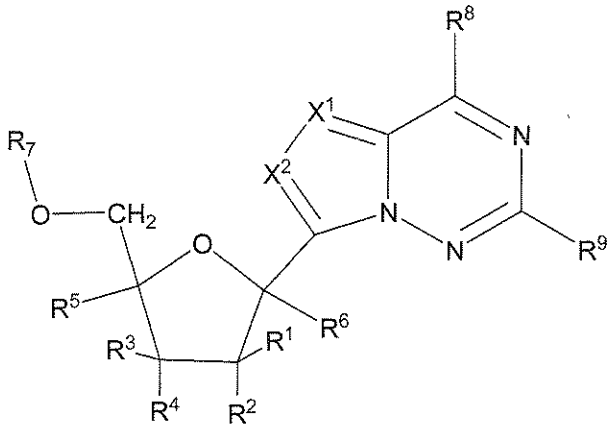
SUMMARY ~~OF THE INVENTION~~

Provided are compounds that inhibit viruses of the *Flaviviridae* family. The ~~invention~~disclosure also comprises compounds of Formula I or Formula IV-VI that inhibit viral nucleic acid polymerases, particularly HCV RNA-dependent RNA polymerase (RdRp), rather than cellular nucleic acid polymerases. The compounds of Formula I or Formula IV-VI have been discovered to be efficacious against both wild type and S282T mutant strains of HCV virus. Therefore, a compound of Formula I or Formula IV-VI are useful for treating *Flaviviridae* infections in humans and other animals.

In one embodiment, provided are compounds of Formula I:



Formula I

or a pharmaceutically acceptable salt, thereof;

wherein:

R^1 is $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl$(C_1$-$C_8)$alkyl;

R^2 is halogen;

each R^3, R^4, or R^5 is independently H, OR^a, $N(R^a)_2$, N_3, CN, NO_2, $S(O)_nR^a$, halogen, $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl$(C_1$-$C_8)$alkyl;

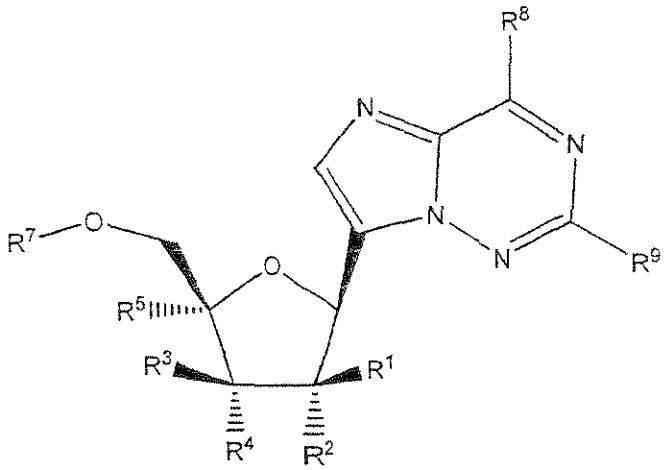
each R^8 is halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, N_3, NO, NO_2, CHO, CN, -CH(=NR^{11}), -CH=$NNHR^{11}$, -CH=$N(OR^{11})$, -$CH(OR^{11})_2$, -C(=O)$NR^{11}R^{12}$, -C(=S)$NR^{11}R^{12}$, -C(=O)OR^{11}, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, $(C_4$–$C_8)$carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, -C(=O)$(C_1$-$C_8)$alkyl, -$S(O)_n(C_1$-$C_8)$alkyl, aryl$(C_1$-$C_8)$alkyl, OR^{11} or SR^{11};

each R^9 or R^{10} is independently H, halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, N_3, NO, NO_2, CHO, CN, -CH(=NR^{11}), -CH=$NHNR^{11}$, -CH=$N(OR^{11})$, -$CH(OR^{11})_2$, -C(=O)$NR^{11}R^{12}$, -C(=S)$NR^{11}R^{12}$, -C(=O)OR^{11}, R^{11}, OR^{11} or SR^{11};

each R^{11} or R^{12} is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, $(C_4$–$C_8)$carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, -C(=O)$(C_1$-$C_8)$alkyl, -$S(O)_n(C_1$-$C_8)$alkyl 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- or –NR^a-;

wherein each $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl or aryl$(C_1$-$C_8)$alkyl of each R^1, R^3, R^4, R^5, R^6, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^a)_2$ or OR^a; and wherein one or more of the non-terminal carbon atoms of each said $(C_1$-$C_8)$alkyl may be optionally replaced with -O-, -S- or –NR^a-.

In one aspect, there is provided a compound of Formula IV:



Formula IV

or a pharmaceutically acceptable salt, thereof;

wherein:

R^1 is CH_3 or CH_2CH_3;

R^2 is F;

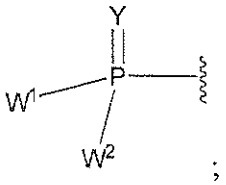
R^3, R^4, and R^5 are each independently H, halogen, OR^a, $N(R^a)_2$, N_3, CN, NO_2, $S(O)_nR^a$, $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl$(C_1$-$C_8)$alkyl;

or any two of R^3, R^4 or R^5 on adjacent carbon atoms when taken together are –O(CO)O- or when taken together with the ring carbon atoms to which they are attached form a double bond;

each n is independently 0, 1, or 2;

each R^a is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, or $–SO_2NR^{11}R^{12}$;

R^7 is H, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, $–SO_2NR^{11}R^{12}$, or



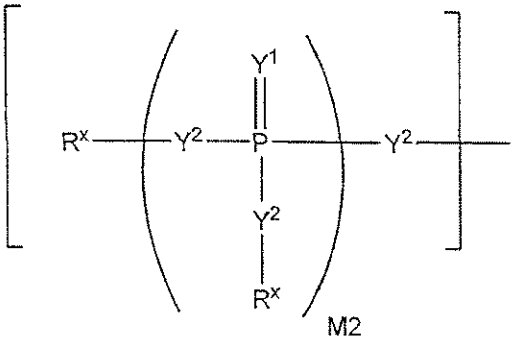
;

Y is O, S, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), or N–NR_2;

W^1 and W^2, when taken together, are $-Y^3(C(R^y)_2)_3Y^3-$; or

one of W^1 or W^2 together with either R^3 or R^4 is $-Y^3-$ and the other of W^1 or W^2 is Formula IVa; or

W^1 and W^2 are each, independently, a group of Formula IVa:



Formula IVa

wherein:

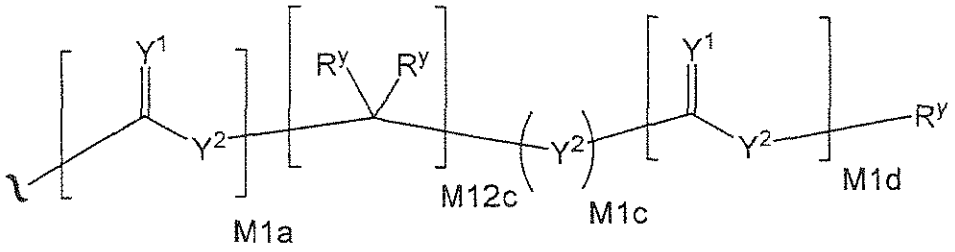
each Y^1 is, independently, O, S, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), or N–NR_2;

each Y^2 is independently a bond, O, CR_2, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), N–NR_2, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula IVb:



Formula IVb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, -C(=Y^1)R, -C(=Y^1)R^{13}, -C(=Y^1)OR, -C(=Y^1)N(R_2), -N(R_2), -$^+$N(R_3), -SR, -S(O)R, -S(O)$_2$R, -S(O)$_2$$R^{13}$, -S(O)(OR), -S(O)$_2$(OR), -OC(=$Y^1$)R, -OC(=$Y^1$)OR, -OC(=$Y^1$)(N($R_2$)), -SC(=$Y^1$)R, -SC(=$Y^1$)OR, -SC(=$Y^1$)(N($R_2$)), -N(R)C(=$Y^1$)R, -N(R)C(=$Y^1$)OR, -N(R)C(=$Y^1$)N($R_2$), $-SO_2NR_2$, –OR, (C_1-C_8) alkyl, C_3–C_{20} carbocyclyl, heteroarylalkyl;

wherein each (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6–C_{20} aryl, C_3–C_{20} carbocyclyl, C_2–C_{20} heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

or when taken together, two R^y on the same carbon atom form a carbocyclic ring of 3 to 7 carbon atoms;

each R is independently H, (C_1-C_8) alkyl,C_3–C_{20} carbocyclyl;

each R^8 is halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, OR^{11} or $S(O)_nR^{11}$;

each R^9 is independently H, halogen, $NR^{11}R^{12}$ or $S(O)_nR^{11}$;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4–C_8)carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, -C(=O)(C_1-C_8)alkyl, -S(O)$_n$(C_1-C_8)alkyl 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- or –NR^b-;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, $-S(O)R$, $-S(O)_2R$, $-S(O)(OR)$, $-S(O)_2(OR)$, $-C(=Y^1)R$, $-C(=Y^1)OR$, or $C(=Y^1)N(R)_2$;

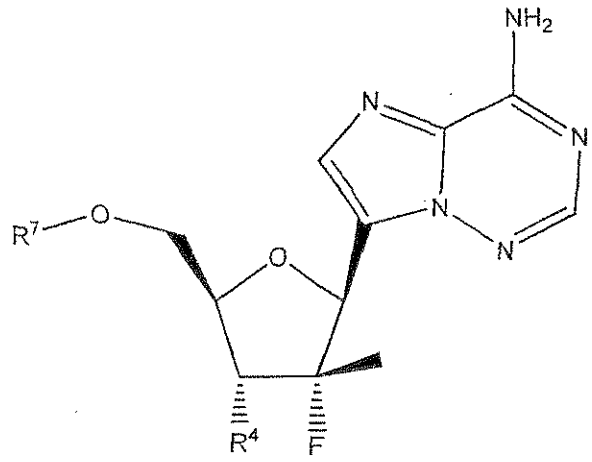
wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or aryl(C_1-C_8)alkyl of each R^1, R^3, R^4, R^5, R^6, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said (C_1-C_8)alkyl may be optionally replaced with -O-, -S- or $-NR^b$;

each R^b 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_4-C_8)carbocyclylalkyl, $-C(=O)R^{21}$, $-C(=O)OR^{21}$, $-C(=O)NR^{21}R^{22}$, $-C(=O)SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)(OR^{21})$, $-S(O)_2(OR^{21})$, or $-SO_2NR^{21}R^{22}$; and

each R^{21} or R^{22} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)(C_1-C_8)$alkyl, $-S(O)_n(C_1-C_8)$alkyl or aryl(C_1-C_8)alkyl.

In another embodiment, provided are compounds of Formula I or Formula IV-VI and pharmaceutically acceptable salts thereof and all racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and amorphous forms thereof.

In one aspect, there is provided a compound of Formula VI:



Formula VI

or a pharmaceutically acceptable salt, thereof;

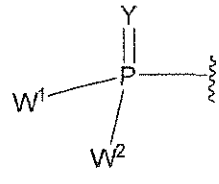
wherein:

R^4 is OR^a;

each n is independently 0, 1, or 2;

each R^a is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_4$–$C_8)$carbocyclylalkyl, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, or –$SO_2NR^{11}R^{12}$;

R^7 is H, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, –$SO_2NR^{11}R^{12}$, or



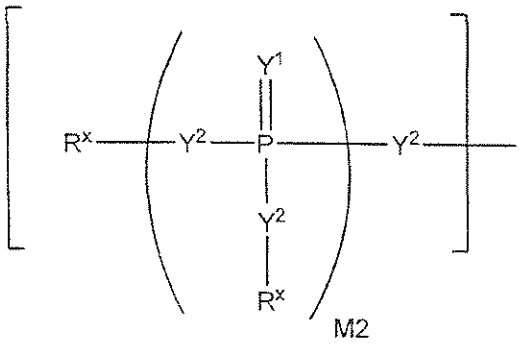
;

Y is O, S, NR, $^+$N(O)(R), N(OR), $^+$N(O)(OR), or N–NR_2;

W^1 and W^2, when taken together, are $–Y^3(C(R^y)_2)_3Y^3$-; or

one of W^1 or W^2 together with R^4 is $–Y^3$- and the other of W^1 or W^2 is Formula VIa; or

W^1 and W^2 are each, independently, a group of Formula VIa:



Formula VIa

wherein:

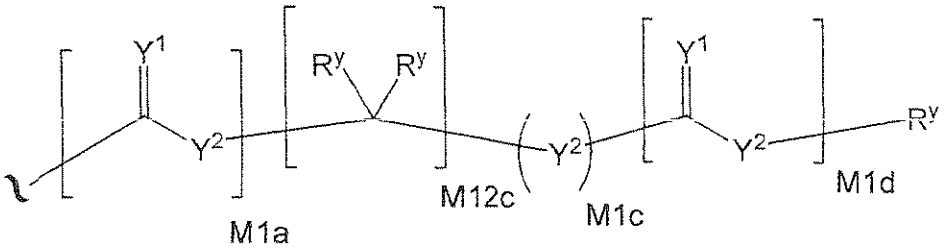
each Y^1 is, independently, O, S, NR, $^+N(O)(R)$, N(OR), $^+N(O)(OR)$, or $N–NR_2$;

each Y^2 is independently a bond, O, CR_2, NR, $^+N(O)(R)$, N(OR), $^+N(O)(OR)$, $N–NR_2$, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula VIb:



Formula VIb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, F, Cl, Br, I, OH, $-C(=Y^1)R$, $-C(=Y^1)R^{13}$, $-C(=Y^1)OR$, $-C(=Y^1)N(R)_2$, $-N(R)_2$, $-^+N(R)_3$, -SR, -S(O)R, $-S(O)_2R$, $-S(O)_2R^{13}$, -S(O)(OR), $-S(O)_2(OR)$, $-OC(=Y^1)R$, $-OC(=Y^1)OR$, $-OC(=Y^1)(N(R)_2)$, $-SC(=Y^1)R$, -

$SC(=Y^1)OR$, $-SC(=Y^1)(N(R)_2)$, $-N(R)C(=Y^1)R$, $-N(R)C(=Y^1)OR$, $-N(R)C(=Y^1)N(R)_2$, $-SO_2NR_2$, –CN, $–N_3$, $–NO_2$, –OR, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, $C_6–C_{20}$ aryl, $C_3–C_{20}$ carbocyclyl, $C_2–C_{20}$ heterocyclyl, arylalkyl, heteroarylalkyl;

wherein each (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, $C_6–C_{20}$ aryl, $C_3–C_{20}$ carbocyclyl, $C_2–C_{20}$ heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

each R is independently H, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, $C_6–C_{20}$ aryl, $C_3–C_{20}$ carbocyclyl, $C_2–C_{20}$ heterocyclyl, or arylalkyl;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, $(C_4–C_8)$carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)(C_1-C_8)$alkyl, $-S(O)_n(C_1-C_8)$alkyl or aryl(C_1-C_8)alkyl;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

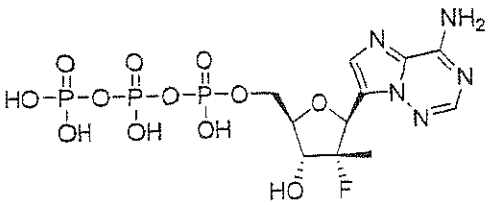
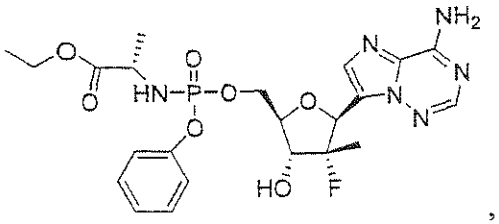
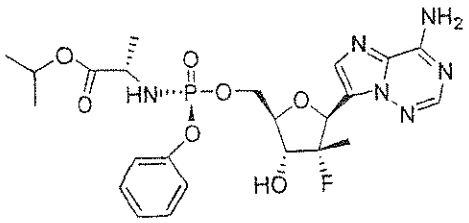
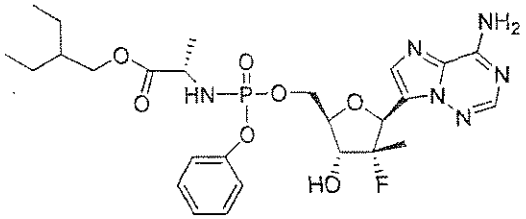
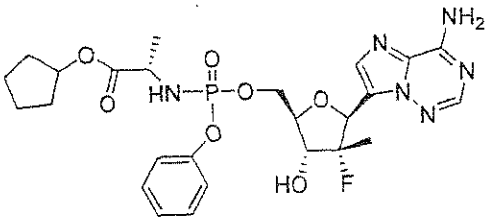
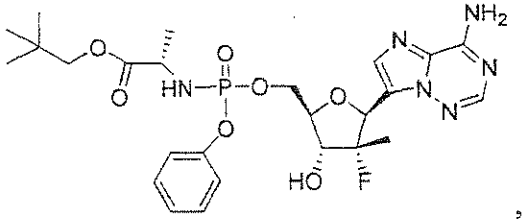
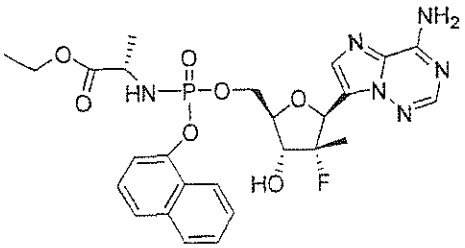
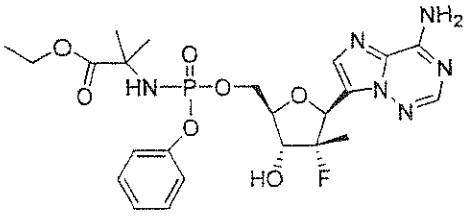
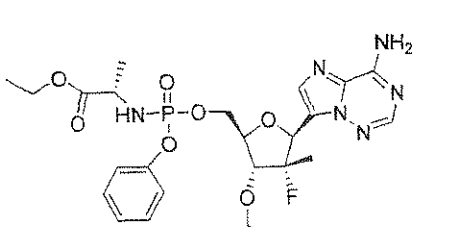
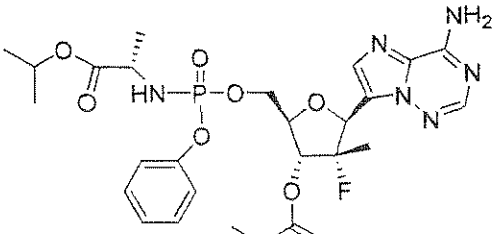
each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, $-S(O)R$, $-S(O)_2R$, $-S(O)(OR)$, $-S(O)_2(OR)$, $-C(=Y^1)R$, $-C(=Y^1)OR$, or $C(=Y^1)N(R)_2$;

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or aryl(C_1-C_8)alkyl of each R^4, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said (C_1-C_8)alkyl may be optionally replaced with -O-, -S- or $–NR^b$;

each R^b is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, $(C_4–C_8)$carbocyclylalkyl, $-C(=O)R^{21}$, $-C(=O)OR^{21}$, $-C(=O)NR^{21}R^{22}$, $-C(=O)SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)(OR^{21})$, $-S(O)_2(OR^{21})$, or $–SO_2NR^{21}R^{22}$; and

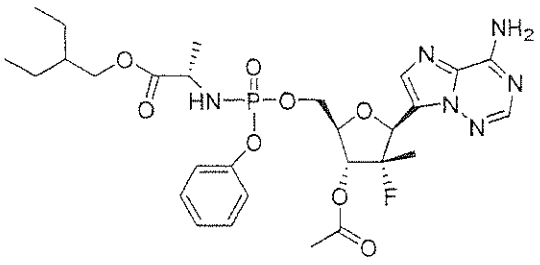
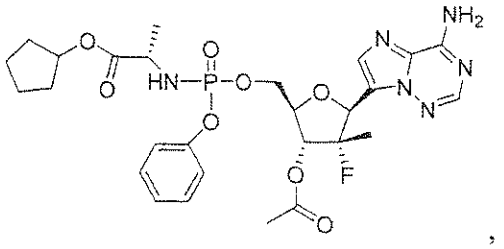
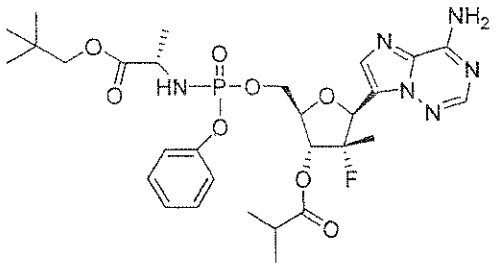
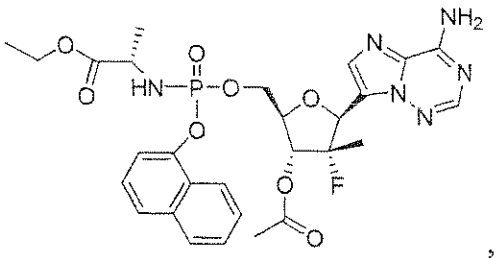
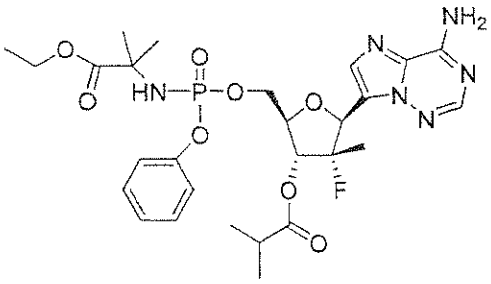
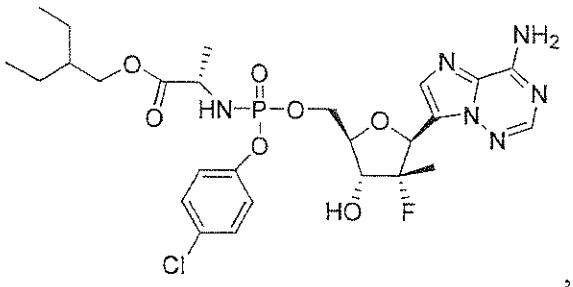
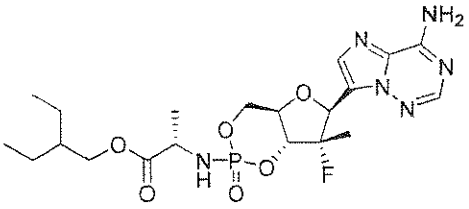
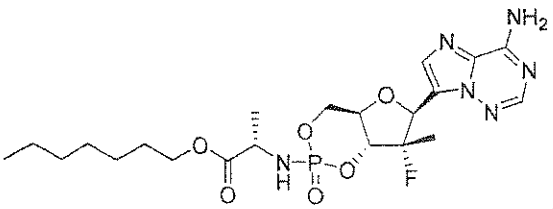
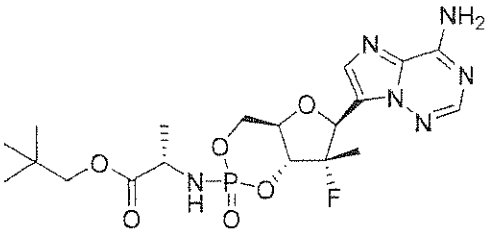
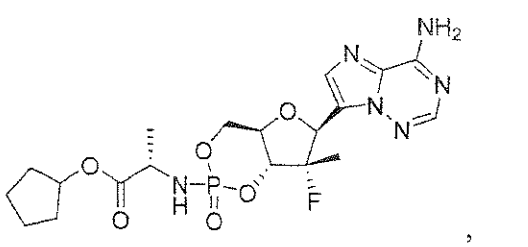
each R^{21} or R^{22} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, $(C_4–C_8)$carbocyclylalkyl, $-C(=O)(C_1-C_8)$alkyl, $-S(O)_n(C_1-C_8)$alkyl or aryl(C_1-C_8)alkyl.

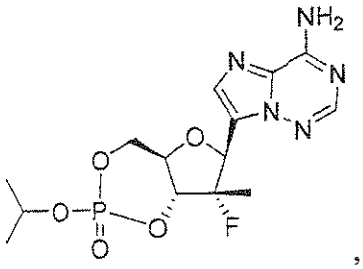
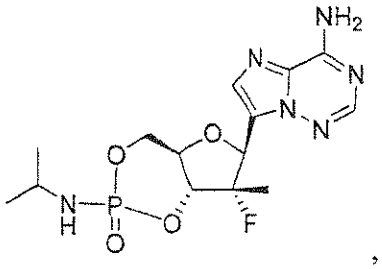
In one aspect, there is provided a compound having a structure:

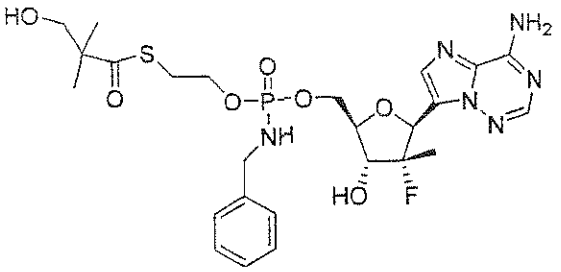

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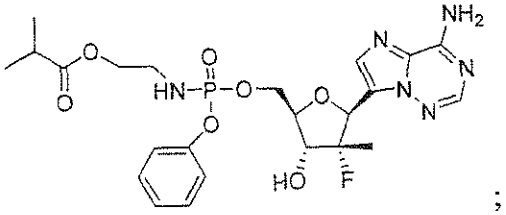
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or a pharmaceutically acceptable salt, thereof.

In another embodiment, provided are novel compounds of Formula I or Formula IV-VI with activity against infectious *Flaviviridae* viruses. Without wishing to be bound by theory, the compounds of the ~~invention~~disclosure may inhibit viral RNA-dependent RNA polymerase and thus inhibit the replication of the virus. They are useful for treating human patients infected with a human virus such as hepatitis C.

In another embodiment, provided are pharmaceutical compositions comprising an effective amount of a Formula I or a Formula IV-VI compound, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable diluent or carrier.

In one aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as described herein and a pharmaceutically acceptable carrier.

In another embodiment, the present application provides for combination pharmaceutical agent comprising:

a) a first pharmaceutical composition comprising a compound of Formula I or Formula IV-VI; or a pharmaceutically acceptable salt, solvate, or ester thereof; and

b) a second pharmaceutical composition comprising at least one additional therapeutic agent selected from the group consisting of interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, NS5a inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, mevalonate decarboxylase antagonists, antagonists of the renin-angiotensin system, other anti-fibrotic agents, endothelin antagonists, nucleoside or nucleotide inhibitors of HCV NS5B polymerase, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophillin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers and other drugs for treating HCV; or mixtures thereof.

In another embodiment, the present application provides for a method of inhibiting HCV polymerase, comprising contacting a cell infected with HCV with an effective amount of a compound of Formula I or Formula IV-VI; or a pharmaceutically acceptable salts, solvate, and/or ester thereof.

In another embodiment, the present application provides for a method of inhibiting HCV polymerase, comprising contacting a cell infected with HCV with an effective amount of a compound of Formula I or Formula IV-VI; or a pharmaceutically acceptable salts, solvate, and/or ester thereof; and at least one additional therapeutic agent.

In another embodiment, the present application provides for a method of treating and/or preventing a disease caused by a viral infection wherein the viral infection is caused by a virus selected from the group consisting of dengue virus,

yellow fever virus, West Nile virus, Japanese encephalitis virus, tick-borne encephalitis virus, Junjin virus, Murray Valley encephalitis virus, St Louis encephalitis virus, Omsk hemorrhagic fever virus, bovine viral diarrhea virus, Zika virus and Hepatitis C virus; by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I or Formula IV-VI, or a pharmaceutically acceptable salt thereof.

In another embodiment, the present application provides for a method of treating HCV in a patient, comprising administering to said patient a therapeutically effective amount of a compound of Formula I or Formula IV-VI; or a pharmaceutically acceptable salt, solvate, and/or ester thereof.

In another embodiment, the present application provides for a method of treating HCV in a patient, comprising administering to said patient a therapeutically effective amount of a compound of Formula I or Formula IV-VI; or a pharmaceutically acceptable salt, solvate, and/or ester thereof; and at least one additional therapeutic agent.

Another ~~aspect~~embodiment of the ~~invention~~disclosure provides a method for the treatment or prevention of the symptoms or effects of an HCV infection in an infected animal which comprises administering to, i.e. treating, said animal with a pharmaceutical combination composition or formulation comprising an effective amount of a Formula I compound or Formula IV-VI, and a second compound having anti-HCV properties.

In another ~~aspect~~embodiment, the ~~invention~~disclosure also provides a method of inhibiting HCV, comprising administering to a mammal infected with HCV an amount of a Formula I or Formula IV-VI compound, effective to inhibit the replication of HCV in infected cells in said mammal.

In another aspect, there is provided ~~is~~ the use of a compound as described herein in the preparation~~of Formula I or Formula IV-VI for the manufacture~~ of a medicament for the treatment of *Flaviviridae* virus~~viral~~ infections. In another ~~aspect~~embodiment, provided is a compound of Formula I or Formula IV-VI for use in treating a *Flaviviridae* viral infection. In one embodiment, the *Flaviviridae* viral infection is acute or chronic HCV infection. In one embodiment of each aspect

of use and compound, the treatment results in the reduction of one or more of the viral loads or clearance of RNA in the patient.

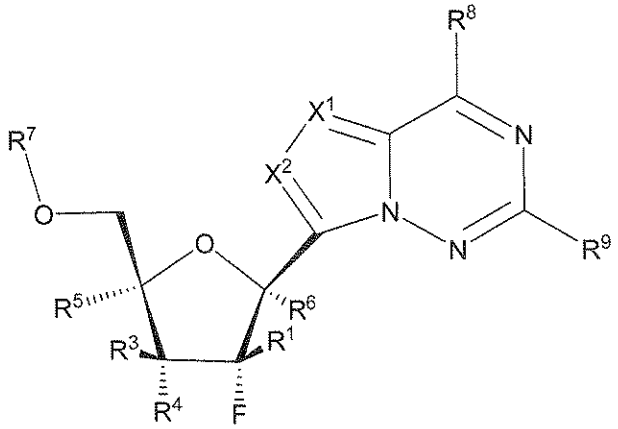
In another ~~aspect~~embodiment, the ~~invention~~disclosure also provides processes and novel intermediates disclosed herein which are useful for preparing Formula I or Formula IV-VI compounds of the ~~invention~~disclosure.

In other ~~aspects~~embodiments, novel methods for synthesis, analysis, separation, isolation, purification, characterization, and testing of the compounds of this ~~invention~~disclosure are provided.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

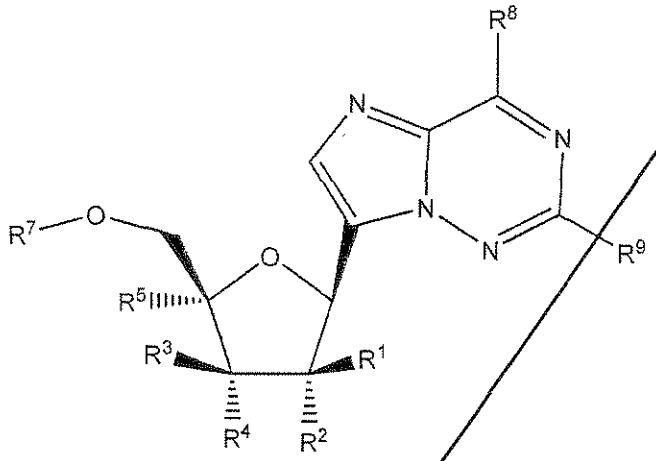
Reference will now be made in detail to certain embodiments of the invention, examples of which are illustrated in the accompanying description, structures and formulas. While the invention will be described in conjunction with the enumerated embodiments, it will be understood that they are not intended to limit the invention to those embodiments. On the contrary, the invention is intended to cover all alternatives, modifications, and equivalents, which may be included within the scope of the present invention.

In another aspect, compounds of Formula I are represented by Formula II:



What is claimed is

1. A compound of Formula IV:



Formula IV

or a pharmaceutically acceptable salt, thereof;

wherein:

R^1 is $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl$(C_1$-$C_8)$alkyl;

R^2 is halogen;

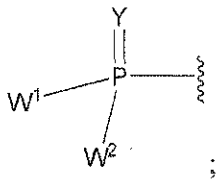
R^3, R^4, and R^5 are each independently H, halogen, OR^a, $N(R^a)_2$, N_3, CN, NO_2, $S(O)_nR^a$, $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl$(C_1$-$C_8)$alkyl;

or any two of R^3, R^4 or R^5 on adjacent carbon atoms when taken together are –O(CO)O- or when taken together with the ring carbon atoms to which they are attached form a double bond;

each n is independently 0, 1, or 2;

each R^a is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, or $–SO_2NR^{11}R^{12}$;

R^7 is H, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)N$R^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2$(OR^{11}), –$SO_2NR^{11}R^{12}$, or



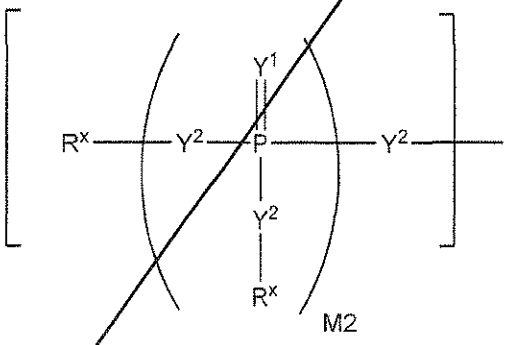
;

Y is O, S, NR, $^+$N(O)(R), N(OR), $^+$N(O)(OR), or N–NR_2;

W^1 and W^2, when taken together, are $–Y^3(C(R^y)_2)_3Y^3$-; or

one of W^1 or W^2 together with either R^3 or R^4 is $–Y^3$- and the other of W^1 or W^2 is Formula Ia; or

W^1 and W^2 are each, independently, a group of Formula IVa:



Formula IVa

wherein:

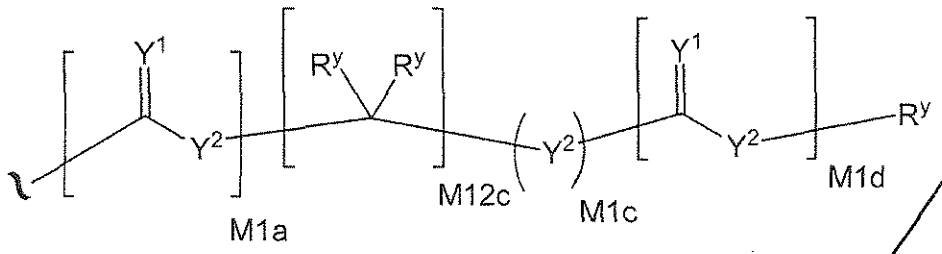
each Y^1 is, independently, O, S, NR, $^+$N(O)(R), N(OR), $^+$N(O)(OR), or N–NR_2;

each Y^2 is independently a bond, O, CR_2, NR, $^+$N(O)(R), N(OR), $^+$N(O)(OR), N–NR_2, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula IVb:



Formula IVb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, F, Cl, Br, I, OH, $-C(=Y^1)R$, $-C(=Y^1)R^{13}$, $-C(=Y^1)OR$, $-C(=Y^1)N(R)_2$, $-N(R)_2$, $-^+N(R)_3$, -SR, $-S(O)R$, $-S(O)_2R$, $-S(O)_2R^{13}$, $-S(O)(OR)$, $-S(O)_2(OR)$, $-OC(=Y^1)R$, $-OC(=Y^1)OR$, $-OC(=Y^1)(N(R)_2)$, $-SC(=Y^1)R$, $-SC(=Y^1)OR$, $-SC(=Y^1)(N(R)_2)$, $-N(R)C(=Y^1)R$, $-N(R)C(=Y^1)OR$, $-N(R)C(=Y^1)N(R)_2$, $-SO_2NR_2$, $-CN$, $-N_3$, $-NO_2$, $-OR$, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, heteroarylalkyl;

wherein each (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

or when taken together, two R^y on the same carbon atom form a carbocyclic ring of 3 to 7 carbon atoms;

each R is independently H, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, or arylalkyl;

each R^8 is halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, N_3, NO, NO_2, OR^{11} or $S(O)_nR^{11}$;

each R^9 is independently H, halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, N_3, NO, NO_2, CHO, CN, $-CH(=NR^{11})$, $-CH=NHNR^{11}$, $-CH=N(OR^{11})$, $-CH(OR^{11})_2$, $-C(=O)NR^{11}R^{12}$, $-C(=S)NR^{11}R^{12}$, $-C(=O)OR^{11}$, R^{11}, OR^{11} or $S(O)_nR^{11}$;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4-C_8)carbocyclylalkyl, optionally substituted aryl, optionally

substituted heteroaryl, -C(=O)(C_1-C_8)alkyl, -S(O)$_n$(C_1-C_8)alkyl 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- or –NR^b-;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, -S(O)R, -$S(O)_2$R, -S(O)(OR), -$S(O)_2$(OR), -C(=Y^1)R, -C(=Y^1)OR, or C(=Y^1)$N(R)_2$;

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or aryl(C_1-C_8)alkyl of each R^1, R^3, R^4, R^5, R^6, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said (C_1-C_8)alkyl may be optionally replaced with -O-, -S- or –NR^b;

each R^b 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_4–C_8)carbocyclylalkyl, -C(=O)R^{21}, -C(=O)OR^{21}, -C(=O)$NR^{21}R^{22}$, -C(=O)SR^{21}, -S(O)R^{21}, -$S(O)_2R^{21}$, -S(O)(OR^{21}), -$S(O)_2$(OR^{21}), or –$SO_2NR^{21}R^{22}$; and

each R^{21} or R^{22} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4–C_8)carbocyclylalkyl, -C(=O)(C_1-C_8)alkyl, -S(O)$_n$(C_1-C_8)alkyl or aryl(C_1-C_8)alkyl.

2. The compound according to claim 1 wherein each Y and Y^1 is O.

3. The compound according to claim 2 wherein R^8 is halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, OR^{11} or $S(O)_nR^{11}$.

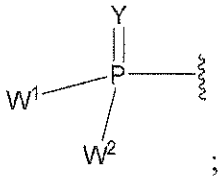
4. The compound according to claim 3 wherein R^9 is H, halogen, $S(O)_nR^{11}$ or $NR^{11}R^{12}$.

5. The compound according to claim 4 wherein R^4 is OR^a.

6. The compound according to claim 5 wherein R^1 is CH_3.

7. The compound according to claim 6 wherein R^2 is F.

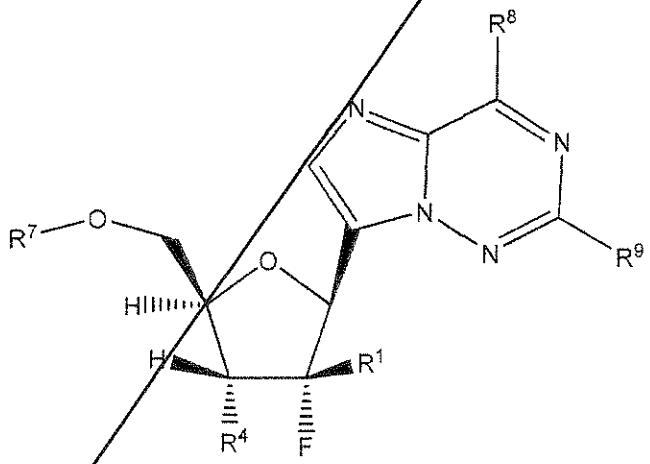
8. The compound according to claim 7 wherein R^7 is



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wherein Y is –O-; W^1 is Formula Ia and W^2 together with R^4 is –O-.

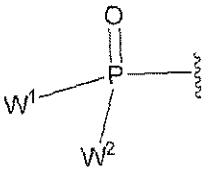
9. The compound according to claim 1 represented by Formula V:



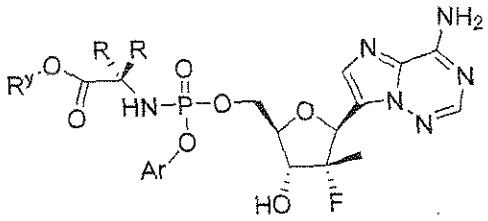
Formula V

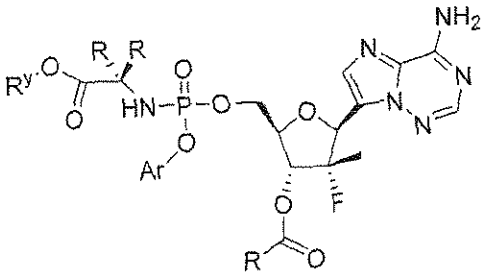
wherein R^1 is methyl or ethynyl, and R^4 is OR^a.

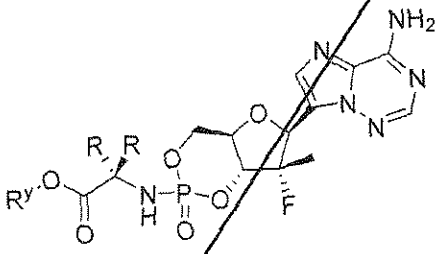
10. The compound according to claim 9 wherein R^7 is H or

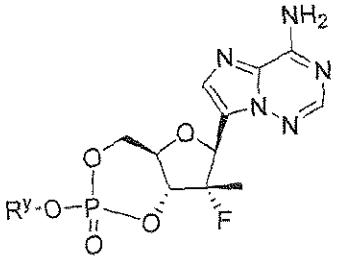


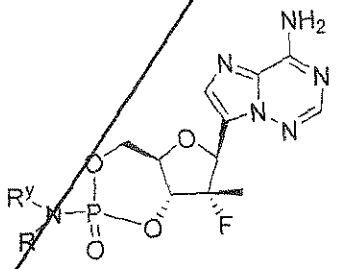
11. The compound according to claim 1 with the following structures:

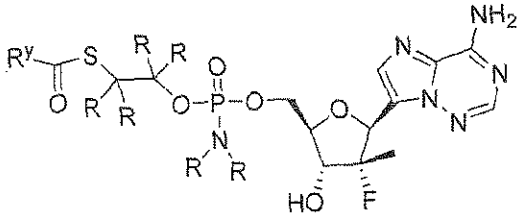


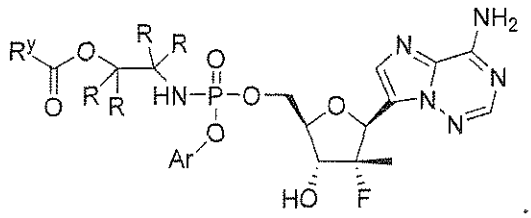




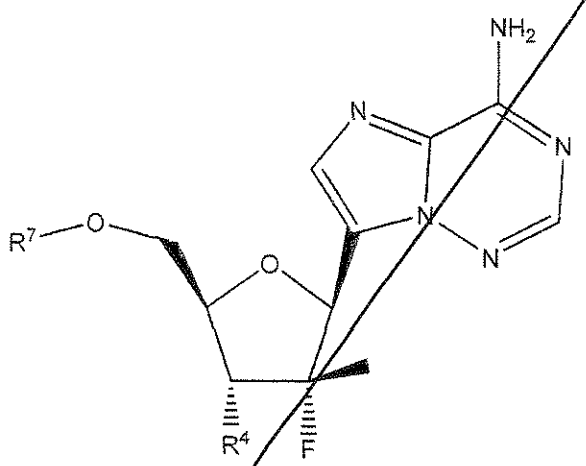








12. A compound of Formula VI:



Formula VI

or a pharmaceutically acceptable salt, thereof;

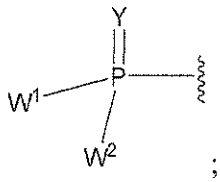
wherein:

R^4 is OR^a;

each n is independently 0, 1, or 2;

each R^a is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_4$–$C_8)$carbocyclylalkyl, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, or –$SO_2NR^{11}R^{12}$;

R^7 is H, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, –$SO_2NR^{11}R^{12}$, or



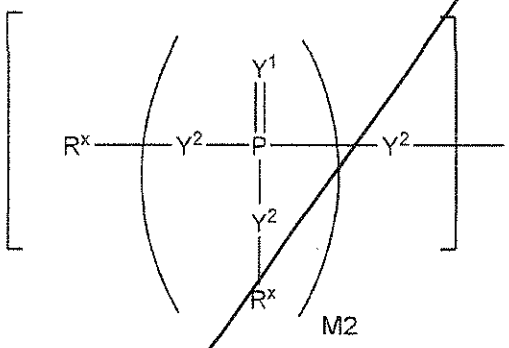
;

Y is O, S, NR, $^{+}N(O)(R)$, N(OR), $^{+}N(O)(OR)$, or N–NR_2;

W^1 and W^2, when taken together, are $-Y^3(C(R^y)_2)_3Y^3-$; or

one of W^1 or W^2 together with R^4 is $-Y^3-$ and the other of W^1 or W^2 is Formula Ia; or

W^1 and W^2 are each, independently, a group of Formula VIa:



Formula VIa

wherein:

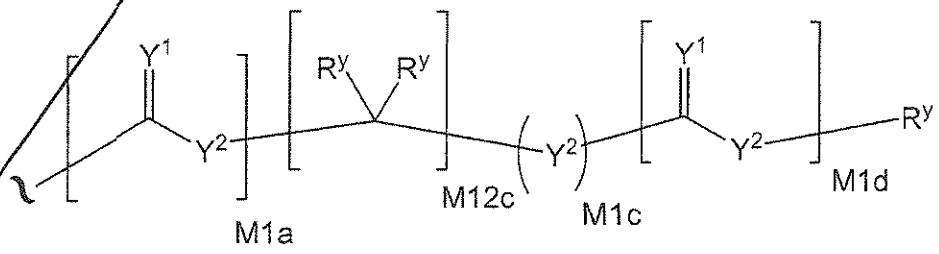
each Y^1 is, independently, O, S, NR, $^{+}N(O)(R)$, N(OR), $^{+}N(O)(OR)$, or N–NR_2;

each Y^2 is independently a bond, O, CR_2, NR, $^{+}N(O)(R)$, N(OR), $^{+}N(O)(OR)$, N–NR_2, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula VIb:



Formula VIb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, F, Cl, Br, I, OH, $-C(=Y^1)R$, $-C(=Y^1)R^{13}$, $-C(=Y^1)OR$, $-C(=Y^1)N(R)_2$, $-N(R)_2$, $-^+N(R)_3$, -SR, $-S(O)R$, $-S(O)_2R$, $-S(O)_2R^{13}$, $-S(O)(OR)$, $-S(O)_2(OR)$, $-OC(=Y^1)R$, $-OC(=Y^1)OR$, $-OC(=Y^1)(N(R)_2)$, $-SC(=Y^1)R$, $-SC(=Y^1)OR$, $-SC(=Y^1)(N(R)_2)$, $-N(R)C(=Y^1)R$, $-N(R)C(=Y^1)OR$, $-N(R)C(=Y^1)N(R)_2$, $-SO_2NR_2$, $-CN$, $-N_3$, $-NO_2$, $-OR$, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, heteroarylalkyl;

wherein each (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

each R is independently H, (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, or arylalkyl;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4-C_8)carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)(C_1-C_8)$alkyl, $-S(O)_n(C_1-C_8)$alkyl or aryl(C_1-C_8)alkyl;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, $-S(O)R$, $-S(O)_2R$, $-S(O)(OR)$, $-S(O)_2(OR)$, $-C(=Y^1)R$, $-C(=Y^1)OR$, or $C(=Y^1)N(R)_2$;

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or aryl(C_1-C_8)alkyl of each R^4, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said (C_1-C_8)alkyl may be optionally replaced with -O-, -S- or $-NR^b$;

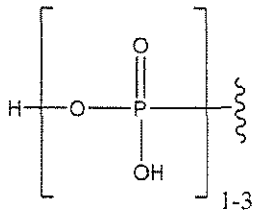
each R^b is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)R^{21}$, $-C(=O)OR^{21}$, $-C(=O)NR^{21}R^{22}$, $-C(=O)SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)(OR^{21})$, $-S(O)_2(OR^{21})$, or $-SO_2NR^{21}R^{22}$; and

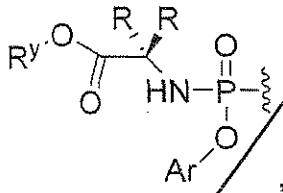
each R^{21} or R^{22} is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, $(C_4$–$C_8)$carbocyclylalkyl, -C(=O)$(C_1$-$C_8)$alkyl, -S(O)$_n(C_1$-$C_8)$alkyl or aryl$(C_1$-$C_8)$alkyl.

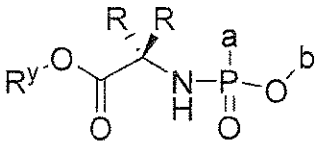
13. The compound according to claim 12 wherein:

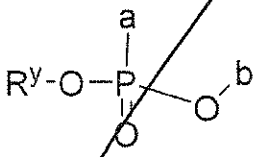
R^a is H, $(C_1$-$C_8)$alkyl, or -C(=O)$(C_1$-$C_6)$alkyl;

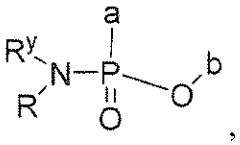
R^7 or R^7 together with R^4 is



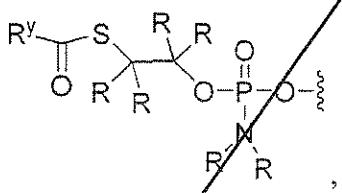
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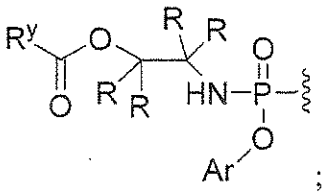
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, or


;

wherein

a is the point of attachement to R^7;

b is the point of attachement to R^4;

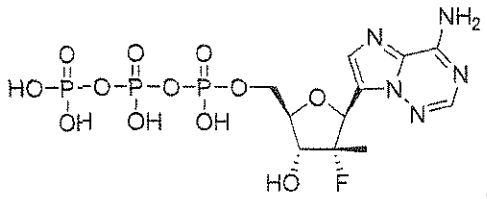
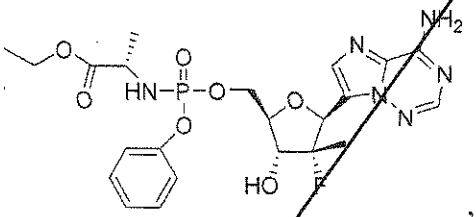
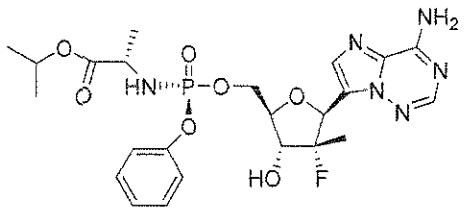
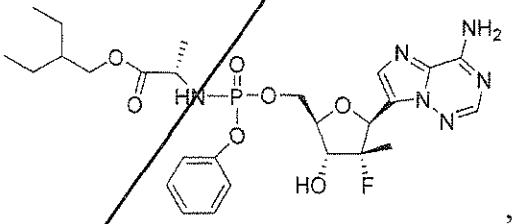
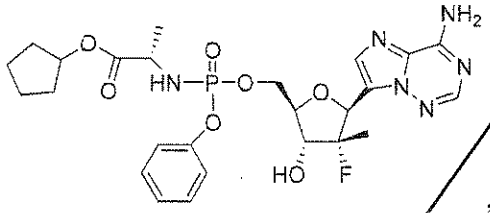
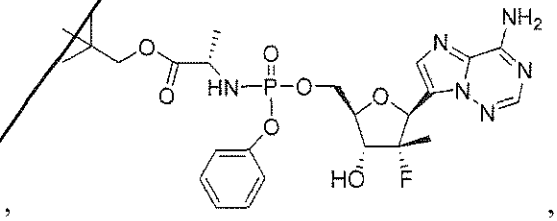
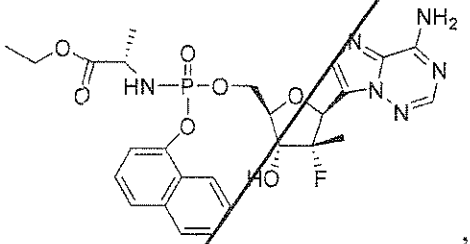
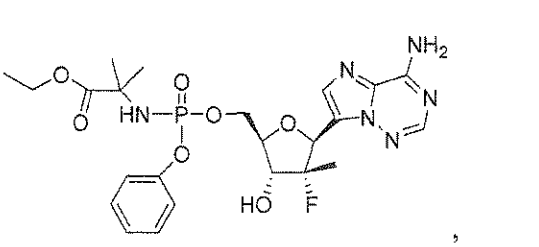
Ar is phenyl or naphthyl, wherein the phenyl and naphthyl are optionally substituted with 1-3 R^{20} groups;

each R^y is independently $(C_1$-$C_8)$ alkyl or C_5–C_6 carbocyclyl, wherein the alkyl and carbocyclyl are optionally substituted with 1-3 R^{20} groups;

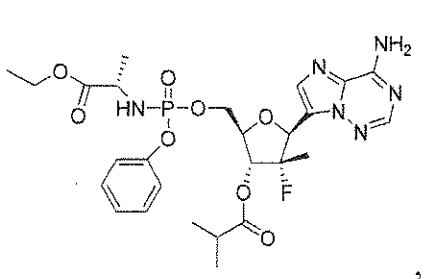
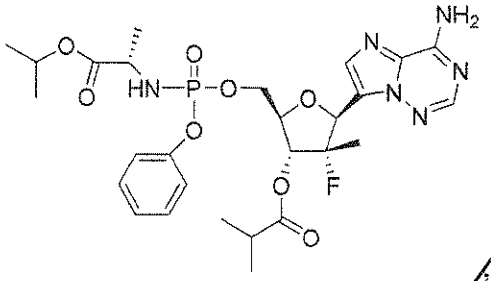
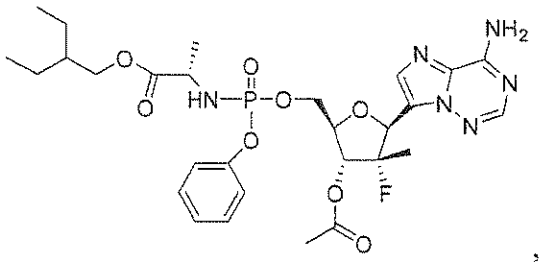
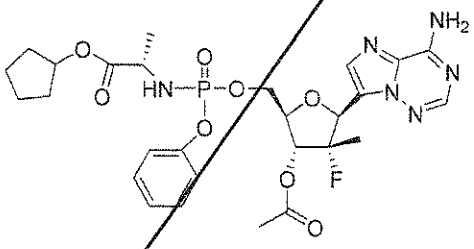
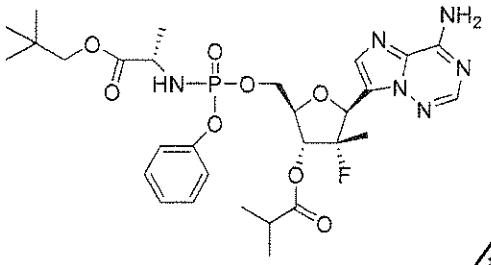
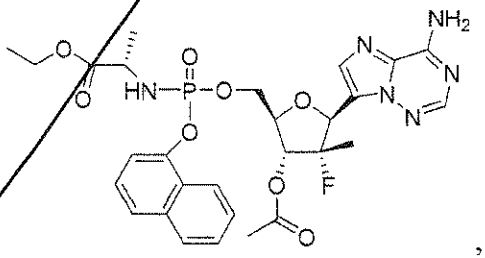
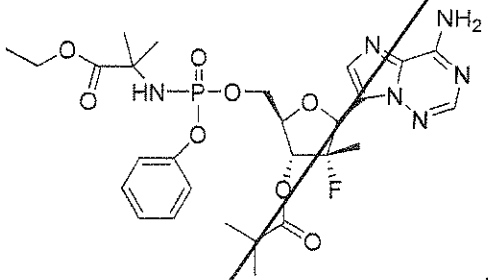
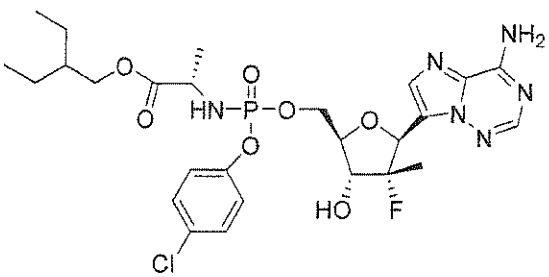
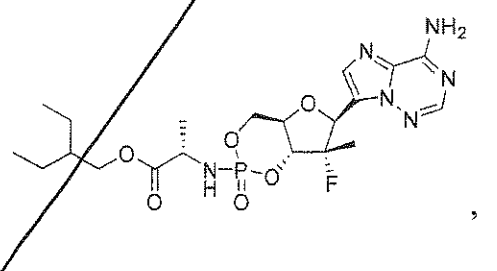
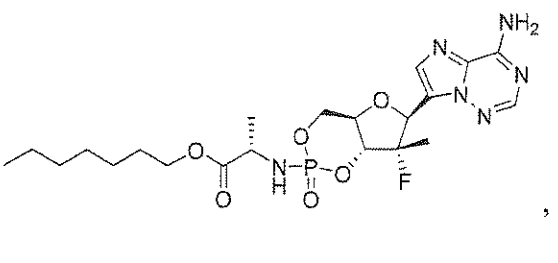
each R is independently H, $(C_1$-$C_6)$ alkyl, or arylalkyl; and

each R^{20} is independently halogen, CN, $N(R)_2$, OR, -SR, -S(O)R, $-S(O)_2R$, -S(O)(OR), $-S(O)_2(OR)$, -C(=O)R, -C(=O)OR, or $C(=O)N(R)_2$.

14. A compound having a structure:

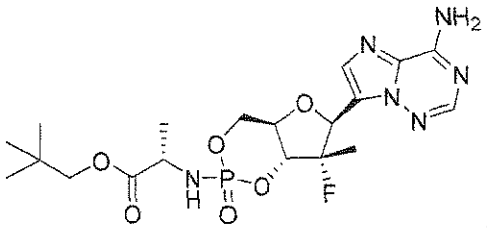
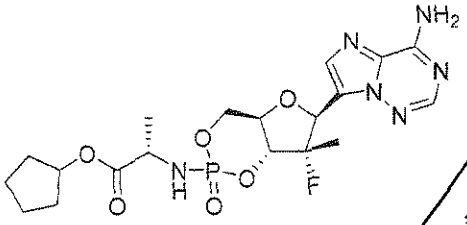
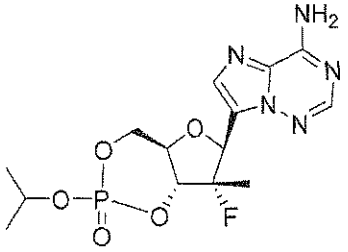
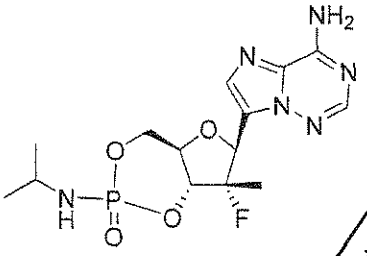
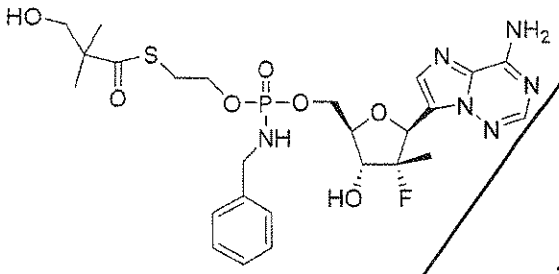
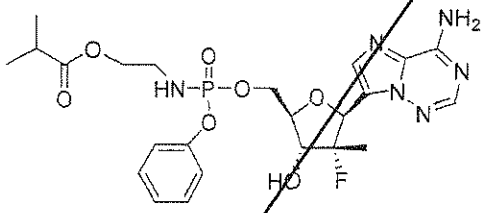









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or a pharmaceutically acceptable salt, thereof.

15. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15 further comprising at least one additional therapeutic agent selected from the group consisting of interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, NS5a inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, mevalonate decarboxylase antagonists, antagonists of the renin-angiotensin system, endothelin antagonists, other anti-fibrotic agents, nucleoside or nucleotide inhibitors of HCV NS5B polymerase, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophillin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers and other drugs for treating HCV; or mixtures thereof.

17. Use of a compound of claim 1 for the preparation of a medicament for treating a *Flaviviridae* virus infection in a mammal in need thereof.

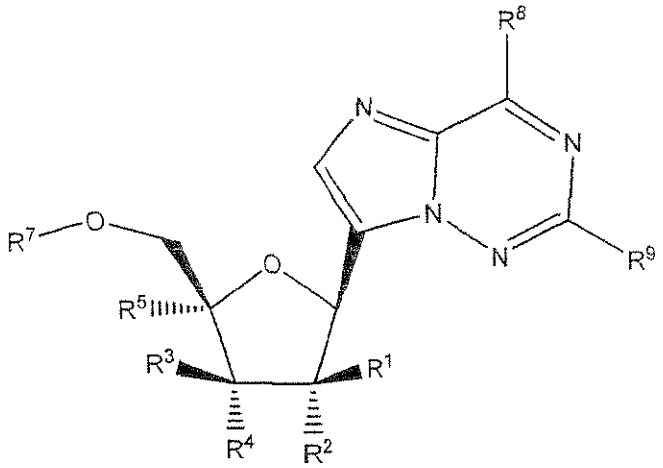
18. The use of claim 17 wherein the viral infection is a Hepatitis C virus infection.

19. The use of claim 18 wherein the viral infection is caused by a S282T mutant of Hepatitis C virus.

20. The use of claim 17 wherein the medicament is to be further administered with at least one additional therapeutic agent selected from the group consisting of interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, NS5a inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, mevalonate decarboxylase antagonists, antagonists of the renin-angiotensin system, endothelin antagonists, other anti-fibrotic agents, nucleoside or nucleotide inhibitors of HCV NS5B polymerase, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophillin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers and other drugs for treating HCV; or mixtures thereof.

5 CLAIMS

1. A compound of Formula IV:



Formula IV

or a pharmaceutically acceptable salt, thereof;

wherein:

R^1 is CH_3 or CH_2CH_3;

R^2 is F;

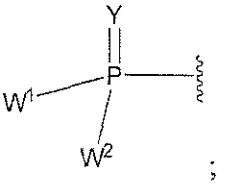
R^3, R^4, and R^5 are each independently H, halogen, OR^a, $N(R^a)_2$, N_3, CN, NO_2, $S(O)_nR^a$, $(C_1–C_8)$alkyl, $(C_4–C_8)$carbocyclylalkyl, $(C_1–C_8)$substituted alkyl, $(C_2–C_8)$alkenyl, $(C_2–C_8)$substituted alkenyl, $(C_2–C_8)$alkynyl, $(C_2–C_8)$substituted alkynyl, or aryl(C_1-C_8)alkyl;

or any two of R^3, R^4 or R^5 on adjacent carbon atoms when taken together are –O(CO)O- or when taken together with the ring carbon atoms to which they are attached form a double bond;

each n is independently 0, 1, or 2;

each R^a is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, $(C_4–C_8)$carbocyclylalkyl, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, or $–SO_2NR^{11}R^{12}$;

R^7 is H, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, $–SO_2NR^{11}R^{12}$, or



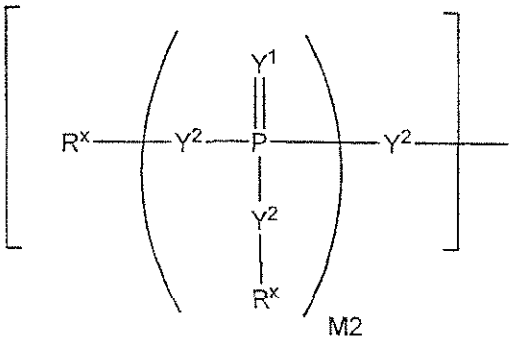
;

Y is O, S, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), or N–NR_2;

W^1 and W^2, when taken together, are $-Y^3(C(R^y)_2)_3Y^3-$; or

one of W^1 or W^2 together with either R^3 or R^4 is $-Y^3-$ and the other of W^1 or W^2 is Formula IVa; or

W^1 and W^2 are each, independently, a group of Formula IVa:



Formula IVa

wherein:

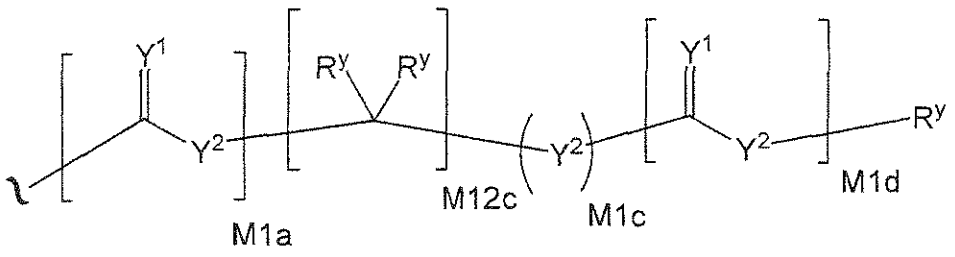
each Y^1 is, independently, O, S, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), or N–NR_2;

each Y^2 is independently a bond, O, CR_2, NR, $^{+}$N(O)(R), N(OR), $^{+}$N(O)(OR), N–NR_2, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula IVb:



Formula IVb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, -C(=Y^1)R, -C(=Y^1)R^{13}, -C(=Y^1)OR, -C(=Y^1)N(R)$_2$, -N(R)$_2$, -$^+$N(R)$_3$, -SR, -S(O)R, -S(O)$_2$R, -S(O)$_2$$R^{13}$, -S(O)(OR), -S(O)$_2$(OR), -OC(=$Y^1$)R, -OC(=$Y^1$)OR, -OC(=$Y^1$)(N(R)$_2$), -SC(=$Y^1$)R, -SC(=$Y^1$)OR, -SC(=$Y^1$)(N(R)$_2$), -N(R)C(=$Y^1$)R, -N(R)C(=$Y^1$)OR, -N(R)C(=$Y^1$)N(R)$_2$, $-SO_2NR_2$, –OR, (C_1-C_8) alkyl, C_3–C_{20} carbocyclyl, heteroarylalkyl;

wherein each (C_1-C_8) alkyl, (C_2-C_8)alkenyl, (C_2-C_8) alkynyl, C_6–C_{20} aryl, C_3–C_{20} carbocyclyl, C_2–C_{20} heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

or when taken together, two R^y on the same carbon atom form a carbocyclic ring of 3 to 7 carbon atoms;

each R is independently H, (C_1-C_8) alkyl,C_3–C_{20} carbocyclyl;

each R^8 is halogen, $NR^{11}R^{12}$, $N(R^{11})OR^{11}$, $NR^{11}NR^{11}R^{12}$, OR^{11} or $S(O)_nR^{11}$;

each R^9 is independently H, halogen, $NR^{11}R^{12}$ or $S(O)_nR^{11}$;

each R^{11} or R^{12} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4–C_8)carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, -C(=O)(C_1-C_8)alkyl, -S(O)$_n$(C_1-C_8)alkyl 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- or –NR^b-;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, -S(O)R, $-S(O)_2R$, -S(O)(OR), $-S(O)_2(OR)$, $-C(=Y^1)R$, $-C(=Y^1)OR$, or $C(=Y^1)N(R)_2$;

wherein each (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or aryl(C_1-C_8)alkyl of each R^1, R^3, R^4, R^5, R^6, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said (C_1-C_8)alkyl may be optionally replaced with -O-, -S- or $-NR^b$;

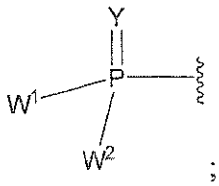
each R^b is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, aryl(C_1-C_8)alkyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)R^{21}$, $-C(=O)OR^{21}$, $-C(=O)NR^{21}R^{22}$, $-C(=O)SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)(OR^{21})$, $-S(O)_2(OR^{21})$, or $-SO_2NR^{21}R^{22}$; and

each R^{21} or R^{22} is independently H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)(C_1-C_8)$alkyl, $-S(O)_n(C_1-C_8)$alkyl or aryl(C_1-C_8)alkyl.

2. The compound according to claim 1 wherein each Y and Y^1 is O.

3. The compound according to claim 1 or claim 2 wherein R^4 is OR^a.

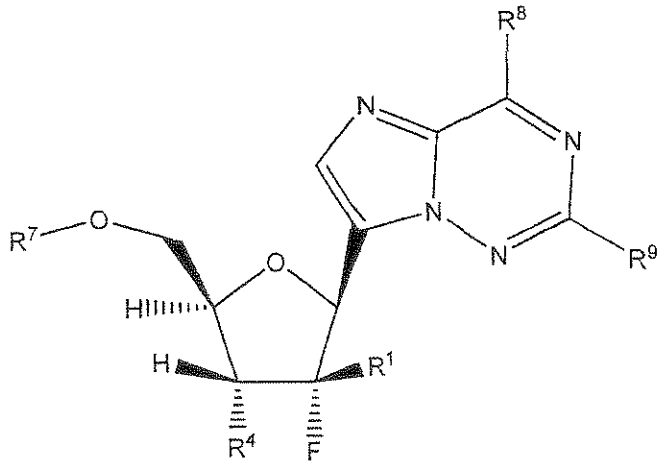
4. The compound according to claim 1 wherein R^7 is



;

wherein Y is –O-; W^1 is Formula IVaand W^2 together with R^4 is –O-.

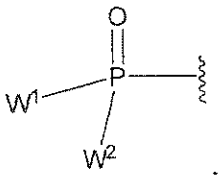
5. The compound according to claim 1 represented by Formula V:



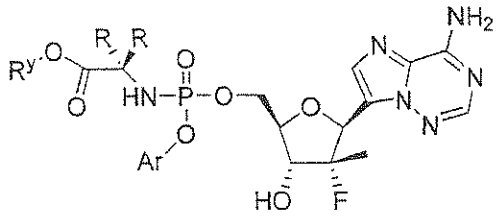
Formula V

wherein R^1 is methyl or ethynyl, and R^4 is OR^a.

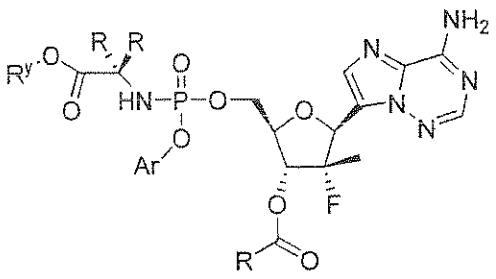
6. The compound according to claim 5 wherein R^7 is H or



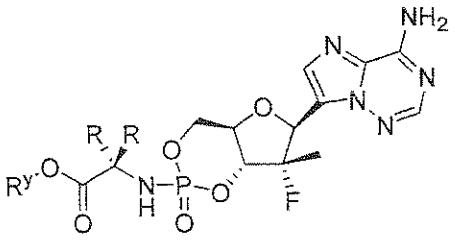
7. The compound according to claim 1 with the following structures:



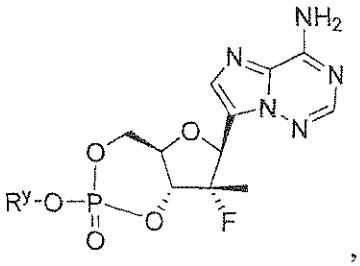
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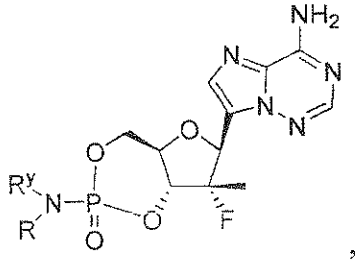
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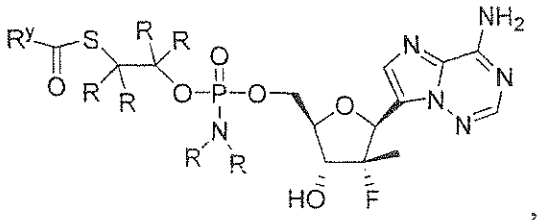
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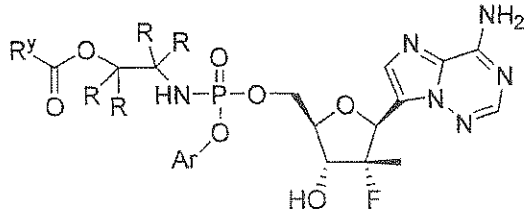
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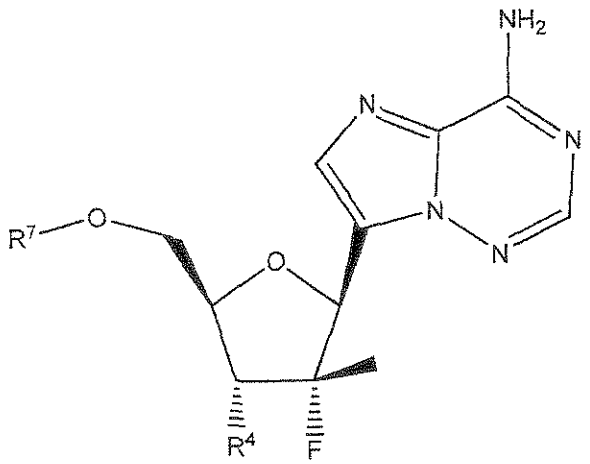


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8. A compound of Formula VI:



Formula VI

or a pharmaceutically acceptable salt, thereof;

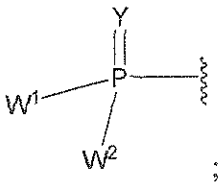
wherein:

R^4 is OR^a;

each n is independently 0, 1, or 2;

each R^a is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_4$–$C_8)$carbocyclylalkyl, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, or –$SO_2NR^{11}R^{12}$;

R^7 is H, -C(=O)R^{11}, -C(=O)OR^{11}, -C(=O)$NR^{11}R^{12}$, -C(=O)SR^{11}, -S(O)R^{11}, -$S(O)_2R^{11}$, -S(O)(OR^{11}), -$S(O)_2(OR^{11})$, –$SO_2NR^{11}R^{12}$, or



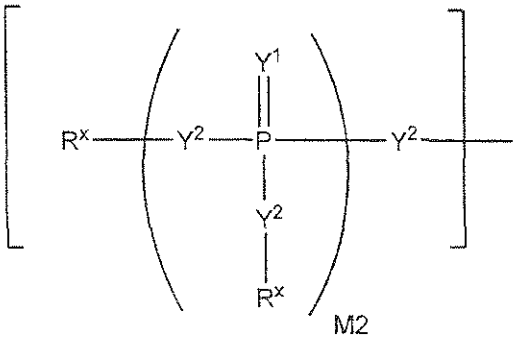
;

Y is O, S, NR, $^+$N(O)(R), N(OR), $^+$N(O)(OR), or N–NR_2;

W^1 and W^2, when taken together, are $–Y^3(C(R^y)_2)_3Y^3$-; or

one of W^1 or W^2 together with R^4 is $–Y^3$- and the other of W^1 or W^2 is Formula VIa; or

W^1 and W^2 are each, independently, a group of Formula VIa:



Formula VIa

wherein:

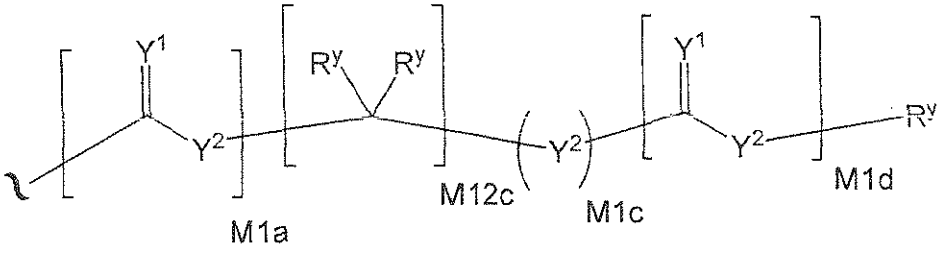
each Y^1 is, independently, O, S, NR, $^+N(O)(R)$, N(OR), $^+N(O)(OR)$, or N–NR_2;

each Y^2 is independently a bond, O, CR_2, NR, $^+N(O)(R)$, N(OR), $^+N(O)(OR)$, N–NR_2, S, S–S, S(O), or $S(O)_2$;

each Y^3 is independently O, S, or NR;

M2 is 0, 1 or 2;

each R^x is a group of Formula VIb:



Formula VIb

wherein:

each M1a, M1c, and M1d is independently 0 or 1;

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

each R^y is independently H, F, Cl, Br, I, OH, -C(=Y^1)R, -C(=Y^1)R^{13}, -C(=Y^1)OR, -C(=Y^1)$N(R)_2$, -$N(R)_2$, -$^+N(R)_3$, -SR, -S(O)R, -$S(O)_2$R, -$S(O)_2R^{13}$, -S(O)(OR), -$S(O)_2$(OR), -OC(=Y^1)R, -OC(=Y^1)OR, -OC(=Y^1)($N(R)_2$), -SC(=Y^1)R, -

$SC(=Y^1)OR$, $-SC(=Y^1)(N(R)_2)$, $-N(R)C(=Y^1)R$, $-N(R)C(=Y^1)OR$, $-N(R)C(=Y^1)N(R)_2$, $-SO_2NR_2$, $-CN$, $-N_3$, $-NO_2$, $-OR$, $(C_1\text{-}C_8)$ alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$ alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, heteroarylalkyl;

wherein each $(C_1\text{-}C_8)$ alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$ alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, arylalkyl, or heteroarylalkyl is optionally substituted with 1-3 R^{20} groups;

each R is independently H, $(C_1\text{-}C_8)$ alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$ alkynyl, C_6-C_{20} aryl, C_3-C_{20} carbocyclyl, C_2-C_{20} heterocyclyl, or arylalkyl;

each R^{11} or R^{12} is independently H, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, (C_4-C_8)carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)(C_1\text{-}C_8)$alkyl, $-S(O)_n(C_1\text{-}C_8)$alkyl or aryl$(C_1\text{-}C_8)$alkyl;

each R^{13} is independently a carbocycle or heterocycle optionally substituted with 1-3 R^{20} groups;

each R^{20} is independently, halogen, CN, N_3, $N(R)_2$, OR, -SR, -S(O)R, $-S(O)_2R$, -S(O)(OR), $-S(O)_2(OR)$, $-C(=Y^1)R$, $-C(=Y^1)OR$, or $C(=Y^1)N(R)_2$;

wherein each $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl or aryl$(C_1\text{-}C_8)$alkyl of each R^4, R^{11} or R^{12} is, independently, optionally substituted with one or more halo, hydroxy, CN, N_3, $N(R^b)_2$ or OR^b; and wherein one or more of the non-terminal carbon atoms of each said $(C_1\text{-}C_8)$alkyl may be optionally replaced with -O-, -S- or $-NR^b$;

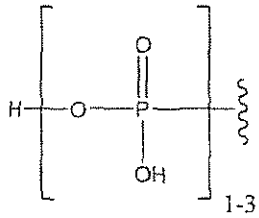
each R^b is independently H, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, aryl$(C_1\text{-}C_8)$alkyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)R^{21}$, $-C(=O)OR^{21}$, $-C(=O)NR^{21}R^{22}$, $-C(=O)SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)(OR^{21})$, $-S(O)_2(OR^{21})$, or $-SO_2NR^{21}R^{22}$; and

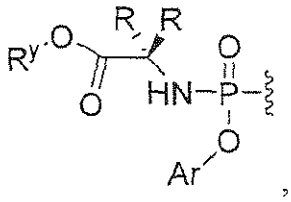
each R^{21} or R^{22} is independently H, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, (C_4-C_8)carbocyclylalkyl, $-C(=O)(C_1\text{-}C_8)$alkyl, $-S(O)_n(C_1\text{-}C_8)$alkyl or aryl$(C_1\text{-}C_8)$alkyl.

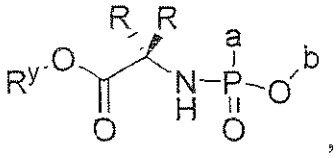
9. The compound according to claim 8 wherein:

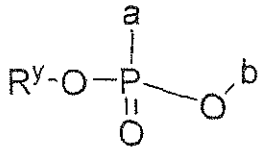
R^a is H, $(C_1\text{-}C_8)$alkyl, or $-C(=O)(C_1\text{-}C_6)$alkyl;

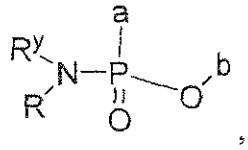
R^7 or R^7 together with R^4 is

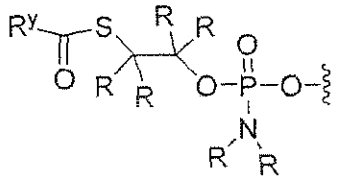


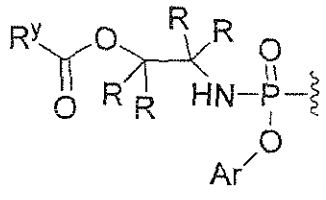
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, or


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wherein

a is the point of attachement to R^7;

b is the point of attachement to R^4;

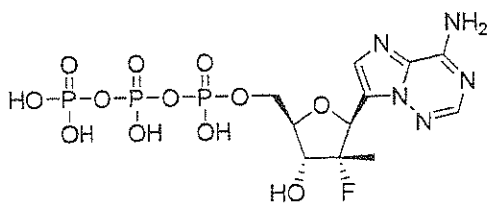
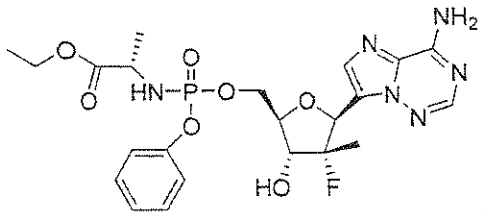
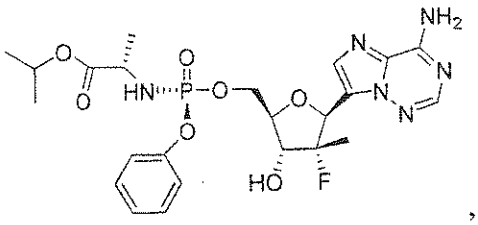
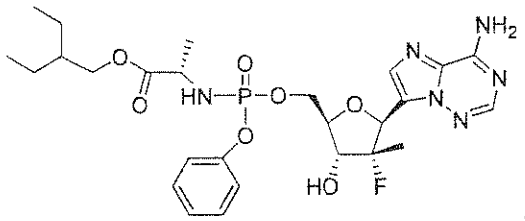
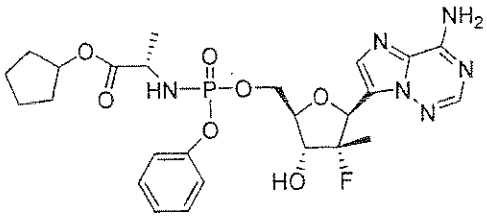
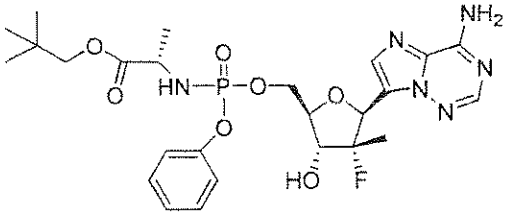
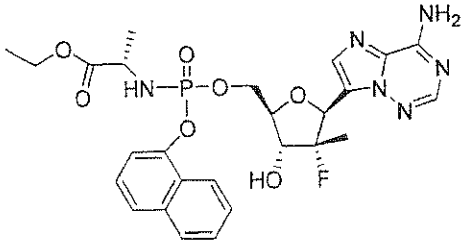
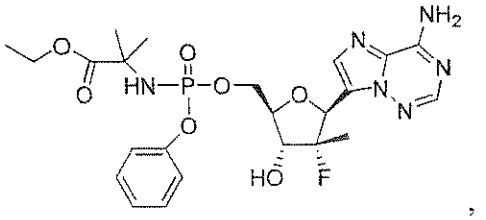
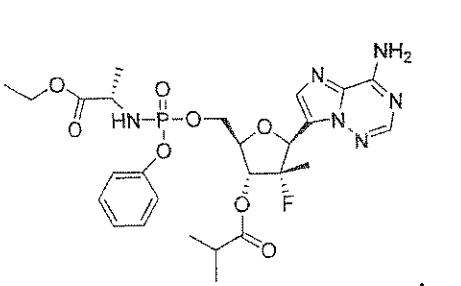
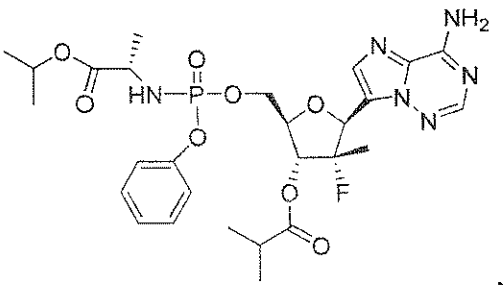
Ar is phenyl or naphthyl, wherein the phenyl and naphthyl are optionally substituted with 1-3 R^{20} groups;

each R^y is independently $(C_1$-$C_8)$ alkyl or C_5–C_6 carbocyclyl, wherein the alkyl and carbocyclyl are optionally substituted with 1-3 R^{20} groups;

each R is independently H, $(C_1$-$C_6)$ alkyl, or arylalkyl; and

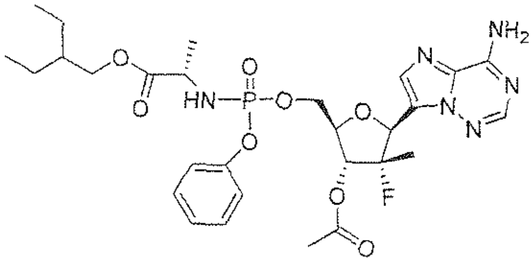
each R^{20} is independently halogen, CN, $N(R)_2$, OR, -SR, -S(O)R, $-S(O)_2R$, -S(O)(OR), $-S(O)_2(OR)$, -C(=O)R, -C(=O)OR, or $C(=O)N(R)_2$.

10. A compound having a structure:

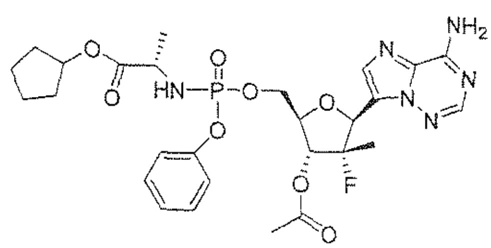

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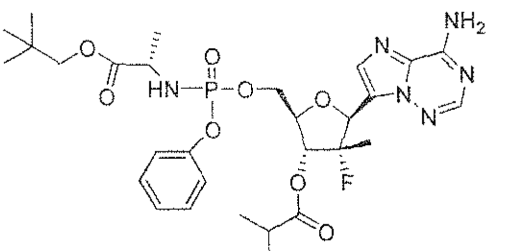
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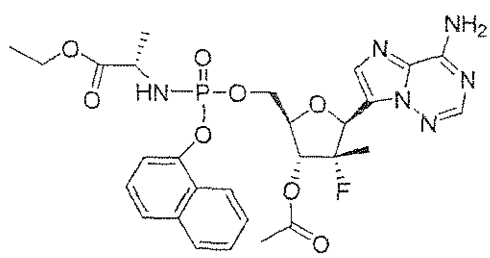
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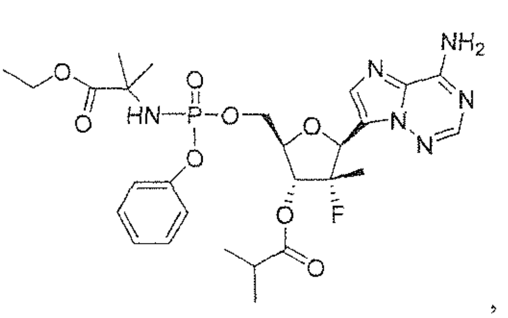
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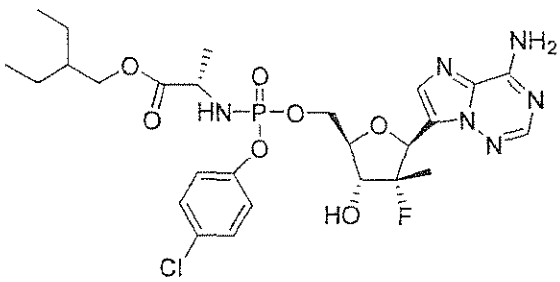
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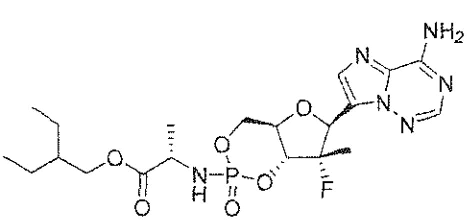
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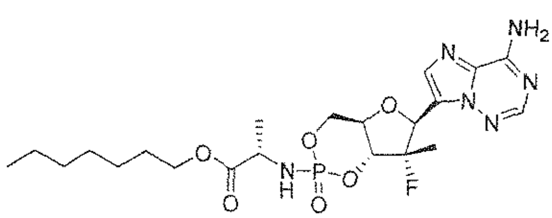
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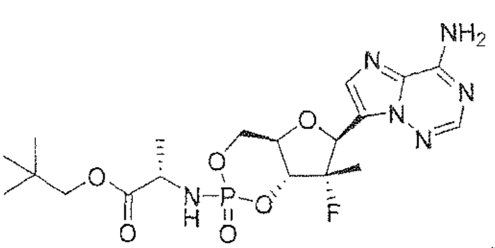
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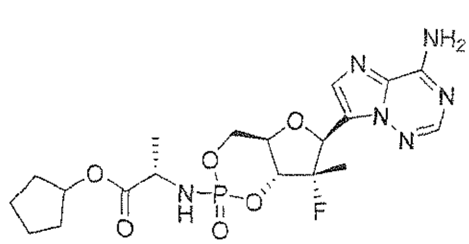
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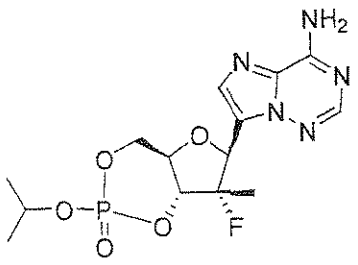
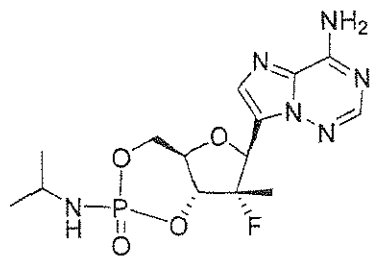
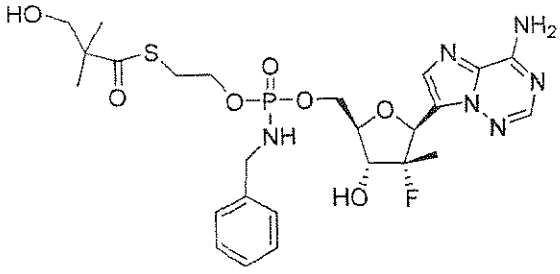
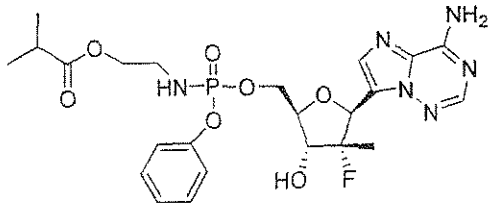
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or a pharmaceutically acceptable salt, thereof.

11. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 10 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11 further comprising at least one additional therapeutic agent selected from the group consisting of interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, NS5a inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, mevalonate decarboxylase antagonists, antagonists of the renin-angiotensin system, endothelin antagonists, other anti-fibrotic agents, nucleoside or nucleotide inhibitors of HCV NS5B polymerase,

non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophillin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers and other drugs for treating HCV; or mixtures thereof.

13. Use of a compound of any one of claims I to 10 in the preparation of a medicament for the treatment of *Flaviviridae* virus infection.

14. Use according to claim 13, wherein the viral infection is a Hepatitis virus infection.

15. Use according to claim 14, wherein the viral infection is caused by a S282T mutant of Hepatitis C virus.

16. Use according to claim 13, wherein the viral infection is a Hepatitis C virus infection.

17. Use according to any one of claims 13 to 16, wherein the medicament is to be administered with at least one additional therapeutic agent selected from the group consisting of interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, NS5a inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, mevalonate decarboxylase antagonists, antagonists of the renin-angiotensin system, endothelin antagonists, other anti-fibrotic agents, nucleoside or nucleotide inhibitors of HCV NS5B polymerase, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophillin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers and other drugs for treating HCV; or mixtures thereof.