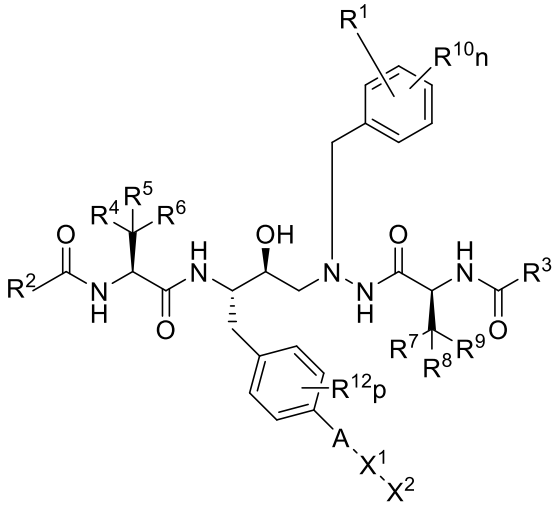
CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is a 5 to 10-membered heterocycle having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 10-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 5 to 10-membered heterocycle or 5 to 10-membered heteroaryl is optionally substituted with 1 to 5 R^a groups;

R^2 and R^3 are each independently C_{1-4}alkyl, C_{3-6}cycloalkyl, O-R^{2A}, C_{1-2}alkyl-O-R^{2A}, N-$(R^{3A})_2$, or C_{1-2}alkyl-N-$(R^{3A})_2$,

wherein each R^{2A} is independently C_{1-4}alkyl, C_{3-6}cycloalkyl, or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S,

wherein each R^{3A} is independently hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, or COO(R^e),

and wherein each C_{3-6}cycloalkyl or 4 to 10-membered heterocyclyl is optionally substituted by 1 to 3 R^f groups, wherein each R^f is independently C_{1-2}alkyl or halogen;

R^4 is hydrogen, halo, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, or C_{1-4}haloalkoxy;

R^7 is hydrogen, halo, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, or C_{1-4}haloalkoxy;

R^5, R^6, R^8, and R^9 are each independently hydrogen, halo, C_{1-2}alkyl, C_{1-2}haloalkyl, or C_{3-6}cycloalkyl;

and wherein two or more of R^4, R^5 and R^6 or two or more of R^7, R^8, and R^9 optionally join together to form one or more C_{3-6}cycloalkyl groups that are optionally substituted with 1 to 4 groups selected from halogen, C_{1-2}alkyl, and C_{1-2}haloalkyl;

each R^{10} is independently halogen, cyano, C_{1-4}alkoxy, C_{1-6}alkyl, or C_{3-6}cycloalkyl;

n is 0 to 4;

each R^a is independently halogen, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{3-6}cycloalkyl, 4 to 10-membered heterocyclyl, or O-R^{3B}, wherein the C_{1-4}alkyl is optionally substituted with 1 to 2 groups selected from hydroxyl and C_{1-4}alkoxy, the 4 to 10-membered heterocyclyl has 1 to 5 heteroatoms selected from N, O, and S, and the 4 to 10-membered heterocyclyl is optionally substituted with R^{a1},

wherein R^{3B} is C_{3-6}cycloalkyl optionally substituted with R^{a1} or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S optionally substituted with R^{a1},

wherein each R^{a1} is independently C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}haloalkyl, or 4 to 8-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S;

A is ethynyl or a bond;

X^1 is a 6 to 10-membered aryl or a 5 to 10-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein each 6 to 10-membered aryl or 5 to 10-membered heteroaryl is optionally substituted with 1 to 4 R^b groups;

X^2 is hydrogen or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 4 to 10-membered heterocyclyl is optionally substituted with one R^{11} and optionally substituted with 1 to 5 R^b groups;

R^{11} is C=O(R^c), CH_2(R^d), S(O)$_{1-2}$(C_{1-4}alkyl), S(O)$_{1-2}C_{3-6}$cycloalkyl, a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 9-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein each 4 to 10-membered heterocyclyl or 5 to 9-membered heteroaryl is optionally substituted with 1 to 5 R^b groups;

each R^b is independently halogen, oxo, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, or $COO(R^e)$, wherein the C_{1-4}alkyl is optionally substituted with 1 to 2 groups selected from hydroxyl and C_{1-4}alkoxy;

R^c is C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, $N(R^e)_2$, C_{3-6}cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6}cycloalkyl and the 4 to 6-membered heterocyclyl are optionally substituted by 1 to 5 R^b groups;

R^d is $COO(R^e)$, $N(R^e)_2$, C_{3-6}cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6}cycloalkyl and the 4 to 6-membered heterocyclyl is optionally substituted by 1 to 5 R^b groups;

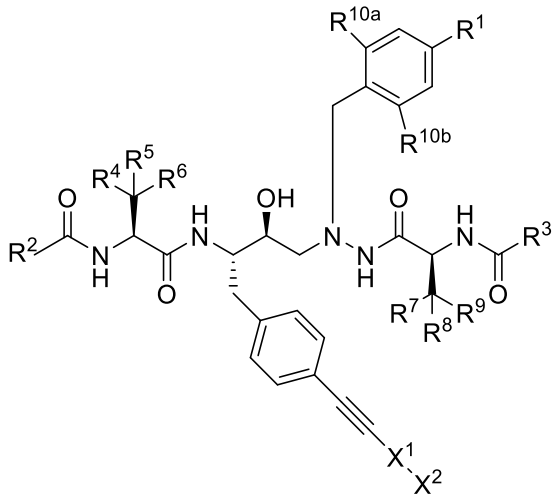
each R^{12} is C_{1-2}alkyl, halo, $-OC_{1-2}$alkyl, or cyano;

each p is 0 to 4;

and each R^e is independently hydrogen or C_{1-4}alkyl.

2. The compound of claim 1, wherein the compound of Formula (I) is a compound of:

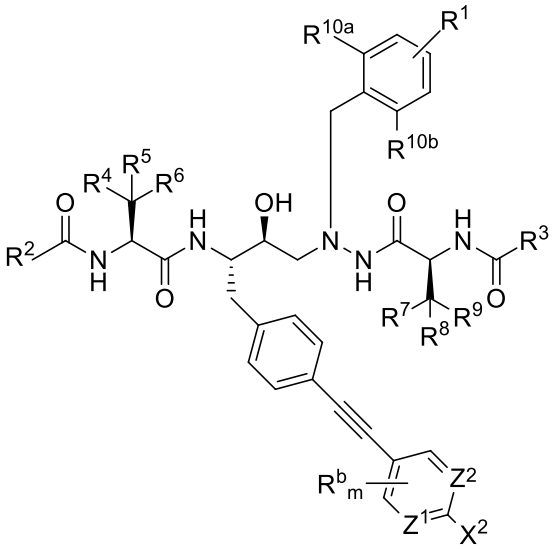
(i) Formula (Ia):



(Ia)

wherein R^{10a} and R^{10b} are independently halogen, cyano, C_{1-4}alkoxy, C_{1-6}alkyl, or C_{3-6}cycloalkyl, or a pharmaceutically acceptable salt thereof; or

(ii) Formula (Ib):



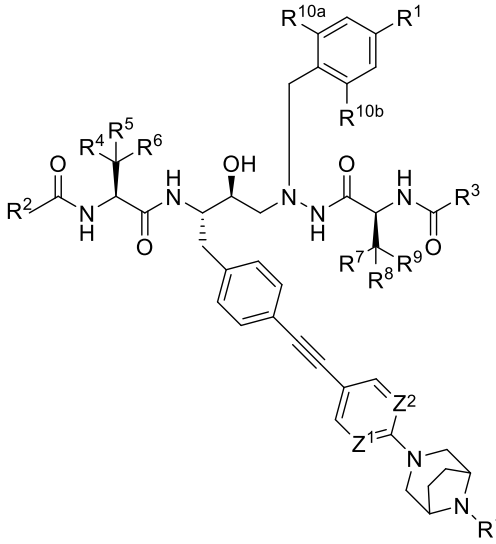
(Ib)

or a pharmaceutically acceptable salt thereof, wherein:

Z^1 and Z^2 are independently N or CH; and

m is 0 to 2; or

Formula (Ic):

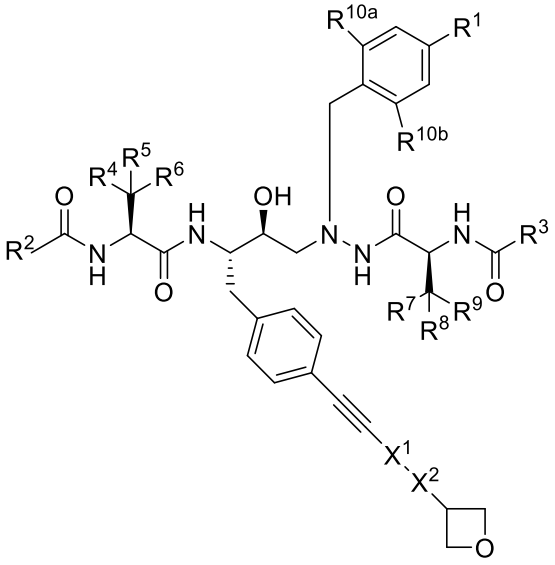


(Ic)

or a pharmaceutically acceptable salt thereof, wherein:

Z^1 and Z^2 are independently N or CH; or

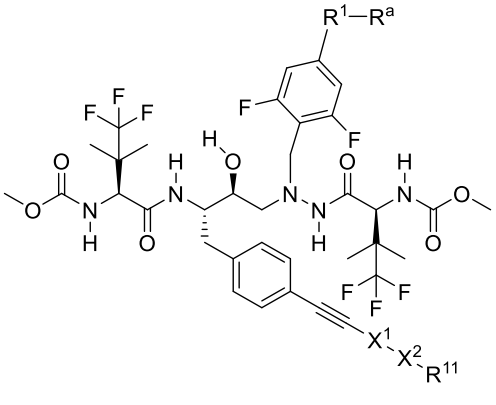
Formula (Id):



(Id)

or a pharmaceutically acceptable salt thereof; or

Formula (Ie):

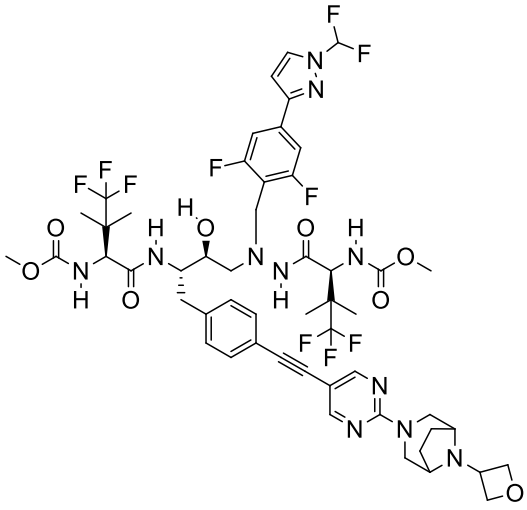


(Ie)

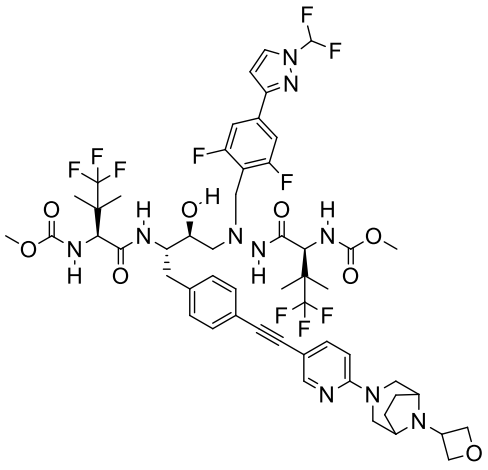
or a pharmaceutically acceptable salt thereof.

3. A compound of any of Examples 1-245, or a pharmaceutically acceptable salt thereof.

4. The compound of any one of claims 1 to 3, which is


; or a pharmaceutically acceptable salt thereof.

5. The compound of any one of claims 1 to 3, which is


; or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

7. The pharmaceutical composition of claim 6, further comprising one, two, three, or four additional therapeutic agents.

8. The pharmaceutical composition of claim 7, wherein the additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs

for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof.

9. The pharmaceutical composition of claim 7 or 8, wherein the additional therapeutic agents are selected from the group consisting of:

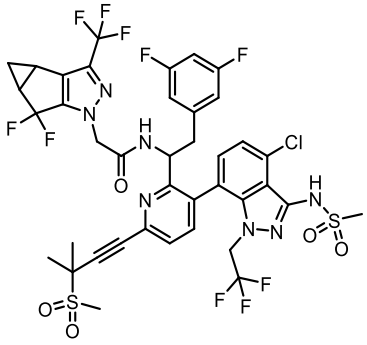
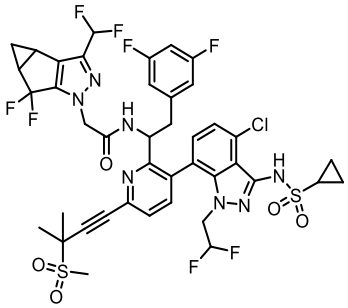
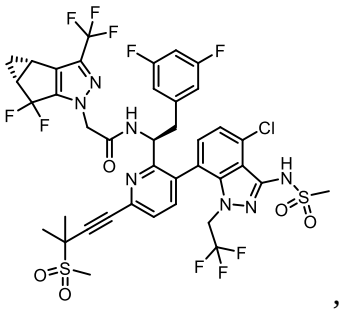
i) abacavir sulfate, bictegravir, cabotegravir, dolutegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate; or

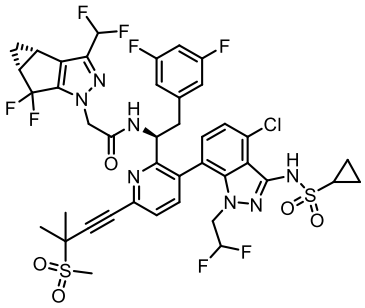
ii) tenofovir alafenamide, tenofovir alafenamide fumarate and tenofovir alafenamide hemifumarate; or

iii) abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir; or

iv) bictegravir, emtricitabine, and GS-9131; or

v) a compound selected from:


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and , or a pharmaceutically acceptable salt thereof.

10. Use of a compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a human immunodeficiency virus (HIV) infection in a subject in need thereof.

11. The use according to claim 10, wherein said medicament comprises one, two, three or four additional therapeutic agents in a unitary dosage form for simultaneous administration.

12. The use according to claim 10, wherein said medicament is for co-administration with one, two, three or four additional therapeutic agents.

13. The use according to claim 11 or 12, wherein the additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase,

HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof.

14. The use according to claim 11 or 12, wherein said compound is combined with:

i) abacavir sulfate, bictegravir, cabotegravir, dolutegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, or tenofovir alafenamide hemifumarate; or

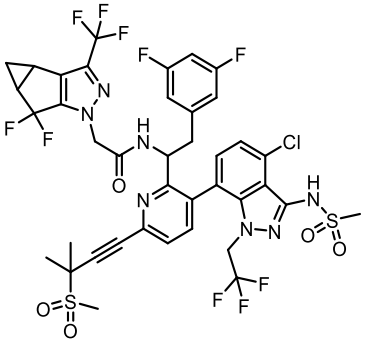
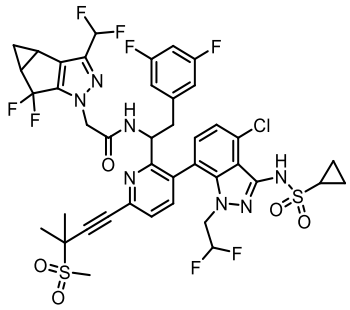
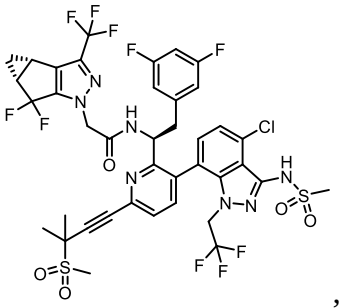
ii) tenofovir alafenamide, tenofovir alafenamide fumarate or tenofovir alafenamide hemifumarate; or

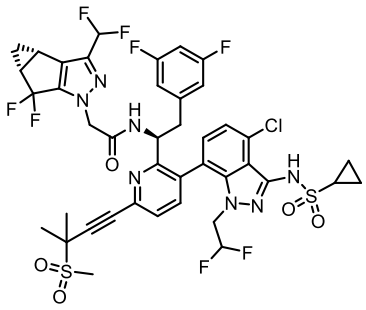
iii) tenofovir disoproxil, tenofovir disoproxil hemifumarate or tenofovir disoproxil fumarate; or

iv) abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir; or

v) bictegravir, emtricitabine, and GS-9131; or

vi) a compound selected from:


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,

,


and , or a pharmaceutically acceptable salt thereof.

15. The use according to claim 11, wherein said compound is combined with:

i) a first additional therapeutic agent selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, and a second additional therapeutic agent selected from the group consisting of emtricitabine and lamivudine; or

ii) a first additional therapeutic agent selected from the group consisting of tenofovir alafenamide fumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, and a second additional therapeutic agent, wherein the second additional therapeutic agent is emtricitabine; or

iii) a first additional therapeutic agent selected from the group consisting of tenofovir disoproxil fumarate, tenofovir disoproxil, and tenofovir disoproxil hemifumarate, and a second additional therapeutic agent, wherein the second additional therapeutic agent is emtricitabine.