hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₃₋₆ alkenyl, an optionally substituted C₃₋₆ cycloalkyl, -C(=O)R^{a11} and -C(=O)OR^{a12}; R^{a9} is selected from hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₃₋₆ alkenyl, an optionally substituted C₃₋₆ cycloalkyl, -C(=O)R^{a13} and -C(=O)OR^{a14}; R^{a10} is selected from hydrogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₃₋₆ alkenyl, an optionally substituted C₃₋₆ cycloalkyl, -C(=O)R^{a15} and -C(=O)OR^{a16}; X^{a1} is N or -CR^{a17}; R^{a17} is selected from hydrogen, halogen, an optionally substituted C₁₋₆ alkyl, an optionally substituted C₂₋₆ alkenyl and an optionally substituted C₂₋₆ alkynyl; R^{a11}, R^{a12}, R^{a13}, R^{a14}, R^{a15} and R^{a16} are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkenyl, C₆₋₁₀ aryl, heteroaryl, heterocyclyl, aryl(C₁₋₆ alkyl), heteroaryl(C₁₋₆ alkyl) and heterocyclyl(C₁₋₆ alkyl); then R^{3A} is selected from H, halo, and an optionally substituted O-linked amino acid; and R^{4A} is selected from OH, halo, -OC(=O)R^{3A} and an optionally substituted O-linked amino acid; or then R^{4A} is an optionally substituted O-linked amino acid; and R^{3A} is selected from H, halo, OH, -OC(=O)R^{3A} and an optionally substituted O-linked amino acid; or then R^{3A} and R^{4A} are both an oxygen atom connected via a carbonyl to form a 5-membered ring; or then R^{1A} is

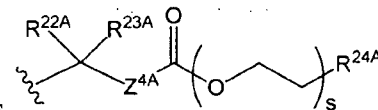


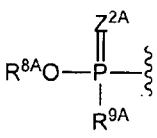
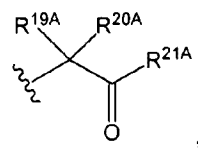
oxygens connected to R^{6A} and R^{7A} , the phosphorus and the moiety form a six-membered to ten-membered ring system. In some embodiments, when R^{2A} is halo (such as fluoro); ----- are each a single bond; then R^{4A} is $-\text{OC}(=\text{O})\text{R}^{3A}$ or an optionally substituted O-linked amino acid. In some embodiments, when R^{2A} is an unsubstituted C_{1-4} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-4} alkynyl, $-(\text{CH}_2)_{1-6}$ halogen or $-(\text{CH}_2)_{1-6}\text{N}_3$; ----- are both absent; Z^1 is absent; O^1 is OR^{1A} ; R^{3A} is OH , $-\text{OC}(=\text{O})\text{R}^{3A}$ or an optionally substituted O-linked amino acid; and R^{4A} is halo; then R^{5A} is selected from an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl. In some embodiments, when R^{2A} is an unsubstituted C_{1-4} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-4} alkynyl, $-(\text{CH}_2)_{1-6}$ halogen or $-(\text{CH}_2)_{1-6}\text{N}_3$; ----- are both absent; Z^1 is absent; O^1 is OR^{1A} ; R^{4A} is halo; and R^{5A} is H or halo; then R^{3A} is H or halo. In some embodiments, when R^{2A} is an unsubstituted C_{1-4} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-4} alkynyl, $-(\text{CH}_2)_{1-6}$ halogen or $-(\text{CH}_2)_{1-6}\text{N}_3$; ----- are both absent; Z^1 is absent; O^1 is OR^{1A} ; R^{3A} is OH , $-\text{OC}(=\text{O})\text{R}^{3A}$ or an optionally substituted O-linked amino

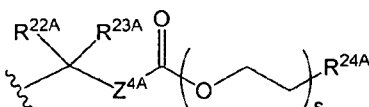
acid; R^{4A} is halo; R^{5A} is H or halo; and R^{1A} is  then at least one of R^{6A} and R^{7A}

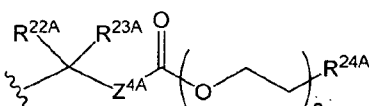
is , wherein R^{21A} is independently selected from an optionally substituted O-heteroaryl and an optionally substituted O-monocyclic heterocyclyl; or then at least one

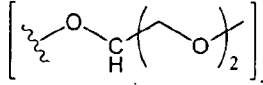
of R^{6A} and R^{7A} is , wherein s is 1, 2 or 3; or then at least one

of R^{6A} and R^{7A} is , wherein s is 0 and R^{24A} is an optionally substituted O-heteroaryl or an optionally substituted O-monocyclic heterocyclyl. In some embodiments, when R^{2A} is an unsubstituted C_{1-4} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-4} alkynyl, $-(\text{CH}_2)_{1-6}$ halogen or $-(\text{CH}_2)_{1-6}\text{N}_3$; ----- are both absent; Z^1 is absent; O^1 is OR^{1A} ; R^{3A} is OH , $-\text{OC}(=\text{O})\text{R}^{3A}$ or an optionally substituted O-linked amino

acid; R^{4A} is halo; R^{5A} is H or halo; and R^{1A} is ; then R^{8A} is  , wherein R^{21A} is independently selected from an optionally substituted -O-heteroaryl and an optionally substituted -O-monocyclic heterocyclyl; or then R^{8A} is

 , wherein s is 1, 2 or 3; or then R^{8A} is

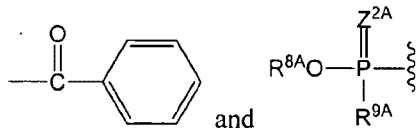
 , wherein s is 0 and R^{24A} is an optionally substituted -O-

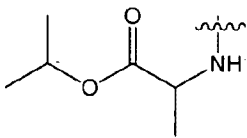
heteroaryl, an optionally substituted -O-monocyclic heterocyclyl or .

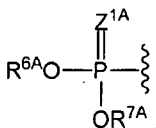
In some embodiments, when ----- are both absent; Z^1 is absent; O^1 is OH; R^{2A} is methyl; R^{3A} is OH; then R^{4A} is halo, $-OC(=O)R^{3B}$ or an optionally substituted O-linked amino acid.

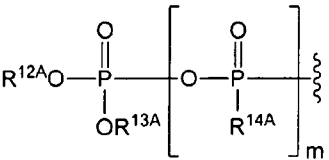
In some embodiments, when ----- are both absent; Z^1 is absent; O^1 is OR^{1A} ; R^{2A} is halo (for example, F); R^{3A} is OH or $-OC(=O)R^{3A}$; R^{4A} is halo (for example, F); and R^{5A} is methyl,

ethyl or ethenyl; then R^{1A} cannot be selected from H,

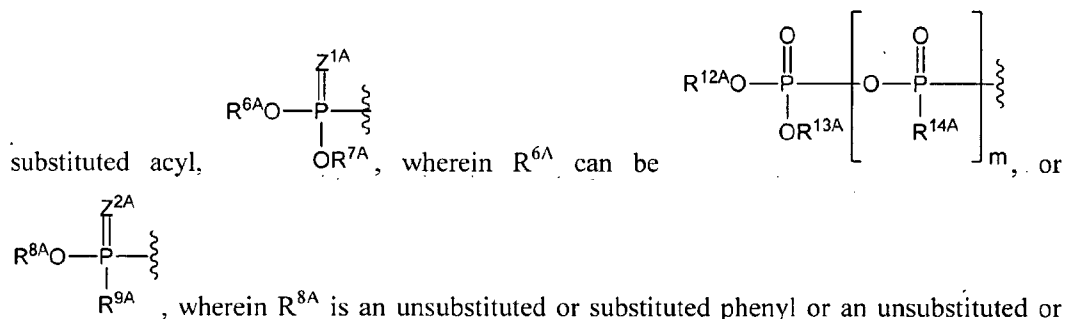


wherein R^{8A} is an unsubstituted aryl; R^{9A} is  and Z^{2A} is oxygen. In some embodiments, R^{1A} is not hydrogen (H), for example, when R^{3A} is halo (such as fluoro)

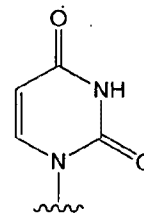
and R^{4A} is OH. In some embodiments, R^{1A} is not , wherein Z^{1A} is O and R^{6A} is

, for example, when R^{4A} is halo (such as fluoro) and R^{3A} is OH.

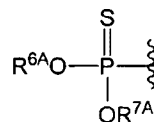
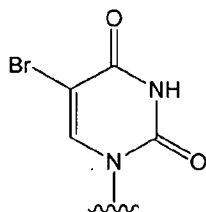
In some embodiments, R^{2A} is not hydrogen (H). In some embodiments, R^{2A} is not halogen. In some embodiments, R^{2A} is not fluoro (F). In some embodiments, R^{2A} is not -CN. In some embodiments, R^{2A} is not -CHF₂. In some embodiments, R^{5A} is not hydrogen or halo. In some embodiments, R^{5A} is not -OH. In some embodiments, R^{4A} is not hydrogen (H). In some embodiments, R^{4A} is not halo. In some embodiments, R^{4A} is not fluoro (F). In some embodiments, R^{4A} is not chloro (Cl). In some embodiments, R^{2A} is not an unsubstituted C₁₋₄ alkyl. In some embodiments, R^{2A} is not an unsubstituted C₂₋₄ alkenyl. In some embodiments, R^{2A} is not an unsubstituted C₂₋₄ alkynyl. In some embodiments, R^{2A} is not -(CH₂)₁₋₆ halogen. In some embodiments, R^{2A} is not -(CH₂)₁₋₆N₃. In some embodiments, R^{4A} is not hydrogen, when R^{5A} is fluoro. In some embodiments, R^{6A} is not an optionally substituted aryl. In some embodiments, R^{6A} is not an unsubstituted aryl. In some embodiments, R^{9A} is not N-alanine isopropyl ester. In some embodiments, R^{5A} is not an optionally substituted C₁₋₆ alkyl. For example, R^{5A} is not an unsubstituted C₁₋₆ alkyl, such as methyl. In some embodiments, B^{1A} is not an optionally substituted uracil, for example, a halo-substituted uracil. In some embodiments, when R^{1A} is hydrogen, an optionally



then B^{1A} cannot be an optionally substituted pyrimidine base, such as

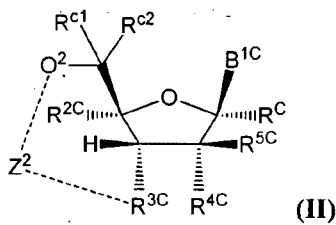


or



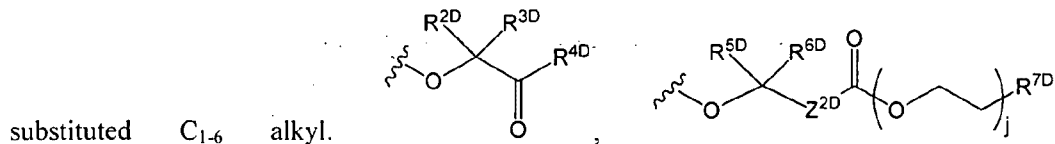
. In some embodiments, when R^{1A} is $R^{6A}O-P(=S)(OR^{7A})$, R^{2A} is H, R^{3A} is OH and R^{4A} is OH or halogen (such as F), then R^{5A} is not an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl or an optionally substituted C_{2-6} alkynyl.

[0231] Some embodiments disclosed herein relate to a compound of Formula (II), or a pharmaceutically acceptable salt thereof, and a use of a compound of Formula (II), or a pharmaceutically acceptable salt thereof:

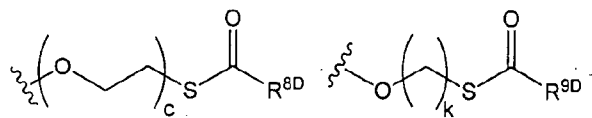


wherein: B^{1C} can be an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group; ----- can be absent or a single bond, provided that both ----- are absent or both ----- are a single bond; when ----- are both absent, then Z^2 can be absent, O^2 can be OR^{1C} , R^{3C} can be selected from H, halo, OH, N_3 , $-OC(=O)R^{3C}$, an optionally substituted O-linked amino acid and $NR^{3D1}R^{3D2}$, R^{4C} can be selected from H, OH, halo, $-OC(=O)R^{4D}$, an optionally substituted O-linked amino acid and $NR^{4D1}R^{4D2}$, or R^{3C} and R^{4C} can be both an oxygen atom connected via a carbonyl to form a

5-membered ring; when ----- are each a single bond, then Z^2 can be $R^{1D}P(=Z^{1D})(R^{2D})$, O^2 can be O, R^{3C} can be O; R^{4C} can be selected from OH, halo, N_3 , $-OC(=O)R^{4D}$ and an optionally substituted O-linked amino acid; and R^{1D} can be selected from O, OH, an -O-optionally

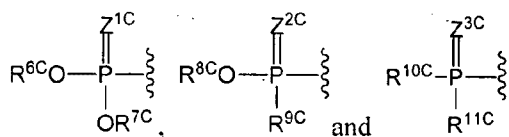


substituted C_{1-6} alkyl.



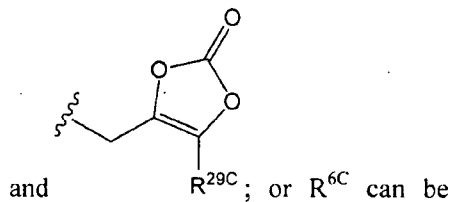
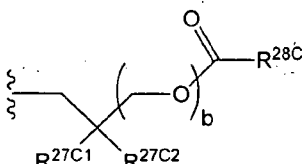
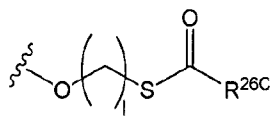
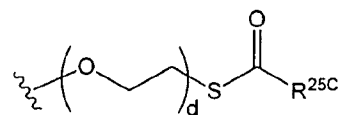
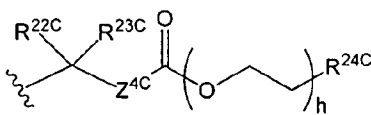
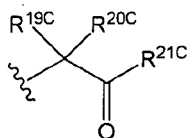
, an optionally substituted N-linked amino

acid and an optionally substituted N-linked amino acid ester derivative; R^{c1} and R^{c2} can be independently hydrogen or deuterium; R^c can be hydrogen, deuterium, an unsubstituted C_{1-3} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-3} alkynyl or cyano; R^{1c} can be selected from hydrogen, an optionally substituted acyl, an optionally substituted O-linked

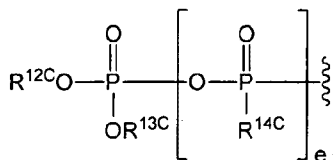


amino acid,

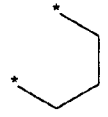
R^{2c} can be halo, an unsubstituted C_{1-4} alkyl, an unsubstituted C_{2-4} alkenyl, an unsubstituted C_{2-4} alkynyl, $-\text{CHF}_2$, $-(\text{CH}_2)_{1-6}$ halogen, $-(\text{CH}_2)_{1-6}\text{N}_3$, $-(\text{CH}_2)_{1-6}\text{NH}_2$ or $-\text{CN}$; R^{5c} can be selected from H, halo, OH, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{2-6} alkenyl and an optionally substituted C_{2-6} alkynyl; R^{6c} , R^{7c} and R^{8c} can be independently selected from absent, hydrogen, an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted $-(\text{CR}^{15c}\text{R}^{16c})_f\text{-O-}C_{1-24}$ alkyl, an optionally substituted $-(\text{CR}^{17c}\text{R}^{18c})_g\text{-O-}C_{1-24}$ alkenyl,

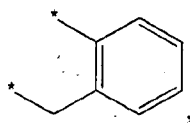


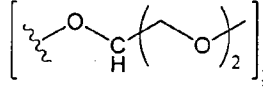
and R^{6c} can be



and R^{7c} can be absent or hydrogen; or R^{6c} and R^{7c} can be

taken together to form a moiety selected from an optionally substituted  and an

optionally substituted , wherein the oxygens connected to R^{6C} and R^{7C}, the phosphorus and the moiety form a six-membered to ten-membered ring system; R^{9C} can be independently selected from an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl, NR^{30C}R^{31C}, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative; R^{10C} and R^{11C} can be independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative; R^{12C} and R^{13C} can be independently absent or hydrogen; R^{14C} can be O⁻, OH or methyl; each R^{15C}, each R^{16C}, each R^{17C} and each R^{18C} can be independently hydrogen, an optionally substituted C₁₋₂₄ alkyl or an alkoxy; R^{19C}, R^{20C}, R^{22C}, R^{23C}, R^{21D}, R^{3D}, R^{5D} and R^{6D} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl and an optionally substituted aryl; R^{21C} and R^{4D} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted aryl, an optionally substituted -O-C₁₋₂₄ alkyl, an optionally substituted -O-aryl, an optionally substituted -O-heteroaryl and an optionally substituted -O-monocyclic heterocyclyl; R^{24C} and R^{7D} can be independently selected from of hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted aryl, an optionally substituted -O-C₁₋₂₄ alkyl, an optionally substituted -O-aryl, an optionally substituted -O-heteroaryl, an

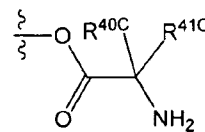
optionally substituted -O-monocyclic heterocyclyl and ; R^{25C}, R^{26C}, R^{29C}, R^{8D} and R^{9D} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl and an optionally substituted aryl; R^{27C1} and R^{27C2} can be independently selected from -C≡N, an optionally substituted C₂₋₈ organylcarbonyl, an optionally substituted C₂₋₈ alkoxy carbonyl and an optionally substituted C₂₋₈ organylaminocarbonyl; R^{28C} can be selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl and

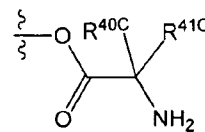
an optionally substituted C₃₋₆ cycloalkenyl; R^{30C} and R^{31C} can be independently selected from hydrogen, an optionally substituted C₁₋₂₄ alkyl, an optionally substituted C₂₋₂₄ alkenyl, an optionally substituted C₂₋₂₄ alkynyl, an optionally substituted C₃₋₆ cycloalkyl, an optionally substituted C₃₋₆ cycloalkenyl and an optionally substituted aryl(C₁₋₄ alkyl); R^{32C} and each R^{33D} can be independently an optionally substituted C₁₋₂₄ alkyl; each R^{34D1} and each R^{34D2} can be independently hydrogen or an optionally substituted C₁₋₆ alkyl; c, d and e can be independently 0 or 1; f and g can be independently 1, 2 or 3; h and j can be independently 0, 1, 2 or 3; b can be 1 or 2; k and l can be independently 3, 4 or 5; and Z^{1C}, Z^{2C}, Z^{3C}, Z^{4C}, Z^{1D} and Z^{2D} can be independently oxygen (O) or sulfur (S).

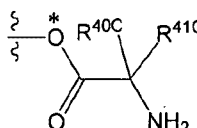
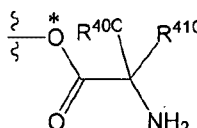
[0232] A compound of Formula (II) can be a nucleoside, a nucleotide (including a monophosphate, a diphosphate, a triphosphate, thiomonophosphate, alpha-thiodiphosphate and/or alpha-thiotriphosphate) or a nucleotide prodrug. In some embodiments, ----- can be both absent, Z² can be absent, O² can be OR^{1C}, R^{3C} can be selected from H, halo, OH, -OC(=O)R^{3C} and an optionally substituted O-linked amino acid, R^{4C} can be selected from OH, halo, -OC(=O)R^{3D} and an optionally substituted O-linked amino acid, or R^{3C} and R^{4C} can be both an oxygen atom connected via a carbonyl to form a 5-membered ring.

[0233] A variety of substituents can be attached to the 5'-position of Formula (II) when both ----- are absent. In some embodiments, R^{1C} can be hydrogen. In some embodiments, R^{1C} can be an optionally substituted acyl. For example, R^{1C} can be -C(=O)R^{39C}, wherein R^{39C} can be selected from an optionally substituted C₁₋₁₂ alkyl, an optionally substituted C₂₋₁₂ alkenyl, an optionally substituted C₂₋₁₂ alkynyl, an optionally substituted C₃₋₈ cycloalkyl, an optionally substituted C₅₋₈ cycloalkenyl, an optionally substituted C₆₋₁₀ aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted aryl(C₁₋₆ alkyl), an optionally substituted heteroaryl(C₁₋₆ alkyl) and an optionally substituted heterocyclyl(C₁₋₆ alkyl). In some embodiments, R^{39C} can be a substituted C₁₋₁₂ alkyl. In other embodiments, R^{39C} can be an unsubstituted C₁₋₁₂ alkyl. In some embodiments, R^{1C} can be -C(=O)-unsubstituted C₁₋₄ alkyl. In some embodiments, both R^{c1} and R^{c2} can be hydrogen. In other embodiments, R^{c1} can be hydrogen and R^{c2} can be deuterium. In still other embodiments, both R^{c1} and R^{c2} can be deuterium.

[0234] In still other embodiments, R^{1C} can be an optionally substituted O-linked amino acid. Examples of suitable O-linked amino acids include alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. Additional examples of suitable amino acids include, but are not limited to, ornithine, hypusine, 2-aminoisobutyric acid, dehydroalanine, gamma-aminobutyric acid, citrulline, beta-alanine, alpha-ethyl-glycine, alpha-propyl-glycine and norleucine. In some

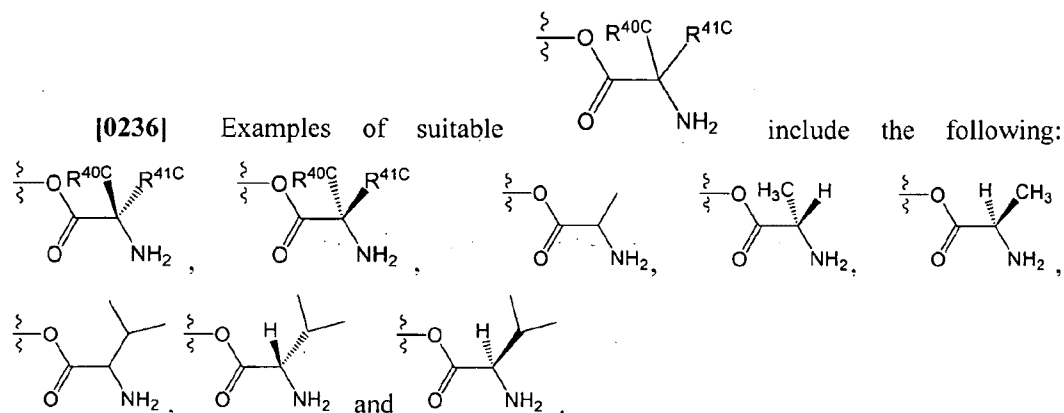


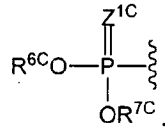
embodiments, the O-linked amino acid can have the structure , wherein R^{40C} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_6 aryl, an optionally substituted C_{10} aryl and an optionally substituted aryl(C_{1-6} alkyl); and R^{41C} can be hydrogen or an optionally substituted C_{1-4} alkyl; or R^{40C} and R^{41C} can be taken together to form an optionally substituted C_{3-6} cycloalkyl. Those skilled in the art understand that when R^{1C} is an optionally substituted O-linked amino acid, the oxygen of $R^{1C}O-$ of Formula (II) is part of the optionally substituted O-linked amino acid. For example, when

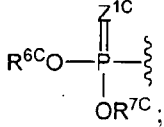
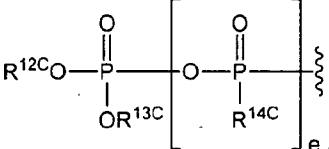
 R^{1C} is , the oxygen indicated with "*" is the oxygen of $R^{1C}O-$ of Formula (I).

[0235] When R^{40C} is substituted, R^{40C} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{40C} can be an unsubstituted C_{1-6} alkyl, such as those described herein. In some embodiments, R^{40C} can be hydrogen. In other embodiments, R^{40C} can be methyl. In some embodiments, R^{41C} can be hydrogen. In other embodiments, R^{41C} can be an optionally substituted C_{1-4} alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In some embodiments, R^{41C} can be methyl. Depending on the groups that are selected for R^{40C} and R^{41C} , the carbon to which R^{40C} and R^{41C} are attached may be a chiral center. In some embodiment, the carbon to which R^{40C} and R^{41C} are attached may be a (*R*)-chiral

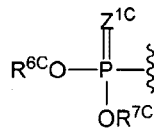
center. In other embodiments, the carbon to which R^{40C} and R^{41C} are attached may be a (*S*)-chiral center.



[0237] In some embodiments, R^{1C} can be . In some embodiments, R^{6C} and R^{7C} can be both hydrogen. In other embodiments, R^{6C} and R^{7C} can be both absent. In still other embodiments, at least one R^{6C} and R^{7C} can be absent. In yet still other embodiments, at least one R^{6C} and R^{7C} can be hydrogen. Those skilled in the art understand that when R^{6C} and/or R^{7C} are absent, the associated oxygen(s) will have a negative charge. For example, when R^{6C} is absent, the oxygen associated with R^{6C} will have a negative charge. In some embodiments, Z^{1C} can be O (oxygen). In other embodiments, Z^{1C} can be S (sulfur). In some embodiments, R^{1C} can be a monophosphate. In other embodiments, R^{1C} can be a monothiophosphate.

[0238] In some embodiments, R^{1C} can be ; R^{6C} can be ; R^{7C} can be absent or hydrogen; R^{12C} and R^{13C} can be independently absent or hydrogen; R^{14C} can be O, OH or methyl; and e can be 0 or 1. In some embodiments, e can be 0, and R^{7C} , R^{12C} and R^{13C} can be independently absent or

hydrogen. In other embodiments, e can be 1, and R^{7C} , R^{12C} and R^{13C} can be independently absent or hydrogen; and R^{14C} can be O⁻, OH or methyl. In some embodiments, e can be 1, and R^{7C} , R^{12C} and R^{13C} can be independently absent or hydrogen; and R^{14C} can be O⁻ or OH. In other embodiments, e can be 1, and R^{7C} , R^{12C} and R^{13C} can be independently absent or hydrogen; and R^{14C} can be methyl. Those skilled in the art understand that when e is 0, R^{6C} can be a diphosphate, when Z^{1C} is oxygen, or an alpha-thiodiphosphate, when Z^{1C} is sulfur. Likewise, those skilled in the art understand that when e is 1, R^{6C} can be a triphosphate, when Z^{1C} is oxygen, or an alpha-thiotriphosphate, when Z^{1C} is sulfur.



[0239] In some embodiments, when R^{1C} is $R^{6C}O-P(OR^{7C})(Z^{1C})$, one of R^{6C} and R^{7C} can be hydrogen, and the other of R^{6C} and R^{7C} can be selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted aryl(C_{1-6} alkyl). In some embodiments, one of R^{6C} and R^{7C} can be hydrogen, and the other of R^{6C} and R^{7C} can be an optionally substituted C_{1-24} alkyl. In other embodiments, both R^{6C} and R^{7C} can be independently selected from an optionally substituted C_{1-24} alkyl, an optionally substituted C_{2-24} alkenyl, an optionally substituted C_{2-24} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted aryl(C_{1-6} alkyl). In some embodiments, both R^{6C} and R^{7C} can be an optionally substituted C_{1-24} alkyl. In other embodiments, both R^{6C} and R^{7C} can be an optionally substituted C_{2-24} alkenyl. In some embodiments, R^{6C} and R^{7C} can be independently an optionally substituted group selected from the following: myristoleyl, myristyl, palmitoleyl, palmityl, sapienyl, oleyl, elaidyl, vaccenyl, linoleyl, α -linolenyl, arachidonyl, eicosapentaenyl, erucyl, docosahexaenyl, caprylyl, capryl, lauryl, stearyl, arachidyl, behenyl, lignoceryl and cerotyl.

[0240] In some embodiments, at least one of R^{6C} and R^{7C} can be $*(CR^{15C}R^{16C})_r-O-C_{1-24}$ alkyl. In other embodiments, R^{6C} and R^{7C} can be both $*(CR^{15C}R^{16C})_r-O-C_{1-24}$ alkyl. In some embodiments, each R^{15C} and each R^{16C} can be hydrogen. In other embodiments, at least one of R^{15C} and R^{16C} can be an optionally substituted C_{1-24} alkyl. In

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LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 283

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 283

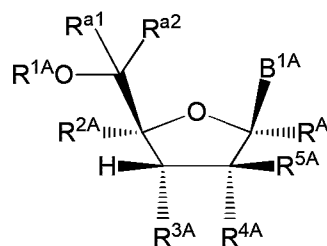
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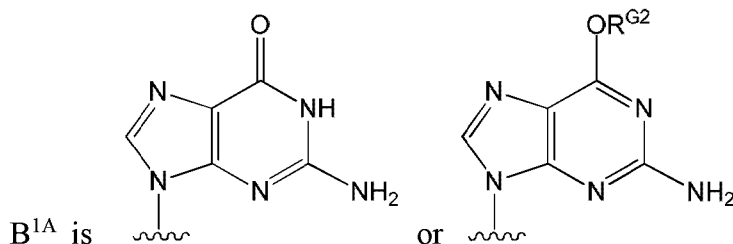
WHAT IS CLAIMED IS:

1. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating a *Picornaviridae* viral infection, wherein the compound of Formula (I) has the structure:



(I)

wherein:



B^{1A} is  or , wherein R^{G2} is an unsubstituted C_{1-6} alkyl;

R^{2A} is halo;

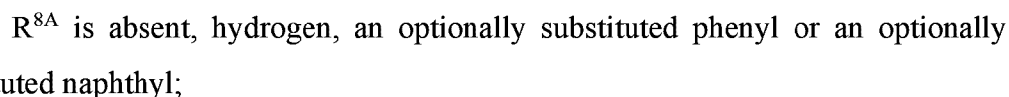
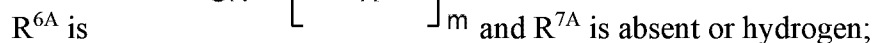
R^{5A} is selected from the group consisting of an unsubstituted C_{1-6} alkyl, an unsubstituted C_{2-6} alkenyl and an unsubstituted C_{2-6} alkynyl;

R^{3A} is selected from the group consisting of halo, OH, $-OC(=O)R''^A$ and an unsubstituted O-linked α -amino acid;

R^{4A} is selected from the group consisting of OH and halo;

R^{a1} and R^{a2} are independently hydrogen or deuterium;

R^A is hydrogen or deuterium;



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leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine;

R^{10A} and R^{11A} are independently an optionally substituted N-linked amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine, or an optionally substituted N-linked amino acid ester derivative, wherein the optionally substituted N-linked α -amino acid ester derivative is an unsubstituted C_{1-6} alkyl ester, an optionally substituted C_{3-6} cycloalkyl ester, an optionally substituted C_6 aryl ester, an optionally substituted C_{10} aryl ester or an optionally substituted benzyl ester of an N-linked α -amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine;

R^{12A} and R^{13A} are independently absent or hydrogen;

R^{14A} is O^- , OH or methyl;

R^{22A} and R^{23A} are each hydrogen;

R^{24A} is selected from the group consisting of hydrogen, an unsubstituted C_{1-24} alkyl and an unsubstituted $-O-C_{1-24}$ alkyl;

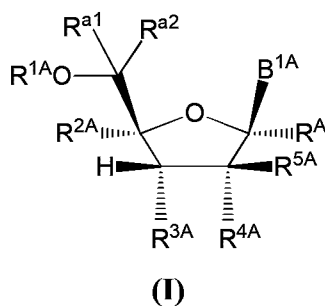
R^{25A} is an unsubstituted C_{1-24} alkyl;

m is 0 or 1;

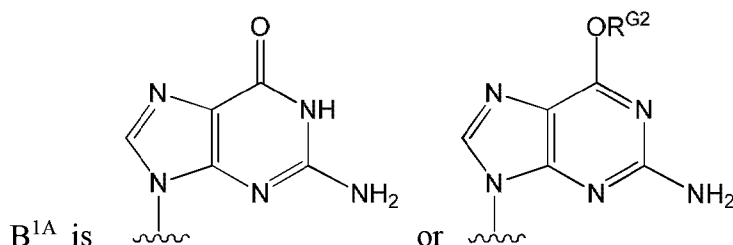
s is 0, 1, 2 or 3;

Z^{1A} , Z^{2A} , Z^{3A} and Z^{4A} are each O.

2. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for ameliorating or treating a *Picornaviridae* viral infection, wherein the compound of Formula (I) has the structure:



wherein:



unsubstituted C_{1-6} alkyl;

R^{2A} is halo;

R^{5A} is selected from the group consisting of an unsubstituted C_{1-6} alkyl, an unsubstituted C_{2-6} alkenyl and an unsubstituted C_{2-6} alkynyl;

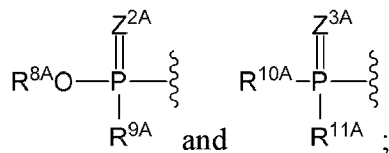
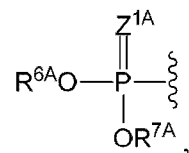
R^{3A} is selected from the group consisting of halo, OH, $-OC(=O)R^{''A}$ and an unsubstituted O-linked α -amino acid;

R^{4A} is selected from the group consisting of OH and halo;

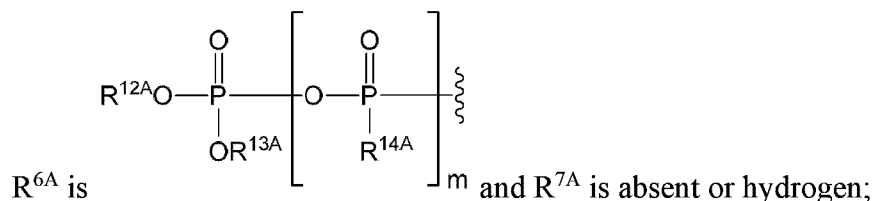
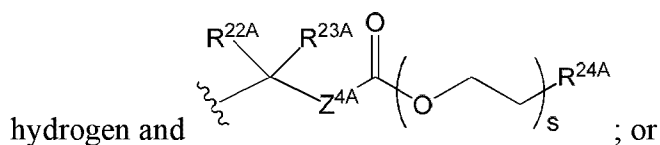
R^{a1} and R^{a2} are independently hydrogen or deuterium;

R^A is hydrogen or deuterium;

R^{1A} is selected from the group consisting of hydrogen,



R^{6A} and R^{7A} are independently selected from the group consisting of absent,



R^{8A} is absent, hydrogen, an optionally substituted phenyl or an optionally substituted naphthyl;

R^{9A} is an optionally substituted N-linked amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine, or an optionally substituted N-linked amino acid ester derivative, wherein the optionally substituted N-linked α -amino acid ester derivative is an unsubstituted C_{1-6} alkyl ester, an optionally substituted C_{3-6} cycloalkyl ester, an optionally substituted C_6 aryl ester, an optionally substituted C_{10} aryl ester or an optionally substituted benzyl ester of an N-linked α -amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine;

R^{10A} and R^{11A} are independently an optionally substituted N-linked amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine,

N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine, or an optionally substituted N-linked amino acid ester derivative, wherein the optionally substituted N-linked α -amino acid ester derivative is an unsubstituted C₁₋₆ alkyl ester, an optionally substituted C₃₋₆ cycloalkyl ester, an optionally substituted C₆ aryl ester, an optionally substituted C₁₀ aryl ester or an optionally substituted benzyl ester of an N-linked α -amino acid selected from the group consisting of N-linked alanine, N-linked asparagine, N-linked aspartate, N-linked cysteine, N-linked glutamate, N-linked glutamine, N-linked glycine, N-linked proline, N-linked serine, N-linked tyrosine, N-linked arginine, N-linked histidine, N-linked isoleucine, N-linked leucine, N-linked lysine, N-linked methionine, N-linked phenylalanine, N-linked threonine, N-linked tryptophan and N-linked valine;

R^{12A} and R^{13A} are independently absent or hydrogen;

R^{14A} is O⁻, OH or methyl;

R^{22A} and R^{23A} are each hydrogen;

R^{24A} is selected from the group consisting of hydrogen, an unsubstituted C₁₋₂₄ alkyl and an unsubstituted -O-C₁₋₂₄ alkyl;

R^{25A} is an unsubstituted C₁₋₂₄ alkyl;

m is 0 or 1;

s is 0, 1, 2 or 3;

Z^{1A}, Z^{2A}, Z^{3A} and Z^{4A} are each O.

3. The use of any one of claims 1 and 2, wherein the Picornaviridae virus is selected from the group consisting of an Aphthovirus, an Enterovirus, a Rhinovirus, a Hepatovirus and a Parechovirus.

4. The use of Claim 3, wherein the Enterovirus is selected from the group consisting of an enterovirus A, enterovirus B, enterovirus C, enterovirus D, enterovirus E, enterovirus F, enterovirus G, enterovirus H and enterovirus J.

5. The use of Claim 3, wherein the Enterovirus is selected from the group consisting of rhinovirus A, rhinovirus B and rhinovirus C.

6. The use of any one of Claims 1-5, wherein:

R^{2A} is F;

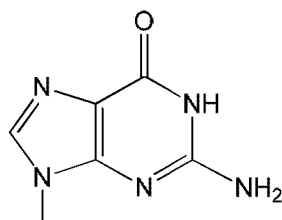
R^{3A} is OH or F;

R^{4A} is OH or F;

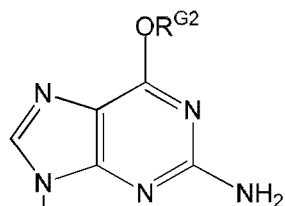
R^{5A} is methyl or ethynyl;

R^A is hydrogen; and

R^{a1} and R^{a2} are both hydrogen.

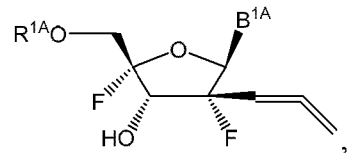
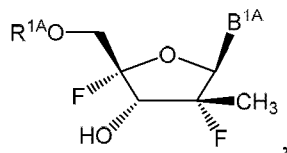
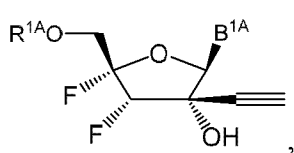
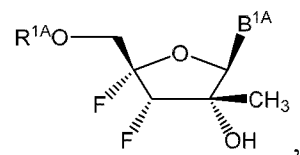
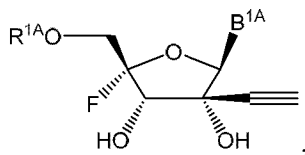
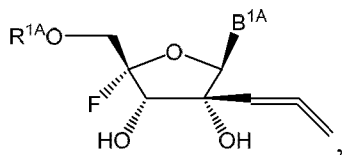
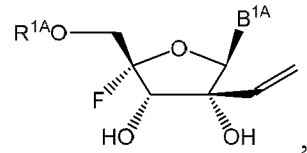
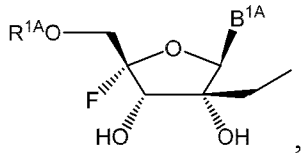
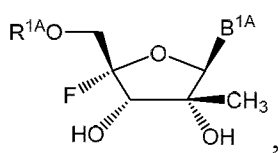


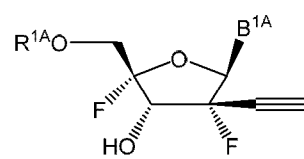
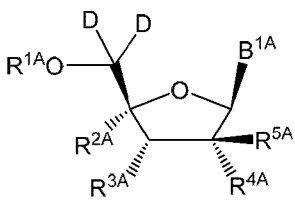
7. The use of Claim 6, wherein B^{1A} is .



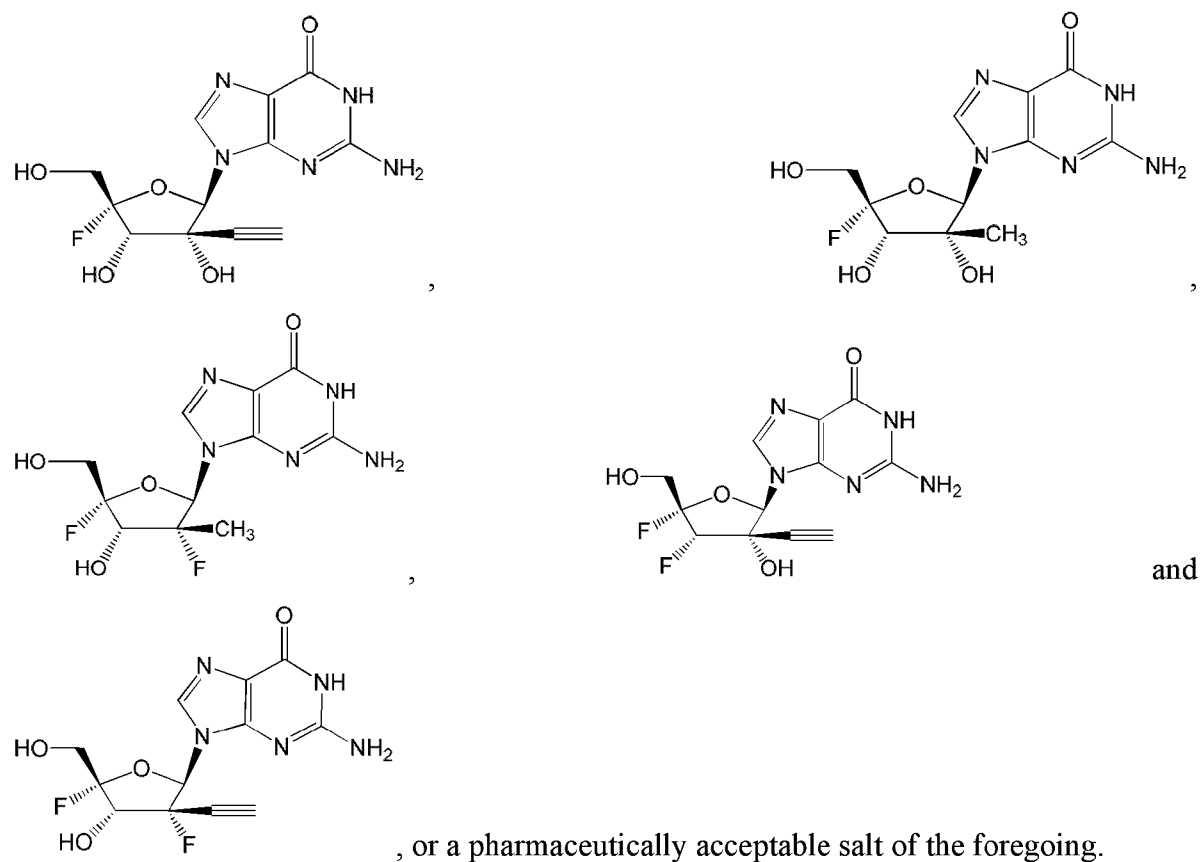
8. The use of Claim 6, wherein B^{1A} is , wherein R^{G2} is $-CH_2CH_3$.

9. The use of any one of Claims 1-5, wherein the compound of Formula (I) is selected from the group consisting of:

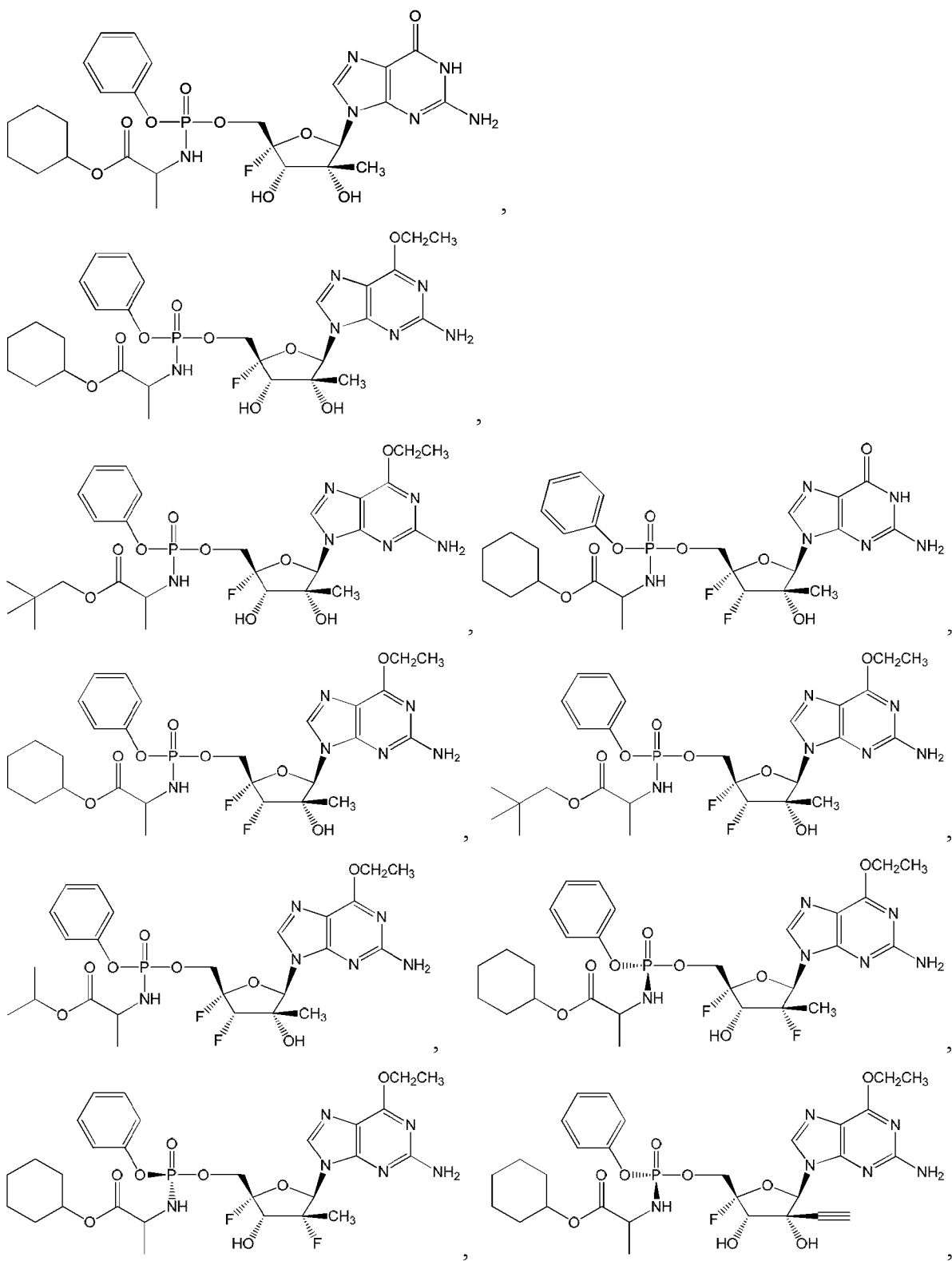


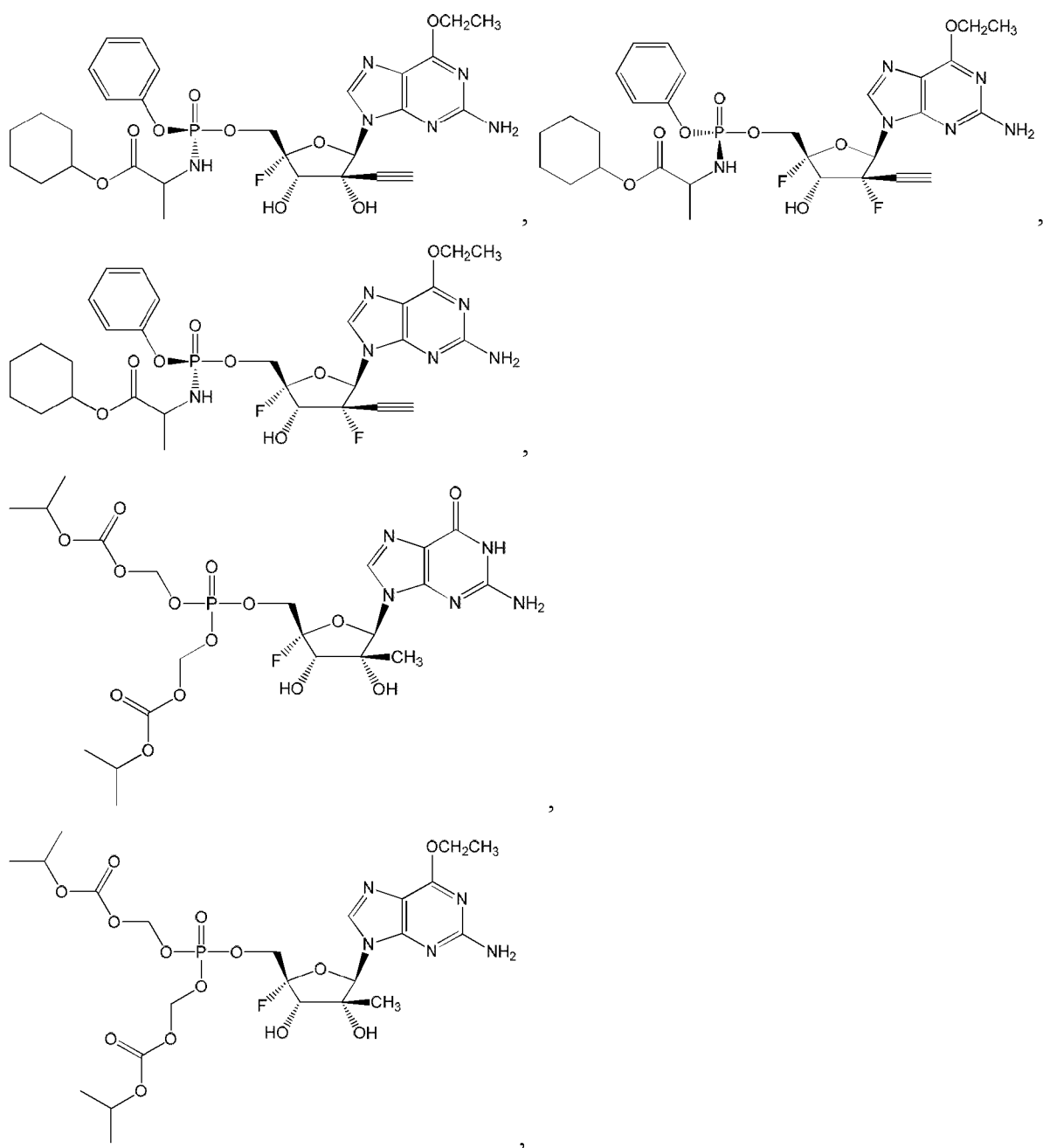


 and , or a pharmaceutically acceptable salt of any of the foregoing.

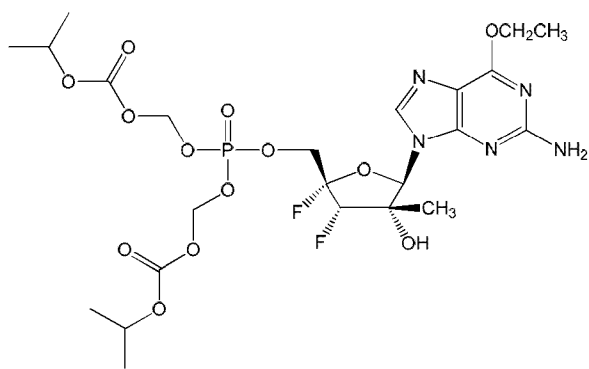
10. The use of any one of Claims 1-5, wherein the compound is selected from the group consisting of:



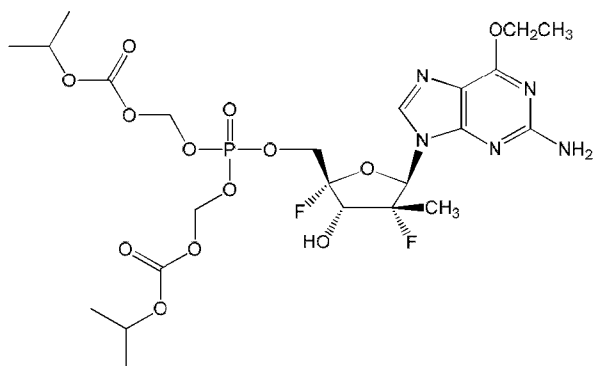
11. The use of any one of Claims 1-5, wherein the compound is selected from the group consisting of:



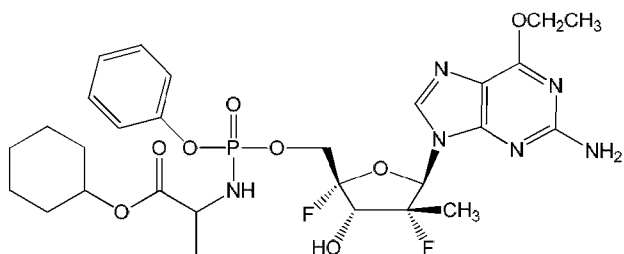




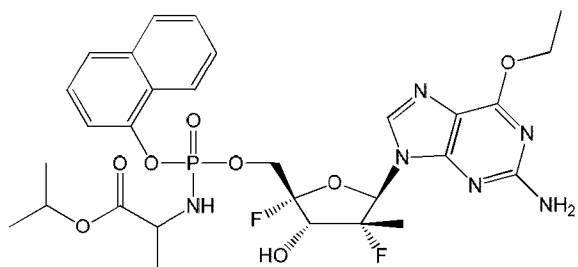
,



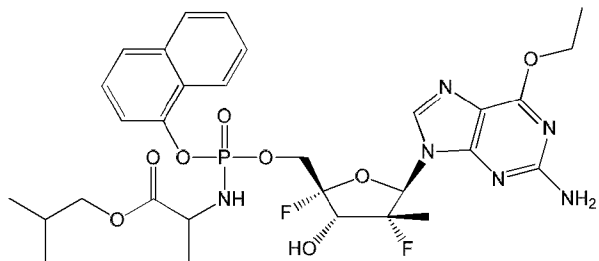
,



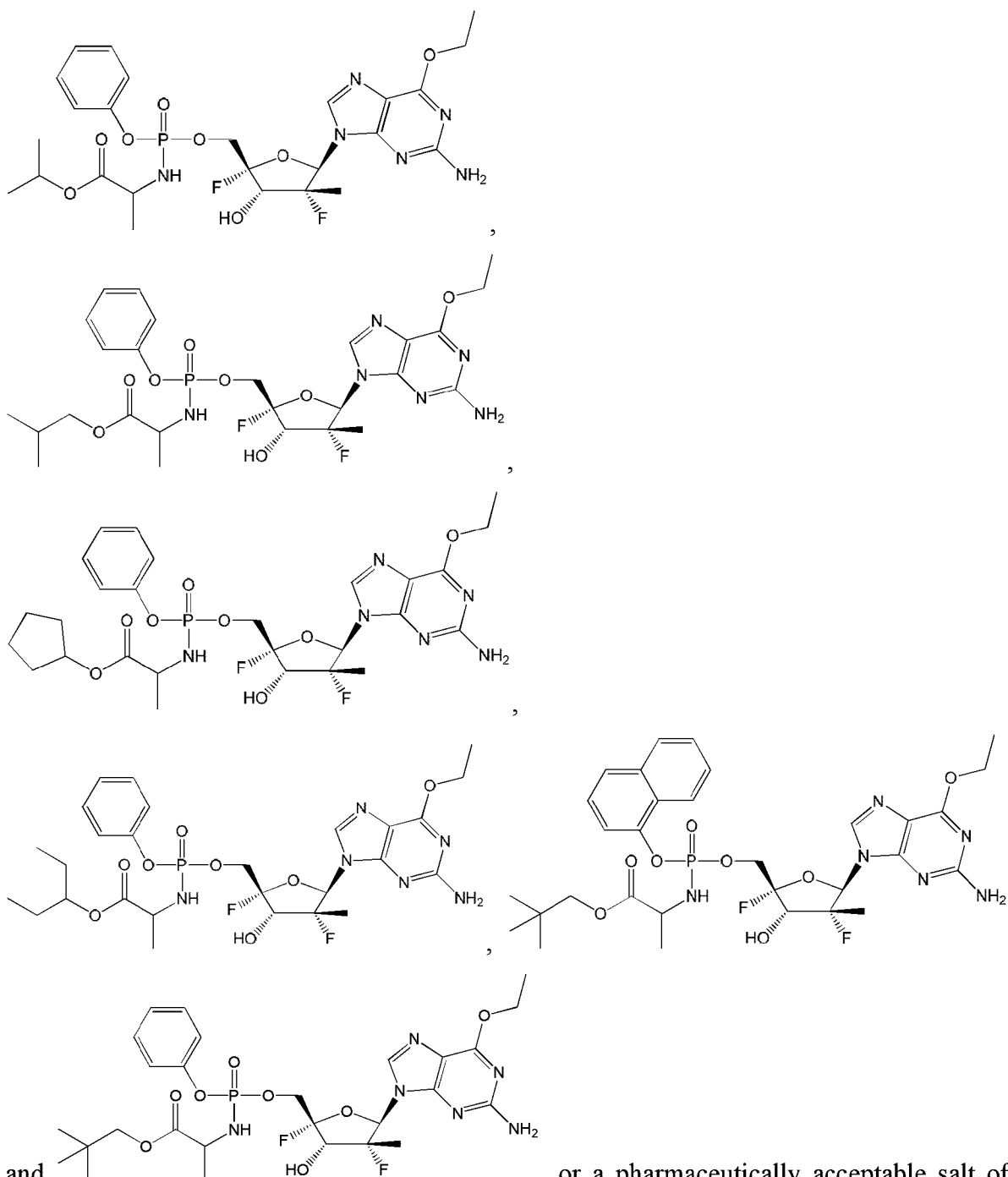
,



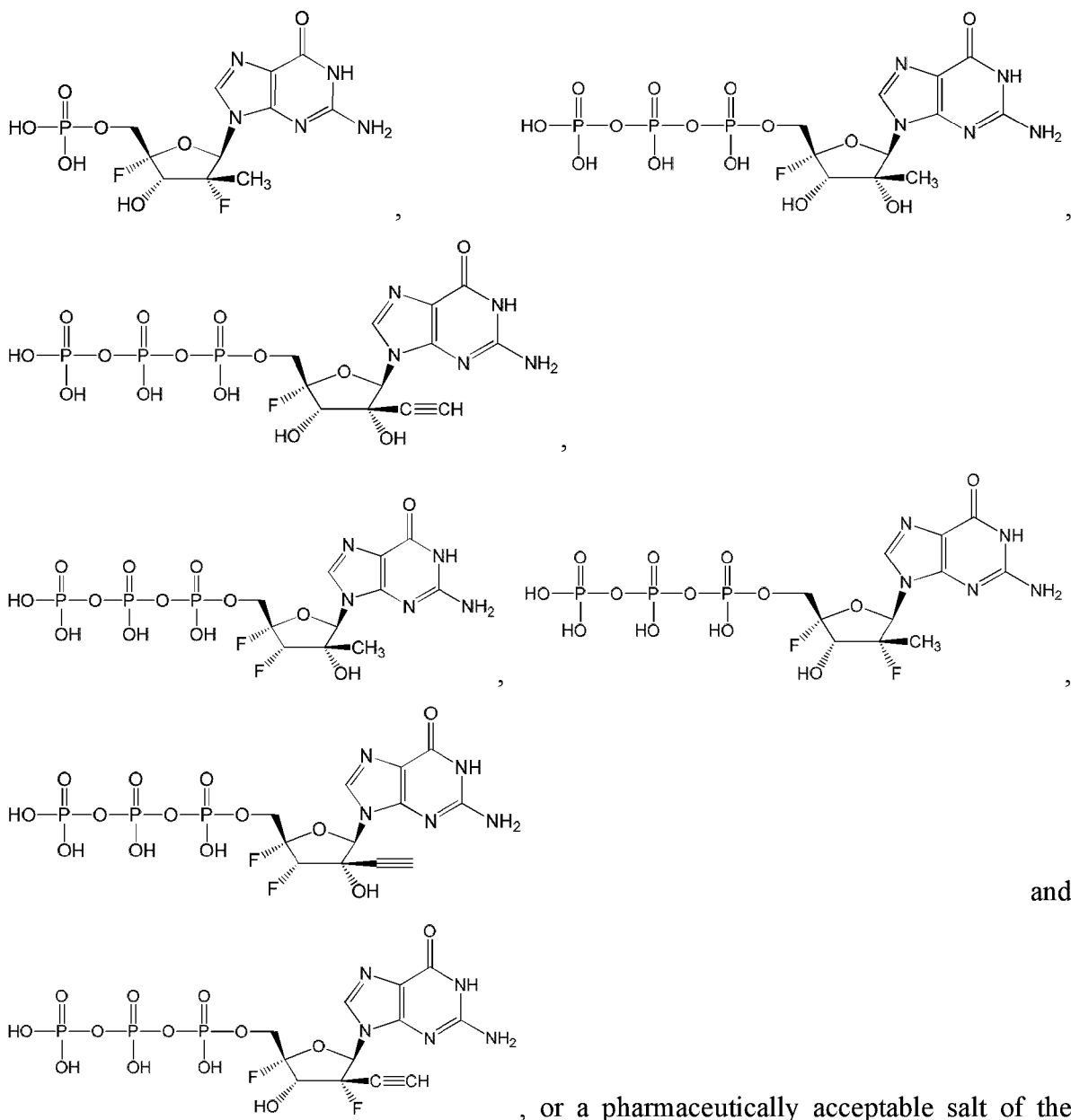
,



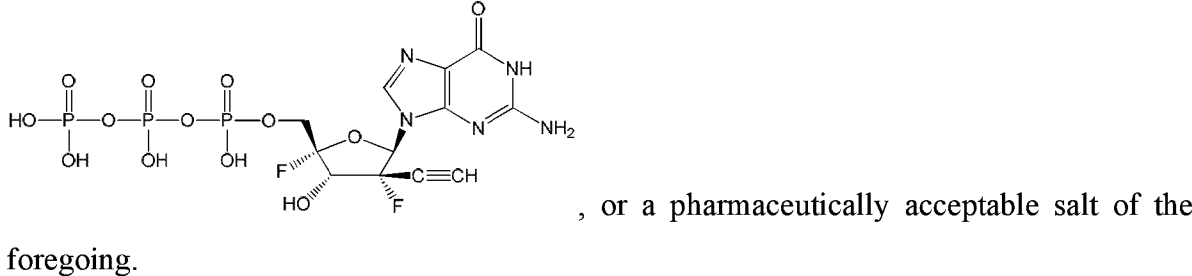
,



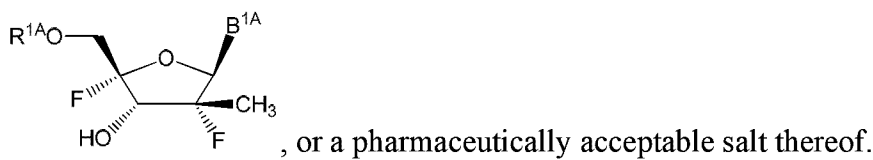
12. The use of any one of Claims 1-5, wherein the compound is selected from the group consisting of:



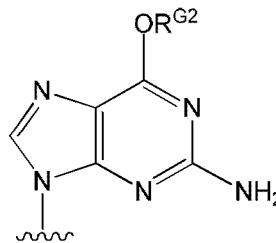
and



13. The use of any one of Claims 1-5, wherein the compound of Formula (I) is

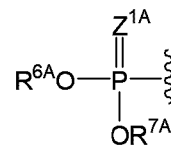


, or a pharmaceutically acceptable salt thereof.

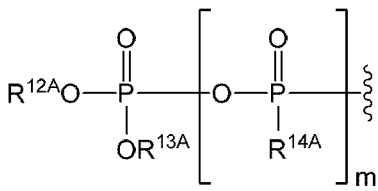


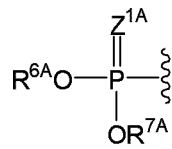
14. The use of Claim 13, wherein B^{1A} is , wherein R^{G2} is -CH₂CH₃.

15. The use of Claim 13, wherein R^{1A} is H.

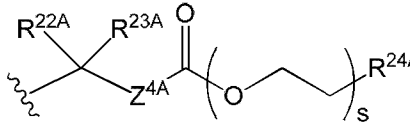


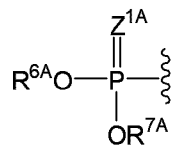
16. The use of Claim 13, wherein R^{1A} is ; R^{6A} is

; R^{7A}, R^{12A} and R^{13A} are independently absent or hydrogen; m is 1; and R^{14A} is O⁻ or OH.

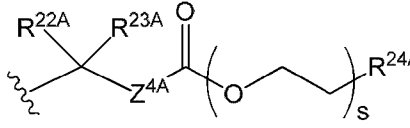


17. The use of Claim 13, wherein R^{1A} is , R^{6A} and R^{7A} are each

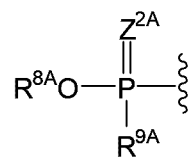
; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted tert-butyl.



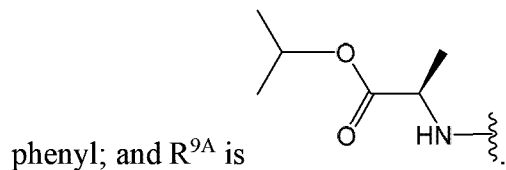
18. The use of Claim 13, wherein R^{1A} is , R^{6A} and R^{7A} are each

; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted O-isopropyl.

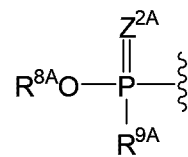
19. The use of Claim 13, wherein R^{1A} is



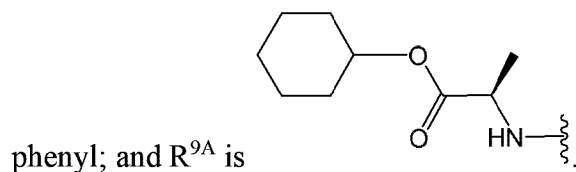
, R^{8A} is an unsubstituted



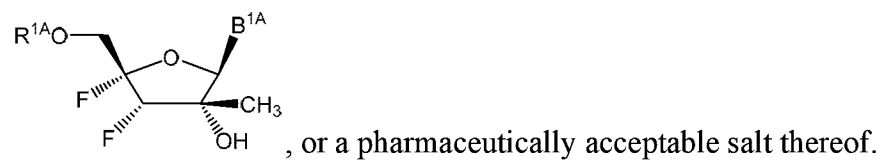
20. The use of Claim 13, wherein R^{1A} is



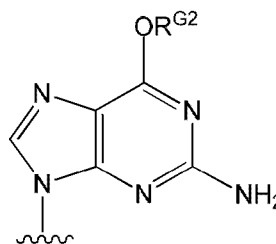
, R^{8A} is an unsubstituted



21. The use of any one of Claims 1-5, wherein the compound of Formula (I) is



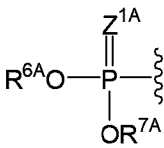
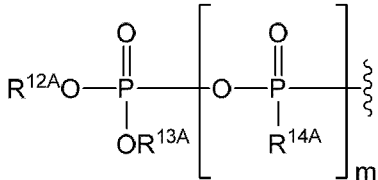
22. The use of Claim 21, wherein B^{1A} is

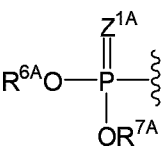
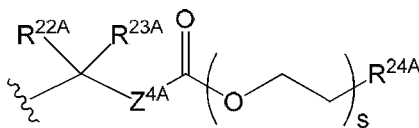


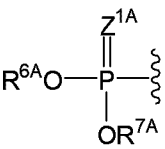
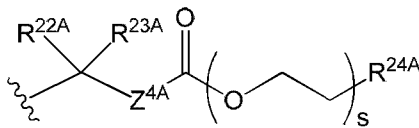
, wherein R^{G2} is -

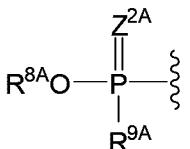
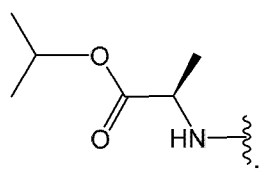
CH₂CH₃.

23. The use of Claim 21, wherein R^{1A} is H.

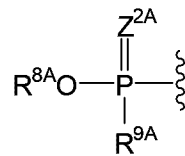
24. The use of Claim 21, wherein R^{1A} is ; R^{6A} is ; R^{7A} , R^{12A} and R^{13A} are independently absent or hydrogen; m is 1; and R^{14A} is O^- or OH .

25. The use of Claim 21, wherein R^{1A} is ; R^{6A} and R^{7A} are each ; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted tert-butyl.

26. The use of Claim 21, wherein R^{1A} is ; R^{6A} and R^{7A} are each ; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted O-isopropyl.

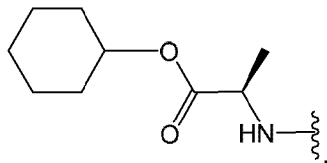
27. The use of Claim 21, wherein R^{1A} is ; R^{8A} is an unsubstituted phenyl; and R^{9A} is .

28. The use of Claim 21, wherein R^{1A} is

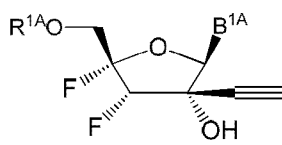


, R^{8A} is an unsubstituted

phenyl; and R^{9A} is

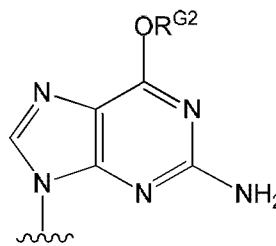


29. The use of any one of Claims 1-5, wherein the compound of Formula (I) is



, or a pharmaceutically acceptable salt thereof.

30. The use of Claim 29, wherein B^{1A} is

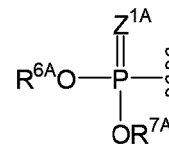


, wherein R^{G2} is -

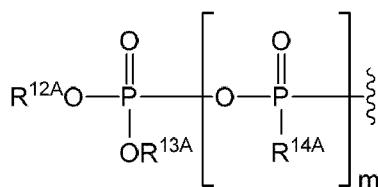
CH_2CH_3 .

31. The use of Claim 29, wherein R^{1A} is H.

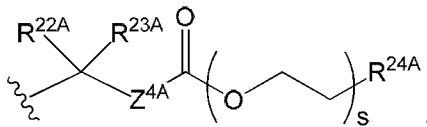
32. The use of Claim 29, wherein R^{1A} is

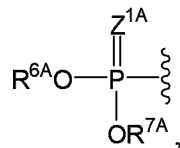


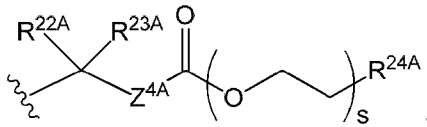
R^{6A} is

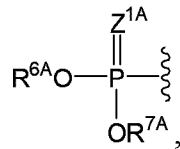


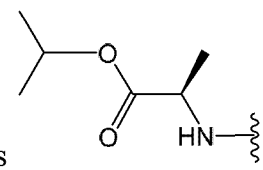
m ; R^{7A} , R^{12A} and R^{13A} are independently absent or hydrogen; m is 1; and R^{14A} is O^- or OH .

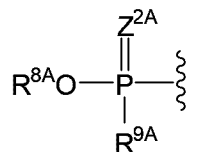
33. The use of Claim 29, wherein R^{1A} is ; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted tert-butyl.

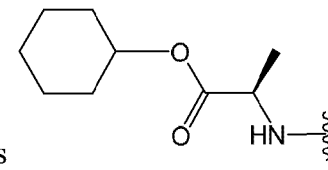


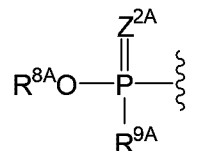
34. The use of Claim 29, wherein R^{1A} is ; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted O-isopropyl.

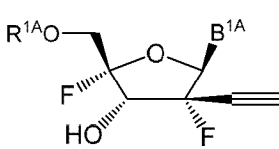


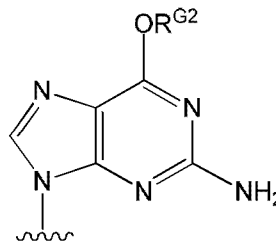
35. The use of Claim 29, wherein R^{1A} is phenyl; and R^{9A} is



36. The use of Claim 29, wherein R^{1A} is phenyl; and R^{9A} is

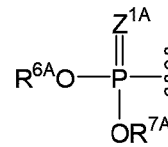


37. The use of any one of Claims 1-5, wherein the compound of Formula (I) is , or a pharmaceutically acceptable salt thereof.

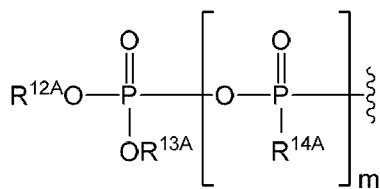


38. The use of Claim 37, wherein B^{1A} is , wherein R^{G2} is -CH₂CH₃.

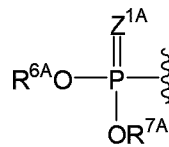
39. The use of Claim 37, wherein R^{1A} is H.



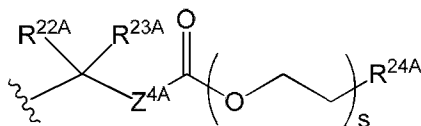
40. The use of Claim 37, wherein R^{1A} is , R^{6A} is



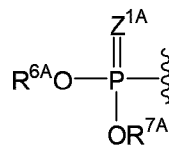
; R^{7A}, R^{12A} and R^{13A} are independently absent or hydrogen; m is 1; and R^{14A} is O⁻ or OH.



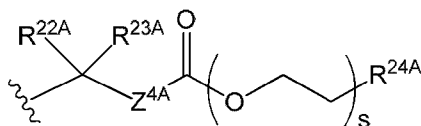
41. The use of Claim 37, wherein R^{1A} is , R^{6A} and R^{7A} are each



; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted tert-butyl.

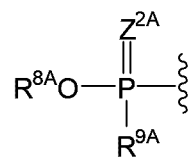


42. The use of Claim 37, wherein R^{1A} is , R^{6A} and R^{7A} are each



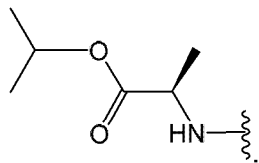
; s is 0; R^{22A} and R^{23A} are each hydrogen; and R^{24A} is an unsubstituted O-isopropyl.

43. The use of Claim 37, wherein R^{1A} is

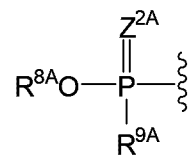


, R^{8A} is an unsubstituted

phenyl; and R^{9A} is

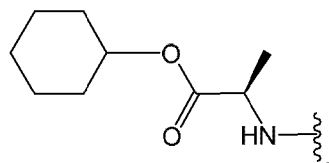


44. The use of Claim 37, wherein R^{1A} is

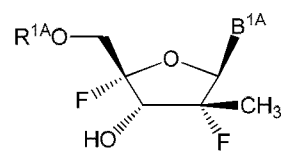


, R^{8A} is an unsubstituted

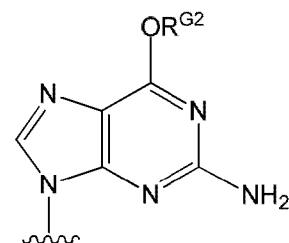
phenyl; and R^{9A} is



45. The use of any one of Claims 1-5, wherein the compound is

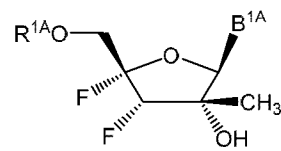


, or a pharmaceutically acceptable salt thereof, wherein B^{1A} is

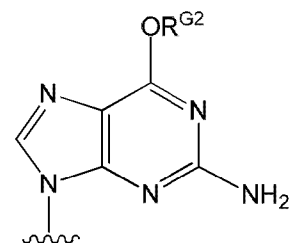


; R^{G2} is -CH₂CH₃; and R^{1A} is hydrogen.

46. The use of any one of Claims 1-5, wherein the compound is

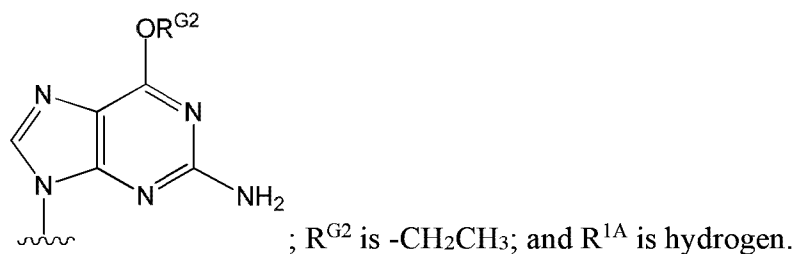
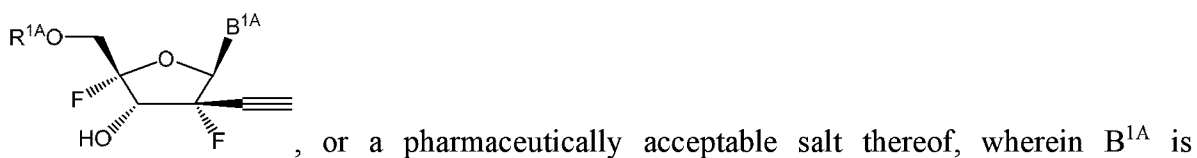


, or a pharmaceutically acceptable salt thereof, wherein B^{1A} is

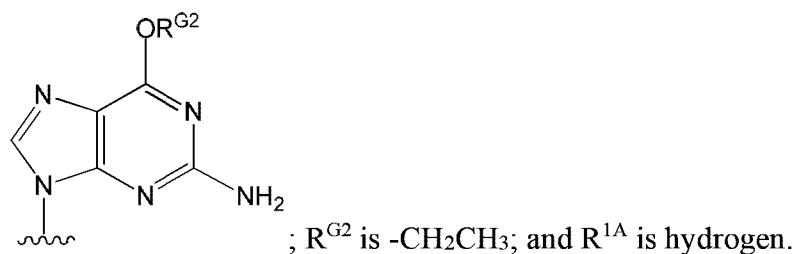
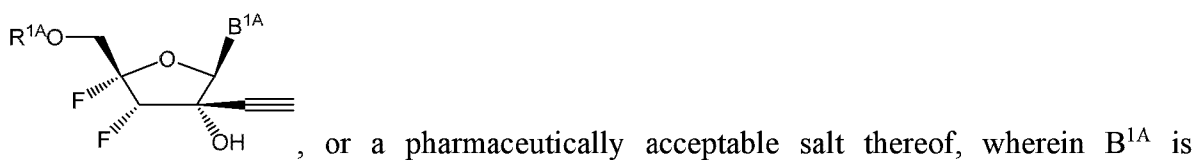


; R^{G2} is -CH₂CH₃; and R^{1A} is hydrogen.

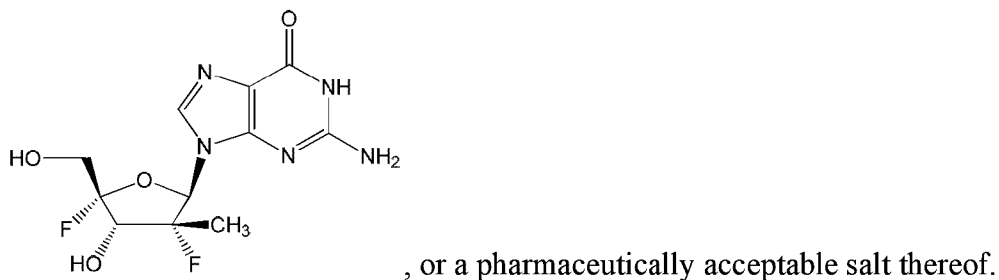
47. The use of any one of Claims 1-5, wherein the compound is



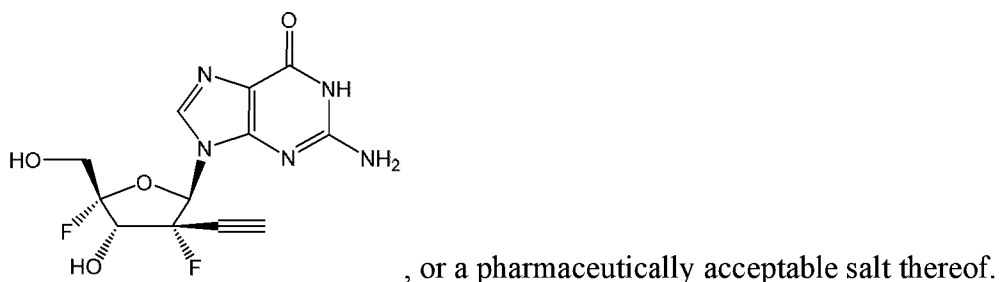
48. The use of any one of Claims 1-5, wherein the compound is



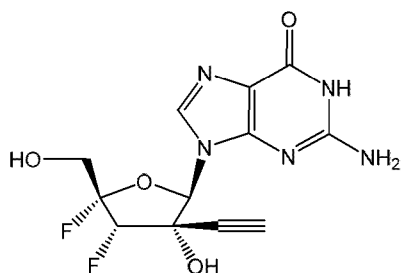
49. The use of any one of Claims 1-5, wherein the compound is



50. The use of any one of Claims 1-5, wherein the compound is

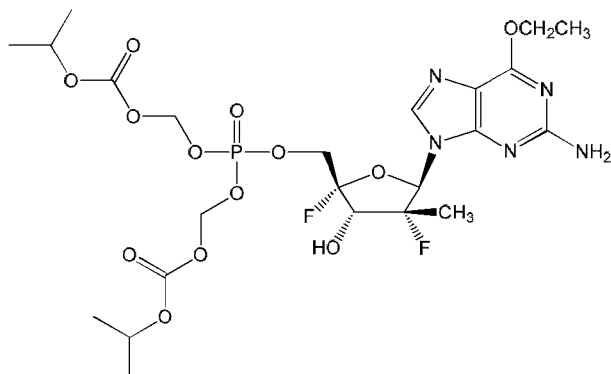


51. The use of any one of Claims 1-5, wherein the compound is



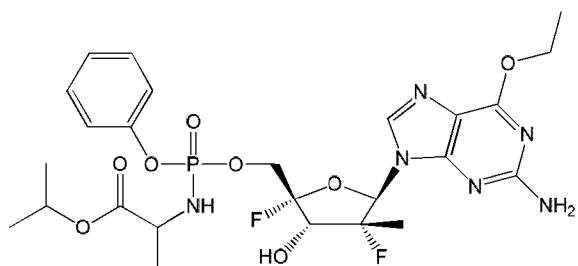
, or a pharmaceutically acceptable salt thereof.

52. The use of any one of Claims 1-5, wherein the compound is



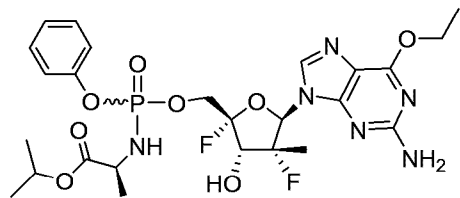
, or a pharmaceutically acceptable salt thereof.

53. The use of any one of Claims 1-5, wherein the compound is



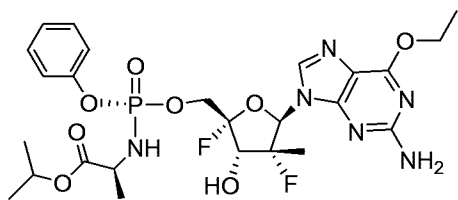
, or a pharmaceutically acceptable salt thereof.

54. The use of Claim 53, wherein the compound is



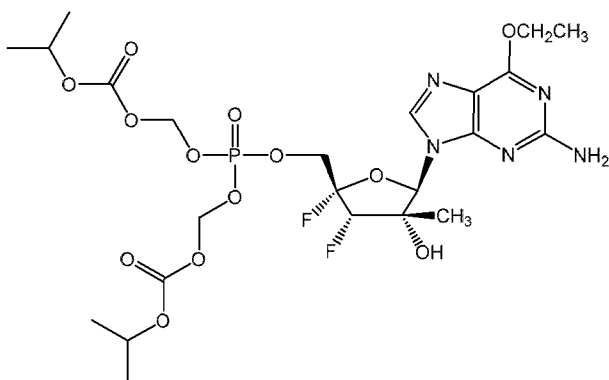
, or a pharmaceutically acceptable salt thereof.

55. The use of Claim 53, wherein the compound is



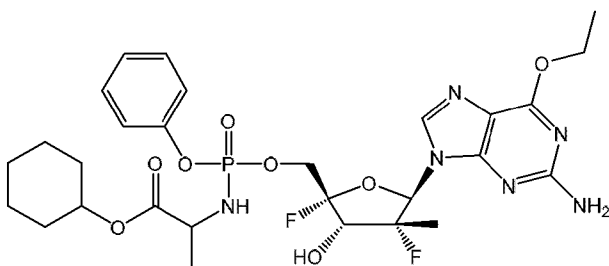
, or a pharmaceutically acceptable salt thereof.

56. The use of any one of Claims 1-5, wherein the compound is



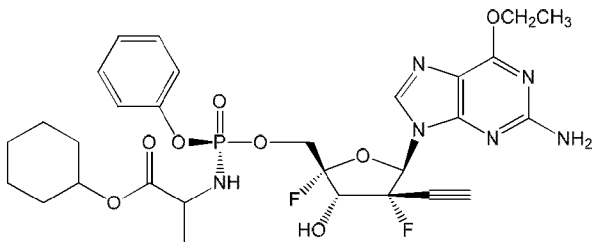
, or a pharmaceutically acceptable salt thereof.

57. The use of any one of Claims 1-5, wherein the compound is



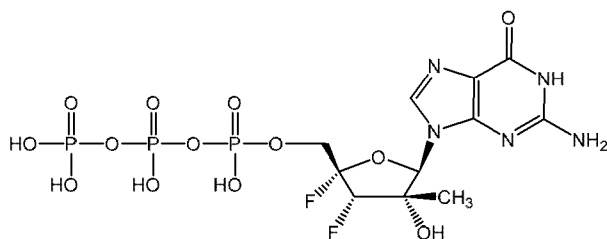
, or a pharmaceutically acceptable salt thereof.

58. The use of any one of Claims 1-5, wherein the compound is



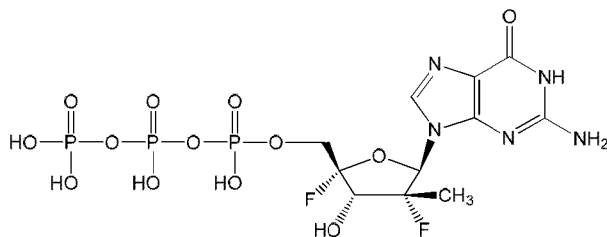
, or a pharmaceutically acceptable salt thereof.

59. The use of any one of Claims 1-5, wherein the compound is



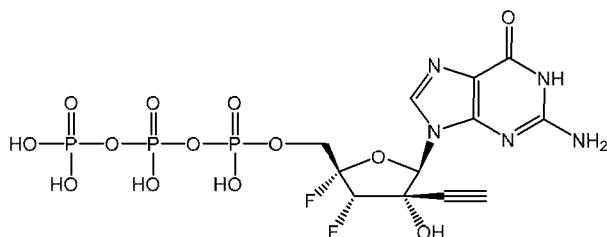
, or a pharmaceutically acceptable salt thereof.

60. The use of any one of Claims 1-5, wherein the compound is



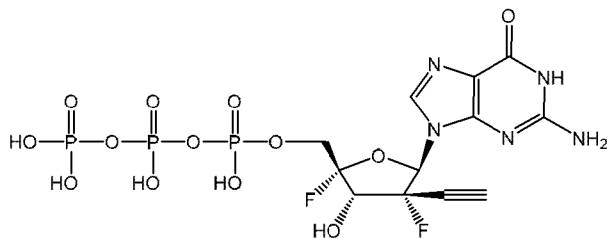
, or a pharmaceutically acceptable salt thereof.

61. The use of any one of Claims 1-5, wherein the compound is



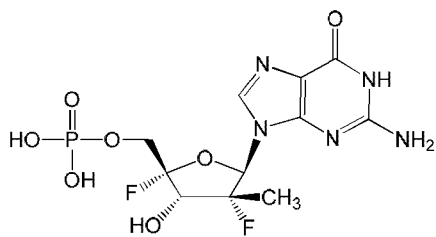
, or a pharmaceutically acceptable salt thereof.

62. The use of any one of Claims 1-5, wherein the compound is



, or a pharmaceutically acceptable salt thereof.

63. The use of any one of Claims 1-5, wherein the compound is



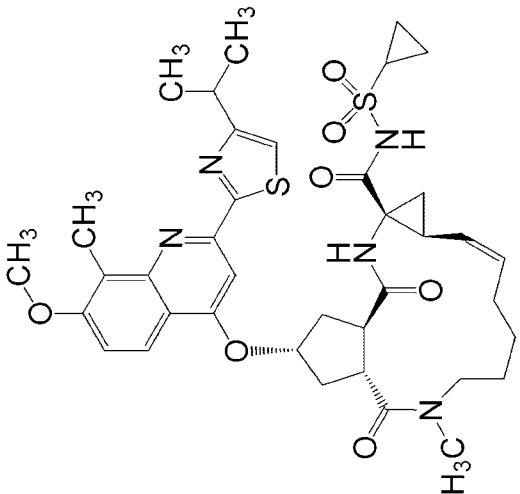
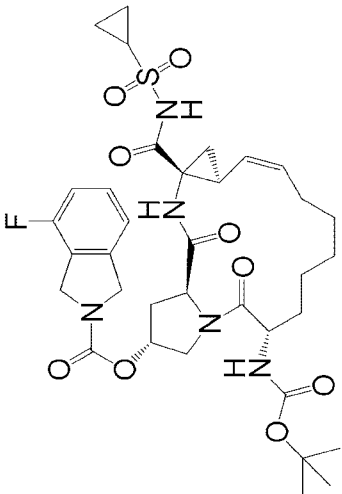
, or a pharmaceutically acceptable salt thereof.

Figure 1: HCV Protease Inhibitors

#	Name	Structure
1001	Telaprevir VX-950	
1002	MK-5172	
1003	ABT-450	
1004	BILN-2061	
1005	BI-201335 BI335	

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Figure 1 (cont.): HCV Protease Inhibitors

#	Name	Structure
1013	TMC-435 TMC-435350	
1014	Danoprevir ITMN-191 RG7227 RO5190591	

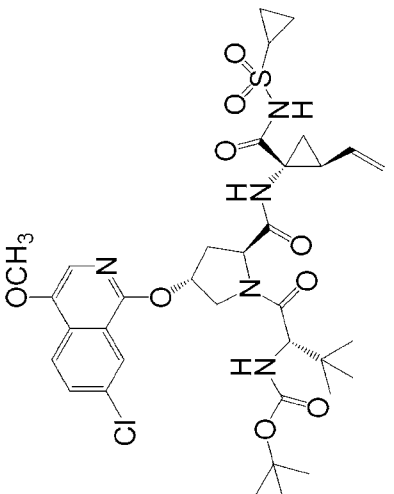
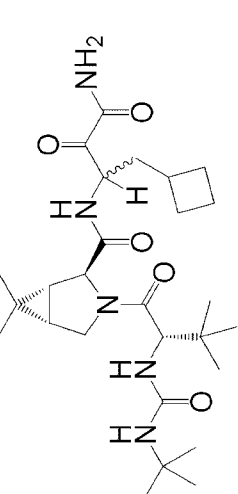
#	Name	Structure
1006	BMS-650032 BM032 Asunaprevir	
1007	Boceprevir SCH 503034	
1008	GS-9256	
1009	GS-9451	
1010	IDX-320	
1011	ACH-1625	
1012	ACH-2684	

Figure 1 (cont.): HCV Protease Inhibitors

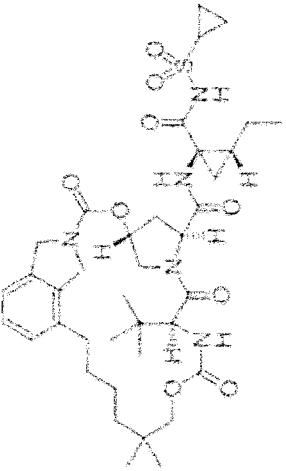
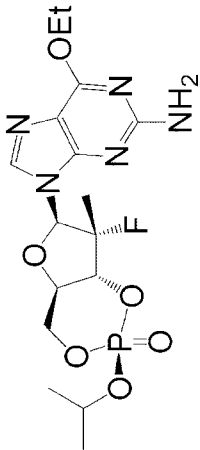
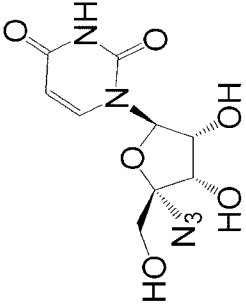
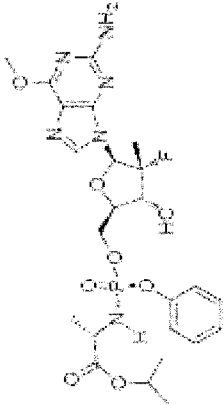
<u>#</u>	<u>Name</u>	<u>Structure</u>
1015	MK-7009 Vaniprevir	
1016	PHX1766	

Figure 2: HCV Polymerase Inhibitors – Nucleosides, Nucleotides and Analogs Thereof

#	Name	Structure
2004	PSI-352938 GS-938	
2005	4'-azidouridine and its prodrugs	
2006	PSI-661	
2007	GS-6620	
2008	TMC649128	

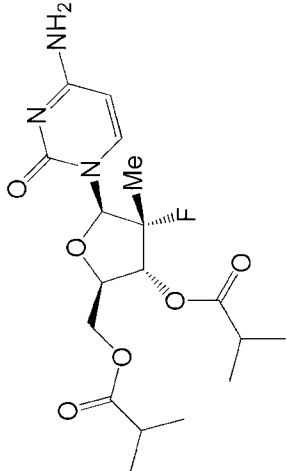
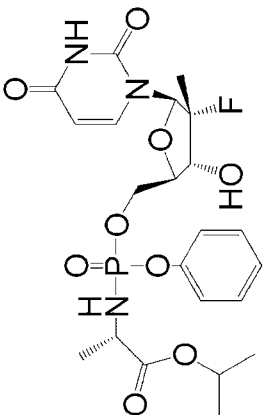
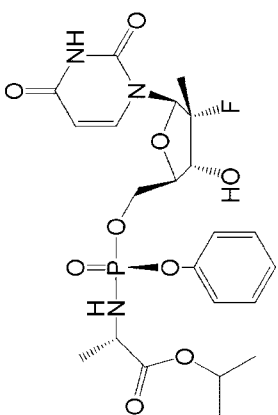
#	Name	Structure
2001	RG7128 Mericitabine	
2002	PSI-7851	
2003	PSI-7977 GS-7977, Sofosbuvir	

Figure 2 (cont.): HCV Polymerase Inhibitors – Nucleosides, Nucleotides and Analogs Thereof

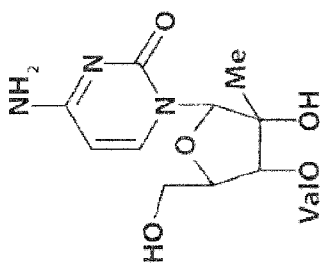
<u>#</u>	<u>Name</u>	<u>Structure</u>
2009	NM283	
2010	BCX5191	
2011	IDX19368	
2012	IDX19370	

Figure 3: HCV Polymerase Inhibitors – Non-Nucleosides

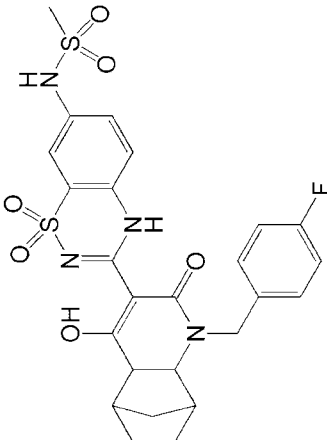
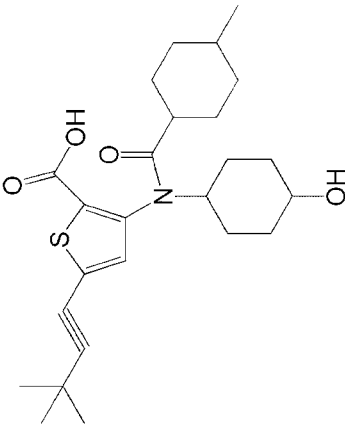
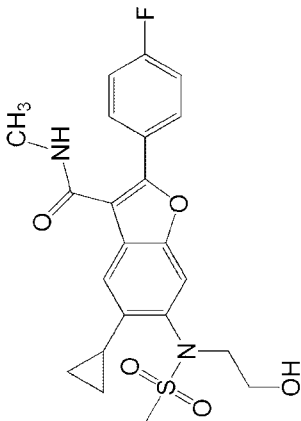
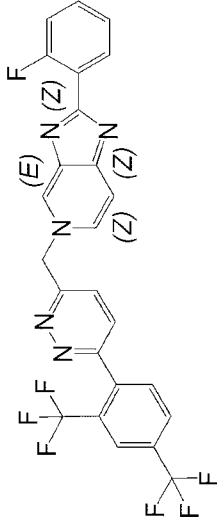
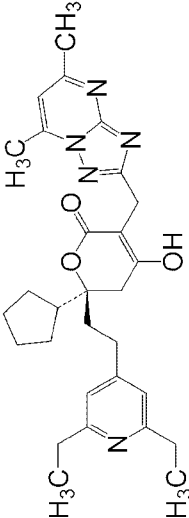
#	Name	Structure
3001	ABT-333	
3002	ANA-598 Setrobuvir	
3003	VX-222 S1480 VCH-222	
3004	HCV-796	
3005	BI-207127	
3006	GS-9190	
3007	Filibuvir PF-00868554	

Figure 3 (cont.): HCV Polymerase Inhibitors – Non-Nucleosides

#	Name	Structure
3011	TMC647055	
3012	BMS-791325	
3013	PPI-383	
3014	GS9669	

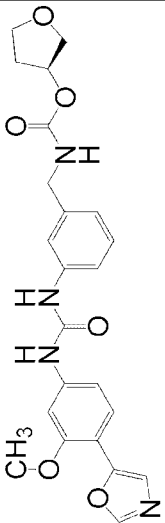
#	Name	Structure
3008	VX-497	
3009	ABT-072	
3010	MK-3281	

Figure 4: NSA Inhibitors

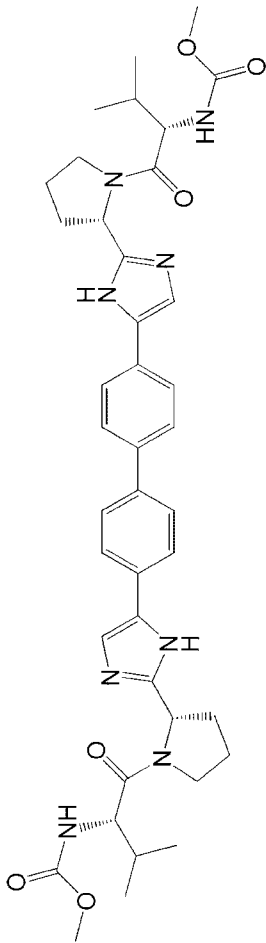
#	Name	Structure
4001	BMS-790052 BMS052 S1482 Daclatasvir	
4002	PPI-461	
4003	ACH-2928	
4004	GS-5885	
4005	BMS-824393	
4006	ABT 267	
4007	ACH-3102	
4008	AZD-7295	
4009	IDX719	
4010	PPI-668	
4011	MK8742	
4012	GSK805	

Figure 5: Other Antivirals

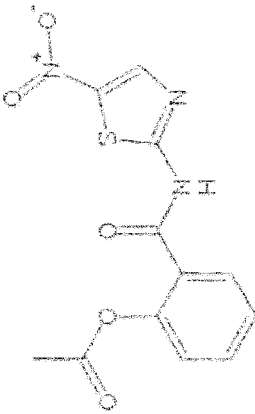
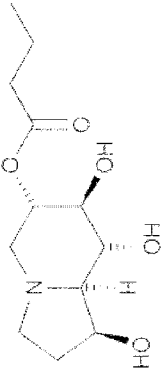
#	Name	Structure
5001	Debio-025 Alisporivir	
5002	MIR-122 inhibitor	
5003	clemizole	
5004	ITX 5061	
5005	BIT225	
5006	NIM811	
5007	SCY-635	
5008	Nitazoxanide	
5009	Miravirsen	
5010	Celgosivir	
5011	GS9620	

Figure 6: Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6002	
6003	
6004	

#	Structure
6000	
6001	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6005	
6006	
6007	
6008	

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Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6011	
6012	
6013	
6009	
6010	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6014	
6015	
6016	
6017	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6021	
6022	
6023	
6018	
6019	
6020	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

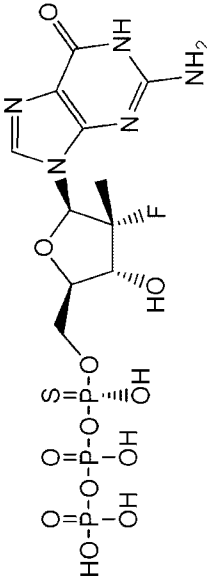
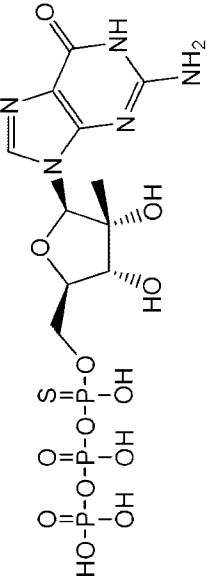
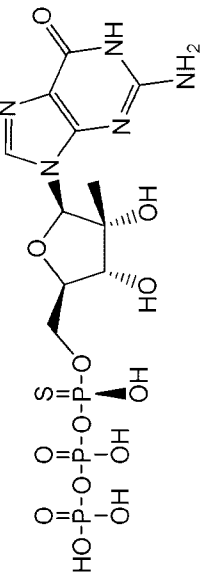
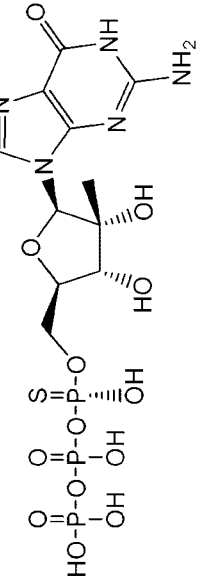
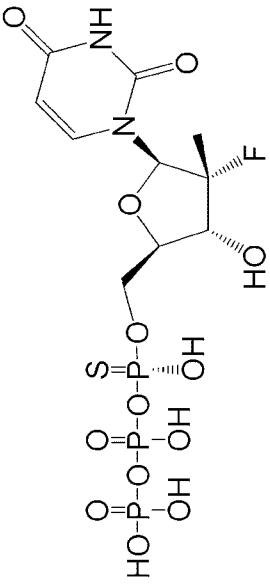
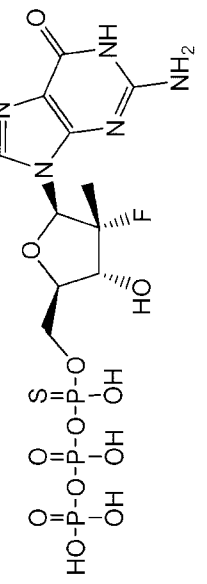
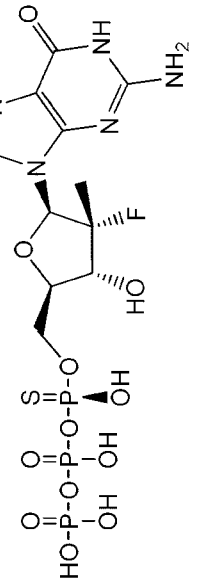
#	Structure
6027	
6028	
6029	
6030	
6024	
6025	
6026	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6031	
6032	
6033	
6034	
6035	
6036	

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Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6040	
6041	
6042	
6037	
6038	
6039	

#	Structure
6043	
6044	
6045	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6051	
6052	
6049	
6050	

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Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

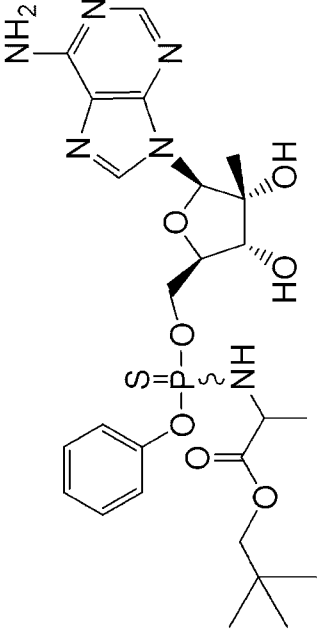
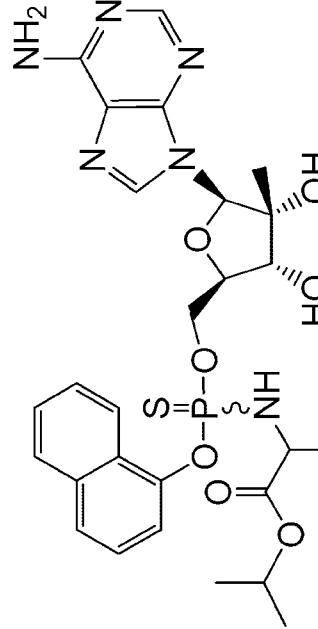
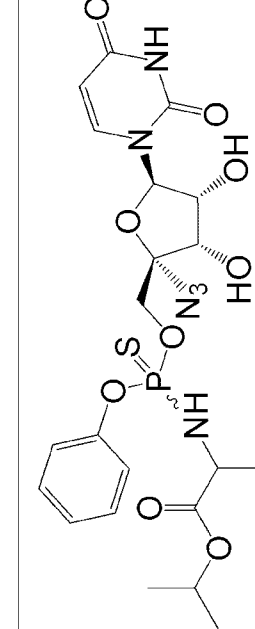
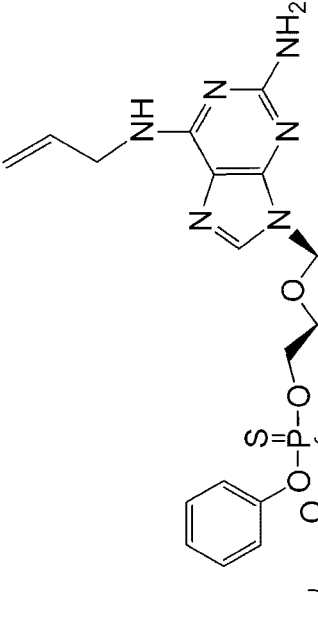
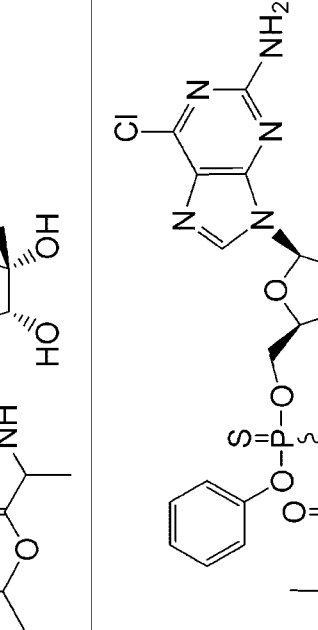
#	Structure
6055	
6056	
6057	
6053	
6054	

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6060	
6061	
6062	
6058	
6059	

22/99

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6066	
6067	
6068	
6063	
6064	
6065	

23/99

Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6072	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1cccnc1)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>
6073	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1ccccc1)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>
6074	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1ccccc1)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>
6069	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1ccc(C)cc1)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>
6070	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1ccc(OC)cc1)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>
6071	 <chem>CC(C)OC(=O)NC(=O)COP(=S)(Oc1ccc2ncccc12)O[C@H]2C[C@@H](O)[C@H](N3C=NC(=O)NC3=O)[C@H]2O</chem>

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Figure 6 (cont.): Compounds of Formula (CC) and alpha-thiotriphosphates thereof

#	Structure
6077	
6078	
6075	
6076	

Figure 7: Compounds of Formula (AA)

#	Structure
7000	
7001	
7002	
7003	

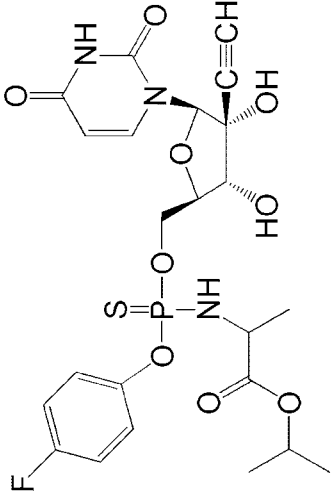
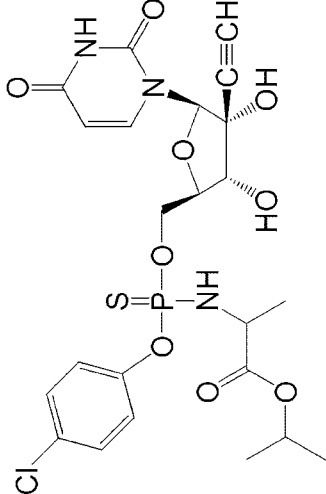
26/99

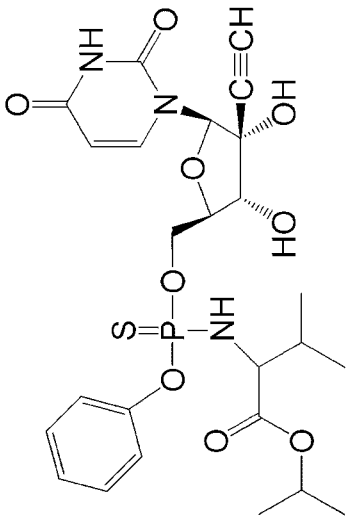
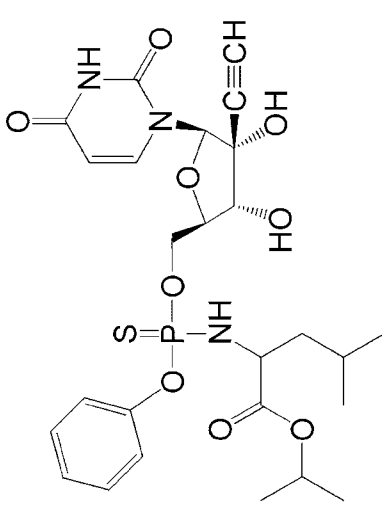
Figure 7 (cont.): Compounds of Formula (AA)

#	Structure
7006	
7007	
7004	
7005	

27/99

Figure 7 (cont.): Compounds of Formula (AA)

#	Structure
7010	
7011	

#	Structure
7008	
7009	

#	Structure
7012	
7013	

29/99

Figure 7 (cont.): Compounds of Formula (AA)

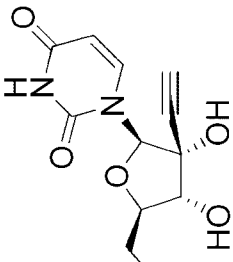
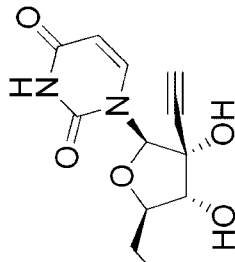
#	Structure
7018	
7019	
7016	
7017	

30/99

Figure 7 (cont.): Compounds of Formula (AA)

#	Structure
7020	
7021	
7022	
7023	

Figure 7 (cont.): Compounds of Formula (AA)

#	Structure
7026	
7027	

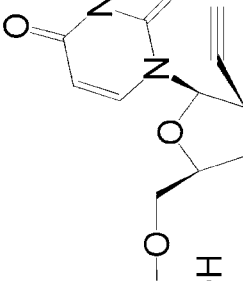
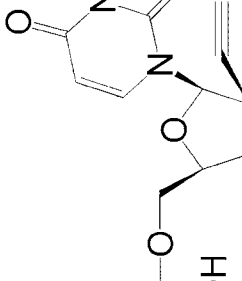
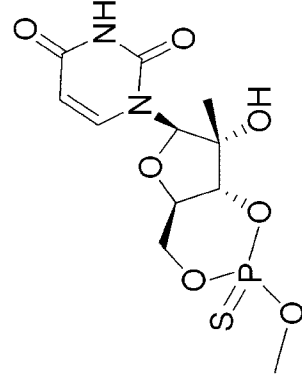
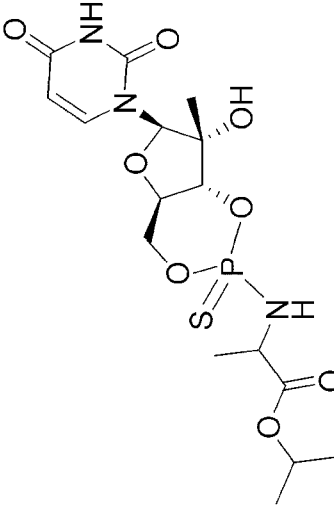
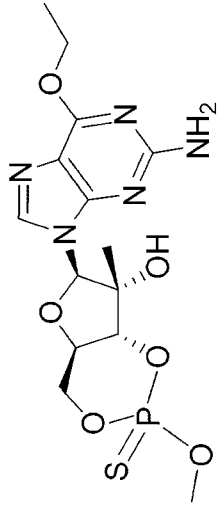
#	Structure
7024	
7025	

Figure 8: Compounds of Formula (BB)

#	Structure
8003	
8004	
8005	

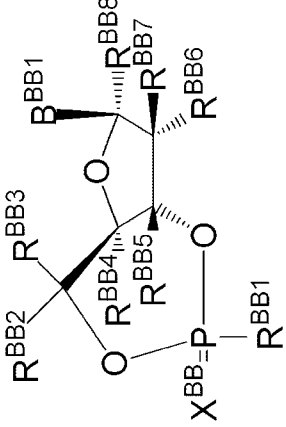
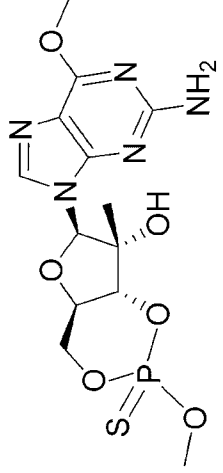
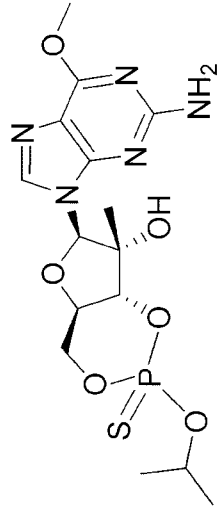
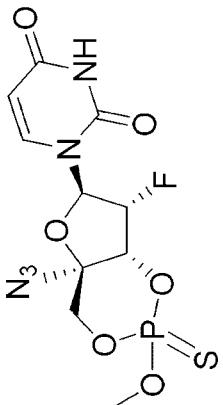
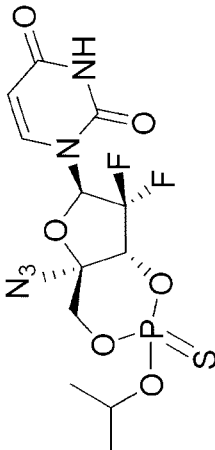
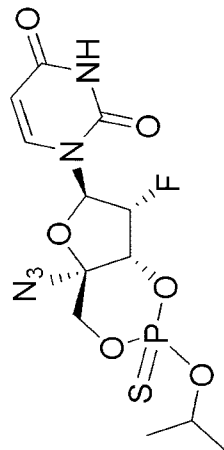
#	Structure
8000	
8001	
8002	

Figure 8 (cont.): Compounds of Formula (BB)

#	Structure
8009	
80010	
8011	

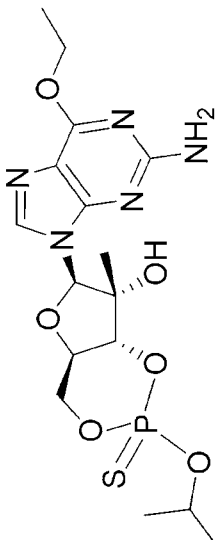
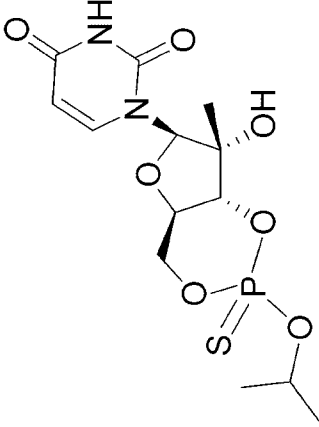
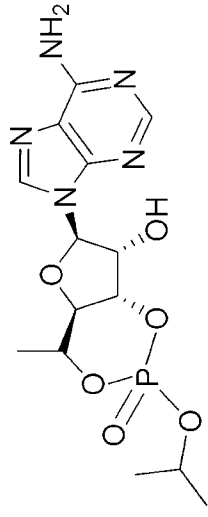
#	Structure
8006	
8007	
8008	

Figure 8 (cont.): Compounds of Formula (BB)

#	Structure
8015	
8016	

#	Structure
8012	
8013	
8014	

Figure 9: Compounds of Formula (I)

#	Structure
9000	
9001	
9002	
9003	
9004	
9005	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9008	
9009	

#	Structure
9006	
9007	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9013	
9014	

#	Structure
9010	
9011	
9012	

Figure 9 (cont.): Compounds of Formula (I)

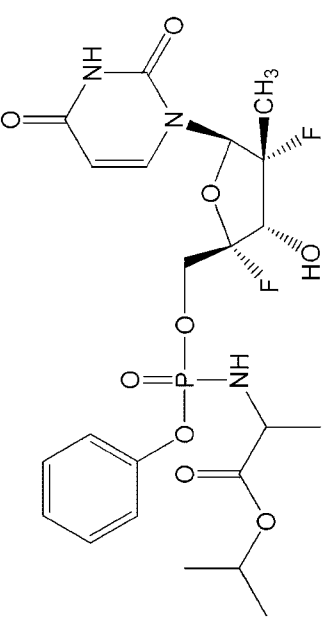
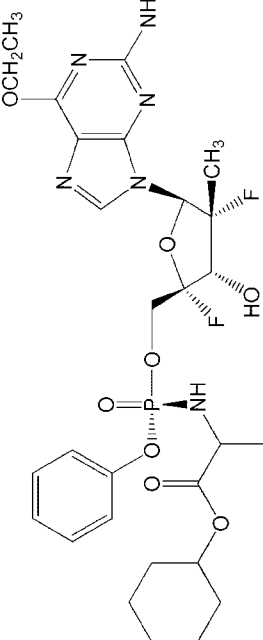
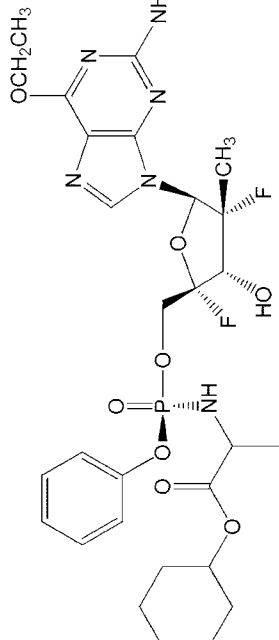
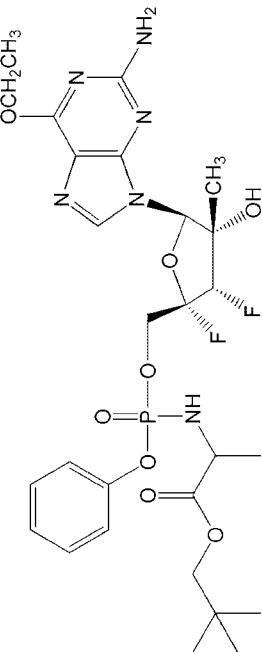
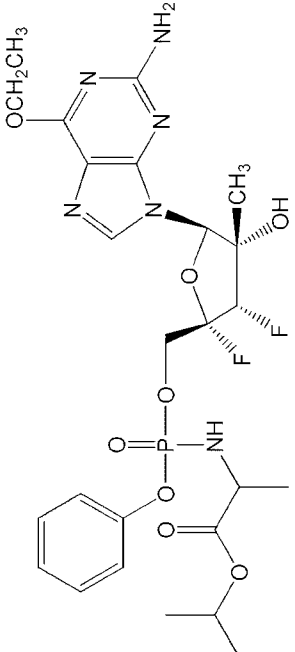
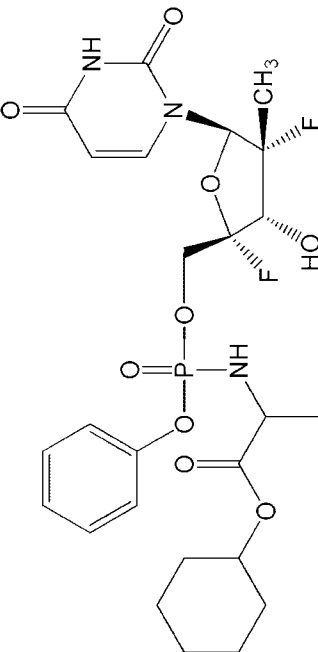
#	Structure
9017	
9018	
9015	
9016	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9022	
9023	
9024	
9019	
9020	
9021	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9028	
9029	
9030	
9025	
9026	
9027	

#	Structure
9031	
9032	
9033	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9040	
9041	
9042	
9037	
9038	
9039	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9045	
9046	
9043	
9044	

44/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9049	
9050	

#	Structure
9047	
9048	

45/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9053	
9054	
9051	
9052	

46/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9057	
9058	
9055	
9056	

47/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9061	
9062	
9059	
9060	

48/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9065	
9066	
9063	
9064	

49/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9069	
9070	
9067	
9068	

50/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9073	
9074	
9071	
9072	

51/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9077	
9078	

#	Structure
9075	
9076	

52/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9081	
9082	
9079	
9080	

53/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9085	
9086	

#	Structure
9083	
9084	

54/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9089	
9090	

#	Structure
9087	
9088	

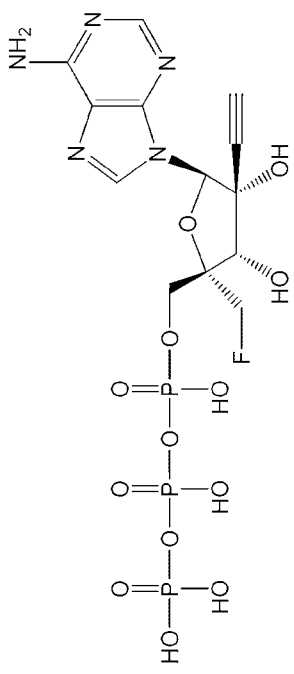
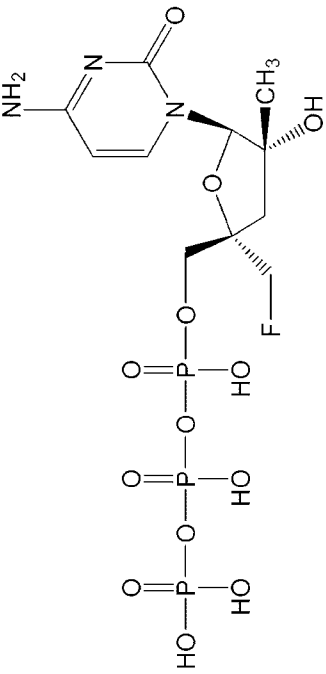
55/99

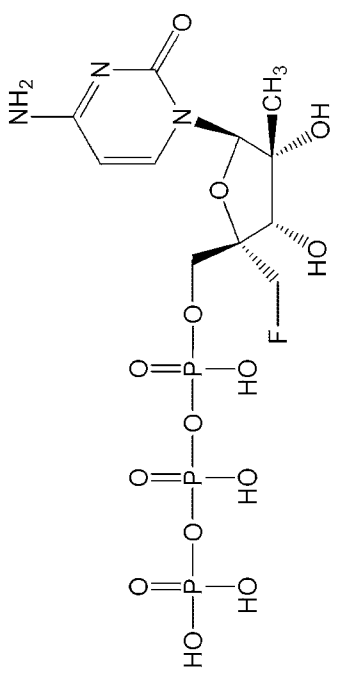
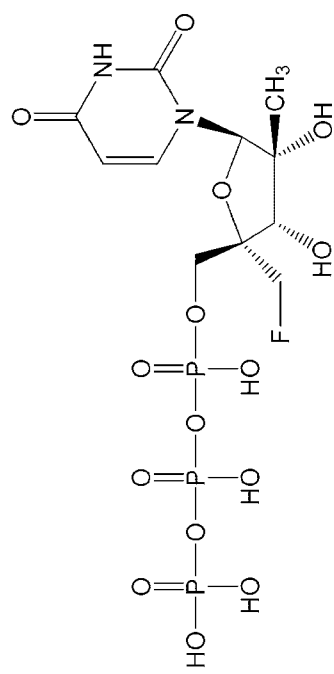
Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9093	
9094	
9091	
9092	

56/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9097	
9098	

#	Structure
9095	
9096	

57/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9101	
9102	
9099	
9100	

58/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9105	
9106	
9107	
9103	
9104	

59/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9111	
9112	

#	Structure
9108	
9109	
9110	

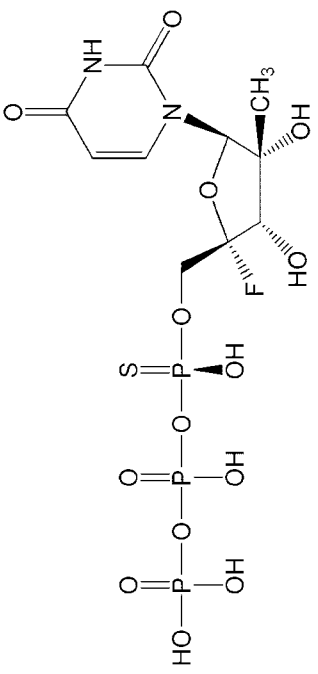
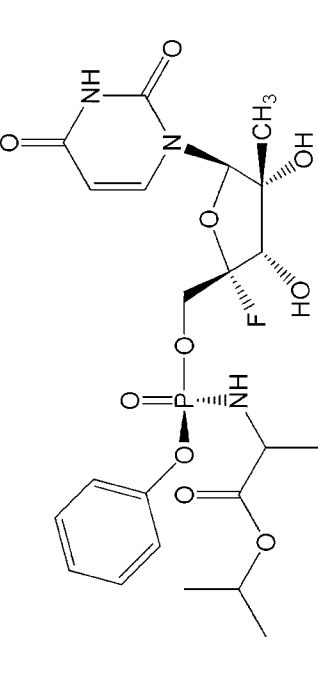
60/99

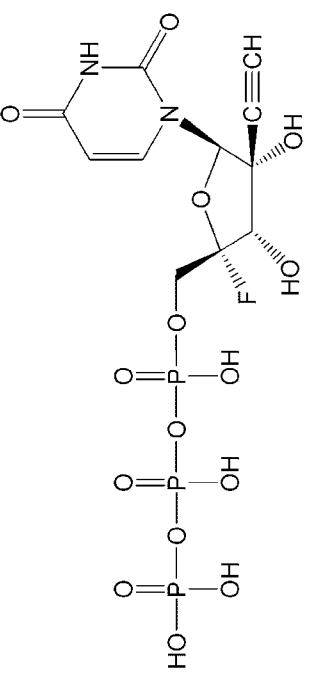
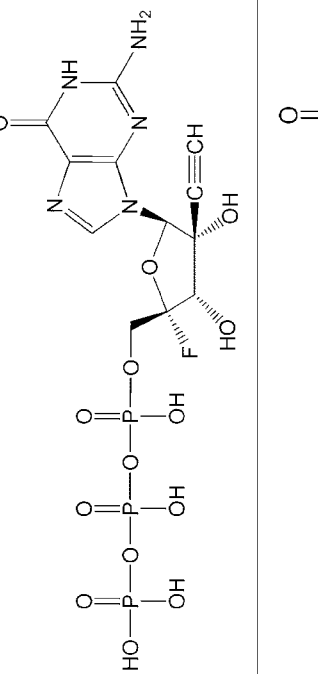
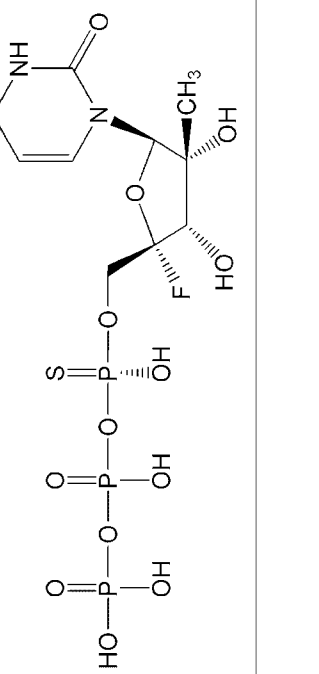
Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9113	
9114	
9115	
9116	
9117	

61/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9121	
9122	

#	Structure
9118	
9119	
9120	

62/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9125	
9126	
9123	
9124	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9130	
9131	
9132	
9127	
9128	
9129	

64/99

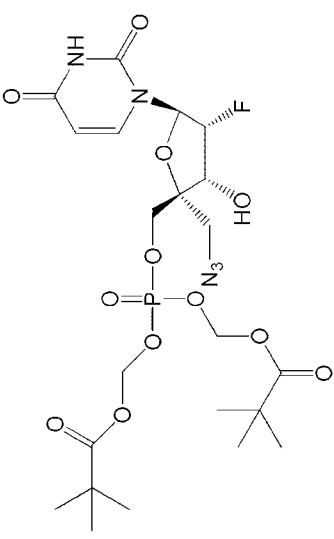
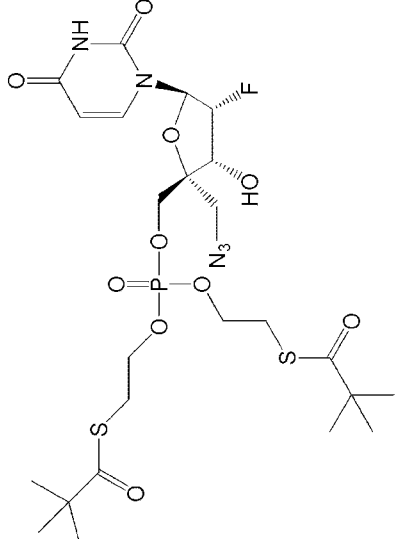
Figure 9 (cont.): Compounds of Formula (I)

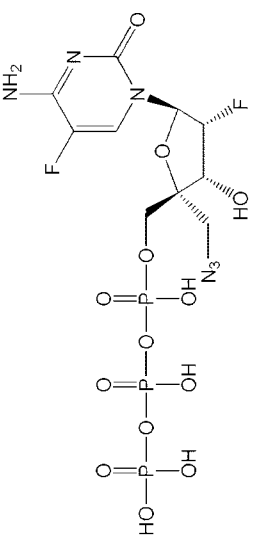
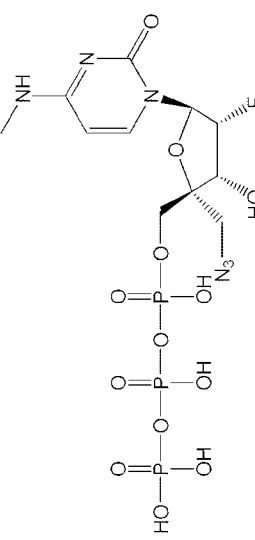
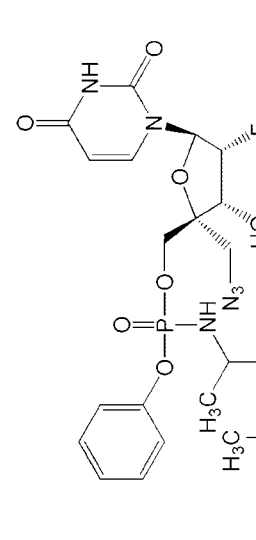
#	Structure
9136	
9137	
9138	

#	Structure
9133	
9134	
9135	

65/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9142	
9143	

#	Structure
9139	
9140	
9141	

#	Structure
9144	 Chemical structure of compound 9144. It consists of a pyrimidine ring connected to a sugar moiety with a fluorine atom and a hydroxyl group. The sugar is linked to a phosphonate group, which is further connected to a cyclohexane ring and a methyl group.
9145	 Chemical structure of compound 9145. It is similar to 9144 but features a different substituent on the cyclohexane ring, specifically a methyl group.
9146	 Chemical structure of compound 9146. It is similar to 9144 but features a different substituent on the cyclohexane ring, specifically a cyclohexyl group.

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9152	
9153	

#	Structure
9150	
9151	

68/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9156	
9157	

#	Structure
9154	
9155	

69/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9160	
9161	

#	Structure
9158	
9159	

70/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9164	
9165	
9162	
9163	

71/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9169	
9170	
9171	
9166	
9167	
9168	

72/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9174	
9175	
9172	
9173	

73/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9178	
9179	
9176	
9177	

74/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9180	
9181	
9182	
9183	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9186	
9187	
9188	
9184	
9185	

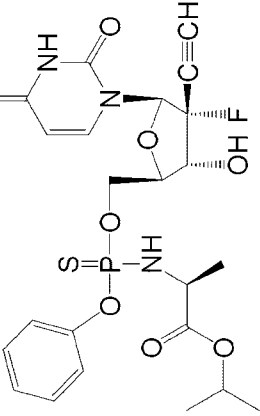
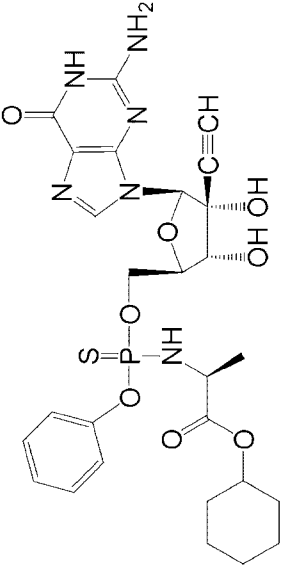
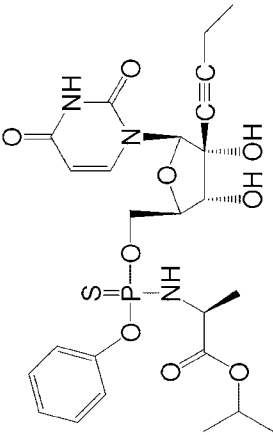
76/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9192	
9193	

#	Structure
9189	
9190	
9191	

#	Structure
9194	
9195	
9196	

#	Structure
9200	
9201	
9202	

79/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9209	
9210	

#	Structure
9206	
9207	
9208	

80/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9214	
9215	
9216	
9211	
9212	
9213	

81/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9220	
9221	
9222	
9217	
9218	
9219	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9226	
9227	

#	Structure
9223	
9224	
9225	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9230	
9231	

#	Structure
9228	
9229	

84/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9235	
9236	
9237	

#	Structure
9232	
9233	
9234	

85/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9241	
9242	
9243	
9238	
9239	
9240	

86/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9247	
9248	

#	Structure
9244	
9245	
9246	

87/99

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9252	
9253	

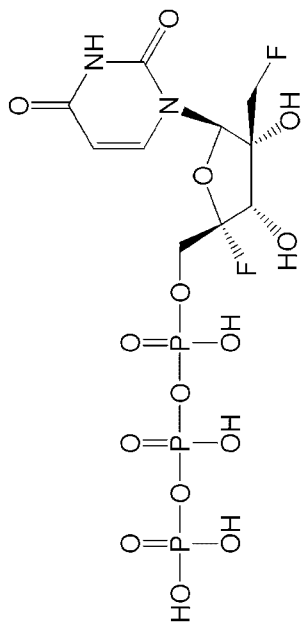
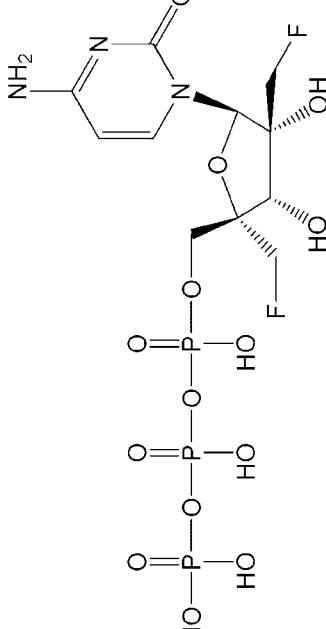
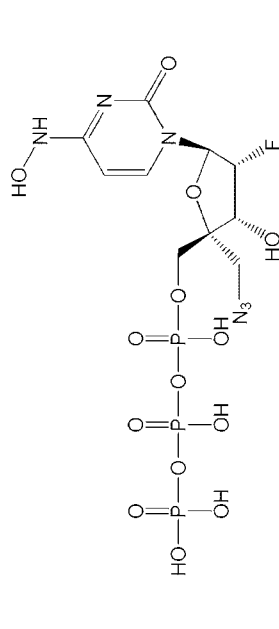
#	Structure
9249	
9250	
9251	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9256	
9257	
9258	
9254	
9255	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9261	
9262	
9263	

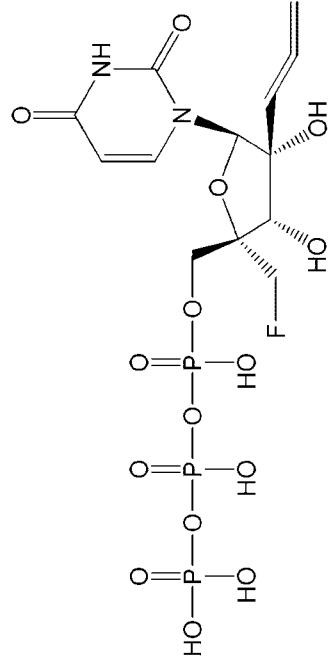
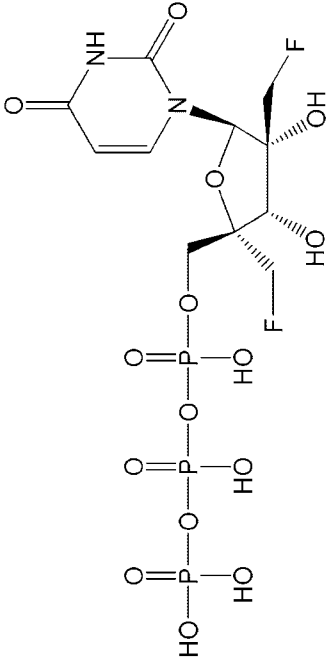
#	Structure
9259	
9260	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9267	
9268	

#	Structure
9264	
9265	
9266	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9271	
9272	
9273	
9269	
9270	

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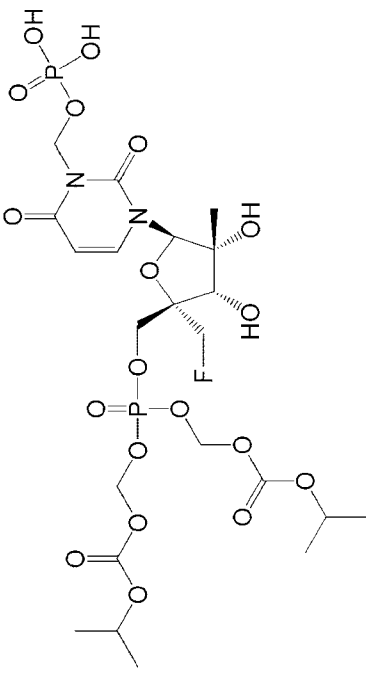
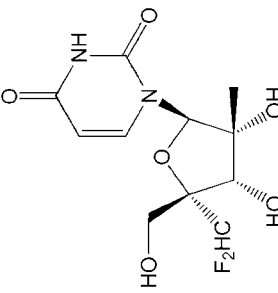
Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9277	
9278	

#	Structure
9274	
9275	
9276	

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Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9281	
9282	

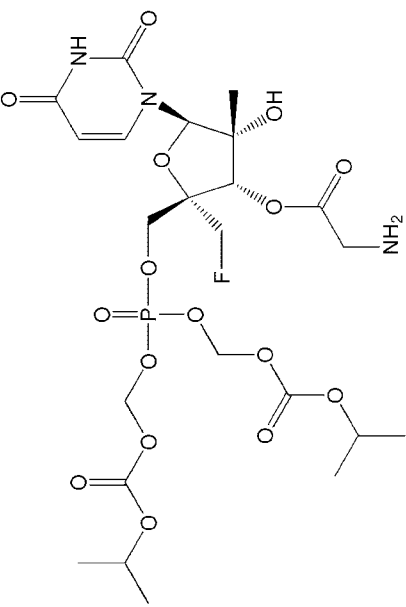
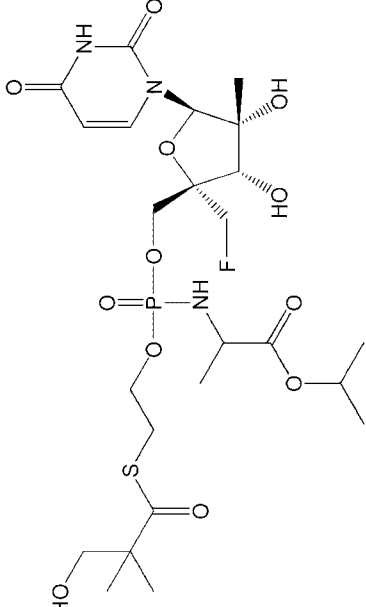
#	Structure
9279	
9280	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9285	
9286	

#	Structure
9283	
9284	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9289	
9290	

#	Structure
9287	
9288	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9293	
9294	
9295	
9291	
9292	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure	#	Structure
9299		9300	
9296		9297	
9301		9298	

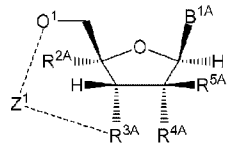
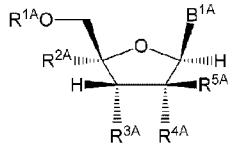
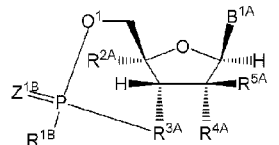
Figure 9 (cont.): Compounds of Formula (I)

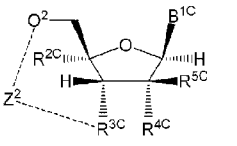
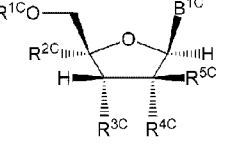
#	Structure
9305	
9306	
9307	
9302	
9303	
9304	

Figure 9 (cont.): Compounds of Formula (I)

#	Structure
9310	
9308	
9309	

Compounds of Formula (I)

#	Structure
9000	
9001	
9002	

#	Structure
9003	
9004	
9005	