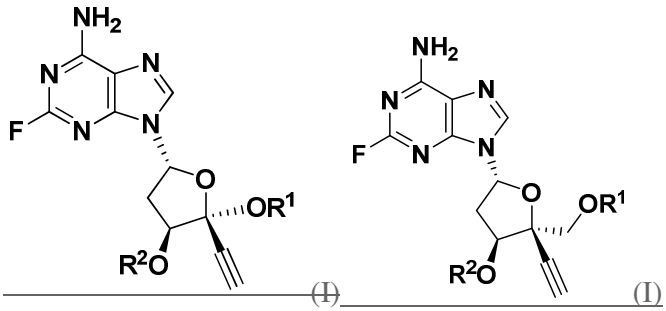


(I)

(I)

wherein

R^1 is H or is X-L_m, wherein m = 1 or 2, and wherein X-L_m is -C(=O)L, -C(=O)OL, -C(=O)NH(L), -C(=O)$N(L)_2$, -CH(R)OC(=O)L, -C(=O)CH(R)-NH(L), -C(=O)CH(R)-$N(L)_2$, -P(=O)$(NHL)_2$, -P(=O)(NHL)(NL_2), or -P(=O)$(NL_2)_2$, and each independently selected L is $(C_{1\text{-}22})$alkyl, $(C_{3\text{-}22})$alkenyl wherein the alkenyl can comprise 1-6 unsaturations, $(C_{3\text{-}7})$cycloalkyl, $(CHR)_n$-phenyl wherein n=0 or 1, or -CHR-$N(R)_2$, or R^1 is -OCH(R)OP(=O)$(OH)_2$ or R^1 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a phophoroboranoate

R is H, $(C_{1\text{-}22})$alkyl, or $(C_{3\text{-}22})$alkenyl wherein the alkenyl can comprise 1-6 unsaturations, or is $(C_{3\text{-}7})$cycloalkyl;

R^2 is H or is X-L_m, or R^2 is - OCH(R)OP(=O)$(OH)_2$ or R^2 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a phophoroboranoate;

excluding following combinations:(a) $R^1 = R^2$ = acetyl, (b) $R^1 = R^2$ = H, and (c) R^2 = H when R^1 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a phophoroboranoate;

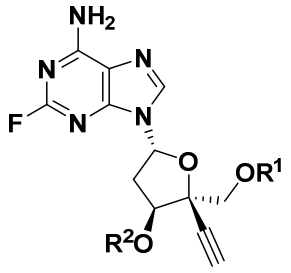
or a pharmaceutically acceptable salt thereof.

In various embodiments, a compound of Formula (I) can be any of the specific compounds **2** - **51**, shown in Table 1.

The invention further provides, in various embodiments, a method of inhibiting viral reverse transcriptase bioactivity, comprising contacting a virus expressing an enzyme with

CLAIMS

1. A compound of Formula (I)



(I)

wherein:

R^1 is H or is X-L_m, wherein m = 1 or 2, and wherein X-L_m is -C(=O)L, -C(=O)OL, -C(=O)NH(L), -C(=O)N$(L)_2$, -CH(R)OC(=O)L, -C(=O)CH(R)-NH(L), -C(=O)CH(R)-N$(L)_2$, -P(=O)$(NHL)_2$, -P(=O)(NHL)(NL_2), or -P(=O)$(NL_2)_2$, and each independently selected L is $(C_{1\text{-}22})$alkyl, $(C_{3\text{-}22})$alkenyl wherein the alkenyl can comprise 1-6 unsaturations, $(C_{3\text{-}7})$cycloalkyl, $(CHR)_n$-phenyl wherein n=0 or 1, or -CHR-N$(R)_2$, or R^1 is -OCH(R)OP(=O)$(OH)_2$ or R^1 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a ~~phophoroboranoate~~phosphoroboranoate;

R is H, $(C_{1\text{-}22})$alkyl, or $(C_{3\text{-}22})$alkenyl wherein the alkenyl can comprise 1-6 unsaturations, or is $(C_{3\text{-}7})$cycloalkyl;

R^2 is H or is X-L_m, or R^2 is - OCH(R)OP(=O)$(OH)_2$ or R^2 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a phosphoroboranoate~~phophoroboranoate~~;

excluding following combinations:(a) $R^1 = R^2$ = acetyl, (b) $R^1 = R^2$ = H, and (c) R^2 = H when R^1 is a phosphate residue or its derivative residue comprising a monophosphate, a diphosphate, a triphosphate, a phosphonate, a phosphate polyester, a phosphate amidate (mono and di), a phosphorothioate, a phosphoroselenoate, or a phosphoroboranoate~~phophoroboranoate~~;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein R^1 and R^2 both are -C(=O)L.

3. The compound of claim 1, wherein at least one of R^1 and R^2 is -C(=O)L.

4. The compound of claim 1, wherein one of R^1 and R^2 is H.

5. The compound of claim 1, wherein one of R^1 and R^2 is -C(=O)L and one of R^1 and R^2 is H.

6. The compound of any one of claims 2 to 5, wherein L is (C_{1-22})alkyl.

7. The compound of any one of claims 2 to 5, wherein L is (C_{3-22})alkenyl wherein the alkenyl can comprise 1-6 unsaturations.

8. The compound of any one of claims 2 to 5, wherein L is (C_{3-7})cycloalkyl.

9. The compound of any one of claims 2 to 5, wherein L is $(CHR)_n$-phenyl, wherein n=0 or 1.

10. The compound of claim 9, wherein n=0.

11. The compound of claim 9, wherein n=1.

12. A formulation comprising a compound of any one of claims 1 to 11, suspended in an aqueous suspension comprising 0.25% sodium carboxymethyl cellulose and 0.1% polyoxyethlene (20) sorbitan monooleate.

13. A formulation comprising a compound of any one of claims 1 to 11, suspended in an aqueous suspension comprising 0.25% sodium carboxymethyl cellulose and 0.5% polyoxyethlene (20) sorbitan monooleate.

14. A pharmaceutical composition comprising an effective amount of a compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. ~~A method of inhibiting viral reverse transcriptase bioactivity, comprising contacting a virus expressing an enzyme with reverse transcriptase bioactivity with~~ Use of an effective amount or concentration of a compound of any one of claims 1 to 11 in the manufacture of a medicament for the treatment of a viral infection, wherein the medicament is for inhibiting viral reverse transcriptase bioactivity.

16. ~~A method of treatment of a viral infection in a patient wherein inhibition of a reverse transcriptase is medically indicated, comprising administering to the patient~~ Use of an effective amount or concentration of a compound of any one of claims 1 to 11 in the manufacture of a medicament for treating a viral infection in a patient wherein inhibition of a reverse transcriptase is medically indicated, and wherein the compound is to be administered to the patient.

17. ~~A method for prophylaxis of a viral infection, comprising administering to the patient~~ Use of an effective amount or concentration of a compound of any one of claims 1 to 11 in the manufacture of a medicament for prophylaxis of a viral infection, wherein the compound is to be administered to the patient.

18. The ~~method~~ use of any one of claims 16 to 17, wherein administration of the compound provides for slow or controlled or sustained release of EFdA from the compound.

19. The use~~method~~ of any one of claims 16 to 17, wherein the route of administration for compound is selected from the group consisting of oral, parenteral, subcutaneous injections, intravenous, intramuscular, intrastemal injection, infusion, and release from an implant.

20. The use~~method~~ of any one of claims 15 to 17, wherein the compound is formulated as aqueous suspension, a solution, or encapsulated in particles for slow-release.

21. The use~~method~~ of any one of claims 15 to 20, wherein the viral infection is caused by HIV.

22. The use~~method~~ of any one of claims 15 to 20, wherein the viral infection is caused by HBV.

23. Use of an effective amount or concentration of a compound of any one of claims 1 to 11 ~~The method of any one of claims 15 to 22, further comprising administering~~ and an additional anti-HIV and/or anti-HBV agent in the manufacture of a medicament for the treatment of a viral infection, wherein the medicament is for inhibiting viral reverse transcriptase bioactivity.

24. Use of an effective amount or concentration of a compound of any one of claims 1 to 11 and an additional anti-HIV and/or anti-HBV agent in the manufacture of a medicament for treating a viral infection in a patient wherein inhibition of a reverse transcriptase is medically indicated.

25. Use of an effective amount or concentration of a compound of any one of claims 1 to 11 and an additional anti-HIV and/or anti-HBV agent in the manufacture of a medicament for prophylaxis of a viral infection.

~~24~~26. The ~~method~~ use of any one of claims 23-25, wherein the additional agent is selected from the group consisting of cabotegravir, dolutegravir, doravirine, elvitegravir, lersiverine, tenofovir disoproxil fumarate, tenofovir alafenamide fumarate, and lamivudine.

~~25. Use of a compound of any one of claims 1 to 11 for treatment and prevention of a viral infection of HIV or HBV.~~