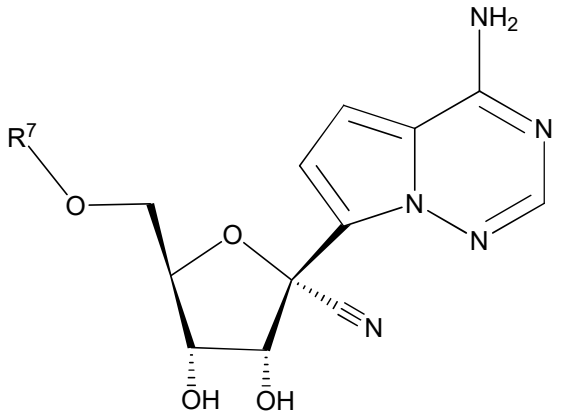
WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of a compound of Formula IV:



Formula IV

or a pharmaceutically acceptable salt or ester, thereof, in the preparation of a medicament for treating a *Coronaviridae* infection in a human in need thereof;

wherein:

R^7 is selected from the group consisting of

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

wherein

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, $(C_4\text{–}C_8)$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; 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 $-NR^a$-;

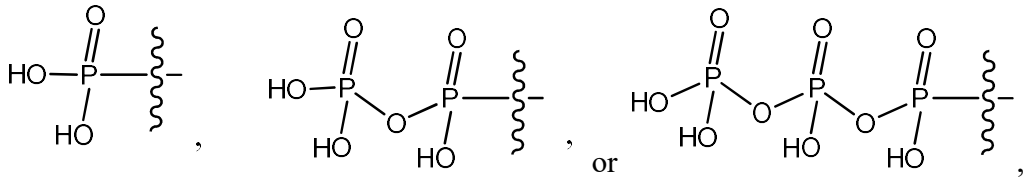
each R^a is independently H, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, aryl$(C_1\text{-}C_8)$alkyl, $(C_4\text{–}C_8)$carbocyclylalkyl, -C(=O)R, -C(=O)OR, -

$C(=O)NR_2$, -C(=O)SR, -S(O)R, $-S(O)_2R$, -S(O)(OR), $-S(O)_2(OR)$, or $-SO_2NR_2$;

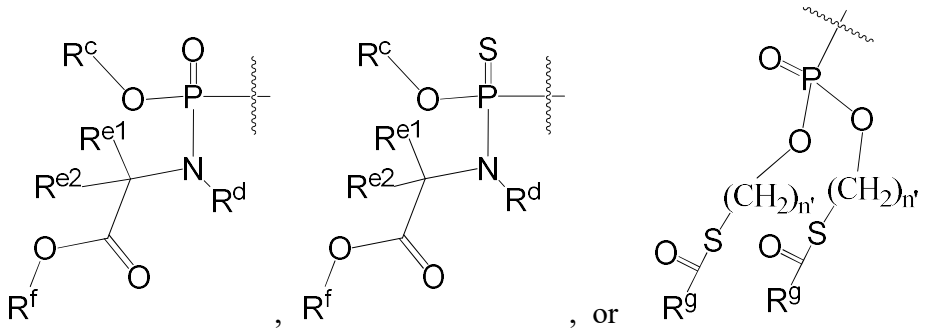
wherein each R is independently H, $(C_1\text{-}C_8)$ alkyl, $(C_1\text{-}C_8)$ substituted alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$ substituted alkenyl, $(C_2\text{-}C_8)$ alkynyl, $(C_2\text{-}C_8)$ substituted alkynyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heterocyclyl,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

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^{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 $(C_1\text{-}C_8)$alkyl may be optionally replaced with -O-, -S- or $-NR^a$-,

b)

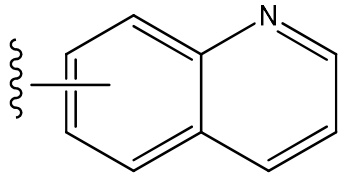


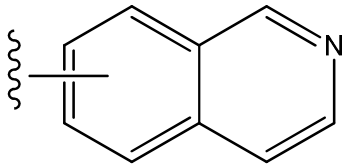
c)



wherein:

R^c is selected from phenyl, 1-naphthyl, 2-naphthyl,



and


;

R^d is H or CH_3;

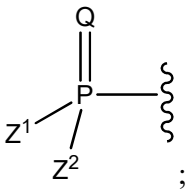
R^{e1} and R^{e2} are each independently H, C_1-C_6 alkyl or benzyl;

R^f is selected from H, C_1-C_8 alkyl, benzyl, C_3-C_6 cycloalkyl, and –CH_2-C_3-C_6 cycloalkyl;

R^g is selected from C_1-C_8 alkyl, -O-C_1-C_8 alkyl, benzyl, -O-benzyl, -CH_2-C_3-C_6 cycloalkyl, -O-CH_2-C_3-C_6 cycloalkyl, and CF_3; and

n' is selected from 1, 2, 3, and 4; and

d) a group of the formula:



;

wherein

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

Z^1 and Z^2, when taken together, are –$Q^1(C(R^y)_2)_3Q^1$-;

wherein

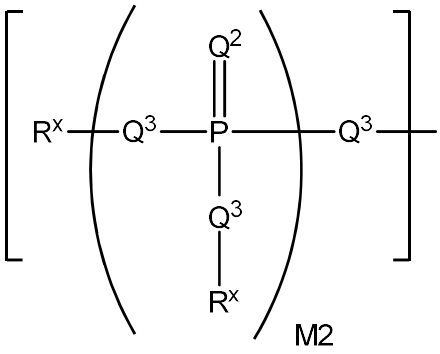
each Q^1 is independently O, S, or NR; and

each R^y is independently H, F, Cl, Br, I, OH, R, -C(=Q^2)R, -C(=Q^2)OR, -C(=Q^2)N($R)_2$, -N($R)_2$, -$^+$N($R)_3$, -SR, -S(O)R, -S(O)$_2$R, -S(O)(OR), -S(O)$_2$(OR), -OC(=Q^2)R, -OC(=Q^2)OR, -OC(=Q^2)(N($R)_2$), -SC(=Q^2)R, -SC(=Q^2)OR, -SC(=Q^2)(N($R)_2$), -N(R)C(=Q^2)R, -N(R)C(=Q^2)OR, -N(R)C(=Q^2)N($R)_2$, –SO_2NR_2, –CN, –N_3, –NO_2, –OR, or Z^3; or when taken together, two R^y on the same carbon atom form a carbocyclic ring of 3 to 7 carbon atoms;

each Q^2 is independently, O, S, NR, $^+N(O)(R)$, N(OR),

$^+N(O)(OR)$, or $N–NR_2$;or

Z^1 and Z^2 are each, independently, a group of the Formula Ia:



Formula Ia

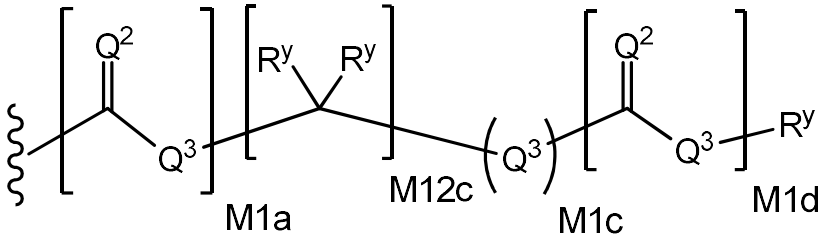
wherein:

each Q^3 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 $S(O)_2$;

M2 is 0, 1 or 2;

each R^x is independently R^y or the formula:



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;

Z^3 is Z^4 or Z^5;

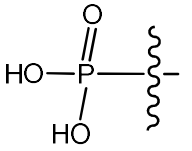
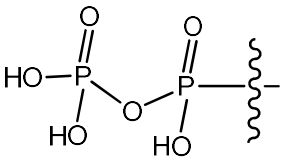
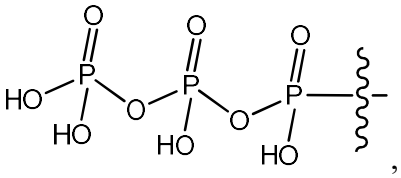
Z^4 is R, $-C(Q^2)R^y$, $-C(Q^2)Z^5$, $-SO_2R^y$, or $-SO_2Z^5$; and

Z^5 is a carbocycle or a heterocycle wherein Z^5 is independently substituted with 0 to 3 R^y groups.

2. The use of claim 1 wherein R^7 is selected from the group of

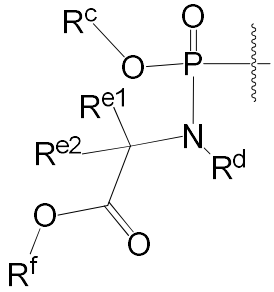
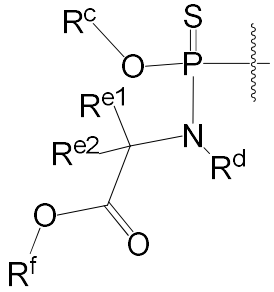
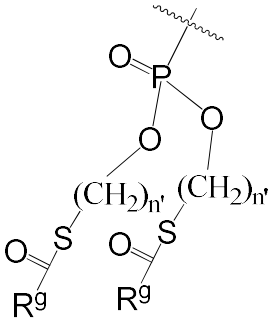
a) $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)(OR^{11})$, $-S(O)_2(OR^{11})$, $-SO_2NR^{11}R^{12}$,

b)


,

,
or

,

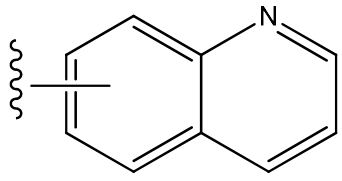
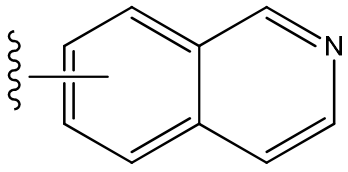
and

c)


,

,
or


wherein:

R^c is selected from phenyl, 1-naphthyl, 2-naphthyl,


and

;

R^d is H or CH_3;

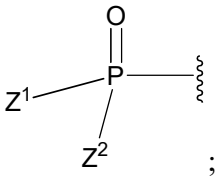
R^{e1} and R^{e2} are each independently H or C_1-C_6 alkyl;

R^f is selected from H, C_1-C_8 alkyl, benzyl, C_3-C_6 cycloalkyl, and –CH_2-C_3-C_6 cycloalkyl;

R^g is selected from C_1-C_8 alkyl, -O-C_1-C_8 alkyl, benzyl, -O-benzyl, -CH_2-C_3-C_6 cycloalkyl, -O-CH_2-C_3-C_6 cycloalkyl, and CF_3; and

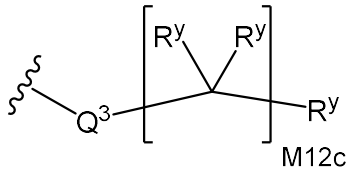
n' is selected from 1, 2, 3, and 4.

3. The use of claim 1 wherein R^7 is



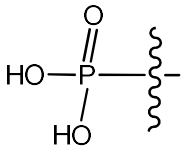
;

wherein Z^1 and Z^2 are each, independently, a group having the structure:

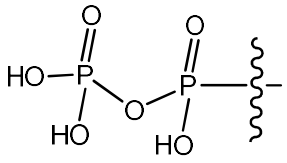


and Z^3 is Z^5.

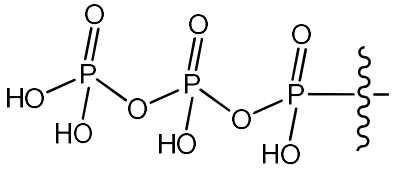
4. The use of any of claims 1 to 3 wherein R^7 is



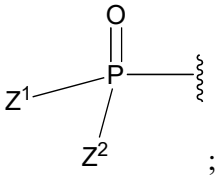
,



,

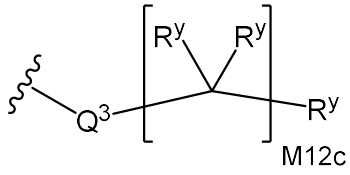


, or



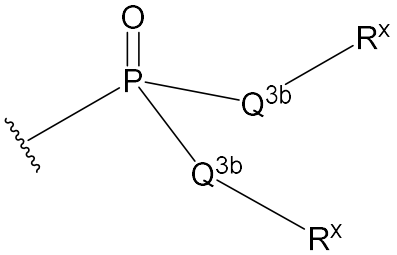
;

wherein Z^1 and Z^2 are each, independently, a group having the structure:



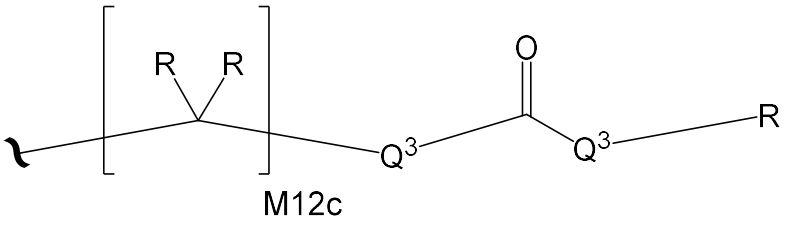
and Z^3 is Z^5.

5. The use of claim 1 wherein R^7 is



wherein each Q^{3b} is, independently, O or N(R).

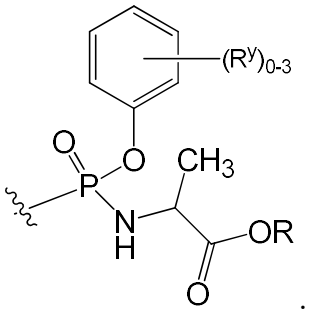
6. The use of claim 5 wherein each Q^{3b} is O and each R^x is independently:



M12c

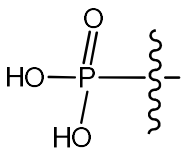
wherein M12c is 1, 2 or 3 and each Q^3 is independently a bond, O, CR_2, or S.

7. The use of any of claims 1 or 4-5 wherein R^7 is

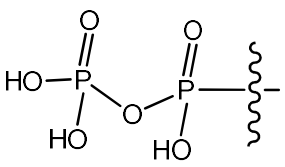


.

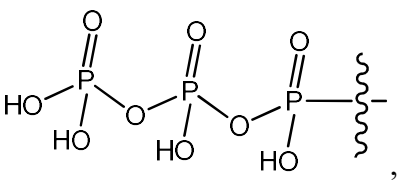
8. The use of any of claims 1, 2 or 4 wherein R^7 is



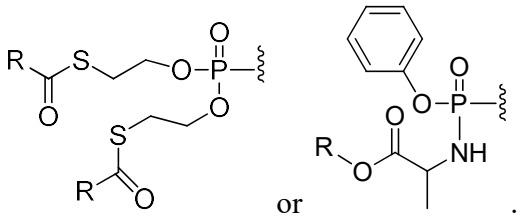
,



,

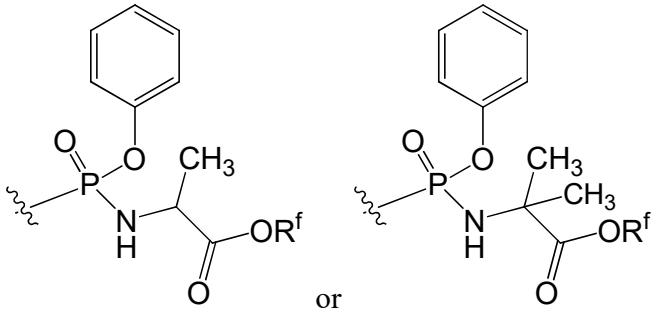


,



or .

9. The use of claim 1 or 2 wherein R^7 is



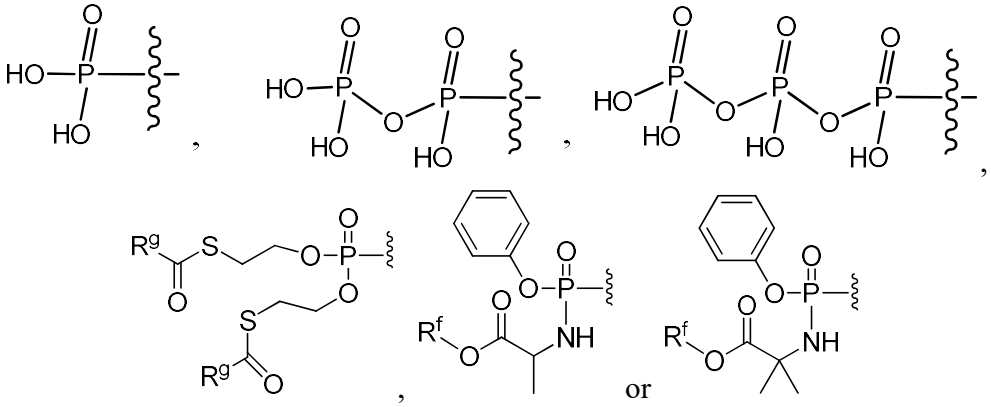
or

wherein

R^f is selected from the group of from H, C_1-C_8 alkyl, benzyl, C_3-C_6 cycloalkyl, and –CH_2-C_3-C_6 cycloalkyl.

10. The use of claim 9 wherein R^f is C_1-C_8 alkyl.

11. The use of claim 1 or 2 wherein R^7 is

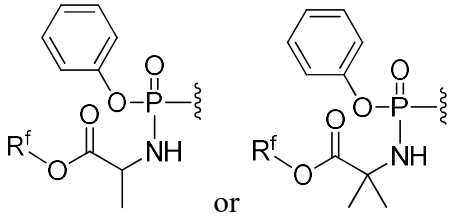


wherein

R^f is selected from H, C_1-C_8 alkyl, benzyl, C_3-C_6 cycloalkyl, and –CH_2-C_3-C_6 cycloalkyl; and

R^g is selected from C_1-C_8 alkyl, -O-C_1-C_8 alkyl, benzyl, -O-benzyl, -CH_2-C_3-C_6 cycloalkyl, -O-CH_2-C_3-C_6 cycloalkyl, and CF_3.

12. The use of any of claims 1, 2 or 11 wherein R^7 is



or

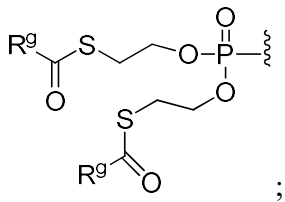
wherein

R^f is selected from H, C_1-C_8 alkyl, benzyl, C_3-C_6 cycloalkyl, and –CH_2-C_3-C_6 cycloalkyl.

13. The use of claim 12 wherein R^f is C_1-C_8 alkyl.

14. The use of claim 12 wherein R^f is C_1-C_6 alkyl.

15. The use of claims 1, 2 or 11 wherein R^7 is:



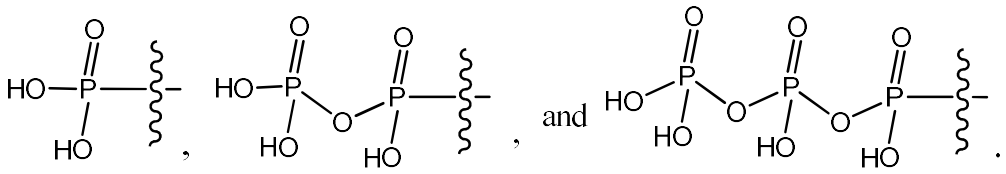
;

wherein

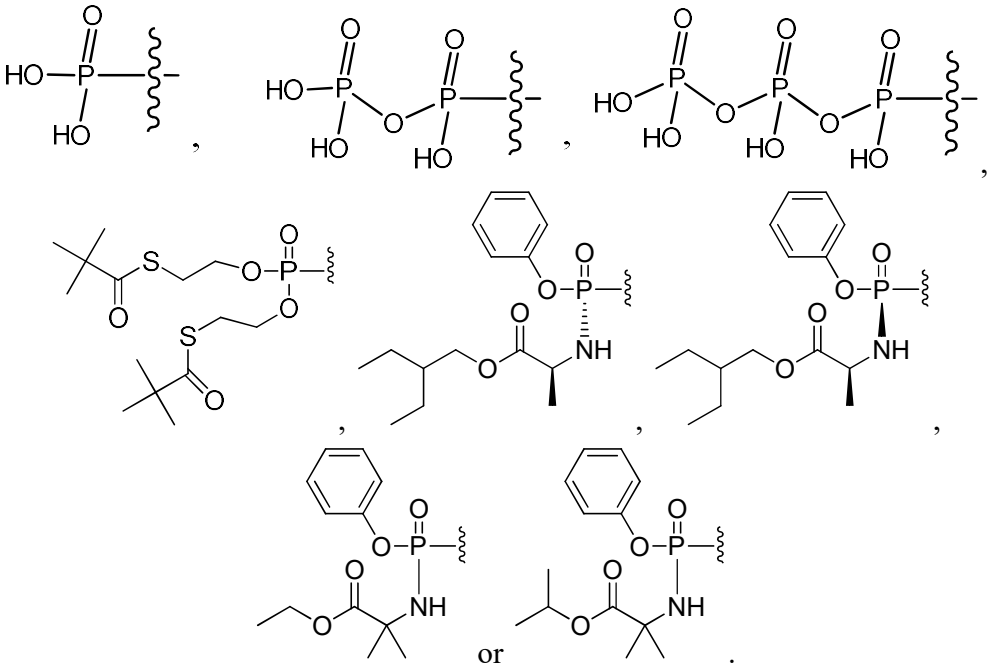
R^g is selected from C_1-C_8 alkyl, -O-C_1-C_8 alkyl, benzyl, -O-benzyl, -CH_2-C_3-C_6 cycloalkyl, -O-CH_2-C_3-C_6 cycloalkyl, and CF_3.

16. The use of claim 15 wherein R^g is C_1-C_8 alkyl.

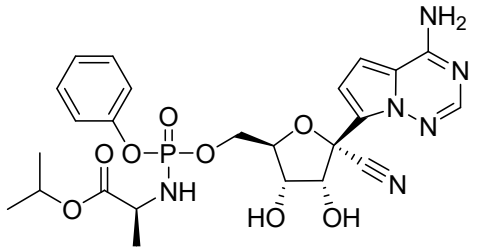
17. The use of any of claims 1, 2, 4, 8 or 11 wherein R^7 is selected from the group of:

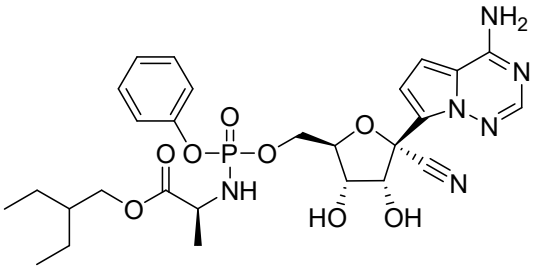
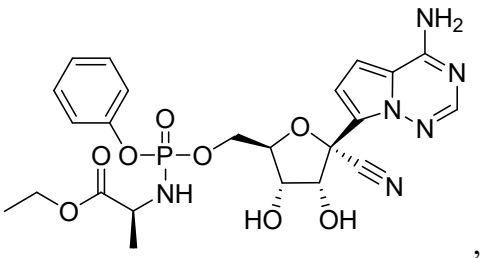
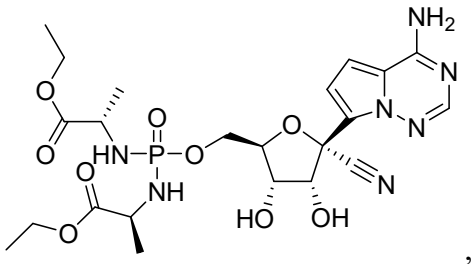
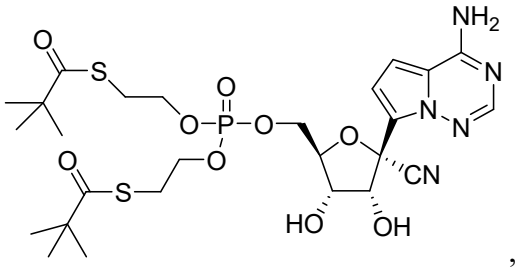
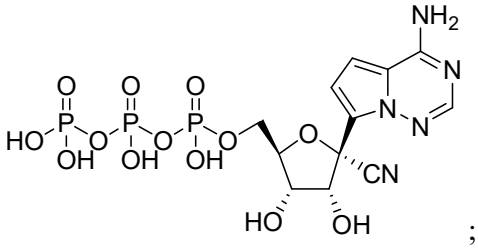


18. The use of any of claims 1, 2, 4, 8 or 11 wherein R^7 is

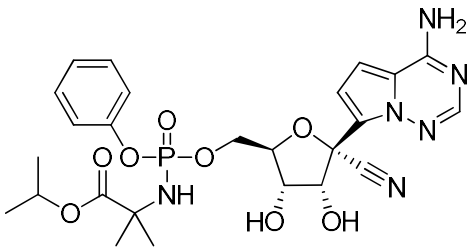
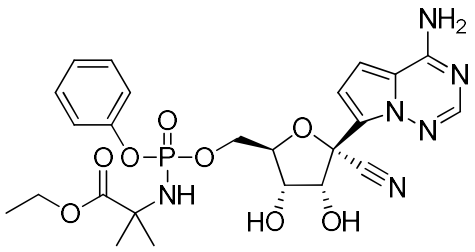
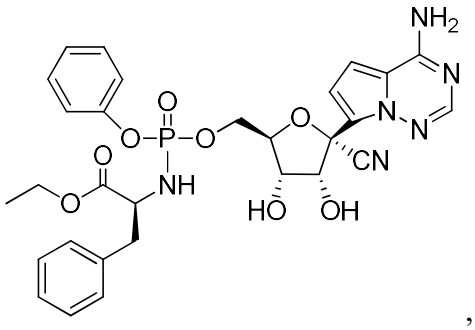
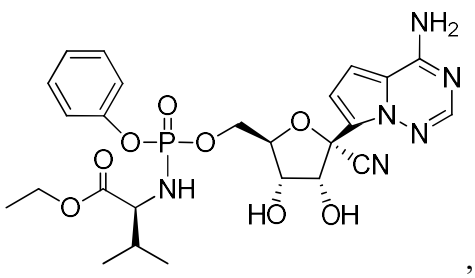


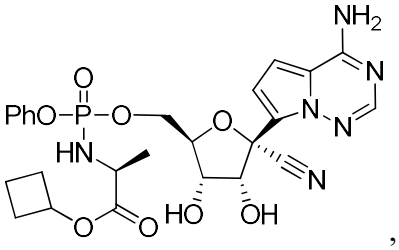
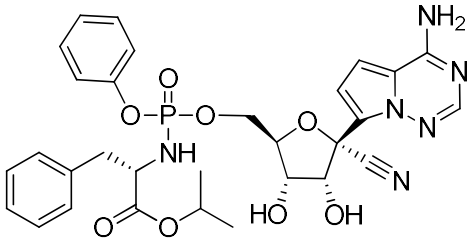
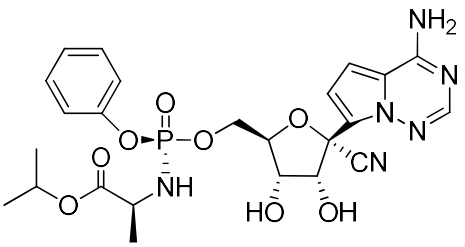
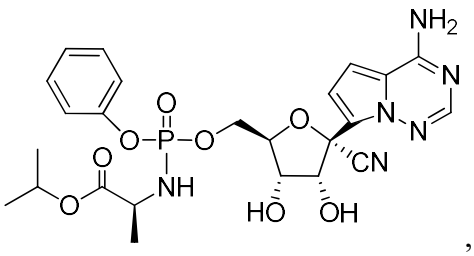
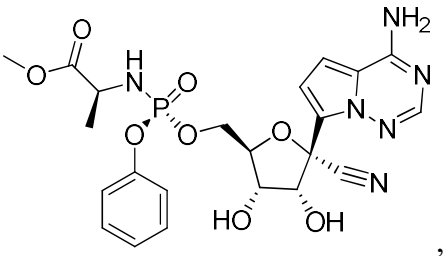
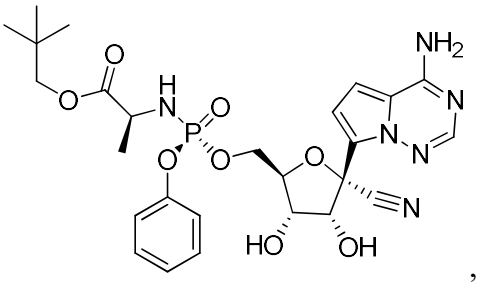
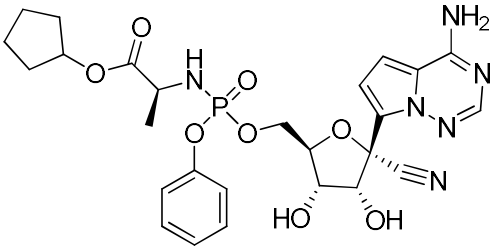
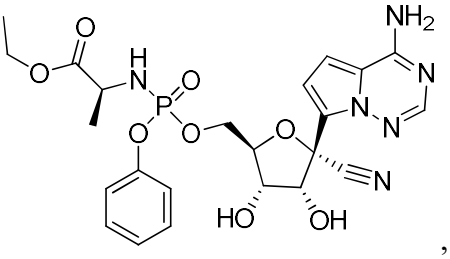
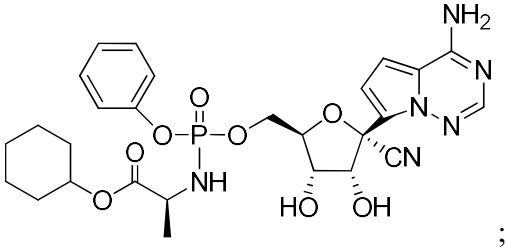
19. The use of claim 1 wherein the compound of Formula IV is:




,

,

,

, or

;
or a pharmaceutically acceptable salt or ester thereof.

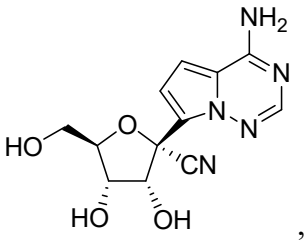
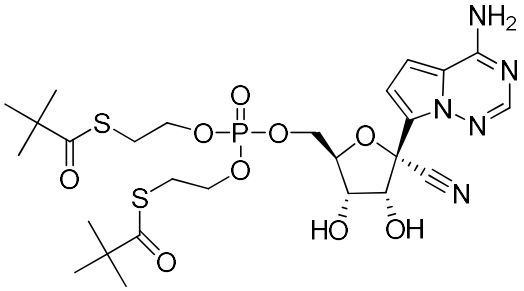
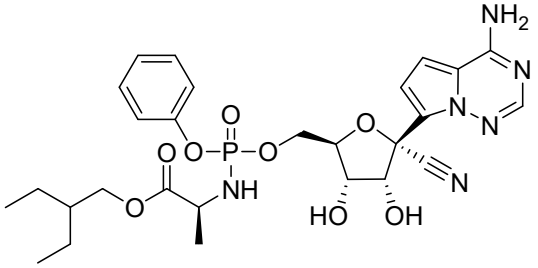
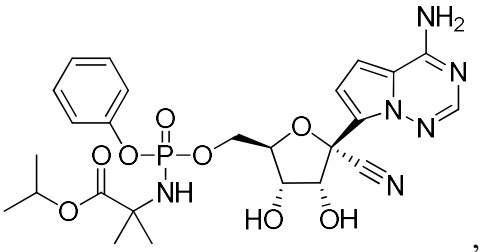
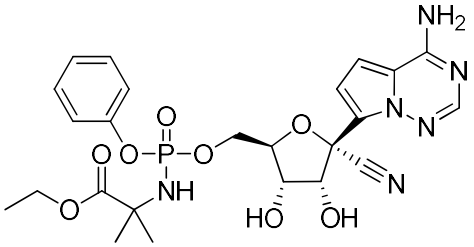
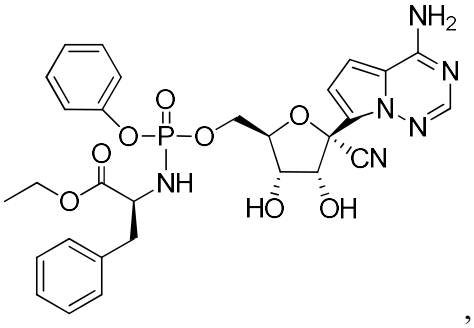
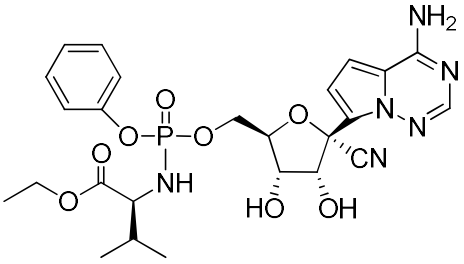
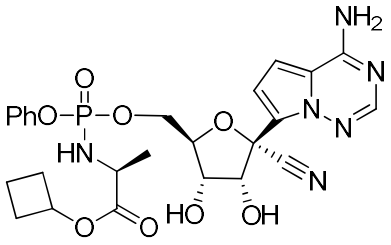
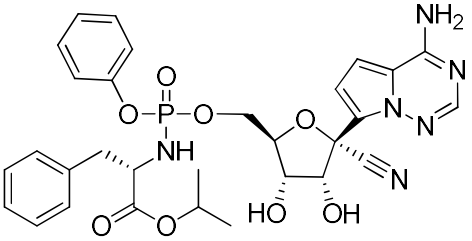
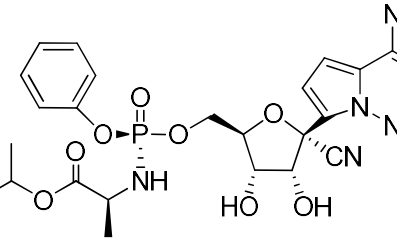
20. The use of claim 1 wherein the compound of Formula IV is:

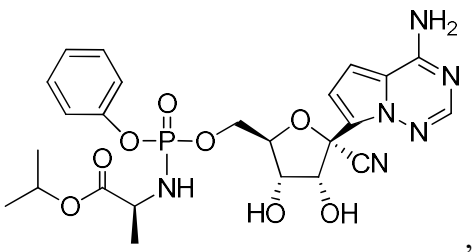
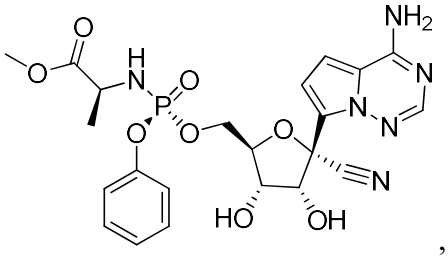
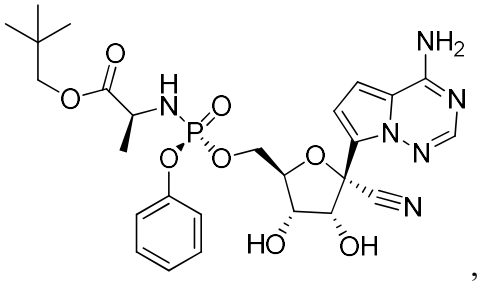
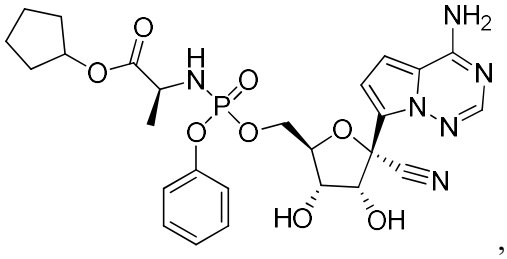
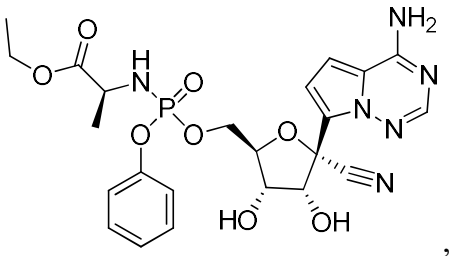
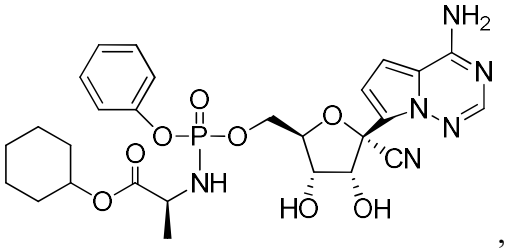
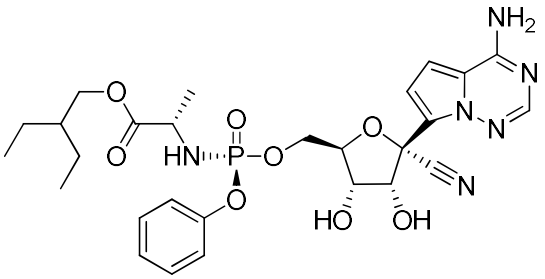
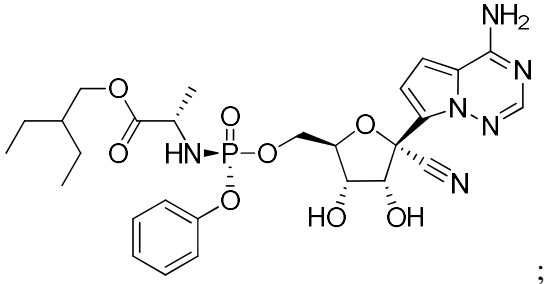

,

,

,

,


,

,

,

,

,

,

,

,

or ;

or a pharmaceutically acceptable salt or ester thereof.

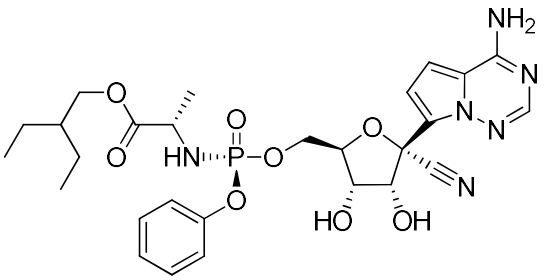
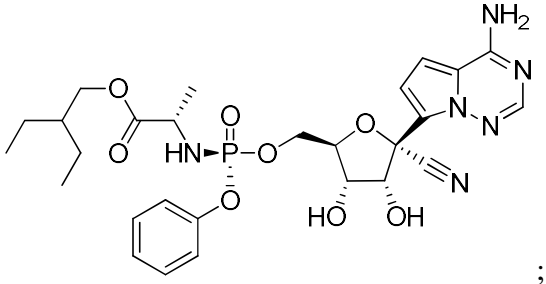
21. The use of claim 1 wherein the compound of Formula IV is:


,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

or

;

or a pharmaceutically acceptable salt or ester thereof.

22. The use of claim 21 wherein the compound of Formula IV is:


or

;

or a pharmaceutically acceptable salt or ester thereof.

23. The use of any of claims 1-22 further comprising a pharmaceutically acceptable carrier or excipient.

24. The use of any of claims 1-22 wherein the medicament further comprises a therapeutically effective amount of at least one other thereapeutic agent or composition thereof selected from the group consisting of a corticosteroid, an anti-inflammatory signal transduction modulator, a β2-adrenoreceptor agonist bronchodilator, an anticholinergic, a mucolytic agent, hypertonic saline and other drugs for treating a *Coronaviridae* virus infections; or mixtures thereof.

25. The use of any of claims 1-22 wherein the *Coronaviridae* infection is caused by a *Coronaviridae* virus selected from SARS, MERS, 229E, NL63, OC43, and HKU1.

26. The method of any of claims 1-22 wherein a *Coronaviridae* polymerase is inhibited.

27. A kit comprising one or more individual dosage units of a compound selected from those described in claims 1-22, or a pharmaceutically acceptable salt, ester, stereoisomer, hydrate, solvate, mixture of stereoisomers, or tautomer thereof, and directions for their use in treating a *Coronaviridae* viral infection in a human.