COMBINATION THERAPY FOR TREATING A PARAMYXOVIRUS

INCORPORATION BY REFERENCE TO ANY PRIORITY APPLICATIONS

[0001] Any and all applications for which a foreign or domestic priority claim is identified, for example, in the Application Data Sheet or Request as filed with the present application, are hereby incorporated by reference under 37 CFR 1.57, and Rules 4.18 and 20.6.

REFERENCE TO SEQUENCE LISTING

[0002] The present application is filed with a Sequence Listing in Electronic format. The Sequence Listing is provided as a file entitled ALIOS086.txt, created August 3, 2015, which is approximately 4 kb in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

BACKGROUND

Field

[0003] The present application relates to the fields of chemistry, biochemistry and medicine. More particularly, disclosed herein are a combination of compounds that can be used to ameliorate, treat and/or prevent a paramyxovirus viral.

Description

[0004] Respiratory viral infections, including upper and lower respiratory tract viral infections, infects and is the leading cause of death of millions of people each year. Upper respiratory tract viral infections involve the nose, sinuses, pharynx and/or larynx. Lower respiratory tract viral infections involve the respiratory system below the vocal cords, including the trachea, primary bronchi and lungs.

[0005] Nucleoside analogs are a class of compounds that have been shown to exert antiviral 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

[0006] Some embodiments disclosed herein relate to a method for ameliorating or treating a paramyxovirus virus infection that can include administering to a subject infected with the paramyxovirus virus an effective amount of a combination of one or more of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, wherein the paramyxovirus virus infection can be selected from a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

[0007] Other embodiments disclosed herein relate to a method for ameliorating or treating a paramyxovirus virus infection comprising contacting a cell infected with the paramyxovirus virus with an effective amount of a combination of one or more of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, wherein the paramyxovirus virus infection can be selected from a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

[0008] Still other embodiments disclosed herein relate to use of an effective amount of a combination of one or more of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, for ameliorating or treating a paramyxovirus virus infection, wherein the paramyxovirus virus infection can be selected from a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection

[0009] Yet still other embodiments disclosed herein relate to use of an effective amount of a combination of one or more of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, for ameliorating or treating a paramyxovirus virus infection, wherein the paramyxovirus virus infection can be selected from a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Figure 1 shows example anti-RSV agents.

DETAILED DESCRIPTION

[0011] *Paramyxoviridae* family is a family of single stranded RNA viruses. Several genera of the *paramyxoviridae* family include respirovirus, rubulavirus, pneumovirus and metapneumovirus. These viruses can be transmitted person to person via direct or close contact with contaminated respiratory droplets or fomites.

[0012] Human Respiratory Syncytial Virus (RSV) is a species of pneumovirus and a negative single-stranded RNA virus. RSV can cause respiratory infections, and can be associated with bronchiolitis and pneumonia. Symptoms of an RSV infection include coughing, sneezing, runny nose, fever, decrease in appetite, sore throat, headache and wheezing. RSV is the most common cause of bronchiolitis and pneumonia in children under one year of age in the world, and can be the cause of tracheobronchitis in older children and adults. In the United States, between 75,000 and 125,000 infants are hospitalized each year with RSV. Among adults older than 65 years of age, an estimated 14,000 deaths and 177,000 hospitalizations have been attributed to RSV.

[0013] Treatment options for people infected with RSV are currently limited. Antibiotics, usually prescribed to treat bacterial infections, and over-the-counter medication are not effective in treating RSV and may help only to relieve some of the symptoms. In severe cases, a nebulized bronchodilator, such as albuterol, may be prescribed to relieve some of the symptoms, such as wheezing. RespiGam® (RSV-IGIV, MedImmune, approved for high risk children younger than 24 months of age) and Synagis® (palivizumab, MedImmune, approved for high risk children younger than 24 months of age) have been approved for prophylactic use against RSV, and Virzole® (ribavirin by aerosol, ICN pharmaceuticals) have been approved for the treatment of RSV.

[0014] Parainfluenza viruses are typically negative-sense RNA viruses. Species of respirovirus include human parainfluenza viruses 1 and 3; and species of rubulavirus include human parainfluenza viruses 2 and 4. Human parainfluenza virus includes four serotypes types (HPIV-1, HPIV-2, HPIV-3 and HPIV-4), and human parainfluenza virus 4 (HPIV-4) include two antigenic subgroups, A and B. Human parainfluenza viruses can cause

upper and lower respiratory tract infections. Human parainfluenza virus 1 (HPIV-1) and human parainfluenza virus 2 (HPIV-2) can be associated with croup; human parainfluenza virus 3 (HPIV-3) can be associated with bronchiolitis and pneumonia. According to the Centers of Disease Control and Prevention (CDC), there are no vaccines against human parainfluenza viruses.

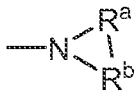
[0015] A species of metapneumovirus is human metapneumovirus. Human metapneumovirus is a negative single-stranded RNA virus. Human metapneumovirus can cause respiratory tract infections, such as upper and lower respiratory tract infections in human, for example young children.

[0016] Respiratory infections include colds, croup, pneumonia, bronchitis, tracheobronchitis and bronchiolitis. Symptoms can include a cough, runny nose, nasal congestion, sore throat, fever, difficulty breathing, abnormally rapid breathing, wheezing vomiting, diarrhea and ear infections.

Definitions

[0017] 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. All patents, applications, published applications and other publications referenced herein are incorporated by reference in their entirety unless stated otherwise. In the event that there are a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

[0018] As used herein, any "R" group(s) such as, without limitation, R^{1A}, R^{2A}, R^{3A}, R^{4A}, R^{5A}, R^{6A}, R^{7A}, R^{8A}, R^{9A}, R^{10A}, R^{11A}, R^{12A}, R^{13A}, R^{14A}, R^{15A}, R^{16A}, R^{17A}, R^{18A}, R^{19A}, R^{20A}, R^{21A}, R^{22A}, R^{23A}, R^{24A}, R^{25A}, R^{26A}, R^{27A}, R^{28A}, R^{29A}, R^{30A}, R^{31A}, R^{32A}, R^{33A}, R^{34A}, R^{35A}, R^{36A}, R^{37A} and R^{38A} 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.

[0019] 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 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, cycloalkynyl, 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, sulfenyl, sulfinyl, sulfonyl, haloalkyl, haloalkoxy, an amino, a mono-substituted amino group and a di-substituted amino group.

[0020] 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 heteroalicyclyl group. That is, the alkyl, alkenyl, alkynyl, ring(s) of the cycloalkyl, ring(s) of the cycloalkenyl, ring(s) of the aryl, ring(s) of the heteroaryl or ring(s) of the heteroalicyclyl can contain from "a" to "b", inclusive, carbon atoms. Thus, for example, a "C_1 to C_4 alkyl" group refers to all alkyl groups having from 1 to 4 carbons, that is, CH_3-, CH_3CH_2-, $CH_3CH_2CH_2$-, $(CH_3)_2CH$-, $CH_3CH_2CH_2CH_2$-, $CH_3CH_2CH(CH_3)$- and $(CH_3)_3C$-. If no "a" and "b" are designated with regard to an alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, aryl, heteroaryl or heteroalicyclyl group, the broadest range described in these definitions is to be assumed.

[0021] 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 "C_1-C_4 alkyl" or similar designations. By way of example only, "C_1-C_4 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.

[0022] 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.

[0023] 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.

[0024] 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.

[0025] 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. Cycloalkenyl groups 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.

[0026] As used herein, "aryl" refers to a carbocyclic (all carbon) monocyclic or multicyclic 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 C_6-C_{14} aryl group, a C_6-C_{10} aryl group, or a C_6 aryl group. Examples of aryl groups include, but are not limited to, benzene, naphthalene and azulene. An aryl group may be substituted or unsubstituted.

[0027] 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.

[0028] 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 heteroalicyclic 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).

[0029] 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 aralkyl may be substituted or unsubstituted. Examples include but are not limited to benzyl, 2-phenyl(alkyl), 3-phenyl(alkyl), and naphthyl(alkyl).

[0030] 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.

[0031] A "(heteroalicyclyl)alkyl" and "(heterocyclyl)alkyl" refer to a heterocyclic or a heteroalicyclylic group connected, as a substituent, via a lower alkylene group. The lower alkylene and heterocyclyl of a heterocyclyl(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).

[0032] "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."

[0033] As used herein, "alkoxy" refers to the formula –OR wherein R is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, aralkyl, heteroaryl(alkyl) or heterocyclyl(alkyl) is defined herein. A non-limiting list of alkoxys 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.

[0034] As used herein, "acyl" refers to a hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl) connected, as substituents, via a carbonyl group. Examples include formyl, acetyl, propanoyl, benzoyl, and acryl. An acyl may be substituted or unsubstituted.

[0035] 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.

[0036] 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.

[0037] As used herein, "haloalkoxy" refers to an –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.

[0038] A "sulfenyl" group refers to an "-SR" group in which R can be hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). A sulfenyl may be substituted or unsubstituted.

[0039] 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.

[0040] A "sulfonyl" group refers to an "SO_2R" group in which R can be the same as defined with respect to sulfenyl. A sulfonyl may be substituted or unsubstituted.

[0041] An "O-carboxy" group refers to a "RC(=O)O-" group in which R can be hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl), as defined herein. An O-carboxy may be substituted or unsubstituted.

[0042] 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.

[0043] 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.

[0044] A "trihalomethanesulfonyl" group refers to an "X_3CSO_2-" group wherein each X is a halogen.

[0045] A "trihalomethanesulfonamido" group refers to an "$X_3CS(O)_2N(R_A)$-" group wherein each X is a halogen, and R_A hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heteroalicyclyl, aralkyl, (heteroaryl)alkyl or (heteroalicyclyl)alkyl.

[0046] The term "amino" as used herein refers to a $-NH_2$ group.

[0047] As used herein, the term "hydroxy" refers to a –OH group.

[0048] A "cyano" group refers to a "-CN" group.

[0049] The term "azido" as used herein refers to a $-N_3$ group.

[0050] An "isocyanato" group refers to a "-NCO" group.

[0051] A "thiocyanato" group refers to a "-CNS" group.

[0052] An "isothiocyanato" group refers to an " -NCS" group.

[0053] A "mercapto" group refers to an "-SH" group.

[0054] A "carbonyl" group refers to a C=O group.

[0055] An "S-sulfonamido" group refers to a "$-SO_2N(R_AR_B)$" group in which R_A and R_B can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An S-sulfonamido may be substituted or unsubstituted.

[0056] An "N-sulfonamido" group refers to a "$RSO_2N(R_A)$-" group in which R and R_A can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-sulfonamido may be substituted or unsubstituted.

[0057] An "O-carbamyl" group refers to a "$-OC(=O)N(R_AR_B)$" group in which R_A and R_B can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An O-carbamyl may be substituted or unsubstituted.

[0058] An "N-carbamyl" group refers to an "$ROC(=O)N(R_A)$-" group in which R and R_A can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-carbamyl may be substituted or unsubstituted.

[0059] An "O-thiocarbamyl" group refers to a "$-OC(=S)-N(R_AR_B)$" group in which R_A and R_B can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An O-thiocarbamyl may be substituted or unsubstituted.

[0060] An "N-thiocarbamyl" group refers to an "$ROC(=S)N(R_A)$-" group in which R and R_A can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-thiocarbamyl may be substituted or unsubstituted.

[0061] A "C-amido" group refers to a "$-C(=O)N(R_AR_B)$" group in which R_A and R_B can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a

cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). A C-amido may be substituted or unsubstituted.

[0062] An "N-amido" group refers to a "RC(=O)N(R_A)-" group in which R and R_A can be independently hydrogen, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkenyl, aryl, heteroaryl, heterocyclyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl) or heterocyclyl(alkyl). An N-amido may be substituted or unsubstituted.

[0063] 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.

[0064] 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, "C_1-C_3 alkoxyphenyl" may include one or more of the same or different alkoxy groups containing one, two or three atoms.

[0065] 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)).

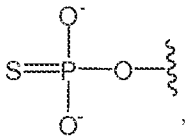
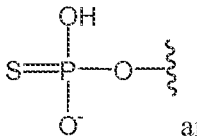
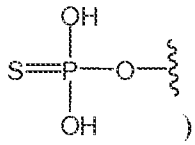
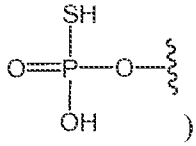
[0066] The term "–N–linked amino acid" refers to an amino acid that is attached to the indicated moiety via a main-chain amino or mono-substituted amino group. When the amino acid is attached in an –N–linked amino acid, one of the hydrogens that is part of the main-chain amino or mono-substituted amino group is not present and the amino acid is attached via the nitrogen. N-linked amino acids can be substituted or unsubstituted.

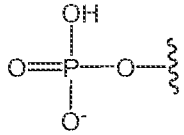
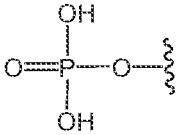
[0067] The term "–N–linked amino acid ester derivative" refers to an amino acid in which a main-chain carboxylic acid group has been converted to an ester group. In some embodiments, the ester group has a formula selected from alkyl-O-C(=O)-, cycloalkyl-O-C(=O)-, aryl-O-C(=O)- and aryl(alkyl)-O-C(=O)-. 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.

[0068] 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.

[0069] 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.

[0070] The term "interferon" is used herein as is commonly understood by one of ordinary skill in the art. Several types of interferons are known to those skilled in the art, such as Type I interferons, Type 2 interferons and Type 3 interferons. A non-limiting list of examples include: alpha-interferons, beta-interferons, delta-interferons, gamma interferons, lambda interferons, omega-interferons, tau-interferons, x-interferons, consensus interferons and asialo-interferons. Interferons can be pegylated. Examples of type 1 interferons include interferon alpha 1A, interferon alpha 1B, interferon alpha 2A, interferon alpha 2B, pegylated-interferon alpha 2a (PEGASYS, Roche), recombinant interferon alpha 2a (ROFERON, Roche), inhaled interferon alpha 2b (AERX, Aradigm), pegylated-interferon alpha 2b (ALBUFERON, Human Genome Sciences/Novartis, PEGINTRON, Schering), recombinant interferon alpha 2b (INTRON A, Schering), pegylated interferon alpha 2b (PEG-INTRON, Schering, VIRAFERONPEG, Schering), interferon beta-1a (REBIF, Serono, Inc. and Pfizer), consensus interferon alpha (INFERGEN, Valeant Pharmaceutical). Examples of type 2 interferons include interferon gamma 1, interferon gamma 2 and pegylated interferon gamma; and examples of type 3 interferons include interferon lambda 1, interferon lambda 2 and interferon lambda 3.

[0071] The terms "phosphorothioate" and "phosphothioate" refer to a compound of the general formula  its protonated forms (for example,  and ) and its tautomers (such as ).

[0072] 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,  and ). 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.

[0073] 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, both of which are hereby incorporated by reference 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-butyldimethylsilyl, tri-*iso*-propylsilyloxymethyl, [2-(trimethylsilyl)ethoxy]methyl or t-butyldiphenylsilyl); esters (e.g. benzoate ester); carbonates (e.g. methoxymethylcarbonate); 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).

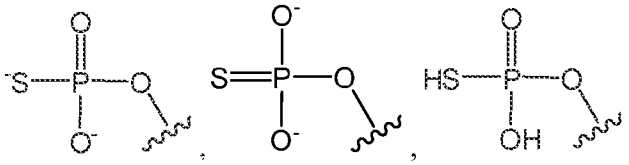
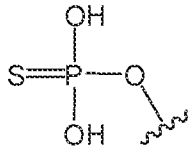
[0074] The term "pharmaceutically acceptable salt" refers to a salt of a compound that does not cause significant irritation to an organism to which it is administered and does not abrogate the biological activity and properties of the compound. In some embodiments, the salt is an acid addition salt 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-toluensulfonic, 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, C_1-C_7 alkylamine, cyclohexylamine, triethanolamine, ethylenediamine, and salts with amino acids such as arginine and lysine.

[0075] 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.

[0076] 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.

[0077] 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.

[0078] 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 phosphorothioate include the following: , . 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.

[0079] 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).

[0080] 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.

[0081] 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.

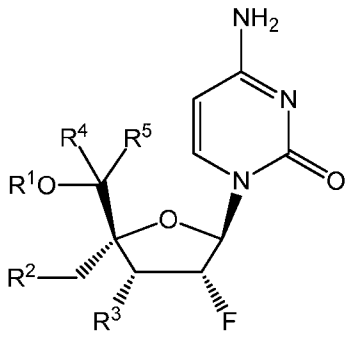
Solvates contain either stoichiometric or non-stoichiometric amounts of a solvent, and may be formed during the process of crystallization with pharmaceutically acceptable solvents such as water, ethanol, or the like. Hydrates are formed when the solvent is water, or alcoholates are formed when the solvent 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.

[0082] 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.

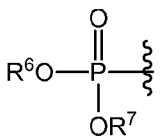
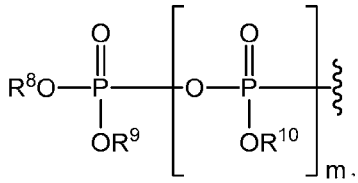
Compounds

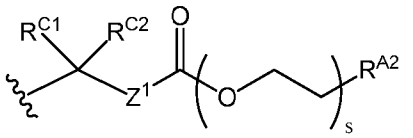
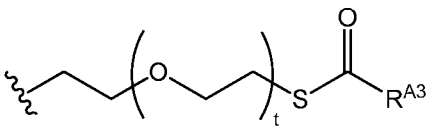
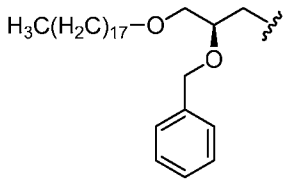
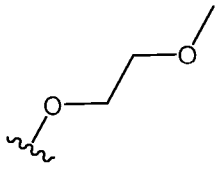
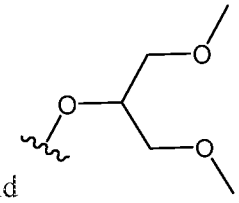
Compound (A)

[0083] Some embodiments described herein relate generally to the use of Compound (A), or a pharmaceutically acceptable salt thereof, wherein:



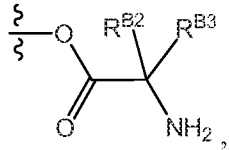
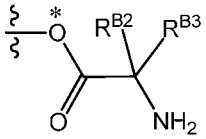
(A)

wherein: R^1 can be selected from H (hydrogen), an optionally substituted acyl, an optionally substituted O-linked amino acid,  and ; R^2 can be chloro (Cl) or azido (N_3); R^3 can be selected from OH, $-OC(=O)R^{A1}$ and an optionally substituted O-linked amino acid; R^4 and R^5 can be independently H (hydrogen) or D (deuterium); R^6 and R^7 can be independently absent, H (hydrogen),



and

; R^8, R^9 and each R^{10} can be independently absent or H (hydrogen); R^{A1} can be an optionally substituted C_{1-24} alkyl; R^{A2} can be independently selected from H (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^{A3} can be selected from H (hydrogen), an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{C1} and R^{C2} can be independently selected from H (hydrogen), an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; m can be 1 or 2; s can be 0, 1, 2 or 3; t can be 0 or 1; and Z^1 can be O (oxygen) or S (sulfur).

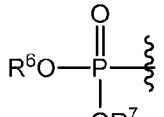
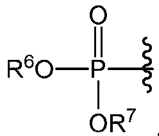
[0084] In some embodiments, R^1 can be H (hydrogen). When R^1 is H, Compound (A) can be a nucleoside. In other embodiments, R^1 can be an optionally substituted acyl. In other embodiments, R^1 can be –C(=O)R^{B1}, wherein R^{B1} can be selected from an optionally substituted C_{1-12} alkyl, an optionally substituted C_{2-12} alkenyl, an optionally substituted C_{2-12} alkynyl, an optionally substituted C_{3-8} cycloalkyl, an optionally substituted C_{5-8} 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^{B1} can be a substituted C_{1-12} alkyl. In other embodiments,

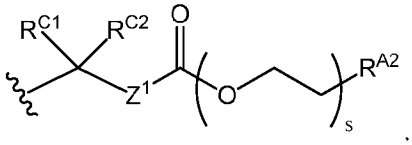
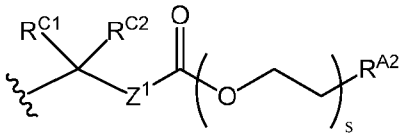
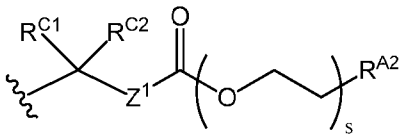
R^{B1} can be an unsubstituted C_{1-12} alkyl. In some embodiments, R^{B1} can be an unsubstituted C_{1-6} alkyl.

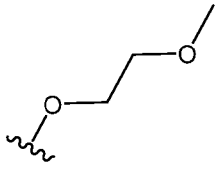
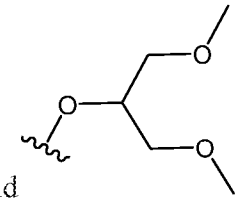
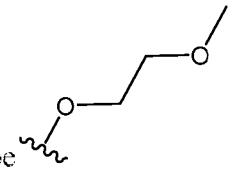
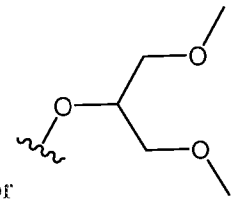
[0085] In still other embodiments, R^1 can be an optionally substituted O-linked amino acid. Examples of suitable O-linked amino acids include alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, 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^{B2} 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^{B3} can be hydrogen or an optionally substituted C_{1-4}-alkyl; or R^{B2} and R^{B3} can be taken together to form an optionally substituted C_{3-6} cycloalkyl. Those skilled in the art understand that when R^1 is an optionally substituted O-linked amino acid, the oxygen of R^1O- of Compound (A) is part of the optionally substituted O-linked amino acid. For example, when R^1 is , the oxygen indicated with "*" is the oxygen of R^1O- of Compound (A).

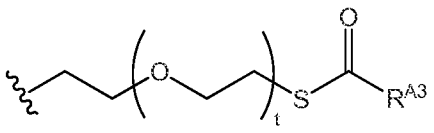
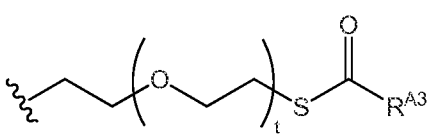
[0086] When R^{B2} is substituted, R^{B2} can be substituted with one or more substituents selected from N-amido, mercapto, alkylthio, an optionally substituted aryl, hydroxy, an optionally substituted heteroaryl, O-carboxy and amino. In some embodiments, R^{B2} can be an unsubstituted C_{1-6}-alkyl, such as those described herein. In some embodiments, R^{B2} can be hydrogen. In other embodiments, R^{B2} can be methyl. In some embodiments, R^{B3} can be hydrogen. In other embodiments, R^{B3} can be an optionally substituted C_{1-4}-alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In an embodiment, R^{B3} can be methyl. Depending on the groups that are selected for R^{B2} and R^{B3}, the carbon to which R^{B2} and R^{B3} are attached may be a chiral center. In some

embodiment, the carbon to which R^{B2} and R^{B3} are attached may be a (R)-chiral center. In other embodiments, the carbon to which R^{B2} and R^{B3} are attached may be a (S)-chiral center.

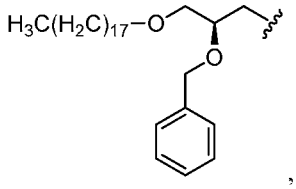
[0087] In yet still other embodiments, R^1 can be . When R^1 is , in some embodiments, at least one of R^6 and R^7 can be absent or H. In other embodiments, both R^6 and R^7 can be independently absent or H. Those skilled in the art understand that when both R^6 and R^7 can be independently absent or H, Compound (A) can be a monophosphate. Those skilled in the art also understand that when R^6 and/or R^7 are absent, then the oxygen(s) associated with R^6 and/or R^7 will have a negative charge. For example, when R^6 is absent, the oxygen associated with R^6 will have an associated negative charge.

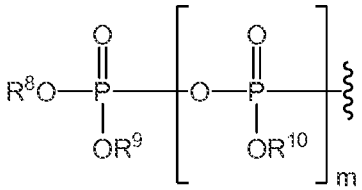
[0088] In some embodiments, at least one of R^6 and R^7 can be . In some embodiments, both R^6 and R^7 can be . When one or both of R^6 and R^7 are , R^{C1} and R^{C2} can be independently selected from hydrogen, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl; R^{A2} can 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 ; and Z^1 can be independently O (oxygen) or S (sulfur). In some embodiments, R^{C1} and R^{C2} can be hydrogen. In other embodiments, at least one of R^{C1} and R^{C2} can be an optionally substituted C_{1-24} alkyl or an optionally substituted aryl. In some embodiments, R^{A2} can be an optionally substituted C_{1-24} alkyl. In other embodiments, R^{A2} can be an optionally substituted aryl. In still other embodiments, R^{A2} can be an optionally substituted –O–C_{1-24} alkyl or an optionally substituted –O–aryl. In yet still other embodiments, R^{A2} can be an optionally substituted –O–heteroaryl or an optionally substituted –O–monocyclic heterocyclyl. In some embodiments, Z^1 can be O (oxygen). In other embodiments, Z^1 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, s can be 0, and R^{A2} can be  or . In some embodiments, one or both of R^6 and R^7 can be isopropyloxycarbonyloxymethyl (POC). In some embodiments, one or both of R^6 and R^7 can be pivaloyloxymethyl (POM). In some embodiments, R^6 and R^7 can be both an optionally substituted isopropyloxycarbonyloxymethyl group, and form an optionally substituted bis(isopropyloxycarbonyloxymethyl) (bis(POC)) prodrug. In some embodiments, R^6 and R^7 can be both an optionally substituted pivaloyloxymethyl group, and form an optionally substituted bis(pivaloyloxymethyl) (bis(POM)) prodrug.

[0089] In some embodiments, R^6 and R^7 can be both . In some embodiments, at least one of R^6 and R^7 can be . In some embodiments, R^{A3} can be hydrogen. In other

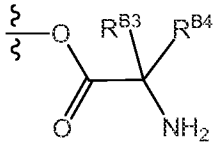
embodiments, R^{A3} can be an optionally substituted C_{1-24} alkyl. In still other embodiments, R^{A3} can be an optionally substituted aryl. In some embodiments, R^{A3} can be a C_{1-6} alkyl, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, pentyl (branched and straight-chained) and hexyl (branched and straight-chained). In some embodiments, t can be 0. In other embodiments, t can be 1. In some embodiments, one or both of R^6 and R^7 can be an optionally substituted S-acylthioethyl (SATE) and form an optionally substituted SATE ester prodrug.

[0090] In some embodiments, one of R^6 and R^7 can be , and the other of R^6 and R^7 can be absent or H.

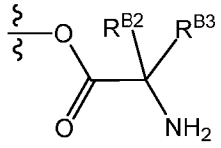
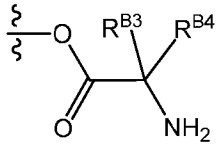
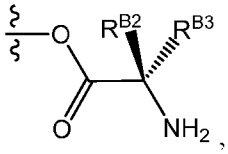
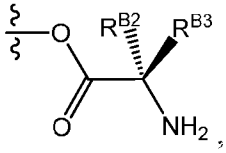
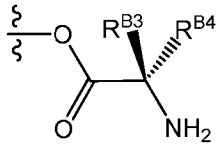
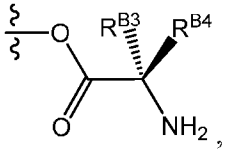
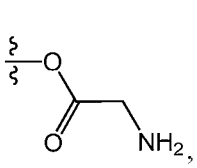
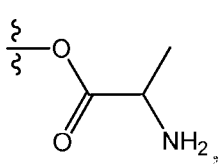
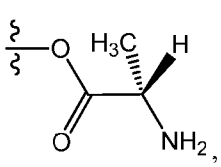
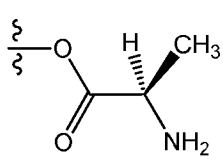
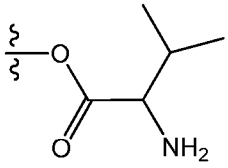
[0091] In some embodiments, R^1 can be , R^8, R^9 and each R^{10} can be independently absent or hydrogen; and m can be 1 or 2. In some embodiments, m can be 1, and R^8, R^9 and R^{10} can be independently absent or hydrogen. In other embodiments, m can be 2, and R^8, R^9 and each R^{10} can be independently absent or hydrogen. Those skilled in the art understand that when m is 1, R^1 can be diphosphate. Likewise, those skilled in the art understand that when m is 2, R^1 can be triphosphate. When R^8, R^9 and/or R^{10} are absent, those skilled in the art understand that the oxygen associated with R^8, R^9 and/or R^{10} will have an associated negative charge. For example, when R^8 is absent, the oxygen associated with R^8 will have a negative charge, which can be indicated as O^-.

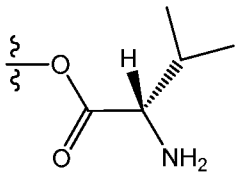
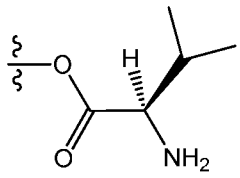
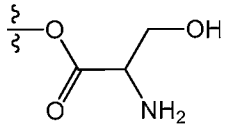
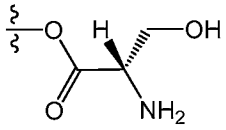
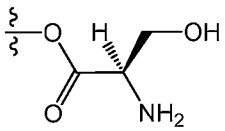
[0092] In some embodiments, R^2 can be chloro, such that the 2'-position is substituted with a chloromethyl group. In other embodiments, R^2 can be azido, such that the 2'-position is substituted with an azidomethyl group.

[0093] The groups attached to the 3'-position of the ring can vary. In some embodiments, R^3 can be OH. In other embodiments, R^3 can be $-OC(=O)R^{A1}$. In some embodiments, R^{A1} can be an optionally substituted C_{1-6} alkyl. In still other embodiments, R^3

can be an optionally substituted O-linked amino acid, such as a O-linked alpha-amino acid. When R^3 is an optionally substituted O-linked amino acid, R^3 can have the structure , wherein R^{B3} 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^{B4} can be hydrogen or an optionally substituted C_{1-4}-alkyl; or R^{B3} and R^{B4} can be taken together to form an optionally substituted C_{3-6} cycloalkyl.

[0094] When R^{B3} is substituted, R^{B3} 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^{B3} can be an unsubstituted C_{1-6}-alkyl, such as those described herein. In some embodiments, R^{B3} can be hydrogen. In other embodiments, R^{B3} can be methyl. In some embodiments, R^{B4} can be hydrogen. In other embodiments, R^{B4} can be an optionally substituted C_{1-4}-alkyl, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. In an embodiment, R^{B4} can be methyl. Depending on the groups that are selected for R^{B3} and R^{B4}, the carbon to which R^{B3} and R^{B4} are attached may be a chiral center. In some embodiment, the carbon to which R^{B3} and R^{B4} are attached may be a (R)-chiral center. In other embodiments, the carbon to which R^{B3} and R^{B4} are attached may be a (S)-chiral center.

[0095] Examples of suitable  and  include the following: , , , , , , , , .





and


[0096] In some embodiments, R^4 and R^5 can be both hydrogen (H). In other embodiments, R^4 and R^5 can be both deuterium (D). In still other embodiments, one of R^4 and R^5 can be hydrogen, and the other of R^4 and R^5 can be deuterium.

[0097] As described herein, at any position of Compound (A) that has a hydrogen, the hydrogen can be an isotope of hydrogen, such as hydrogen-2 (deuterium). In some embodiments, Compound (A) can be Compound (A1). Some embodiments of Compound (A1) are provided in Table A.

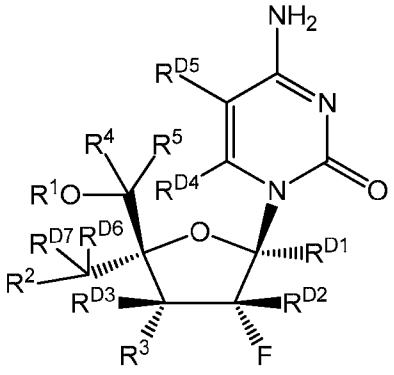

(A1)

Table A

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	DD	D	D	D	D	D	DD
Cl	DD	D	D	D	D	D	HD
Cl	DD	D	D	D	H	D	DD
Cl	DD	D	D	D	D	H	DD
Cl	DD	D	D	D	D	D	HH
Cl	DD	D	D	D	H	D	HD
Cl	DD	D	D	D	D	H	HD
Cl	DD	D	D	D	H	H	DD
Cl	DD	D	D	D	H	D	HH
Cl	DD	D	D	D	D	H	HH

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	DD	D	D	D	H	H	HD
Cl	DD	D	D	D	H	H	HH
Cl	HD	D	D	D	D	D	DD
Cl	HD	D	D	D	D	D	HD
Cl	HD	D	D	D	H	D	DD
Cl	HD	D	D	D	D	H	DD
Cl	HD	D	D	D	D	D	HH
Cl	HD	D	D	D	H	D	HD
Cl	HD	D	D	D	D	H	HD
Cl	HD	D	D	D	H	H	DD
Cl	HD	D	D	D	H	D	HH
Cl	HD	D	D	D	D	H	HH

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	HD	D	D	D	H	H	HD
Cl	HD	D	D	D	H	H	HH
Cl	HH	D	D	D	D	D	DD
Cl	HH	D	D	D	D	D	HD
Cl	HH	D	D	D	H	D	DD
Cl	HH	D	D	D	D	H	DD
Cl	HH	D	D	D	D	D	HH
Cl	HH	D	D	D	H	D	HD
Cl	HH	D	D	D	D	H	HD
Cl	HH	D	D	D	H	H	DD
Cl	HH	D	D	D	H	D	HH
Cl	HH	D	D	D	D	H	HH
Cl	HH	D	D	D	H	H	HD
Cl	HH	D	D	D	H	H	HH
Cl	DD	H	D	D	D	D	DD
Cl	DD	H	D	D	D	D	HD
Cl	DD	H	D	D	H	D	DD
Cl	DD	H	D	D	D	H	DD
Cl	DD	H	D	D	D	D	HH
Cl	DD	H	D	D	H	D	HD
Cl	DD	H	D	D	D	H	HD
Cl	DD	H	D	D	H	H	DD
Cl	DD	H	D	D	H	D	HH
Cl	DD	H	D	D	D	H	HH
Cl	DD	H	D	D	H	H	HD
Cl	DD	H	D	D	H	H	HH
Cl	HD	H	D	D	D	D	DD
Cl	HD	H	D	D	D	D	HD
Cl	HD	H	D	D	H	D	DD
Cl	HD	H	D	D	D	H	DD
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Cl	HD	H	D	D	H	H	DD
Cl	HD	H	D	D	H	D	HH
Cl	HD	H	D	D	D	H	HH
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Cl	HD	H	D	D	H	H	HH
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Cl	HH	H	D	D	D	D	HD
Cl	HH	H	D	D	H	D	DD
Cl	HH	H	D	D	D	H	DD
Cl	HH	H	D	D	D	D	HH
Cl	HH	H	D	D	H	D	HD
Cl	HH	H	D	D	D	H	HD
Cl	HH	H	D	D	H	H	DD
Cl	HH	H	D	D	H	D	HH

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	HH	H	D	D	D	H	HH
Cl	HH	H	D	D	H	H	HD
Cl	HH	H	D	D	H	H	HH
Cl	DD	D	H	D	D	D	DD
Cl	DD	D	H	D	D	D	HD
Cl	DD	D	H	D	H	D	DD
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Cl	DD	D	H	D	D	D	HH
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Cl	DD	D	H	D	H	H	HH
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Cl	DD	D	D	H	D	D	DD
Cl	DD	D	D	H	D	D	HD
Cl	DD	D	D	H	H	D	DD
Cl	DD	D	D	H	D	H	HD
Cl	DD	D	D	H	H	H	DD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	DD	D	D	H	H	D	HH
Cl	DD	D	D	H	D	H	HH
Cl	DD	D	D	H	H	H	HD
Cl	DD	D	D	H	H	H	HH
Cl	HD	D	D	H	D	D	DD
Cl	HD	D	D	H	D	D	HD
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Cl	HD	H	H	D	D	H	DD
Cl	HD	H	H	D	D	D	HH
Cl	HD	H	H	D	H	D	HD
Cl	HD	H	H	D	D	H	HD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	HD	H	H	D	H	H	DD
Cl	HD	H	H	D	H	D	HH
Cl	HD	H	H	D	D	H	HH
Cl	HD	H	H	D	H	H	HD
Cl	HD	H	H	D	H	H	HH
Cl	HH	H	H	D	D	D	DD
Cl	HH	H	H	D	D	D	HD
Cl	HH	H	H	D	H	D	DD
Cl	HH	H	H	D	D	H	DD
Cl	HH	H	H	D	D	D	HH
Cl	HH	H	H	D	H	D	HD
Cl	HH	H	H	D	D	H	HD
Cl	HH	H	H	D	H	H	DD
Cl	HH	H	H	D	H	D	HH
Cl	HH	H	H	D	D	H	HH
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Cl	HH	D	H	H	D	D	DD
Cl	HH	D	H	H	D	D	HD
Cl	HH	D	H	H	H	D	DD
Cl	HH	D	H	H	D	H	DD
Cl	HH	D	H	H	D	D	HH
Cl	HH	D	H	H	H	D	HD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	HH	D	H	H	D	H	HD
Cl	HH	D	H	H	H	H	DD
Cl	HH	D	H	H	H	D	HH
Cl	HH	D	H	H	D	H	HH
Cl	HH	D	H	H	H	H	HD
Cl	HH	D	H	H	H	H	HH
Cl	DD	H	D	H	D	D	DD
Cl	DD	H	D	H	D	D	HD
Cl	DD	H	D	H	H	D	DD
Cl	DD	H	D	H	D	H	DD
Cl	DD	H	D	H	D	D	HH
Cl	DD	H	D	H	H	D	HD
Cl	DD	H	D	H	D	H	HD
Cl	DD	H	D	H	H	H	DD
Cl	DD	H	D	H	H	D	HH
Cl	DD	H	D	H	D	H	HH
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Cl	DD	H	D	H	H	H	HH
Cl	HD	H	D	H	D	D	DD
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Cl	HD	H	D	H	D	H	DD
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Cl	HH	H	D	H	H	D	HH
Cl	HH	H	D	H	D	H	HH
Cl	HH	H	D	H	H	H	HD
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Cl	DD	H	H	H	D	D	DD
Cl	DD	H	H	H	D	D	HD
Cl	DD	H	H	H	H	D	DD
Cl	DD	H	H	H	D	H	DD
Cl	DD	H	H	H	D	D	HH

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
Cl	DD	H	H	H	H	D	HD
Cl	DD	H	H	H	D	H	HD
Cl	DD	H	H	H	H	H	DD
Cl	DD	H	H	H	H	D	HH
Cl	DD	H	H	H	D	H	HH
Cl	DD	H	H	H	H	H	HD
Cl	DD	H	H	H	H	H	HH
Cl	HD	H	H	H	D	D	DD
Cl	HD	H	H	H	D	D	HD
Cl	HD	H	H	H	H	D	DD
Cl	HD	H	H	H	D	H	DD
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Cl	HD	H	H	H	D	H	HD
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N_3	HD	D	D	D	D	D	DD
N_3	HD	D	D	D	D	D	HD
N_3	HD	D	D	D	H	D	DD
N_3	HD	D	D	D	D	H	DD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
N_3	HD	D	D	D	D	D	HH
N_3	HD	D	D	D	H	D	HD
N_3	HD	D	D	D	D	H	HD
N_3	HD	D	D	D	H	H	DD
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N_3	HD	H	D	D	H	H	HH
N_3	HH	H	D	D	D	D	DD
N_3	HH	H	D	D	D	D	HD
N_3	HH	H	D	D	H	D	DD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
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N_3	HH	H	D	D	D	D	HH
N_3	HH	H	D	D	H	D	HD
N_3	HH	H	D	D	D	H	HD
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N_3	HH	D	H	D	H	H	HD
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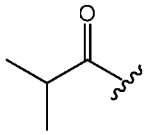
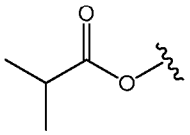
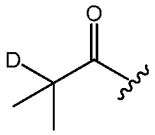
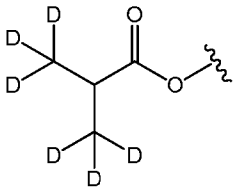
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N_3	DD	D	D	H	D	H	DD
N_3	DD	D	D	H	D	D	HH
N_3	DD	D	D	H	H	D	HD
N_3	DD	D	D	H	D	H	HD
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N_3	DD	D	D	H	D	H	HH
N_3	DD	D	D	H	H	H	HD
N_3	DD	D	D	H	H	H	HH
N_3	HD	D	D	H	D	D	DD
N_3	HD	D	D	H	D	D	HD
N_3	HD	D	D	H	H	D	DD
N_3	HD	D	D	H	D	H	DD
N_3	HD	D	D	H	D	D	HH
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N_3	DD	H	H	D	H	H	HD
N_3	DD	H	H	D	H	H	HH
N_3	HD	H	H	D	D	D	DD

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
N_3	HD	H	H	D	D	D	HD
N_3	HD	H	H	D	H	D	DD
N_3	HD	H	H	D	D	H	DD
N_3	HD	H	H	D	D	D	HH
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N_3	HD	D	H	H	D	H	HH
N_3	HD	D	H	H	H	H	HD
N_3	HD	D	H	H	H	H	HH

R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
N_3	HH	D	H	H	D	D	DD
N_3	HH	D	H	H	D	D	HD
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N_3	HH	D	H	H	D	H	DD
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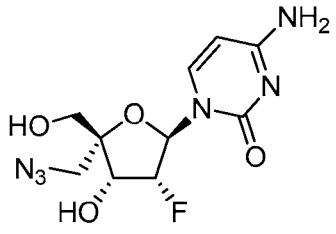
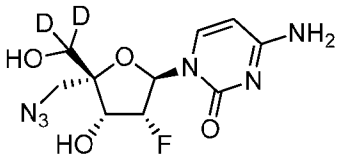
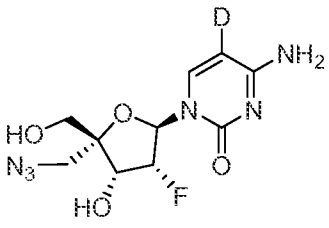
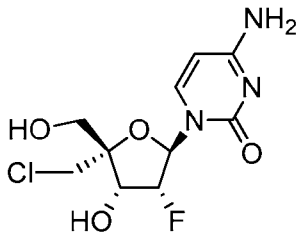
R^2	R^4 R^5	R^{D1}	R^{D2}	R^{D3}	R^{D4}	R^{D5}	R^{D6} R^{D7}
N_3	HH	H	D	H	H	H	DD
N_3	HH	H	D	H	H	D	HH
N_3	HH	H	D	H	D	H	HH
N_3	HH	H	D	H	H	H	HD
N_3	HH	H	D	H	H	H	HH
N_3	DD	H	H	H	D	D	DD
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N_3	HH	H	H	H	H	D	HH
N_3	HH	H	H	H	D	H	HH
N_3	HH	H	H	H	H	H	HD
N_3	HH	H	H	H	H	H	HH

[0098] In some embodiments of Table A, R^1 can be hydrogen. In some embodiments of Table A, R^1 can be deuterium. In still other embodiments of Table A, R^1

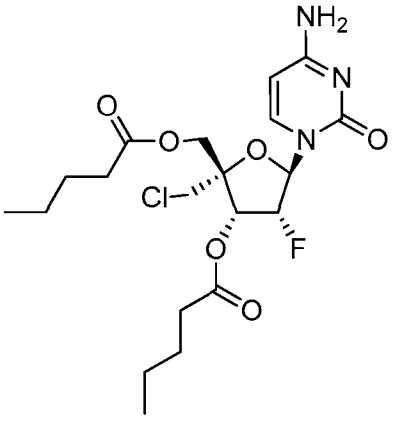
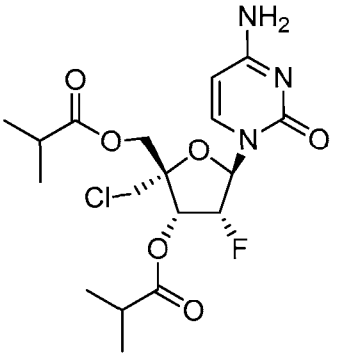
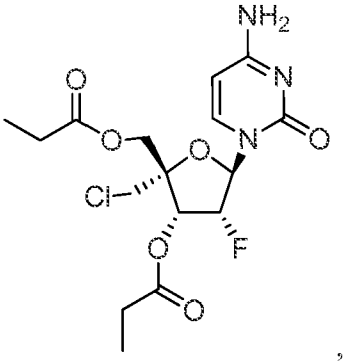
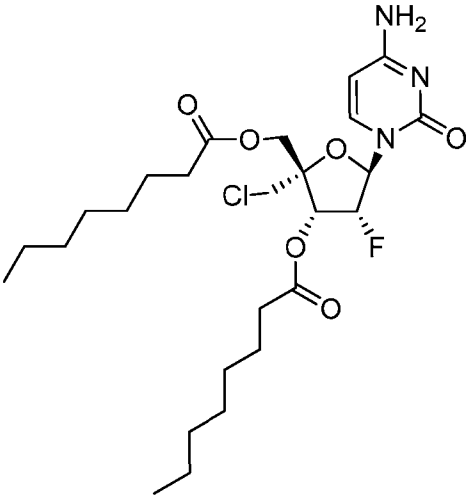
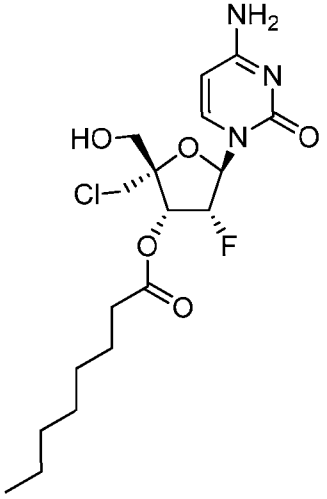
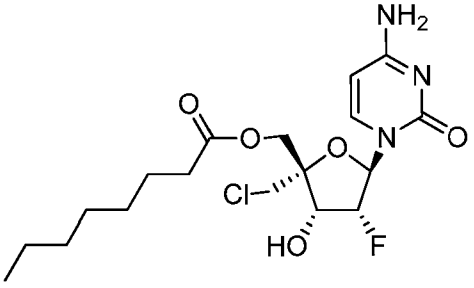
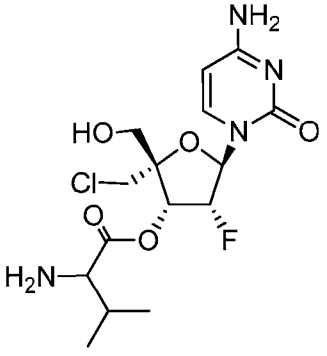
can be an optionally substituted acyl, for example, R^1 can be $-C(=O)C_{1-6}$ alkyl. In some embodiments of Table A, R^3 can be OH. In other embodiments of Table A, R^3 can be $-OC(=O)R^{A1}$. In some embodiments of Table A, R^1 can be hydrogen and R^3 can be OH. In other embodiments of Table A, R^1 can be an optionally substituted acyl and R^3 can be $-OC(=O)R^{A1}$. In some embodiments of Table A, R^1 can be $-C(=O)C_{1-6}$ alkyl and R^3 can be $-OC(=O)C_{1-6}$ alkyl. In some embodiments of Table A, R^1 can be  and R^3 can be . In some embodiments, R^1 and/or R^3 can include one or more deuterium atoms. For example, R^1 can be deuterium or R^1 can be , and/or R^3 can be  or R^3 can be OD.

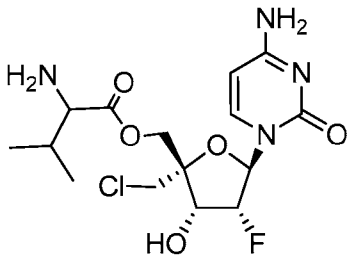
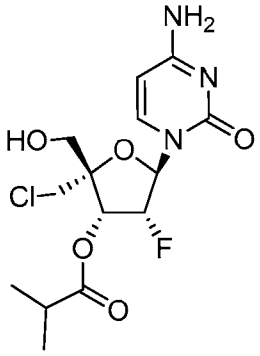
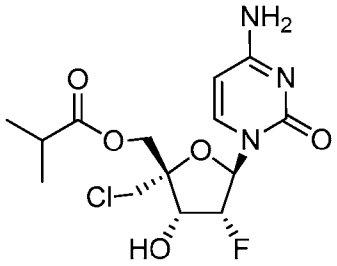
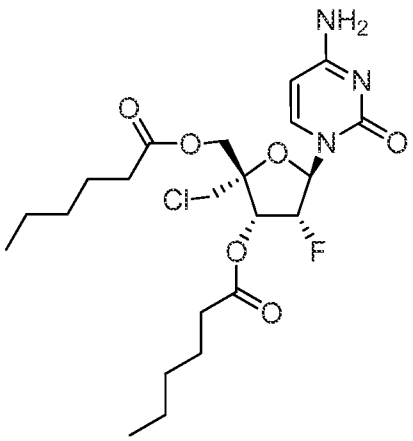
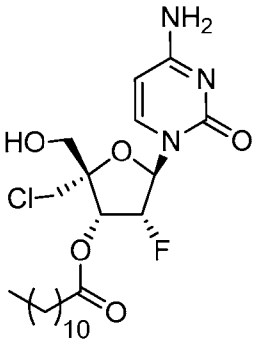
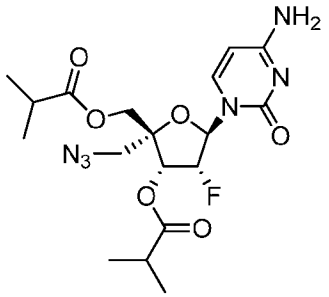
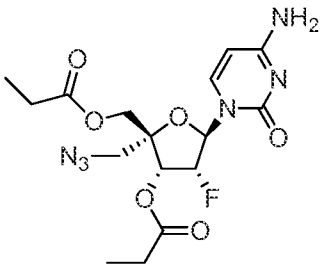
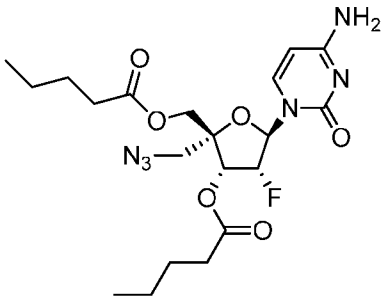
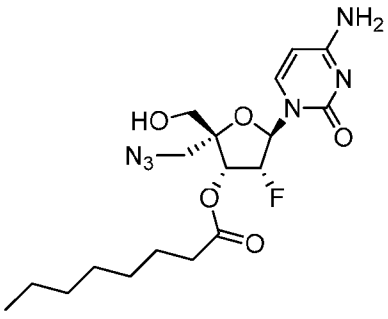
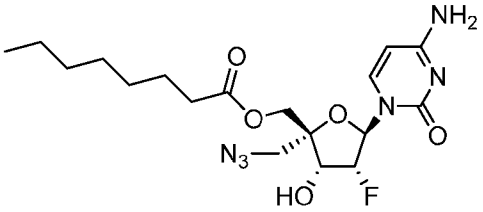
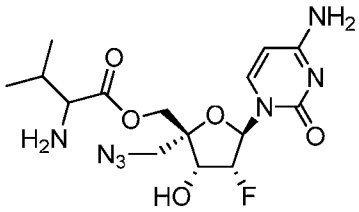
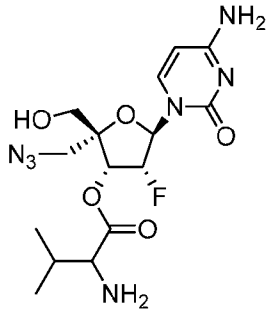
[0099] Compound (A), or a pharmaceutically acceptable salt thereof, can act as a chain-terminator and inhibit replication of a virus, such as a paramyxovirus.

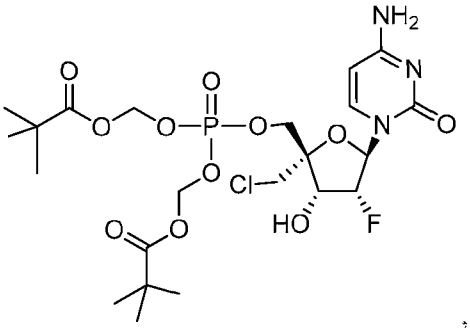
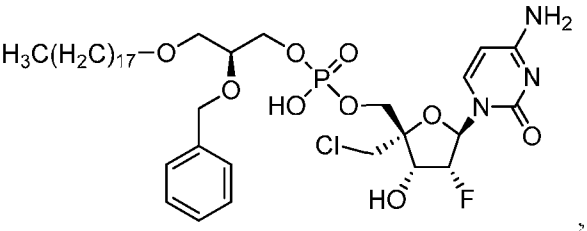
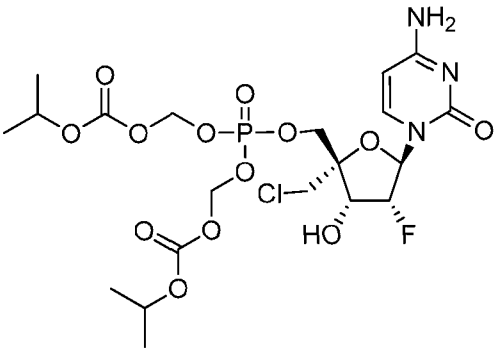
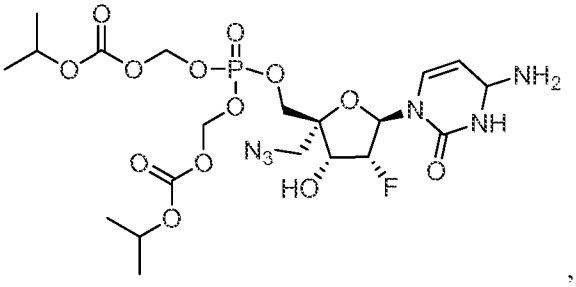
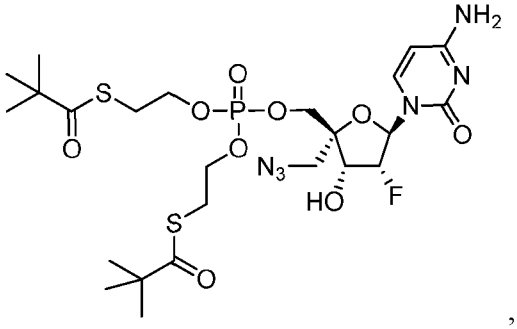
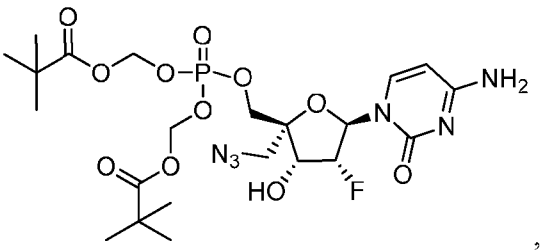
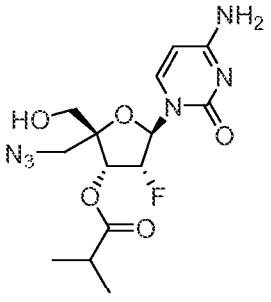
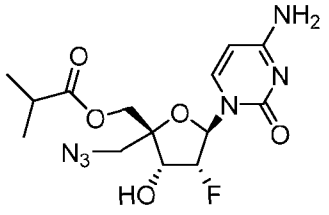
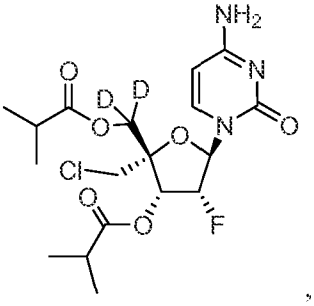
[0100] Examples of Compound (A), or a pharmaceutically acceptable salt thereof, include the following:

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

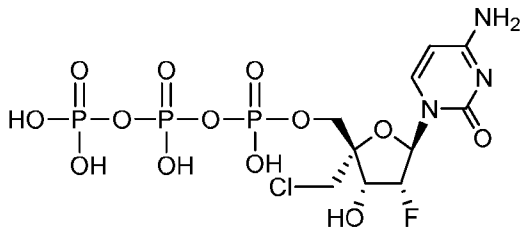
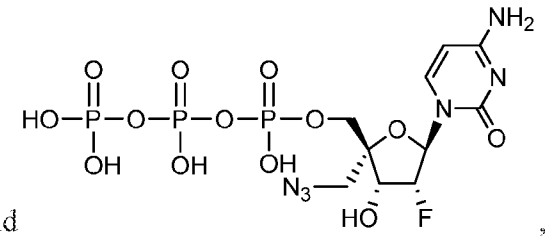
[0101] Further examples of Compound (A), or a pharmaceutically acceptable salt thereof, include:


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and

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

[0102] Additional examples of Compound (A), or a pharmaceutically acceptable salt thereof, include the following:

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

Compound (B)

[0103] A variety of compounds can be compound (B), or a pharmaceutically acceptable salt thereof. In some embodiments, compound (B), or a pharmaceutically acceptable salt thereof, can be selected from an anti-RSV antibody, a fusion protein inhibitor, an N-protein inhibitor, a RSV polymerase inhibitor, an IMPDH inhibitor, an interferon and an other compound that inhibits the RSV virus, or a pharmaceutically acceptable salt of any of the foregoing.

[0104] In some embodiments, compound (B), or a pharmaceutically acceptable salt thereof, can be an anti-RSV agent. In some embodiments, compound (B) can be an anti-RSV antibody, or a pharmaceutically acceptable salt thereof. Examples of anti-RSV antibodies include, but are not limited to, RSV-IGIV (RespiGam®), palivizumab (Synagis®, a chimeric humanized IgG monoclonal antibody) and motavizumab (MEDI-524, humanized monoclonal antibody), and pharmaceutically acceptable salts of the foregoing.

[0105] In some embodiments, compound (B) can be a fusion protein inhibitor, or a pharmaceutically acceptable salt thereof. A non-limiting list of fusion protein inhibitors include the following: 1-cyclopropyl-3-[[1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]imidazo[4,5-c]pyridin-2-one (BMS-433771), 4,4"-bis-{4,6-bis-[3-(bis-carbamoylmethyl-sulfamoyl)-phenylamino]-(1,3,5)triazin-2-ylamino}-biphenyl-2,2"-disulfonic-acid (RFI-641), 4,4'-Bis[4,6-di[3-aminophenyl-N,N-bis(2-carbamoylethyl)-sulfonilimino]-1,3,5-triazine-2-ylamino]-biphenyl-2,2'-disulfonic acid, disodium salt (CL387626), 2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-4-methyl-1H-benzimidazol-1-yl]-6-methyl-3-pyridinol (JNJ-2408068), 2-[[6-[[[2-(3-Hydroxypropyl)-5-methylphenyl]amino]methyl]-2-[[3-(morpholin-4-yl)propyl]amino]benzimidazol-1-yl]methyl]-6-methylpyridin-3-ol (TMC-353121), 5,5'-bis[1-(((5-amino-1H-

tetrazolyl)imino)methyl)]2,2′,4″-methylidynetrisphenol (VP-14637, MDT-637), N-(2-hydroxyethyl)-4-methoxy-N-methyl-3-(6-methyl-[1,2,4]triazolo[3,4-a]phthalazin-3-yl)benzenesulfonamide (P13), 2-((2-((1-(2-aminoethyl)piperidin-4-yl)amino)-4-methyl-1H-benzo[d]imidazol-1-yl)methyl)-6-methylpyridin-3-ol (R170591), 1,4-bis(3-methylpyridin-4-yl)-1,4-diazepane (C15), (R)-9b-(4-chlorophenyl)-1-(4-fluorobenzoyl)-2,3-dihydro-1H-imidazo[1',2':1,2]pyrrolo[3,4-c]pyridin-5(9bH)-one (BTA9981), [2,2-bis(docosyloxy-oxymethyl)propyl-5-acetaoamido-3,5-dideoxy-4,7,8,9-tetra-O-(sodium-oxysulfonyl)-D-glycero-D-galacto-2-nonulopyranosid]onate (MBX-300), BTA-C286, N-(2-((S)-2-(5-((S)-3-aminopyrrolidin-1-yl)-6-methylpyrazolo[1,5-a]pyrimidin-2-yl)piperidine-1-carbonyl)-4-chlorophenyl)methanesulfonamide (GS-5806), an anti-RSV nanobody (e.g., ALX-0171 (a trivalent nanobody, for example, those described in U.S. Publication No. 2012/0128669, filed June 7, 2010, which is hereby incorporated by reference for the limited purpose of its description of nanobodies), Ablynx) and a peptide fusion inhibitor (such as a peptide having the sequence DEFDASISQVNEKINQSLAFIRKSDELL (T-67, SEQ ID NO: 1, U.S. Patent No. 6,623,741, filed Feb. 29, 2000), and a peptide having the sequence FDASISQVNEKINQSLAFIRKSDELLHNVNAGKST (T-118, SEQ ID NO: 2, U.S. Patent No. 6,623,741, filed Feb. 29, 2000), and pharmaceutically acceptable salts of the foregoing. U.S. Patent No. 6,623,741 is hereby incorporated by reference for the limited purpose of its description of peptide fusion inhibitors.

[0106] In some embodiments, compound (B) can be an N-protein inhibitor, or a pharmaceutically acceptable salt thereof. An exemplary N-protein inhibitor is (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea (RSV-604), STP-92 (siRNA delivered through nanoparticle based delivery systems, Sirnaomics) and iKT-041 (Inhibikase), and a pharmaceutically acceptable salt thereof.

[0107] In some embodiments, compound (B) can be a RSV polymerase inhibitor, or a pharmaceutically acceptable salt thereof. Examples of RSV polymerase inhibitors include, but are not limited to, 6-{4-[(biphenyl-2-ylcarbonyl) amino]benzoyl}-N-cyclopropyl-5,6-dihydro-4H-thieno[3,2-d][1]benzazepine-2-carboxamide (YM-53403), N-cyclopropyl-5-(4-(2-(pyrrolidin-1-yl)benzamido)benzoyl)-5,6,7,10-tetrahydrobenzo[b]cyclopenta[d]azepine-9-carboxamide, 6-(4-(2-(2-oxa-7-azaspiro[3.5]nonan-7-yl)nicotinamido)benzoyl)-N-cyclopropyl-5,6-dihydro-4H-

benzo[b]thieno[2,3-d]azepine-2-carboxamide, 4-amino-8-(3-{[2-(3,4-dimethoxyphenyl)ethyl]amino}propyl)-6,6-dimethyl-2-(4-methyl-3-nitrophenyl)-1H-imidazo[4,5-h]-isoquinoline-7,9(6H,8H)-dione (CAS Reg. No. 851658-10-1) and 6-(4-(2-(2-oxa-7-azaspiro[3.5]nonan-7-yl)nicotinamido)benzoyl)-N-cyclopropyl-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide (AZ27), and pharmaceutically acceptable salts of the foregoing.

[0108] In some embodiments, compound (B) can be an IMPDH inhibitor, or a pharmaceutically acceptable salt thereof. A non-limiting list of IMPDH inhibitors include: ribavirin, 5-ethynyl-1-beta-D-ribofuranosylimidazole-4-carboxamide (EICAR), 4-hydroxy-3-beta-D-ribofuranosylpyrazole-5-carboxamide (pyrazofurin), 1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1H-1,2,4-triazole-3-carboximidamide (Taribavirin, viramidine), 1,3,4-thiadiazol-2-ylcyanamide (LY253963), tetrahydrofuran-3-yl-3-(3-(3-methoxy-4-(oxazol-5-yl)phenyl)ureido)benzylcarbamate (VX-497), (4E)-6-(4-Hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydro-2-benzofuran-5-yl)-4-methylhex-4-enoic acid (Mycophenolic acid) and 2-morpholin-4-ylethyl-(E)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1H-2-benzofuran-5-yl)-4-methylhex-4-enoate (Mycophenolate Mofetil), or a pharmaceutically acceptable salt of any of the foregoing.

[0109] In some embodiments, compound (B) can be an interferon, or a pharmaceutically acceptable salt thereof. Examples of interferons are described herein. In some embodiments, the interferon can be a pegylated interferon. In some embodiments, the interferon can be a Type 1 interferon, for example, an alpha-interferon (IFN-α). Exemplary alpha-interferons include Pegylated interferon-alpha-2a (PEGASYS®), Pegylated interferon-alpha-2b (PEG-INTRON®) and interferon alfacon-1 (INFERGEN®). In other embodiments, the Type 1 interferon can be a beta-interferon (IFN-β). In some embodiments, the interferon can be a Type 2 interferon. In other embodiments, the interferon can be Type 3 interferon, such as a lambda-interferon (IFN-λ) and pegylated interferon lambda.

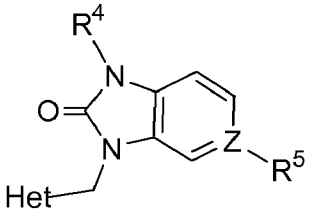
[0110] In some embodiments, compound (B) can be an other compound that inhibits the RSV virus, or a pharmaceutically acceptable salt thereof. Examples of other compounds that inhibits the RSV virus include, but are not limited to, a double stranded RNA oligonucleotide, 5-methyl-N-[4-(trifluoromethyl) phenyl]-isoxazole-4-carboxamide (leflumomide), N-(2-chloro-4-methylphenyl)-2-((1-(4-methoxyphenyl)-1H-

benzo[d]imidazol-2-yl)thio)propanamide (JMN3-003), Medi-559, Medi-534, Medi-557, an intratracheal formulation of recombinant human CC10 (CG-100), high titer, human immunoglobulin (RI-001, ADMA Biologics Inc.) and a non-neutralizing mAb against the G protein (mAb 131-2G), or a pharmaceutically acceptable salt of any of the foregoing. A non-limiting list of double stranded RNA oligonucleotides are ALN-RSV01 (an siRNA agent with the sense strand sequence (5' to 3') GGCUCUUAGCAAAGUCAAGdTdT (SEQ ID NO. 3) and the antisense strand sequence (5' to 3') CUUGACUUUGCUAAGAGCCdTdT (SEQ ID NO. 4) and ALN-RSV02. Additional information regarding ALN-RSV01 and/or ALN-RSV02 can be found in U.S. Publication No. 2009/0238772, filed Dec. 15, 2008 (Alnylam Pharmaceuticals).

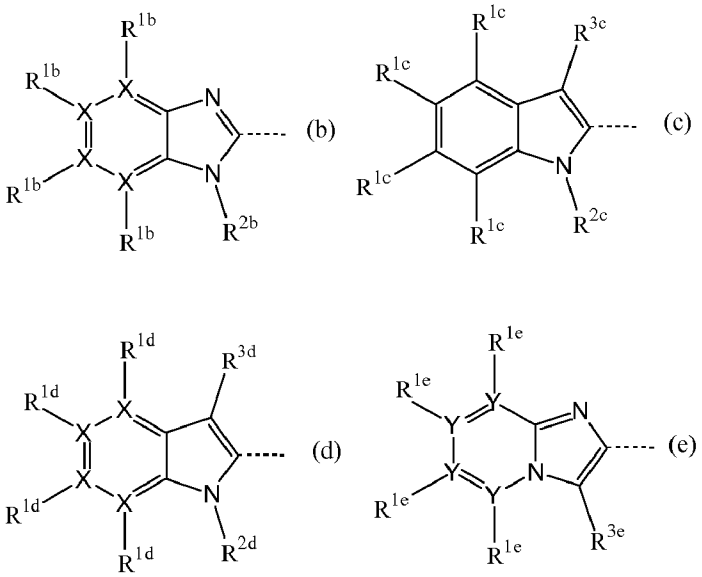
[0111] Additional compounds for Compound (B) include compounds that can be encompassed by the following formulae/compounds. For each of the following formulae/compounds, each variable pertains only to each individual section. For example for Compounds of Formula (B1), the variables listed under Compounds of Formula (B1) refer only to Compounds of Formula (B1) and not Compounds of Formula (B2) or any of the other formulae/compounds provided in this section, unless stated otherwise.

Compounds of Formula (B1)

[0112] Compounds of the general Formula (B1) are described in PCT Publication No. WO 2013/186333, published December 19, 2013, which is hereby incorporated by reference in its entirety. Formula (B1) has the structure:



or a stereoisomeric form thereof, wherein: Het can be a heterocycle having formula (b), (c), (d) or (e):

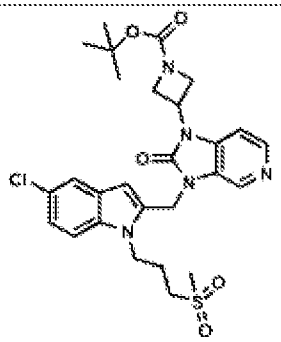
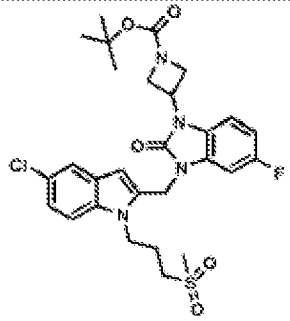
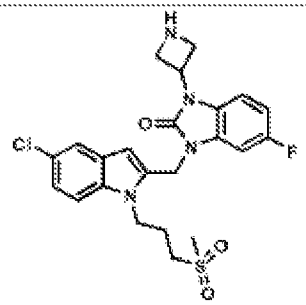
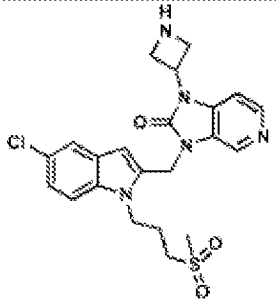


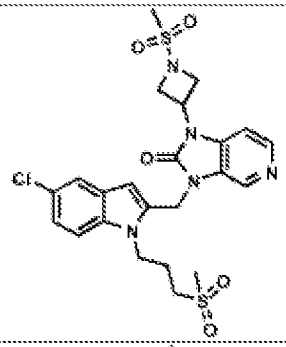
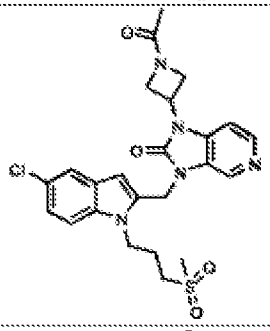
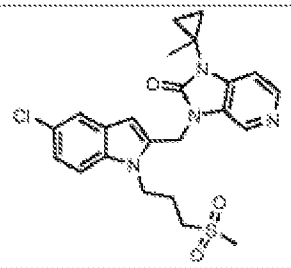
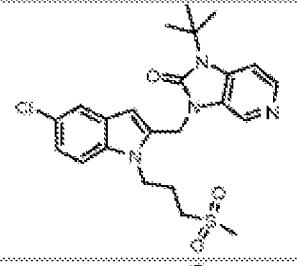
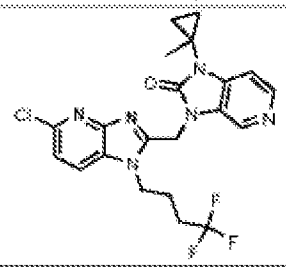
each X independently can be C or N; provided that at least one X is N; R^{1b} can be present when Het has formula (b) and X is C; each R^{1b} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1b} is absent when the X to which it is bound is N; R^{2b} can be $-(CR^8R^9)_m\text{-}R^{10b}$; each R^6 can be independently selected from H, C_1-C_6 alkyl, $COOCH_3$ and $CONHSO_2CH_3$; each R^7 can be independently selected from OH, C_1-C_6 alkyloxy, NH_2, $NHSO_2N(C_1\text{-}C_6$ alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1\text{-}C_6$ alkyl), $NHSO_2(C_3\text{-}C_7$ cycloalkyl) and $N(C_1\text{-}C_6$ alkyl$)_2$; each R^8 and R^9 can be independently chosen from H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^8 and R^9 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains one or more heteroatoms selected from N, S and O; R^{10b} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, O-Benzyl, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$, and a 4 to 6 membered saturated ring containing one oxygen atom; m can be an integer from 2 to 6; R^{11} can be selected from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; R^{12} can be selected from phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{12} can be C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents

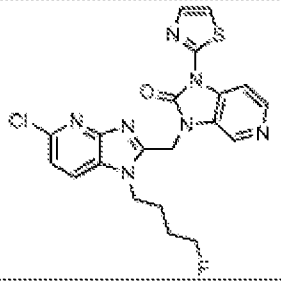
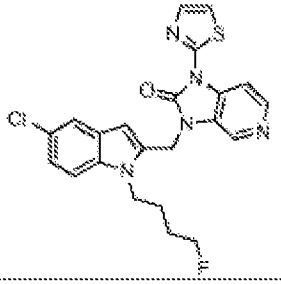
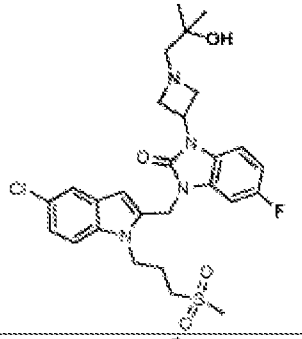
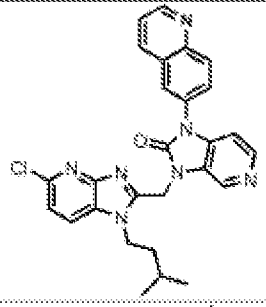
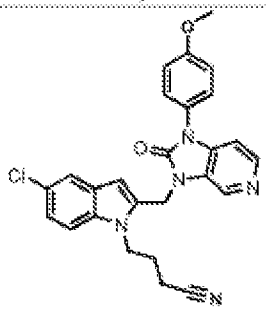
each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; R^{1c} can be present when Het has formula (c); each R^{1c} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^{7c})$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{3c} can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy and $CO(R^{7c})$; R^{2c} can be $-(CR^8R^9)_m\text{-}R^{10c}$; R^{7c} can be selected from OH, $O(C_1$-C_6 alkyl$)$, NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl$)$, $NHSO_2(C_3$-C_7 cycloalkyl$)$, $N(C_1$-C_6 alkyl$)_2$, NR^8R^9 and NR^9R^{10c}; R^{10c} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; R^{1d} can be present when Het has formula (d) and X is C; each R^{1d} is selected independently from H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1d} is absent when the X to which it is bound is N; R^{3d} can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, and $CO(R^7)$; R^{2d} can be $-(CR^8R^9)_m\text{-}R^{10d}$; R^{10d} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR_9, $OCOR^8$,$NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; each Y independently can be C or N; R^{1e} can be present when Het has formula (e) and Y is C; each R^{1e} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1e} is absent when the Y to which it is bound is N; R^{3e} can be selected from H, halogen, $-(CR^8R^9)_m\text{-}R^{10e}$, $C\equiv C\text{-}CH_2\text{-}R^{10e}$, $C\equiv C\text{-}R^{10e}$ and $C=C\text{-}R^{10e}$; R^{10e} can be selected from H, R^{11}, C_1-C_6 alkyloxy, OH, CN, F, CF_2H,CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; R^4 can be selected from tert-butyl, Het^1, aryl, Het^2, $CH(CH_3)(CF_3)$, and C_3-C_7 cycloalkyl substituted with one or more substituents selected from halo and C_1-C_4 alkyl; aryl can represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from halo C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, CF_30, $CONR^8R^9$, $COOR^8$,$CON(R^8)SO_2R^9$,

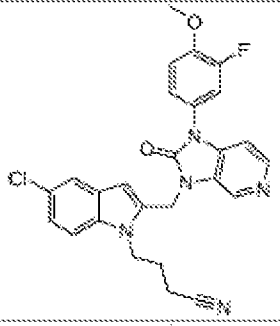
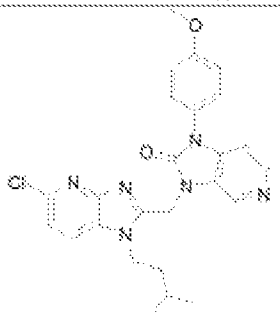
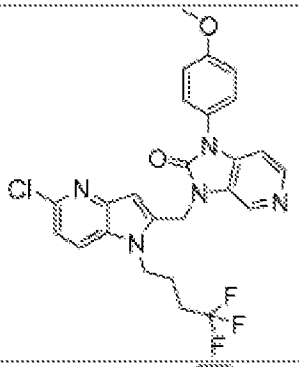
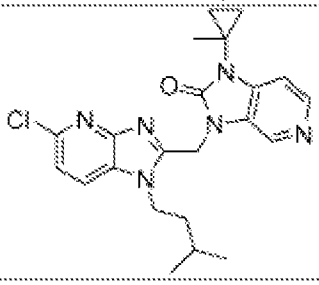
$CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$,$SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$; or C_1-C_4 alkyloxyC_1-C_4 alkyloxy; Het^1 can represents a 4 to 6 membered saturated ring containing one N atom, optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, SO_2R^8 , C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), (C=O)NH(C_1-C_4 alkyl), (C=S)NH(C_1-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy; or Het^1 can represents a 4 to 6 membered saturated ring containing one O atom, substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, CF_3, NH(C=O)(C_1-C_4 alkyl), (C=O)NH(C_1-C_4 alkyl) and C_1-C_4 alkyl; or Het represents a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N, optionally substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, SO_2R^8, C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), (C=O)NH(C_1-C_4 alkyl), (C=S)NH(C_1-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy; Het^2 can represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONRV^2$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$; Z can be C or N; R^5 is present where Z is C, whereby R^5 can be selected form hydrogen, CF_3 and halogen; R^5 is absent where Z is N; or a pharmaceutically acceptable addition salt or a solvate thereof.

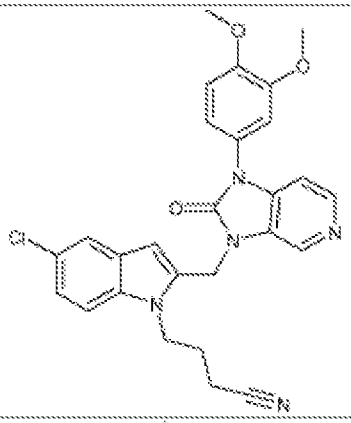
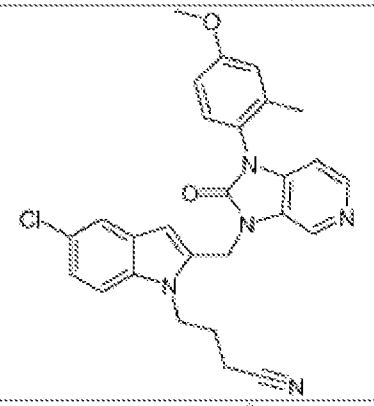
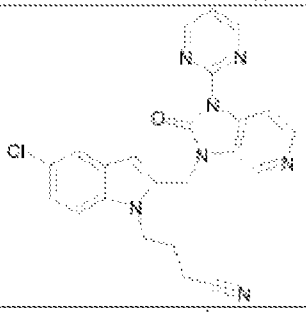
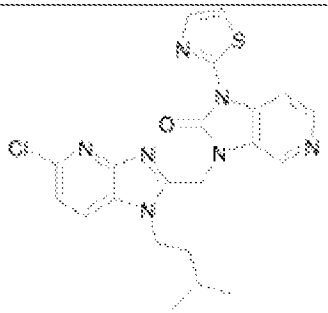
[0113] Examples of Compounds of Formula (B1) include:

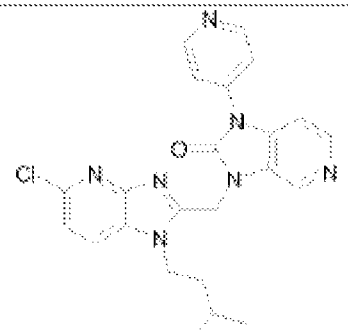
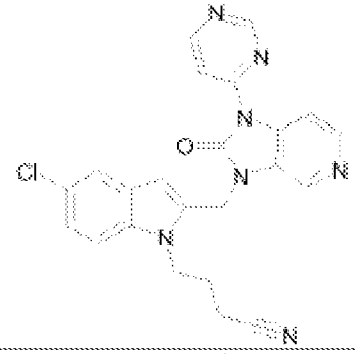
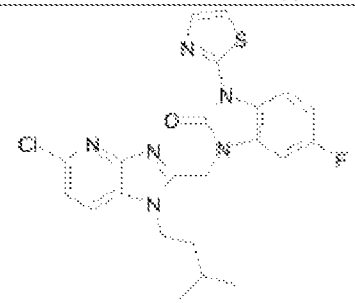
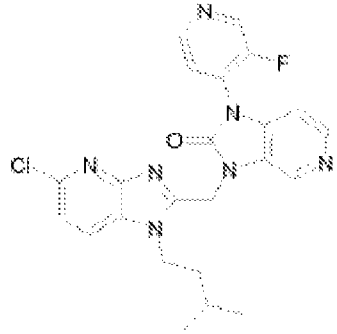
	Structure
P1	
P2	
P3	 .0.17 CF_3COOH
P4	 .CF_3COOH

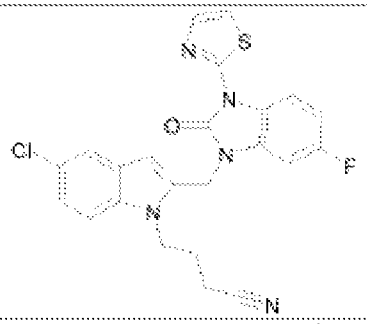
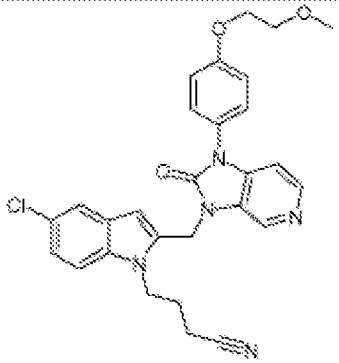
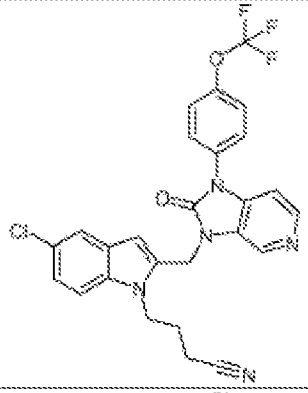
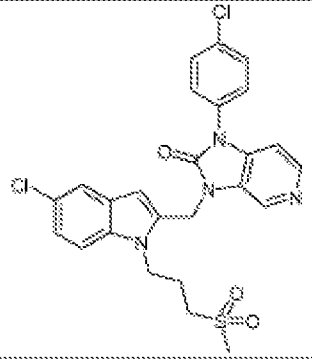
	Structure
P5	
P6	
P7	
P8	
P9	

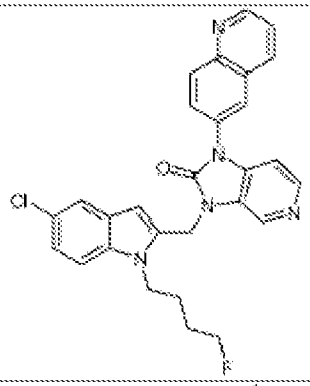
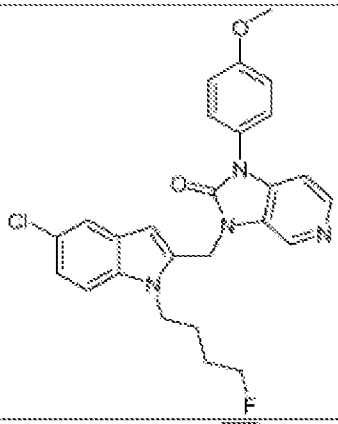
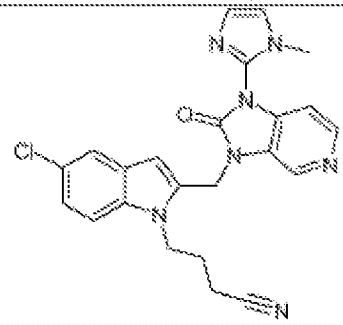
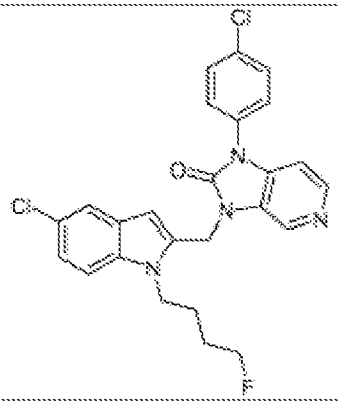
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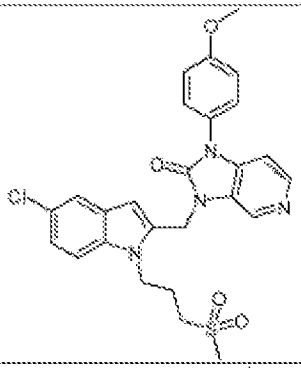
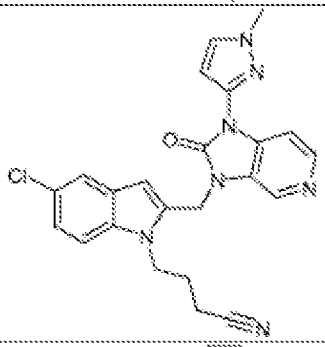
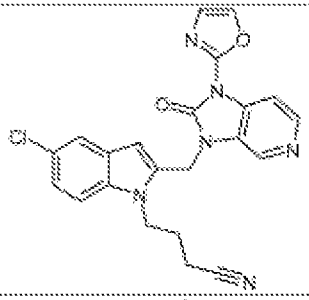
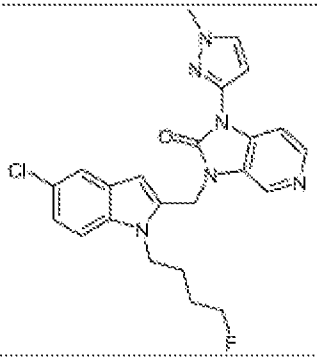
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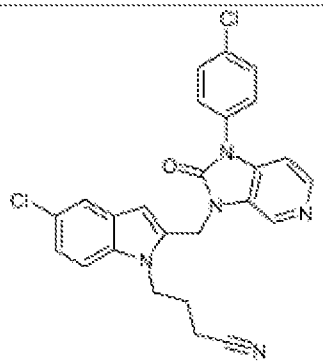
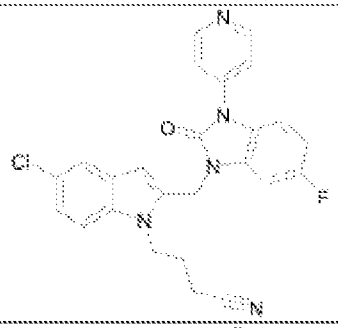
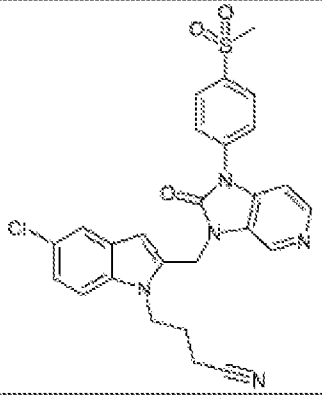
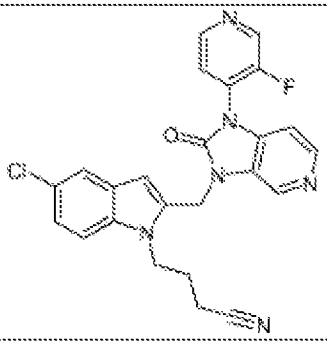
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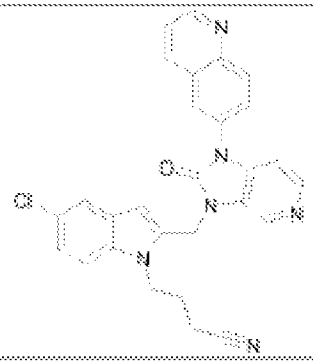
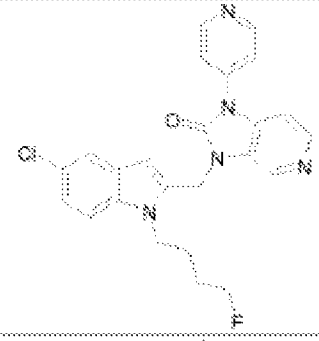
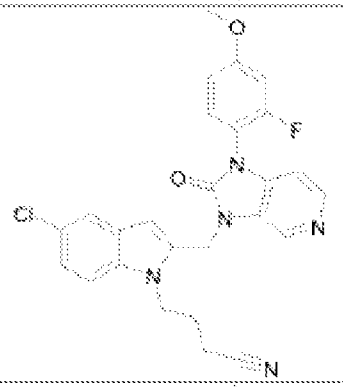
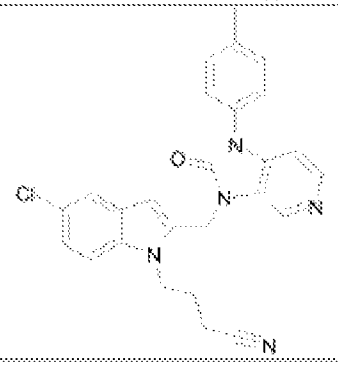
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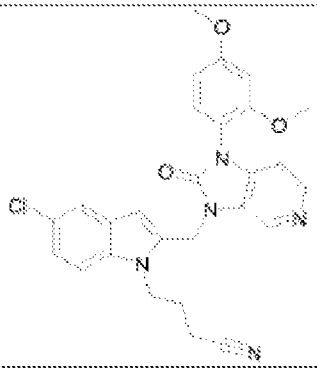
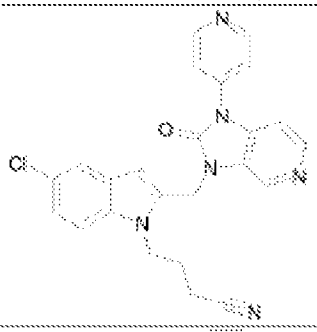
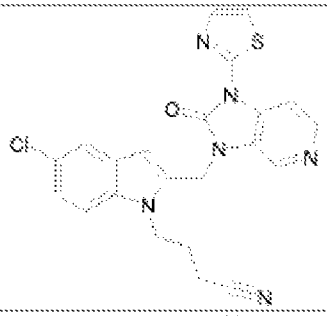
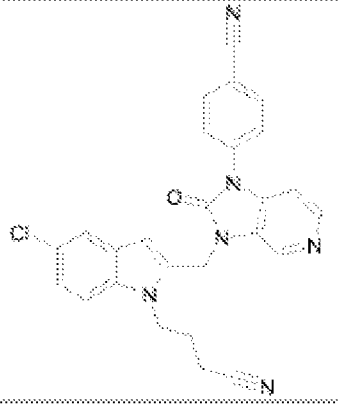
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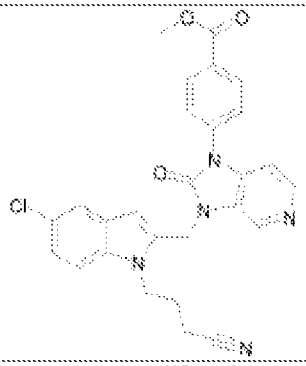
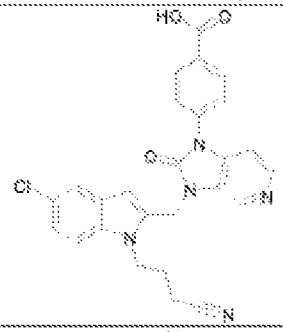
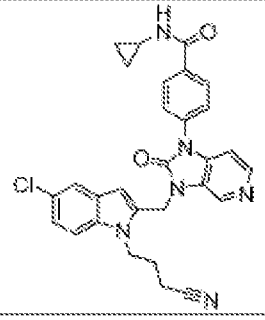
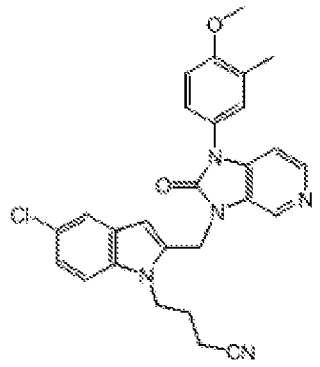
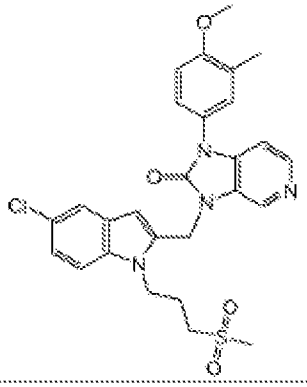
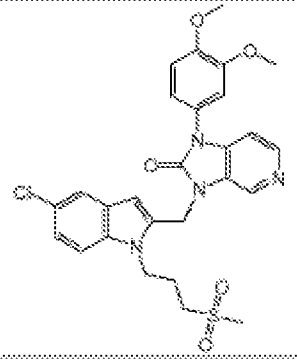
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	Structure
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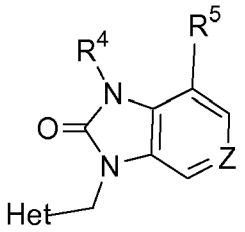
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	Structure
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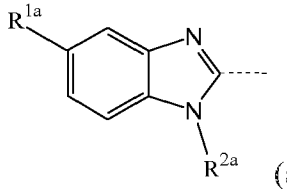
	Structure
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Compounds of Formula (B2)

[0114] Compounds of the general Formula (B2) are described in PCT Publication No. WO 2013/186332, published December 19, 2013, which is hereby incorporated by reference in its entirety. Formula (B2) has the structure:



a tautomer or a stereoisomeric form thereof, wherein: Het can be a heterocycle having formula (a):

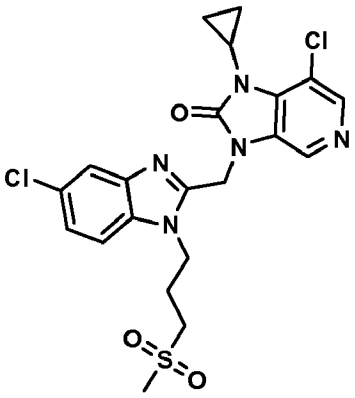
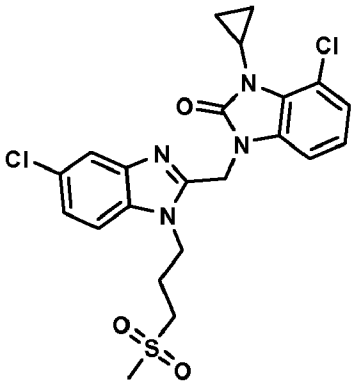
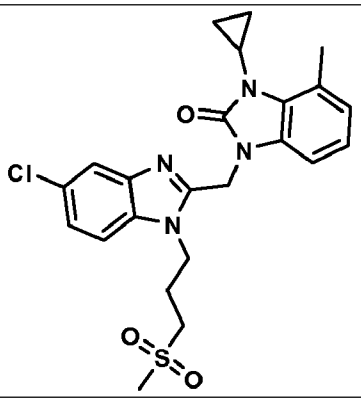


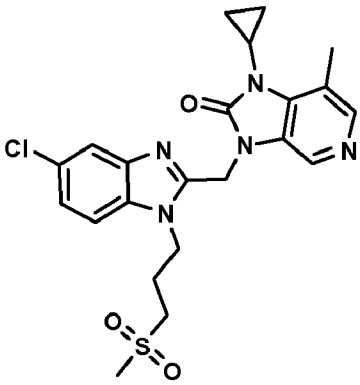
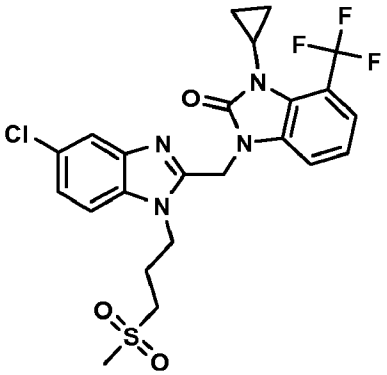
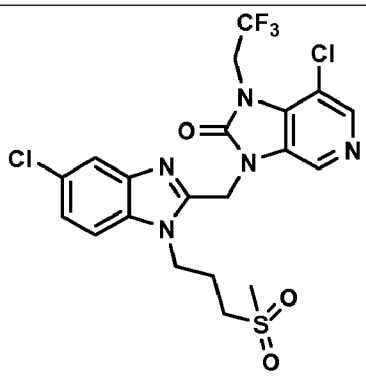
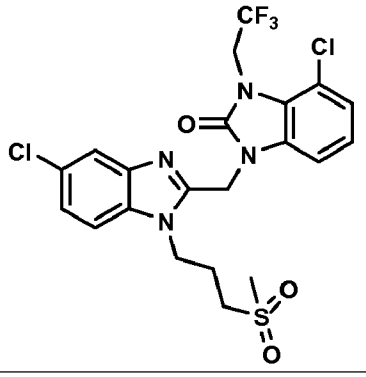
(a)

R^{1a} can be Br or Cl; R^{2a} can be $-(CR^{8a}R^{9a})_n-R^{10a}$; each R^{8a} and R^{9a} can be independently chosen from H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^{8a} and R^{9a} can be taken together form a 4 to 6 membered aliphatic ring; wherein the 4 to 6 membered aliphatic ring optionally contains one or more heteroatoms selected from N, S and O; R^{10a} can be selected from H, C_1-C_6 alkyl, R^{11}, OH, CF_3, CHF_2, F, Cl, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR^{8a}SO_2R^{8a}$, $SO_2NR^{8a}R^{9a}$, $NR^{8a}SO_2C_3$-C_7 cycloalkyl, CN, $NR^{8a}R^{9a}$, COOH, $COOR^{8a}$, $CONR^{8a}R^{9a}$, $OCOC_1$-C_6 alkyl, $CONR^{8a}SO_2R^{9a}$, $CONR^{8a}SO_2NR^{8a}R^{9a}$, a 4 to 6 membered aliphatic ring and a 5 to 6 membered aromatic ring; wherein the aliphatic or aromatic ring optionally contains one or more heteroatoms selected from N, S and O; R^{11} can be selected from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; n can be an integer having a value from 1 to 6; R^5 can be selected from C_1-C_6 alkyl, C_1-C_6 alkyloxy, CN, CF_3 and halo; R^4 can be selected from hydrogen, tert-butyl, C_3-C_7 cycloalkyl, $CH(CH_3)(CF_3)$, C_2-C_{10} alkenyl, CH_2CF_3, SO_2CH_3, $-CH_2$-p-fluorophenyl, aryl, Het^1, Het^2 and C_3-C_7 cycloalkyl substituted with one or more substituents selected from halo and C_1-C_4 alkyl; aryl can represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11a}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11a}$, and C_1-C_4 alkyl; Het^1 can represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; or a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; said Het^1 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, SO_2R^{8a} C_1-C_4 alkylcarbonyl,

C_1-C_4 alkyloxycarbonyl, CO(aryl), $COHet^2$, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), $NH(C{=}O)(C_1$-C_4 alkyl), $(C{=}O)NH(C_1$-C_4 alkyl), $(C{=}S)NH(C_1$-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy; Het^2 can represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$,$NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11a}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11a}$ and C_1-C_4 alkyl; R^{11a} can be selected from phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{11a} can be C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; Z can be CH or N; or a pharmaceutically acceptable addition salt or a solvate thereof.

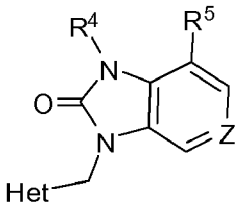
[0115] Examples of Compounds of Formula (B2) include:

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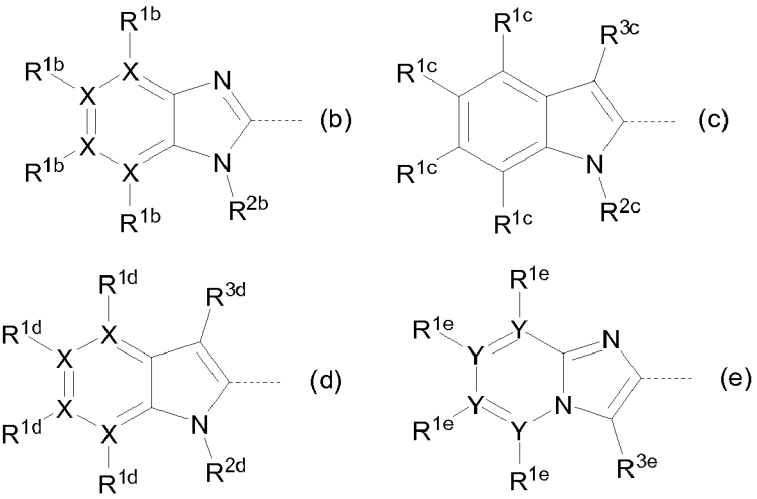
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Compounds of Formula (B3)

[0116] Compounds of the general Formula (B3) are described in PCT Publication No. WO 2013/186335, published December 19, 2013, which is hereby incorporated by reference in its entirety. Formula (B3) has the structure:



a tautomer or a stereoisomeric form thereof, wherein: Het can be a heterocycle having formula (b), (c), (d) or (e):

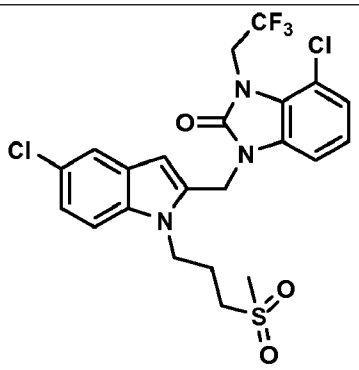
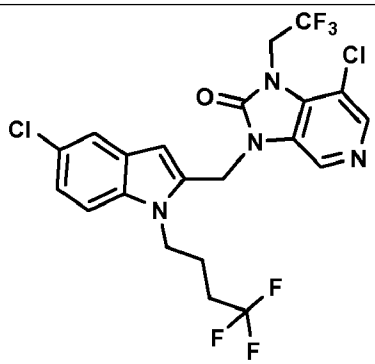
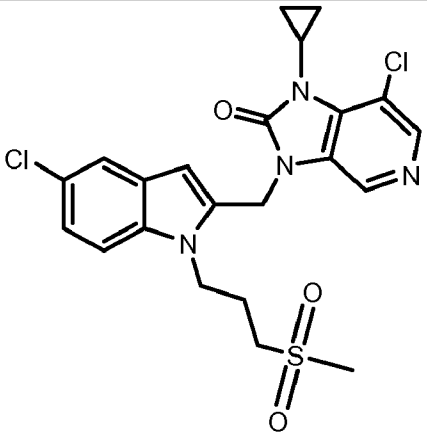


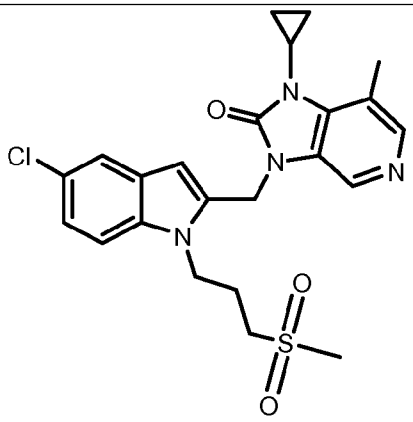
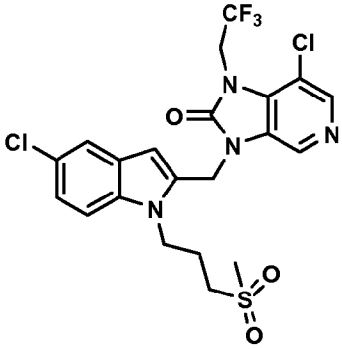
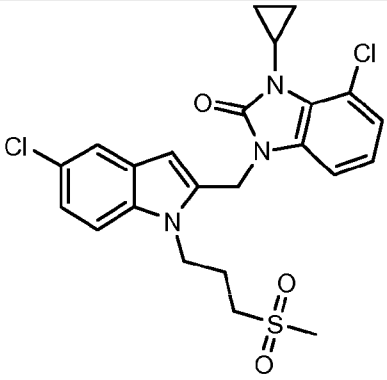
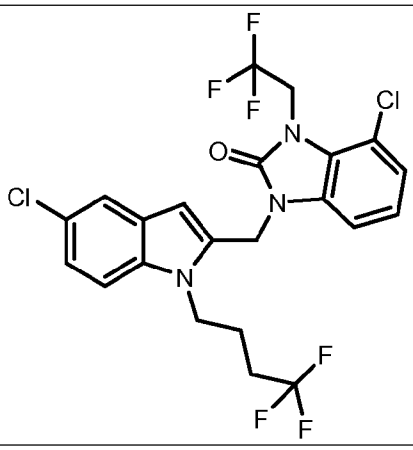
each X independently can be C or N; provided that at least one X is N; R^{1b} can be present when Het has formula (b) and X is C; each R^{1b} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1b} can be absent when the X to which it is bound is N; R^{2b} can be $-(CR^8R^9)_m\text{-}R^{10b}$; each R^6 can be independently selected from can be H, C_1-C_6 alkyl, $COOCH_3$ and $CONHSO_2CH_3$; each R^7 can be independently selected from OH, C_1-C_6 alkyloxy, NH_2, $NHSO_2N(C_1\text{-}C_6\text{ alkyl})_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1\text{-}C_6\text{ alkyl})$, $NHSO_2(C_3\text{-}C_7$ cycloalkyl) and $N(C_1\text{-}C_6\text{-alkyl})_2$; each R^8 and R^9 can be independently chosen from H, C_1-C_6 alkyl and C_3-C_7 cycloalkyl; or R^8 and R^9 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains one or more heteroatoms selected from N, S and O; R^{10b} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, O-Benzyl, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8,

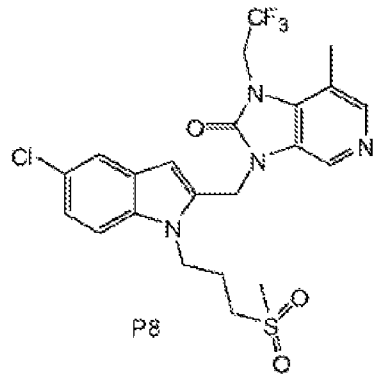
$OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$ and a 4 to 6 membered saturated ring containing one oxygen atom; R^{11} can be selected from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; R^{12} can be selected from phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{12} can be C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; m can be an integer from 2 to 6; R^{1c} can be present when Het has formula (c); each R^{1c} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^{7c})$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6alkyl)_2$; R^{3c} can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy and $CO(R^{7c})$; R^{2c} can be $-(CR^8R^9)_m$-R^{10c}; R^{7c} can be selected from OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), $N(C_1$-C_6-alkyl$)_2$, NR^8R^9 and NR^9R^{10c}; R^{10c} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; R^{1d} can be present when Het has formula (d) and X is C; each R^{1d} can be selected independently from H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1d} is absent when the X to which it is bound is N; R^{3d} can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, and $CO(R^7)$; R^{2d} can be $-(CR^8R^9)_m$-R^{10d}; R^{10d} can be selected from H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; each Y independently can be C or N; R^{1e} can be present when Het has formula (e) and Y is C; each R^{1e} can be selected independently from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1e} is absent when the Y to which it is bound is N; R^{3e} can be selected from H, halogen, $-(CR^8R^9)_m$-R^{10e}, $C\equiv C\text{-}CH_2$- R^{10e}, $C\equiv C\text{-}R^{10e}$ and $C=C\text{-}R^{10e}$; R^{10e} can be selected from H, R^{11}, C_1-C_6 alkyloxy, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom; R^5 can be

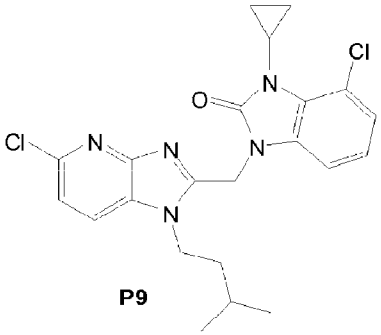
selected from C_1-C_6 alkyl, C_1-C_6 alkyloxy, CN, CF_3 and halogen; R^4 can be selected from hydrogen, C_3-C_7 cycloalkyl, tert-butyl, C_2-C_{10} alkenyl, CH_2CF_3, $CH(CH_3)(CF_3)$, SO_2CH_3, -CH_2-p-fluorophenyl, aryl, Het^1, Het^2 and C_3-C_7 cycloalkyl substituted with one or more substituents selected from halo and C_1-C_4 alkyl; aryl can represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4alkyloxy, C_1-C_4alkyl, OH, CN, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$ and $N(R^8)COOR^{12}$; Het^1 can represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; or a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; said Het^1 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, SO_2R, C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl)$_2$, $SO_2NH(C_1$-C_4 alkyl),$NH(C{=}O)(C_1$-C_4 alkyl), $(C{=}O)NH(C_1$-C_4 alkyl), $(C{=}S)NH(C_1$-C_4 alkyl) and C_1-C_4 alkyl; Het^2 can represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, CONRV, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$ and $N(R^8)COOR^{12}$; Z can be CH or N; or a pharmaceutically acceptable addition salt or a solvate thereof.

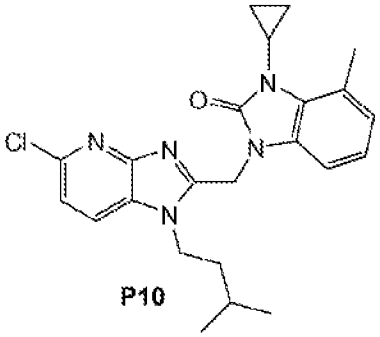
[0117] Examples of Compounds of Formula (B3) include:

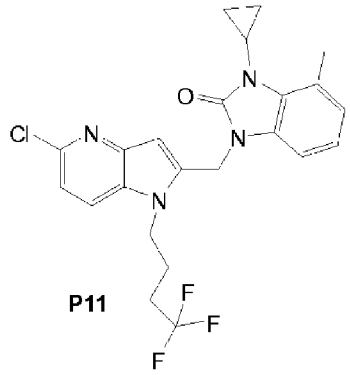
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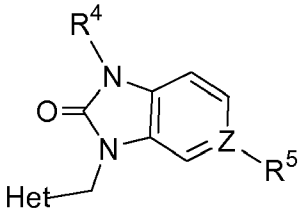

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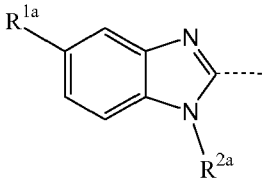

P11

Compounds of Formula (B4)

[0118] Compounds of the general Formula (B4) are described in PCT Publication No. WO 2013/186334, published December 19, 2013, which is hereby incorporated by reference in its entirety. Formula (B4) has the structure:



or a stereoisomeric form thereof, wherein: Het can be a heterocycle having formula (a):

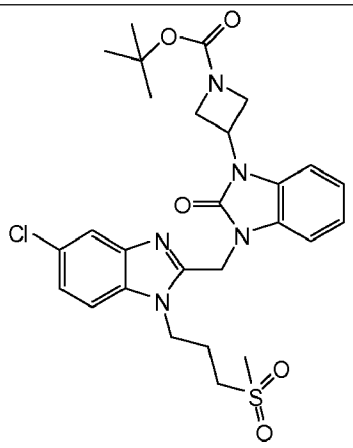

(a)

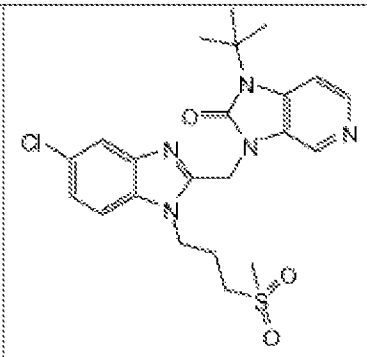
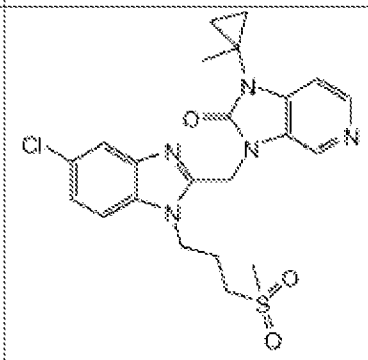
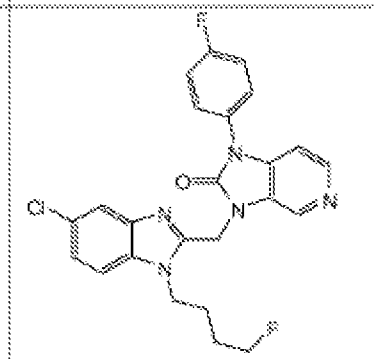
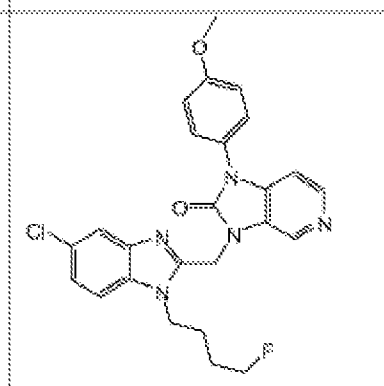
R^{1a} can be Br or Cl; R^{2a} can be $-(CR^{8a}R^{9a})_n-R^{10a}$; each R^{8a} and R^{9a} can be independently chosen from H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^{8a} and R^{9a} can be taken together form a 4 to 6 membered aliphatic ring; wherein the 4 to 6 membered aliphatic ring optionally contains one or more heteroatoms selected N, S and O; R^{10a} can be selected from H, C_1-C_6 alkyl, R^{11}, OH, CF_3,

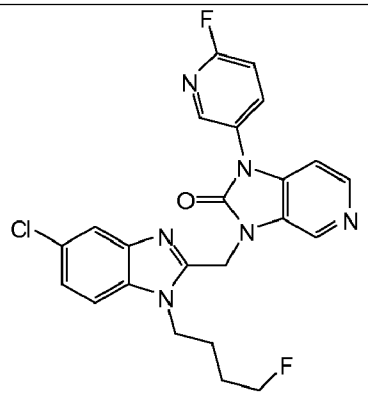
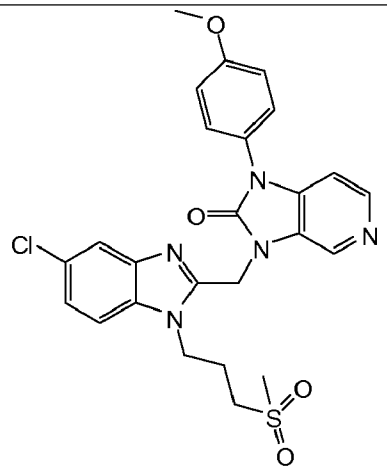
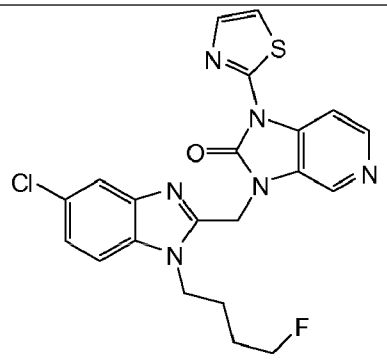
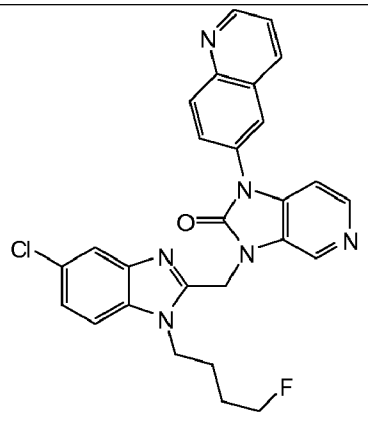
CHF_2, F, Cl, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR^{8a}SO_2R^{8a}$, $SO_2NR^{8a}R^{9a}$, $NR^{8a}SO_2C_3$-C_7 cycloalkyl, CN, $NR^{8a}R^{9a}$, COOH, $COOR^{8a}$, $CONR^{8a}R^{9a}$, $OCOC_1$-C_6 alkyl, $CONR^{8a}SO_2R^{9a}$, $CONR^{8a}SO_2NR^{8a}R^{9a}$, a 4 to 6 membered aliphatic ring and a 5 to 6 membered aromatic ring; wherein the aliphatic or aromatic ring optionally contains one or more heteroatoms selected from N, S and O; R^{11} can be selected from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; n can be an integer having a value from 1 to 6; R^4 can be selected from tert-butyl, $CH(CH_3)(CF_3)$, aryl, Het^1, Het^2 and C_3-C_7 cycloalkyl substituted with one or more substituents selected from halo and C_1-C_4 alkyl; aryl represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11b}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11b}$, and C_1-C_4 alkyl; Het^1 can represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; or a bicyclic 7 to 1 1 non-aromatic heterocycle containing one or two heteroatoms each independently selected from O, S and N; said Het^1 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, SO_2R^{8a} C_1-C_4 alkylcarbonyl, C_1-C_4 alkyloxycarbonyl, CO(aryl), $COHet^2$, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), NH(C=O)(C_1-C_4 alkyl), (C=O)NH(C_1-C_4 alkyl), (C=S)NH(C_1-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy; Het^2 can represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11b}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11b}$ and C_1-C_4 alkyl; R^{11b} can be selected from phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{11b} can be C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from CF_3, CH_3, OCH_3, OCF_3 and halogen; Z can be C or N; R^5 is present where Z is C,

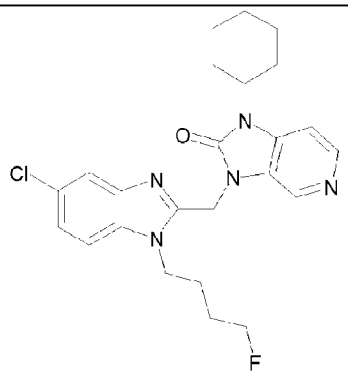
whereby R^5 can be selected from hydrogen, CF_3 and halogen; R^5 is absent where Z is N; or a pharmaceutically acceptable addition salt or a solvate thereof.

[0119] Examples of Compounds of Formula (B4) include:

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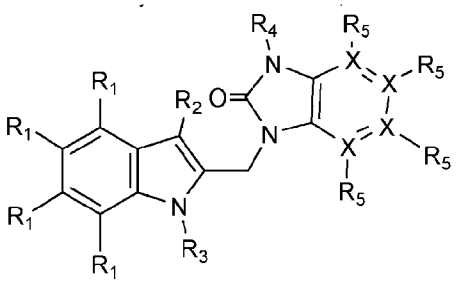
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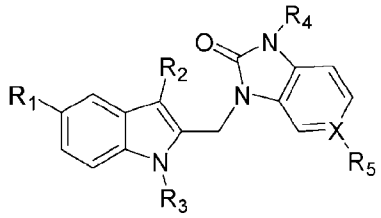
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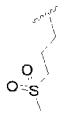
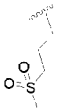
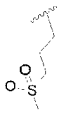
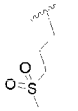
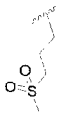
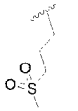
[0120] Compounds of the general Formula (B5) are described in PCT Publication No. WO 2012/080447, published June 21, 2012, which is hereby incorporated by reference in its entirety. Formula (B5) has the structure:

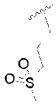
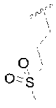
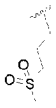
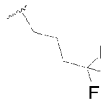


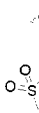
or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: each X independently can be C or N; R_1 can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_6)_2$, $CO(R_7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R_2 can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, and $CO(R_7)$; R_3 can be $-(CR_8R_9)_n\text{-}R_{10}$; R_4 can be selected from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_8$, CH_2CF_3, SO_2CH_3 or a 4 to 6 membered saturated ring containing an oxygen atom; R_5 is present where X is C, and can be selected from H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen; R_5 is absent where X is N; R_6 can be selected from H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$; R_7 can be selected from OH, $O(C_1\text{-}C_6$ alkyl), NH_2, $NHSO_2N(C_1\text{-}C_6$ alkyl$)_2$, $NHSO_2NCH_3$, $NHSO_2(C_1\text{-}C_6$ alkyl), $NHSO_2(C_3\text{-}C_7$ cycloalkyl), and $N(C_1\text{-}C_6$ alkyl$)_2$, NR_8R_9, NR_9R_{10}; n can be an integer from 2 to 6; R_8 and R_9 can be each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_8 and R_9 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains one or more heteroatoms selected from N, S, O; R_{10} can be selected from H, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR_8R_9$, $COOR_8$, $CONR_8SO_2R_9$, $CON(R_8)SO_2N(R_8R_9)$, NR_8R_9, NR_8COOR_9, $OCOR_8$, $NR_8SO_2R_9$, $SO_2NR_8R_9$, SO_2NR_8 or a 4 to 6 membered saturated ring containing an oxygen atom.

[0121] Examples of Compounds of Formula (B5) include:

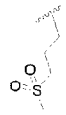
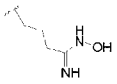
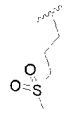
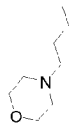


	R_1	R_2	R_3	R_4	X-R_5
P20	F	H			N
P21	Br	H			C-H
P22	F	H			N
P23	CF_3	H			N
P24	H	H			N
P25	H	H			N

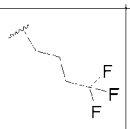
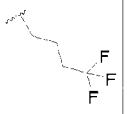
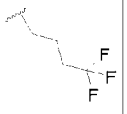
P26	F	H			C-H
P27	F	H			C-F
P28	H	H			C-H
P29	F	H			N
P30	Cl	H			N
P31	Br	H			C-H
P32	Br	H			N
P33	Cl	H			N

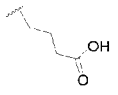
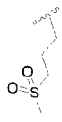
P34	F	H			C-H
P35	Cl	H			C-H
P36	Cl	H			N
P37	Cl	H			C-F
P38	Cl	H			C-H
P39	Cl	H			C-F
P40	Cl	H			C-H
P41	F	H			C-OCH$_3$

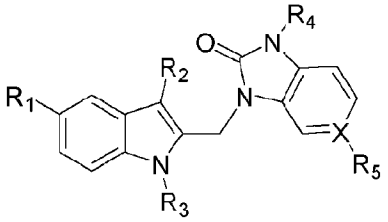
P42	Cl	H			C-H
P43	CN	H			N
P44	Cl	H			C-CONHMe
P45	Br	H			N
P46	H	H			N
P47	H	H			N
P48	Cl	H			N
P49	Cl	H			N

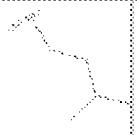
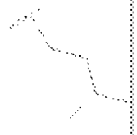
P50	Cl	H			C-F
P51	Cl	H			N
P52	Cl	H			N
P53	Cl	COOH			N
P54	Cl	CONH2			N
P55	Cl	H			N
P57	Cl	H			N
P58	Cl	H			N

P59	Cl	COOH			N
P60	Cl	COOH			C-F
P61	Cl	CONH2			N
P62	Cl	H			N
P63	Cl	CONH2			C-F
P64	Cl	CONHMe			N
P65	Cl	CONH2			C-F
P66	Cl	H			N

P67	Cl	H			N
P68	Cl	CONHcyclopropyl			N
P69	Cl	CONHMe			N
P70	Cl	$CONH_2$			N
P71	CN	H			C-H
P72	Cl	H			N
P73	Cl	H			N
P74	Cl	H			N

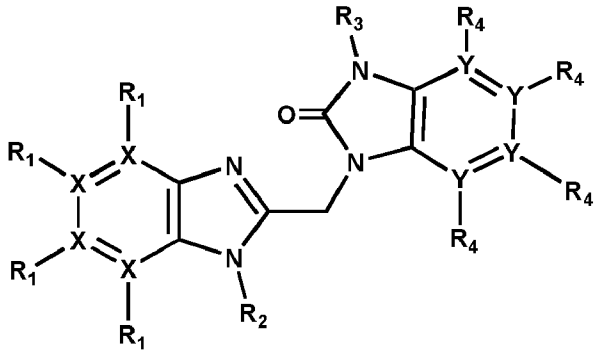
P75	Cl	H			C-F
P79	Cl	H			C-F
P80	Cl	H			N
P81	Cl	H			C-H



	R_1	R_2	R_3	R_4	X-R_5
P82 P83 P84	Cl	$CONH_2$			N CH CF
P85 P86 P87	Cl	$CONH_2$			N CH CF
P88 P89 P90	Cl	$CONH_2$			N CH CF
P91 P92 P93	Cl	$CONH_2$			N CH CF
P94 P95 P96	Cl	$CONH_2$			N CH CF
P97 P98 P99	Cl	$CONH_2$			N CH CF
P100 P101 P102	Cl	$CONH_2$			N CH CF
P103 P104 P105	Cl	$CONH_2$			N CH CF

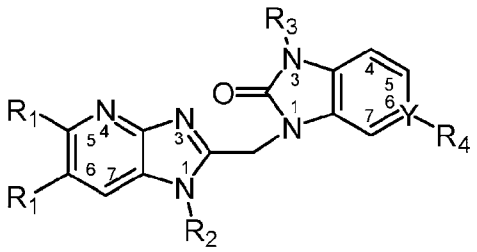
Compounds of Formula (B6)

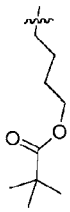
[0122] Compounds of the general Formula (B6) are described in PCT Publication No. WO 2012/080449, published June 21, 2012, which is hereby incorporated by reference in its entirety. Formula (B6) has the structure:

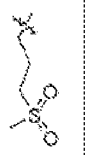
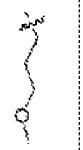
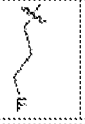


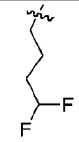
or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: each X independently can be C or N; at least one X = N; each Y independently can be C or N; R_1 is present when X = C and R_1 can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_5)_2$, $CO(R_6)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R_1 is absent when X = N; R_2 can be $-(CR_7R_8)_n\text{-}R_9$; R_3 can be selected from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_7$, CH_2CF_3 or a 4 to 6 membered saturated ring containing an oxygen atom; R_4 can be present where Y is C and is selected from H, C_1-C_6 alkyl, C_1-C_6 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, $COO(R_7)$, CF_3 and halogen, R_5 can be selected from H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$; R_6 can be selected from OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), and $N(C_1$-C_6-alkyl$)_2$; R_7 and R_8 can be each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_7 and R_8 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains a heteroatom selected from N, S, O; R_9 can be selected from H, R_{10}, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $CONR_7R_8$, $COOR_7$, $CON(R_7)SO_2R_8$, $CON(R_7)SO_2N(R_7R_8)$, NR_7R_8, NR_7COOR_8, $OCOR_7$, O-Benzyl, $NR_7SO_2R_8$, $SO_2R_7R_8$, SO_2R_7, $OCONR_7R_8$, $OCONR_7R_{10}$, $N(R_7)CON(R_7R_8)$, $N(R_7)COOC$; phtalimido, 2-methyl-benzothiophene(1,1)di oxide, or a 4 to 6 membered saturated ring containing an oxygen atom; n can be an integer from 2 to 6; R_{10} can be selected from C_1-C_6 alkyl, C_3-C_7 cycloalkyl , phenyl, pyridine or pyrazole, optionally substituted with one or more substituents selected from CF_3, CH_3, OCH_3, OCF_3 or halogen.

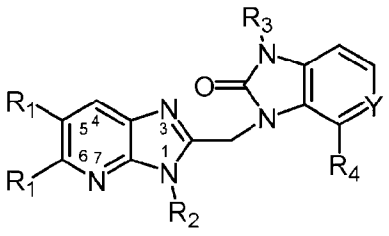
[0123] Examples of Compounds of Formula (B6) include:

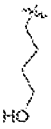


N°	Name	C_5-R_1	C_6-R_1	R_2	R_3	Y-R_4
1	3-((5-chloro-1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Cl	C-H			N
2	3-((5-chloro-1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Cl	C-H			N
3	4-(5-chloro-2-((1-cyclopropyl-2-oxo-1*H*-imidazo[4,5-*c*]pyridin-3(2*H*)-yl)methyl)-1*H*-imidazo[4,5-*b*]pyridin-1yl)butyl pivalate	C-Cl	C-H			N
4	1-cyclopropyl-3-((1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-H	C-H			C-H
5	1-cyclopropyl-3-((1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
6	3-((5-chloro-1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-5-fluoro-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-Cl	C-H			C-F

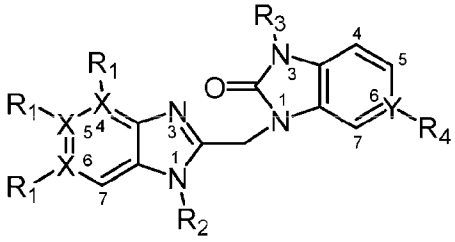
7	1-cyclopropyl-3-((1-(3-(methylsulfonyl)propyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
8	1-cyclopropyl-5-fluoro-3-((1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-H	C-H			C-F
9	3-((1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
10	1-cyclopropyl-3-((1-(3-(methoxypropyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
11	1-cyclopropyl-3-((1-(3-(fluoropropyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
12	3-((1-(3-methoxypropyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			N
13	3-((5-chloro-1-isopentyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-3-cyclopropyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-Cl	C-H			C-H
14	3-((5-chloro-1-(4-hydroxybutyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Cl	C-H			N
15	1-cyclopropyl-5-fluoro-3-((1-(3-methoxypropyl)-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-H	C-H			C-F

39	3-({5-chloro-1-(4,4,4-trifluorobutyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1-cyclopropyl-1H-imidazo[4,5-b]pyridin-2(3*H*)-one	C-Cl	C-H			N
40	3-({5-chloro-1-(4-fluorobutyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1-cyclopropyl-1H-imidazo[4,5-b]pyridin-2(3*H*)-one	C-Cl	C-H			N
41	1-cyclopropyl-3-({1-(4,4,4-trifluorobutyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one	C-H	C-H			N
42	1-cyclopropyl-3-({1-(4-fluorobutyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1H-imidazo[4,5-c]pyridin-2(3*H*)-one	C-H	C-H			N
43	1-cyclopropyl-3-((1-(4,4-difluorobutyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1H-imidazo[4,5-c]pyridin-2(3*H*)-one	C-H	C-H			N
44	1-cyclopropyl-3-((1-isopentyl-5-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-2-yl)methyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one	C-CF_3	C-H			N

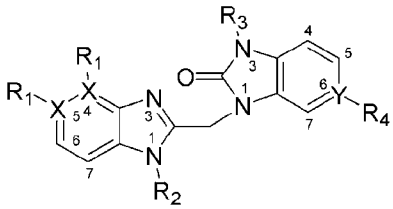


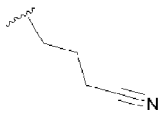
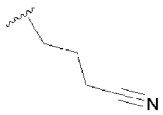
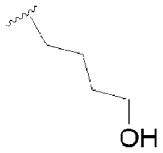
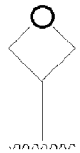
N°	Name	C_5-R_1	C_6-R_1	R_2	R_3	R_4	Y
16	3-((6-bromo-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Br	C-H			H	N
17	3-((6-(aminomethyl)-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridine-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-CH_2NH_2	C-H			H	N
18	3-((6-bromo-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Br	C-H			H	N
19	3-((6-bromo-3-(4-hydroxybutyl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Br	C-H			H	N
20	3-((6-bromo-3-(4-hydroxybutyl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Br	C-H			H	N
21	3-((6-chloro-3-(4-hydroxybutyl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Cl	C-H			H	N

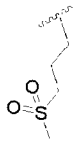
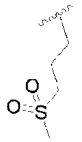
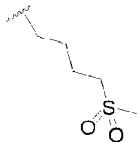
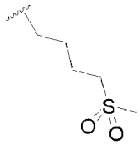
22	1-cyclopropyl-3-((6-fluoro-3-(4-hydroxybutyl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-F	C-H			H	N
23	2-((1-cyclopropyl-2-oxo-1*H*-imidazo[4,5-*c*]pyridin-3(2*H*)-yl)methyl)-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-6-ylboronic acid	C-B(OH)$_2$	C-H			H	N
24	1-cyclopropyl-3-((3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			H	N
25	4-chloro-3-((3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-isopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H			Cl	N
26	methyl 2-((1-cyclopropyl-2-oxo-1*H*-imidazo[4,5-*c*]pyridin-3(2*H*)-yl)methyl)-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridine-6-carboxylate	C-CO$_2$Me	C-H			H	N
27	2-((1-cyclopropyl-2-oxo-1*H*-imidazo[4,5-*c*]pyridin-3(2*H*)-yl)methyl)-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridine-6-carbonitrile	C-CN	C-H			H	N
28	2-((1-cyclopropyl-2-oxo-1*H*-imidazo[4,5-*c*]pyridin-3(2*H*)-yl)methyl)-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid	C-CO$_2$H	C-H			H	N
29	3-((3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-1-isopropyl-2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridine-4-carbonitrile	C-H	C-H			CN	N
30	1-((6-bromo-3-isopentyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl)-3-cyclopropyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-Br	C-H			H	CH

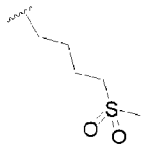
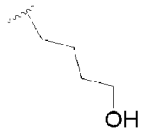
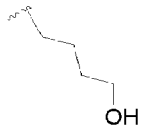
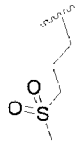


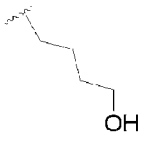
N°	Name	X_4-R_1	X_5-R_1	X_6-R_1	R_2	R_3	Y-R_4
31	1-cyclopropyl-3-((1-isopentyl-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-H	N	C-H			C-H
32	1-cyclopropyl-5-fluoro-3-((1-isopentyl-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one	C-H	N	C-H			C-F
33	1-cyclopropyl-3-((1-isopentyl-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	N	C-H			N
34	1-cyclopropyl-3-((3-isopentyl-3*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	C-H	N			N
35	1-cyclopropyl-3-((1-(4-hydroxybutyl)-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	N	C-H			N
36	3-((1-isopentyl-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1-(oxetan-3-yl)-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-H	N	C-H			N
37	1-cyclopropyl-3-((4-(dimethylamino)-1-(4-hydroxybutyl)-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-NMe_2	N	C-H			N
38	3-((1-(4-benzyloxy)butyl)-4-chloro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)methyl-1-cyclopropyl-1*H*-imidazo[4,5-*c*]pyridin-2(3*H*)-one	C-Cl	N	C-H			N

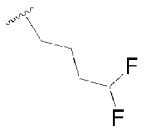
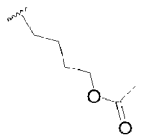
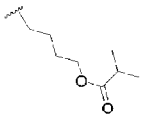
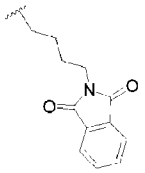


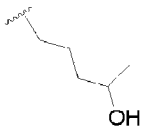
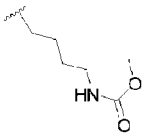
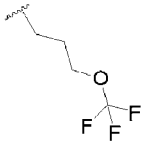
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100	N	C-Cl		
101	N	C-Cl		

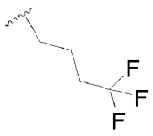
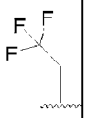
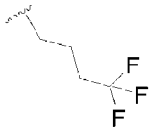
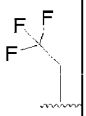
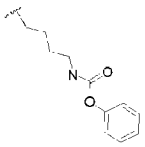
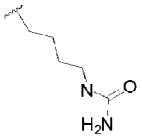
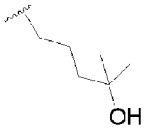
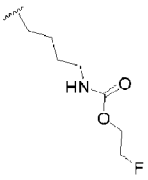
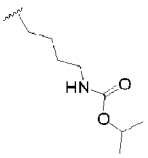
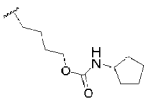
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102	N	C-Cl			N
103	N	C-Cl			C-F
45	N	C-Cl			N
46	N	C-Cl			C-F
47	N	C-Cl			N

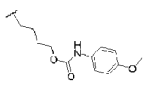
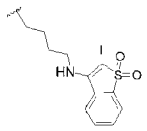
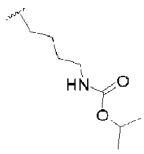
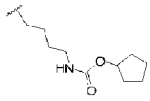
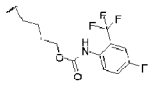
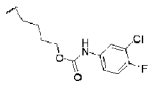
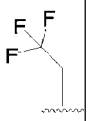
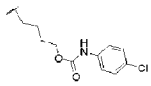
48	N	C-Cl			C-H
50	N	C-H		H	N
51	N	C-H			N
54	N	C-Cl			C-H

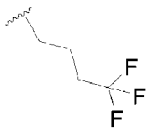
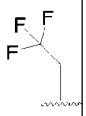
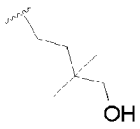
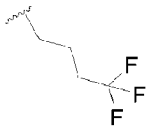
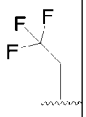
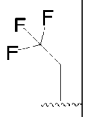
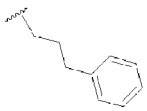
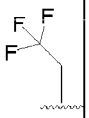
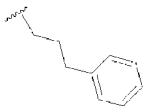
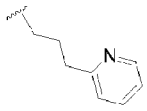
55	N	C-Cl			C-COOEt
56	N	C-Cl			C-COOEt
57	N	C-Cl			C-COOH
58	N	C-Cl			C-F

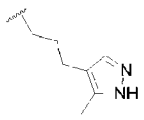
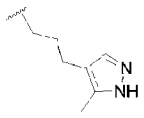
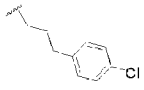
43	N	C-H			N
64	N	C-Cl			N
65	N	C-Cl			N
66	N	C-Cl			N

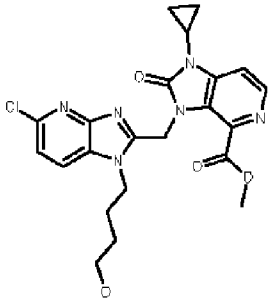
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68	N	C-Cl			N
69	N	C-F			N
70	N	C-H			N

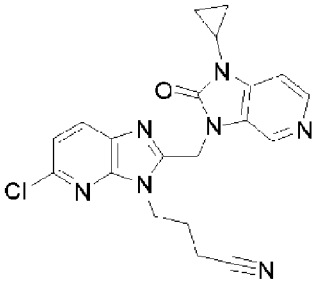
71	N	C-Cl			N
72	N	C-H			N
73	N	C-Cl			N
74	N	C-Cl			N
75	N	C-Cl			N
76	N	C-Cl			N
77	N	C-Cl			N
78	N	C-Cl			N

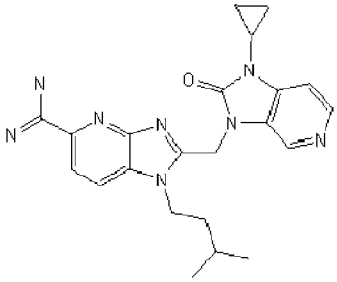
79	N	C-Cl			N
80	N	C-Cl			N
81	N	C-H			N
82	N	C-Cl			N
83	N	C-Cl			N
84	N	C-Cl			N
85	N	C-H			N
86	N	C-Cl			N

87	N	C-Cl			C-F
88	N	C-Cl			N
89	N	C-H			C-F
90	N	C-Cl			N
91	N	C-H			N
92	N	C-Cl			C-F
93	N	C-H			C-F
94	N	C-H			N

95	N	C-H			C-F
96	N	C-H			N
97	N	CMe_2NH_2			N
98	N	C-H			N

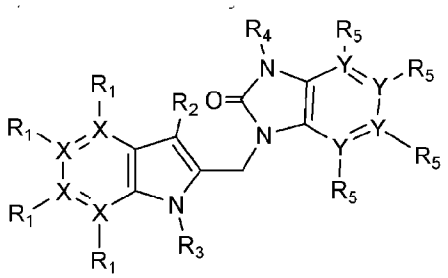






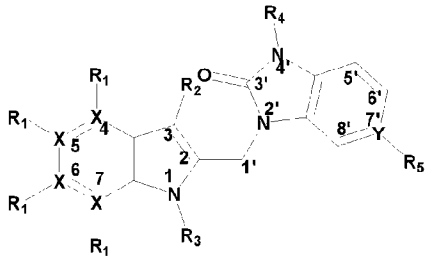
Compounds of Formula (B7)

[0124] Compounds of the general Formula (B7) are described in PCT Publication No. WO 2012/080450, published June 21, 2012, which is hereby incorporated by reference in its entirety. Formula (B7) has the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: each X independently can be C or N with at least one X being N; R_1 is present where X = C and R_1 can be selected from H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, NH_2, $CO(R_7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R_2 can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, and $CO(R_7)$; R_3 can be $-(CR_8R_9)_n\text{-}R_{10}$; R_4 can be selected from H, C_1-C_{10} alkyl, CH_2CF_3 C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_8$, or a 4 to 6 membered saturated ring containing an oxygen atom; R_5 is present where Y is C, and can be selected from H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen; R_5 is absent where X is N; R_6 can be selected from H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$; R_7 can be selected from OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$,N HSO_2NHCH_3, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), and $N(C_1$-C_6-alkyl$)_2$; n can be an integer from 2 to 6; R_8 and R_9 can be each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_8 and R_9 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains a heteroatom selected from N, S, O; R_{10} can be selected from H, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $CONR_8R_9$, $COOR_8$, $CONR_8SO_2R_9$, $CON(R_8)SO_2N(R_8R_9)$, NR_8R_9, NR_8COOR_9, $OCOR_8$, $NR_8SO_2R_9$, $SO_2NR_8R_9$, SO_2R_8 or a 4 to 6 membered saturated ring containing an oxygen atom.

[0125] Examples of Compounds of Formula (B7) include:



	Compound name	X_4-R_1	X_5-R_1	X_6-R_1	X_7-R_1	R_2	R_3	R_4	Y_7-R_5
P1	1-Cyclopropyl-3-{[1-(4-hydroxybutyl)-1H-pyrrolo[3,2-c]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	C-H	N	C-H	C-H	H			N
P2	3-{[5-Chloro-1-(4-hydroxybutyl)-1H-pyrrolo[3,2-b]pyridin-2-yl]methyl}-1-cyclopropyl-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	N	C-Cl	C-H	C-H	H			N
P3	1-Cyclopropyl-3-{[1-(3-methylbutyl)-1H-pyrrolo[3,2-b]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	N	C-H	C-H	C-H	H			N

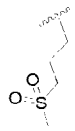
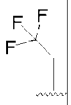
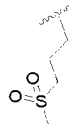
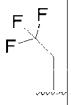
P4	1-Cyclopropyl-3-{[1-(4-hydroxybutyl)-1H-pyrrolo[2,3-c]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	C-H	C-H	N	C-H	H			N
P5	1-Cyclopropyl-3-{[1-(4-hydroxybutyl)-1H-pyrrolo[3,2-b]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	N	C-H	C-H	C-H	H			N
P6	1-Cyclopropyl-3-{[1-(4-hydroxybutyl)-5-methoxy-1H-pyrrolo[3,2-b]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	N	C-OMe	C-H	C-H	H			N
P8	1-Cyclopropyl-3-{[5-hydroxy-1-(4-hydroxybutyl)-1H-pyrrolo[3,2-b]pyridin-2-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	N	C-OH	C-H	C-H	H			N

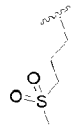
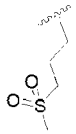
P9	4-{2-[(1-Cyclopropyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)methyl]-5-hydroxy-1H-pyrrolo[3,2-b]pyridin-1-yl}butyl 2,2-dimethylpropanoate	N	C-OH	C-H	C-H	H			N
P10	1-Cyclopropyl-3-{[1-(3-methylbutyl)-1H-pyrrolo[2,3-b]pyridin-3-yl]methyl}-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one	C-H	C-H	C-H	N	H			N

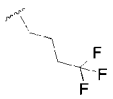
	X_4-R_1	X_5-R_1	X_6-R_1	R_2	R_3	R_4	Y_7, -R_5
P11	CH	C-Cl	N	H			N
P12	CH	C-Cl	N	H			N

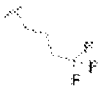
P13	CH	C-Cl	N	H			N
P14	CH	C-Cl	N	H			C-F
P15	CH	C-Cl	N	H			N
P16	CH	C-Cl	N	H			C-F
P17	CH	N	CH	Br			N
P18	CH	N	CH	H			N

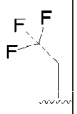
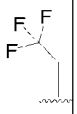
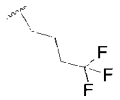
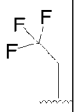
P19	CH	N	CH	H			N
P20	CH	N	CH	H			N
P21	CH	N	CH	H			N
P22	CH	N	CH	Cl			N

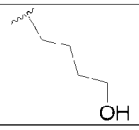
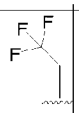
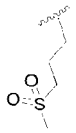
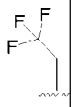
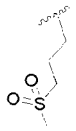
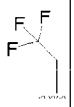
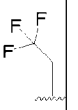
P23	CH	N	CH	F			N
P25	CH	N	CH	Me			N
P26	CH	N	CH	I			N
P29	CH	N	CH	Br			C-F
P30	CH	N	CH	H			C-F
P32	N	Cl	CH	H			N

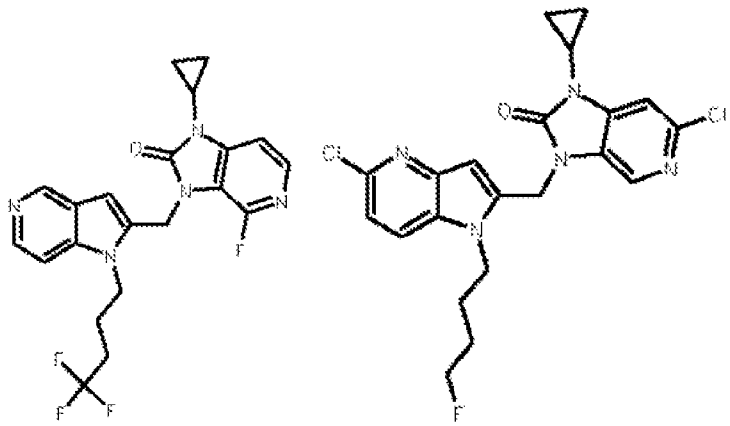
P33	**N**	**Cl**	**CH**	**H**			**N**
P34	**N**	**Cl**	**CH**	**H**			**N**
P35	**N**	**Cl**	**CH**	**H**			**C-H**
P36	**N**	**Cl**	**CH**	**H**			**N**

P37	N	Cl	CH	H			C-F
P38	N	Cl	CH	H			C-F
P39	N	Cl	CH	H			C-H
P40	N	Cl	CH	H			N
P42	N	Cl	CH	H			N

P43	N	Cl	CH	H			C-H
P45	N	CH	CH	H			N
P46	N	CF_3	CH	H			N

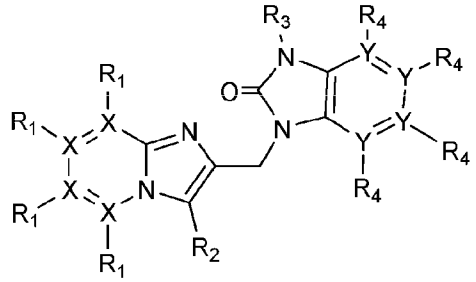
P47	**N**	**Cl**	**CH**	**H**			**C-F**
P48	**N**	**Cl**	**CH**	**H**			**N**
P49	**N**	**Cl**	**CH**	**H**			**N**

P50	**N**	**Cl**	**CH**	**H**			**N**
P51	**N**	**Cl**	**CH**	**H**			**C-H**
P52	**N**	**Cl**	**CH**	**H**			**N**
P53	**N**	**Cl**	**CH**	**H**			**N**
P54	**N**	**Cl**	**CH**	**H**			**N**



Compounds of Formula (B8)

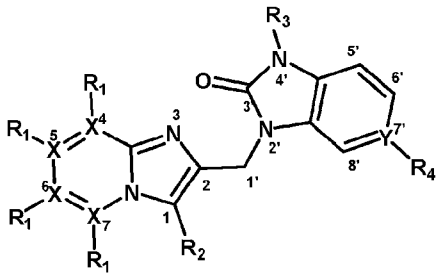
[0126] Compounds of the general Formula (B8) are described in PCT Publication No. WO 2012/080451, published June 21, 2012, which is hereby incorporated by reference in its entirety. Formula (B8) has the structure:

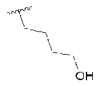


or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: each X independently can be C or N; each Y independently can be C or N; R_1 is present when X = C and R_1 can be selected from H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_5)_2$, $CO(R_6)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R_1 is absent when X = N; R_2 can be selected from H, halogen, $-(CR_7R_8)_n\text{-}R_9$, $C\equiv C\text{-}CH_2\text{-}R_9$ and $C\equiv C\text{-}R_9$, $C=C\text{-}R_9$; R_3 can be selected from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_7$, or a 4 to 6 membered saturated ring containing an oxygen atom; R_4 is present where Y is C and can be selected from H, C_1-C_6 alkyl, C_1-C_6 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen, R_5 can be selected from H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$; R_6 can be selected from OH, $O(C_1\text{-}C_6\text{ alkyl})$, NH_2, $NHSO_2N(C_1\text{-}C_6\text{ alkyl})_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1\text{-}C_6\text{ alkyl})$, $NHSO_2(C_3\text{-}C_7\text{ cycloalkyl})$, and $N(C_1\text{-}C_6\text{-alkyl})_2$; R_7 and R_8 can be each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_7 and R_8 can be taken together form a 4 to 6 membered aliphatic ring that optionally contains at least one heteroatom selected from N, S, O; R_9 can be selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl OH, CN, F, CF_2H, CF_3, $CONR_7R_8$, $COOR_7$, $CON(R_7)SO_2R_8$, $CON(R_7)SO_2N(R_7R_8)$,

NR_7R_8, NR_7COOR_8, $OCOR_7$, $NR_7SO_2R_8$, $SO_2NR_7R_8$, SO_2R_7 or a 4 to 6 membered saturated ring containing an oxygen atom; n can be an integer from 2 to 6.

[0127] Examples of Compounds of Formula (B8) include:

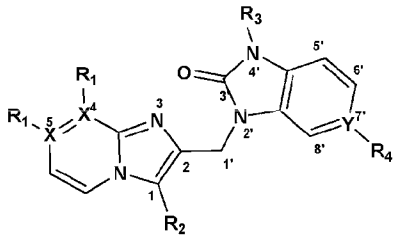


	X_4-R_1	X_5-R_1	X_6-R_1	X_7-R_1	R_2	R_3	Y_7-R_4
P1	C-H	C-Cl	C-H	C-H			N
P2	C-H	C-Cl	C-H	C-H			N
P3	C-H	C-H	C-H	C-H			N
P4	C-H	C-H	C-H	C-H			N

P5	C-H	C-H	C-H	C-H			N
P6	C-H	C-Cl	C-H	C-H			N
P7	C-H	C-H	C-H	C-H			C-H
P8	C-H	C-H	C-H	C-H			N
P9	C-H	C-H	C-H	C-H			C-H

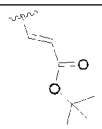
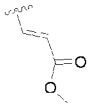
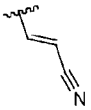
P10	C-H	C-C_3H_6OH	C-H	C-H			N
P11	C-H	C-H	C-H	C-H			C-H
P12	C-H	C-H	C-H	C-H			C-H

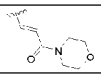
	X_4-R_1	X_5-R_1	X_6-R_1	X_7-R_1	R_2	R_3	Y_7-R_4
P13	C-H	C-H	C-H	C-H			N
P14	C-H	N	C-H	C-H			N



	X_4-R_1	X_5-R_1	R_2	R_3	Y_7-R_4
P15	CH	N			N
P16	CH	N			N

	X_4-R_1	X_5-R_1	R_2	R_3	Y_7-R_4
P17	CH	N			N
P18	CH	N			N

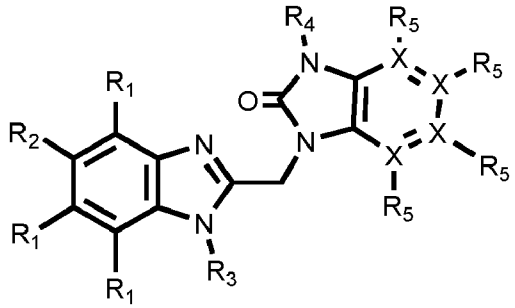
	X_4-R_1	X_5-R_1	R_2	R_3	Y_7-R_4
P19	CH	C-Cl			N
P20	CH	C-Cl			N
P21	CH	C-Cl			N

	X_4-R_1	X_5-R_1	R_2	R_3	Y_7-R_4
P22	CH	C-Cl			N
P23	CH	C-Cl			N
P24	CH	C-Cl			N
P25	CH	CH			N

	X_4-R_1	X_5-R_1	R_2	R_3	Y_7-R_4
P26	CH	C-Cl			N
P27	CH	CH			N

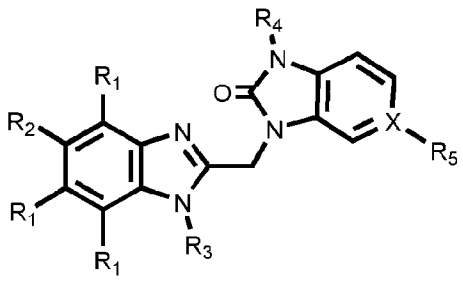
Compounds of Formula (B9)

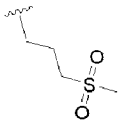
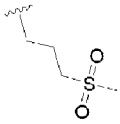
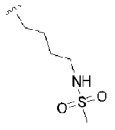
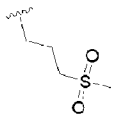
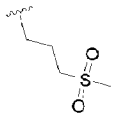
[0128] Compounds of the general Formula (B9) are described in PCT Publication No. WO 2012/080446, published June 21, 2012, which is hereby incorporated by reference in its entirety. Formula (B9) has the structure:

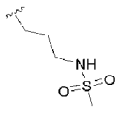
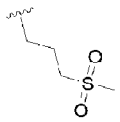
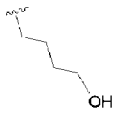
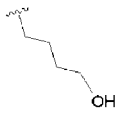
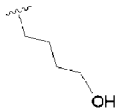


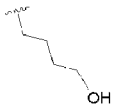
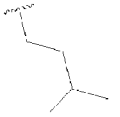
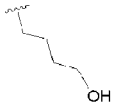
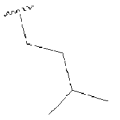
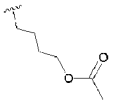
or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: each X independently can be C or N; R_1 can be H; R_2 can be selected from Br and Cl; R_3 can be $-(CR_6R_7)_n-R_8$; R_4 can be selected from H, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $-(CR_6R_7)_n-R_8$, $-CH_2$-p-Fluorophenyl, CH_2CF_3 and $-SO_2CH_3$; R_5 is present where X is C, whereby each R_5 can be selected, each independently, from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, and CN; R_5 is absent where X is N; R_6 and R_7 can be each independently chosen from H and C_1-C_{10} alkyl, C_3-C_7 cycloalkyl; or R_6 and R_7 can be taken together form a 5 to 6 membered aliphatic or aromatic ring that optionally contains one or more heteroatoms selected from the group N, S, O; R_8 can be selected from H, OH, CF_3, CHF_2, F, CI, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR_6SO_2R_6$, $SO_2R_6R_7$, $R_6SO_2C_3$-C_7 cycloalkyl, CN, NR_6R_7, COOH, $COOR_6$, $CONR_6R_7$, $OCOC_1$-C_6 alkyl, $CONR_6SOR_7$, CONH-R_6-SO_2R_7 , CONH-R_6-$SO_2NR_6R_7CONR_6SO_2NR_6R_7$, phtalimido or a 5 to 6 membered aliphatic or aromatic ring that optionally contains one or more heteroatoms selected from the group N, S, O; n can be an integer having a value from 1 to 6.

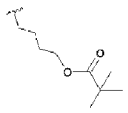
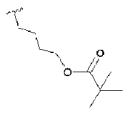
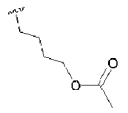
[0129] Examples of Compounds of Formula (B9) include:

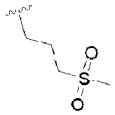
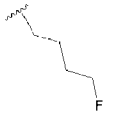
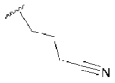
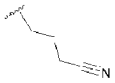


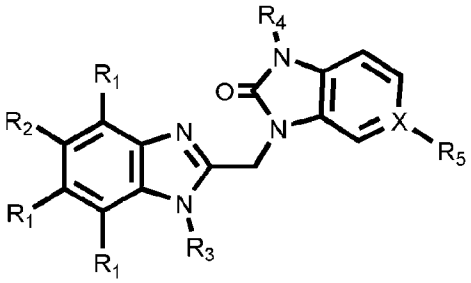
	R_1	R_2	R_3	R_4	$X\text{-}R_5$
P1	H	Br			N
P2	H	Br			N
P3	H	Br			C-F
P4	H	Br			N
P5	H	Br			N
P6	H	Cl			N
P7	H	Br			C-H
P8	H	Br			N

	R_1	R_2	R_3	R_4	$X\text{-}R_5$
P9	H	Br			N
P10	H	Cl			C-F
P11	H	Cl			C-F
P12	H	Cl			C-H
P13	H	Cl			N

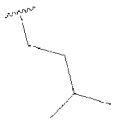
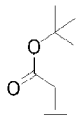
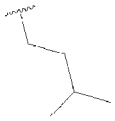
	R_1	R_2	R_3	R_4	$X\text{-}R_5$
P14	H	Br			N
P15	H	Cl			N
P16	H	Br			C-F
P17	H	Br			N
P18	H	Br			N

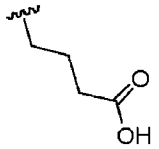
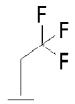
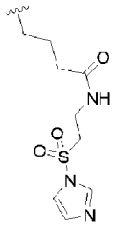
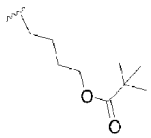
	R_1	R_2	R_3	R_4	X-R_5
P19	H	Cl			C-H
P20	H	Cl			C-F
P21	H	Br			N
P22	H	Br			C-F
P23	H	Br			C-F

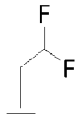
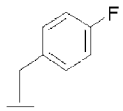
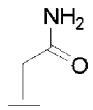
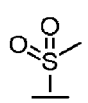
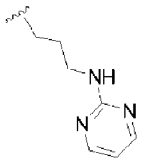
	R_1	R_2	R_3	R_4	X-R_5
P24	H	Cl			C-H
P25	H	Cl			C-H
P26	H	Cl			N
P27	H	Br			N

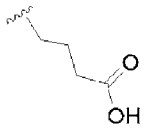
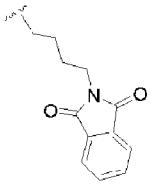
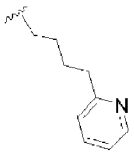
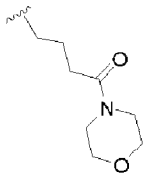


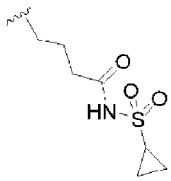
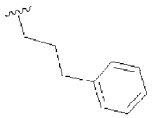
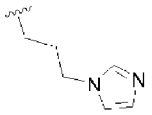
	R_1	R_2	R_3	R_4	X-R_5
P28	H	Cl			C-F
P29	H	Cl			N
P30	H	Cl			N

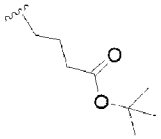
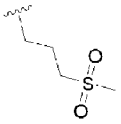
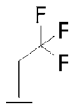
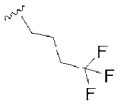
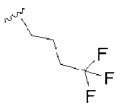
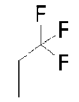
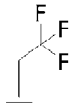
	R_1	R_2	R_3	R_4	X-R_5
P31	H	Cl			N
P32	H	Br			C-F
P33	H	Cl			N
P34	H	Cl			N
P35	H	Cl			CH

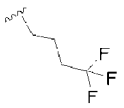
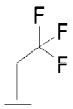
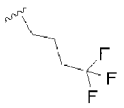
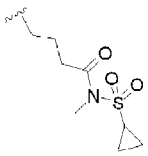
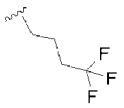
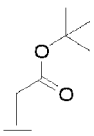
	R_1	R_2	R_3	R_4	X-R_5
P36	H	Br			N
P37	H	Cl			N
P38	H	Br			N
P39	H	Cl			N

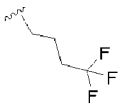
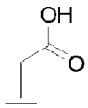
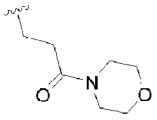
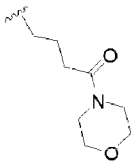
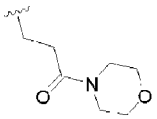
	R_1	R_2	R_3	R_4
P40	H	Cl		
P41	H	Cl		
P42	H	Cl		
P43	H	Cl		
P44	H	Cl		

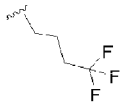
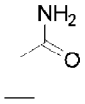
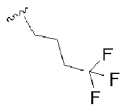
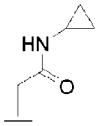
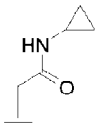
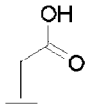
	R_1	R_2	R_3	R_4
P45	H	Cl		
P46	H	Cl		
P47	H	Cl		
P48	H	Br		

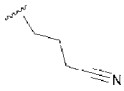
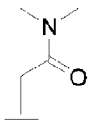
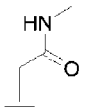
	R_1	R_2	R_3	R_4
P49	H	Cl		
P50	H	Cl		
P51	H	Cl		

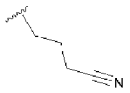
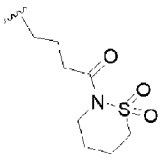
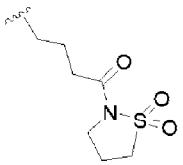
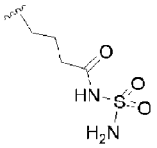
	R_1	R_2	R_3	R_4	X-R_5
P52	H	Cl			N
P53	H	Cl			C-F
P54	H	Cl			N
P55	H	Cl			N
P56	H	Cl			C-F

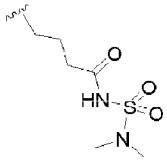
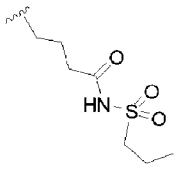
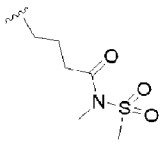
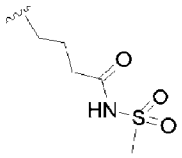
	R_1	R_2	R_3	R_4	X-R_5
P57	H	Cl			C-F
P58	H	Cl			C-F
P59	H	Cl			N
P60	H	Cl			N

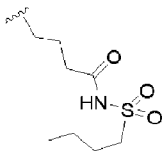
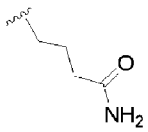
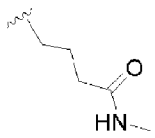
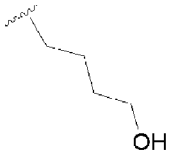
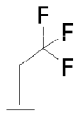
	R_1	R_2	R_3	R_4	X-R_5
P61	H	Cl			N
P62	H	Cl			C-F
P63	H	Cl			N
P64	H	Cl			N

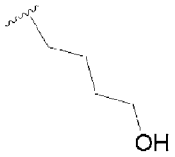
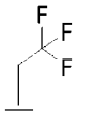
	R_1	R_2	R_3	R_4	X-R_5
P65	H	Cl			N
P66	H	Cl			N
P67	H	Cl			N
P68	H	Cl			N

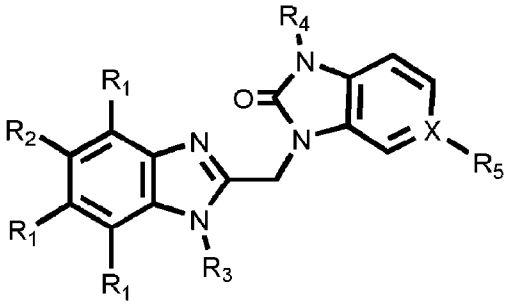
	R_1	R_2	R_3	R_4	X-R_5
P69	H	Cl			C-F
P70	H	Cl			CH
P71	H	Cl			N
P72	H	Cl			N

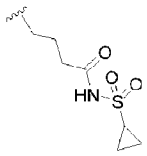
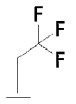
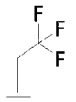
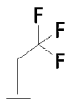
	R_1	R_2	R_3	R_4	X-R_5
P73	H	Cl			C-F
P74	H	Br			N
P75	H	Br			N
P76	H	Br			N

	R_1	R_2	R_3	R_4	X-R_5
E. P77	F. H	G. Br	H. 		N
P78	H	Br			N
P79	H	Br			N
P80	H	Br			N

	R_1	R_2	R_3	R_4	X-R_5
P81	H	Br			N
P82	H	Br			N
P83	H	Br			N
P84	H	Cl			N

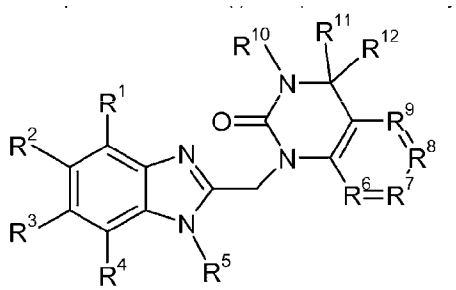
	R_1	R_2	R_3	R_4	X-R_5
P85	H	Cl			C-F



	R_1	R_2	R_3	R_4	X-R_5
P86	H	Cl			C-F
P87	H	Cl			C-F
P88	H	Cl			C-H
P89	H	Cl			N

Compounds of Formula (B10)

[0130] Compounds of the general Formula (B10) are described in PCT Publication No. WO 2010/103306, published September 16, 2010, which is hereby incorporated by reference in its entirety. Formula (B10) has the structure:



wherein: R^1, $R^3$and R^4 each independently can represent H, C1-6 alkyl or halogen; R^2 can represent H, CN, CH_2NH_2, $CH_2NH(CH_2)_3NH_2$, $C(=NH)NH_2$ or $C(=NOH)NH_2$; R^5 can represent C1-6 alkyl; said C1-6 alkyl being optionally substituted with one or more of OR^{13}, CF_3, CN or $NR^{14}R^{15}$ wherein R^{13} can represent H or C1-6 alkyl and R^{14} and R^{15} independently can represent H, C1-6 alkyl or C3-

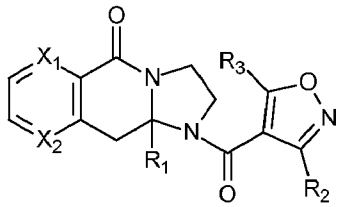
7 cycloalkyl; or the group -$NR^{14}R^{15}$ together can represent a 5 to 7 membered azacyclic ring optionally incorporating one further heteroatom selected from O, S and NR^{19} wherein R^{19} can represent H or C1-6 alkyl; R^6, R^7, R^8 and R^9 each independently can represent CH, C-F, C-Cl, C-CF_3 or N; R^{10} can represent aryl, heteroaryl, C3-7 cycloalkyl or C1-6 alkyl; said C1-6 alkyl or C3-7 cycloalkyl being optionally substituted with one or more of aryl, C3-7 cycloalkyl, OR^{16}, SR^{16}, halogen or $NR^{17}R^{18}$, wherein R^{16} can represent H or C1-6 alkyl and R^{17} and R^{18} each independently can represent H, C1-6 alkyl or C3-7 cycloalkyl; or the group -$NR^{17}R^1$ together represents a 5 to 7 membered azacyclic ring optionally incorporating one heteroatom selected from O, S and NR^{20} wherein R^{20} can represent H or C1-6 alkyl; and R^{11} and R^{12} each independently can represent H or C1-6 alkyl.

[0131] Examples of Compounds of Formula (B10) include: 3-methyl-1-[(1-isopentylbenzimidazol-2-yl)methyl]-4H-quinazolin-2-one; 3-isopentyl-1-[(1-isopentylbenzimidazol-2-yl)methyl]-4H-quinazolin-2-one; 3-cyclopropyl-1-[(1-isopentylbenzimidazol-2-yl)methyl]-4-methyl-4H-quinazolin-2-one; 3-cyclopropyl-1-[(1-isopentylbenzimidazol-2-yl)methyl]-4,4-dimethyl-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-methyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-propyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-tert-butyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopentyl-4H-quinazolin- 2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-benzyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-phenethyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4H-pyrido[2,3- d]pyrimidin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-(2-methoxyethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-isopentyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-isobutyl-4H-quinazolin-2- one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-(cyclopropylmethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-(3-pyrrolidin-1-ylpropyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-(2-methylsulfanylethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-(cyclohexylmethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4-methyl-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-

isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4,4-dimethyl-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-5-(trifluoromethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-5-fluoro-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]-3-methyl-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]-3-cyclopropyl-4H- quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]-3-(2-methoxyethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]-3-(cyclohexylmethyl)-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4,4,4-trifluorobutyl)benzimidazol-2-yl]methyl]-3-cyclopropyl-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4,4,4-trifluorobutyl)benzimidazol-2-yl]methyl]-3-cyclopropyl-4-methyl-4H-quinazolin-2-one; 1-[[5-(aminomethyl)-1-(4,4,4-trifluorobutyl)benzimidazol-2-yl]methyl]-3-cyclopropyl-4,4- dimethyl-quinazolin-2-one; 1-[[5-[(3 -aminopropylamino)methyl]-1-isopentyl-benzimidazol-2-yl]methyl]-3-methyl-4H-quinazolin-2-one; 1-[[5-[(3-aminopropylamino)methyl]-1-isopentyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4H-quinazolin-2-one; 1-[[5-[(3-aminopropylamino)methyl]-1-isopentyl-benzimidazol-2-yl]methyl]-3-(2-methoxyethyl)-4H-quinazolin-2-one; 1-[[5-[(3-aminopropylamino)methyl]-1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]-3- methyl-4H-quinazolin-2-one; 2-[(3-cyclopropyl-2-oxo-4H-quinazolin-1-yl)methyl]-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4-methyl-2-oxo-4H-quinazolin-1-yl)methyl]-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4,4-dimethyl-2-oxo-quinazolin-1-yl)methyl]-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-2-oxo-4H-quinazolin-1-yl)methyl]-N'-hydroxy-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4-methyl-2-oxo-4H-quinazolin-1-yl)methyl]-N'-hydroxy-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4,4-dimethyl-2-oxo-quinazolin-1-yl)methyl]-N'-hydroxy-1-isopentyl-benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-2-oxo-4H-quinazolin-1-yl)methyl]-1-(4,4,4-trifluorobutyl)benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4-methyl-2-oxo-4H-quinazolin-1-yl)methyl]-1-(4,4,4-trifluorobutyl)benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4,4-dimethyl-2-oxo-quinazolin-1-yl)methyl]-1-(4,4,4-trifluorobutyl)benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4-methyl-2-oxo-4H-quinazolin-1-yl)methyl]-N'-hydroxy-1-(4,4,4-trifluorobutyl)benzimidazole-5-carboxamidine; 2-[(3-cyclopropyl-4,4-dimethyl-2-oxo-quinazolin-1-yl)methyl]-N'-hydroxy-1-(4,4,4-trifluorobutyl)benzimidazole-5-carboxamidine; and 1-[[5-(aminomethyl)-1-isopentyl-6-methyl-benzimidazol-2-yl]methyl]-3-cyclopropyl-4H-quinazolin-2-one.

Compounds of Formula (B11)

[0132] Compounds of the general Formula (B11) are described in PCT Publication No. WO 2012/068622, published May 31, 2012, which is hereby incorporated by reference in its entirety. Formula (B11) has the structure:



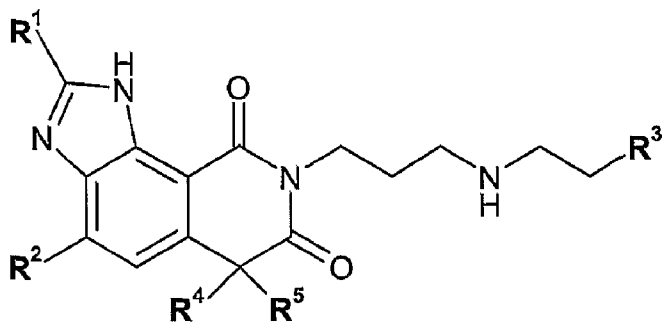
or racemates, isomers and/or salts thereof, wherein: X_1 and X_2 can be independently selected from CH and N wherein at least one of X_1 and X_2 is N; R_1 is optionally substituted and can be selected from a carbocyclic, heterocyclic and aromatic ring; R_2 can be selected from C_1-$_6$ alkyl, haloC_1-$_3$alkyl and C_1-$_3$alkoxy; and R_3 can be H or an optional substituent.

[0133] Examples of Compounds of Formula (B11) include: 5a-(4-chlorophenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8-tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; 10a-(4-chlorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(4-methoxyphenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(4-fluorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a- tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 5a-(4-fluorophenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8-tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; 10a-(4-fluoro-3-methylphenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(3,4-difluorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 5a-(3,4-difluorophenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8- tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; 5a-(4-fluoro-3-methylphenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8-tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; 10a-(2-chlorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-cyclohexyl-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a- tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(4,4-difluorocyclohexyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(4-chlorophenyl)-1-{[3-(trifluoromethyl)-1,2-oxazol-4-yl]carbonyl}-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; 10a-(2,3-dihydro-1-benzofuran-5-yl)-1-[(3-methyl-1,2-oxazol-4-

yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)- one; (5aS)-5a-(4-chlorophenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8-tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; (10aS)-10a-(4-chlorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]- 2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; (10aS)-10a-(4-fluorophenyl)-1-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one; (5aS)-5a-(4-fluorophenyl)-6-[(3-methyl-1,2-oxazol-4-yl)carbonyl]-5a,6,7,8-tetrahydroimidazo[1',2':1,6]pyrido[3,4-b]pyrazin-10(5H)-one; and (10aS)-10a-(4-fluoro-3-methylphenyl)-1-[(3-methyl-1,2-oxazol-4- yl)carbonyl]-2,3,10,10a-tetrahydroimidazo[2,1-g][1,7]naphthyridin-5(1H)-one.

Compounds of Formula (B12)

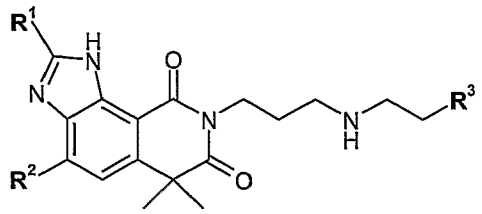
[0134] Compounds of the general Formula (B12) are described in PCT Publication No. WO 2005/042530, published May 12, 2005, which is hereby incorporated by reference in its entirety. Formula (B12) has the structure:

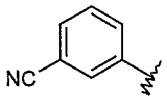
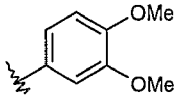
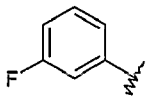
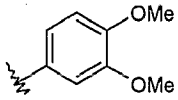
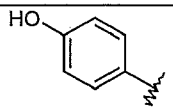
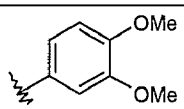
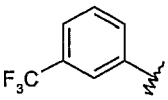
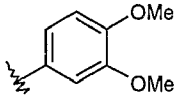


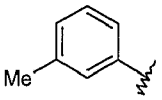
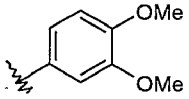
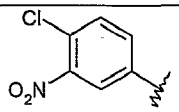
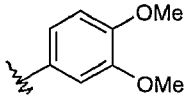
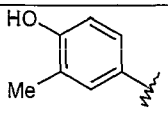
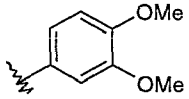
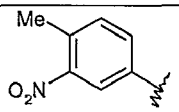
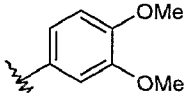
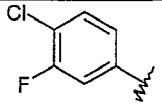
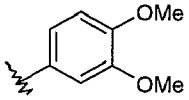
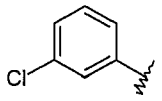
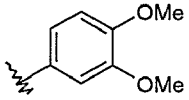
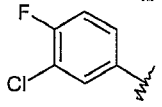
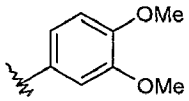
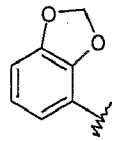
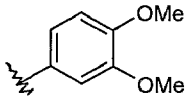
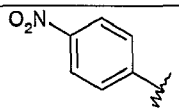
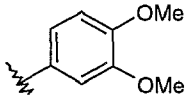
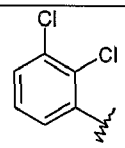
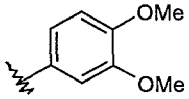
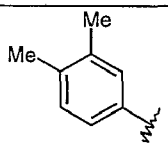
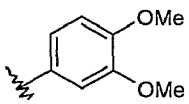
or an enantiomer or a salt thereof, wherein: R^1 can be -(CH=CH)$_{0-1}$-(C_6 or C_{10})aryl or -(CH=CH)$_{0-1}$-5-, 6-, 9- or 10- membered heteroaryl, said aryl or heteroaryl being optionally substituted with one, two or three substituents, each independently selected from: (C_{1-6})alkyl optionally substituted with amino, halo, (C_{1-6})haloalkyl, hydroxy, (C_{1-6})alkoxy, (C_{1-6})alkylthio, nitro, azido, cyano, amino,(C_{1-6})alkylamino, di((C_{1-6})alkyl)amino, aryl and heteroaryl; R^2 can be H, (C_{1-6})alkyl, hydroxy, halo, (C_{1-6})haloalkyl, amino, (C_{1-6})alkylamino. di((C_{1-6})alkyl)amino, or (C_{2-6})alkynyl; R^3 can be (C_6, C_{10} or C_{14})aryl or 5-, 6-, 9- or 10-membered heteroaryl, each of which being optionally substituted with one, two or three substituents, each independently selected from: (C_{1-6})alkyl, halo, (C_{1-6})haloalkyl, hydroxy, (C_{1-6})alkoxy, (C_{1-6})alkylthio, nitro, amino, (C_{1-6})alkylamino, di((C_{1-6})alkyl)amino and COO(C_{1-6})alkyl; and R^4 and R^5 can be each independently H or (C_{1-6})alkyl; or R^4 and R^5 can be linked, together with the carbon atom to which they are attached, to form a (C_{3-7})cycloalkyl group;

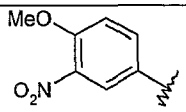
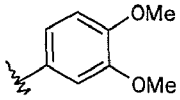
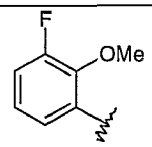
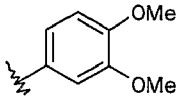
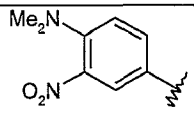
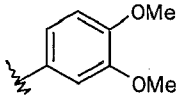
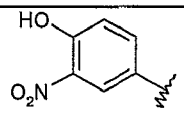
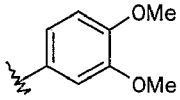
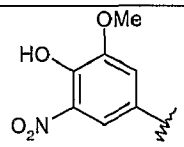
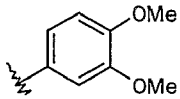
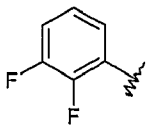
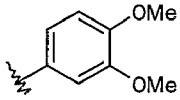
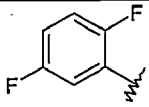
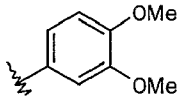
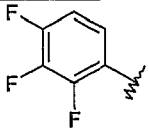
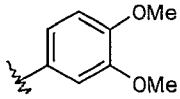
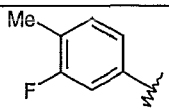
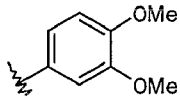
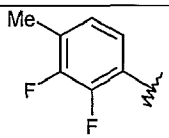
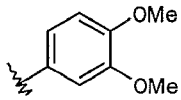
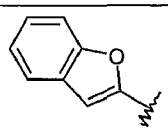
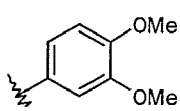
with the proviso that R^1 is not 2-methoxyphenyl, when R^2 is H, R^3 is 3,4-dimethoxyphenyl, R^4 is CH_3 and R^5 is CH_3.

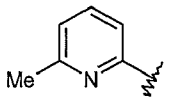
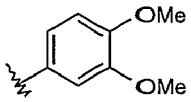
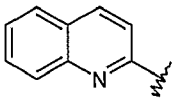
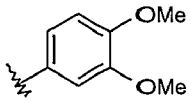
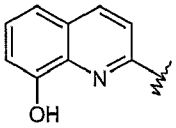
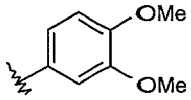
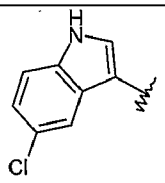
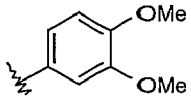
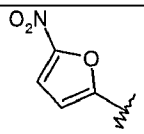
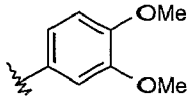
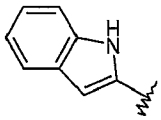
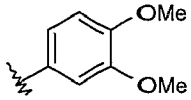
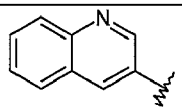
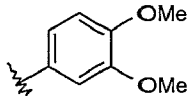
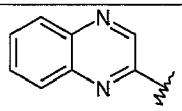
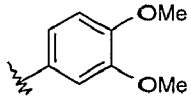
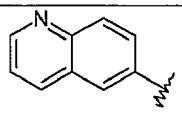
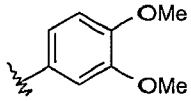
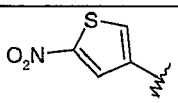
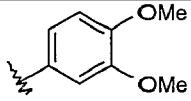
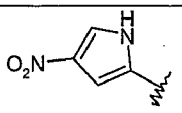
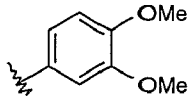
[0135] Examples of Compounds of Formula (B12) include:

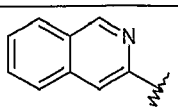
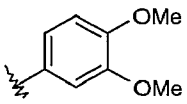
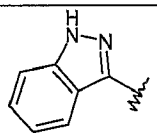
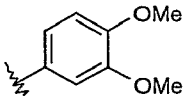
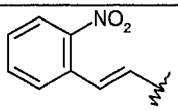
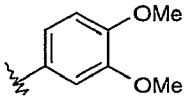
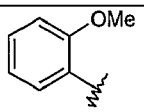
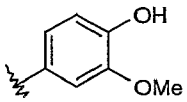
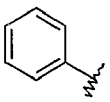
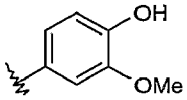
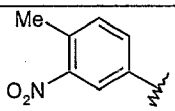
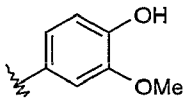
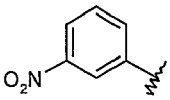
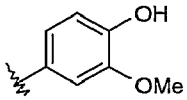
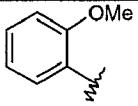
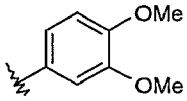
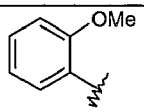
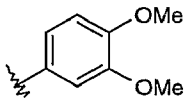
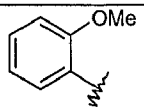
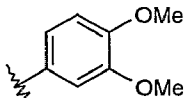
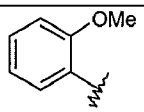
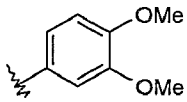
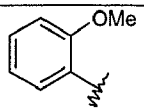
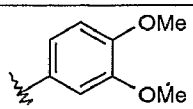


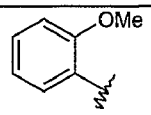
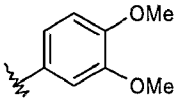
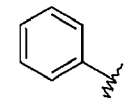
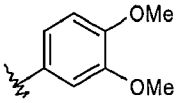
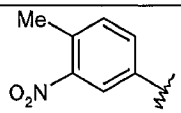
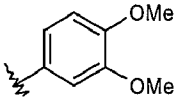
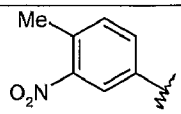
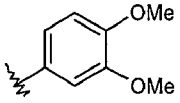
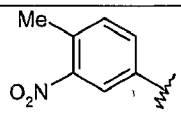
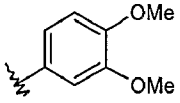
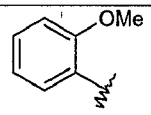
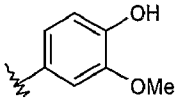
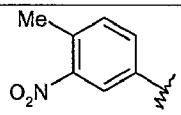
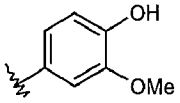
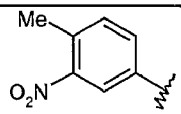
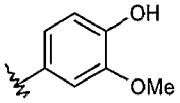
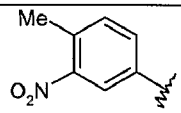
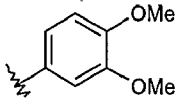
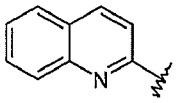
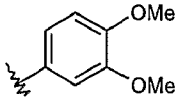
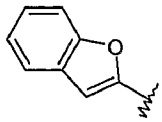
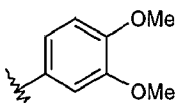
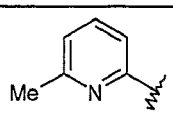
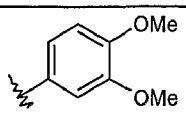
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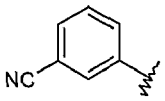
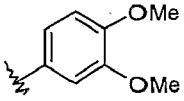
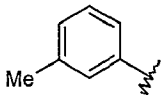
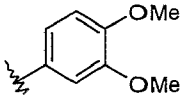
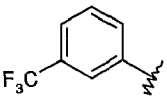
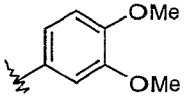
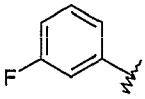
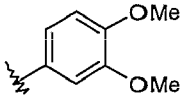
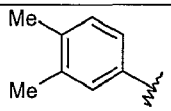
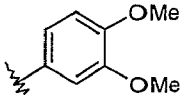
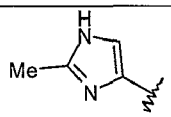
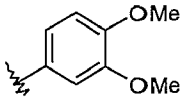
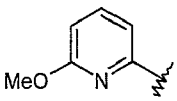
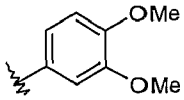
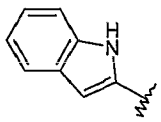
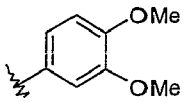
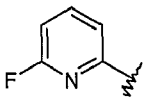
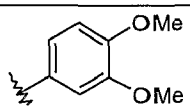
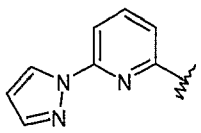
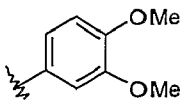
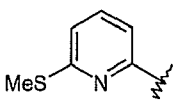
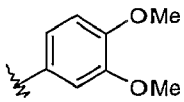
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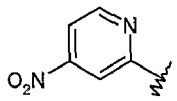
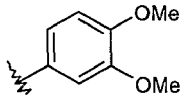
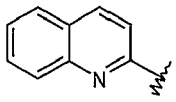
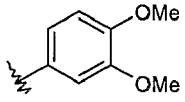
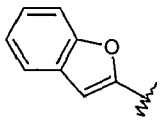
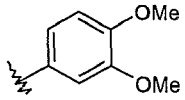
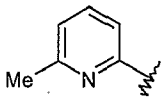
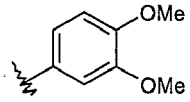
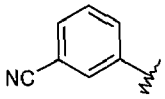
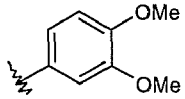
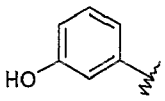
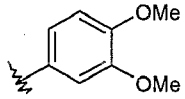
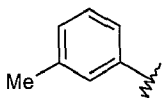
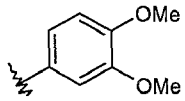
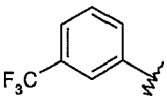
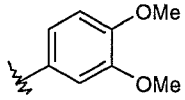
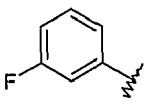
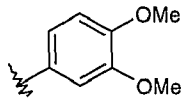
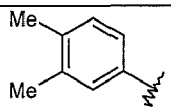
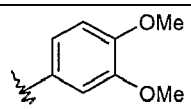
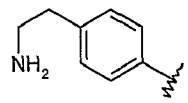
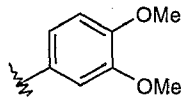
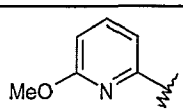
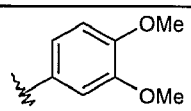
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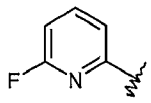
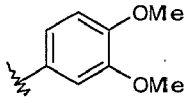
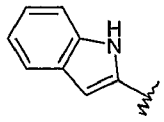
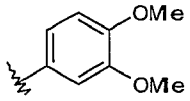
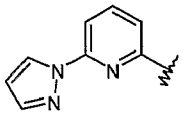
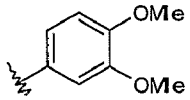
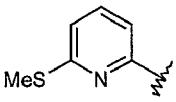
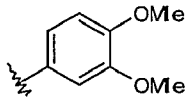
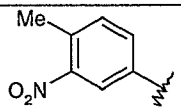
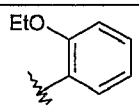
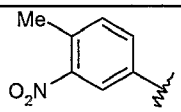
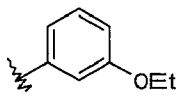
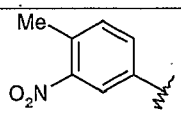
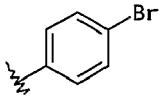
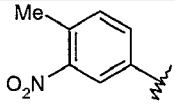
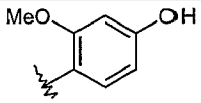
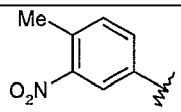
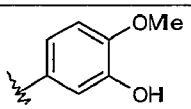
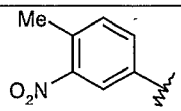
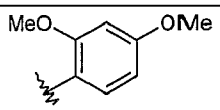
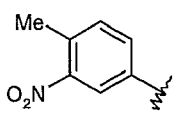
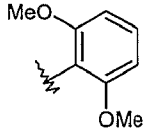
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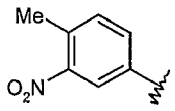
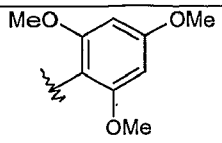
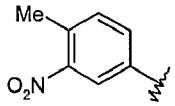
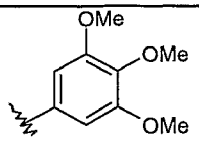
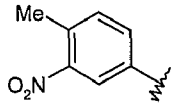
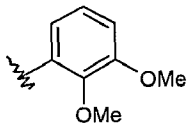
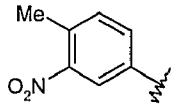
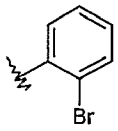
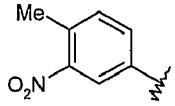
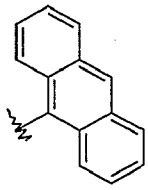
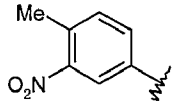
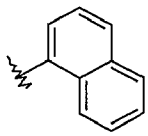
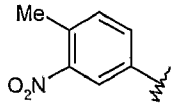
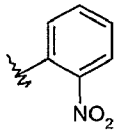
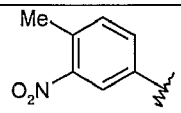
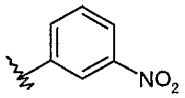
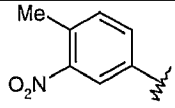
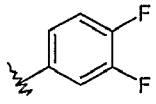
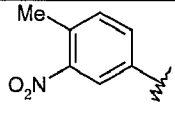
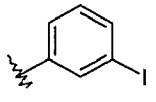
Cpd entry #	R^1	R^2	R^3
1039		H	
1040		H	
1041		H	
1042		H	
1043		H	
1044		H	
1045		H	
1046		Br	
1047		Et	
1048		NH_2	
1049		C≡CH	
1050		NHMe	

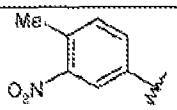
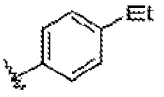
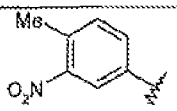
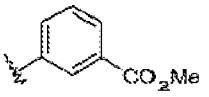
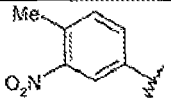
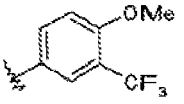
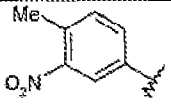
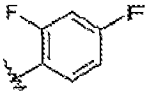
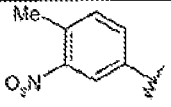
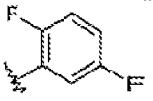
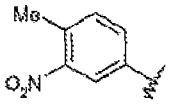
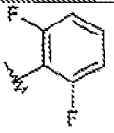
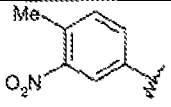
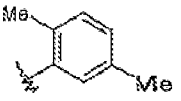
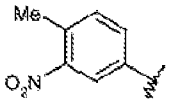
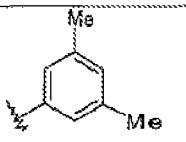
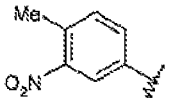
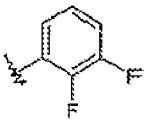
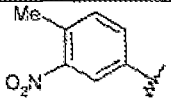
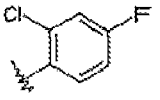
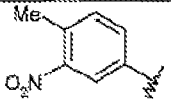
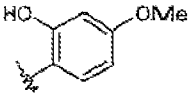
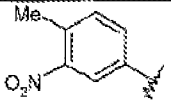
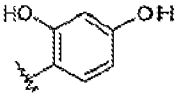
Cpd entry #	R^1	R^2	R^3
1051		Me	
1052		Br	
1053		Br	
1054		Cl	
1055		OH	
1056		Br	
1057		Br	
1058		NH_2	
1059		NH_2	
1060		Br	
1061		Br	
1062		Br	

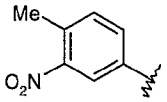
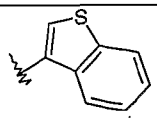
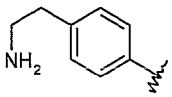
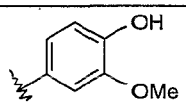
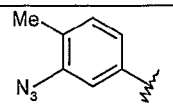
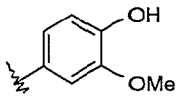
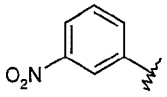
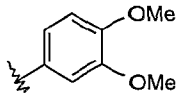
Cpd entry #	R^1	R^2	R^3
1063		Br	
1064		Br	
1065		Br	
1066		Br	
1067		Br	
1068		Br	
1069		Br	
1070		Br	
1071		Br	
1072		Br	
1073		Br	

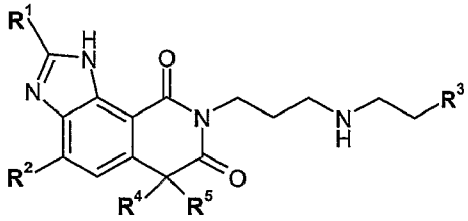
Cpd entry #	R^1	R^2	R^3
1074		Br	
1075		NH_2	
1076		NH_2	
1077		NH_2	
1078		NH_2	
1079		NH_2	
1080		NH_2	
1081		NH_2	
1082		NH_2	
1083		NH_2	
1084		NH_2	
1085		NH_2	

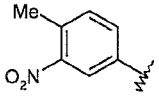
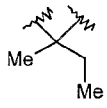
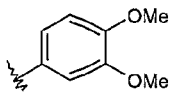
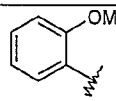
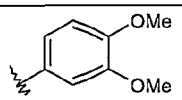
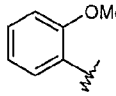
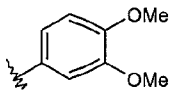
Cpd entry #	R^1	R^2	R^3
1086		NH_2	
1087		NH_2	
1088		NH_2	
1089		NH_2	
1090		Br	
1091		Br	
1092		Br	
1093		Br	
1094		Br	
1095		Br	
1096		Br	

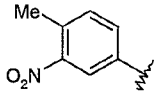
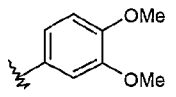
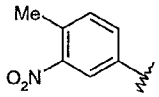
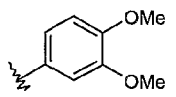
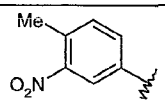
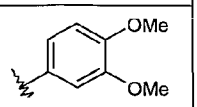
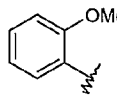
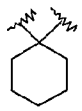
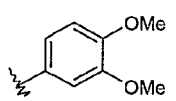
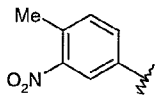
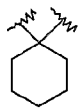
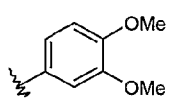
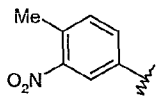
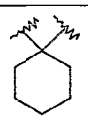
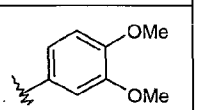
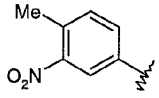
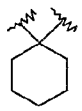
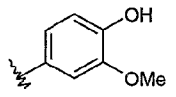
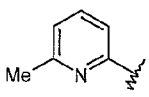
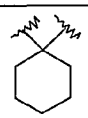
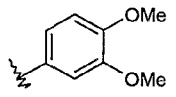
Cpd entry #	R^1	R^2	R^3
1097		Br	
1098		Br	
1099		Br	
1100		Br	
1101		Br	
1102		Br	
1103		Br	
1104		Br	
1105		Br	
1106		Br	

Cpd entry #	R^1	R^2	R^3
1107		Br	
1108		Br	
1109		Br	
1110		Br	
1111		Br	
1112		Br	
1113		Br	
1114		Br	
1115		Br	
1116		Br	
1117		Br	
1118		Br	

Cpd entry #	R^1	R^2	R^3
1129		Br	
1130		NH_2	
1131		NH_2	
1132		H	

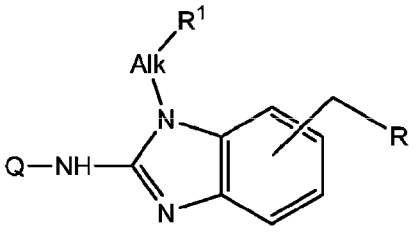


Cpd entry #	R^1	R^2	R^4 R^5	R^3
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2002		H		
2003		H		

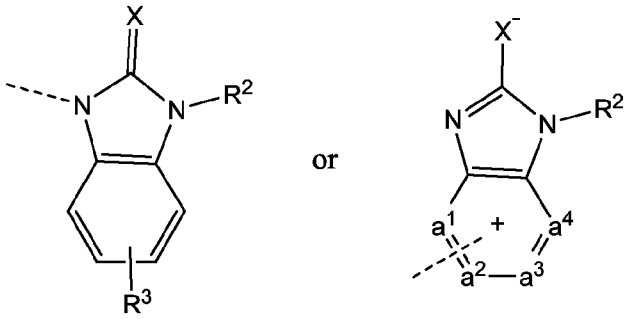
Cpd entry #	R^1	R^2	R^4 R^5	R^3	
2004		H			;
2005		Br			;
2006		NH_2			;
2007		H			;
2008		Br			;
2009		NH_2			;
2010		NH_2			or
2011		NH_2			.

Compounds of Formula (B13)

[0136] Compounds of the general Formula (B13) are described in PCT Publication No. WO 2006/136561, published December 28, 2006, which is hereby incorporated by reference in its entirety. Formula (B13) has the structure:



or a salt or a stereochemically isomeric form thereof, wherein: R can be a radical of formula

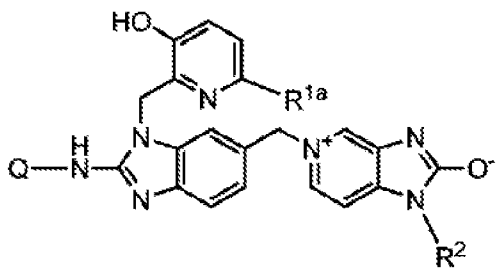


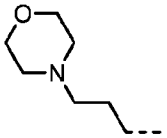
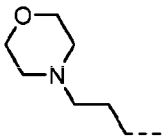
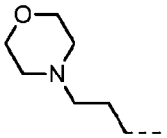
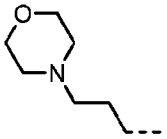
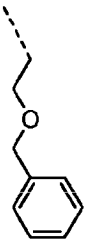
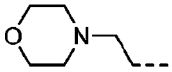
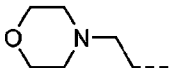
(a) (b)

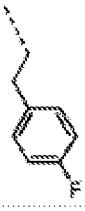
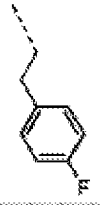
Q can be hydrogen or C_{1-6}alkyl optionally substituted with a heterocycle or Q is C_{1-6}alkyl substituted with both a radical -OR^4 and a heterocycle; wherein said heterocycle is selected from oxazolidine, thiazolidine, 1-oxo-thiazolidine, 1,1-dioxothiazolidine, morpholinyl, thiomorpholinyl, 1-oxo-thiomorpholinyl,1,1-dioxothiomorpholinyl, hexahydrooxazepine, hexahydrothiazepine, 1-oxo- hexahydrothiazepine, 1,1-dioxo-hexahydrothiazepine, pyrrolidine, piperidine, homopiperidine, piperazine; wherein each of said heterocycle may be optionally substituted with one or two substituents selected from the group consisting of C_{1-6}alkyl, hydroxyC_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, hydroxy, carboxyl, C_{1-6} alkyloxycarbonyl, aminocarbonyl, mono- or di(C_{1-6}alkyl)aminocarbonyl, C_{1-6}alkylcarbonylamino, aminosulfonyl and mono- or di(C_{1-6}alkyl)aminosulfonyl; Alk can be C_{1-6} alkanediyl; X can be O or S; -a^1=a^2-a^3=a^4- can be a bivalent radical of formula -N=CH-CH=CH-, -CH=N-CH=CH-, -CH=CH-N=CH- or -CH=CH-CH=N-; wherein one of the nitrogen atoms bears the chemical bond linking radical (b) with the rest of the molecule; R^1 can be Ar or a heterocycle selected from pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl,

benzoxazolyl, benzothiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]- pyridinyl, imidazo[1,2-a]pyridinyl and 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl; wherein each of said heterocycle may optionally be substituted with 1, 2, or 3 substituents each independently selected from halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, hydroxyC_{1-6}alkyloxy, (C_{1-6}alkyl-oxy)C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkyloxycarbonyl, aminocarbonyl, mono- and di- C_{1-6}alkylaminocarbonyl; R^2 can be hydrogen, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, Ar-C_{1-6}alkyloxy-C_{1-6}alkyl, C_{3-7} cycloalkyl, cyano-C_{1-6}alkyl, Ar-C_{1-6}alkyl, Het-C_{1-6}alkyl; R^3 can be hydrogen, C_{1-6}alkyl, cyano, aminocarbonyl, polyhaloC_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl; R^4 can be hydrogen or C_{1-6}alkyl; each Ar independently can be phenyl or phenyl substituted with 1 to 5, such as 1, 2, 3 or 4, substituents selected from halo, hydroxy, amino, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkylcarbonylamino, C_{1-6}alkylsulfonylamino, cyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, aminoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxy, polyhaloC_{1-6}alkyloxy, phenoxy, aminocarbonyl, mono- or di(C_{1-6}alkyl)aminocarbonyl, hydroxycarbonyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkylcarbonyl, amino sulfonyl, mono- and di(C_{1-6}alkyl)- aminosulfonyl; Het can be a heterocycle selected from pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, iuranyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyridinyl and 2,3-dihydro-1,4-dioxino-[2,3-b]pyridyl; wherein each Het may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, amino, mono- or di(C_{1-6}alkyl)amino, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkyloxy.

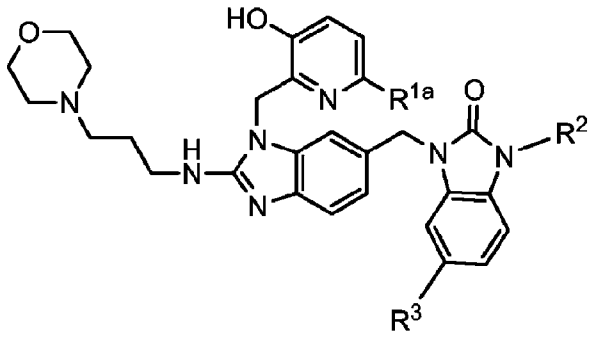
[0137] Examples of Compounds of Formula (B13) include:

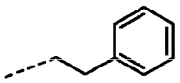
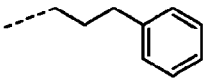


Comp. Nr.	Q	R^{1a}	R^2
a-6			
c-4			
b-4			
d-5			
e-7			
m-9			
n-7			

Comp. Nr.	Q	R^{1a}	R^2
i-3			
h-4			
o-3			
p-3			
g-7			
q-3			
j-4			

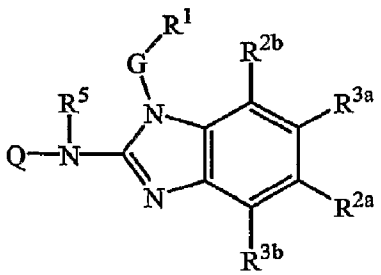
and



Comp. Nr.	R^{1a}	R^2	R^3
k-3			
l-3			
l-4			
f-6			

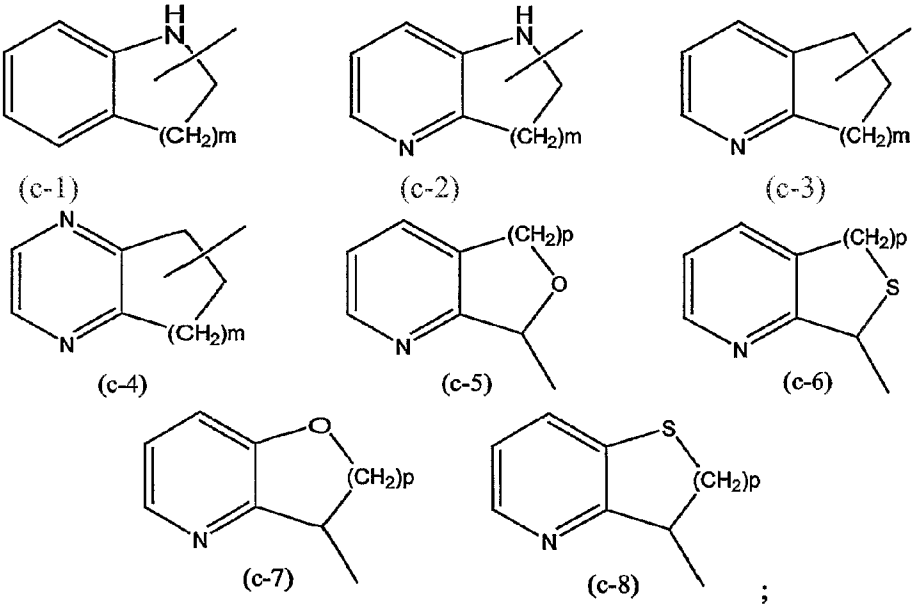
Compounds of Formula (B14)

[0138] Compounds of the general Formula (B14) are described in PCT Publication No. WO 2005/058869, published June 30, 2005, which is hereby incorporated by reference in its entirety. Formula (B14) has the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof, wherein: G can be a direct bond or C_{1-10}alkanediyl optionally substituted with one or more substituents independently selected from hydroxy, C_{1-6}alkyloxy, Ar^1 C_{1-6}alkyloxy,C_{1-6}alkylthio, Ar^1 C_{1-6}alkylthio,$HO(-CH_2-CH_2-O)_n-$, C_{1-6}alkyloxy$(-CH_2-CH_2-O)_a-$ or Ar^1 C_{1-6}alkyloxy$(-CH_2-CH_2-O)n-$; each n independently can be 1, 2, 3 or 4; R^1 can be Ar^1 or a monocyclic or bicyclic heterocycle being selected from piperidinyl, piperazinyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydro- furanyl, thienyl, pynolyl, thiazolyl, oxazolyl,

imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]- pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula



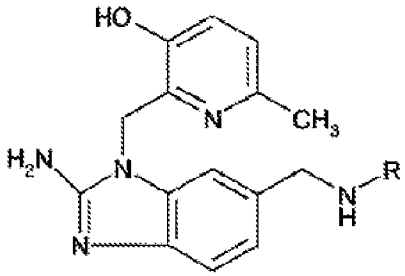
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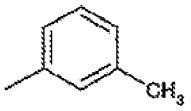
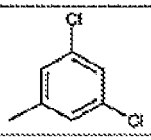
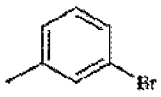
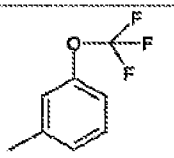
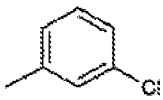
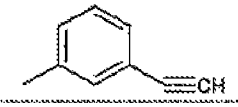
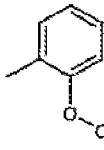
wherein each of said monocyclic or bicyclic heterocycles may optionally be substituted with 1 or where possible more, such as 2, 3, 4 or 5, substituents independently selected from halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyCi-ealkyl, Ar^1, Ar^1C_{1-6}alkyl, Ar^1C_{1-6}alkyloxy, hydroxyC_{1-6}alkyl,mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino,C_{1-6}alkyl-SO_2-NR^{5c}-, Ar^1-SO_2-NR^{5c}-, C_{1-6}alkyloxycarbonyl, -C(=O)-$NR^{5c}R^{5d}$, HO(-CH_2-CH_2-O)$_n$-, halo(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$-, Ar^1C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$- and mono-or di(C_{1-6}alkyl)amino(-CH_2-CH_2-O)$_n$-; each m independently can be 1 or 2; each p independently can be 1 or 2; each t independently can be 0, 1 or 2; Q can be hydrogen, amino or mono- or di(C_{1-4}alkyl)amino; one of R^{2a} and R^{3a} can be selected from halo, optionally mono- or polysubstituted C_{1-6}alkyl, optionally mono- or polysubstituted C_{2-6}alkenyl, nitro, hydroxy, Ar^2, N($R^{4a}R^4$), N($R^{4a}R^{4b}$)sulfonyl, N($R^{4a}R^4$)carbonyl, C_{1-6}alkyloxy, Ar^2oxy, Ar^2C_{1-6}alkyloxy,carboxyl, C_{1-6}alkyloxycarbonyl, or -C(=Z)Ar^2; and the other one of R^{2a} and R^{3a} is hydrogen; wherein =Z is =O, =CH-C(=O) -$NR^{5a}R^{5b}$, =CH_2, =CH- C_{1-6}alkyl, =N-OH or =N-O- C_{1-6}alkyl; and the optional substituents on C_{1-6}alkyl and C_{2-6} alkenyl can be the same or can be different relative to one another, and are each independently selected from hydroxy, cyano, halo, nitro, N($R^{4a}R^{4b}$), N($R^{4a}R^{4b}$)sulfonyl, Het, Ar^2, C_{1-6}alkyloxy, C_{1-6}alkyl-S(=O)$_t$, Ar^2oxy, Ar^2-S(=O)$_t$, Ar^2C_{1-6}alkyloxy, Ar^2C_{1-6}alkyl-S(=O)$_t$, Het-oxy, Het-

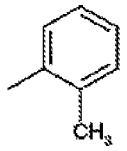
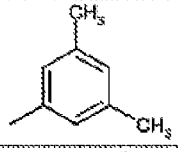
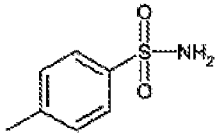
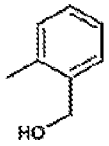
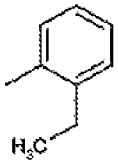
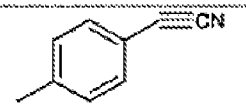
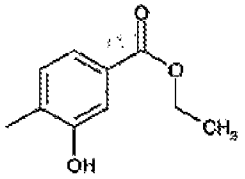
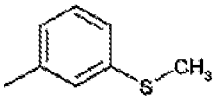
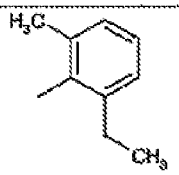
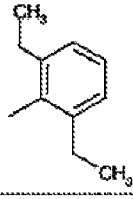
$S(=O)_t$,HetC_{1-6}alkyloxy, HetC_{1-6}alkyl-$S(=O)_t$, carboxyl, C_{1-6}alkyloxycarbonyl and -C(=Z)Ar^2; in case R^{2a} is different from hydrogen then R^{2b} is hydrogen, C_{1-6}alkyl or halogen and R^{3b} is hydrogen; in case R^{3a} is different from hydrogen then R^{3b} is hydrogen, C_{1-6}alkyl or halogen and R^{2b} is hydrogen; R^{4a} and R^{4b} can be the same or can be different relative to one another, and can be each independently selected from hydrogen, C_{1-6}alkyl, Ar^2C_{1-6}alkyl, (Ar^2)(hydroxy) C_{1-6}alkyl, Het-C_{1-6}alkyl, hydroxyC_{1-6}alkyl, mono- and di-(C_{1-6}alkyloxy)C_{1-6}alkyl, (hydroxyC_{1-6}alkyl)oxyC_{1-6}alkyl, Ar^1C_{1-6}alkyloxy-C_{1-6}alkyl, dihydroxyC_{1-6}alkyl, (C_{1-6}alkyloxy)(hydroxy)C_{1-6}alkyl, (Ar^1C_{1-6}alkyloxy)(hydroxy) C_{1-6}alkyl, Ar^1oxy-C_{1-6}alkyl, (Ar^1oxy)(hydroxy)-C_{1-6}alkyl, aminoC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)amino-C_{1-6}alkyl, carboxyl- C_{1-6}alkyl, C_{1-6}alkyloxycarbonylC_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminocarbonylC_{1-6}alkyl, C_{1-6}alkylcarbonylC_{1-6}alkyl, (C_{1-4}alkyloxy)$_2$-P(=O)-C_{1-6}alkyl, (C_{1-4}alkyloxy)$_2$P(=O)-O-C_{1-6}alkyl, aminosulfonyl-C_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminosulfonyl-C_{1-6}alkyl, C_{1-6}alkylcarbonyl, Ar^2carbonyl, Het-carbonyl, Ar^2C_{1-6}alkylcarbonyl, Het-C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, aminosulfonyl, mono- and di(C_{1-6}alkyl)aminosulfonyl, Ar^2sulfonyl, Ar^2C_{1-6}alkylsulfonyl, Ar^2, Het, Het-sulfonyl, HetC_{1-6}alkylsulfonyl; R^{5a} and R^{5b} can be the same or can be different relative to one another, and are each independently hydrogen or C_{1-6}alkyl; or R^{5a} and R^{5b} taken together may form a bivalent radical of formula -$(CH_2)_s$- wherein s is 4 or 5; R^{5c} and R^{5d} can be the same or can be different relative to one another, and are each independently hydrogen or C_{1-6}alkyl; or R^{5c} and R^{5d} taken together may form a bivalent radical of formula -$(CH_2)_s$- wherein s is 4 or 5; R^{6a} can be hydrogen, C_{1-6}alkyl, Ar^1, Ar^1C_{1-6}alkyl, C_{1-6}alkylcarbonyl, Ar^1carbonyl, Ar^1C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, Ar^1sulfonyl, Ar^1C_{1-6}alkylsulfonyl, C_{1-6}alkyloxyC_{1-6}alkyl, aminoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, hydroxyC_{1-6}alkyl, (carboxyl)-C_{1-6}alkyl, (C_{1-6}alkyloxycarbonyl)-C_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminocarbonylC_{1-6}alkyl, aminosulfonyl-C_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminosulfonyl-C_{1-6}alkyl, Het, Het-C_{1-6}alkyl, Het-carbonyl, Het-sulfonyl, Het-C_{1-6}alkylcarbonyl; R^{6b} can be hydrogen, C_{1-6}alkyl, Ar^1 or Ar^1C_{1-6}alkyl; R^{6c} can be C_{1-6}alkyl, Ar^1 or Ar^1C_{1-6}alkyl; Ar^1 can be phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, and C_{1-6}alkyloxy; Ar^2 can be phenyl, phenyl annelated with C_{5-7} cycloalkyl, or phenyl substituted with 1 or more, such as 2, 3, 4 or 5, substituents selected from halo, cyano, C_{1-6}alkyl, Het-C_{1-6}alkyl, Ar^1C_{1-6}alkyl, cyanoC_{1-6}alkyl, C_{2-6}alkenyl, cyanoC_{2-6}alkenyl, R^{6b}-O-C_{3-6}alkenyl, C_{2-6}alkynyl, cyanoC_{2-6}alkynyl, R^{6b}-O-C_{3-6}alkynyl, Ar^1, Het, R^{6b}-O-, R^{6b}-S-, R^{6c}-SO-, R^{6c}-SO_2-, R^{6b}-O-C_{1-6}alkyl-SO_2-, -$N(R^{6a}R^{6b})$, polyhalo-C_{1-6}alkyl, polyhaloC_{1-6}alkyloxy, polyhaloC_{1-6}alkylthio, R^{6c}-C(=O)-, R^{6b}-O-

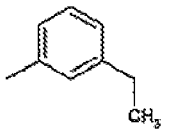
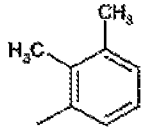
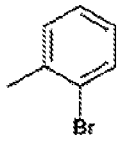
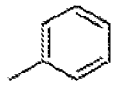
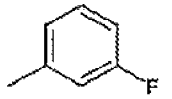
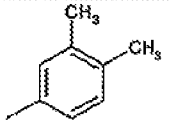
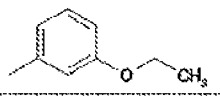
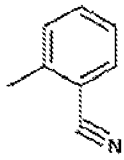
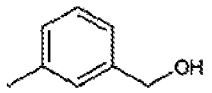
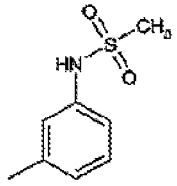
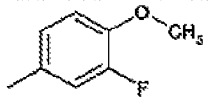
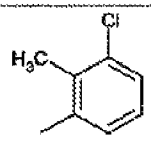
C(=O)-, -N($R^{6a}R^{6b}$)-C(=O)-, R^{6b}-O-C_{1-10}alkyl, R^{6b}-S-C_{1-6}alkyl, R^{6c}-S(=O)$_2$-C_{1-6}alkyl, -N($R^{6a}R^{6b}$)-C_{1-6}alkyl, R^{6c}-C(=O) -C_{1-6}alkyl, R^{6b}-O-C(=O)-C_{1-6}alkyl, N($R^{6a}R^{6}$)-C(=O)-C_{1-6}alkyl, R^{6c}-C(=O)-NR^{6} -, R^{6c}-C(=O) --O-, R^{6c}-C(=O) --$NR^{6b}C_{1-6}$alkyl, R^{6c}-C(=O) --O-C_{1-6}alkyl, N($R^{6a}R^{6b}$)-S(=O)$_2$-, H_2N-C(=NH)-; Het can be a heterocycle being selected from tetrahydrofuranyl, tetrahydrothienyl, pynolidinyl, pynolidinonyl, furanyl, thienyl, pynolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, piperidinyl, homopiperidinyl, piperazinyl, moφholinyl, pyridyl, pyrazinyl, pyridazinyl, pyrirmdinyl, tetrahydroquinolinyl, quinolinyl, isoquinolinyl, benzodioxanyl, benzodioxolyl, indolinyl, indolyl, each of said heterocycle may optionally be substituted with oxo, amino, Ar^{J}, C_{1-4}alkyl, aminoC_{1-4}alkyl, $Ar^{J}C_{1-4}$alkyl, mono- or di(C_{1-6}alkyl)ammoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)amino, (hydroxyC_{1-6}alkyl)amino, and optionally further with one or two C_{1-4}alkyl radicals.

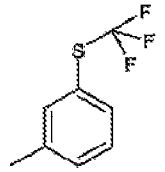
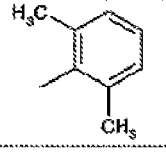
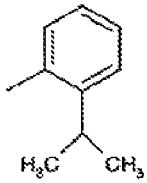
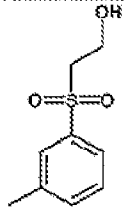
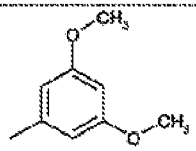
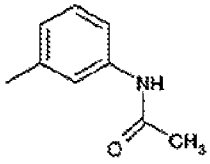
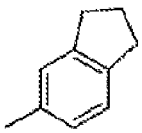
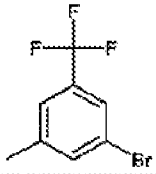
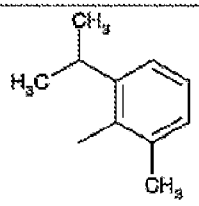
[0139] Examples of Compounds of Formula (B14) include:

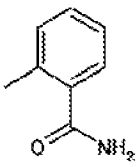
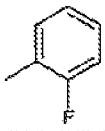
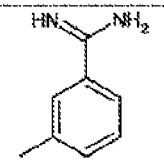
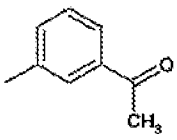
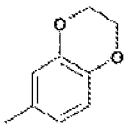
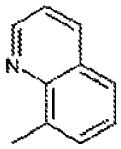
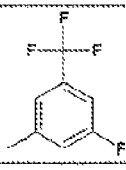
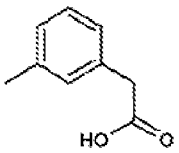
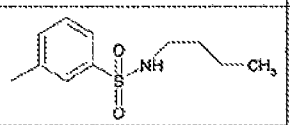
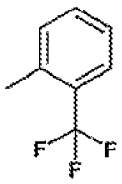


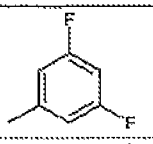
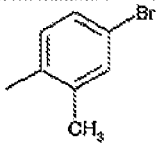
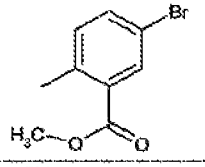
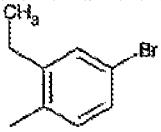
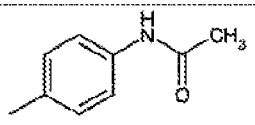
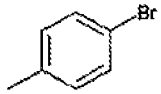
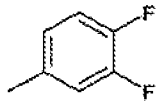
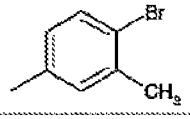
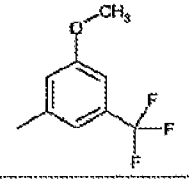
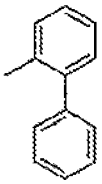
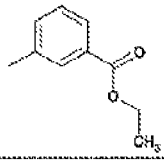
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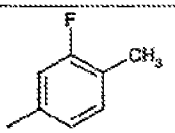
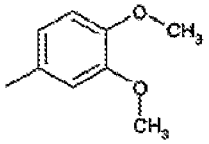
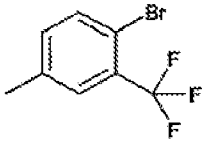
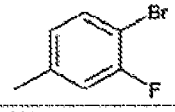
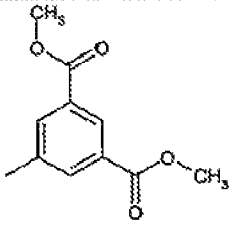
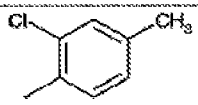
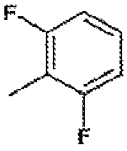
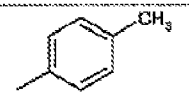
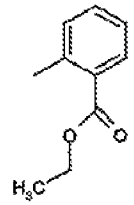
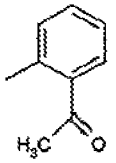
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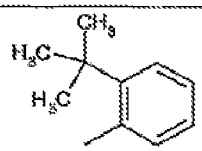
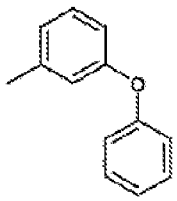
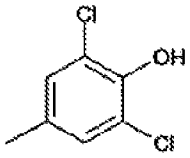
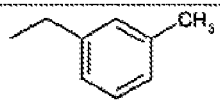
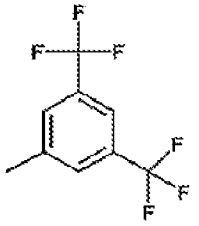
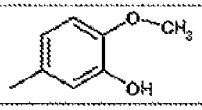
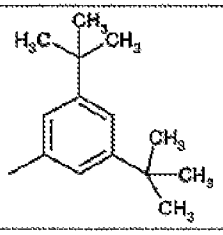
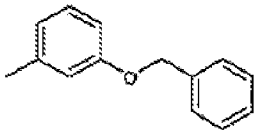
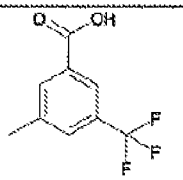
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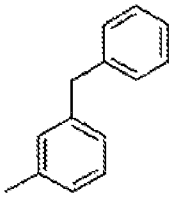
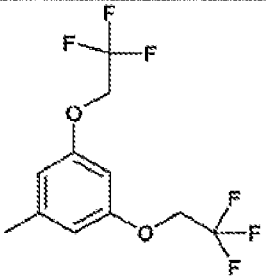
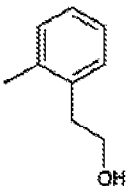
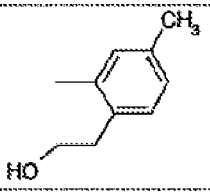
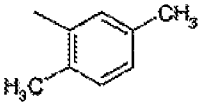
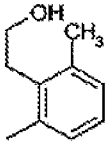
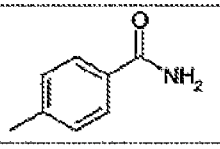
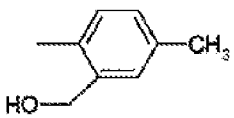
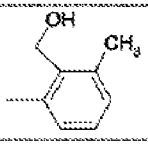
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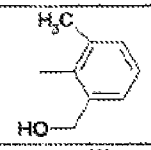
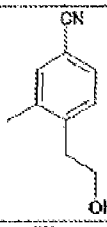
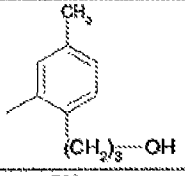
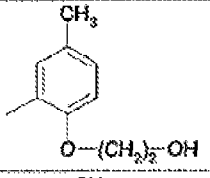
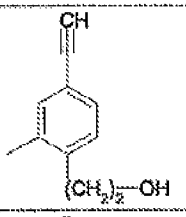
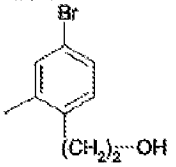
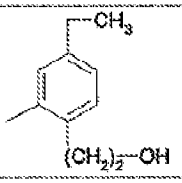
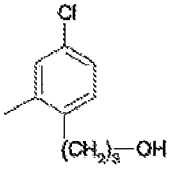
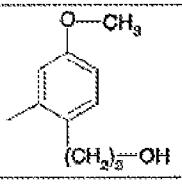
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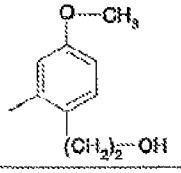
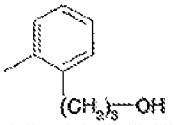
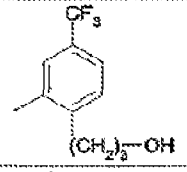
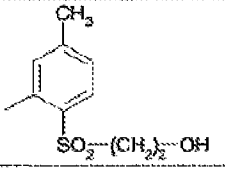
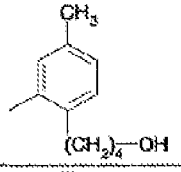
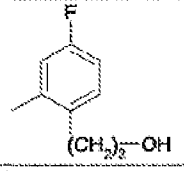
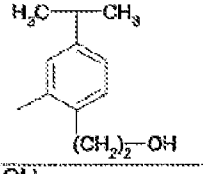
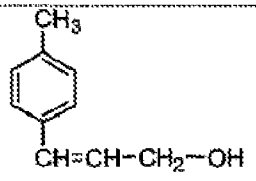
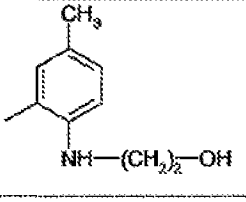
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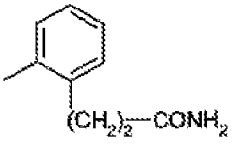
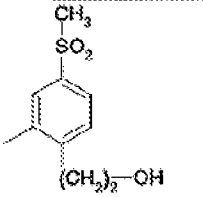
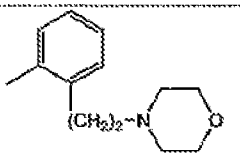
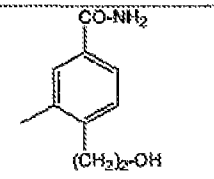
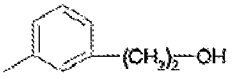
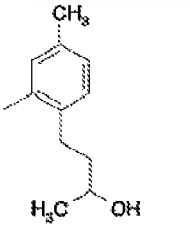
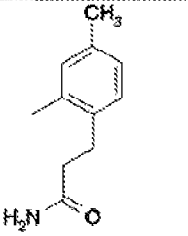
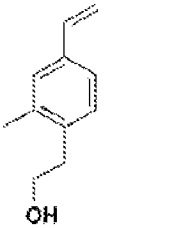
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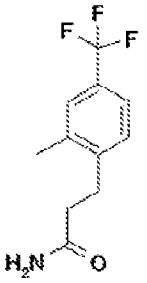
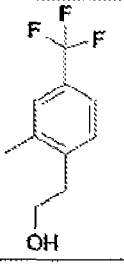
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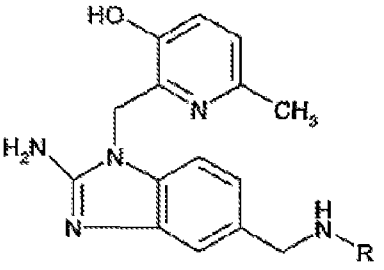
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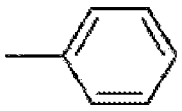
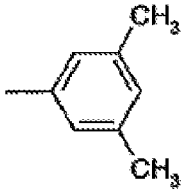
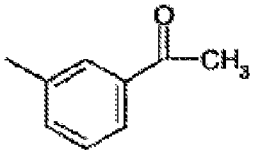
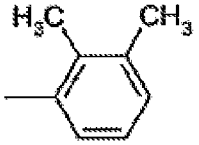
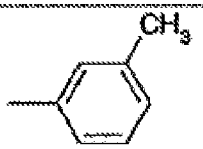
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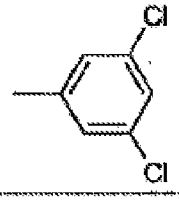
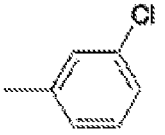
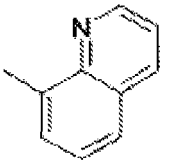
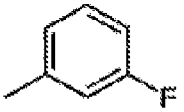
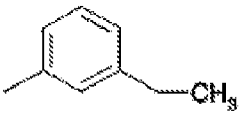
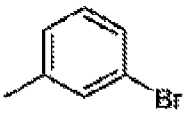
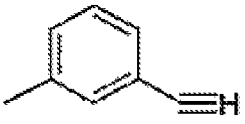
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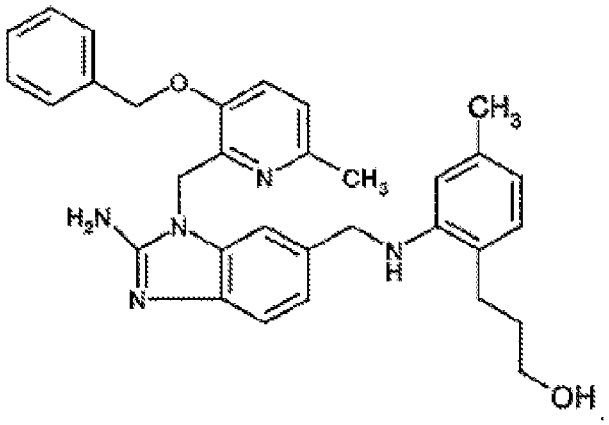
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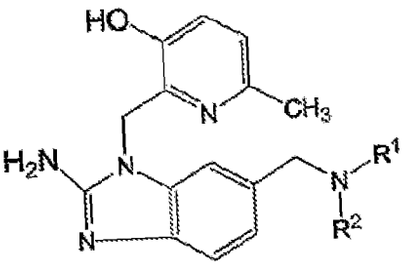


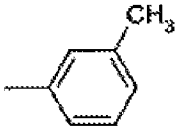
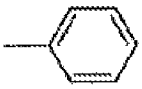
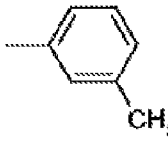
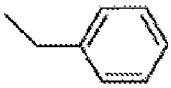
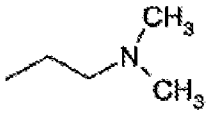
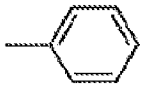
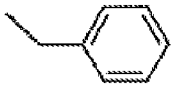
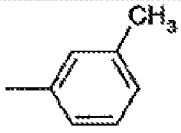
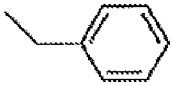
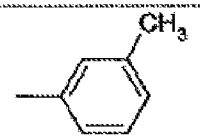
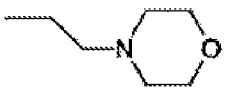
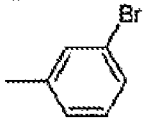
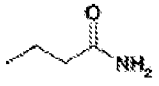
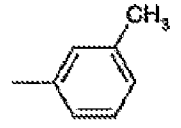
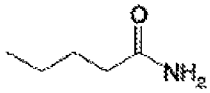
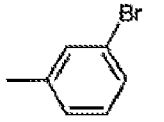
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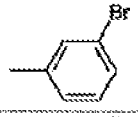
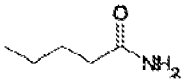
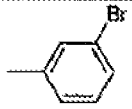
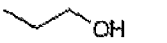
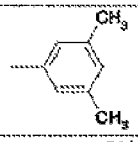
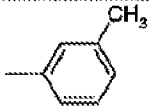
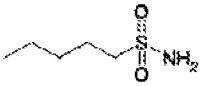
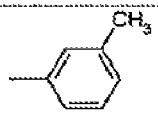
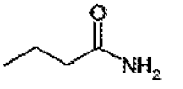
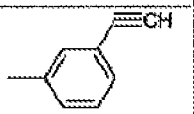
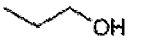
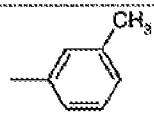
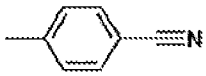
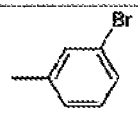
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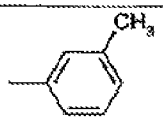
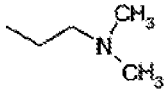
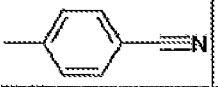
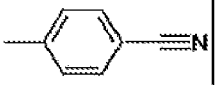
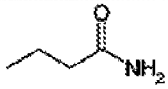
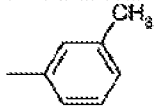
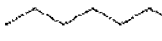
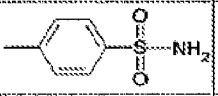
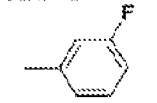
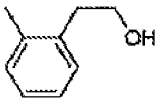
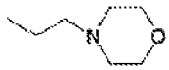
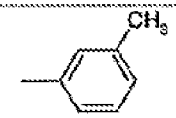
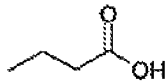
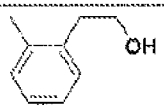
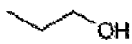
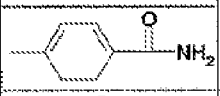
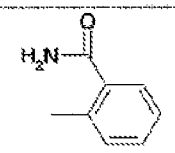
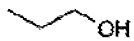
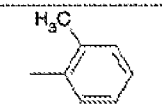
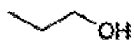
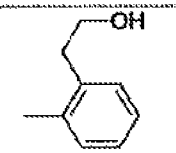
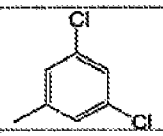


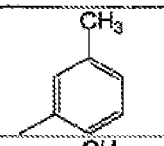
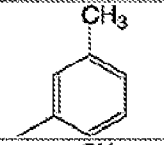
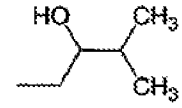
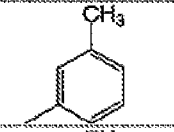
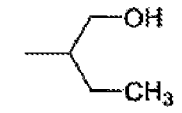
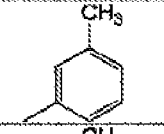
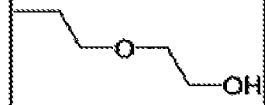
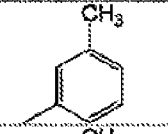
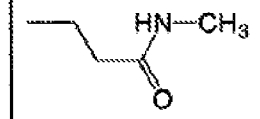
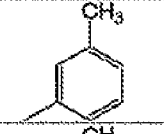
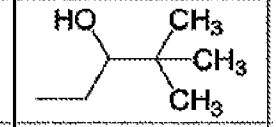
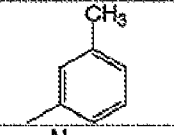
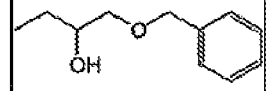
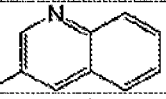
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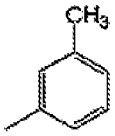
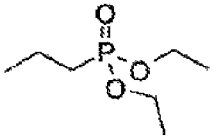
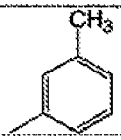
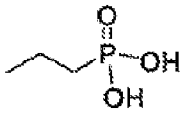

HO
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CH3
H2N
N
N
N
R1
R2

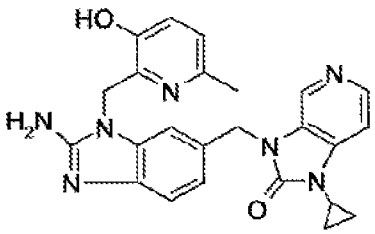
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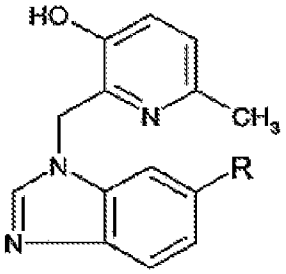
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156		
157		
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162		
163		
164		
165		
166		$-CH_3$
167		$-(CH_2)_2-CO-NH_2$

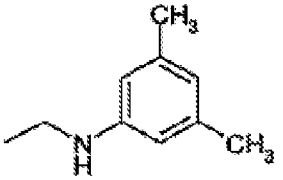
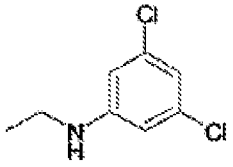
Comp. No.	R^1	R^2
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169		
170		
171		
172		
173		
174		
175		$-(CH_2)_2-OH$
176		
177		
178		$-(CH_2)_2-OH$
179		$-(CH_2)_2-OH$
180		

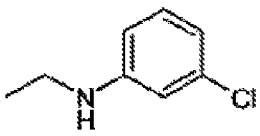
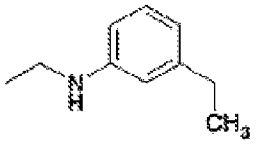
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182		

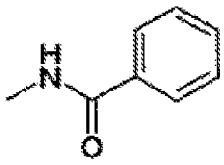
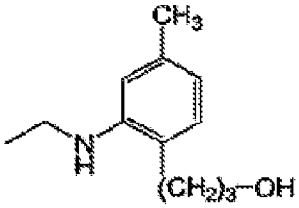
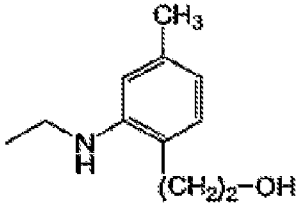
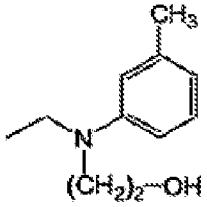


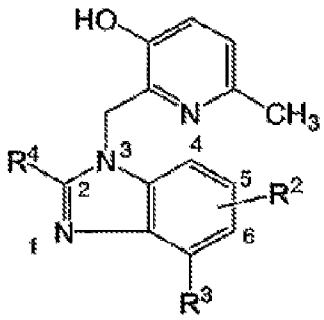
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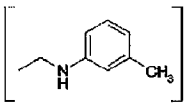
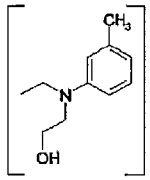
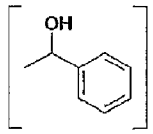
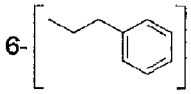
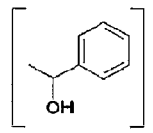
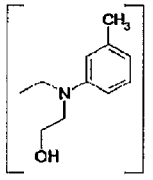


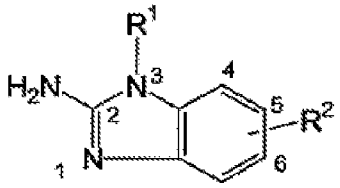
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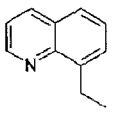
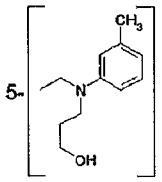
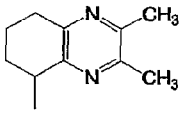
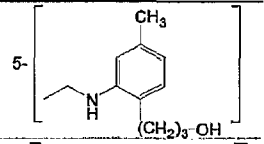
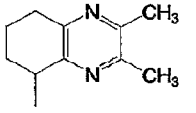
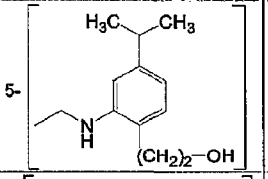
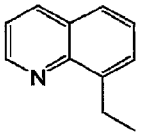
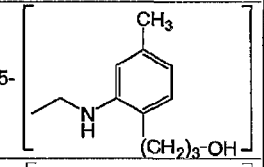
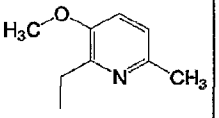
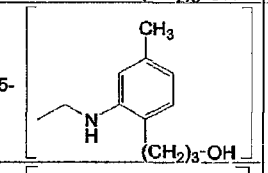
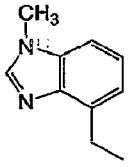
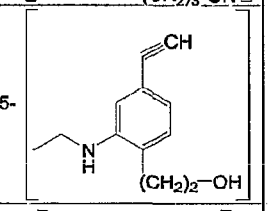
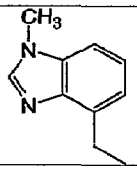
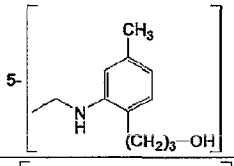
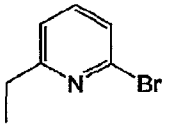
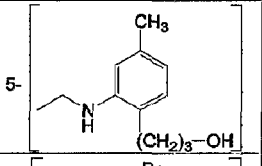
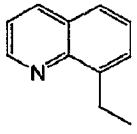
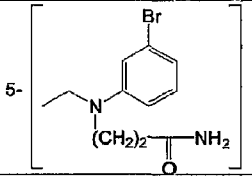
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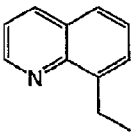
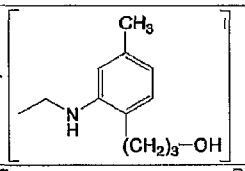
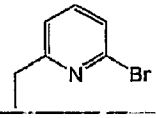
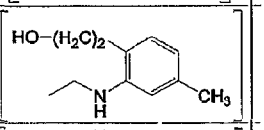
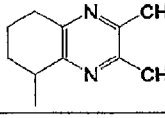
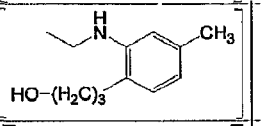
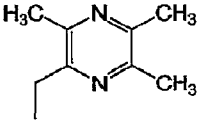
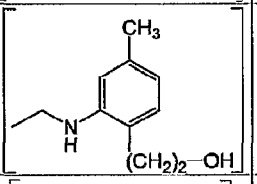
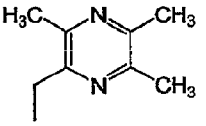
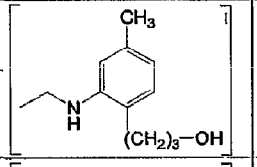
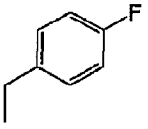
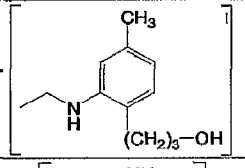
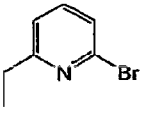
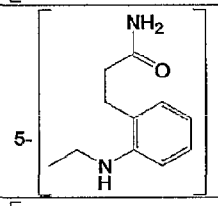
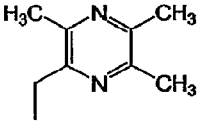
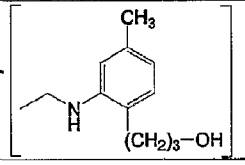
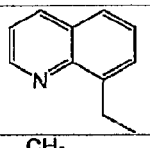
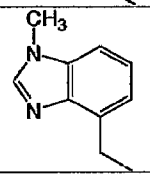
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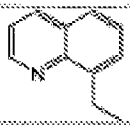
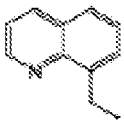
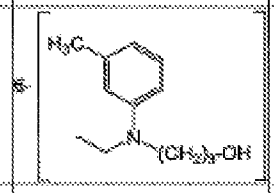
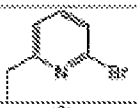
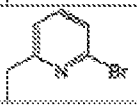
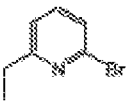
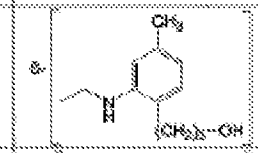
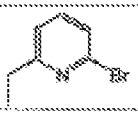
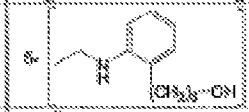
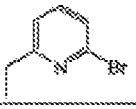
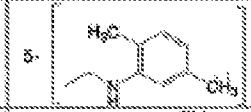
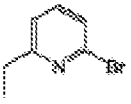
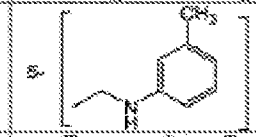
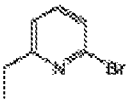
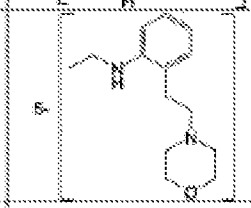
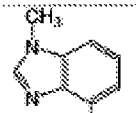
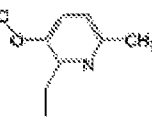
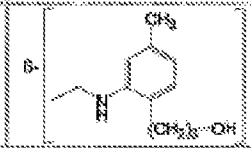


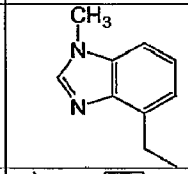
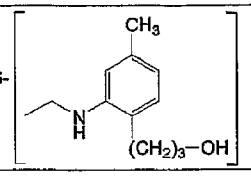
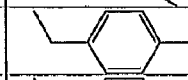
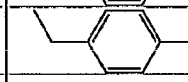
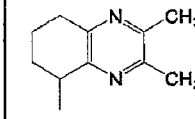
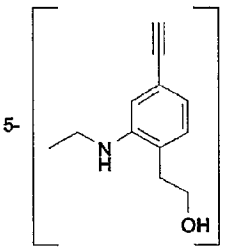
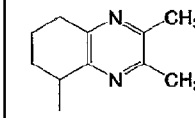
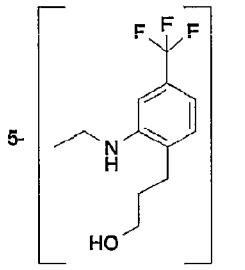
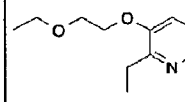
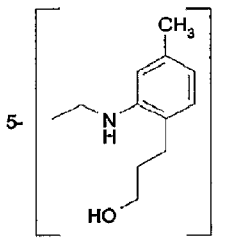
Comp. No.	R^2	R^3	R^4
194	5-	$-CH_3$	$-NH_2$
195	5-	H	$-NH-CH_3$
196	5-[$-(CH_2)_3-NH_2$]	H	$-NH_2$
197	5-	H	$-NH_2$
198	5- [$-(CH_2)_2-CN$]	H	$-NH_2$
199	5- [$-CH_3$]	$-CH_3$	$-NH_2$
200	5- [$-CH_2-OH$]	H	$-NH-CH_3$
201	6-	H	$-NH_2$
202	6- [CH_2-OH]	H	$-NH-CH_3$
203	6-	H	$-NH_2$
204	6-	H	$-NH-CH_3$

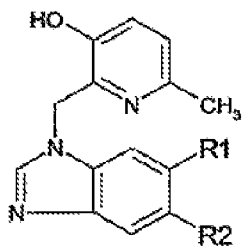


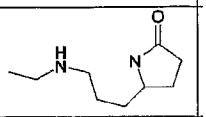
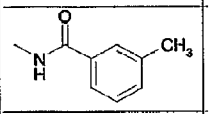
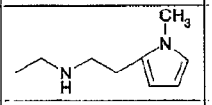
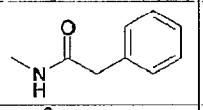
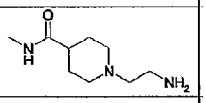
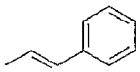
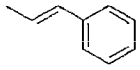
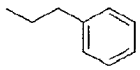
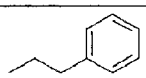
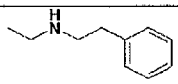
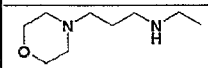
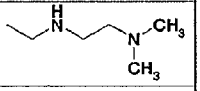
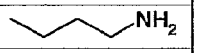
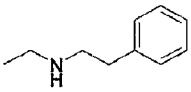
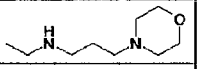
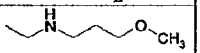
Comp. No.	R^1	R^2
205		
206		
207		
208		
209		
210		
211		
212		
213		

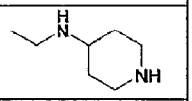
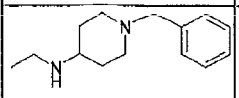
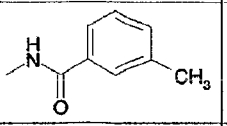
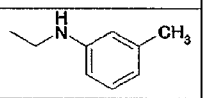
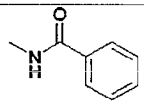
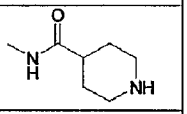
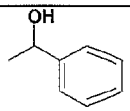
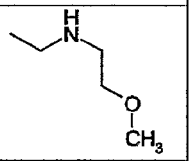
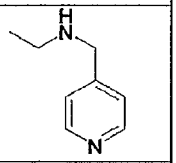
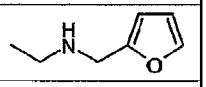
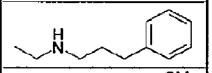
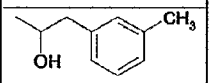
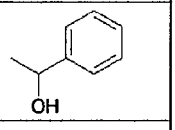
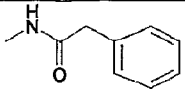
Comp. No.	R^1	R^2
214		
215		
216		
217		
218		
219		
220		
221		
222		5-(CH_2-OH)
223		5-(CH_2-OH)

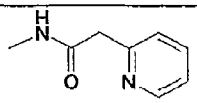
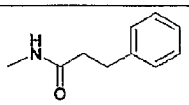
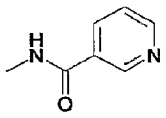
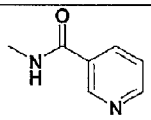
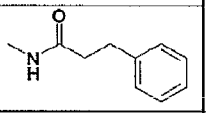
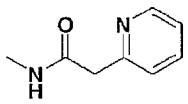
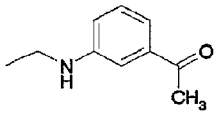
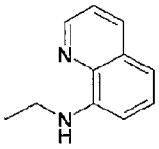
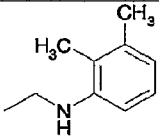
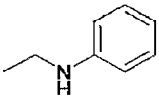
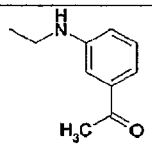
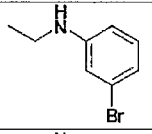
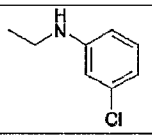
Comp. No.	R^1	R^2
224		6-(CH_2-OH)
225		
226		5-(CH_2-OH)
227		6-(CH_2-OH)
228		
229		
230		
231		
232		
233		6-(CH_2-OH)
234		

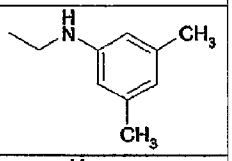
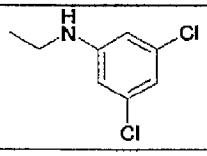
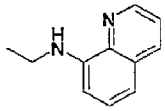
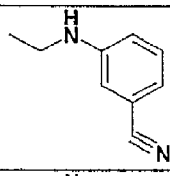
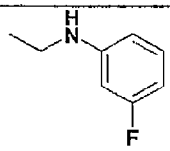
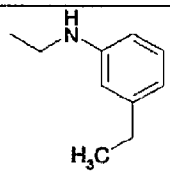
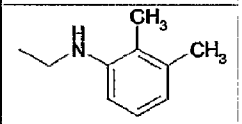
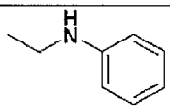
Comp. No.	R^1	R^2
235		
236		5-(CH_2-OH)
237		6-(CH_2-OH)
238		
239		
240		



Comp. No.	R1	R2
241	H	
242	H	
243	H	
244	H	
245	H	
246	H	$-CH_2-OH$
247	$-CH_2-OH$	H
248		H
249	H	
250	H	
251		H
252	H	-CH=CH-CN
253	H	
254		H
255	H	
256	H	
257		H
258	H	
259	H	$-NH_2$
260	H	
261	$-NH_2$	H

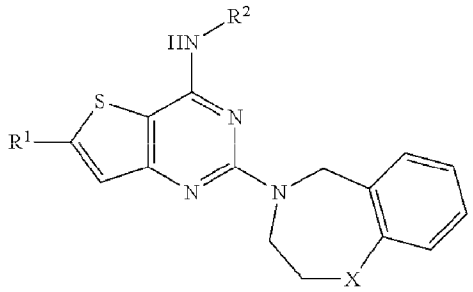
Comp. No.	R1	R2
262	H	
263		H
264		H
265	H	
266	H	
267	H	
268		H
269	H	
270	H	
271	H	
272	H	
273	H	
274	H	
275		H

Comp. No.	R1	R2
276		H
277		H
278		H
279	H	
280	H	
281	H	
282		H
283		H
284		H
285		H
286	H	
287	H	
288	H	

Comp. No.	R1	R2
289	H	
290	H	
291	H	
292	H	
293	H	
294	H	
295	H	
296	H	

Compounds of Formula (B15)

[0140] Compounds of the general Formula (B15) are described in U.S. Publication No. 2013/0090328, published April 11, 2013, which is hereby incorporated by reference in its entirety. Formula (B15) has the structure:



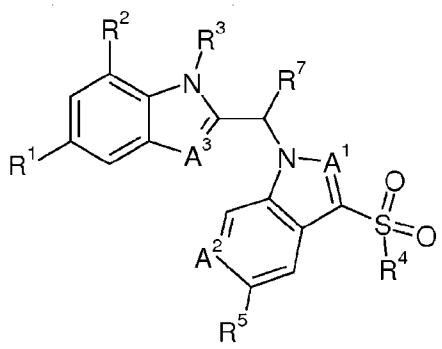
or a pharmaceutically acceptable salt or stereoisomer thereof, wherein: R^1 can be hydrogen or a C_{1-6}alkyl; R^2 can be (1) amino$(CH_2)_{2-6}$; (2) amino$(CH_2)_{1-6}$difluoromethyl$(CH_2)_{1-6}$; (3) amino$(CH_2)_{1-6}$fluoromethyl$(CH_2)_{1-6}$; (4) amino$(CH_2)_{0-6}$oxetanyl$(CH_2)_{1-6}$; (5) amino$(CH_2)_{1-6}$oxetanyl$(CH_2)_{0-6}$; or (6) pyrrolidin-3-yl, unsubstituted or 4-substituted by halogen; and X can be –O–, –S–, –S(=O) –, –$S(O_2)$ –, –CH_2–, –CF_2– or –NH–.

[0141] Examples of Compounds of Formula (B15) include: N-[2-(1,1-dioxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]-2,2-difluoropropane-1,3-diamine; N-[2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)-6-methylthieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(1,1-dioxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)-6-methylthieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(1,1-dioxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[(3-aminooxetan-3-yl)methyl]-2-(1,1-dioxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-amine; N-[3-(aminomethyl)oxetan-3-yl]-2-(1,1-dioxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-amine; N-[(3-aminooxetan-3-yl)methyl]-2-[(1R)-1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl]thieno[3,2-d]pyrimidin-4-amine; N-[(3-aminooxetan-3-yl)methyl]-2-[(1S)-1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl]thieno[3,2-d]pyrimidin-4-amine; N-[(3-aminooxetan-3-yl)methyl]-6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-amine; 2-fluoro-N-[6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]ethane-1,2-diamine;

N-{[3-(aminomethyl)oxetan-3-yl]methyl}-6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-amine; N-[6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[trans-(±)-4-fluoropyrrolidin-3-yl]-6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-amine; 6-methyl-2-(1-oxido-2,3-dihydro-1,4-benzothiazepin-4(5H)-yl)-N-(pyrrolidin-3-yl)thieno[3,2-d]pyrimidin-4-amine; N-[6-methyl-2-(1,2,3,5-tetrahydro-4H-1,4-benzodiazepin-4-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(1,2,3,5-tetrahydro-4H-1,4-benzodiazepin-4-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(2,3-dihydro-1,4-benzoxazepin-4(5H)-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(5,5-difluoro-1,3,4,5-tetrahydro-2H-2-benzazepin-2-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-{[3-(aminomethyl)oxetan-3-yl]methyl}-2-(5,5-difluoro-1,3,4,5-tetrahydro-2H-2-benzazepin-2-yl)thieno[3,2-d]pyrimidin-4-amine; N-[2-(1,3,4,5-tetrahydro-2H-2-benzazepin-2-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(2,3-dihydro-1,4-benzoxazepin-4(5H)-yl)-6-methylthieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; N-[2-(5,5-difluoro-1,3,4,5-tetrahydro-2H-2-benzazepin-2-yl)-6-methylthieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine; and N-[6-methyl-2-(1,3,4,5-tetrahydro-2H-2-benzazepin-2-yl)thieno[3,2-d]pyrimidin-4-yl]propane-1,3-diamine.

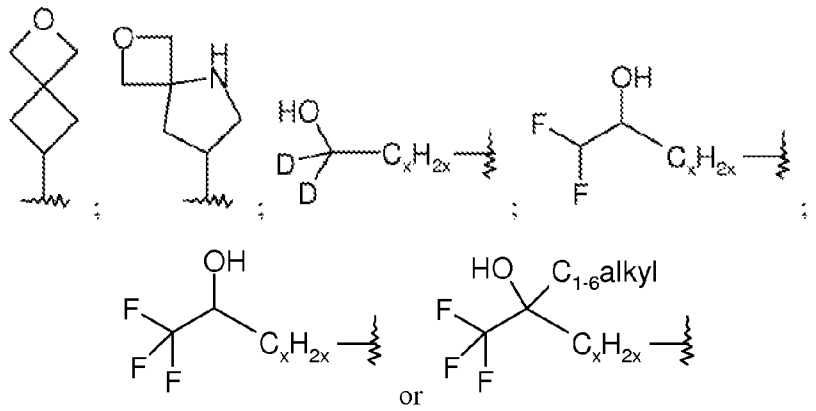
Compounds of Formula (B16)

[0142] Compounds of the general Formula (B16) are described in PCT Publication No. WO 2014/009302, published January 16, 2014, which is hereby incorporated by reference in its entirety. Formula (B16) has the structure:



or pharmaceutically acceptable salts thereof, wherein: R^1 can be hydrogen or halogen; R^2 can be hydrogen or halogen; R^3 can be azetidinyl; $C_{1\text{-}6}$alkoxypyridinyl; $C_{1\text{-}6}$alkylsulfonyl-C_xH_{2x}-; carboxycycloalkyl; difluorocycloalkyl; 1,1-dioxo-tetrahydrothienyl; halopyridinyl; hydroxy-C_yH_{2y}-; hydroxy-C_xH_{2x}- cycloalkyl; hydroxy-C_yH_{2y}-O-C_yH_{2y}-; hydroxycycloalkyl-C_zH_{2z}-, unsubstituted or substituted by $C_{1\text{-}3}$alkyl, hydroxy or hydroxy-C_xH_{2x}-; 4-hydroxypiperidin-1-yl-C_yH_{2y}-; 3-hydroxy-

pyrrolidin-1- yl-C_yH_{2y}-; morpholinyl-C_yH_{2y}-; oxetanyl; oxetanyl-C_xH_{2x}-, unsubstituted or substituted by C_{1-3}alkyl; piperidinyl; oxo-piperidinyl; oxo-pyrrolidinyl; pyrrolidinyl, unsubstituted or substituted by C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, hydroxy- C_yH_{2y}-, hydroxy-C_xH_{2x}-carbonyl, amino-C_xH_{2x}-carbonyl or trifluoromethyl- C_xH_{2x}-; tetrahydrofuran-3-yl- C_zH_{2z}-; tetrahydropyranyl; trifluoromethyl- C_xH_{2x}-;



or

R^4 can be C_{1-6}alkyl or cycloalkyl; R^5 can be hydrogen or halogen; R^7 can be hydrogen or C_{1-6}alkyl; A^1 can be -N- or -CH; A^2 can be -N-, -NO or -CH; A^3 can be -N- or -CH; x can be 1-6; y can be 2-6; z can be 0-6.

[0143] Examples of Compounds of Formula (B16) include: 1-[2-(methylsulfonyl)ethyl]-2-{[3-(methylsulfonyl)-1H-indol-1-yl]methyl}-1H-benzimidazole; 5-chloro-2-{[3-(methylsulfonyl)-1H-indol-1-yl]methyl}-1-[3-(methylsulfonyl)propyl]-1H-benzimidazole; 5-chloro-2-{[5-fluoro-3-(methylsulfonyl)-1H-indol-1-yl]methyl}-1-[3-(methylsulfonyl)propyl]-1H-benzimidazole; 5-chloro-1-[3-(methylsulfonyl)propyl]-2-{[3-(methylsulfonyl)-1H-pyrrolo[2,3-c]pyridin-1-yl]methyl}-1H-benzimidazole; 5-chloro-2-{[3-(ethylsulfonyl)-1H-indol-1-yl]methyl}-1-[3-(methylsulfonyl)propyl]-1H-benzimidazole; 5-chloro-1-[3-(methylsulfonyl)propyl]-2-{[3-(propan-2-ylsulfonyl)-1H-indol-1-yl]methyl}-1H-benzimidazole; 5-chloro-2-{[3-(cyclopropylsulfonyl)-1H-indol-1-yl]methyl}-1-[3-(methylsulfonyl)propyl]-1H-benzimidazole; 1-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-indazole; 1-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-benzimidazol-2-yl}methyl)-3-(propan-2-ylsulfonyl)-1H-indazole; 1-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-benzimidazol-2-yl}methyl)-3-(ethylsulfonyl)-1H-indazole; 1-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[2-(methylsulfonyl)ethyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-indazole; 1-({5-chloro-1-[2-(methylsulfonyl)ethyl]-1H-benzimidazol-2-yl}methyl)-3-(propan-2-ylsulfonyl)-1H-

indazole; 1-({5-chloro-1-[(3R)-1,1-dioxidotetrahydrothiophen-3-yl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(1,1-dioxidotetrahydrothiophen-3- yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(oxetan-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin- 1-yl]methyl}-1H-benzimidazol-1-yl)piperidin-2- one; 1-{[5-chloro-1-(oxetan-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-benzimidazol-2- yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(tetrahydrofuran-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(3,3-difluorocyclopentyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(3,3-difluorocyclopentyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclohexanol; 3-(5-chloro-2-{[3-(methylsulfonyl)-6-oxido-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclopentanol; 1-{[5-chloro-1-(pyrrolidin-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[1-(azetidin-3-yl)-5-chloro-1H-benzimidazol-2- yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(piperidin-4-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)- 1H-indazole; 1-[3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]ethanone; 1-[3-(5-chloro-2-{ [3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]-2-hydroxyethanone; 2-amino-1-[3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]ethanone; 1-({5-chloro-1-[(*3S*)-1-(2,2,2-trifluoroethyl)pyrrolidin-3-yl]-1H-benzimidazol-2- yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[(*3R*)-1-(2,2,2-trifluoroethyl)pyrrolidin-3-yl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H- pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(3,3,3-trifluoropropyl)-1H-benzimidazol-2-yl] methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(oxetan-3-ylmethyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[2-(oxetan-3-yl)ethyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(6-fluoropyridin-3-yl)-1H-benzimidazol-2-yl] methyl}-3-(methylsulfonyl)-1H- indazole; 1-{[5-chloro-1-(6-fluoropyridin-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-

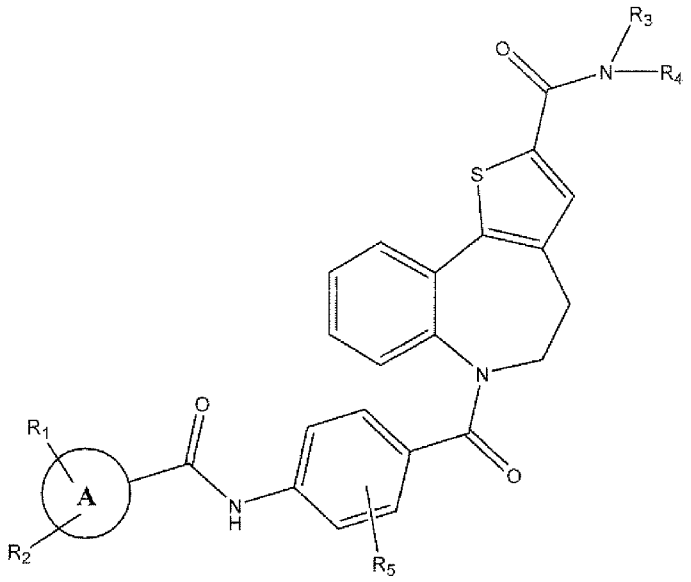
(6-fluoropyridin-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine 6-oxide; 1-{[5-chloro-1-(6-methoxypyridin-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(6-chloropyridin-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(4,4,4-trifluorobutyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-indazole; 1-{[5-chloro-1-(4,4,4-trifluorobutyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine 6-oxide; 1-{[5-chloro-1-(4,4,4-trifluorobutyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-7-fluoro-1-(3,3,3-trifluoropropyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-7-fluoro-1-(4,4,4-trifluorobutyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-{[5-chloro-1-(2-oxaspiro[33]hept-6-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[2-(3-methyloxetan-3-yl)ethyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; *trans*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1-methylcyclobutanol; 3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)propan-1-ol; 1-{[5-chloro-1-(tetrahydrofuran-3-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-2-methylbutan-2-ol; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)butan-1-ol; 1-{[5-chloro-1-(tetrahydrofuran-3-ylmethyl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; *trans*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclobutanol; *cis*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1-methylcyclobutanol; 1-[2-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)ethyl]cyclopropanol; 2-[2-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)ethoxy]ethanol; *trans*'-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclopentanol; *cis*'-4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1-methylcyclohexanol; 5-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-2-methylpentan-2-ol; 2-[*trans*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclobutyl]propan-2-ol; 1-({5-chloro-1-[2-(morpholin-4-yl)ethyl]-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-

c]pyridine; *trans*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo [3,4-c]pyridin-1-yl] methyl}-1H-benzimidazol-1-yl)cyclobutanecarboxylic acid; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1- yl]methyl}-1H-benzimidazol-1-yl)-1,1,1-trifluorobutan-2-ol; *cis*-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1-methylcyclopentanol; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1- yl]methyl}-1H-benzimidazol-1-yl)-1,1-difluorobutan-2-ol; *trans*'-4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclopentane-1,2-diol; *trans*'-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1-(hydroxymethyl)cyclobutanol; 1-[(*3R*)-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]ethanone; 1-[3-(5-chloro-2-{[3-(methylsulfonyl)-1H-indazol-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]ethanone; 1-[(*3R*)-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-indazol-1- yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]propan-1-one; 1-[(*3R*)-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1- yl]-2-methylpropan-1-one; 1-[(*3R*)-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]-2-hydroxy-2-methylpropan-1-one; 1-({5-chloro-1-[(*3R*)-1-(methylsulfonyl)pyrrolidin-3-yl]-1H-benzimidazol-2- yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 2-[(*3R*)-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-1-yl]ethanol; 4-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)pyrrolidin-2-one; 1-{[5-chloro-1-(2-oxa-5-azaspiro[3.4]oct-7-yl)-1H-benzimidazol-2-yl]methyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[2-(methylsulfonyl)ethyl]-1H-indol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-indol-2-yl}methyl)-3-(methylsulfonyl)-1H- pyrazolo[3,4-c]pyridine; 1-({5-chloro-7-fluoro-1-[2-(methylsulfonyl)ethyl]-1H-indol-2- yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 1-[2-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)ethyl]pyrrolidin-3-ol; 1-[2-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1- yl]methyl}-1H-benzimidazol-1-yl)ethyl]piperidin-4-ol; [*trans*'-3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)cyclobutyl]methanol; 1-({5-chloro-1-[(*3R*)-1,1-dioxidotetrahydrothiophen-3-yl]-7-fluoro-1H-benzimidazol-2-yl}methyl)-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; 3-(5-chloro-2-{[3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)(1,1-H_2)propan-1-ol; 4-(5-chloro-2-{[3-

(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl]methyl}-1H-benzimidazol-1-yl)-1,1,1-trifluoro-2-methylbutan-2-ol; 1-{(*1R*)-1-[5-chloro-1-(3,3,3- trifluoropropyl)-1H-benzimidazol-2-yl]ethyl}-3-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine; and 1-{(*1S*)-1-[5-chloro-1-(3,3,3-trifluoropropyl)-1H-benzimidazol-2-yl]ethyl}-3- (methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine.

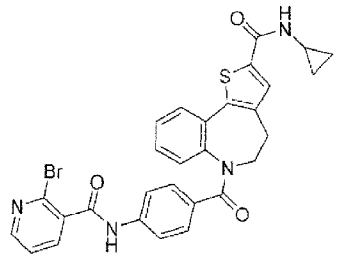
Compounds of Formula (B17)

[0144] Compounds of the general Formula (B17) are described in PCT Publication No. WO 2011/005842, published January 13, 2011, which is hereby incorporated by reference in its entirety. Formula (B17) has the structure:

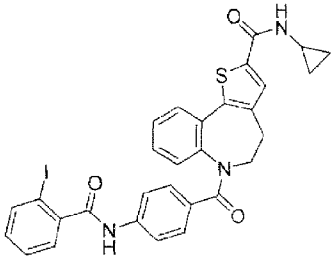


or a pharmaceutically acceptable salt thereof, wherein: A can be aryl or heteroaryl; R_1 can be alkyl, alkoxy, haloalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, said heterocyclyl is optionally substituted by one to three substituents independently selected from halo, hydroxyl, haloalkyl, alkoxy, alkyl, alkoxy-alkyl-,hydroxyl-alkyl-, CN, alky-NH-; said aryl or heteroaryl can be optionally substituted by one to three substituents independently selected from halo, cyano, nitro, hydroxyl, alkyl, alkoxy, alkyl-NH-, with the proviso that when A is aryl, R_1 is not unsubstituted aryl; R_2 can be hydrogen, alkyl, alkoxy, amino, alkyl-NH-, CN, alkyl-SO_2-, or halo; R_3 can be hydrogen, alkyl, heterocyclyl, heteroaryl, heteroaryl-alkyl-, or cycloalkyl, said alkyl is optionally substituted by one substituent selected from NH_2-C(O)-, halo, hydroxyl, NH_2-SO_2-, alkoxy-alkyl-, heterocyclyl; aryl, heteroaryl, CN, alkyl-NH-; R_4 can be hydrogen, or alkyl; or haloalkyl; R_3 and R_4 can be taken together with the nitrogen atom to which they are attached optionally form a 3- to 7-membered ring; R_5 can be hydrogen, alkyl, alkoxy, haloalkyl, or halo.

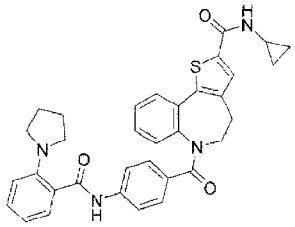
[0145] Examples of Compounds of Formula (B17) include:



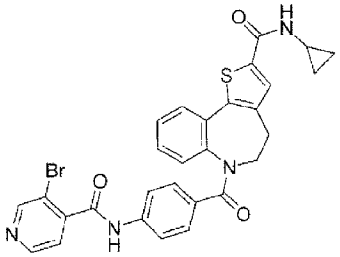
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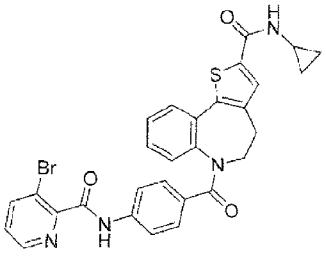
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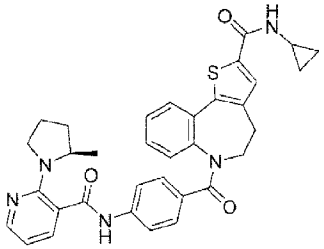
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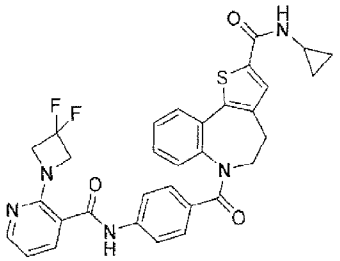
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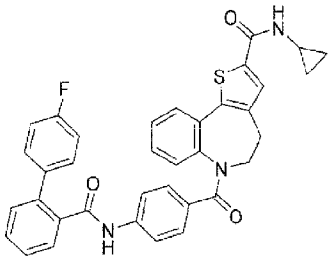


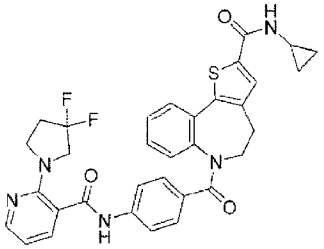
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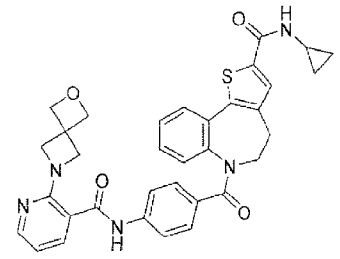


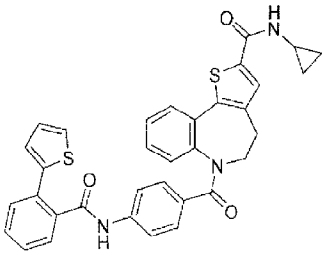
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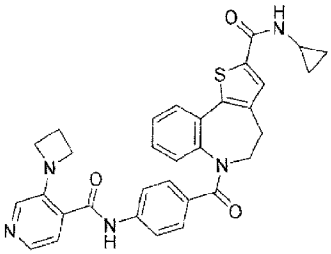


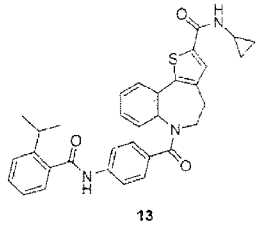




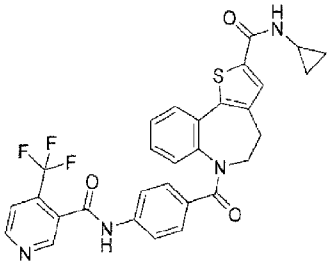


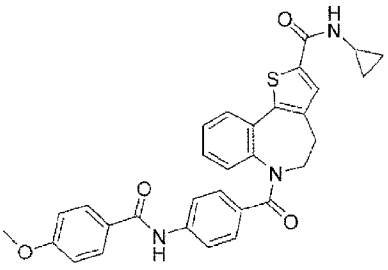


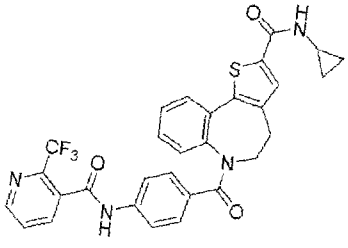
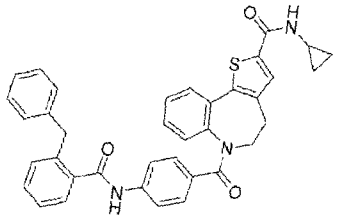
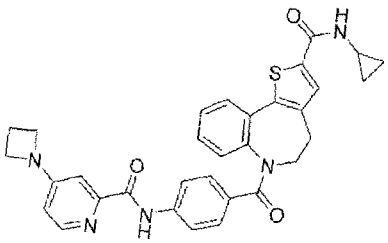


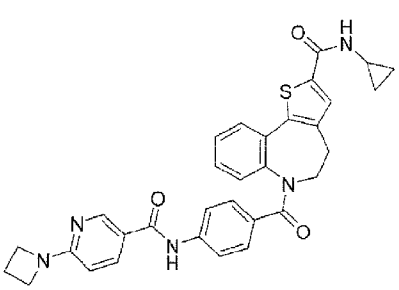
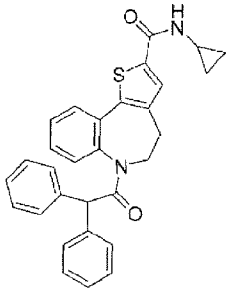
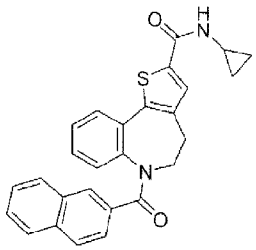
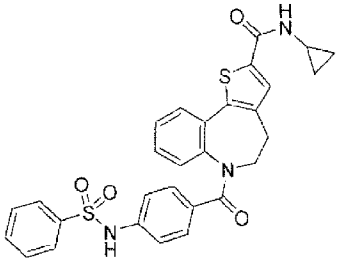
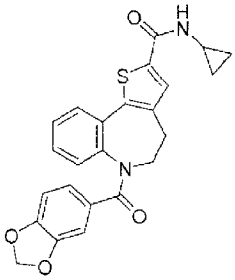
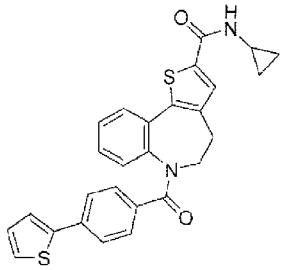
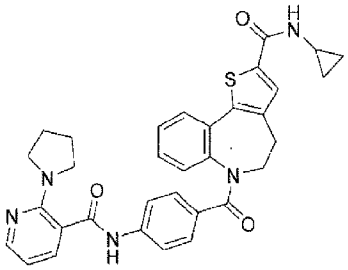
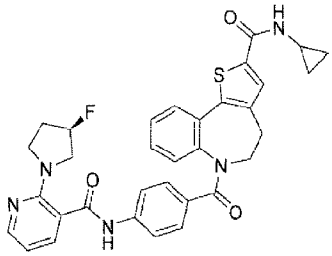
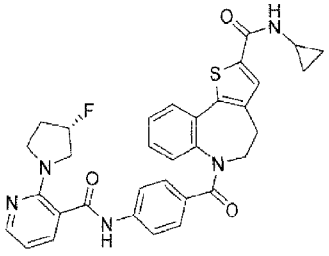
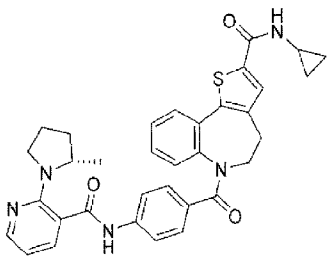
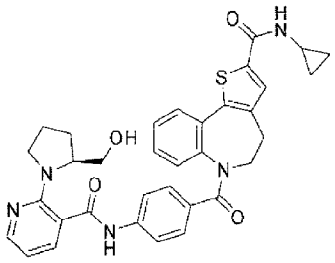
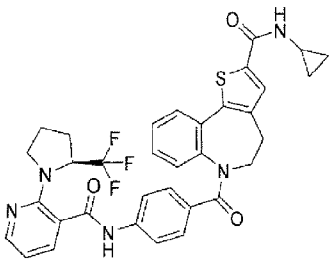
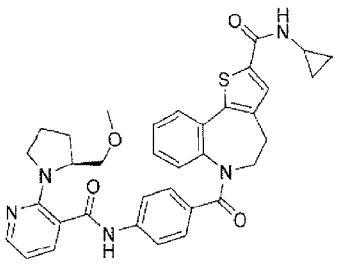
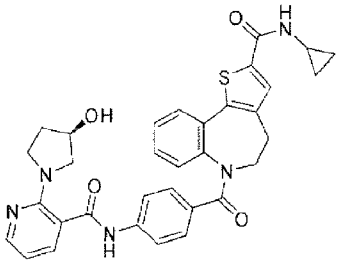
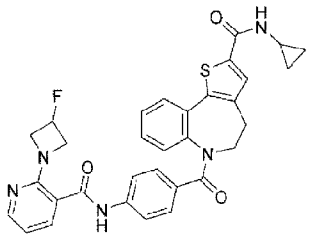
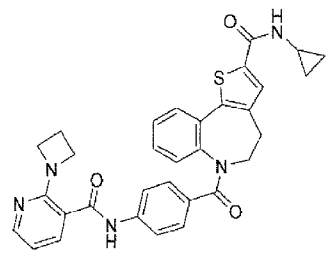
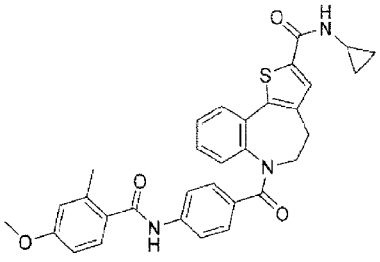
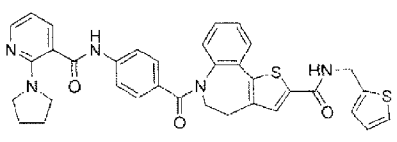


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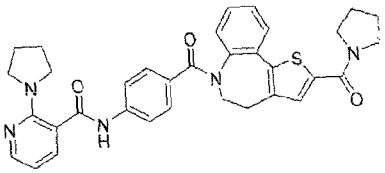


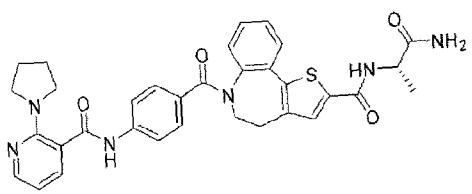


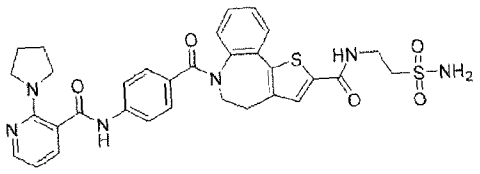




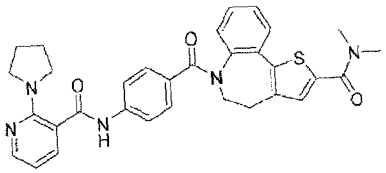



















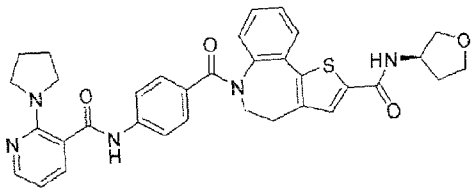
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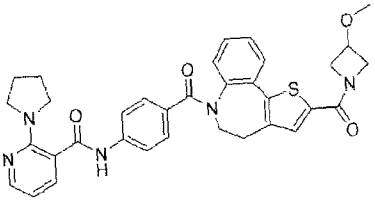


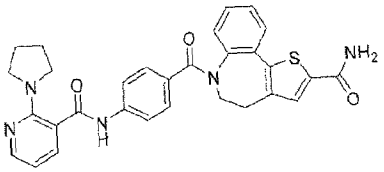


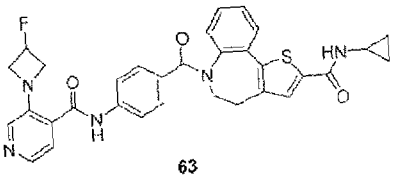




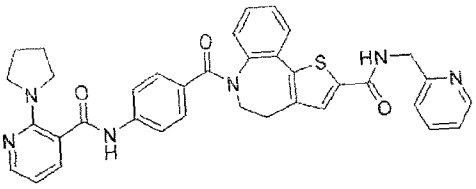


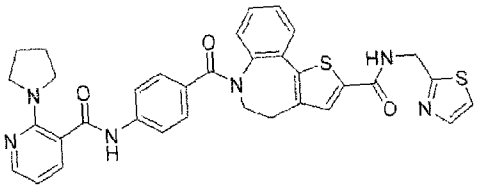


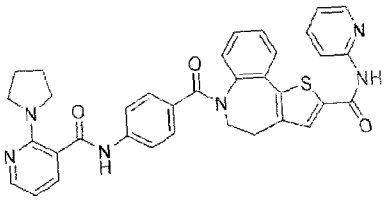


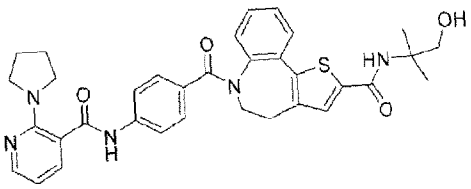


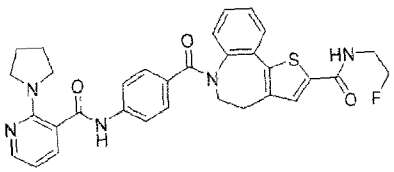
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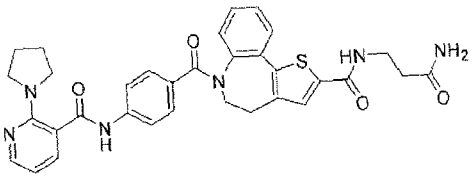


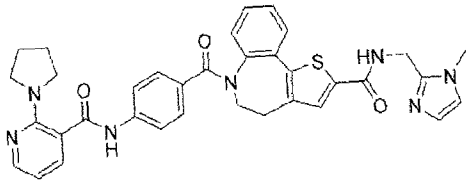


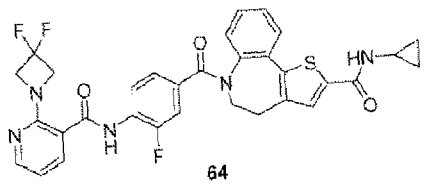




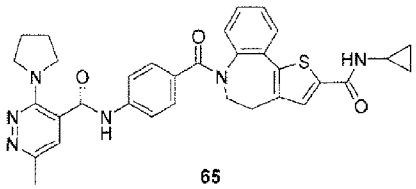




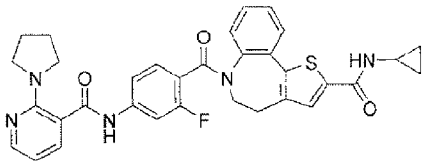


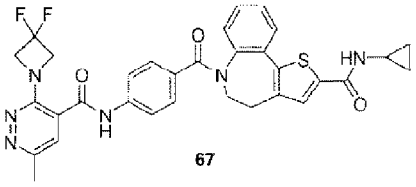


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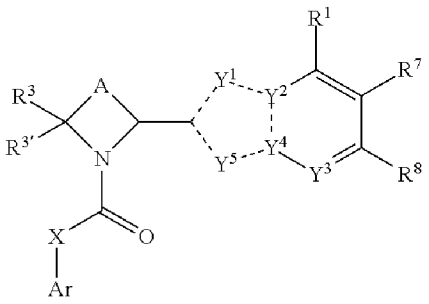


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Compounds of Formula (B18)

[0146] Compounds of the general Formula (B18) are described in U.S. Publication No. 2013/0273037, published October 17, 2013, which is hereby incorporated by reference in its entirety. Formula (B18) has the structure:

I



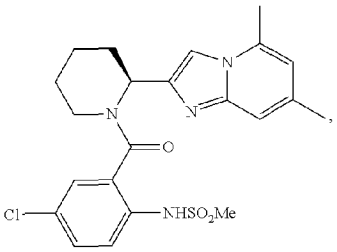
or a pharmaceutically acceptable salt thereof, wherein: a) Y^1 can be N, NH or CH, Y^2 is C, Y^3 is N or $CR^{8'}$, Y^4 is N or C and Y^5 is N, $NR^{2'}$ or CR^2, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$; or b) Y^1 can be N, NH or CH, Y^2 is N or C, Y^3 is N or $CR^{8'}$, Y^4 is N or C, and Y^5 is N or $NR^{2'}$, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$; or c) Y^1 can be N, NH or CH, Y^2 is N or C, Y^3 is $CR^{8'}$, Y^4 is N or C, and Y^5 is N, $NR^{2'}$ or CR^2, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$; the dashed bonds ---- can be selected from single bonds and double bonds so as to provide an aromatic ring system; A can be $-(CR^4R^{4'})_n-$ wherein any one $CR^4R^{4'}$ of said $-(CR^4R^{4'})_n-$ may be optionally replaced with –O-, -S-, $-S(O)_p-$, NH or NR^a; n can be 3, 4, 5 or 6; each p can be 1 or 2; Ar can be a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1 to 5 R^6; X can be $-C(R^{13})(R^{14})-$, $-N(CH_2R^{14})-$ or –NH-, or X is absent; R^1 can be H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-R^{11}$, $-S(O)_pR^a$, $NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-

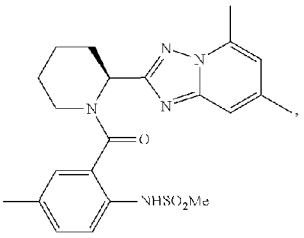
C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; R^2 can be H, CN, NO_2, halogen or (C_1-C_8)alkyl; $R^{2'}$ can be H or (C_1-C_8)alkyl; R^3 can be H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; $R^{3'}$ can be H, $-OR^{11}$, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; each R^4 can be independently H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; and each $R^{4'}$ can be independently H, OR^{11}, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; or two R^4 on adjacent carbon atoms, when taken together, may form a double bond between the two carbons to which they are attached or may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –S(O)$_p$–, –NH– or –NR^a–; or two R^4 on non-adjacent carbon atoms, when taken together, may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –S(O)$_p$–, –NH– or –NR^a–; or two R^4 and two $R^{4'}$ on adjacent carbon atoms, when taken together, may form an optionally substituted C_6 aryl ring; or one R^4 and one $R^{4'}$ on the same carbon atom, when taken together, may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –S(O)$_p$–, –NH– or –NR^a–; each R^5 can be independently H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; each $R^{5'}$ can be independently H, $-OR^{11}$, (C_1-C_8)alkyl, (C_2-C_8)alkenyl,

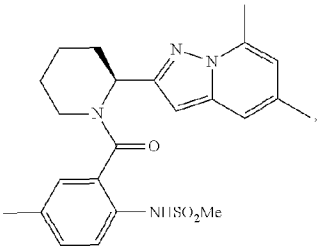
(C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; each R^6 can be independently H, oxo, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$NR^{11}C(O)OR^{11}$, -$NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, -SR^{11}, -$S(O)_pR^a$, -$NR^{11}S(O)_pR^a$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)SR^{11}$, -$S(O)_p(OR^{11})$, -$SO_2NR^{11}R^{12}$, -$NR^{11}S(O)_p(OR^{11})$, -$NR^{11}SO_pNR^{11}R^{12}$, -$NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclykC$_1$-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; or two R^6 on adjacent carbon atoms, when taken together, may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –$S(O)_P$–, –NH– or –NR^a–; or any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^3, may form a bond or a -$(CR^5R^{5'})_m$- group wherein m is 1 or 2; or any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^2 or $R^{2'}$ may form a bond; R^7 can be H, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$NR^{11}C(O)OR^{11}$, -$NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, -SR^{11}, -$S(O)_pR^a$, -$NR^{11}S(O)_pR^a$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)SR^{11}$, -$S(O)_p(OR^{11})$, -$SO_2NR^{11}R^{12}$, -$NR^{11}S(O)_p(OR^{11})$, -$NR^{11}SO_pNR^{11}R^{12}$, -$NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; R^8 can be H, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$NR^{11}C(O)OR^{11}$, -$NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, -SR^{11}, -$S(O)_pR^a$, -$NR^{11}S(O)_pR^a$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)SR^{11}$, -$S(O)_p(OR^{11})$, -$SO_2NR^{11}R^{12}$, -$NR^{11}S(O)_p(OR^{11})$, -$NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; $R^{8'}$ can be H, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$NR^{11}C(O)OR^{11}$, -$NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, -SR^{11}, -$S(O)_pR^a$, -$NR^{11}S(O)_pR^a$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)SR^{11}$, -$S(O)_p(OR^{11})$, -$SO_2NR^{11}R^{12}$, -$NR^{11}S(O)_p(OR^{11})$, -$NR^{11}SO_pNR^{11}R^{12}$, -$NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl; each R^a can be independently (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl wherein any (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl or (C_2-C_8)alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_3-

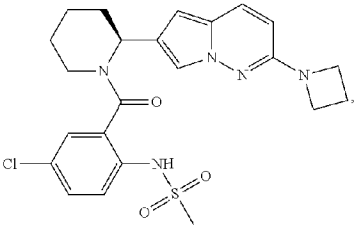
C_7)cycloalkyl(C_1-C_8)alkyl of R^a is optionally substituted with one or more -OH, -NH_2, CO_2H, C_2-C_{20} heterocyclyl or (C_1-C_8)alkyl; each R^{11} or R^{12} can be independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_8)alkyl, -C(=O)R^a or -$S(O)_pR^a$; or when R^{11} and R^{12} are attached to a nitrogen they may optionally can be taken together with the nitrogen to which they are both attached to form a 3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, –$S(O)_p$–, –NH–, –NR^a– or –C(O)–; R^{13} can be H or (C_1-C_8)alkyl; R^{14} can be H, (C_1-C_8)alkyl, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, $NR^{11}S(O)_pR^a$, –$NR^{11}S(O)_p(OR^{11})$ or $NR^{11}SO_pNR^{11}R^{12}$; and wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl of each R^1, R^2, $R^{2'}$, R^3, $R^{3'}$, R^4, $R^{4'}$, R^5, $R^{5'}$, R^6, R^7, R^8, $R^{8'}$ or R^{12} can be independently, optionally substituted with one or more oxo, halogen, hydroxy, –NH_2, CN, N_3, –$N(R^a)_2$, –NHR^a, –SH, –SR^a, –$S(O)_pR^a$, –OR^a, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, –C(O)R^a, –C(O)H, –C(=O)OR^a, –C(=O)OH, –C(=O)$N(R^a)_2$, –C(=O)NHR^a, –C(=O)NH_2, –$NHS(O)_pR^a$, –$NR^aS(O)_pR^a$, –$NHC(O)R^a$, –$NR^aC(O)R^a$, –$NHC(O)OR^a$, –$NR^aC(O)OR^a$, –$NR^aC(O)NHR^a$, –$NR^aC(O)N(R^a)_2$, –$NR^aC(O)NH_2$, –$NHC(O)NHR^a$, –$NHC(O)N(R^a)_2$, –$NHC(O)NH_2$, =NH, =NOH, =NOR^a, –$NR^aS(O)_pNHR^a$, —$NR^aS(O)_pN(R^a)_2$, —$NR^aS(O)_pNH_2$, —$NHS(O)_pNHR^a$, —$NHS(O)_pN(R^a)_2$, —$NHS(O)_pNH_2$, –$OC(=O)R^a$, –$OP(O)(OH)_2$ or R^a.

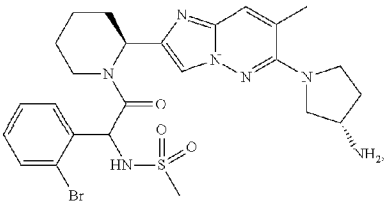
[0147] Examples of Compounds of Formula (B18) include:

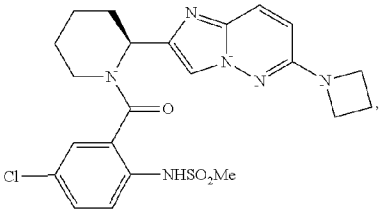


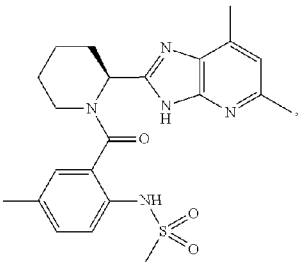


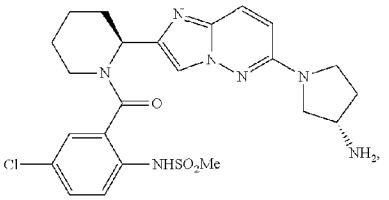


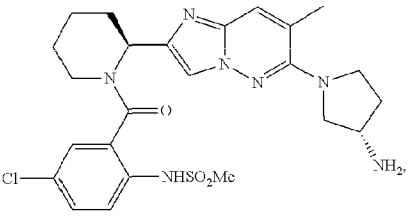


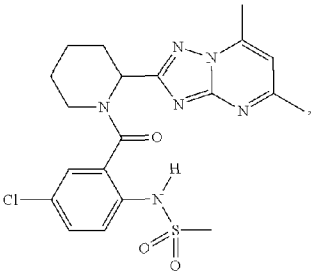


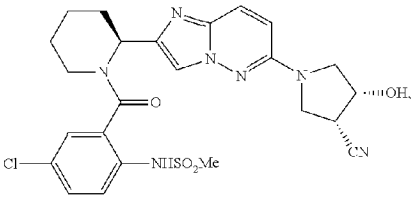


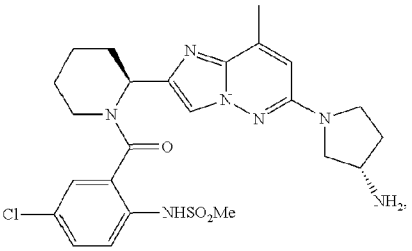


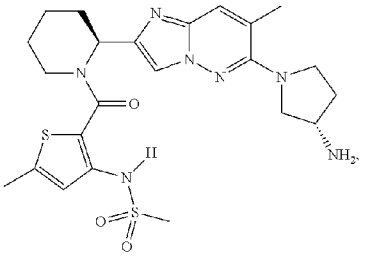


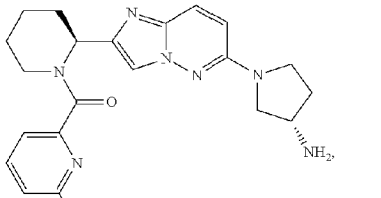


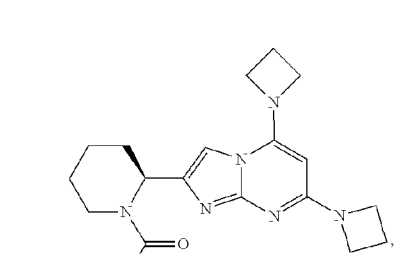


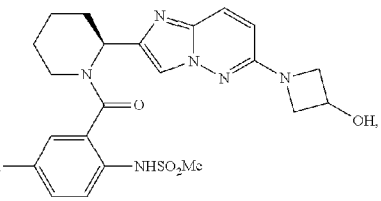


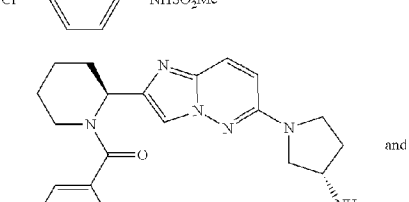


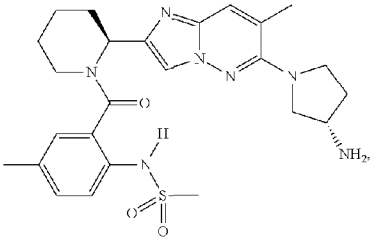




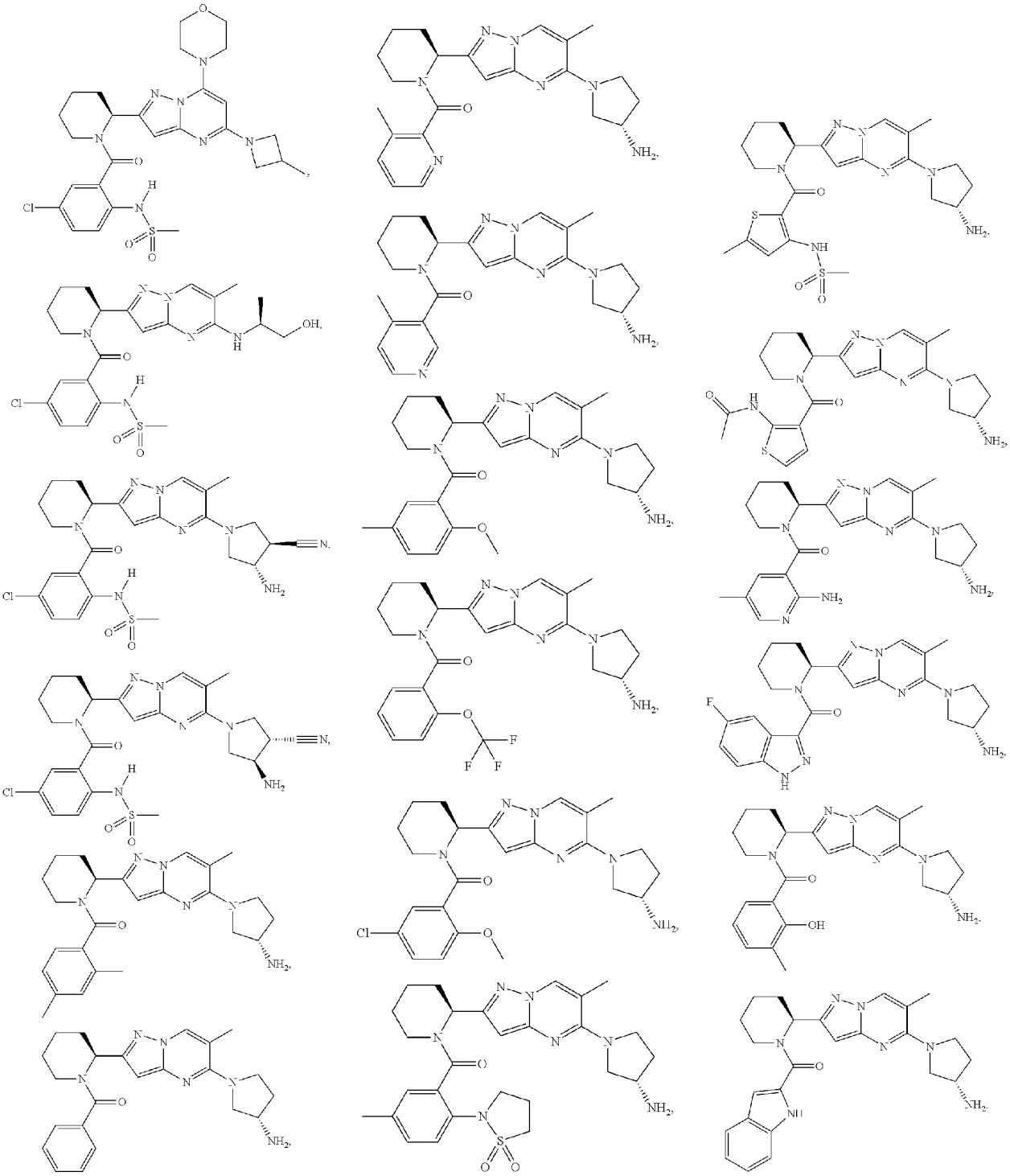


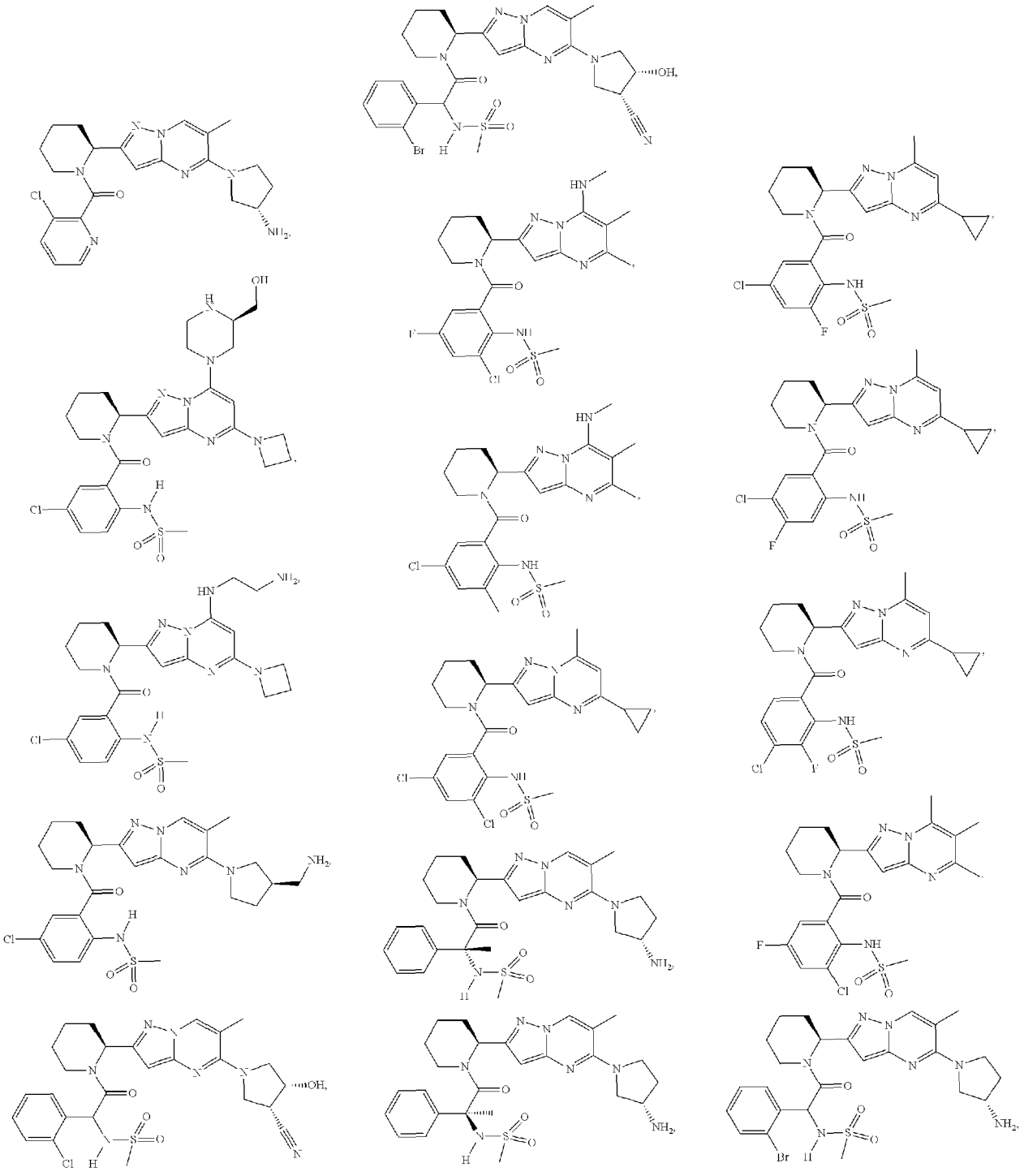


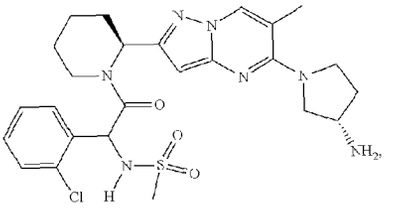
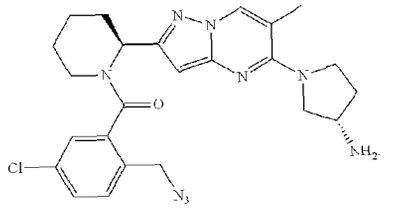
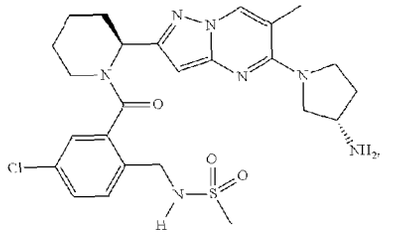
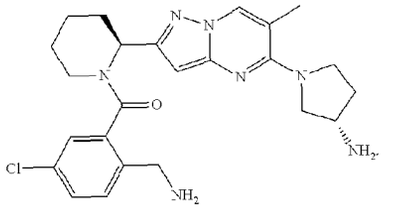
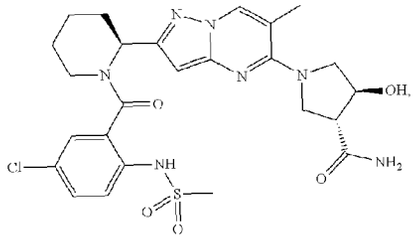
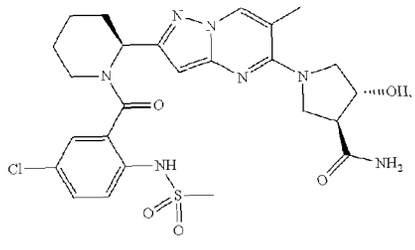
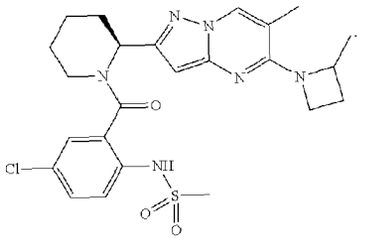
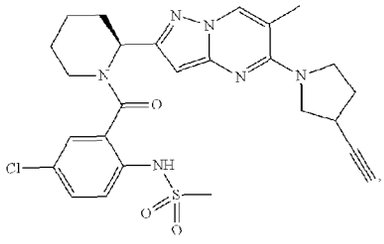
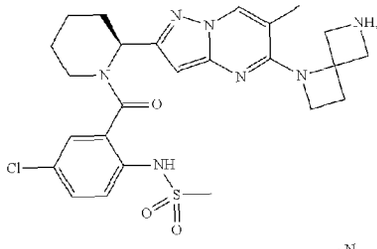
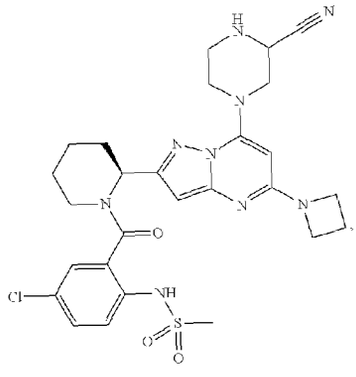
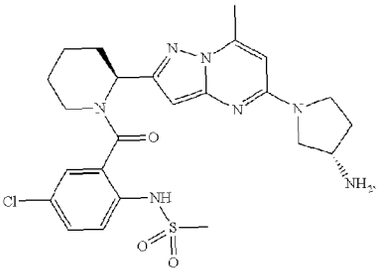
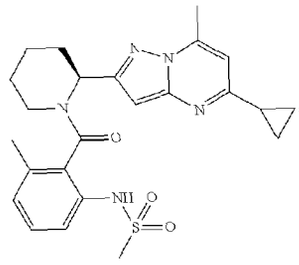
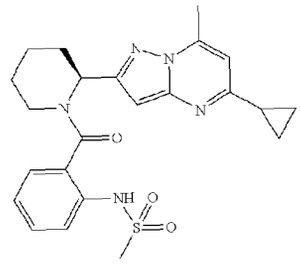
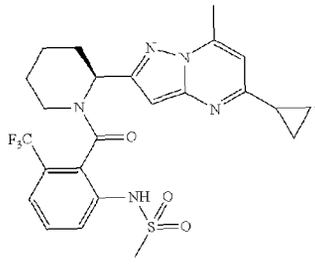
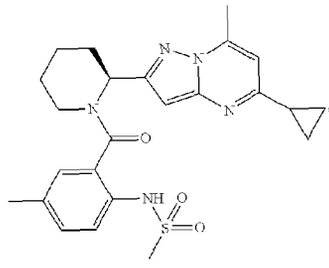
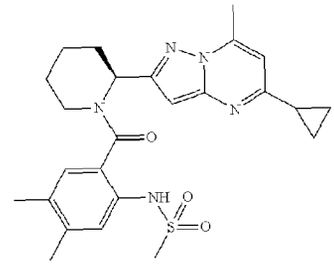


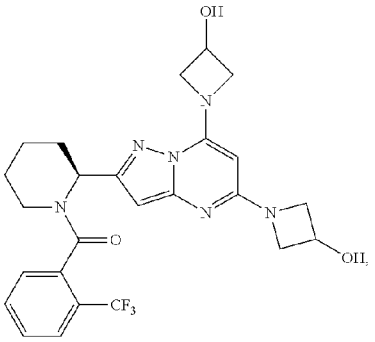


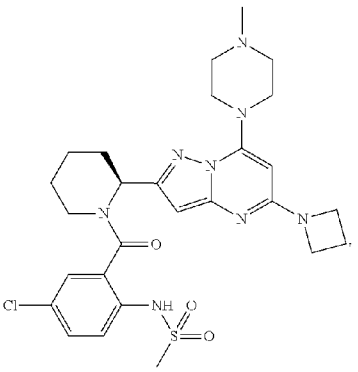
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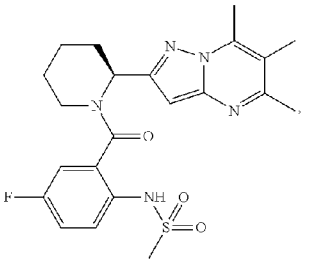


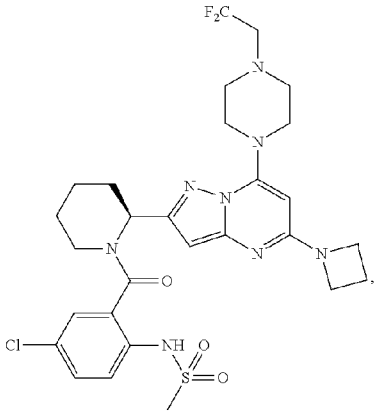


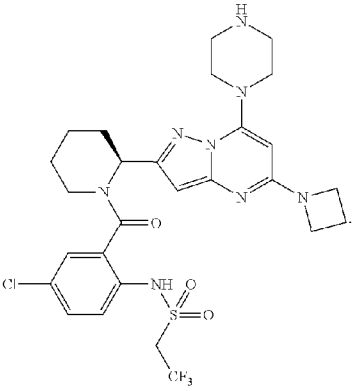

















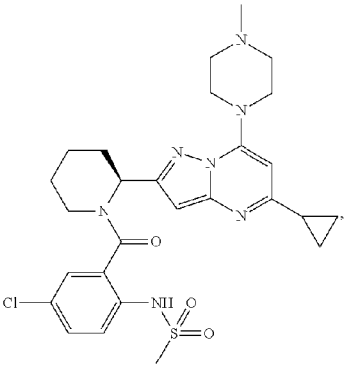


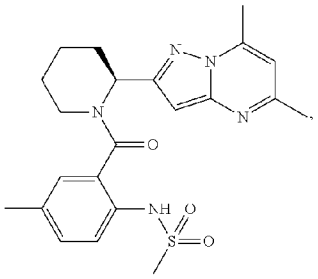


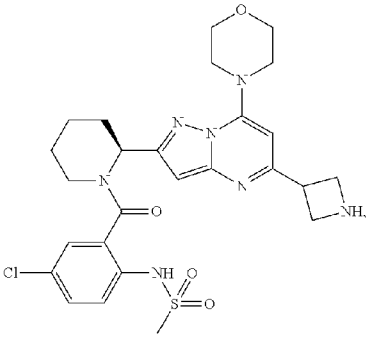


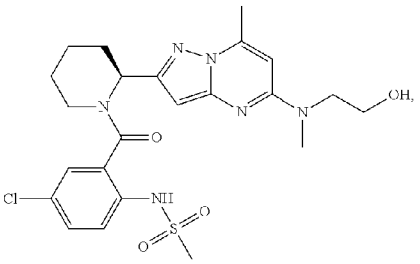


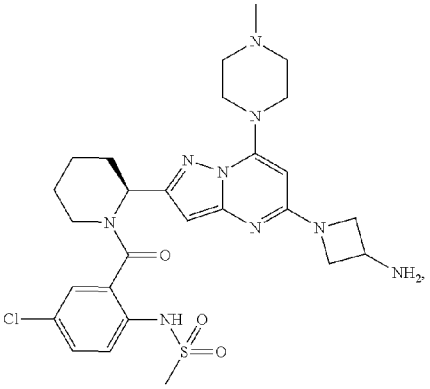


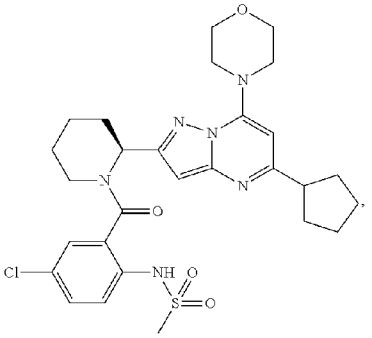


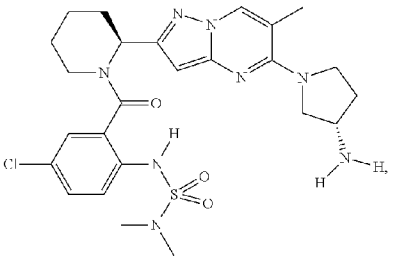


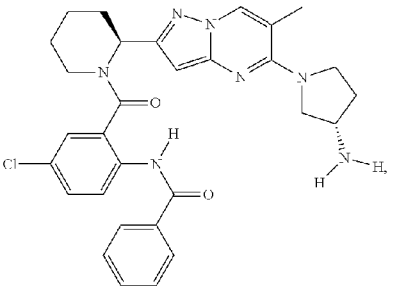


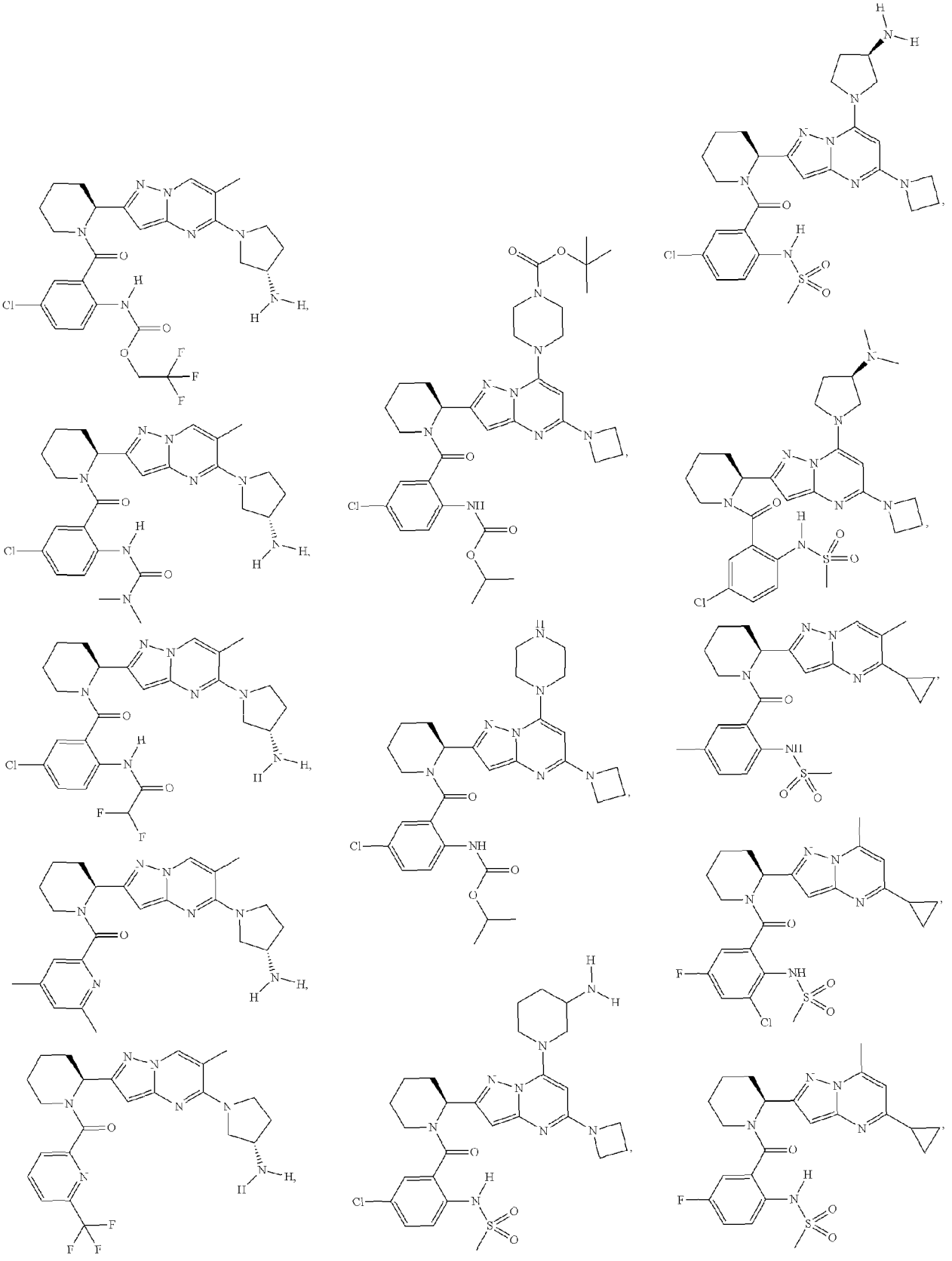


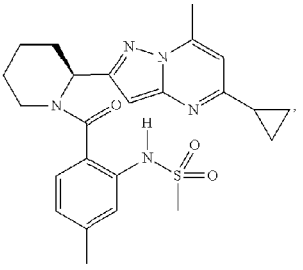
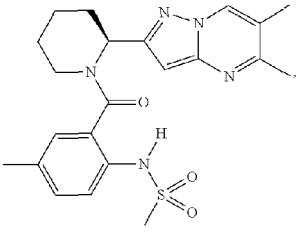
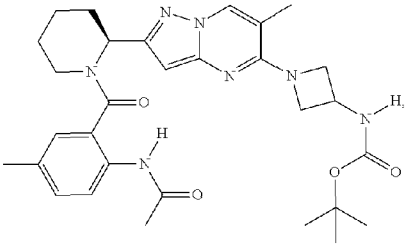
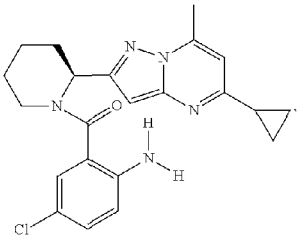
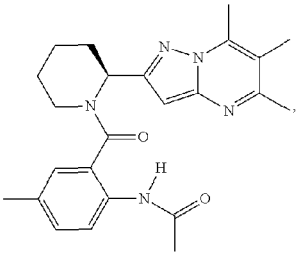
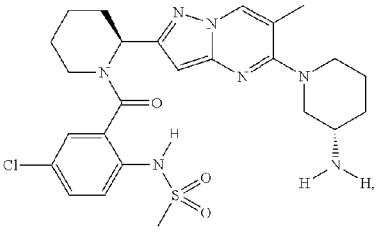
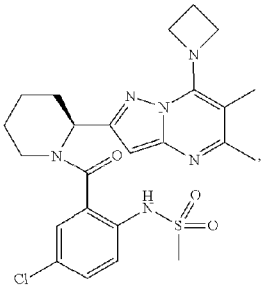
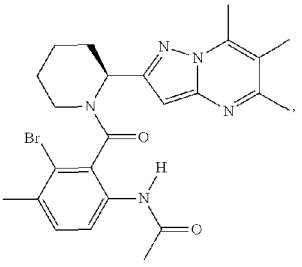
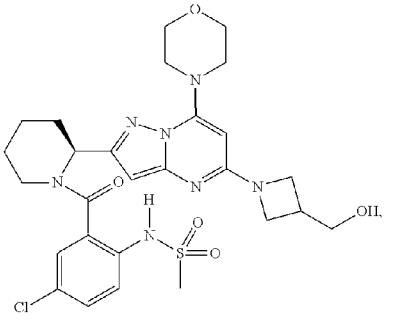
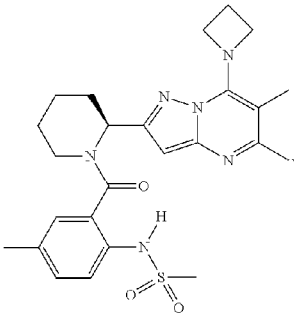
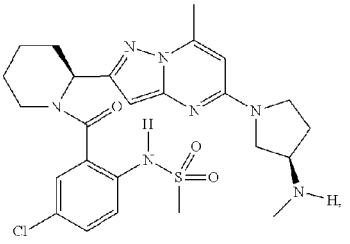
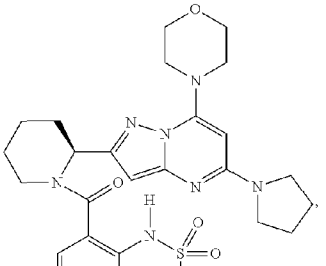
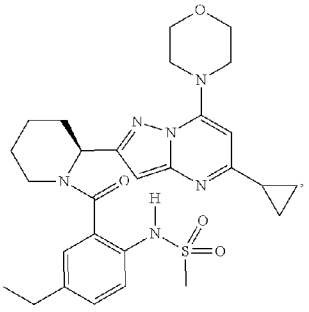
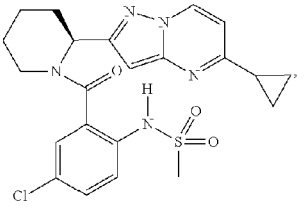
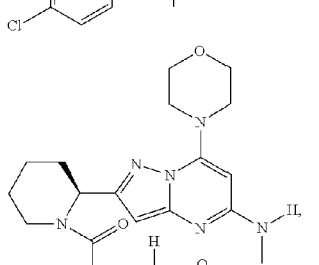


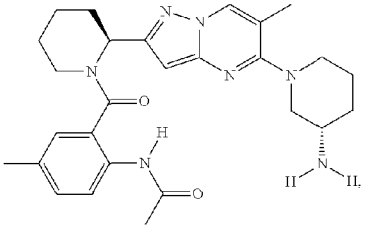


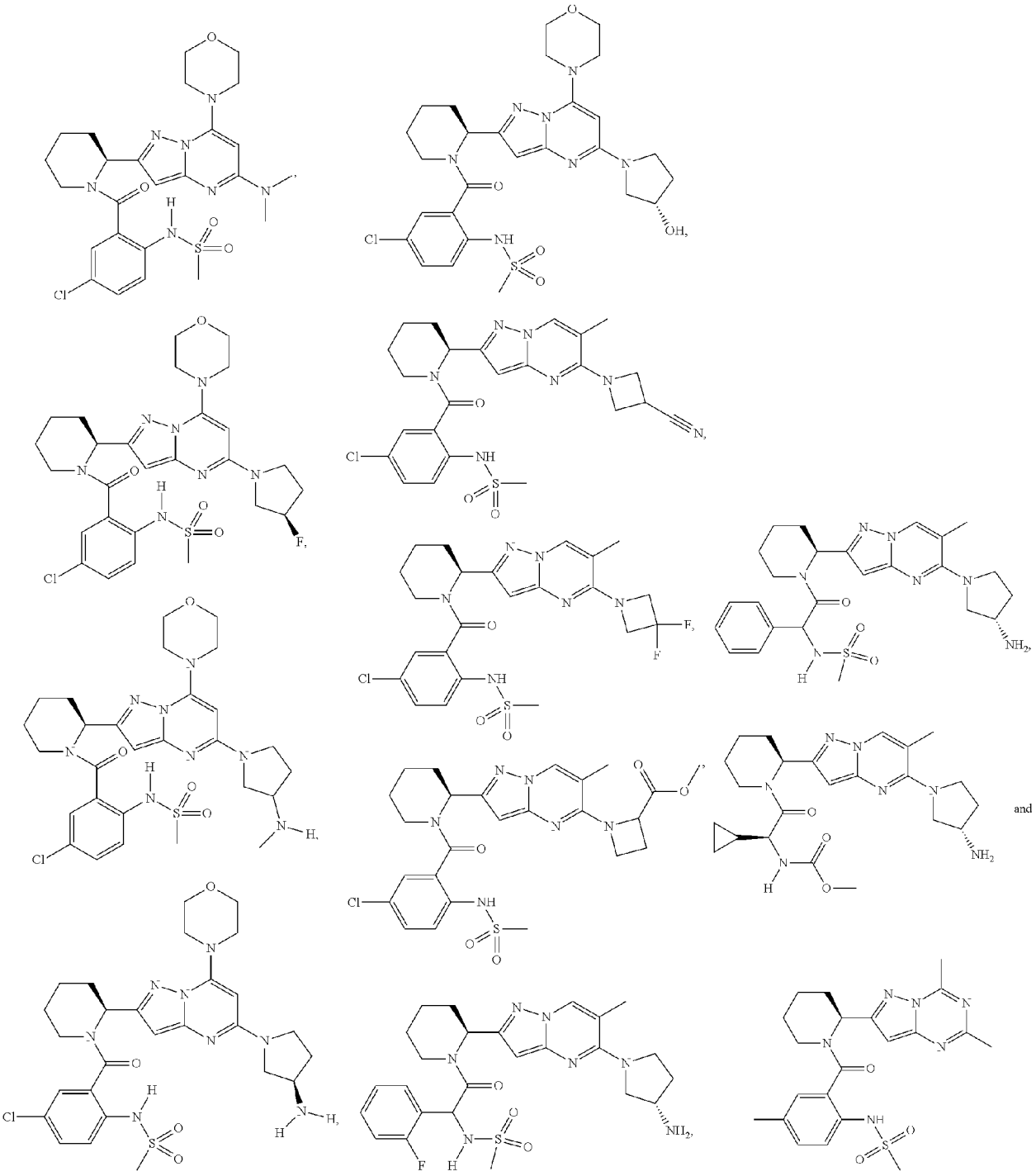








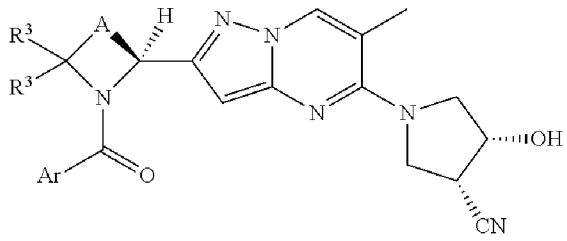


and

Compounds of Formula (B19)

[0148] Compounds of the general Formula (B19) are described in U.S. Publication No. 2013/0164280, published June 27, 2013, which is hereby incorporated by reference in its entirety. Formula (B19) has the structure:

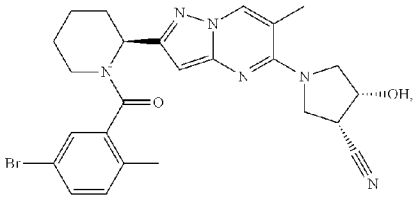
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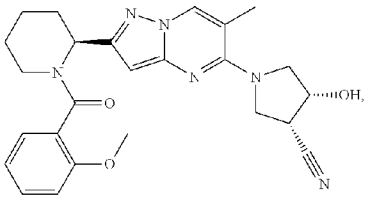


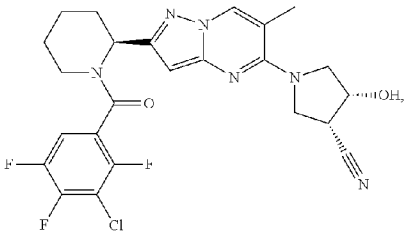
or a salt or ester thereof, wherein: A can be -$(C(R^4)_2)_n$- wherein any one $C(R^4)_2$ of said -$(C(R^4)_2)_n$- may be optionally replaced with –O–, –S–, –$S(O)_p$–, NH or NR^a; n can be 3,4, 5 or 6; each p can be 1 or 2; Ar can be a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1, 2, 3, 4 or 5 R^6; each R^3, R^4 or R^6 can be independently H, oxo, OR^{11}, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $S(O)_pR^a$, $NR^{11}S(O)_pR^a$, –$C(=O)R^{11}$, –$C(=O)OR^{11}$, –$C(=O)NR^{11}R^{12}$, –$C(=O)SR^{11}$, –$S(O)_p(OR^{11})$, –$SO_2NR^{11}R^{12}$, –$NR^{11}S(O)_p(OR^{11})$, –$NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl; or two R^4 on adjacent carbon atoms, when taken together, may optionally form a double bond between the two carbons to which they are attached or may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –$S(O)_p$–, –NH– or –NR^a–; or four R^4 on adjacent carbon atoms, when taken together, may optionally form an optionally substituted C_6 aryl ring; or two R^4 on the same carbon atom, when taken together, may optionally form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –$S(O)_p$–, –NH– or –NR^a–; or two R^6 on adjacent carbon atoms, when taken together, may optionally form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –$S(O)_p$–, –NH– or –NR^a–; each R^a can be independently (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl wherein any (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl or (C_2-C_8)alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl or (C_1-C_8)alkyl; each R^{11} or R^{12} can be independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl, (C_4-C_8)carbocyclylalkyl, —C(=O)R^a, —$S(O)_pR^a$ or aryl(C_1-C_8)alkyl; or R^{11} and R^{12} can be taken together with a nitrogen to which they are both attached form a

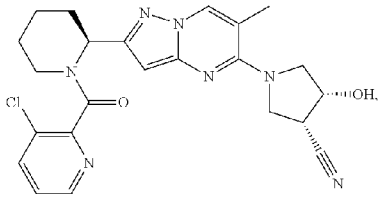
3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, $–S(O)_p–$, –NH–, $–NR^a–$;or –C(O) –; and wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl of each R^6, R^{11} or R^{12} can be, independently, optionally substituted with one or more oxo, halogen, hydroxy, NH_2, CN, N_3, $N(R^a)_2$, NHR^a, SH, SR^a, $S(O)_pR^a$, OR^a, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, $–C(O)R^a$, –C(O)H, $–C(=O)OR^a$, –C(=O)OH, $–C(=O)N(R^a)_2$, $–C(=O)NHR^a$, $–C(=O)NH_2$, $NHS(O)_pR^a$, $NR^aS(O)_pR^a$, $NHC(O)R^a$, $NR^aC(O)R^a$, $NHC(O)OR^a$, $NR^aC(O)OR^a$, $NR^aC(O)NHR^a$, $NR^aC(O)N(R^a)_2$, $NR^aC(O)NH_2$, $NHC(O)NHR^a$, $NHC(O)N(R^a)_2$, $NHC(O)NH_2$, =NH, =NOH, $=NOR^a$, $NR^aS(O)_pNHR^a$, $NR^aS(O)_pN(R^a)_2$, $NR^aS(O)_pNH_2$, $NHS(O)_pNHR^a$, $NHS(O)_pN(Ra)_2$, $NHS(O)_pNH_2$, $–OC(=O)R^a$, $–OP(O)(OH)_2$ or R^a.

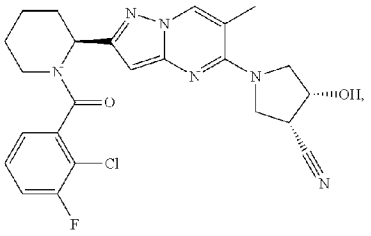
[0149] Examples of Compounds of Formula (B19) include:

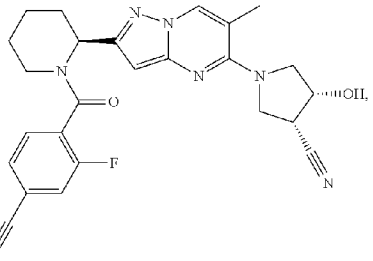


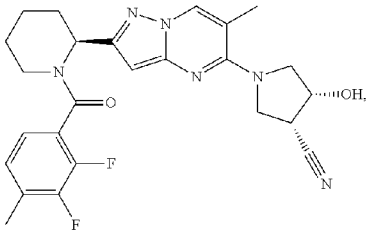


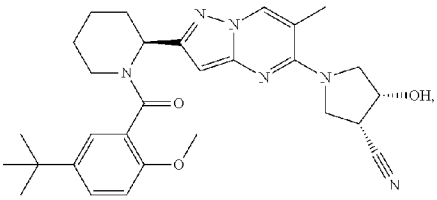


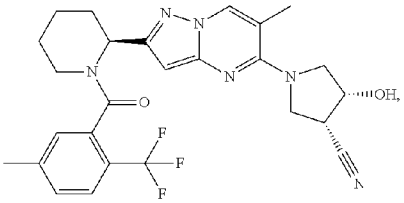


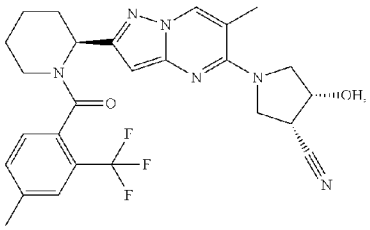


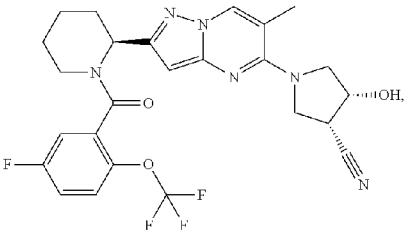


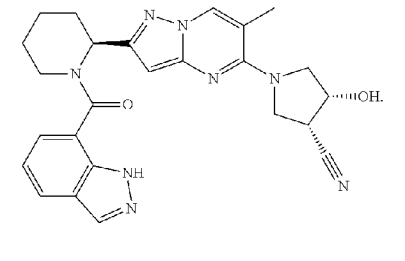


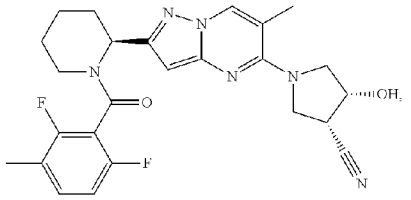


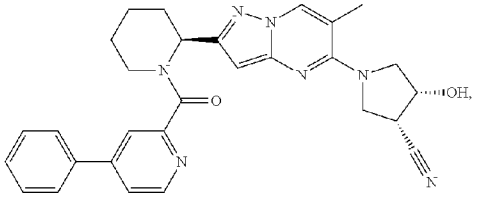


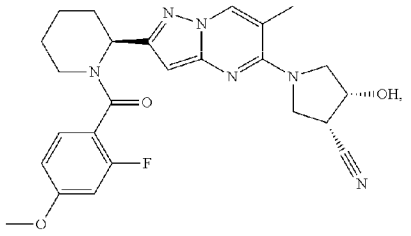


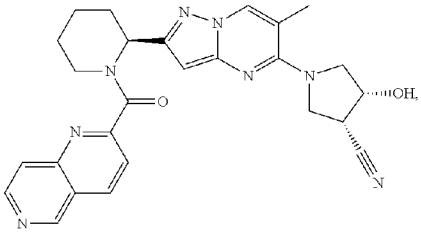


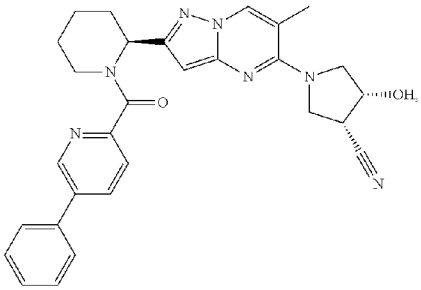


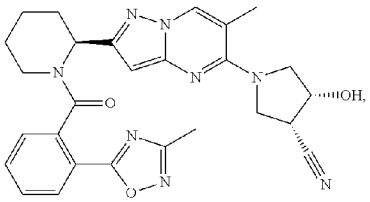


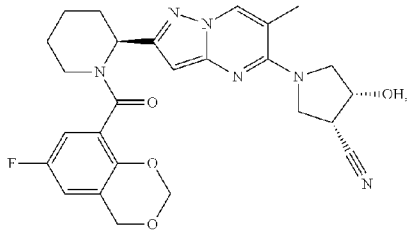


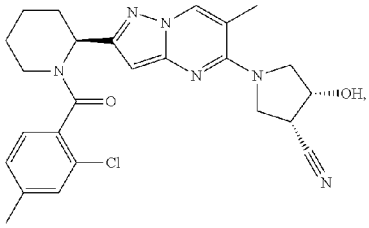


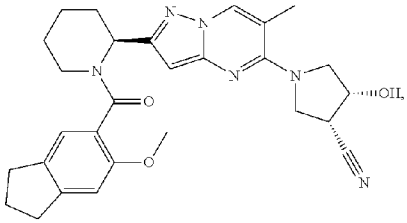


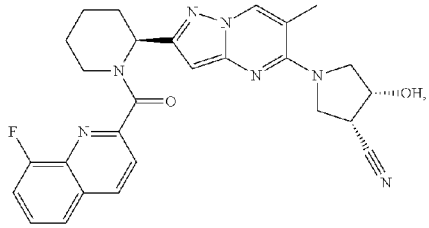


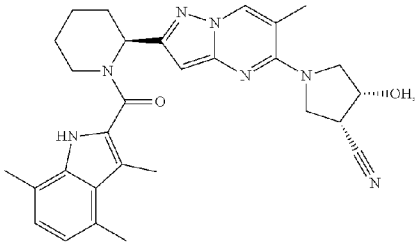


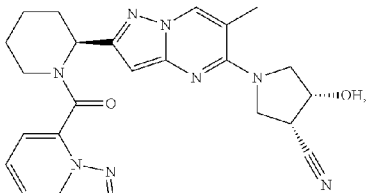


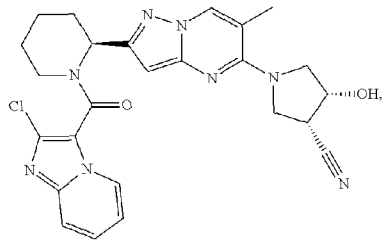


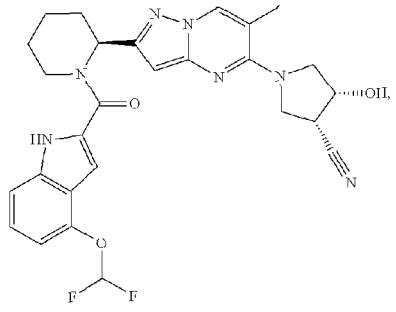


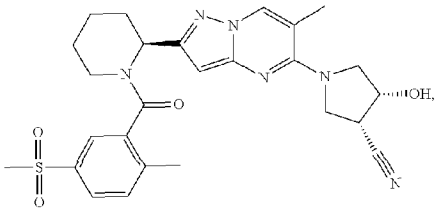


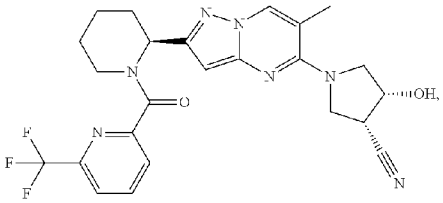


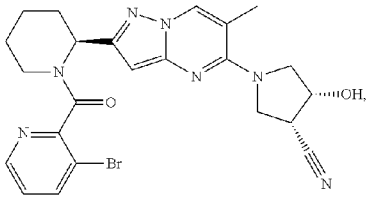


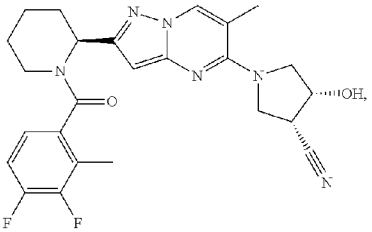


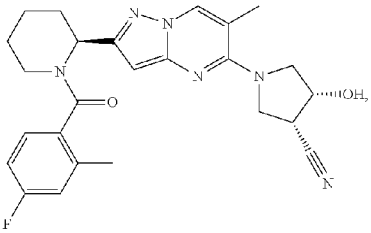


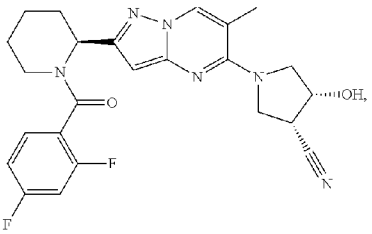


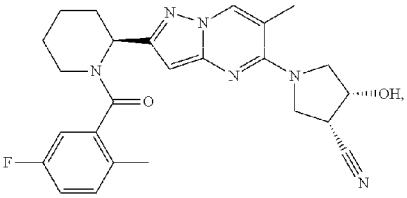


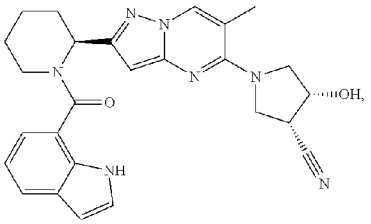


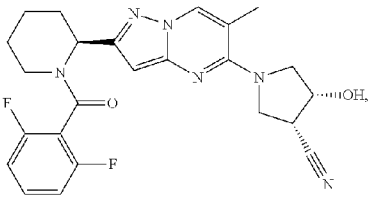


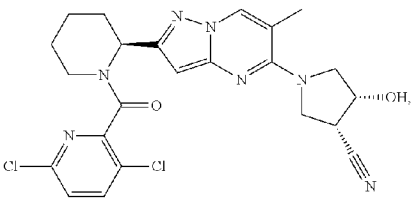


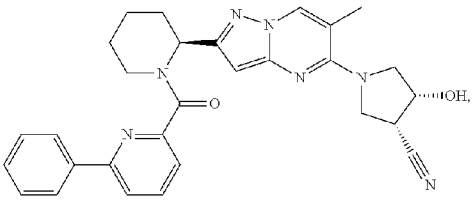


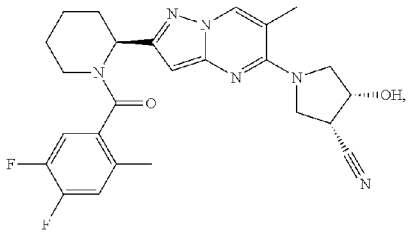


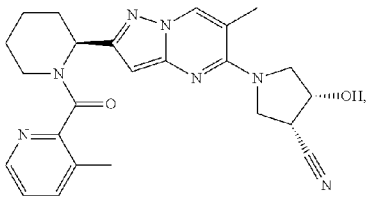


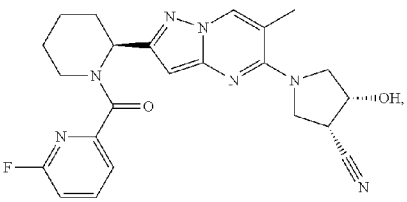


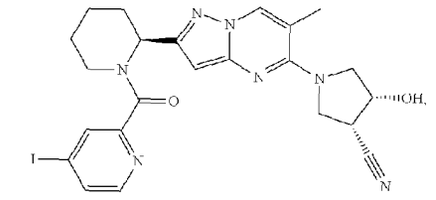


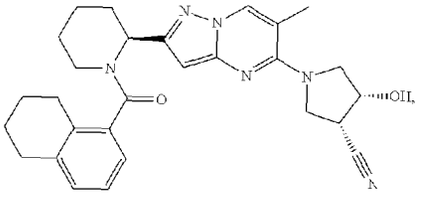


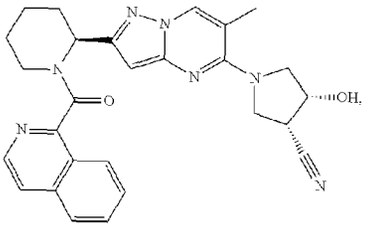


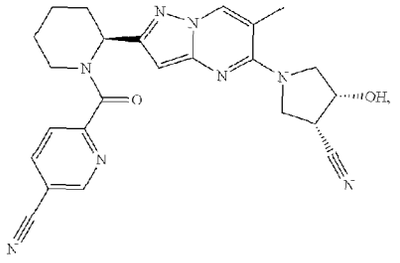


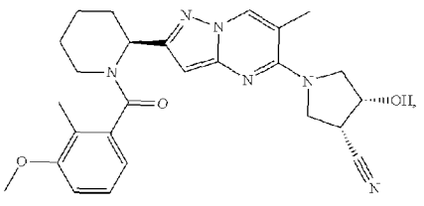


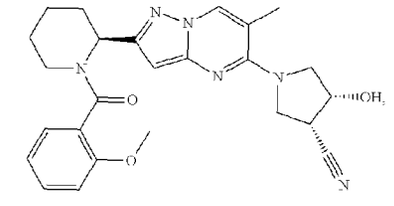


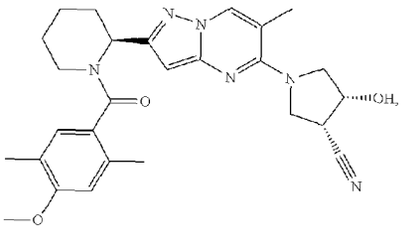


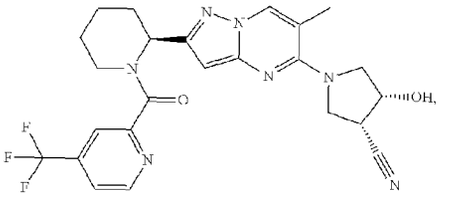


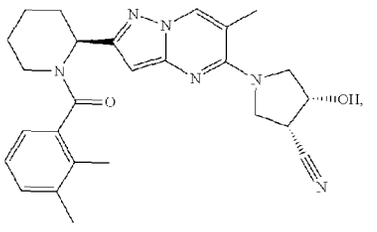


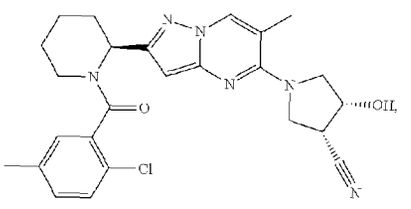


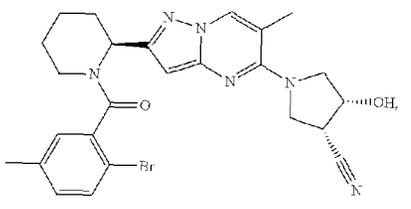


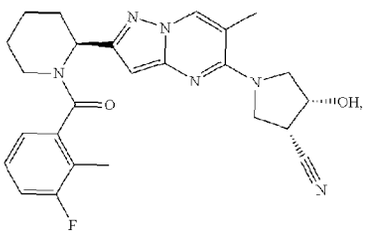


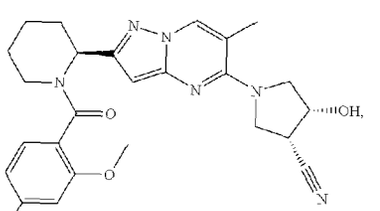




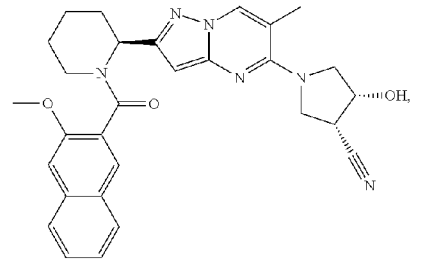


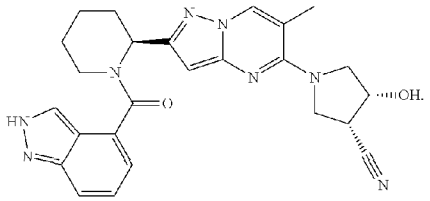


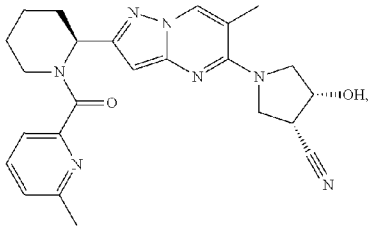


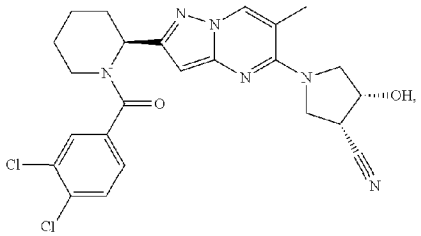


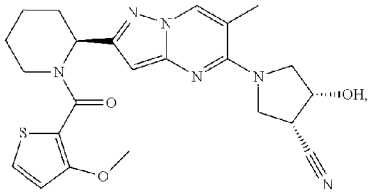


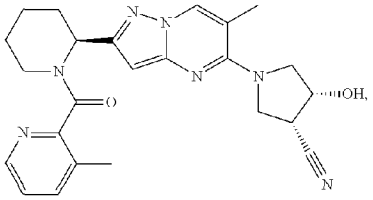


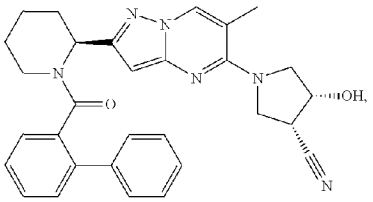


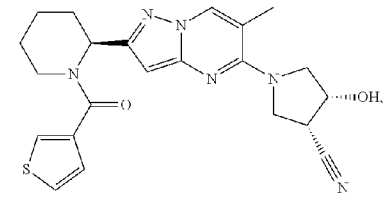


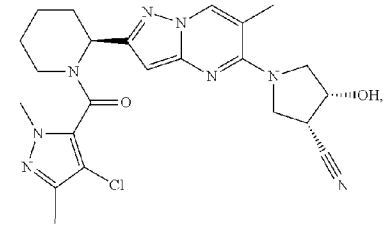


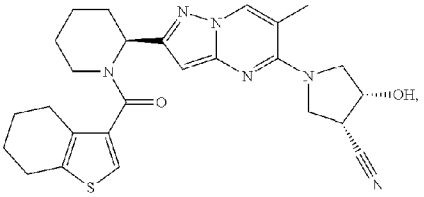


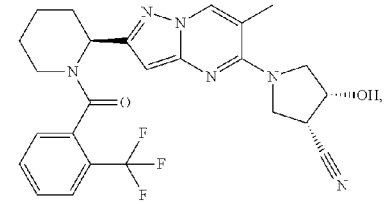


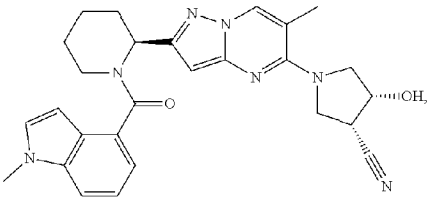


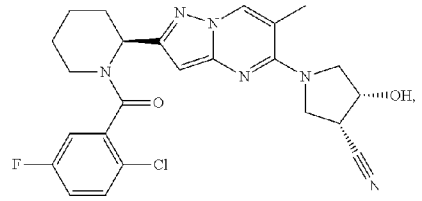


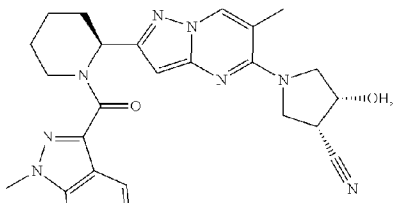


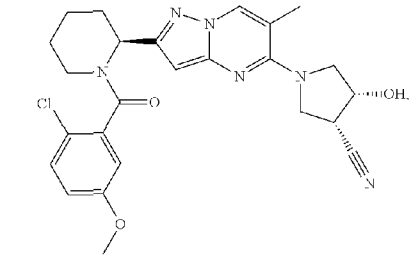


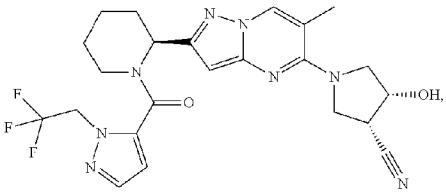


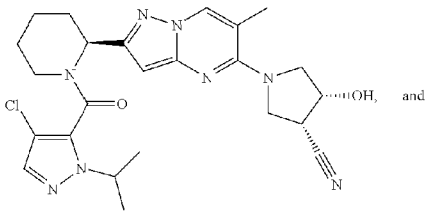




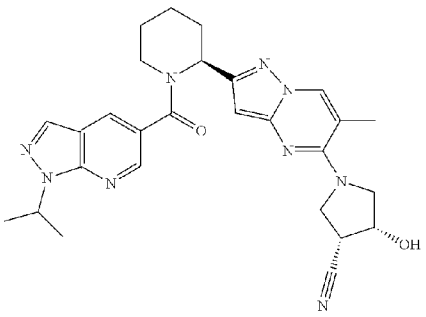


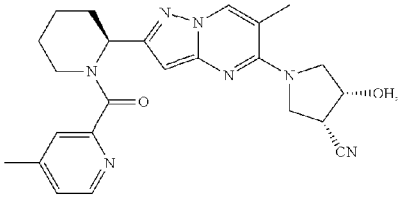


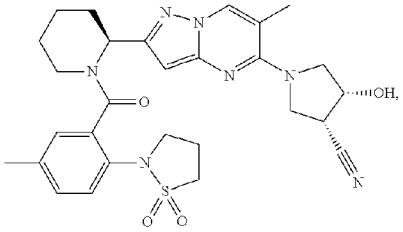


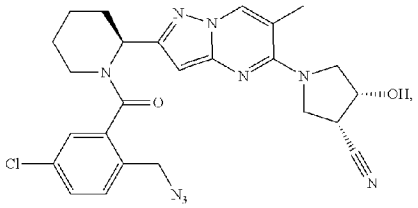


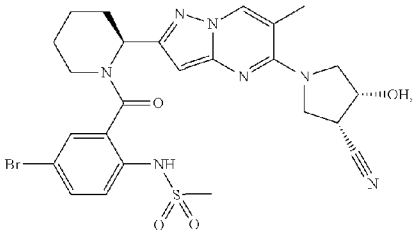
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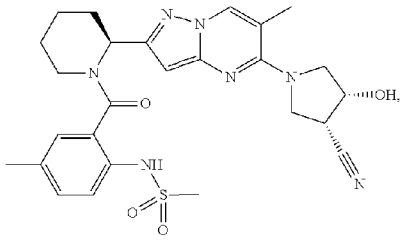


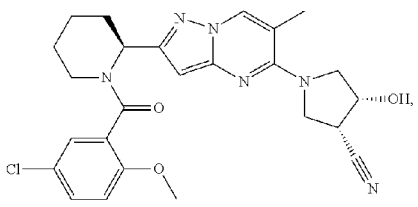


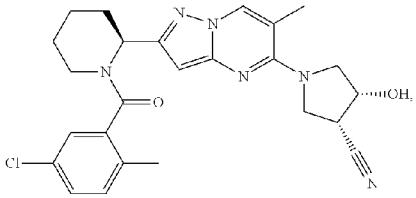


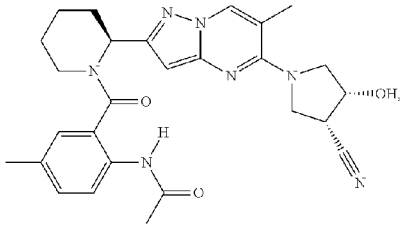


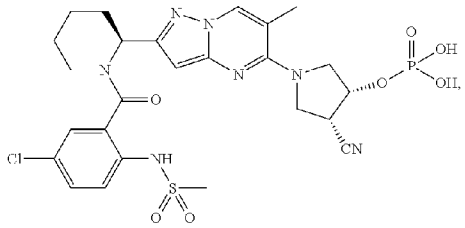


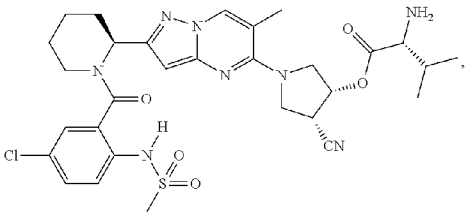


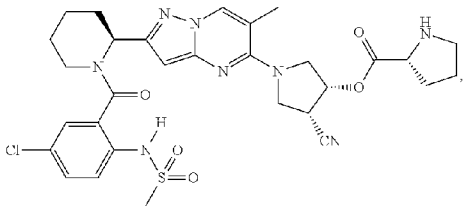


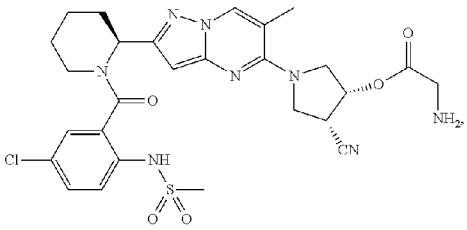


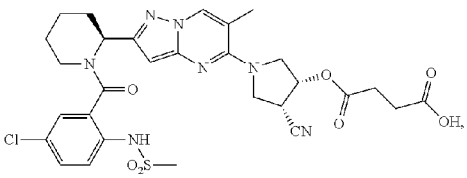


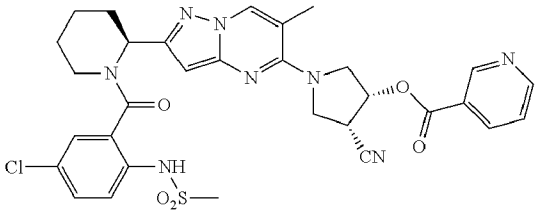




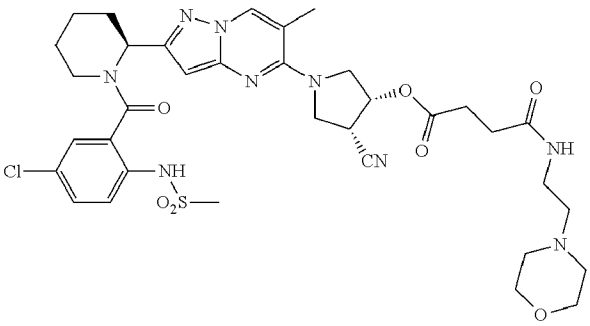


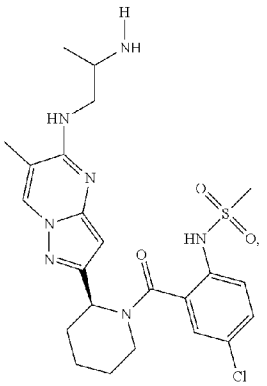


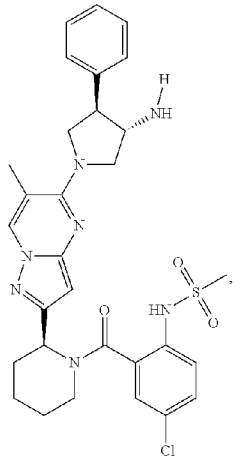


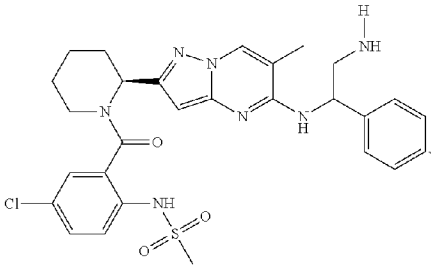


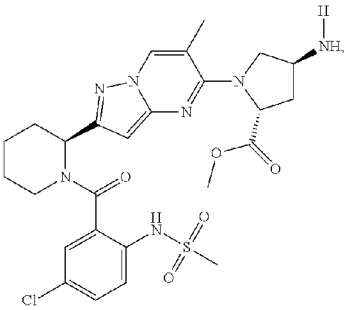
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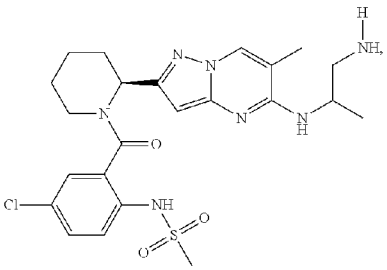


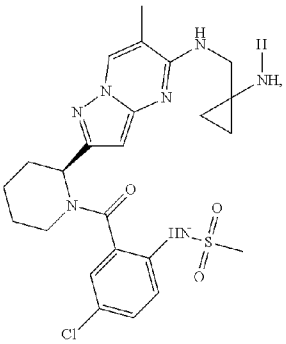


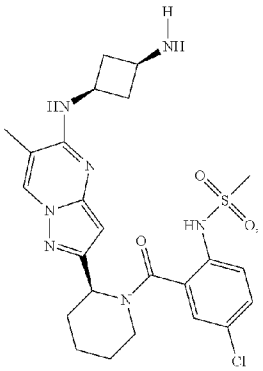


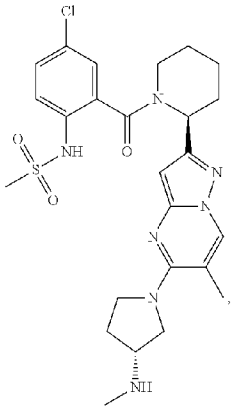


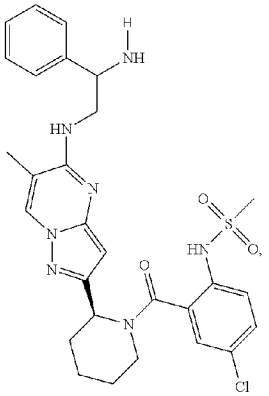


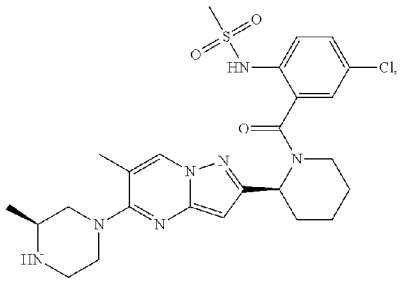


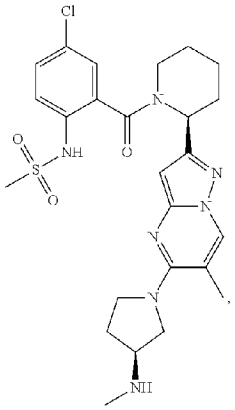


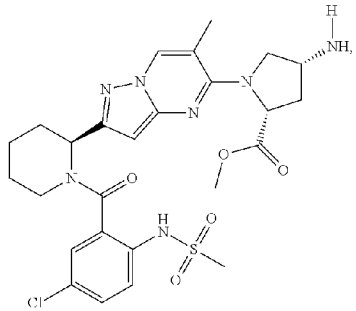


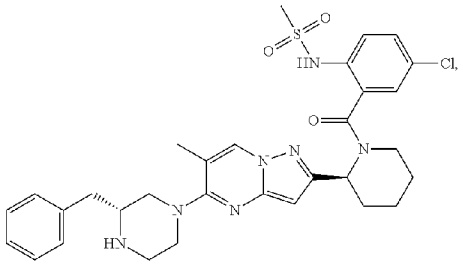


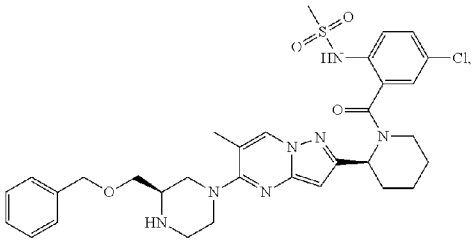


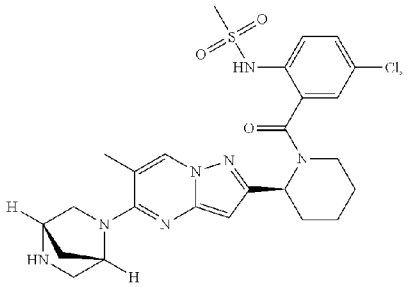


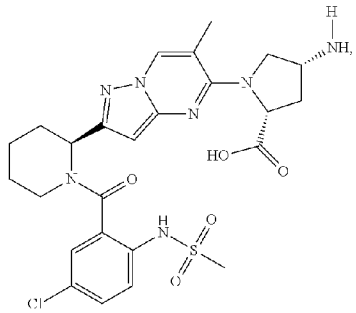


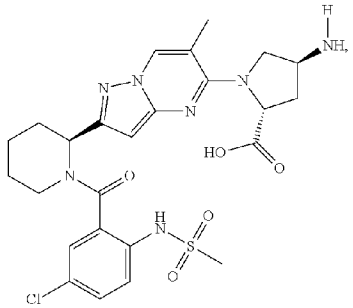


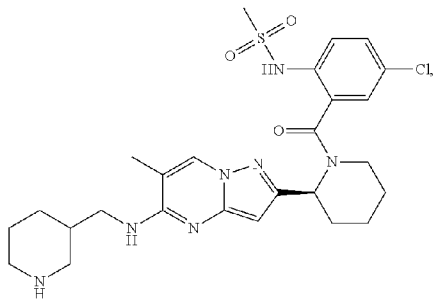


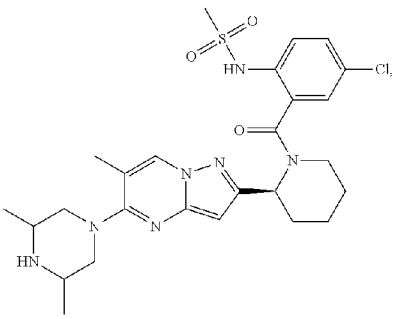


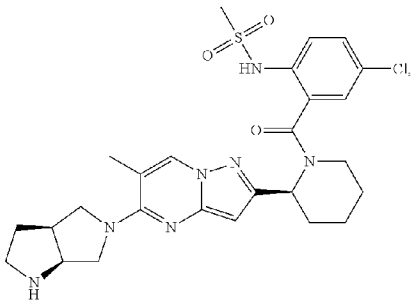


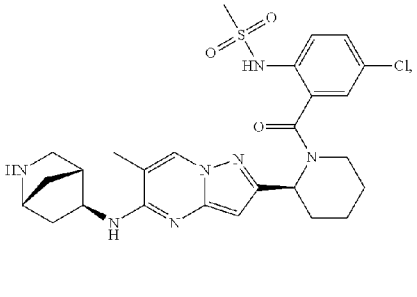


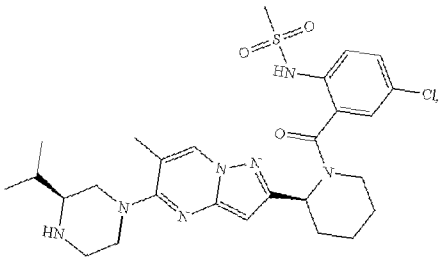


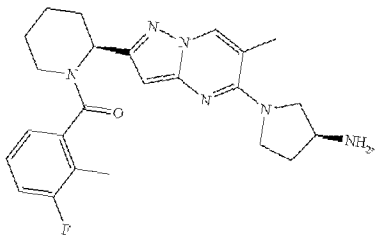


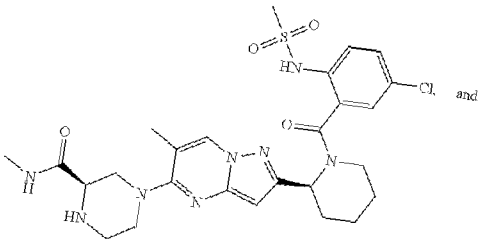




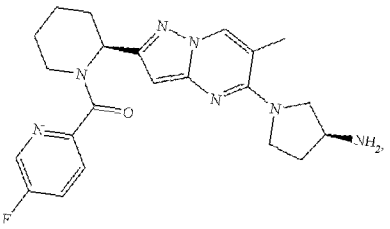


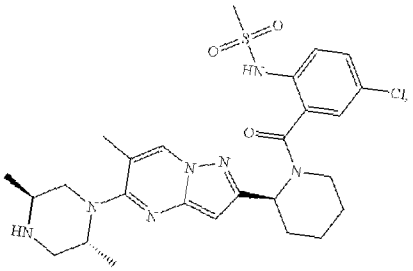


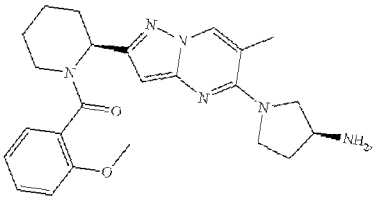


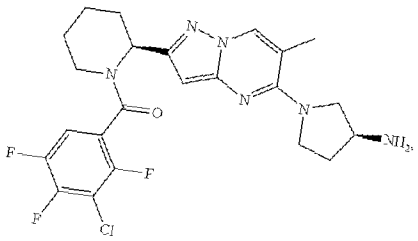


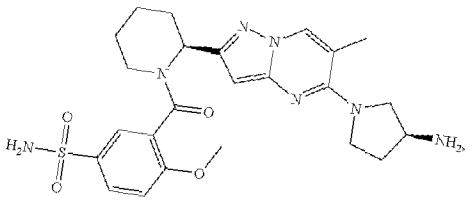
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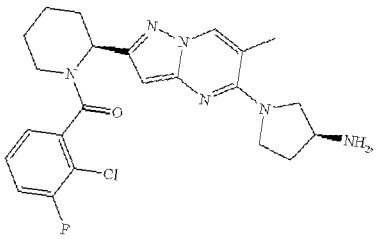


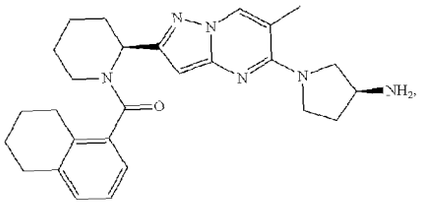


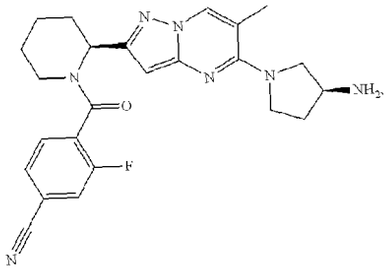


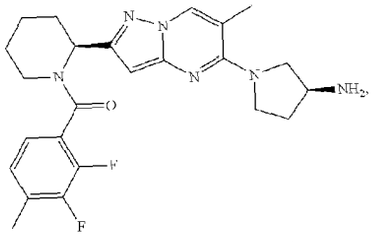


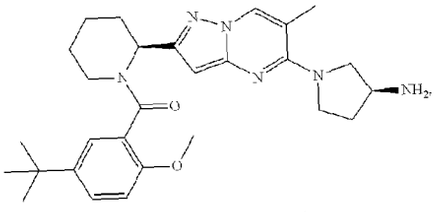


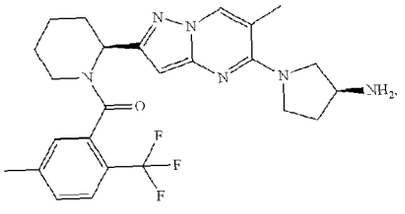


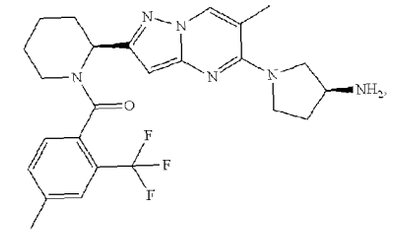


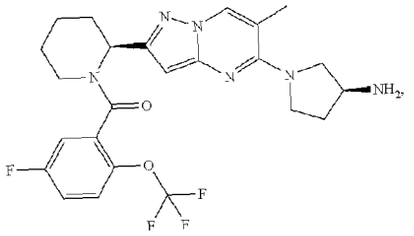


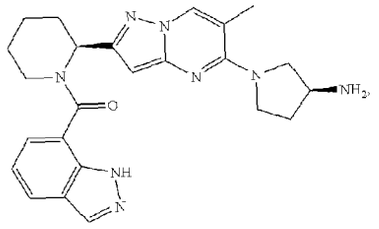


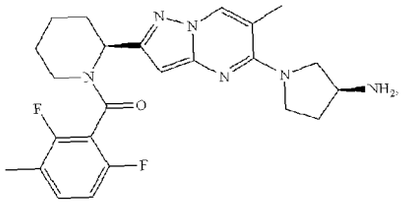


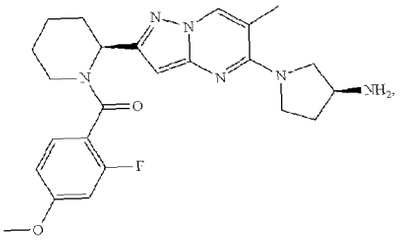


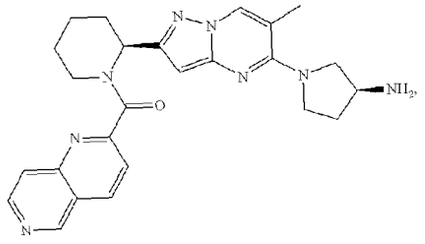


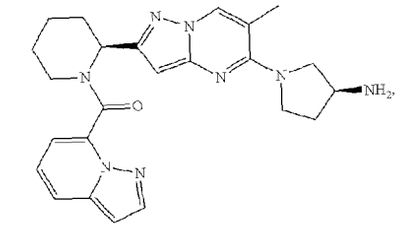


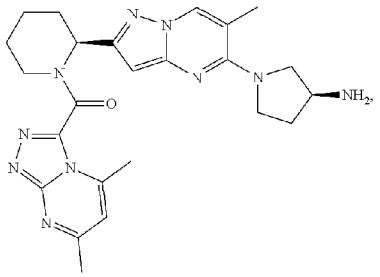


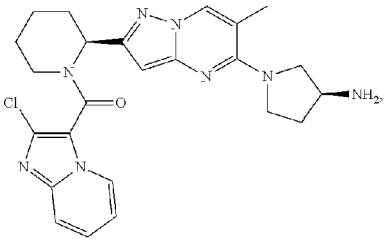


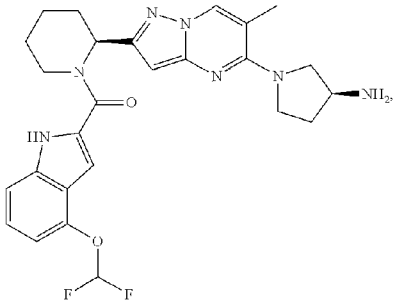


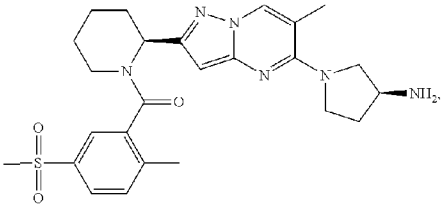


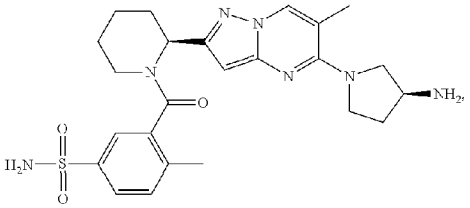


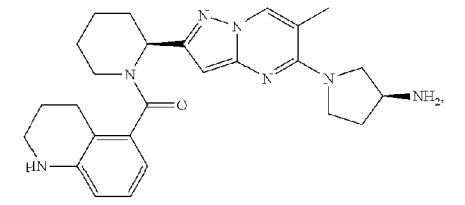


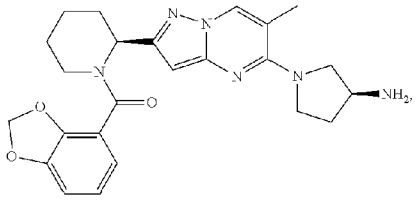


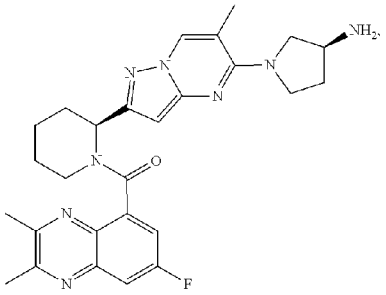


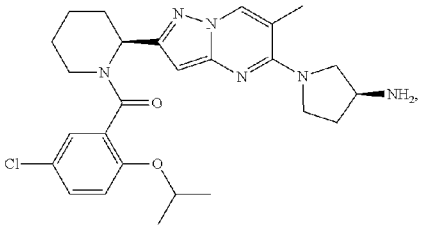


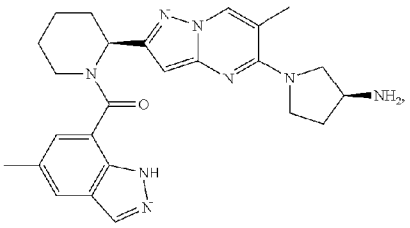


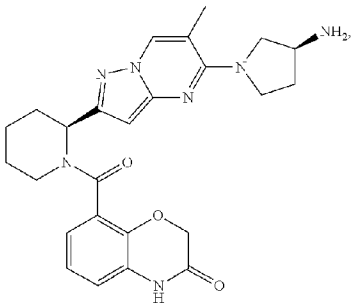


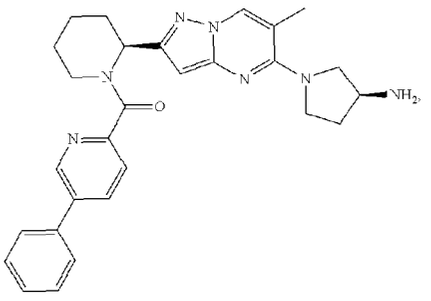


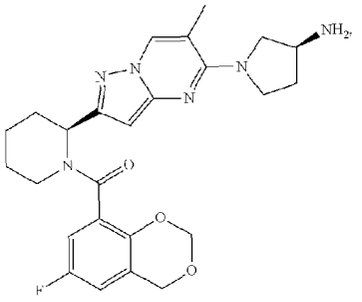


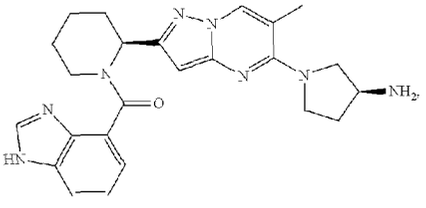


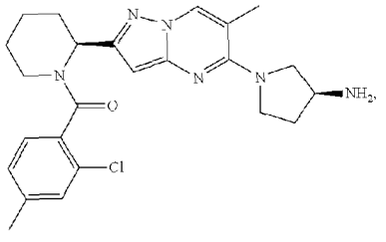


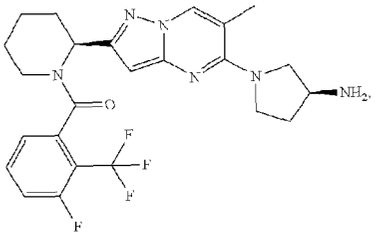


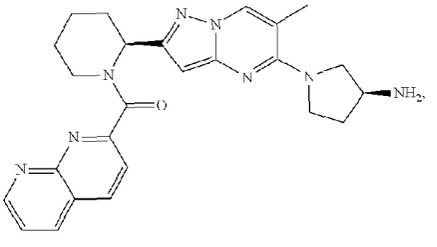


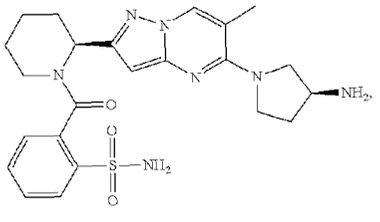


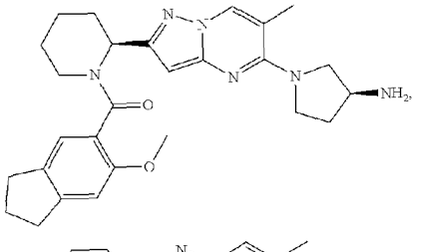


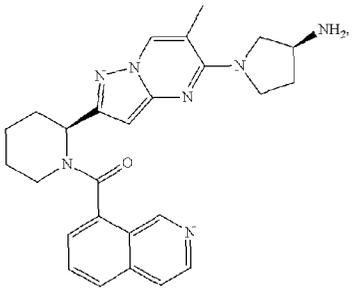


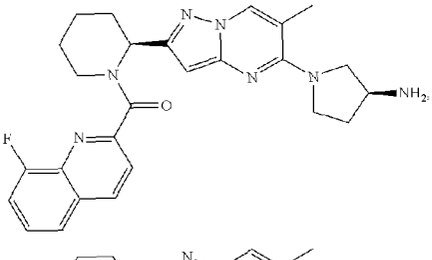


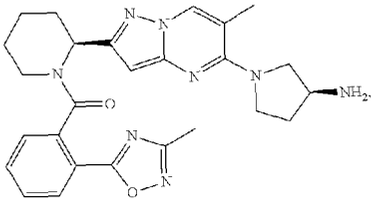


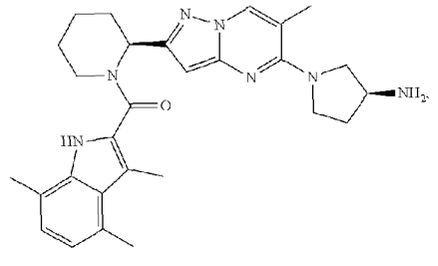


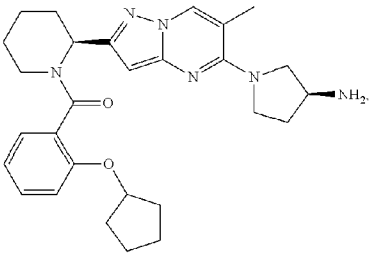


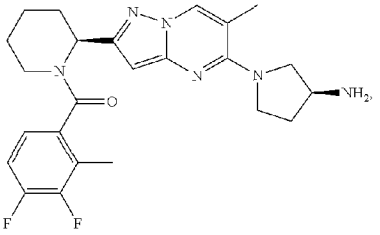


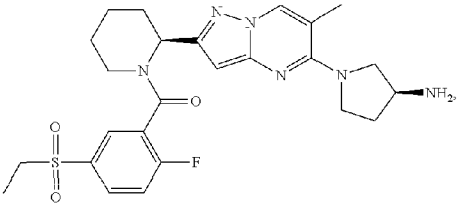


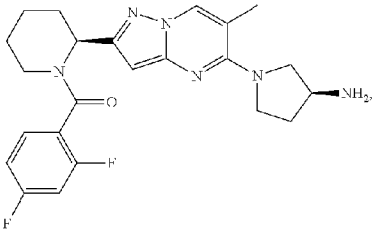


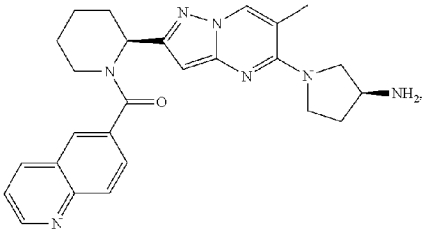


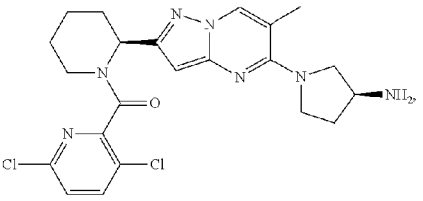


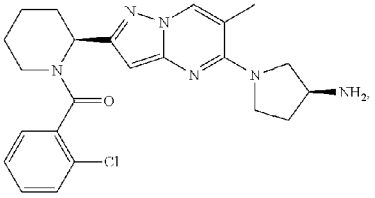


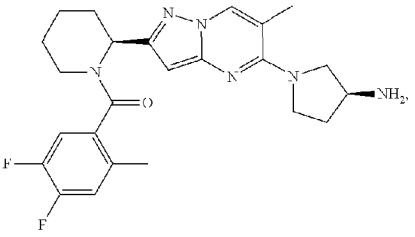


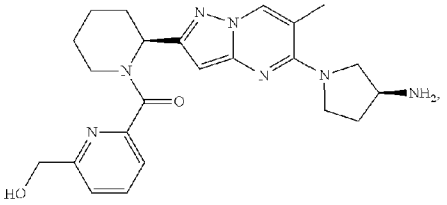


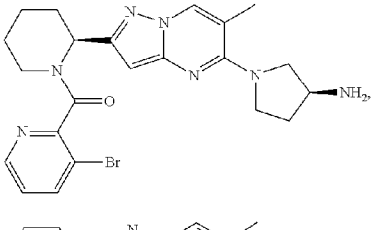


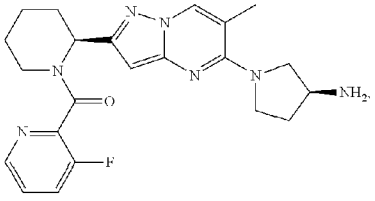


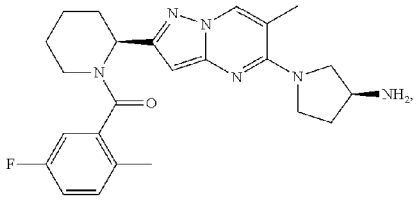


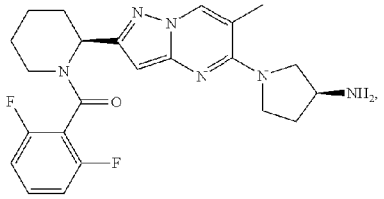


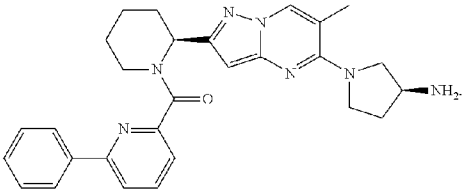


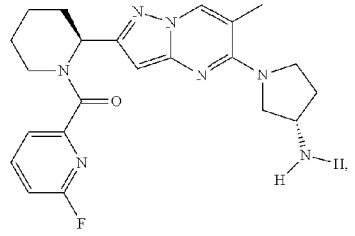


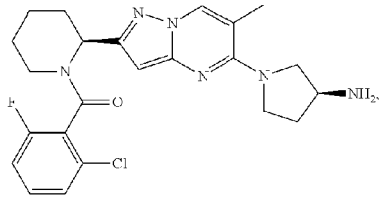


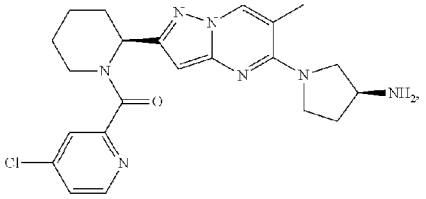


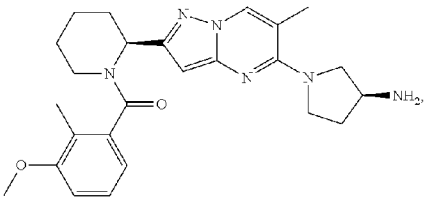


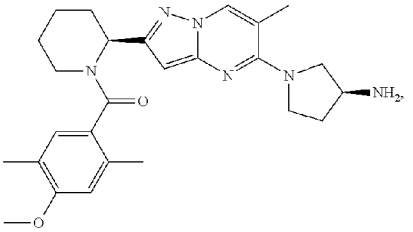


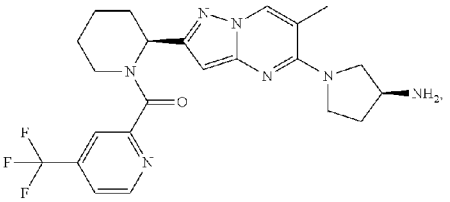


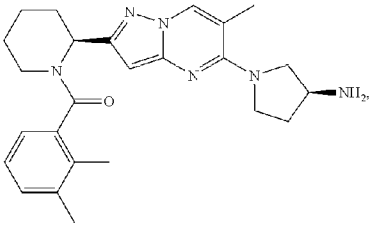


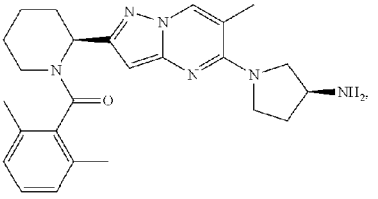


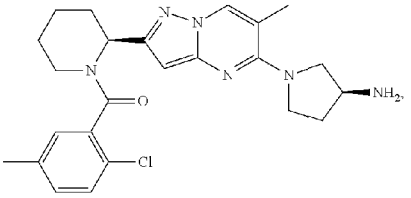


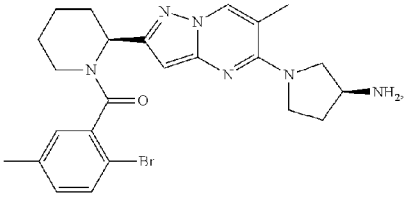


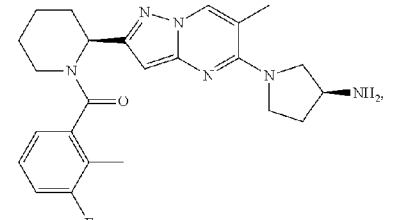




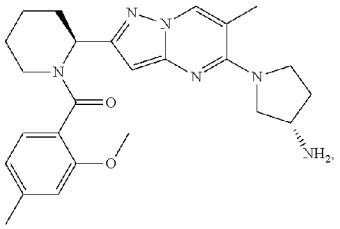


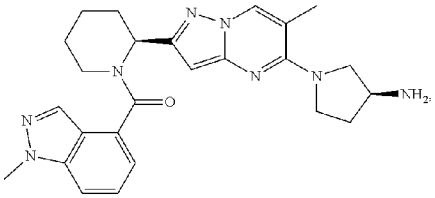


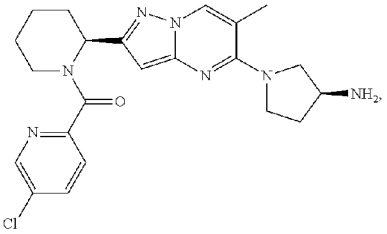


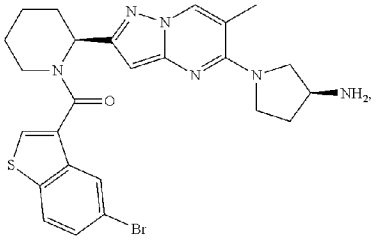


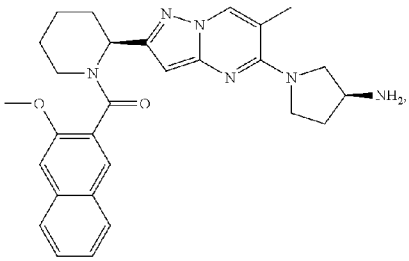


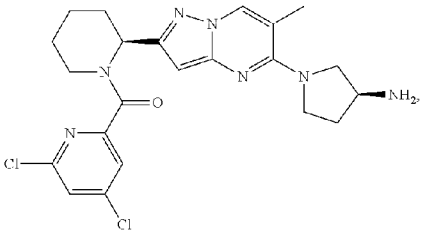


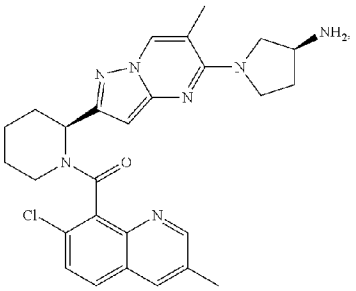


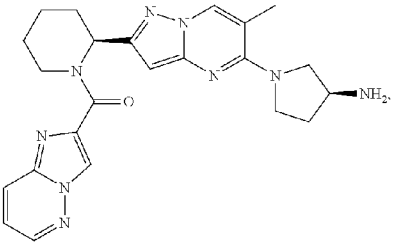


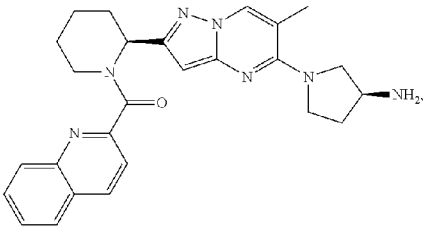


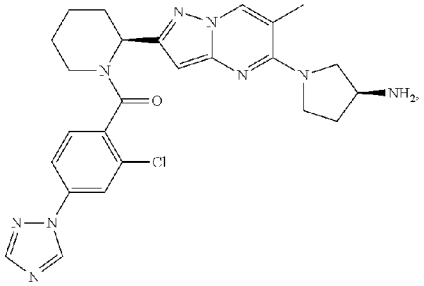


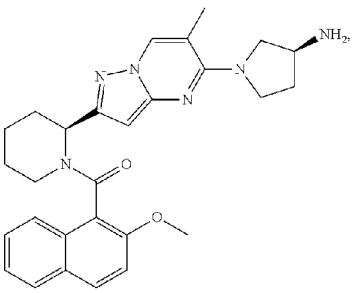


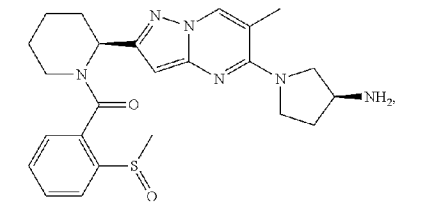


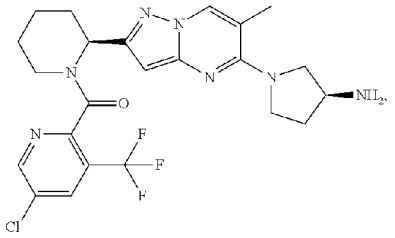


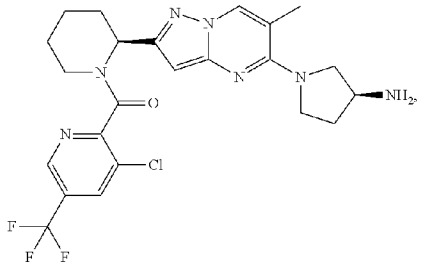


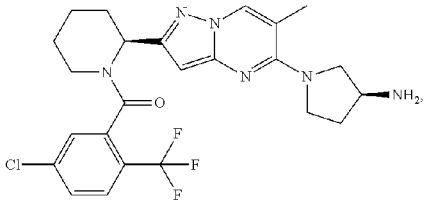


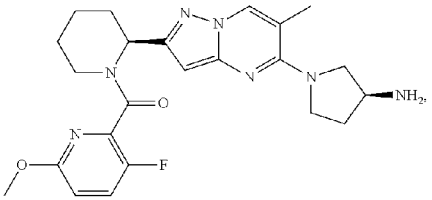


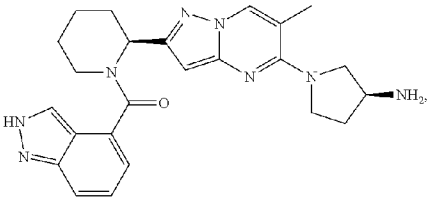


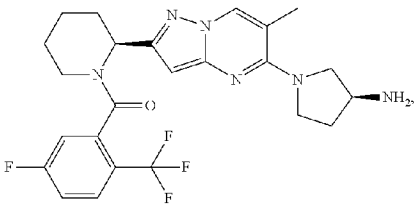


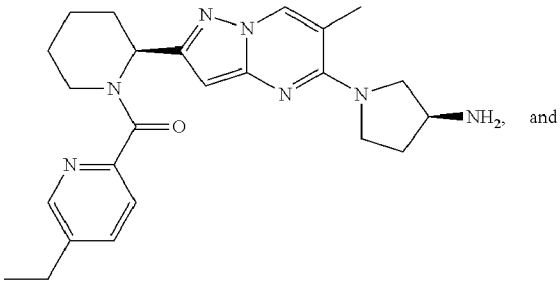




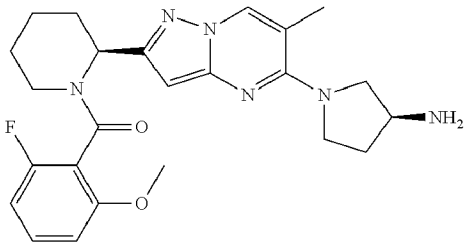






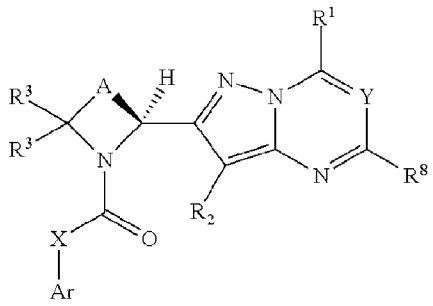
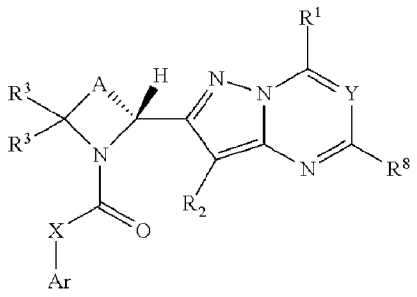


and



Compounds of Formula (B20)

[0150] Compounds of the general Formula (B20) are described in U.S. Publication No. 2014/0072554, published March 13, 2014, which is hereby incorporated by reference in its entirety. Formula (B20) has a structure selected from:

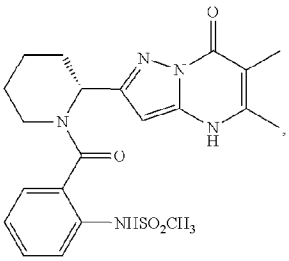
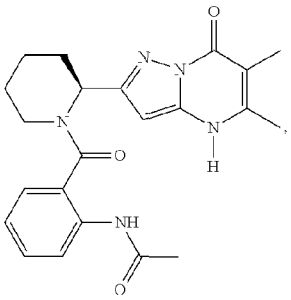
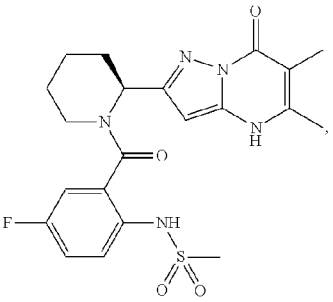
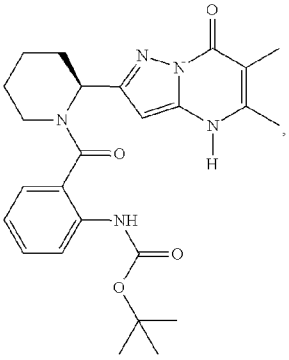
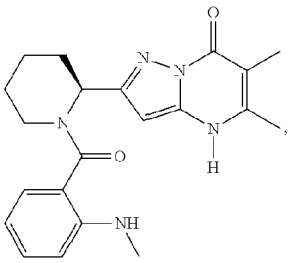
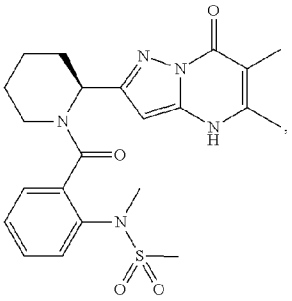
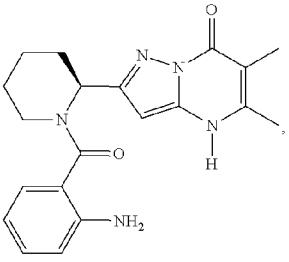
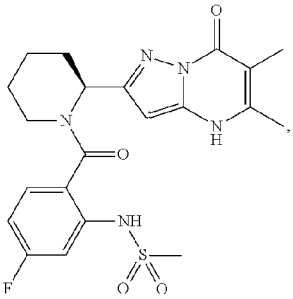
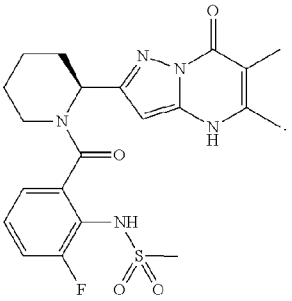
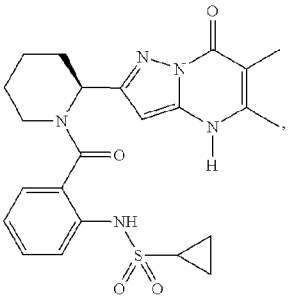
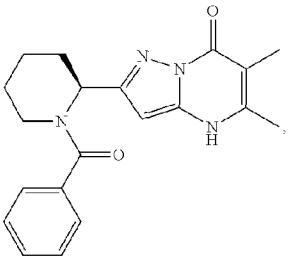
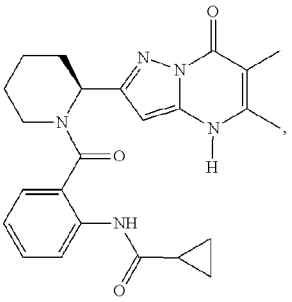
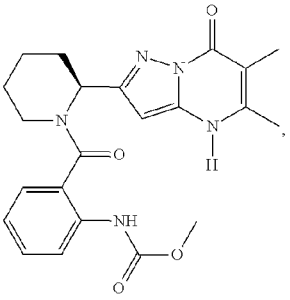
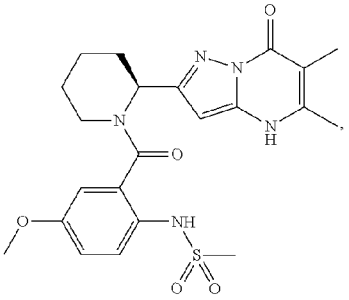
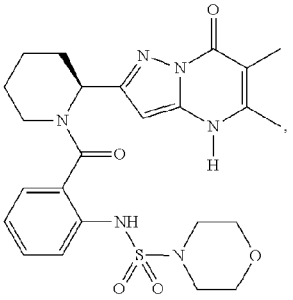



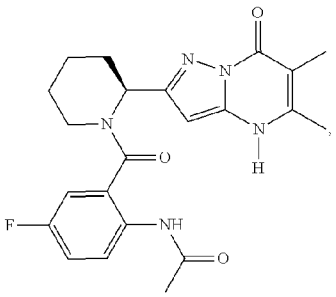
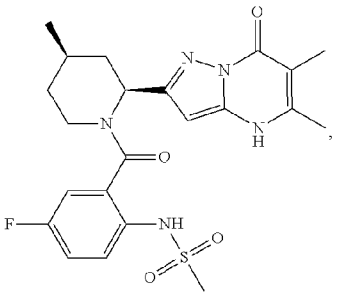
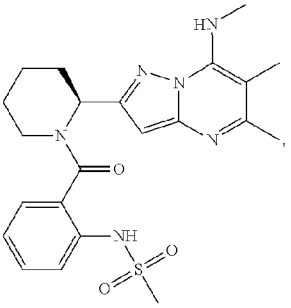
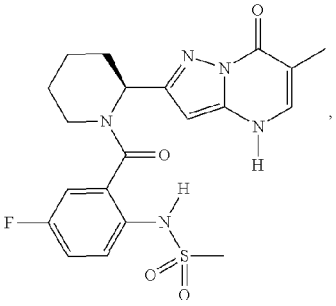
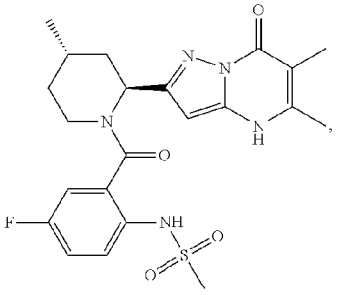
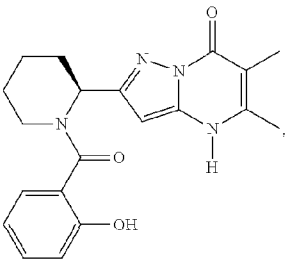
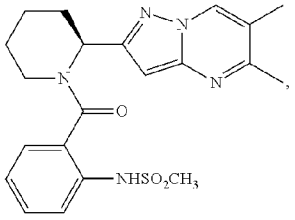
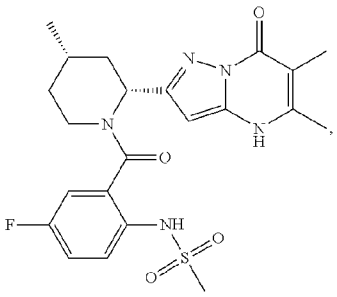
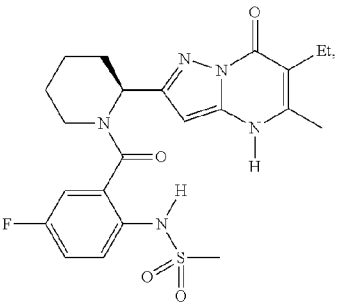
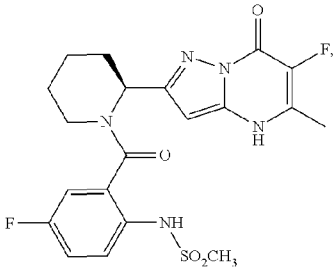
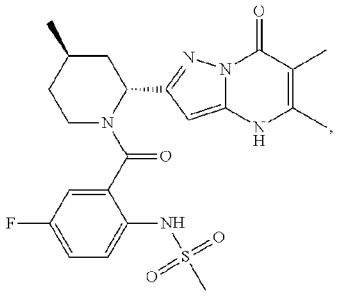
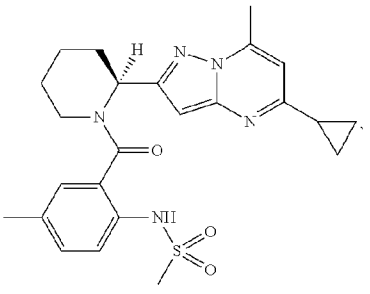
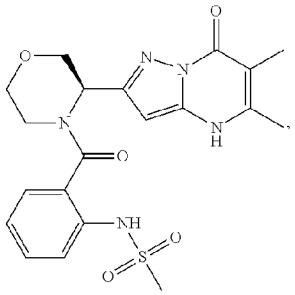
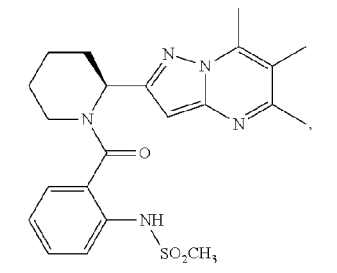
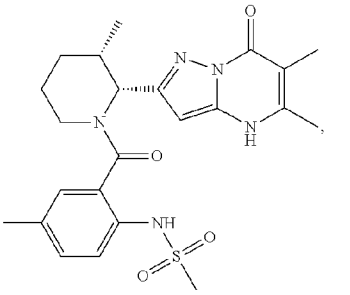
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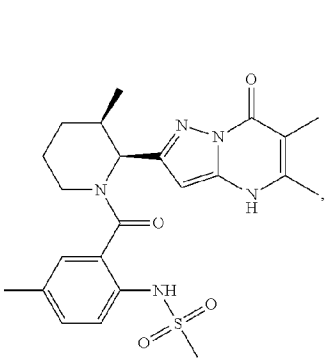
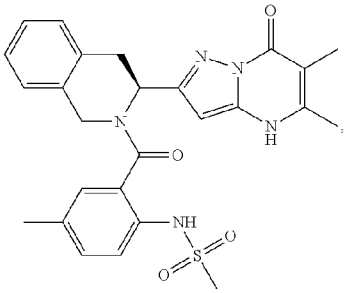
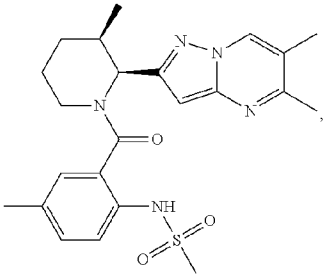
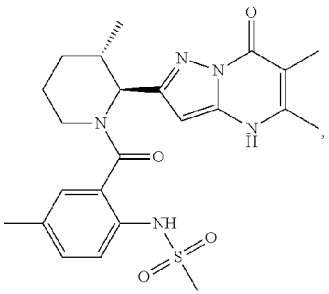
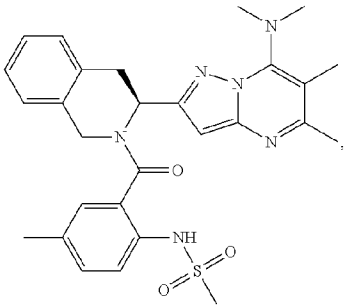
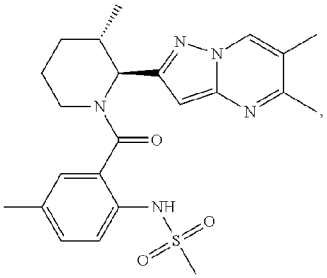
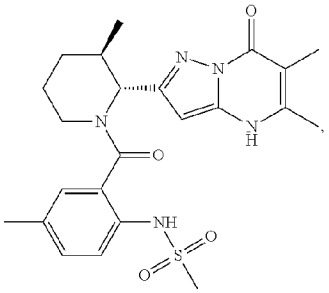
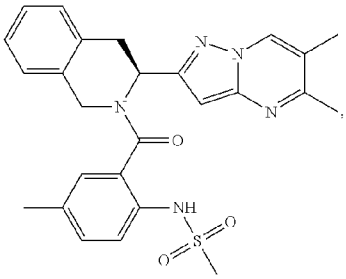
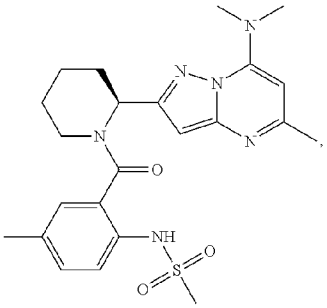
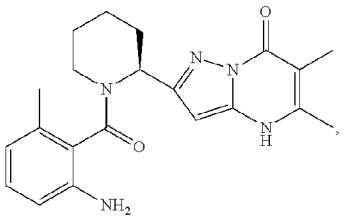
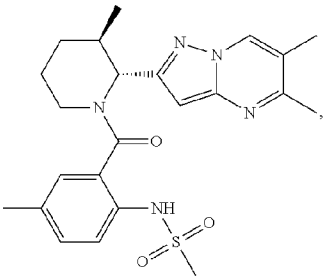
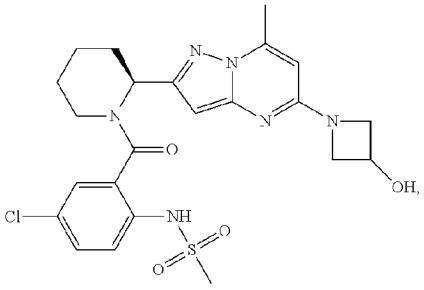
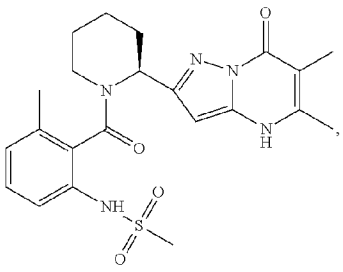
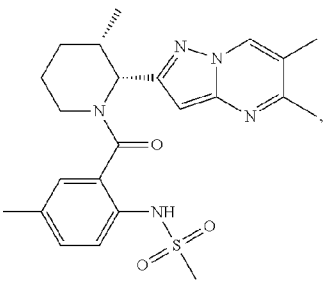
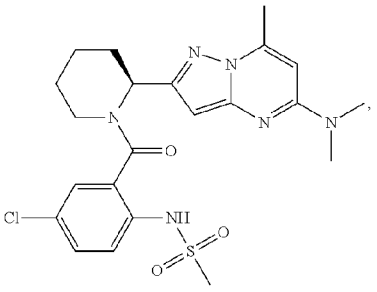
a pharmaceutically acceptable salt or ester, wherein: A can be $-(C(R^4)_2)_n-$ wherein any one $C(R^4)_2$ of said $-(C(R^4)_2)_n-$ may be optionally replaced with –O–, –S–, $-S(O)_p-$, NH or NR^a; n can be 3, 4, 5 or 6; each p can be 1 or 2; Ar can be a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1 to 5 R^6; X can be $-C(R^{13})(R^{14})-$, $-N(CH_2R^{14})-$ or X is absent; Y can be N or CR^7; each R^1, R^2, R^3, R^4, R^5, R^6, R^7 or R^8 can be independently H, oxo, OR^{11}, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $S(O)_pR^a$, $NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl; two R^4 on adjacent carbon atoms, when taken together, may form a double bond between the two carbons to which they are attached or may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p-$, –NH– or $-NR^a-$; four R^4 on adjacent carbon atoms, when taken together, may form an optionally substituted C_6 aryl ring; two R^4 on the same carbon atom, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p-$, –NH– or $-NR^a-$; two R^6 on adjacent carbon atoms, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p-$, –NH– or $-NR^a-$; any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^3, may form a bond or a $-(C(R^5)_2)_m-$ group wherein m is 1 or 2; any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^2, may form a bond; each R^a can be independently $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl wherein any $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $(C_2$-$C_8)$alkenyl or $(C_2$-$C_8)$alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl of R^a is

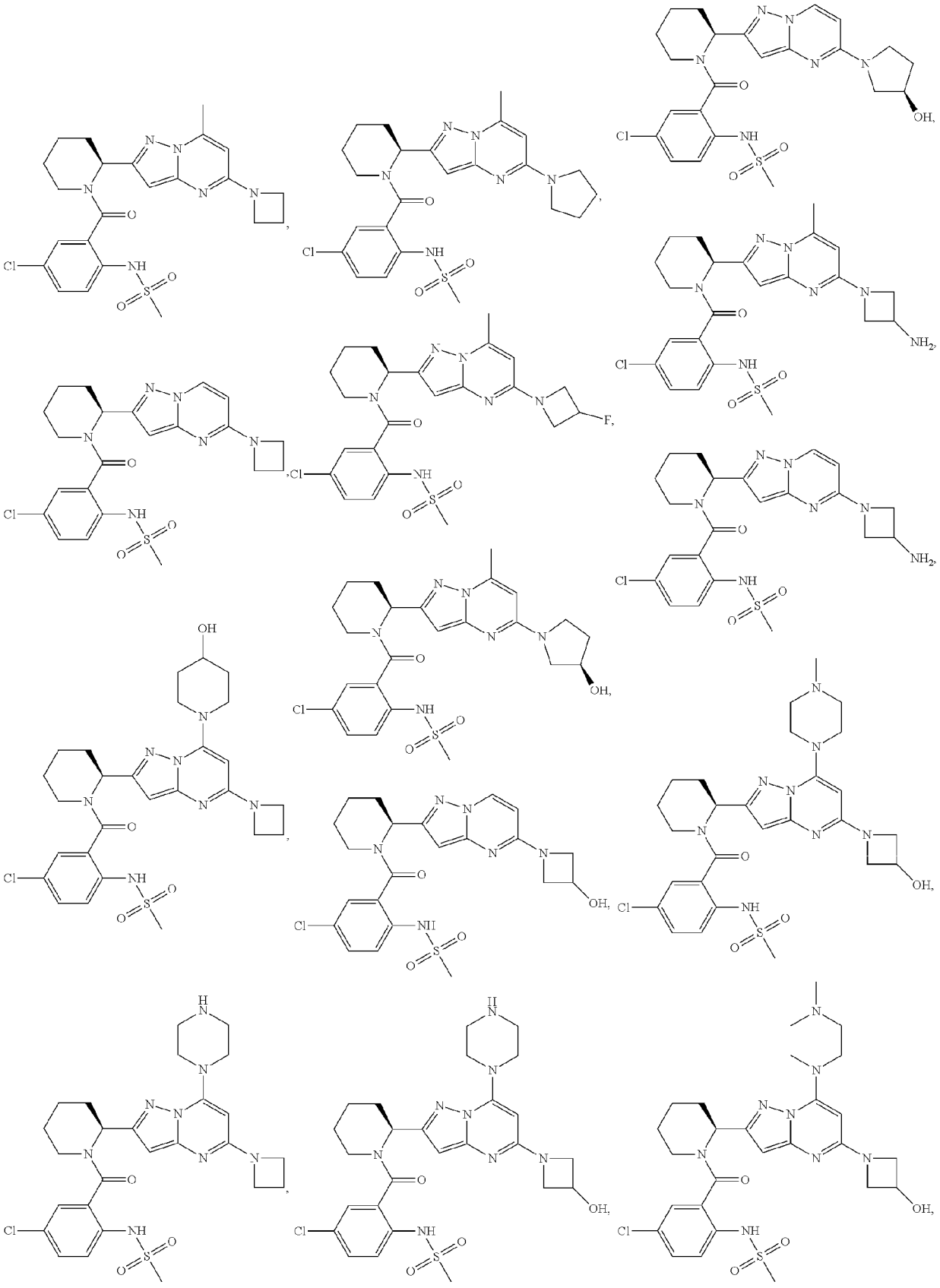
optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl or (C_1-C_8)alkyl; each R^{11} or R^{12} can be independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl, (C_4-C_8)carbocyclylalkyl, –C(=O)R^a, –S(O)$_p$$R^a$, or aryl($C_1$-$C_8$)alkyl; or R^{11} and R^{12} can be taken together with a nitrogen to which they are both attached form a 3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, –S(O)$_p$–, –NH–, –NR^a– or –C(O) –; R^{13} can be H or (C_1-C_8)alkyl; R^{14} can be H, (C_1-C_8)alkyl, $NR^{11}R^{12}$, NR^{11}C(O)R^{11}, NR^{11}C(O)OR^{11}, NR^{11}C(O)$NR^{11}R^{12}$, NR^{11}S(O)$_p$$R^a$, –$NR^{11}$S(O)$_p$($OR^{11}$) or $NR^{11}SO_pNR^{11}R^{12}$; and wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl of each R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11} or R^{12} can be, independently, optionally substituted with one or more oxo, halogen, hydroxy, NH_2, CN, N_3, N(R^a)$_2$, NHR^a, SH, SR^a, S(O)$_p$$R^a$, O$R^a$, ($C_1$-$C_8$)alkyl, ($C_1$-$C_8$)haloalkyl, –C(O)$R^a$, –C(O)H, –C(=O)O$R^a$, –C(=O)OH, –C(=O)N($R^a$)$_2$, –C(=O)NH$R^a$, –C(=O)$NH_2$, NHS(O)$_p$$R^a$, NR^aS(O)$_p$$R^a$, NHC(O)$R^a$, NR^aC(O)R^a, NHC(O)OR^a, NR^aC(O)OR^a, NR^aC(O)NHR^a, NR^aC(O)N(R^a)$_2$, NR^aC(O)NH_2, NHC(O)NHR^a, NHC(O)N(R^a)$_2$, NHC(O)NH_2, =NH, =NOH, =NOR^a, NR^aS(O)$_p$NHR^a, NR^aS(O)$_p$N(R^a)$_2$, NR^aS(O)$_p$$NH_2$, NHS(O)$_pNHR^a$, NHS(O)$_p$N($R^a$)$_2$, NHS(O)$_p$$NH_2$, –OC(=O)$R^a$, –OP(O)$(OH)_2$ or R^a.

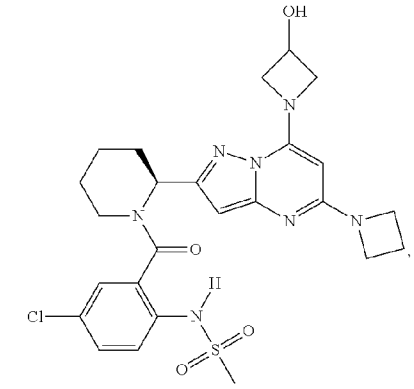
[0151] Examples of Compounds of Formula (B20) include:

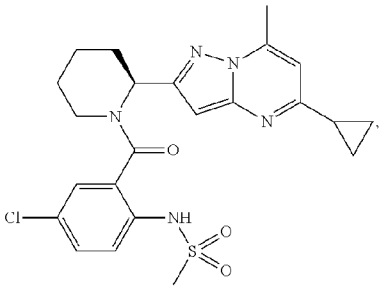
















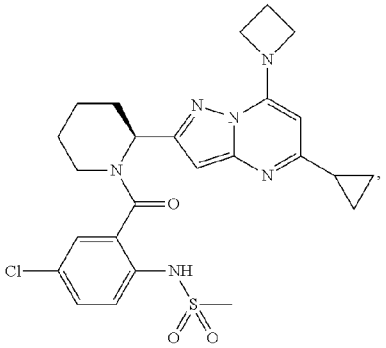
















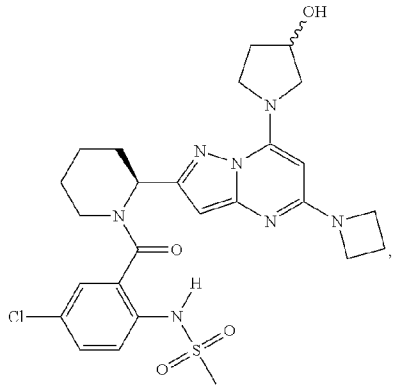
















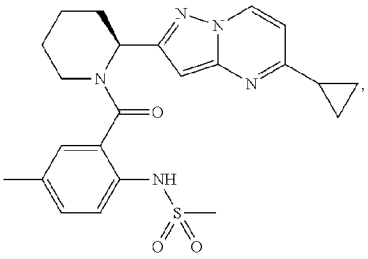


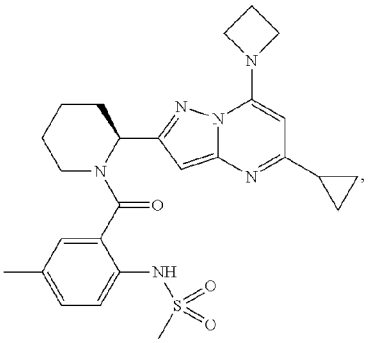


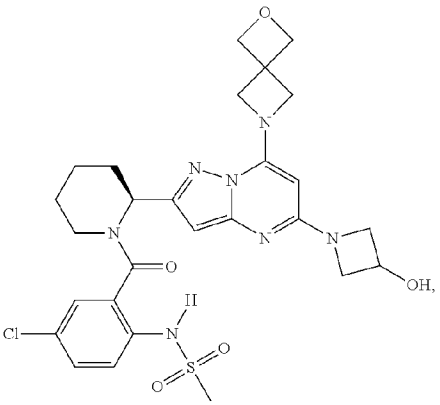


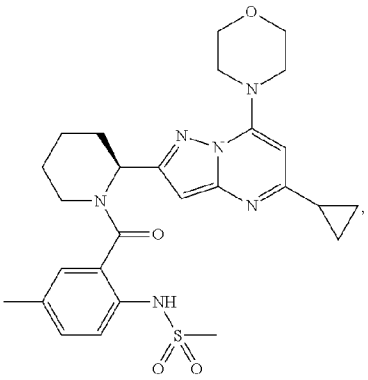


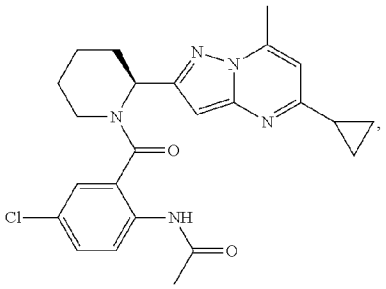


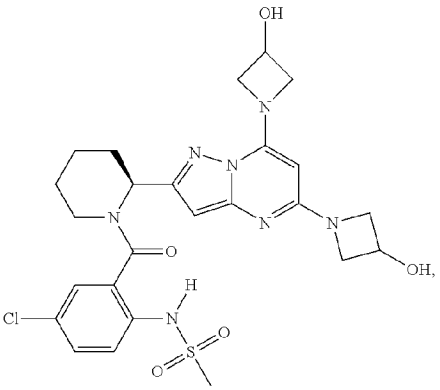


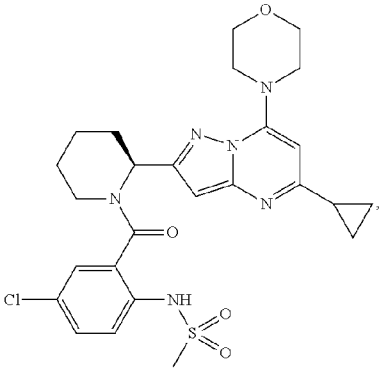


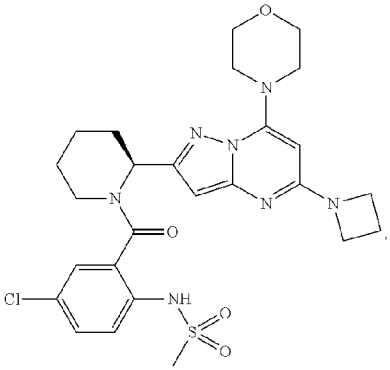


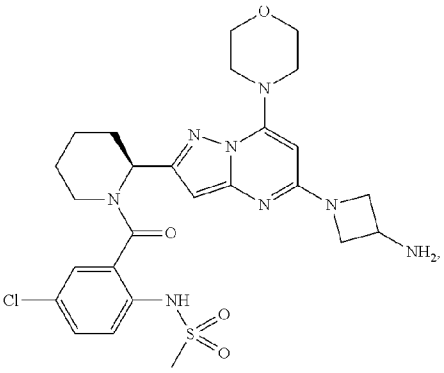


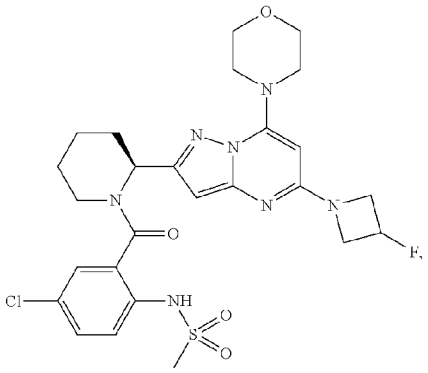


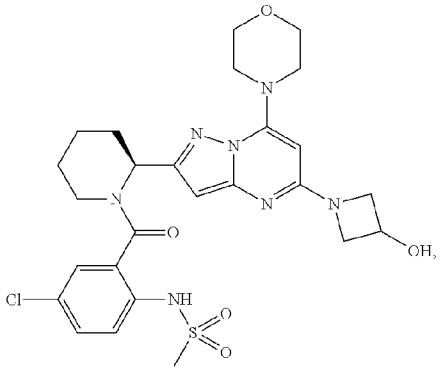


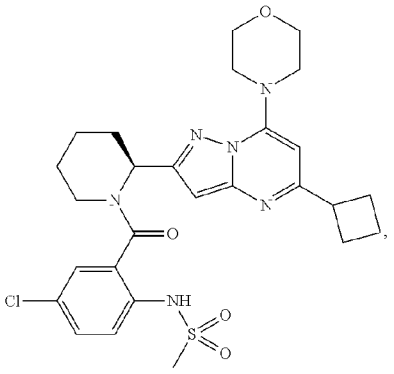


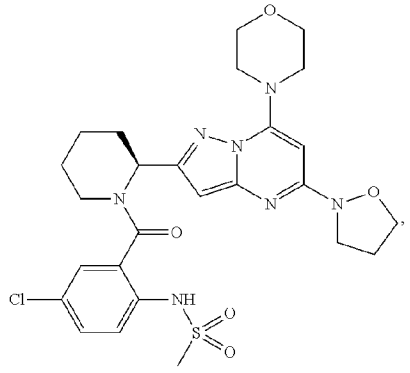


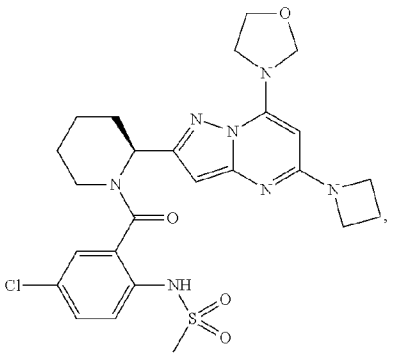


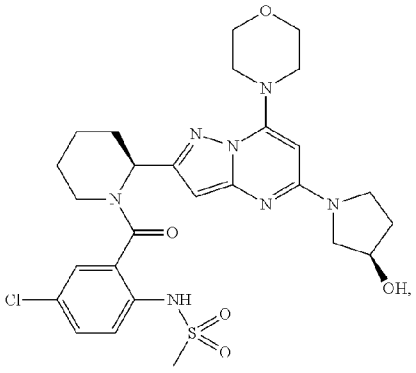


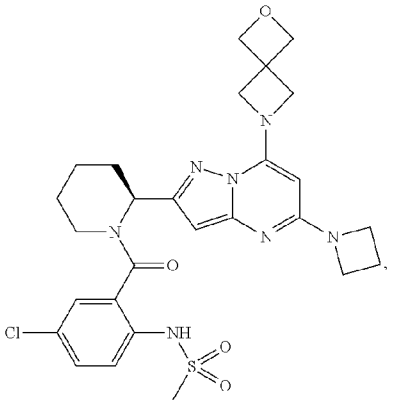


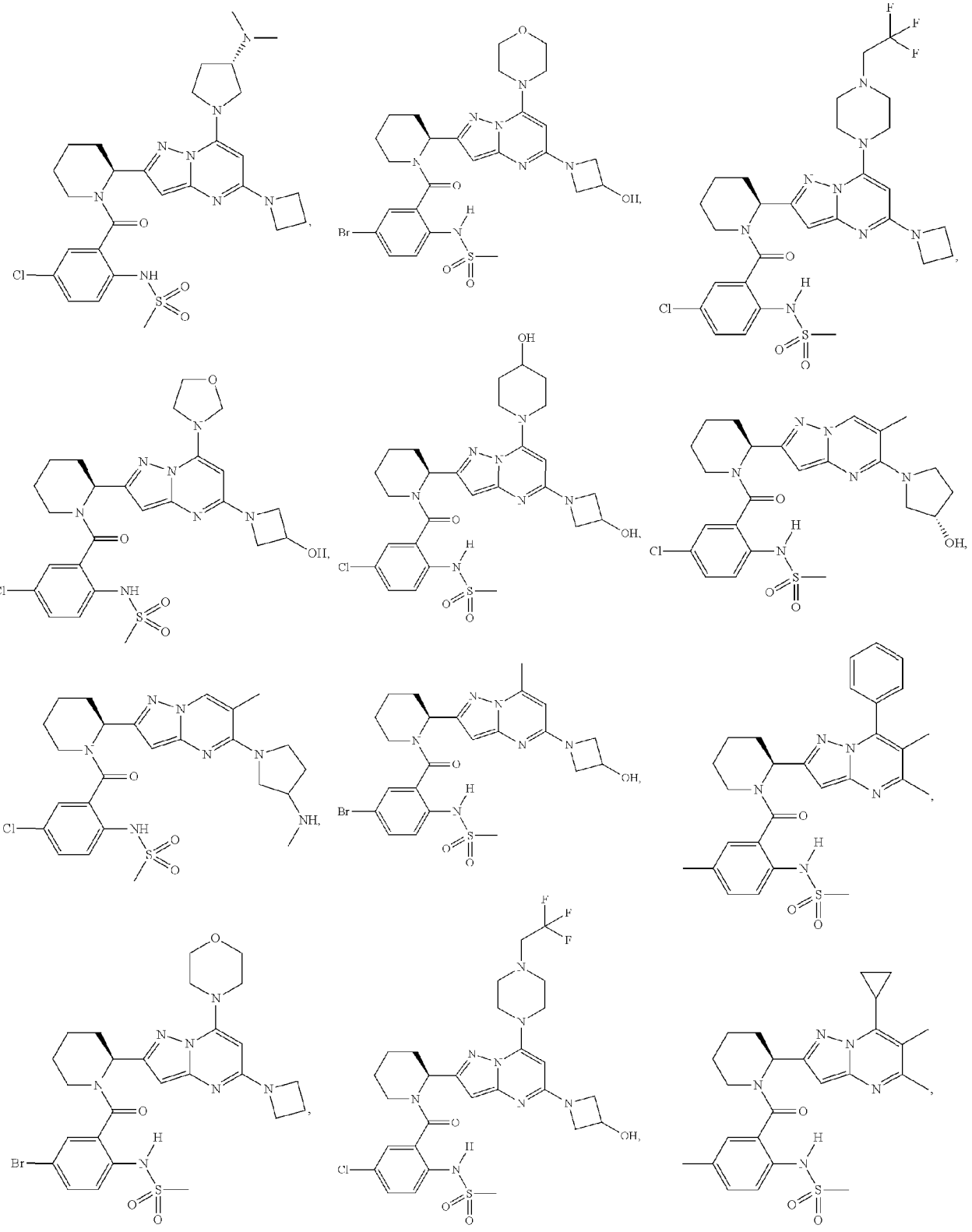


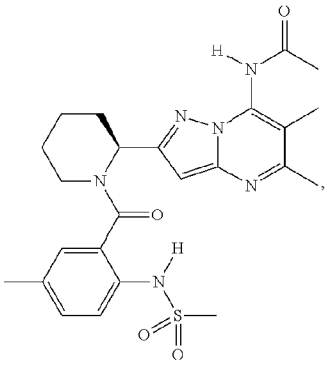


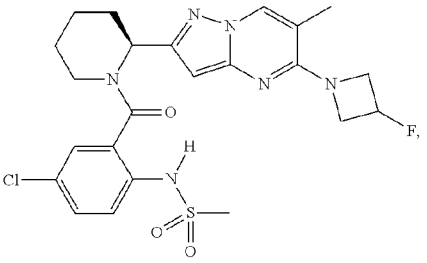


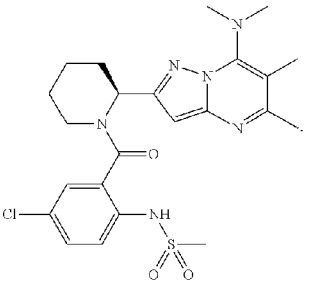


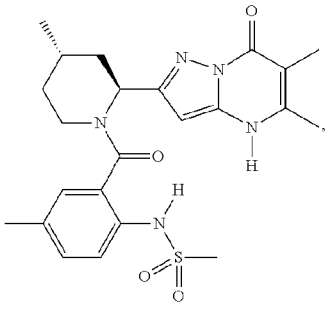


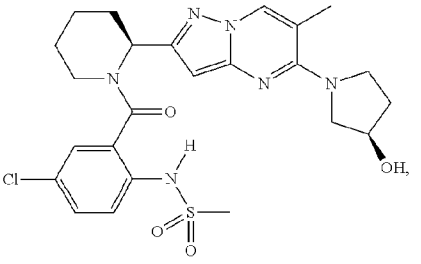


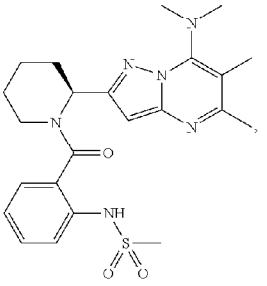


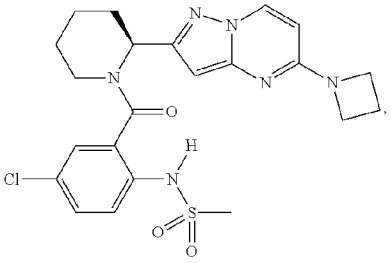


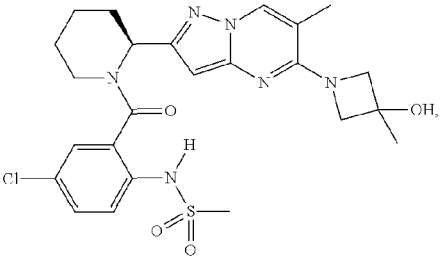


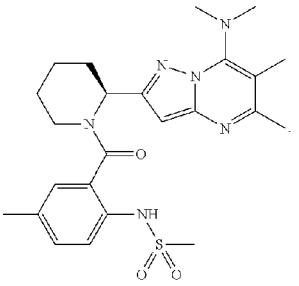


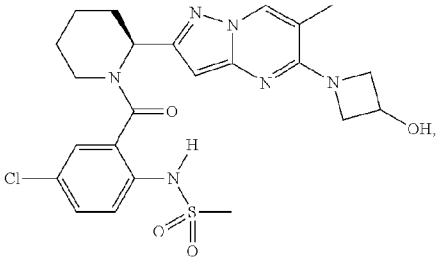


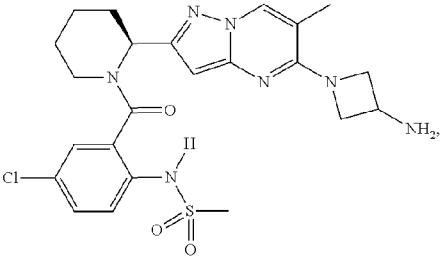


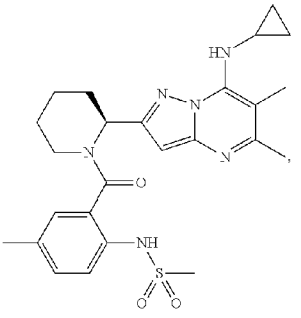


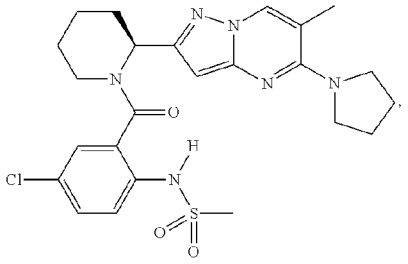


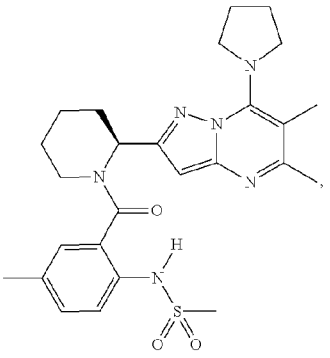


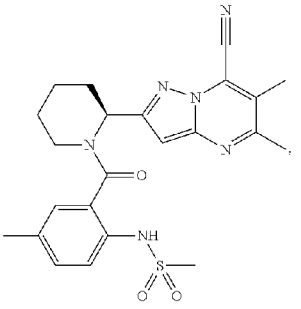


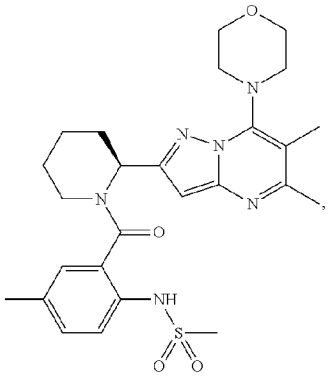


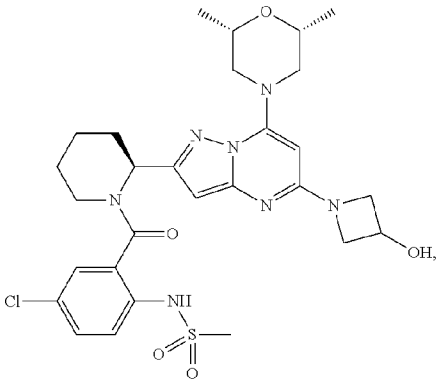


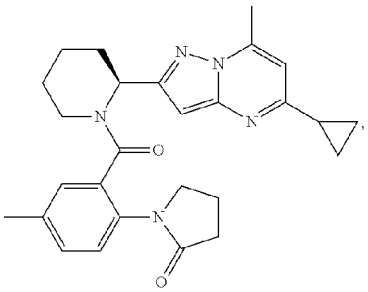


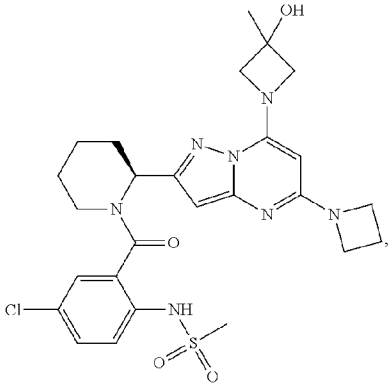


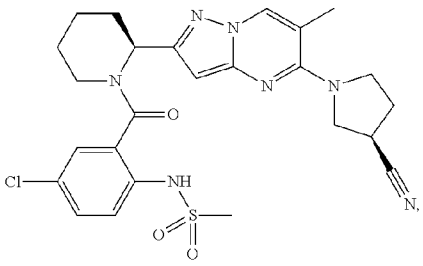


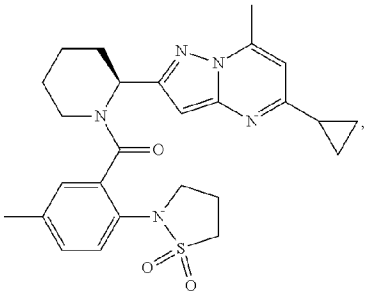


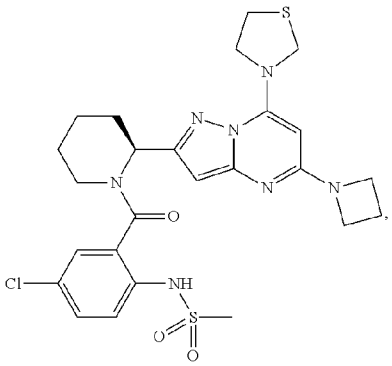


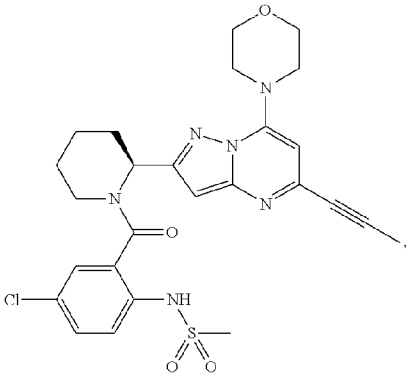


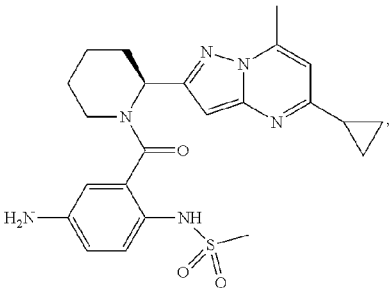


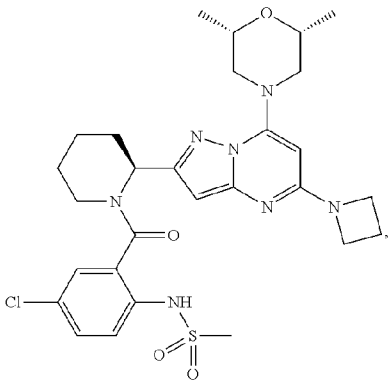


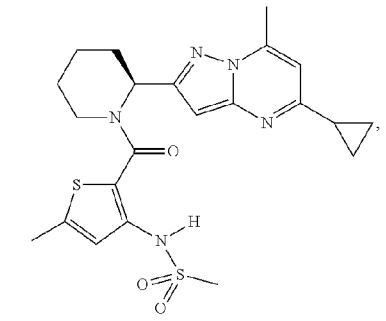


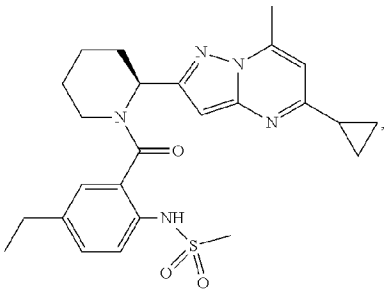


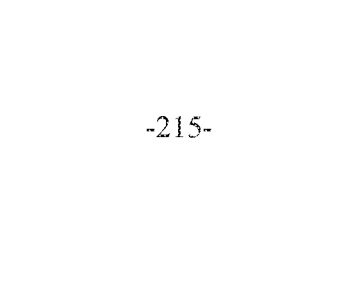


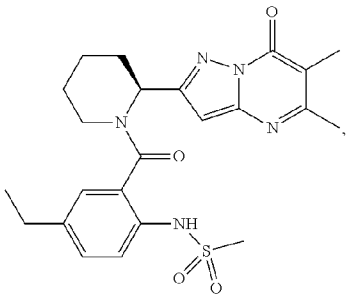


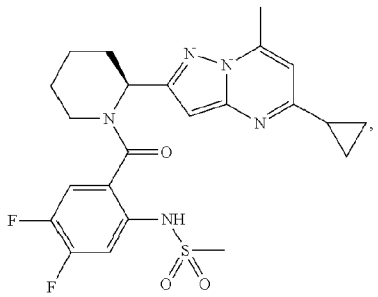
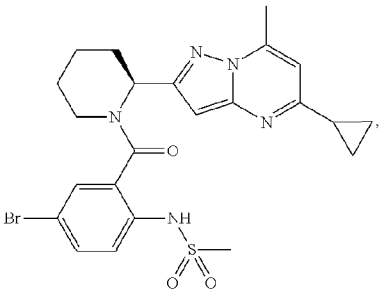
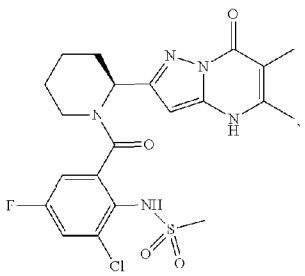
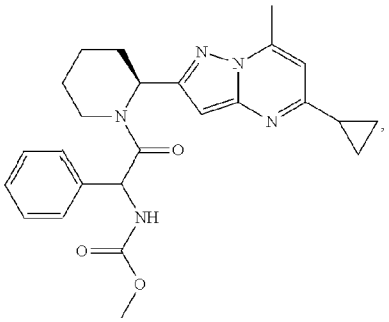
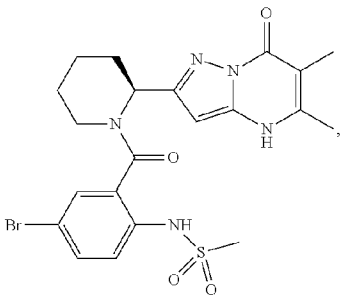
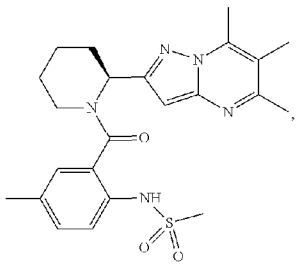
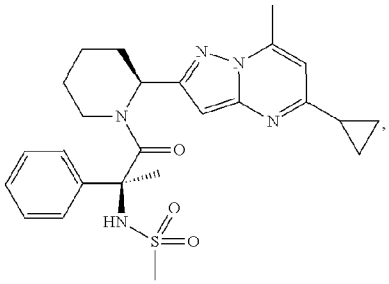
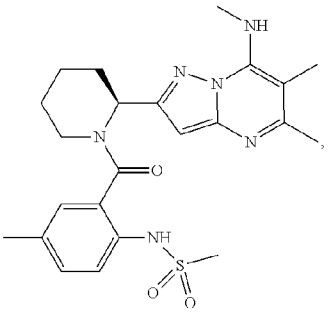
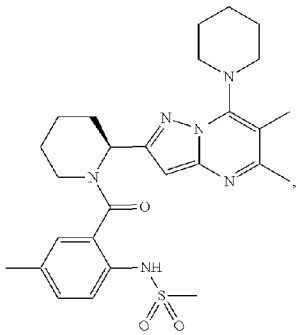
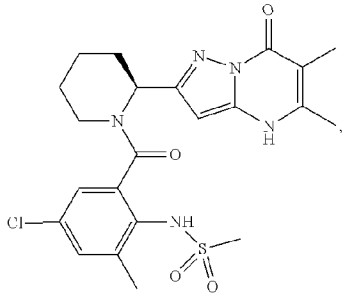
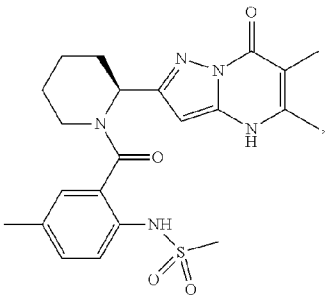
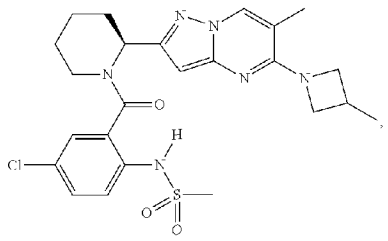
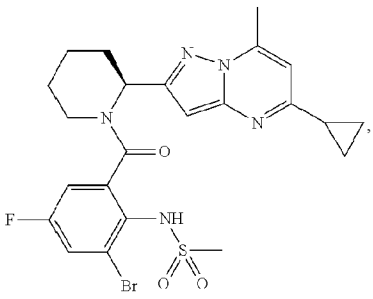
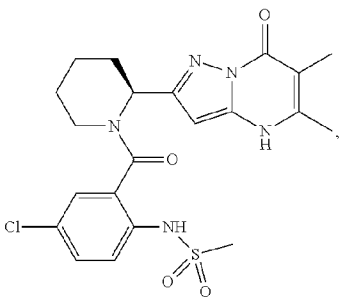
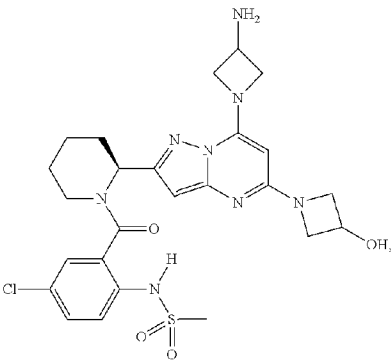


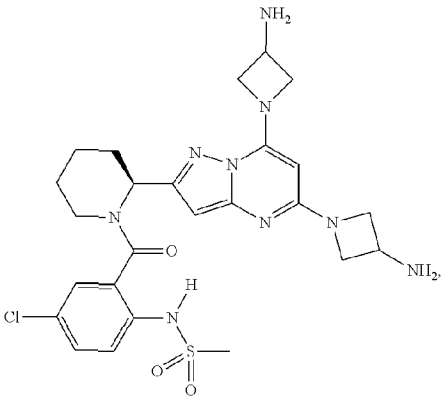


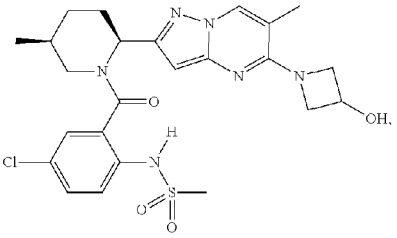


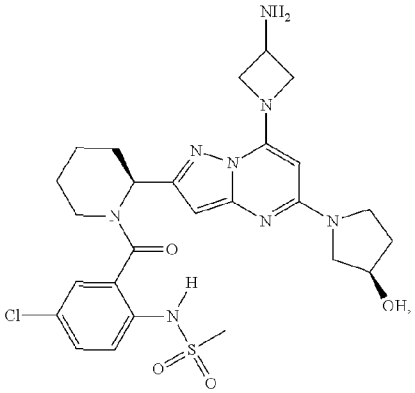


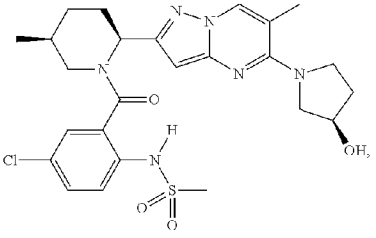


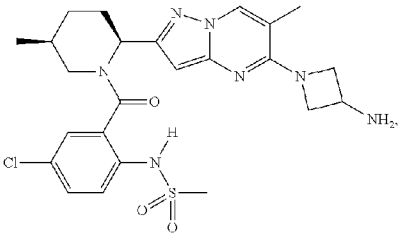
















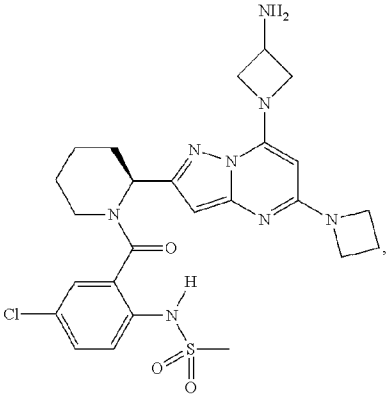


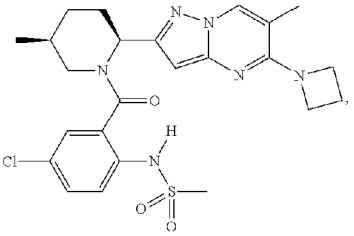


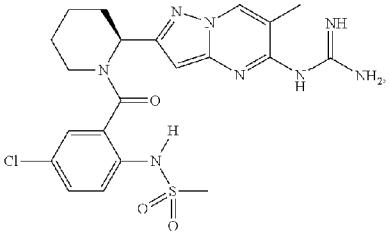


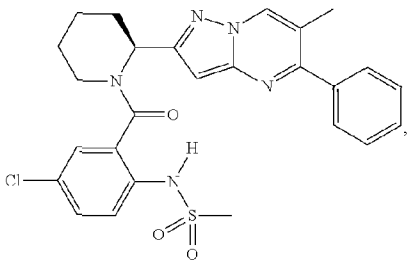


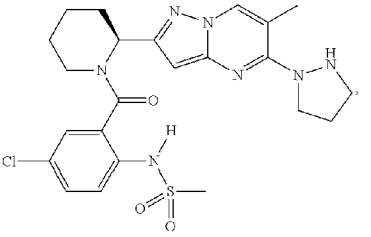


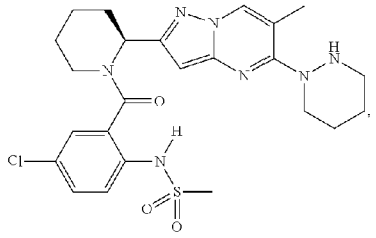


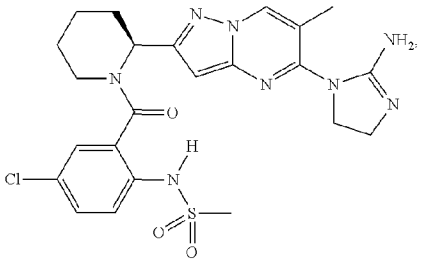


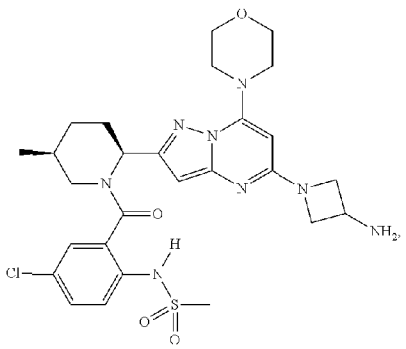


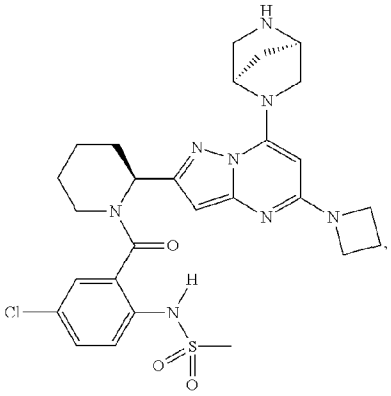


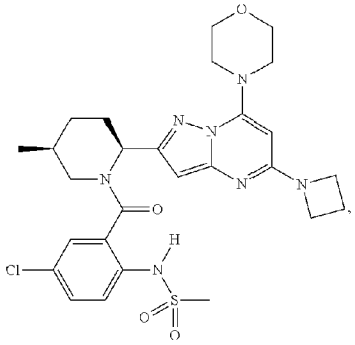


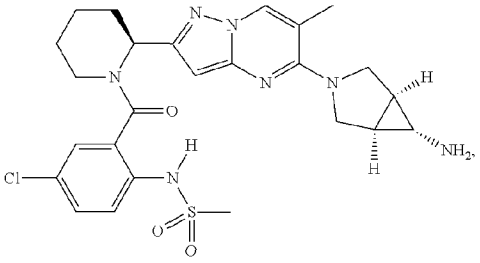


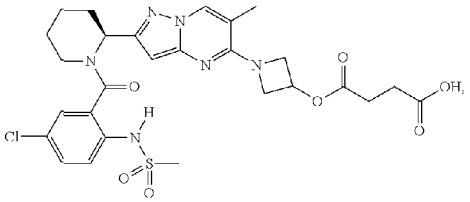


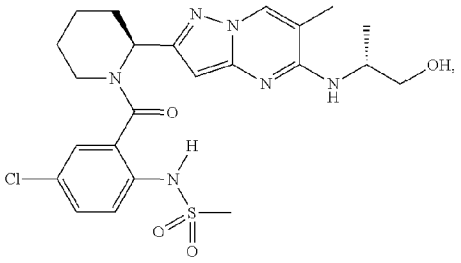


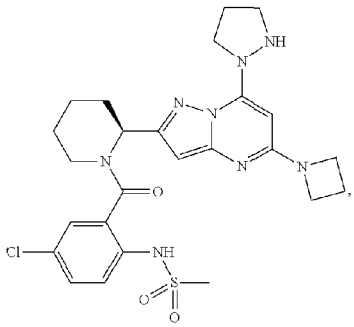


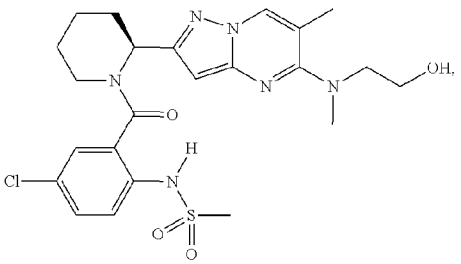


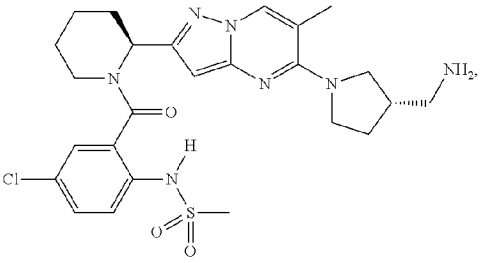


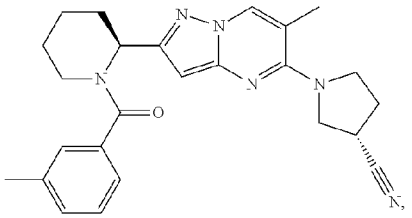


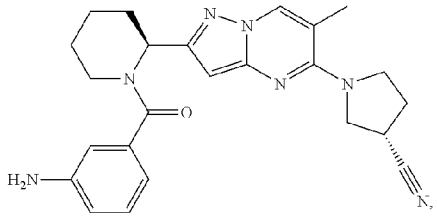


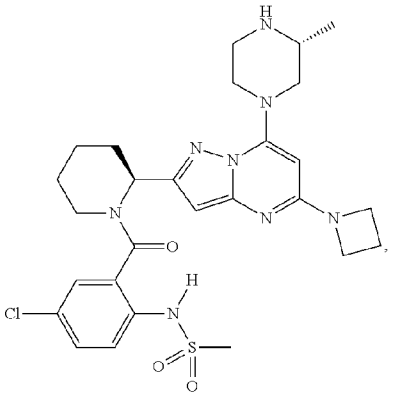


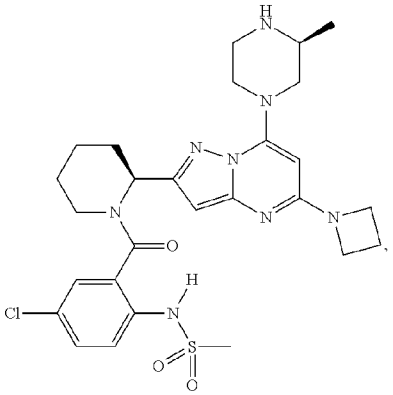


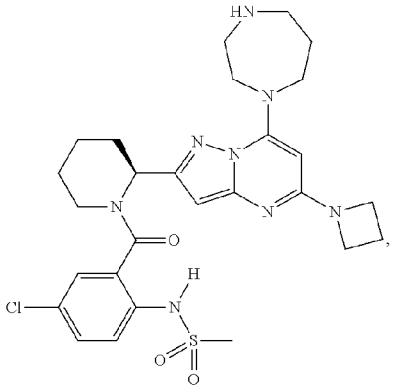


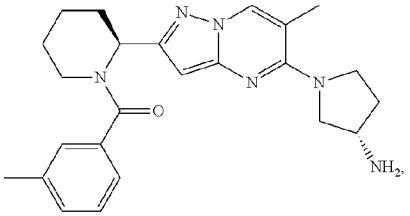


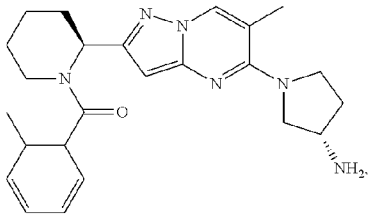


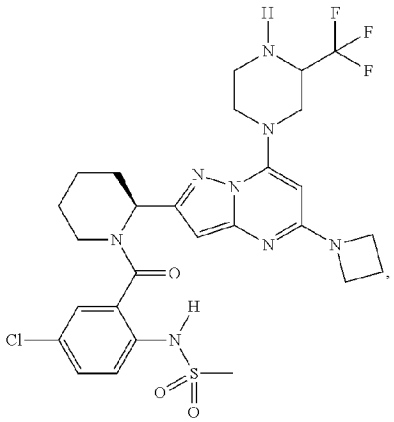


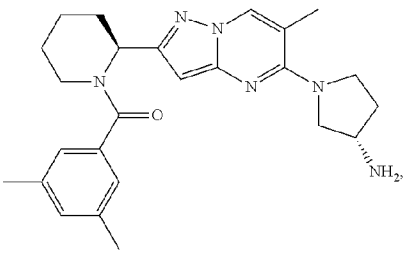


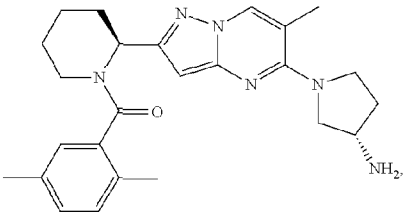


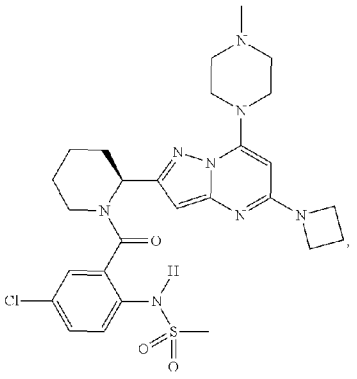


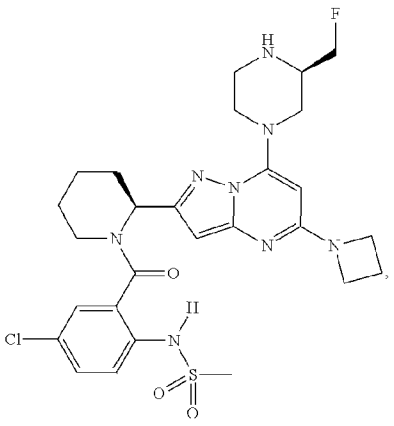


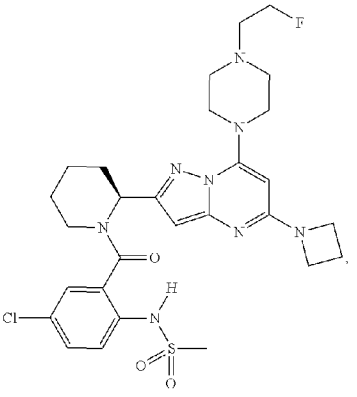


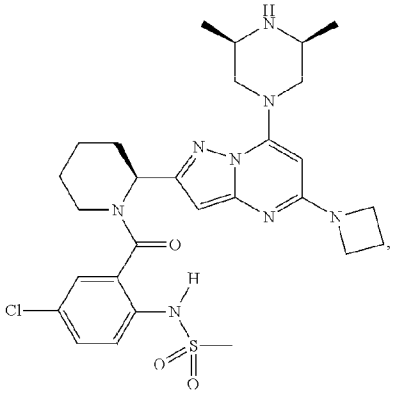


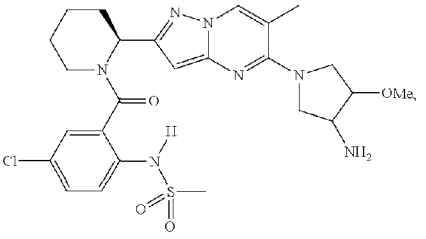


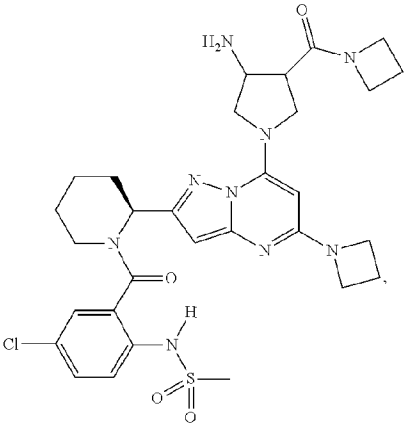


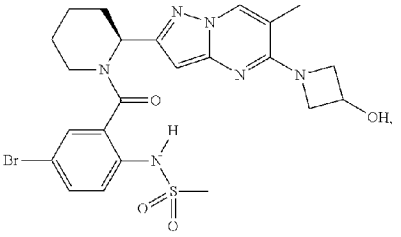


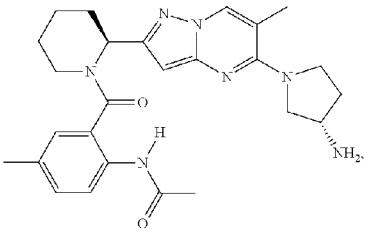


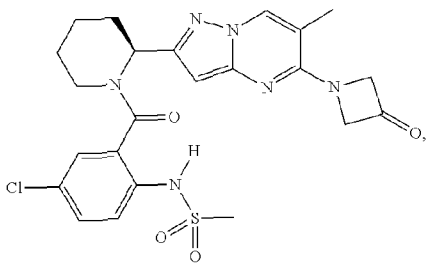


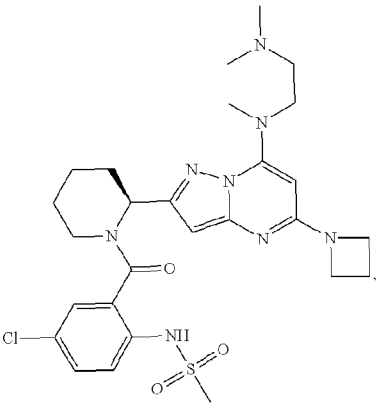


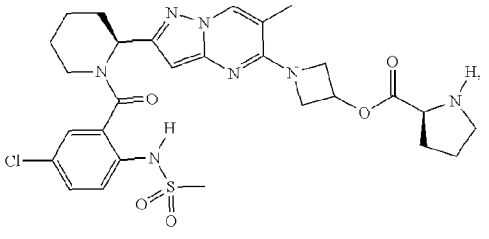


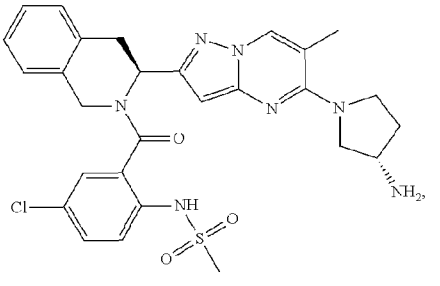


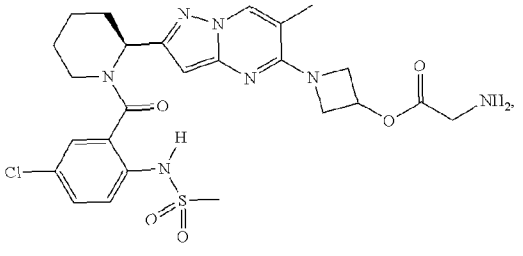


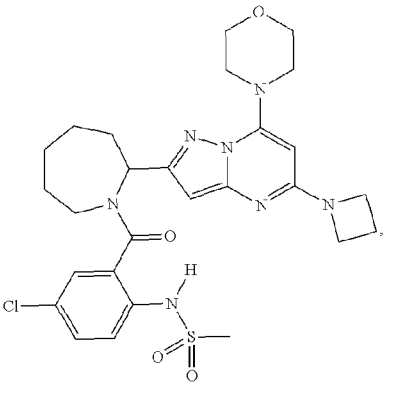


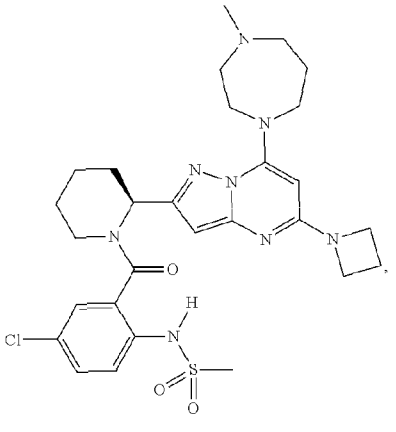


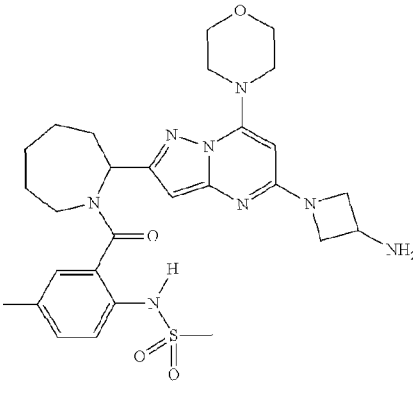


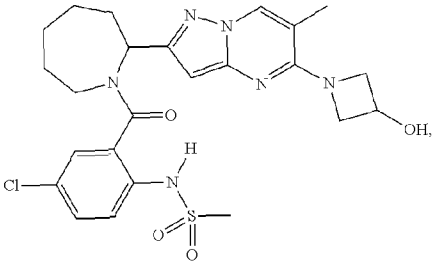


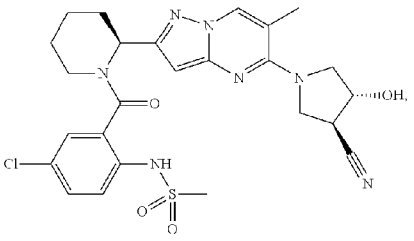


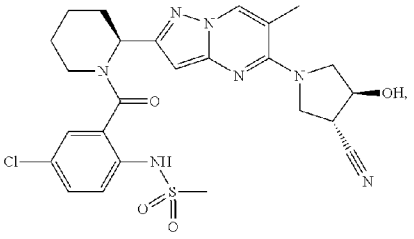


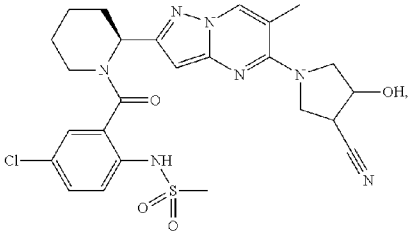


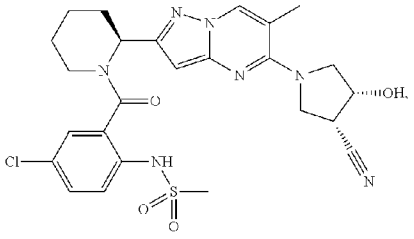


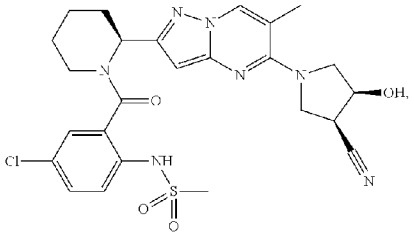


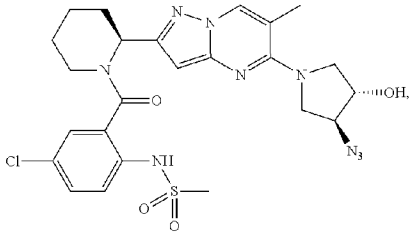


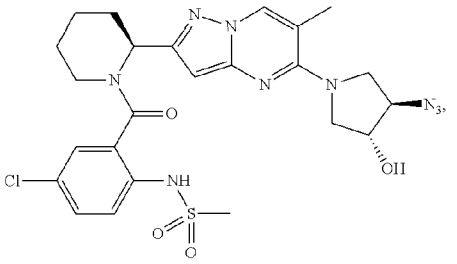


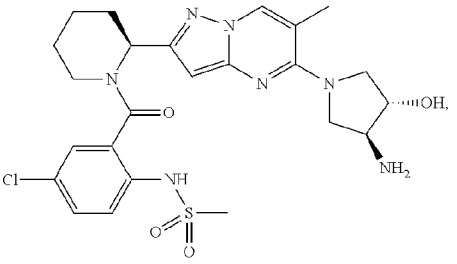


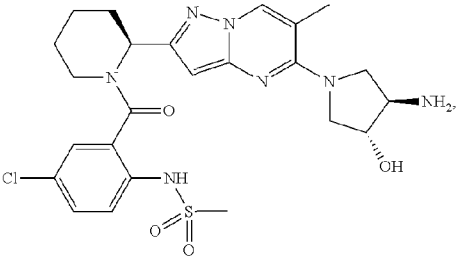


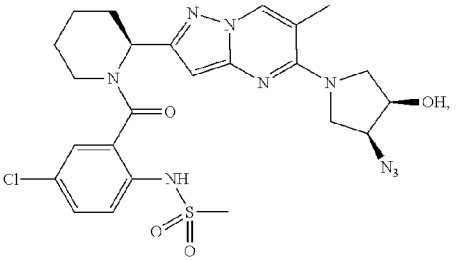


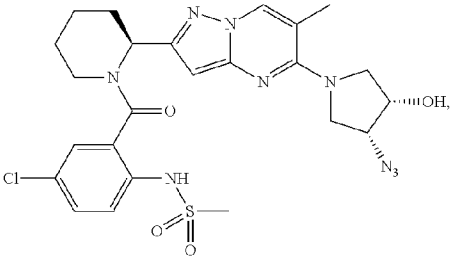


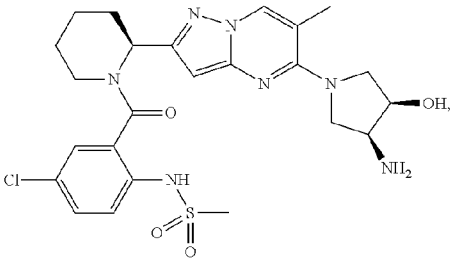


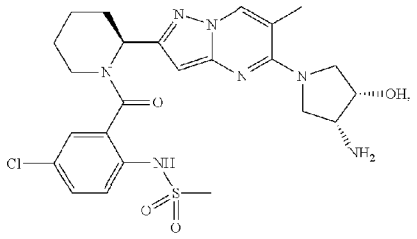


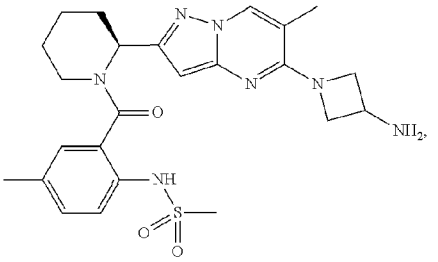


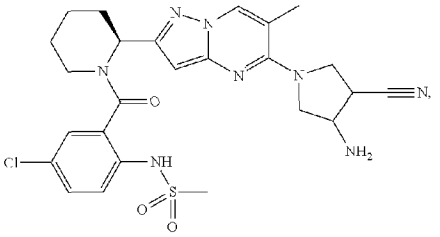


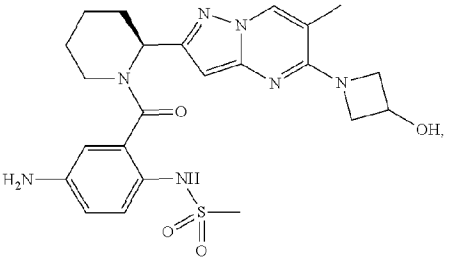


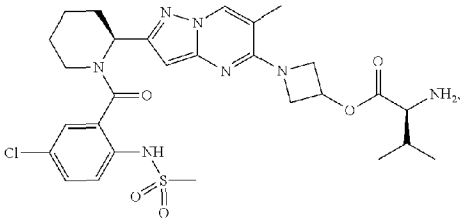


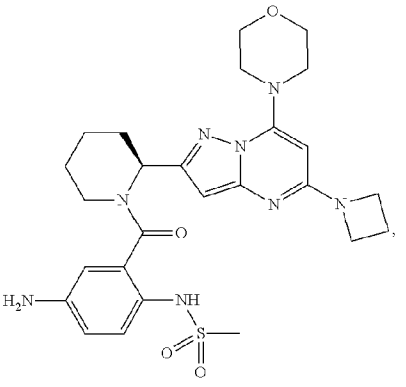


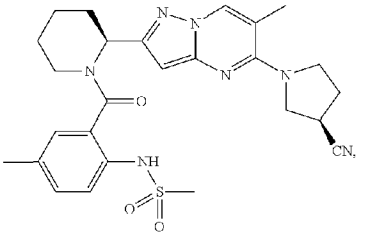


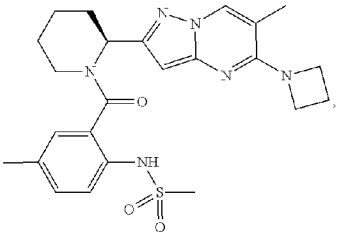


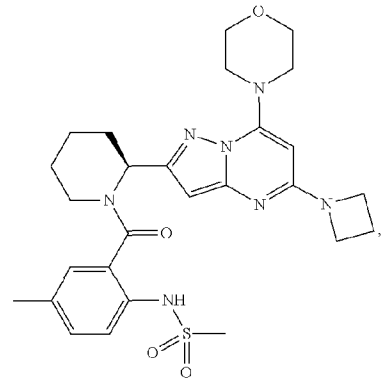


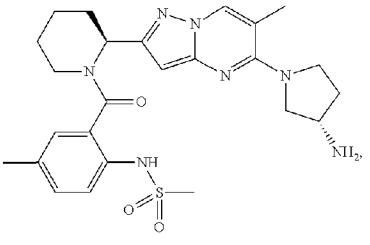


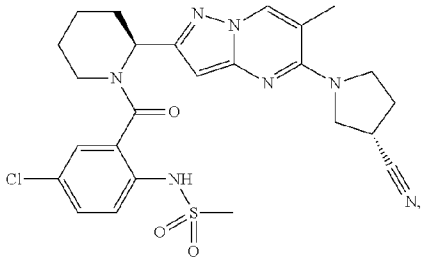


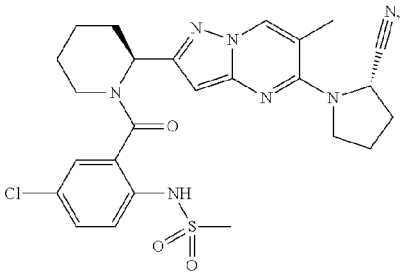


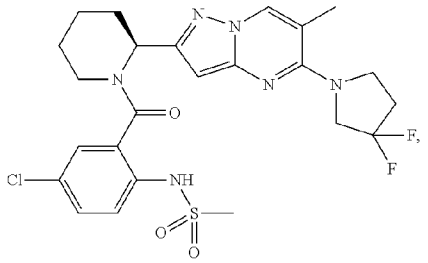


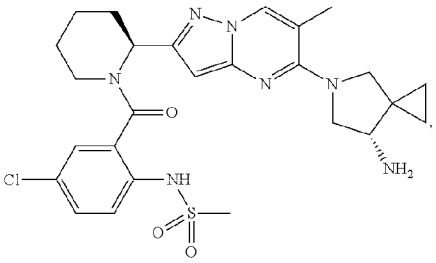


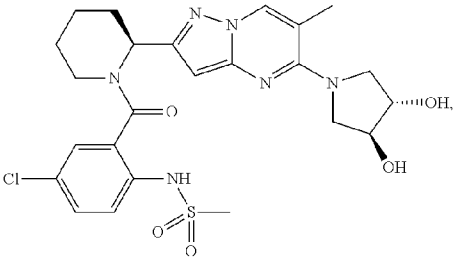


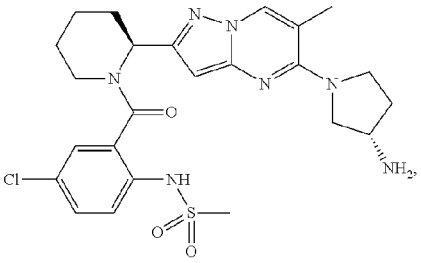


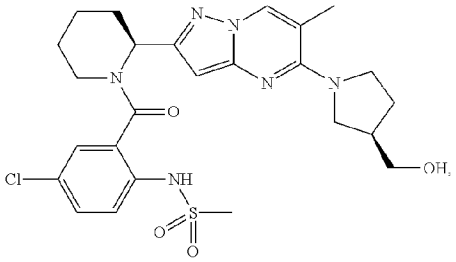


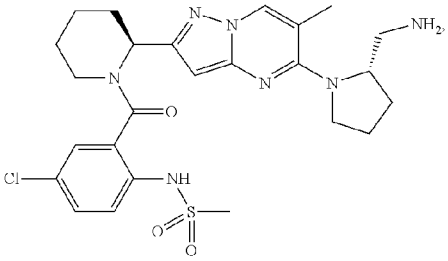


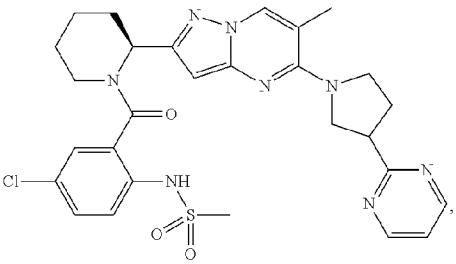


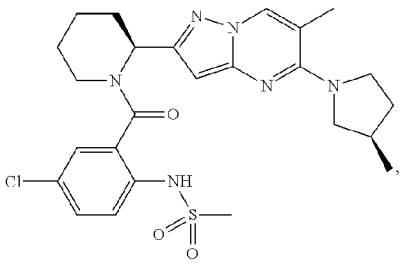


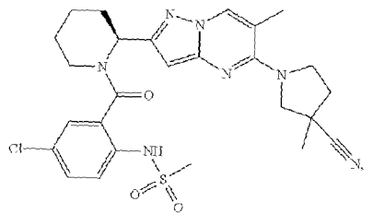
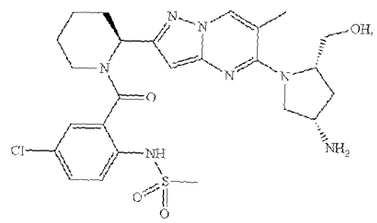
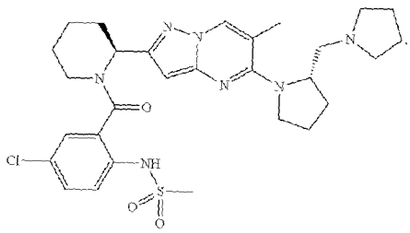
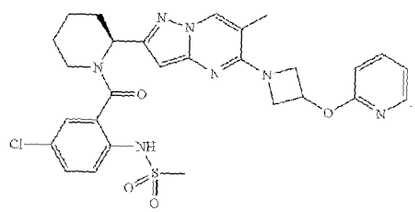
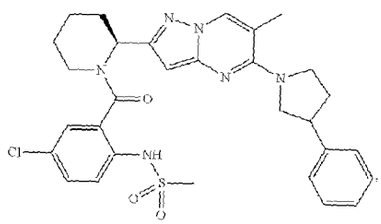
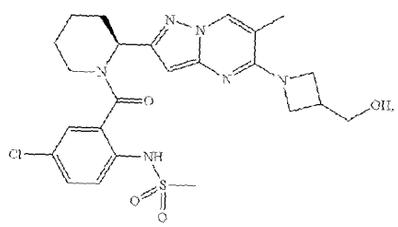
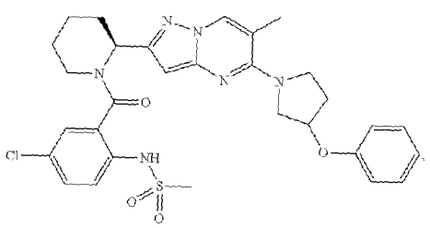
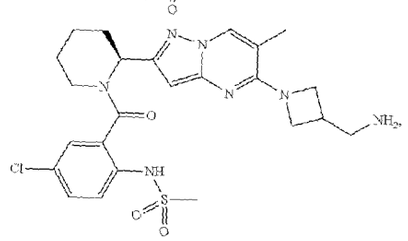
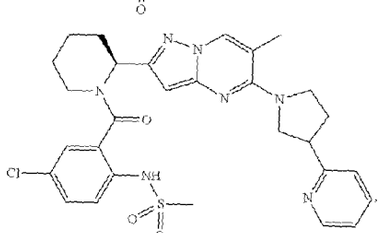
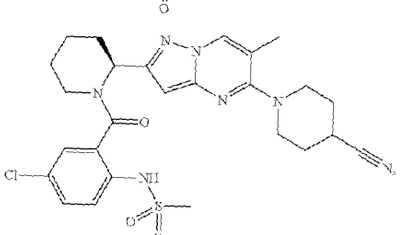
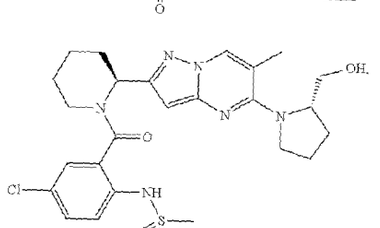
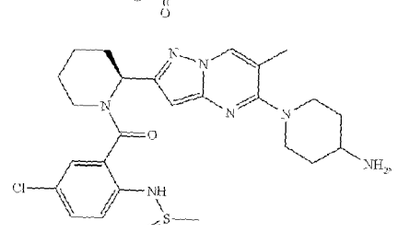
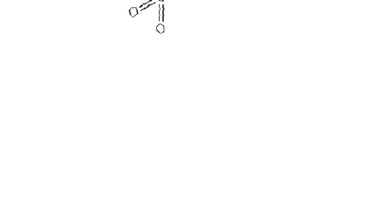
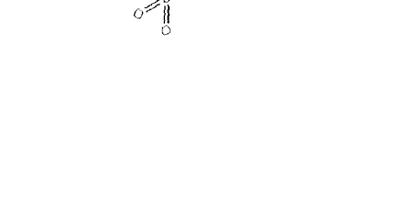


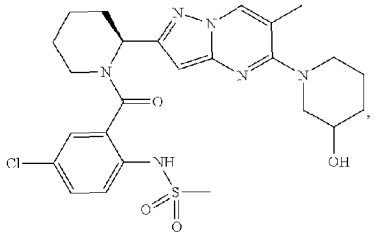


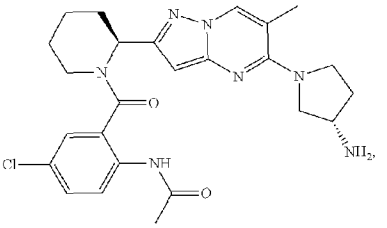


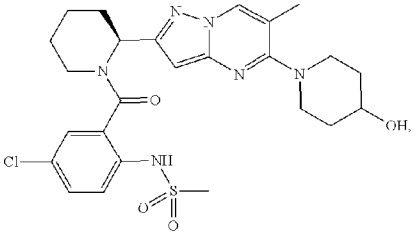


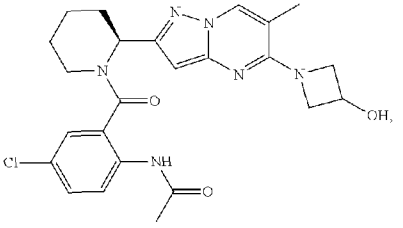


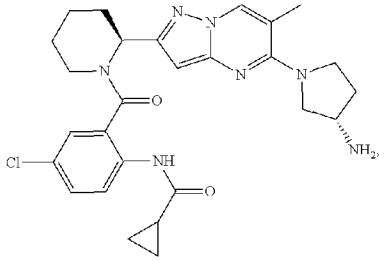















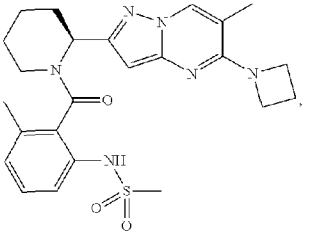


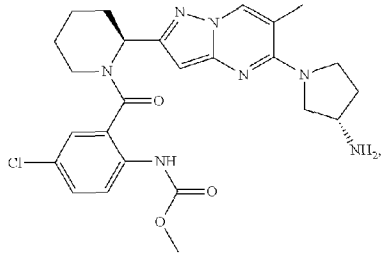


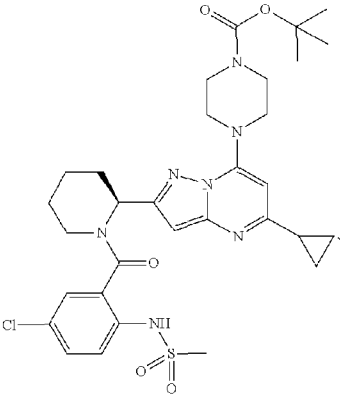


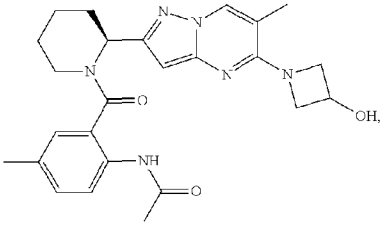


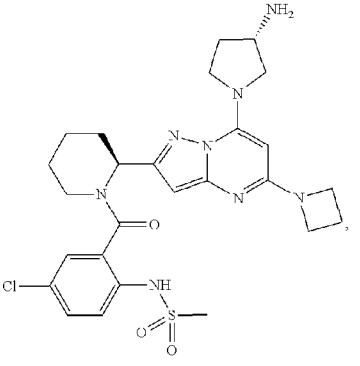


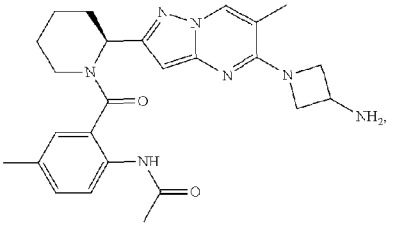


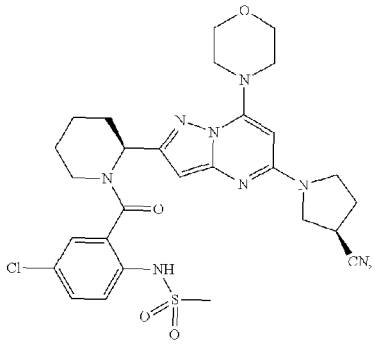


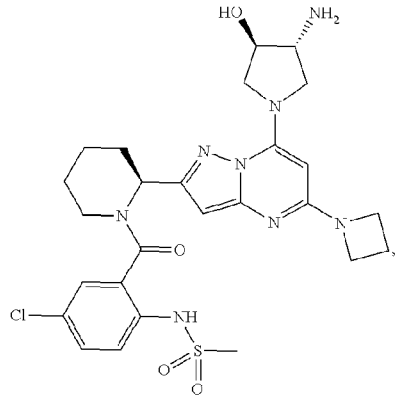


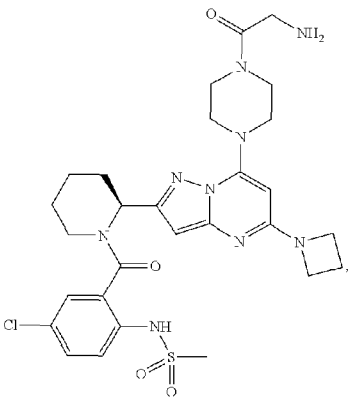


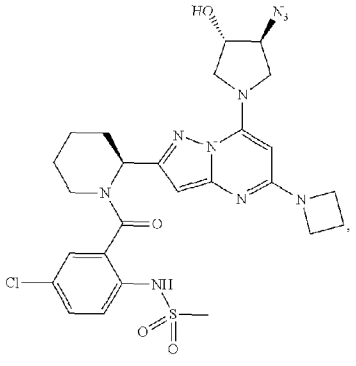


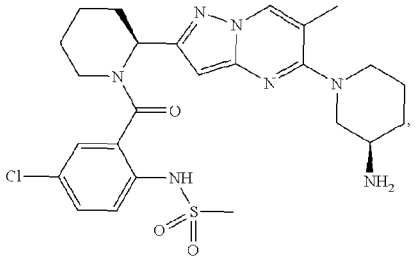


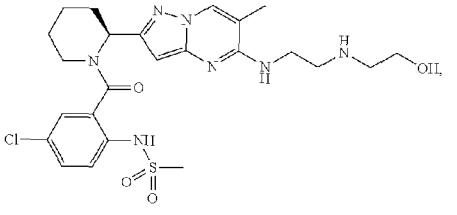


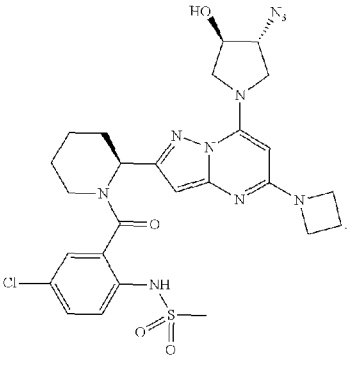


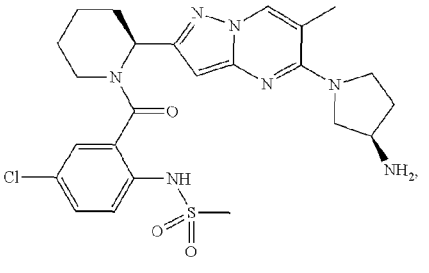


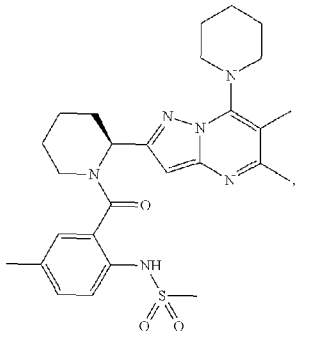


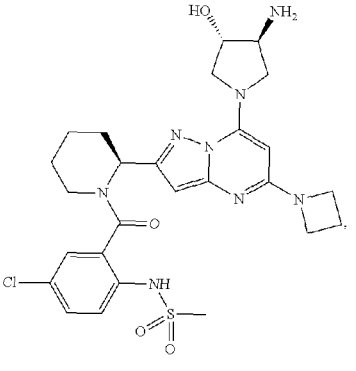


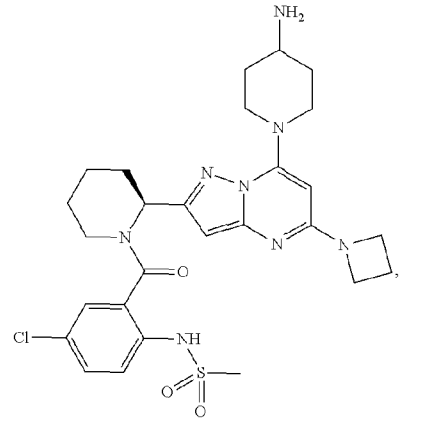


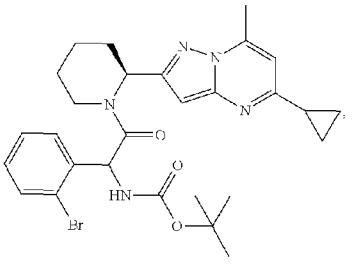


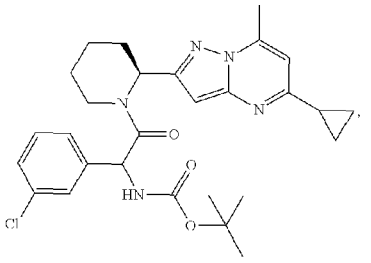


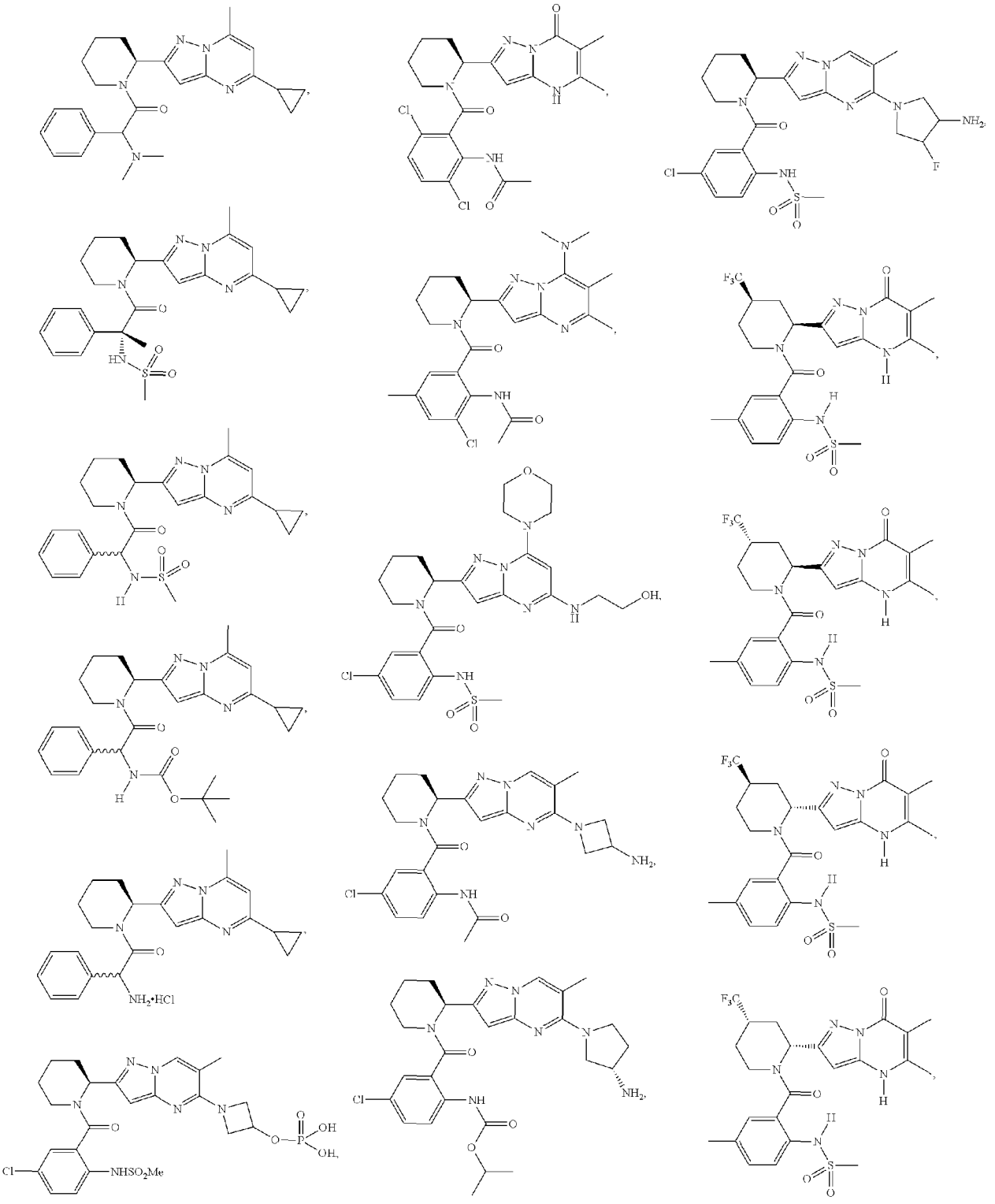


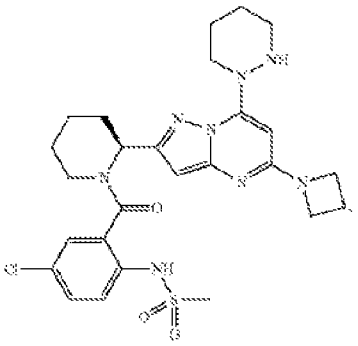


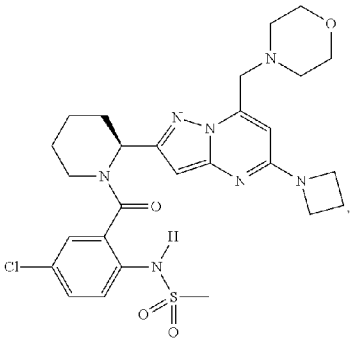


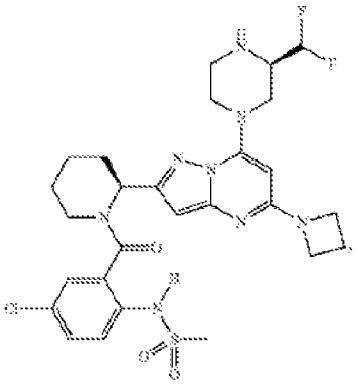


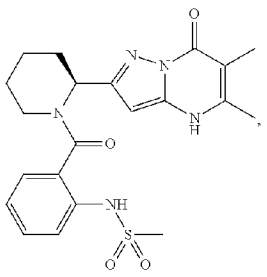


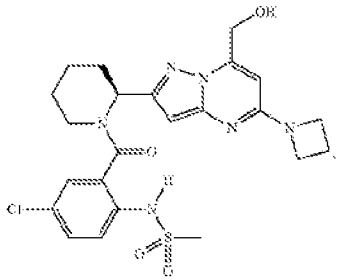


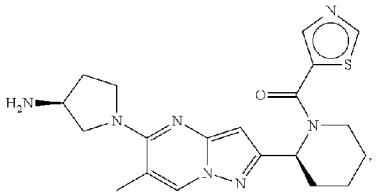


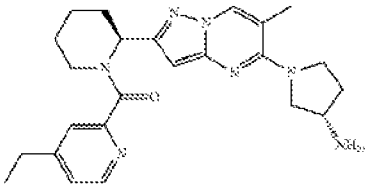


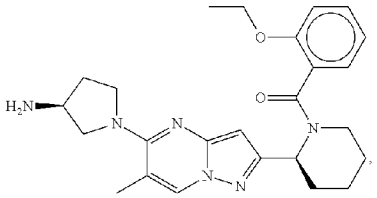


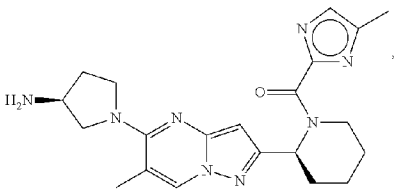


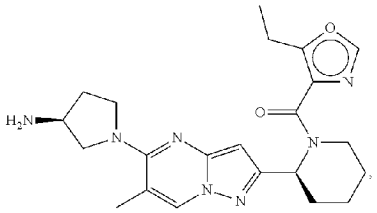


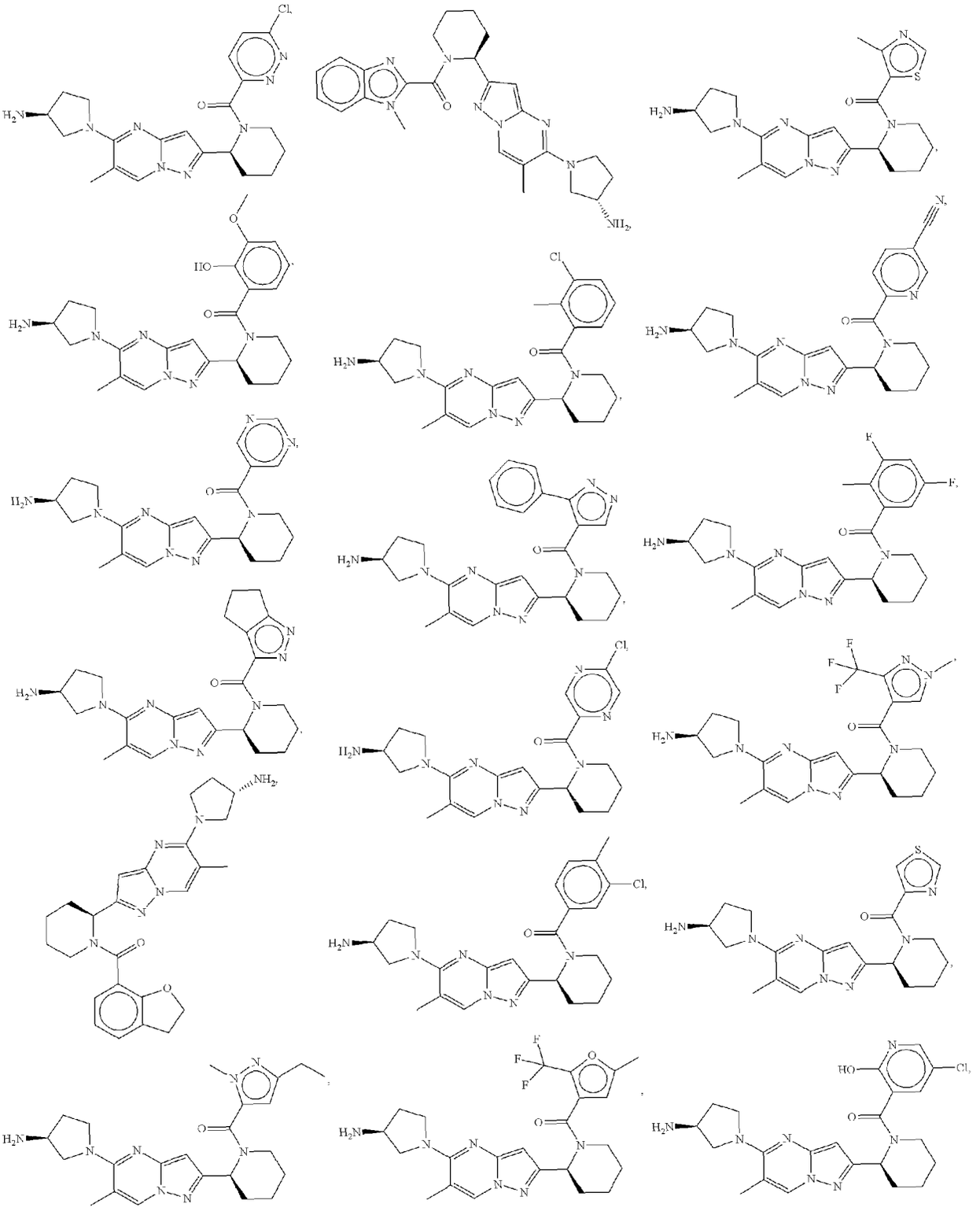


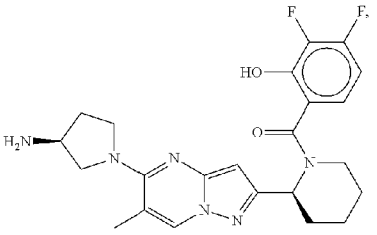


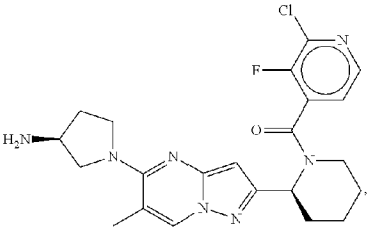


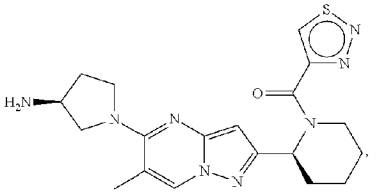


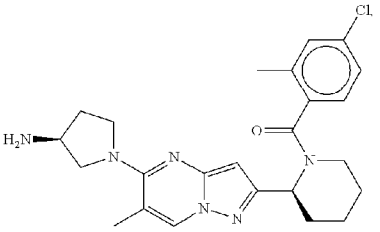


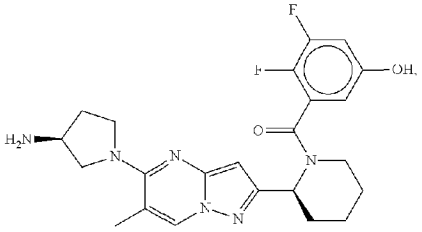


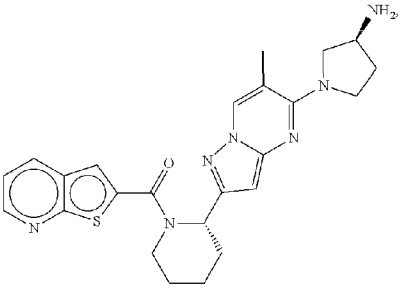


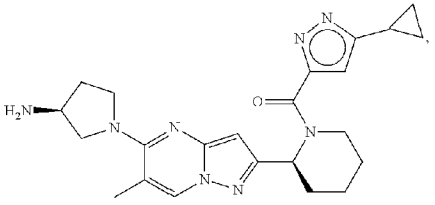


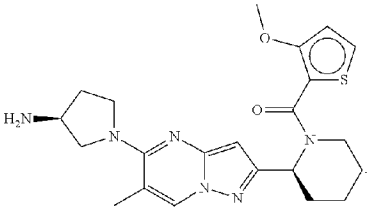


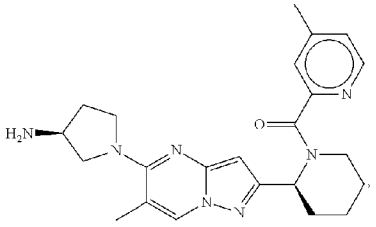


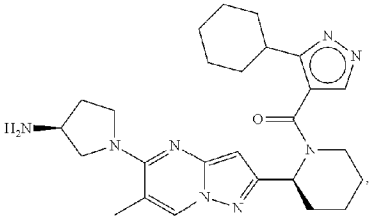


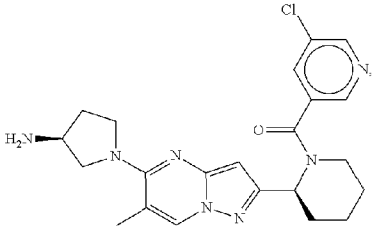


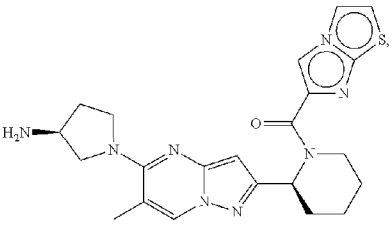


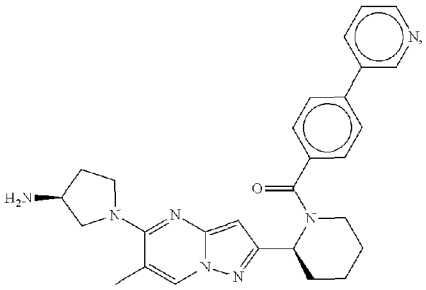


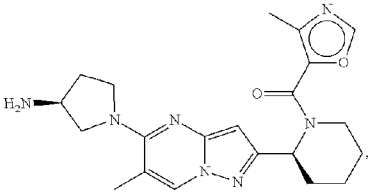


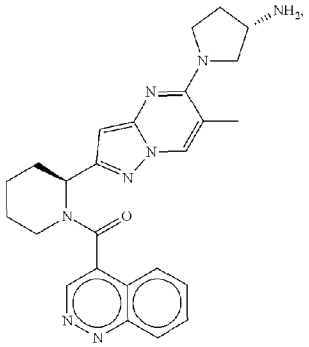


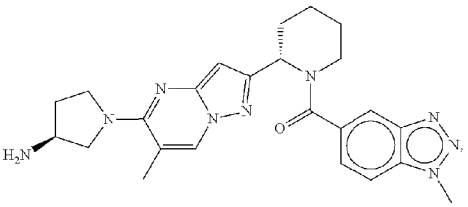


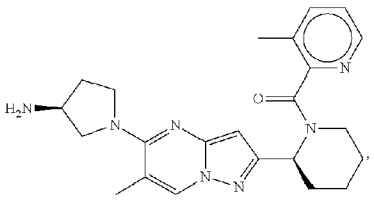


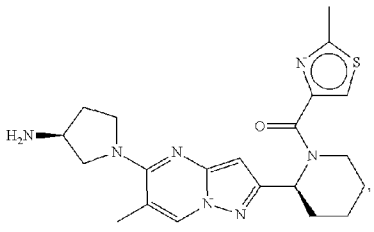


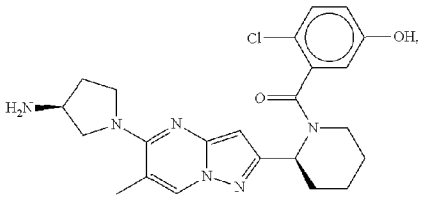


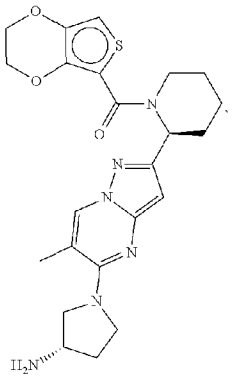


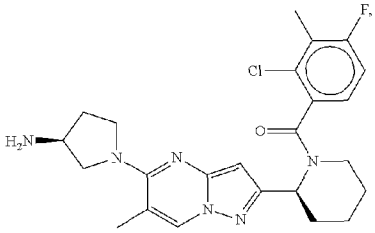


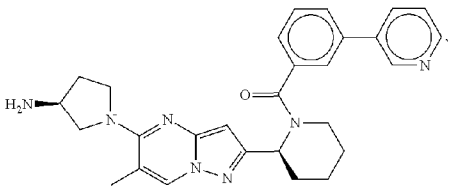


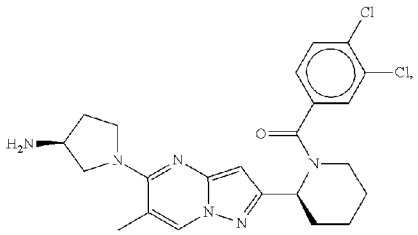


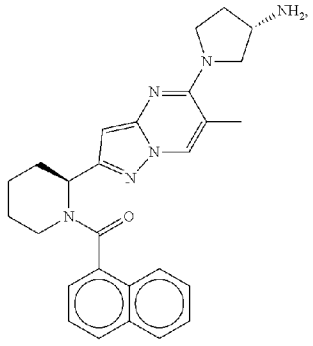


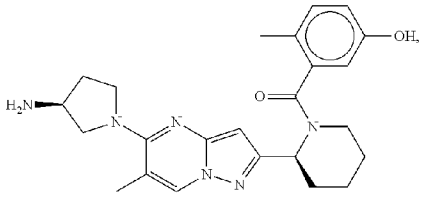


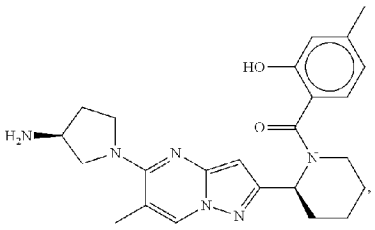


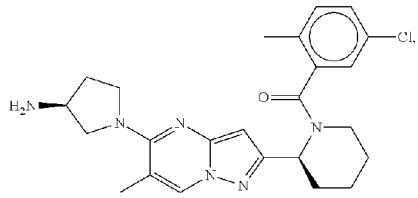


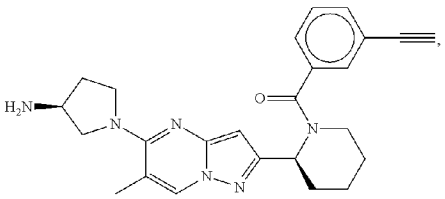


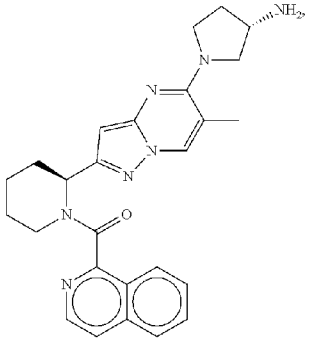


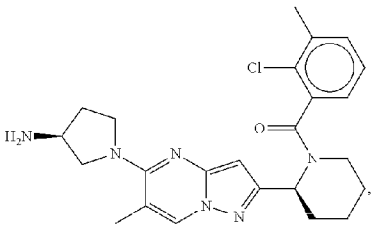


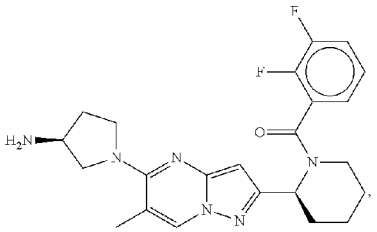


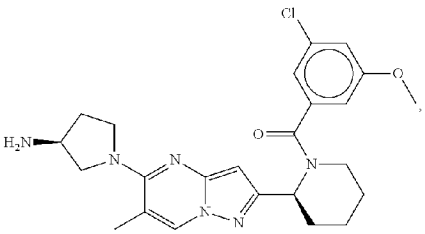


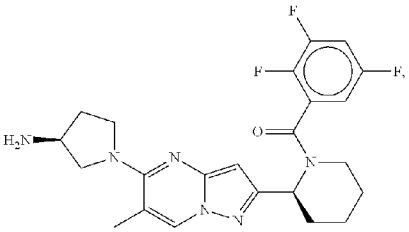


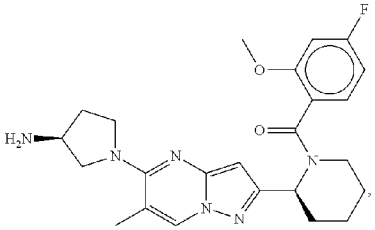


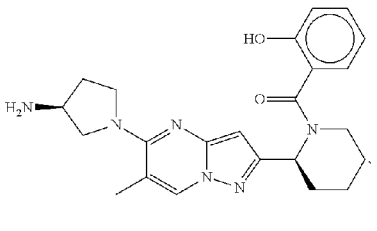


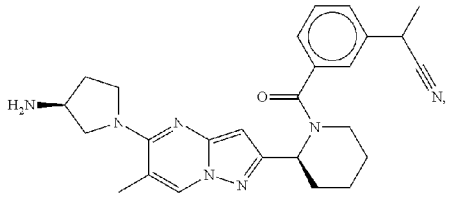


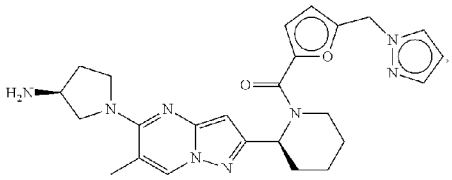


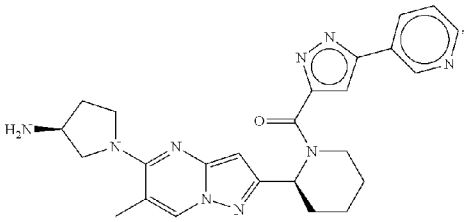


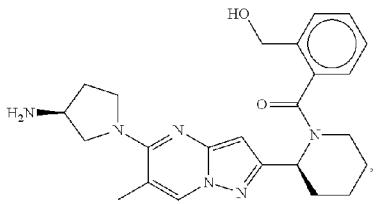


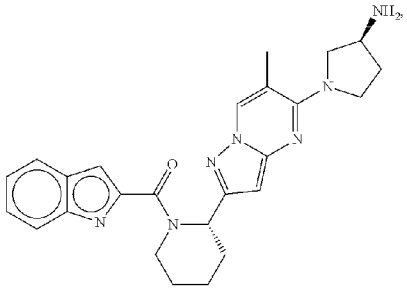


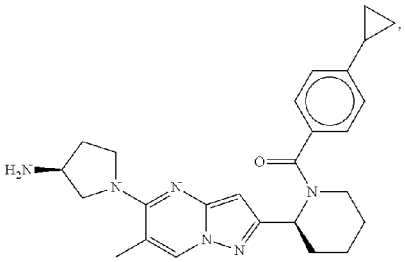


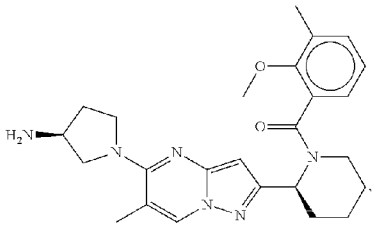


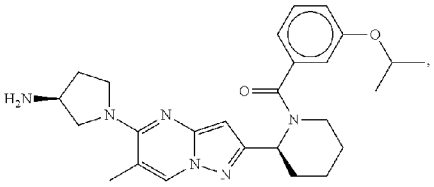


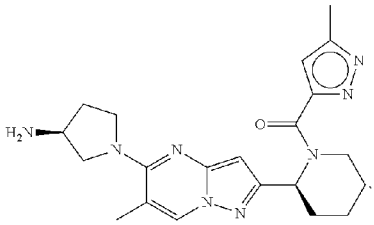


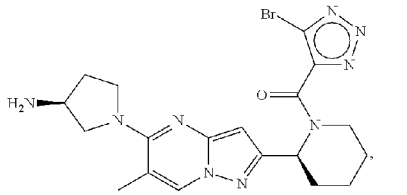


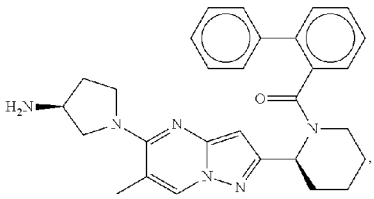


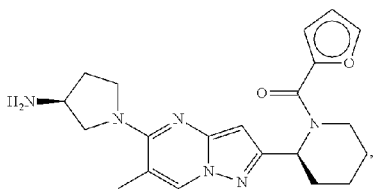


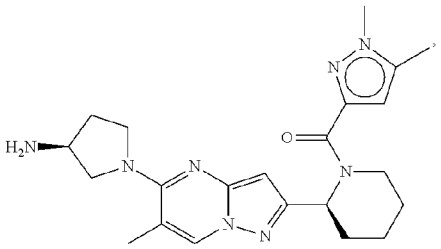


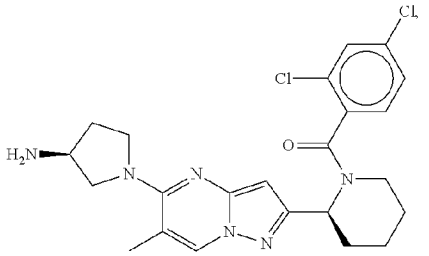


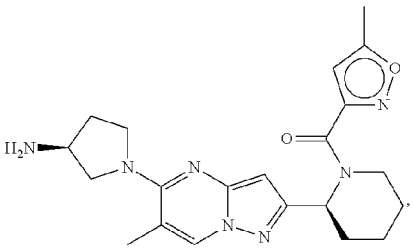


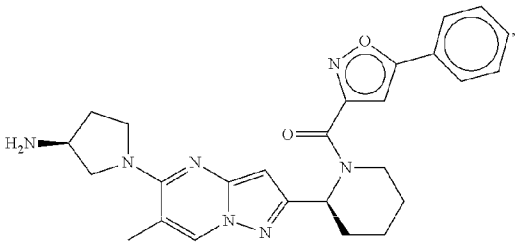


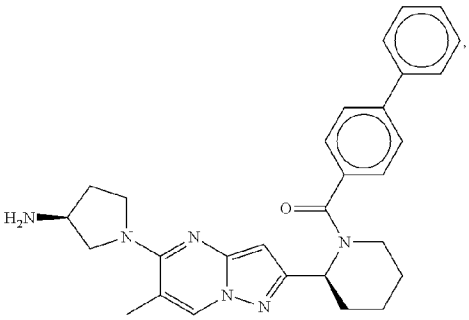


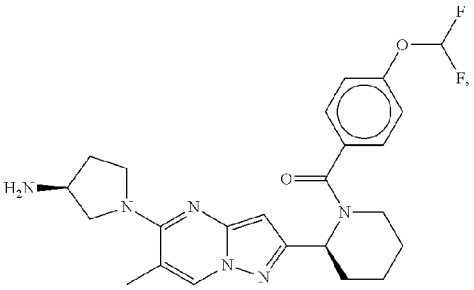


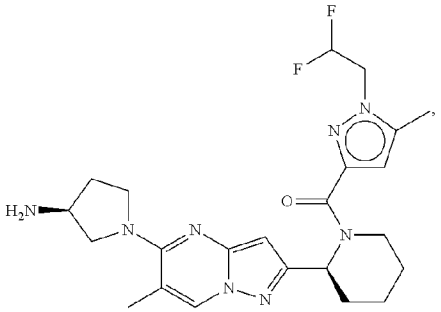


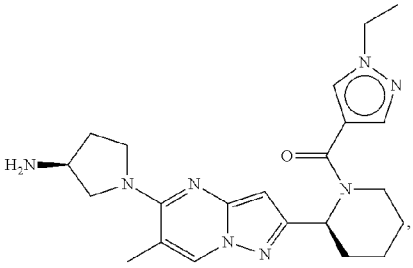


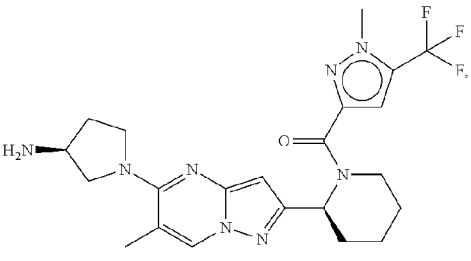


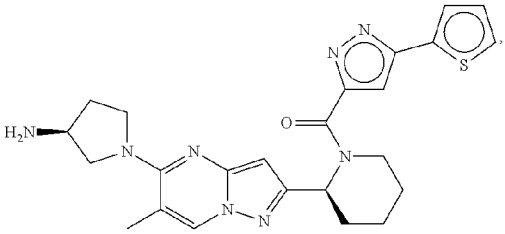


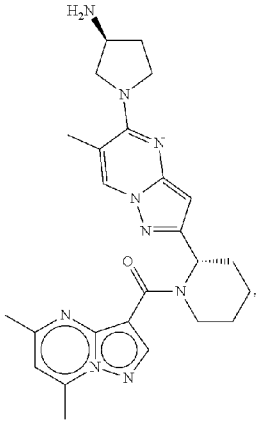


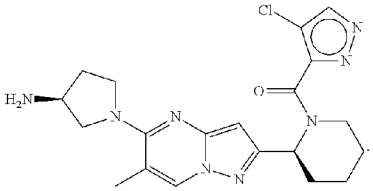


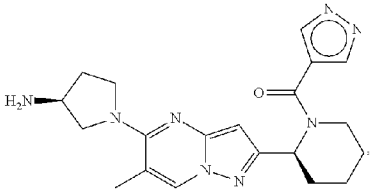


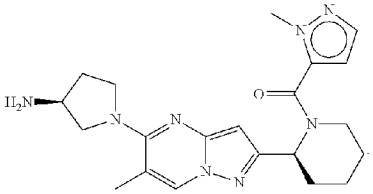


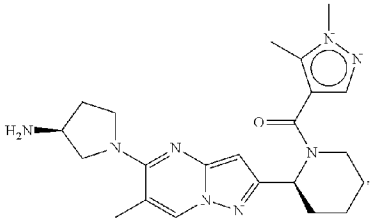


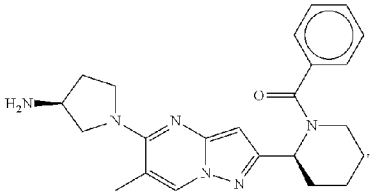


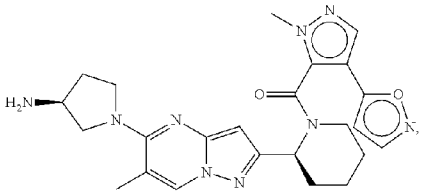


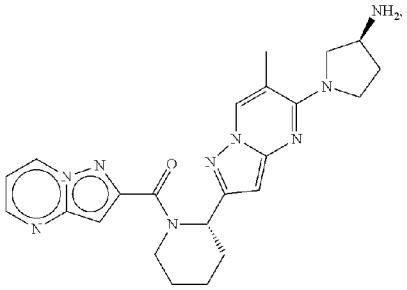


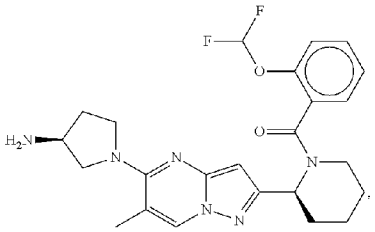


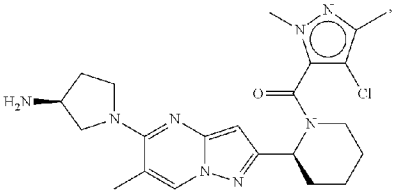


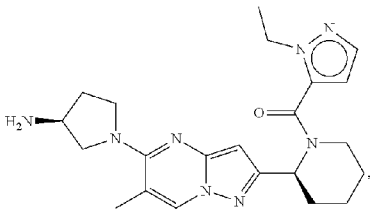


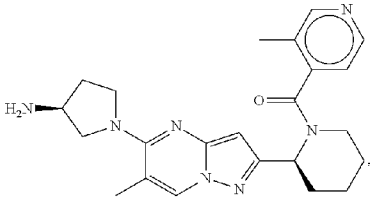


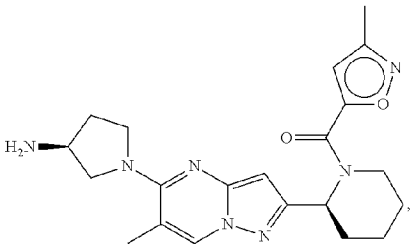


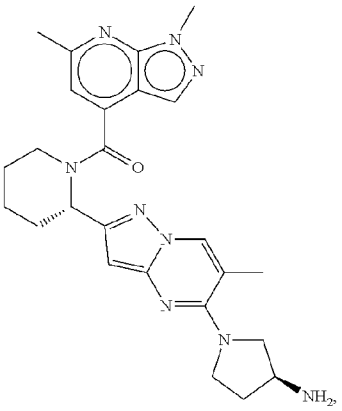


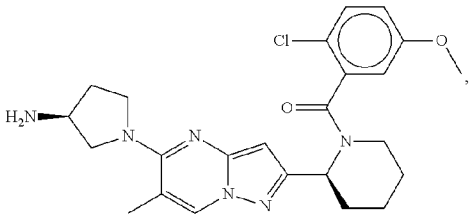


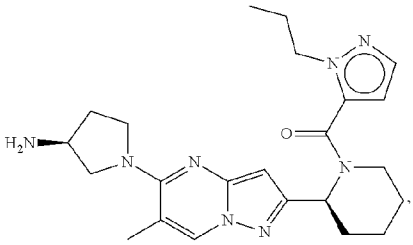


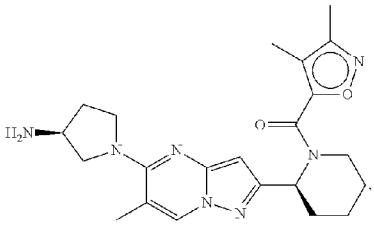


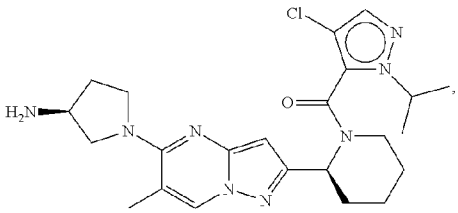


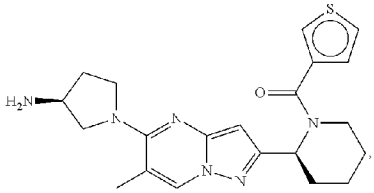


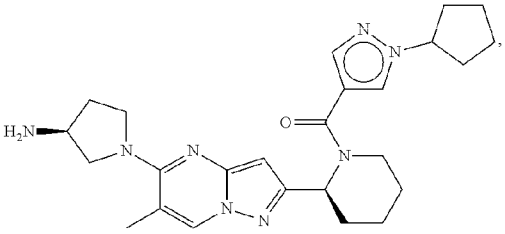


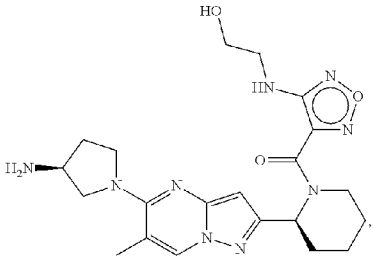


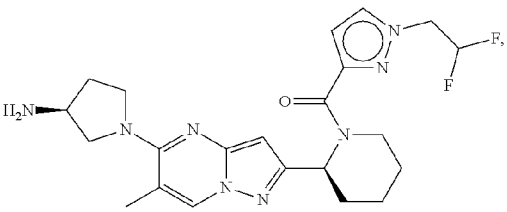


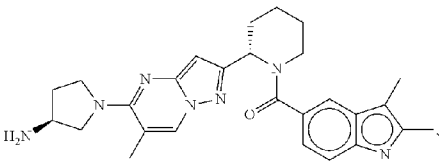


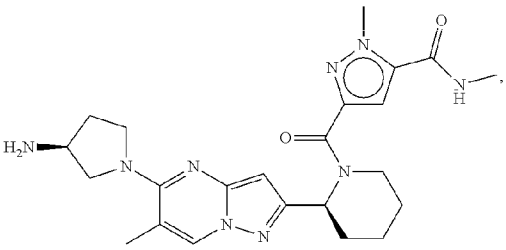


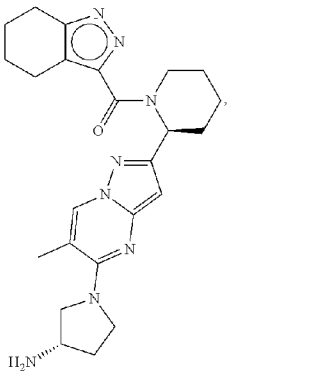


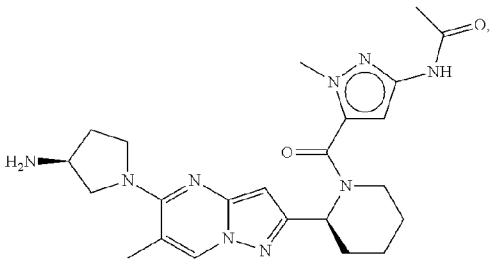


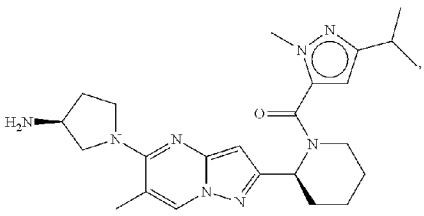


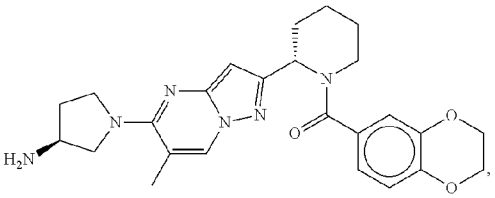


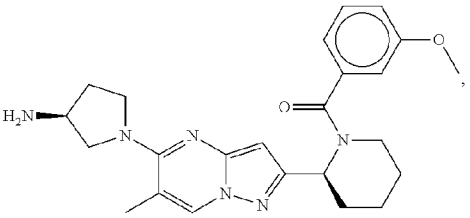


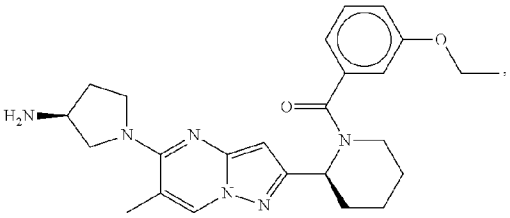


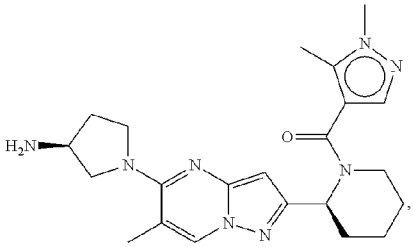


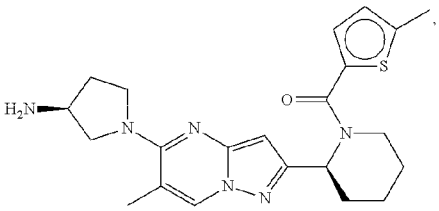


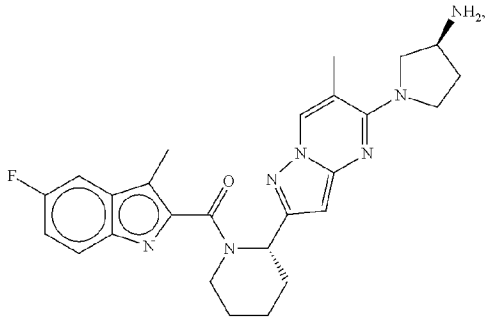


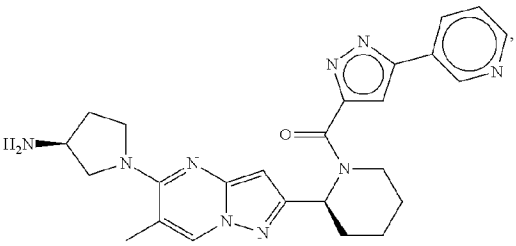


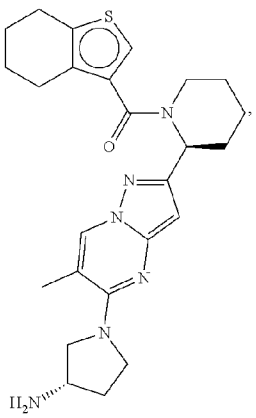


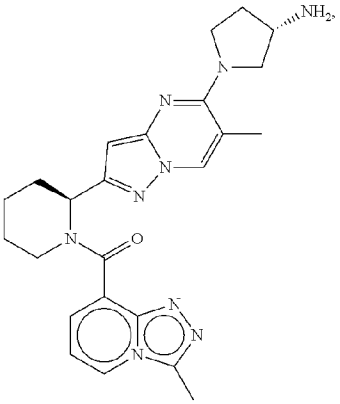


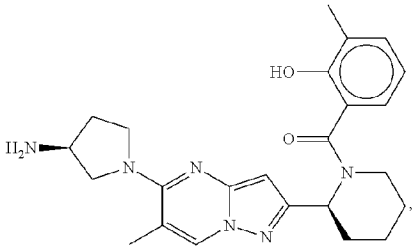


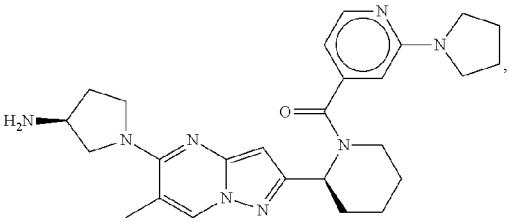


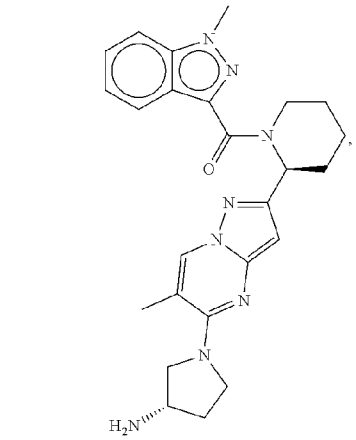


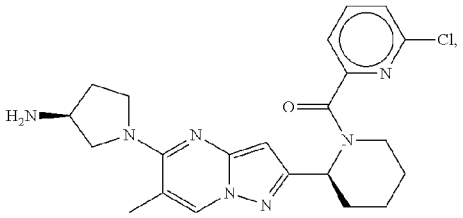


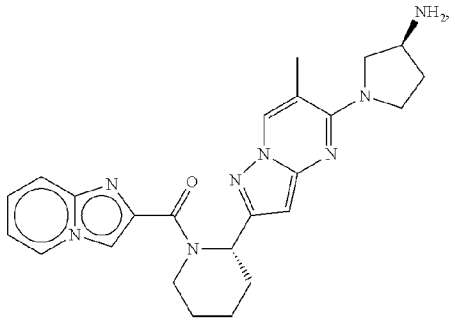


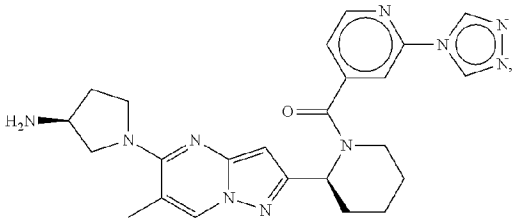


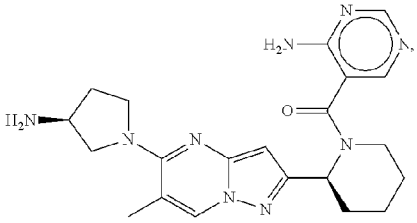


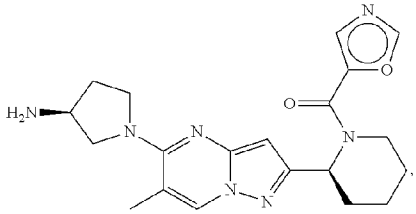


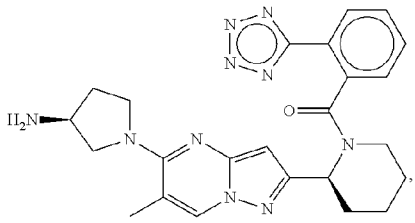


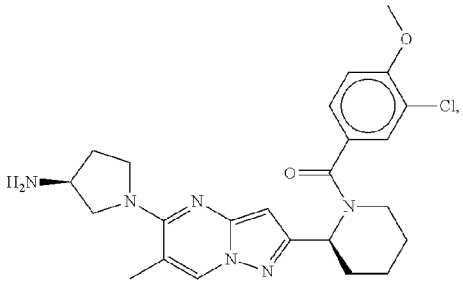


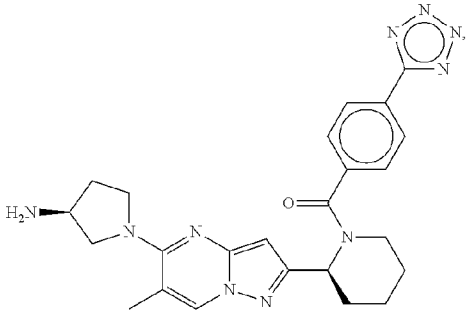


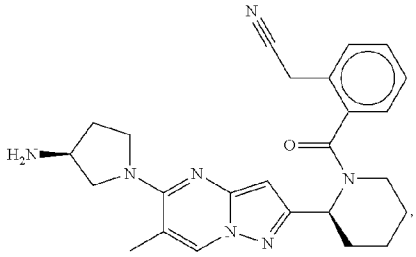


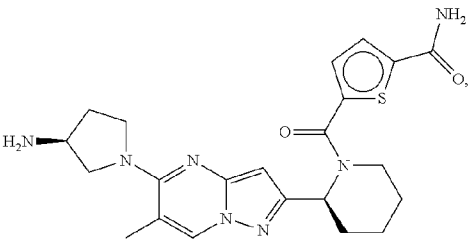


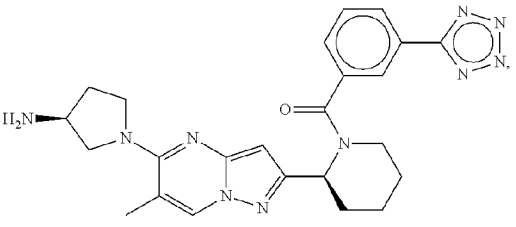


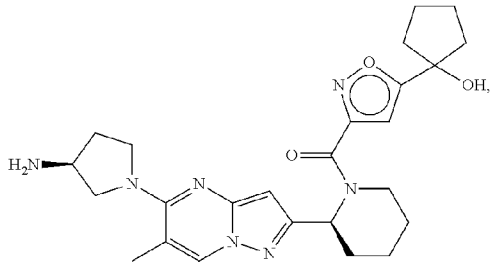


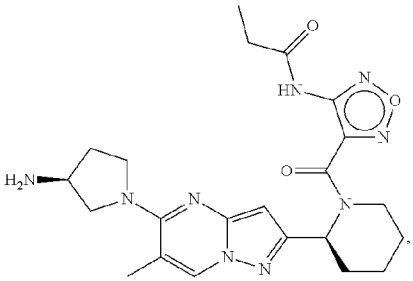


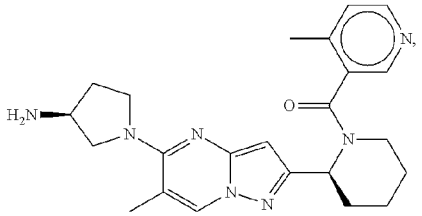


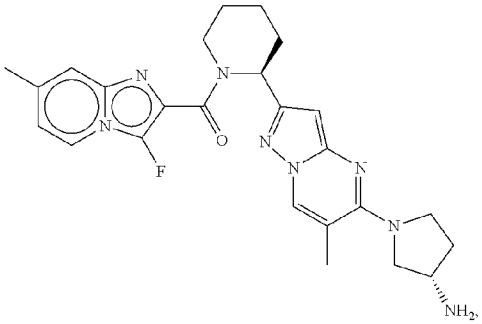


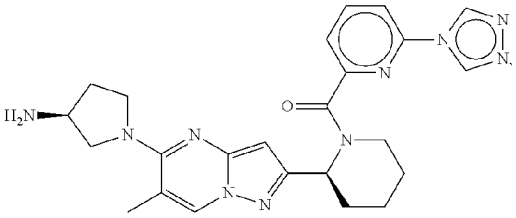


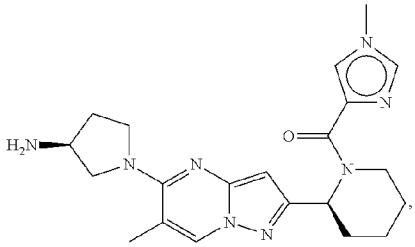


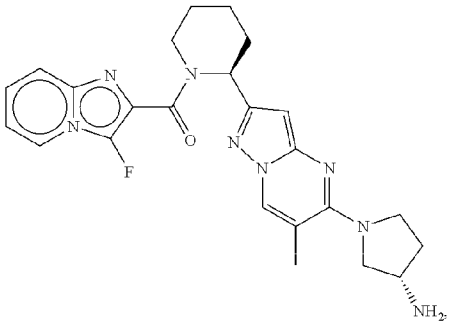


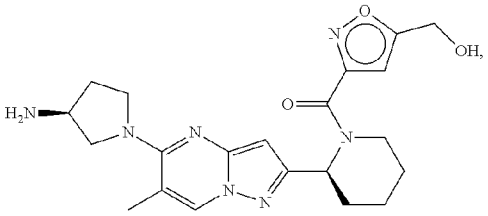


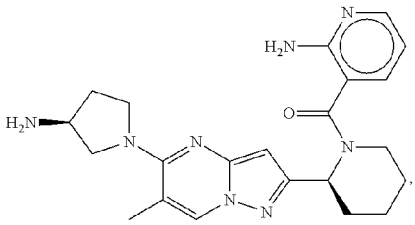


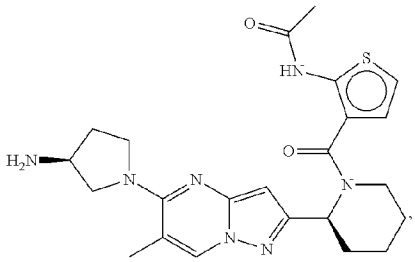


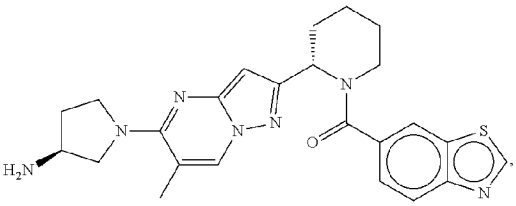


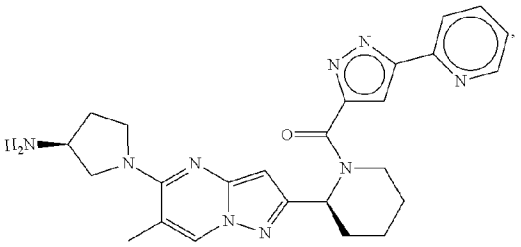


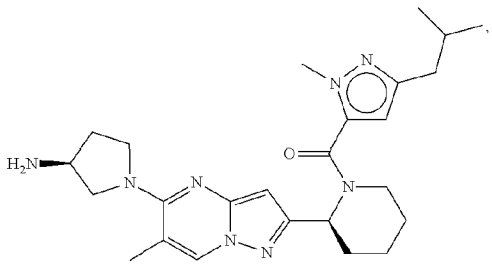


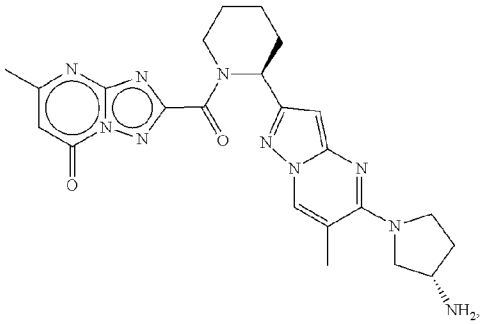


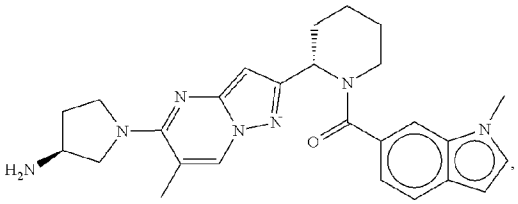


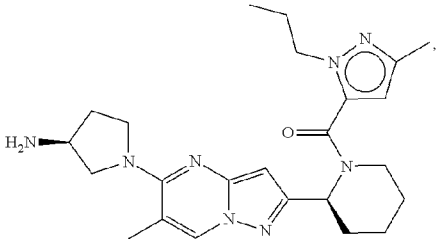


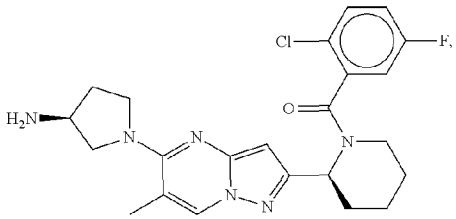


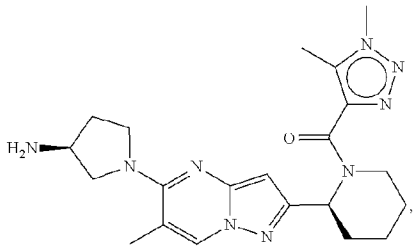


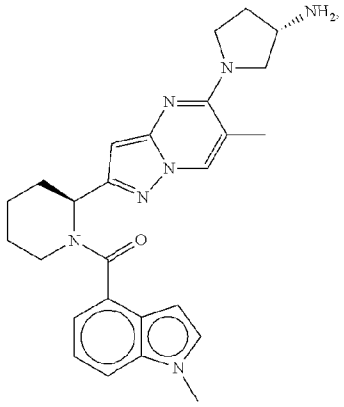


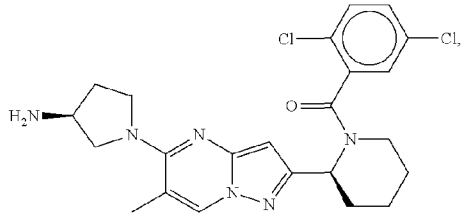


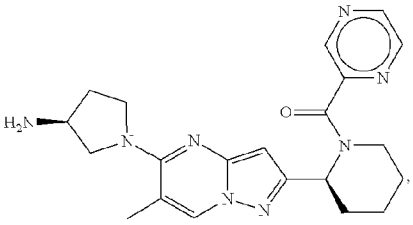


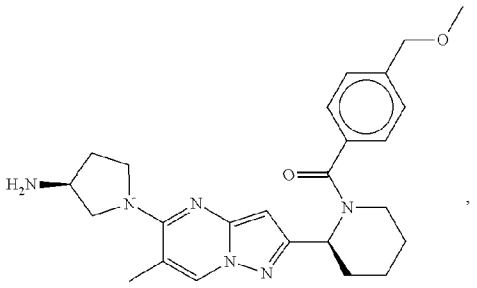


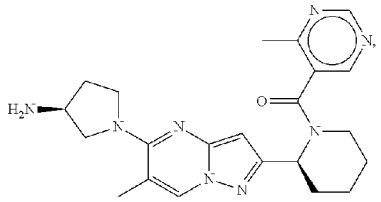


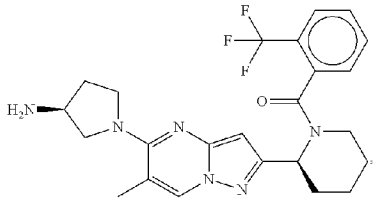


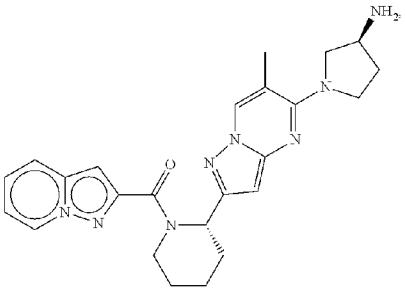


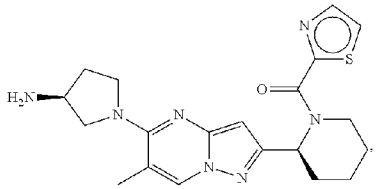


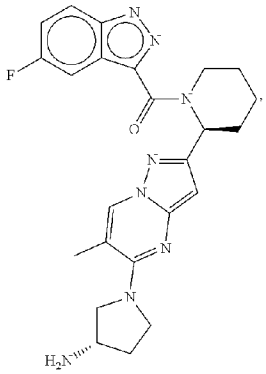


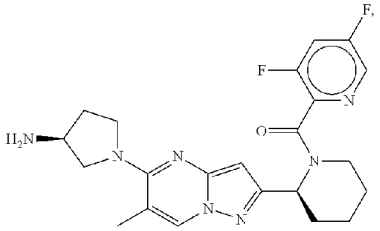


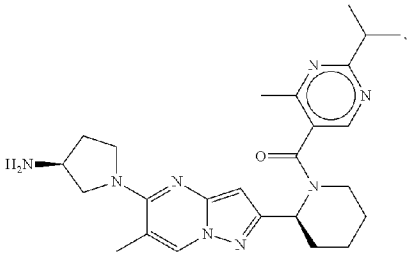


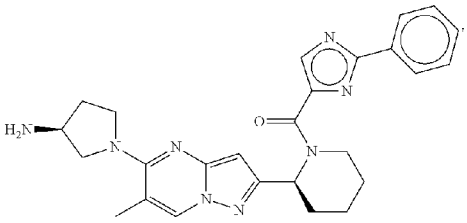


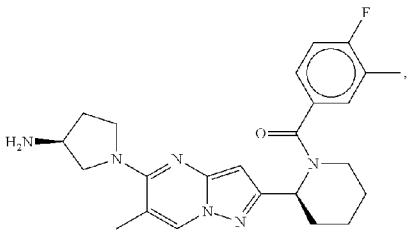


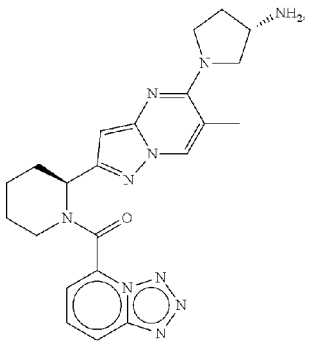


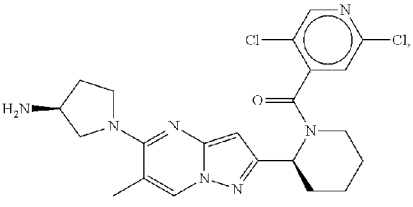


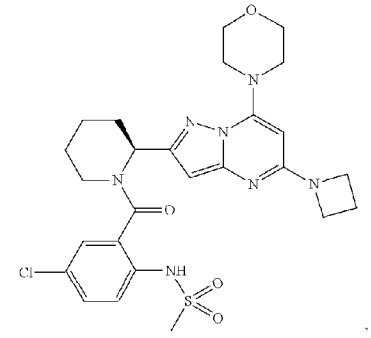


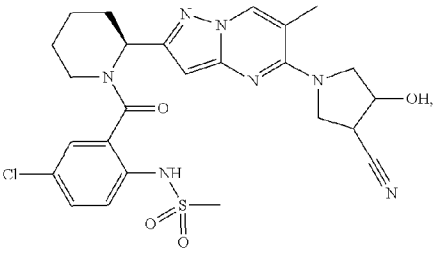


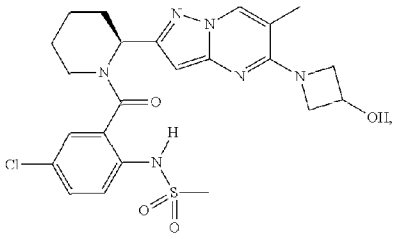


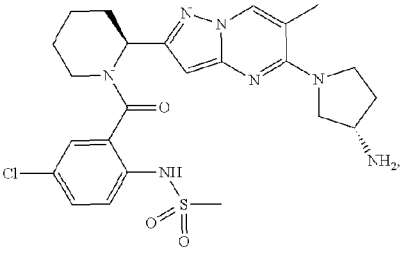


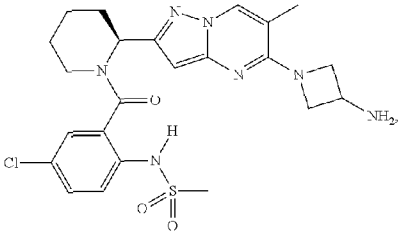


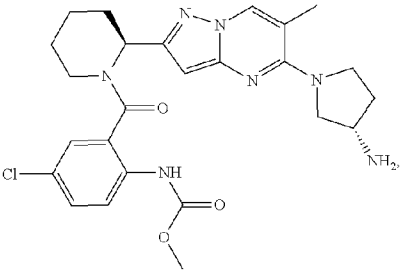


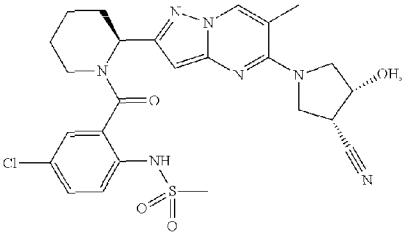


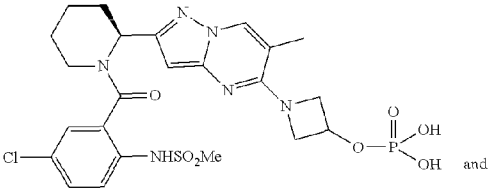


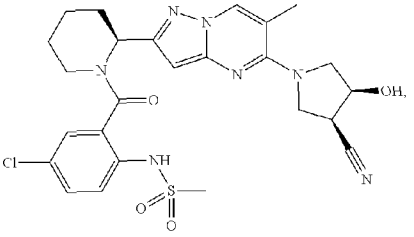


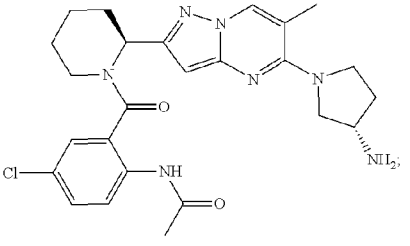


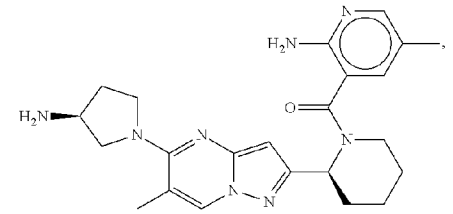


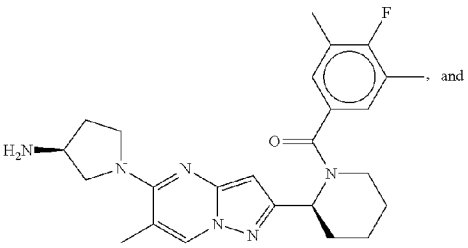


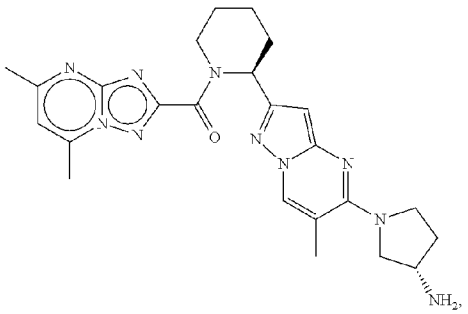

and





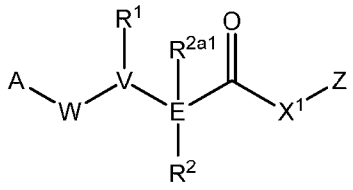






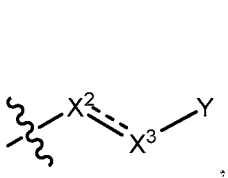
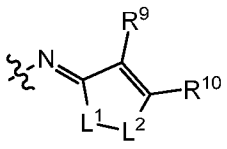
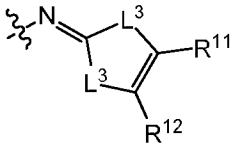
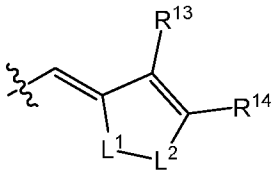
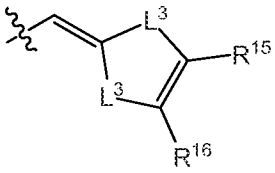
Compounds of Formula (B21)

[0152] Compounds of the general Formula (B21) are described in PCT Publication No. WO 2014/031784, published February 27, 2014, which is hereby incorporated by reference in its entirety. Formula (B21) has the structure:



(I)

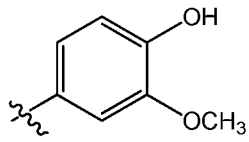
or a pharmaceutically acceptable salt thereof, wherein: A can be selected from an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-2} alkyl), an optionally substituted heteroaryl and an optionally substituted heterocyclyl; W can be O, S, C=O, C=S, NR^{3a3}, S=O, $S(=O)_2$ or $-C(R^{1a1})(R^{1a2})-$; V can be N or CH; E can be C or N; provided that when E is N, then R^{2a1} is absent; Z can be selected from





and


; Y can be selected from an optionally substituted acylalkyl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl; -------- between X^2 and X^3 can represent a single or double bond between X^2 and X^3; wherein when ------ is a double bond, then X^1 can be NR^{3a1} or $CR^{3a2}R^6$, X^2 is N (nitrogen) or CR^{7a1}, and X^3 can be N (nitrogen) or CR^4; and when -------- is a single bond, then X^1 can be NR^{3a1} or $CR^{3a2}R^6$, X^2 can be O, NR^7, C(=O) or $C(R^{7a2})(R^{7a3})$, and X^3 can be NR^4, C(=O), CR^4R^8 or $CH_2CH_2C(=O)$; or X^1, X^2 and X^3 can be each independently C (carbon), N (nitrogen), O (oxygen) or C(=O), and form a mono-cyclic ring selected from an optionally substituted mono-cyclic heteroaryl and an optionally substituted mono-cyclic heterocyclyl by joining X^1 and X^3 together; and provided that at least one of X^1, X^2 and X^3 comprises a nitrogen atom, with the proviso that the valencies of X^1, X^2 and X^3 are satisfied with a substituent selected from hydrogen and an optionally substituted C_{1-4} alkyl; and X^1, X^2 and X^3 are uncharged; L^1 can be $-C(R^{17})_2-$, $-C(R^{18})_2C(R^{18a1})_2-$, $-C(R^{18a2})=C(R^{18a3})-$ or $-C(R^{19})_2N(R^{19a1})-$; L^2 can be $-C(R^{20})_2-$, $-N(R^{21})-$, S, or O; each L^3 can be independently $-C(R^{22})_2-$, $-C(R^{23})_2C(R^{23a1})_2-$ or $-C(R^{23a2})=C(R^{23a3})-$; provided that when L^1 is $-C(R^{19})_2N(R^{19a1})-$, then L^2 is $-C(R^{20})_2-$; R^1 can be hydrogen or an unsubstituted C_{1-4} alkyl; R^{1a1} and R^{1a2} can be each independently hydrogen, hydroxy or an unsubstituted C_{1-4} alkyl; R^2 and R^{2a1} can be each independently selected from hydrogen, an optionally substituted C_{1-4} alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, hydroxy, 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); or R^1 and R^2, together with the atoms to which they are attached, can be joined to form an optionally substituted 5-membered heterocyclic ring or an optionally substituted 6-membered heterocyclic ring, R^{2a1} can be selected from hydrogen, an optionally substituted C_{1-4} alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, hydroxy, 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); R^{3a1}, R^{3a2} and R^{3a3} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^4 can be selected from hydrogen, an optionally substituted C_{1-8} alkyl, an

optionally substituted C_{2-8} alkenyl, an optionally substituted C_{2-8} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted C_{3-6} cycloalkyl(C_{1-6} alkyl), an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl(C_{1-6} alkyl), an optionally substituted heterocyclyl(C_{1-6} alkyl), halo(C_{1-8} alkyl), an optionally substituted hydroxyalkyl, an optionally substituted alkoxyalkyl and cyano; R^6, R^7, and R^{7a1} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^{7a2} and R^{7a3} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^8 can be hydrogen or optionally substituted C_{1-4} alkyl; R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15} and R^{16} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; or R^9 and R^{10}, R^{11} and R^{12}, R^{13} and R^{14}, and R^{15} and R^{16}, are each independently taken together form an optionally substituted cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl or an optionally substituted heterocyclyl; and each R^{17}, each R^{18}, each R^{18a1}, R^{18a2}, R^{18a3}, each R^{19}, R^{19a1}, each R^{20}, R^{21}, each R^{22}, each R^{23}, each R^{23a1}, R^{23a2} and R^{23a3} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl;

[0153] In some embodiments, Formula (B21) includes the following: provided that when X^1 is NR^{3a1}, X^2=X^3 is N=CR^4, Y is an optionally substituted indolyl, then R^4 is selected from of hydrogen, cyano, an optionally substituted C_{2-6} alkyl, an optionally substituted acylalkyl, an optionally substituted hydroxyalkyl, an optionally substituted alkoxy(alkyl), an optionally substituted C_{2-6} alkenyl, an optionally substituted C_{2-6} alkynyl, haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkyl(C_{1-6} alkyl), an optionally substituted 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).

[0154] In some embodiments, Formula (B21) includes the following: provided that when X^1 is NR^{3a1}, X^2=X^3 is N=CR^4, Y is 

, then R^4 is selected from cyano, halo(C_{1-8}alkyl), an optionally substituted acylalkyl, an optionally substituted C_{1-8} alkyl, an optionally substituted hydroxyalkyl, an optionally substituted alkoxy(alkyl), an optionally substituted C_{2-8} alkenyl, an optionally substituted C_{2-8} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{3-6} cycloalkyl(C_{1-6} alkyl), an optionally substituted 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).

[0155] In some embodiments, a compound of Formula (B21) can be selected from the following: 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 242, 244, 245, 246A, 246B, 247, 300, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 415, 416, 417, 419, 422, 423, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 437, 438, 439, 440, 441, 442, 443, 444, 445, 448A, 448B, 449, 450, 453, 454, 455A, 455B, 456, 457, 458A, 458B, 459, 460, 461, 462A, 462B, 463A, 463B, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 400-1, 400-2, 400-3, 400-4, 400-5, 400-6, 400-7, 400-8, 400-9, 400-10, 400-11, 400-12, 400-13, 400-14, 400-15, 400-16, 400-17, 400-18, 400-19, 400-20, 400-21, 400-22, 400-24, 400-25, 400-26, 400-27, 400-28, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514A, 514B, 600, 601, 602, 603A, 603B, 604, 605, 606, 650, 651, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 901, 1206, 1352, 2300, 2301, 2302, 2303, 2304, 2400, 2401, 4105, 4304, 4305, 4306 , 4307, 4308, 4309, 4310, 4311, 4312, 4313 and 4314.

[0156] In some embodiments, a compound of Formula (B21) can be selected from the following: 1200, 1202, 1204, 1209, 1211, 1213, 1214, 1216, 1217, 1220, 1221, 1223, 1224, 1225, 1226, 1227, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1242, 1243, 1244, 1245, 1246, 1247, 1248, 1249, 1250, 1251, 1252, 1253, 1255, 1256, 1257, 1258, 1300, 1301, 1302, 1303, 1304, 1307, 1308, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1318, 1319, 1320, 1321, 1322, 1323, 1325, 1326, 1327, 1328, 1329, 1330, 1331, 1332, 1333, 1334, 1335, 1336, 1340, 1341, 1343, 1344, 1345, 1346, 1359, 1360, 1401, 1402, 1403, 1404, 1405, 1501, 1502, 1503, 1504, 1505, 1506, 1507, 1508, 1509, 1510, 1511, 1512, 1513, 1514, 1515, 1516, 1517, 1518, 1519, 1520, 1521, 1522, 1523, 1524, 1525, 1526, 1527, 1528, 1529, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 1540, 1541, 1601, 1602, 1603, 1604, 1605, 1606, 1607, 1608, 1609, 1610, 1611, 1612, 1613, 1614, 1615, 1616, 1617, 1618, 1619, 1620, 1621, 1622, 1623, 1800, 1802, 1803, 1804, 1805, 1806, 1807, 1808, 1809, 1810, 1811, 1812, 1813, 1814, 1815, 1816, 1817, 1818, 1819, 1820, 1821, 1822, 1823, 1824, 1825, 1826, 1829, 1830, 1831, 1832, 1833, 1834, 1835, 1836, 1837, 1838, 1839, 1900, 1901, 1902, 1903, 2000, 2100, 2101, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2111, 2112,

2113, 2114, 2115, 2504, 2506, 2507, 2508, , 2601, 2602, 2603, 2604, 2605, 2613, 2615, 2617, 2618, 2619, 2620, 2621, 2622, 2624, 2626, 2627, 2638, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2654, 3302, 3800, 3903, 4002, 4201, 4202, 4203, 4204, 4205, 4206, 4207, 4208, 4209, 4210, 4212 and 4216.

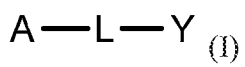
[0157] In some embodiments, a compound of Formula (B21) can be selected from the following: 840, 1100, 1101, 1201, 1205, 1210, 1215, 1219, 1222, 1228, 1240, 1241, 2204, 2205, 2800, 2801, 3200, 3401, 3500, 3501, 3900 and 4303.

[0158] In some embodiments, a compound of Formula (B21) can be selected from the following: 900, 902, 903, 904, 908, 910, 917, 1000, 2803, 3300 and 4302.

[0159] In some embodiments, a compound of Formula (B21) can be selected from the following: 239, 240, 241, 2305, 2306 and 2802.

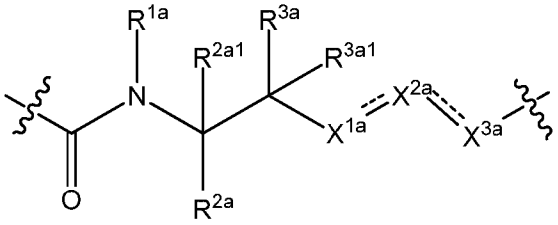
Compounds of Formula (B22)

[0160] Compounds of the general Formula (B22) are described in PCT Publication No. WO 2015/026792, filed August 19, 2014, which is hereby incorporated by reference in its entirety. Formula (B22) has the structure:

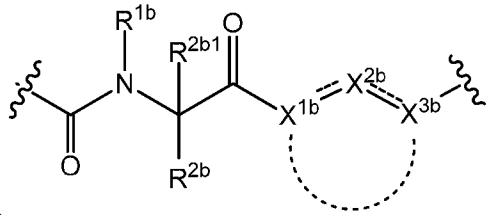


(I)

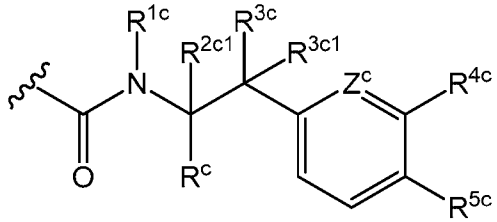
or a pharmaceutically acceptable salt thereof, wherein: L can be selected from:



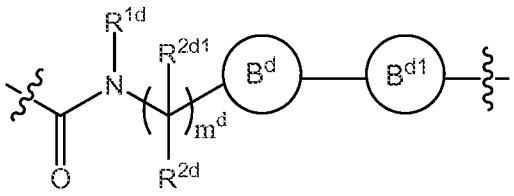
(Ia),



(Ib),

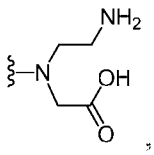


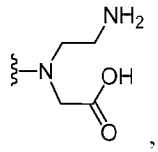
(Ic) and

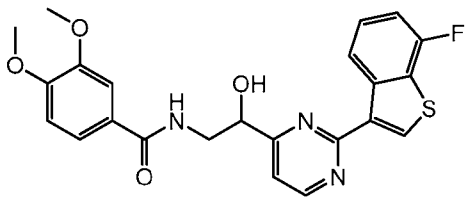


(Id);

A can be selected from an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-2} alkyl), an optionally substituted heteroaryl and an optionally substituted heterocyclyl; Y can be selected from an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl; R^{1a}, R^{1b}, R^{1c} and R^{1d} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^{2a}, R^{2a1}, R^{2b}, R^{2b1}, R^{2c}, R^{2c1},

R^{2d} and R^{2d1} can be each independently selected from can be hydrogen, an optionally substituted C_{1-4} alkyl, an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heterocyclyl(C_{1-6} alkyl), an alkoxyalkyl, an aminoalkyl, a hydroxyalkyl and hydroxy; or R^{2a1} can be hydrogen, and R^{1a} and R^{2a} can be joined together with the atoms to which they are attached to form an optionally substituted 5 membered heterocyclyl or an optionally substituted 6 membered heterocyclyl, R^{2b1} can be hydrogen, and R^{1b} and R^{2b} can be joined together with the atoms to which they are attached to form an optionally substituted 5 membered heterocyclyl or an optionally substituted 6 membered heterocyclyl; --------- between X^{1a} and X^{2a} can represent a single or double bond between X^{1a} and X^{2a}; --------- between X^{2a} and X^{3a} can represent a single or double bond between X^{2a} and X^{3a}; provided that --------- between X^{1a} and X^{2a} and --------- between X^{2a} and X^{3a} cannot be both double bonds and at least one of --------- is a double bond; when --------- between X^{1a} and X^{2a} represents a double bond and --------- between X^{2a} and X^{3a} represents a single bond, then X^{1a} can be N or CR^{4a1}, X^{2a} can be N or CR^{5a} and X^{3a} can be NR^{6a1}, C(=O) or $CR^{6a2}R^{6a3}$; and when --------- between X^{1a} and X^{2a} represents a single bond and --------- between X^{2a} and X^{3a} represents a double bond, then X^{1a} can be NR^{4a} or $CR^{4a2}R^{4a3}$, X^{2a} can be N or CR^{5a} and X^{3a} can be N or CR^{6a}; or X^{1a}, X^{2a} and X^{3a} can be each independently C, N, O or C(=O), and form a ring or ring system selected from an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl by joining X^{1a} and X^{3a} together; with the proviso that the valencies of X^{1a}, X^{2a} and X^{3a} can be each independently satisfied with a substituent selected from hydrogen and an optionally substituted C_{1-4} alkyl, and X^{1a}, X^{2a} and X^{3a} are uncharged; R^{3a} and R^{3a1} can be each independently selected from hydrogen, hydroxy, halogen, amino, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{2-4} alkenyl, an optionally substituted C_{2-4} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{1-4} alkoxy, -O-carboxy, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, CHF_2, CF_3 and , provided that R^{3a} and R^{3a1} cannot be both hydrogen; or R^{3a} and R^{3a1} can together form =N-OR^a; or R^{3a} and R^{3a1} together with the atom to which they are attached can be joined to form an optionally substituted 3 membered ring, an optionally substituted 4 membered ring, an optionally substituted 5 membered ring or an optionally substituted 6 membered ring; R^{4a}, R^{4a1}, R^{4a2} and R^{4a3} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^{5a} and R^{5a1} can be each independently be hydrogen or an unsubstituted C_{1-4} alkyl; R^{6a} and R^{6a1} can be each independently hydrogen, an optionally substituted C_{1-4} alkyl or

an optionally substituted alkoxyalkyl; R^{6a2} and R^{6a3} can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; X^{1b}, X^{2b} and X^{3b} can be each independently C, N, O or C(=O), and form indicates a bi-cyclic ring selected from an optionally substituted bi-cyclic heteroaryl and an optionally substituted bi-cyclic heterocyclyl by joining X^{1b} and X^{3b} together, wherein -------- between X^{1b} and X^{2b} represents a single or double bond between X^{1b} and X^{2b}; -------- between X^{2b} and X^{3b} represents a single or double bond between X^{2b} and X^{3b}; and provided that at least one of X^{1b}, X^{2b} and X^{3b} comprises a nitrogen atom and both -------- cannot be double bonds; with the proviso that the valencies of X^{1b}, X^{2b} and X^{3b} can be each independently satisfied with a substituent selected from hydrogen and an optionally substituted C_{1-4} alkyl; and X^{1b}, X^{2b} and X^{3b} are uncharged; R^{3c} and R^{3c1} can be each independently selected from hydrogen, hydroxy, halogen, amino, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{2-4} alkenyl, an optionally substituted C_{2-4} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{1-4} alkoxy, -O-carboxy, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, CHF_2, CF_3 and , provided that R^{3c} and R^{3c1} cannot be both hydrogen; or R^{3c} and R^{3c1} together form =N-OR^c; or R^{3c} and R^{3c1} together with the atom to which they are attached can be joined to form an optionally substituted 3 membered ring, an optionally substituted 4 membered ring, an optionally substituted 5 membered ring or an optionally substituted 6 membered ring; R^a and R^c can be each independently hydrogen or an unsubstituted C_{1-4} alkyl; R^{4c} and R^{5c} can be taken together to form an unsubstituted aryl, an unsubstituted heteroaryl or an optionally substituted heterocyclyl; Z^c can be N or CH; m^d can be 0 or 1; ring B^d can be an optionally substituted C_5 cycloalkyl; ring B^{d1} can be an optionally substituted pyridinyl; and provided that when L is Formula (IIc), then Y is absent.

[0161] In some embodiments, Formula (B22) is not .

[0162] In some embodiments, a compound of Formula (B22) can be selected from the following: 1, 13-1, 100, 101, 102, 103, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 116a, 116b, 117, 117a, 117b, 118, 118a, 118b, 119, 120, 120a, 120b, 121, 122, 122a, 122b, 123,

124, 125, 126, 127, 128, 129, 131, 132, 133, 134, 138, 139, 142, 143, 144, 145, 146, 147, 148, 151, 152, 153, 154, 155, 158, 159, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 218, 219, 221, 223, 224, 225, 226, 227, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 306, 307, 308, 309, 310, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498a, 498b, 498c, 498d, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604a, 604b, 604c, 604d, 605a, 605b, 605c, 605d, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623a, 623b, 624a, 624b, 625, 626, 627, 628, 629, 630, 631, 632, 633a, 633b, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 680, 681 and 682, or a pharmaceutically acceptable salt of the foregoing.

[0163] In some embodiments, a compound of Formula (B22) can be selected from the following: 629, 630, 631 and 632, or a pharmaceutically acceptable salt of the foregoing.

[0164] In some embodiments, a compound of Formula (B22) can be selected from the following: 149, 150, 156, 157, 160, 217, 220, 222, 229, 287, 302, 303, 304, 305, 311, 401, 473 and 474, or a pharmaceutically acceptable salt of the foregoing.

[0165] In some embodiments, a compound of Formula (B22) can be selected from the following: 130, 135, 140 and 141, or a pharmaceutically acceptable salt of the foregoing.

[0166] In some embodiments, a compound of Formula (B22) can be 104 or 161, or a pharmaceutically acceptable salt of the foregoing, as provided in (B22).

[0167] In some embodiments, a compound of Formula (B22) can be 136 or 137, or a pharmaceutically acceptable salt of the foregoing, as provided in (B22).

Methods of Use

[0168] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used to treat and/or ameliorate a paramyxovirus infection. In some embodiments, a combination of compounds described herein can be used to prevent a paramyxovirus infection. In some embodiments, a combination of compounds described herein can be used to inhibit the replication of a paramyxovirus. In some embodiments, a combination of compounds described herein can be used to inhibit the paramyxovirus polymerase complex.

[0169] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used to treat and/or ameliorate a respiratory syncytial viral (RSV) infection. In some embodiments, a combination of compounds described herein can be used to prevent a respiratory syncytial viral infection. In some embodiments, a combination of compounds described herein can be used to inhibit the replication of a respiratory syncytial virus. In some embodiments, a combination of compounds described herein can be used to inhibit the RSV polymerase complex. In some embodiments, the RSV can be Type A. In other embodiments, the RSV can be Type B. In still other embodiments, the RSV can be Type A and B.

[0170] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used to treat and/or ameliorate a HPIV-1 infection and/or HPIV-3 infection. In some embodiments, a combination of compounds described herein can be used to prevent a HPIV-1 infection and/or HPIV-3 infection. In some embodiments, a

combination of compounds described herein can be used to inhibit the replication of HPIV-1 and/or HPIV-3. In some embodiments, a combination of compounds described herein can be used to inhibit the HPIV-1 polymerase complex and/or HPIV-3 polymerase complex.

[0171] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used to treat and/or ameliorate a HPIV-2 infection and/or HPIV-4 infection. In some embodiments, a combination of compounds described herein can be used to prevent a HPIV-2 infection and/or HPIV-4 infection. In some embodiments, a combination of compounds described herein can be used to inhibit the replication of HPIV-2 and/or HPIV-4. In some embodiments, a combination of compounds described herein can be used to inhibit the HPIV-2 polymerase complex and/or HPIV-4 polymerase complex.

[0172] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used to treat and/or ameliorate a metapneumoviral infection. In some embodiments, a combination of compounds described herein can be used to prevent a metapneumoviral infection. In some embodiments, a combination of compounds described herein can be used to inhibit the replication of a metapneumovirus. In some embodiments, a combination of compounds described herein can be used to inhibit the metapneumovirus polymerase complex. In some embodiments, including those of this paragraph, the metapneumovirus can be a human metapneumovirus.

[0173] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used treat and/or ameliorate an upper respiratory viral infection caused by a paramyxovirus infection. In some embodiments, a combination of compounds described herein can be used treat and/or ameliorate a lower respiratory viral infection caused by a paramyxovirus infection. In some embodiments, a combination of compounds described herein can be used treat and/or ameliorate one or more symptoms of an infection caused by a paramyxovirus infection (such as those described herein). Respiratory infections include colds, croup, pneumonia, bronchitis and bronchiolitis. Symptoms can include a cough, runny nose, nasal congestion, sore throat, fever, difficulty breathing, abnormally rapid breathing, wheezing vomiting, diarrhea and ear infections. In some embodiments, a combination described herein can be used treat and/or ameliorate one or more symptoms of an infection caused

by a virus selected from a RSV virus, a parainfluenza virus and a metapneumovirus (such as those described herein).

[0174] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be used treat and/or ameliorate bronchiolitis and/or tracheobronchitis due to a paramyxovirus infection. In some embodiments, a combination described herein can be used treat and/or ameliorate pneumonia due to a paramyxovirus infection. In some embodiments, a combination described herein can be used treat and/or ameliorate croup due to a paramyxovirus infection.

[0175] As used herein, the terms "prevent" and "preventing," mean lowering the efficiency of viral replication and/or inhibiting viral replication to a greater degree in a subject who receives the compound compared to a subject who does not receive the compound. Examples of forms of prevention include prophylactic administration to a subject who has been or may be exposed to an infectious agent, such as a paramyxovirus (e.g., RSV).

[0176] As used herein, the terms "treat," "treating," "treatment," "therapeutic," and "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 subject's overall feeling of well-being or appearance.

[0177] 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, a therapeutically 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 therapeutically 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.

[0178] Various indicators for determining the effectiveness of a method for treating a paramyxovirus 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 of disease response.

[0179] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can reduce viral titers to undetectable levels, for example, less than 1.7 $\log_{10}$ plaque forming units equivalents (PFUe)/mL, or less than 0.3 $\log_{10}$ plaque forming units equivalents (PFUe)/mL. In some embodiments, a combination of compounds described herein can reduce the viral load compared to the viral load before administration of the combination (for example, 60 hours after receiving the initial dosage of the combination). In some embodiments, a combination of compounds described herein can reduce the viral load to lower than 1.7 $\log_{10}$ (PFUe)/mL, or lower than 0.3 $\log_{10}$ (PFUe)/mL. In some embodiments, a combination of compounds described herein can achieve a reduction in 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 combination. For example, the viral load is measure before administration of the combination, and several hours after receiving the initial dosage of the combination (for example, 60 hours after receiving the initial dosage of the combination).

[0180] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical 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 a paramyxovirus relative to pre-treatment levels in a subject, as determined several hours after receiving the initial dosage of the combination (for example, 60 hours after receiving the initial dosage of the combination). In some embodiments, a combination of compounds described herein can result in a reduction of the replication of a paramyxovirus 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 combination of compounds described herein can result in a reduction of a paramyxovirus 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 a paramyxovirus replication compared to the

reduction of a paramyxovirus reduction achieved by ribavirin (Virazole®), or may achieve the same reduction as that of ribavirin (Virazole®) therapy in a shorter period of time, for example, in one day, two days, three days, four days, or five days, as compared to the reduction achieved after 5 days of ribavirin (Virazole®) therapy.

[0181] 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 combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can be administered to a subject infected with RSV that is resistant to one or more different anti-RSV agents (for example, ribavirin). In some embodiments, development of resistant RSV strains can be delayed when subjects are treated with combination of compounds described herein compared to the development of RSV strains resistant to other anti-RSV drugs administered as monotherapy.

[0182] In some embodiments, a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) can decrease the percentage of subjects that experience complications from a RSV viral infection compared to the percentage of subjects that experience complication being treated with ribavirin. For example, the percentage of subjects being treated with a combination of compounds described herein that experience complications can be 10%, 25%, 40%, 50%, 60%, 70%, 80% and 90% less compared to subjects being treated with ribavirin.

[0183] In some embodiments, a combination of compounds can include one or more of compound (A), or a pharmaceutically acceptable salt thereof. In some embodiments, a combination of compounds can include one or more of compound (B), or a pharmaceutically acceptable salt thereof. In some embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered with one or more of compound (B), or a pharmaceutically acceptable salt thereof, in a single pharmaceutical composition. In some embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered with one or more of compound (B), or a pharmaceutically acceptable salt thereof, as two or more separate

pharmaceutical compositions. For example, compound (A), or a pharmaceutically acceptable salt thereof, can be administered in one pharmaceutical composition, and compound (B), or a pharmaceutically acceptable salt thereof, can be administered in a second pharmaceutical composition. In some embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered with at least one of compound (B), or a pharmaceutically acceptable salt thereof.

[0184] The order of administration of compound (A), or a pharmaceutically acceptable salt thereof, with compound (B), or a pharmaceutically acceptable salt thereof, can vary. In some embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered prior all of compound (B), or a pharmaceutically acceptable salt thereof. In other embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered prior to at least one compound (B), or a pharmaceutically acceptable salt thereof. In still other embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered concomitantly with one or more of compound (B), or a pharmaceutically acceptable salt thereof. In yet still other embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered subsequent to the administration of at least one compound (B), or a pharmaceutically acceptable salt thereof. In some embodiments, one or more of compound (A), or a pharmaceutically acceptable salt thereof, can be administered subsequent to the administration of all of compound (B), or a pharmaceutically acceptable salt thereof.

[0185] A potential advantage of utilizing a combination of compounds described herein (for example, a combination of one or more of compound (A) and one or more of compound (B), or a pharmaceutical acceptable salt of the foregoing) may be a reduction in the required amount(s) of one or more of compound (A), or a pharmaceutically acceptable salt thereof, and/or one or more of compound (B), or a pharmaceutically acceptable salt thereof, that is effective in treating a disease condition disclosed herein (for example, RSV), as compared to the amount required to achieve same therapeutic result when one or more of compound (B), or a pharmaceutically acceptable salt thereof, and/or one or more of compound (A), or a pharmaceutically acceptable salt thereof. For example, the amount of a one or more of compound (A), or a pharmaceutically acceptable salt thereof, and/or one or more of compound (B), or a pharmaceutically acceptable salt thereof, can be less compared to the amount of the aforementioned compounds needed to achieve the same viral load reduction when administered as a monotherapy. Another potential advantage of utilizing a combination

described herein 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. Additional advantages of utilizing a combination described herein may include little to no cross resistance between the compounds of the combination; different routes for elimination of the compounds of the combination; little to no overlapping toxicities between the compounds of the combination; little to no significant effects on cytochrome P450; and/or little to no pharmacokinetic interactions between the compounds of the combination.

[0186] 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.

[0187] 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.

[0188] 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 ED_{50} or ID_{50} values, or other appropriate values derived from *in vitro* or *in vivo* studies, as qualified by toxicity studies and efficacy studies in animals.

[0189] 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.

[0190] 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.

[0191] 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 administrated 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.

[0192] 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.

Pharmaceutical Compositions

[0193] Some embodiments described herein relates to one or more pharmaceutical compositions, that can include one or more of compound (A), or a pharmaceutically acceptable salt thereof and/or one or more of compound (B), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

[0194] The term "pharmaceutical composition" refers to a mixture of one or more of compounds disclosed herein with other chemical components, such as diluents or carriers. The pharmaceutical composition facilitates administration of the compound to an organism. Pharmaceutical compositions can also be obtained by reacting compounds with inorganic or organic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, and salicylic acid. Pharmaceutical compositions will generally be tailored to the specific intended route of administration.

[0195] The term "physiologically acceptable" defines a carrier, diluent or excipient that does not abrogate the biological activity and properties of the compound.

[0196] As used herein, a "carrier" refers to a compound that facilitates the incorporation of a compound into cells or tissues. For example, without limitation, dimethyl sulfoxide (DMSO) is a commonly utilized carrier that facilitates the uptake of many organic compounds into cells or tissues of a subject.

[0197] As used herein, a "diluent" refers to an ingredient in a pharmaceutical composition that lacks pharmacological activity but may be pharmaceutically necessary or desirable. For example, a diluent may be used to increase the bulk of a potent drug whose mass is too small for manufacture and/or administration. It may also be a liquid for the dissolution of a drug to be administered by injection, ingestion or inhalation. A common form of diluent in the art is a buffered aqueous solution such as, without limitation, phosphate buffered saline that mimics the composition of human blood.

[0198] As used herein, an "excipient" refers to an inert substance that is added to a pharmaceutical composition to provide, without limitation, bulk, consistency, stability, binding ability, lubrication, disintegrating ability etc., to the composition. A "diluent" is a type of excipient.

[0199] The pharmaceutical compositions described herein can be administered to a human patient *per se*, or in pharmaceutical compositions where they are mixed with other active ingredients, as in combination therapy, or carriers, diluents, excipients or combinations thereof. Proper formulation is dependent upon the route of administration chosen. Techniques for formulation and administration of the compounds described herein are known to those skilled in the art.

[0200] The pharmaceutical compositions disclosed herein may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or tableting processes. Additionally, the active ingredients are contained in an amount effective to achieve its intended purpose. Many of the compounds used in the pharmaceutical combinations disclosed herein may be provided as salts with pharmaceutically compatible counterions.

[0201] Multiple techniques of administering a compound exist in the art including, but not limited to, oral, rectal, topical, aerosol, injection and parenteral delivery, including intramuscular, subcutaneous, intravenous, intramedullary injections, intrathecal, direct intraventricular, intraperitoneal, intranasal and intraocular injections.

[0202] One may also administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into the infected area, often in a depot or sustained release formulation. Furthermore, one may administer the compound in a targeted drug delivery system, for example, in a liposome coated with a tissue-specific antibody. The liposomes will be targeted to and taken up selectively by the organ.

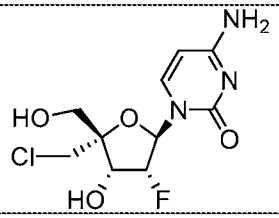
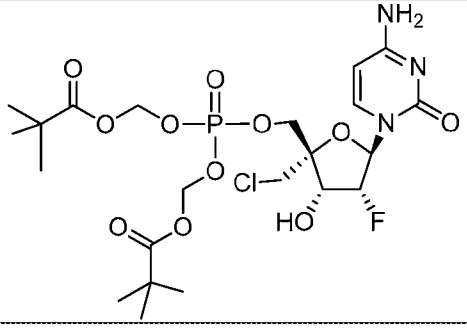
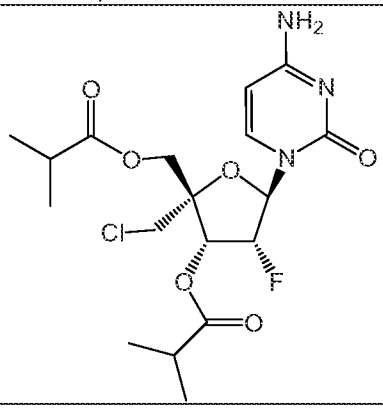
[0203] The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may for example comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. The pack or dispenser may also be accompanied with a notice associated with the container in form prescribed by a governmental agency regulating the manufacture, use, or sale of pharmaceuticals, which notice is reflective of approval by the agency of the form of the drug for human or veterinary administration. Such notice, for example, may be the labeling approved by the U.S. Food and Drug Administration for

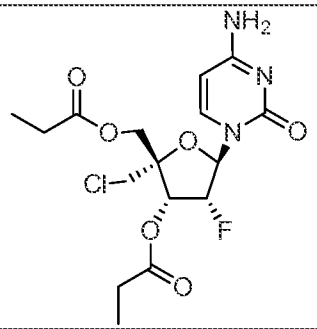
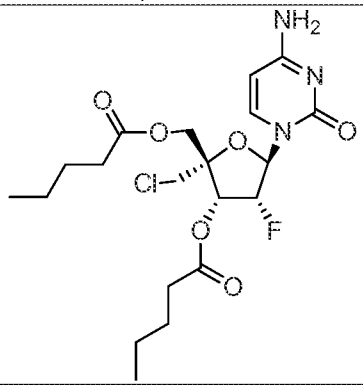
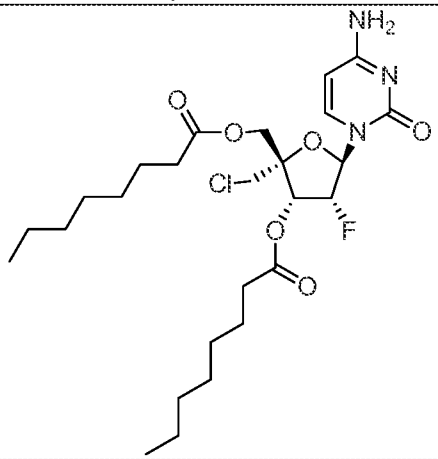
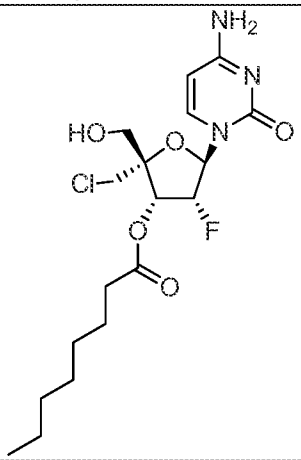
prescription drugs, or the approved product insert. Compositions that can include a compound described herein formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

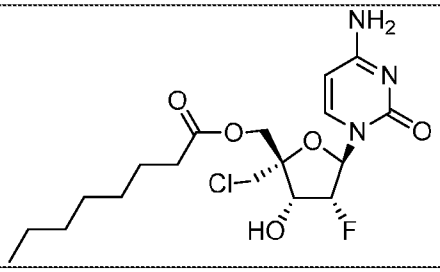
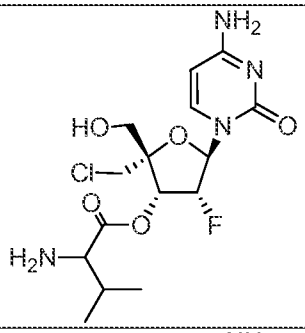
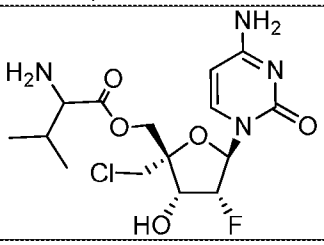
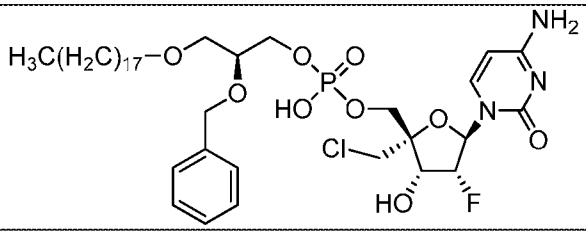
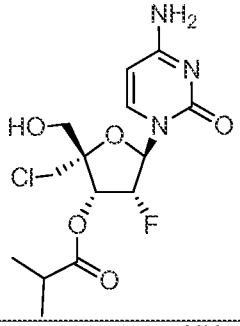
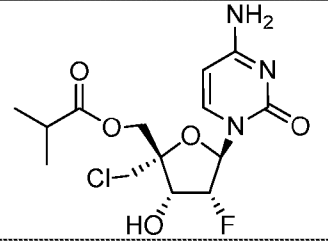
EXAMPLES

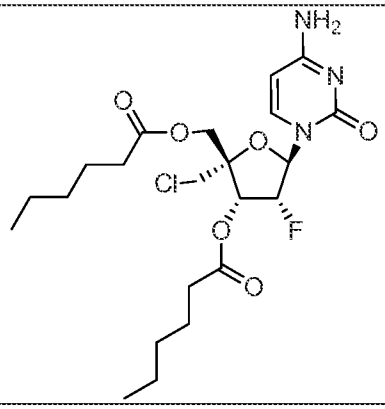
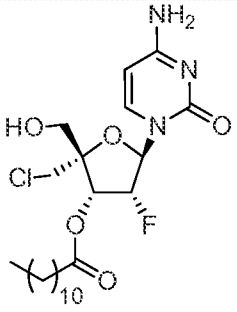
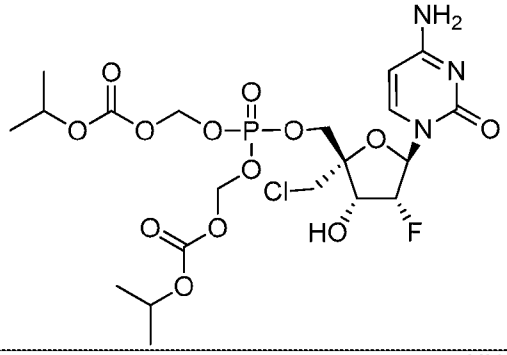
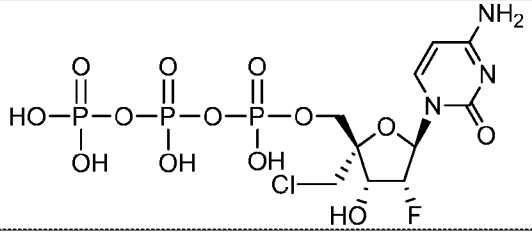
[0204] Additional embodiments are disclosed in further detail in the following examples, which are not in any way intended to limit the scope of the claims.

EXAMPLE 1
Preparation of Compounds 1-17

Compound No.	Structure	Analytical Data
1		294 $[M+H]^+$, 587 $[2M+H]^+$
2		646 [M+46-1].
3		434 [M+1]

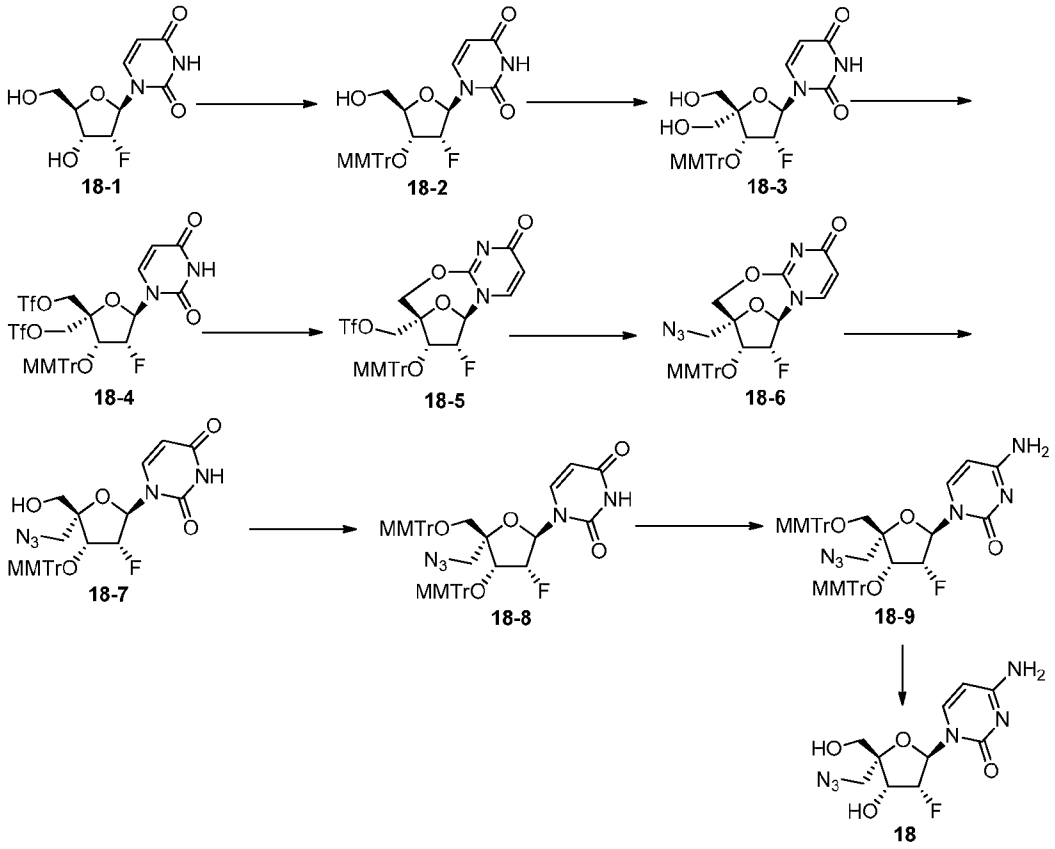
Compound No.	Structure	Analytical Data
4		404 [M-1]
5		462 [M+1]
6		544 [M-1]
7		418 [M-1]

Compound No.	Structure	Analytical Data
8		418 [M-1]
9		391 [M-1]
10		391 [M-1]
11		788.3 $[M-H]^+$
12		362.1 [M+1]
13		364 [M+1]

Compound No.	Structure	Analytical Data
14		488 [M-1]
15		474 [M-1]
16		606 [M+1]
17		532.1 [M-1]

[0205] Compounds 1-17 were prepared as described in U.S. Publication No. 2013/0165400, filed December 20, 2012, PCT Publication WO 2013/096679, filed December 20, 2012 and Publication No. WO 2013/142525, March 19, 2013, which are hereby incorporated by reference in their entireties.

EXAMPLE 2
Preparation of Compound 18



[0206] Preparation of (18-2): To a solution of **18-1** (50 g, 203 mmol) in anhydrous pyridine (200 mL) was added TBDPS-Cl (83.7 g, 304 mmol). The reaction was allowed to proceed overnight at R.T. The solution was concentrated under low pressure to give a residue, which was partitioned between ethyl acetate and water. The organic layer was separated, washed with brine, dried over magnesium sulfate and concentrated under reduced pressure to give 5'-OTBDPS ether as a white foam (94 g).

[0207] To a solution of the 5'-OTBDPS ether (94.0 g, 194.2 mmol) in anhydrous DCM (300 mL) were added silver nitrate (66.03 g, 388.4 mmol) and collidine (235 mL, 1.94 mol). The mixture was stirred at R.T. After 15 mins, the mixture was cooled to 0°C, and monomethoxytrityl chloride (239.3 g, 776.8 mmol) was added as a single portion. After being stirred overnight at R.T., the mixture was filtered through Celite and the filtrate was diluted with TBME. The solution was washed successively with 1M citric acid, diluted brine and 5% sodium bicarbonate. The organic solution was dried over sodium sulfate and concentrated under vacuum to give the fully protected intermediate as a yellow foam.

[0208] This fully protected intermediate was dissolved in toluene (100 mL) and the solution was concentrated under reduced pressure. The residue was dissolved in anhydrous THF (250 mL) and treated with TBAF (60 g, 233 mmol). The mixture was stirred for 2 h at R.T., and the solvent was removed under reduced pressure. The residue was taken into ethyl acetate and the solution was washed first with saturated sodium bicarbonate and then with brine. After being dried over magnesium sulfate, the solvent was removed in vacuum and the residue was purified by column chromatography (50% EA in PE) to give **18-2** (91 g, 86.4%) as a white foam.

[0209] Preparation of (18-3): To a solution of **18-2** (13.5 g, 26 mmol) in DCM (100 mL) was added pyridine (6.17 mL, 78 mmol). The solution was cooled to 0°C, and Dess-Martin periodinane (33.8 g, 78 mmol) was added as a single portion. The reaction mixture was stirred for 4 h at R.T., and quenched by the addition of $Na_2S_2O_3$ solution (4%) and sodium bicarbonate aqueous solution (4%) (the solution was adjusted to pH 6, ~150 mL). The mixture was stirred for 15 mins. The organic layer was separated, washed with diluted brine and concentrated under reduced pressure. The residue was dissolved in dioxane (100 mL) and the solution was treated with 37% aqueous formaldehyde (21.2 g, 10 eq.) and 2N aqueous sodium hydroxide (10 eq.). The reaction mixture was stirred at R.T., overnight. After stirring for 0.5 h at R.T., the excess of aqueous sodium hydroxide was removed with saturated NH_4Cl (~150 mL). The mixture was concentrated under reduced pressure, and the residue was partitioned between ethyl acetate and 5% sodium bicarbonate. The organic phase was separated, washed with brine, dried over magnesium sulfate and concentrated. The residue was purified by column chromatography (2% MeOH in DCM) to give the diol **18-3** (9.2 g, 83.6%) as a white foam.

[0210] Preparation of (18-4): Compound **18-3** (23 g, 42.0 mmol) was co-evaporated with toluene twice. The residue was dissolved in anhydrous DCM (250 mL) and pyridine (20 mL). The solution was cooled to 0°C, and triflic anhydride (24.9 g, 88.1 mmol) was added dropwise over 10 mins. At this temperature, the reaction was stirred for 40 mins. The reaction was monitored by TLC (PE: EA= 2:1 and DCM: MeOH= 15:1). After completion, the reaction mixture was quenched with water (50 mL) at 0°C. The mixture was stirred for 30 mins, and extracted with EA. The organic phase was dried over Na_2SO_4 and filtered through a silica gel pad. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (50% EA in PE) to give **18-4** (30.0 g, 88.3%) as a brown foam.

[0211] Preparation of (18-5): To a stirred solution of **18-4** (4.4 g, 5.42mmol) in anhydrous DMF (50 mL) was added NaH (260 mg, 6.5 mmol) at 0°C under nitrogen atmosphere.

The solution was stirred at R.T., for 1.5 h. The solution was used for the next step without any further workup.

[0212] Preparation of (18-6): To the stirred solution was added NaN_3 (1.5 g, 21.68 mmol) at 0°C under nitrogen atmosphere, and the resulting solution was stirred at R.T. for 1.5 h. The reaction was quenched with water, extracted with EA, washed with brine, and dried over $MgSO_4$. The concentrated organic phase was used for the next step without further purification.

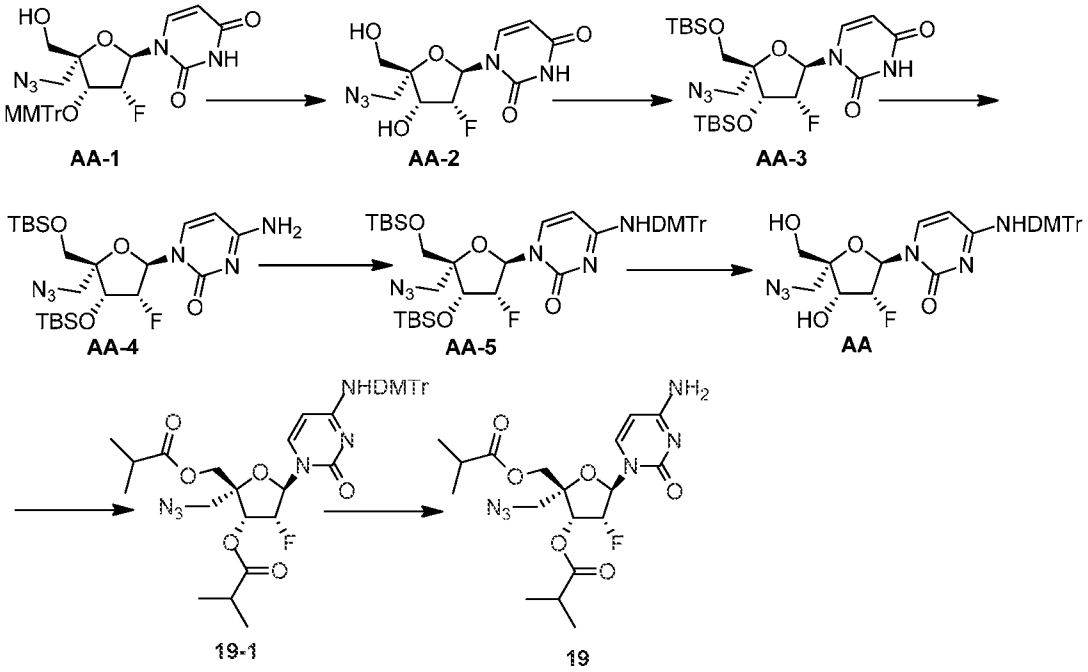
[0213] Preparation of (18-7): To a solution of **18-6** (3.0 g, 5.4 mmol) in anhydrous 1,4-dioxane (18 mL) was added NaOH (5.4 mL, 2M in water) at R.T. The reaction mixture was stirred at R.T. for 3 h. The reaction was diluted with EA, washed with brine, and dried over $MgSO_4$. The concentrated organic phase was purified on a silica gel column (30% EA in PE) to give **1-7** (2.9 g, 93%) as a white foam.

[0214] Preparation of (18-8): To a stirred solution of **18-7** (1.1 g, 2.88 mmol) in anhydrous DCM (10 mL) was added MMTrCl (1.77 g, 5.76 mmol), $AgNO_3$ (1.47 g, 8.64 mmol) and collidine (1.05 g, 8.64 mmol) at 25 °C under a N_2 atmosphere. The reaction was refluxed for 12 h. MeOH (20 mL) was added and the solvent was removed to dryness. The residue was purified on a silica gel column (20% EA in PE) to give **18-8** (1.6 g, 85.1%) as a white foam.

[0215] Preparation of (18-9): To a stirred solution of **18-8** (800 mg, 0.947 mmol) in anhydrous MeCN (10 mL) were added TPSCl (570 mg, 1.89 mmol), DMAP (230 mg, 1.89 mmol) and TEA (190 mg, 1.89 mmol) at R.T. The mixture was stirred for 12 h. NH_4OH (25 mL) was added and the mixture was stirred for 2 h. The solvent was removed, and the residue was purified on a silica gel column as a yellow foam. Further purification by prep-TLC gave **18-9** (700 mg, 87.1%) as a white solid.

[0216] Preparation of (18): Compound **18-9** (300 mg, 0.355 mmol) was dissolved in 80% of HCOOH (5 mL) at R.T. The mixture was stirred for 3 h, and monitored by TLC. The solvent was then removed and the residue was treated with MeOH and toluene (3 times). NH_3/MeOH was added and the mixture was stirred at R.T., for 5 mins. The solvent was removed and the residue was purified by column chromatography to give **18** (124 mg, 82.6%) as a white solid. ESI-LCMS: m/z 301.0 $[M+H]^+$, 601.0 $[2M+H]^+$.

EXAMPLE 3
Preparation of Compound 19



[0217] Preparation of (AA-2): **AA-1** (2.20 g, 3.84 mmol) was dissolved in 80% HCOOH (40 mL) at R.T. (18 °C). The mixture was stirred at R.T. for 12 h. The solvent was removed at low pressure. The residue was purified by column chromatography using 50% EA in Hexane to give **AA-2** (1.05 g, 91.3%) as a white solid.

[0218] Preparation of (AA-3): To a stirred solution of **AA-2** (1 g, 3.32 mmol) in anhydrous pyridine (20 mL) was added TBSCl (747 mg, 4.98 mmol) and imidazole (451 mg, 6.64 mmol) at R.T. (16 °C) under N_2 atmosphere. The mixture was stirred at R.T. for 4 h. The resulting solution was concentrated to dryness under reduced pressure, and the residue was dissolved in EA (100 mL). The solution was washed with sat. $NaHCO_3$ solution and brine, and dried over anhydrous $MgSO_4$. The solution was concentrated to dryness, and the residue was purified on a silica gel column using 20% EA in Hexane to give **AA-3** (1.4 g, 79.5%) as a white solid.

[0219] Preparation of (AA-4): To a stirred solution of **AA-3** (1.50 g, 2.83 mmol, 1.00 eq.) in anhydrous CH_3CN (28 mL) was added TPSCl (1.71 g, 5.80 mmol, 2.05 eq.), DMAP (691.70 mg, 5.66 mmol, 2.00 eq.) and TEA (573.00 mg, 5.66 mmol, 2.00 eq.) at R.T. (15 °C). The mixture was stirred for 2 h. $NH_3.H_2O$ (20 mL) was added, and the mixture was stirred for 3 h. The mixture was extracted with EA (3 x 60 mL). The organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated at low pressure. The residue was purified on a silica gel column (30% EA in PE) to give **AA-4** (2.3 g, crude) as a yellow foam.

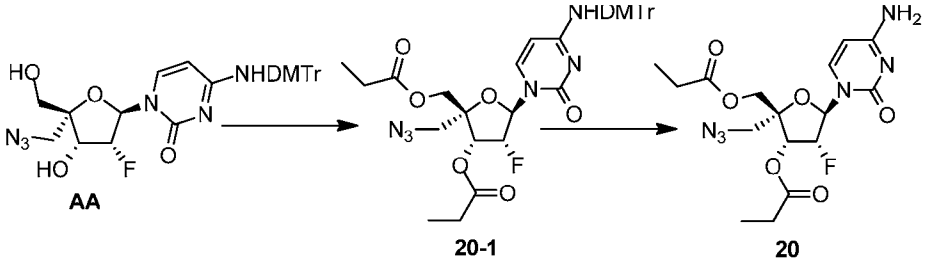
[0220] Preparation of (AA-5): To a stirred solution of **AA-4** (1.90 g, 2.34 mmol) in anhydrous DCM (20 mL) was added DMTrCl (1.82 g, 3.49 mmol) and 2,4,6-trimethylpyridine (1.00 g, 8.25 mmol) at R.T. (15 °C) under N_2 atmosphere. The mixture was stirred at R.T. for 12 h. MeOH (20 mL) was added. The mixture was filtered, and the filtrate was concentrated to dryness. The residue was dissolved in EA (80 mL). The solution was washed with brine, dried over anhydrous Na_2SO_4 and concentrated at low pressure. The residue was purified on a silica gel column (5% MeOH in DCM) to give **AA-5** (1.4 g, crude) as a white solid.

[0221] Preparation of (AA): **AA-5** (2.40 g, 2.60 mmol) was dissolved in TBAF (10 mL, 1M in THF). The mixture was stirred at R.T. (15 °C) for 30 mins. The mixture was concentrated to dryness, and the residue was dissolved in EA (60 mL). The solution was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified on a silica gel column (5% MeOH in DCM) to give **AA** (1.50 g, 95.8%) as a white solid. ESI-MS: m/z 625.3 $[M+Na]^+$.

[0222] Preparation of (19-1): To a solution of **AA** (60.0 mg, 99.57 μmol, 1.00 eq.) in pyridine (1 mL) was added isobutyric anhydride (31.50 mg, 199.13 μmol, 2.00 eq.) in 1 portion at R.T. (15 °C) under N_2 atmosphere. The mixture was stirred at R.T. for 12 h. The mixture was concentrated, and the residue was partitioned between EA and water. The combined organic phases were washed with water and brine, and dried over anhydrous Na_2SO_4. The mixture was filtered, and the filtrate was concentrated to dryness. The residue was purified by silica gel chromatography (30% EA in PE) to afford **19-1** (59.00 mg, 79.77%) as a white solid.

[0223] Preparation of (19): **19-1** (57.00 mg, 76.74 μmol, 1.00 eq.) was dissolved in 80% CH_3COOH (8 mL). The solution was stirred at R.T. (15 °C) for 12 h. The mixture was concentrated to dryness. The residue was purified on a silica gel column (2.5% MeOH in DCM) to give **19** (23.00 mg, 68.05%) as a white foam. ESI-MS: m/z 441.2 $[M+H]^+$, 463.2 $[M+Na]^+$.

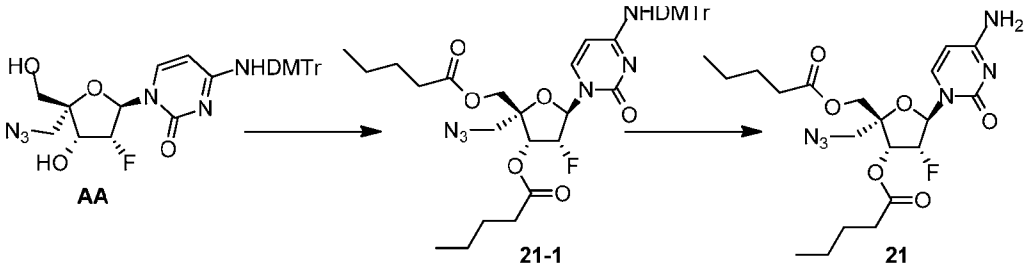
EXAMPLE 4
Preparation of Compound 20



[0224] Preparation of (20-1): **20-1** was prepared in similar manner as **19-1** using **AA** (60.00 mg, 99.57 μmol, 1.00 eq.) in pyridine (1 mL) and propionic anhydride (25.92 mg, 199.13 μmol, 2.00 eq.). **20-1** (white solid, 56.00 mg, 78.69%).

[0225] Preparation of (20): Compound **20** was prepared in similar manner as **19** using **20-1** (54.00 mg, 75.55 μmol, 1.00 eq.) **20** (white foam, 18.00 mg, 57.78%). ESI-MS: m/z 413.1 $[M+H]^+$.

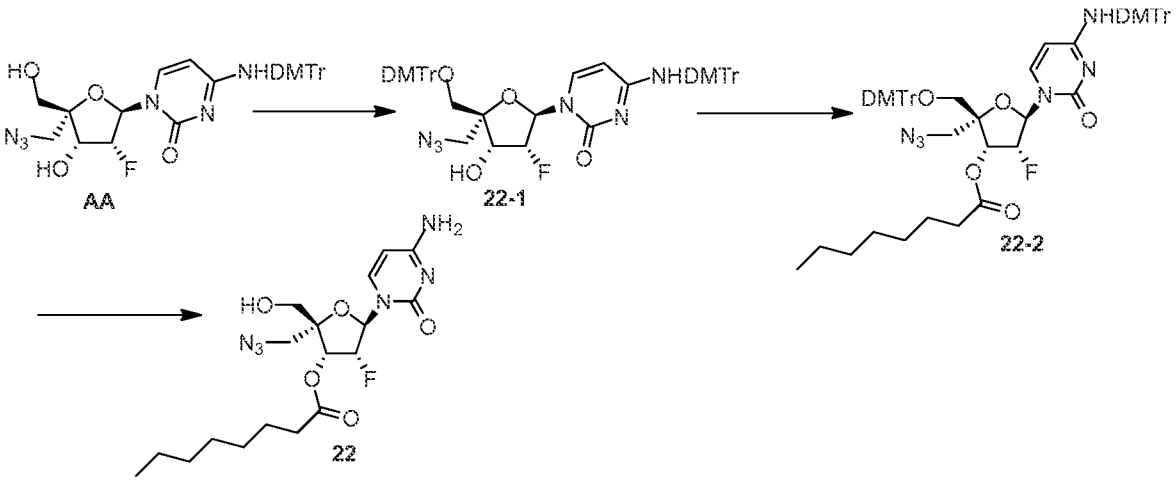
EXAMPLE 5
Preparation of Compound 21



[0226] Preparation of (21-1): **21-1** was prepared in similar manner as **19-1** using **AA** (62.00 mg, 102.89 μmol, 1.00 eq.) in pyridine (1 mL) and pentanoic anhydride (38.32 mg, 205.77 μmol, 2.00 eq.). **21-1** (white solid, 60.00 mg, 75.65%).

[0227] Preparation of (21): Compound **21** was prepared in similar manner as **19** using **21-1** (75.00 mg, 97.30 μmol, 1.00 eq.) **21** (white foam, 28.00 mg, 61.43%). ESI-MS: m/z 469.2 $[M+H]^+$.

EXAMPLE 6
Preparation of Compound 22

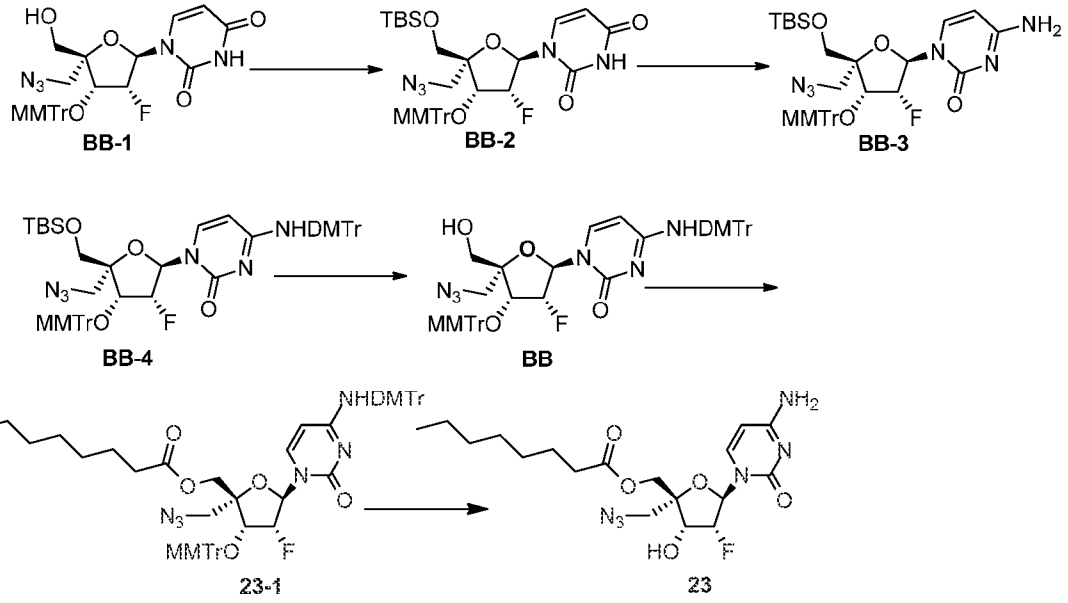


[0228] Preparation of (22-1): To a stirred solution of **AA-1** (300.0 mg, 497.83 μmol) in anhydrous pyridine (0.5 mL) was added DMTrCl (337.36 mg, 995.66 μmol) at R.T. (17 °C) under N_2 atmosphere. The solution was stirred at 50 °C~60 °C for 12 h. The mixture was concentrated to dryness under reduced pressure, and the residue was dissolved in EA (40 mL). The solution was washed with brine, dried over anhydrous $MgSO_4$, and concentrated to dryness at low pressure. The residue was purified on a silica gel column using 20% EA in PE to give **22-1** (300 mg, 66.59%) as a white solid.

[0229] Preparation of (22-2): To a stirred solution of **22-1** (100.00 mg, 110.50 μmol) in anhydrous pyridine (0.5 mL) was added DMAP (6.75 mg, 55.25 μmol), DCC (22.80 mg, 110.50 μmol) and n-actanoic acid (31.87 mg, 221.00 μmol) at R.T. (18 °C) under N_2 atmosphere. The solution was stirred at R.T. for 12 h. The solution was concentrated to dryness under reduced pressure. The residue was purified on a silica gel column using 15% EA in PE to give **22-2** (98.00 mg, 86.0%) as a white foam.

[0230] Preparation of (22): **22-2** (90.00 mg, 87.28 μmol) was dissolved in 80% CH_3COOH (20 mL) at R.T. (16 °C). The mixture was stirred R.T. for 12 h. The reaction was quenched with MeOH, and the mixture was concentrated to dryness. The residue was purified on a silica gel column (5% MeOH in DCM) to give **22** (33.00 mg, 88.7%) as a white solid. ESI-MS: m/z 427.2 $[M+H]^+$.

EXAMPLE 7
Preparation of Compound 23



[0231] Preparation of (BB-2): To a stirred solution of **BB-1** (500.00 mg, 0.87 mmol) in anhydrous pyridine (1 mL) was added TBSCl (236.5 mg, 1.57 mmol) at 20 °C under N_2. The solution was stirred at 50 °C~60 °C for 12 h. The solution was concentrated to dryness under reduced pressure. The residue was dissolved in EA (50 mL). The solution was washed with sat. $NaHCO_3$ solution and brine, and dried over anhydrous $MgSO_4$. The solution was filtered, and the filtrate was concentrated to dryness. The residue was purified on a silica gel column to give **BB-2** (510.00 mg, 85.06%) as a white solid.

[0232] Preparation of (BB-3): To a stirred solution of **BB-2** (430.00 mg, 625.15 mmol) in anhydrous MeCN (6 mL) was added TPSCl (368.65 mg, 1.25 mmol), DMAP (152.75 mg, 1.25 mmol) and TEA (126.52 mg, 1.25 mmol) at R.T. The mixture was stirred for 2 h. NH_4OH (8 mL) was added, and the mixture stirred for 3 h. The mixture was extracted with EA (3 x 40 mL). The organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated at low pressure. The residue was purified on a silica gel column (25% EA in PE) to give **BB-3** (500 mg of crude) as a yellow foam.

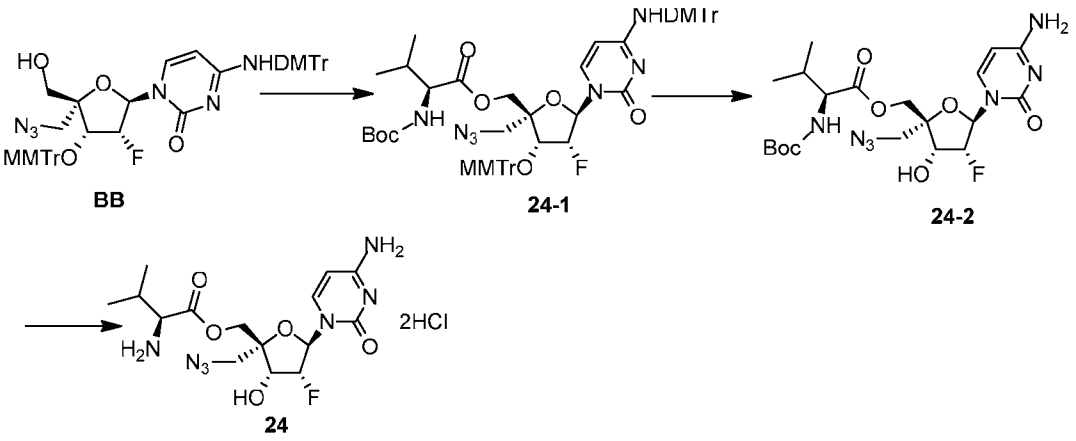
[0233] Preparation of (BB-4): To a stirred solution of **BB-3** (500 mg of crude, 0.72 mmol) in anhydrous DCM (7 mL) was added DMTrCl (365 mg, 1.0 mmol) and collidine (305 mg, 2.5 mmol) and $AgNO_3$ (184 mg, 1.08 mmol) at R.T. (15 °C) under N_2 atmosphere. The mixture was stirred at R.T. for 12 h. MeOH (5 mL) was added. The mixture was filtered, and the filtrate was concentrated to dryness. The residue was dissolved in EA (50 mL). The solution was washed with brine, dried over anhydrous Na_2SO_4 and concentrated at low pressure. The residue was purified on a silica gel column (5% MeOH in DCM) to give **BB-4** (500 mg, 70.3%) as a white solid.

[0234] Preparation of (BB): **BB-4** (1.00 g, 1.01 mmol) was dissolved in TBAF (5 mL, 1M in THF) and stirred at R.T. for 30 mins. The mixture was diluted with EA (100 mL). The mixture was washed with water and brine, and dried over anhydrous $MgSO_4$. The organic phase was concentrated to dryness. The residue was purified on the silica gel column (30% EA in PE) to give **BB** (0.80 g, 91.5%) as a white solid. ESI-MS: m/z 873.7 $[M+1]^+$.

[0235] Preparation of (23-1): To a solution of **BB** (100.00 mg, 114.29 μmol) in anhydrous pyridine (1.5 mL) was added DMAP (2.79 mg, 22.86 μmol), DCC (70.75 mg, 342.88 μmol) and n-octanoic acid (49.45 mg, 342.88 μmol) at R.T. (18 °C) under N_2 atmosphere. The solution was stirred at R.T. for 12 h. The solution was concentrated to dryness under reduced pressure. The residue was purified on a silica gel column using 15% EA in PE to give **23-1** (95.00 mg, 83.03%) as a white foam.

[0236] Preparation of (23): **23-1** (110.00 mg, 109.87 μmol) was dissolved in 80% CH_3COOH (25 mL) at R.T. (15°C). The mixture was stirred for 12 h. The reaction was quenched with MeOH, and the solution was concentrated to dryness. The residue was purified on a silica gel column (5% MeOH in DCM) to give **23** (30.00 mg, 64.03%) as a white solid. ESI-MS: m/z 427.2 $[M+H]^+$.

EXAMPLE 8
Preparation of Compound 24



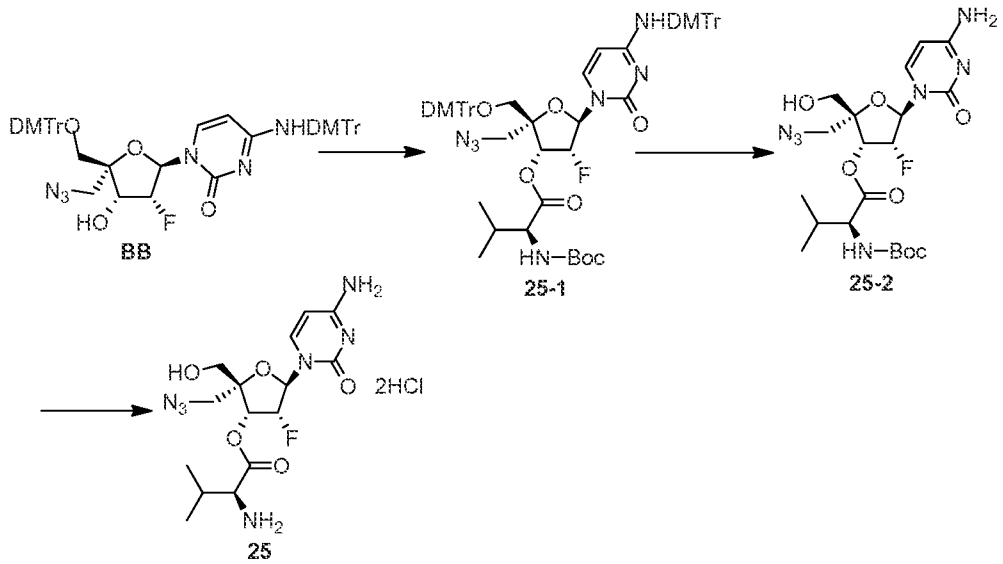
[0237] Preparation of (24-1): To a solution of N-Boc-L-Valine (620.78 mg, 2.86 mmol) and TEA (144.57 mg, 1.43 mmol) in anhydrous THF (2.5 mL) was added **BB** (250.00 mg, 285.73 μmol). The mixture was co-evaporated with pyridine and toluene to remove water. The residue was dissolved in THF (2.5 mL). DIPEA (369.28 mg, 2.86 mmol) was added, followed by addition of BOP-Cl (363.68 mg, 1.43 mmol) and 3-nitro-1H-1,2,4-triazole (162.95 mg, 1.43 mmol) at R.T. (18 °C). The mixture was stirred at R.T. for 12 h and then diluted with EA (40 mL). The solution was washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness at low pressure. The residue was purified on a silica gel column (30% EA in PE) to give **24-1** (220 mg, crude) as a white foam.

[0238] Preparation of (24-2): **24-1** (250.0 mg, 232.73 μmol) was dissolved in 80% CH_3COOH (30 mL). The solution was heated to 50 °C and stirred for 12 h. The reaction was quenched with MeOH, and the solution was concentrated to dryness. The residue was purified on a silica gel column (5% MeOH in DCM) to give **24-2** (80.00 mg, 68.82%) as a white foam.

[0239] Preparation of (24): **24-2** (78.00 mg, 156.16 μmol) was dissolved in HCl/dioxane (1.5 mL) and EA (1.5 mL) at R.T. (19 °C). The mixture was stirred at R.T. for 30

mins. The solution was concentrated to dryness at low pressure The residue was purified by prep-HPLC to give **24** (23 mg, 31.25%) as a white solid. ESI-MS: m/z 400.20 $[M+H]^+$,799.36 $[2M+H]^+$.

EXAMPLE 9
Preparation of Compound 25

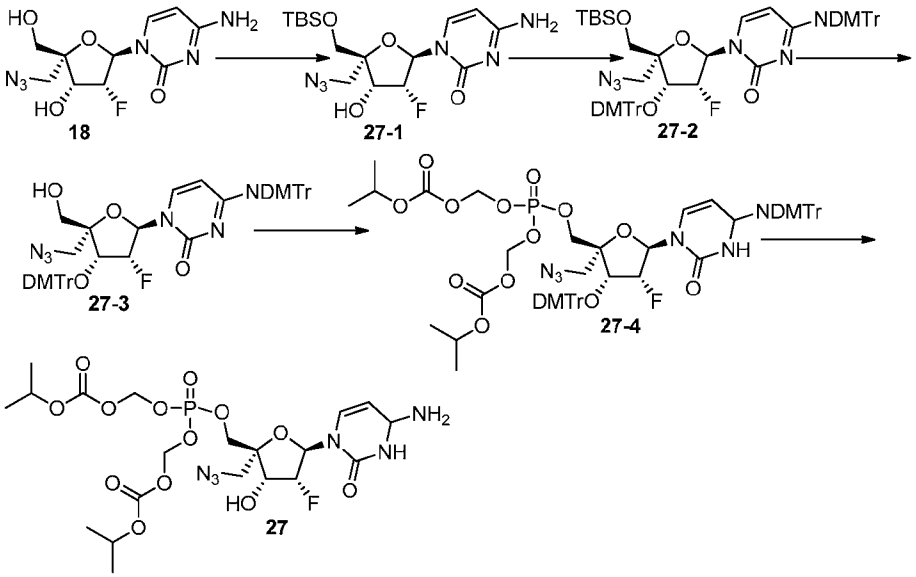


[0240] Preparation of (25-1): **25-1** was prepared in similar manner as **24-1** using **BB** (250.0 mg, 276.25 μmol), (2S)-2-(tert-butoxycarbonylamino)-3-methyl-butanoic acid (360.11 mg, 1.66 mmol) and TEA (83.86 mg, 828.75 μmol). **25-1** (white foam, 220.0 mg, 72.12%).

[0241] Preparation of (25-2): **25-2** was prepared in similar manner as **24-2** using **25-1** (230.00 mg, 208.29 μmol, 1.00 eq.). **25-2** (white foam, 80.00 mg, 77.66%).

[0242] Preparation of (25): **25** was prepared in similar manner as **24** using **25-2** (100.00 mg, 200.20 μmol, 1.00 eq.). **25** (white solid, 56 mg, 59.57 %). ESI-MS: m/z 400.0 $[M+H]^+$, 422.1 $[M+Na]^+$; 799.1 $[2M+H]^+$, 821.2 $[2M+Na]^+$.

EXAMPLE 10
Preparation of Compound 27



[0243] Preparation of (27-1): To a solution of **18** (200 mg, 0.67 mmol) in anhydrous pyridine (5 mL) was added TBSCl (120 mg, 0.8 mmol) at R.T. The mixture was stirred overnight, and the reaction mixture was diluted with EA. The mixture was washed with $NaHCO_3$ aq. solution and brine. The organic layer was dried, filtered and concentrated to give residue, which was purified by silica gel column chromatography (5% MeOH in DCM to 25% MeOH in DCM to give **27-1** (153 mg, 55%) as a white solid.

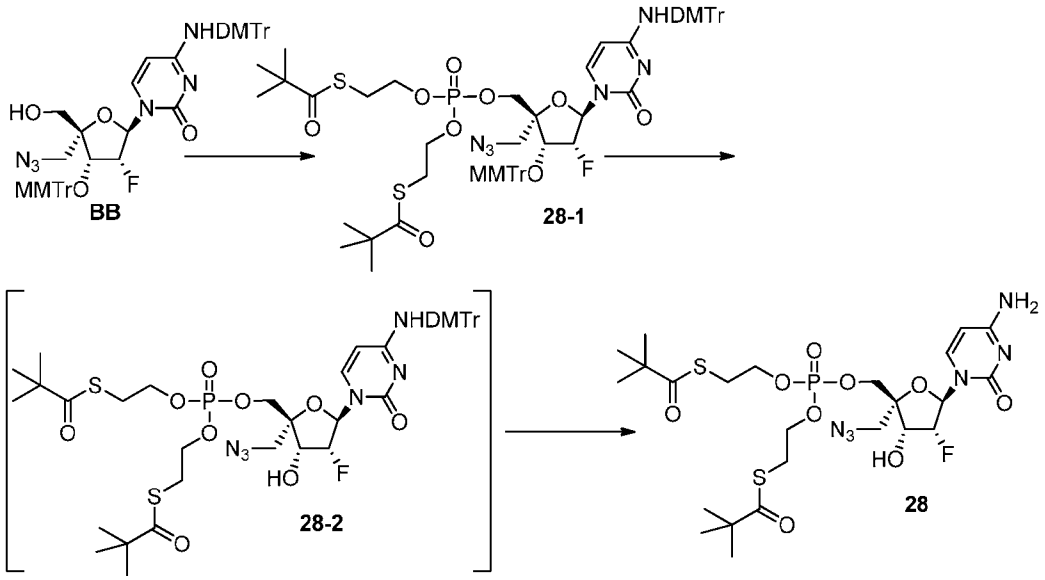
[0244] Preparation of (27-2): To a solution of **27-1** (54 mg, 0.13 mmol) in anhydrous DCM (2 mL) was added collidine (95 μL, 0.78 mmol), DMTrCl (262 mg, 0.78 mmol) and $AgNO_3$ (66 mg, 0.39 mmol) at R.T. The mixture was stirred overnight, and then diluted wit DCM (5 mL). The mixture was filtered through a pre-packed celite funnel, and the filtrate was washed with $NaHCO_3$ aq. solution, 1.0 M citric acid solution and then brine. The organic layer was dried over Na_2SO_4, and concentrated at low pressure to give a residue. The residue was purified by silica gel column chromatography (25% EA in PE to 100 %EA) to give **27-2** (83.5 mg, 63.6%).

[0245] Preparation of (27-3): To a solution of **27-2** (83 mg, 0.081 mmol) in THF (1 mL), was added a 1M solution of TBAF in THF (0.122 mL, 0.122 mmol) at ice bath temperature. The mixture was stirred for 1.5 h. The mixture was diluted with EA, and washed with water and brine. The organic layer was dried and concentrated to give the crude product, which was purified by silica gel column chromatography (DCM to 5% MeOH in DCM) to give **27-3** (66.6 mg, 91%) as a white foam.

[0246] Preparation of (27-4): Compound **27-3** (66.6 mg, 0.074 mmol) was co-evaporated with toluene and THF (3x). Bis(POC)phosphate (33 mg, 0.96 mmol) was added, and then co-evaporated with toluene (3x). The mixture was dissolved in anhydrous THF (1.5 mL) and cooled in an ice bath (0 to 5 0C). 3-nitro-1,2,4-triazole (13 mg, 0.11 mmol), diisopropylethyl amine (54 µL, 0.3 mmol), and BOP-Cl (28 mg, 0.11 mmol) were added successively. The mixture was stirred 2 h at 0 to 5 ^{0}C, diluted with EtOAc, washed with 1.0M citric acid, sat. aq. $NaHCO_3$ and brine, and dried with Na_2SO_4. The residue was purified on silica (10 g column) with CH_2Cl_2:i-PrOH (4-10% gradient) to give **27-4** (68 mg, 76%) as a white solid.

[0247] Preparation of (27): **27-4** (68 mg, 0.07 mmol) was dissolved in 80% HCOOH. The mixture was stirred at R.T. for 2 h. The solvents were evaporated at R.T. and co-evaporated with toluene (3x). The residue was dissolved in 50% CH_3CN/H_2O, was purified on a reverse-phase HPLC (C18) using CH_3CN and H_2O. The product was lyophilization to give **27** (4.8 mg, 14%) as a white foam. ESI-LCMS: m/z = 613.1 $[M+H]^+$, 1225.2 $[2M+H]^+$.

EXAMPLE 11
Preparation of Compound 28

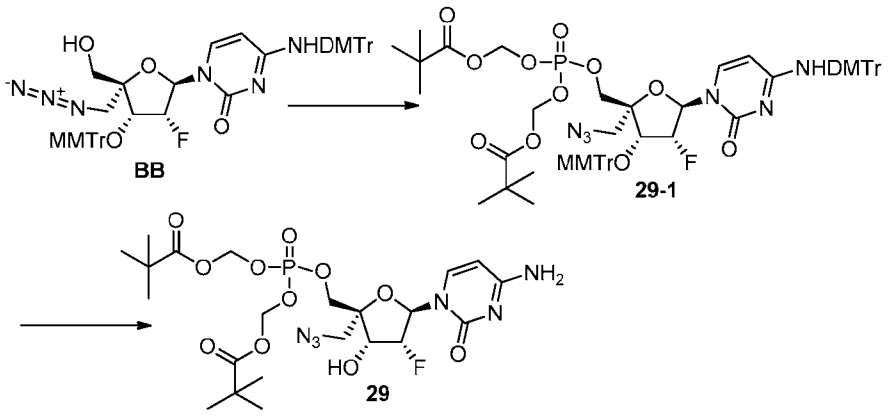


[0248] Preparation of (28-1): To a solution of **BB** (100mg, 0.114 mmol) in anhydrous CH_3CN (2 mL) were added a solution of bis-SATE-phosphoramidate (62.2 mg, 0.14 mmol) in CH_3CN (1 mL) followed by 5-ethylthio-1H-tetrazole in CH_3CN (0.25M; 0.56 mL, 0.14 mmol) at 0 to 5 ^{0}C dropwise. The mixture was stirred 2 h at 0 to 5 ^{0}C under Ar. A solution of 77% m-CPBA (49 mg, 0.22 mmol) in DCM (1 mL) was added, and the mixture was stirred 2 h at 0 to 5 ^{0}C under Ar. The mixture was diluted with EtOAc (50 mL), washed with 1.0M citric acid, sat. $NaHCO_3$, and

brine, and dried with $MgSO_4$. The mixture was filtered and the solvents were evaporated in vacuo. The residue was purified on silica (10 g column) with EA/hexanes (10-100% gradient) to give **28-1** (72 mg, 50.8 %) as a white solid.

[0249] Preparation of (28): **28-1** (72 mg, 0.056 mmol) was dissolved in anhydrous CH_3CN (1.0 mL), and 4N HCl in dioxane (87 μL, 0.35 mmol) was added at 0 to 5 °C. The mixture was stirred at R.T. for 2 h. Intermediate **28-2** was observed by LCMS. The solvents were evaporated at R.T. and co-evaporated with toluene (3x). The residue obtained was re-dissolved in 80% HCOOH (2 mL). The mixture was stirred at R.T. for 4.5 h. The solvents were evaporated at R.T. and co-evaporated with toluene (3x). Anhydrous EtOH (3 x 5 mL) was added. The residue was dissolved in 50% CH_3CN/H_2O, purified on a reverse-phase HPLC (C18) using CH_3CN and H_2O, and lyophilized to give **28** (19.2 mg) as a white foam. ESI-LCMS: m/z = 669.2 $[M+H]^+$, 1337.25 $[2M+H]^+$.

EXAMPLE 12
Preparation of Compound 29

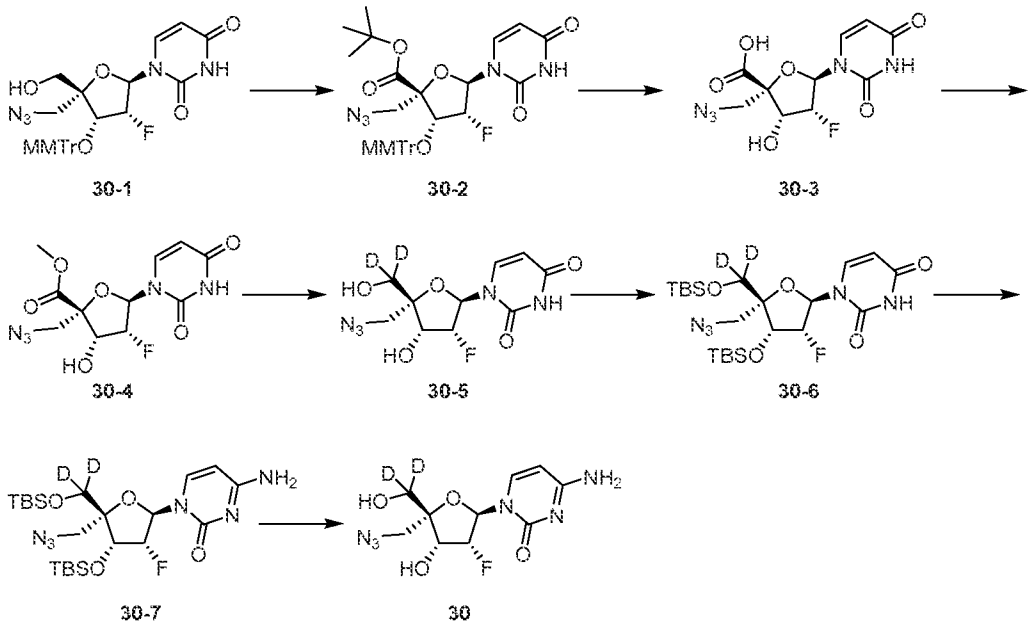


[0250] Preparation of (29-1): **29-1** (98 mg, 72.6 %) was prepared in the same manner from **BB** (100 mg, 0.114 mmol) and bis(tert-butoxycarbonyloxymethyl)phosphate (83mg, 0.35 mmol) with DIPEA (126 μL, 0.69 mmol), BOP-Cl (87 mg, 0.34 mmol), and 3-nitro-1,2,4-triazole (39 mg, 0.34 mmol) in THF (1.5 mL) in the same manner as **27-4**.

[0251] Preparation of (29): **29-1** (98 mg, 0.083 mmol) was dissolved in anhydrous CH_3CN (0.5 mL), and 4N HCl in dioxane (34 μL, 0.135 mmol) was added at 0 to 5 °C. The mixture was stirred at R.T. for 3 h. Anhydrous EtOH (200 μL) was added. The solvents were evaporated at R.T. and co-evaporated with toluene (3x). The residue was purified on silica (10 g

column) with MeOH/CH_2Cl_2 (5-7% gradient) and lypholized give **29** (30.2 mg, 60%). ESI-LCMS: m/z = 609.15 $[M+H]^+$, 1217.3 $[2M+H]^+$.

EXAMPLE 13
Preparation of Compound 30



[0252] To a stirred solution of **30-1** (3.00 g, 5.23 mmol) in anhydrous DCM (36 mL) was added PDC (3.94 g, 10.46 mmol), Ac_2O (5.34 g, 52.30 mmol) and 2-methylpropan-2-ol (7.75 g, 104.60 mmol) at RT. The mixture was stirred at RT for 15 h. The mixture was loaded on a very short silica gel column and eluted with EA. The fractions containing the product were combined and concentrated under reduced pressure. The residue was purified by column chromatography (20% EA in PE) to give **30-2** (2.40 g, 71.3%) as a white foam.

[0253] To a stirred solution of **30-2** (2.00 g, 3.26 mmol) in DCM (30 mL) was added TFA (15 mL). The mixture was stirred at RT for 1.5 h. The mixture was concentrated under reduced pressure to give **30-3** (1.00 g, crude), which was used in the next step without further purification.

[0254] Crude **30-3** (1.00 g, crude) was dissolved in a mixture of toluene (25 mL) and MeOH (20 mL). TMS-diazomethane (2 M, 3.17 mL) was added. After stirring for 2 h, the mixture was concentrated under reduced pressure at RT. The residue was diluted with EA (25 mL), washed with water (25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (2% MeOH in DCM) to give **30-4**

(451 mg, 43.2%) as a white solid. The aqueous phase was concentrated to give **30-3** (500 mg, 50.0%) as a white solid.

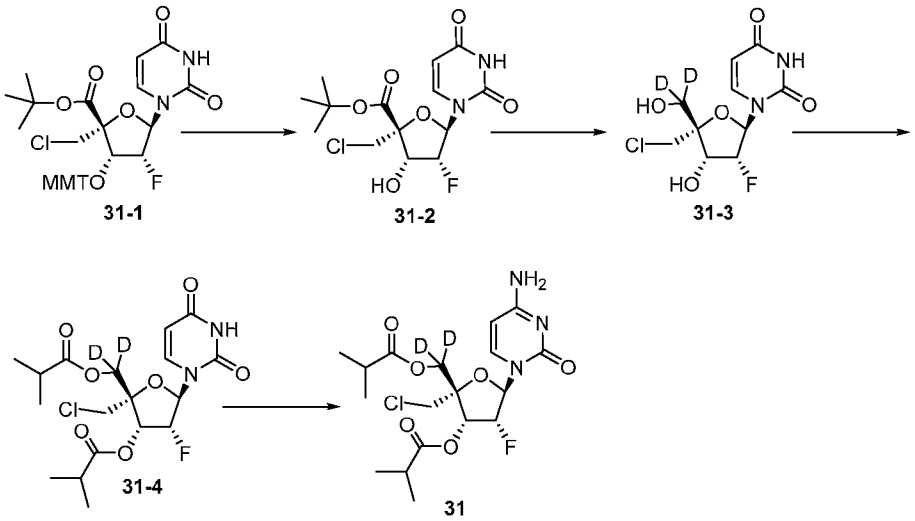
[0255] To a solution of **30-4** (451 mg, 1.37 mmol) in anhydrous CD_3OD (18 mL) was added $NaBD_4$ (344 mg, 8.22 mmol) at RT. The mixture was stirred at RT for 1 h. The reaction was quenched with CD_3OD (0.2 mL) and neutralized with AcOH (0.2 mL). The mixture was concentrated under reduced pressure. The residue was purified by column chromatography (4% MeOH in DCM) to give **30-5** (410 mg, 98.7%) as a white solid.

[0256] To a stirred solution of **30-5** (410 mg, 1.35 mmol) in pyridine (2.5 mL) was added imidazole (459 mg, 6.75 mmol) and TBSCl (610 mg, 4.05 mmol) at RT. The mixture was stirred at 60 °C for 10 h. The mixture was concentrated under reduced pressure. The residue was diluted with EA (20 mL) and washed with brine (20 mL). The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (10% EA in PE) to give **30-6** (440 mg, 61.3%) as a white solid.

[0257] To a solution of **30-6** (440 mg, 827 μmol) in anhydrous MeCN (4 mL) were added DMAP (253 mg, 2.07 mmol), Et_3N (209.32 mg, 2.07 mmol) and 2,4,6-triisopropylbenzene-1-sulfonyl chloride (626.50 mg, 2.07 mmol) at RT. The mixture was stirred at RT for 16 h. $NH_3 \cdot H_2O$ (2 mL) was added, and the mixture was stirred for 1 h. The mixture was diluted with EA (20 mL) and washed with sat. aq. NH_4Cl (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (2% MeOH in DCM) to give the crude product. The crude product was purified by TLC (10% MeOH in DCM) to give **30-7** (420 mg, 95.63%) as a white solid.

[0258] To a solution of **30-7** (420 mg, 791 μmol) in MeOH (4 mL) was added NH_4F (586 mg, 15.83 mmol) at RT. The mixture was stirred at 90-100 °C for 10 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (10% MeOH in DCM) to give the crude product. The crude product was purified by prep-HPLC (neutral condition) to give **30** (201 mg, 61.8% yield, 100% deuterium) as a white solid. ESI-TOF-MS: m/z 303.1 $[M+H]^+$, 605.2 $[2M+H]^+$.

EXAMPLE 14
Preparation of Compound 31



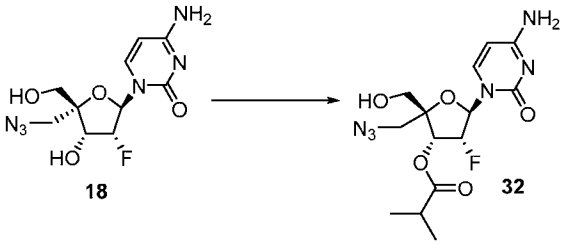
[0259] A solution of **31-1** (0.68 g, 1.07 mmol) in AcOH (10 mL) and TFA (0.25 mL) was stirred 1 h at RT. The mixture was evaporated, and the residue coevaporated with MeCN and toluene. Purification on silica column with MeOH:CH_2Cl_2 solvent system (2-12% gradient) afforded **31-1** (0.32 g, 82%).

[0260] A mixture of **31-1** (0.32 g, 0.9 mmol) in THF (9 mL) and $LiBH_4$ (94 mg, 3.6 mmol) was stirred 2 d at RT. The reaction was quenched with AcOH:EtOH, and the mixture evaporated. Purification on silica column with MeOH:CH_2Cl_2 solvent system (4-15% gradient) afforded **31-2** (80 mg, 30%).

[0261] A mixture of **31-2** (80 mg, 0.27 mmol) in pyridine (3 mL) and isobutyric anhydride (90 µL, 0.55 mmol) was stirred overnight at RT. The mixture was evaporated, and the residue coevaporated with toluene. Purification on silica column with EtOAc:hexanes solvent system (30-100% gradient) yielded **31-3** (72 mg, 61%) as a white solid.

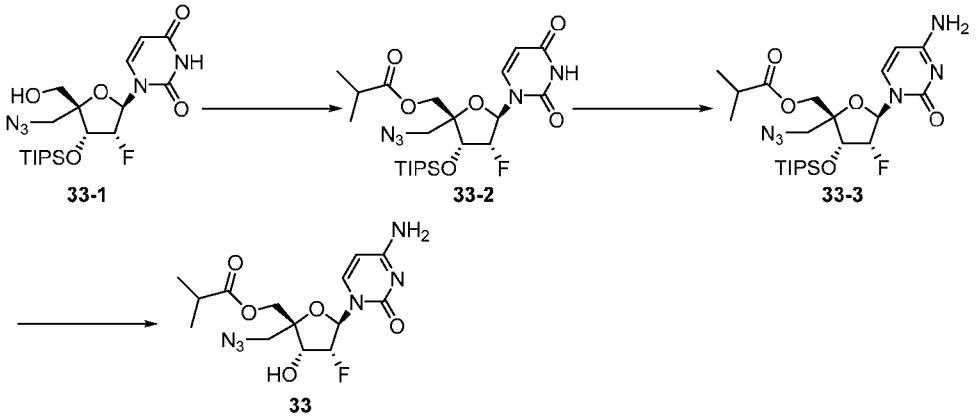
[0262] To a solution of **31-3** (72 mg, 0.17 mmol) in MeCN (2 mL) were added triisopropylphenylsulfonyl chloride (102 mg, 0.34 mmol), DMAP (41 mg, 0.34 mmol) and Et_3N (47 µL, 0.34 mmol). The mixture was stirred at RT for 90 mins, and then ammonia was quickly bubbled (<1 min) through. The mixture was stirred for 10 mins. The mixture was diluted with CH_2Cl_2, washed with 0.1 N HCl, sat. aq. $NaHCO_3$, and brine, and dried with Na_2SO_4. Purification on silica column with MeOH:CH_2Cl_2 solvent system (4-12% gradient) afforded **31** (46 mg, 60%). MS: m/z = 434.00 [M-1].

EXAMPLE 15
Preparation of Compound 32



[0263] To a solution of isobutiric acid (278 µL, 3 mmol) in THF (5 mL) was added CDI (486 mg, 3 mmol). After 1 h the solution of isobutiric acid imidazolide was added to a stirred solution of **18** (600 mg, 2 mmol), triethylamine (560 µL, 4 mmol) and DMAP (0.2 mmol) in DMF (5 mL). The solution was left overnight at RT. The reaction was partitioned between isopropyl acetate and sat. aq. ammonium chloride. The organic phase was washed with water and concentrated under reduced pressure. **32** (500 mg, 67%) was isolated by column chromatography (10 to 15% MeOH in DCM) followed by crystallization from isopropanol:hexane (1:2) as a white solid. MS: m/z 371 $[M+H]^+$.

EXAMPLE 16
Preparation of Compound 33



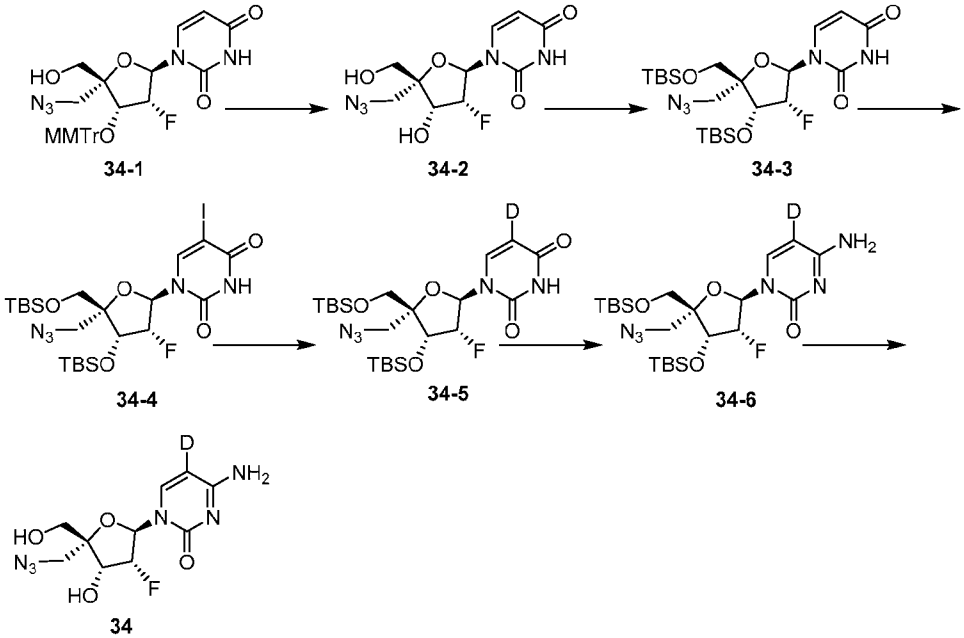
[0264] To a stirred solution of **33-1** (2.16 g, 4.73 mmol) in ACN (20 mL) were added triethylamine (1.9 mL, 15 mmol), DMAP (60 mg, 0.5 mmol) and isobutyric anhydride (1.08 mL, 6.5 mmol). The mixture was stirred at RT for 1 h, and then partitioned between isopropyl acetate and sat. aq. sodium bicarbonate solution. The organic phase was separated, washed with water and concentrated. **33-2** (2.1 g, 84%) was isolated by column chromatography using 25 to 50% EA in hexane as a white foam. MS: m/z 528 $[M+H]^+$.

[0265] **33-2** (2.1g, 3.98 mmol) was dissolved in ACN (15 mL,) and the solution was cooled to 0 °C. Triethylamine (1.1 mL, 8 mmol) and DMAP (537 mg, 4.4 mmol) were added to the solution followed by addition of triisopropylbenzenesulfonil chloride (1.33 g, 4.4 mmol). The mixture was warmed to RT and then stirred for 1 h. The reaction was quenched with ammonium hydroxide (1 mL). The mixture was stirred for 2 h at RT, diluted with isopropyl acetate and filtered from ammonium salts. The filtrate was washed with water and aq. sodium bicarbonate and then concentrated under reduced pressure. **33-3** (2.1 g, ~100%) was isolated by column chromatography using 4-10% MeOH in CH_2Cl_2 as a yellowish foam. MS: m/z 527 $[M+H]^+$.

[0266] **33-3** (1.10 g, 2.09 mmol) was dissolved in THF (6 mL). The solution was cooled to 0 °C and treated with 1M TBAF solution in THF (2.1 mL, 2.1 mmol). The reaction was allowed to proceed for 1 h, and then quenched by the addition of a sat. aq. ammonium chloride solution. **33** (450 mg, 58%) was extracted with isopropyl acetate and isolated by column chromatography in 5-15% MeOH in CH_2Cl_2 as an off-white foam, MS: m/z 371 $[M+H]^+$.

EXAMPLE 184

Preparation of Compound 34



[0267] To a solution of **34-1** (1.2 g, 2.09 mmol) in DCE (40 mL) was added TFA (2 mL). The mixture was stirred at RT for 1 h. The mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (3% MeOH in DCM) to give **34-2** (600 mg, 95.3%) as a white solid.

[0268] To a solution of **34-2** (600 mg, 1.99 mmol) in pyridine (4 mL) was added imidazole (677 mg, 9.95 mmol) and TBSCl (900 mg, 5.97 mmol) at RT. The mixture was stirred at 60 °C for 16 h, and then concentrated under reduced pressure. The residue was diluted with EA (40 mL) and washed with brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (10% EA in PE) to give **34-3** (700 mg, 65.7%) as a white solid.

[0269] To a solution of **34-3** (700 mg, 1.32 mmol) in DCM (52 mL) was added NIS (356 mg, 1.58 mmol) and TFA (1.3 mL). The mixture was stirred at 60 °C for 3 h. After cooling to RT, the solution was extracted with DCM (30 mL), washed with sat. aq. $NaHCO_3$ and brine (20 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (10% EA in PE) to give **34-4** (400 mg, 46.2%) as a white solid.

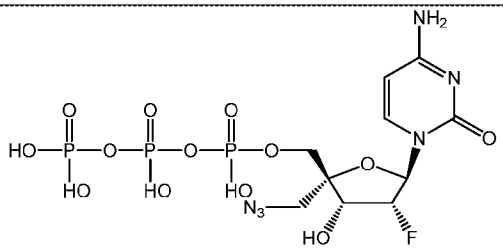
[0270] A mixture of **34-4** (327 mg, 498 μmol), Bu_3SnH (174 mg, 598 μmol) and 2,2'-azobis(2,4-dimethylvaleronitrile) (25 mg, 100 μmol) in THF-d_8 (10 mL) was stirred at 90-100 °C for 3 h. The mixture was concentrated under reduced pressure. and the residue was purified by column chromatography (10% EA in PE) to give **34-5** (180 mg, 68.00%) as a white solid.

[0271] To a solution of **34-5** (210 mg, 395 μmol) in anhydrous MeCN (2 mL) were added DMAP (121 mg, 989 μmol), Et_3N (100 mg, 989 μmol) and 2,4,6-triisopropylbenzene-1-sulfonyl chloride (299 mg, 989 μmol) at RT. The mixture was stirred at RT for 16 h. $NH_3 \cdot H_2O$ (1 mL) was added, and the mixture was stirred for 1 h. The mixture was diluted with EA (15 mL) and washed with sat. aq. NH_4Cl (15 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (2% MeOH in DCM) to give the crude product. The crude product was purified by prep-TLC (10% MeOH in DCM) to give **34-6** (200 mg, 95.42%) as a white solid.

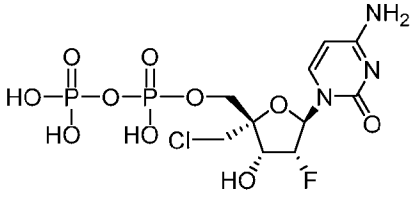
[0272] To a solution of **34-6** (200 mg, 0.38 mmol) in MeOH (2 mL) was added NH_4F (210 mg, 5.66 mmol) at RT. The mixture was stirred at 90-100 °C for 16 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (10% MeOH in DCM) to give the crude product. The crude product was purified by prep-HPLC (neutral condition) to give **34** (70 mg, 61.8% yield, 78.4% deuterium) as a white solid. ESI-TOF-MS: m/z = 302.1 $[M+H]^+$, 603.2 $[2M+H]^+$.

EXAMPLE 18
Preparation of Compound 35

[0273] Dry nucleoside (0.05 mmol) was dissolved in a mixture of $PO(OMe)_3$ (0.7 mL) and pyridine (0.3 mL). The mixture was evaporated in vacuum for 15 mins at a bath temperature of 42^0C, and then cooled down to R.T. N-Methylimidazole (0.009 mL, 0.11 mmol) was added followed by $POCl_3$ (9ul, 0.11 mmol), and the mixture was kept at R.T. for 40 mins. The reaction was controlled by LCMS and monitored by the appearance of the corresponding nucleoside 5'-monophosphate. After more than 50% of transformation was achieved, tetrabutylammonium salt of pyrophosphate (150 mg) was added, followed by DMF (0.5 mL) to get a homogeneous solution. After 1.5 hours at ambient temperature, the reaction was diluted with water (10 mL) and loaded on the column HiLoad 16/10 with Q Sepharose High Performance. Separation was done in a linear gradient of NaCl from 0 to 1N in 50 mM TRIS-buffer (pH7.5). Triphosphate was eluted at 75-80%B. Corresponding fractions were concentrated. Desalting was achieved by RP HPLC on Synergy 4 micron Hydro-RP column (Phenominex). A linear gradient of methanol from 0 to 30% in 50 mM triethylammonium acetate buffer (pH 7.5) was used for elution. The corresponding fractions were combined, concentrated and lyophilized 3 times to remove excess of buffer.

Compound	^{31}P NMR Pα	^{31}P NMR Pβ	^{31}P NMR Pγ	MS (M-1)
 **35**	-5.36(d)	-20.72(t)	-11.40(d)	539.3

EXAMPLE 19
Preparation of Compound 36



36

[0274] The diphosphate, **36**, can be prepared using a similar procedure to preparing the triphosphate of Example 18 with the replacement of tetrabutylammonium salt of pyrophosphate

with tetrabutylammonium phosphate (75 mg) and using 0.3 mL of DMF to get the homogeneous solution.

EXAMPLE 20
RSV Assay

[0275] The RSV subgenomic replicon 395 HeLa was licensed from Apath (Brooklyn, NY) and was originally developed by Dr. Mark Meeples of Center for Vaccines & Immunity, the Research Institute at Nationwide Children's Hospital in Columbus, Ohio. To generate subgenomic RSV replicon, three glycoprotein genes, those for SH, G, and F, from a full-length recombinant GFP-expressing (rg) RSV antigenomic cDNA were deleted. In their place, a blasticidin S deaminase (*bsd*) gene was inserted. Through multiple steps, the RSV replicon was established in HeLa cells. The 395 HeLa cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) containing 4500 mg/L D-glucose, L-glutamine, and 110 mg/L sodium pyruvate (Invitrogen, Cat. #11995-040). The medium was further supplemented with 10% (v/v) fetal bovine serum (FBS) (Mediatech, Cat. #35-010-CV), 1% (v/v) penicillin/streptomycin (Mediatech, Cat. #30-002-CI), and 10 μg/mL of Blasticidin (BSD) (Invivogen, Cat. code ant-bl-1). Cells were maintained at 37 °C in a humidified 5% CO_2 atmosphere.

[0276] Determination of 50% inhibitory concentration (EC_{50}), 90% inhibitory concentration (EC_{90}) and 50% cytotoxic concentration (CC_{50}) in RSV replicon cells were performed by the following procedure. On the first day, 5000 RSV replicon cells per well were plated in a 96-well plate. On the following day, compounds to be tested were solubilized in 100% DMSO to 100X the desired final testing concentration. Each compound was serially diluted (1:3) up to 9 distinct concentrations. Compounds in 100% DMSO were reduced to 10% (v/v) DMSO by diluting 1:10 in cell culture media. A 10 μL sample of the compounds diluted to 10% (v/v) DMSO with cell culture media was used to treat the RSV replicon cells in 96-well format. The final DMSO concentration was 1% (v/v). Cells were incubated with compounds for 7 days at 37 °C in a 5% CO_2 atmosphere. In each assay, positive control that was previously characterized in the RSV replicon assay was included.

[0277] The *Renilla* Luciferase Assay System (Promega, Cat. #E2820) was used to measure anti-RSV replicon activity. Assay plates were set up as stated above. Luminescence was recorded using a Perkin Elmer multilabel counter Victor3V. EC_{50}, the concentration of the drug required for reducing RSV replicon RNA by 50% in relation to the untreated cell control value, was

calculated from the plot of percentage reductions of the optical density (OD) value against the drug concentrations using the Microsoft Excel forecast function.

[0278] 395 HeLa cell proliferation assay (Promega; CellTiter-Glo Luminescent Cell Viability Assay, Cat. #G7572) was used to measure cell viability. The CellTiter-Glo® Luminescent Cell Viability Assay is a homogeneous method to determine the number of viable cells in culture based on quantitation of the ATP present, which signals the presence of metabolically active cells. Assay plates were set up in the same format as noted above for the replicon assay. CellTiter-Glo reagent (100 µL) was added to each well and incubated at room temperature for 8 minutes. Luminescence was recorded using a Perkin Elmer multilabel counter Victor3V. The CC_{50}, the concentration of the drug required for reducing viable cells by 50% in relation to the untreated cell control value, was calculated from the plot of percentage reductions of the luminescence value against the drug concentrations using the Microsoft Excel forecast function.

[0279] Compounds 31 and 34 each had an EC_{50} value less than 1 µM.

EXAMPLE 21
Combination Studies

RSV with Renilla Reporter

[0280] RSV expressing Renilla luciferase (A2-RL-line19F) was generated by Dr. Martin Moore of Emory University, Atlanta, GA, USA. The *in vitro* viral kinetics of A2-RL-line19F is similar to that of wild type RSV (See Hotard, A.L., Virology (2012) 434(1):129–136).

[0281] Host cell HEp-2 was purchased from ATCC (Cat. #CCL-23) and cells were cultured in DMEM/Ham's F-12 50/50 1× containing L-glutamine and 15 mM HEPES (Mediatech, Cat. #10-092-CM). The medium was further supplemented with 5% (v/v) FBS (Mediatech, Cat. #35-010-CV) and 1% (v/v) penicillin/streptomycin (Mediatech, Cat. #30-002-CI). HEp-2 cells were maintained at 37 °C in a humidified 5% CO_2 atmosphere.

Drug Treatment and Viral Dosing

[0282] To determine the effect of a combination of compounds, the following procedure was followed. On the first day, 20,000 HEp-2 cells were plated per well in a 96-well plate. On the following day, test articles were solubilized in 100% DMSO (for chemicals) or 1 x PBS (for biologics) to 200x the desired final testing concentration. Subsequently, Compound (A), or a pharmaceutically acceptable salt thereof, was serially diluted (1:3) to 9 distinct concentrations

"horizontally" in a 96-well plate, and Compound (B), or a pharmaceutically acceptable salt thereof, was serially diluted (1:3) to 7 distinct concentrations "vertically" in 96-well plate. The serially diluted 200x test articles were then diluted 1:10 into cell culture media to generate 20x test articles. A 5 μL aliquot of the 20x test articles was added in a checkerboard fashion to the cells with 90 μL existing media. Space was also allotted for titrations of each of the compounds alone to be used as reference controls. After 12 hour pre-incubation of test articles, A2-RL-line19F at an MOI of 0.5 was added to the plate and further incubated for 2 days at 37 °C in a 5% CO_2.

Determination of Anti-RSV Activity

[0283] The *Renilla* Luciferase Assay System (Promega, Cat. # E2820) was used to measure anti-RSV replicon activity. Assay plates were set up as stated above. Luminescence was recorded using a Perkin Elmer multilabel counter Victor3V.

Cell Viability Assay

[0284] Promega CellTiter-Glo Luminescent Cell Viability Assay, Cat. #G7572) was used to measure cell viability. The CellTiter-Glo® Luminescent Cell Viability Assay is a homogeneous method to determine the number of viable cells in culture based on quantitation of the adenosine triphosphate (ATP) present, which signals the presence of metabolically active cells. Assay plates were set up in the same format the anti-RSV assay, except that no virus was added to the cell viability assay. A 100-μL aliquot of CellTiter-Glo reagent was added to each well and incubated at room temperature for 8 minutes. Luminescence was recorded using a Perkin Elmer multilabel counter Victor3V.

Data Analysis

[0285] Each experiment was performed at N=5 for both anti-RSV activity and cell viability. Mean percent inhibition of the replicon values from the 5 experiments was generated and for anti-RSV activity, it was analyzed using two drug interaction analysis models, Isobologram Analysis and/or Prichard's Model.

Isobologram Analysis

[0286] The effects of drug-drug combinations were evaluated by the Loewe additivity model in which the experimental data were analyzed using CalcuSyn (Biosoft, Ferguson, MO), a

computer program based on the method of Chou and Talalay. The combination index (CI) value and the isobologram for each experimental combination were calculated. CI values of <1, 1, and >1 indicate synergy, additive effect, and antagonism, respectively. Under the synergy category, CI<0.1 is considered very strong synergism; CI 0.1-0.3 strong synergism; CI 0.3-0.7 synergism and CI 0.7-0.85 moderate synergism. The isobologram analysis, which graphically represents additive, synergistic, and antagonistic drug effects, was also used to model the interaction of antiviral activities. In this representation, an effective concentration (EC) value of one drug is plotted on one axis and corresponding EC value of a second drug is plotted on the second axis; the line connecting these two points represents the amount of each drug in a combination that would be required to reach the equivalent EC value, given that their effects are additive.

Prichard's Model (MacSynergy II)

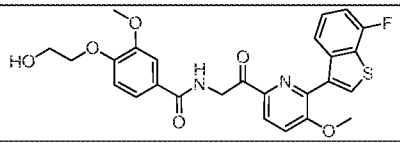
[0287] MacSynergy II software was kindly provided by Dr. M. Prichard (University of Michigan). This program allows the three-dimensional examination of drug interactions of all data points generated from the checkerboard combination of two inhibitors with Bliss-Independence model. Confidence bounds are determined from replicate data. If the 95% confidence limits (CL) do not overlap the theoretic additive surface, then the interaction between the two drugs differs significantly from additive. The volumes of synergy or antagonism can be determined and graphically depicted in three dimensions and represent the relative quantity of synergism or antagonism per change in the two drug concentrations. Synergy and antagonism volumes are based on the Bliss independence model, which assumes that both compounds act independently on different targets. A set of predicted fractional responses *faAB* under the Bliss independence model is calculated as $faAB = faA + faB - faA \cdot faB$ with *faA* and *faB* representing the fraction of possible responses, e.g. % inhibition, of compounds *A* and *B* at amounts *dA* and *dB*, respectively, and describes the % inhibition of a combination of compounds *A* and *B* at amount *(dA+dB)*. If $faAB > faA + faB - faA \cdot faB$ then we have Bliss synergy; if $faAB < faA + faB - faA \cdot faB$ then we have Bliss antagonism. The 95% synergy/antagonism volumes are the summation of the differences between the observed inhibition and the 95% confidence limit on the prediction of *faAB* under the Bliss independence model. Table 1 shows the volumes and corresponding volume descriptions for the results of the Bliss Independence Analysis. MacSynergy II was used for data analysis.

[0288] The synergy volume results for the combinations are provided in Table 2.

Table 1. MacSynergy II Volume Descriptions

Volume ($\mu M^2\%$)	Volume Description
<25	Additive
25-50	Minor synergism
50-100	Significant synergism
>100	Strong synergism

Table 2.

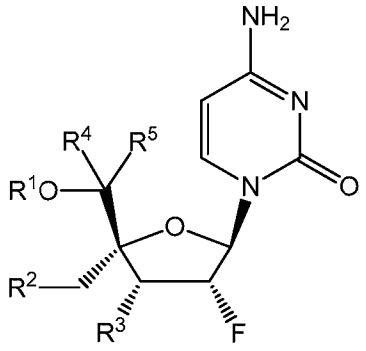
Compound (A)	Compound (B)	Class of Compound (B)	Synergy Volume ($\mu M^2\%$)	Observed Result
1	Palivizumab	Anti-RSV Antibody	115	strongly synergistic
1	BMS-433771	Fusion Inhibitor	320	strongly synergistic
1		Polymerase Inhibitor	12.2	Additive
1	Ribavirin	IMPDH Inhibitor	4.7	Additive
1	interferon alfacon-1	interferon	81	Significant synergism

[0289] Although the foregoing has been described in some detail by way of illustrations and examples for purposes of clarity and understanding, it will be understood by those of skill in the art that numerous and various modifications can be made without departing from the spirit of the present disclosure. Therefore, it should be clearly understood that the forms disclosed herein are illustrative only and are not intended to limit the scope of the present disclosure, but rather to also cover all modification and alternatives coming with the true scope and spirit of the invention.

WHAT IS CLAIMED IS:

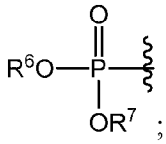
1. A method for ameliorating or treating a paramyxovirus virus infection comprising administering to a subject infected with the paramyxovirus virus an effective amount of a combination of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, wherein:

the Compound (A) has the structure:



(A),

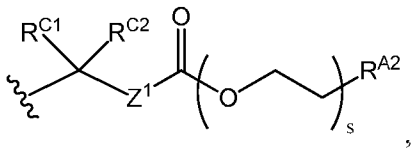
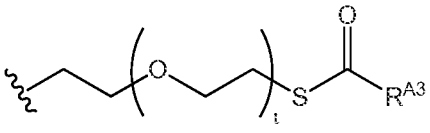
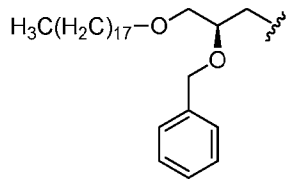
wherein:

R^1 is selected from the group consisting of H, an optionally substituted acyl, an optionally substituted O-linked amino acid and ;

R^2 is chloro or azido;

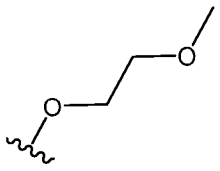
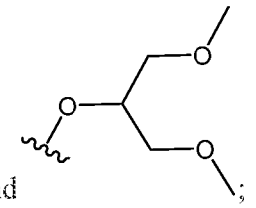
R^3 is selected from the group consisting of OH, $-OC(=O)R^{A1}$ and an optionally substituted O-linked amino acid;

R^4 and R^5 are independently H or D;

R^6 and R^7 is independently absent, H, ,  and ;

R^{A1} is an optionally substituted C_{1-24} alkyl;

R^{A2} is independently selected from the group consisting of H, 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^{A3} is selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

R^{C1} and R^{C2} are independently selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

s is 0, 1, 2 or 3;

t is 0 or 1; and

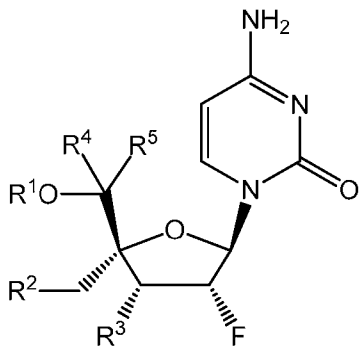
Z^1 is O or S;

one or more of Compound (B) is selected from the group consisting of an anti-RSV antibody, a fusion protein inhibitor, an N-protein inhibitor, a RSV polymerase inhibitor, an IMPDH inhibitor, an interferon and an other compound that inhibits the RSV virus, or a pharmaceutically acceptable salt of any of the foregoing; and

the paramyxovirus virus infection is selected from the group consisting of a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

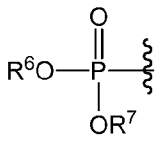
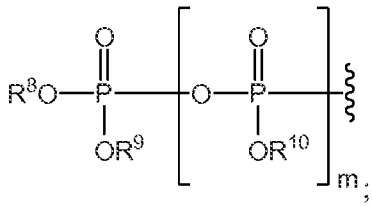
2. A method for ameliorating or treating a paramyxovirus virus infection comprising contacting a cell infected with the paramyxovirus virus with an effective amount of a combination of Compound (A) and one or more of Compound (B) , or a pharmaceutical acceptable salt of any of the foregoing, wherein:

the Compound (A) has the structure:



(A),

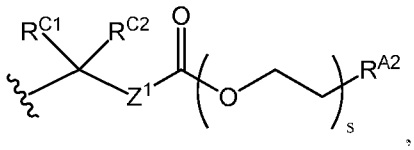
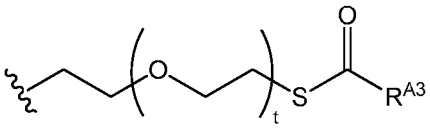
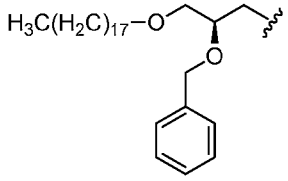
wherein:

R^1 is selected from the group consisting of H, an optionally substituted acyl, an optionally substituted O-linked amino acid,  and ;

R^2 is chloro or azido;

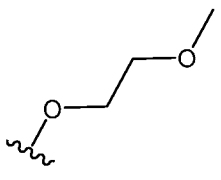
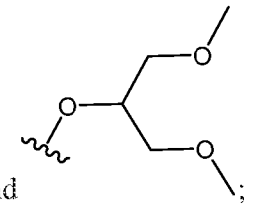
R^3 is selected from the group consisting of OH, $-OC(=O)R^{A1}$ and an optionally substituted O-linked amino acid;

R^4 and R^5 are independently H or D;

R^6 and R^7 is independently absent, H, ,  and ;

R^8, R^9 and each R^{10} are independently absent or H;

R^{A1} is an optionally substituted C_{1-24} alkyl;

R^{A2} is independently selected from the group consisting of H, 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^{A3} is selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

R^{C1} and R^{C2} are independently selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

m is 1 or 2;

s is 0, 1, 2 or 3;

t is 0 or 1; and

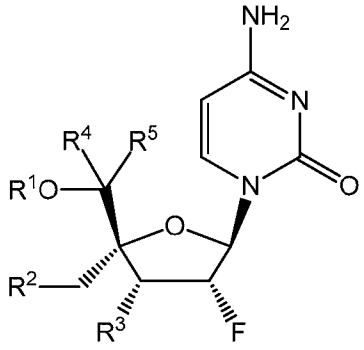
Z^1 is O or S;

one or more of Compound (B) is selected from the group consisting of an anti-RSV antibody, a fusion protein inhibitor, an N-protein inhibitor, a RSV polymerase inhibitor, an IMPDH inhibitor, an interferon and an other compound that inhibits the RSV virus, or a pharmaceutically acceptable salt of any of the foregoing; and

the paramyxovirus virus infection is selected from the group consisting of a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

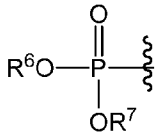
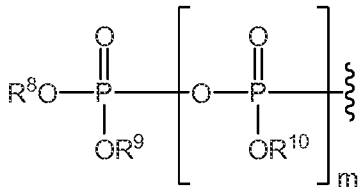
3. Use of an effective amount of a combination of Compound (A) and one or more of Compound (B), or a pharmaceutical acceptable salt of any of the foregoing, in the preparation of a medicament for ameliorating or treating a paramyxovirus virus infection wherein:

the Compound (A) has the structure:



(A),

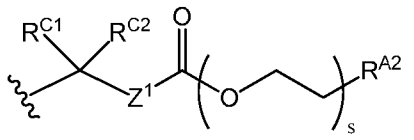
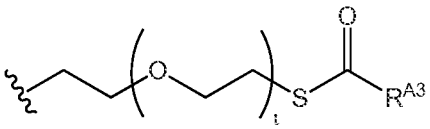
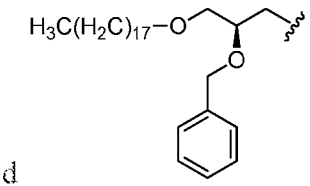
wherein:

R^1 is selected from the group consisting of H, an optionally substituted acyl, an optionally substituted O-linked amino acid,  and ;

R^2 is chloro or azido;

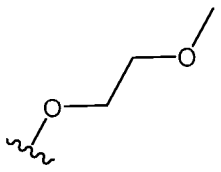
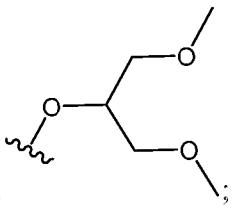
R^3 is selected from the group consisting of OH, $-OC(=O)R^{A1}$ and an optionally substituted O-linked amino acid;

R^4 and R^5 are independently H or D;

R^6 and R^7 is independently absent, H, ,  and ;

R^8, R^9 and each R^{10} are independently absent or H;

R^{A1} is an optionally substituted C_{1-24} alkyl;

R^{A2} is independently selected from the group consisting of H, 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^{A3} is selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

R^{C1} and R^{C2} are independently selected from the group consisting of H, an optionally substituted C_{1-24} alkyl and an optionally substituted aryl;

m is 1 or 2;

s is 0, 1, 2 or 3;

t is 0 or 1; and

Z^1 is O or S;

one or more of Compound (B) is selected from the group consisting of an anti-RSV antibody, a fusion protein inhibitor, an N-protein inhibitor, a RSV polymerase inhibitor, an IMPDH inhibitor, an interferon and an other compound that inhibits the RSV virus, or a pharmaceutically acceptable salt of any of the foregoing; and

the paramyxovirus virus infection is selected from the group consisting of a respiratory syncytial virus infection, a parainfluenza virus infection and a metapneumovirus infection.

4. The method or use of any one of Claims 1-3, wherein the paramyxovirus virus infection is a respiratory syncytial virus infection.

5. The method or use of Claim 4, wherein the RSV is Type A.

6. The method or use of Claim 4, wherein the RSV is Type B.

7. The method or use of any one of Claims 1-3, wherein the paramyxovirus virus infection is a parainfluenza virus infection.

8. The method or use of any one of Claims 1-3, wherein the paramyxovirus virus infection is a metapneumovirus infection.

9. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is an anti-RSV antibody.

10. The method or use of Claim 9, wherein the anti-RSV antibody is selected from the group consisting of

RSV-IGIV (RespiGam®)

palivizumab (Synagis®, a chimeric humanized IgG monoclonal antibody) and

motavizumab (MEDI-524, humanized monoclonal antibody).

11. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is a fusion protein inhibitor.

12. The method or use of Claim 11, wherein the fusion protein inhibitor is selected from the group consisting of

1-cyclopropyl-3-[[1-(4-hydroxybutyl)benzimidazol-2-yl]methyl]imidazo[4,5-c]pyridin-2-one (BMS-433771),

4,4"-bis-{4,6-bis-[3-(bis-carbamoylmethyl-sulfamoyl)-phenylamino]-(1,3,5)triazin-2-ylamino}-biphenyl-2,2"-disulfonic-acid (RFI-641),

4,4'-Bis[4,6-di[3-aminophenyl-N,N-bis(2-carbamoylethyl)-sulfonilimino]-1,3,5-triazine-2-ylamino]-biphenyl-2,2'-disulfonic acid, disodium salt (CL387626),

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-4-methyl-1H-benzimidazol-1-yl]-6-methyl-3-pyridinol (JNJ-2408068),

2-[[6-[[[2-(3-Hydroxypropyl)-5-methylphenyl]amino]methyl]-2-[[3-(morpholin-4-yl)propyl]amino]benzimidazol-1-yl]methyl]-6-methylpyridin-3-ol (TMC-353121),

5,5′-bis[1-(((5-amino-1H-tetrazolyl)imino)methyl)]2,2′,4″-methylidynetrisphenol (VP-14637, MDT-637),

N-(2-hydroxyethyl)-4-methoxy-N-methyl-3-(6-methyl-[1,2,4]triazolo[3,4-a]phthalazin-3-yl)benzenesulfonamide (P13),

2-((2-((1-(2-aminoethyl)piperidin-4-yl)amino)-4-methyl-1H-benzo[d]imidazol-1-yl)methyl)-6-methylpyridin-3-ol (R170591),

1,4-bis(3-methylpyridin-4-yl)-1,4-diazepane (C15),

(R)-9b-(4-chlorophenyl)-1-(4-fluorobenzoyl)-2,3-dihydro-1H-imidazo[1',2':1,2]pyrrolo[3,4-c]pyridin-5(9bH)-one (BTA9981),

[2,2-bis(docosyloxy-oxymethyl)propyl-5-acetaoamido-3,5-dideoxy-4,7,8,9-tetra-O-(sodium-oxysulfonyl)-D-glycero-D-galacto-2-nonulopyranosid]onate (MBX-300),

BTA-C286,

N-(2-((S)-2-(5-((S)-3-aminopyrrolidin-1-yl)-6-methylpyrazolo[1,5-a]pyrimidin-2-yl)piperidine-1-carbonyl)-4-chlorophenyl)methanesulfonamide (GS-5806),

an anti-RSV nanobody and

a peptide fusion inhibitor,

or a pharmaceutically acceptable salt of any of the foregoing.

13. The method or use of Claim 12, wherein peptide fusion inhibitor is selected from the group consisting of:

a peptide having the sequence DEFDASISQVNEKINQSLAFIRKSDELL (T-67), and

a peptide having the sequence FDASISQVNEKINQSLAFIRKSDELLHNVNAGKST (T-118).

14. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is an N-protein inhibitor.

15. The method or use of Claim 14, wherein the N-protein inhibitor is selected from the group consisting of (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea (RSV-604), STP-92 (siRNA delivered through nanoparticle based delivery systems, Sirnaomics) and iKT-041 (Inhibikase), or a pharmaceutically acceptable salt thereof.

16. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is a RSV polymerase inhibitor.

17. The method or use of Claim 16, wherein the RSV polymerase inhibitor is selected from the group consisting of

6-{4-[(biphenyl-2-ylcarbonyl)amino]benzoyl}-N-cyclopropyl-5,6-dihydro-4H-thieno[3,2-d][1]benzazepine-2-carboxamide (YM-53403),

N-cyclopropyl-5-(4-(2-(pyrrolidin-1-yl)benzamido)benzoyl)-5,6,7,10-tetrahydrobenzo[b]cyclopenta[d]azepine-9-carboxamide,

6-(4-(2-(2-oxa-7-azaspiro[3.5]nonan-7-yl)nicotinamido)benzoyl)-N-cyclopropyl-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide,

4-amino-8-(3-{[2-(3,4-dimethoxyphenyl)ethyl]amino}propyl)-6,6-dimethyl-2-(4-methyl-3-nitrophenyl)-1H-imidazo[4,5-h]-isoquinoline-7,9(6H,8H)-dione and

6-(4-(2-(2-oxa-7-azaspiro[3.5]nonan-7-yl)nicotinamido)benzoyl)-N-cyclopropyl-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide (AZ27),

or a pharmaceutically acceptable salt of any of the foregoing.

18. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is an IMPDH inhibitor.

19. The method or use of Claim 18, wherein the IMPDH inhibitor is selected from the group consisting of

ribavirin,

5-ethynyl-1-beta-D-ribofuranosylimidazole-4-carboxamide (EICAR),

4-hydroxy-3-beta-D-ribofuranosylpyrazole-5-carboxamide (pyrazofurin),

1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1H-1,2,4-triazole-3-carboximidamide (Taribavirin, viramidine),

1,3,4-thiadiazol-2-ylcyanamide (LY253963),

tetrahydrofuran-3-yl-3-(3-(3-methoxy-4-(oxazol-5-yl)phenyl)ureido)benzylcarbamate (VX-497),

(4E)-6-(4-Hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydro-2-benzofuran-5-yl)-4-methylhex-4-enoic acid (Mycophenolic acid) and

2-morpholin-4-ylethyl-(E)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1H-2-benzofuran-5-yl)-4-methylhex-4-enoate (Mycophenolate Mofetil),

or a pharmaceutically acceptable salt of any of the foregoing.

20. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is an interferon.

21. The method or use of Claim 20, wherein the interferon is a pegylated interferon.

22. The method or use of any one of Claims 20-21, wherein the interferon is a Type 1 interferon.

23. The method or use of Claim 22, wherein the Type 1 interferon is an alpha-interferon (IFN-α).

24. The method or use of Claim 23, wherein the IFN-α is selected from the group consisting of Pegylated interferon-alpha-2a (PEGASYS®), Pegylated interferon-alpha-2b (PEG-INTRON®) and interferon alfacon-1 (INFERGEN®).

25. The method or use of any one of Claims 20-21, wherein the Type 1 interferon is a beta-interferon (IFN-β).

26. The method or use of any one of Claims 20-21, wherein the interferon is a Type 2 interferon.

27. The method or use of any one of Claims 20-21, wherein the interferon is a Type 3 interferon.

28. The method or use of Claim 27, wherein the Type 3 interferon is a lambda-interferon (IFN-λ).

29. The method or use of Claim 28, wherein the IFN-λ is pegylated interferon lambda.

30. The method or use of any one of Claims 1-8, wherein one or more of Compound (B) is an other compound that inhibits the RSV virus.

31. The method or use of Claim 30, wherein the other compound is selected from the group consisting of

a double stranded RNA oligonucleotide,

5-methyl-N-[4-(trifluoromethyl) phenyl]-isoxazole-4-carboxamide (leflumomide),

N-(2-chloro-4-methylphenyl)-2-((1-(4-methoxyphenyl)-1H-benzo[d]imidazol-2-yl)thio)propanamide (JMN3-003),

Medi-559,

Medi-534,

Medi-557,

an intratracheal formulation of recombinant human CC10 (CG-100),

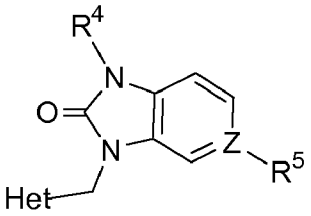
high titer, human immunoglobulin (RI-001, ADMA Biologics Inc.) and

a non-neutralizing mAb against the G protein (mAb 131-2G),

or a pharmaceutically acceptable salt of any of the foregoing.

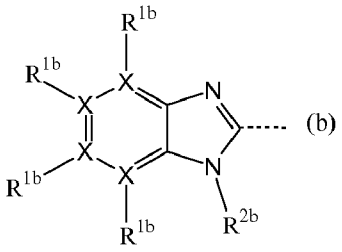
32. The method or use of Claim 31, wherein the double stranded RNA oligonucleotide is ALN-RSV01 or ALN-RSV02.

33. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B1) having the structure:

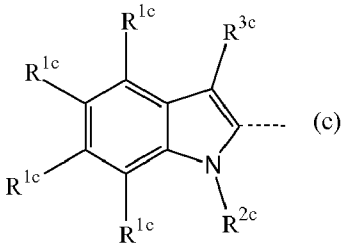


or a stereoisomeric form thereof, wherein

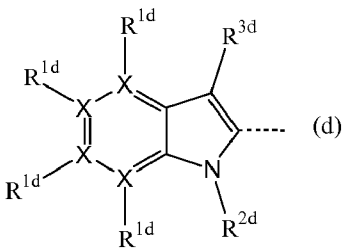
Het is a heterocycle having formula (b), (c), (d) or (e)



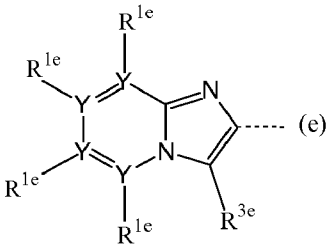
(b)



(c)



(d)



(e)

each X independently is C or N; provided that at least one X is N;

R^{1b} is present when Het has formula (b) and X is C; each R^{1b} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1b} is absent when the X to which it is bound is N;

R^{2b} is $-(CR^8R^9)_m-R^{10b}$;

each R^6 is independently selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$ and $CONHSO_2CH_3$;

each R^7 is independently selected from the group consisting of OH, C_1-C_6 alkyloxy, NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl) and $N(C_1$-C_6 alkyl$)_2$;

each R^8 and R^9 are independently chosen from the group consisting of H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^8 and R^9 taken together form a 4 to 6 membered aliphatic ring that optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{10b} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, O-Benzyl, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$, and a 4 to 6 membered saturated ring containing one oxygen atom;

m is an integer from 2 to 6;

R^{11} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

R^{12} is selected from the group consisting of phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{12} is C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

R^{1c} is present when Het has formula (c);

each R^{1c} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^{7c})$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O$-C_1-C_6 alkyl$)_2$;

R^{3c} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy and $CO(R^{7c})$;

R^{2c} is $-(CR^8R^9)_m$-R^{10c};

R^{7c} is selected from the group consisting of OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), $N(C_1$-C_6 alkyl$)_2$, NR^8R^9 and NR^9R^{10c};

R^{10c} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9,

NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

R^{1d} is present when Het has formula (d) and X is C; each R^{1d} is selected independently from the group consisting of H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1d} is absent when the X to which it is bound is N;

R^{3d} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, and $CO(R^7)$;

R^{2d} is $-(CR^8R^9)_m\text{-}R^{10d}$;

R^{10d} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR_9, $OCOR^8$,$NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

each Y independently is C or N;

R^{1e} is present when Het has formula (e) and Y is C; each R^{1e} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1e} is absent when the Y to which it is bound is N;

R^{3e} is selected from the group consisting of H, halogen, $-(CR^8R^9)_m\text{-}R^{10e}$, $C\equiv C\text{-}CH_2\text{-}R^{10e}$, $C\equiv C\text{-}R^{10e}$ and $C=C\text{-}R^{10e}$;

R^{10e} is selected from the group consisting of H, R^{11}, C_1-C_6 alkyloxy, OH, CN, F, CF_2H,CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

R^4 is selected from the group consisting of tert-butyl, Het^1, aryl, Het^2, $CH(CH_3)(CF_3)$, and C_3-C_7 cycloalkyl substituted with one or more substituents selected from the group consisting of halo and C_1-C_4 alkyl;

aryl represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from the group consisting of halo C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, CF_30, $CONR^8R^9$, $COOR^8$,$CON(R^8)SO_2R^9$,

$CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$,$SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$; or C_1-C_4 alkyloxyC_1-C_4 alkyloxy;

Het^1 represents a 4 to 6 membered saturated ring containing one N atom, optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, SO_2R^8 , C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), $(C=O)NH(C_1$-C_4 alkyl), $(C=S)NH(C_1$-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy; or

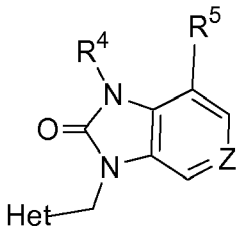
Het^1 represents a 4 to 6 membered saturated ring containing one O atom, substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, CF_3, $NH(C=O)(C_1$-C_4 alkyl), $(C=O)NH(C_1$-C_4 alkyl) and C_1-C_4 alkyl; or Het represents a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N, optionally substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, SO_2R^8, C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), $(C=O)NH(C_1$-C_4 alkyl), $(C=S)NH(C_1$-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy;

Het^2 represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONRV^2$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$;

Z is C or N; R^5 is present where Z is C, whereby R^5 is selected form the group consisting of hydrogen, CF_3 and halogen; R^5 is absent where Z is N;

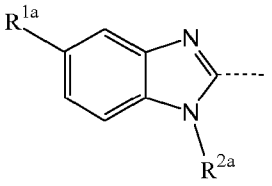
or a pharmaceutically acceptable addition salt or a solvate thereof.

34. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B2) having the structure:



a tautomer or a stereoisomeric form thereof, wherein

Het is a heterocycle having formula (a)



(a)

R^{1a} is Br or Cl;

R^{2a} is $-(CR^{8a}R^{9a})_n-R^{10a}$;

each R^{8a} and R^{9a} are independently chosen from the group consisting of H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^{8a} and R^{9a} taken together form a 4 to 6 membered aliphatic ring; wherein the 4 to 6 membered aliphatic ring optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{10a} is selected from the group consisting of H, C_1-C_6 alkyl, R^{11}, OH, CF_3, CHF_2, F, Cl, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR^{8a}SO_2R^{8a}$, $SO_2NR^{8a}R^{9a}$, $NR^{8a}SO_2C_3$-C_7 cycloalkyl, CN, $NR^{8a}R^{9a}$, COOH, $COOR^{8a}$, $CONR^{8a}R^{9a}$, $OCOC_1$-C_6 alkyl, $CONR^{8a}SO_2R^{9a}$, $CONR^{8a}SO_2NR^{8a}R^{9a}$, a 4 to 6 membered aliphatic ring and a 5 to 6 membered aromatic ring; wherein the aliphatic or aromatic ring optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{11} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

n is an integer having a value from 1 to 6;

R^5 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkyloxy, CN, CF_3 and halo;

R^4 is selected from the group consisting of hydrogen, tert-butyl, C_3-C_7 cycloalkyl, $CH(CH_3)(CF_3)$, C_2-C_{10} alkenyl, CH_2CF_3, SO_2CH_3, $-CH_2$-p-fluorophenyl, aryl, Het^1, Het^2 and

C_3-C_7 cycloalkyl substituted with one or more substituents selected from the group consisting of halo and C_1-C_4 alkyl;

aryl represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11a}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11a}$, and C_1-C_4 alkyl;

Het^1 represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; said Het^1 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, SO_2R^{8a} C_1-C_4 alkylcarbonyl, C_1-C_4 alkyloxycarbonyl, CO(aryl), $COHet^2$, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), $NH(C{=}O)(C_1$-C_4 alkyl), $(C{=}O)NH(C_1$-C_4 alkyl), $(C{=}S)NH(C_1$-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy;

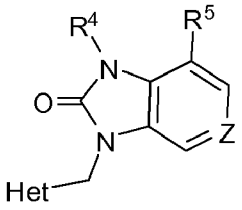
Het^2 represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$,$NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11a}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11a}$ and C_1-C_4 alkyl;

R^{11a} is selected from the group consisting of phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{11a} is C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

Z is CH or N;

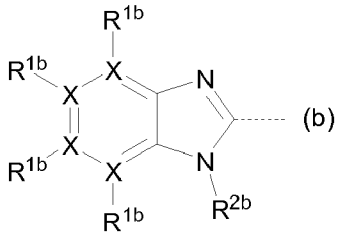
or a pharmaceutically acceptable addition salt or a solvate thereof.

35. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B3) having the structure:

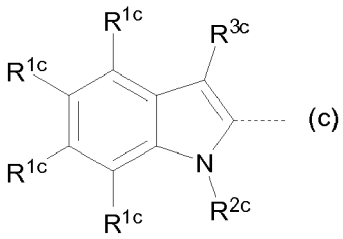


a tautomer or a stereoisomeric form thereof, wherein

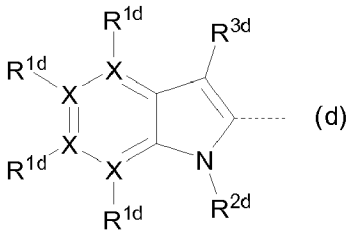
Het is a heterocycle having formula (b), (c), (d) or (e)



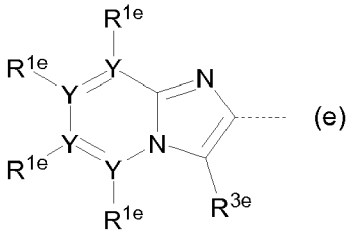
(b)



(c)



(d)



(e)

each X independently is C or N; provided that at least one X is N;

R^{1b} is present when Het has formula (b) and X is C; each R^{1b} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R^{1b} is absent when the X to which it is bound is N;

R^{2b} is $-(CR^8R^9)_m\text{-}R^{10b}$;

each R^6 is independently selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$ and $CONHSO_2CH_3$; each R^7 is independently selected from the group consisting of OH, C_1-C_6 alkyloxy, NH_2, $NHSO_2N(C_1\text{-}C_6$ alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1\text{-}C_6$ alkyl), $NHSO_2(C_3\text{-}C_7$ cycloalkyl) and $N(C_1\text{-}C_6\text{-}$alkyl$)_2$;

each R^8 and R^9 are independently chosen from the group consisting of H, C_1-C_6 alkyl and C_3-C_7 cycloalkyl; or R^8 and R^9 taken together form a 4 to 6 membered aliphatic ring that

optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{10b} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, O-Benzyl, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$, $N(R^8)COOR^{12}$ and a 4 to 6 membered saturated ring containing one oxygen atom;

R^{11} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

R^{12} is selected from the group consisting of phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

or R^{12} is C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

m is an integer from 2 to 6;

R^{1c} is present when Het has formula (c);

each R^{1c} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^{7c})$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{alkyl})_2$;

R^{3c} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy and $CO(R^{7c})$;

R^{2c} is $-(CR^8R^9)_m\text{-}R^{10c}$;

R^{7c} is selected from the group consisting of OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl)$_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), $N(C_1$-C_6-alkyl)$_2$, NR^8R^9 and NR^9R^{10c};

R^{10c} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

R^{1d} is present when Het has formula (d) and X is C; each R^{1d} is selected independently from the group consisting of H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl,

C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1d} is absent when the X to which it is bound is N;

R^{3d} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, and $CO(R^7)$;

R^{2d} is $-(CR^8R^9)_m\text{-}R^{10d}$;

R^{10d} is selected from the group consisting of H, R^{11}, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CONR^8SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

each Y independently is C or N;

R^{1e} is present when Het has formula (e) and Y is C; each R^{1e} is selected independently from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyloxy, $N(R^6)_2$, $CO(R^7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, $B(OH)_2$ and $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$; R^{1e} is absent when the Y to which it is bound is N;

R^{3e} is selected from the group consisting of H, halogen, $-(CR^8R^9)_m\text{-}R^{10e}$, $C\equiv C\text{-}CH_2\text{-}R^{10e}$, $C\equiv C\text{-}R^{10e}$ and $C=C\text{-}R^{10e}$;

R^{10e} is selected from the group consisting of H, R^{11}, C_1-C_6 alkyloxy, OH, CN, F, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8 and a 4 to 6 membered saturated ring containing one oxygen atom;

R^5 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkyloxy, CN, CF_3 and halogen;

R^4 is selected from the group consisting of hydrogen, C_3-C_7 cycloalkyl, tert-butyl, C_2-C_{10} alkenyl, CH_2CF_3, $CH(CH_3)(CF_3)$, SO_2CH_3, $-CH_2$-p-fluorophenyl, aryl, Het^1, Het^2 and C_3-C_7 cycloalkyl substituted with one or more substituents selected from the group consisting of halo and C_1-C_4 alkyl;

aryl represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4alkyloxy, C_1-C_4alkyl, OH, CN, CF_2H, CF_3, $CONR^8R^9$, $COOR^8$, $CON(R^8)SO_2R^9$,

$CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$ and $N(R^8)COOR^{12}$;

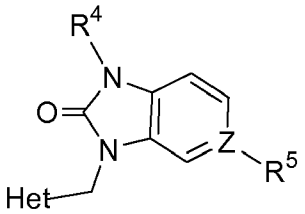
Het^1 represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 7 to 11 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; said Het^1 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, SO_2R, C_1-C_4 alkylcarbonyl, CO(aryl), $COHet^2$, C_1-C_4 alkyloxycarbonyl, pyridinyl, CF_3, $SO_2N(C_1$-C_4 $alkyl)_2$, $SO_2NH(C_1$-C_4 alkyl),$NH(C{=}O)(C_1$-C_4 alkyl), $(C{=}O)NH(C_1$-C_4 alkyl), $(C{=}S)NH(C_1$-C_4 alkyl) and C_1-C_4 alkyl;

Het^2 represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, C_1-C_4 alkyl, OH, CN, CF_2H, CF_3, CONRV, $COOR^8$, $CON(R^8)SO_2R^9$, $CON(R^8)SO_2N(R^8R^9)$, NR^8R^9, NR^8COOR^9, $OCOR^8$, $NR^8SO_2R^9$, $SO_2NR^8R^9$, SO_2R^8, $OCONR^8R^9$, $OCONR^8R^{12}$, $N(R^8)CON(R^8R^9)$ and $N(R^8)COOR^{12}$;

Z is CH or N;

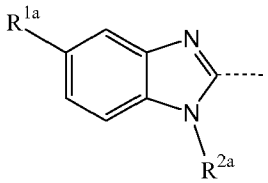
or a pharmaceutically acceptable addition salt or a solvate thereof.

36. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B4) having the structure:



or a stereoisomeric form thereof, wherein

Het is a heterocycle having formula (a)



(a)

R^{1a} is Br or Cl;

R^{2a} is $-(CR^{8a}R^{9a})_n-R^{10a}$;

each R^{8a} and R^{9a} are independently chosen from the group consisting of H, C_1-C_{10} alkyl and C_3-C_7 cycloalkyl; or R^{8a} and R^{9a} taken together form a 4 to 6 membered aliphatic ring; wherein the 4 to 6 membered aliphatic ring optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{10a} is selected from the group consisting of H, C_1-C_6 alkyl, R^{11}, OH, CF_3, CHF_2, F, Cl, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR^{8a}SO_2R^{8a}$, $SO_2NR^{8a}R^{9a}$, $NR^{8a}SO_2C_3$-C_7 cycloalkyl, CN, $NR^{8a}R^{9a}$, COOH, $COOR^{8a}$, $CONR^{8a}R^{9a}$, $OCOC_1$-C_6 alkyl, $CONR^{8a}SO_2R^{9a}$, $CONR^{8a}SO_2NR^{8a}R^{9a}$, a 4 to 6 membered aliphatic ring and a 5 to 6 membered aromatic ring; wherein the aliphatic or aromatic ring optionally contains one or more heteroatoms selected from the group consisting of N, S and O;

R^{11} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, phenyl, pyridinyl and pyrazolyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

n is an integer having a value from 1 to 6;

R^4 is selected from the group consisting of tert-butyl, $CH(CH_3)(CF_3)$, aryl, Het^1, Het^2 and C_3-C_7 cycloalkyl substituted with one or more substituents selected from the group consisting of halo and C_1-C_4 alkyl; aryl represents phenyl or naphthalenyl; said aryl optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11b}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11b}$, and C_1-C_4 alkyl;

Het^1 represents a monocyclic 4 to 6 membered non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 7 to 11 non-aromatic heterocycle containing one or two heteroatoms each independently selected from the group consisting of O, S and N; said Het^1 optionally being

substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, SO_2R^{8a} C_1-C_4 alkylcarbonyl, C_1-C_4 alkyloxycarbonyl, CO(aryl), $COHet^2$, pyridinyl, CF_3, $SO_2N(C_1$-C_4 alkyl$)_2$, $SO_2NH(C_1$-C_4 alkyl), $NH(C{=}O)(C_1$-C_4 alkyl), $(C{=}O)NH(C_1$-C_4 alkyl), $(C{=}S)NH(C_1$-C_4 alkyl), C_1-C_4 alkyl and C_1-C_4 alkyl substituted with one hydroxy;

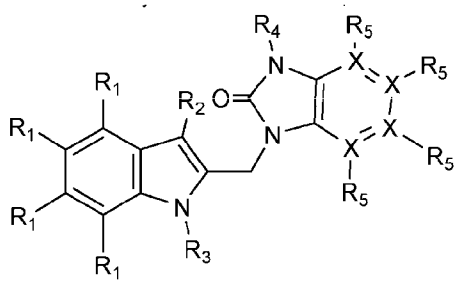
Het^2 represents a monocyclic 5 to 6 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; or a bicyclic 8 to 12 membered aromatic heterocycle containing one or more heteroatoms each independently selected from the group consisting of O, S and N; said Het^2 optionally being substituted with one or more substituents each independently selected from the group consisting of halo, C_1-C_4 alkyloxy, OH, CN, CF_2H, CF_3, $CONR^{8a}R^{9a}$, $COOR^{8a}$, $CON(R^{8a})SO_2R^{9a}$, $CON(R^{8a})SO_2N(R^{8a}R^{9a})$, $NR^{8a}R^{9a}$, $NR^{8a}COOR^{9a}$, $OCOR^{8a}$, $NR^{8a}SO_2R^{9a}$, $SO_2NR^{8a}R^{9a}$, SO_2R^{8a}, $OCONR^{8a}R^{9a}$, $OCONR^{8a}R^{11b}$, $N(R^{8a})CON(R^{8a}R^{9a})$, $N(R^{8a})COOR^{11b}$ and C_1-C_4 alkyl;

R^{11b} is selected from the group consisting of phenyl, pyridinyl and pyrazolyl; each optionally substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen; or R^{11b} is C_1-C_6 alkyl or C_3-C_7 cycloalkyl; each substituted with one or more substituents each independently selected from the group consisting of CF_3, CH_3, OCH_3, OCF_3 and halogen;

Z is C or N; R^5 is present where Z is C, whereby R^5 is selected from the group consisting of hydrogen, CF_3 and halogen; R^5 is absent where Z is N;

or a pharmaceutically acceptable addition salt or a solvate thereof.

37. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B5) having the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

each X independently is C or N;

R_1 is selected from the group of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_6)_2$, $CO(R_7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6\text{ alkyl})_2$;

R_2 is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, and $CO(R_7)$;

R_3 is $-(CR_8R_9)_n\text{-}R_{10}$;

R_4 is selected from the group consisting of H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_8$, CH_2CF_3, SO_2CH_3 or a 4 to 6 membered saturated ring containing an oxygen atom;

R_5 is present where X is C, and is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen; R_5 is absent where X is N;

R_6 is selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$;

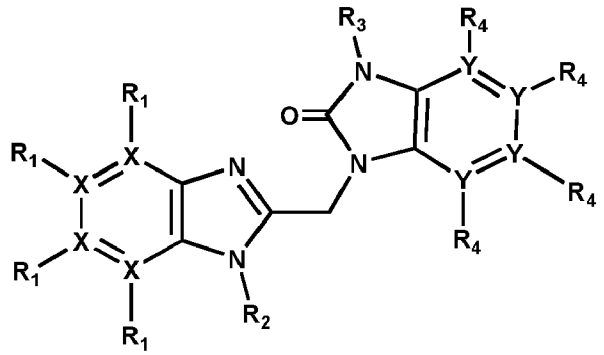
R_7 is selected from the group consisting of OH, $O(C_1\text{-}C_6\text{ alkyl})$, NH_2, $NHSO_2N(C_1\text{-}C_6\text{ alkyl})_2$, $NHSO_2NCH_3$, $NHSO_2(C_1\text{-}C_6\text{ alkyl})$, $NHSO_2(C_3\text{-}C_7\text{ cycloalkyl})$, and $N(C_1\text{-}C_6\text{ alkyl})_2$, NR_8R_9, NR_9R_{10};

n is an integer from 2 to 6;

R_8 and R_9 are each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_8 and R_9 taken together form a 4 to 6 membered aliphatic ring that optionally contains one or more heteroatoms selected from the group N, S, O;

R_{10} is selected from the group consisting of H, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $C(=NOH)NH_2$, $CONR_8R_9$, $COOR_8$, $CONR_8SO_2R_9$, $CON(R_8)SO_2N(R_8R_9)$, NR_8R_9, NR_8COOR_9, $OCOR_8$, $NR_8SO_2R_9$, $SO_2NR_8R_9$, SO_2NR_8 or a 4 to 6 membered saturated ring containing an oxygen atom.

38. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B6) having the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

each X independently is C or N; at least one X = N;

each Y independently is C or N;

R_1 is present when X = C and R_1 is selected from the group of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_5)_2$, $CO(R_6)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6$ alkyl$)_2$; R_1 is absent when X = N;

R_2 is $-(CR_7R_8)_n\text{-}R_9$;

R_3 is selected from the group consisting of H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, $SO_2\text{-}R_7$, CH_2CF_3 or a 4 to 6 membered saturated ring containing an oxygen atom;

R_4 is present where Y is C and is selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, $COO(R_7)$, CF_3 and halogen,

R_5 is selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$;

R_6 is selected from the group consisting of OH, $O(C_1\text{-}C_6$ alkyl), NH_2, $NHSO_2N(C_1\text{-}C_6$ alkyl$)_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1\text{-}C_6$ alkyl), $NHSO_2(C_3\text{-}C_7$ cycloalkyl), and $N(C_1\text{-}C_6\text{-}$alkyl$)_2$;

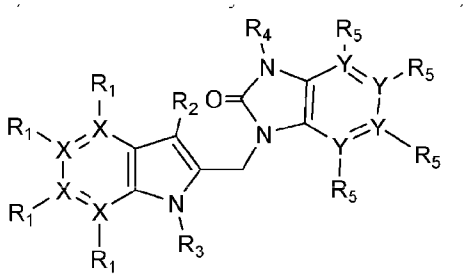
R_7 and R_8 are each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_7 and R_8 taken together form a 4 to 6 membered aliphatic ring that optionally contains a heteroatom selected from the group N, S, O;

R_9 is selected from the group consisting of H, R_{10}, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $CONR_7R_8$, $COOR_7$, $CON(R_7)SO_2R_8$, $CON(R_7)SO_2N(R_7R_8)$, NR_7R_8, NR_7COOR_8, $OCOR_7$, O-Benzyl, $NR_7SO_2R_8$, SO_2 R_7R_8, SO_2R_7, $OCONR_7R_8$, $OCONR_7R_{10}$, $N(R_7)CON(R_7R_8)$, $N(R_7)COOC$; phtalimido, 2-methyl-benzothiophene(1,1)di oxide, or a 4 to 6 membered saturated ring containing an oxygen atom;

n is an integer from 2 to 6;

R_{10} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl , phenyl, pyridine or pyrazole, optionally substituted with one or more substituents selected from the group comprising CF_3, CH_3, OCH_3, OCF_3 or halogen.

39. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B7) having the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

each X independently is C or N with at least one X being N;

R_1 is present where X = C and R_1 selected from the group of H, OH, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, NH_2, $CO(R_7)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O\text{-}C_1\text{-}C_6\ alkyl)_2$;

R_2 is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, and $CO(R_7)$;

R_3 is $-(CR_8R_9)_n\text{-}R_{10}$;

R_4 is selected from the group consisting of H, C_1-C_{10} alkyl, CH_2CF_3 C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, SO_2-R_8, or a 4 to 6 membered saturated ring containing an oxygen atom;

R_5 is present where Y is C, and is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen;

R_5 is absent where X is N;

R_6 is selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$;

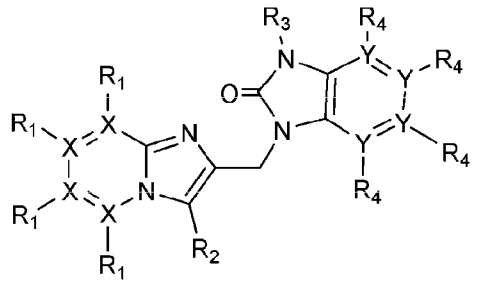
R_7 is selected from the group consisting of OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl)$_2$,N HSO_2NHCH_3, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), and $N(C_1$-C_6-alkyl)$_2$;

n is an integer from 2 to 6;

R_8 and R_9 are each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_8 and R_9 taken together form a 4 to 6 membered aliphatic ring that optionally contains a heteroatom selected from the group N, S, O;

R_{10} is selected from the group consisting of H, C_1-C_6 alkyl, OH, CN, F, CF_2H, CF_3, $CONR_8R_9$, $COOR_8$, $CONR_8SO_2R_9$, $CON(R_8)SO_2N(R_8R_9)$, NR_8R_9, NR_8COOR_9, $OCOR_8$, $NR_8SO_2R_9$, $SO_2NR_8R_9$, SO_2R_8 or a 4 to 6 membered saturated ring containing an oxygen atom.

40. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B8) having the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

each X independently is C or N;

each Y independently is C or N;

R_1 is present when X = C and R_1 is selected from the group of H, halogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, $N(R_5)_2$, $CO(R_6)$, CH_2NH_2, CH_2OH, CN, $C(=NOH)NH_2$, $C(=NOCH_3)NH_2$, $C(=NH)NH_2$, CF_3, OCF_3, and $B(OH)_2$; $B(O$-C_1-C_6 alkyl)$_2$;

R_1 is absent when X = N

R_2 is selected from the group consisting of H, halogen, $-(CR_7R_8)_n$-R_9, $C\equiv C$-CH_2-R_9 and $C\equiv C$-R_9, $C=C$-R_9;

R_3 is selected from the group consisting of H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, SO_2-R_7, or a 4 to 6 membered saturated ring containing an oxygen atom;

R_4 is present where Y is C and is selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 cycloalkyl, C_1-C_6 alkoxy, $CO(R_7)$, CF_3 and halogen,

R_5 is selected from the group consisting of H, C_1-C_6 alkyl, $COOCH_3$, and $CONHSO_2CH_3$;

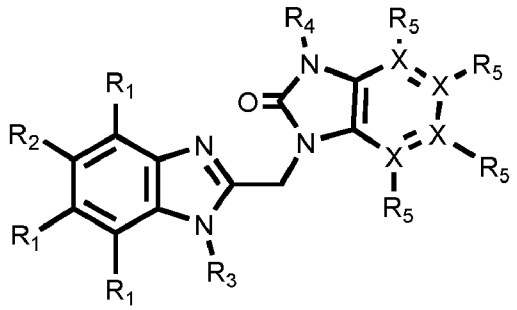
R_6 is selected from the group consisting of OH, $O(C_1$-C_6 alkyl), NH_2, $NHSO_2N(C_1$-C_6 alkyl)$_2$, $NHSO_2NHCH_3$, $NHSO_2(C_1$-C_6 alkyl), $NHSO_2(C_3$-C_7 cycloalkyl), and $N(C_1$-C_6-alkyl)$_2$;

R_7 and R_8 are each independently chosen from H, C_1-C_{10} alkyl, C_3-C_7 cycloalkyl or R_7 and R_8 taken together form a 4 to 6 membered aliphatic ring that optionally contains at least one heteroatom selected from the group N, S, O;

R_9 is selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl OH, CN, F, CF_2H, CF_3, $CONR_7R_8$, $COOR_7$, $CON(R_7)SO_2R_8$, $CON(R_7)SO_2N(R_7R_8)$, NR_7R_8, NR_7COOR_8, $OCOR_7$, $NR_7SO_2R_8$, $SO_2NR_7R_8$, SO_2R_7 or a 4 to 6 membered saturated ring containing an oxygen atom;

n is an integer from 2 to 6.

41. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B9) having the structure:



or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

each X independently is C or N;

R_1 is H;

R_2 is selected from the group consisting of Br and Cl;

R_3 is $-(CR_6R_7)_n$-R_8;

R_4 is selected from the group consisting of H, C_3-C_7 cycloalkyl, C_2-C_{10} alkenyl, -$(CR_6R_7)_n$-R_8, -CH_2-p-Fluorophenyl, CH_2CF_3 and -SO_2CH_3;

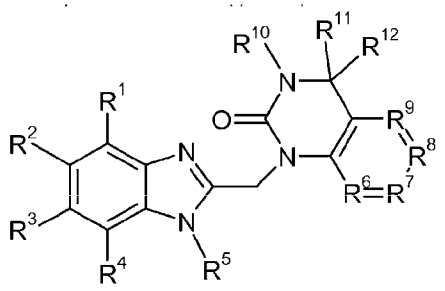
R_5 is present where X is C, whereby each R_5 is selected, each independently, from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, and CN; R_5 is absent where X is N;

R_6 and R_7 are each independently chosen from H and C_1-C_{10} alkyl, C_3-C_7 cycloalkyl; or R_6 and R_7 taken together form a 5 to 6 membered aliphatic or aromatic ring that optionally contains one or more heteroatoms selected from the group N, S, O;

R_8 is selected from the group consisting of H, OH, CF_3, CHF_2, F, Cl, SO_2CH_3, SO_2C_3-C_7 cycloalkyl, $NR_6SO_2R_6$, $SO_2R_6R_7$, $R_6SO_2C_3$-C_7 cycloalkyl, CN, NR_6R_7, COOH, $COOR_6$, $CONR_6R_7$, $OCOC_1$-C_6 alkyl, $CONR_6SOR_7$, CONH-R_6-SO_2R_7 , CONH-R_6-$SO_2NR_6R_7CONR_6SO_2NR_6R_7$, phtalimido or a 5 to 6 membered aliphatic or aromatic ring that optionally contains one or more heteroatoms selected from the group N, S, O;

n is an integer having a value from 1 to 6.

42. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B10) having the structure:



wherein

R^1, $R^3$and R^4 each independently represents H, C1-6 alkyl or halogen;

R^2 represents H, CN, CH_2NH_2, $CH_2NH(CH_2)_3NH_2$, C(=NH)NH_2 or C(=NOH)NH_2;

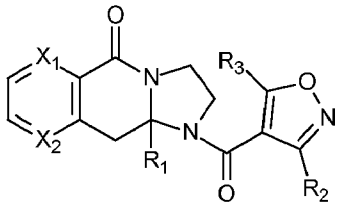
R^5 represents C1-6 alkyl; said C1-6 alkyl being optionally substituted with one or more of OR^{13}, CF_3, CN or $NR^{14}R^{15}$ wherein R^{13} represents H or C1-6 alkyl and R^{14} and R^{15} independently represent H, C1-6 alkyl or C3-7 cycloalkyl; or the group -$NR^{14}R^{15}$ together represents a 5 to 7 membered azacyclic ring optionally incorporating one further heteroatom selected from O, S and NR^{19} wherein R^{19} represents H or C1-6 alkyl;

R^6, R^7, R^8 and R^9 each independently represents CH, C-F, C-Cl, C-CF_3 or N;

R^{10} represents aryl, heteroaryl, C3-7 cycloalkyl or C1-6 alkyl; said C1-6 alkyl or C3-7 cycloalkyl being optionally substituted with one or more of aryl, C3-7 cycloalkyl, OR^{16}, SR^{16}, halogen or $NR^{17}R^{18}$, wherein R^{16} represents H or C1-6 alkyl and R^{17} and R^{18} each independently represents H, C1-6 alkyl or C3-7 cycloalkyl; or the group $-NR^{17}R^{1}$ together represents a 5 to 7 membered azacyclic ring optionally incorporating one heteroatom selected from O, S and NR^{20} wherein R^{20} represents H or C1-6 alkyl; and

R^{11} and R^{12} each independently represents H or C1-6 alkyl.

43. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B11) having the structure:



or racemates, isomers and/or salts thereof,

wherein:

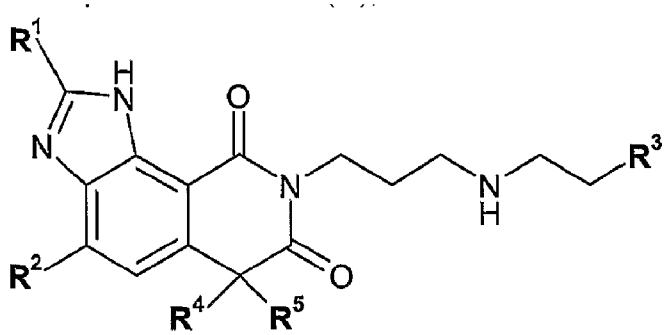
X_1 and X_2 are independently selected from CH and N wherein at least one of X_1 and X_2 is N;

R_1 is optionally substituted and is selected from a carbocyclic, heterocyclic and aromatic ring;

R_2 is selected from C_{1-6} alkyl, haloC_{1-3}alkyl and C_{1-3}alkoxy; and

R_3 is H or an optional substituent.

44. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B12) having the structure:



or an enantiomer or a salt thereof,

wherein:

R^1 is -(CH=CH)$_{0-1}$-(C_6 or C_{10})aryl or -(CH=CH)$_{0-1}$-5-, 6-, 9- or 10- membered heteroaryl, said aryl or heteroaryl being optionally substituted with one, two or three substituents, each independently selected from: (C_{1-6})alkyl optionally substituted with amino, halo, (C_{1-6})haloalkyl, hydroxy, (C_{1-6})alkoxy, (C_{1-6})alkylthio, nitro, azido, cyano, amino,(C_{1-6})alkylamino, di((C_{1-6})alkyl)amino, aryl and heteroaryl;

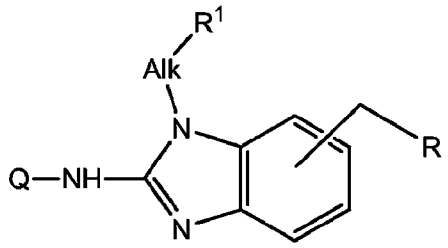
R^2 is H, (C_{1-6})alkyl, hydroxy, halo, (C_{1-6})haloalkyl, amino, (C_{1-6})alkylamino. di((C_{1-6})alkyl)amino, or (C_{2-6})alkynyl;

R^3 is (C_6, C_{10} or C_{14})aryl or 5-, 6-, 9- or 10-membered heteroaryl, each of which being optionally substituted with one, two or three substituents, each independently selected from: (C_{1-6})alkyl, halo, (C_{1-6})haloalkyl, hydroxy, (C_{1-6})alkoxy, (C_{1-6})alkylthio, nitro, amino, (C_{1-6})alkylamino, di((C_{1-6})alkyl)amino and COO(C_{1-6})alkyl; and

R^4 and R^5 are each independently H or (C_{1-6})alkyl; or R^4 and R^5 are linked, together with the carbon atom to which they are attached, to form a (C_{3-7})cycloalkyl group;

with the proviso that R^1 is not 2-methoxyphenyl, when R^2 is H, R^3 is 3,4-dimethoxyphenyl, R^4 is CH_3 and R^5 is CH_3.

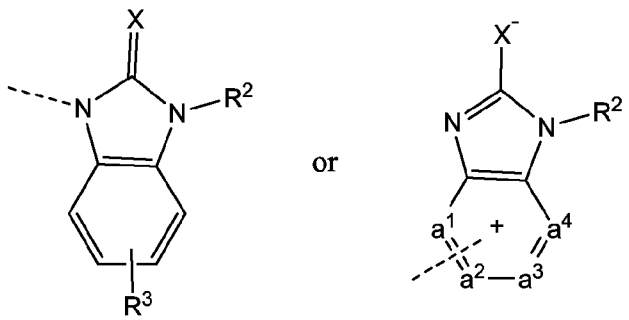
45. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B13) having the structure:



or a salt or a stereochemically isomeric form thereof,

wherein:

R is a radical of formula



(a) (b)

Q is hydrogen or C_{1-6}alkyl optionally substituted with a heterocycle or Q is C_{1-6}alkyl substituted with both a radical -OR^4 and a heterocycle; wherein said heterocycle is selected from the group consisting of oxazolidine, thiazolidine, 1-oxo-thiazolidine, 1,1-dioxothiazolidine, morpholinyl, thiomorpholinyl, 1-oxo-thiomorpholinyl,1,1-dioxothiomorpholinyl, hexahydrooxazepine, hexahydrothiazepine, 1-oxo-hexahydrothiazepine, 1,1-dioxo-hexahydrothiazepine, pyrrolidine, piperidine, homopiperidine, piperazine; wherein each of said heterocyle may be optionally substituted with one or two substituents selected from the group consisting of C_{1-6}alkyl, hydroxyC_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, hydroxy, carboxyl, C_{1-6} alkyloxycarbonyl, aminocarbonyl, mono- or di(C_{1-6}alkyl)aminocarbonyl, C_{1-6}alkylcarbonylamino, aminosulfonyl and mono- or di(C_{1-6}alkyl)aminosulfonyl;

Alk is C_{1-6}alkanediyl;

X is O or S;

-a^1=a^2-a^3=a^4- is a bivalent radical of formula -N=CH-CH=CH-, -CH=N-CH=CH-, -CH=CH-N=CH- or -CH=CH-CH=N-; wherein one of the nitrogen atoms bears the chemical bond linking radical (b) with the rest of the molecule;

R^1 is Ar or a heterocycle selected from pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]- pyridinyl, imidazo[1,2-a]pyridinyl and 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl; wherein each of said heterocycle may optionally be substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, hydroxyC_{1-6}alkyloxy, (C_{1-6}alkyl-oxy)C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkyloxycarbonyl, aminocarbonyl, mono- and di- C_{1-6}alkylaminocarbonyl;

R^2 is hydrogen, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, Ar-C_{1-6}alkyloxy-C_{1-6}alkyl, C_{3-7} cycloalkyl, cyano-C_{1-6}alkyl, Ar-C_{1-6}alkyl, Het-C_{1-6}alkyl;

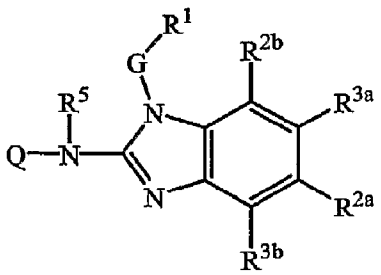
R^3 is hydrogen, C_{1-6}alkyl, cyano, aminocarbonyl, polyhaloC_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl;

R^4 is hydrogen or C_{1-6}alkyl;

each Ar independently is phenyl or phenyl substituted with 1 to 5, such as 1, 2, 3 or 4, substituents selected from halo, hydroxy, amino, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkylcarbonylamino, C_{1-6}alkylsulfonylamino, cyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, aminoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxy, polyhaloC_{1-6}alkyloxy, phenoxy, aminocarbonyl, mono- or di(C_{1-6}alkyl)aminocarbonyl, hydroxycarbonyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkylcarbonyl, amino sulfonyl, mono- and di(C_{1-6}alkyl)- aminosulfonyl;

Het is a heterocycle selected from the group consisting of pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, iuranyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyridinyl and 2,3-dihydro-1,4-dioxino-[2,3-b]pyridyl; wherein each Het may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, amino, mono- or di(C_{1-6}alkyl)amino, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkyloxy.

46. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B14) having the structure:



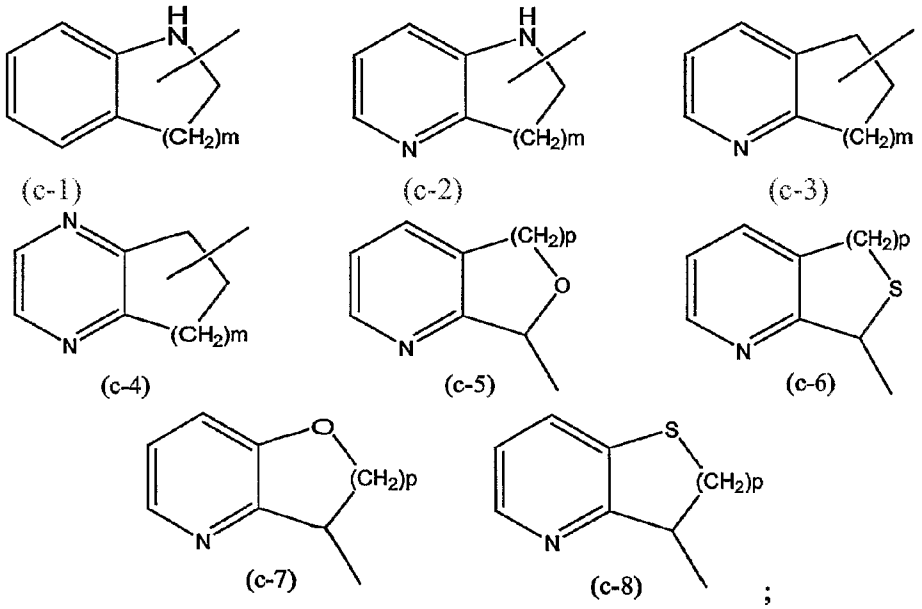
or a prodrug, N-oxide, addition salt, quaternary amine, metal complex, or a stereochemically isomeric form thereof,

wherein:

G is a direct bond or C_{1-10}alkanediyl optionally substituted with one or more substituents independently selected from the group of substituents consisting of hydroxy, C_{1-6}alkyloxy, Ar^1 C_{1-6}alkyloxy,C_{1-6}alkylthio, Ar^1 C_{1-6}alkylthio,HO(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_a$- or Ar^1 C_{1-6}alkyloxy(-CH_2-CH_2-O)n-;

each n independently is 1, 2, 3 or 4;

R^1 is Ar^1 or a monocyclic or bicyclic heterocycle being selected from piperidinyl, piperazinyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydro- furanyl, thienyl, pynolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]- pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula



;

wherein each of said monocyclic or bicyclic heterocycles may optionally be substituted with 1 or where possible more, such as 2, 3, 4 or 5, substituents independently selected from the group of substituents consisting of halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyCi-ealkyl, Ar^1, Ar^1C_{1-6}alkyl, Ar^1C_{1-6}alkyloxy, hydroxyC_{1-6}alkyl,mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino,C_{1-6}alkyl-SO_2-NR^{5c}-, Ar^1-SO_2-NR^{5c}-, C_{1-6}alkyloxycarbonyl, -C(=O)-$NR^{5c}R^{5d}$, HO(-CH_2-CH_2-O)$_n$-, halo(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$-, Ar^1C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$- and mono-or di(C_{1-6}alkyl)amino(-CH_2-CH_2-O)$_n$-;

each m independently is 1 or 2;

each p independently is 1 or 2;

each t independently is 0, 1 or 2;

Q is hydrogen, amino or mono- or di(C_{1-4}alkyl)amino;

one of R^{2a} and R^{3a} is selected from halo, optionally mono- or polysubstituted C_{1-6}alkyl, optionally mono- or polysubstituted C_{2-6}alkenyl, nitro, hydroxy, Ar^2, $N(R^{4a}R^4)$, $N(R^{4a}R^{4b})$sulfonyl, $N(R^{4a}R^4)$carbonyl, C_{1-6}alkyloxy, Ar^2oxy, Ar^2C_{1-6}alkyloxy,carboxyl, C_{1-6}alkyloxycarbonyl, or $-C(=Z)Ar^2$; and the other one of R^{2a} and R^{3a} is hydrogen; wherein =Z is =O, =CH-C(=O) $-NR^{5a}R^{5b}$, $=CH_2$, =CH- C_{1-6}alkyl, =N-OH or =N-O- C_{1-6}alkyl; and the optional substituents on C_{1-6}alkyl and C_{2-6} alkenyl can be the same or can be different relative to one another, and are each independently selected from the group of substituents consisting of hydroxy, cyano, halo, nitro, $N(R^{4a}R^{4b})$, $N(R^{4a}R^{4b})$sulfonyl, Het, Ar^2, C_{1-6}alkyloxy, C_{1-6}alkyl-$S(=O)_t$, Ar^2oxy, Ar^2-$S(=O)_t$, Ar^2C_{1-6}alkyloxy, Ar^2C_{1-6}alkyl-$S(=O)_t$, Het-oxy, Het-$S(=O)_t$,HetC_{1-6}alkyloxy, HetC_{1-6}alkyl-$S(=O)_t$, carboxyl, C_{1-6}alkyloxycarbonyl and $-C(=Z)Ar^2$;

in case R^{2a} is different from hydrogen then R^{2b} is hydrogen, C_{1-6}alkyl or halogen and R^{3b} is hydrogen;

in case R^{3a} is different from hydrogen then R^{3b} is hydrogen, C_{1-6}alkyl or halogen and R^{2b} is hydrogen;

R^{4a} and R^{4b} can be the same or can be different relative to one another, and are each independently selected from the group of substituents consisting of hydrogen, C_{1-6}alkyl, Ar^2C_{1-6}alkyl, (Ar^2)(hydroxy) C_{1-6}alkyl, Het-C_{1-6}alkyl, hydroxyC_{1-6}alkyl, mono- and di-(C_{1-6}alkyloxy)C_{1-6}alkyl, (hydroxyC_{1-6}alkyl)oxyC_{1-6}alkyl, Ar^1C_{1-6}alkyloxy-C_{1-6}alkyl, dihydroxyC_{1-6}alkyl, (C_{1-6}alkyloxy)(hydroxy)C_{1-6}alkyl, (Ar^1C_{1-6}alkyloxy)(hydroxy) C_{1-6}alkyl, Ar^1oxy-C_{1-6}alkyl, (Ar^1oxy)(hydroxy)-C_{1-6}alkyl, aminoC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)amino-C_{1-6}alkyl, carboxyl- C_{1-6}alkyl, C_{1-6}alkyloxycarbonylC_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminocarbonylC_{1-6}alkyl, C_{1-6}alkylcarbonylC_{1-6}alkyl, (C_{1-4}alkyloxy)$_2$-P(=O)-C_{1-6}alkyl, (C_{1-4}alkyloxy)$_2$P(=O)-O-C_{1-6}alkyl, aminosulfonyl-C_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminosulfonyl-C_{1-6}alkyl, C_{1-6}alkylcarbonyl, Ar^2carbonyl, Het-carbonyl, Ar^2C_{1-6}alkylcarbonyl, Het-C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, aminosulfonyl, mono- and di(C_{1-6}alkyl)aminosulfonyl, Ar^2sulfonyl, Ar^2C_{1-6}alkylsulfonyl, Ar^2, Het, Het-sulfonyl, HetC_{1-6}alkylsulfonyl;

R^{5a} and R^{5b} can be the same or can be different relative to one another, and are each independently hydrogen or C_{1-6}alkyl; or

R^{5a} and R^{5b} taken together may form a bivalent radical of formula $-(CH_2)_s-$ wherein s is 4 or 5;

R^{5c} and R^{5d} can be the same or can be different relative to one another, and are each independently hydrogen or C_{1-6}alkyl; or

R^{5c} and R^{5d} taken together may form a bivalent radical of formula $-(CH_2)_s-$ wherein s is 4 or 5;

R^{6a} is hydrogen, C_{1-6}alkyl, Ar^1, Ar^1C_{1-6}alkyl, C_{1-6}alkylcarbonyl, Ar^1carbonyl, Ar^1C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, Ar^1sulfonyl, Ar^1C_{1-6}alkylsulfonyl, C_{1-6}alkyloxyC_{1-6}alkyl, aminoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, hydroxyC_{1-6}alkyl, (carboxyl)-C_{1-6}alkyl, (C_{1-6}alkyloxycarbonyl)-C_{1-6}alkyl, aminocarbonylC_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminocarbonylC_{1-6}alkyl, aminosulfonyl-C_{1-6}alkyl, mono- and di(C_{1-6}alkyl)aminosulfonyl-C_{1-6}alkyl, Het, Het-C_{1-6}alkyl, Het-carbonyl, Het-sulfonyl, Het-C_{1-6}alkylcarbonyl;

R^{6b} is hydrogen, C_{1-6}alkyl, Ar^1 or Ar^1C_{1-6}alkyl;

R^{6c} is C_{1-6}alkyl, Ar^1 or Ar^1C_{1-6}alkyl;

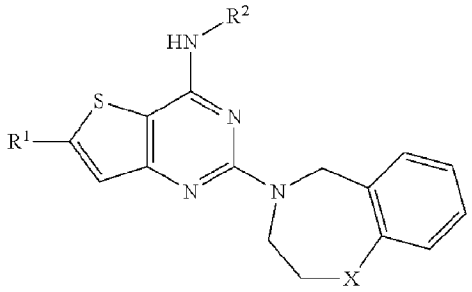
Ar^1 is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, and C_{1-6}alkyloxy;

Ar^2 is phenyl, phenyl annelated with C_{5-7} cycloalkyl, or phenyl substituted with 1 or more, such as 2, 3, 4 or 5, substituents selected from halo, cyano, C_{1-6}alkyl, Het-C_{1-6}alkyl, Ar^1C_{1-6}alkyl, cyanoC_{1-6}alkyl, C_{2-6} alkenyl, cyanoC_{2-6}alkenyl, R^{6b}-O-C_{3-6}alkenyl, C_{2-6}alkynyl, cyanoC_{2-6}alkynyl, R^{6b}-O-C_{3-6}alkynyl, Ar^1, Het, R^{6b}-O-, R^{6b}-S-, R^{6c}-SO-, R^{6c}-SO_2-, R^{6b}-O-C_{1-6}alkyl-SO_2-, -N($R^{6a}R^{6b}$), polyhalo-C_{1-6}alkyl, polyhaloC_{1-6}alkyloxy, polyhaloC_{1-6}alkylthio, R^{6c}-C(=O)-, R^{6b}-O-C(=O)-, -N($R^{6a}R^{6b}$)-C(=O)-, R^{6b}-O-C_{1-10}alkyl, R^{6b}-S-C_{1-6}alkyl, R^{6c}-S(=O)$_2$-C_{1-6}alkyl, -N($R^{6a}R^{6b}$)- C_{1-6}alkyl, R^{6c}-C(=O) -C_{1-6}alkyl, R^{6b}-O-C(=O)-C_{1-6}alkyl, N($R^{6a}R^6$)-C(=O)-C_{1-6}alkyl, R^{6c}-C(=O)-NR^6 -, R^{6c}-C(=O) –O-, R^{6c}-C(=O) –$NR^{6b}$$C_{1-6}$alkyl, R^{6c}-C(=O) –O-C_{1-6}alkyl, N($R^{6a}R^{6b}$)-S(=O)$_2$-, H_2N-C(=NH)-;

Het is a heterocycle being selected from tetrahydrofuranyl, tetrahydrothienyl, pynolidinyl, pynolidinonyl, furanyl, thienyl, pynolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, piperidinyl, homopiperidinyl, piperazinyl, moφholinyl, pyridyl, pyrazinyl, pyridazinyl, pyrirmdinyl, tetrahydroquinolinyl, quinolinyl, isoquinolinyl, benzodioxanyl, benzodioxolyl, indolinyl, indolyl, each of said heterocycle may optionally be substituted with oxo, amino, Ar^1, C_{1-4}alkyl, aminoC_{1-4}alkyl,

Ar^1C_{1-4}alkyl, mono- or di(C_{1-6}alkyl)ammoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)amino, (hydroxyC_{1-6}alkyl)amino, and optionally further with one or two C_{1-4}alkyl radicals.

47. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B15) having the structure:



or a pharmaceutically acceptable salt or stereoisomer thereof,

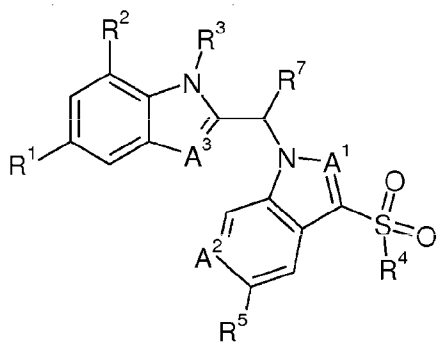
wherein:

R^1 is hydrogen or a C_{1-6}alkyl;

R^2 is (1) amino$(CH_2)_{2-6}$; (2) amino$(CH_2)_{1-6}$difluoromethyl$(CH_2)_{1-6}$; (3) amino$(CH_2)_{1-6}$fluoromethyl$(CH_2)_{1-6}$; (4) amino$(CH_2)_{0-6}$oxetanyl$(CH_2)_{1-6}$; (5) amino$(CH_2)_{1-6}$oxetanyl$(CH_2)_{0-6}$; or (6) pyrrolidin-3-yl, unsubstituted or 4-substituted by halogen; and

X is –O–, –S–, –S(=O) –, –S(O_2) –, –CH_2–, –CF_2– or –NH–.

48. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B16) having the structure:



or pharmaceutically acceptable salts thereof,

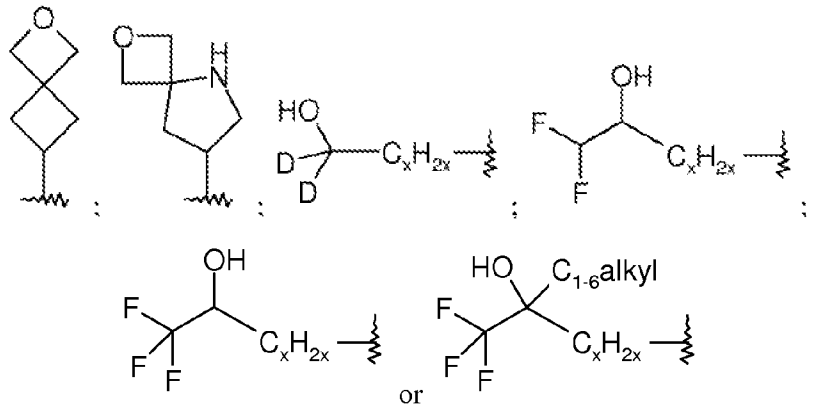
wherein:

R^1 is hydrogen or halogen;

R^2 is hydrogen or halogen;

R^3 is azetidinyl; C_{1-6}alkoxypyridinyl; C_{1-6}alkylsulfonyl-C_xH_{2x}-; carboxycycloalkyl; difluorocycloalkyl; 1,1-dioxo-tetrahydrothienyl; halopyridinyl; hydroxy-C_yH_{2y}-; hydroxy-

C_xH_{2x}- cycloalkyl; hydroxy-C_yH_{2y}-O-C_yH_{2y}-; hydroxycycloalkyl-C_zH_{2z}-, unsubstituted or substituted by C_{1-3}alkyl, hydroxy or hydroxy-C_xH_{2x}-; 4-hydroxypiperidin-1-yl-C_yH_{2y}-; 3-hydroxy-pyrrolidin-1- yl-C_yH_{2y}-; morpholinyl-C_yH_{2y}-; oxetanyl; oxetanyl-C_xH_{2x}-, unsubstituted or substituted by C_{1-3}alkyl; piperidinyl; oxo-piperidinyl; oxo-pyrrolidinyl; pyrrolidinyl, unsubstituted or substituted by C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, hydroxy-C_yH_{2y}-, hydroxy-C_xH_{2x}-carbonyl, amino-C_xH_{2x}-carbonyl or trifluoromethyl- C_xH_{2x}-; tetrahydrofuran-3-yl- C_zH_{2z}-; tetrahydropyranyl; trifluoromethyl- C_xH_{2x}-;



or

R^4 is C_{1-6}alkyl or cycloalkyl;

R^5 is hydrogen or halogen;

R^7 is hydrogen or C_{1-6}alkyl;

A^1 is -N- or -CH;

A^2 is -N-, -NO or -CH;

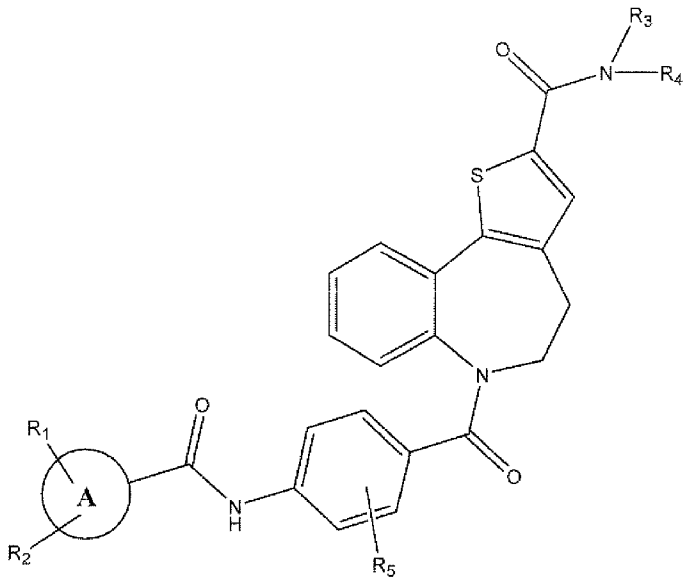
A^3 is -N- or -CH;

x is 1-6;

y is 2-6;

z is 0-6.

49. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B17) having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

A is aryl or heteroaryl;

R_1 is alkyl, alkoxy, haloalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, said heterocyclyl is optionally substituted by one to three substituents independently selected from the group consisting of halo, hydroxyl, haloalkyl, alkoxy, alkyl, alkoxy-alkyl-,hydroxyl-alkyl-, CN, alky-NH- „; said aryl or heteroaryl is optionally substituted by one to three substituents independently selected from the group consisting of halo, cyano, nitro, hydroxyl, alkyl, alkoxy, alkyl-NH-, with the proviso that when A is aryl, R_1 is not unsubstituted aryl;

R_2 is hydrogen, alkyl, alkoxy, amino, alkyl-NH-, CN, alkyl-SO_2-, or halo;

R_3 is hydrogen, alkyl, heterocyclyl, heteroaryl, heteroaryl-alkyl-, or cycloalkyl, said alkyl is optionally substituted by one substituent selected from the group consisting of NH_2-C(O)-, halo, hydroxyl, NH_2-SO_2-, alkoxy-alkyl-, heterocyclyl; aryl, heteroaryl, CN, alkyl-NH-;

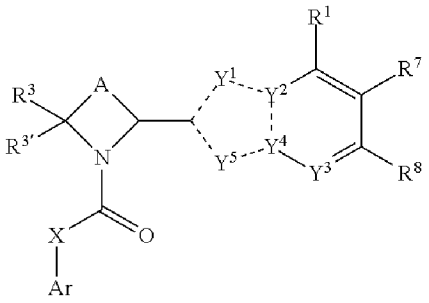
R_4 is hydrogen, or alkyl; or haloalkyl;

R_3 and R_4 taken together with the nitrogen atom to which they are attached optionally form a 3- to 7-membered ring;

R_5 is hydrogen, alkyl, alkoxy, haloalkyl, or halo.

50. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B18) having the structure:

I



or a pharmaceutically acceptable salt thereof,

wherein:

a) Y^1 is N, NH or CH, Y^2 is C, Y^3 is N or $CR^{8'}$, Y^4 is N or C and Y^5 is N, $NR^{2'}$ or CR^2, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$; or

b) Y^1 is N, NH or CH, Y^2 is N or C, Y^3 is N or $CR^{8'}$, Y^4 is N or C, and Y^5 is N or $NR^{2'}$, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$; or

c) Y^1 is N, NH or CH, Y^2 is N or C, Y^3 is $CR^{8'}$, Y^4 is N or C, and Y^5 is N, $NR^{2'}$ or CR^2, wherein at least two of Y^1, Y^2, Y^3, Y^4 and Y^5 are independently N, NH or $NR^{2'}$;

the dashed bonds ---- are selected from single bonds and double bonds so as to provide an aromatic ring system;

A is $-(CR^4R^{4'})_n-$ wherein any one $CR^4R^{4'}$ of said $-(CR^4R^{4'})_n-$ may be optionally replaced with –O-, -S-, $-S(O)_p-$, NH or NR^a;

n is 3, 4, 5 or 6;

each p is 1 or 2;

Ar is a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1 to 5 R^6;

X is $-C(R^{13})(R^{14})-$, $-N(CH_2R^{14})-$ or –NH-, or X is absent;

R^1 is H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-R^{11}$, $-S(O)_pR^a$, $NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl;

R^2 is H, CN, NO_2, halogen or (C_1-C_8)alkyl;

$R^{2'}$ is H or $(C_1$-$C_8)$alkyl;

R^3 is H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

$R^{3'}$ is H, $-OR^{11}$, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

each R^4 is independently H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl; and

each $R^{4'}$ is independently H, OR^{11}, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

or two R^4 on adjacent carbon atoms, when taken together, may form a double bond between the two carbons to which they are attached or may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p$–, –NH– or $-NR^a$–;

or two R^4 on non-adjacent carbon atoms, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p$–, –NH– or $-NR^a$–;

or two R^4 and two $R^{4'}$ on adjacent carbon atoms, when taken together, may form an optionally substituted C_6 aryl ring;

or one R^4 and one $R^{4'}$ on the same carbon atom, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p$–, –NH– or $-NR^a$–;

each R^5 is independently H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

each $R^{5'}$ is independently H, $-OR^{11}$, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

each R^6 is independently H, oxo, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclykC_1-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

or two R^6 on adjacent carbon atoms, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p$–, –NH– or $-NR^a$–;

or any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^3, may form a bond or a $-(CR^5R^{5'})_m$- group wherein m is 1 or 2;

or any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^2 or $R^{2'}$ may form a bond;

R^7 is H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $-NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl$(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$cycloalkyl or $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_8)$alkyl;

R^8 is H, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{11}$, $-NR^{11}C(O)OR^{11}$, $-NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, $-SR^{11}$, $-S(O)_pR^a$, $-NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-

C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl;

$R^{8'}$ is H, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$NR^{11}C(O)OR^{11}$, -$NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, -SR^{11}, -$S(O)_pR^a$, -$NR^{11}S(O)_pR^a$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)SR^{11}$, -$S(O)_p(OR^{11})$, -$SO_2NR^{11}R^{12}$, -$NR^{11}S(O)_p(OR^{11})$, -$NR^{11}SO_pNR^{11}R^{12}$, -$NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl;

each R^a is independently (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl wherein any (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl or (C_2-C_8)alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl of R^a is optionally substituted with one or more -OH, -NH_2, CO_2H, C_2-C_{20} heterocyclyl or (C_1-C_8)alkyl;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_8)alkyl, -$C(=O)R^a$ or -$S(O)_pR^a$; or when R^{11} and R^{12} are attached to a nitrogen they may optionally be taken together with the nitrogen to which they are both attached to form a 3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, –$S(O)_p$–, –NH–, –NR^a– or –C(O)–;

R^{13} is H or (C_1-C_8)alkyl;

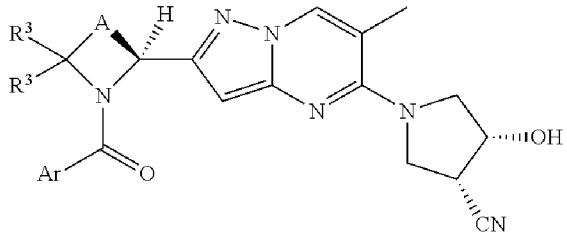
R^{14} is H, (C_1-C_8)alkyl, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, $NR^{11}S(O)_pR^a$, –$NR^{11}S(O)_p(OR^{11})$ or $NR^{11}SO_pNR^{11}R^{12}$; and

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, C_2-C_{20} heterocyclyl(C_1-C_8)alkyl, (C_3-C_7)cycloalkyl or (C_3-C_7)cycloalkyl(C_1-C_8)alkyl of each R^1, R^2, $R^{2'}$, R^3, $R^{3'}$, R^4, $R^{4'}$, R^5, $R^{5'}$, R^6, R^7, R^8, $R^{8'}$ or R^{12} is independently, optionally substituted with one or more oxo, halogen, hydroxy, –NH_2, CN, N_3, –$N(R^a)_2$, –NHR^a, –SH, –SR^a, –$S(O)_pR^a$, –OR^a, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, –$C(O)R^a$, –C(O)H, –$C(=O)OR^a$, –C(=O)OH, –$C(=O)N(R^a)_2$, –$C(=O)NHR^a$, –$C(=O)NH_2$, –$NHS(O)_pR^a$, –$NR^aS(O)_pR^a$, –$NHC(O)R^a$, –$NR^aC(O)R^a$, –$NHC(O)OR^a$, –$NR^aC(O)OR^a$, –$NR^aC(O)NHR^a$, –$NR^aC(O)N(R^a)_2$, –$NR^aC(O)NH_2$, –$NHC(O)NHR^a$, –$NHC(O)N(R^a)_2$, –

$NHC(O)NH_2$, =NH, =NOH, $=NOR^a$, $-NR^aS(O)_pNHR^a$, $—NR^aS(O)_pN(R^a)_2$, $—NR^aS(O)_pNH_2$, $—NHS(O)_pNHR^a$, $—NHS(O)_pN(R^a)_2$, $—NHS(O)_pNH_2$, $–OC(=O)R^a$, $–OP(O)(OH)_2$ or R^a.

51. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B19) having the structure:

I



or a salt or ester thereof,

wherein:

A is $-(C(R^4)_2)_n-$ wherein any one $C(R^4)_2$ of said $-(C(R^4)_2)_n-$ may be optionally replaced with –O–, –S–, $–S(O)_p–$, NH or NR^a;

n is 3,4, 5 or 6;

each p is 1 or 2;

Ar is a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1, 2, 3, 4 or 5 R^6;

each R^3, R^4 or R^6 is independently H, oxo, OR^{11}, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $S(O)_pR^a$, $NR^{11}S(O)_pR^a$, $–C(=O)R^{11}$, $–C(=O)OR^{11}$, $–C(=O)NR^{11}R^{12}$, $–C(=O)SR^{11}$, $–S(O)_p(OR^{11})$, $–SO_2NR^{11}R^{12}$, $–NR^{11}S(O)_p(OR^{11})$, $–NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl;

or two R^4 on adjacent carbon atoms, when taken together, may optionally form a double bond between the two carbons to which they are attached or may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, $–S(O)_p–$, –NH– or $–NR^a–$;

or four R^4 on adjacent carbon atoms, when taken together, may optionally form an optionally substituted C_6 aryl ring;

or two R^4 on the same carbon atom, when taken together, may optionally form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –S(O)$_p$–, –NH– or –NR^a–;

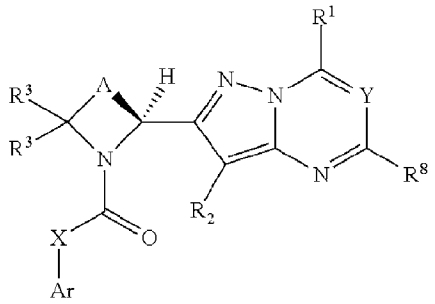
or two R^6 on adjacent carbon atoms, when taken together, may optionally form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, –S(O)$_p$–, –NH– or –NR^a–;

each R^a is independently (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl wherein any (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_2-C_8)alkenyl or (C_2-C_8)alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl or (C_1-C_8)alkyl;

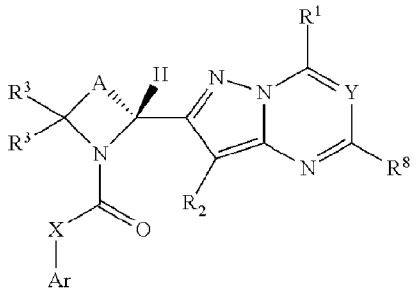
each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl, (C_4-C_8)carbocyclylalkyl, —C(=O)R^a, —S(O)$_p$R^a or aryl(C_1-C_8)alkyl; or R^{11} and R^{12} taken together with a nitrogen to which they are both attached form a 3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, –S(O)$_p$–, –NH–, –NR^a–;or –C(O) –; and

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl of each R^6, R^{11} or R^{12} is, independently, optionally substituted with one or more oxo, halogen, hydroxy, NH_2, CN, N_3, N(R^a)$_2$, NHR^a, SH, SR^a, S(O)$_p$R^a, OR^a, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, –C(O)R^a, –C(O)H, –C(=O)OR^a, –C(=O)OH, –C(=O)N(R^a)$_2$, –C(=O)NHR^a, –C(=O)NH$_2$, NHS(O)$_p$R^a, NR^{a}S(O)$_p$R^a, NHC(O)R^a, NR^{a}C(O)R^a, NHC(O)OR^a, NR^{a}C(O)OR^a, NR^{a}C(O)NHR^a, NR^{a}C(O)N(R^a)$_2$, NR^{a}C(O)NH$_2$, NHC(O)NHR^a, NHC(O)N(R^a)$_2$, NHC(O)NH$_2$, =NH, =NOH, =NOR^a, NR^{a}S(O)$_p$NHR^a, NR^{a}S(O)$_p$N(R^a)$_2$, NR^{a}S(O)$_p$NH$_2$, NHS(O)$_p$NHR^a, NHS(O)$_p$N(Ra)$_2$, NHS(O)$_p$NH$_2$, –OC(=O)R^a, –OP(O)(OH)$_2$ or R^a.

52. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B20) having a structure selected from:



and



a pharmaceutically acceptable salt or ester,

wherein:

A is $-(C(R^4)_2)_n-$ wherein any one $C(R^4)_2$ of said $-(C(R^4)_2)_n-$ may be optionally replaced with –O–, –S–, $-S(O)_p-$, NH or NR^a;

n is 3, 4, 5 or 6;

each p is 1 or 2;

Ar is a C_2-C_{20} heterocyclyl group or a C_6-C_{20} aryl group, wherein the C_2-C_{20} heterocyclyl group or the C_6-C_{20} aryl group is optionally substituted with 1 to 5 R^6;

X is $-C(R^{13})(R^{14})-$, $-N(CH_2R^{14})-$ or X is absent;

Y is N or CR^7;

each R^1, R^2, R^3, R^4, R^5, R^6, R^7 or R^8 is independently H, oxo, OR^{11}, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, N_3, CN, NO_2, SR^{11}, $S(O)_pR^a$, $NR^{11}S(O)_pR^a$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)_p(OR^{11})$, $-SO_2NR^{11}R^{12}$, $-NR^{11}S(O)_p(OR^{11})$, $-NR^{11}SO_pNR^{11}R^{12}$, $NR^{11}C(=NR^{11})NR^{11}R^{12}$, halogen, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, (C_3-C_7)cycloalkyl or (C_4-C_8)carbocyclylalkyl;

two R^4 on adjacent carbon atoms, when taken together, may form a double bond between the two carbons to which they are attached or may form a (C_3-C_7)cycloalkyl ring wherein one carbon atom of said (C_3-C_7)cycloalkyl ring may be optionally replaced by –O–, –S–, $-S(O)_p-$, –NH– or $-NR^a-$;

four R^4 on adjacent carbon atoms, when taken together, may form an optionally substituted C_6 aryl ring;

two R^4 on the same carbon atom, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $–S(O)_p–$, –NH– or $–NR^a–$;

two R^6 on adjacent carbon atoms, when taken together, may form a $(C_3$-$C_7)$cycloalkyl ring wherein one carbon atom of said $(C_3$-$C_7)$cycloalkyl ring may be optionally replaced by –O–, –S–, $–S(O)_p–$, –NH– or $–NR^a–$;

any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^3, may form a bond or a $–(C(R^5)_2)_m–$ group wherein m is 1 or 2;

any R^6 adjacent to the obligate carbonyl group of said Ar, when taken together with R^2, may form a bond;

each R^a is independently $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl wherein any $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $(C_2$-$C_8)$alkenyl or $(C_2$-$C_8)$alkynyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl, and wherein any aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl of R^a is optionally substituted with one or more OH, NH_2, CO_2H, C_2-C_{20} heterocyclyl or $(C_1$-$C_8)$alkyl;

each R^{11} or R^{12} is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl, $(C_4$-$C_8)$carbocyclylalkyl, $–C(=O)R^a$, $–S(O)_pR^a$, or aryl$(C_1$-$C_8)$alkyl; or R^{11} and R^{12} taken together with a nitrogen to which they are both attached form a 3 to 7 membered heterocyclic ring wherein any one carbon atom of said heterocyclic ring can optionally be replaced with –O–, –S–, $–S(O)_p–$, –NH–, $–NR^a–$ or –C(O) –;

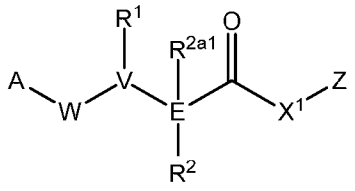
R^{13} is H or $(C_1$-$C_8)$alkyl;

R^{14} is H, $(C_1$-$C_8)$alkyl, $NR^{11}R^{12}$, $NR^{11}C(O)R^{11}$, $NR^{11}C(O)OR^{11}$, $NR^{11}C(O)NR^{11}R^{12}$, $NR^{11}S(O)_pR^a$, $–NR^{11}S(O)_p(OR^{11})$ or $NR^{11}SO_pNR^{11}R^{12}$; and

wherein each $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, C_6-C_{20} aryl, C_2-C_{20} heterocyclyl, $(C_3$-$C_7)$cycloalkyl or $(C_4$-$C_8)$carbocyclylalkyl of each R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11} or R^{12} is, independently, optionally substituted with one or more oxo, halogen, hydroxy, NH_2, CN, N_3, $N(R^a)_2$, NHR^a, SH, SR^a, $S(O)_pR^a$, OR^a, $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $–C(O)R^a$, –C(O)H, $–C(=O)OR^a$, –C(=O)OH, $–C(=O)N(R^a)_2$, $–C(=O)NHR^a$, $–C(=O)NH_2$, $NHS(O)_pR^a$, $NR^aS(O)_pR^a$, $NHC(O)R^a$, $NR^aC(O)R^a$, $NHC(O)OR^a$, $NR^aC(O)OR^a$,

$NR^aC(O)NHR^a$, $NR^aC(O)N(R^a)_2$, $NR^aC(O)NH_2$, $NHC(O)NHR^a$, $NHC(O)N(R^a)_2$, $NHC(O)NH_2$, =NH, =NOH, $=NOR^a$, $NR^aS(O)_pNHR^a$, $NR^aS(O)_pN(R^a)_2$, $NR^aS(O)_pNH_2$, $NHS(O)_pNHR^a$, $NHS(O)_pN(R^a)_2$, $NHS(O)_pNH_2$, $-OC(=O)R^a$, $-OP(O)(OH)_2$ or R^a.

53. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B21) having the structure:



(I)

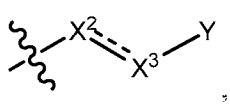
wherein:

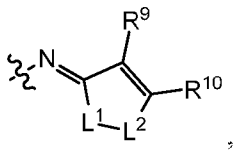
A is selected from the group consisting of an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-2} alkyl), an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

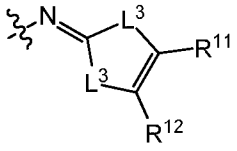
W is O, S, C=O, C=S, NR^{3a3}, S=O, $S(=O)_2$ or $-C(R^{1a1})(R^{1a2})-$;

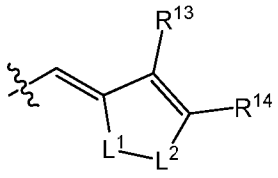
V is N or CH;

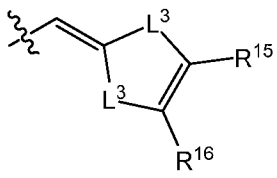
E is C or N; provided that when E is N, then R^{2a1} is absent;

Z is selected from the group consisting of 

, 

, 

, 

and 

;

Y is selected from the group consisting of an optionally substituted acylalkyl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

--------- between X^2 and X^3 represents a single or double bond between X^2 and X^3;

wherein when ------ is a double bond, then X^1 is NR^{3a1} or $CR^{3a2}R^6$, X^2 is N (nitrogen) or CR^{7a1}, and X^3 is N (nitrogen) or CR^4; and when -------- is a single bond, then X^1 is NR^{3a1} or $CR^{3a2}R^6$, X^2 is O, NR^7, C(=O) or $C(R^{7a2})(R^{7a3})$, and X^3 is NR^4, C(=O), CR^4R^8 or $CH_2CH_2C(=O)$; or

X^1, X^2 and X^3 are each independently C (carbon), N (nitrogen), O (oxygen) or C(=O), and form a mono-cyclic ring selected from the group consisting of an optionally substituted mono-cyclic heteroaryl and an optionally substituted mono-cyclic heterocyclyl by joining X^1 and X^3 together; and provided that at least one of X^1, X^2 and X^3 comprises a nitrogen atom, with the proviso that the valencies of X^1, X^2 and X^3 are satisfied with a substituent selected from the group consisting of hydrogen and an optionally substituted C_{1-4} alkyl; and X^1, X^2 and X^3 are uncharged;

L^1 is $-C(R^{17})_2-$, $-C(R^{18})_2C(R^{18a1})_2-$, $-C(R^{18a2})=C(R^{18a3})-$ or $-C(R^{19})_2N(R^{19a1})-$;

L^2 is $-C(R^{20})_2-$, $-N(R^{21})-$, S, or O;

each L^3 is independently $-C(R^{22})_2-$, $-C(R^{23})_2C(R^{23a1})_2-$ or $-C(R^{23a2})=C(R^{23a3})-$;

provided that when L^1 is $-C(R^{19})_2N(R^{19a1})-$, then L^2 is $-C(R^{20})_2-$;

R^1 is hydrogen or an unsubstituted C_{1-4} alkyl;

R^{1a1} and R^{1a2} are each independently hydrogen, hydroxy or an unsubstituted C_{1-4} alkyl;

R^2 and R^{2a1} are each independently selected from the group consisting of hydrogen, an optionally substituted C_{1-4} alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, hydroxy, 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); or

R^1 and R^2, together with the atoms to which they are attached, are joined to form an optionally substituted 5-membered heterocyclic ring or an optionally substituted 6-membered heterocyclic ring, R^{2a1} is selected from the group consisting of hydrogen, an optionally substituted C_{1-4} alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, hydroxy, 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);

R^{3a1}, R^{3a2} and R^{3a3} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^4 is selected from the group consisting of hydrogen, an optionally substituted C_{1-8} alkyl, an optionally substituted C_{2-8} alkenyl, an optionally substituted C_{2-8} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted C_{3-6} cycloalkyl(C_{1-6} alkyl), an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl(C_{1-6} alkyl), an optionally substituted heterocyclyl(C_{1-6} alkyl), halo(C_{1-8} alkyl), an optionally substituted hydroxyalkyl, an optionally substituted alkoxyalkyl and cyano;

R^6, R^7, and R^{7a1} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^{7a2} and R^{7a3} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^8 is hydrogen or optionally substituted C_{1-4} alkyl;

R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15} and R^{16} are each independently hydrogen or an unsubstituted C_{1-4} alkyl; or R^9 and R^{10}, R^{11} and R^{12}, R^{13} and R^{14}, and R^{15} and R^{16}, are each independently taken together form an optionally substituted cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl or an optionally substituted heterocyclyl; and

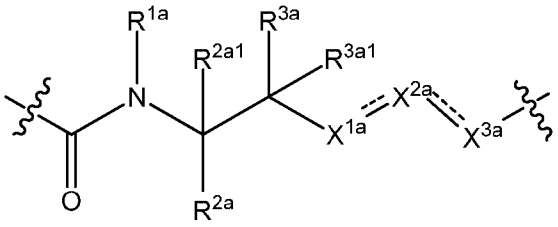
each R^{17}, each R^{18}, each R^{18a1}, R^{18a2}, R^{18a3}, each R^{19}, R^{19a1}, each R^{20}, R^{21}, each R^{22}, each R^{23}, each R^{23a1}, R^{23a2} and R^{23a3} are each independently hydrogen or an unsubstituted C_{1-4} alkyl.

54. The method or use of any one of Claims 1-8, wherein Compound (B) is Formula (B22) having the structure:

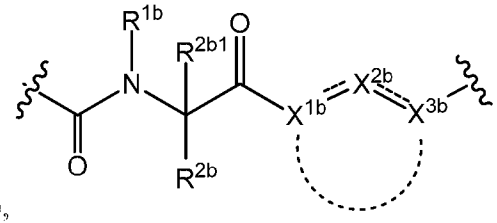


(I)

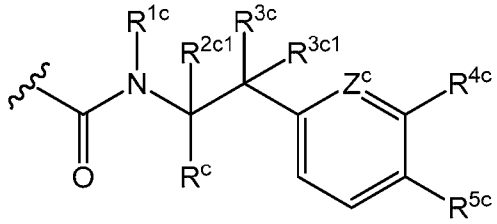
wherein: L is selected from the group consisting of:



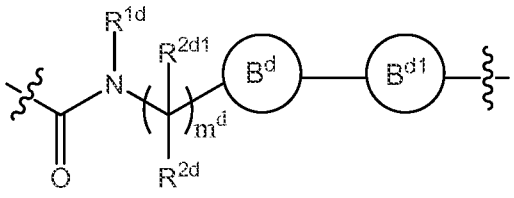
(Ia),



(Ib),



(Ic) and



(Id);

A is selected from the group consisting of an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted aryl(C_{1-2} alkyl), an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

Y is selected from the group consisting of an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

R^{1a}, R^{1b}, R^{1c} and R^{1d} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

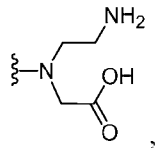
R^{2a}, R^{2a1}, R^{2b}, R^{2b1}, R^{2c}, R^{2c1}, R^{2d} and R^{2d1} are each independently selected from the group consisting of hydrogen, an optionally substituted C_{1-4} alkyl, an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heterocyclyl(C_{1-6} alkyl), an alkoxyalkyl, an aminoalkyl, a hydroxyalkyl and hydroxy; or

R^{2a1} is hydrogen, and R^{1a} and R^{2a} is joined together with the atoms to which they are attached to form an optionally substituted 5 membered heterocyclyl or an optionally substituted 6 membered heterocyclyl, R^{2b1} is hydrogen, and R^{1b} and R^{2b} is joined together with the atoms to which they are attached to form an optionally substituted 5 membered heterocyclyl or an optionally substituted 6 membered heterocyclyl;

--------- between X^{1a} and X^{2a} represents a single or double bond between X^{1a} and X^{2a}; --------- between X^{2a} and X^{3a} represents a single or double bond between X^{2a} and X^{3a}; provided that --------- between X^{1a} and X^{2a} and --------- between X^{2a} and X^{3a} cannot be both double bonds and at least one of --------- is a double bond;

when --------- between X^{1a} and X^{2a} represents a double bond and --------- between X^{2a} and X^{3a} is a single bond, then X^{1a} is N or CR^{4a1}, X^{2a} is N or CR^{5a} and X^{3a} is NR^{6a1}, C(=O) or $CR^{6a2}R^{6a3}$; and when --------- between X^{1a} and X^{2a} represents a single bond and --------- between X^{2a} and X^{3a} is a double bond, then X^{1a} is NR^{4a} or $CR^{4a2}R^{4a3}$, X^{2a} is N or CR^{5a} and X^{3a} is N or CR^{6a}; or

X^{1a}, X^{2a} and X^{3a} are each independently C, N, O or C(=O), and form a ring or ring system selected from an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl by joining X^{1a} and X^{3a} together; with the proviso that the valencies of X^{1a}, X^{2a} and X^{3a} can be each independently satisfied with a substituent selected from hydrogen and an optionally substituted C_{1-4} alkyl, and X^{1a}, X^{2a} and X^{3a} are uncharged;

R^{3a} and R^{3a1} are each independently selected from the group consisting of hydrogen, hydroxy, halogen, amino, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{2-4} alkenyl, an optionally substituted C_{2-4} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{1-4} alkoxy, -O-carboxy, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, CHF_2, CF_3 and , provided that R^{3a} and R^{3a1} cannot be both hydrogen; or R^{3a} and R^{3a1} together form =N-OR^a; or R^{3a} and R^{3a1} together

with the atom to which they are attached can be joined to form an optionally substituted 3 membered ring, an optionally substituted 4 membered ring, an optionally substituted 5 membered ring or an optionally substituted 6 membered ring;

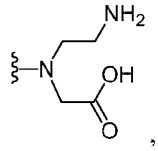
R^{4a}, R^{4a1}, R^{4a2} and R^{4a3} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^{5a} and R^{5a1} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^{6a} and R^{6a1} are each independently hydrogen, an optionally substituted C_{1-4} alkyl or an optionally substituted alkoxyalkyl;

R^{6a2} and R^{6a3} are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

X^{1b}, X^{2b} and X^{3b} are each independently C, N, O or C(=O), and form indicates a bi-cyclic ring selected from an optionally substituted bi-cyclic heteroaryl and an optionally substituted bi-cyclic heterocyclyl by joining X^{1b} and X^{3b} together, wherein --------- between X^{1b} and X^{2b} represents a single or double bond between X^{1b} and X^{2b}; --------- between X^{2b} and X^{3b} represents a single or double bond between X^{2b} and X^{3b}; and provided that at least one of X^{1b}, X^{2b} and X^{3b} comprises a nitrogen atom and both --------- cannot be double bonds; with the proviso that the valencies of X^{1b}, X^{2b} and X^{3b} can be each independently satisfied with a substituent selected from hydrogen and an optionally substituted C_{1-4} alkyl; and X^{1b}, X^{2b} and X^{3b} are uncharged;

R^{3c} and R^{3c1} are each independently selected from the group consisting of hydrogen, hydroxy, halogen, amino, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{2-4} alkenyl, an optionally substituted C_{2-4} alkynyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_{1-4} alkoxy, -O-carboxy, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, CHF_2, CF_3 and , provided that R^{3c} and R^{3c1} cannot be both hydrogen; or R^{3c} and R^{3c1} together form =N-OR^c; or R^{3c} and R^{3c1} together with the atom to which they are attached can be joined to form an optionally substituted 3 membered ring, an optionally substituted 4 membered ring, an optionally substituted 5 membered ring or an optionally substituted 6 membered ring;

R^a and R^c are each independently hydrogen or an unsubstituted C_{1-4} alkyl;

R^{4c} and R^{5c} are taken together to form an unsubstituted aryl, an unsubstituted heteroaryl or an optionally substituted heterocyclyl;

Z^c is N or CH;

m^d is 0 or 1;

ring B^d is an optionally substituted C_5 cycloalkyl;

ring B^{d1} is an optionally substituted pyridinyl; and

provided that when L is Formula (IIc), then Y is absent.

55. The method or use of any one of Claims 1-54, wherein the method comprises one Compound (B), or a pharmaceutically acceptable salt thereof.

56. The method or use of any one of Claims 1-54, wherein the method comprises two of Compound (B), or a pharmaceutically acceptable salt thereof.

57. The method or use of any one of Claims 1-56, wherein R^2 is chloro.

58. The method or use of any one of Claims 1-56, wherein R^2 is azido.

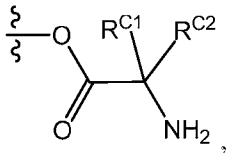
59. The method or use of any one of Claims 1-58, wherein R^3 is OH.

60. The method or use of any one of Claims 1-58, wherein R^3 is $-OC(=O)R^{A1}$.

61. The method or use of Claim 60, wherein R^{A1} is unsubstituted C_{1-8} alkyl.

62. The method or use of any one of Claims 1-58, wherein R^3 is an optionally substituted O-linked amino acid.

63. The method or use of Claim 62, wherein the optionally substituted O-linked amino acid is selected from the group consisting of alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, ornithine, hypusine, 2-aminoisobutyric acid, dehydroalanine, gamma-aminobutyric acid, citrulline, beta-alanine, alpha-ethyl-glycine, alpha-propyl-glycine and norleucine.

64. The method or use of Claim 62, wherein the optionally substituted O-linked amino acid has the structure , wherein R^{C1} 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^{C2} can be hydrogen or an optionally substituted C_{1-4} alkyl; or R^{C1} and R^{C2} can be taken together to form an optionally substituted C_{3-6} cycloalkyl.

65. The method or use of any one of Claims 1-64, wherein R^1 is hydrogen.

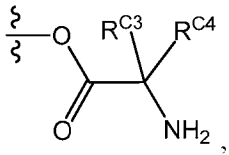
66. The method or use of any one of Claims 1-64, wherein R^1 is an optionally substituted acyl.

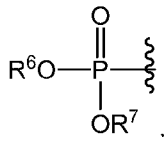
67. The method or use of Claim 66, wherein the optionally substituted acyl is $-C(=O)R^{B1}$, wherein R^{B1} is an optionally substituted C_{1-24} alkyl or an optionally substituted C_{3-6} cycloalkyl.

68. The method or use of Claim 67, wherein R^{B1} is unsubstituted C_{1-8} alkyl.

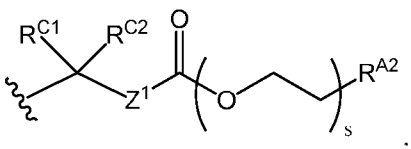
69. The method or use of any one of Claims 1-64, wherein R^1 is an optionally substituted O-linked amino acid.

70. The method or use of Claim 69, wherein the optionally substituted O-linked amino acid is selected from the group consisting of alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, tyrosine, arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, ornithine, hypusine, 2-aminoisobutyric acid, dehydroalanine, gamma-aminobutyric acid, citrulline, beta-alanine, alpha-ethyl-glycine, alpha-propyl-glycine and norleucine.

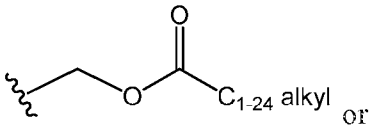
71. The method or use of Claim 69, wherein the optionally substituted O-linked amino acid has the structure , wherein R^{C3} can be selected from hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted C_{1-6} haloalkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted C_6 aryl, an optionally substituted C_{10} aryl and an optionally substituted aryl(C_{1-6} alkyl); and R^{C4} can be hydrogen or an optionally substituted C_{1-4} alkyl; or R^{C3} and R^{C4} can be taken together to form an optionally substituted C_{3-6} cycloalkyl.

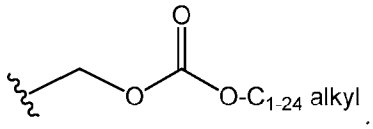
72. The method or use of any one of Claims 1-64, wherein R^1 is .

73. The method or use of Claim 72, wherein R^6 and R^7 are independently absent or H.

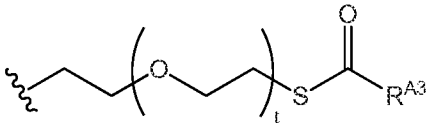
74. The method or use of Claim 72, wherein R^6 and R^7 are independently .

75. The method or use of Claim 74, wherein R^6 and R^7 are independently

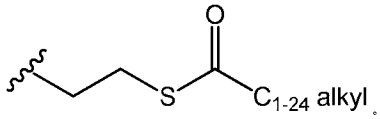


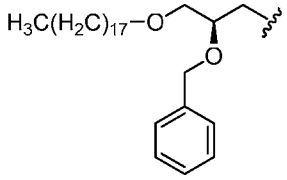
or


76. The method or use of Claim 72, wherein R^6 and R^7 are independently



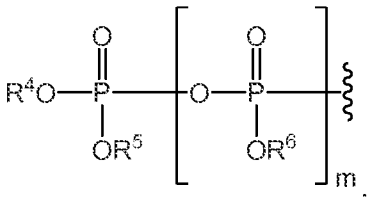
77. The method or use of Claim 76, wherein R^6 and R^7 are independently





78. The method or use of Claim 72, wherein one of R^6 and R^7 is , and the other of R^6 and R^7 is absent or H.

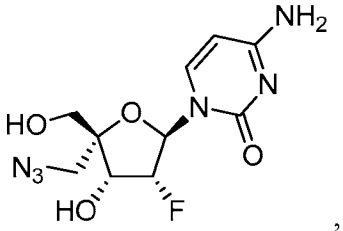
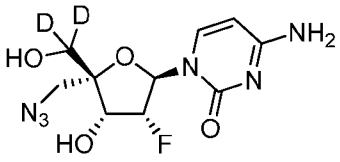
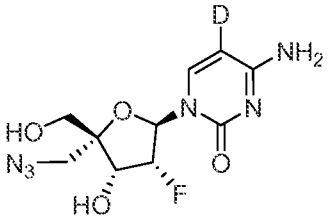
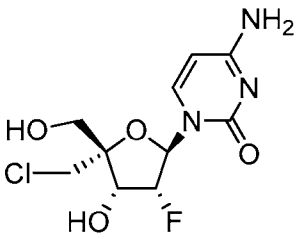
79. The method or use of any one of Claims 2-64, wherein R^1 is



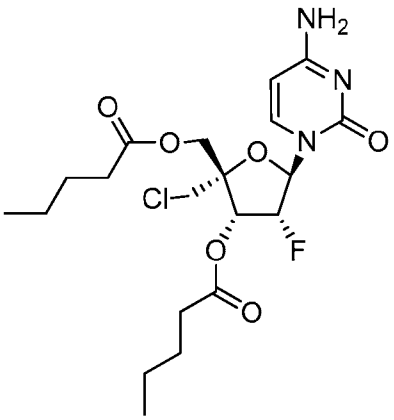
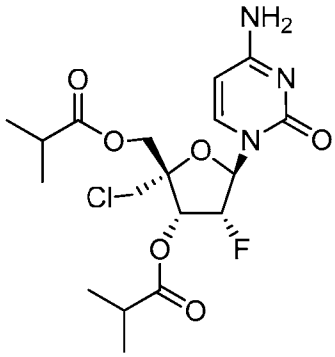
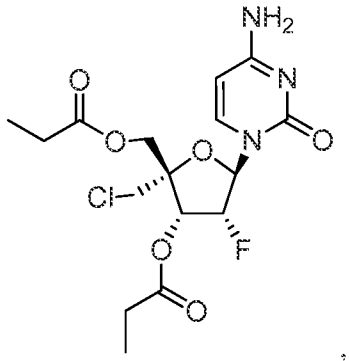
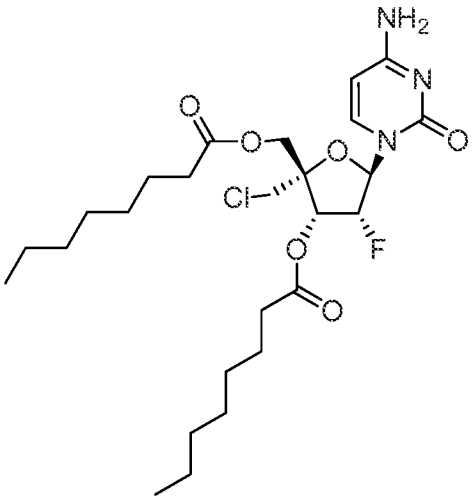
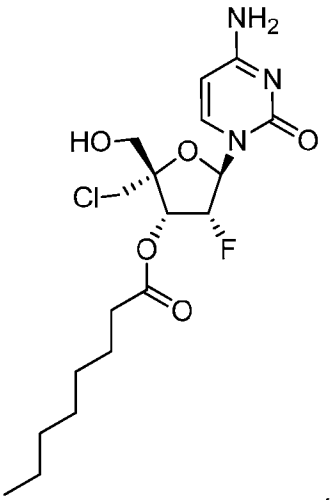
80. The method or use of Claim 79, wherein m is 1.

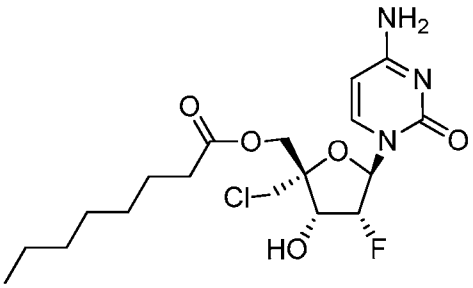
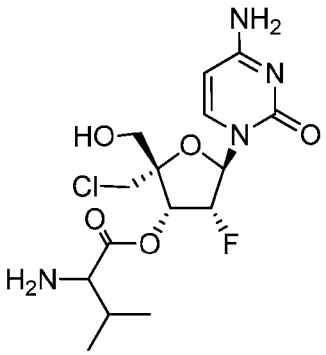
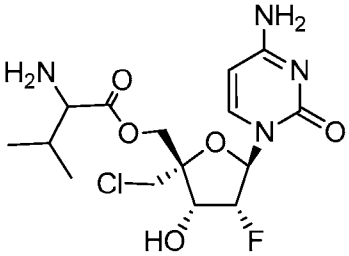
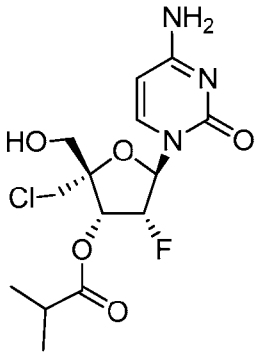
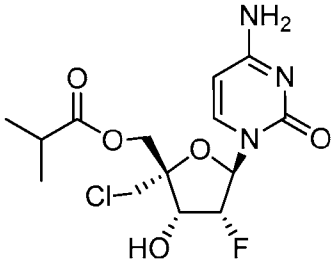
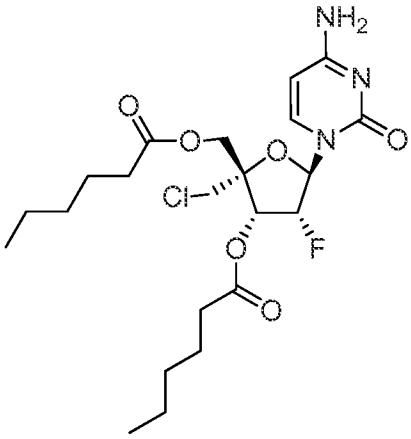
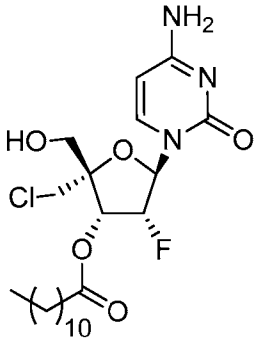
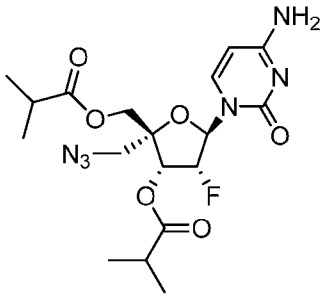
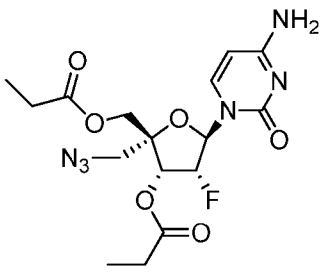
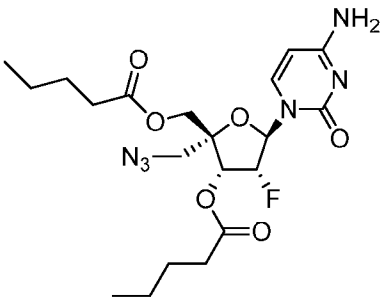
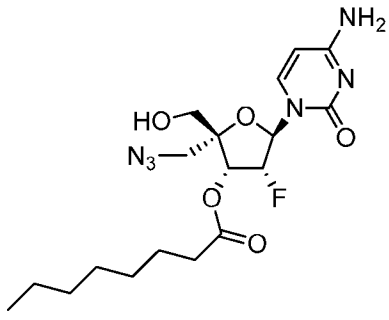
81. The method or use of Claim 79, wherein m is 2.

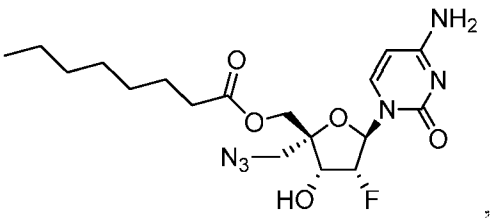
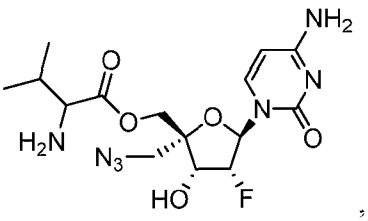
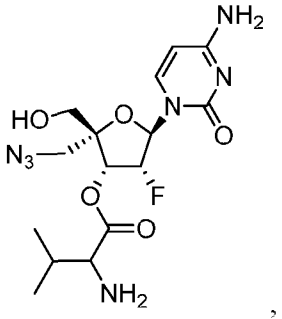
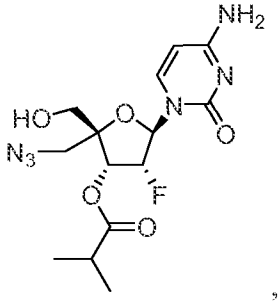
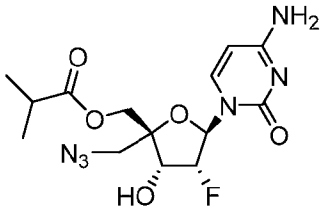
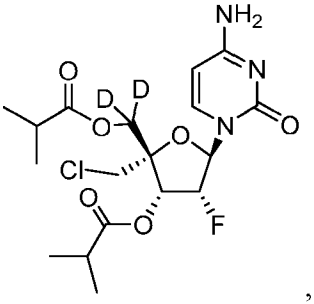
82. The method or use of any one of Claims 1-56, wherein Compound (A) is selected from the group consisting of:


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and

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

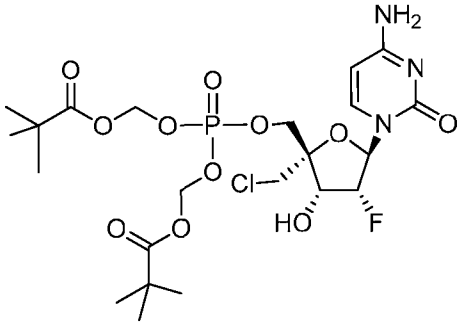
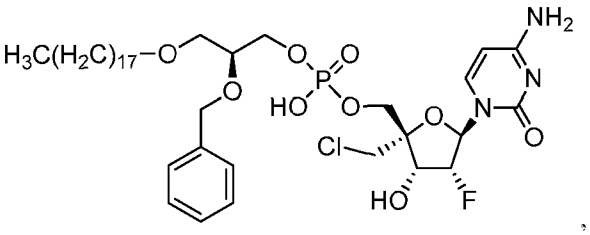
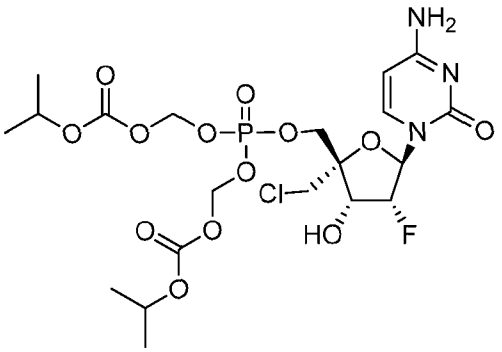
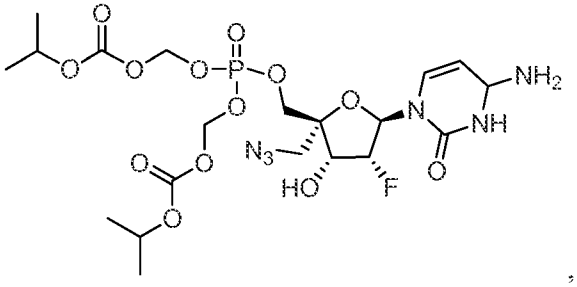
83. The method or use of any one of Claims 1-56, wherein Compound (A) is selected from the group consisting of:

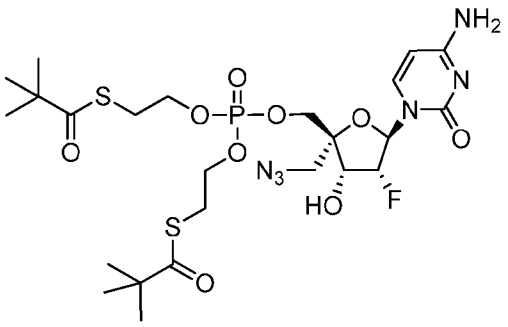

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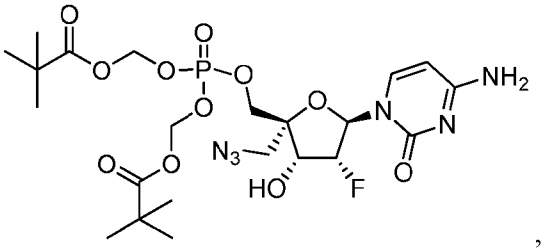

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and

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

84. The method or use of any one of Claims 1-56, wherein Compound (A) is selected from the group consisting of:


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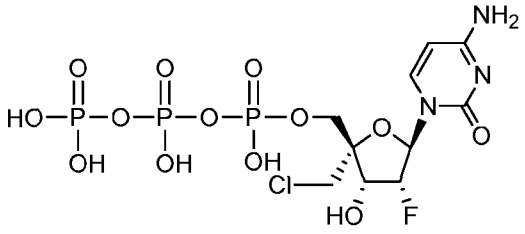


and

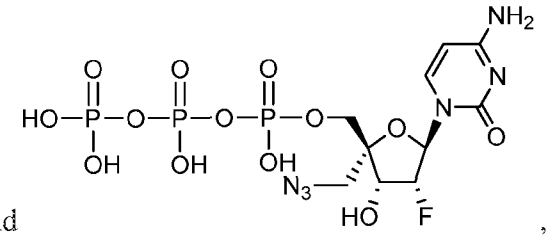


, or a pharmaceutically acceptable salt of any of the foregoing.

85. The method or use of any one of Claims 2-56, wherein Compound (A) is selected from the group consisting of:



and



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