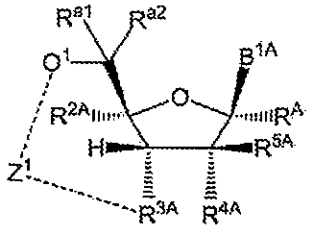
WHAT IS CLAIMED IS:

1. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating a *Picornaviridae* viral infection, wherein the compound of Formula (I) has the structure:

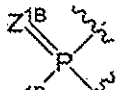


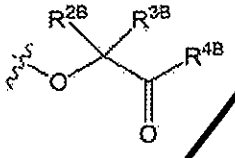
(I)

wherein:

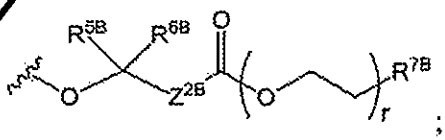
$B^{1A}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

when -------- are both absent, $Z^1$ is absent, $O^1$ is $OR^{1A}$, $R^{3A}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{xA}$ and an optionally substituted O-linked amino acid;

when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or $-CN$, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1-6}$ alkyl,



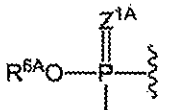
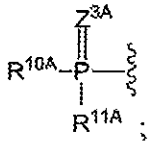
and



;

$R^{a1}$ and $R^{a2}$ are independently hydrogen or deuterium;

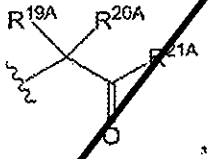
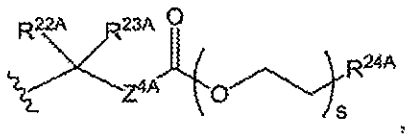
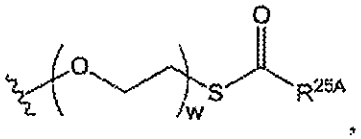
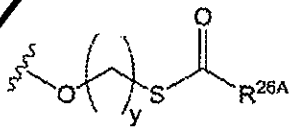
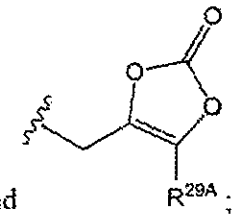
$R^{xA}$ is hydrogen, deuterium, an unsubstituted $C_{1-3}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-3}$ alkynyl or cyano;

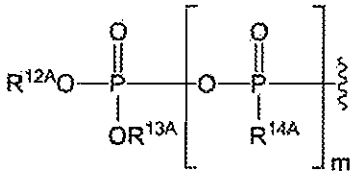
$R^{1A}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  and  ;

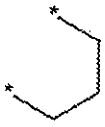
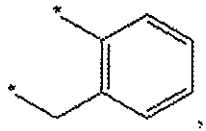
$R^{2A}$ is an unsubstituted $C_{2-4}$ alkyl or $-(CH_2)_{1-6}F$, and $R^{5A}$ is selected from the group consisting of halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; or

$R^{2A}$ is halo, an unsubstituted $C_{2-4}$ alkenyl, $-CH_2$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or -CN, and $R^{5A}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{4A}$ is selected from the group consisting of H, OH, halo, $N_3$, $-OC(=O)R^{"B}$, an optionally substituted O-linked amino acid and $NR^{"B1}R^{"B2}$, or $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

$R^{6A}$, $R^{7A}$ and $R^{8A}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted $*-(CR^{15A}R^{16A})_p-O-C_{1-24}$ alkyl, an optionally substituted $*-(CR^{17A}R^{18A})_q-O-C_{1-24}$ alkenyl,  ,  ,  ,  and  ; or

$R^{6A}$ is  and $R^{7A}$ is absent or hydrogen; or

$R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9A}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

$R^{12A}$ and $R^{13A}$ are independently absent or hydrogen;

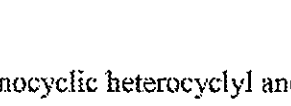
$R^{14A}$ is $O^-$, OH or methyl;

each $R^{15A}$, each $R^{16A}$, each $R^{17A}$ and each $R^{18A}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19A}$, $R^{20A}$, $R^{22A}$ and $R^{23A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an

optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25A}$, $R^{26A}$ and $R^{29A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{30A}$ and $R^{31A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R^{27A}$ and each $R^{27B}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R^{27B1}$ and each $R^{27B2}$ are independently hydrogen and an optionally substituted $C_{1-6}$ alkyl;

$R^{2B}$, $R^{3B}$, $R^{5B}$ and $R^{6B}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4B}$ and $R^{7B}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

m and w are 0 or 1;

p and q are independently 1, 2 or 3;

r and s are independently 0, 1, 2 or 3;

y is 3, 4 or 5; and

$Z^{1A}$, $Z^{2A}$, $Z^{3A}$, $Z^{4A}$, $Z^{1B}$ and $Z^{2B}$ are independently O or S;

2. The use of Claim 1, wherein the Picornaviridae virus is selected from the group consisting of an Aphthovirus, an Enterovirus, a Rhinovirus, a Hepatovirus and a Parechovirus.

3. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of an enterovirus A, enterovirus B, enterovirus C, enterovirus D, enterovirus E, enterovirus F, enterovirus G, enterovirus Henterovirus J.

4. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of poliovirus 1, poliovirus 2, poliovirus 3, CV-A1, CV-A2, CV-A3, CV-A4, CV-A5, CV-A6, CV-A7, CV-A8, CV-A9, CV-A10, CV-A11, CV-A12, CV-A13, CV-A14, CV-A15, CV-A16,

CV-A17, CV-A18, CV-A19, CV-A20, CV-A21, CV-A22, CV-A23, CV-B1, CV-B2, CV-B3, CV-B4, CV-B5, CV-B6, echovirus 1, echovirus 2, echovirus 3, echovirus 4, echovirus 5, echovirus 6, echovirus 7, echovirus 9, echovirus 11, echovirus 12, echovirus 13, echovirus 14, echovirus 15, echovirus 16, echovirus 17, echovirus 18, echovirus 19, echovirus 20, echovirus 21, echovirus 24, echovirus 25, echovirus 26, echovirus 27, echovirus 29, echovirus 30, echovirus 31, echovirus 32, echovirus 33, enterovirus 68, enterovirus 69, enterovirus 70, enterovirus 71 and viluisk human encephalomyelitis virus.

5. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of rhinovirus A, rhinovirus B and rhinovirus C.

6. The use of Claim 2, wherein Hepatovirus is hepatitis A.

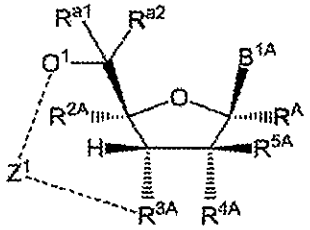
7. The use of Claim 2, wherein the Parechovirus is selected from the group consisting of human parechovirus 1, human parechovirus 2, human parechovirus 3, human parechovirus 4, human parechovirus 5 and human parechovirus 6.

8. The use of Claim 1, wherein the Picornaviridae virus is selected from the group consisting of an Aquamavirus, an Avihepatovirus, a Cardiovirus, a Cosavirus, a Dicipivirus, an Erbovirus, a Kobuvirus, a Megrivirus, a Salivirus, a Sapelovirus, a Senecavirus, a Teschovirus and a Tremovirus.

9. The use of any one of Claims 1-8, wherein $R^{2A}$ is halo or $-CHF_2$, $-(CH_2)_{1-6}Cl$.

10. The use of any one of Claims 1-9, wherein $R^{5A}$ is H.

11. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating a *Flaviviridae* viral infection, wherein the compound of Formula (I) has the structure:

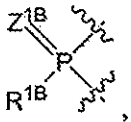


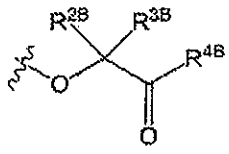
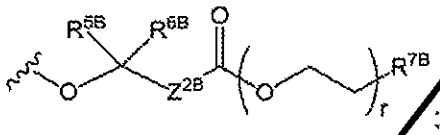

(I)

wherein:

$B^{1A}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

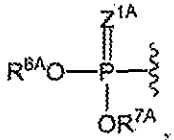
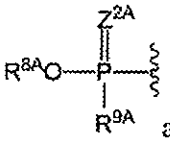
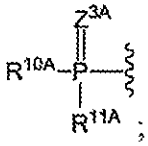
when -------- are both absent, $Z^1$ is absent, $O^1$ is $OR^{1A}$, $R^{3A}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{xA}$ and an optionally substituted O-linked amino acid;

when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or $-CN$, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an $-O-$optionally substituted $C_{1-6}$ alkyl.

 and  ;

$R^{a1}$ and $R^{a2}$ are independently hydrogen or deuterium;

$R^A$ is hydrogen, deuterium, an unsubstituted $C_{1-3}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-3}$ alkynyl or cyano;

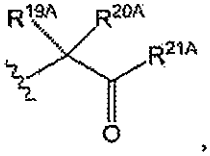
$R^{1A}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  ,  and  ;

$R^{2A}$ is halo, an unsubstituted $C_{2-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, $-(CH_2)_{1-6}F$, or $-CN$, and $R^{5A}$ is selected from the group consisting of OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; or

$R^{2A}$ is $-CHF_2$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$ or $-(CH_2)_{1-6}NH_2$, and $R^{5A}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{4A}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R^{xB}$, an optionally substituted O-linked amino acid and $NR^{xB1}R^{xB2}$, or $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

$R^{6A}$, $R^{7A}$ and $R^{8A}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted *–$(CR^{15A}R^{16A})_p$–O–$C_{1-24}$ alkyl, an optionally substituted *–$(CR^{17A}R^{18A})_q$–O–$C_{1-24}$ alkenyl,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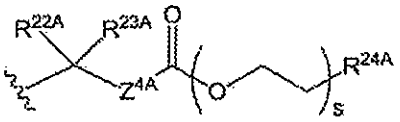
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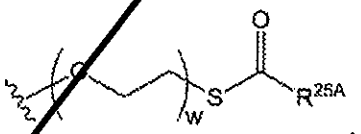
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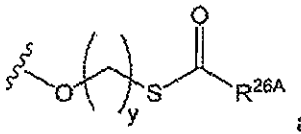
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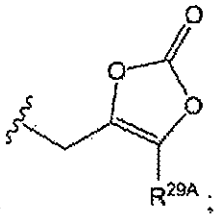
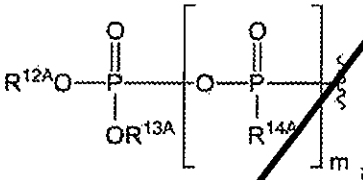
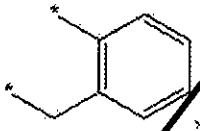

; or



$R^{6A}$ is and $R^{7A}$ is absent or hydrogen; or

$R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9A}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

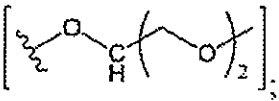
$R^{12A}$ and $R^{13A}$ are independently absent or hydrogen;

$R^{14A}$ is $O^-$, OH or methyl;

each $R^{15A}$, each $R^{16A}$, each $R^{17A}$ and each $R^{18A}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19A}$, $R^{20A}$, $R^{22A}$ and $R^{23A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25A}$, $R^{26A}$ and $R^{29A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{30A}$ and $R^{31A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R^{\prime\prime A}$ and each $R^{\prime\prime B}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R^{\prime\prime B1}$ and each $R^{\prime\prime B2}$ are independently hydrogen and an optionally substituted $C_{1-6}$ alkyl;

$R^{2B}$, $R^{3B}$, $R^{5B}$ and $R^{6B}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4B}$ and $R^{7B}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted

–O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

m and w are 0 or 1;

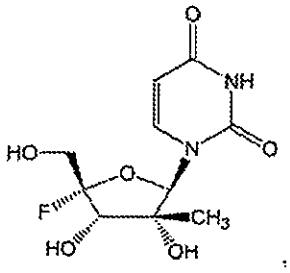
p and q are independently 1, 2 or 3;

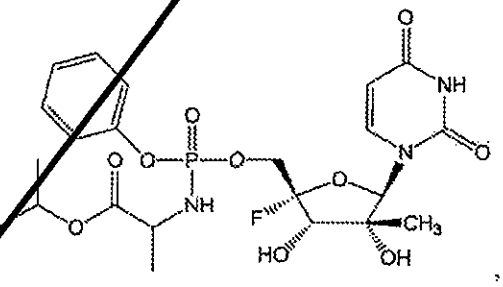
r and s are independently 0, 1, 2 or 3;

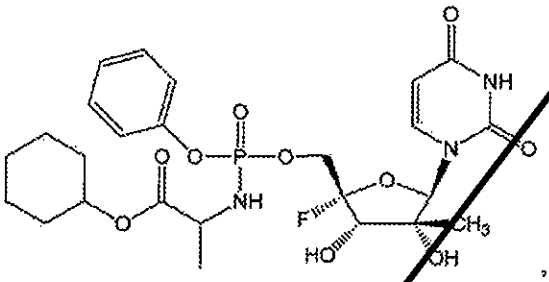
y is 3, 4 or 5; and

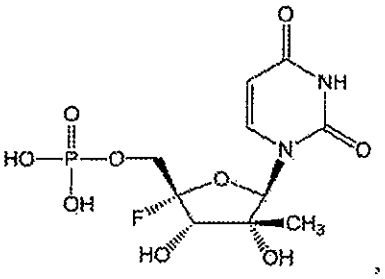
$Z^{1A}$, $Z^{2A}$, $Z^{3A}$, $Z^{4A}$, $Z^{1B}$ and $Z^{2B}$ are independently O or S;

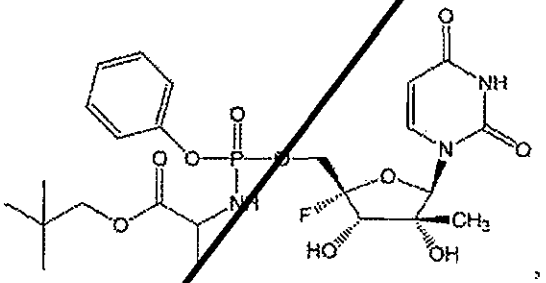
provided that the compound of Formula (I), or a pharmaceutically acceptable salt thereof, cannot be selected from the group consisting of:

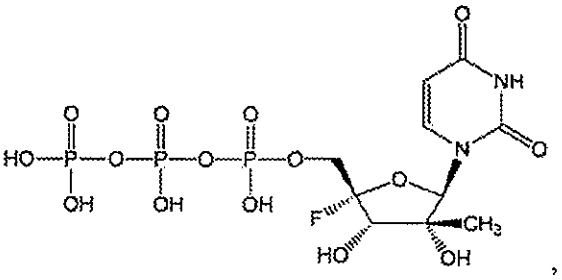


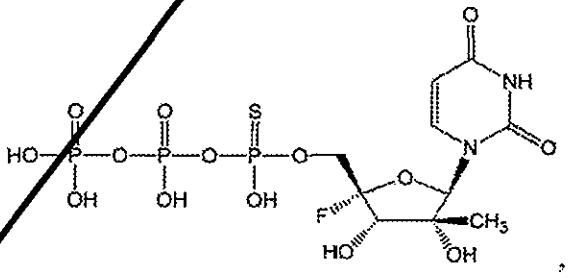


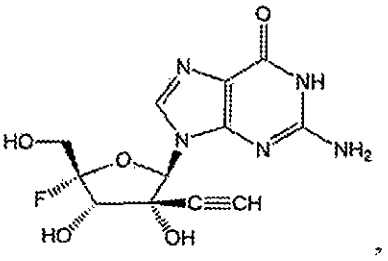


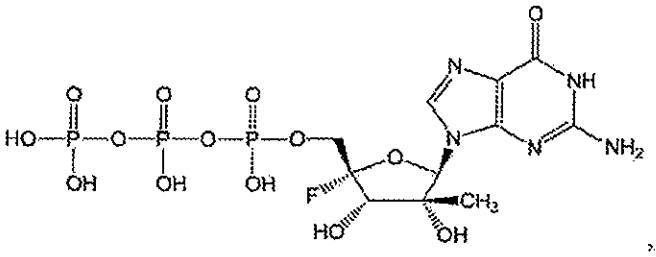


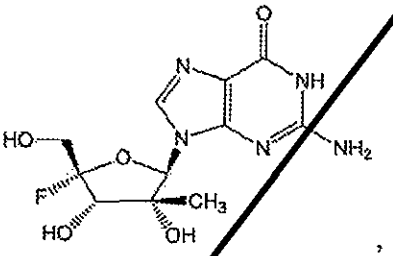


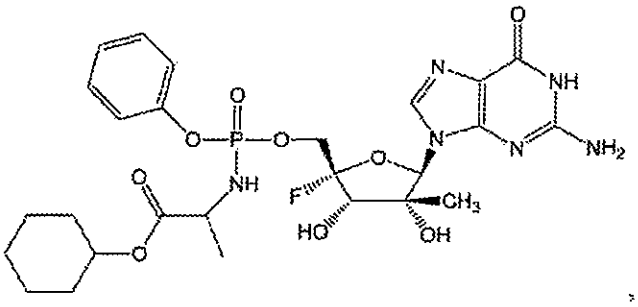


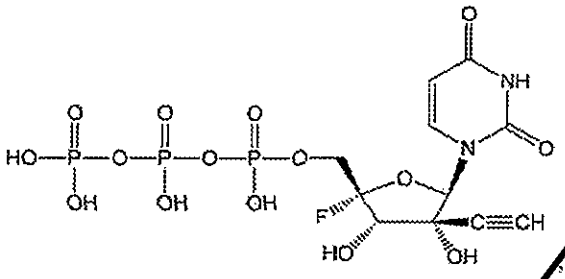


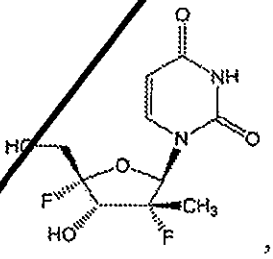


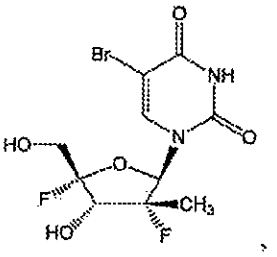


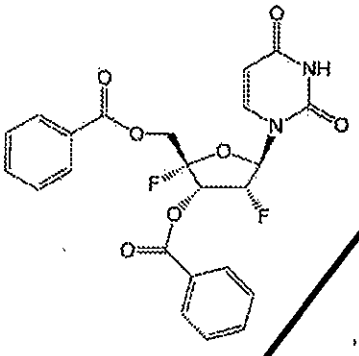


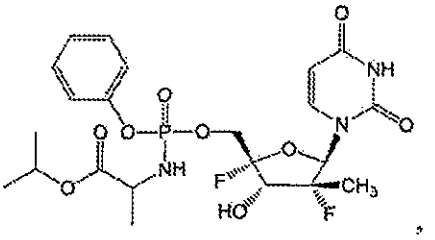


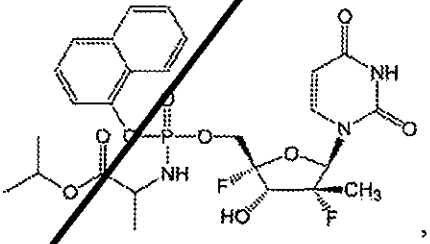


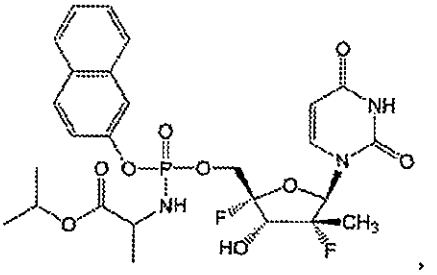


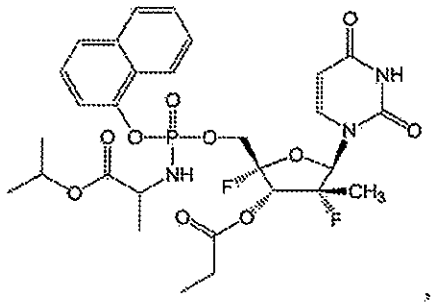


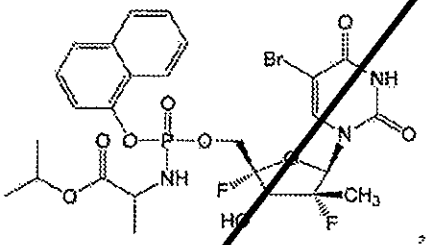


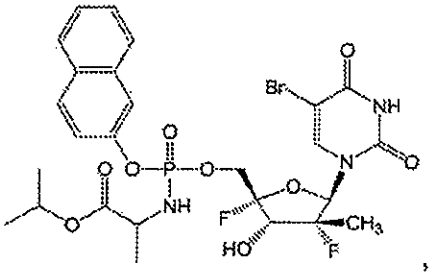


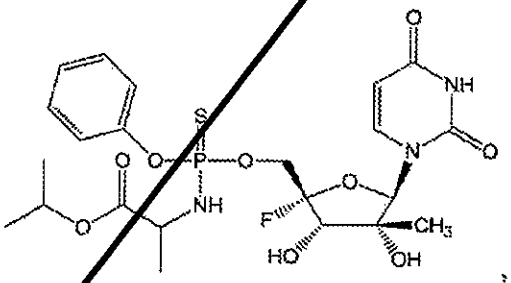


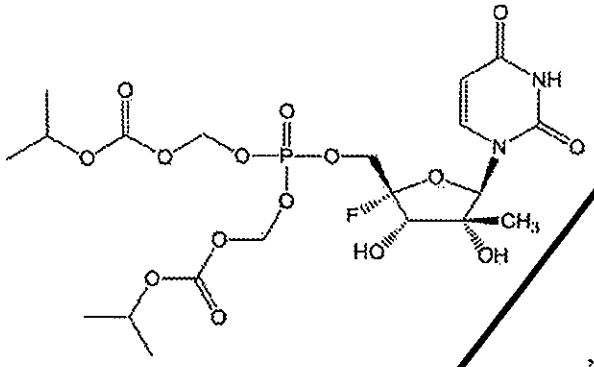


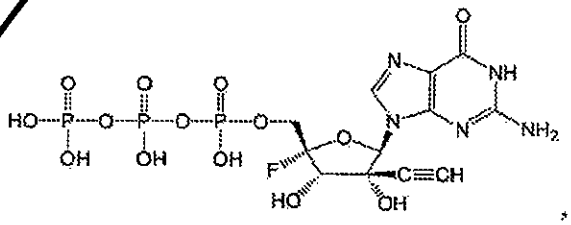


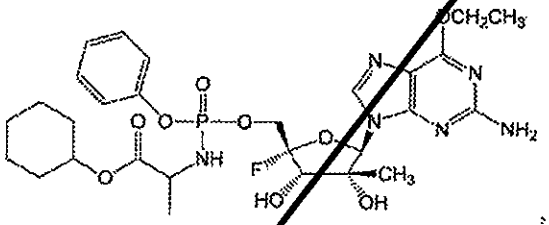


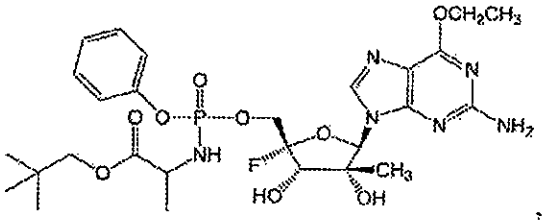


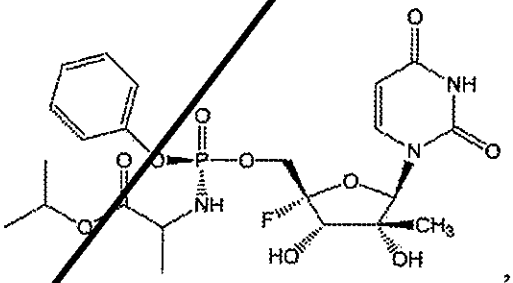


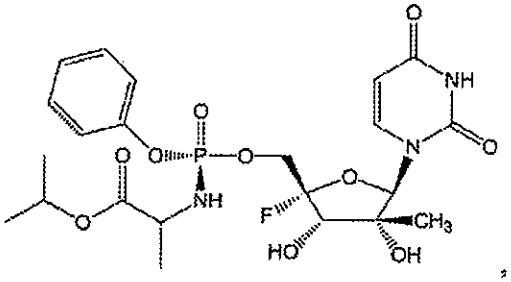


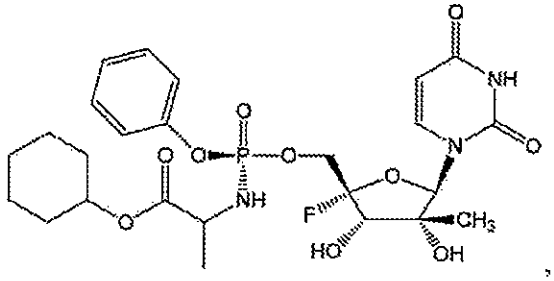


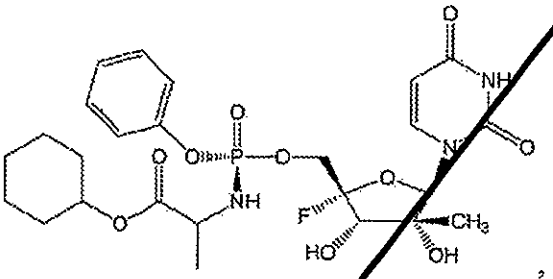


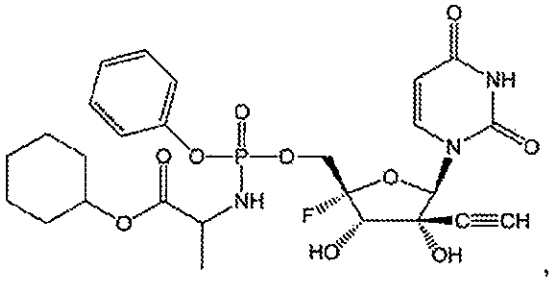


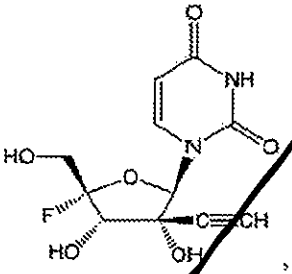


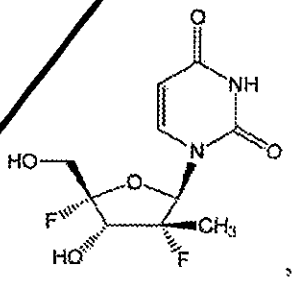


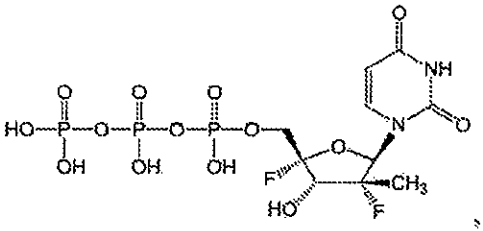


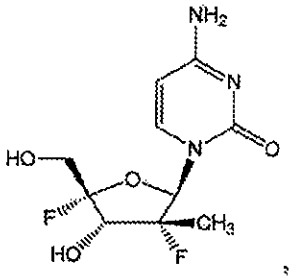


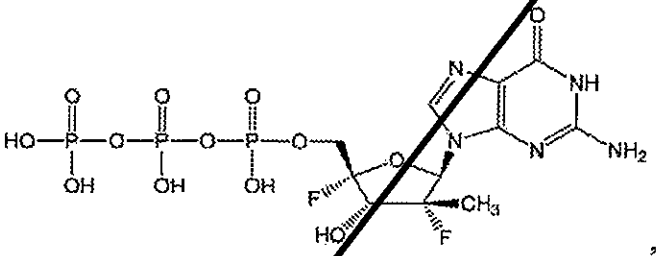


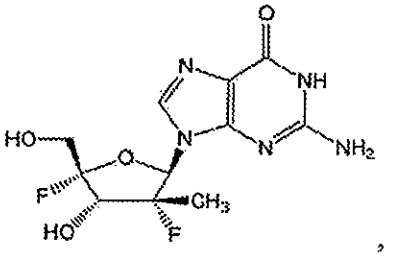


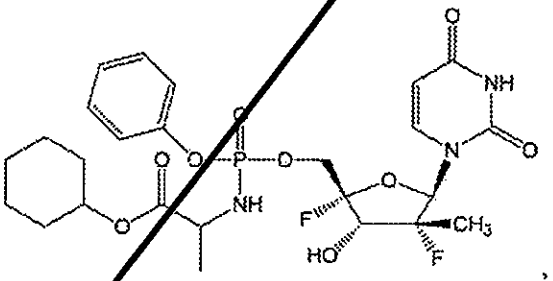


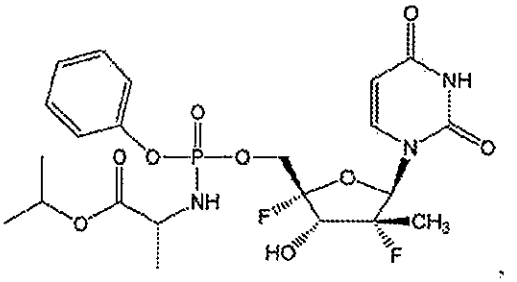


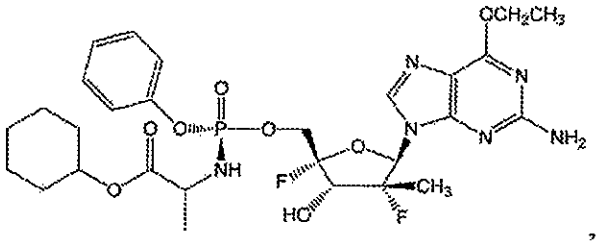


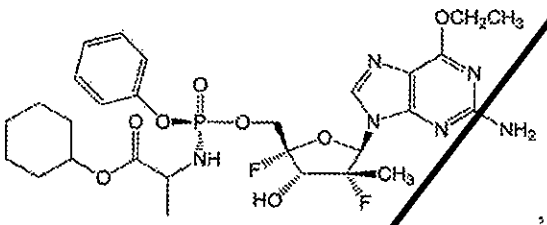


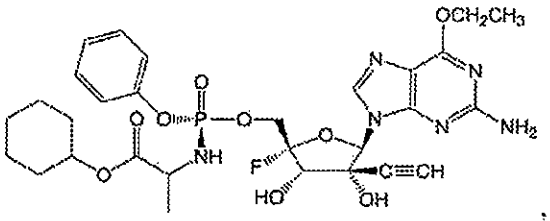


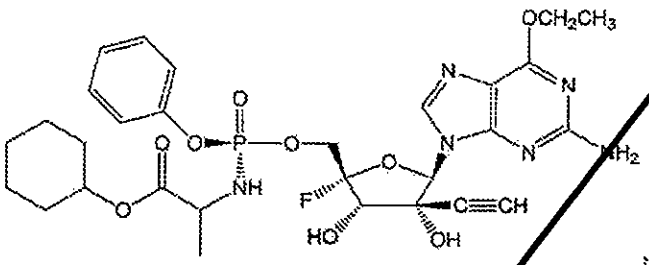


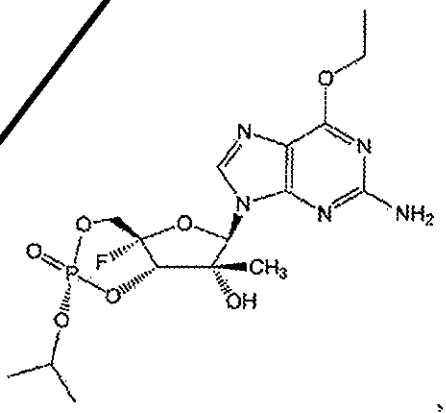


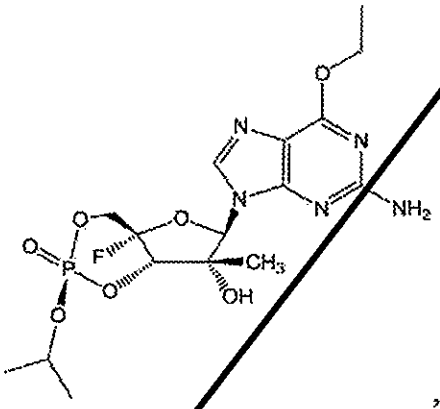


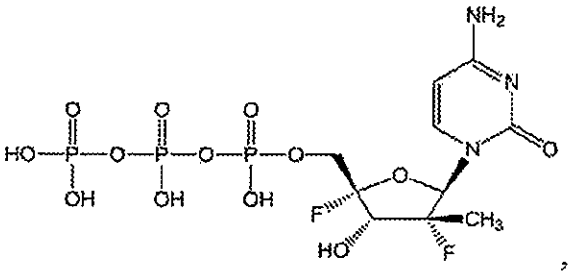


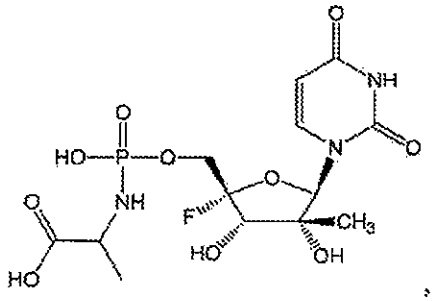


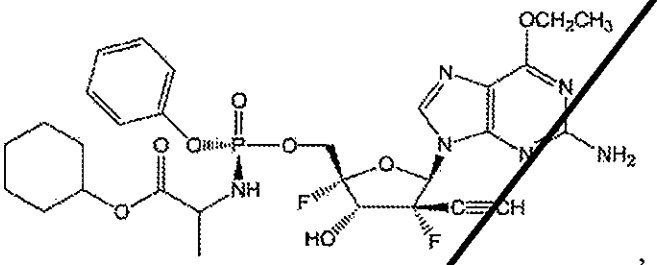


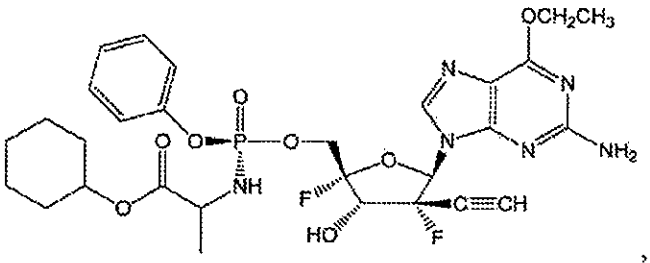


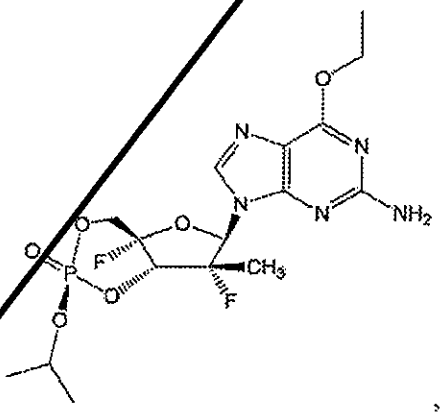


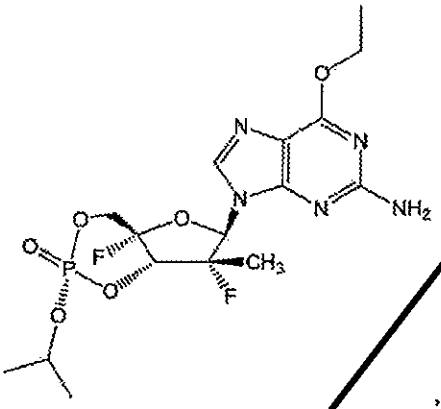


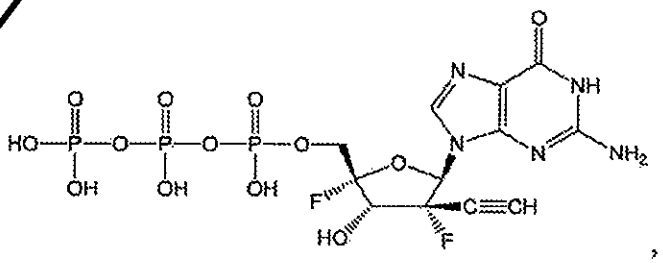


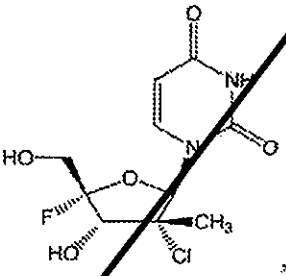


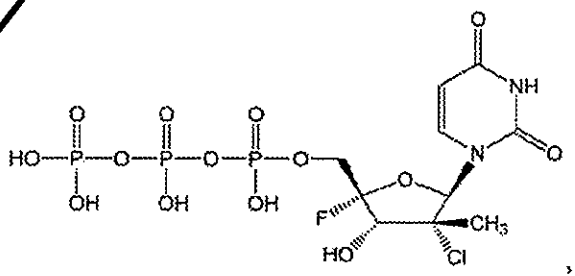


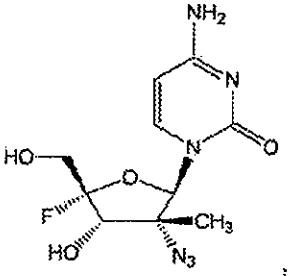


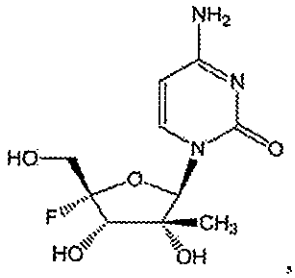


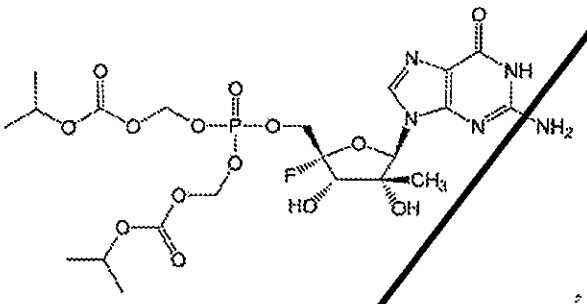


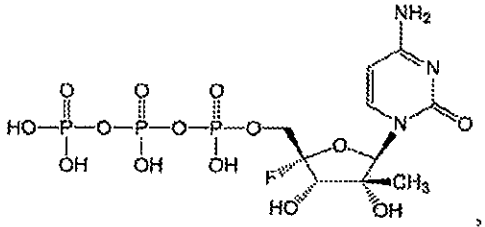


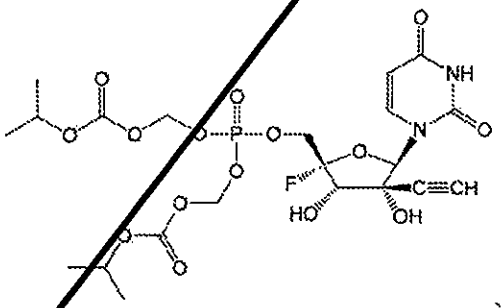


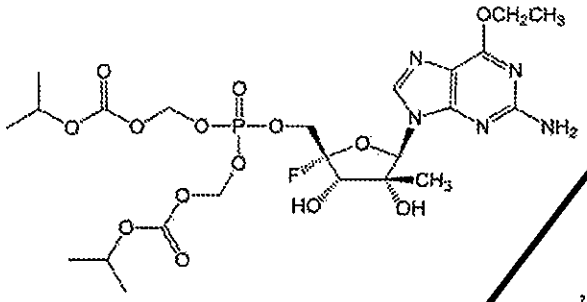


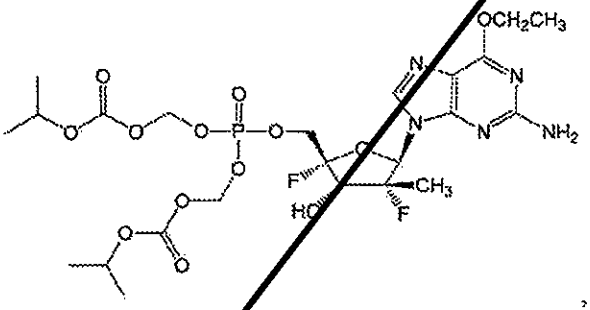


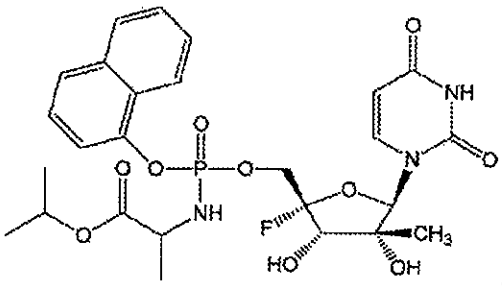


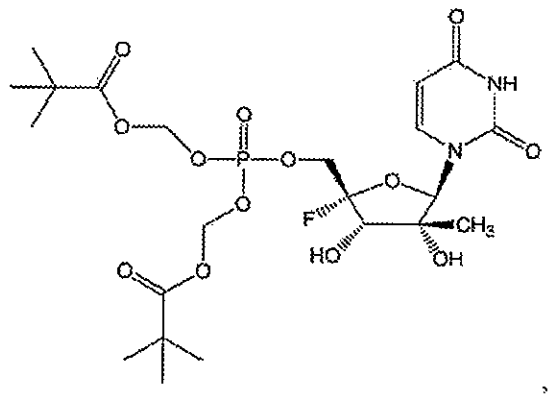


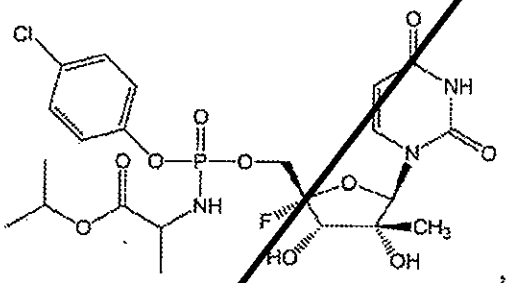


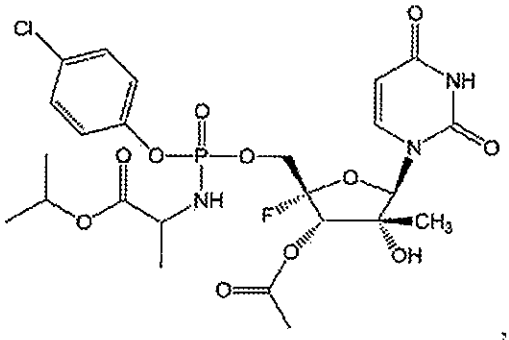


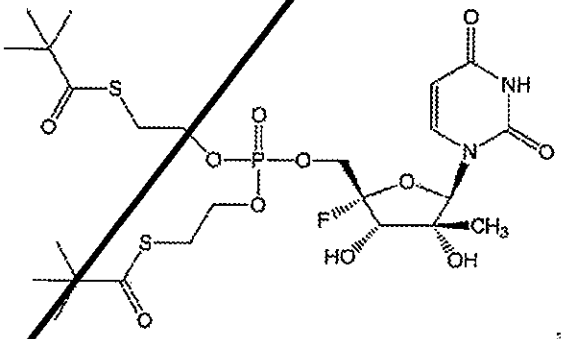


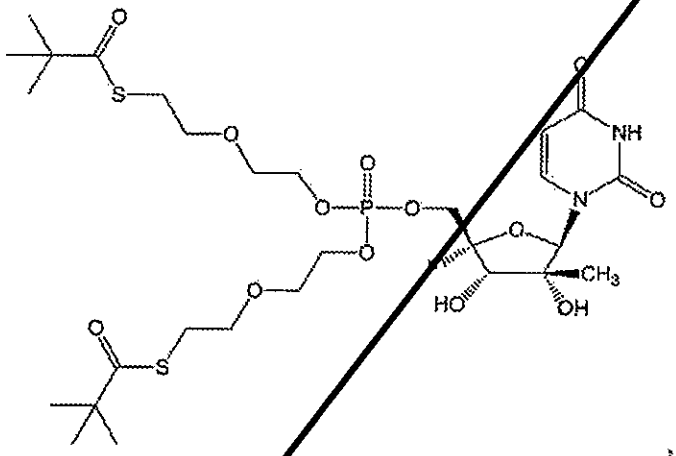


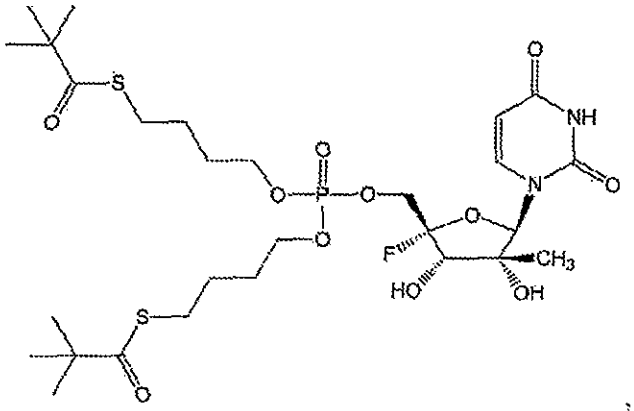


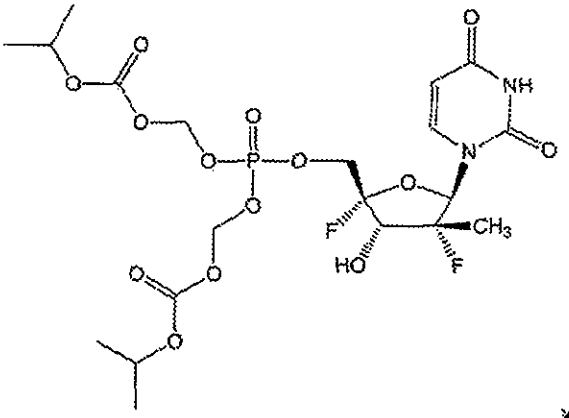


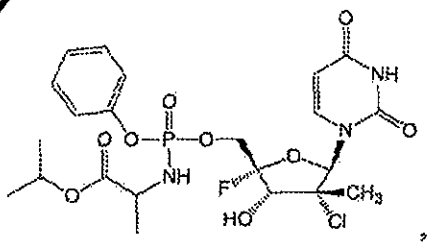


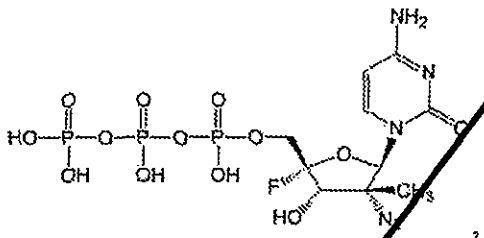


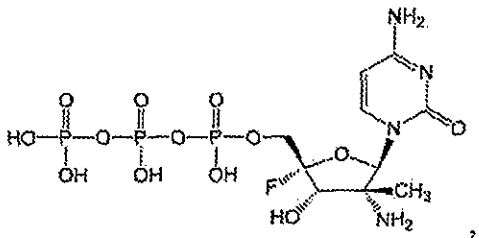


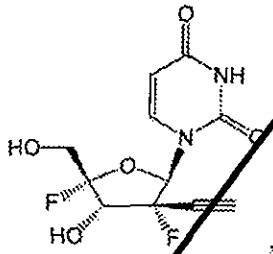


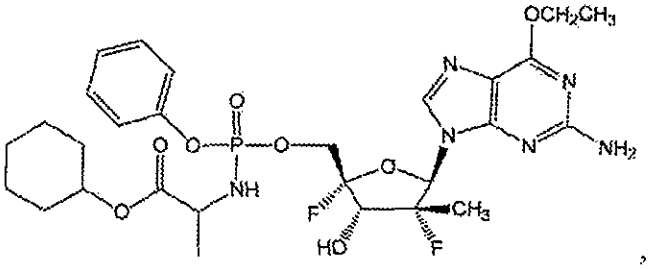


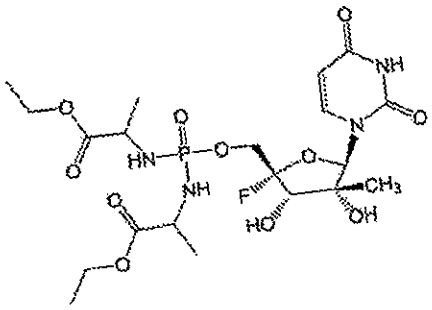


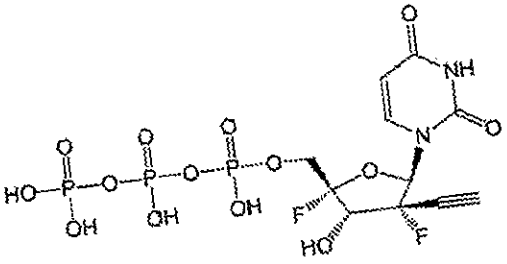


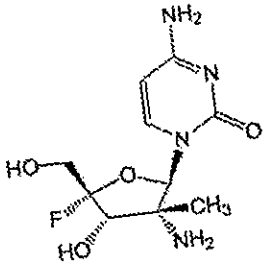


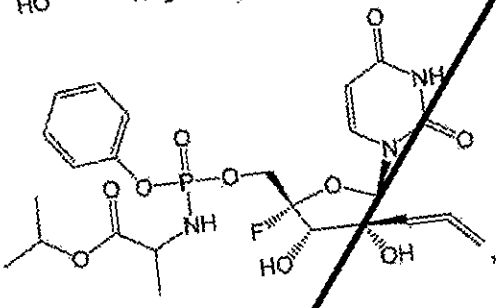


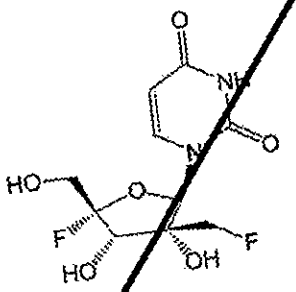


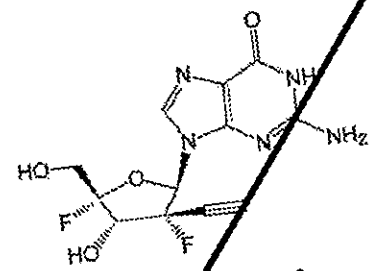


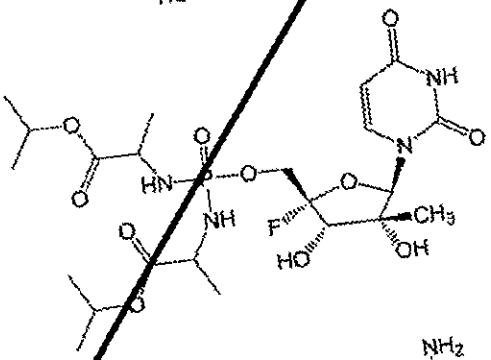


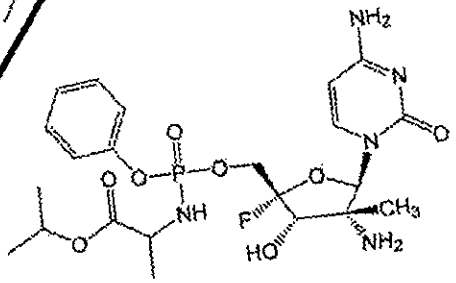


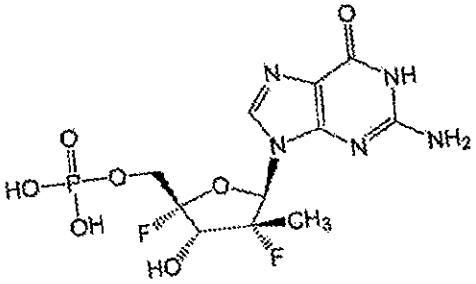


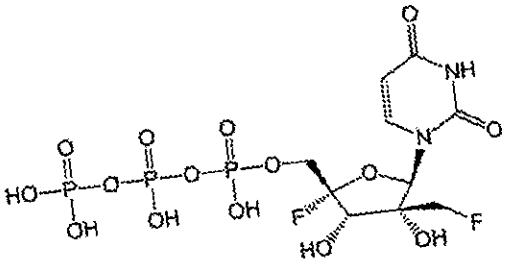


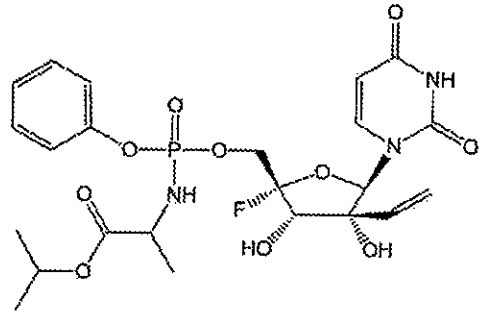


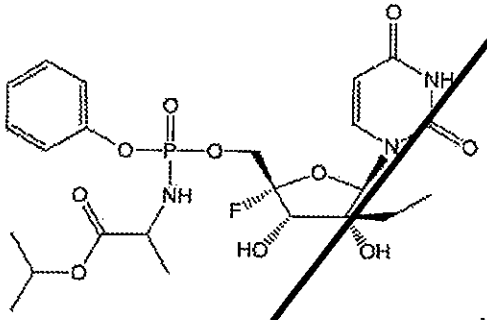


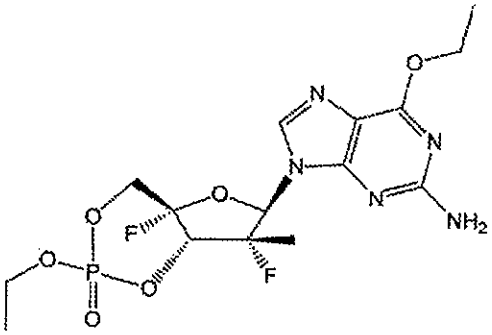


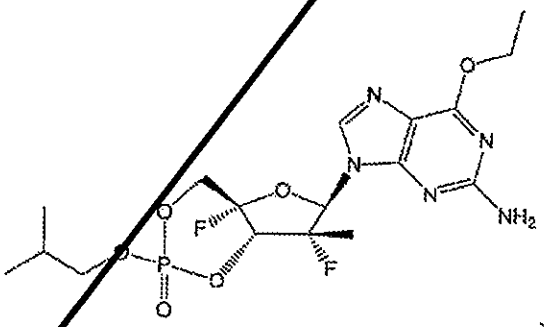


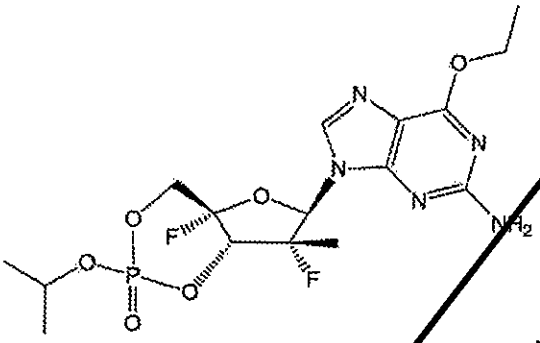


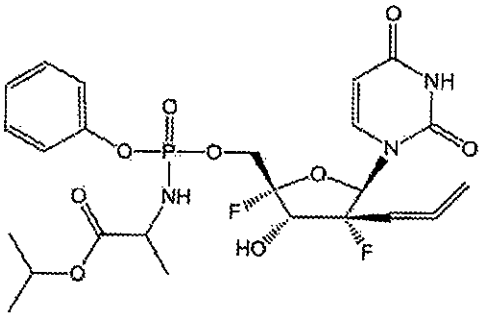


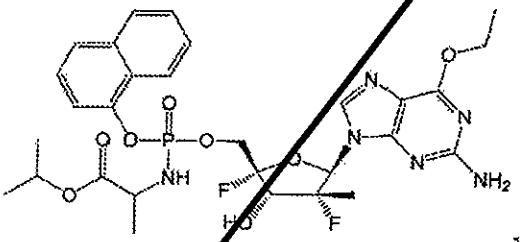


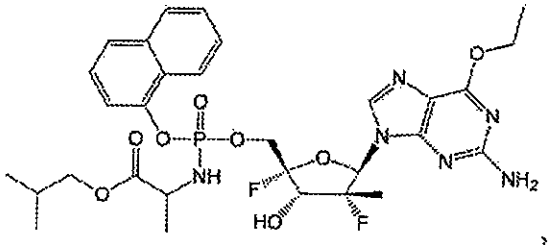


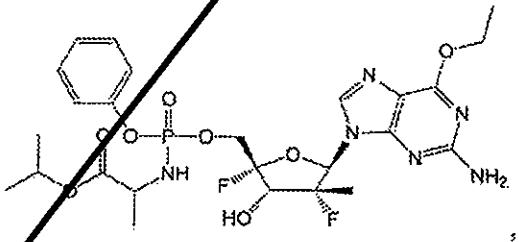


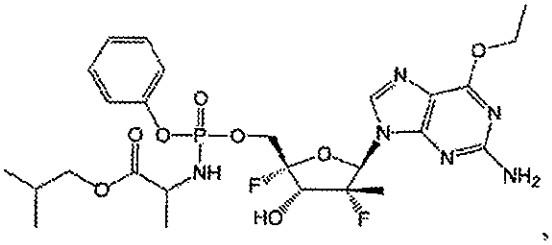


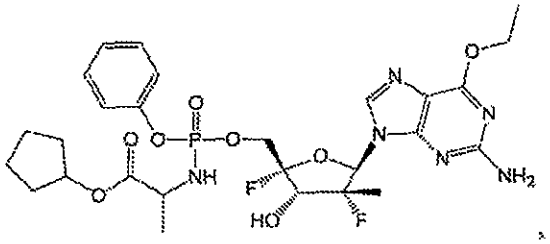
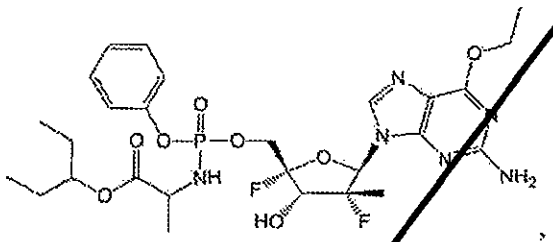


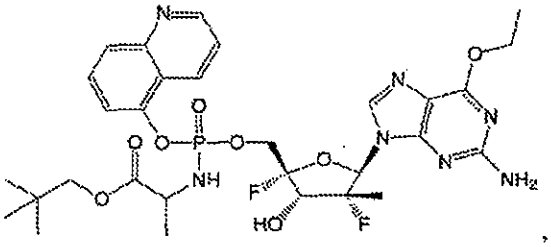
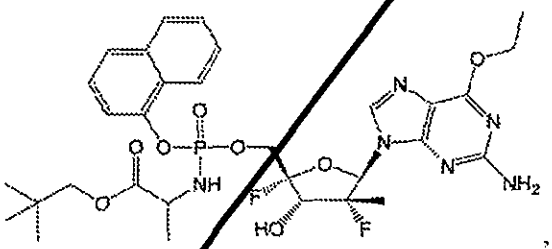


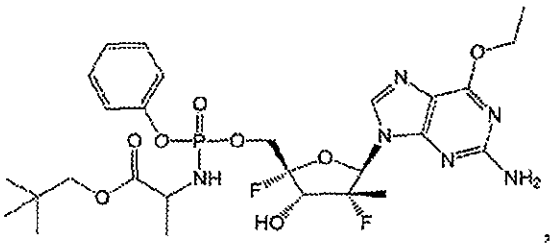
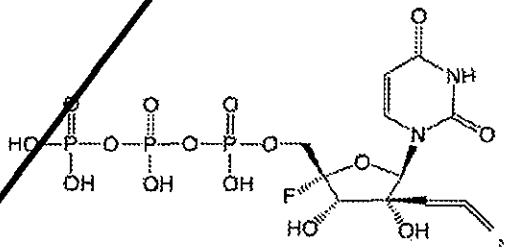


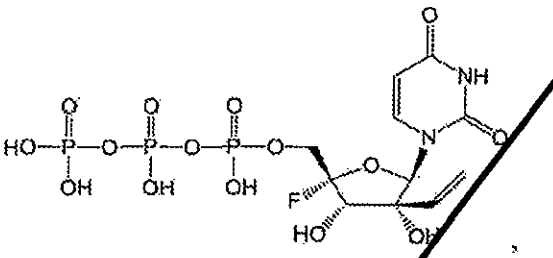
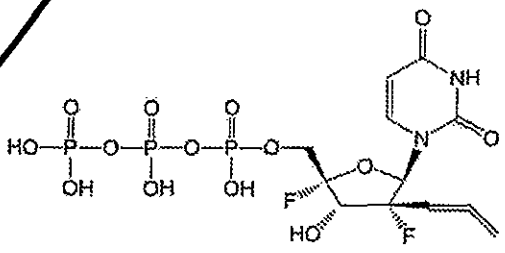


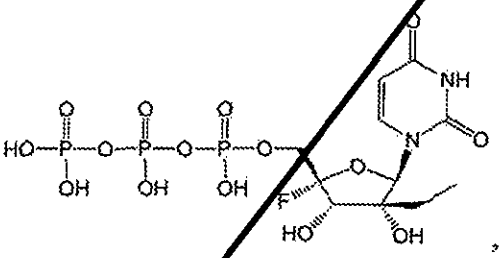


 ,  ,

 ,  ,

 ,  ,

 ,  and

 , or a pharmaceutically acceptable salt of the foregoing.

12. The use of Claim 11, wherein the Flaviviridae virus is selected from the group consisting of a Flavivirus, a Hepacirvirus and a Pestivirus.

13. The use of Claim 11, wherein the Flaviviridae virus is selected from the group consisting of hepatitis C virus (HCV), yellow fever virus (YFV), West Nile virus (WNV), dengue fever virus, an encephalitis virus from within the Flaviviridae family, classic swine fever virus and bovine diarrhea virus.

14. The use of Claim 13, wherein the encephalitis virus from within the Flaviviridae family is selected from the group consisting of Japanese encephalitis virus (JEV) and tick-borne encephalitis virus (TBEV).

15. The use of any one of Claims 1-14, wherein $R^{2A}$ is halo.

16. The use of Claim 15, wherein the halo is fluoro.

17. The use of any one of Claims 1-14, wherein $R^{2A}$ is an unsubstituted $C_{2-4}$ alkyl.

18. The use of any one of Claims 1-14, wherein $R^{2A}$ is an unsubstituted $C_{2-4}$ alkenyl.

19. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-CHF_2$.

20. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}F$.

21. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}Cl$.

22. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}N_3$.

23. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}NH_2$.

24. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-CN$.

25. The use of any one of Claims 1-10, wherein $R^{2A}$ is selected from the group consisting of halo, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, $-CHF_2$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or $-CN$; and $R^{4A}$ is H.

26. The use of any one of Claims 1-24, wherein $R^{4A}$ is OH.

27. The use of any one of Claims 1-24, wherein $R^{4A}$ is halo.

28. The use of Claim 27, wherein the halo is F.

29. The use of Claim 27, wherein the halo is Cl.

30. The use of any one of Claims 1-24, wherein $R^{4A}$ is $-OC(=O)R^{"B}$ or an optionally substituted O-linked amino acid.

31. The use of any one of Claims 1-24, wherein $R^{4A}$ is $N_3$ or $NR^{"B1}R^{"B2}$.

32. The use of any one of Claims 1-19, 21-23 or 26-31, wherein $R^{5A}$ is H.

33. The use of any one of Claims 19, 21-23 or 26-31, wherein $R^{5A}$ is halo.

34. The use of any one of Claims 1-31, wherein $R^{5A}$ is OH.

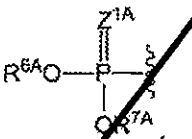
35. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{1-6}$ alkyl.

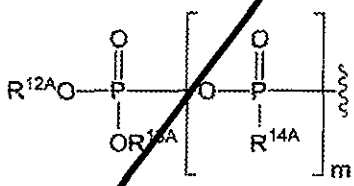
36. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{2-6}$ alkenyl.

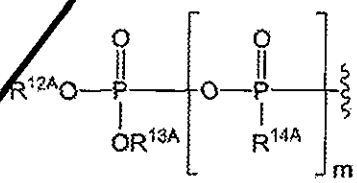
37. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{2-6}$ alkynyl.

38. The use of any one of Claims 1-37, wherein $R^{1A}$ is hydrogen.

39. The use of any one of Claims 1-37, wherein $R^{1A}$ is an optionally substituted acyl or an optionally substituted O-linked amino acid.

40. The use of any one of Claims 1-37, wherein $R^{1A}$ is  .

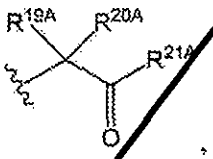
41. The use of Claim 40, wherein $R^{6A}$ is  , $R^{7A}$ is absent or hydrogen and m is 0.

42. The use of Claim 40, wherein $R^{6A}$ is  , $R^{7A}$ is absent or hydrogen and m is 1.

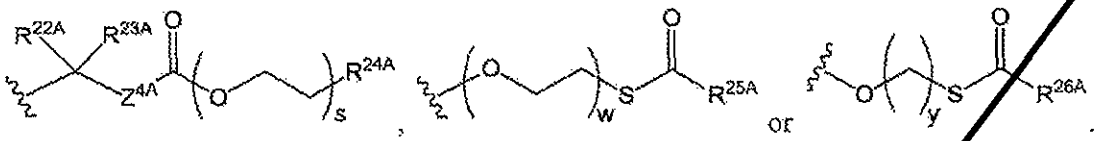
43. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently absent or hydrogen.

44. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl).

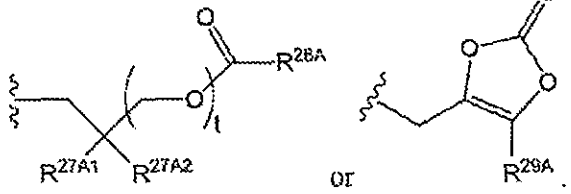
45. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently an optionally substituted *–$(CR^{15A}R^{16A})_p$–O–$C_{1-24}$ alkyl or an optionally substituted *–$(CR^{17A}R^{18A})_q$–O–$C_{1-24}$ alkenyl.

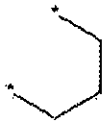
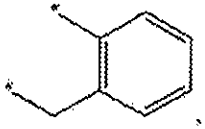


46. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently



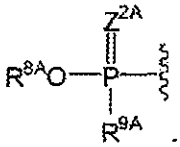
47. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently



48. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten membered ring system.

49. The use of any one of Claims 40-48, wherein $Z^{1A}$ is O.

50. The use of any one of Claims 40-48, wherein $Z^{1A}$ is S.

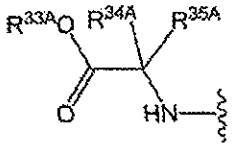


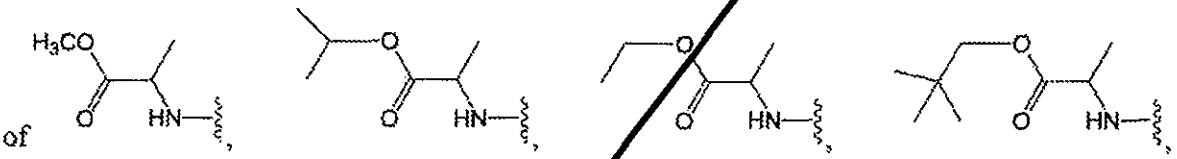
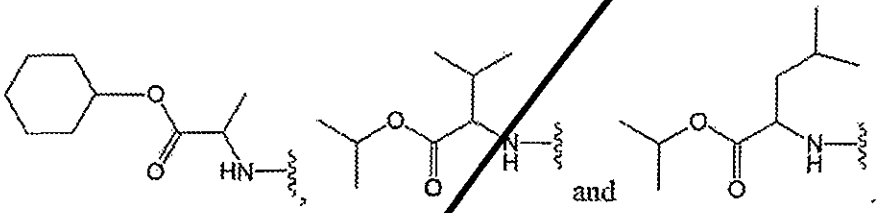
51. The use of any one of Claims 1-37, wherein $R^{1A}$ is .

52. The use of Claim 51, wherein $R^{8A}$ is an optionally substituted aryl.

53. The use of Claim 51, wherein $R^{8A}$ is an optionally substituted heteroaryl.

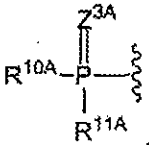
54. The use of any one of Claims 51-53, wherein $R^{9A}$ is an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative.

55. The use of Claim 54, wherein $R^{9A}$ is  wherein $R^{33A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted aryl, an optionally substituted aryl($C_{1-6}$ alkyl) and an optionally substituted haloalkyl; $R^{34A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{1-6}$ haloalkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_6$ aryl, an optionally substituted $C_{10}$ aryl and an optionally substituted aryl($C_{1-6}$ alkyl); and $R^{35A}$ is hydrogen or an optionally substituted $C_{1-4}$ alkyl; or $R^{34A}$ and $R^{35A}$ are taken together to form an optionally substituted $C_{3-6}$ cycloalkyl.

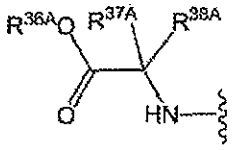
56. The use of Claim 54, wherein $R^{9A}$ is selected from the group consisting of   and .

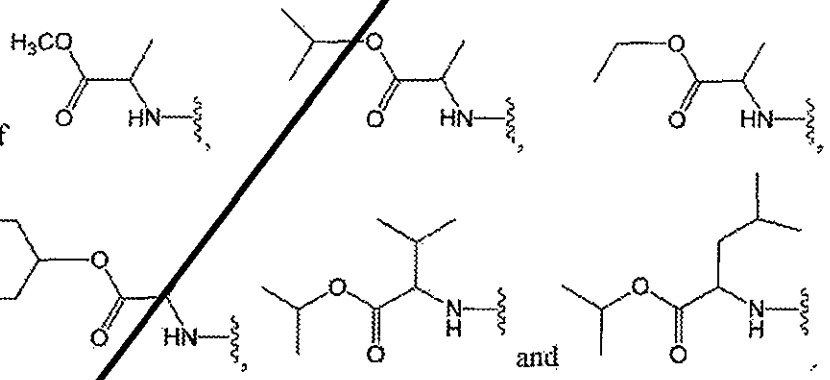
57. The use of any one of Claims 51-56, wherein $Z^{2A}$ is O.

58. The use of any one of Claims 51-56, wherein $Z^{2A}$ is S.

59. The use of any one of Claims 1-37, wherein $R^{1A}$ is  .

60. The use of Claim 59, wherein $R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative.

61. The compound of Claim 59, wherein $R^{10A}$ and $R^{11A}$ are independently  wherein $R^{36A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted aryl, an optionally substituted aryl($C_{1-6}$ alkyl) and an optionally substituted haloalkyl; $R^{37A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{1-6}$ haloalkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_6$ aryl, an optionally substituted $C_{10}$ aryl and an optionally substituted aryl($C_{1-6}$ alkyl); and $R^{38A}$ is hydrogen or an optionally substituted $C_{1-4}$ alkyl; or $R^{37A}$ and $R^{38A}$ are taken together to form an optionally substituted $C_{3-6}$ cycloalkyl.

62. The use of Claim 61, wherein $R^{10A}$ and $R^{11A}$ are independently selected from the group consisting of  and .

63. The use of any one of Claims 59-62, wherein $Z^{3A}$ is O.

64. The use of any one of Claims 59-62, wherein $Z^{3A}$ is S.

65. The use of any one of Claims 37-64, wherein $R^{3A}$ is H.

66. The use of any one of Claims 37-64, wherein $R^{3A}$ is halo.

67. The use of Claim 66, wherein the halo is fluoro.

68. The use of Claim 66, wherein the halo is chloro.

69. The use of any one of Claims 37-64, wherein $R^{3A}$ is OH.

70. The use of any one of Claims 37-64, wherein $R^{3A}$ is $-OC(=O)R^{39A}$ or an optionally substituted O-linked amino acid.

71. The use of any one of Claims 37-64, wherein $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring.

72. The use of any one of Claims 1-71, wherein $R^A$ is hydrogen.

73. The use of any one of Claims 1-71, wherein $R^A$ is deuterium.

74. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{1-3}$ alkyl.

75. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{2-4}$ alkenyl.

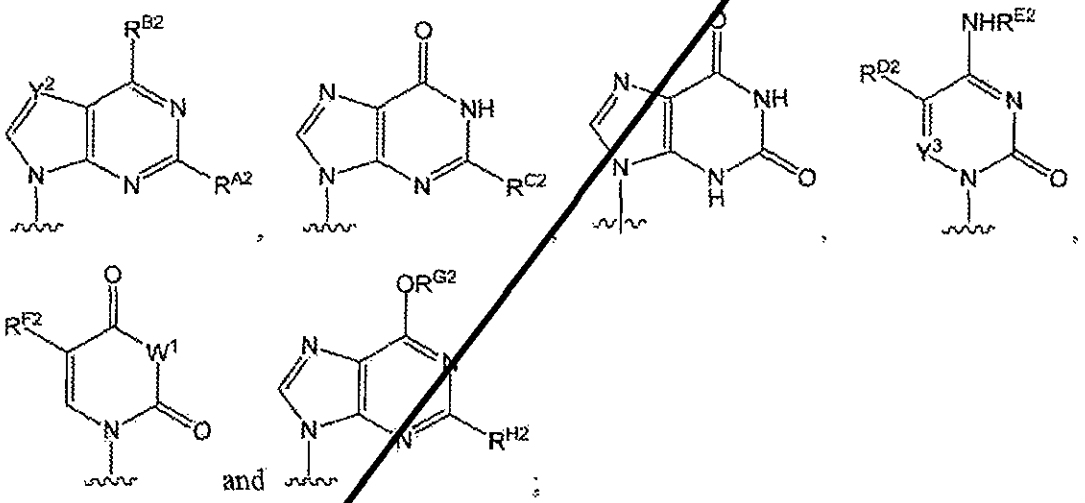
76. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{2-4}$ alkynyl.

77. The use of any one of Claims 1-71, wherein $R^A$ is cyano.

78. The use of any one of Claims 1-77, wherein $R^{a1}$ and $R^{a2}$ are both hydrogen.

79. The use of any one of Claims 1-77, wherein $R^{a1}$ and $R^{a2}$ are both deuterium.

80. The use of any one of Claims 1-79, wherein $B^{1A}$ is selected from the group consisting of:



wherein:

$R^{A2}$ is selected from the group consisting of hydrogen, halogen and $NHR^{J2}$, wherein $R^{J2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{K2}$ and $-C(=O)OR^{L2}$;

$R^{B2}$ is halogen or $NHR^{W2}$, wherein $R^{W2}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{M2}$ and $-C(=O)OR^{N2}$;

$R^{C2}$ is hydrogen or $NHR^{O2}$, wherein $R^{O2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{P2}$ and $-C(=O)OR^{Q2}$;

$R^{D2}$ is selected from the group consisting of hydrogen, deuterium, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{E2}$ is selected from the group consisting of hydrogen, hydroxy, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{R2}$ and $-C(=O)OR^{S2}$;

$R^{F2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

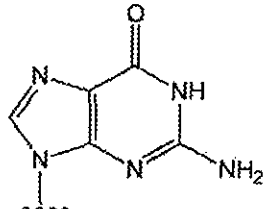
$Y^2$ and $Y^3$ are independently N or $CR^{I2}$, wherein $R^{I2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

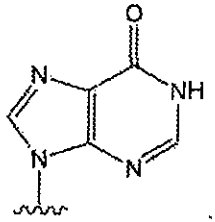
$W^1$ is NH, $-NCH_2$-OC(=O)CH($NH_2$)-CH($CH_3$)$_2$ or $-(CH_2)_{1-2}$-O-P(=O)($OW^{1A}$)$_2$, wherein $W^{1A}$ is selected from the group consisting of absent, hydrogen and an optionally substituted $C_{1-6}$ alkyl;

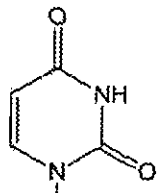
$R^{G2}$ is an optionally substituted $C_{1-6}$ alkyl;

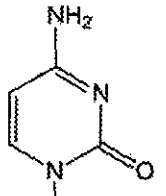
$R^{H2}$ is hydrogen or $NHR^{T2}$, wherein $R^{T2}$ is independently selected from the group consisting of hydrogen, $-C(=O)R^{U2}$ and $-C(=O)OR^{V2}$; and

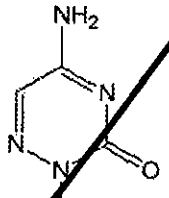
$R^{K2}$, $R^{L2}$, $R^{M2}$, $R^{N2}$, $R^{P2}$, $R^{Q2}$ $R^{R2}$, $R^{S2}$, $R^{U2}$ and $R^{V2}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl).

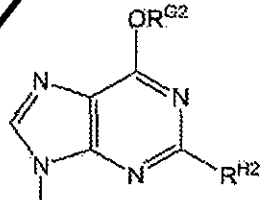
81. The use of Claim 80, wherein $B^{1A}$ is 

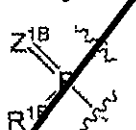
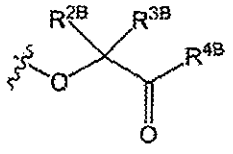
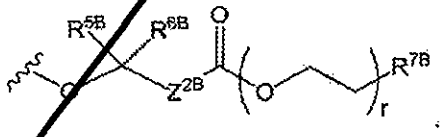
82. The use of Claim 80, wherein $B^{1A}$ is 

83. The use of Claim 80, wherein $B^{1A}$ is  .

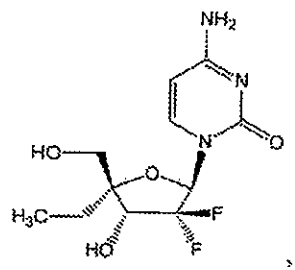
84. The use of Claim 80, wherein $B^{1A}$ is  .

85. The use of Claim 80, wherein $B^{1A}$ is  .

86. The use of Claim 80, wherein $B^{1A}$ is  .

87. The use of any one of Claims 1-37 or 72-86, wherein when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, and $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or $-CN$, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1-6}$ alkyl,  and  .

88. The use of Claim 1, wherein the compound is selected from the group consisting of: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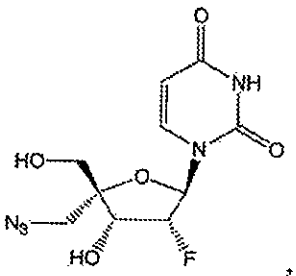
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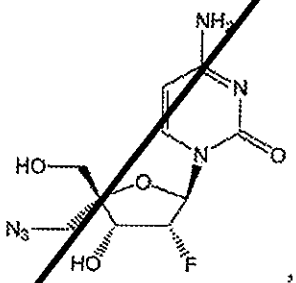
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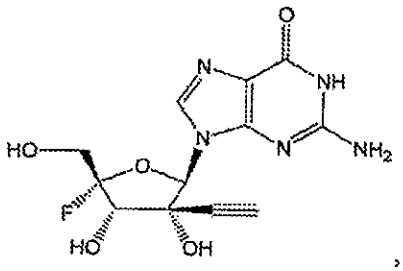
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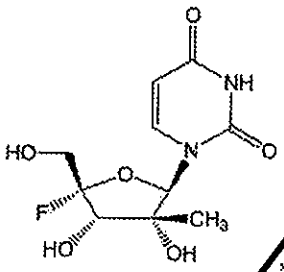
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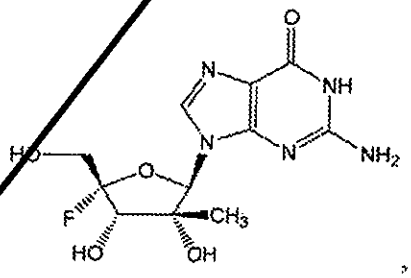
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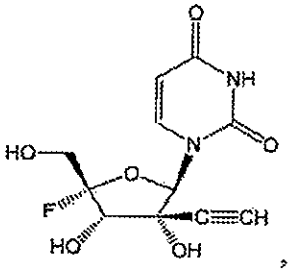
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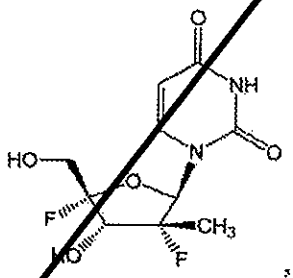
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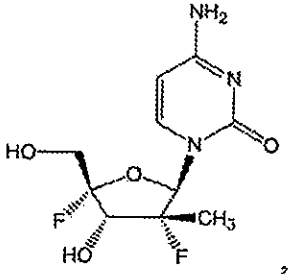
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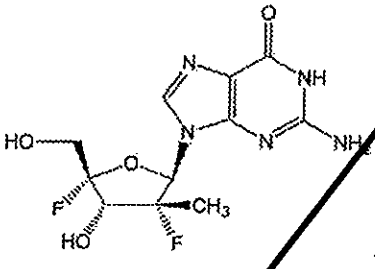
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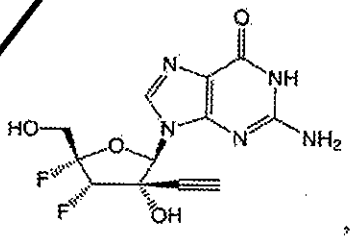
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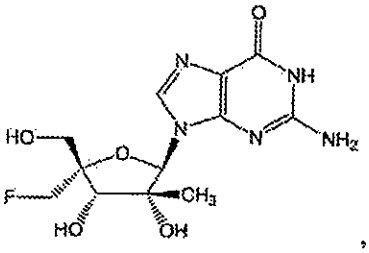
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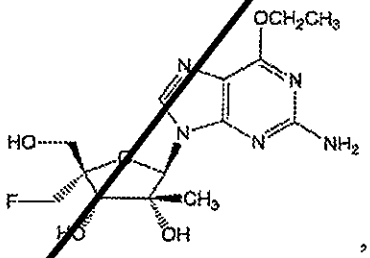
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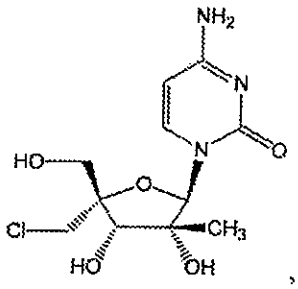
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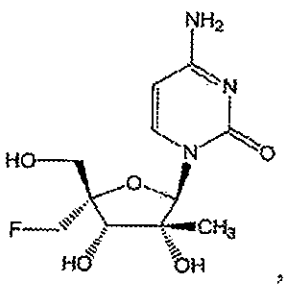
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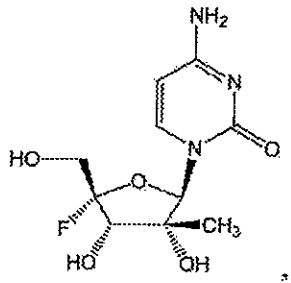
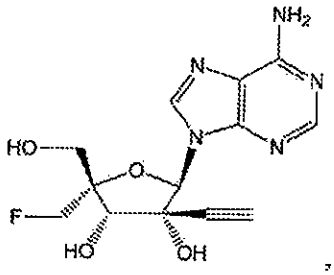
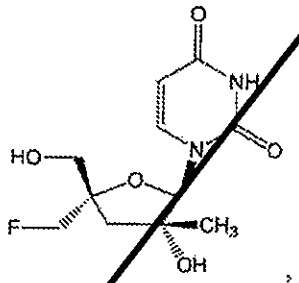
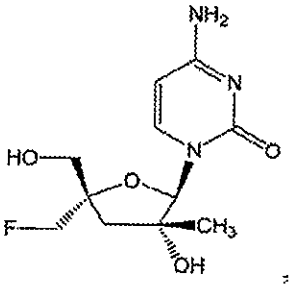
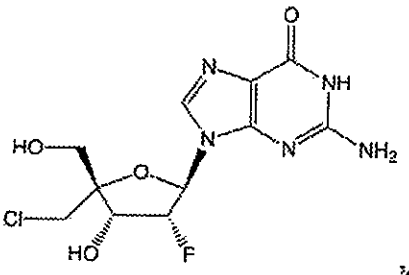
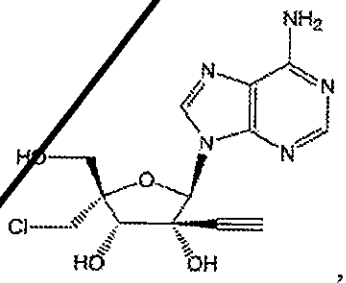
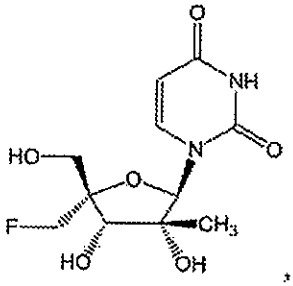
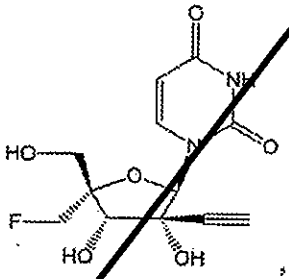
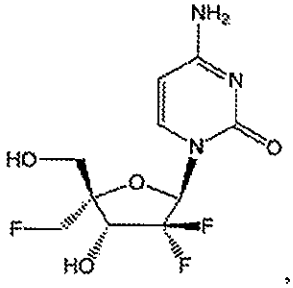
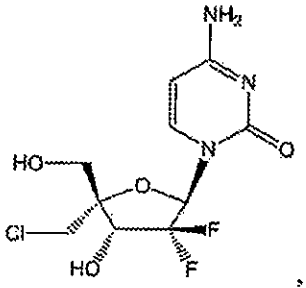
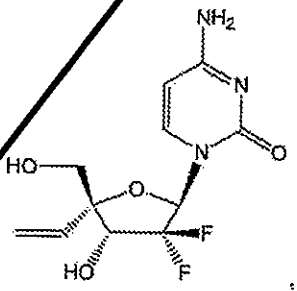
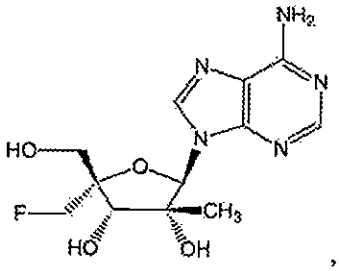
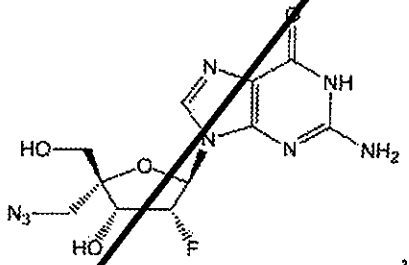
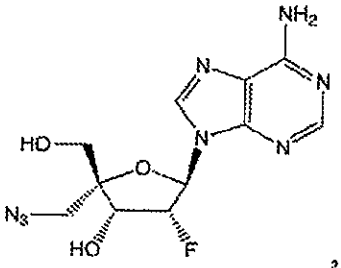
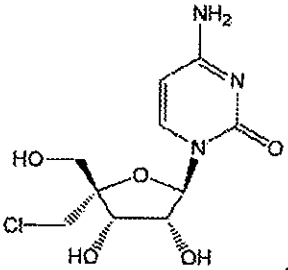

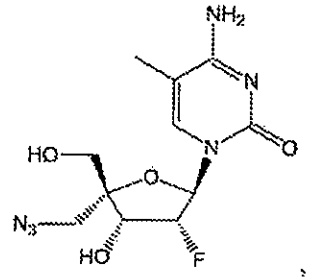
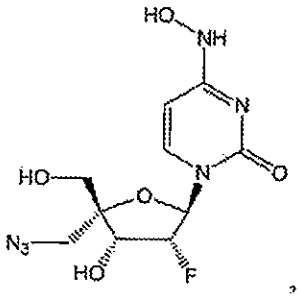
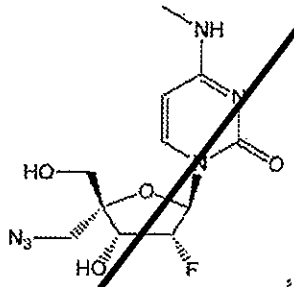
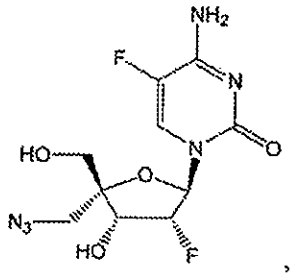
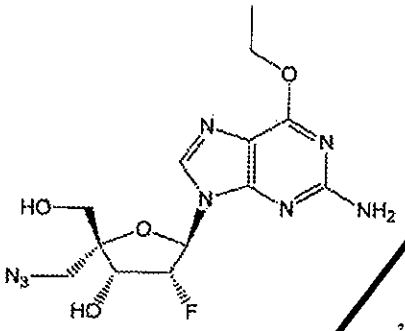
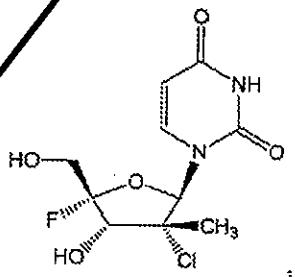
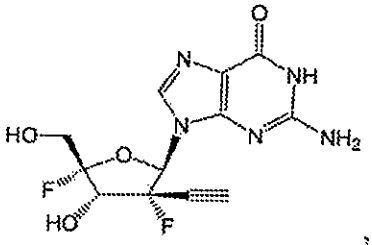
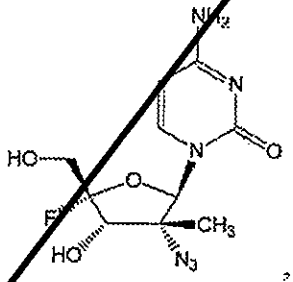
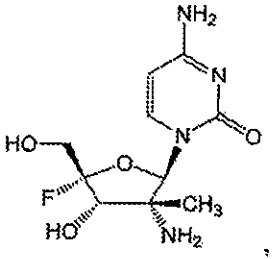
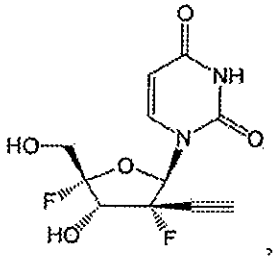
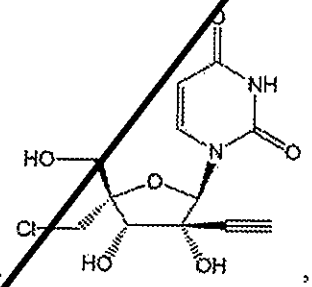
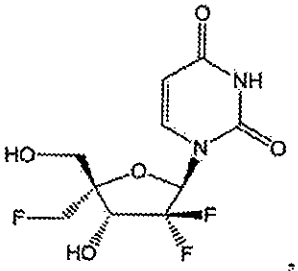
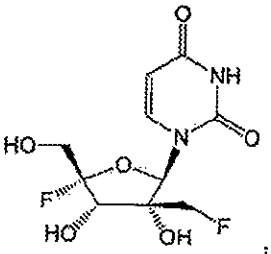
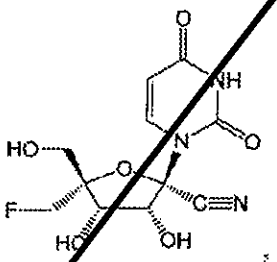
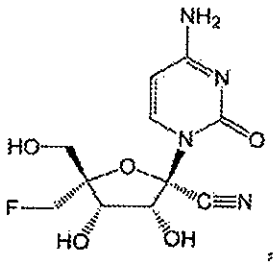
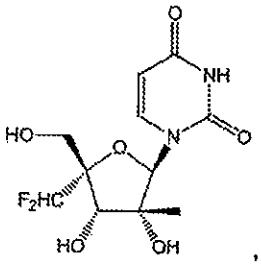
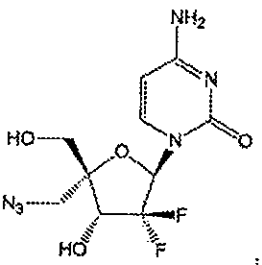

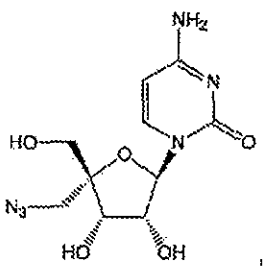
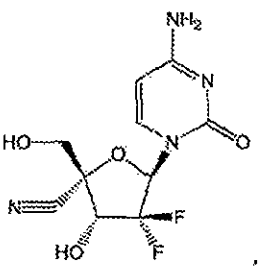
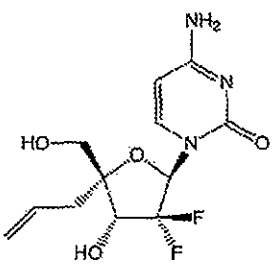
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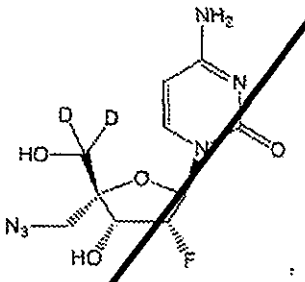
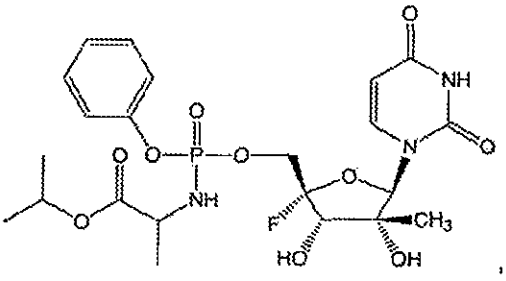
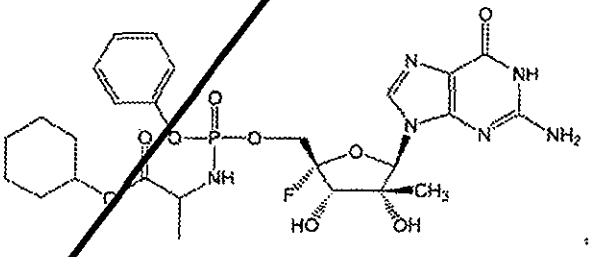
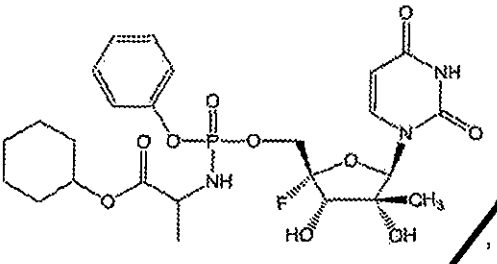
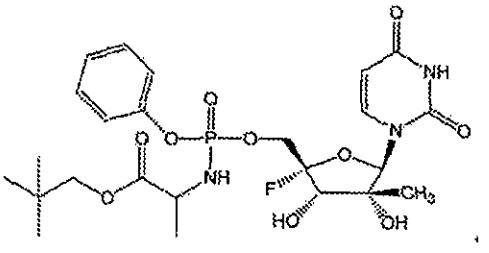
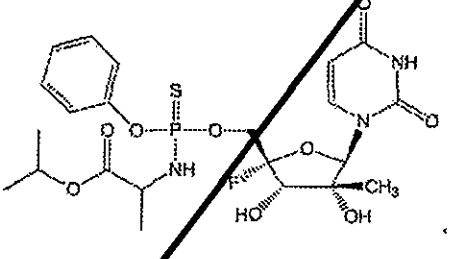
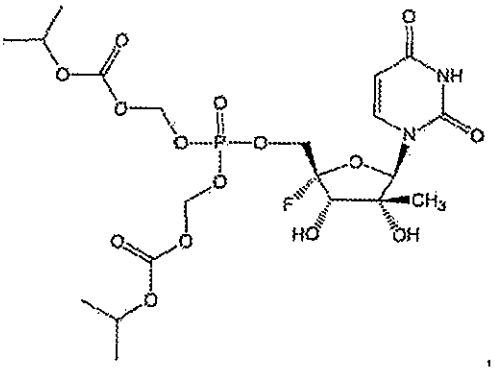
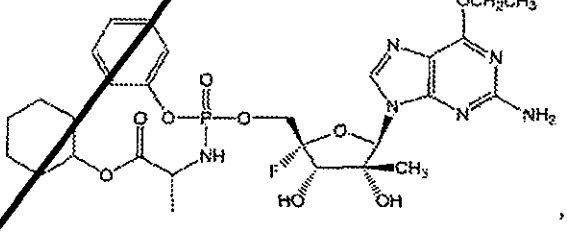
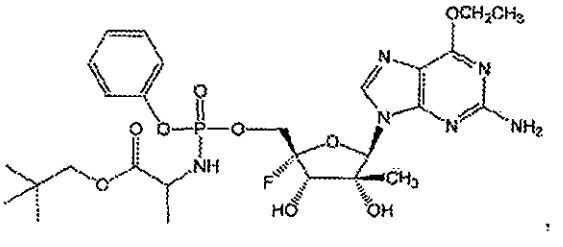
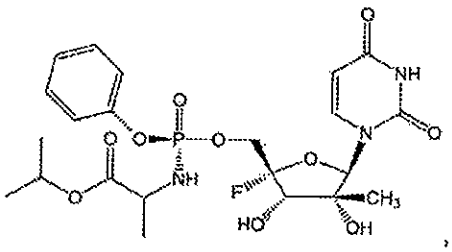
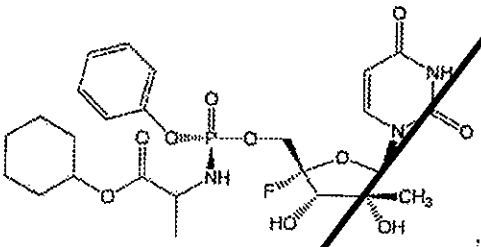
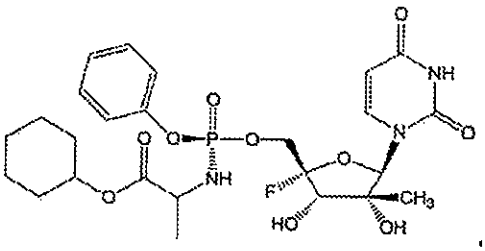
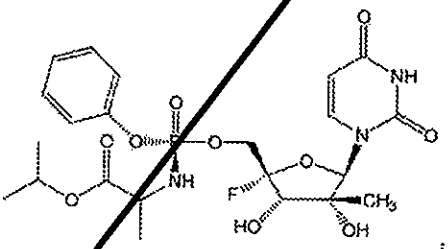
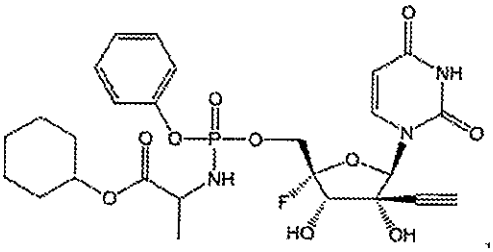
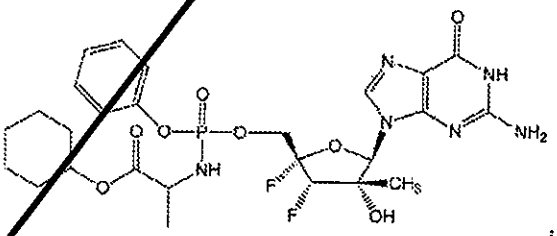
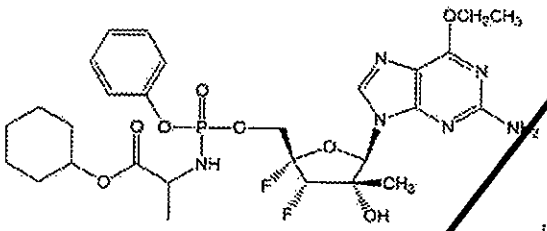
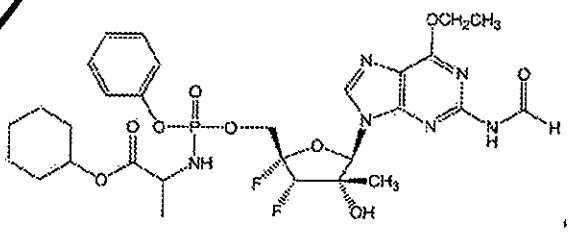
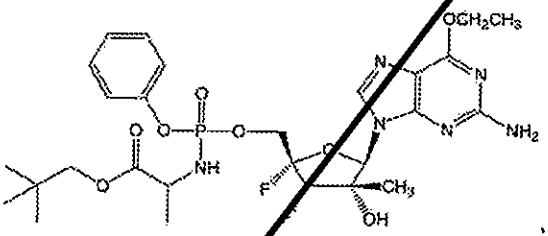
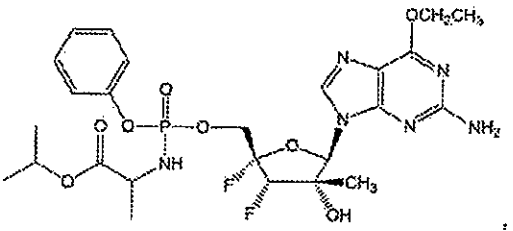
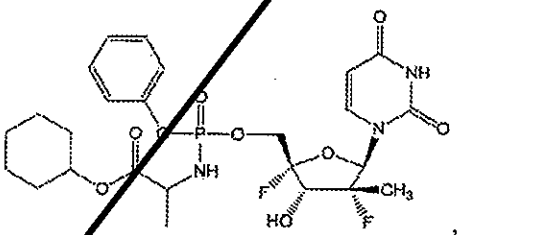
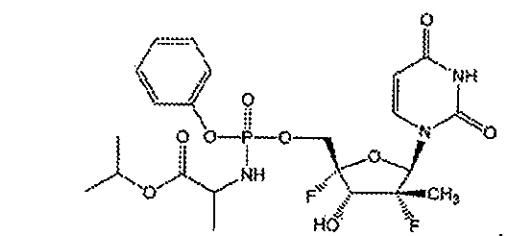
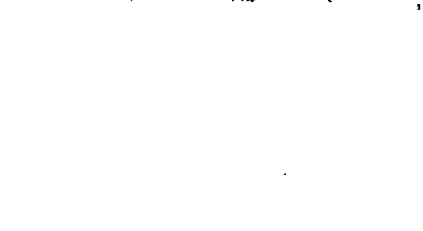


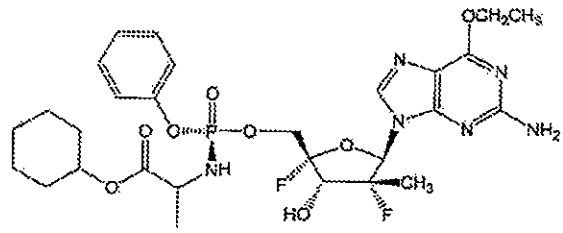
or a pharmaceutically acceptable salt of the foregoing.

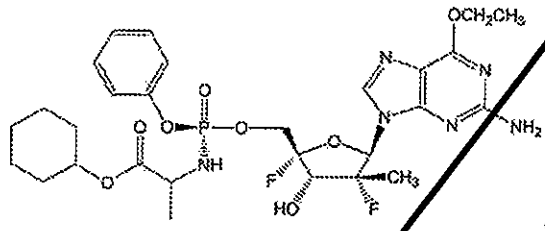
89. The use of Claim 1, wherein the compound is selected from the group consisting of:

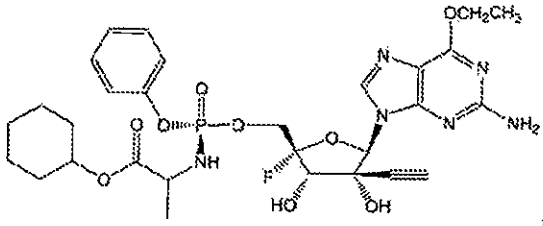









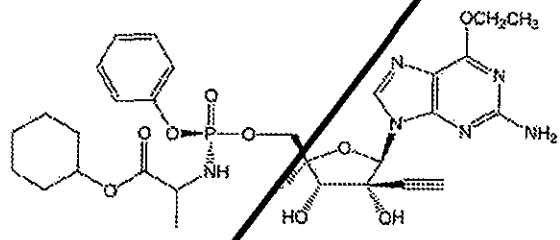













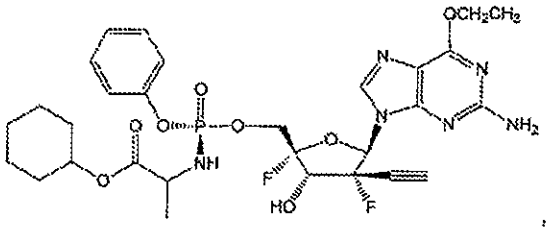


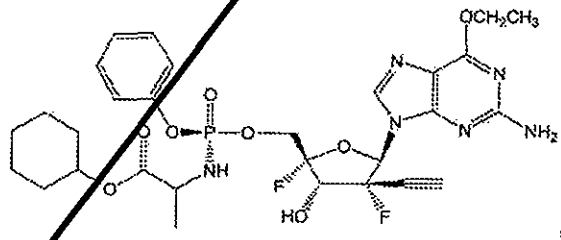


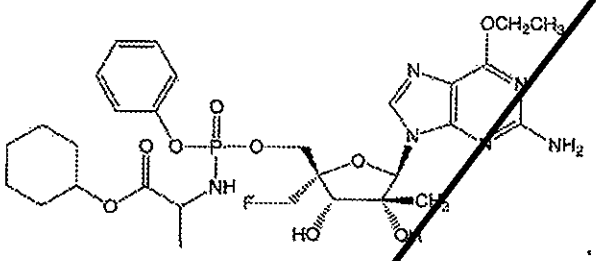


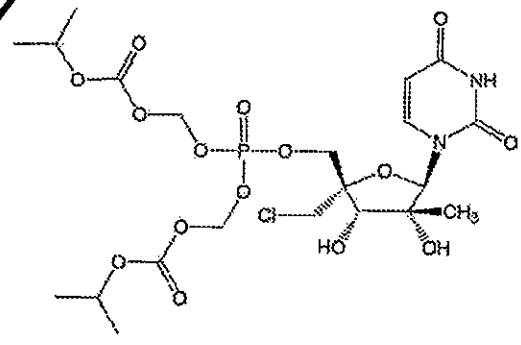


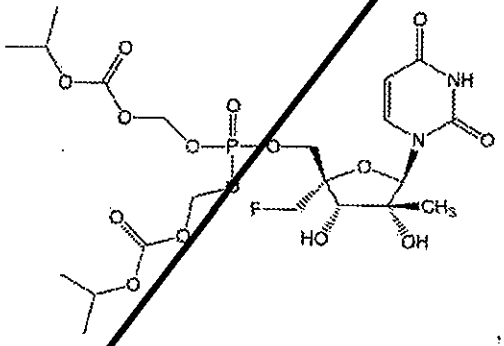


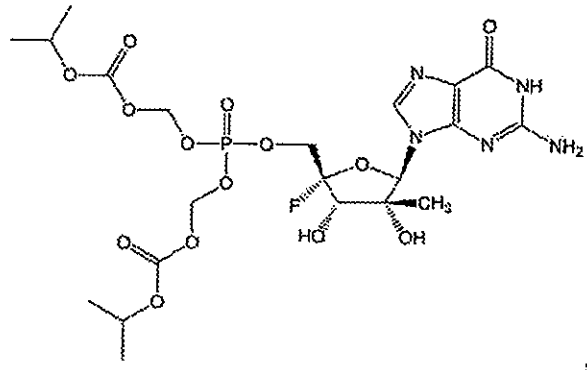


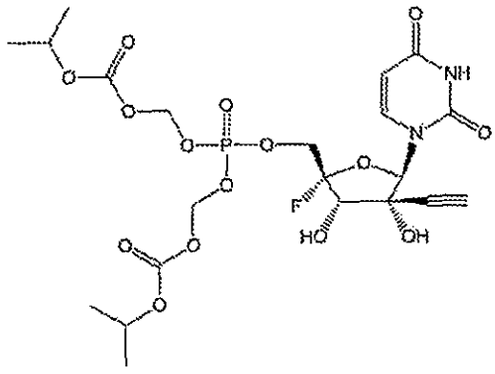


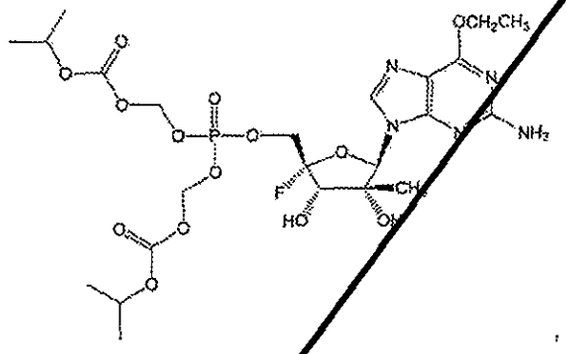


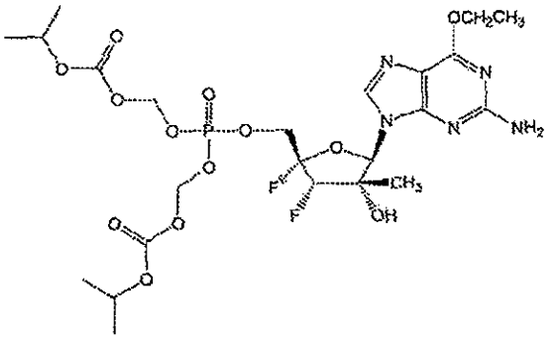


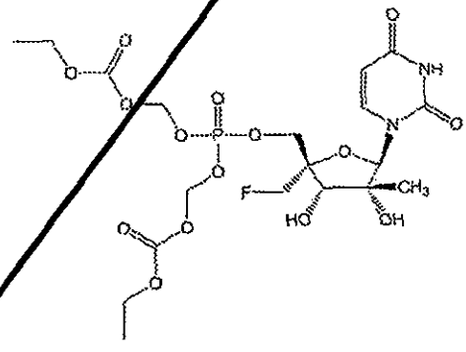


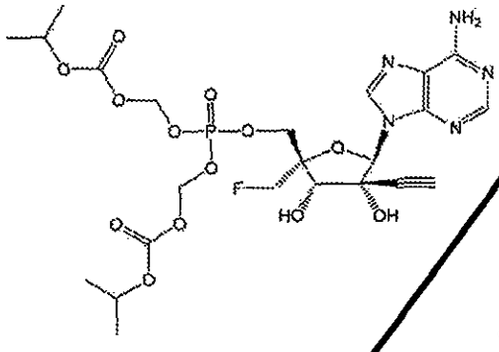


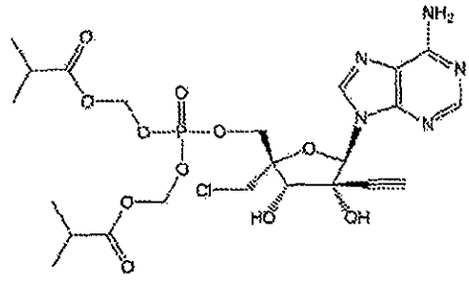


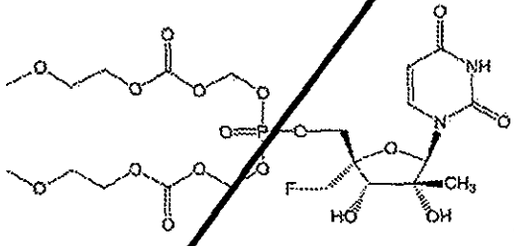


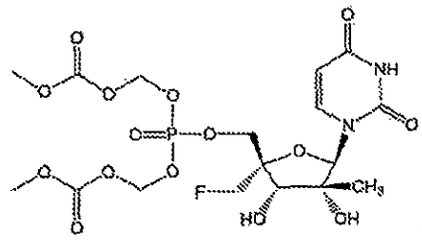


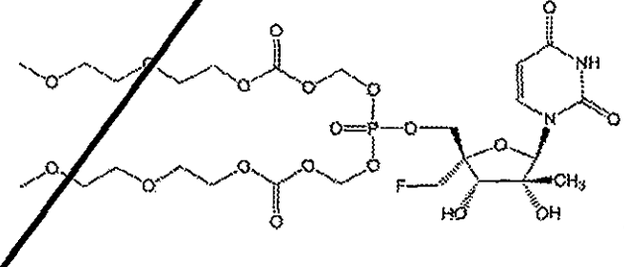


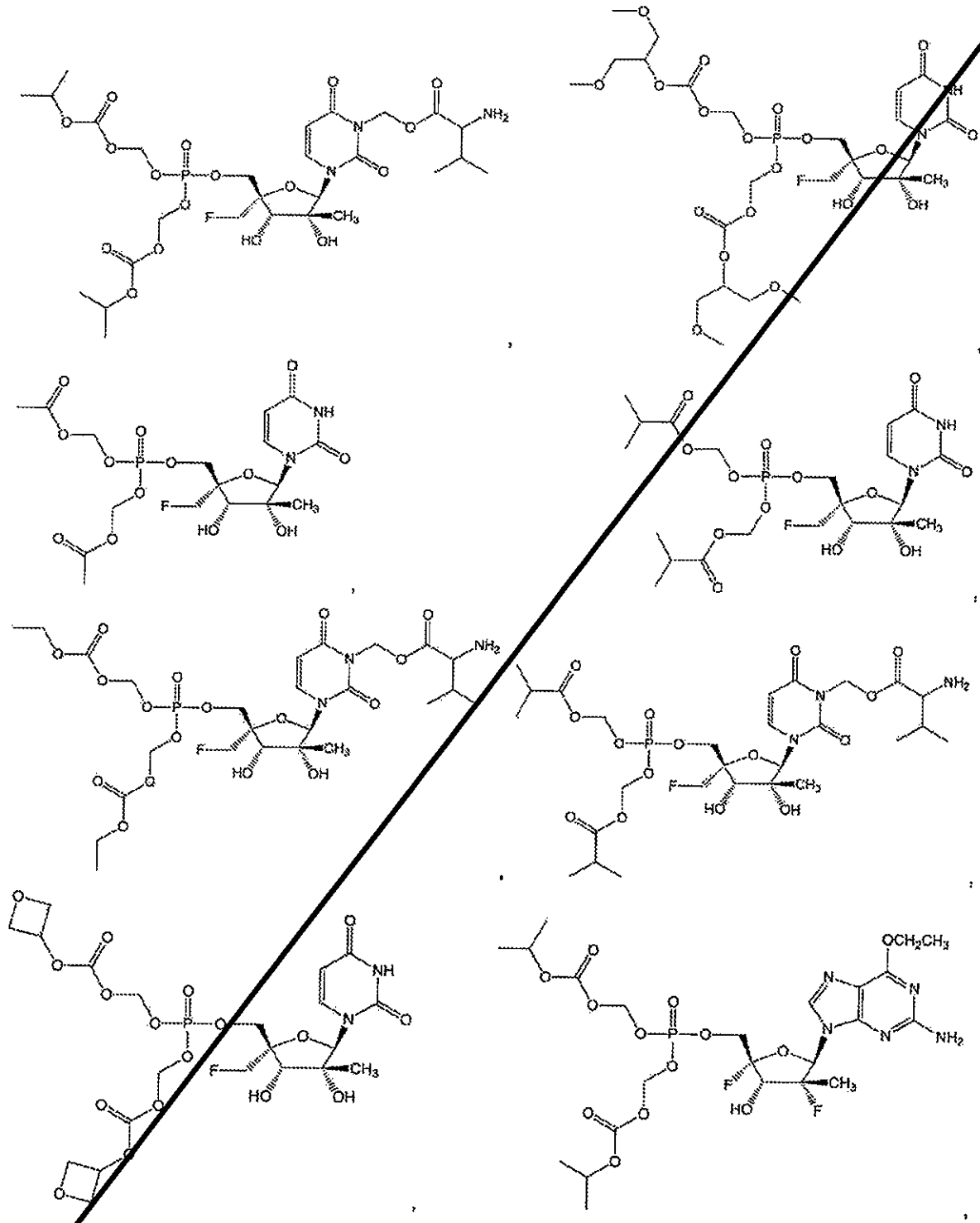


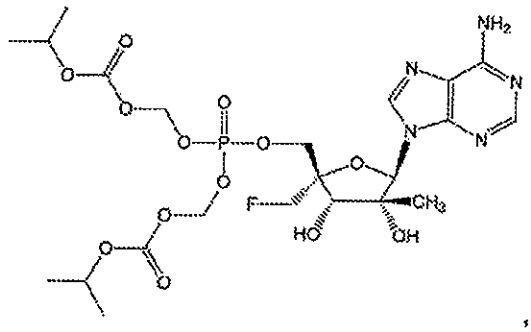


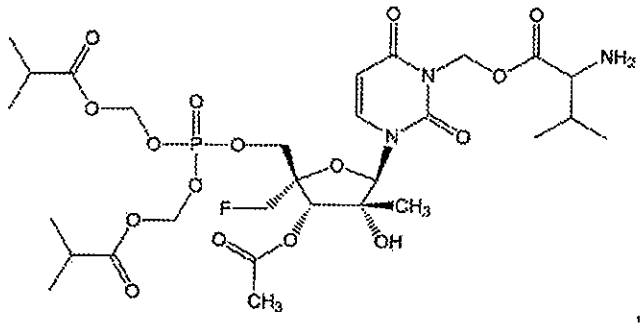


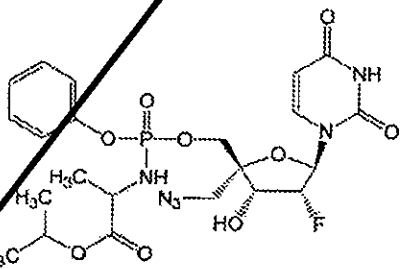


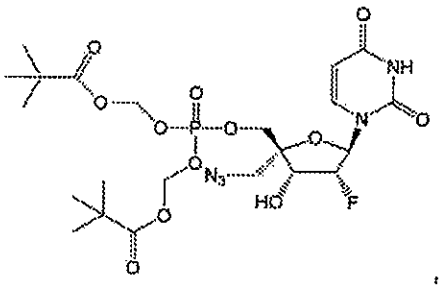


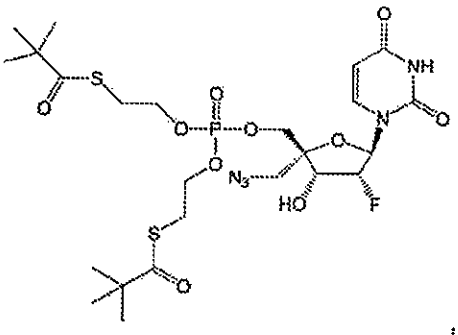


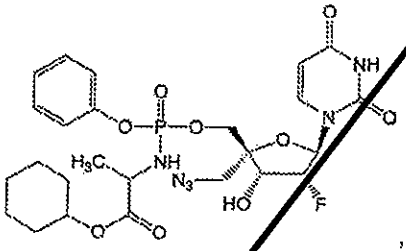


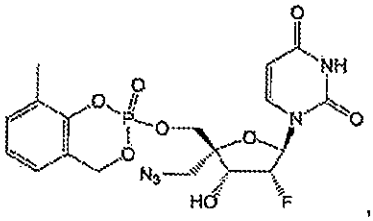


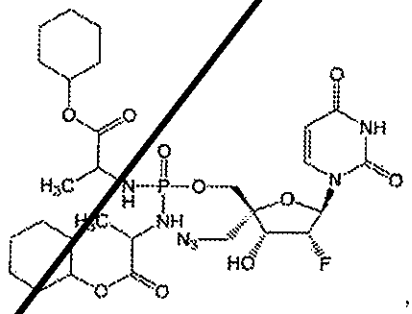


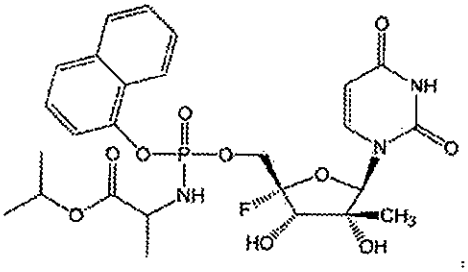


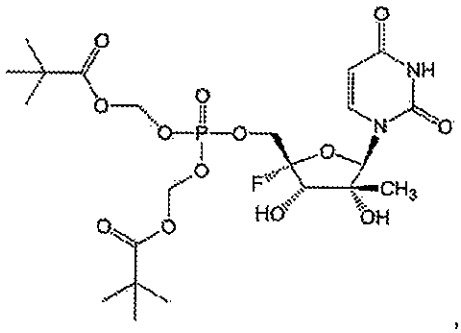


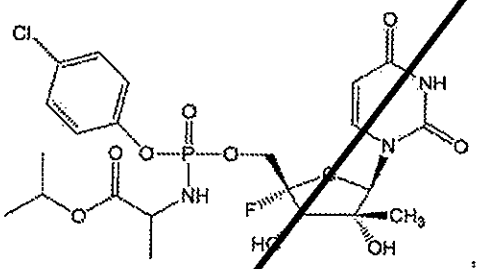


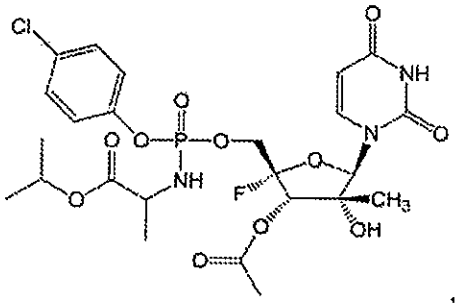


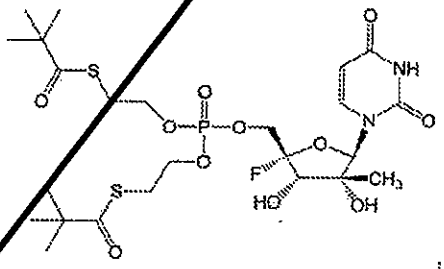


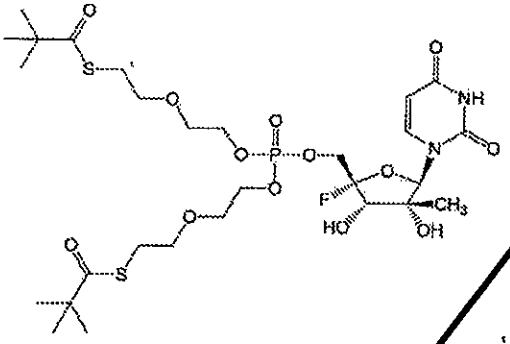


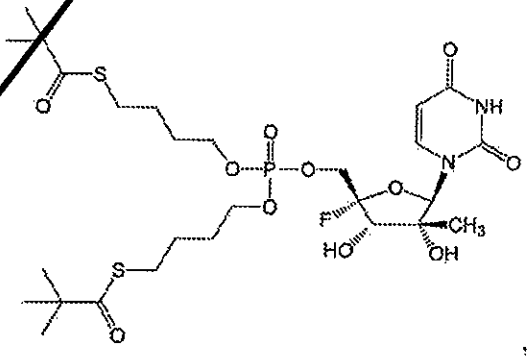


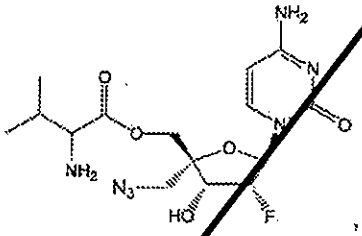


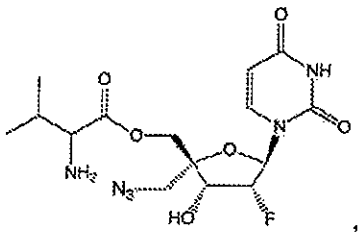


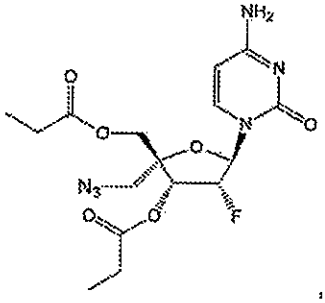


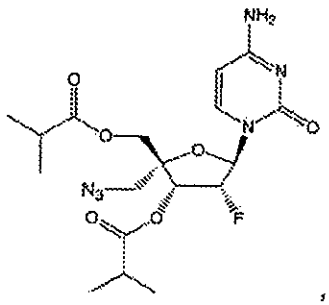


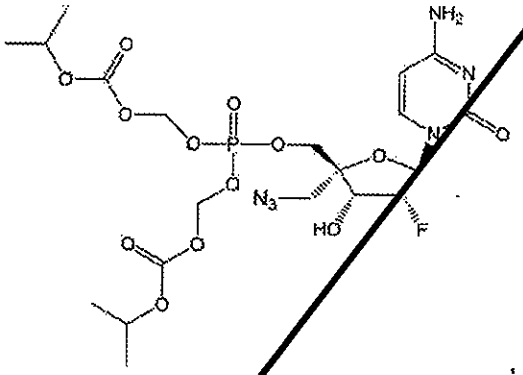


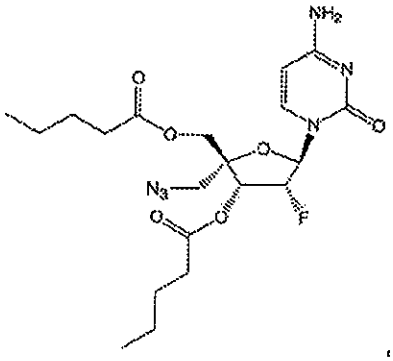


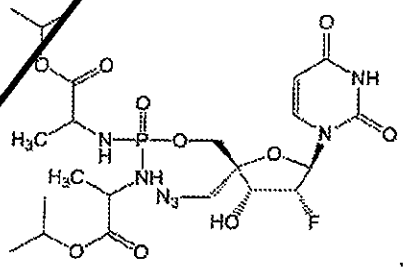


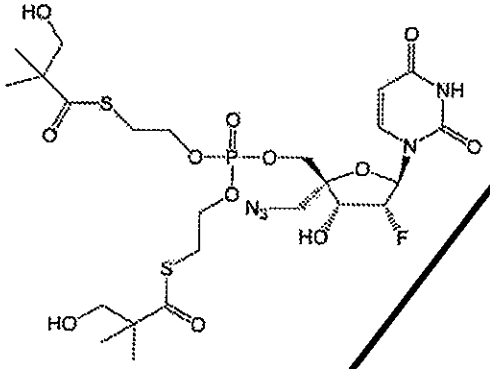


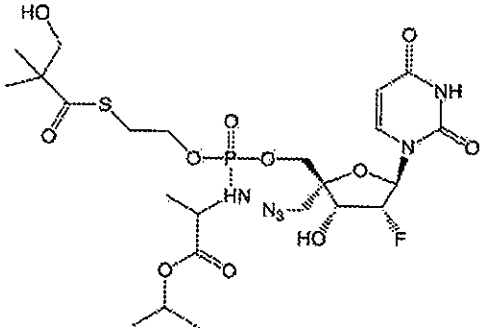


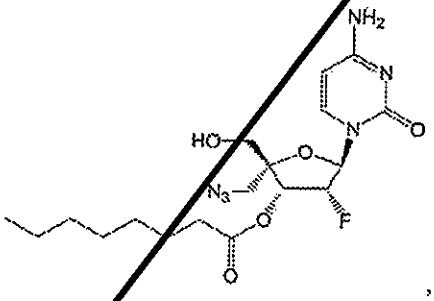


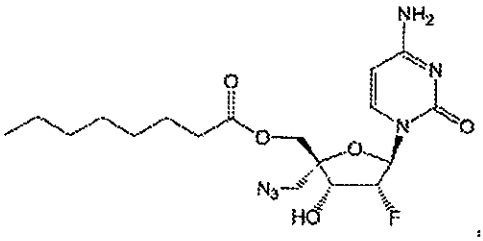


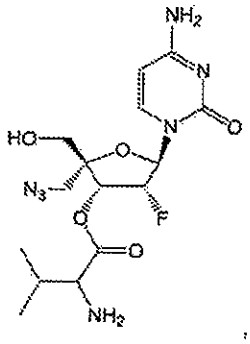


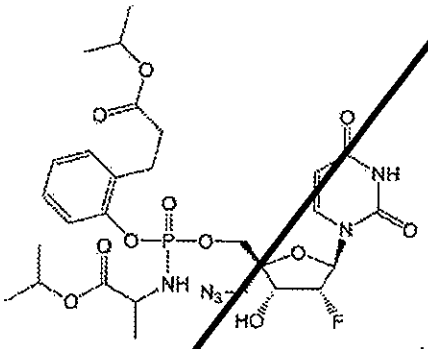


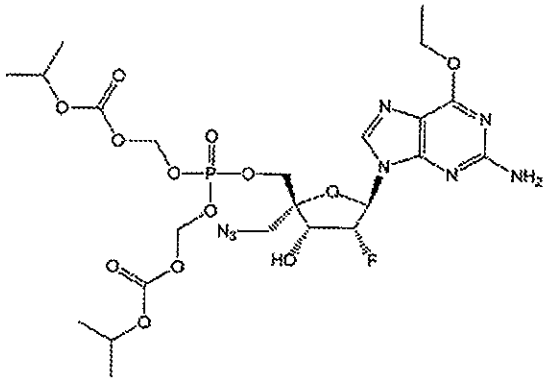


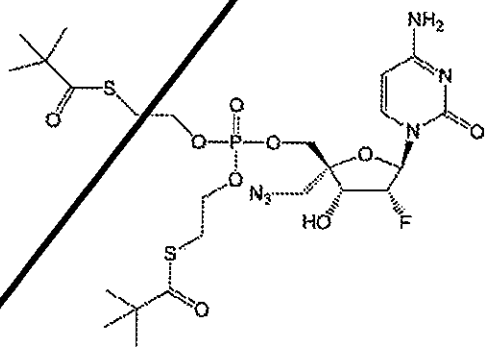


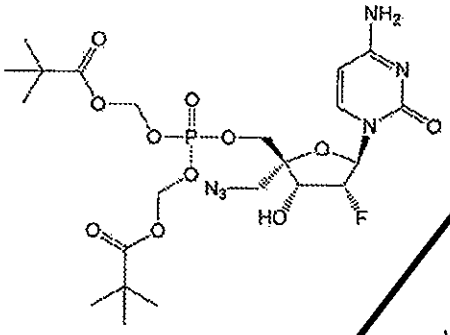


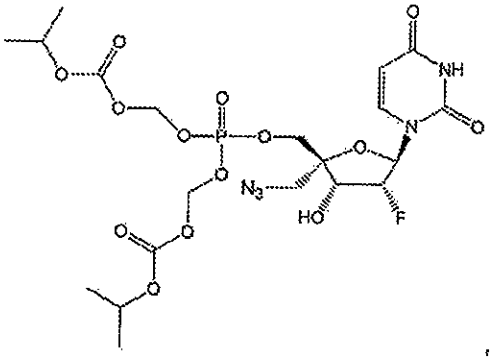


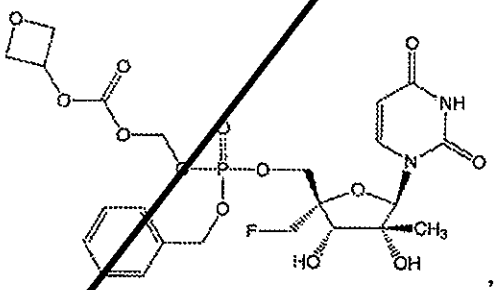


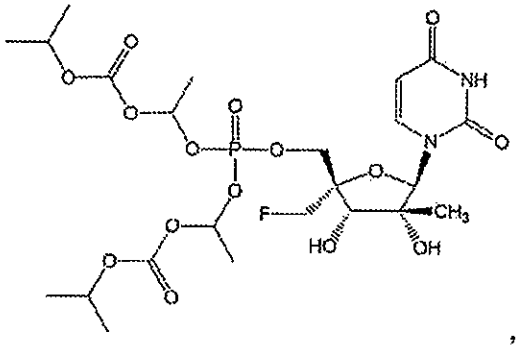


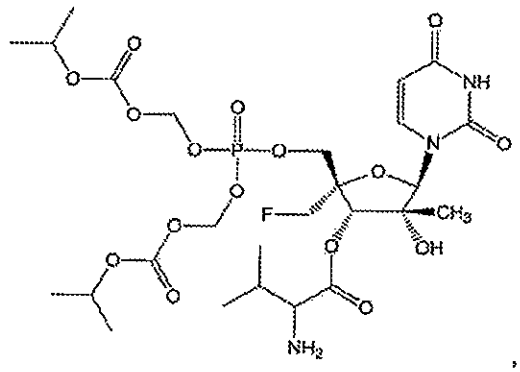


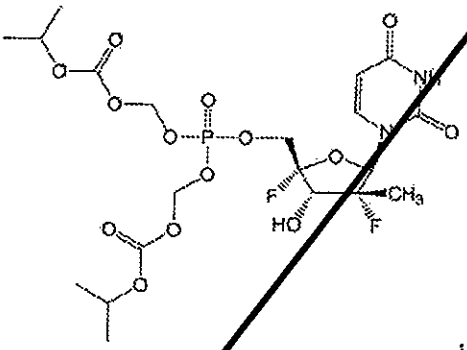


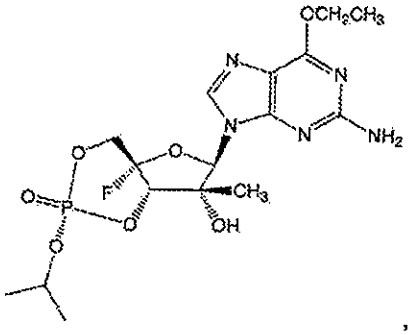


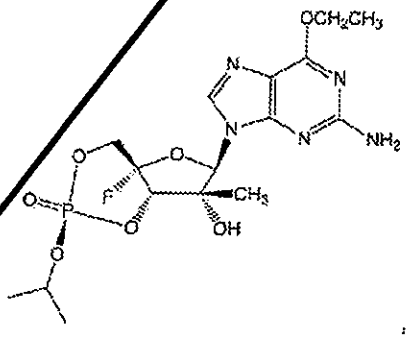


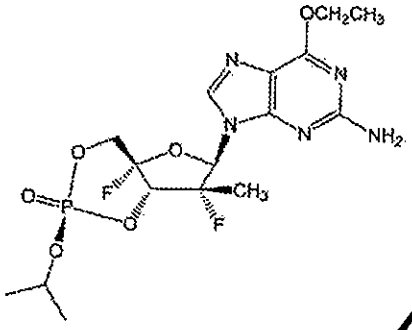


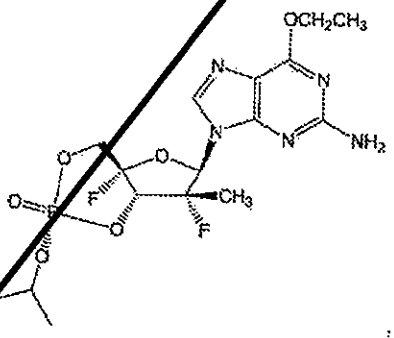


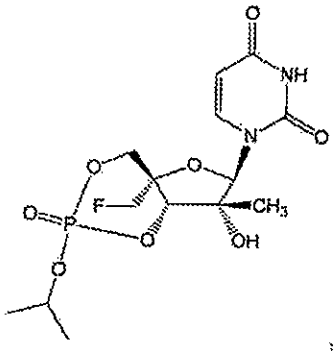


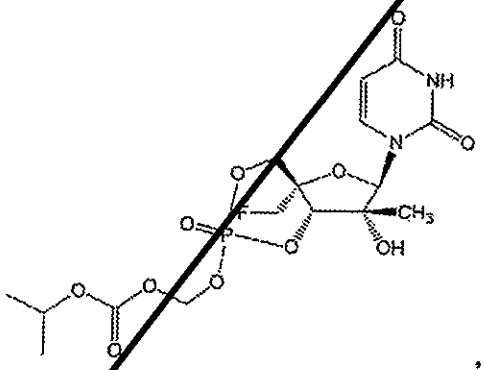


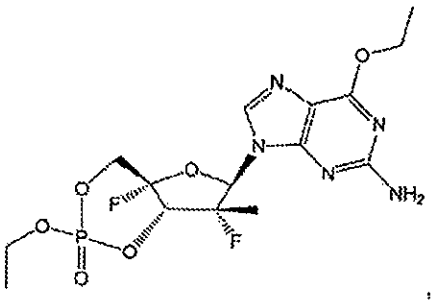


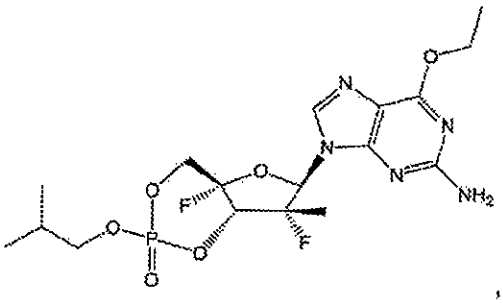


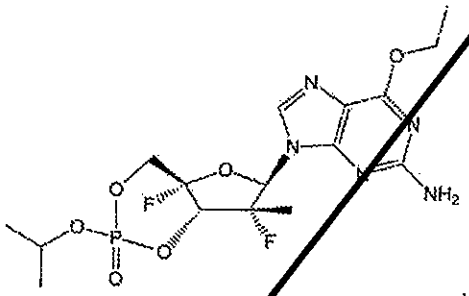


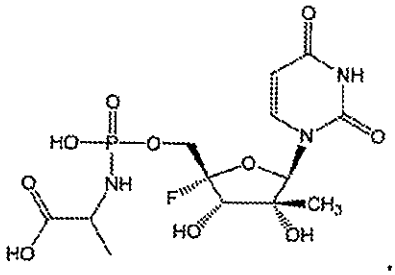


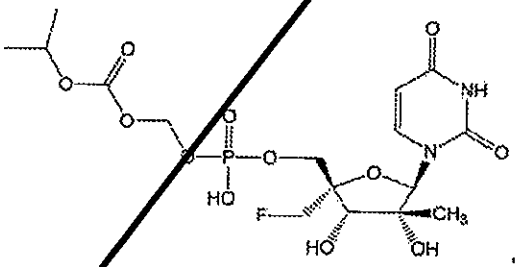


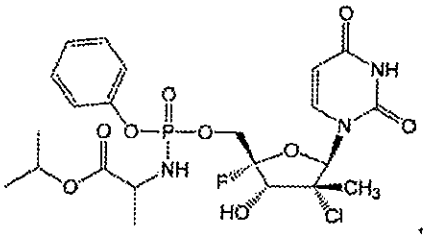


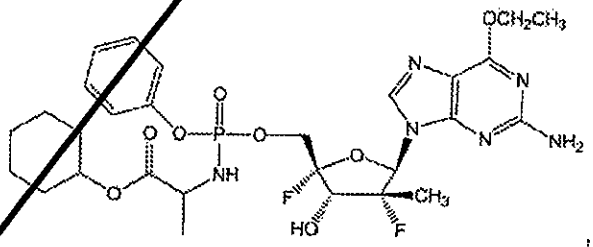


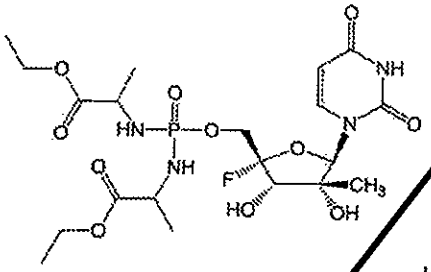


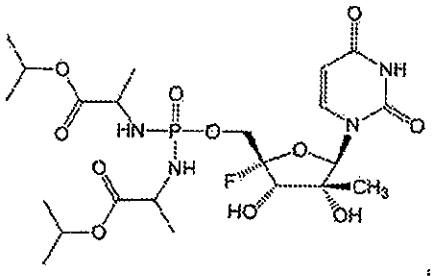


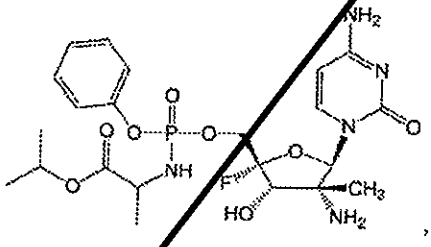


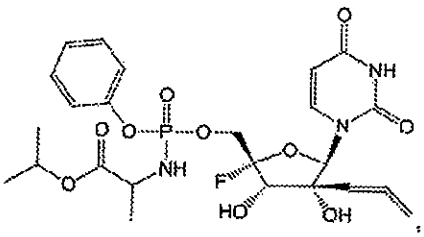


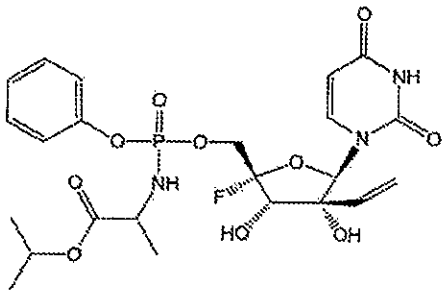


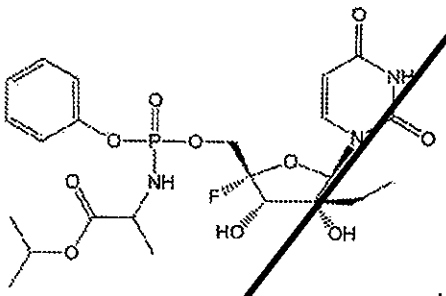


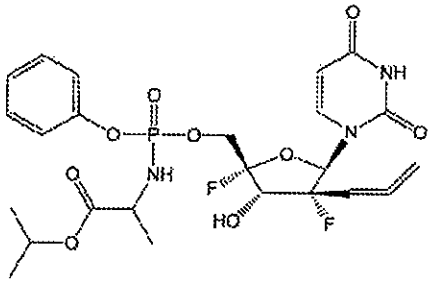


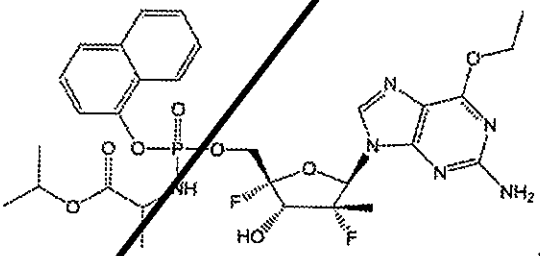


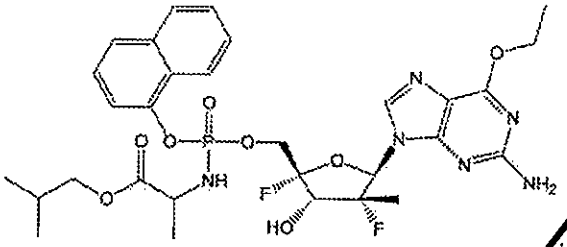


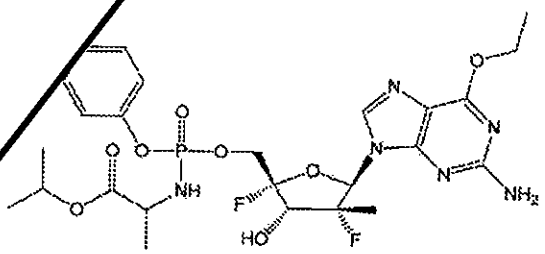


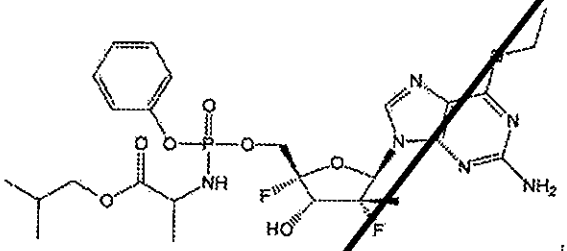


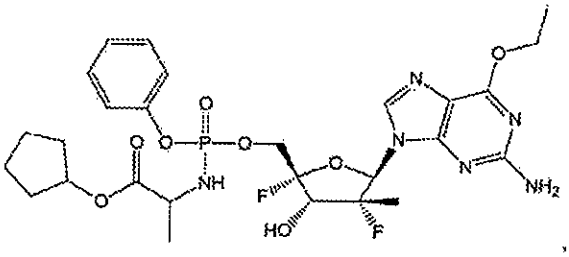


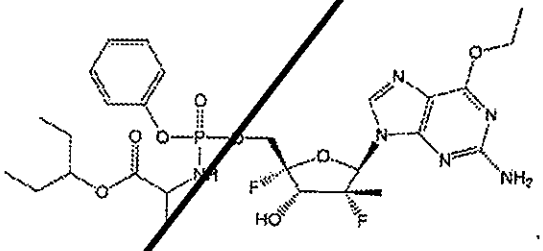


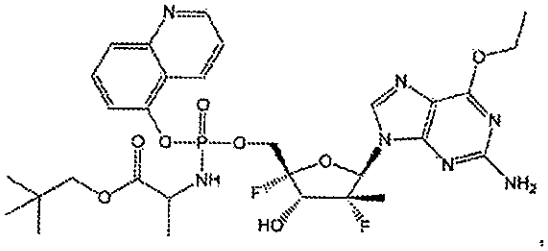


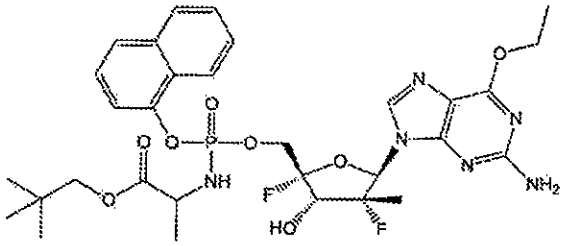


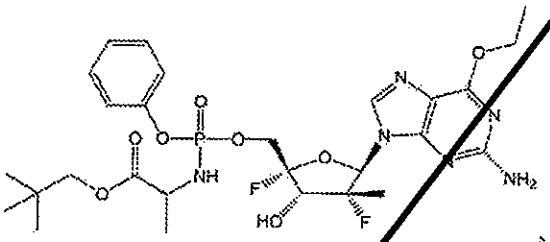


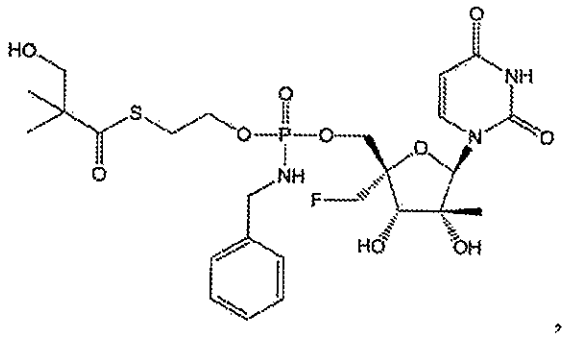


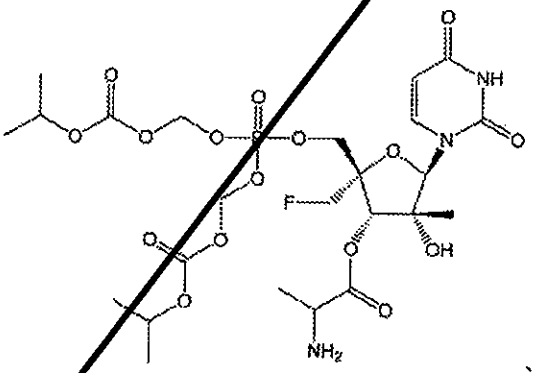


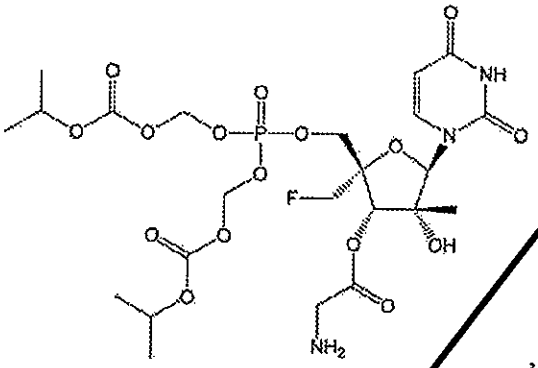


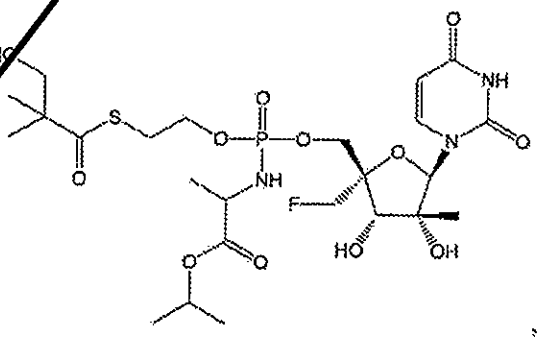


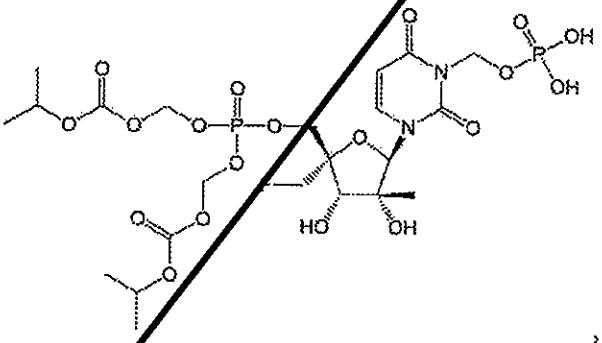


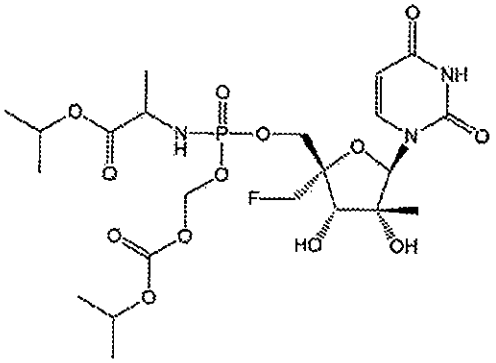


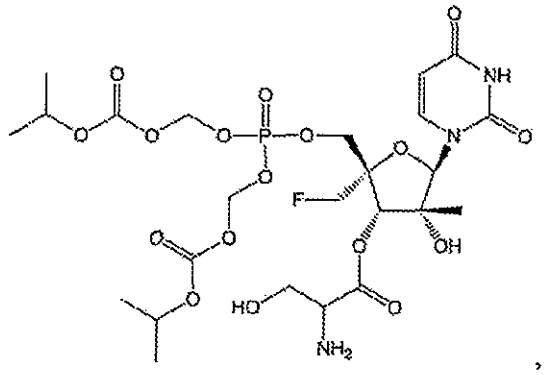








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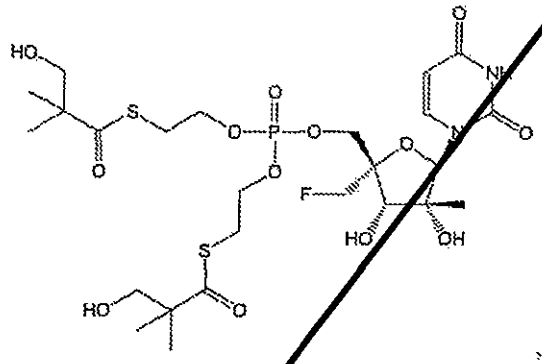
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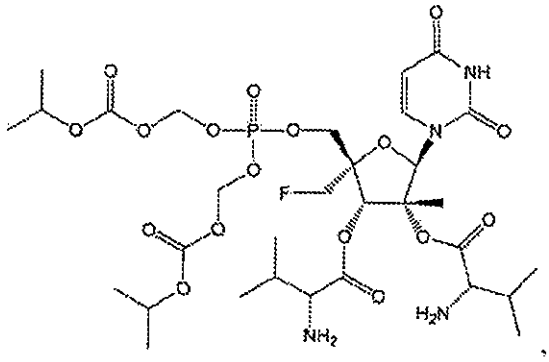
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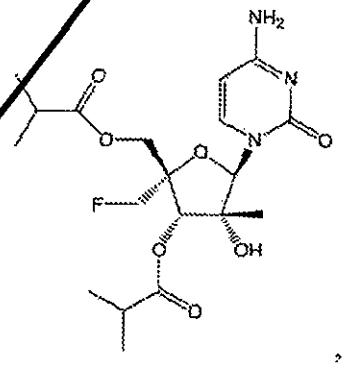
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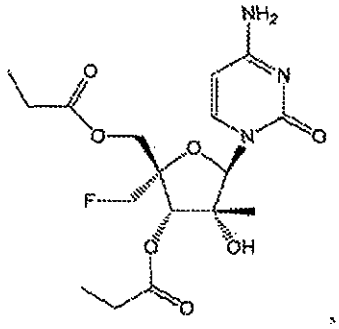
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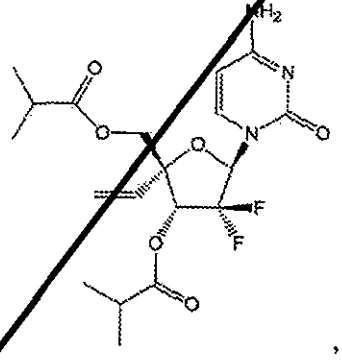
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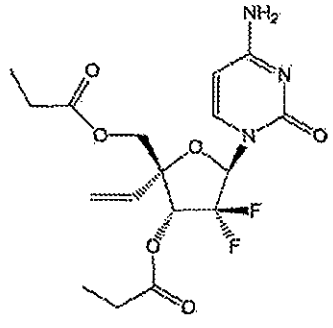
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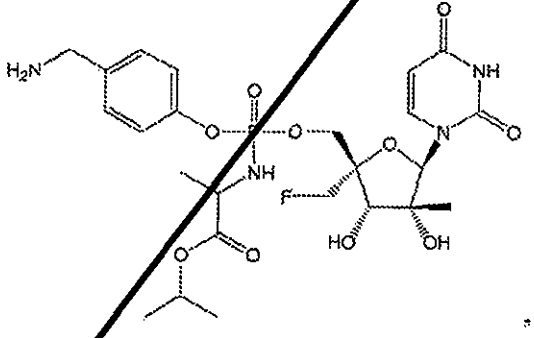
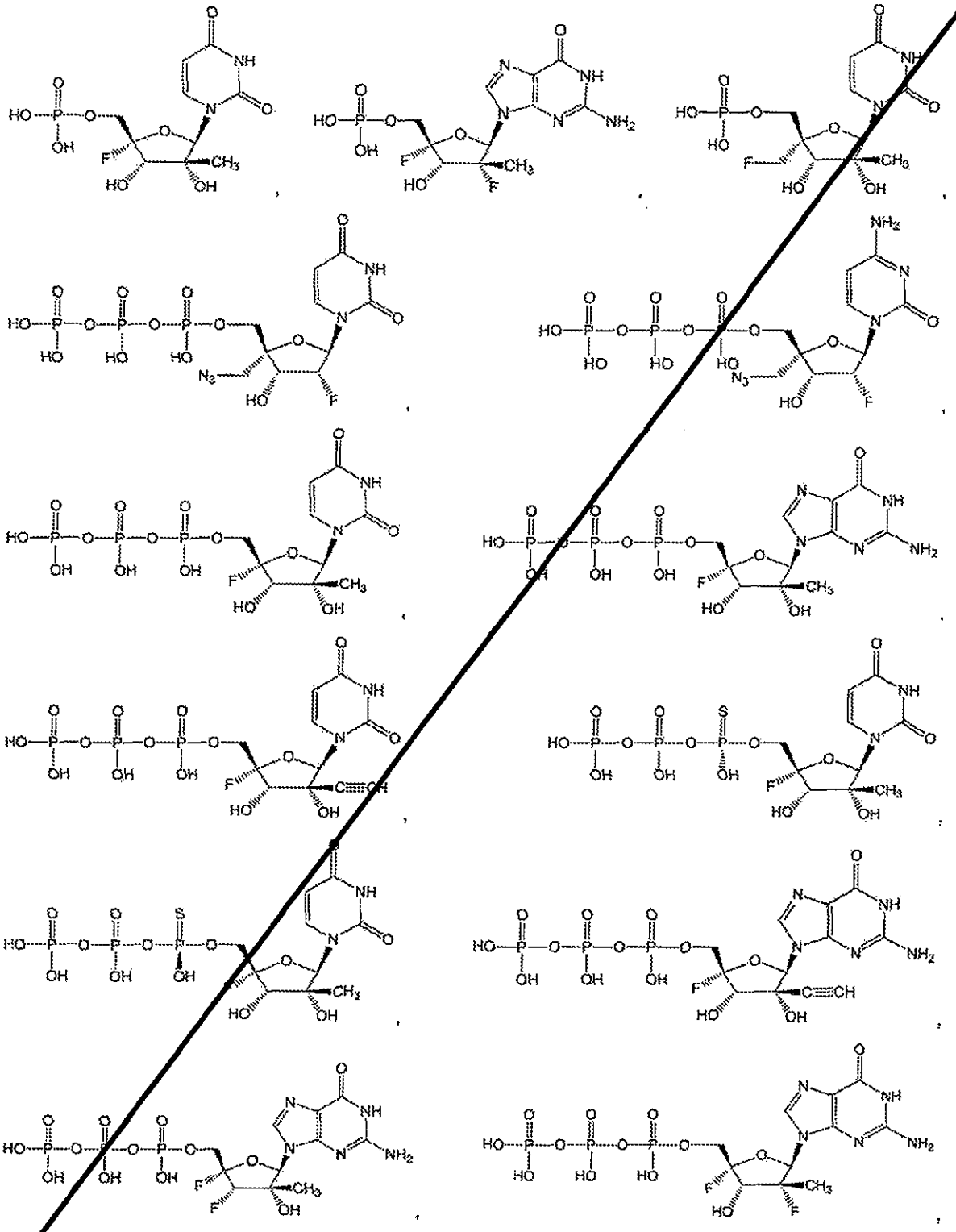
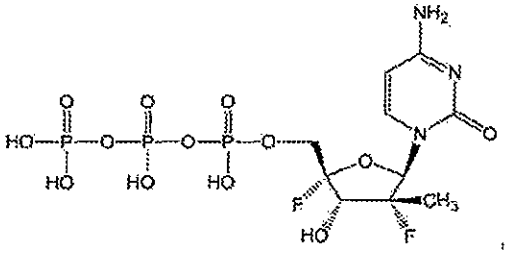
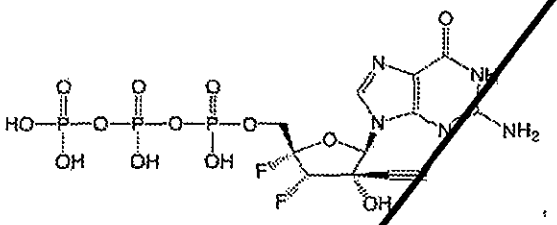
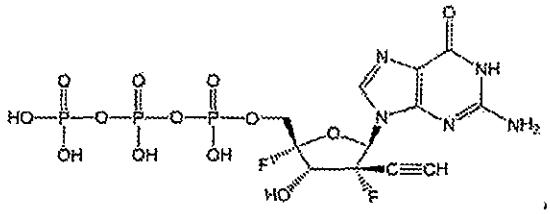

, or a pharmaceutically acceptable salt of the foregoing.

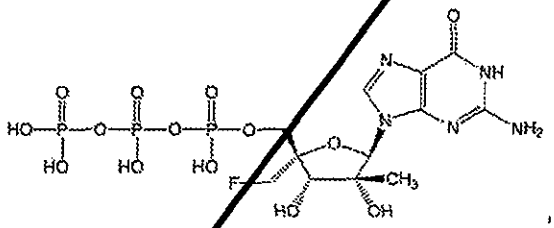
90. The use of Claim 1, wherein the compound is selected from the group consisting of:

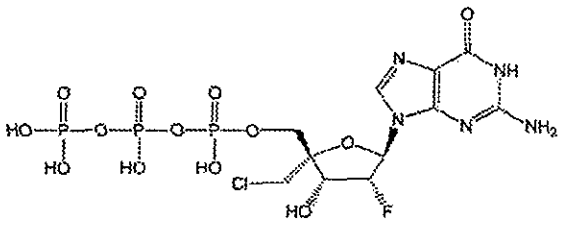


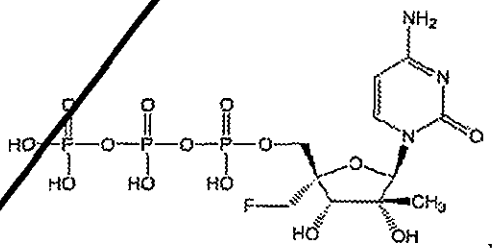


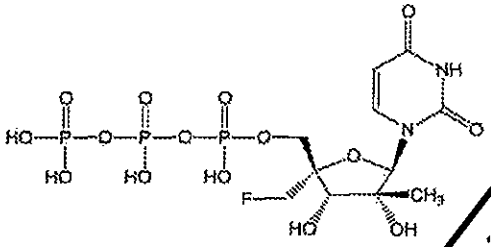


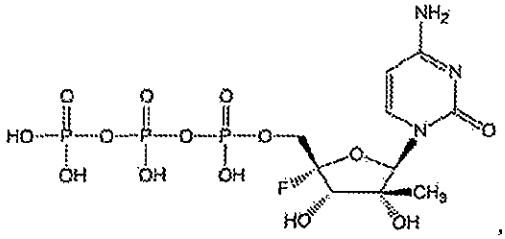


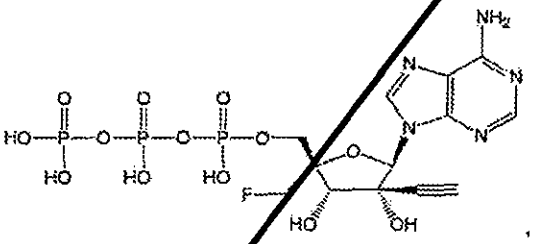


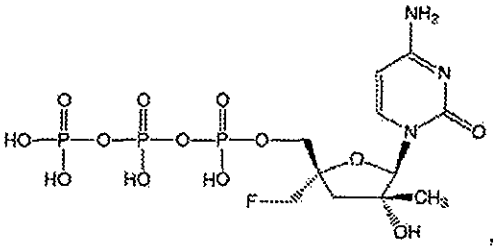


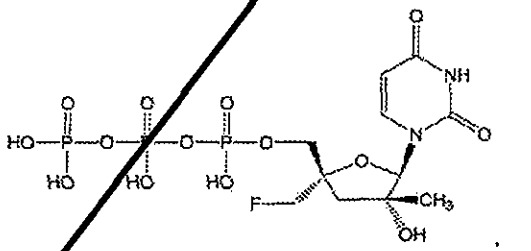


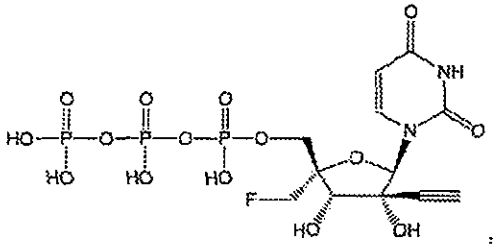




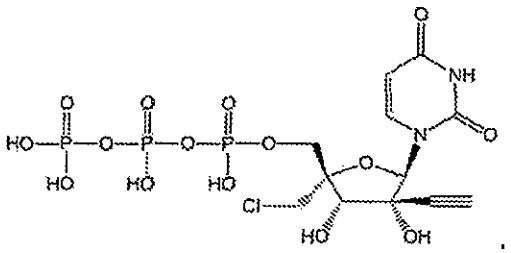


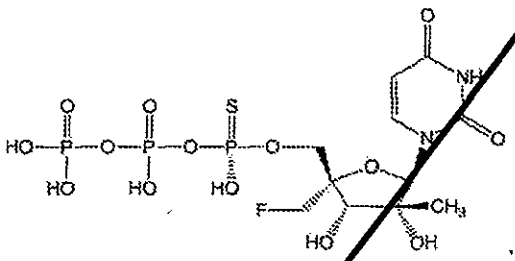


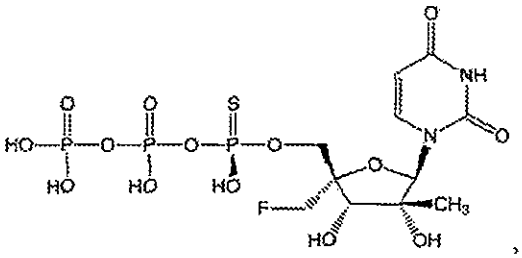


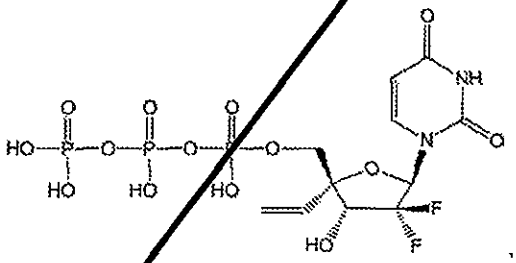


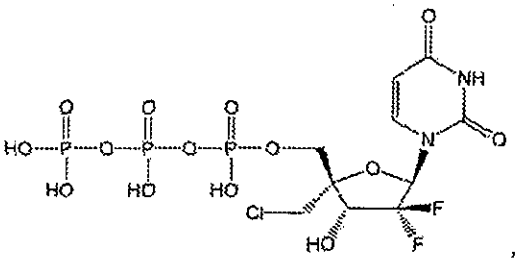


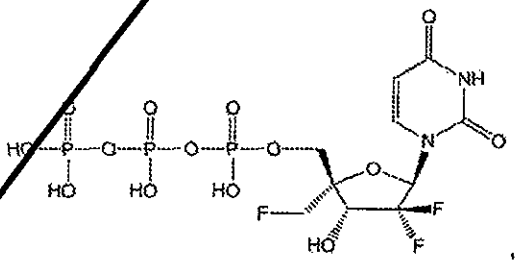


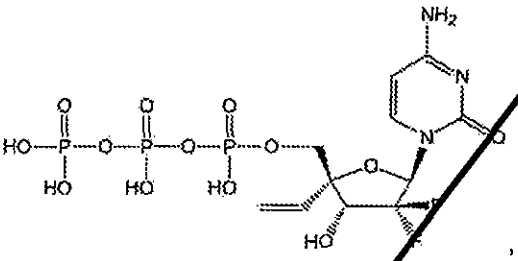


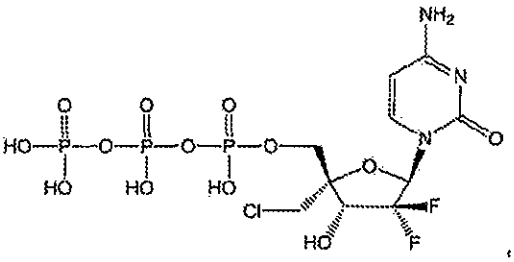


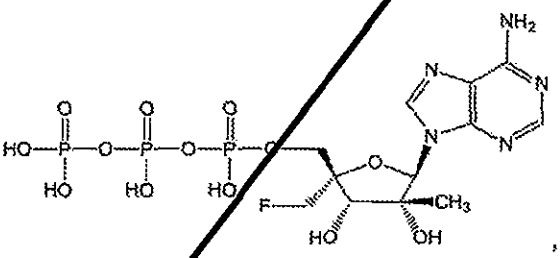


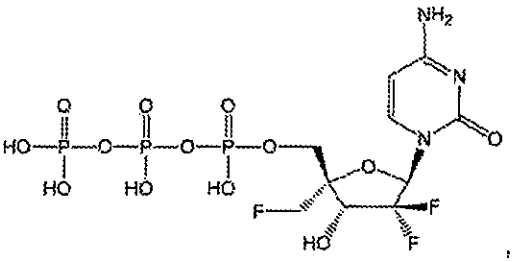


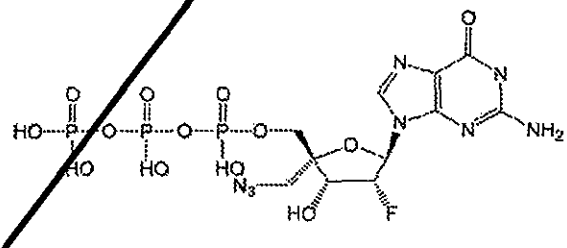


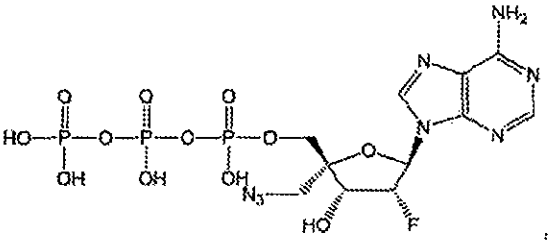


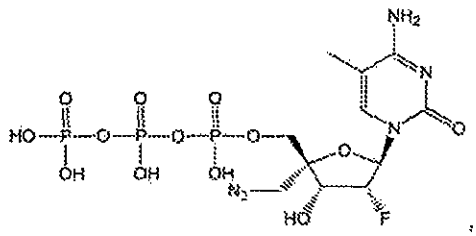


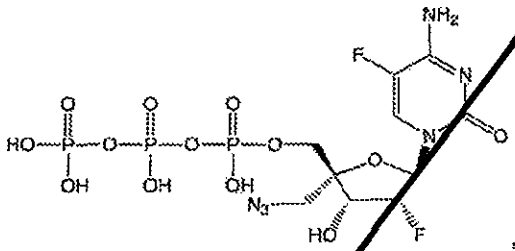


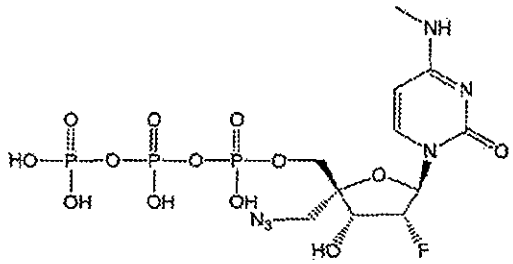


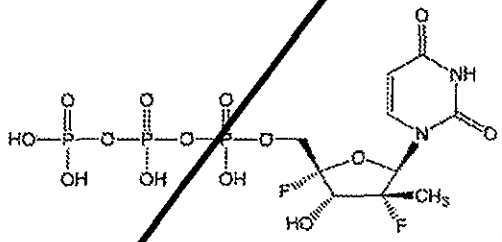


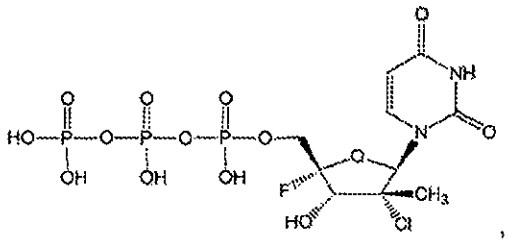


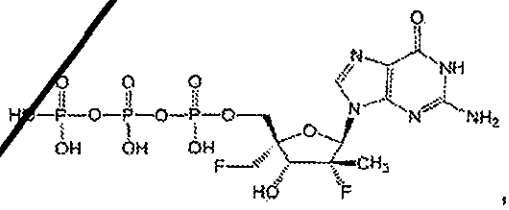


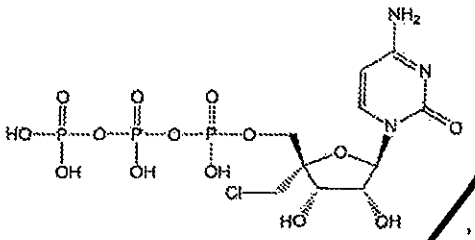


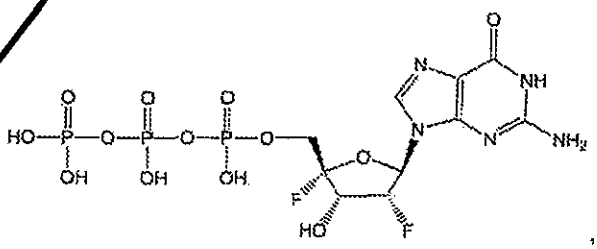


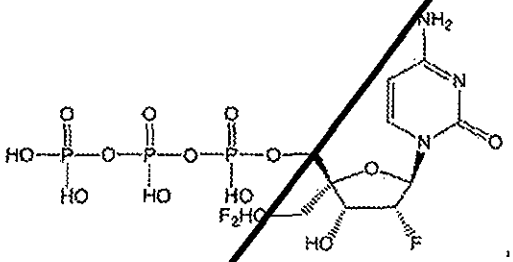


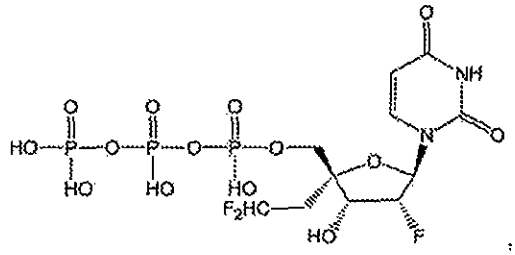


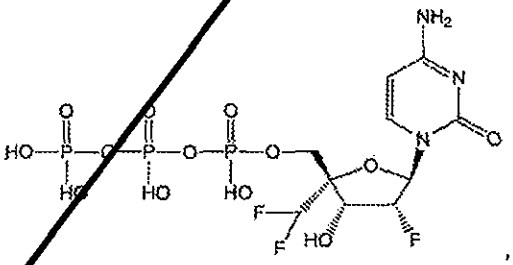


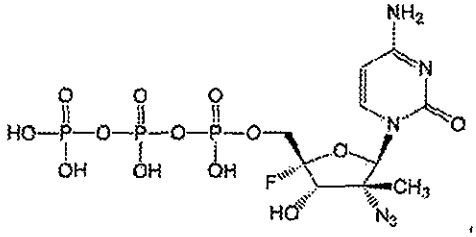


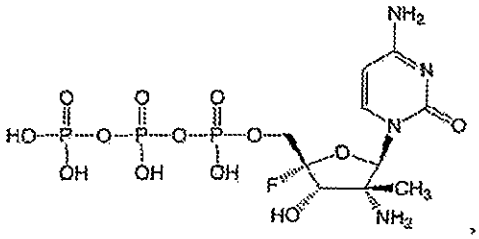


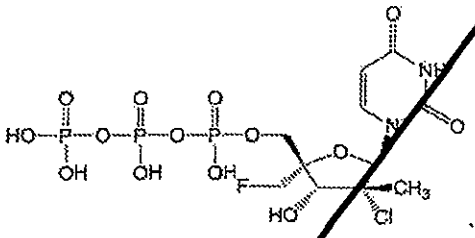


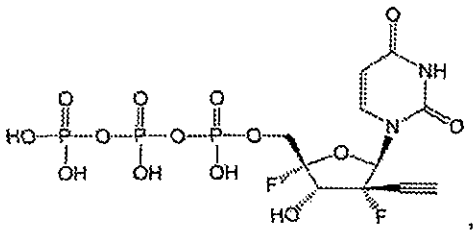


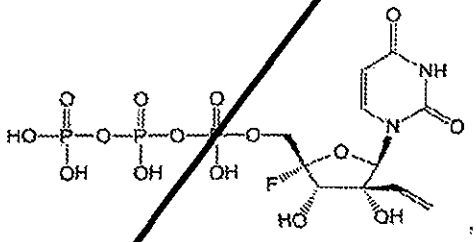


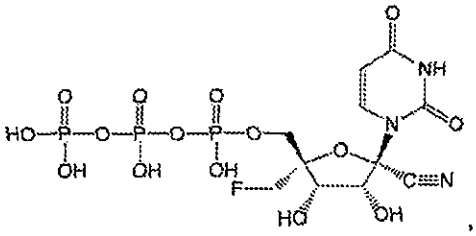


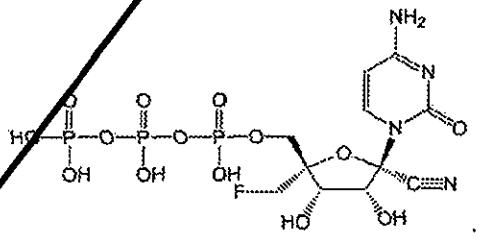


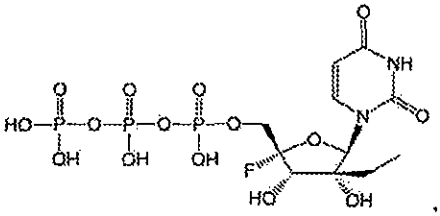


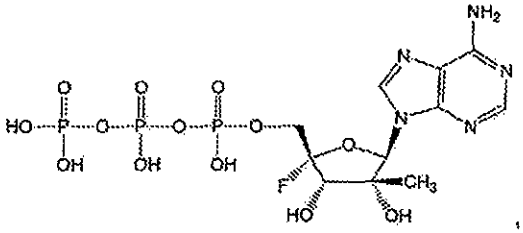


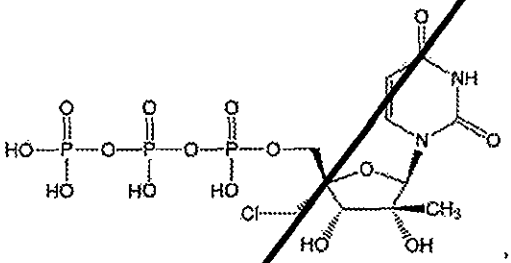


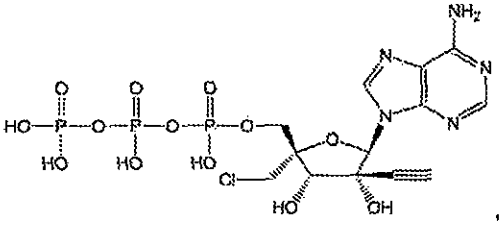


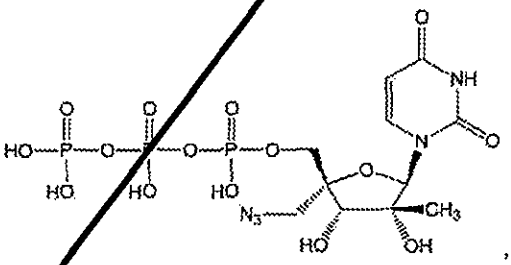


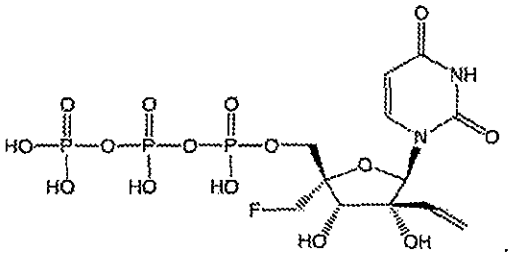


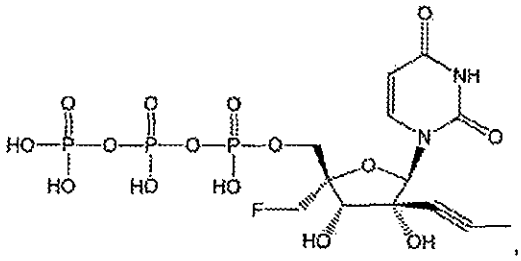


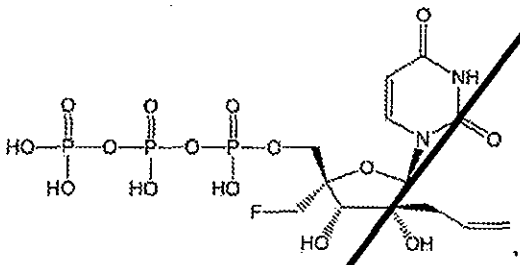


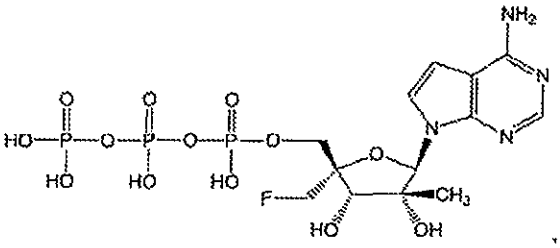


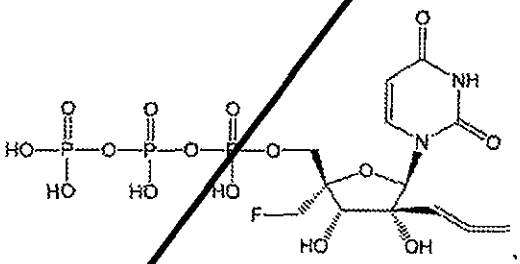


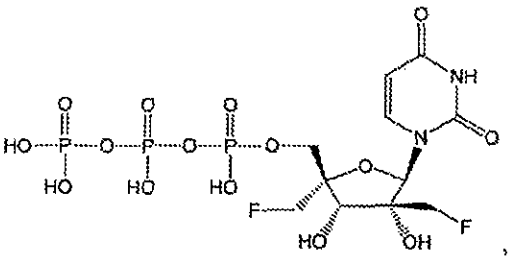


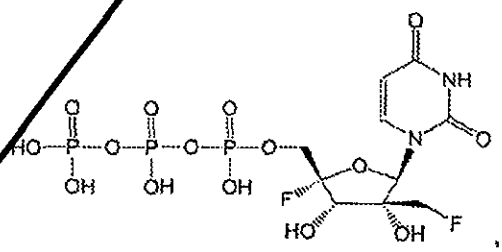


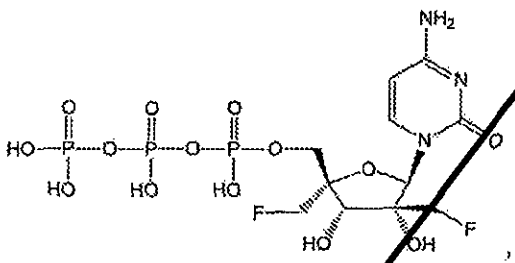


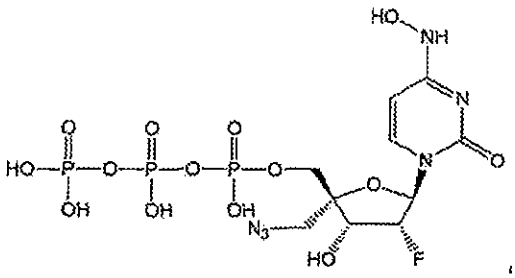


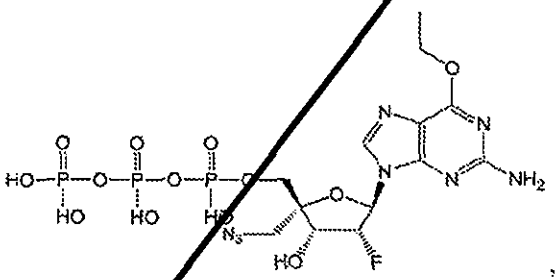


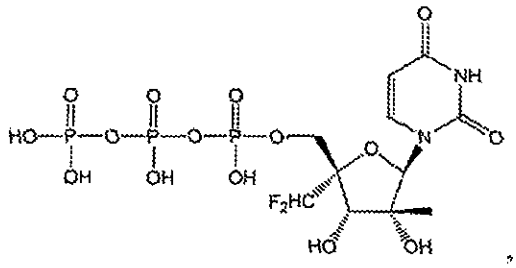


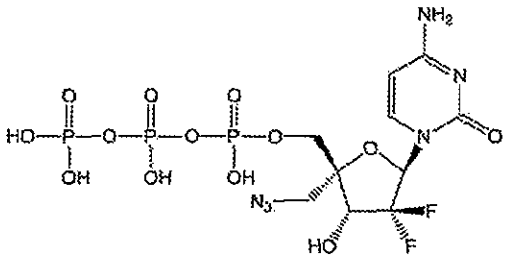








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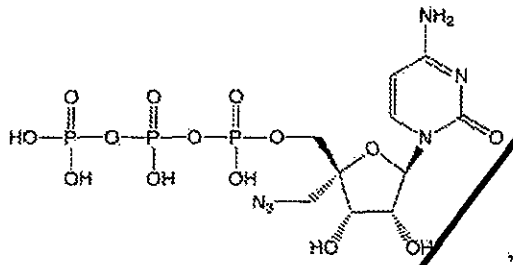
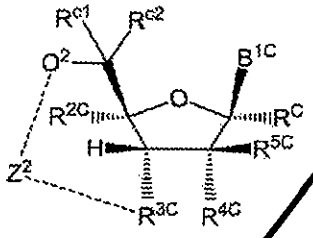

, or a pharmaceutically acceptable salt of the foregoing.

91. A compound of Formula (II), or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (II) has the structure:

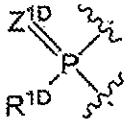
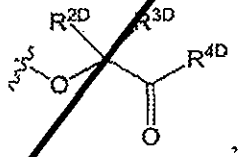
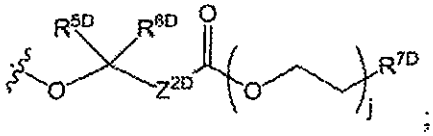


**(II)**

wherein:

$B^{1C}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

when -------- are both absent, then $Z^2$ is absent, $O^2$ is $OR^{1C}$and $R^{3C}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{"C}$ and an optionally substituted O-linked amino acid;

when -------- are each a single bond, then $Z^2$ is  , $O^2$ is O, $R^{3C}$ is O, $R^{2C}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or –CN, and $R^{1D}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1-6}$ alkyl,  ,  ;

$R^{2C}$ is halo, an unsubstituted $C_{2-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}NH_2$, $-(CH_2)_{1-6}N_3$ or -CN, and $R^{5C}$ is selected from the group consisting of an

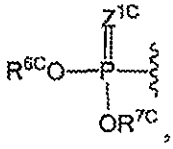
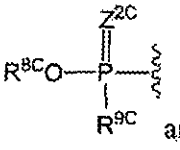
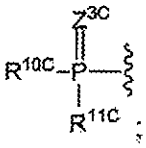
optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl, or

$R^{2C}$ is $-CHF_2$ or $-(CH_2)_{1-6}Cl$, and $R^{5C}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

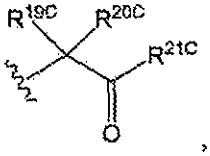
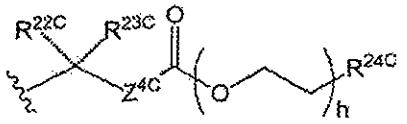
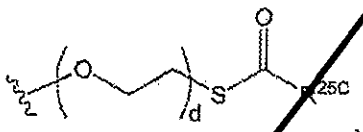
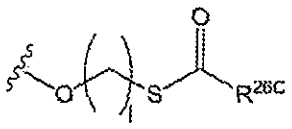
$R^{4C}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R^{aD}$, an optionally substituted O-linked amino acid and $NR^{aD1}R^{aD2}$, or $R^{3C}$ and $R^{4C}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

$R^{c1}$ and $R^{c2}$ are independently hydrogen or deuterium;

$R^{C}$ is hydrogen, deuterium, an unsubstituted $C_{1-3}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-3}$ alkynyl or cyano;

$R^{1C}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  ,  and  ;

$R^{6C}$, $R^{7C}$ and $R^{8C}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted $*-(CR^{15C}R^{16C})_f-O-C_{1-24}$ alkyl, an optionally substituted $*-(CR^{17C}R^{18C})_g-O-C_{1-24}$ alkenyl,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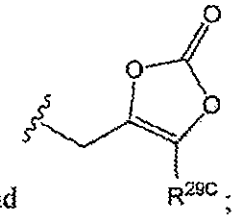
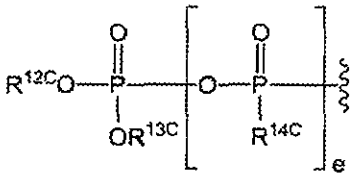
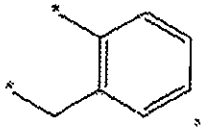

; or



$R^{6C}$ is and $R^{7C}$ is absent or hydrogen; or

$R^{6C}$ and $R^{7C}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6C}$ and $R^{7C}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9C}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30C}R^{31C}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10C}$ and $R^{11C}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

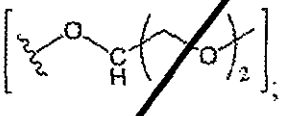
$R^{12C}$ and $R^{13C}$ are independently absent or hydrogen;

$R^{14C}$ is O-, OH or methyl;

each $R^{15C}$, each $R^{16C}$, each $R^{17C}$ and each $R^{18C}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19C}$, $R^{20C}$, $R^{22C}$ and $R^{23C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21C}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24C}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25C}$, $R^{26C}$ and $R^{29C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{30C}$ and $R^{31C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R^{\prime\prime C}$ and each $R^{\prime\prime D}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R^{\prime\prime DJ}$ and each $R^{\prime\prime DJ2}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{2D}$, $R^{3D}$, $R^{5D}$ and $R^{6D}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4D}$ and $R^{7D}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

d and e are independently 0 or 1;

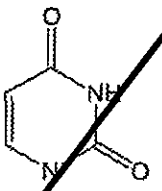
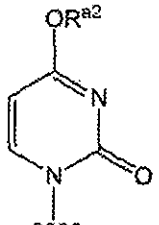
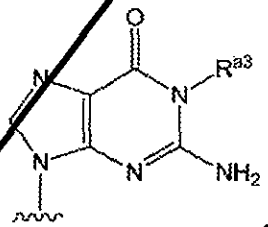
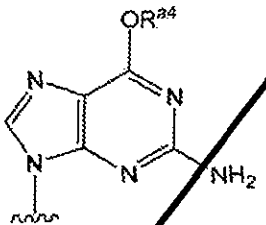
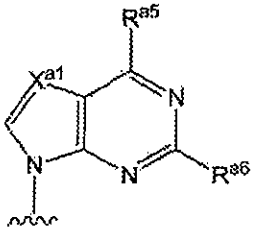
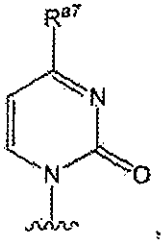
f and g are independently 1, 2 or 3;

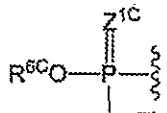
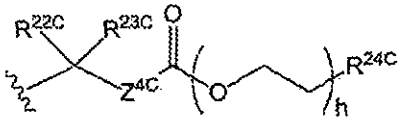
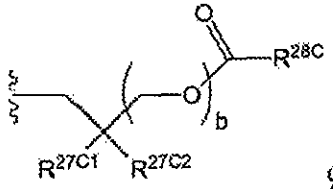
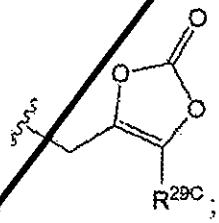
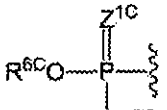
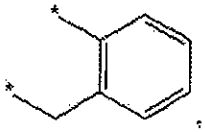
h and j are independently 0, 1, 2 or 3;

l is 3, 4 or 5; and

$Z^{1C}$, $Z^{2C}$, $Z^{3C}$ and $Z^{4C}$ are independently O or S;

provided that when $R^{2C}$ is halo; ------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$;

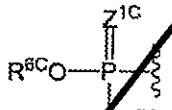
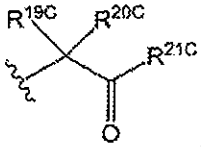
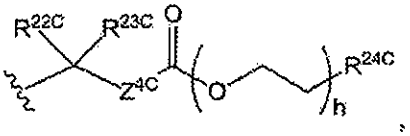
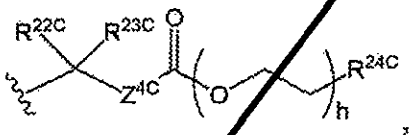
$B^{1C}$ is selected from the group consisting of an optionally substituted  , an optionally substituted  , an optionally substituted  , an optionally substituted  , an optionally substituted  and an optionally substituted  , wherein $R^{a2}$ is an optionally substituted $C_{1-6}$ alkyl or an optionally substituted $C_{3-6}$ cycloalkyl, $R^{a3}$ and $R^{a4}$ are independently selected from the group consisting of hydrogen, an unsubstituted $C_{1-6}$ alkyl, an unsubstituted $C_{3-6}$ alkenyl, an unsubstituted $C_{3-6}$ alkynyl and an unsubstituted $C_{3-6}$ cycloalkyl, $R^{a5}$ is $NHR^{a8}$, and $R^{a6}$ is hydrogen, halogen or $NHR^{a9}$; $R^{a7}$ is $NHR^{a10}$; $R^{a8}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a11}$ and $-C(=O)OR^{a12}$; $R^{a9}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a13}$ and $-C(=O)OR^{a14}$; $R^{a10}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a15}$ and $-C(=O)OR^{a16}$; $X^{a1}$ is N or $-CR^{a17}$;

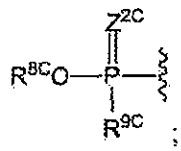
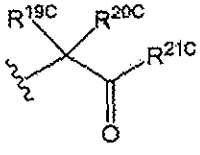
$R^{a17}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; $R^{a11}$, $R^{a12}$, $R^{a13}$, $R^{a14}$, $R^{a15}$ and $R^{a16}$ are independently selected from the group consisting of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl); then $R^{3C}$ is selected from the group consisting of H, halo and an optionally substituted O-linked amino acid; and $R^{4C}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R^{"D}$, an optionally substituted O-linked amino acid and $NR^{"D1}R^{"D2}$; or then $R^{3C}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{"C}$ and an optionally substituted O-linked amino acid and $R^{4C}$ is an optionally substituted O-linked amino acid; or then $R^{1C}$ is  , wherein $R^{6C}$ and $R^{7C}$ are independently  , wherein h is 1, 2 or 3,  or  ; or then $R^{1C}$ is  , wherein $R^{6C}$ and $R^{7C}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6C}$ and $R^{7C}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, $-(CH_2)_{1-6}$halogen,$-(CH_2)_{1-6}N_3$ or $-(CH_2)_{1-6}NH_2$; ------ are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, $-OC(=O)R^{"C}$ or an optionally substituted O-linked amino acid; and $R^{4C}$ is halo; then $R^{5C}$ is selected from the group

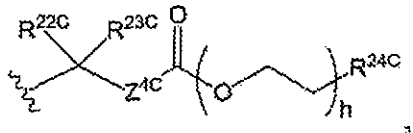
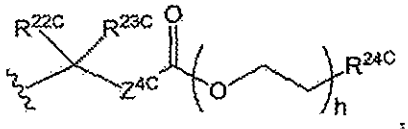
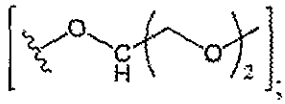
consisting of an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

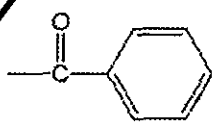
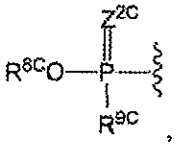
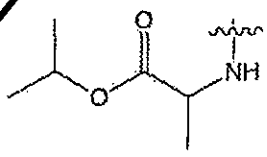
provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, —$(CH_2)_{1-6}$halogen, –$(CH_2)_{1-6}N_3$ or –$(CH_2)_{1-6}NH_2$; ------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{4C}$ is halo; and $R^{5C}$ is H or halo; then $R^{3C}$ is H or halo;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl or —$(CH_2)_{1-6}$halogen; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, –OC(=O)$R^{7C}$ or an optionally substituted O-linked amino acid; $R^{4C}$ is halo; $R^{5C}$ is H or halo; and $R^{1C}$ is  then at least one of $R^{6C}$ and $R^{7C}$ is  , wherein $R^{21C}$ is independently selected from the group consisting of an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl; or then at least one of $R^{6C}$ and $R^{7C}$ is  , wherein s is 1, 2 or 3; or then at least one of $R^{6C}$ and $R^{7C}$ is  , wherein s is 0 and $R^{24C}$ is an optionally substituted –O–heteroaryl or an optionally substituted –O–monocyclic heterocyclyl;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl or —$(CH_2)_{1-6}$halogen; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, –OC(=O)$R^{7C}$ or an optionally substituted O-linked amino acid; $R^{4C}$ is halo; $R^{5C}$ is H or halo; and $R^{1C}$ is  ; then $R^{8C}$ is  , wherein $R^{21C}$ is independently selected from the group consisting of an optionally

substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl; or

then $R^{8C}$ is  , wherein s is 1, 2 or 3; or then $R^{8C}$ is  , wherein s is 0 and $R^{24C}$ is an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl or  ; and

provided that when -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{2C}$ is fluoro; $R^{3C}$ is OH or $-OC(=O)R^{7C}$; $R^{4C}$ is fluoro; and $R^{5C}$ is methyl, ethyl or ethenyl; then $R^{1C}$ cannot be selected from the group consisting of H,  and  , wherein $R^{8C}$ is an unsubstituted aryl; $R^{9C}$ is  and $Z^{2C}$ is oxygen.

92. The compound of Claim 91, wherein $R^{2C}$ is halo.
93. The compound of Claim 92, wherein the halo is fluoro.
94. The compound of Claim 91, wherein $R^{2C}$ is an unsubstituted $C_{2-4}$ alkyl.
95. The compound of Claim 91, wherein $R^{2C}$ is an unsubstituted $C_{2-4}$ alkenyl.
96. The compound of Claim 91, wherein $R^{2C}$ is $-CHF_2$.
97. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}F$.
98. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}Cl$.
99. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}N_3$.
100. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}NH_2$.
101. The compound of Claim 91, wherein $R^{2C}$ is –CN.
102. The compound of any one of Claims 91-101, wherein $R^{3C}$ is halo.
103. The compound of Claim 102, wherein the halo is F.
104. The compound of Claim 102, wherein the halo is Cl.

105. The compound of any one of Claims 91-101, wherein $R^{3C}$ is H.

106. The compound of any one of Claims 91-105, wherein $R^{4C}$ is halo.

107. The compound of Claim 106, wherein the halo is fluoro.

108. The compound of any one of Claims 91-105, wherein $R^{4C}$ is OH.

109. The compound of any one of Claims 91-105, wherein $R^{4C}$ is $-OC(=O)R^{nD}$ or an optionally substituted O-linked amino acid.

110. The compound of any one of Claims 91-105, wherein $R^{4C}$ is $N_3$ or $NR^{nD1}R^{nD2}$.

111. The compound of Claim 110, wherein $R^{4C}$ is $NH_2$.

112. The compound of any one of Claims 91, 96, 98, 99 or 102-111, wherein $R^{5C}$ is H.

113. The compound of any one of Claims 91, 96, 98, 99 or 102-111, wherein $R^{5C}$ is halo.

114. The compound of any one of Claims 91-111, wherein $R^{5C}$ is OH.

115. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{1-6}$ alkyl.

116. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{2-6}$ alkenyl.

117. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{2-6}$ alkynyl.

118. The compound of any one of Claims 91-117, wherein $R^{C}$ is hydrogen.

119. The compound of any one of Claims 91-117, wherein $R^{C}$ is deuterium.

120. The compound of any one of Claims 91-117, wherein $R^{C}$ is an unsubstituted $C_{1-3}$ alkyl.

121. The compound of any one of Claims 91-117, wherein $R^{C}$ is an unsubstituted $C_{2-4}$ alkenyl.

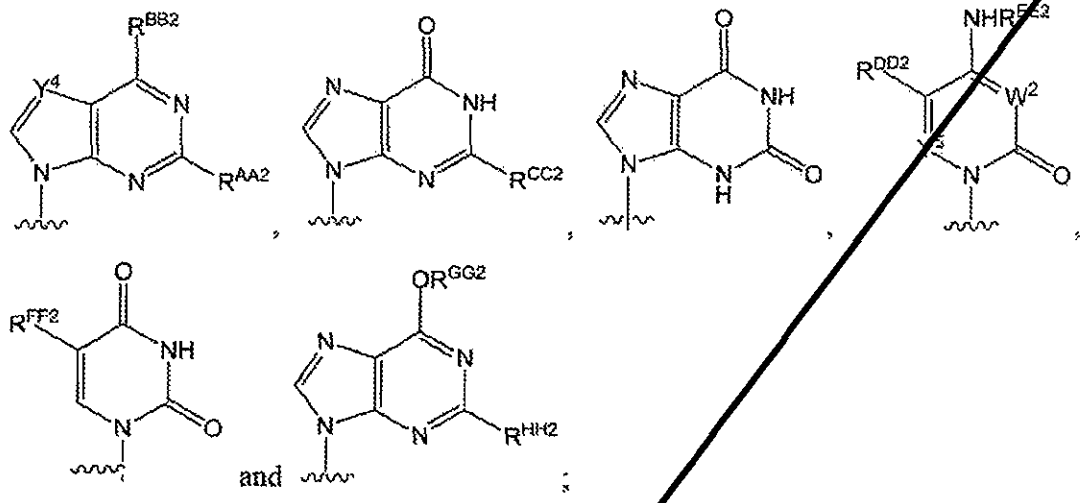
122. The compound of any one of Claims 91-117, wherein $R^{C}$ is an unsubstituted $C_{2-3}$ alkynyl.

123. The compound of any one of Claims 91-117, wherein $R^{C}$ is cyano.

124. The compound of any one of Claims 91-123, wherein $R^{c1}$ and $R^{c2}$ are both hydrogen.

125. The compound of any one of Claims 91-123, wherein $R^{c1}$ and $R^{c2}$ are both deuterium.

126. The compound of any one of Claims 91-125, wherein $B^{1C}$ is selected from the group consisting of:



wherein:

$R^{AA2}$ is selected from the group consisting of hydrogen, halogen and $NHR^{JJ2}$, wherein $R^{JJ2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{KK2}$ and $-C(=O)OR^{LL2}$;

$R^{BB2}$ is halogen or $NHR^{WW2}$, wherein $R^{WW2}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{MM2}$ and $-C(=O)OR^{NN2}$;

$R^{CC2}$ is hydrogen or $NHR^{OO2}$, wherein $R^{O2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{PP2}$ and $-C(=O)OR^{QQ2}$;

$R^{DD2}$ is selected from the group consisting of hydrogen, deuterium, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{EE2}$ is selected from the group consisting of hydrogen, hydroxy, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{RR2}$ and $-C(=O)OR^{SS2}$;

$R^{FF2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

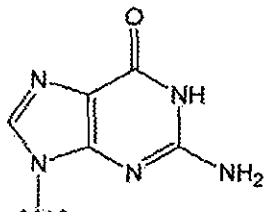
$Y^4$ and $Y^5$ are independently N or $CR^{H2}$, wherein $R^{H2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$-alkenyl and an optionally substituted $C_{2-6}$-alkynyl;

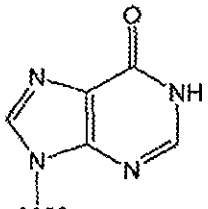
$W^2$ is NH, $-NCH_2$-OC(=O)CH($NH_2$)-CH($CH_3$)$_2$ or $-(CH_2)_{1-2}-O-P(=O)(OW^{2C})_2$, wherein $W^{2C}$ is selected from the group consisting of absent, hydrogen and an optionally substituted $C_{1-6}$ alkyl;

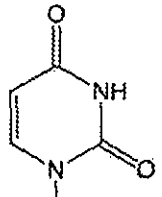
$R^{GG2}$ is an optionally substituted $C_{1-6}$ alkyl;

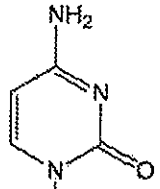
$R^{HH2}$ is hydrogen or $NHR^{TT2}$, wherein $R^{TT2}$ is independently selected from the group consisting of hydrogen, $-C(=O)R^{UU2}$ and $-C(=O)OR^{VV2}$; and

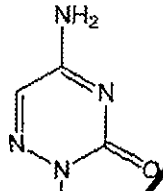
$R^{KK2}$, $R^{LL2}$, $R^{MM2}$, $R^{NN2}$, $R^{PP2}$, $R^{QQ2}$ $R^{RR2}$, $R^{SS2}$, $R^{UU2}$ and $R^{VV2}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl).

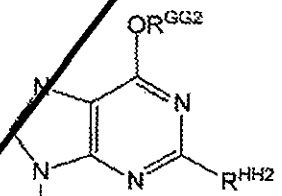
127. The compound of Claim 126, wherein $B^{1C}$ is  .

128. The compound of Claim 126, wherein $B^{1C}$ is  .

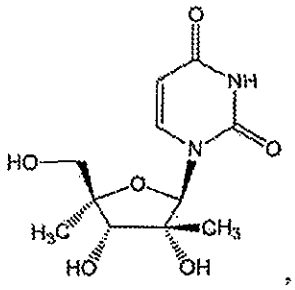
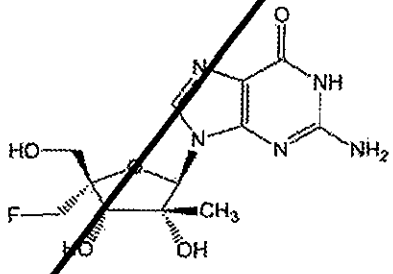
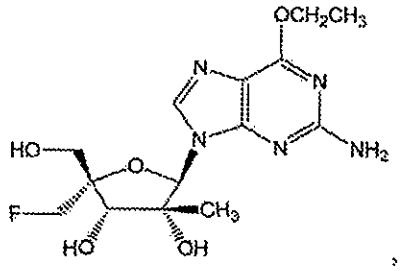
129. The compound of Claim 126, wherein $B^{1C}$ is  .

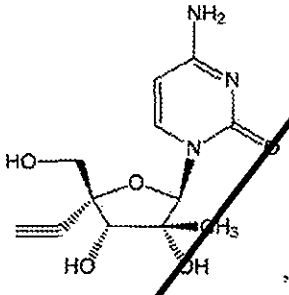
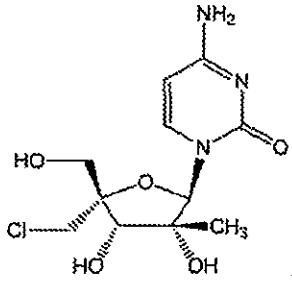
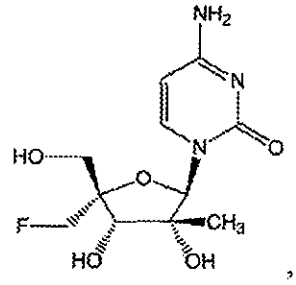
130. The compound of Claim 126, wherein $B^{1C}$ is  .

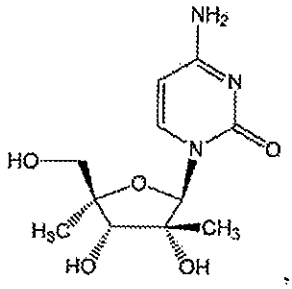
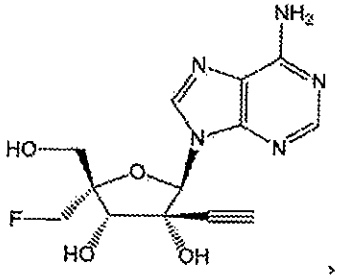
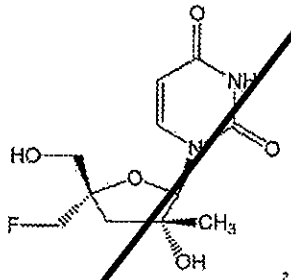
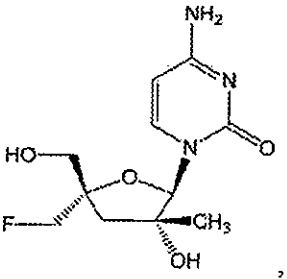
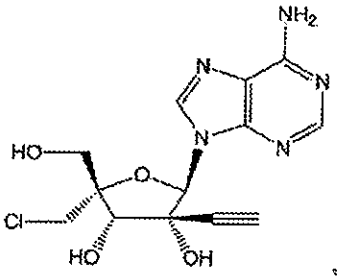
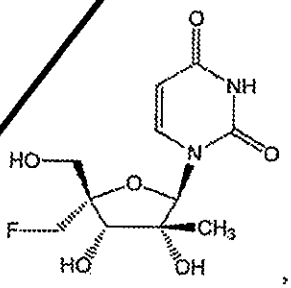
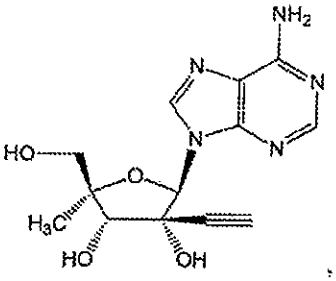
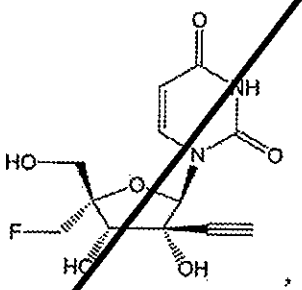
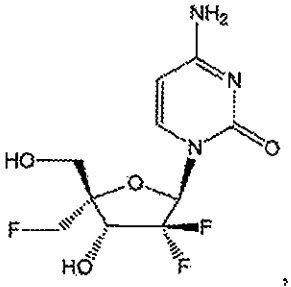
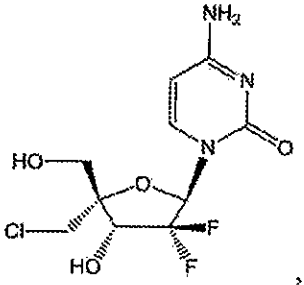
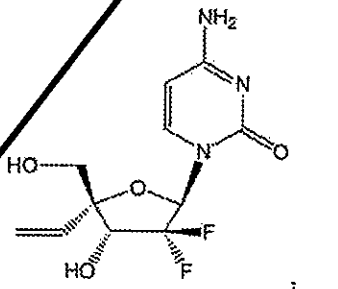
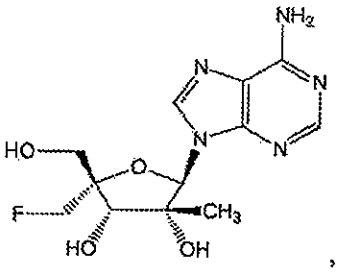
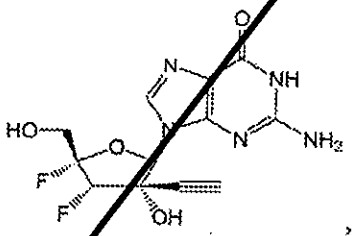
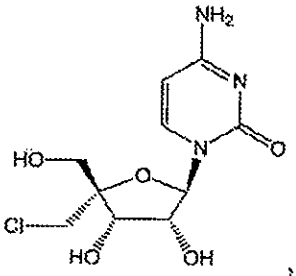
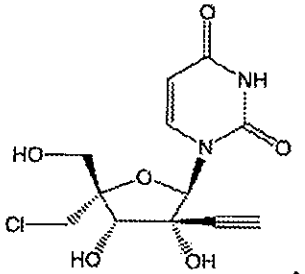
131. The compound of Claim 126, wherein $B^{1C}$ is  .

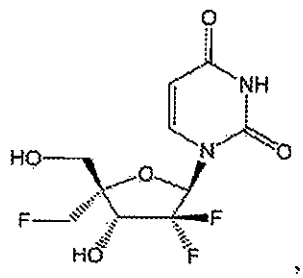
132. The compound of Claim 127, wherein $B^{1C}$ is  .

133. A compound selected from the group consisting of:

 ,  ,  ,

 ,  ,  ,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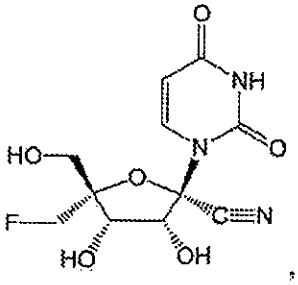
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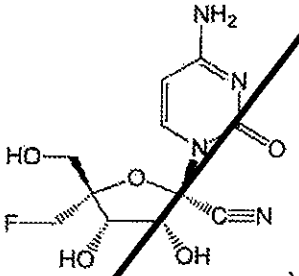
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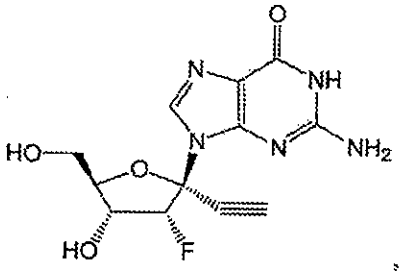
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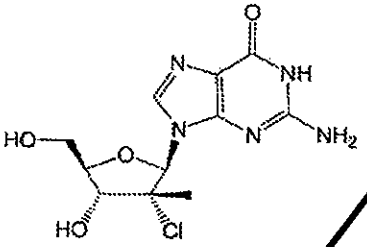
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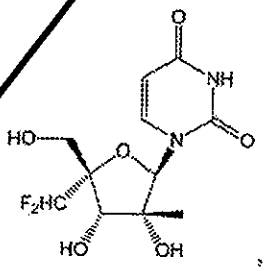
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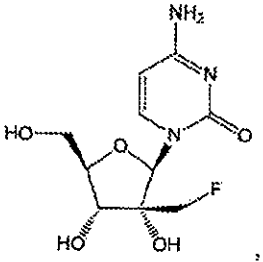
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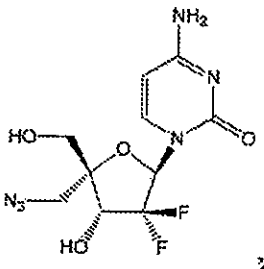
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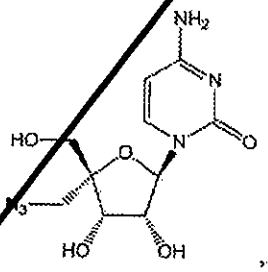
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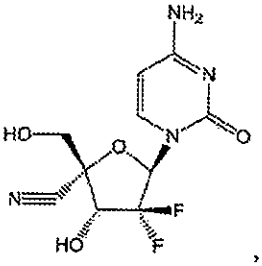
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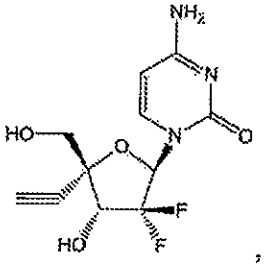
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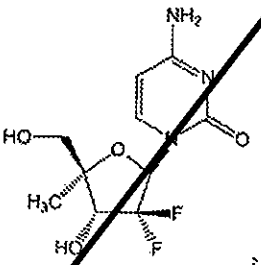
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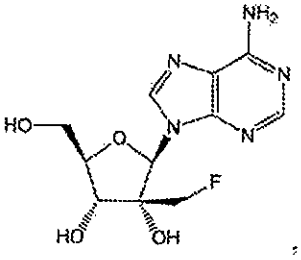
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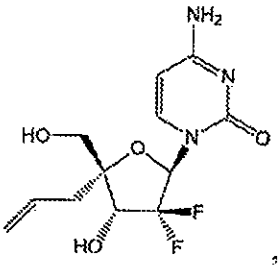
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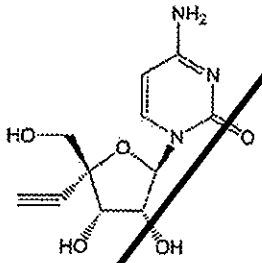
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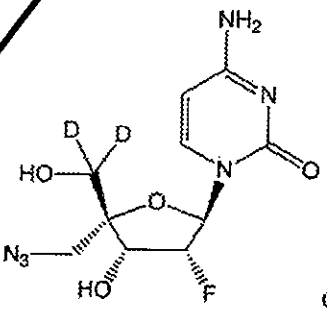
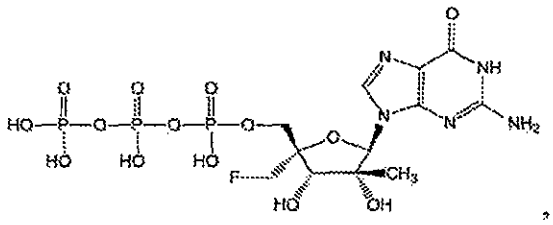
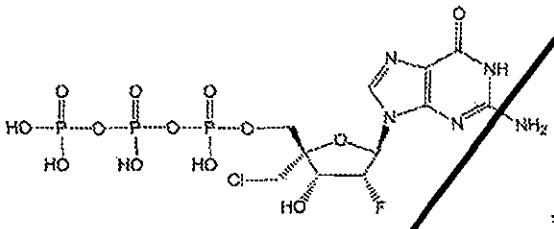
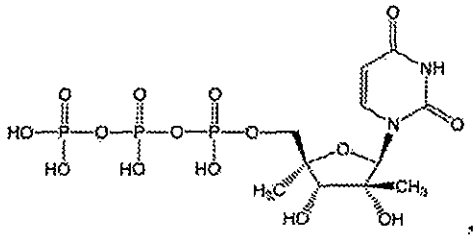
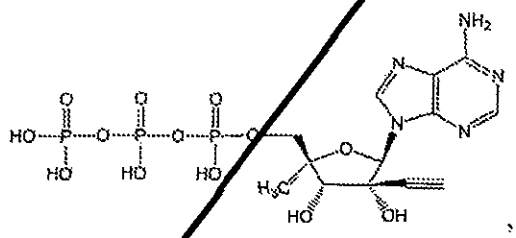

or a pharmaceutically acceptable salt of the foregoing.

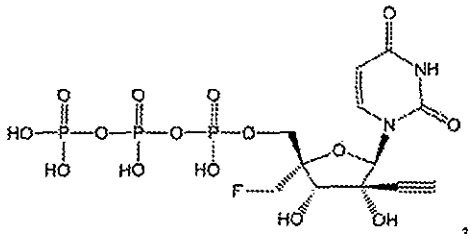
134. A compound selected from the group consisting of:

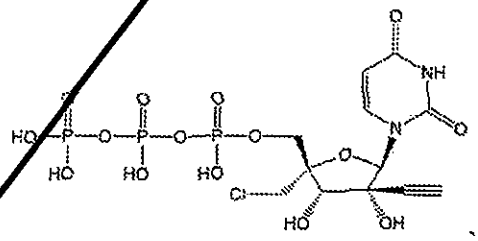


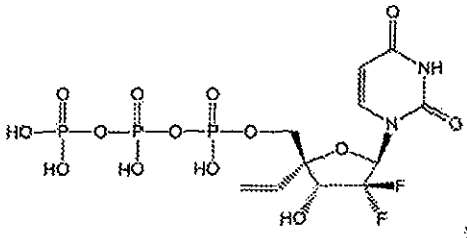


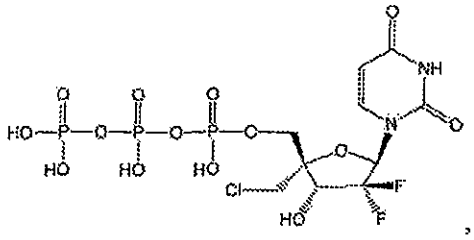


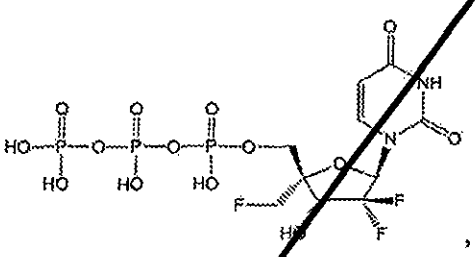


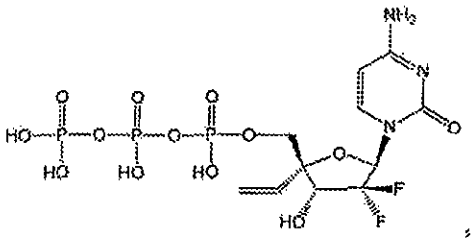


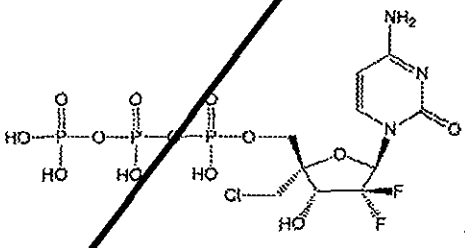


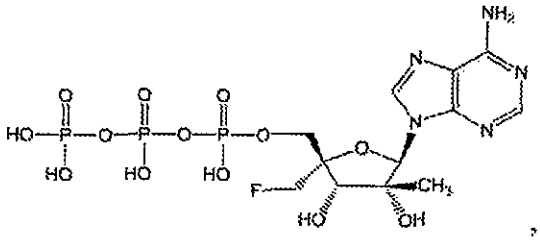


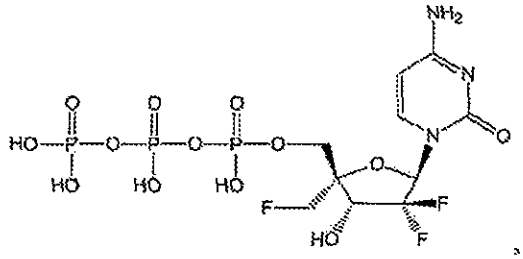


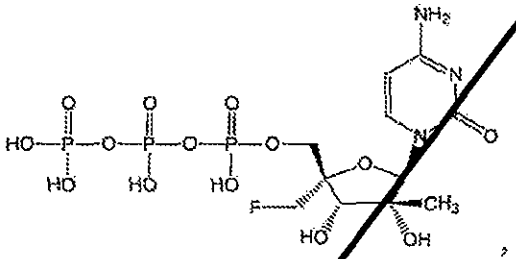


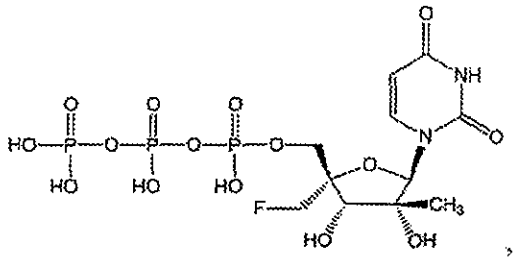


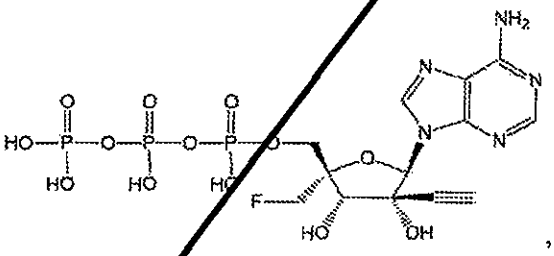


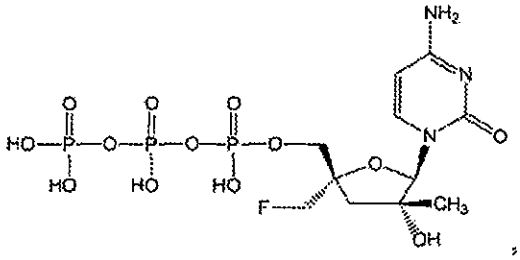


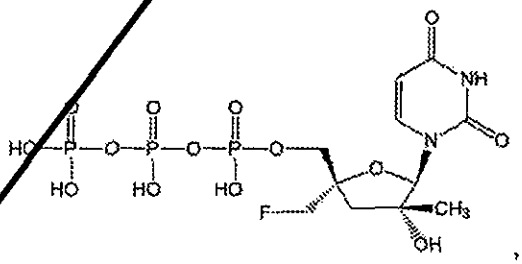


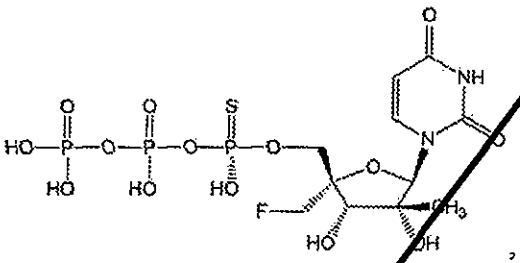


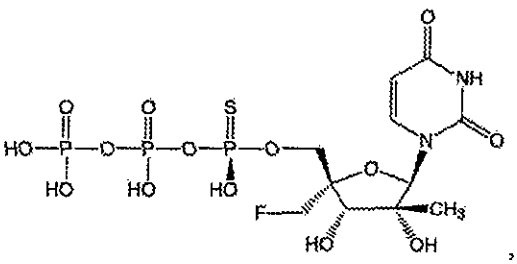


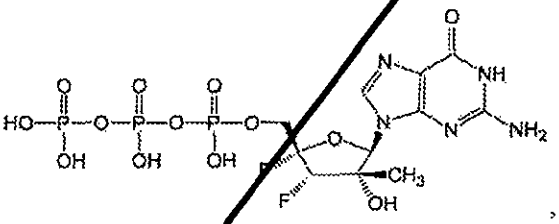


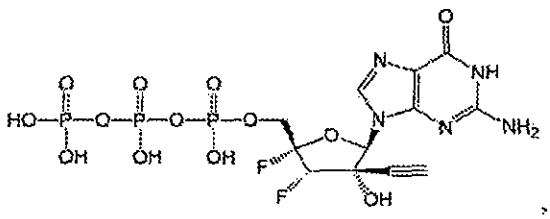


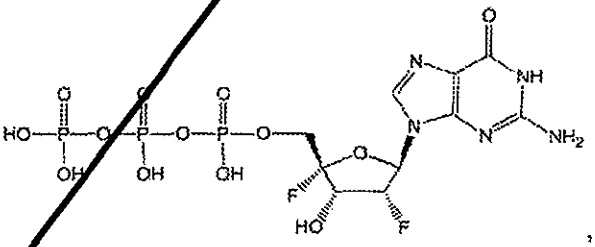


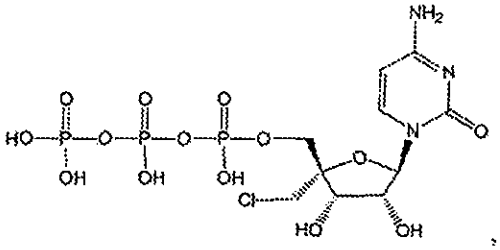


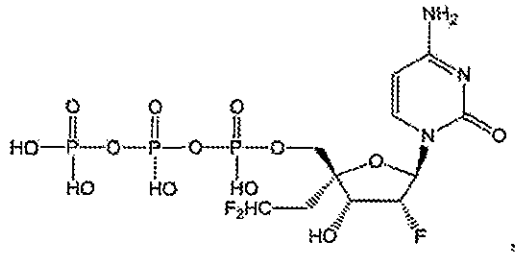


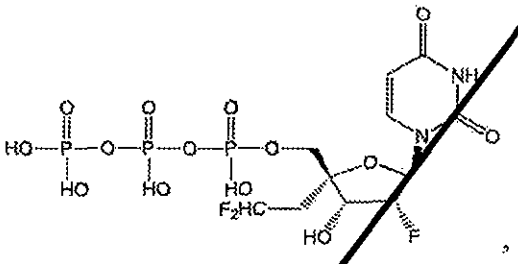


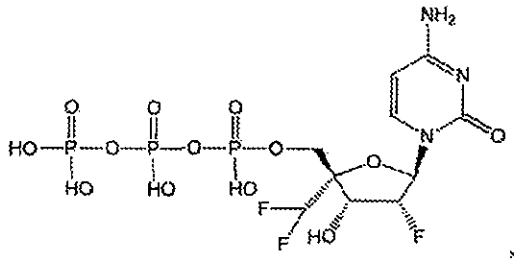


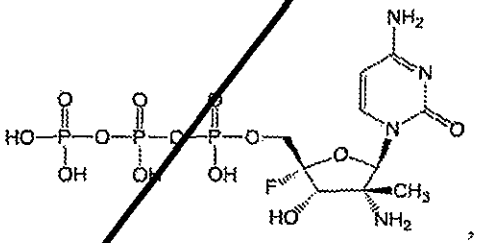


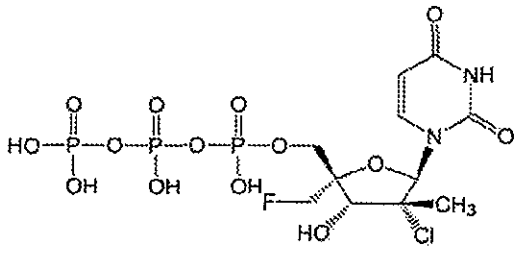


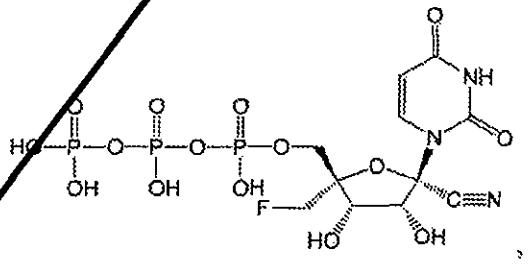


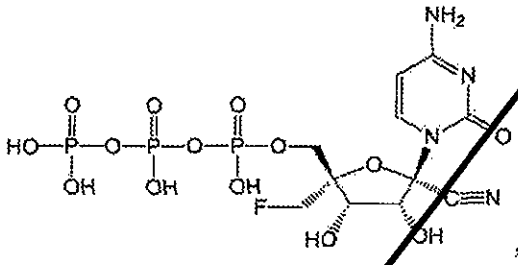


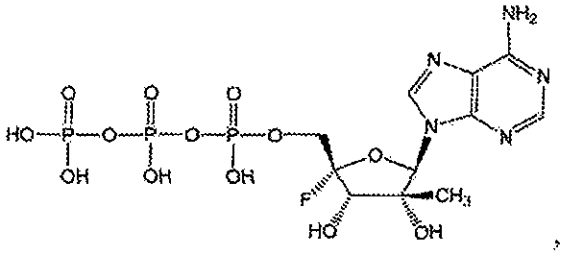


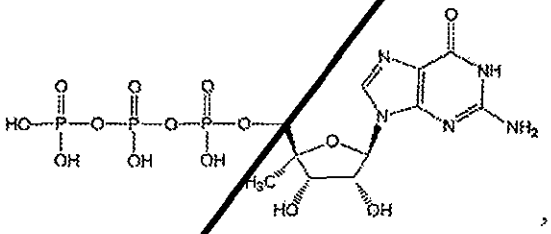


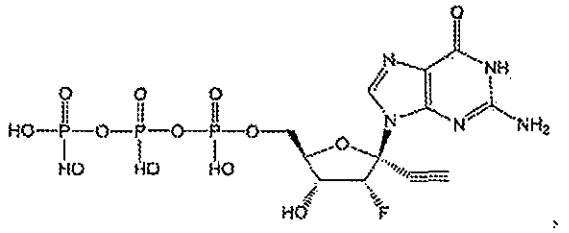


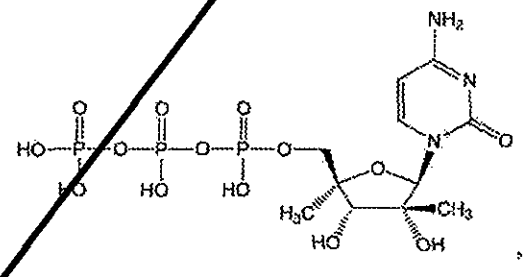


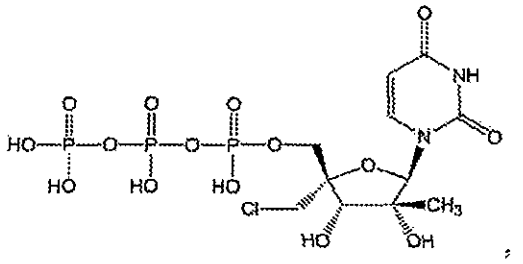


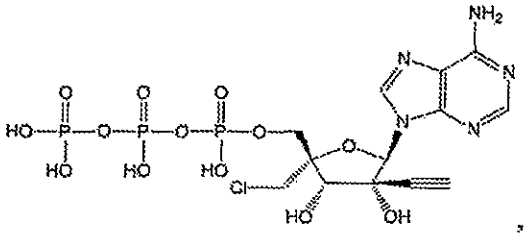


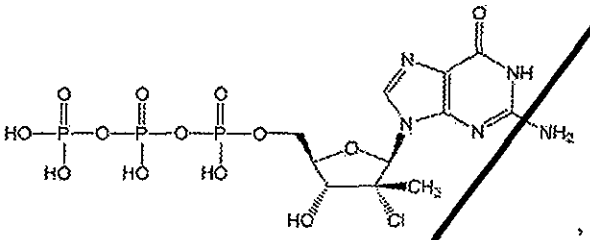


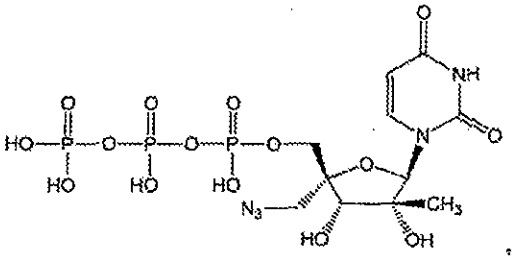


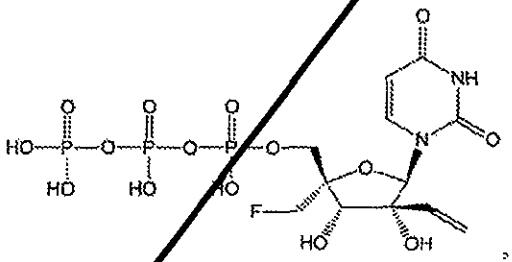


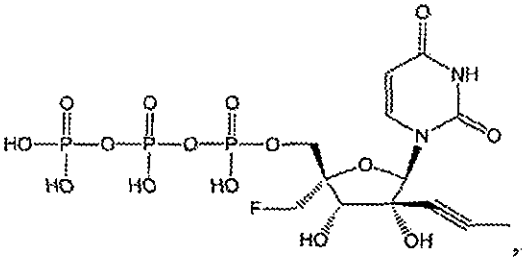


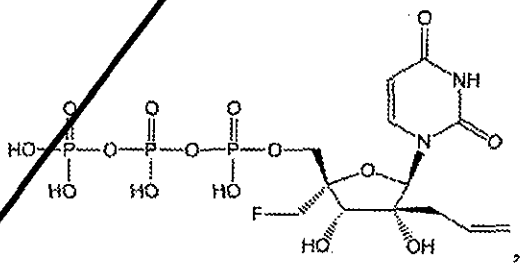


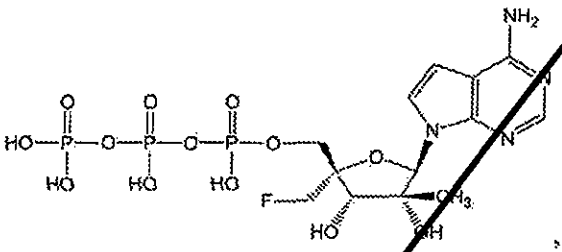


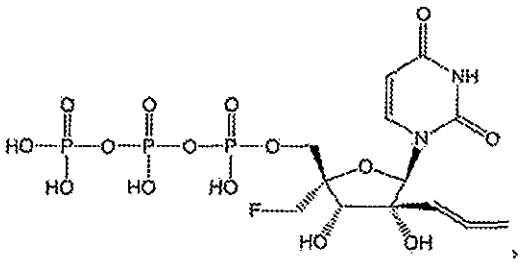


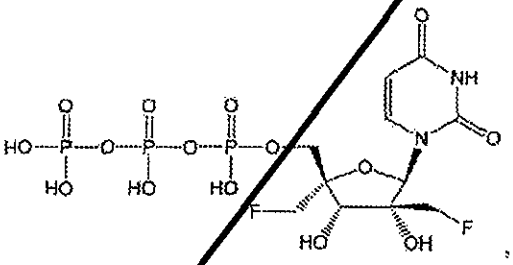


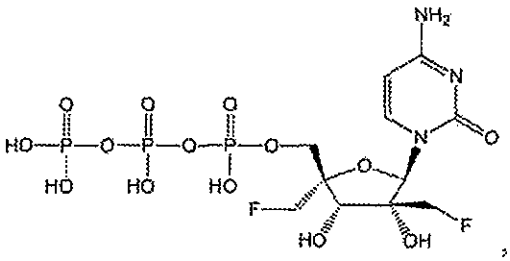


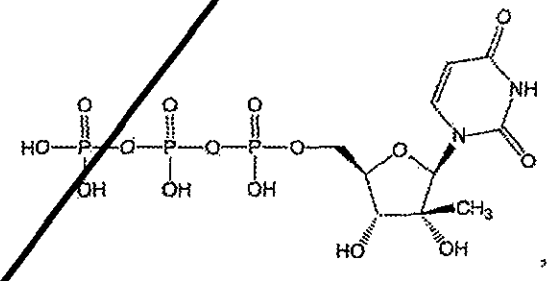


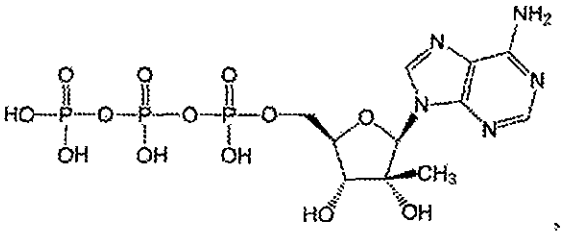


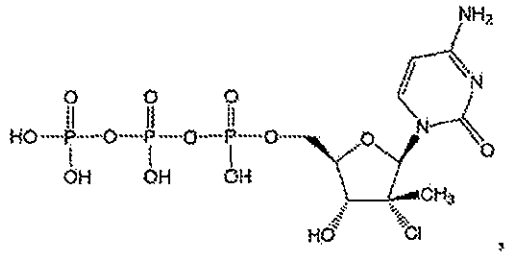








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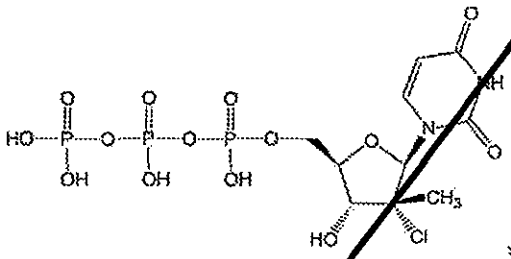
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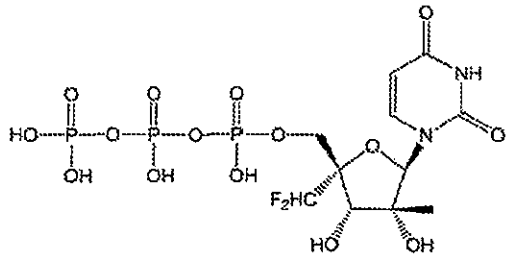
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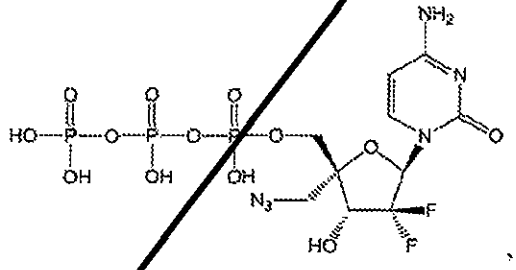
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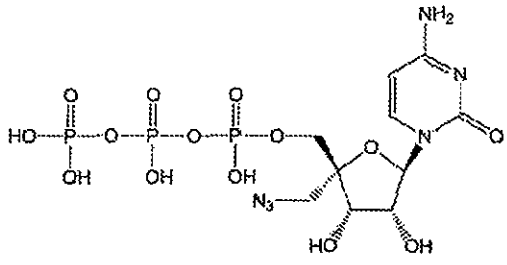
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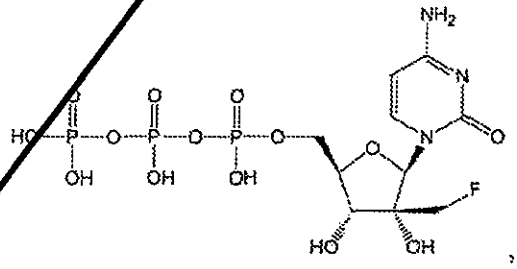
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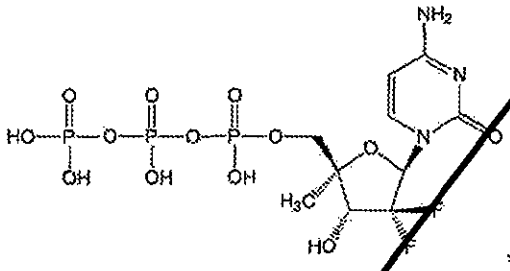
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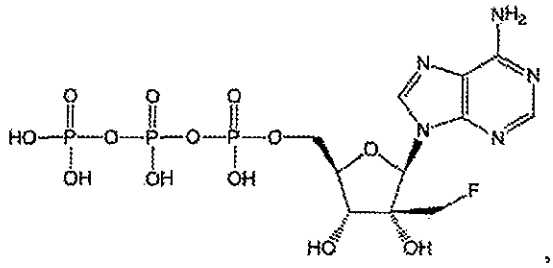
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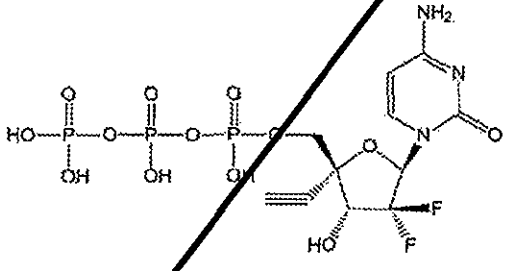
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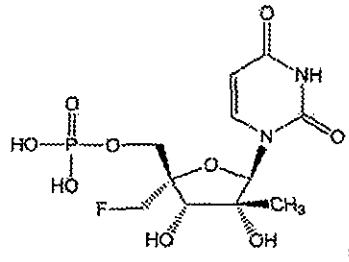
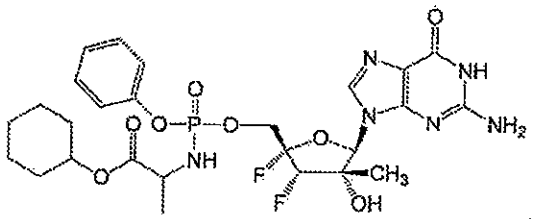
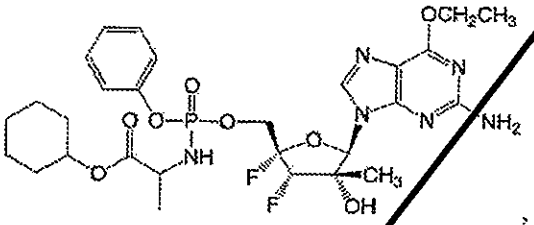
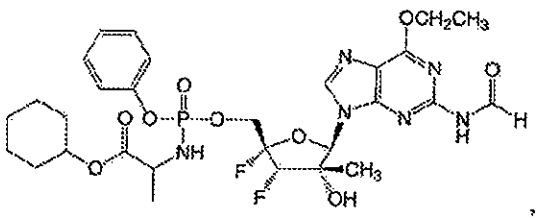
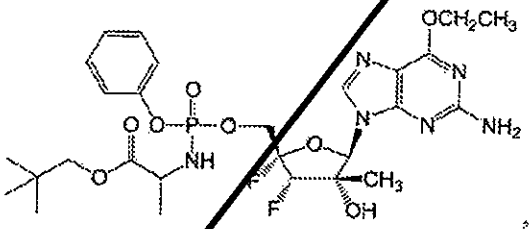

, or a pharmaceutically acceptable salt of the foregoing.

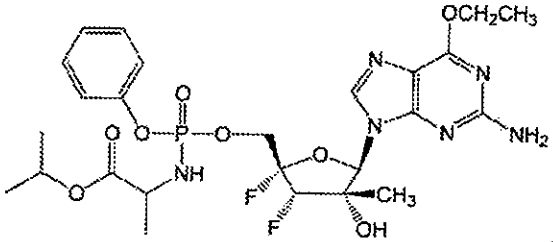
125. A compound selected from the group consisting of:

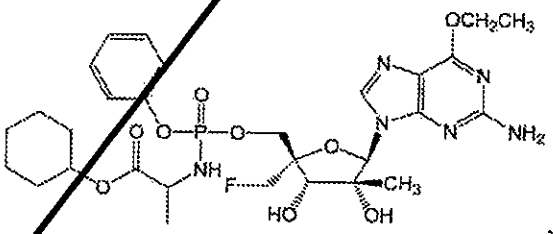


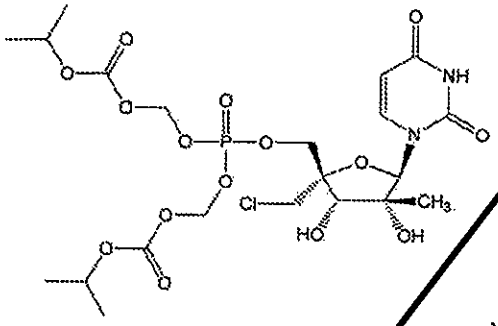


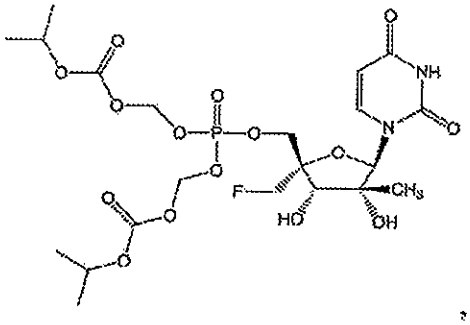


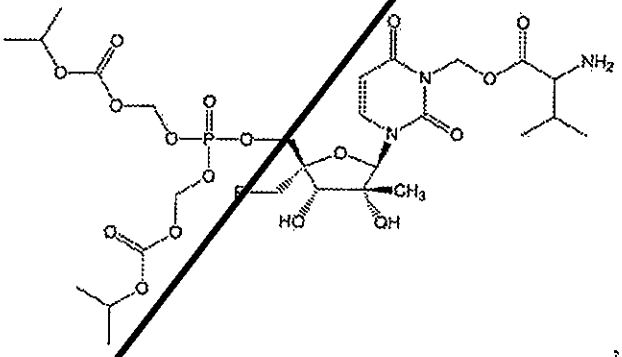


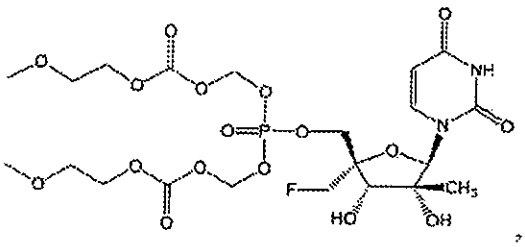


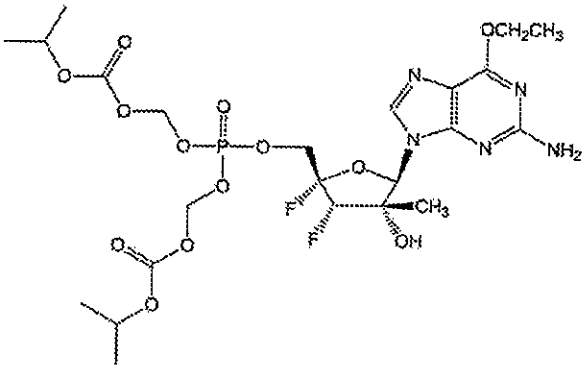


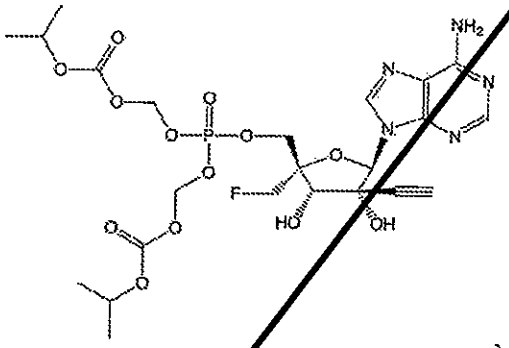


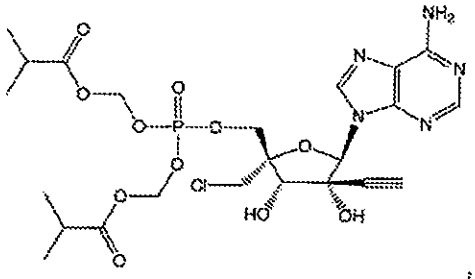


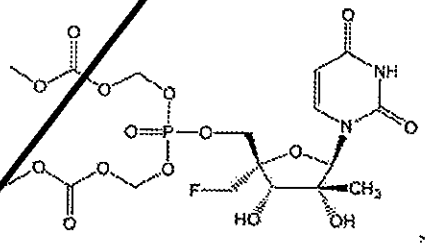


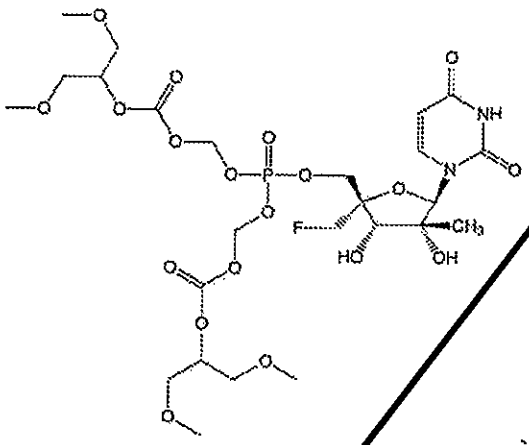


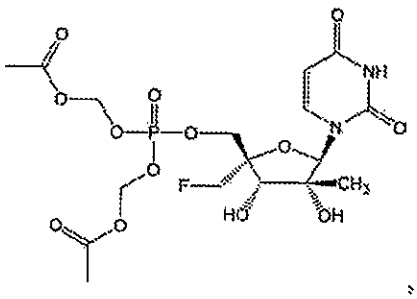


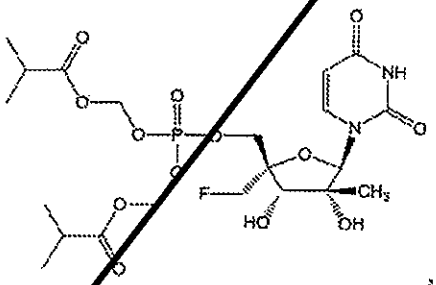


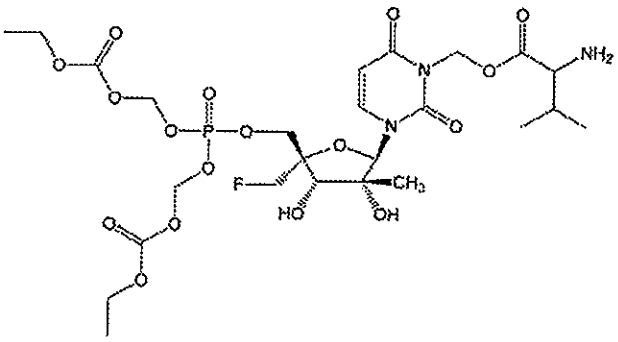


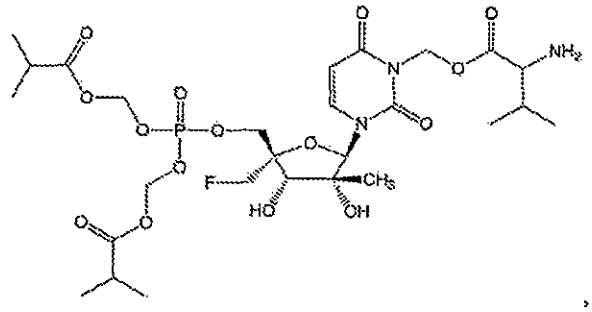


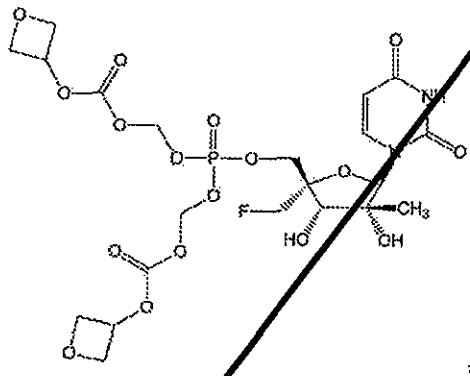


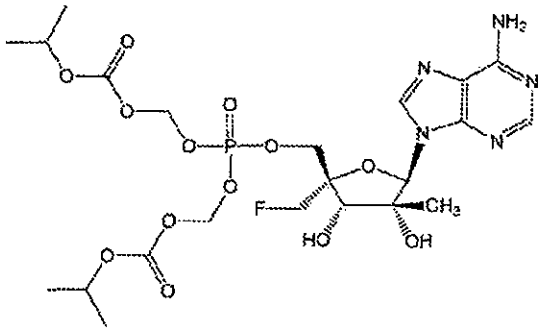


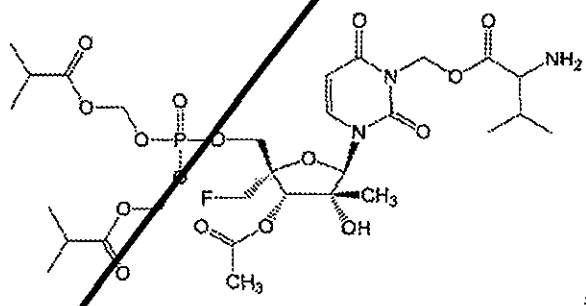


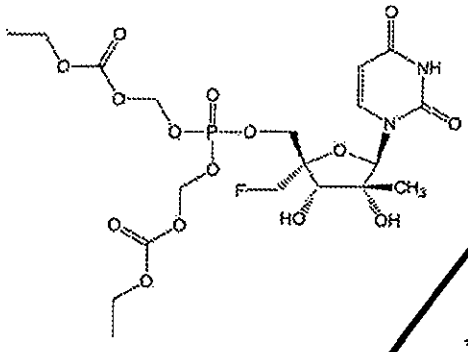


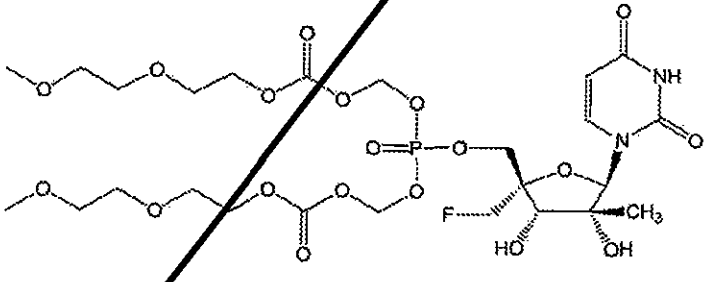


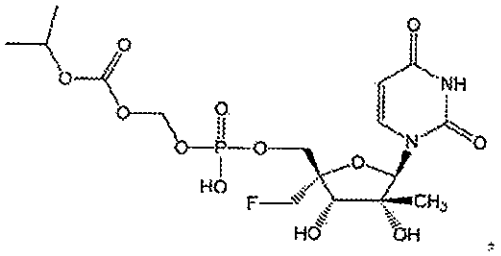


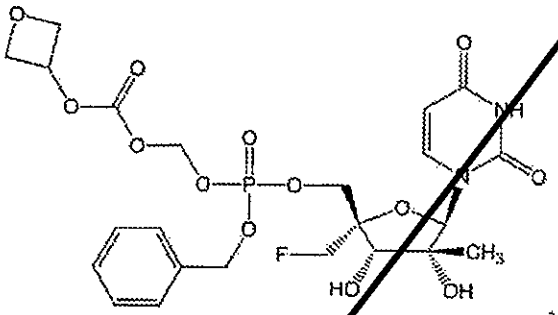


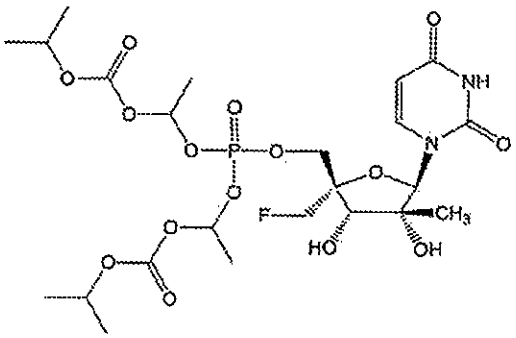


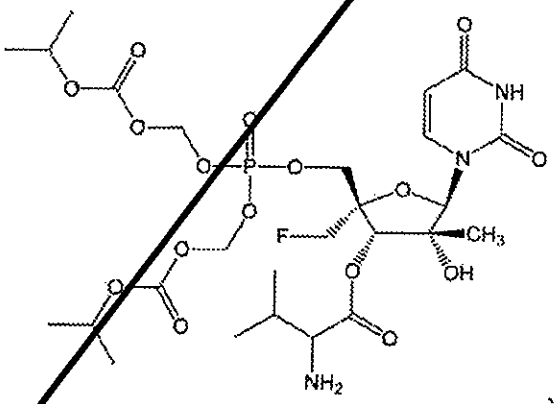


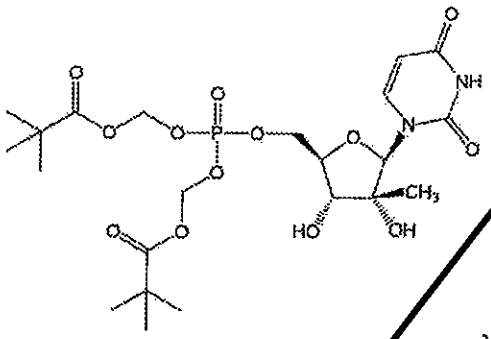


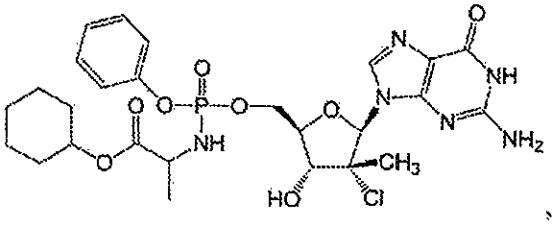


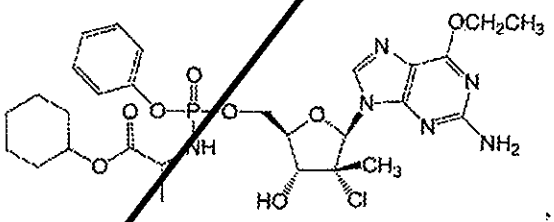


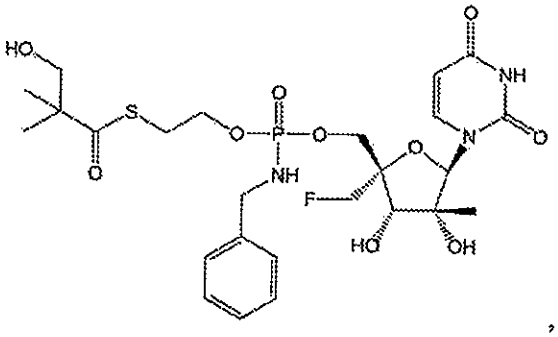


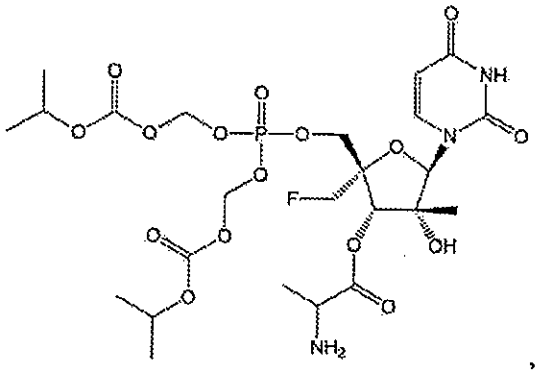


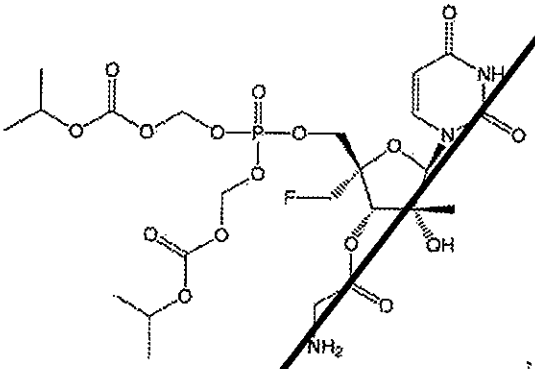


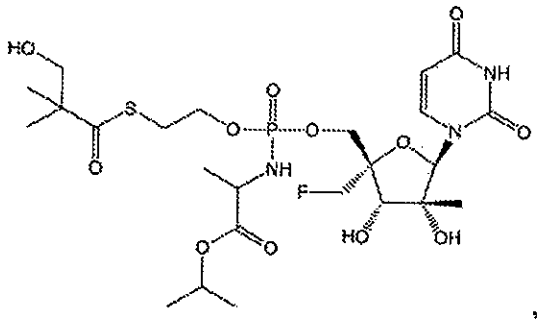


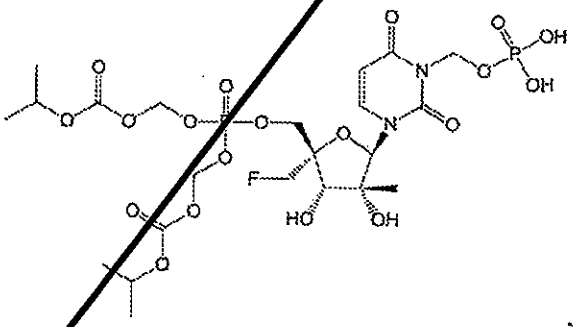


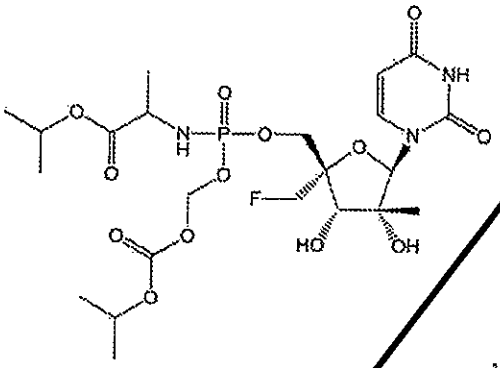


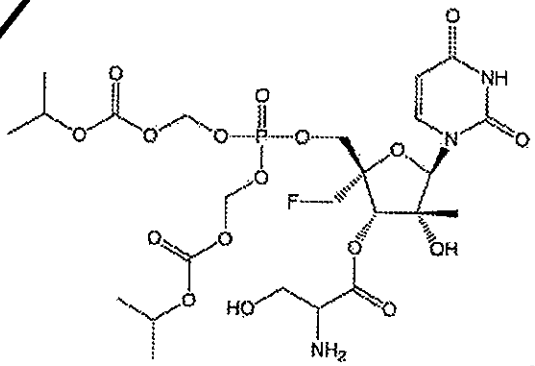


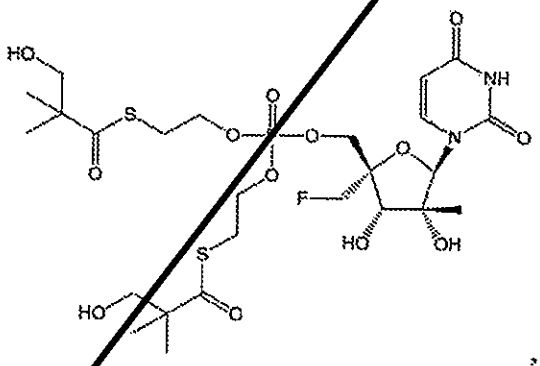


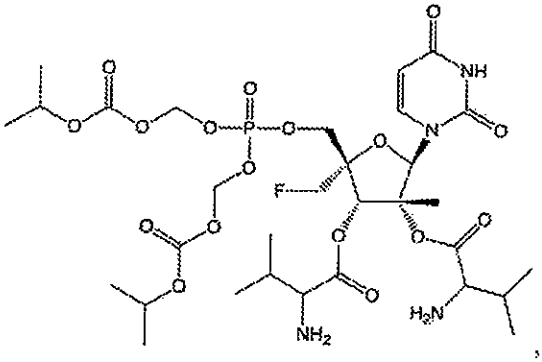


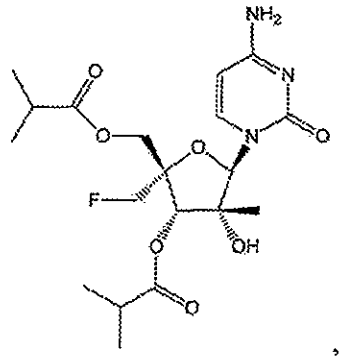
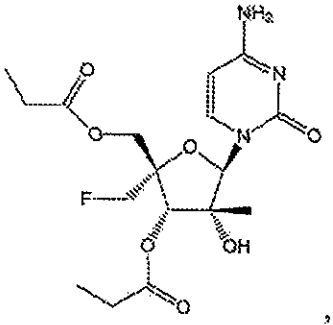
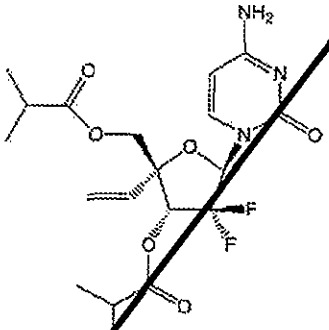
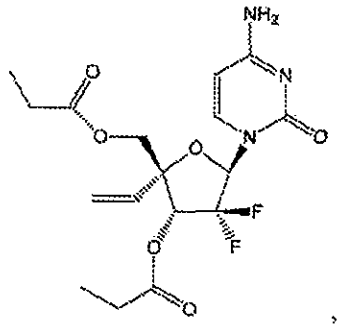
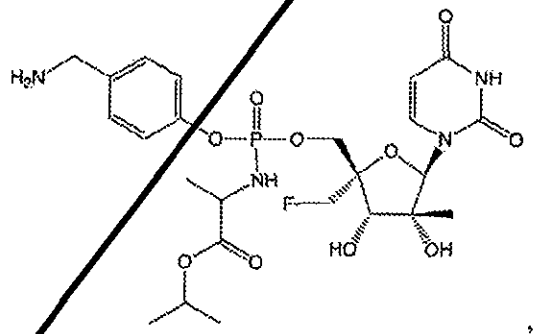
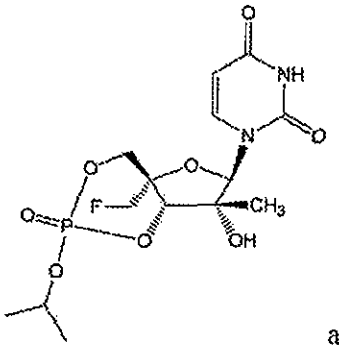
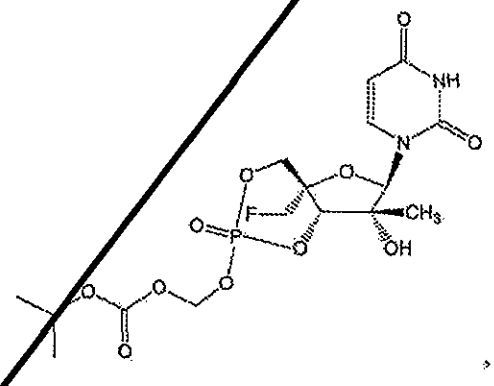










and , or a pharmaceutically acceptable salt of the foregoing.

136. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 91-135, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

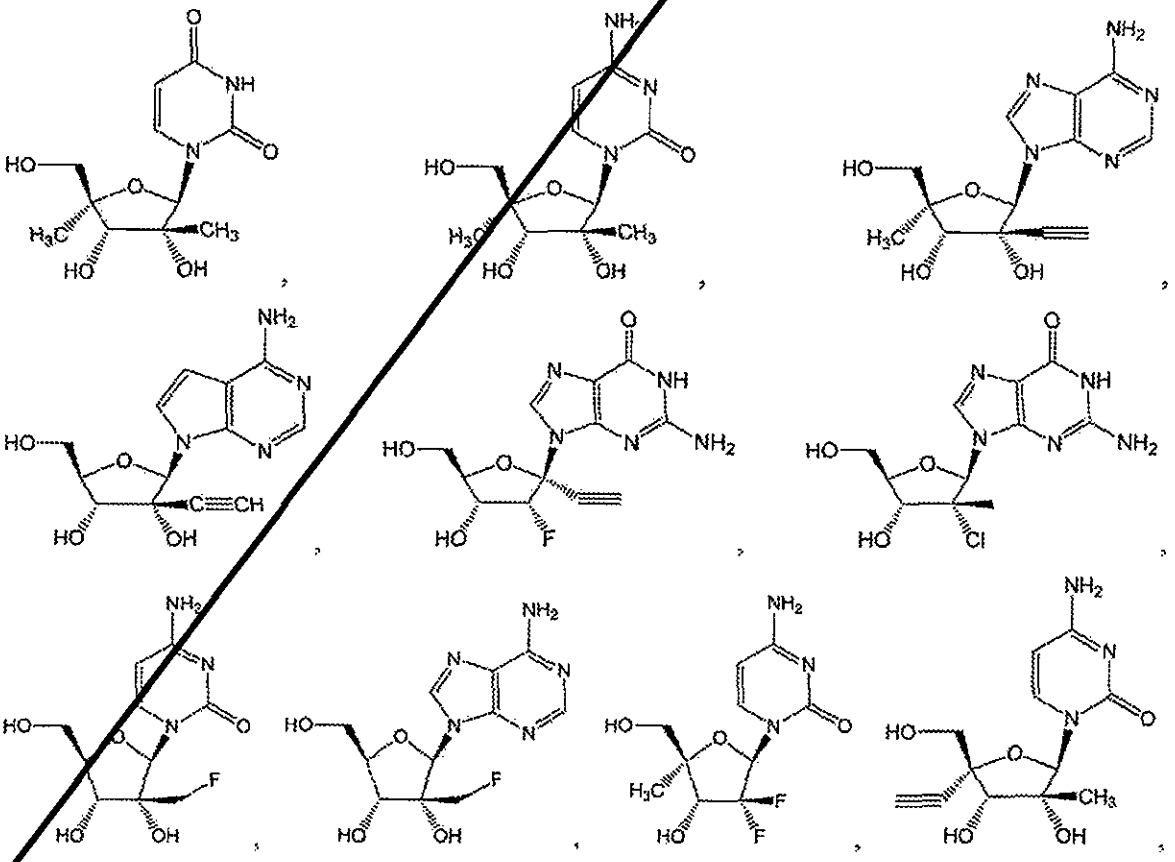
137. Use of a compound of any one of Claims 91-135 in the preparation of a medicament for ameliorating or treating a HCV infection, wherein the medicament is manufactured for use in combination with one or more agents selected from the group consisting of an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB)

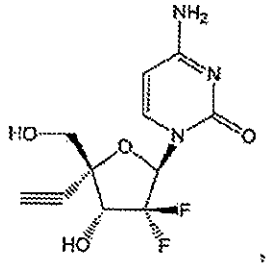
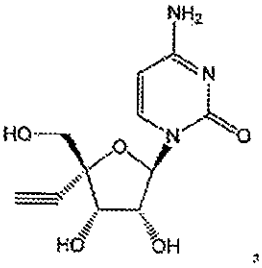
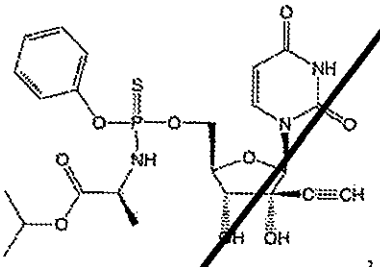
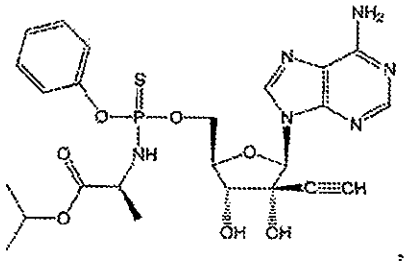
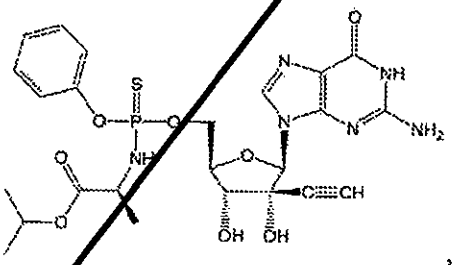
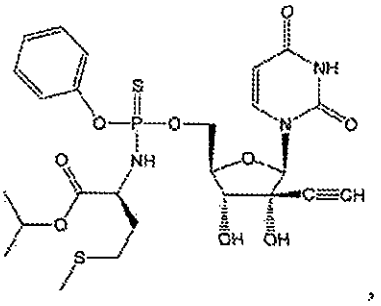
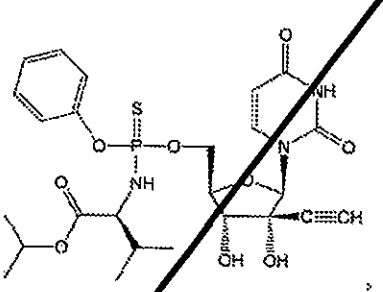
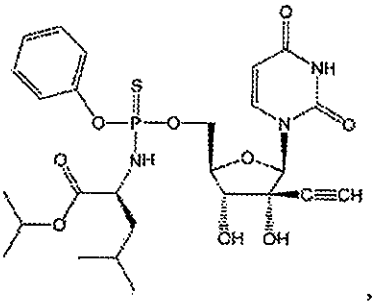
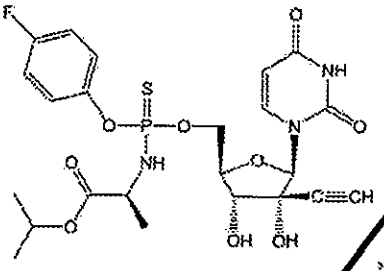
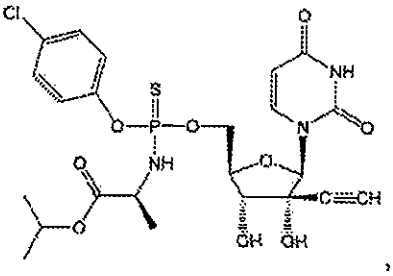
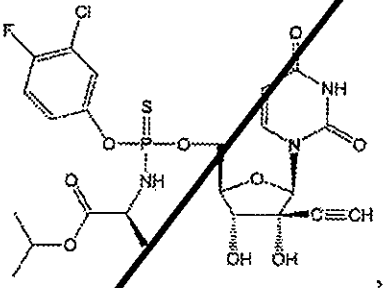
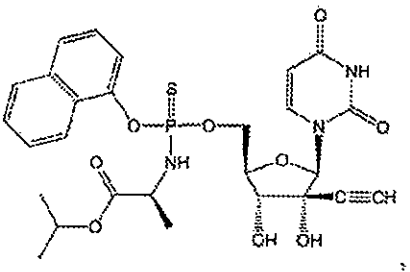
and a compound of Formula (CC), or a pharmaceutically acceptable salt any of the aforementioned compounds.

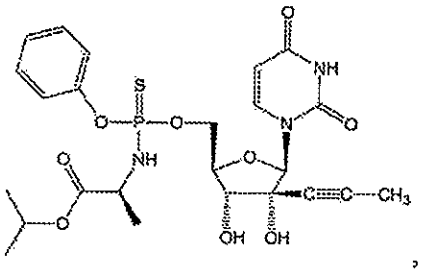
138. Use of a compound of any one of Claims 91-135 in the preparation of a medicament for contacting a cell infected with a hepatitis C virus, wherein the medicament is manufactured for use in combination with one or more agents selected from the group consisting of an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA) , a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt any of the aforementioned compounds.

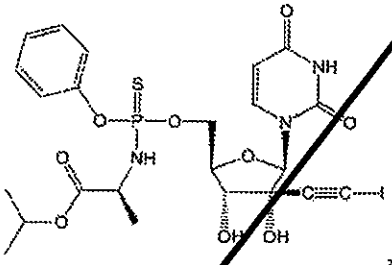
139. The use of any one of Claim 136-138, wherein the one or more agents are selected from the group consisting of Compounds 1001-1016, 2001-2012, 3001-3014, 4001-4012, 5001-5011, 6001-6078, 7000-7027 and 8000-8016, or a pharmaceutically acceptable salt of any of the aforementioned compounds.

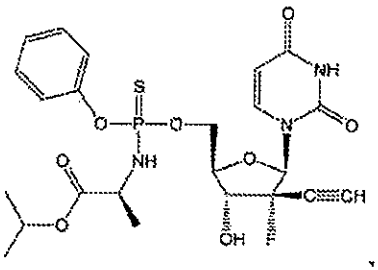
140. Use of a compound selected from the group consisting of:

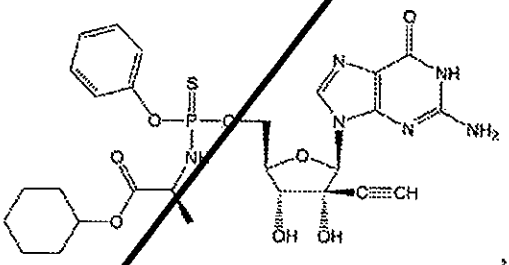


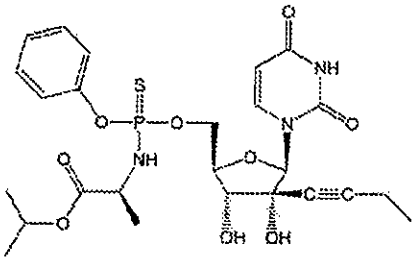













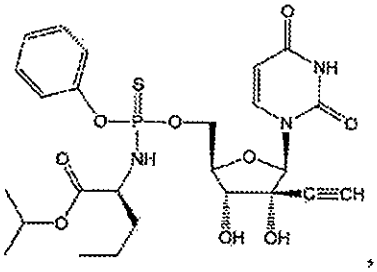


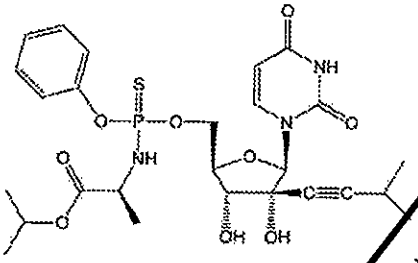


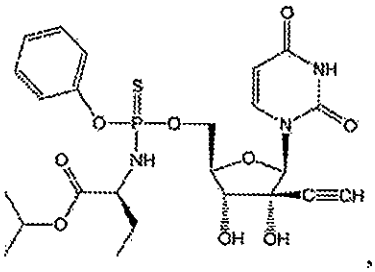


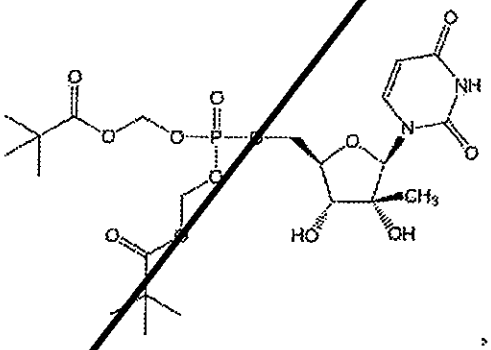


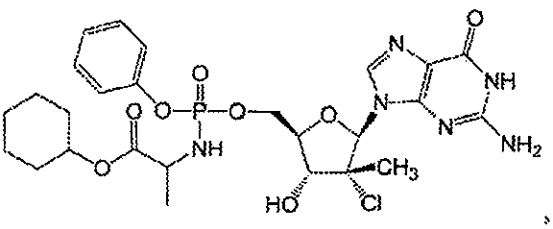


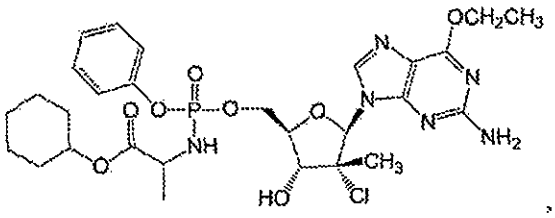


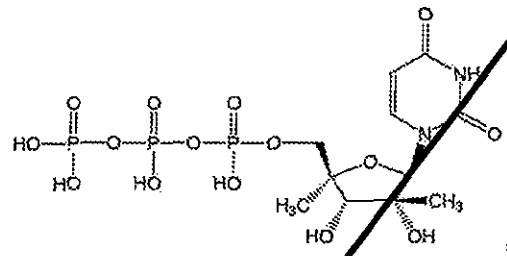


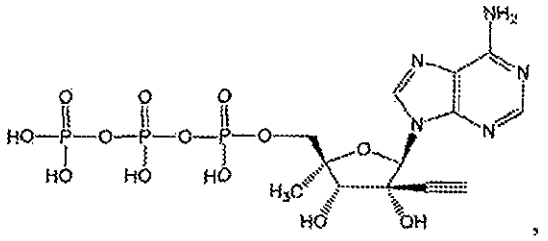


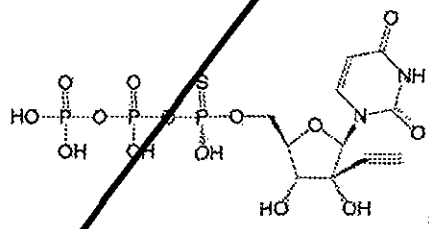


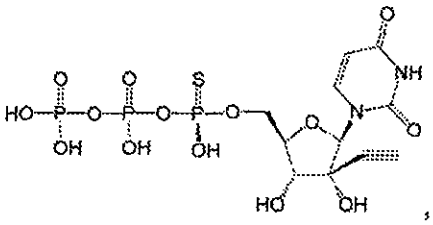


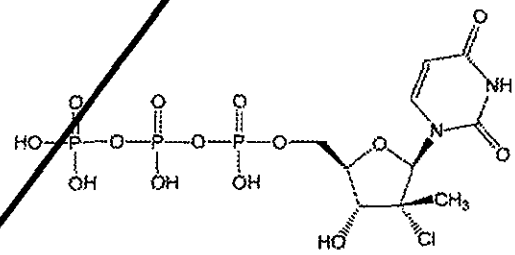


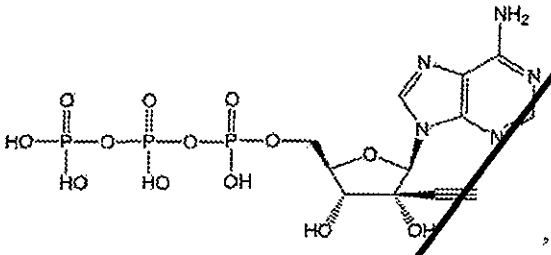


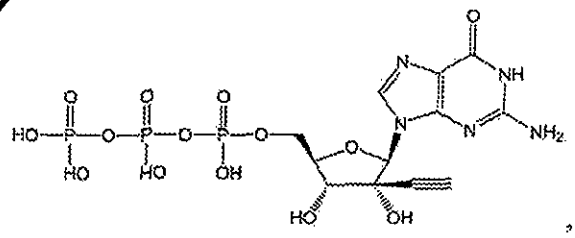


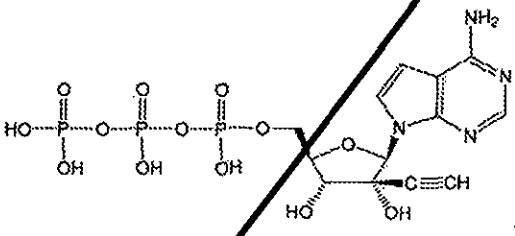


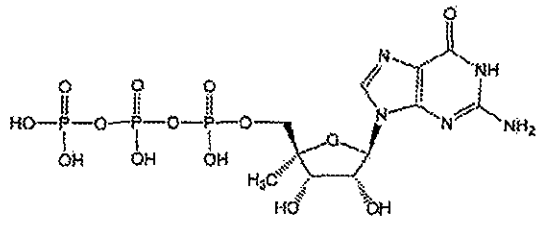


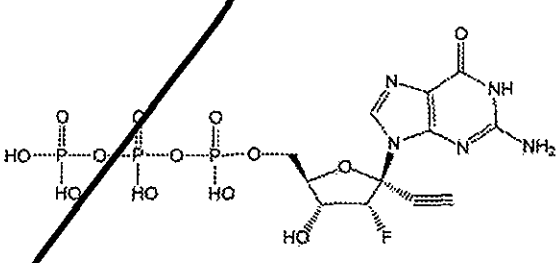


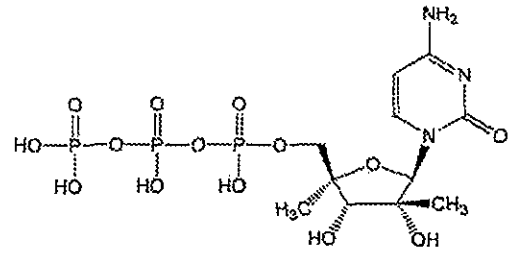


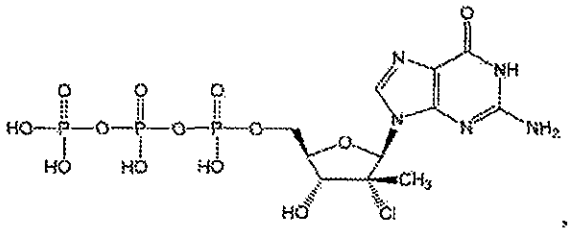












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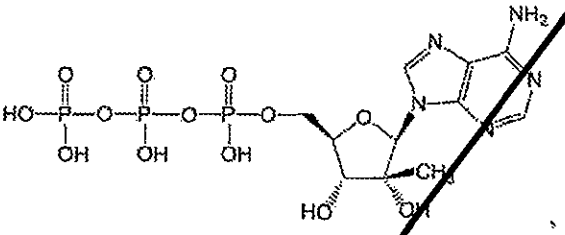

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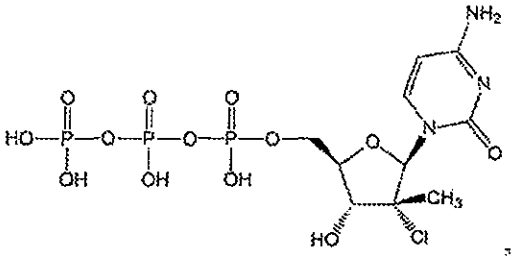

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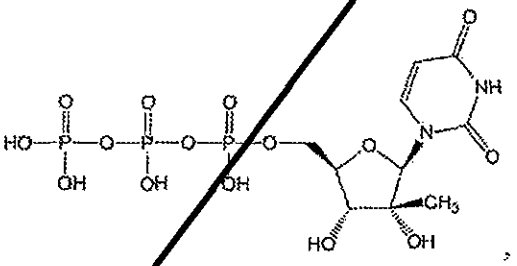

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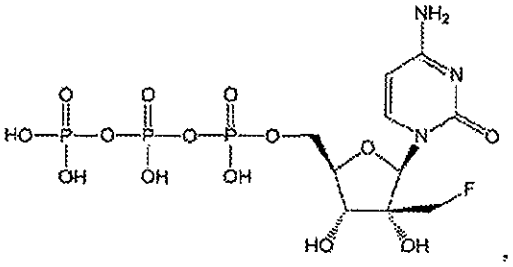

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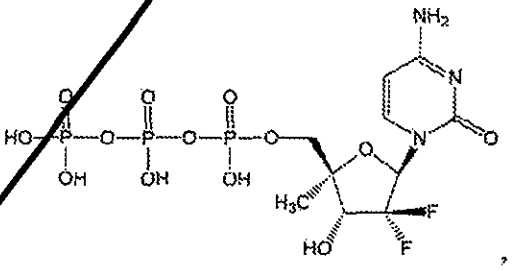

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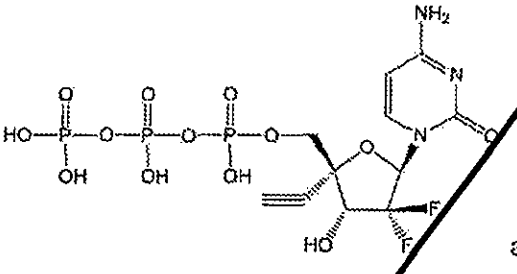

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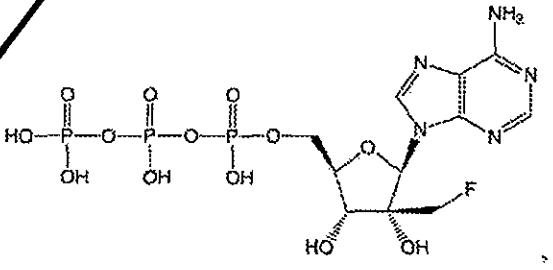
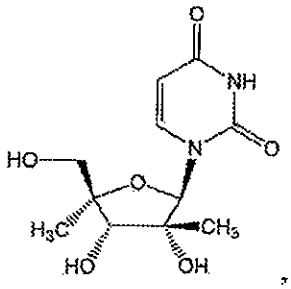
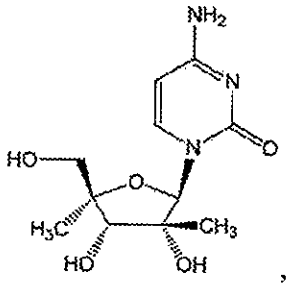
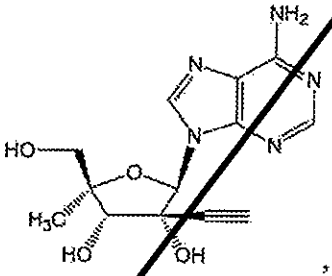
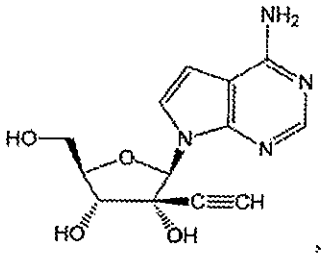
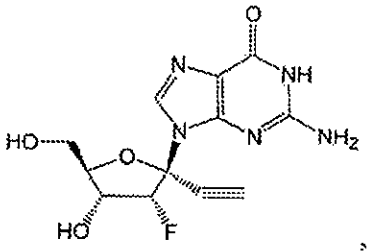
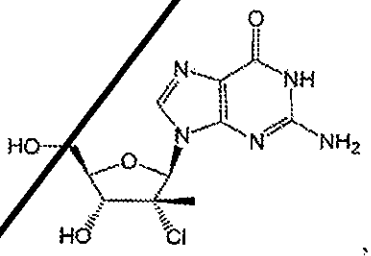
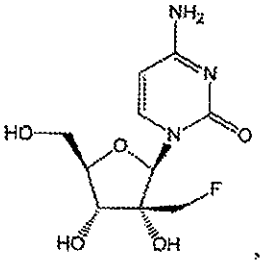
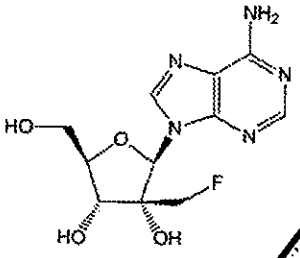
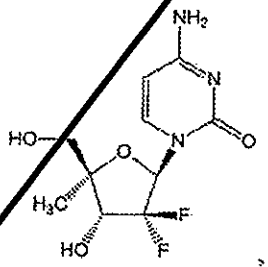
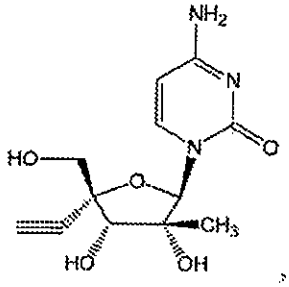
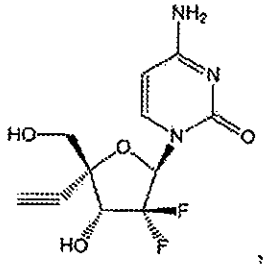
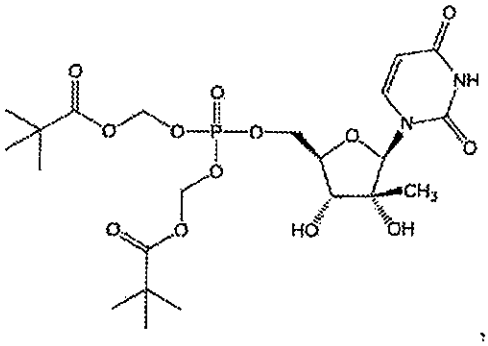
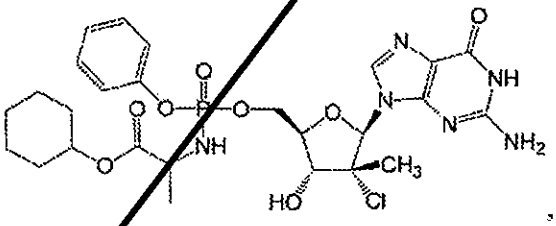
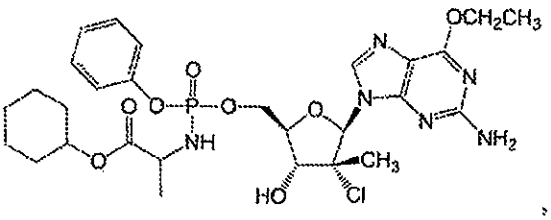
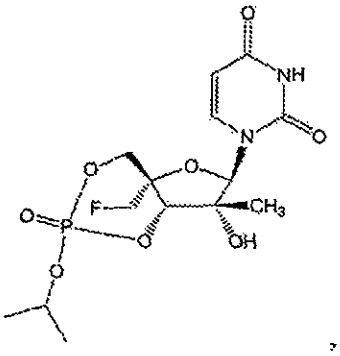
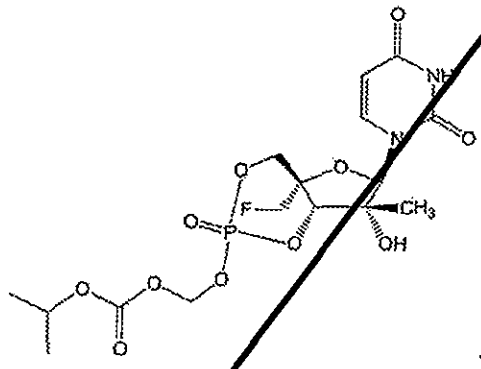


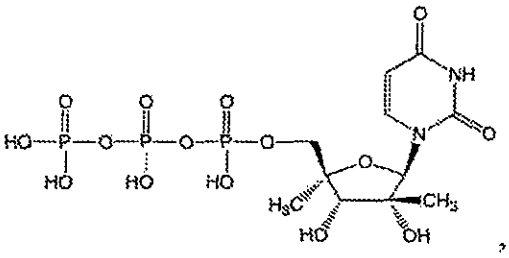
, or a pharmaceutically acceptable salt of the foregoing, in the preparation of a medicament for ameliorating or treating a *Picornaviridae* viral infection.

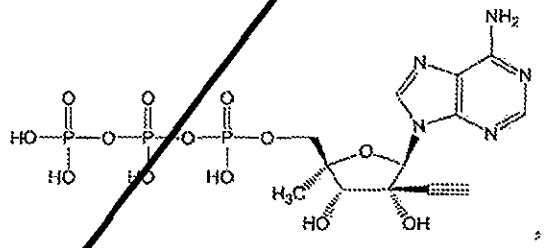
141. Use of a compound selected from the group consisting of:

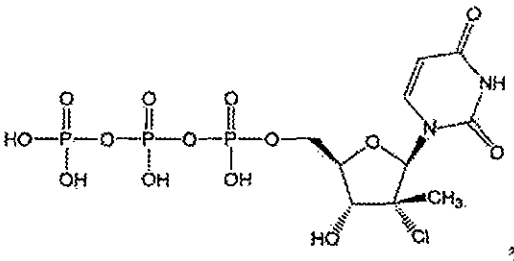















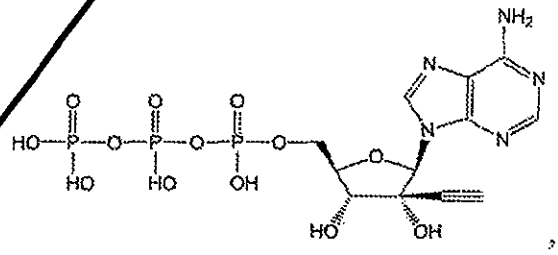


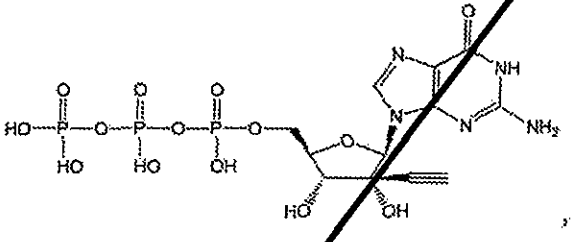


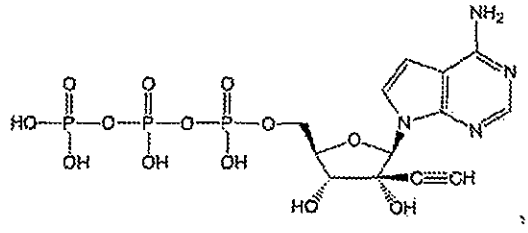


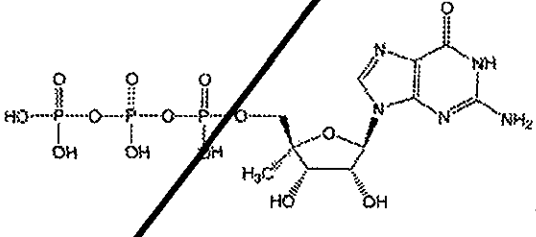


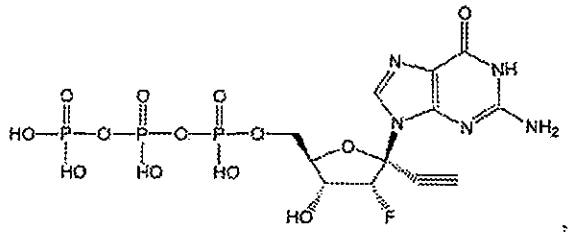












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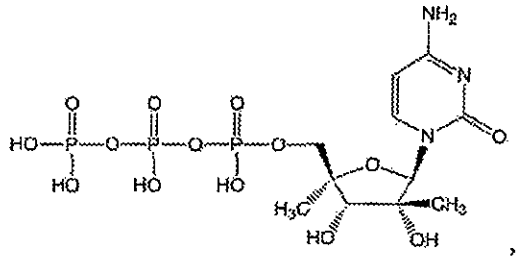
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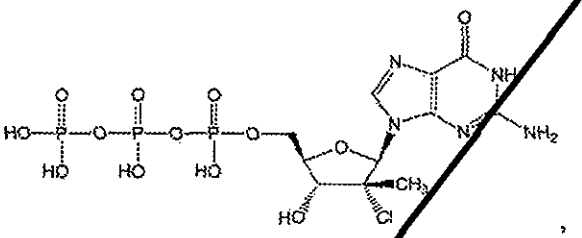
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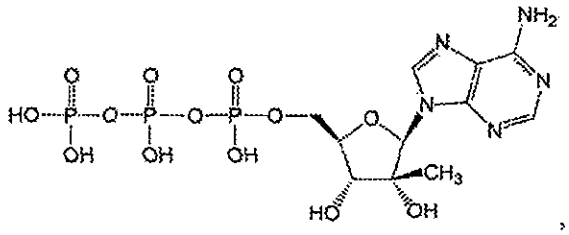
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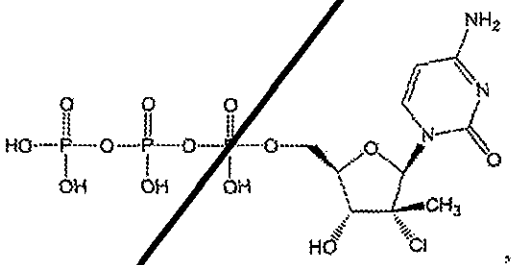
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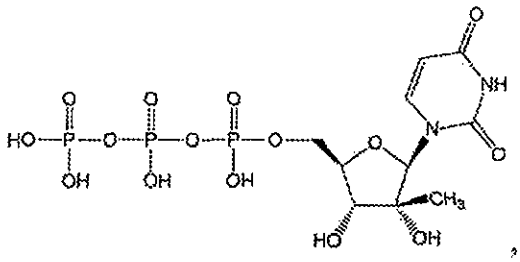
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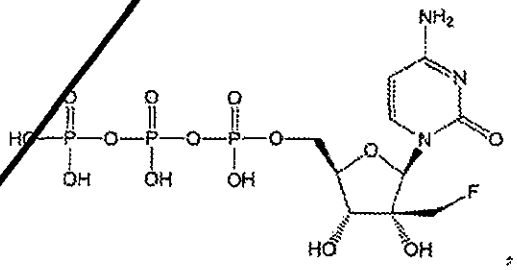
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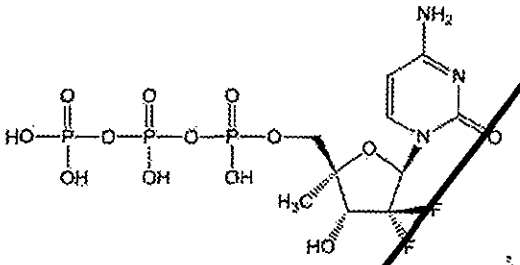
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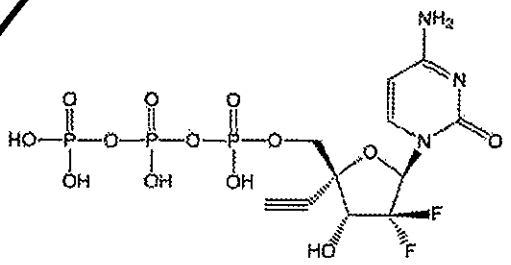
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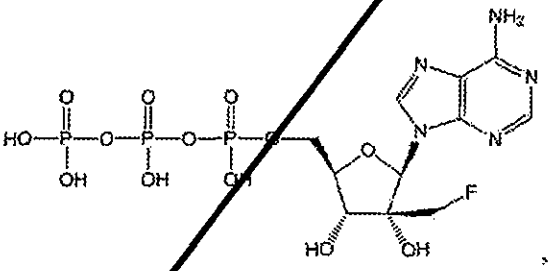
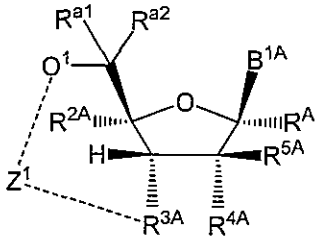

, or a pharmaceutically acceptable salt of the foregoing, in the preparation of a medicament for ameliorating or treating a *Flaviviridae* viral infection.

## CLAIMS

1. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating a *Picornaviridae* viral infection, wherein the compound of Formula (I) has the structure:

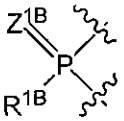


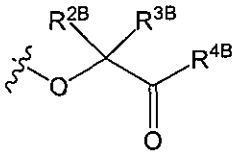
**(I)**

wherein:

$B^{1A}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

when -------- are both absent, then $Z^1$ is absent, $O^1$ is $OR^{1A}$, and $R^{3A}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{"A}$ and an optionally substituted O-linked amino acid, $R^{4A}$ is selected from the group consisting of H, OH, halo, $N_3$, $-OC(=O)R^{"B}$, an optionally substituted O-linked amino acid and $NR^{"B1}R^{"B2}$, or $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1\text{-}6}F$, $-(CH_2)_{1\text{-}6}Cl$, $-(CH_2)_{1\text{-}6}N_3$, $-(CH_2)_{1\text{-}6}NH_2$ or –CN, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1\text{-}6}$ alkyl,



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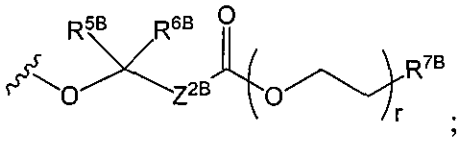
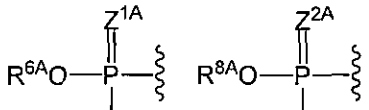
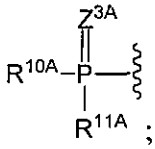


;

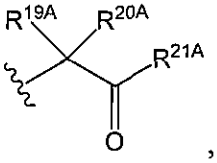
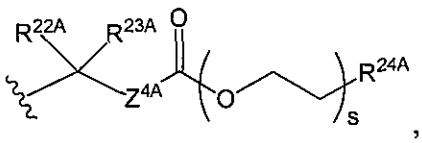
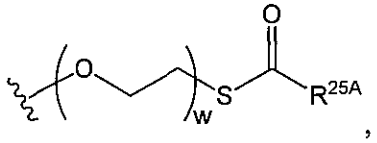
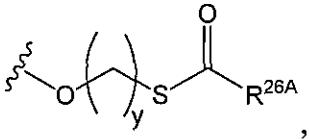
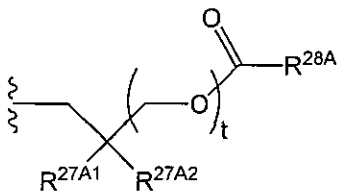
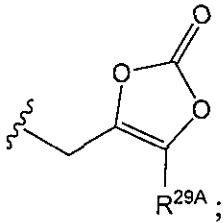
$R^{a1}$ and $R^{a2}$ are independently hydrogen or deuterium;

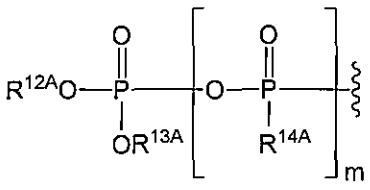
$R^A$ is hydrogen, deuterium, an unsubstituted $C_{1\text{-}3}$ alkyl, an unsubstituted $C_{2\text{-}4}$ alkenyl, an unsubstituted $C_{2\text{-}3}$ alkynyl or cyano;

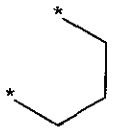
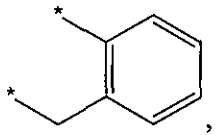
$R^{1A}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  and  ;

$R^{2A}$ is an unsubstituted $C_{2-4}$ alkyl or $-(CH_2)_{1-6}F$, and $R^{5A}$ is selected from the group consisting of halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; or

$R^{2A}$ is halo, an unsubstituted $C_{2-4}$ alkenyl, $-CHF_2$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or -CN, and $R^{5A}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{6A}$, $R^{7A}$ and $R^{8A}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted *$-(CR^{15A}R^{16A})_p-O-C_{1-24}$ alkyl, an optionally substituted *$-(CR^{17A}R^{18A})_q-O-C_{1-24}$ alkenyl,  ,  ,  ,  ,  and  ; or

$R^{6A}$ is  and $R^{7A}$ is absent or hydrogen; or

$R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9A}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

$R^{12A}$ and $R^{13A}$ are independently absent or hydrogen;

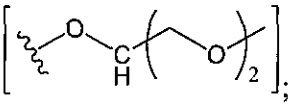
$R^{14A}$ is $O^-$, OH or methyl;

each $R^{15A}$, each $R^{16A}$, each $R^{17A}$ and each $R^{18A}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19A}$, $R^{20A}$, $R^{22A}$ and $R^{23A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an

optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25A}$, $R^{26A}$ and $R^{29A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{27A1}$ and $R^{27A2}$ are independently selected from the group consisting of -C≡N, an optionally substituted $C_{2-8}$ organylcarbonyl, an optionally substituted $C_{2-8}$ alkoxycarbonyl and an optionally substituted $C_{2-8}$ organylaminocarbonyl;

$R^{28A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl and an optionally substituted $C_{3-6}$ cycloalkenyl;

$R^{30A}$ and $R^{31A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R"^{A}$ and each $R"^{B}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R"^{B1}$ and each $R"^{B2}$ are independently hydrogen or an optionally substituted $C_{1-6}$ alkyl;

$R^{2B}$, $R^{3B}$, $R^{5B}$ and $R^{6B}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4B}$ and $R^{7B}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

m and w are independently 0 or 1;

p and q are independently 1, 2 or 3;

r and s are independently 0, 1, 2 or 3;

t is 1 or 2;

y is 3, 4 or 5; and

$Z^{1A}$, $Z^{2A}$, $Z^{3A}$, $Z^{4A}$, $Z^{1B}$ and $Z^{2B}$ are independently O or S;

2. The use of Claim 1, wherein the Picornaviridae virus is selected from the group consisting of an Aphthovirus, an Enterovirus, a Rhinovirus, a Hepatovirus and a Parechovirus.

3. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of enterovirus A, enterovirus B, enterovirus C, enterovirus D, enterovirus E, enterovirus F, enterovirus G, enterovirus H and enterovirus J.

4. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of poliovirus 1, poliovirus 2, poliovirus 3, CV-A1, CV-A2, CV-A3, CV-A4, CV-A5, CV-A6, CV-A7, CV-A8, CV-A9, CV-A10, CV-A11, CV-A12, CV-A13, CV-A14, CV-A15, CV-A16, CV-A17, CV-A18, CV-A19, CV-A20, CV-A21, CV-A22, CV-A23, CV-B1, CV-B2, CV-B3, CV-B4, CV-B5, CV-B6, echovirus 1, echovirus 2, echovirus 3, echovirus 4, echovirus 5, echovirus 6, echovirus 7, echovirus 9, echovirus 11, echovirus 12, echovirus 13, echovirus 14, echovirus 15, echovirus 16, echovirus 17, echovirus 18, echovirus 19, echovirus 20, echovirus 21, echovirus 24, echovirus 25, echovirus 26, echovirus 27, echovirus 29, echovirus 30, echovirus 31, echovirus 32, echovirus 33, enterovirus 68, enterovirus 69, enterovirus 70, enterovirus 71 and viluisk human encephalomyelitis virus.

5. The use of Claim 2, wherein the Enterovirus is selected from the group consisting of rhinovirus A, rhinovirus B and rhinovirus C.

6. The use of Claim 2, wherein Hepatovirus is hepatitis A.

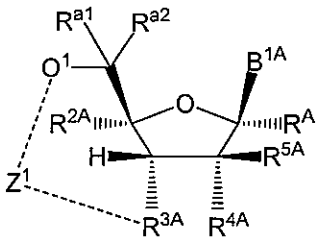
7. The use of Claim 2, wherein the Parechovirus is selected from the group consisting of human parechovirus 1, human parechovirus 2, human parechovirus 3, human parechovirus 4, human parechovirus 5 and human parechovirus 6.

8. The use of Claim 1, wherein the Picornaviridae virus is selected from the group consisting of an Aquamavirus, an Avihepatovirus, a Cardiovirus, a Cosavirus, a Dicipivirus, an Erbovirus, a Kobuvirus, a Megrivirus, a Salivirus, a Sapelovirus, a Senecavirus, a Teschovirus and a Tremovirus.

9. The use of any one of Claims 1-8, wherein $R^{2A}$ is halo, $-CHF_2$ or $-(CH_2)_{1-6}Cl$.

10. The use of any one of Claims 1-9, wherein $R^{5A}$ is H.

11. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating a *Flaviviridae* viral infection, wherein the compound of Formula (I) has the structure:

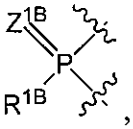


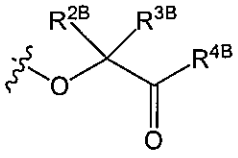
**(I)**

wherein:

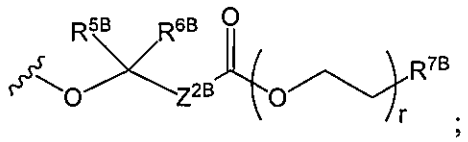
$B^{1A}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

when -------- are both absent, then $Z^1$ is absent, $O^1$ is $OR^{1A}$, and $R^{3A}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R''^{A}$ and an optionally substituted O-linked amino acid, $R^{4A}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R''^{B}$, an optionally substituted O-linked amino acid and $NR''^{B1}R''^{B2}$, or $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or –CN, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1-6}$ alkyl,



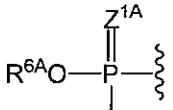
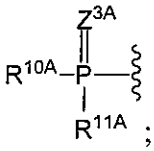
and



;

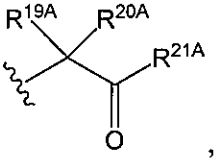
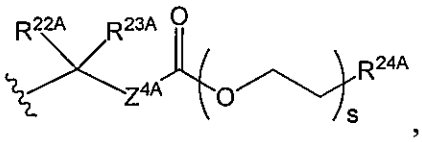
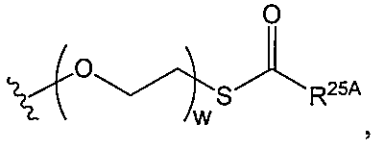
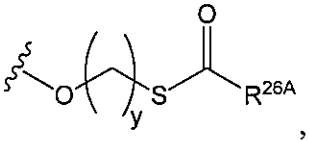
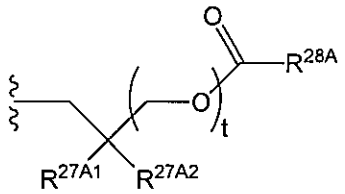
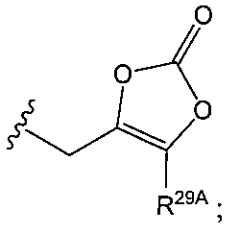
$R^{a1}$ and $R^{a2}$ are independently hydrogen or deuterium;

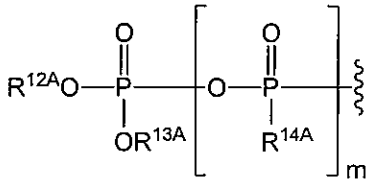
$R^A$ is hydrogen, deuterium, an unsubstituted $C_{1-3}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-3}$ alkynyl or cyano;

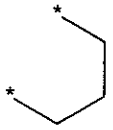
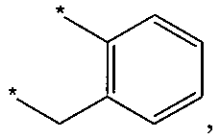
$R^{1A}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  and  ;

$R^{2A}$ is halo, an unsubstituted $C_{2-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, $-(CH_2)_{1-6}F$, or $-CN$, and $R^{5A}$ is selected from the group consisting of OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; or

$R^{2A}$ is $-CHF_2$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$ or $-(CH_2)_{1-6}NH_2$, and $R^{5A}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{6A}$, $R^{7A}$ and $R^{8A}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted *–$(CR^{15A}R^{16A})_p$–O–$C_{1-24}$ alkyl, an optionally substituted *–$(CR^{17A}R^{18A})_q$–O–$C_{1-24}$ alkenyl,  ,  ,  ,  ,  , and  ; or

$R^{6A}$ is  and $R^{7A}$ is absent or hydrogen; or

$R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9A}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30A}R^{31A}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

$R^{12A}$ and $R^{13A}$ are independently absent or hydrogen;

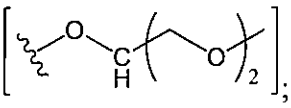
$R^{14A}$ is $O^-$, OH or methyl;

each $R^{15A}$, each $R^{16A}$, each $R^{17A}$ and each $R^{18A}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19A}$, $R^{20A}$, $R^{22A}$ and $R^{23A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an

optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25A}$, $R^{26A}$ and $R^{29A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{27A1}$ and $R^{27A2}$ are independently selected from the group consisting of -C≡N, an optionally substituted $C_{2-8}$ organylcarbonyl, an optionally substituted $C_{2-8}$ alkoxycarbonyl and an optionally substituted $C_{2-8}$ organylaminocarbonyl;

$R^{28A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl and an optionally substituted $C_{3-6}$ cycloalkenyl;

$R^{30A}$ and $R^{31A}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R^{"A}$ and each $R^{"B}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R^{"B1}$ and each $R^{"B2}$ are independently hydrogen or an optionally substituted $C_{1-6}$ alkyl;

$R^{2B}$, $R^{3B}$, $R^{5B}$ and $R^{6B}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4B}$ and $R^{7B}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

m and w are independently 0 or 1;

p and q are independently 1, 2 or 3;

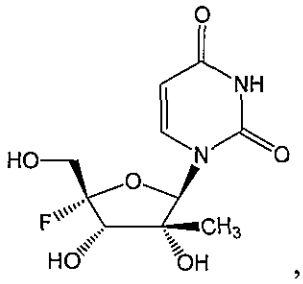
r and s are independently 0, 1, 2 or 3;

t is 1 or 2;

y is 3, 4 or 5; and

$Z^{1A}$, $Z^{2A}$, $Z^{3A}$, $Z^{4A}$, $Z^{1B}$ and $Z^{2B}$ are independently O or S;

provided that the compound of Formula (I), or a pharmaceutically acceptable salt thereof, cannot be selected from the group consisting of: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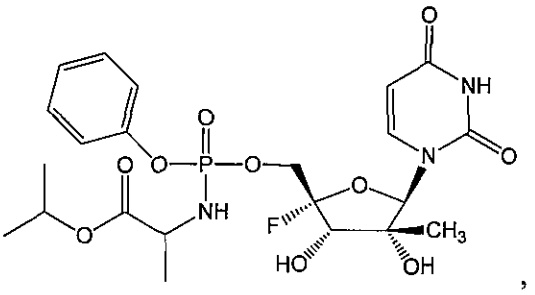
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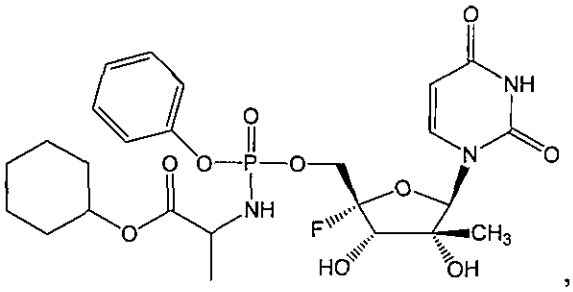
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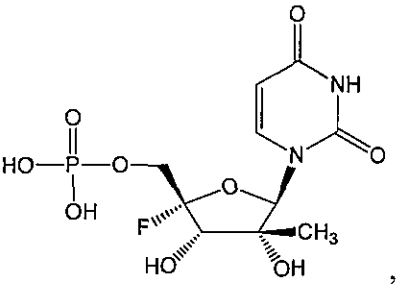
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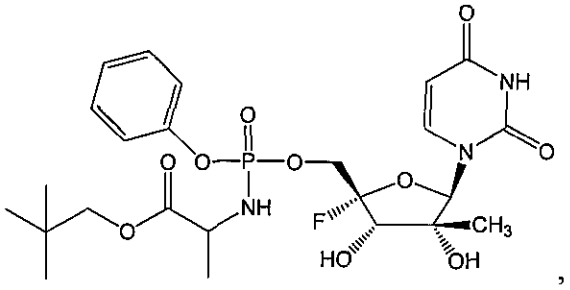
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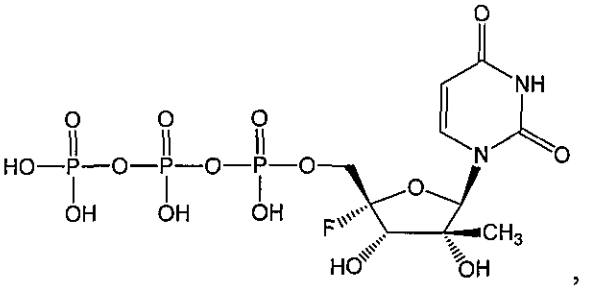
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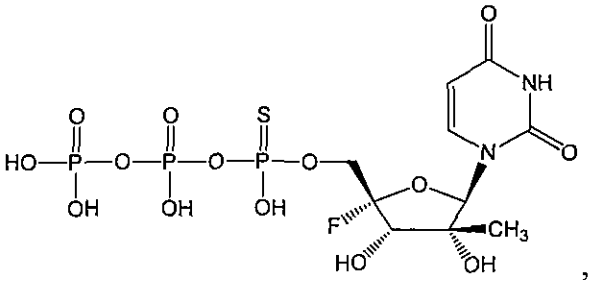
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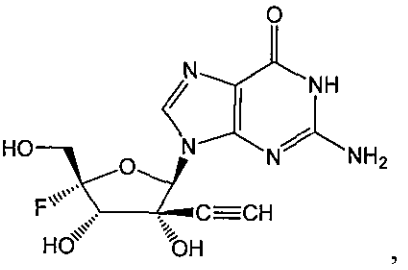
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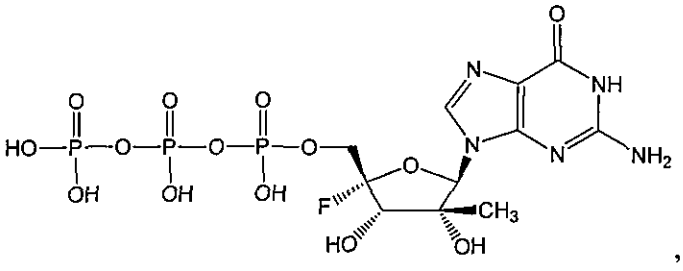
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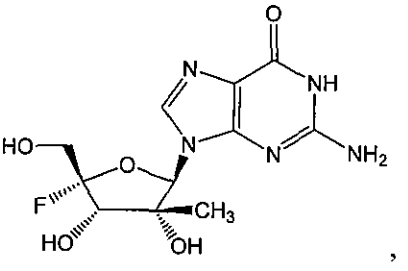
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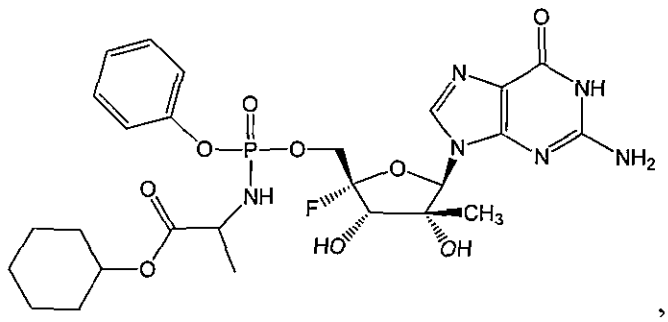

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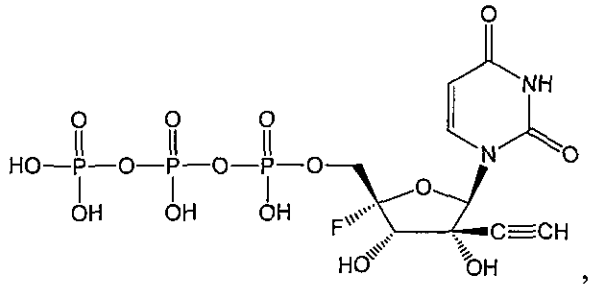

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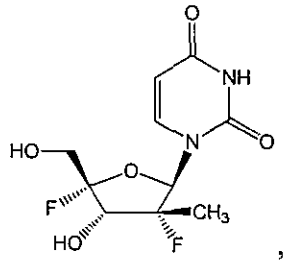

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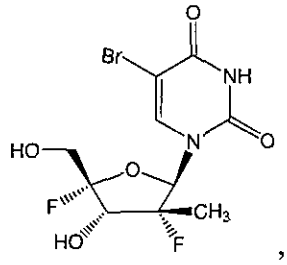

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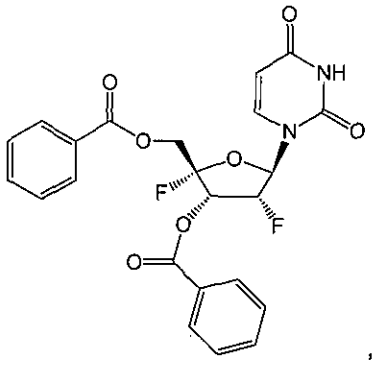

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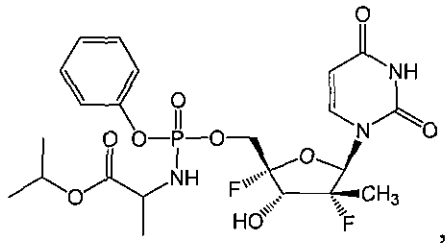

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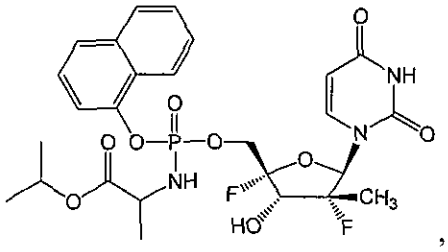

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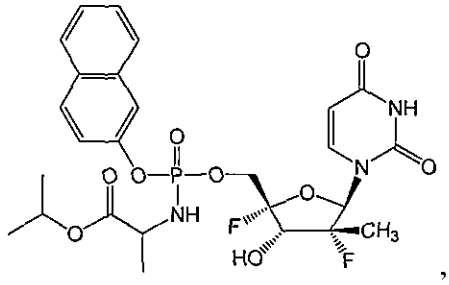

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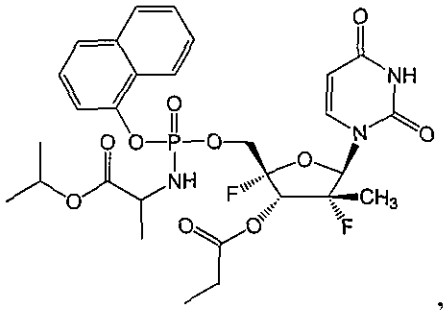

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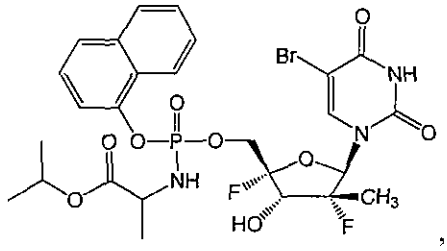

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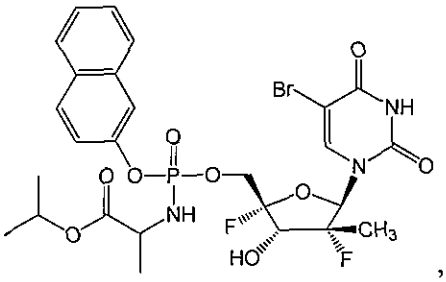
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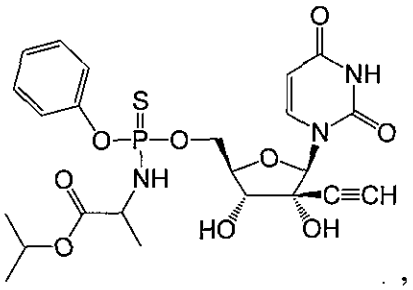
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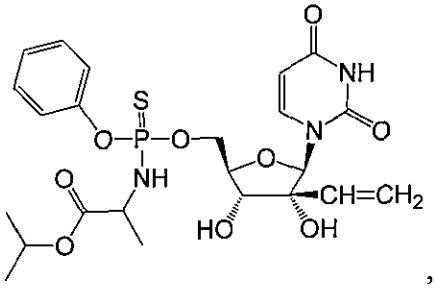
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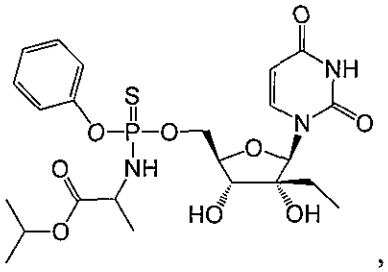
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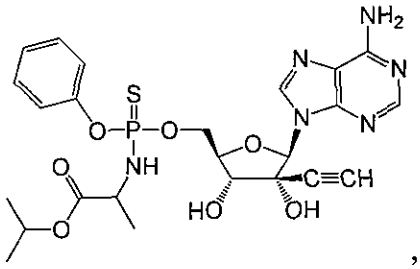
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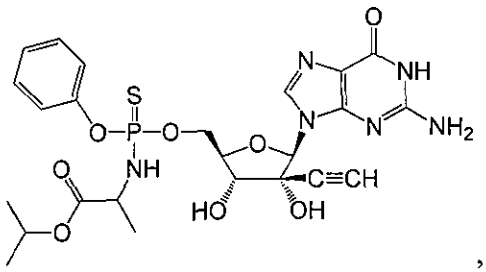
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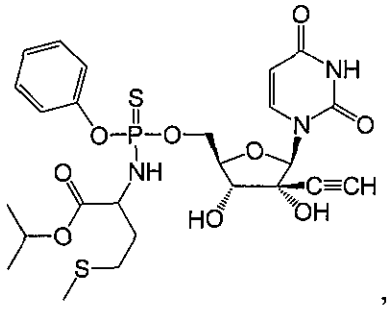
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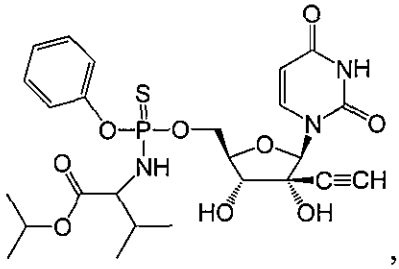
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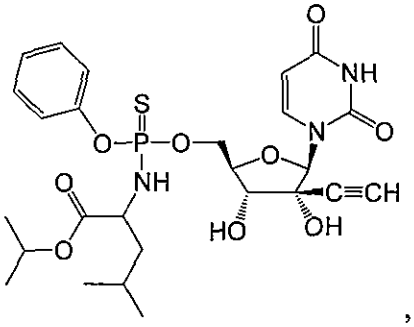
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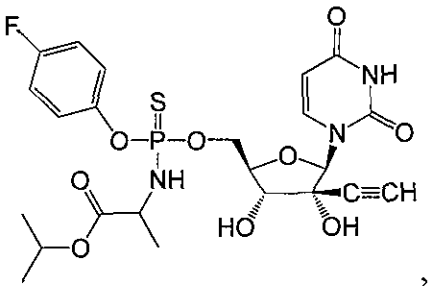
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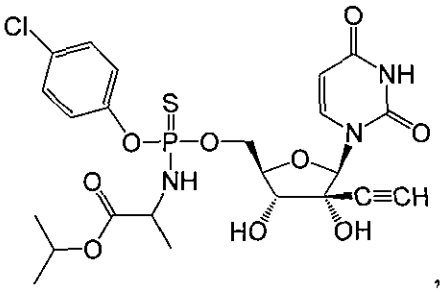
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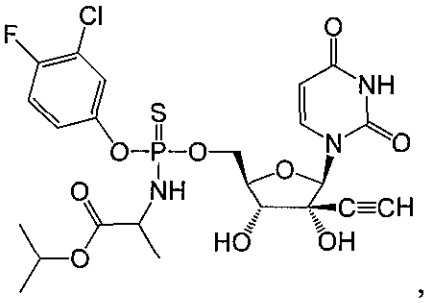
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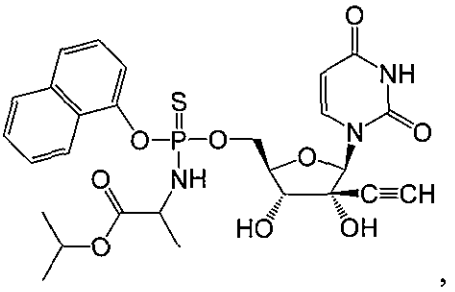
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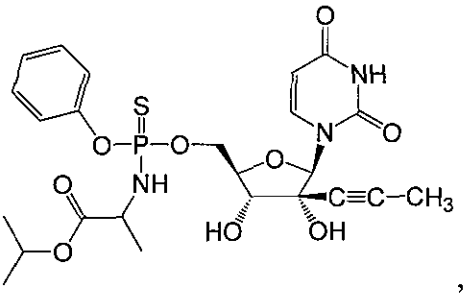
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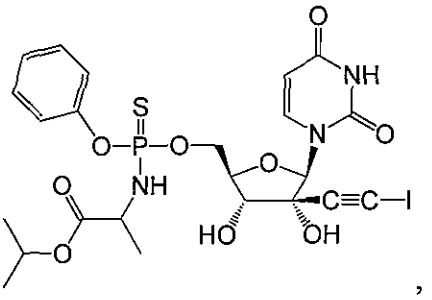
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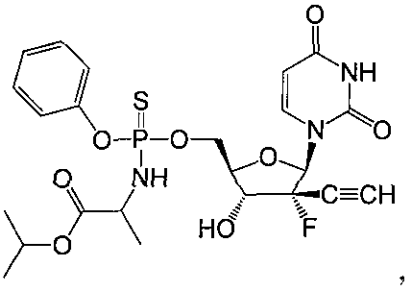
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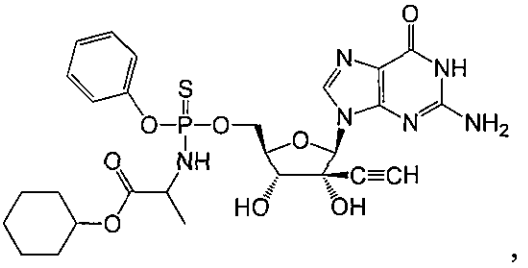
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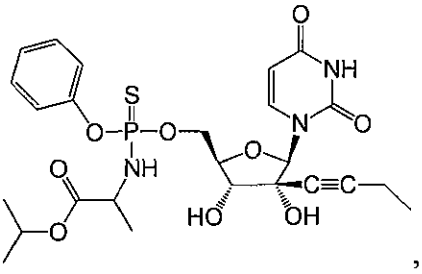
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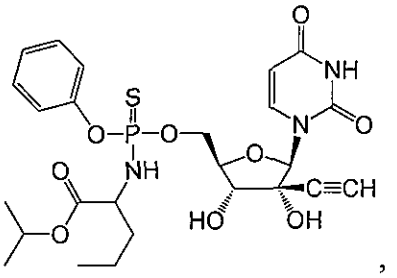
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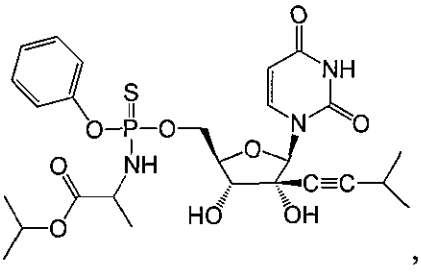
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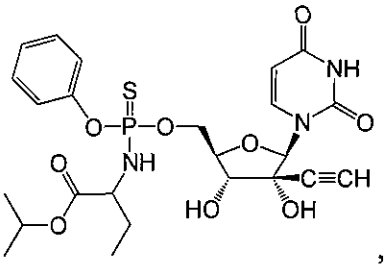
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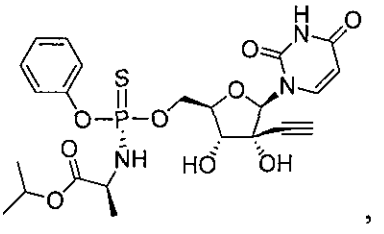
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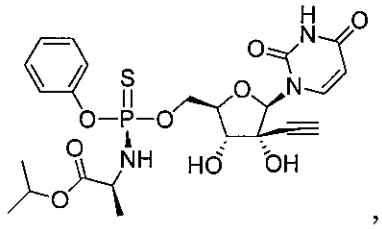
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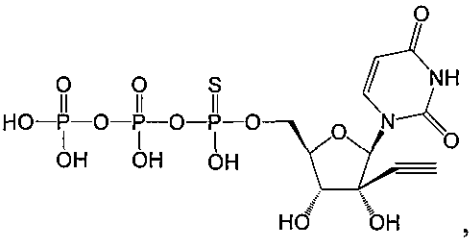
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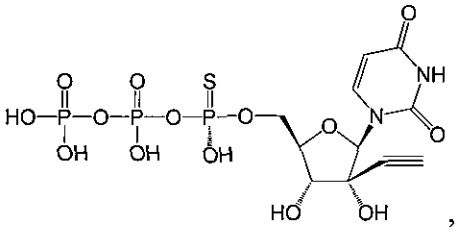
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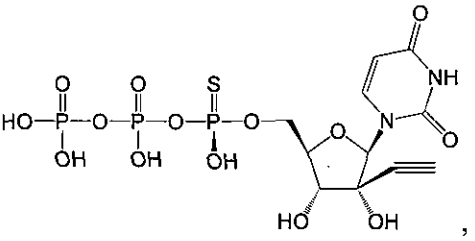
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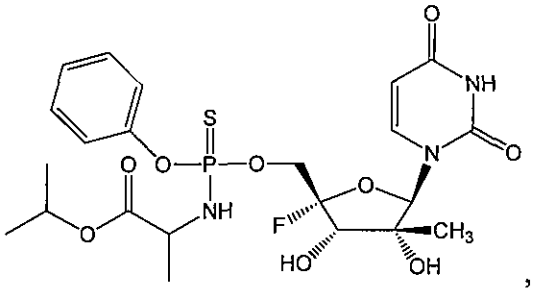
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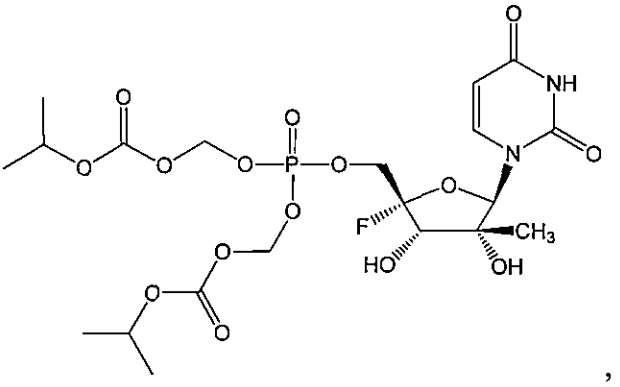
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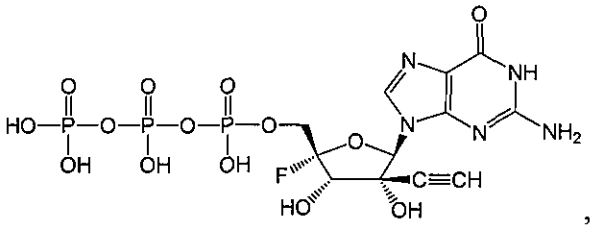
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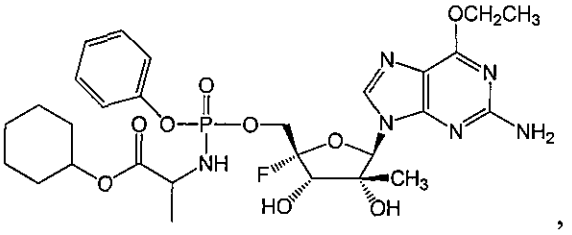
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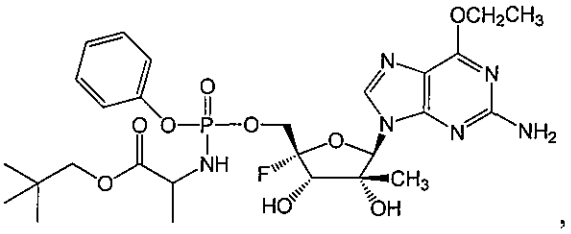
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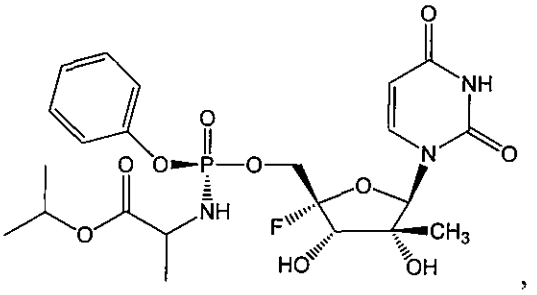
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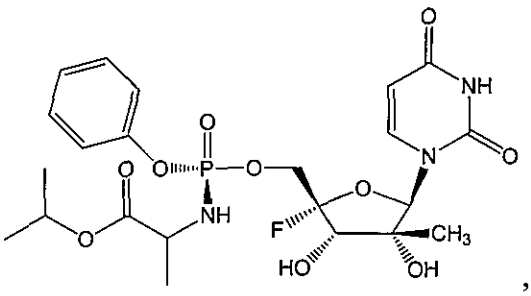
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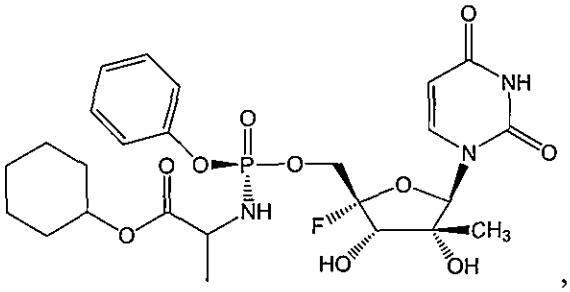
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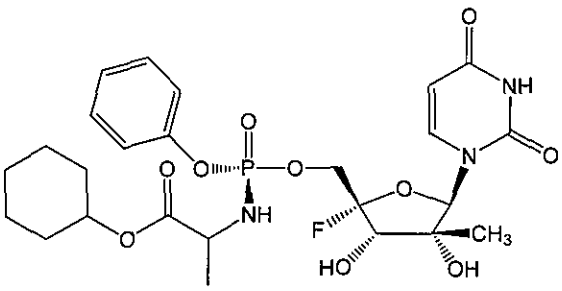
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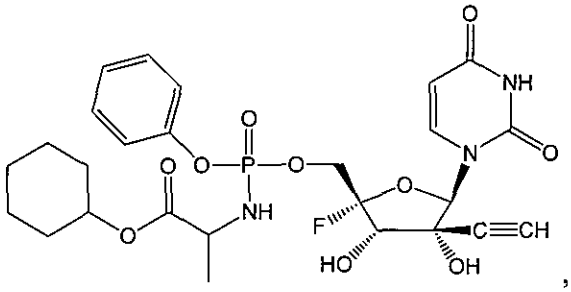
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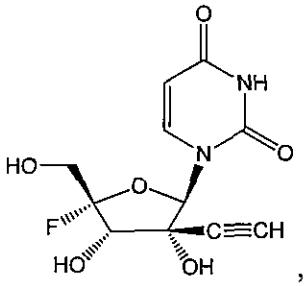
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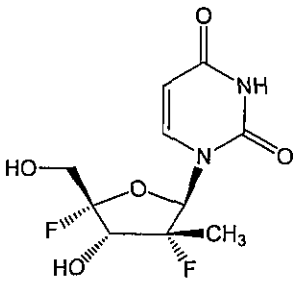
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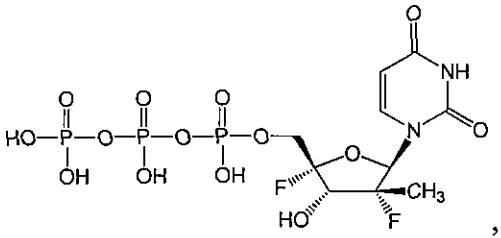
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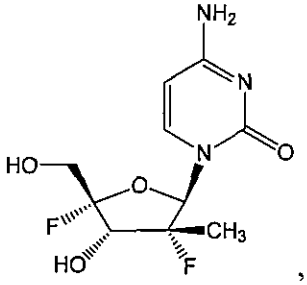
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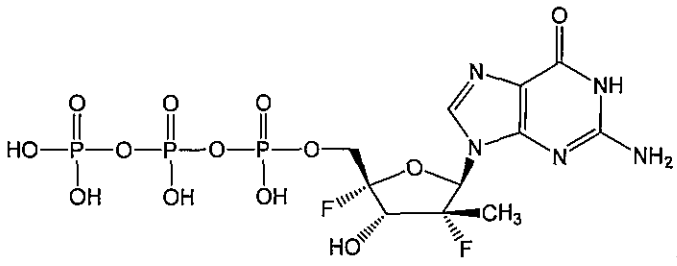
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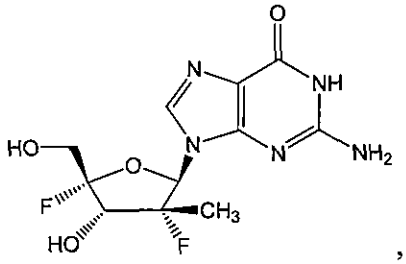
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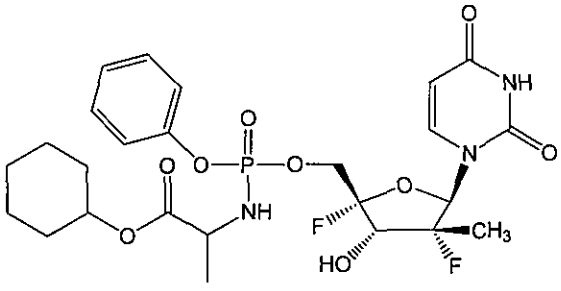
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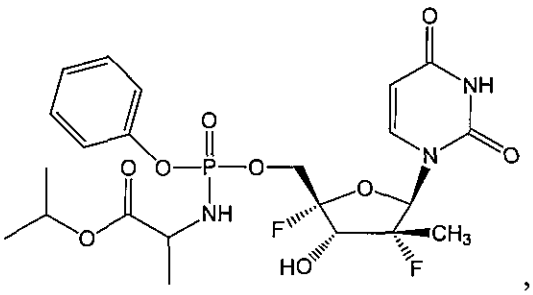
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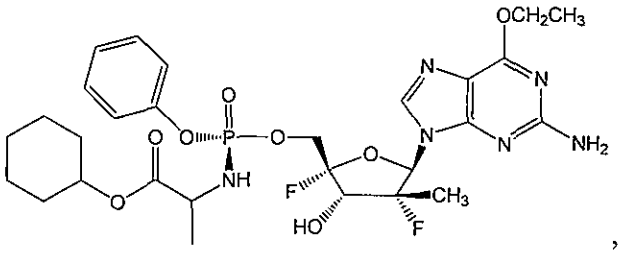
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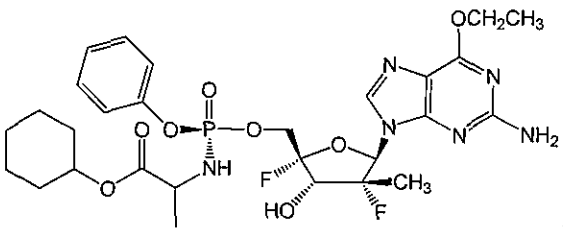
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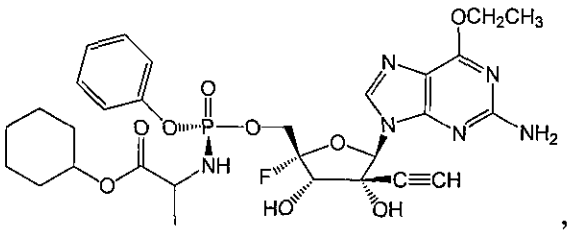
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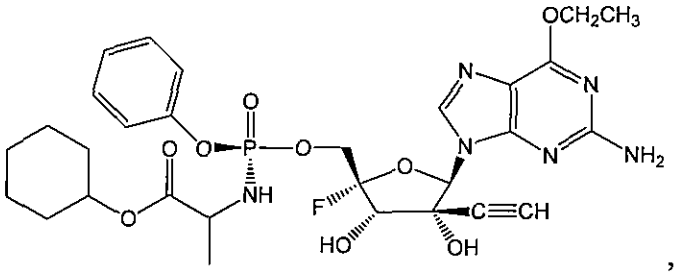
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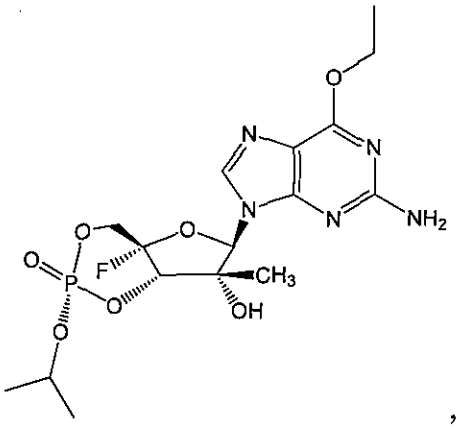
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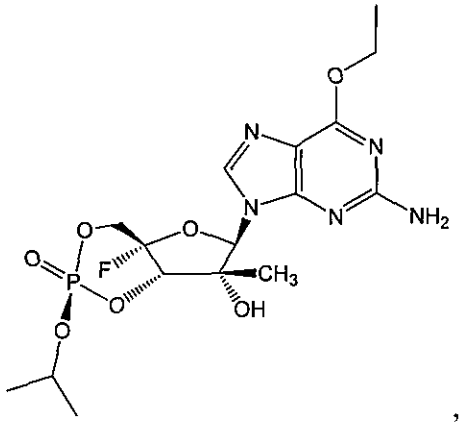
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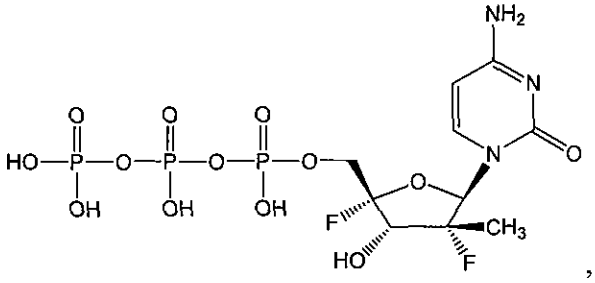
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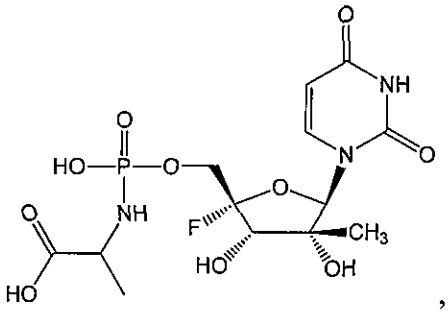
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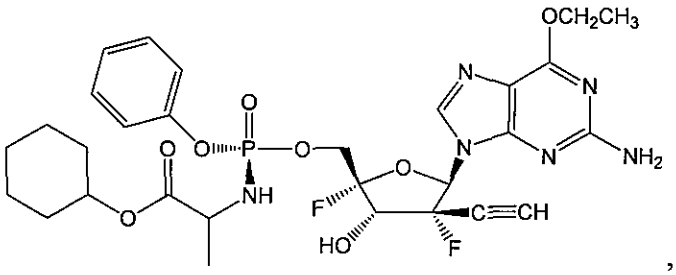
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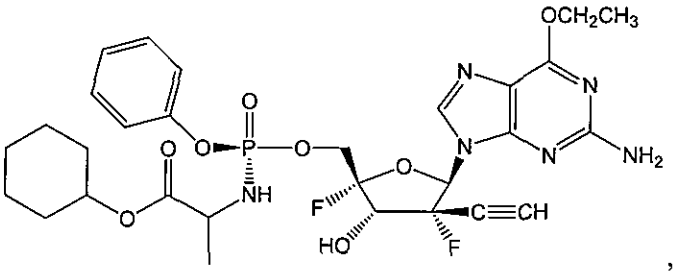
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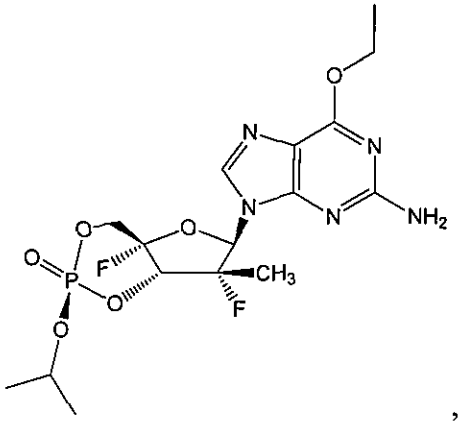
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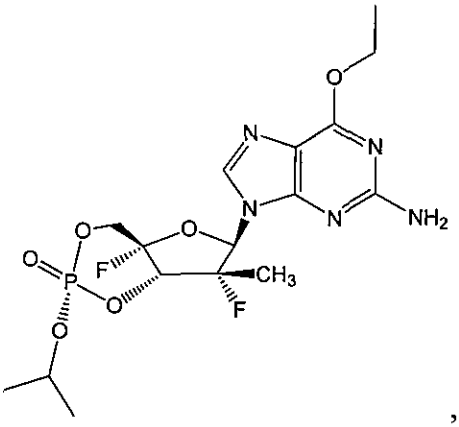
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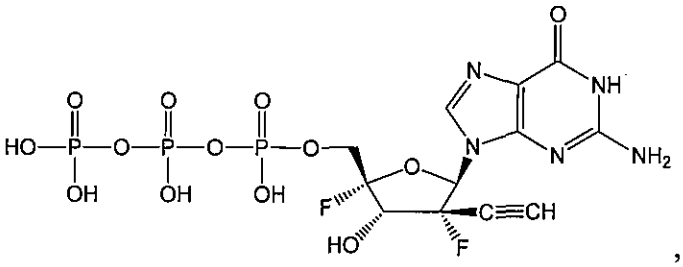
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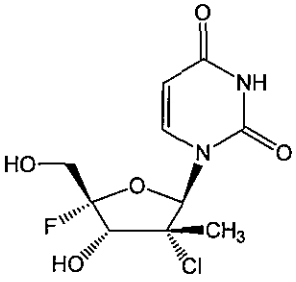
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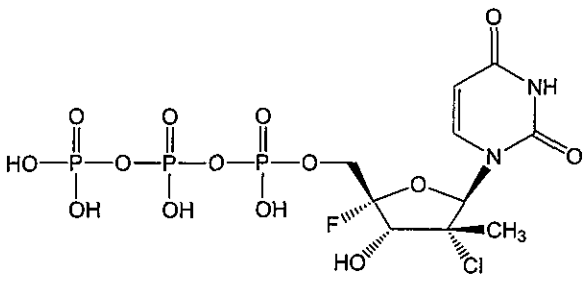
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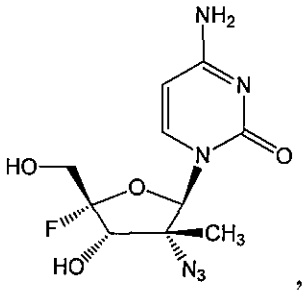
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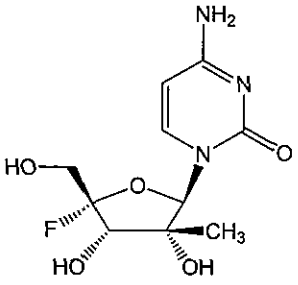

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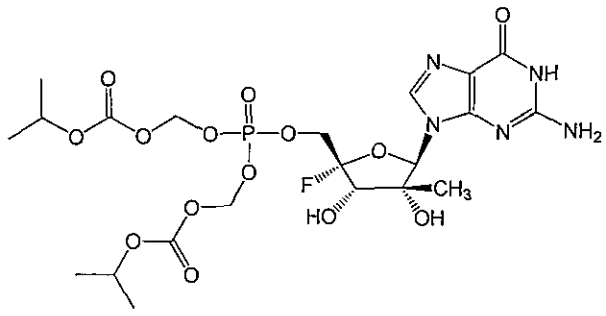

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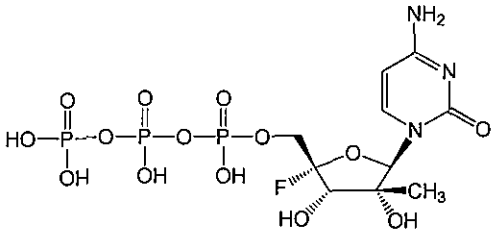

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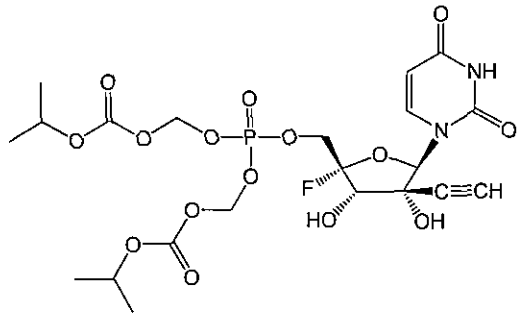

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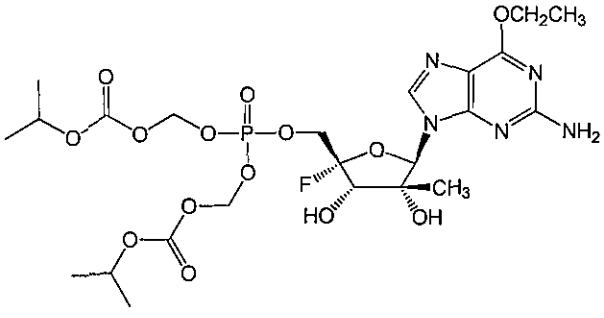

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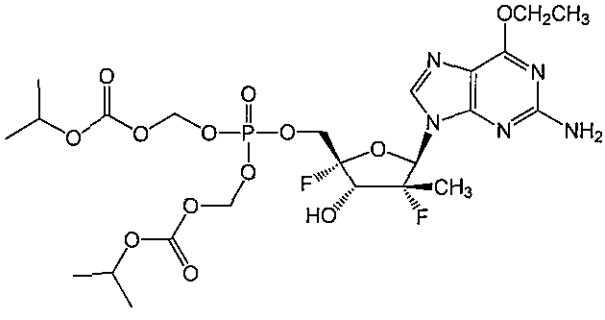

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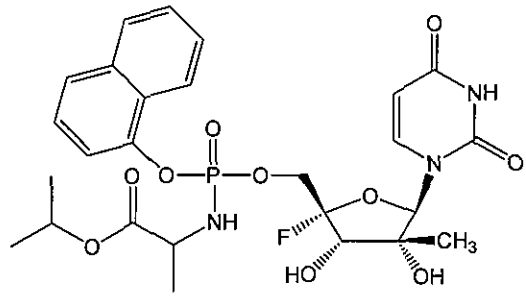

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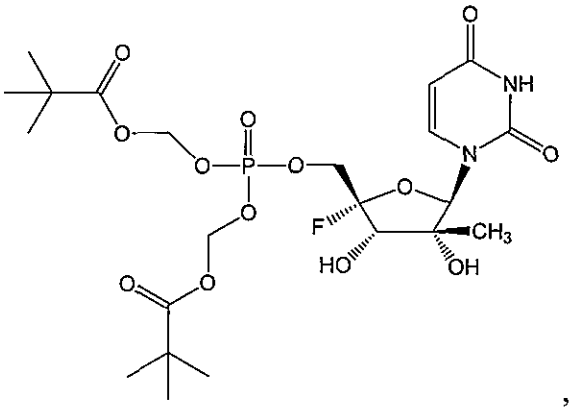
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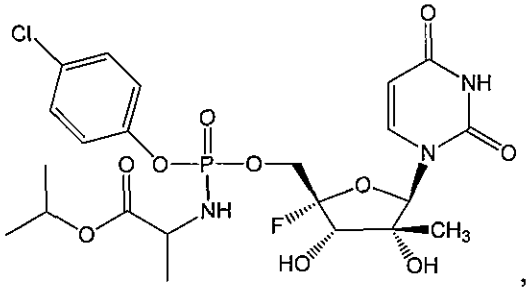
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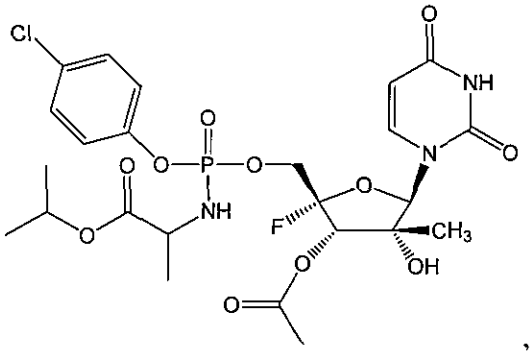
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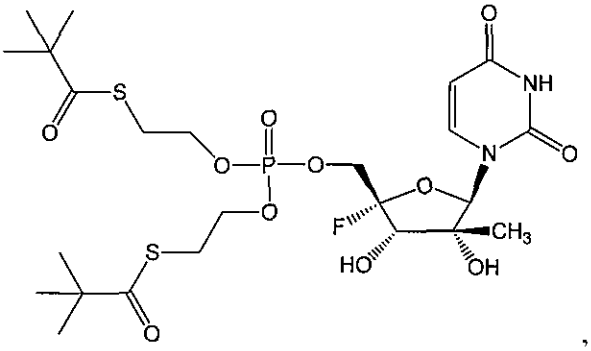
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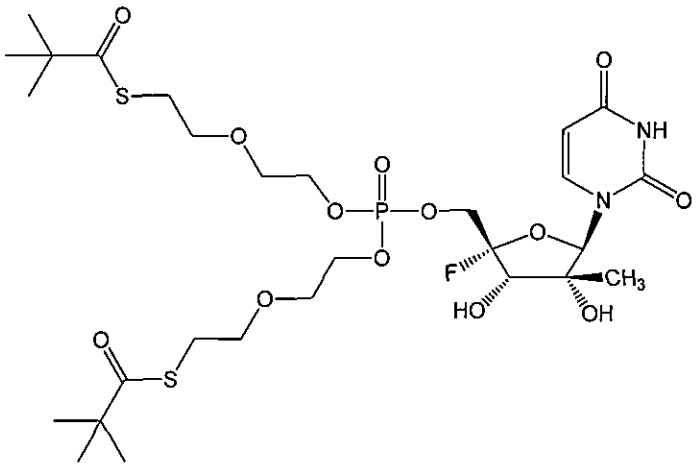
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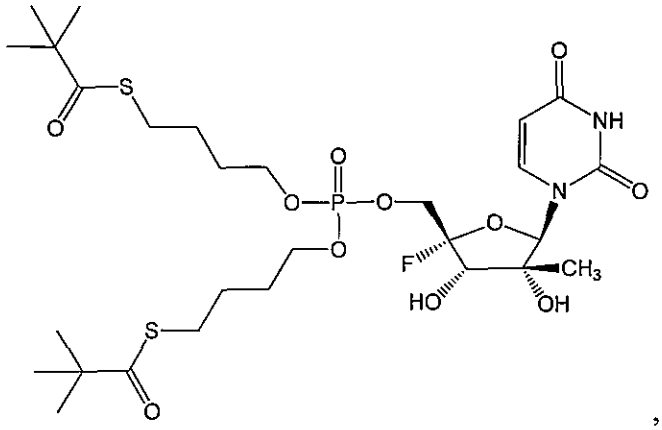

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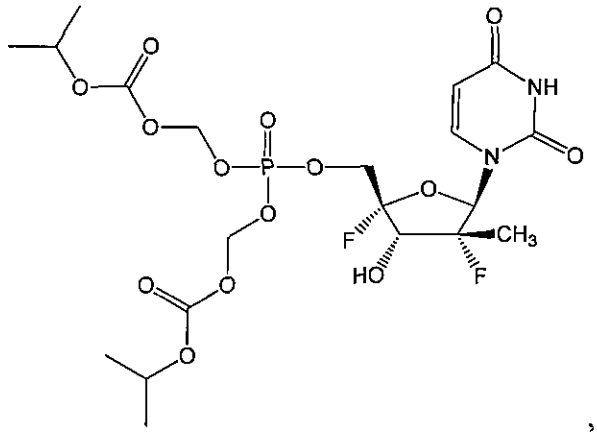

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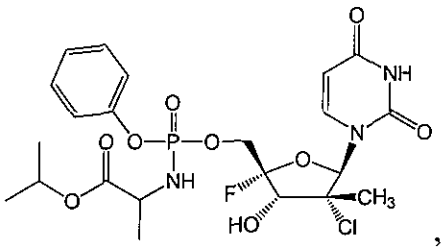

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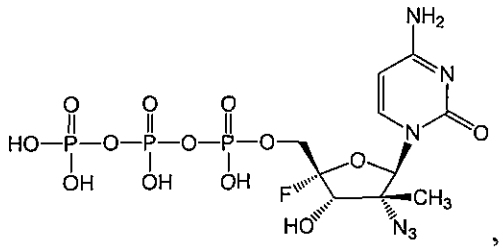

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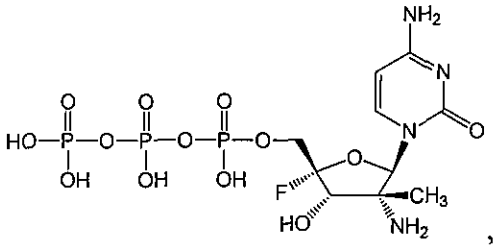

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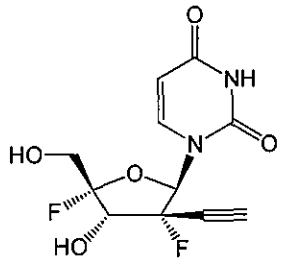

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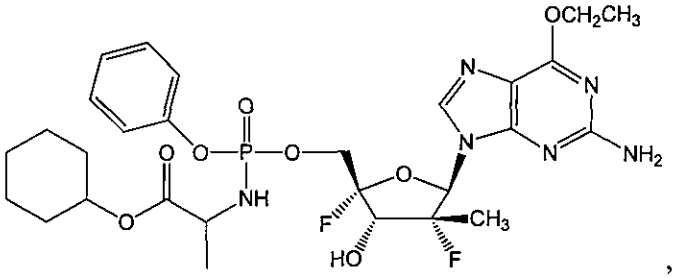

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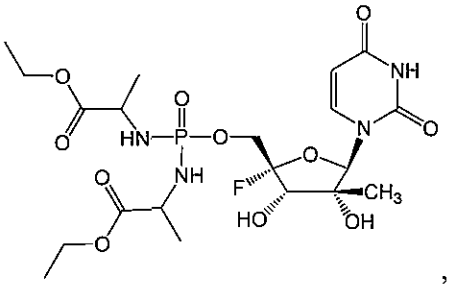
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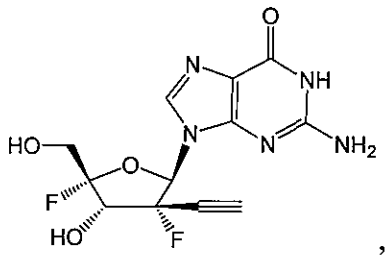
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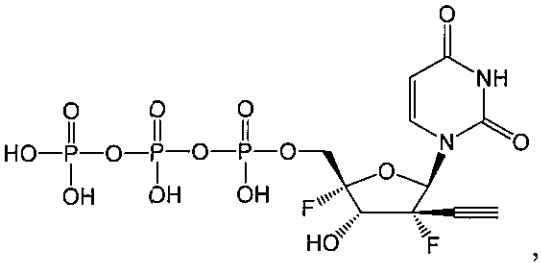
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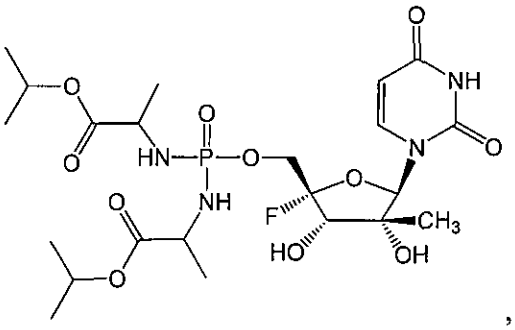
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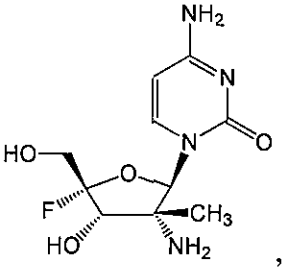
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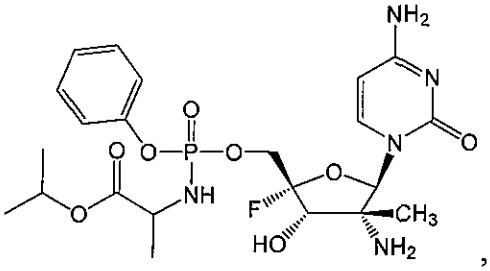
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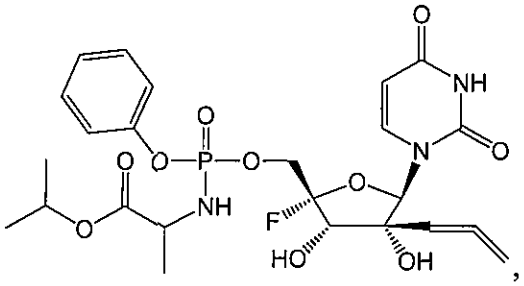
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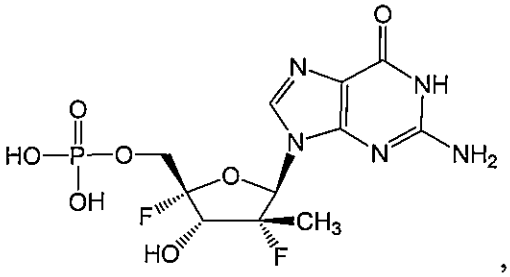
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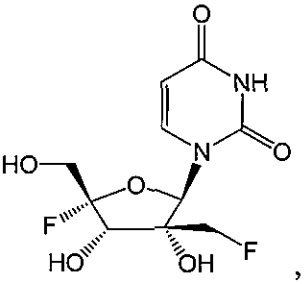
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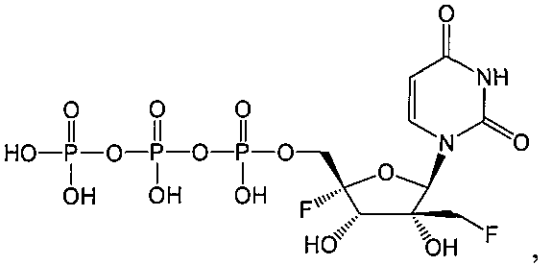
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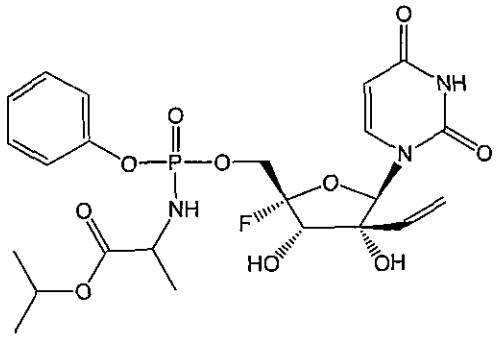
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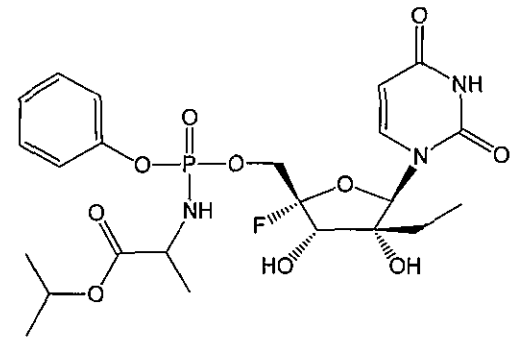
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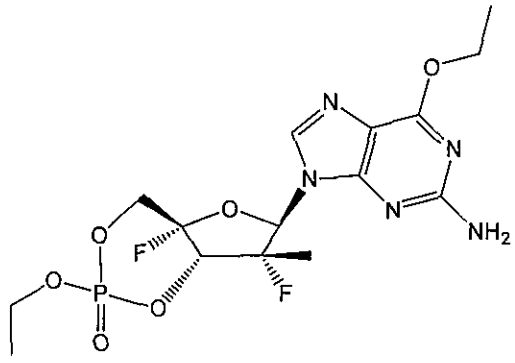
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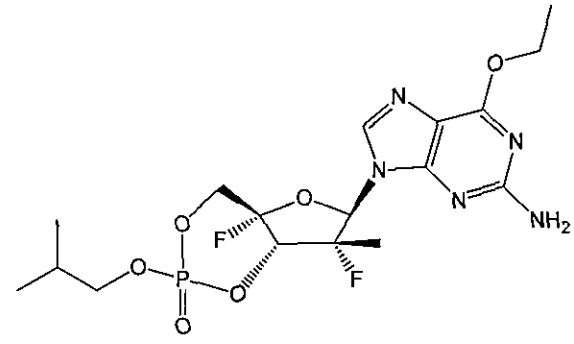
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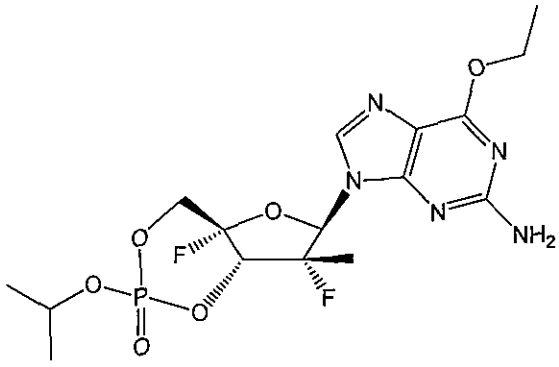
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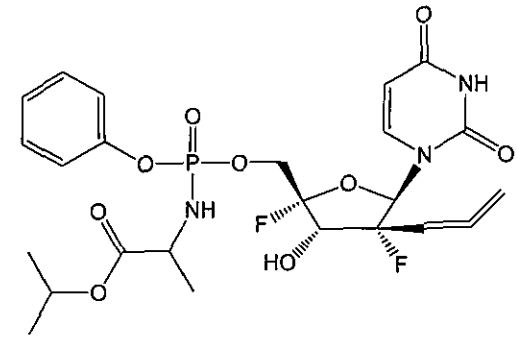
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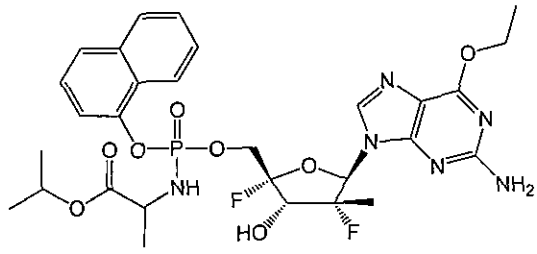
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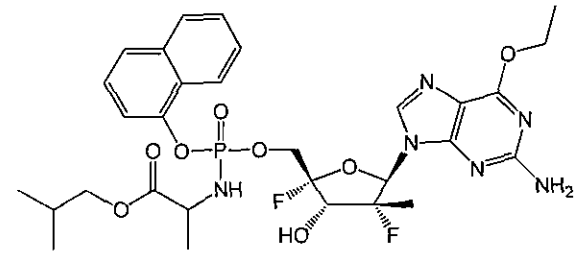
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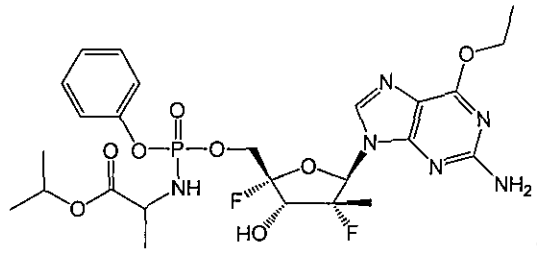
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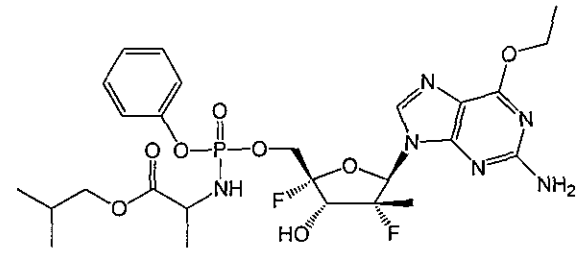
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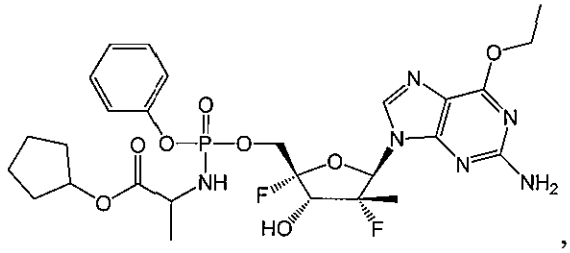
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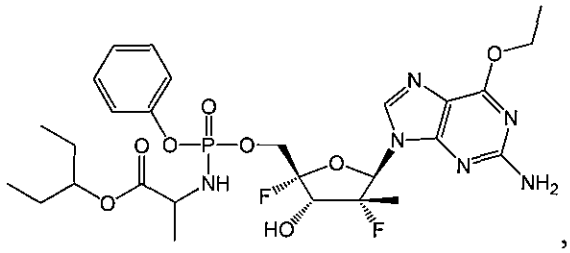
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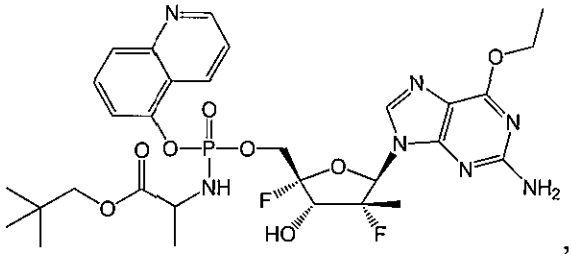
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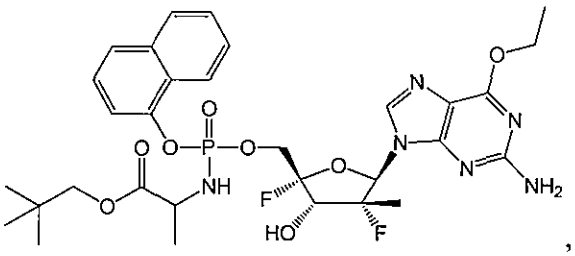
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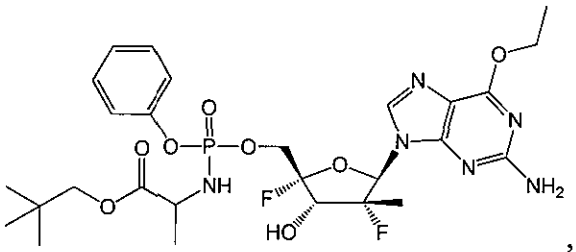
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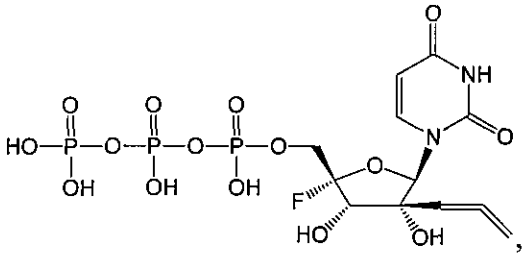
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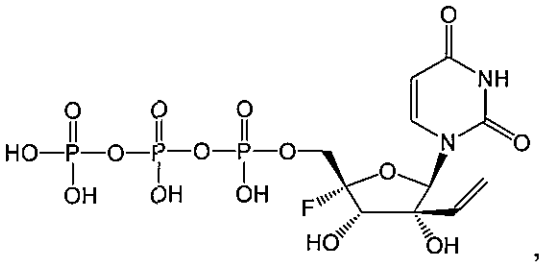
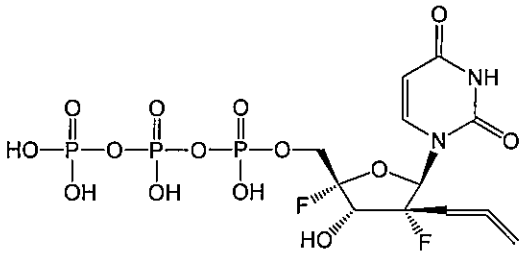
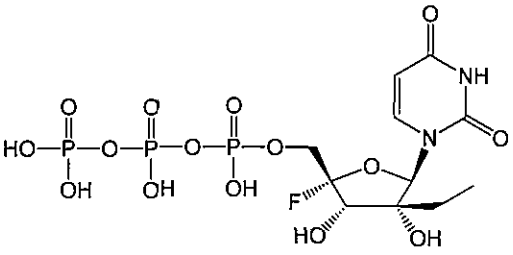

,

and

, or a pharmaceutically acceptable salt of the foregoing.

12. The use of Claim 11, wherein the Flaviviridae virus is selected from the group consisting of a Flavivirus, a Hepacirvirus and a Pestivirus.

13. The use of Claim 11, wherein the Flaviviridae virus is selected from the group consisting of hepatitis C virus (HCV), yellow fever virus (YFV), West Nile virus (WNV), dengue fever virus, an encephalitis virus from within the Flaviviridae family, classic swine fever virus and bovine diarrhea virus.

14. The use of Claim 13, wherein the encephalitis virus from within the Flaviviridae family is selected from the group consisting of Japanese encephalitis virus (JEV) and tick-borne encephalitis virus (TBEV).

15. The use of any one of Claims 1-14, wherein $R^{2A}$ is halo.

16. The use of Claim 15, wherein the halo is fluoro.

17. The use of any one of Claims 1-14, wherein $R^{2A}$ is an unsubstituted $C_{2-4}$ alkyl.

18. The use of any one of Claims 1-14, wherein $R^{2A}$ is an unsubstituted $C_{2-4}$ alkenyl.

19. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-CHF_2$.

20. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}F$.

21. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}Cl$.

22. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}N_3$.

23. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-(CH_2)_{1-6}NH_2$.

24. The use of any one of Claims 1-14, wherein $R^{2A}$ is $-CN$.

25. The use of any one of Claims 1-10, wherein $R^{2A}$ is selected from the group consisting of halo, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, $-CHF_2$, $-(CH_2)_{1-6}$ Cl, $-(CH_2)_{1-6}N_3$ and $-(CH_2)_{1-6}NH_2$ or $-CN$; and $R^{4A}$ is H.

26. The use of any one of Claims 1-24, wherein $R^{4A}$ is OH.

27. The use of any one of Claims 1-24, wherein $R^{4A}$ is halo.

28. The use of Claim 27, wherein the halo is F.

29. The use of Claim 27, wherein the halo is Cl.

30. The use of any one of Claims 1-24, wherein $R^{4A}$ is $-OC(=O)R^{"B}$ or an optionally substituted O-linked amino acid.

31. The use of any one of Claims 1-24, wherein $R^{4A}$ is $N_3$ or $NR^{"B1}R^{"B2}$.

32. The use of any one of Claims 1-16, 18, 19, 21-24 or 26-31, wherein $R^{5A}$ is H.

33. The use of any one of Claims 1-31, wherein $R^{5A}$ is halo.

34. The use of any one of Claims 1-31, wherein $R^{5A}$ is OH.

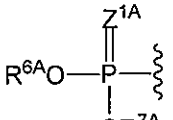
35. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{1-6}$ alkyl.

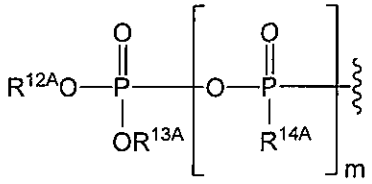
36. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{2-6}$ alkenyl.

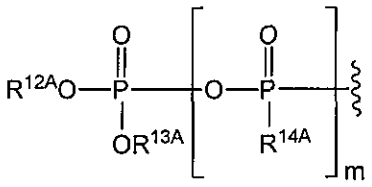
37. The use of any one of Claims 1-31, wherein $R^{5A}$ is an optionally substituted $C_{2-6}$ alkynyl.

38. The use of any one of Claims 1-37, wherein $R^{1A}$ is hydrogen.

39. The use of any one of Claims 1-37, wherein $R^{1A}$ is an optionally substituted acyl or an optionally substituted O-linked amino acid.

40. The use of any one of Claims 1-37, wherein $R^{1A}$ is  .

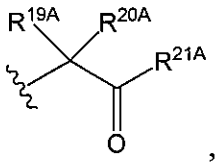
41. The use of Claim 40, wherein $R^{6A}$ is  , $R^{7A}$ is absent or hydrogen and m is 0.

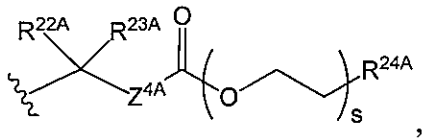
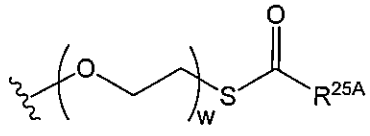
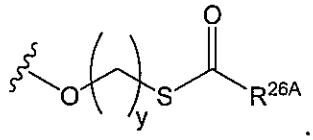
42. The use of Claim 40, wherein $R^{6A}$ is  , $R^{7A}$ is absent or hydrogen and m is 1.

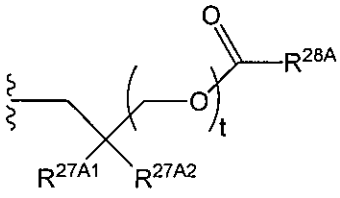
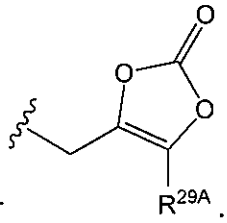
43. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently absent or hydrogen.

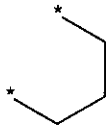
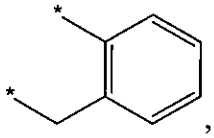
44. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl or an optionally substituted aryl($C_{1-6}$ alkyl).

45. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently an optionally substituted *–$(CR^{15A}R^{16A})_p$–O–$C_{1-24}$ alkyl or an optionally substituted *–$(CR^{17A}R^{18A})_q$–O–$C_{1-24}$ alkenyl.

46. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently  ,

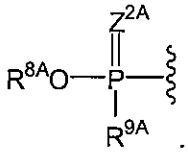
 ,  or  .

47. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are independently  or  .

48. The use of Claim 40, wherein $R^{6A}$ and $R^{7A}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6A}$ and $R^{7A}$, the phosphorus and the moiety form a six-membered to ten-membered ring system.

49. The use of any one of Claims 40-48, wherein $Z^{1A}$ is O.

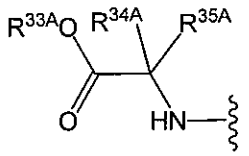
50. The use of any one of Claims 40-48, wherein $Z^{1A}$ is S.

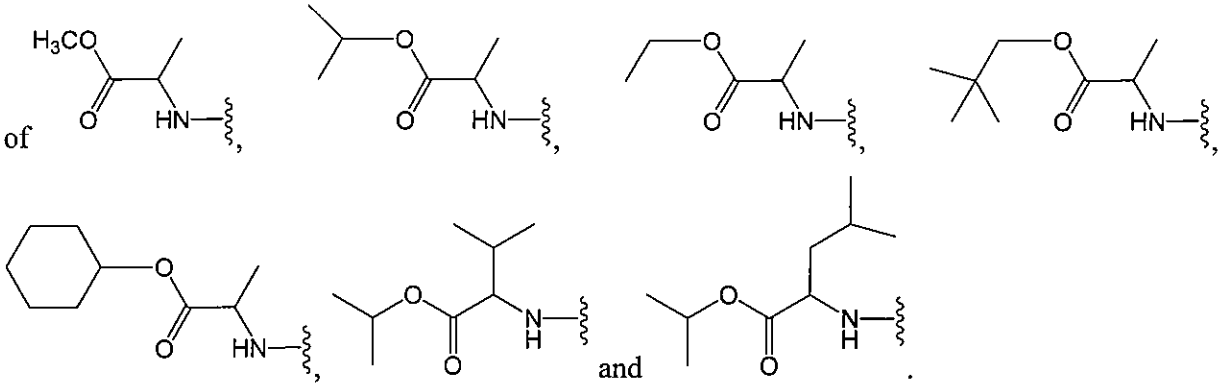
51. The use of any one of Claims 1-37, wherein $R^{1A}$ is  .

52. The use of Claim 51, wherein $R^{8A}$ is an optionally substituted aryl.

53. The use of Claim 51, wherein $R^{8A}$ is an optionally substituted heteroaryl.

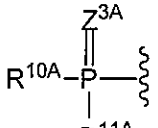
54. The use of any one of Claims 51-53, wherein $R^{9A}$ is an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative.

55. The use of any one of Claims 51-53, wherein $R^{9A}$ is  wherein $R^{33A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted aryl, an optionally substituted aryl($C_{1-6}$ alkyl) and an optionally substituted haloalkyl; $R^{34A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{1-6}$ haloalkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_6$ aryl, an optionally substituted $C_{10}$ aryl and an optionally substituted aryl($C_{1-6}$ alkyl); and $R^{35A}$ is hydrogen or an optionally substituted $C_{1-4}$ alkyl; or $R^{34A}$ and $R^{35A}$ are taken together to form an optionally substituted $C_{3-6}$ cycloalkyl.

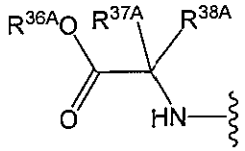
56. The use of Claim 55, wherein $R^{9A}$ is selected from the group consisting of  .

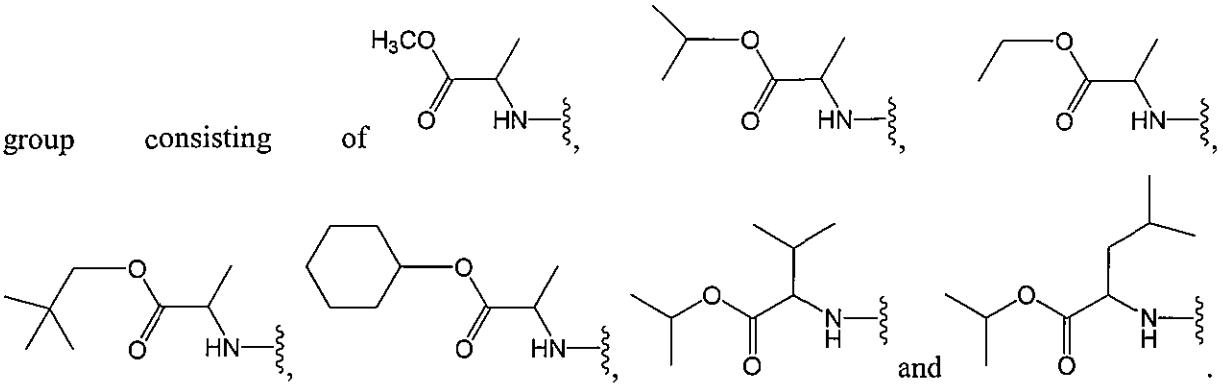
57. The use of any one of Claims 51-56, wherein $Z^{2A}$ is O.

58. The use of any one of Claims 51-56, wherein $Z^{2A}$ is S.

59. The use of any one of Claims 1-37, wherein $R^{1A}$ is  .

60. The use of Claim 59, wherein $R^{10A}$ and $R^{11A}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative.

61. The compound of Claim 59, wherein $R^{10A}$ and $R^{11A}$ are independently  wherein $R^{36A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted aryl, an optionally substituted aryl($C_{1-6}$ alkyl) and an optionally substituted haloalkyl; $R^{37A}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{1-6}$ haloalkyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_6$ aryl, an optionally substituted $C_{10}$ aryl and an optionally substituted aryl($C_{1-6}$ alkyl); and $R^{38A}$ is hydrogen or an optionally substituted $C_{1-4}$ alkyl; or $R^{37A}$ and $R^{38A}$ are taken together to form an optionally substituted $C_{3-6}$ cycloalkyl.

62. The use of Claim 61, wherein $R^{10A}$ and $R^{11A}$ are independently selected from the group consisting of  .

63. The use of any one of Claims 59-62, wherein $Z^{3A}$ is O.

64. The use of any one of Claims 59-62, wherein $Z^{3A}$ is S.

65. The use of any one of Claims 38-64, wherein $R^{3A}$ is H.

66. The use of any one of Claims 38-64, wherein $R^{3A}$ is halo.

67. The use of Claim 66, wherein the halo is fluoro.

68. The use of Claim 66, wherein the halo is chloro.

69. The use of any one of Claims 38-64, wherein $R^{3A}$ is OH.

70. The use of any one of Claims 38-64, wherein $R^{3A}$ is $-OC(=O)R''^{A}$ or an optionally substituted O-linked amino acid.

71. The use of any one of Claims 38-64, wherein $R^{3A}$ and $R^{4A}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring.

72. The use of any one of Claims 1-71, wherein $R^A$ is hydrogen.

73. The use of any one of Claims 1-71, wherein $R^A$ is deuterium.

74. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{1-3}$ alkyl.

75. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{2-4}$ alkenyl.

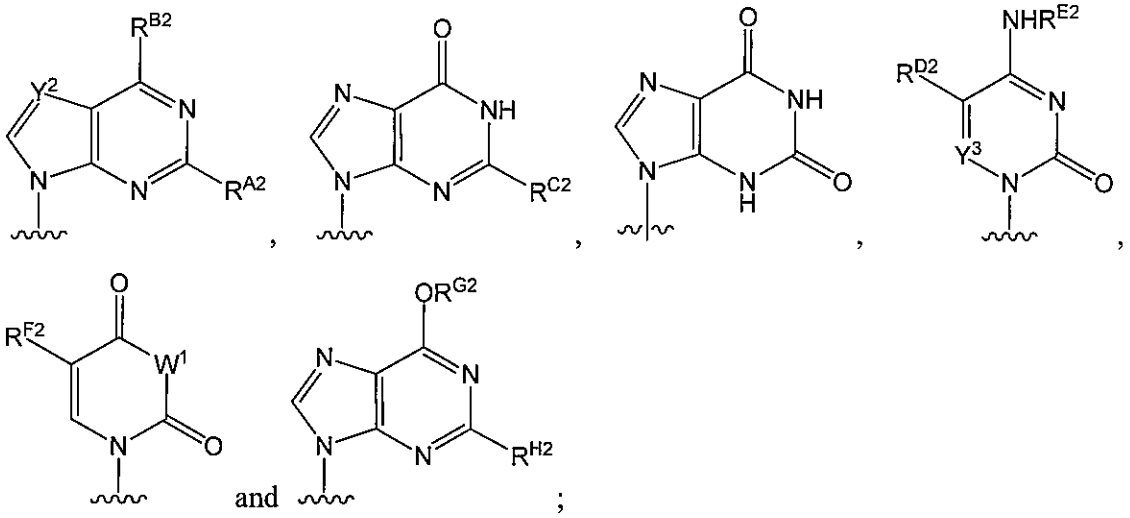
76. The use of any one of Claims 1-71, wherein $R^A$ is an unsubstituted $C_{2-3}$ alkynyl.

77. The use of any one of Claims 1-71, wherein $R^A$ is cyano.

78. The use of any one of Claims 1-77, wherein $R^{a1}$ and $R^{a2}$ are both hydrogen.

79. The use of any one of Claims 1-77, wherein $R^{a1}$ and $R^{a2}$ are both deuterium.

80. The use of any one of Claims 1-79, wherein $B^{1A}$ is selected from the group consisting of:



wherein:

$R^{A2}$ is selected from the group consisting of hydrogen, halogen and $NHR^{J2}$, wherein $R^{J2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{K2}$ and $-C(=O)OR^{L2}$;

$R^{B2}$ is halogen or $NHR^{W2}$, wherein $R^{W2}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{M2}$ and $-C(=O)OR^{N2}$;

$R^{C2}$ is hydrogen or $NHR^{O2}$, wherein $R^{O2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{P2}$ and $-C(=O)OR^{Q2}$;

$R^{D2}$ is selected from the group consisting of hydrogen, deuterium, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{E2}$ is selected from the group consisting of hydrogen, hydroxy, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{R2}$ and $-C(=O)OR^{S2}$;

$R^{F2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

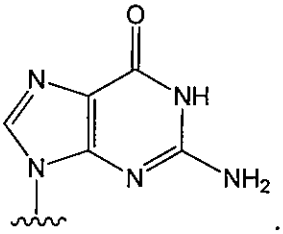
$Y^2$ and $Y^3$ are independently N or $CR^{I2}$, wherein $R^{I2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

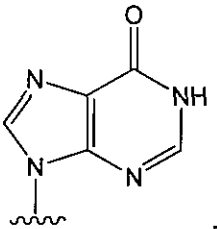
$W^1$ is NH, $-NCH_2\text{-}OC(=O)CH(NH_2)\text{-}CH(CH_3)_2$ or $-(CH_2)_{1-2}-O\text{-}P(=O)(OW^{1A})_2$, wherein $W^{1A}$ is selected from the group consisting of absent, hydrogen and an optionally substituted $C_{1-6}$ alkyl;

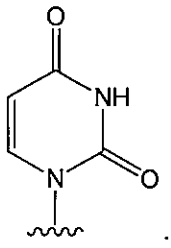
$R^{G2}$ is an optionally substituted $C_{1-6}$ alkyl;

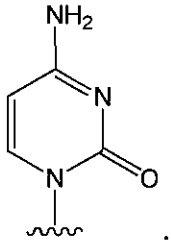
$R^{H2}$ is hydrogen or $NHR^{T2}$, wherein $R^{T2}$ is independently selected from the group consisting of hydrogen, $-C(=O)R^{U2}$ and $-C(=O)OR^{V2}$; and

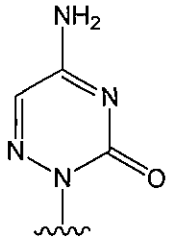
$R^{K2}$, $R^{L2}$, $R^{M2}$, $R^{N2}$, $R^{P2}$, $R^{Q2}$ $R^{R2}$, $R^{S2,}$ $R^{U2}$ and $R^{V2}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl).

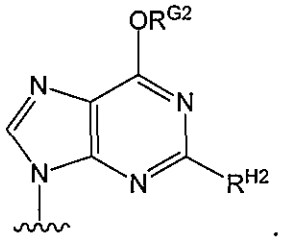
81. The use of Claim 80, wherein $B^{1A}$ is  .

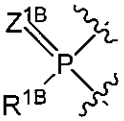
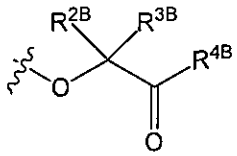
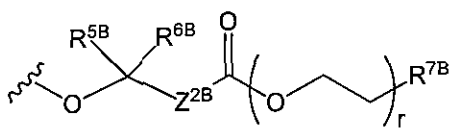
82. The use of Claim 80, wherein $B^{1A}$ is  .

83. The use of Claim 80, wherein $B^{1A}$ is  .

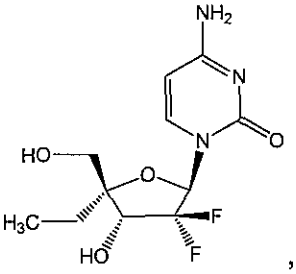
84. The use of Claim 80, wherein $B^{1A}$ is  .

85. The use of Claim 80, wherein $B^{1A}$ is  .

86. The use of Claim 80, wherein $B^{1A}$ is  .

87. The use of any one of Claims 1-37 or 72-86, wherein when -------- are each a single bond, then $Z^1$ is  , $O^1$ is O, $R^{3A}$ is O, $R^{2A}$ is halo, $-CHF_2$, $-(CH_2)_{1\text{-}6}F$, $-(CH_2)_{1\text{-}6}Cl$, $-(CH_2)_{1\text{-}6}N_3$, $-(CH_2)_{1\text{-}6}NH_2$ or –CN, and $R^{1B}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1\text{-}6}$ alkyl.  and  .

88. The use of Claim 1, wherein the compound is selected from the group consisting of: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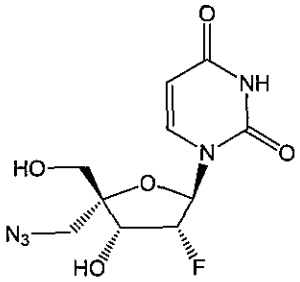
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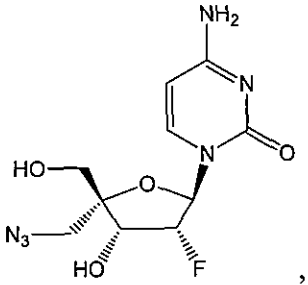
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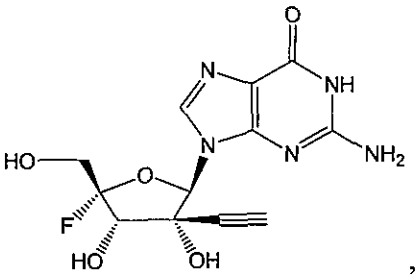
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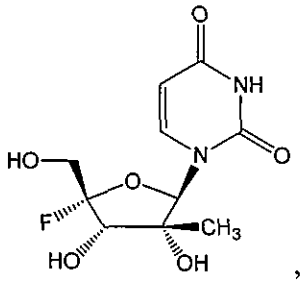
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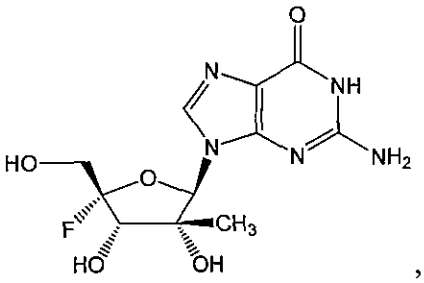
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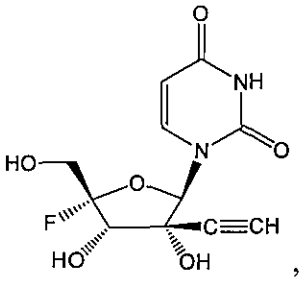
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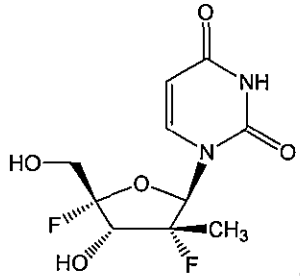
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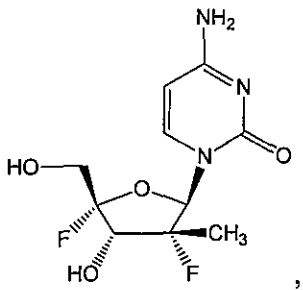
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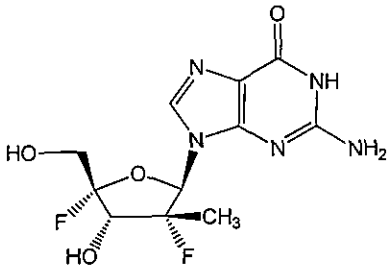
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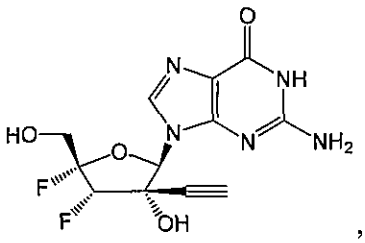
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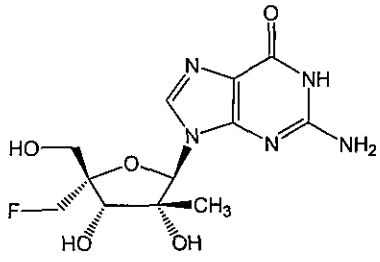
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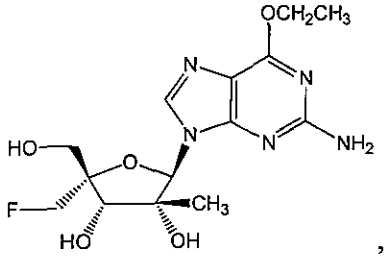
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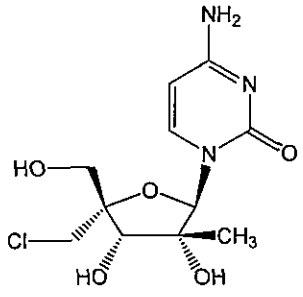
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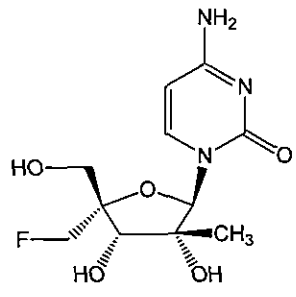
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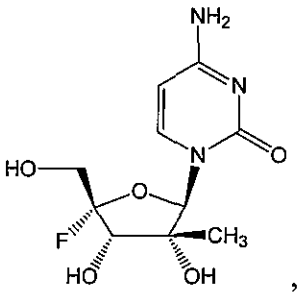
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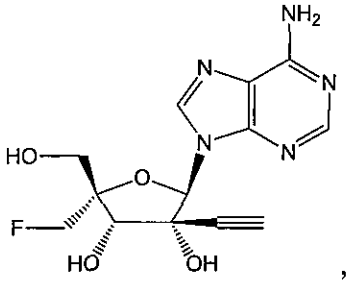
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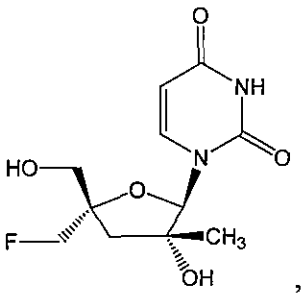
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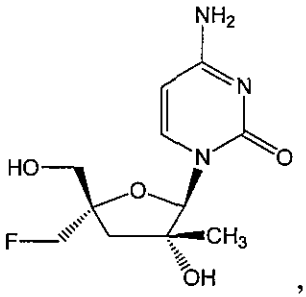
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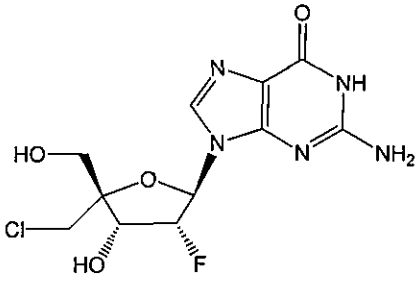
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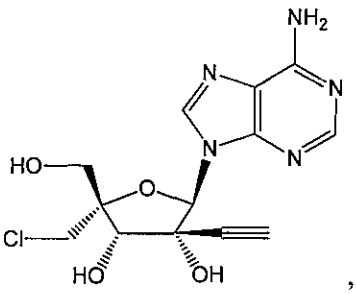
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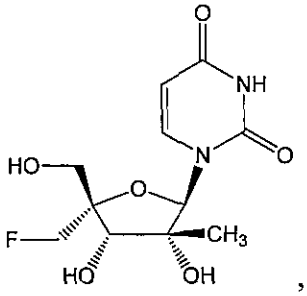
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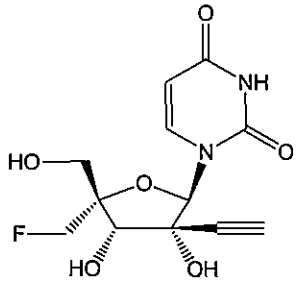
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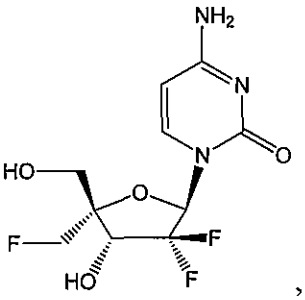
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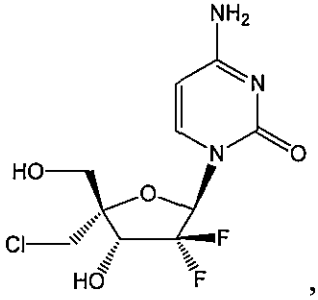
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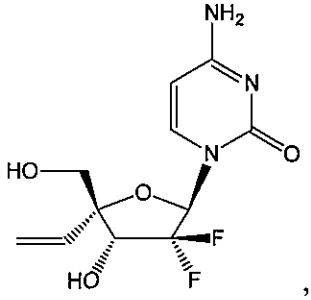
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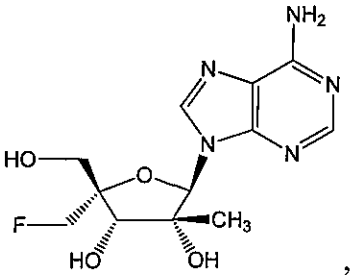
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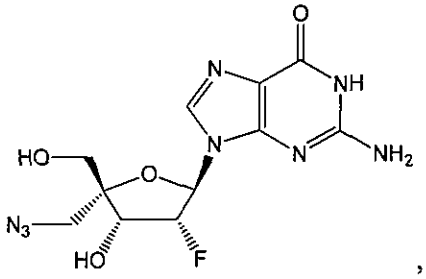
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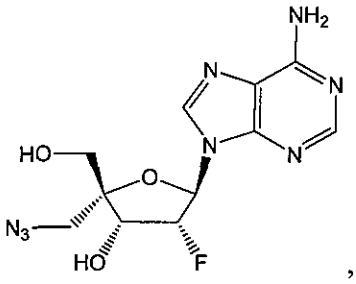
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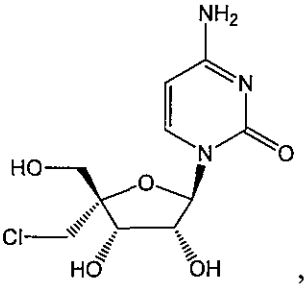
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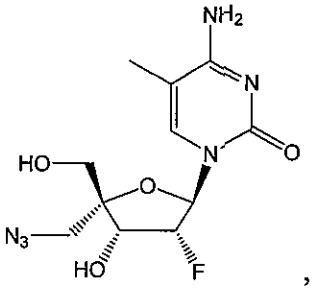
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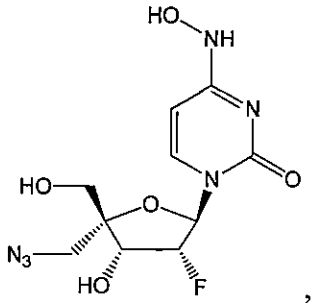
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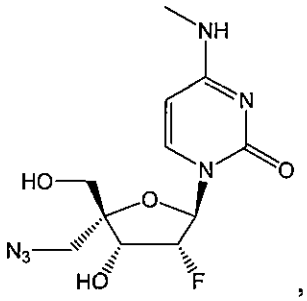
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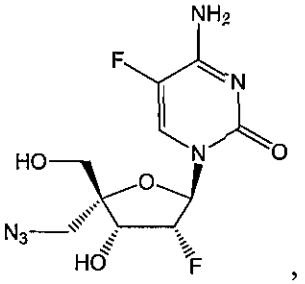
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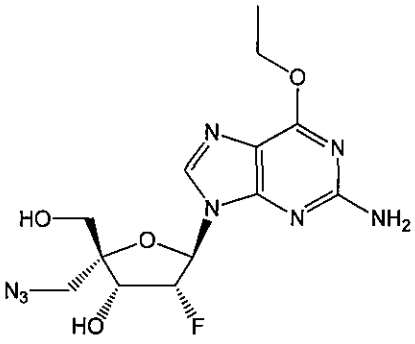
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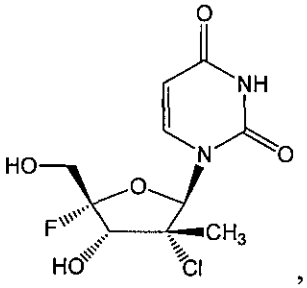
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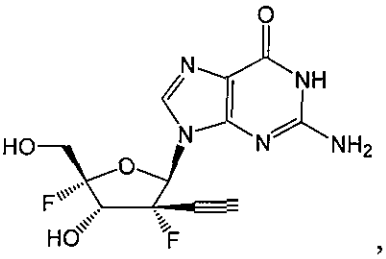
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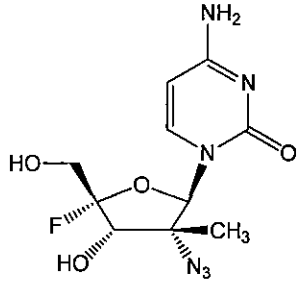
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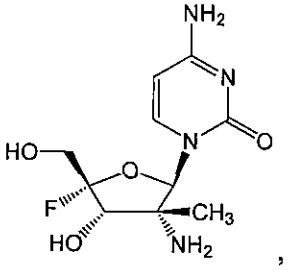
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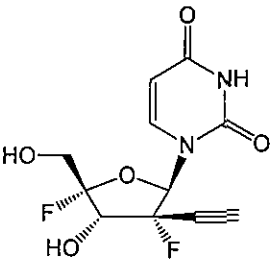
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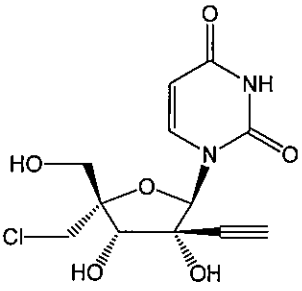
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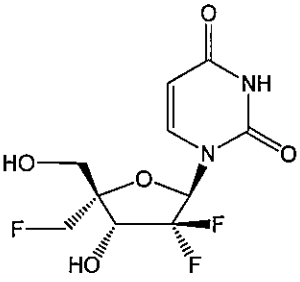
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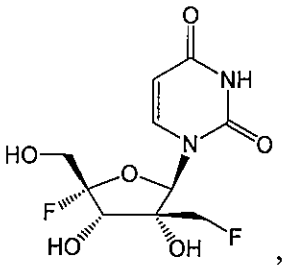
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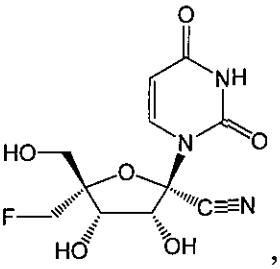
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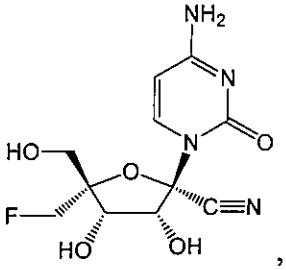
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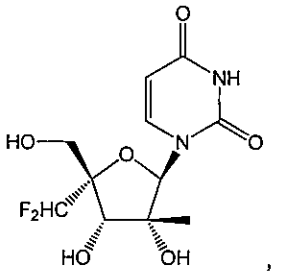
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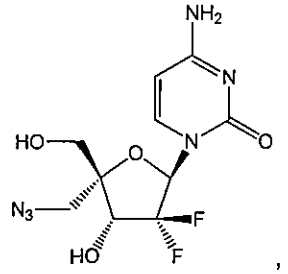
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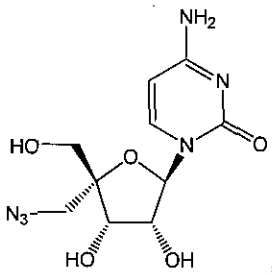
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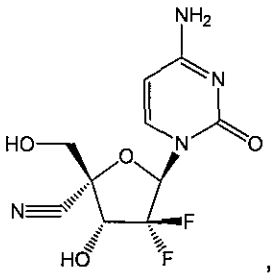
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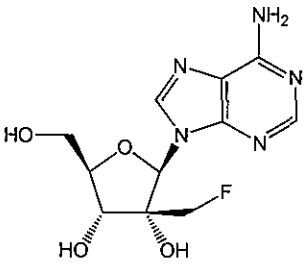
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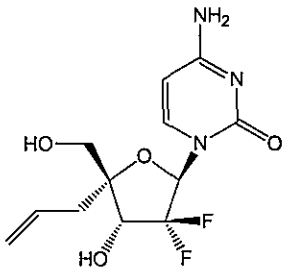
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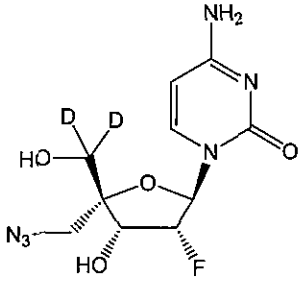
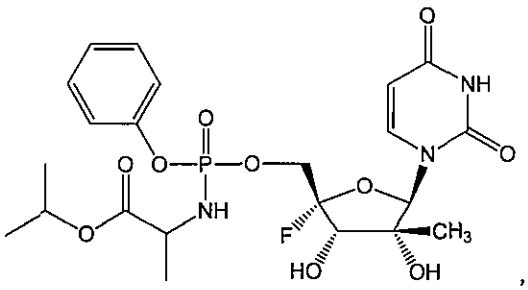

, or a pharmaceutically acceptable salt of the foregoing.

89. The use of Claim 1, wherein the compound is selected from the group consisting of: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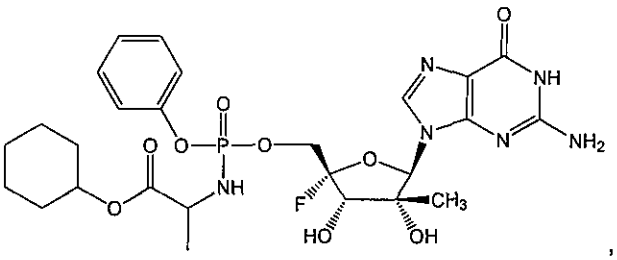
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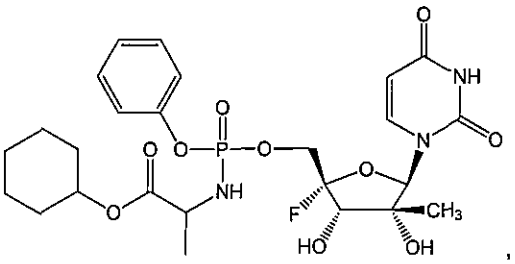
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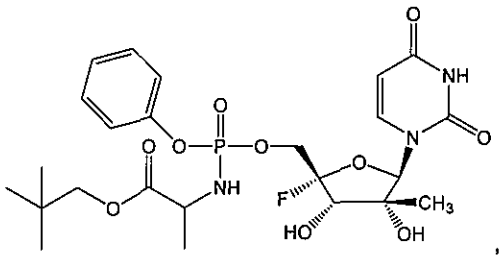
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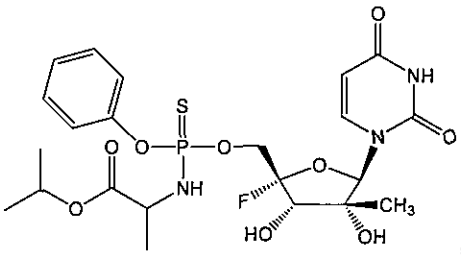
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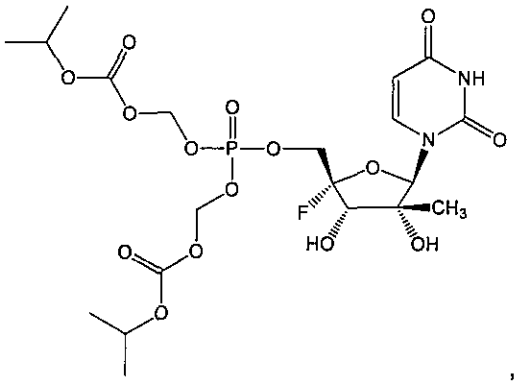
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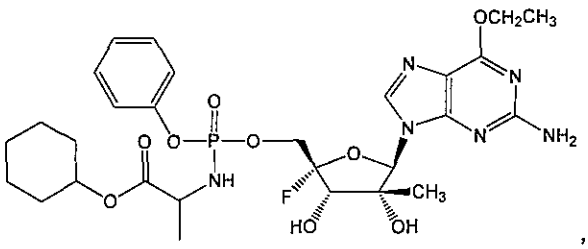
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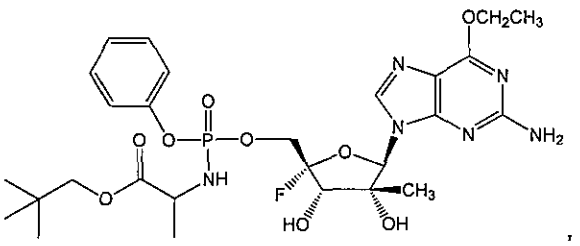
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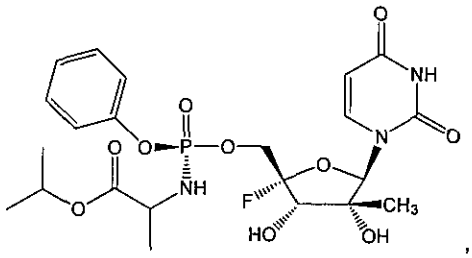
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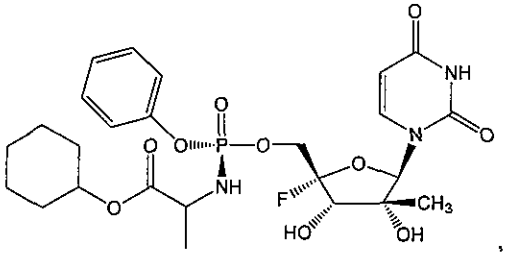
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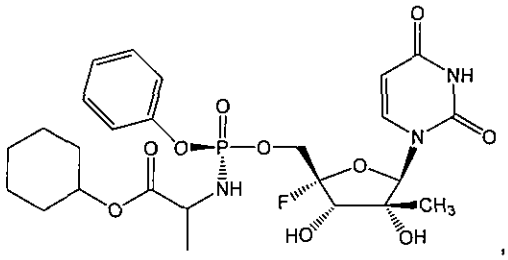
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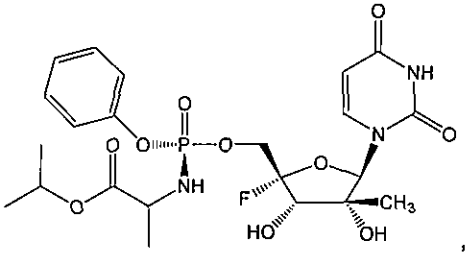
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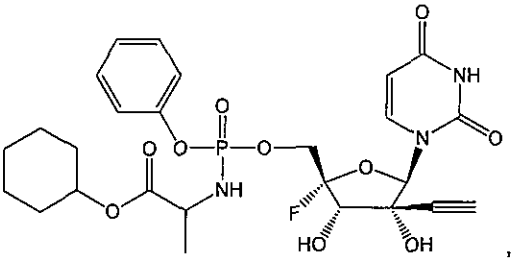
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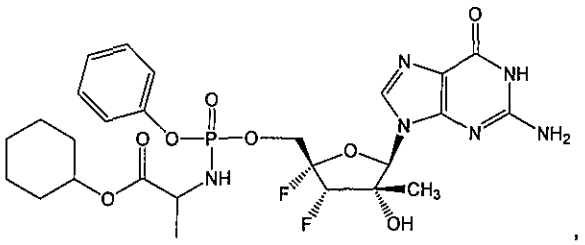
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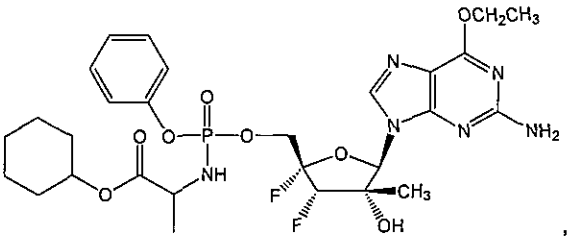
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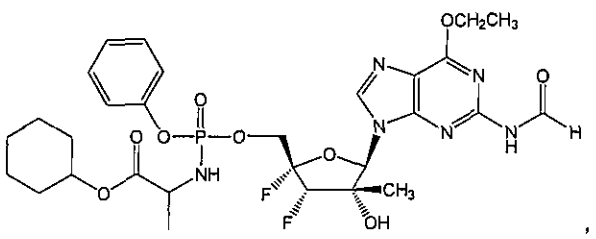
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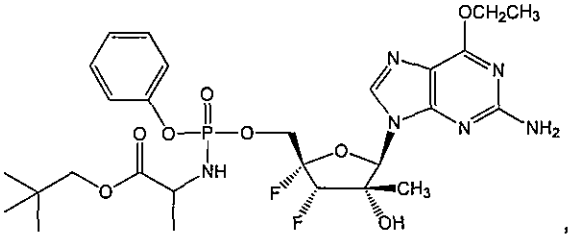
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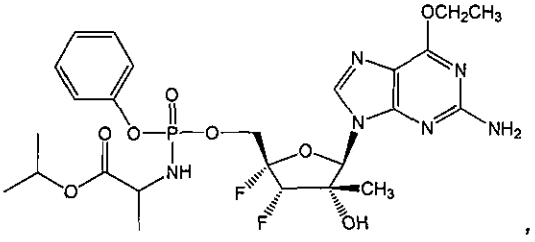
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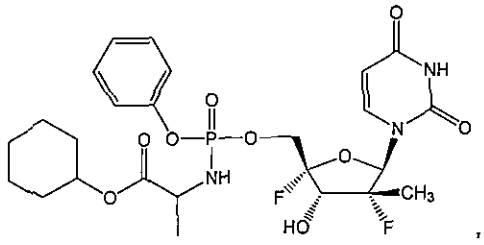

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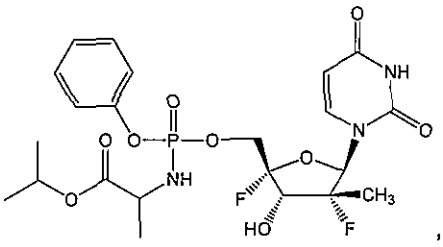

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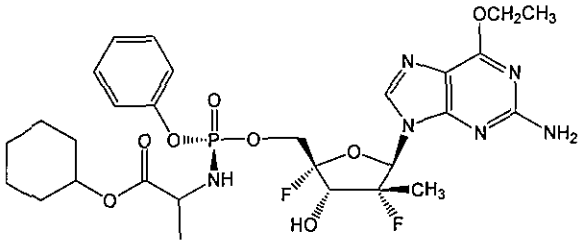

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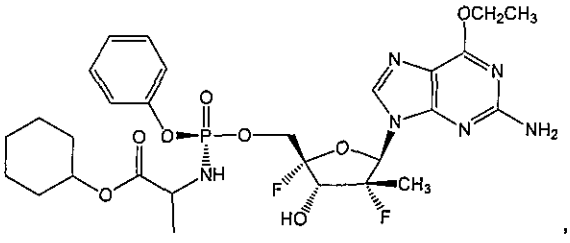

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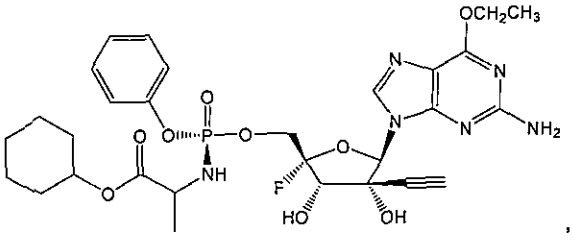

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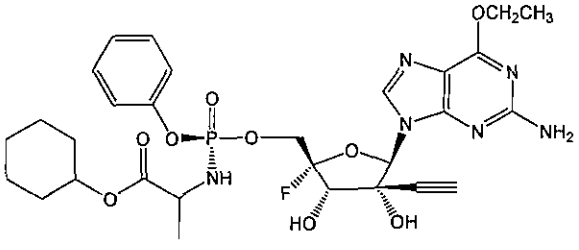

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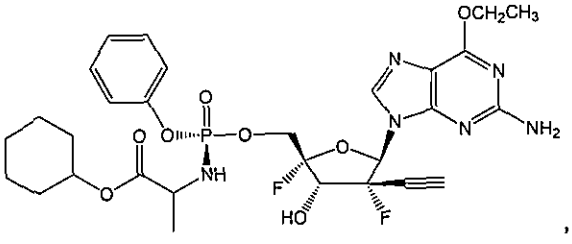

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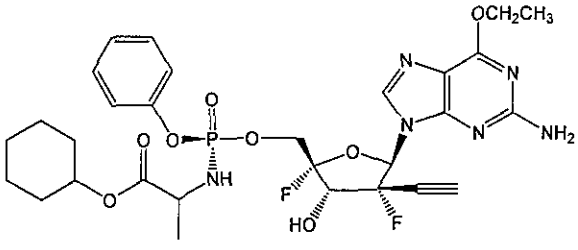

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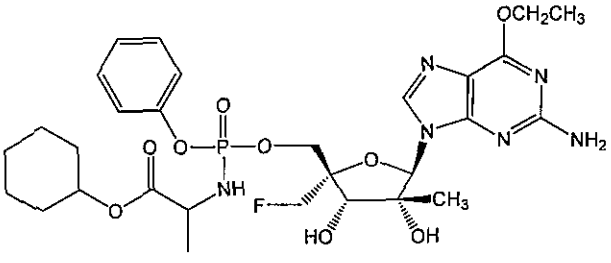

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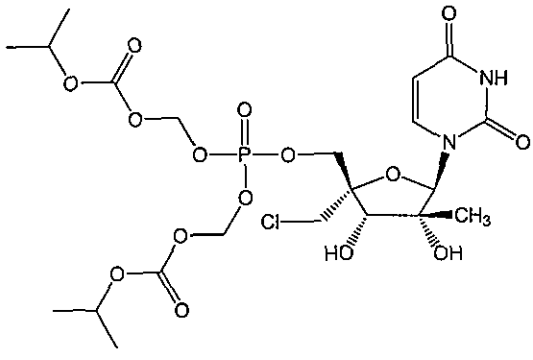

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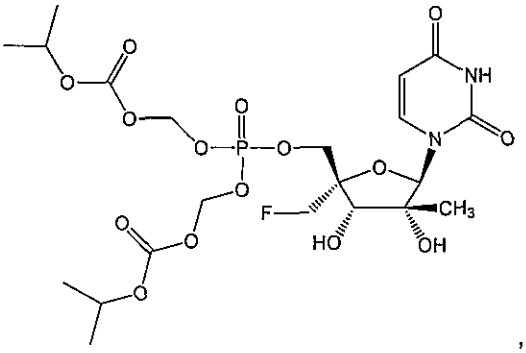

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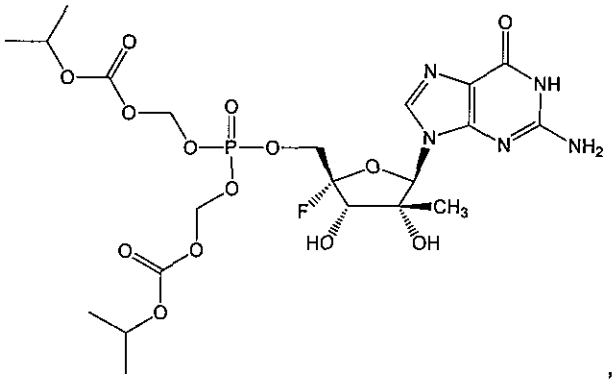

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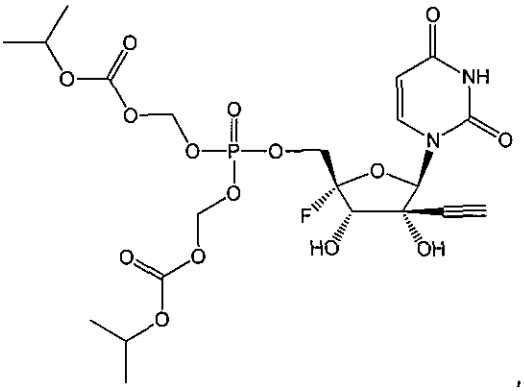

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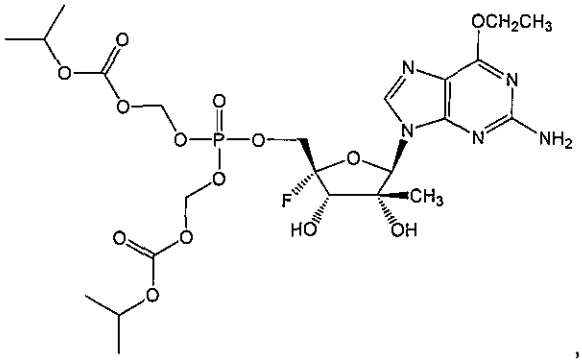

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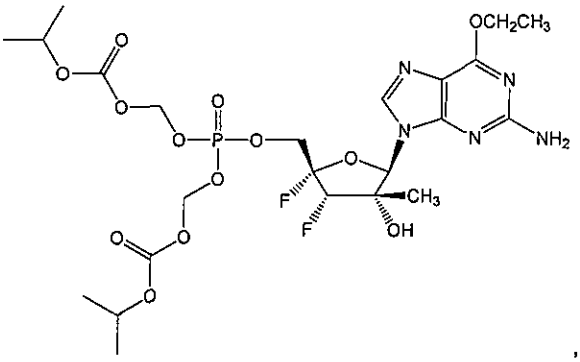

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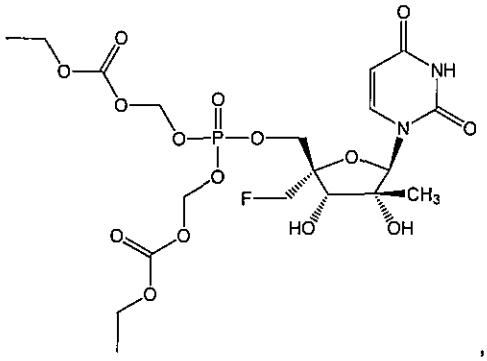

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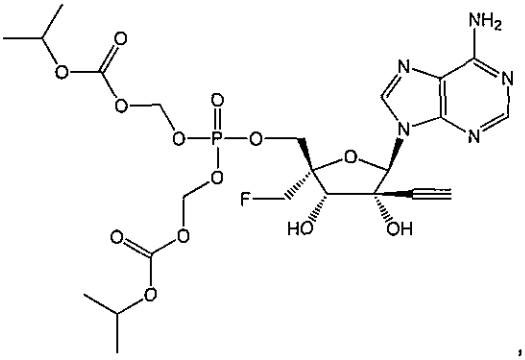

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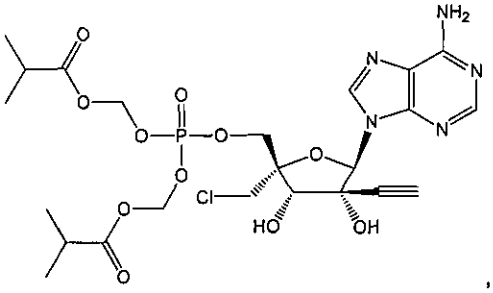

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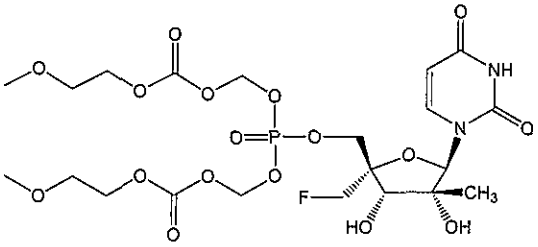

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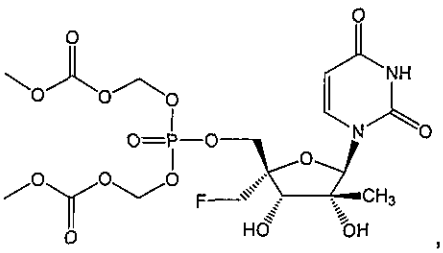

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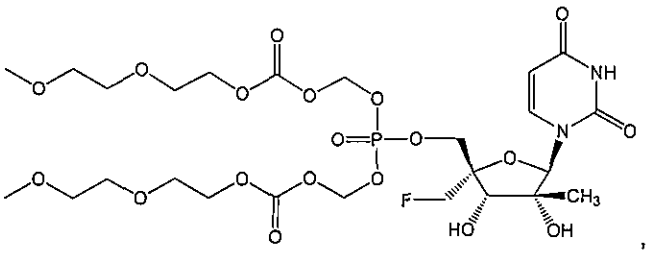

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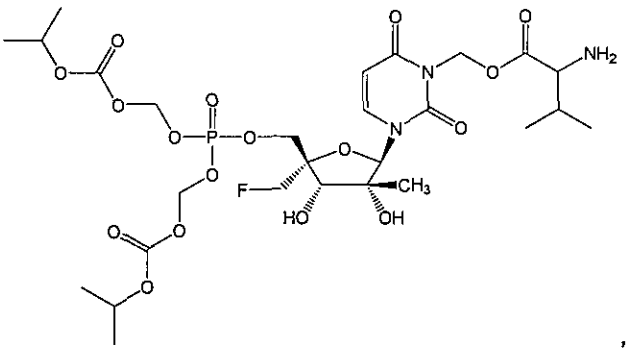

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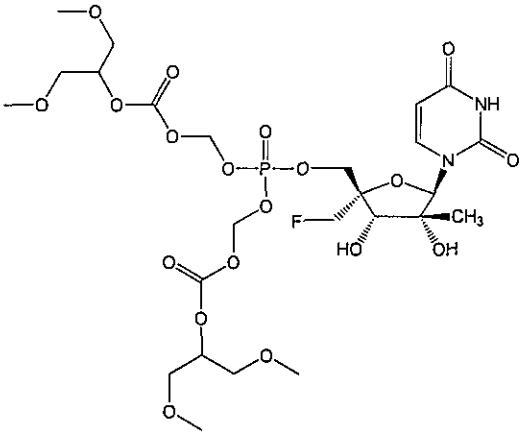

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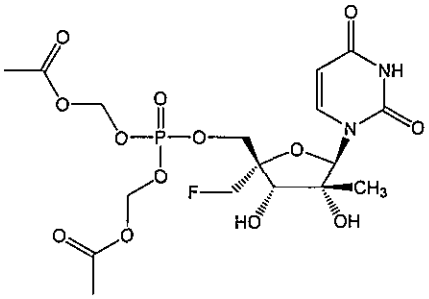

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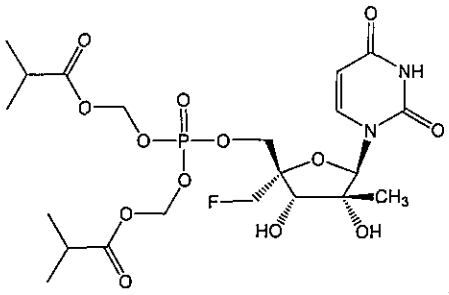

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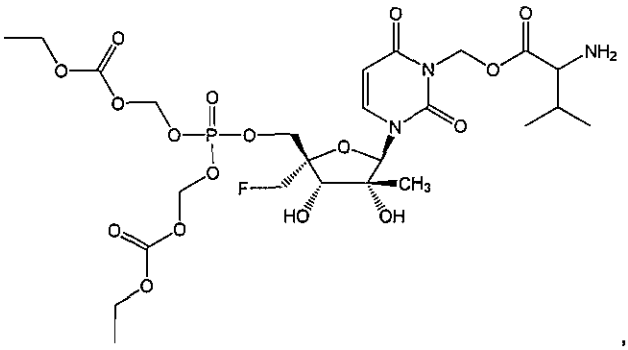

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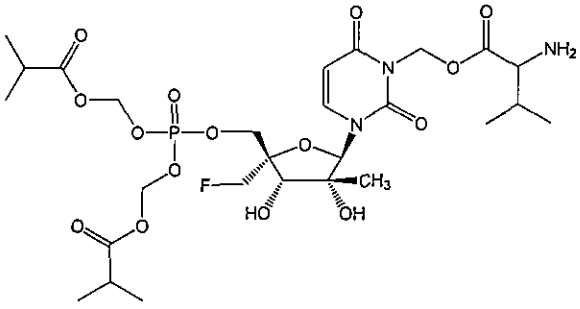

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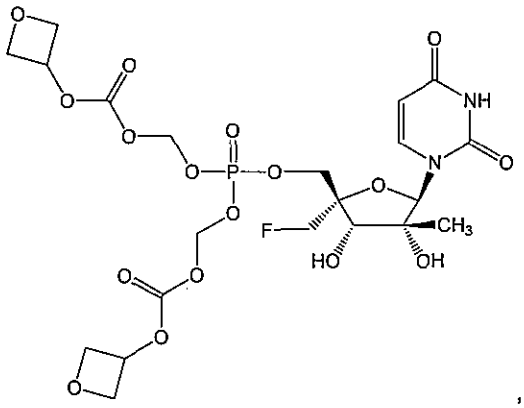

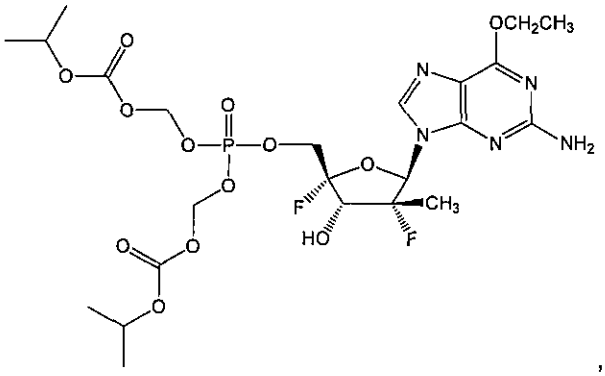

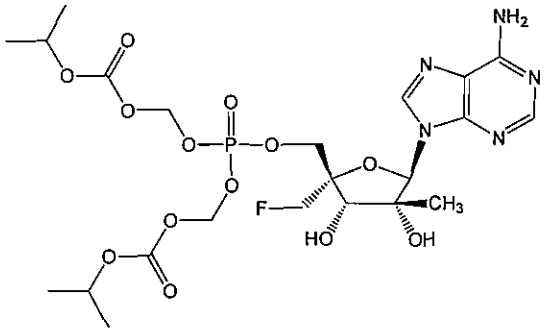

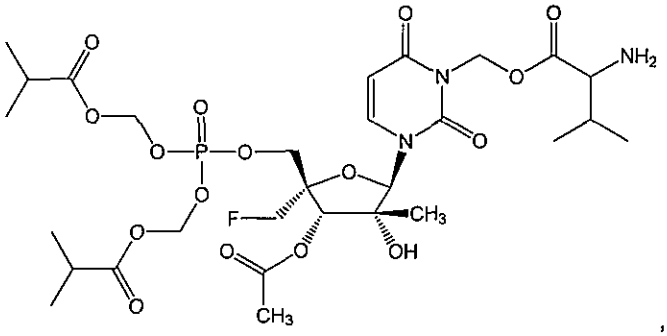

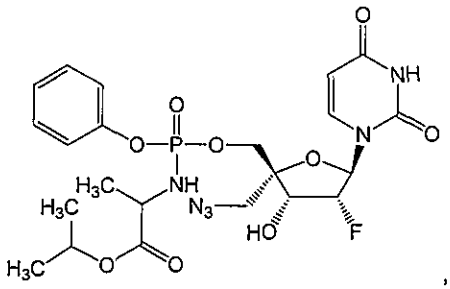

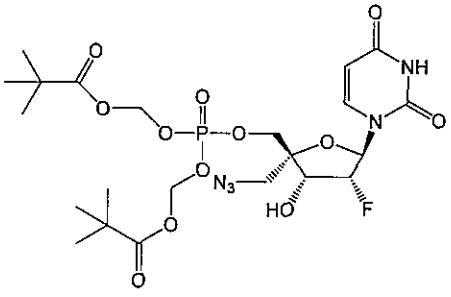

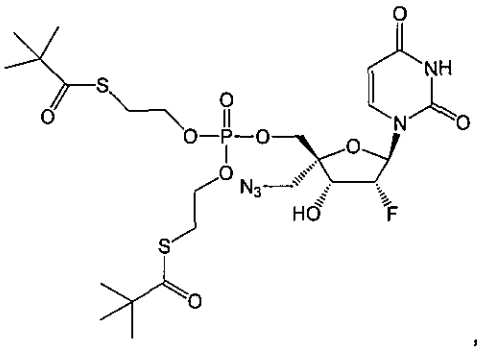

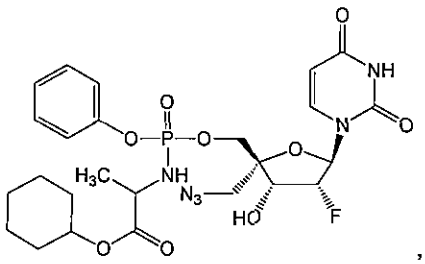

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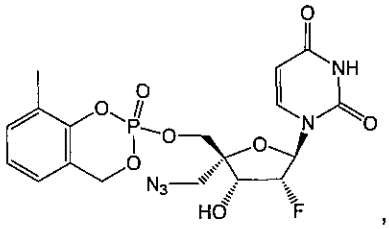

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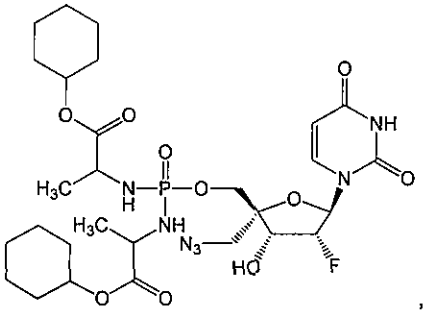

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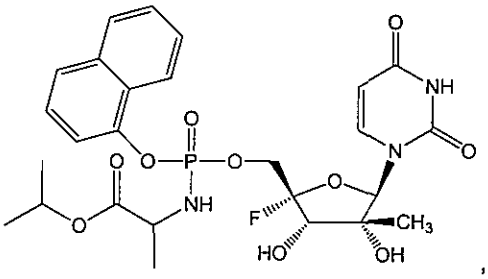

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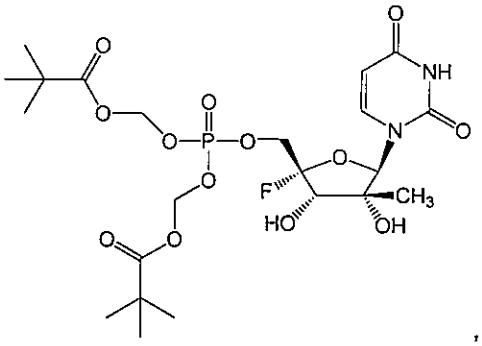

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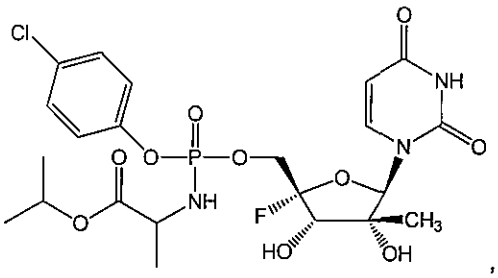

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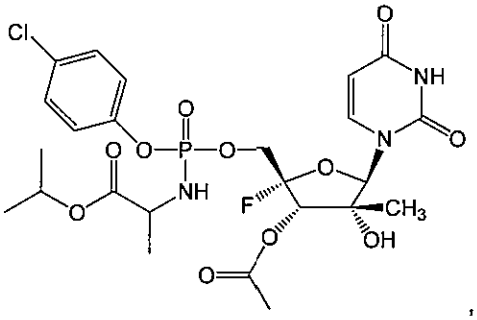

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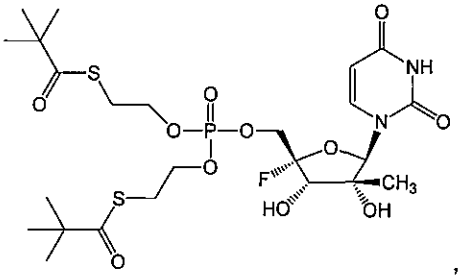

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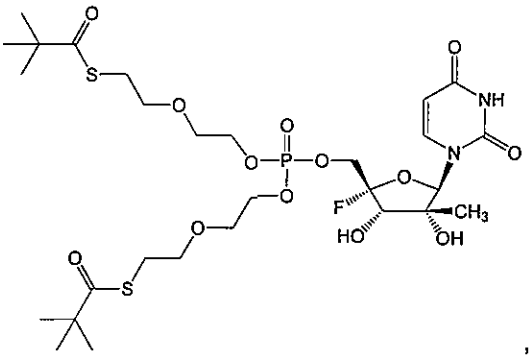

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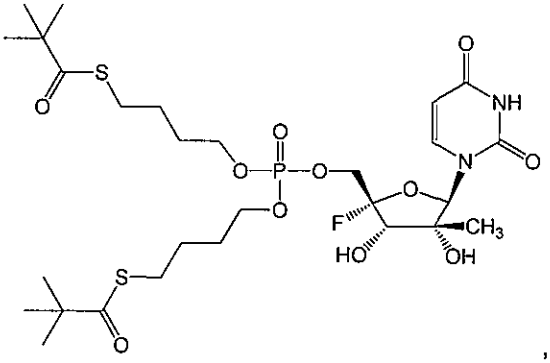

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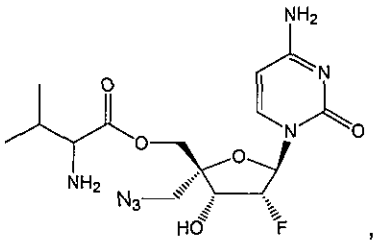
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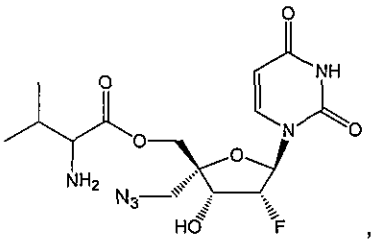
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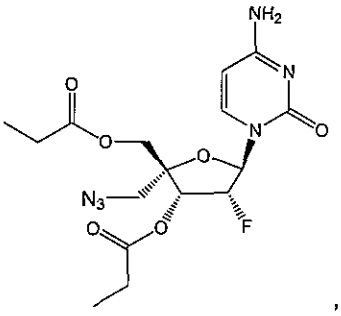
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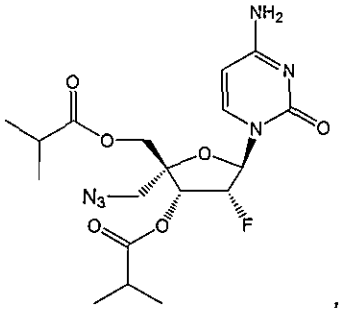
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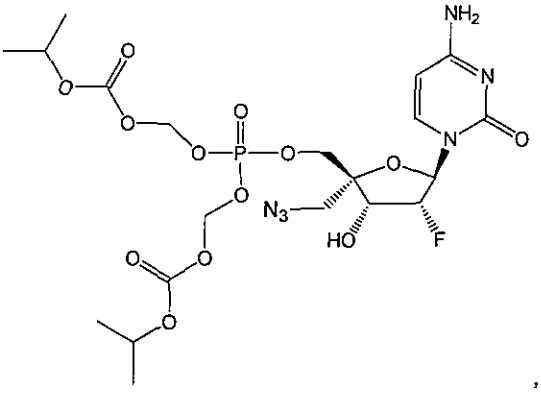
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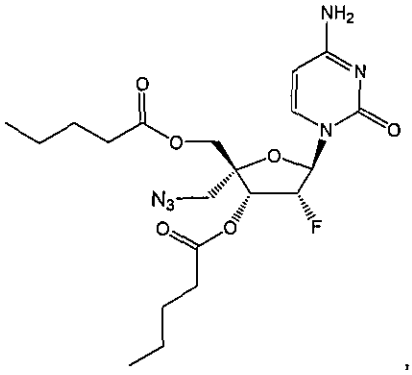
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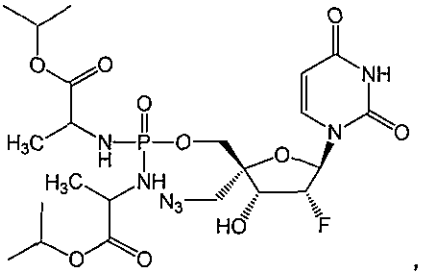
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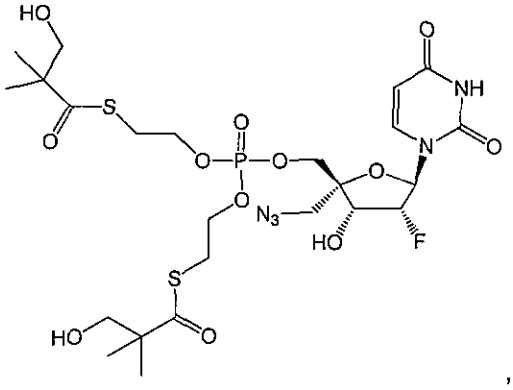
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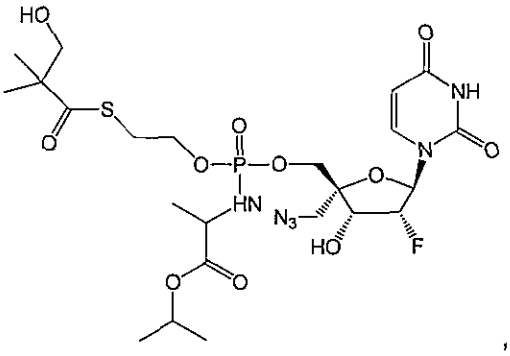
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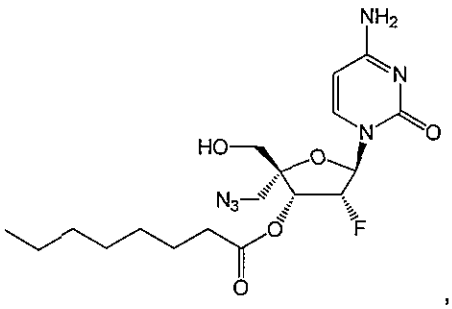

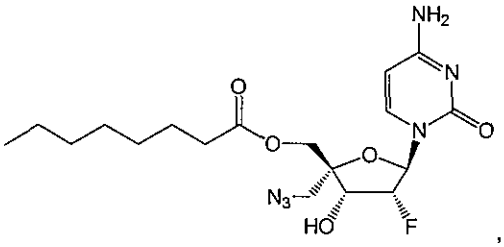

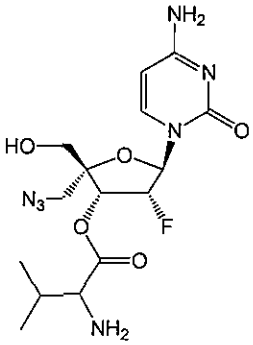

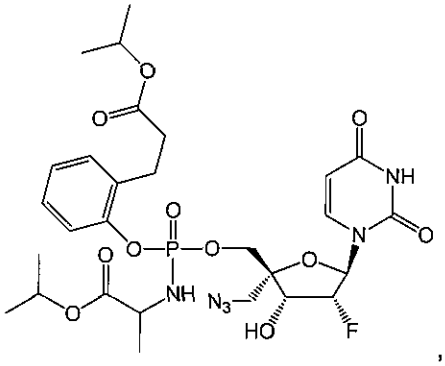

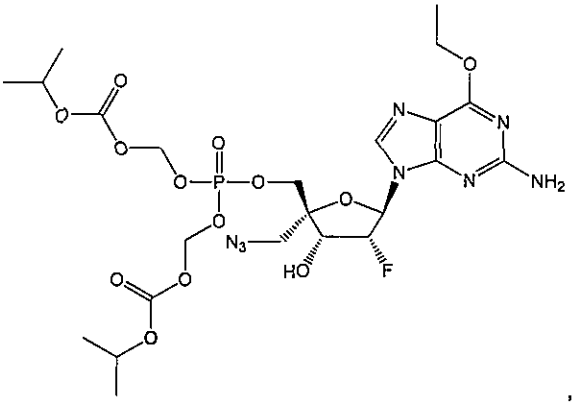

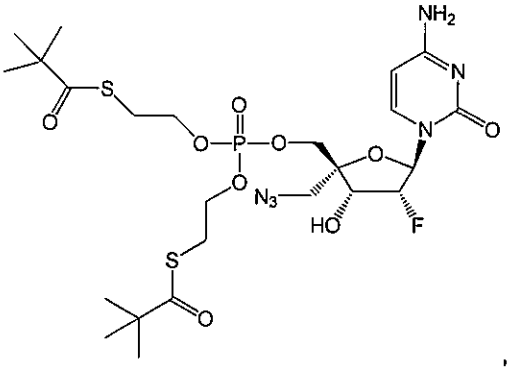

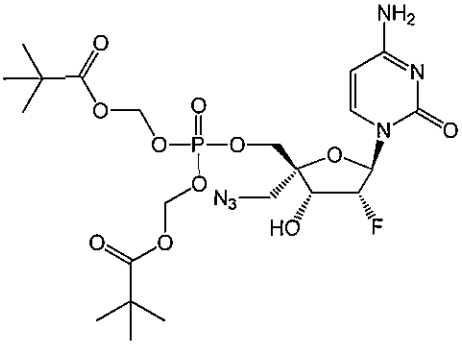

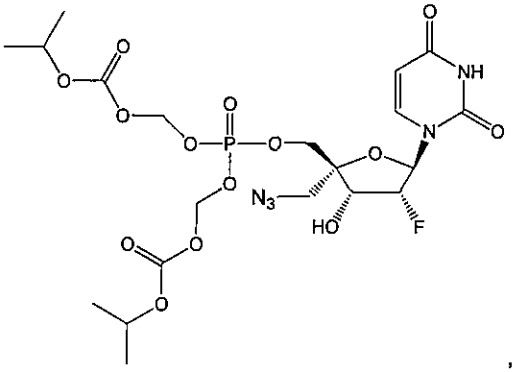

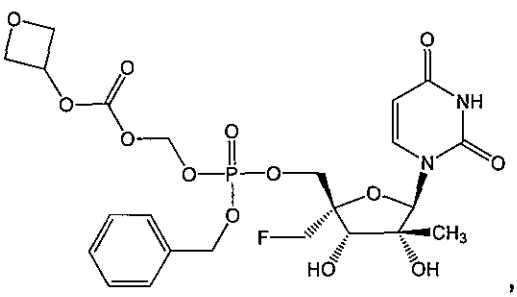

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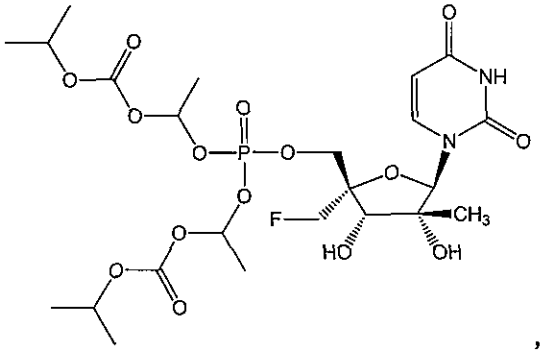

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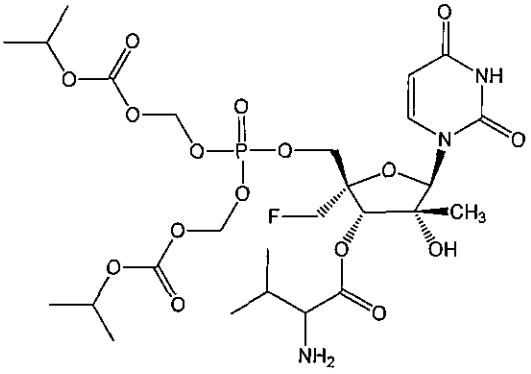

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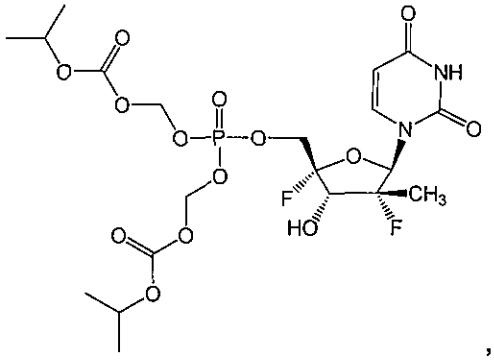

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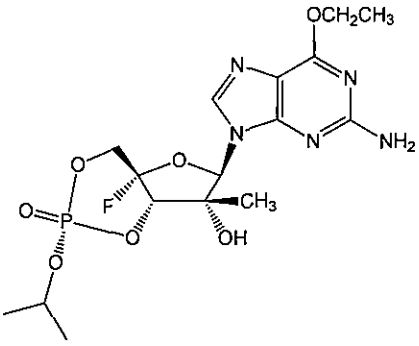

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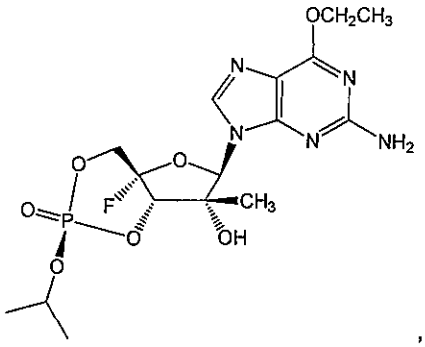

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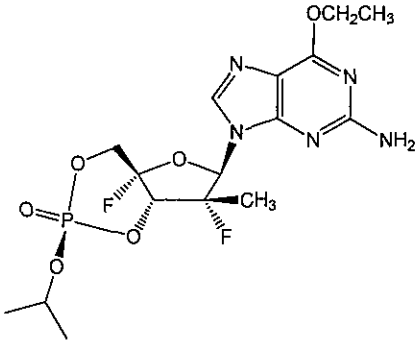

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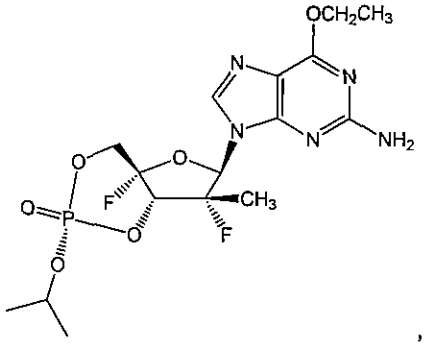

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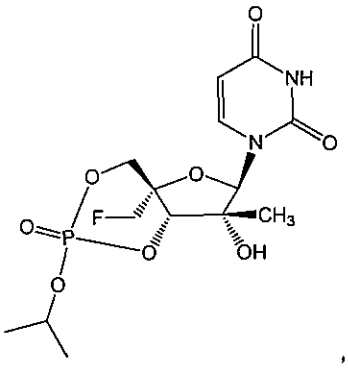

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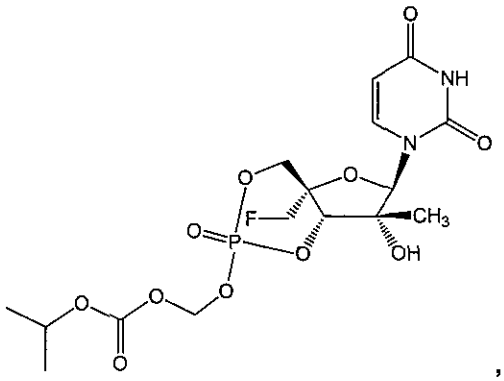

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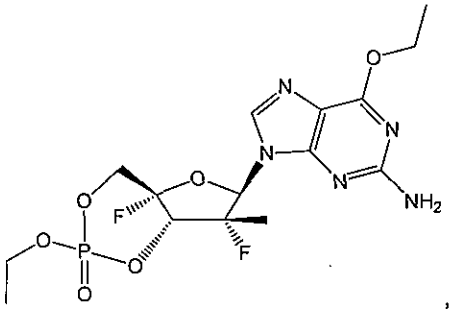

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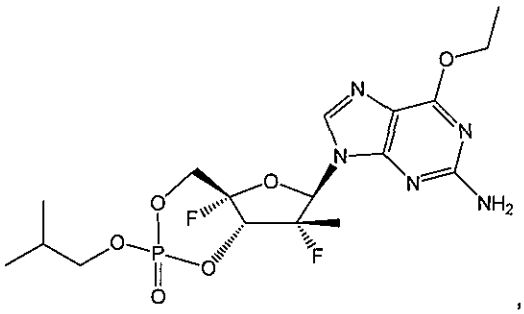

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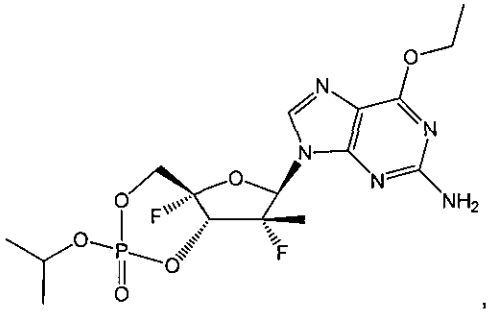

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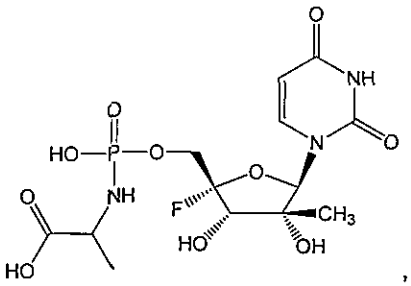

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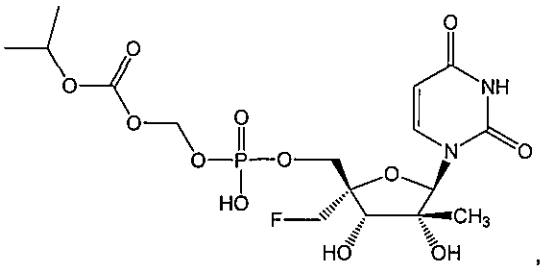

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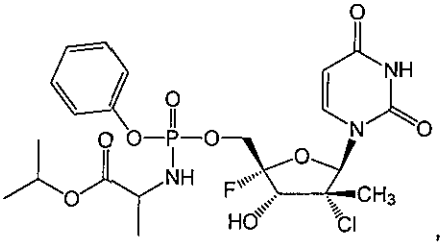

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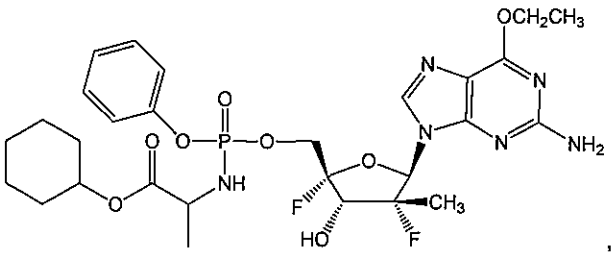

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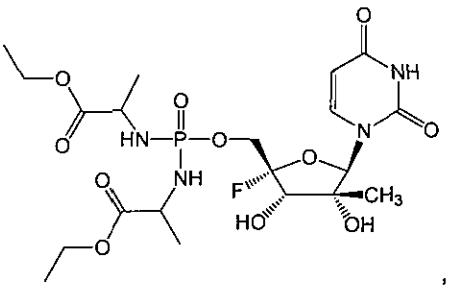

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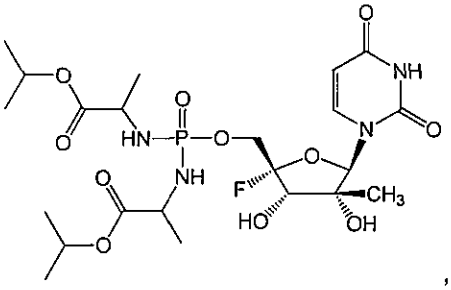

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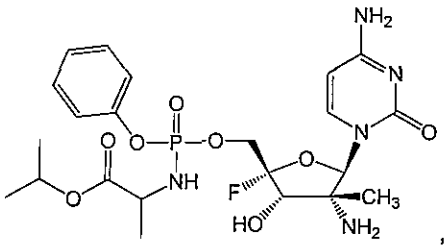

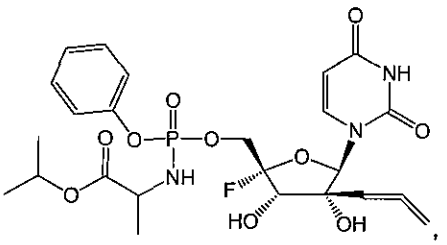

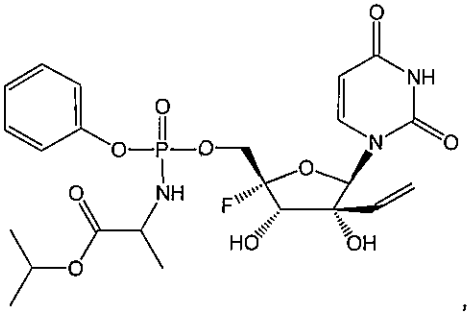

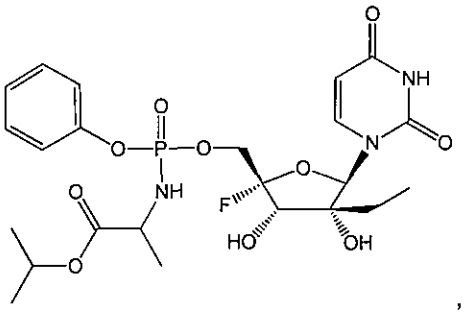

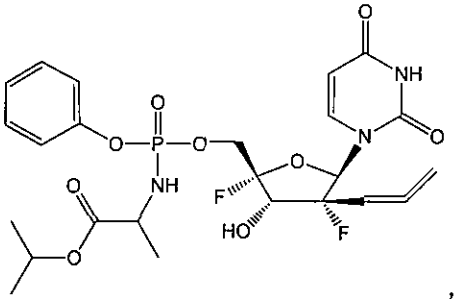

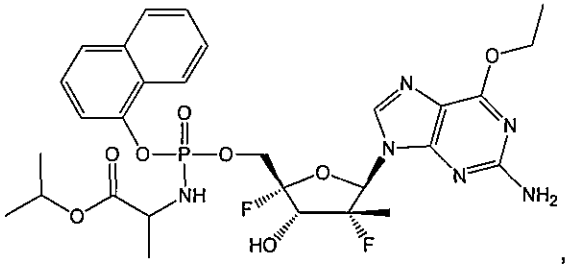

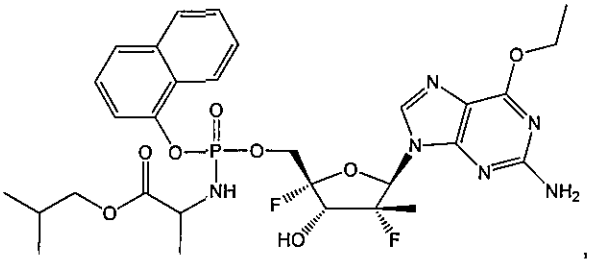

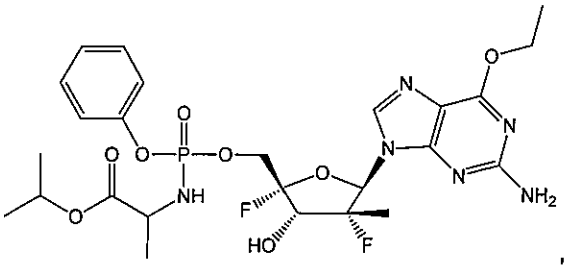

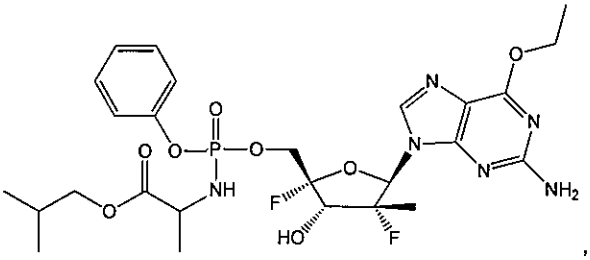

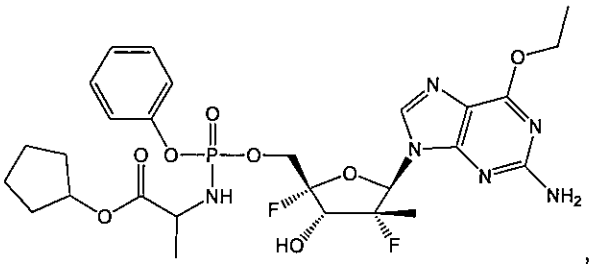

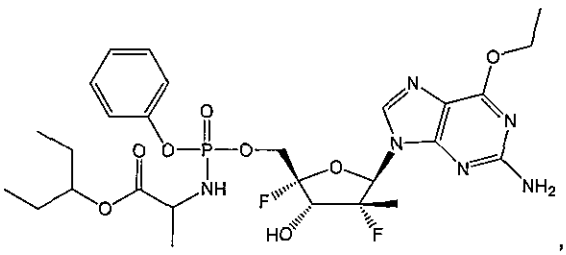
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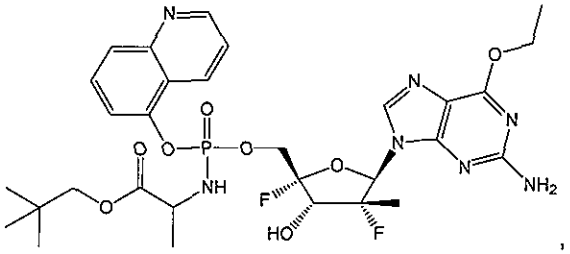
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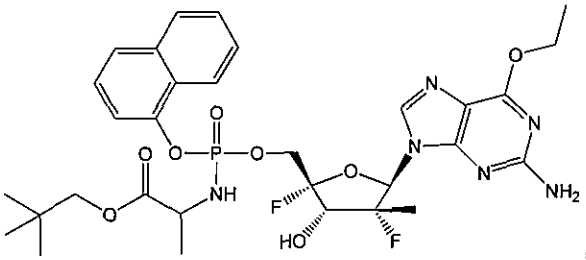
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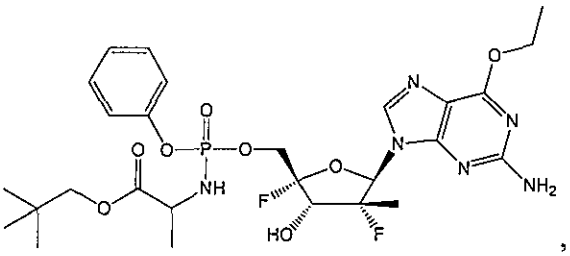
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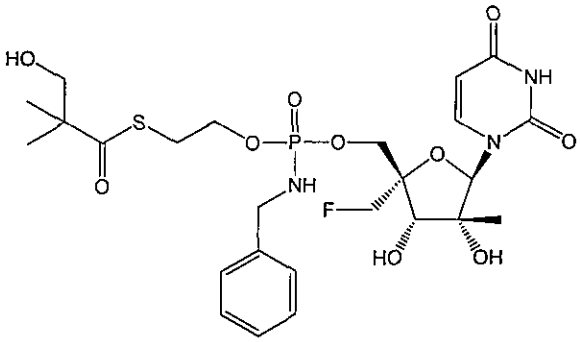
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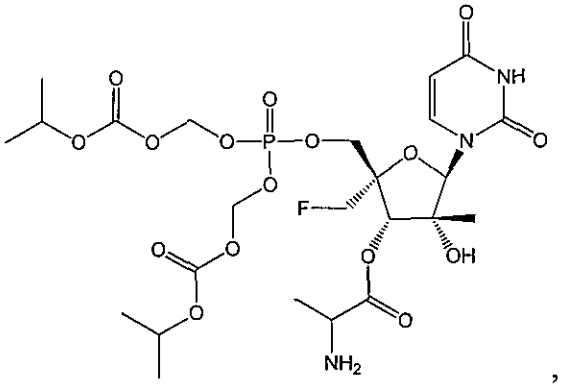
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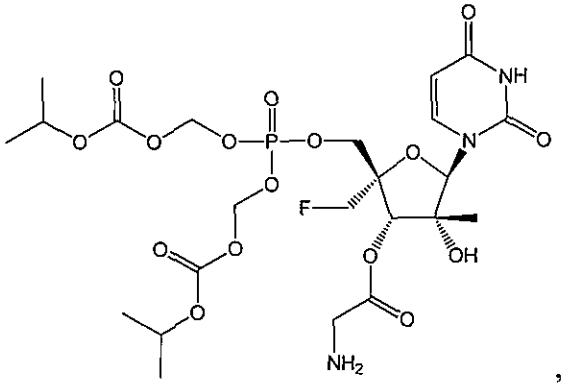
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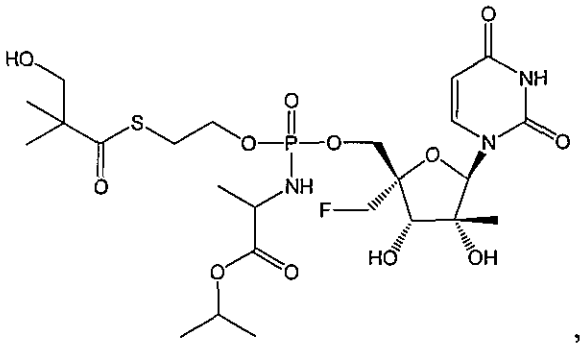
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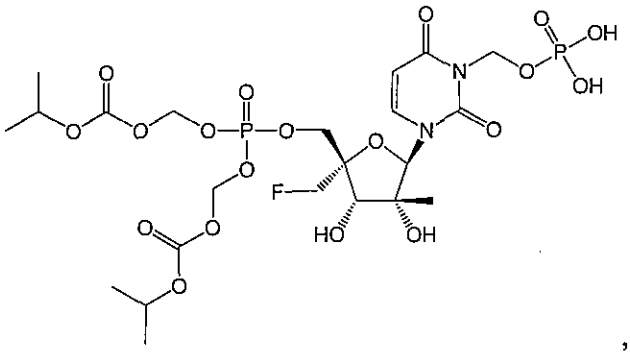
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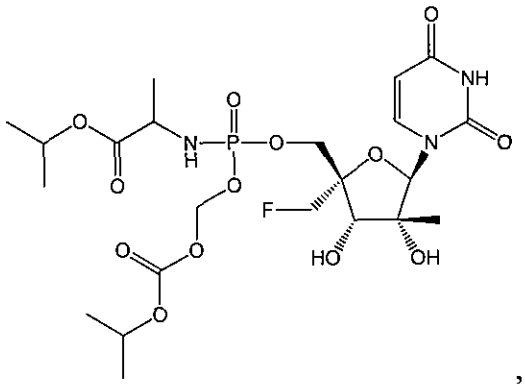
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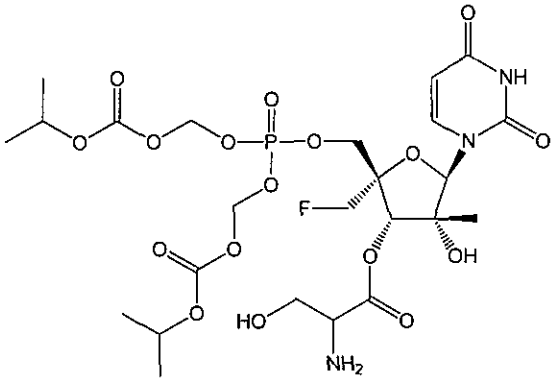
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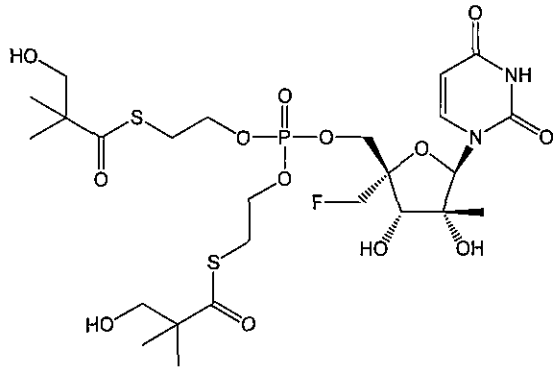
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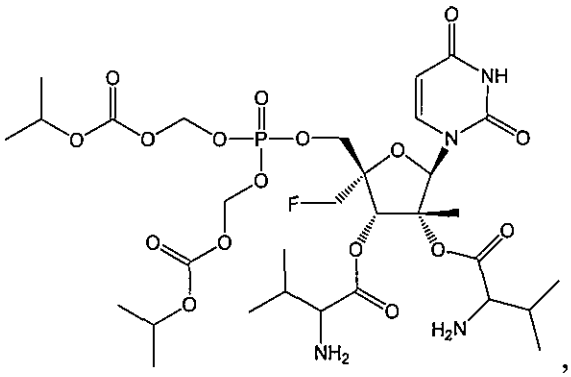
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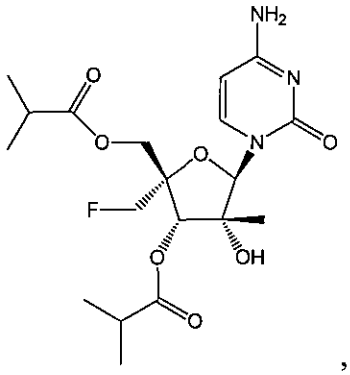
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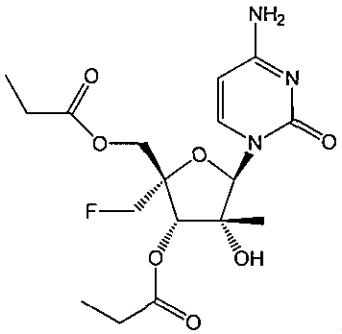
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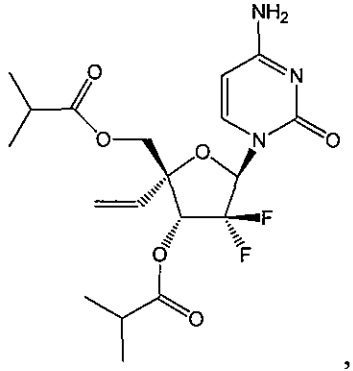
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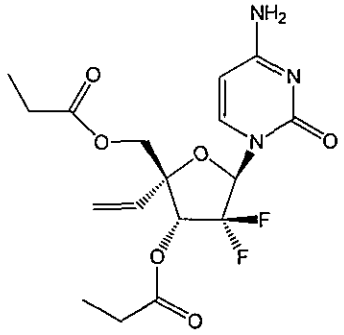
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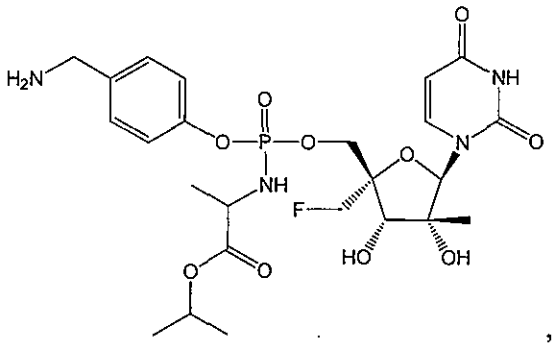
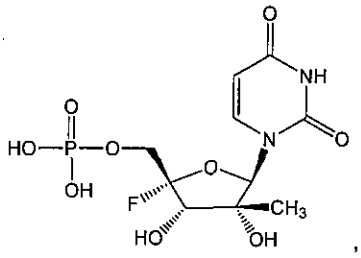


, or a pharmaceutically acceptable salt of the foregoing.

90. The use of Claim 1, wherein the compound is selected from the group consisting of: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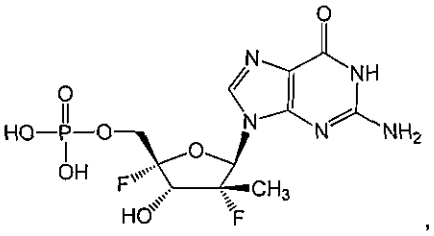
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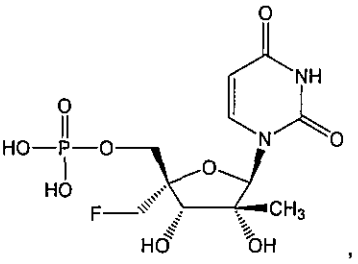
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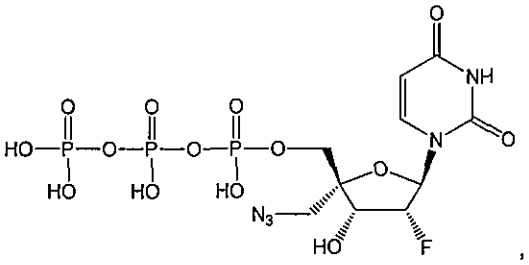
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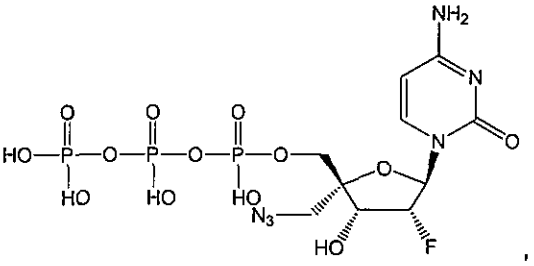
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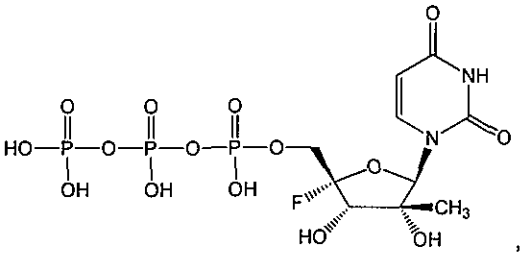
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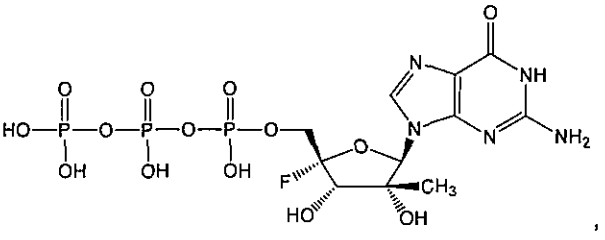
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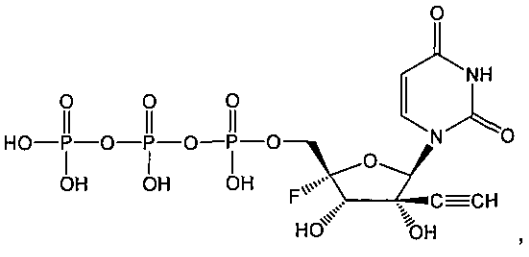
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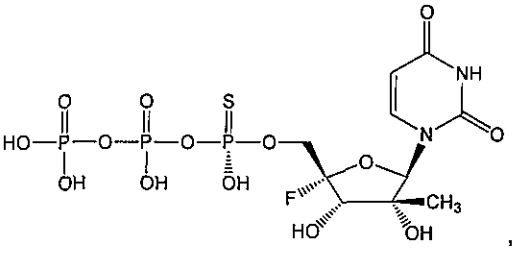
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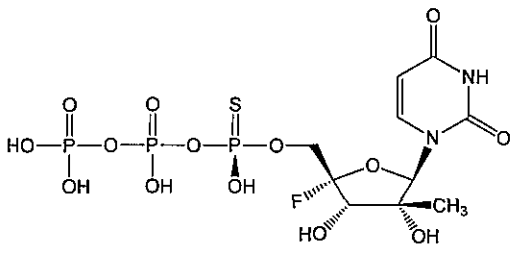

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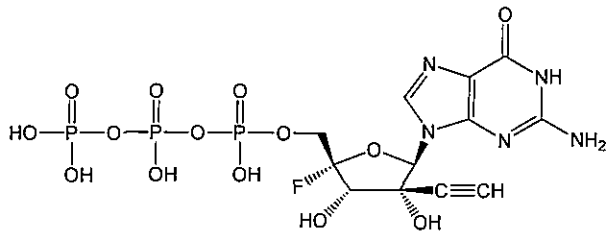

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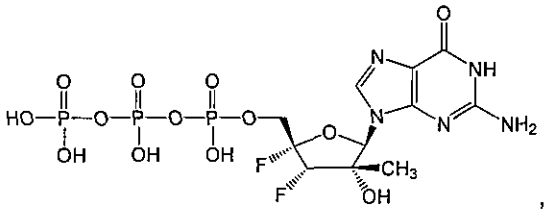

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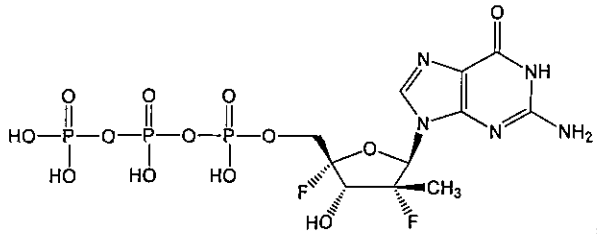

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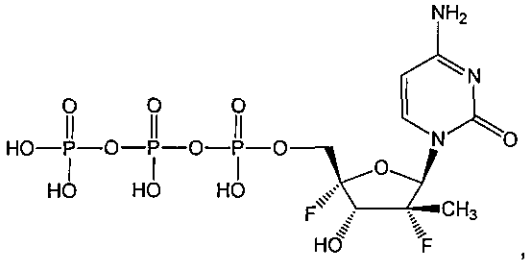

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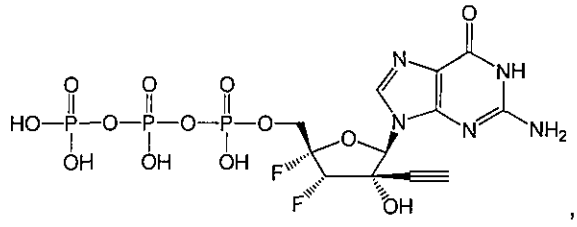

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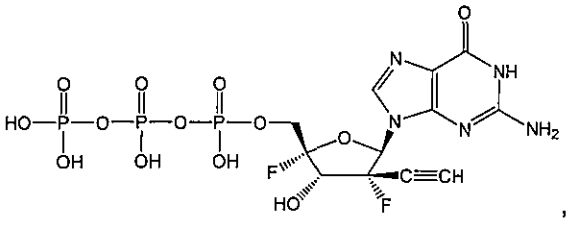

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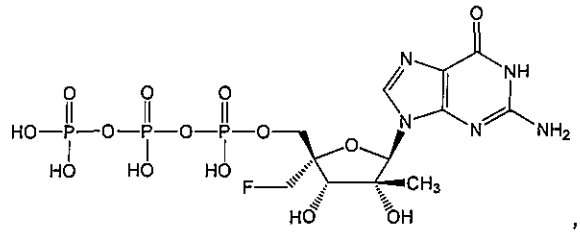

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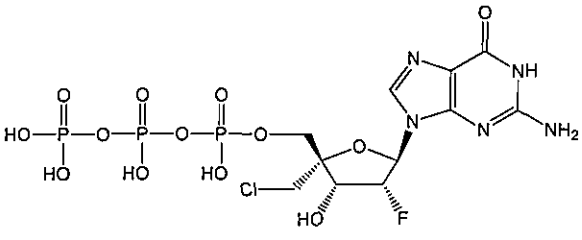

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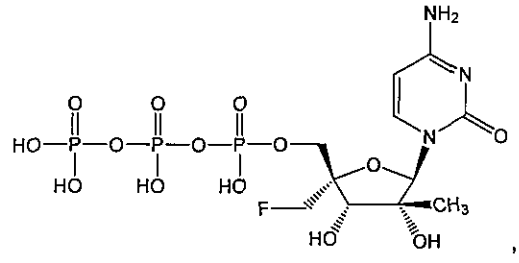

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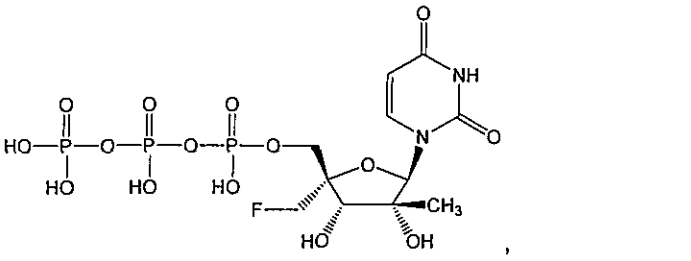

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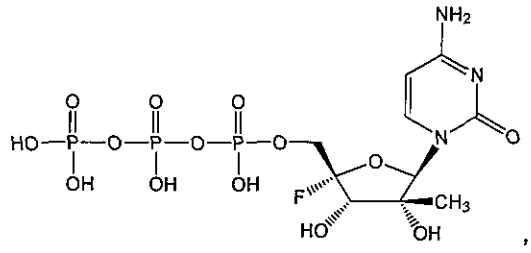

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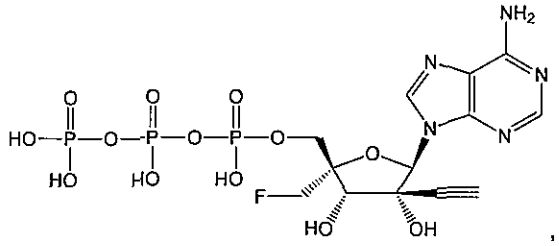

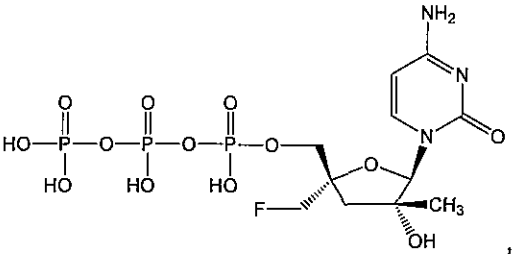

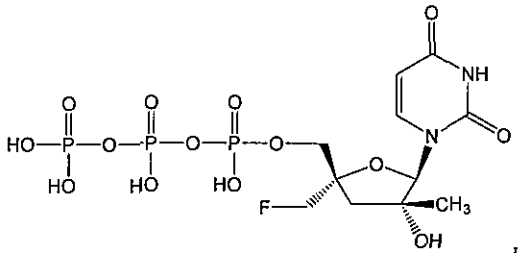

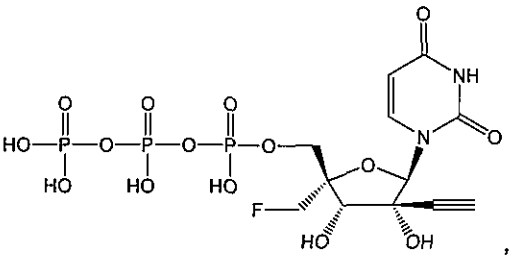

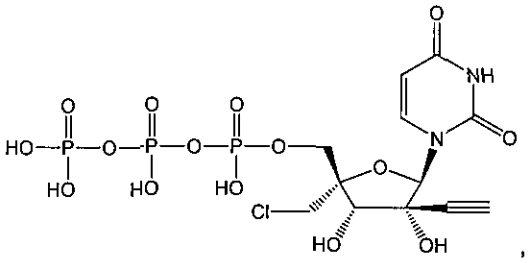

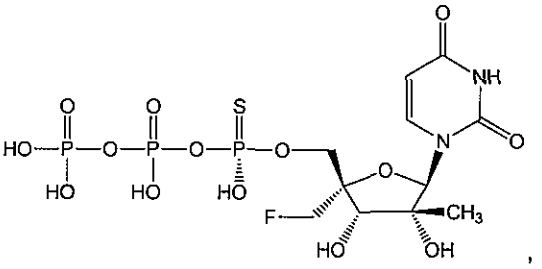

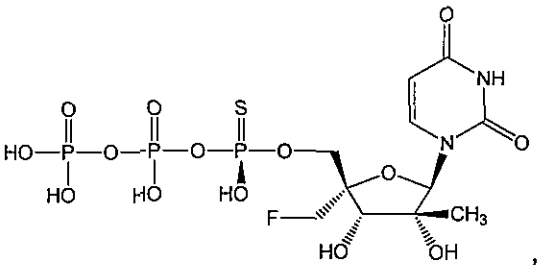

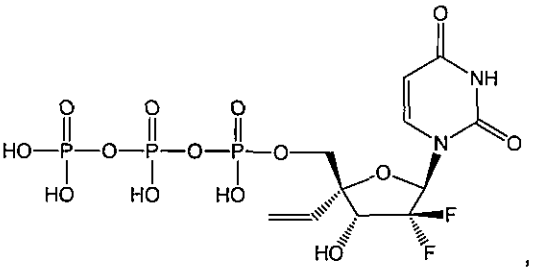

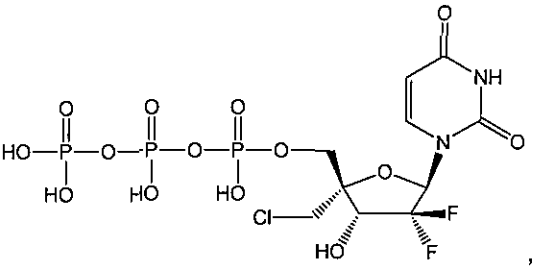

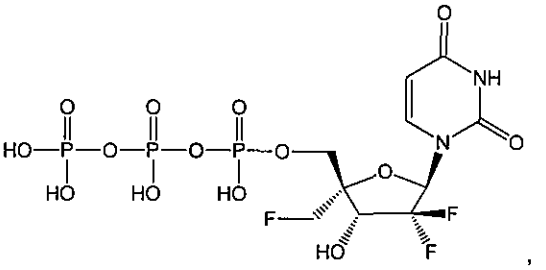

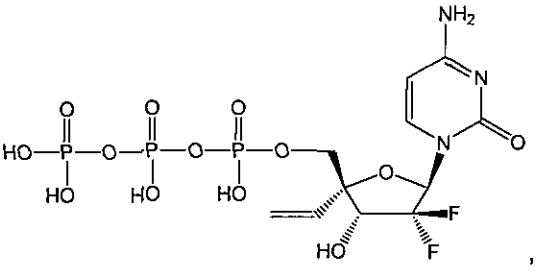

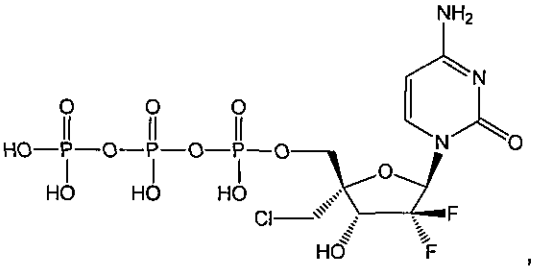

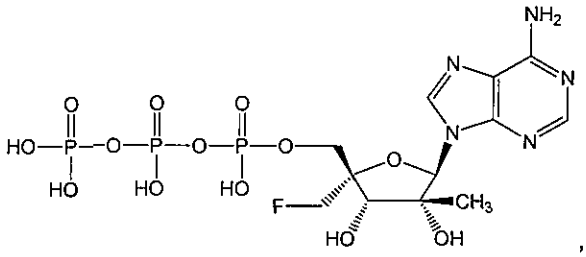

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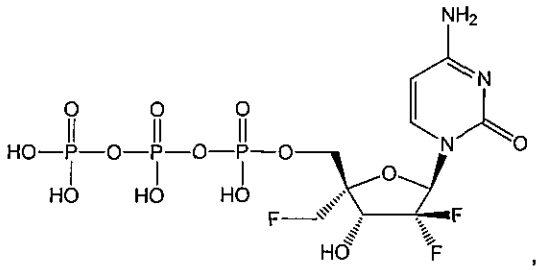

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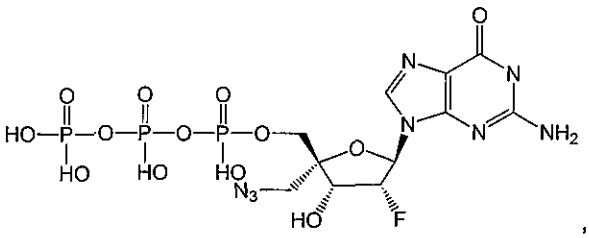

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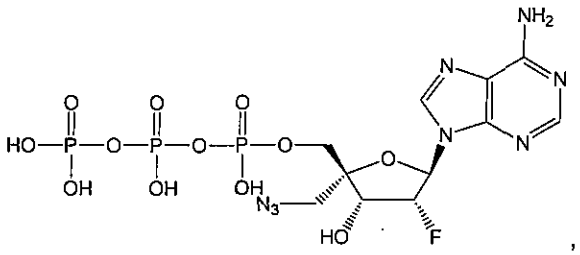

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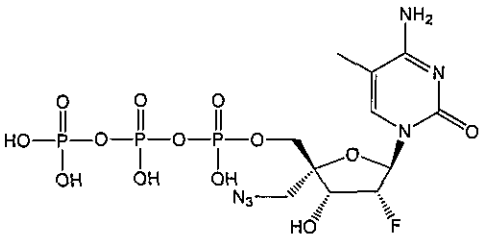

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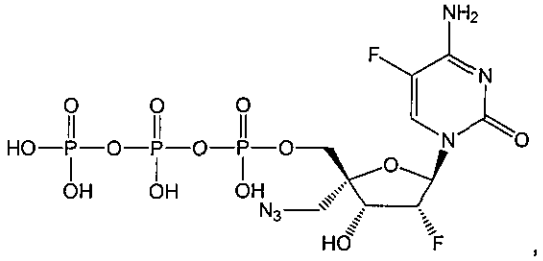

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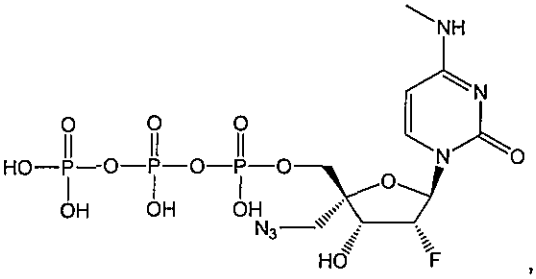

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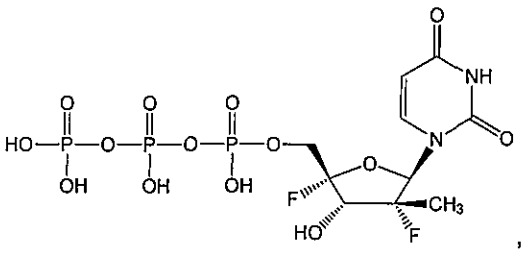

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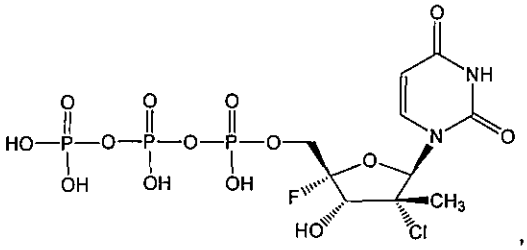

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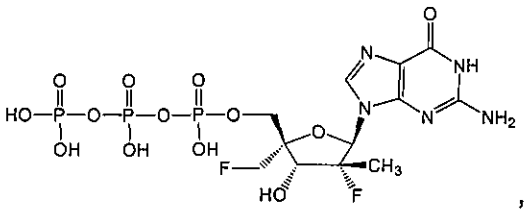

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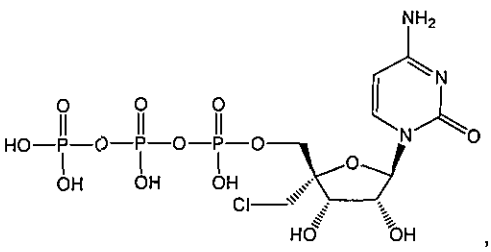

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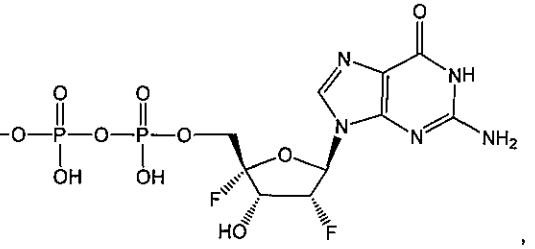

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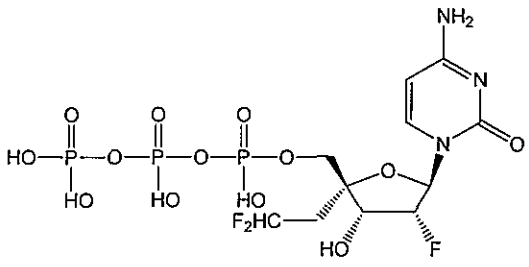

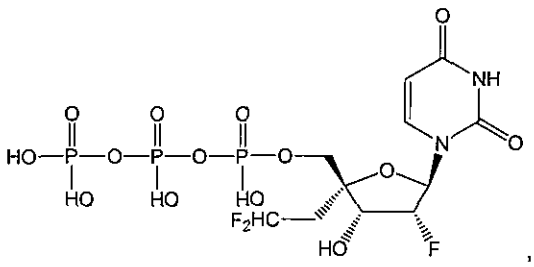

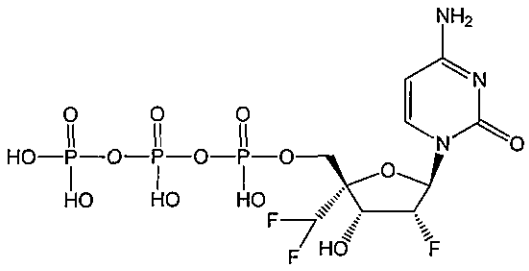

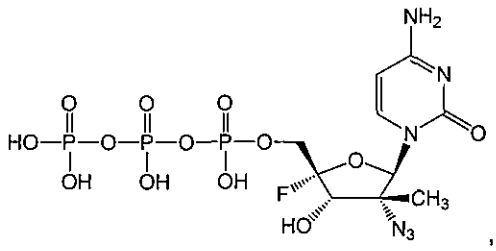

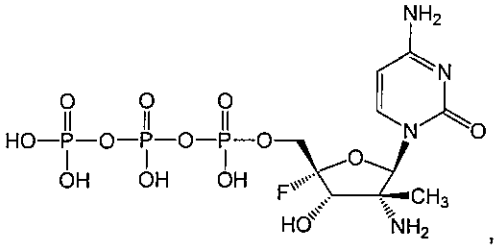

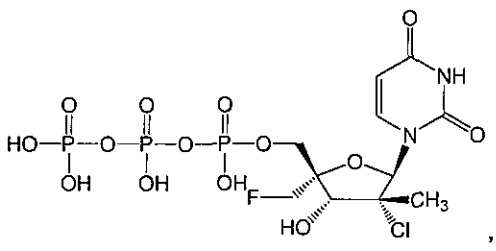

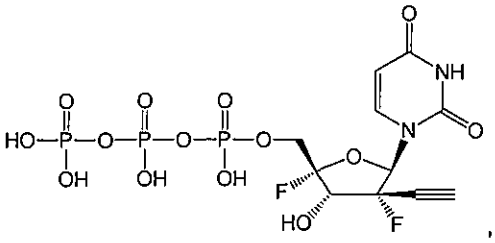

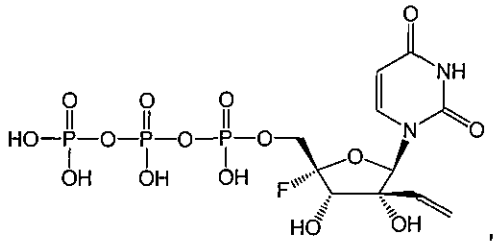

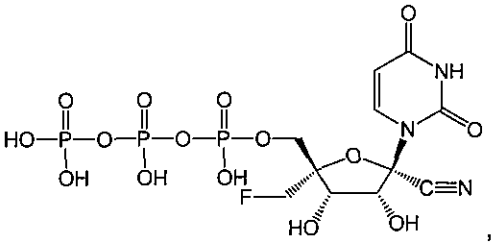

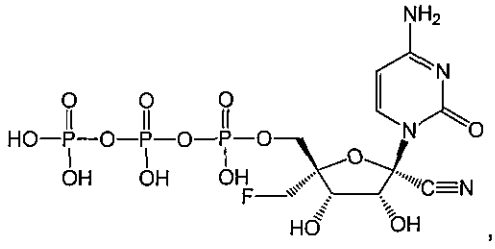

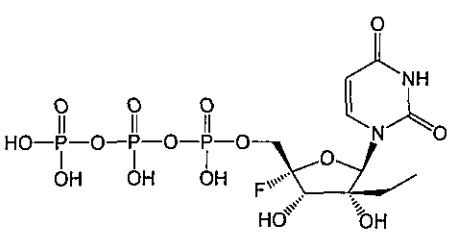

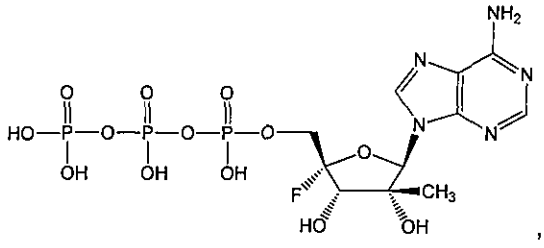

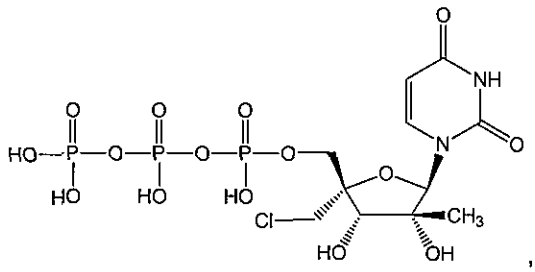

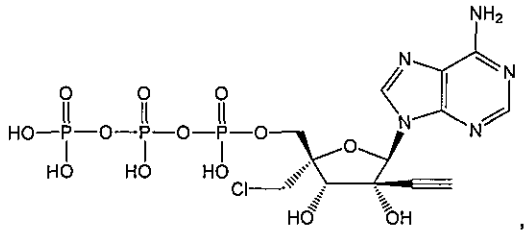

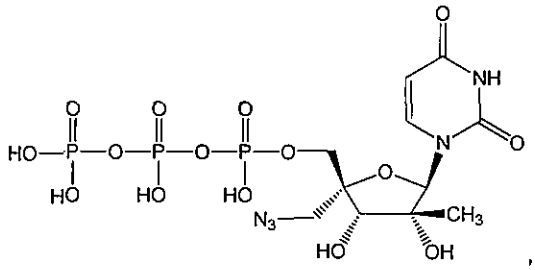

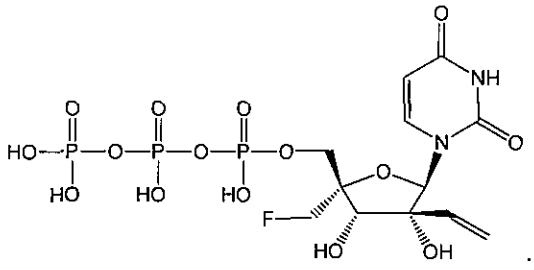

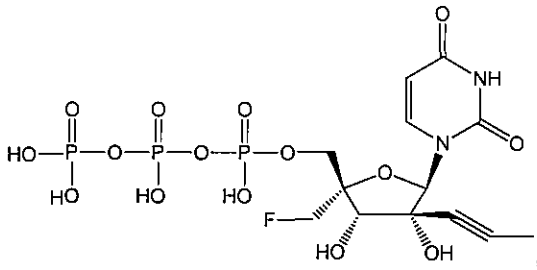

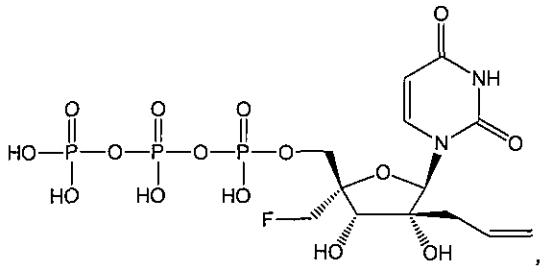

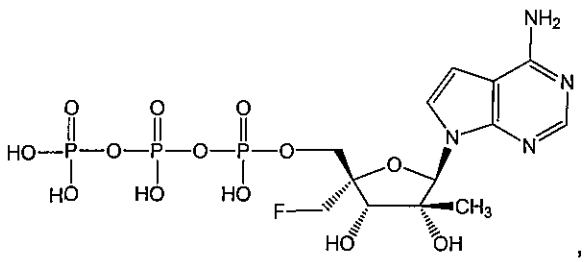

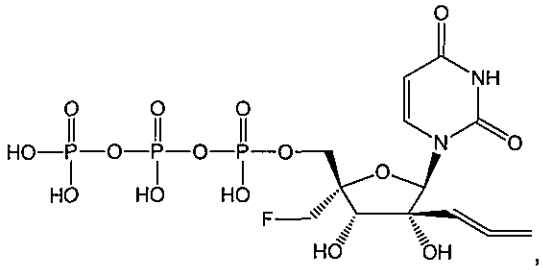

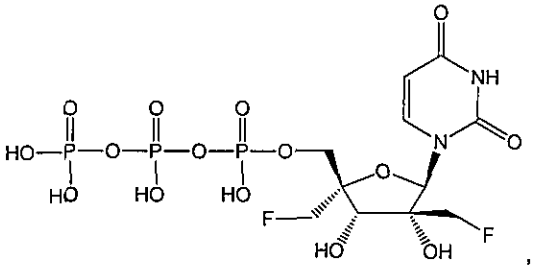

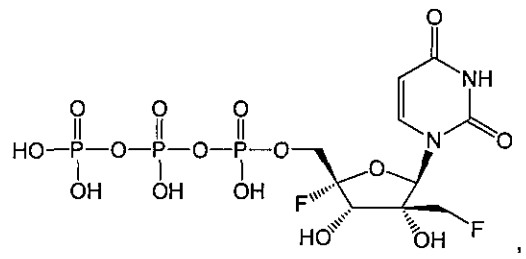

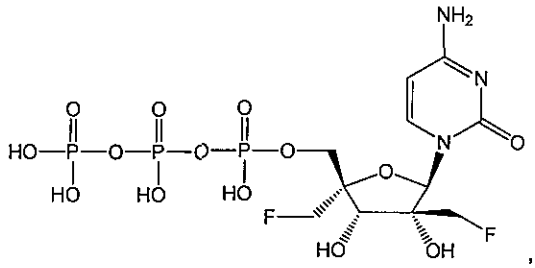
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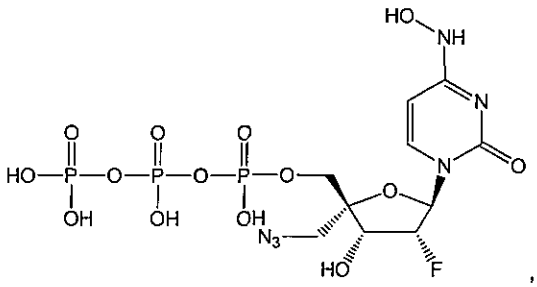
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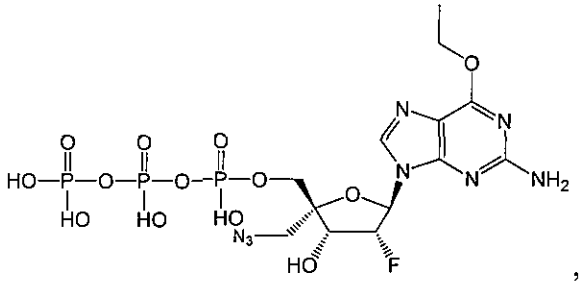
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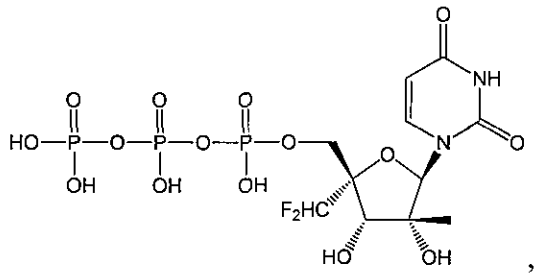
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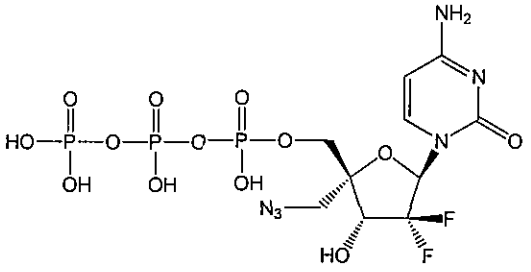
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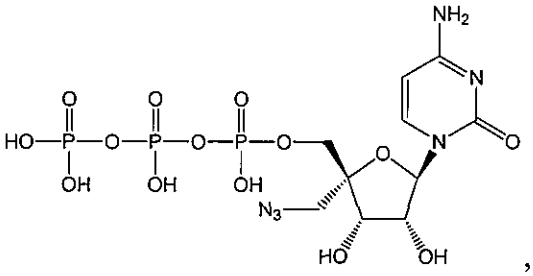
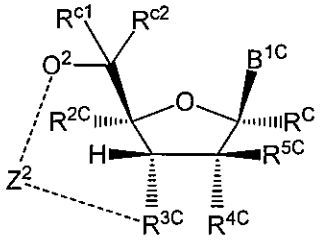

, or a pharmaceutically acceptable salt of the foregoing.

91. A compound of Formula (II), or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (II) has the structure:

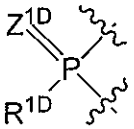


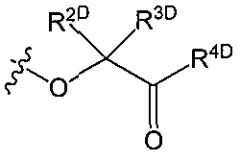
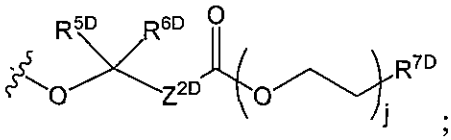
**(II)**

wherein:

$B^{1C}$ is an optionally substituted heterocyclic base or an optionally substituted heterocyclic base with a protected amino group;

when -------- are both absent, then $Z^2$ is absent, $O^2$ is $OR^{1C}$, and $R^{3C}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R''^{C}$ and an optionally substituted O-linked amino acid;

when -------- are each a single bond, then $Z^2$ is  , $O^2$ is O, $R^{3C}$ is O, $R^{2C}$ is halo, $-CHF_2$, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}Cl$, $-(CH_2)_{1-6}N_3$, $-(CH_2)_{1-6}NH_2$ or –CN, and $R^{1D}$ is selected from the group consisting of $O^-$, OH, an –O–optionally substituted $C_{1-6}$ alkyl,

 ,  ;

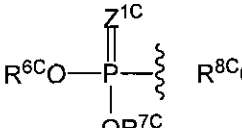
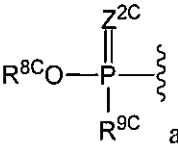
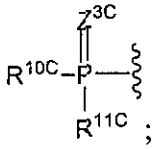
$R^{2C}$ is halo, an unsubstituted $C_{2-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, $-(CH_2)_{1-6}F$, $-(CH_2)_{1-6}NH_2$ or -CN, and $R^{5C}$ is selected from the group consisting of an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl, or

$R^{2C}$ is $-CHF_2$, $-(CH_2)_{1-6}Cl$ or $-(CH_2)_{1-6}N_3$, and $R^{5C}$ is selected from the group consisting of H, halo, OH, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{4C}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R^{"D}$, an optionally substituted O-linked amino acid and $NR^{"D1}R^{"D2}$, or $R^{3C}$ and $R^{4C}$ are both an oxygen atom connected via a carbonyl to form a 5-membered ring;

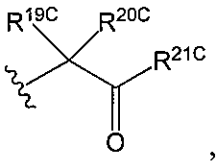
$R^{c1}$ and $R^{c2}$ are independently hydrogen or deuterium;

$R^C$ is hydrogen, deuterium, an unsubstituted $C_{1-3}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-3}$ alkynyl or cyano;

$R^{1C}$ is selected from the group consisting of hydrogen, an optionally substituted acyl, an optionally substituted O-linked amino acid,  ,  and  ;

$R^{6C}$, $R^{7C}$ and $R^{8C}$ are independently selected from the group consisting of absent, hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an

optionally substituted $C_{3-6}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aryl($C_{1-6}$ alkyl), an optionally substituted *–$(CR^{15C}R^{16C})_f$–O–$C_{1-24}$ alkyl, an optionally substituted *–$(CR^{17C}R^{18C})_g$–O–$C_{1-24}$ alkenyl,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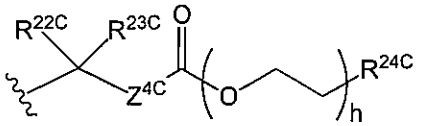
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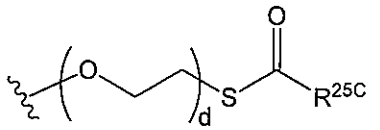
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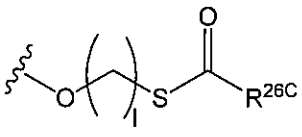
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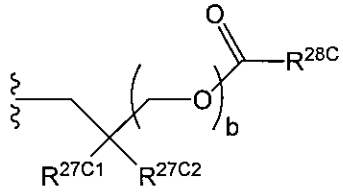
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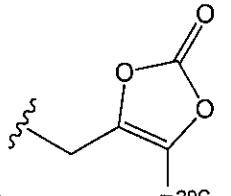
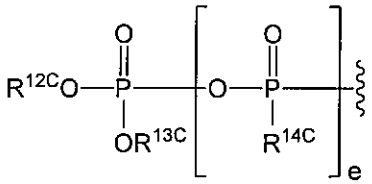
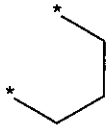
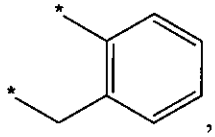

; or


$R^{6C}$ is and $R^{7C}$ is absent or hydrogen; or

$R^{6C}$ and $R^{7C}$ are taken together to form a moiety selected from the group consisting of an optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6C}$ and $R^{7C}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;.

$R^{9C}$ is independently selected from the group consisting of an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl, $NR^{30C}R^{31C}$, an optionally substituted N-linked amino acid and an optionally substituted N-linked amino acid ester derivative;

$R^{10C}$ and $R^{11C}$ are independently an optionally substituted N-linked amino acid or an optionally substituted N-linked amino acid ester derivative;

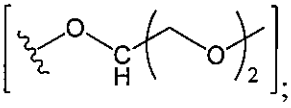
$R^{12C}$ and $R^{13C}$ are independently absent or hydrogen;

$R^{14C}$ is $O^-$, OH or methyl;

each $R^{15C}$, each $R^{16C}$, each $R^{17C}$ and each $R^{18C}$ are independently hydrogen, an optionally substituted $C_{1-24}$ alkyl or an alkoxy;

$R^{19C}$, $R^{20C}$, $R^{22C}$ and $R^{23C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{21C}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

$R^{24C}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted –O–$C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl and  ;

$R^{25C}$, $R^{26C}$ and $R^{29C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl and an optionally substituted aryl;

$R^{27C1}$ and $R^{27C2}$ are independently selected from the group consisting of -C≡N, an optionally substituted $C_{2-8}$ organylcarbonyl, an optionally substituted $C_{2-8}$ alkoxycarbonyl and an optionally substituted $C_{2-8}$ organylaminocarbonyl;

$R^{28C}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl and an optionally substituted $C_{3-6}$ cycloalkenyl;

$R^{30C}$ and $R^{31C}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted $C_{2-24}$ alkenyl, an optionally substituted $C_{2-24}$ alkynyl, an optionally substituted $C_{3-6}$ cycloalkyl, an optionally substituted $C_{3-6}$ cycloalkenyl and an optionally substituted aryl($C_{1-4}$ alkyl);

$R''^{C}$ and each $R''^{D}$ are independently an optionally substituted $C_{1-24}$ alkyl;

each $R''^{D1}$ and each $R''^{D2}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{2D}$, $R^{3D}$, $R^{5D}$ and $R^{6D}$ are independently hydrogen or an optionally substituted $C_{1-24}$ alkyl;

$R^{4D}$ and $R^{7D}$ are independently selected from the group consisting of hydrogen, an optionally substituted $C_{1-24}$ alkyl, an optionally substituted aryl, an optionally substituted $-O-C_{1-24}$ alkyl, an optionally substituted –O–aryl, an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl;

d and e are independently 0 or 1;

f and g are independently 1, 2 or 3;

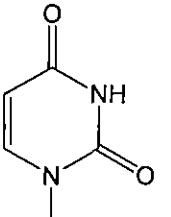
h and j are independently 0, 1, 2 or 3;

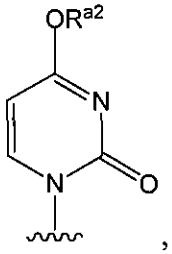
b is 1 or 2;

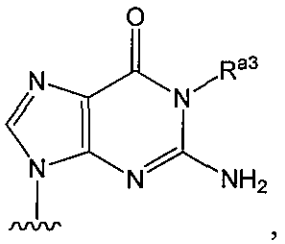
l is 3, 4 or 5; and

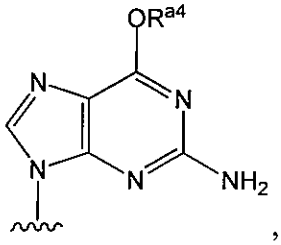
$Z^{1C}$, $Z^{2C}$, $Z^{3C}$, $Z^{4C}$, $Z^{1D}$ and $Z^{2D}$ are independently O or S;

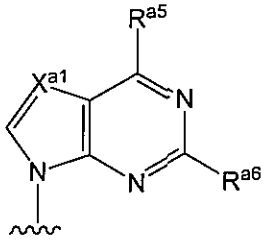
provided that when $R^{2C}$ is halo; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$;

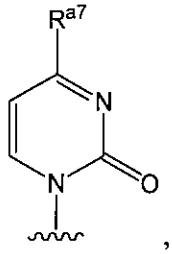
$B^{1C}$ is selected from the group consisting of an optionally substituted 

, an optionally substituted 

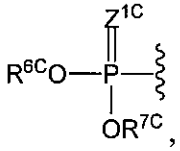
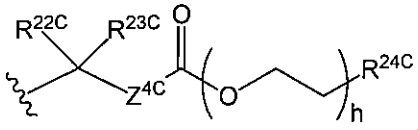
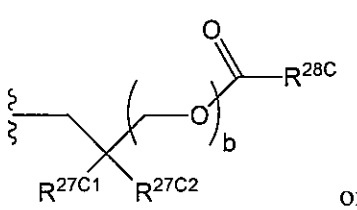
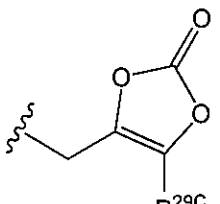
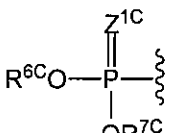
, an optionally substituted 

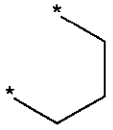
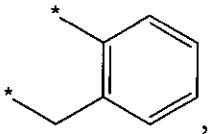
, an optionally substituted 

, an optionally substituted 

and an optionally substituted 

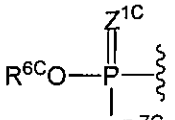
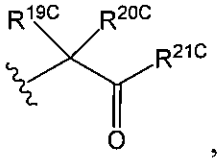
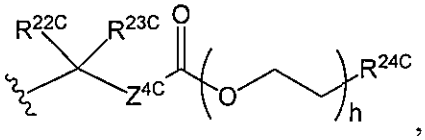
, wherein $R^{a2}$ is an optionally substituted $C_{1-6}$ alkyl or an optionally substituted $C_{3-6}$ cycloalkyl, $R^{a3}$ and $R^{a4}$

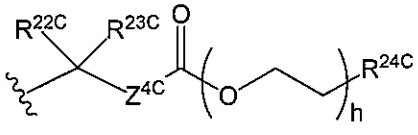
are independently selected from the group consisting of hydrogen, an unsubstituted $C_{1-6}$ alkyl, an unsubstituted $C_{3-6}$ alkenyl, an unsubstituted $C_{3-6}$ alkynyl and an unsubstituted $C_{3-6}$ cycloalkyl, $R^{a5}$ is $NHR^{a8}$, and $R^{a6}$ is hydrogen, halogen or $NHR^{a9}$; $R^{a7}$ is $NHR^{a10}$; $R^{a8}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a11}$ and $-C(=O)OR^{a12}$; $R^{a9}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a13}$ and $-C(=O)OR^{a14}$; $R^{a10}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-6}$ alkenyl, an optionally substituted $C_{3-6}$ cycloalkyl, $-C(=O)R^{a15}$ and $-C(=O)OR^{a16}$; $X^{a1}$ is N or $-CR^{a17}$; $R^{a17}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl; $R^{a11}$, $R^{a12}$, $R^{a13}$, $R^{a14}$, $R^{a15}$ and $R^{a16}$ are independently selected from the group consisting of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl); then $R^{3C}$ is selected from the group consisting of H, halo and an optionally substituted O-linked amino acid; and $R^{4C}$ is selected from the group consisting of OH, halo, $N_3$, $-OC(=O)R^{"D}$, an optionally substituted O-linked amino acid and $NR^{"D1}R^{"D2}$; or then $R^{3C}$ is selected from the group consisting of H, halo, OH, $-OC(=O)R^{"C}$ and an optionally substituted O-linked amino acid and $R^{4C}$ is an optionally substituted O-linked amino acid; or then $R^{1C}$ is  , wherein $R^{6C}$ and $R^{7C}$ are independently  , wherein h is 1, 2 or 3,  or  ; or then $R^{1C}$ is  , wherein $R^{6C}$ and $R^{7C}$ are taken together to form a moiety selected from the group consisting of an

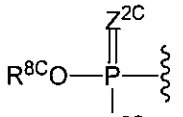
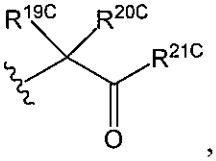
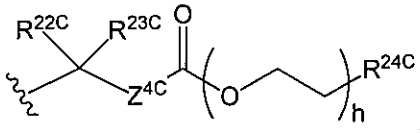
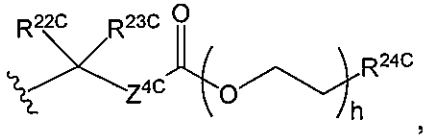
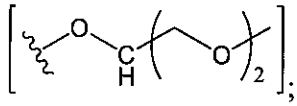
optionally substituted  and an optionally substituted  , wherein the oxygens connected to $R^{6C}$ and $R^{7C}$, the phosphorus and the moiety form a six-membered to ten-membered ring system;

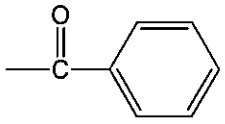
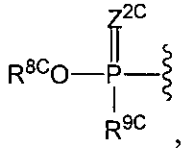
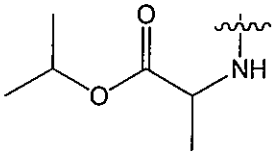
provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, —$(CH_2)_{1-6}$ halogen,–$(CH_2)_{1-6}N_3$ or –$(CH_2)_{1-6}NH_2$; ------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, –OC(=O)R"$^C$ or an optionally substituted O-linked amino acid; and $R^{4C}$ is halo; then $R^{5C}$ is selected from the group consisting of an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl, —$(CH_2)_{1-6}$ halogen, –$(CH_2)_{1-6}N_3$ or –$(CH_2)_{1-6}NH_2$; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{4C}$ is halo; and $R^{5C}$ is H or halo; then $R^{3C}$ is H or halo;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl or —$(CH_2)_{1-6}$ halogen; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, –OC(=O)R"$^C$ or an optionally substituted O-linked amino acid; $R^{4C}$ is halo; $R^{5C}$ is H or halo; and $R^{1C}$ is  then at least one of $R^{6C}$ and $R^{7C}$ is  , wherein $R^{21C}$ is independently selected from the group consisting of an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl; or then at least one of $R^{6C}$ and $R^{7C}$ is  , wherein s is 1, 2 or 3; or then at least one of $R^{6C}$ and $R^{7C}$ is


, wherein s is 0 and $R^{24C}$ is an optionally substituted –O–heteroaryl or an optionally substituted –O–monocyclic heterocyclyl;

provided that when $R^{2C}$ is an unsubstituted $C_{1-4}$ alkyl, an unsubstituted $C_{2-4}$ alkenyl, an unsubstituted $C_{2-4}$ alkynyl or —$(CH_2)_{1-6}$halogen; -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{3C}$ is OH, –OC(=O)$R^{"C}$ or an optionally substituted O-linked amino acid; $R^{4C}$ is halo; $R^{5C}$ is H or halo; and $R^{1C}$ is  ; then $R^{8C}$ is  , wherein $R^{21C}$ is independently selected from the group consisting of an optionally substituted –O–heteroaryl and an optionally substituted –O–monocyclic heterocyclyl; or then $R^{8C}$ is  , wherein s is 1, 2 or 3; or then $R^{8C}$ is  , wherein s is 0 and $R^{24C}$ is an optionally substituted –O–heteroaryl, an optionally substituted –O–monocyclic heterocyclyl or  ; and

provided that when -------- are both absent; $Z^2$ is absent; $O^2$ is $OR^{1C}$; $R^{2C}$ is fluoro; $R^{3C}$ is OH or –OC(=O)$R^{"C}$; $R^{4C}$ is fluoro; and $R^{5C}$ is methyl, ethyl or ethenyl; then $R^{1C}$ cannot be selected from the group consisting of H,  and  ,  wherein $R^{8C}$ is an unsubstituted aryl; $R^{9C}$ is and $Z^{2C}$ is oxygen.

92. The compound of Claim 91, wherein $R^{2C}$ is halo.

93. The compound of Claim 92, wherein the halo is fluoro.

94. The compound of Claim 91, wherein $R^{2C}$ is an unsubstituted $C_{2-4}$ alkyl.

95. The compound of Claim 91, wherein $R^{2C}$ is an unsubstituted $C_{2-4}$ alkenyl.

96. The compound of Claim 91, wherein $R^{2C}$ is $-CHF_2$.

97. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}F$.

98. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}Cl$.

99. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}N_3$.

100. The compound of Claim 91, wherein $R^{2C}$ is $-(CH_2)_{1-6}NH_2$.

101. The compound of Claim 91, wherein $R^{2C}$ is –CN.

102. The compound of any one of Claims 91-101, wherein $R^{3C}$ is halo.

103. The compound of Claim 102, wherein the halo is F.

104. The compound of Claim 102, wherein the halo is Cl.

105. The compound of any one of Claims 91-101, wherein $R^{3C}$ is H.

106. The compound of any one of Claims 91-105, wherein $R^{4C}$ is halo.

107. The compound of Claim 106, wherein the halo is fluoro.

108. The compound of any one of Claims 91-105, wherein $R^{4C}$ is OH.

109. The compound of any one of Claims 91-105, wherein $R^{4C}$ is $-OC(=O)R^{"D}$ or an optionally substituted O-linked amino acid.

110. The compound of any one of Claims 91-105, wherein $R^{4C}$ is $N_3$, or $NR^{"D1}R^{"D2}$.

111. The compound of Claim 110, wherein $R^{4C}$ is $NH_2$.

112. The compound of any one of Claims 91, 96, 98 or 102-111, wherein $R^{5C}$ is H.

113. The compound of any one of Claims 91, 96, 98 or 102-111, wherein $R^{5C}$ is halo.

114. The compound of any one of Claims 91-111, wherein $R^{5C}$ is OH.

115. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{1-6}$ alkyl.

116. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{2-6}$ alkenyl.

117. The compound of any one of Claims 91-111, wherein $R^{5C}$ is an optionally substituted $C_{2-6}$ alkynyl.

118. The compound of any one of Claims 91-117, wherein $R^{C}$ is hydrogen.

119. The compound of any one of Claims 91-117, wherein $R^{C}$ is deuterium.

120. The compound of any one of Claims 91-117, wherein $R^C$ is an unsubstituted $C_{1-3}$ alkyl.

121. The compound of any one of Claims 91-117, wherein $R^C$ is an unsubstituted $C_{2-4}$ alkenyl.

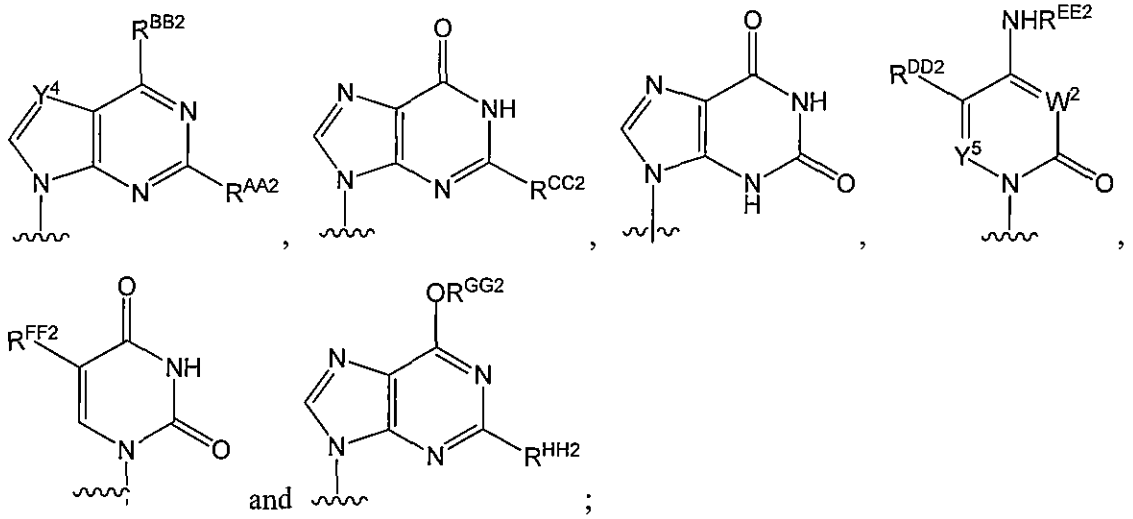
122. The compound of any one of Claims 91-117, wherein $R^C$ is an unsubstituted $C_{2-3}$ alkynyl.

123. The compound of any one of Claims 91-117, wherein $R^C$ is cyano.

124. The compound of any one of Claims 91-123, wherein $R^{c1}$ and $R^{c2}$ are both hydrogen.

125. The compound of any one of Claims 91-123, wherein $R^{c1}$ and $R^{c2}$ are both deuterium.

126. The compound of any one of Claims 91-125, wherein $B^{1C}$ is selected from the group consisting of:




;

wherein:

$R^{AA2}$ is selected from the group consisting of hydrogen, halogen and $NHR^{JJ2}$, wherein $R^{JJ2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{KK2}$ and $-C(=O)OR^{LL2}$;

$R^{BB2}$ is halogen or $NHR^{WW2}$, wherein $R^{WW2}$ is selected from the group consisting of hydrogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{MM2}$ and $-C(=O)OR^{NN2}$;

$R^{CC2}$ is hydrogen or $NHR^{OO2}$, wherein $R^{O2}$ is selected from the group consisting of hydrogen, $-C(=O)R^{PP2}$ and $-C(=O)OR^{QQ2}$;

$R^{DD2}$ is selected from the group consisting of hydrogen, deuterium, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

$R^{EE2}$ is selected from the group consisting of hydrogen, hydroxy, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{3-8}$ cycloalkyl, $-C(=O)R^{RR2}$ and $-C(=O)OR^{SS2}$;

$R^{FF2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$alkyl, an optionally substituted $C_{2-6}$ alkenyl and an optionally substituted $C_{2-6}$ alkynyl;

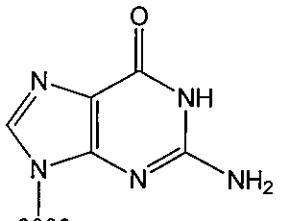
$Y^4$ and $Y^5$ are independently N or $CR^{II2}$, wherein $R^{II2}$ is selected from the group consisting of hydrogen, halogen, an optionally substituted $C_{1-6}$ alkyl, an optionally substituted $C_{2-6}$-alkenyl and an optionally substituted $C_{2-6}$-alkynyl;

$W^2$ is NH, $-NCH_2$-$OC(=O)CH(NH_2)$-$CH(CH_3)_2$ or $-(CH_2)_{1-2}-O-P(=O)(OW^{2C})_2$, wherein $W^{2C}$ is selected from the group consisting of absent, hydrogen and an optionally substituted $C_{1-6}$ alkyl;

$R^{GG2}$ is an optionally substituted $C_{1-6}$ alkyl;

$R^{HH2}$ is hydrogen or $NHR^{TT2}$, wherein $R^{TT2}$ is independently selected from the group consisting of hydrogen, $-C(=O)R^{UU2}$ and $-C(=O)OR^{VV2}$; and

$R^{KK2}$, $R^{LL2}$, $R^{MM2}$, $R^{NN2}$, $R^{PP2}$, $R^{QQ2}$ $R^{RR2}$, $R^{SS2}$, $R^{UU2}$ and $R^{VV2}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkenyl, $C_{6-10}$ aryl, heteroaryl, heterocyclyl, aryl($C_{1-6}$ alkyl), heteroaryl($C_{1-6}$ alkyl) and heterocyclyl($C_{1-6}$ alkyl).

127. The compound of Claim 126, wherein $B^{1C}$ is 

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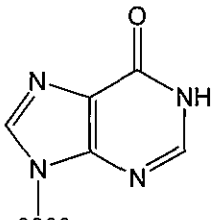
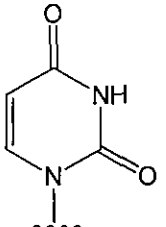
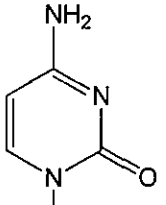
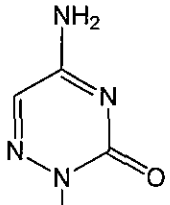
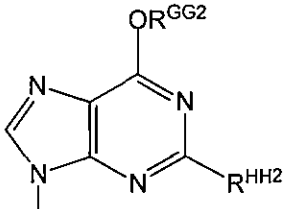
128. The compound of Claim 126, wherein $B^{1C}$ is  .

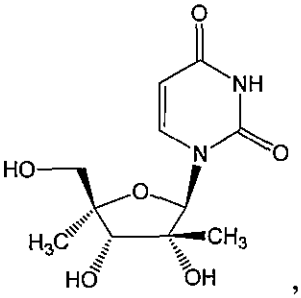
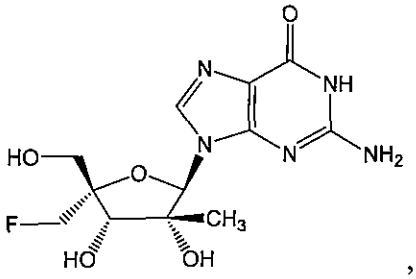
129. The compound of Claim 126, wherein $B^{1C}$ is  .

130. The compound of Claim 126, wherein $B^{1C}$ is  .

131. The compound of Claim 126, wherein $B^{1C}$ is  .

132. The compound of Claim 127, wherein $B^{1C}$ is  .

133. A compound selected from the group consisting of:


,

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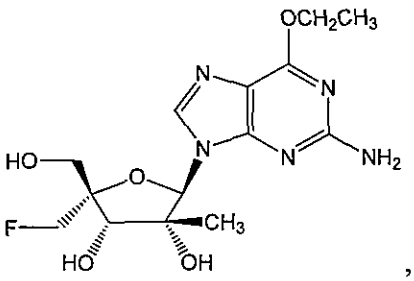
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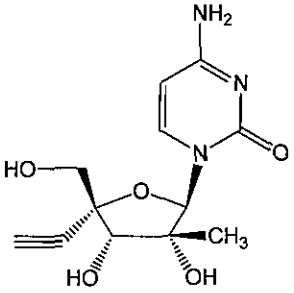
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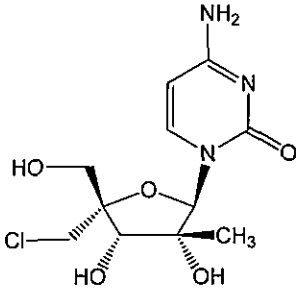
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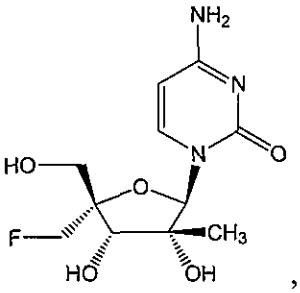
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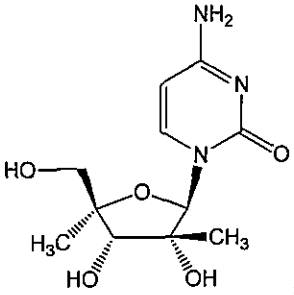
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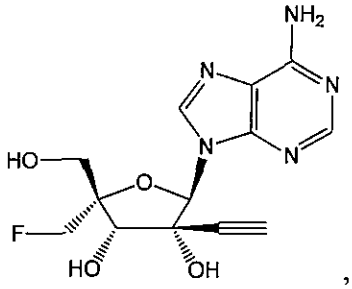
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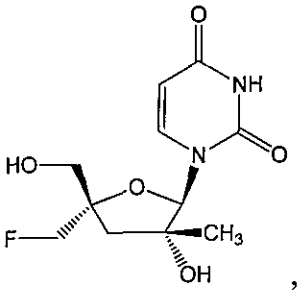
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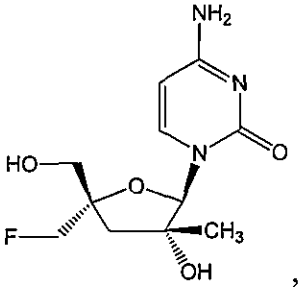
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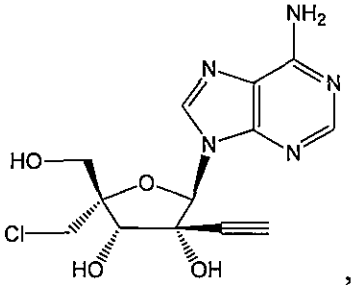
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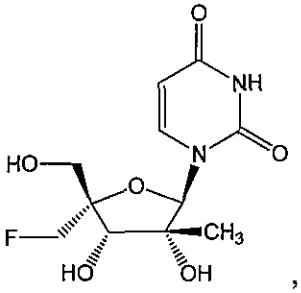
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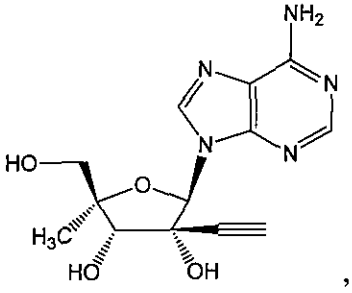
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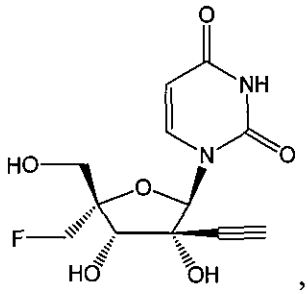
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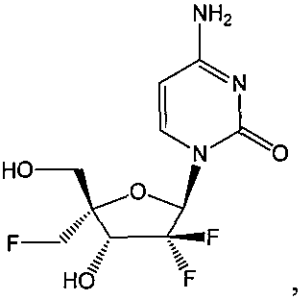

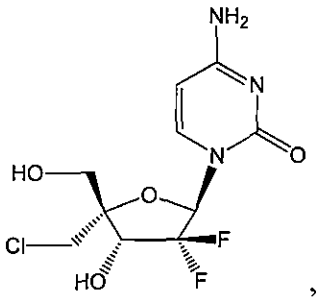
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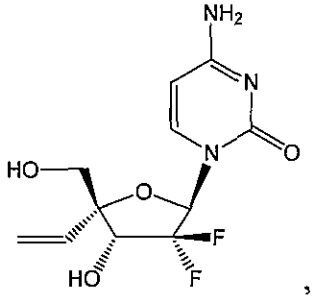
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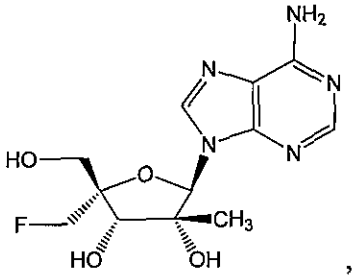
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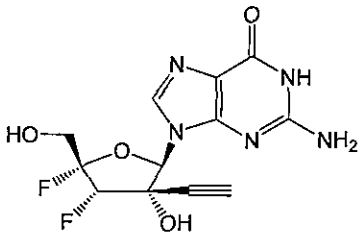
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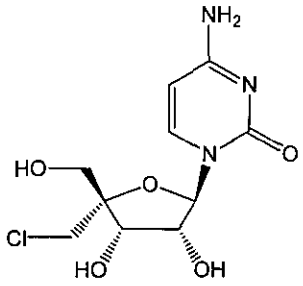
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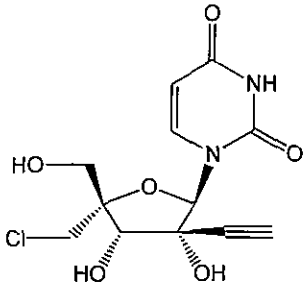
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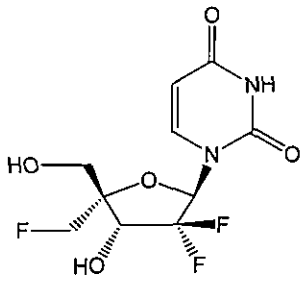
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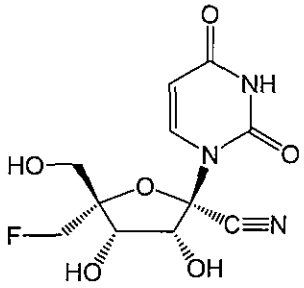
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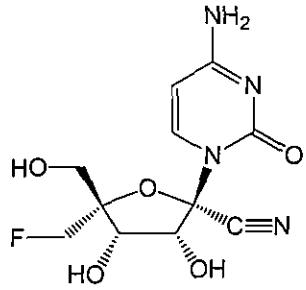
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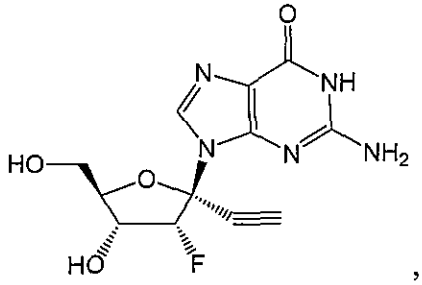
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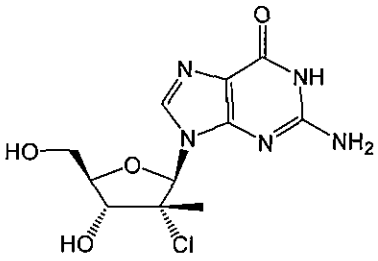
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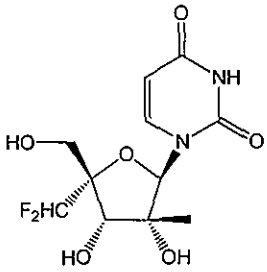
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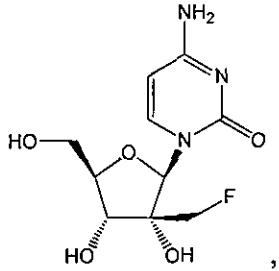
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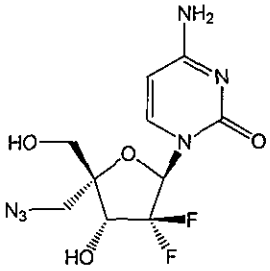
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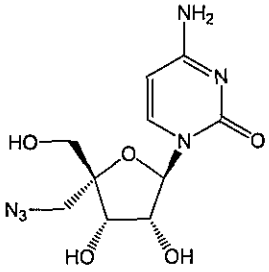
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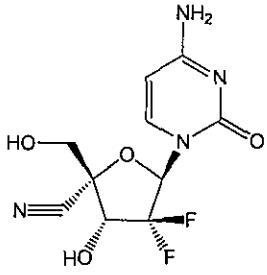
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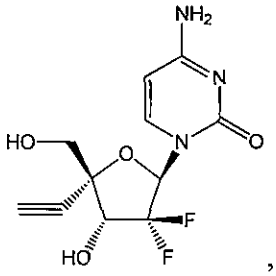
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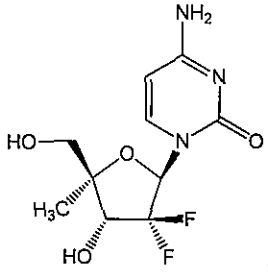
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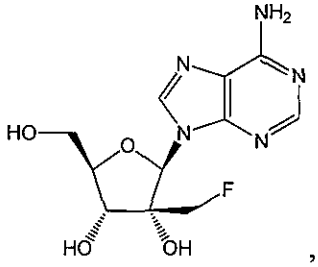
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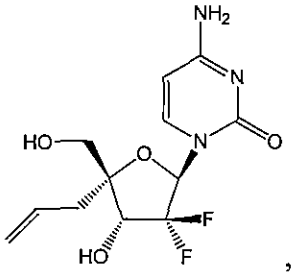
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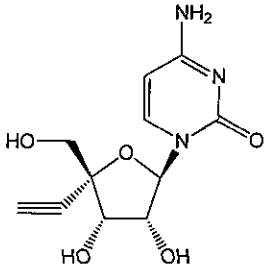
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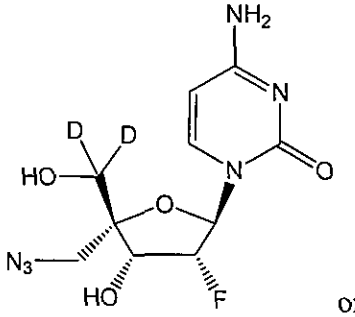
or a pharmaceutically acceptable salt of the foregoing.

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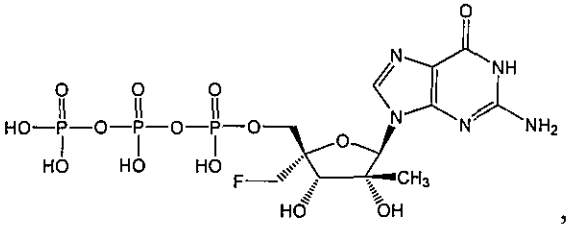
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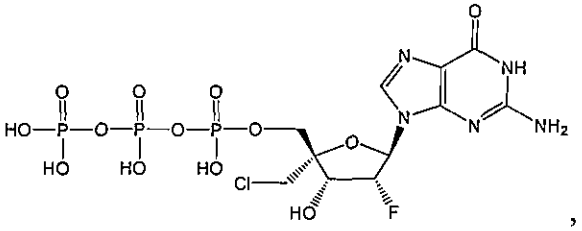
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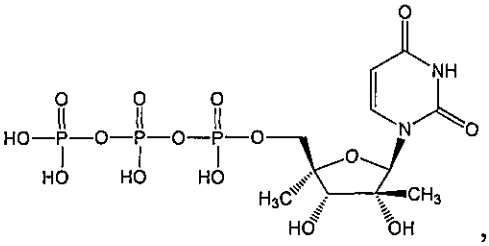
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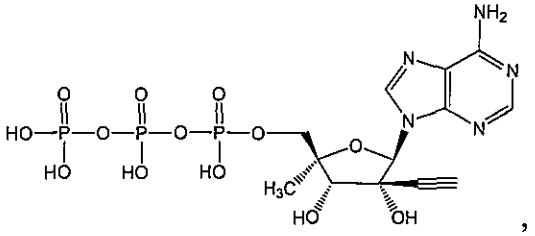
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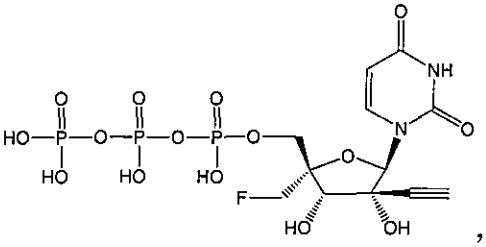
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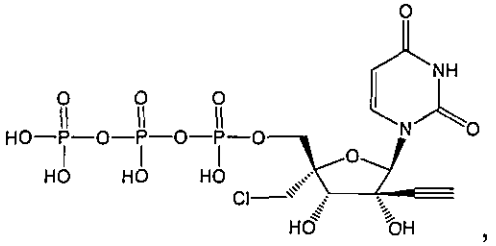
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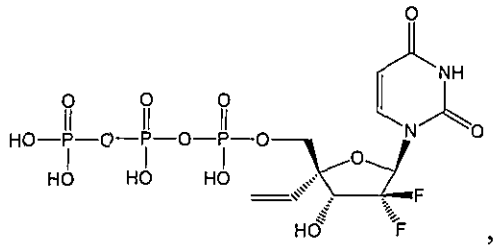
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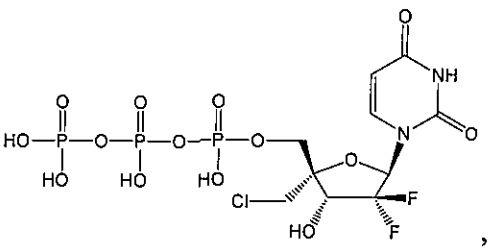
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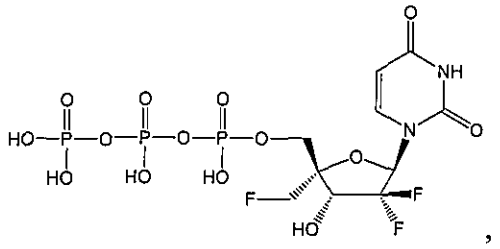
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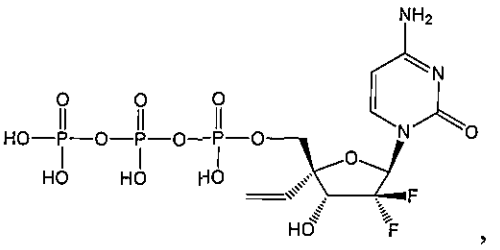
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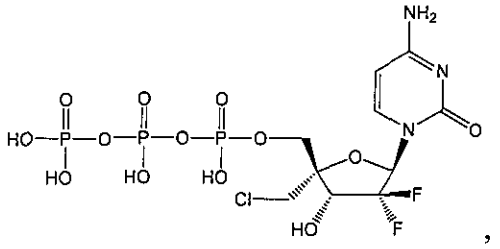
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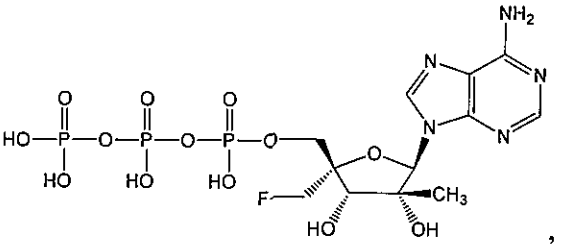
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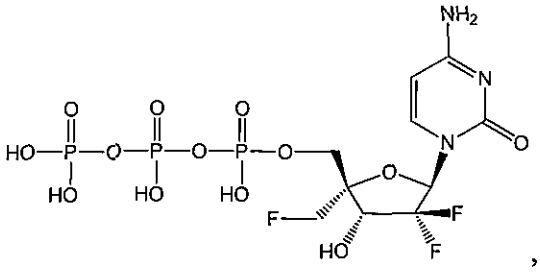
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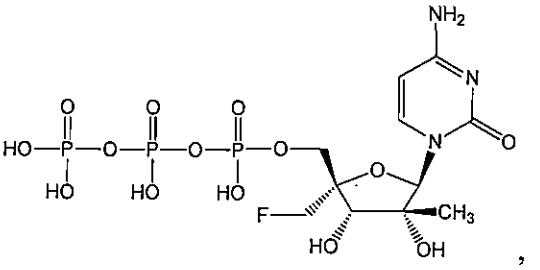
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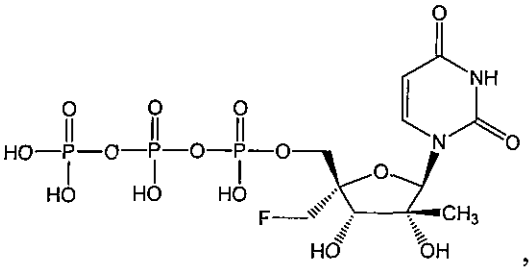
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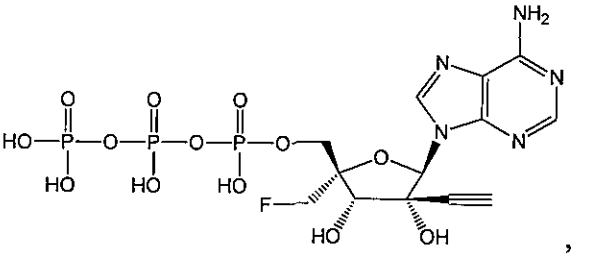
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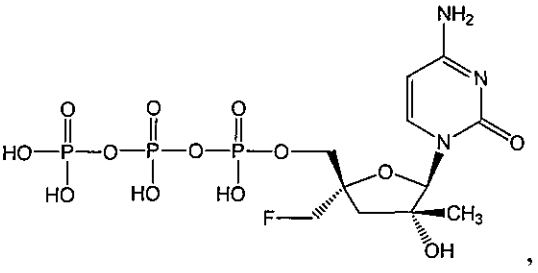
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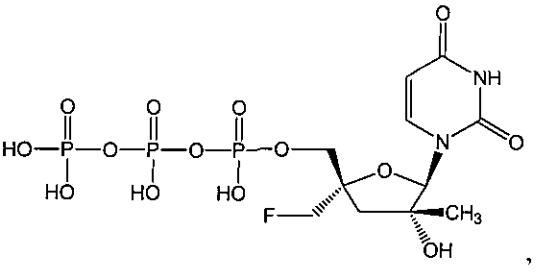
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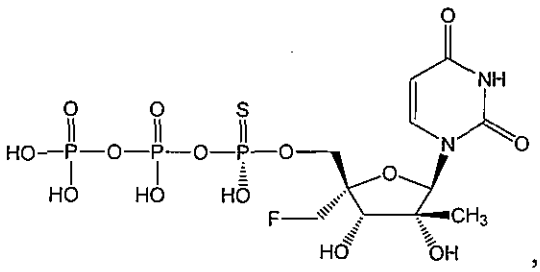
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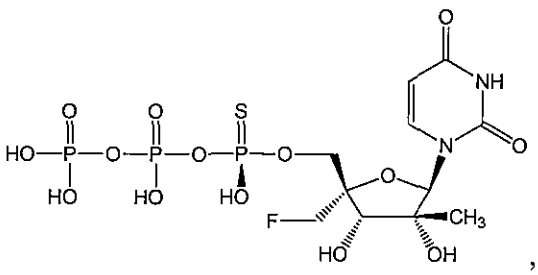
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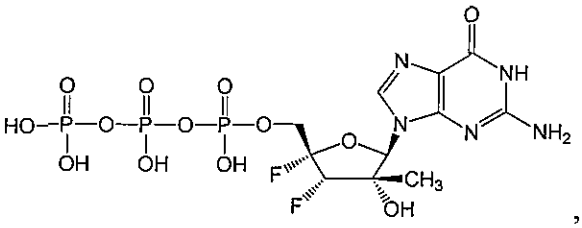
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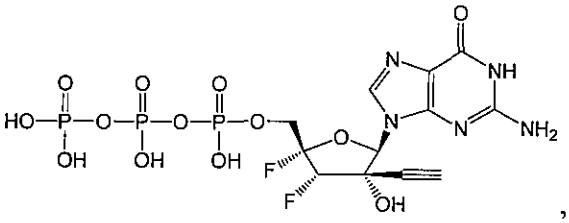
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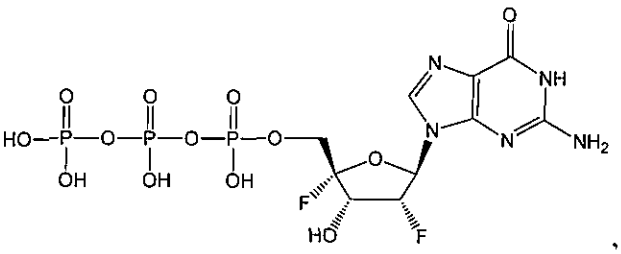
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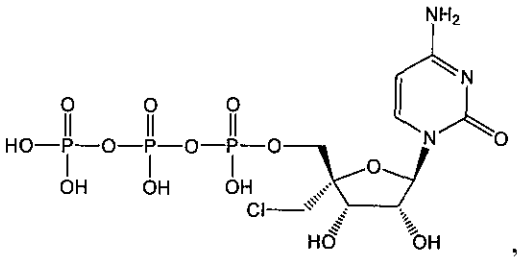
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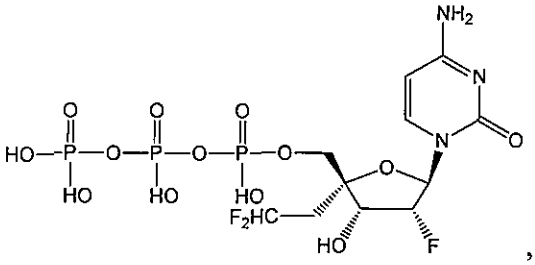
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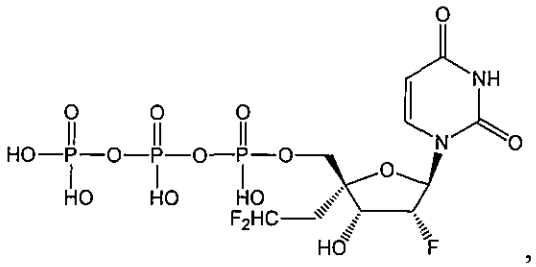
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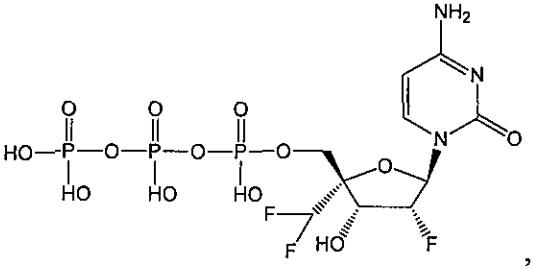
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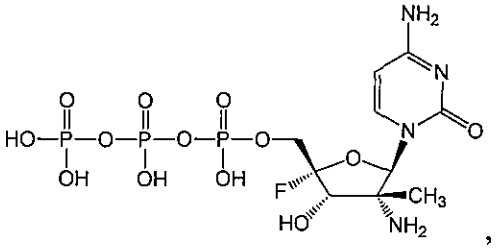
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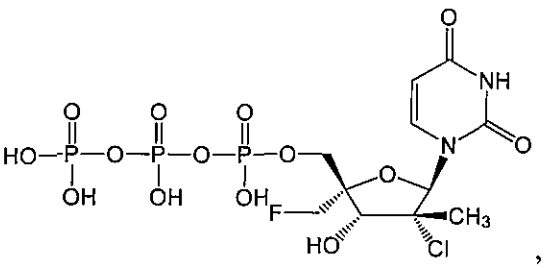
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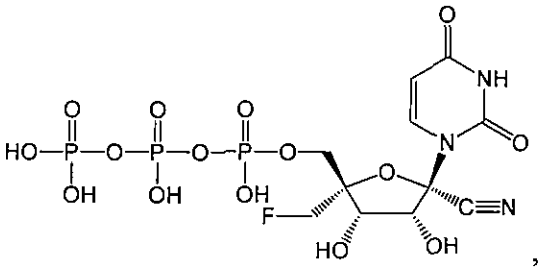
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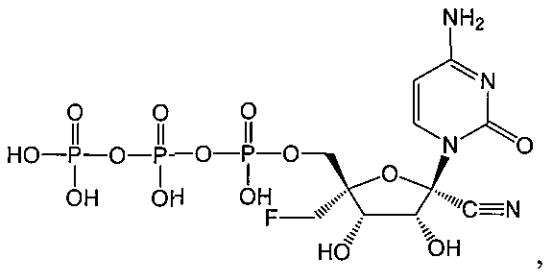
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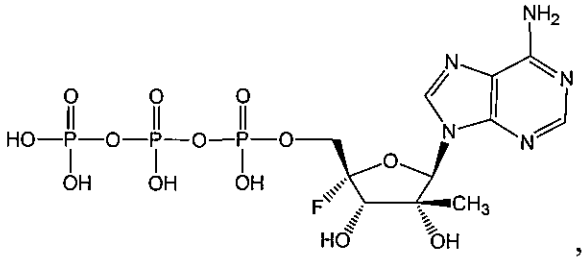
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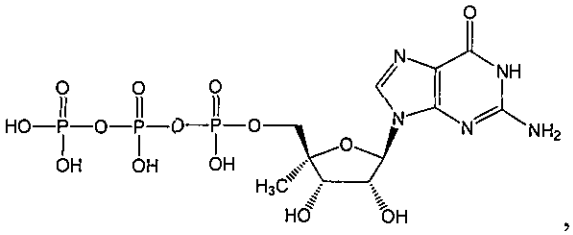
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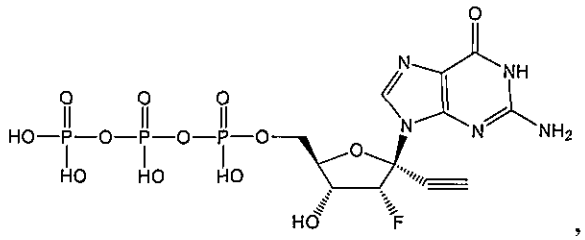
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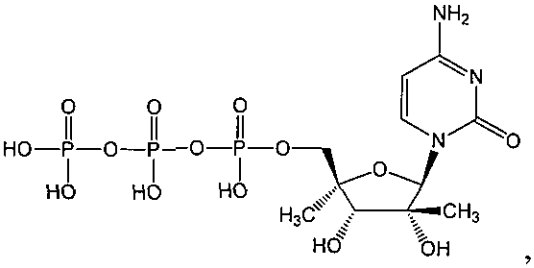
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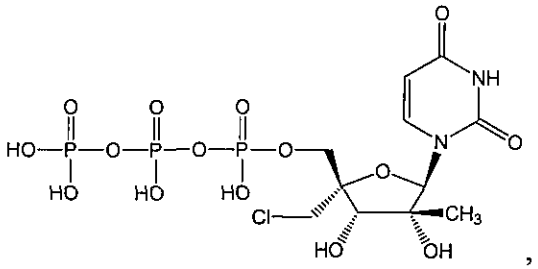
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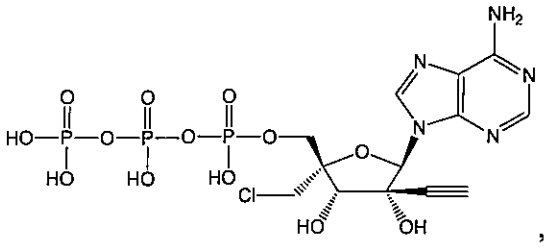
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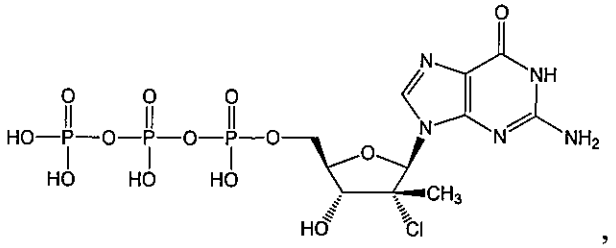
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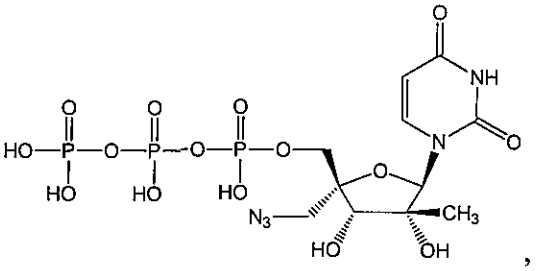
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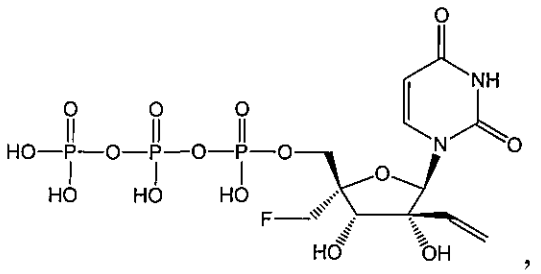
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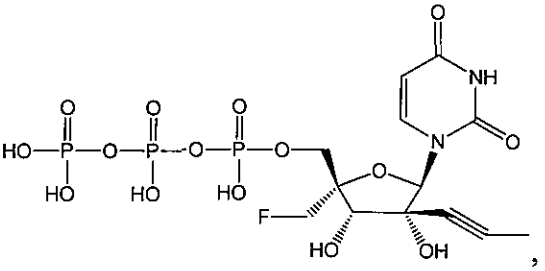
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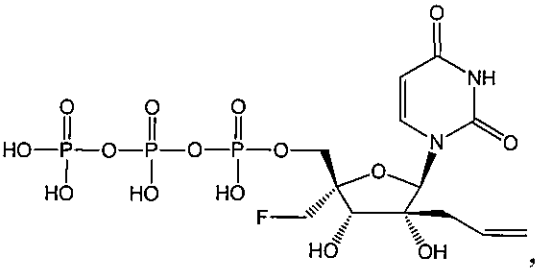
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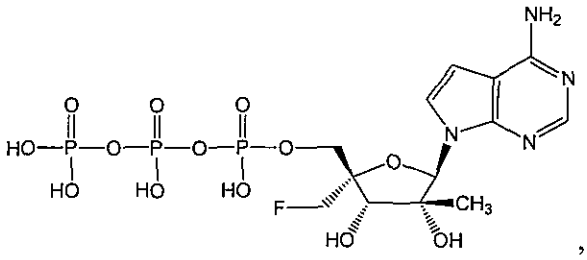
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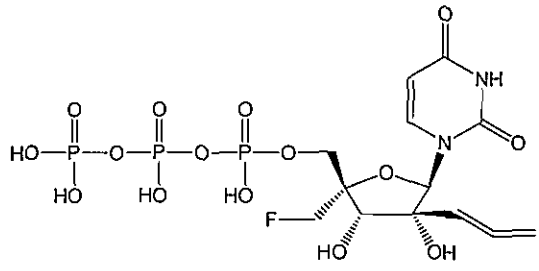
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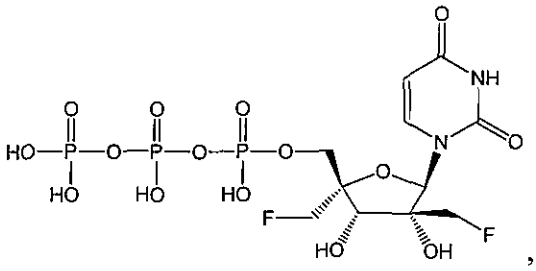
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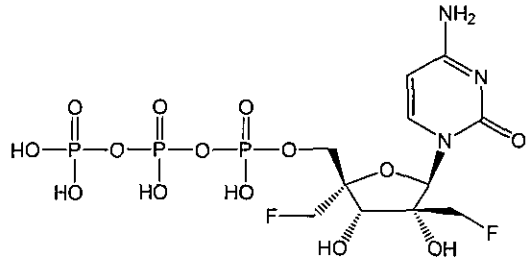
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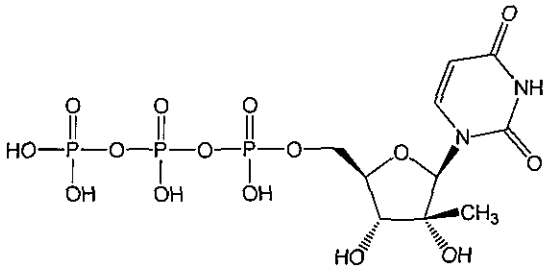
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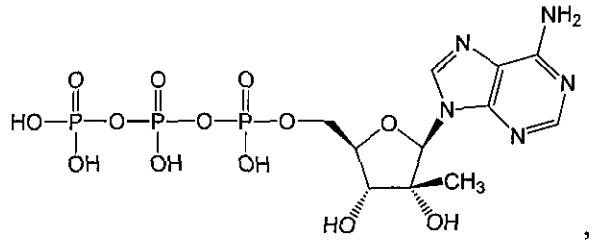
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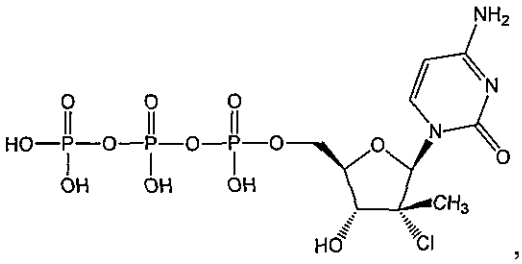
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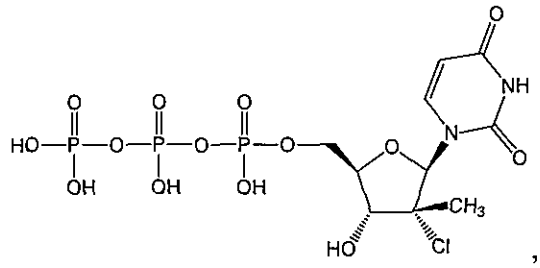
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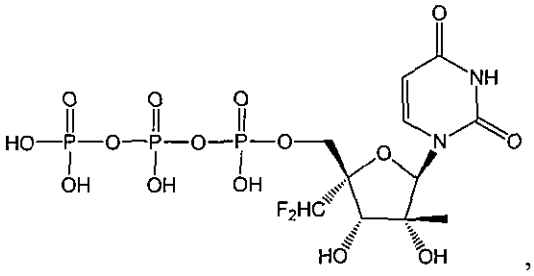
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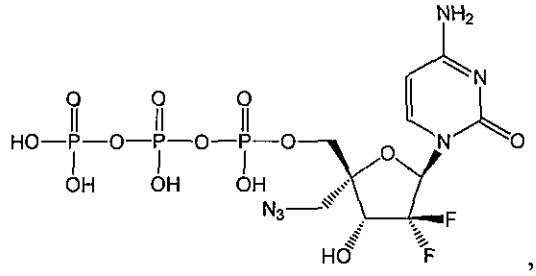
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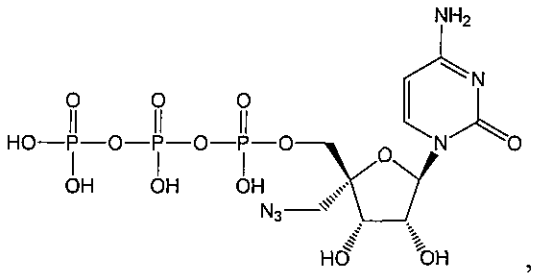
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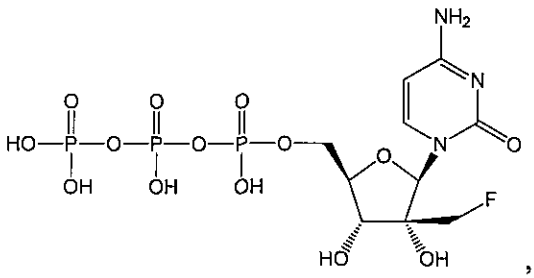
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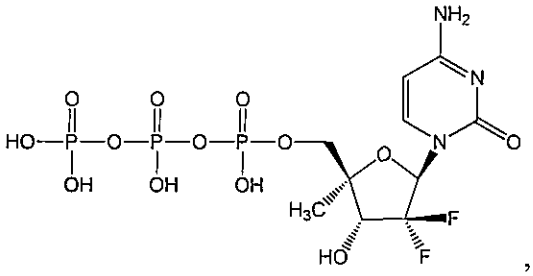
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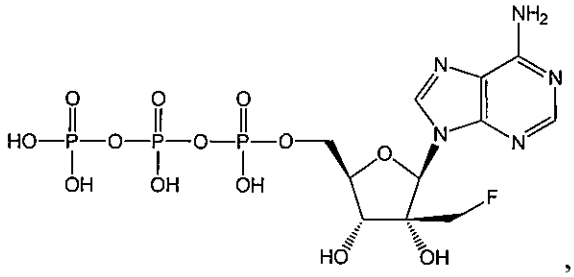
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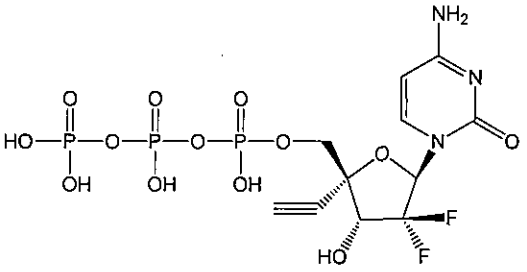
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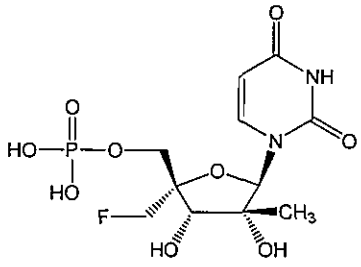
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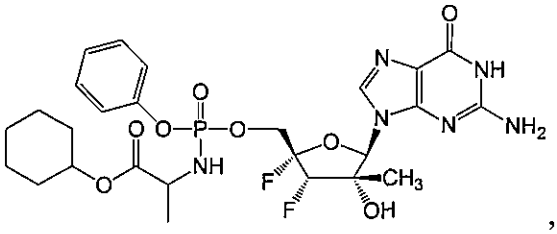
135. A compound selected from the group consisting of: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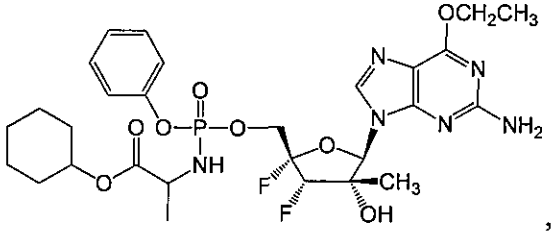
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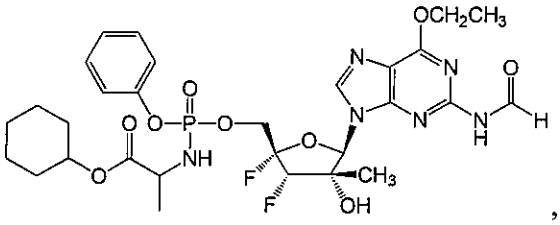
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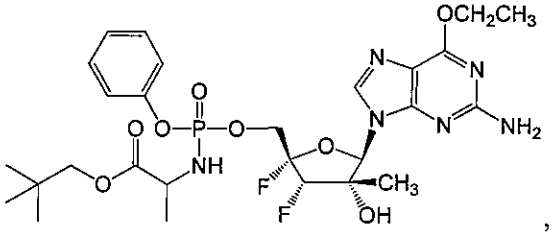
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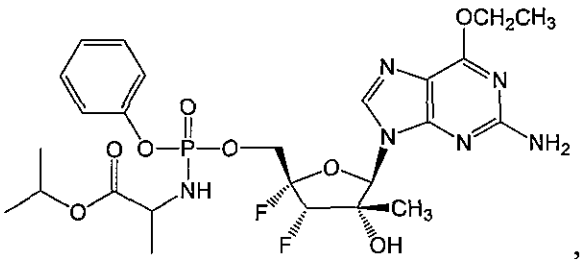
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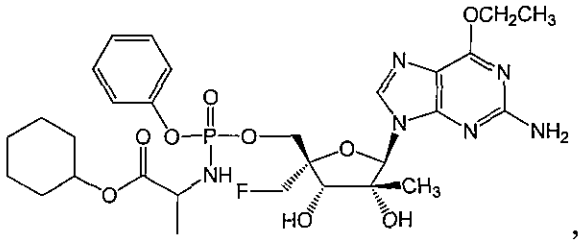
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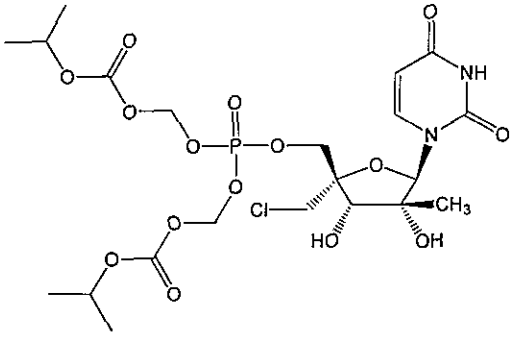
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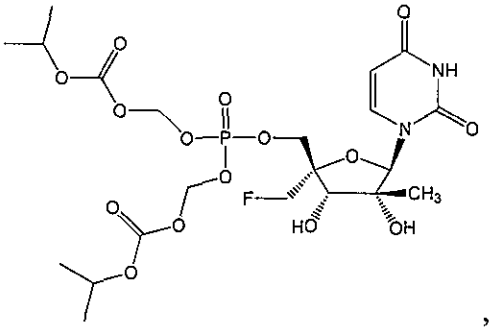
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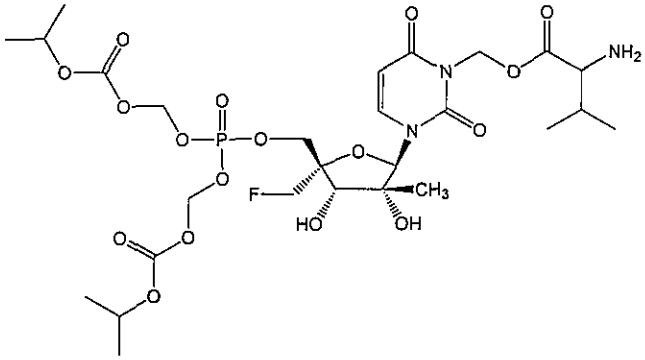
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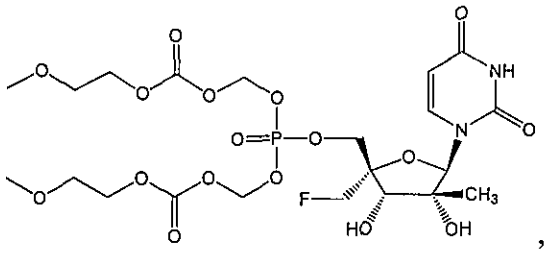
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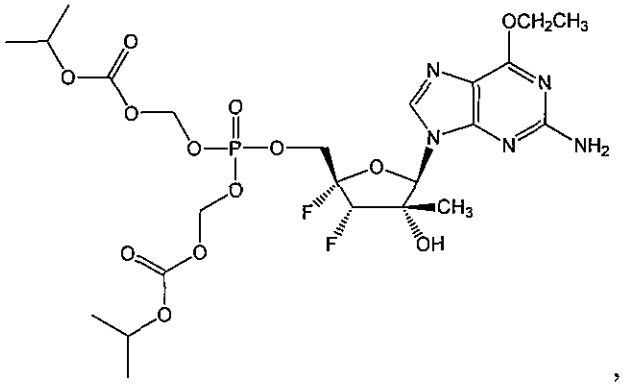
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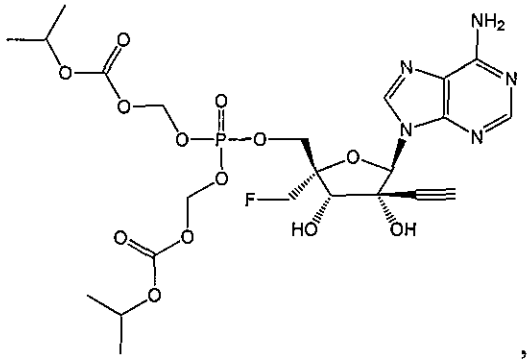
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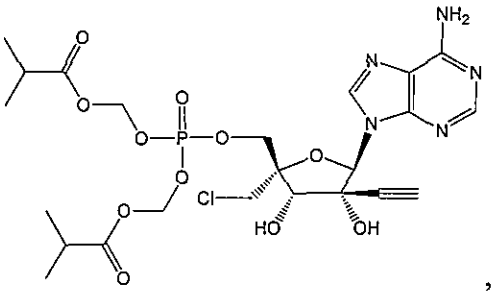

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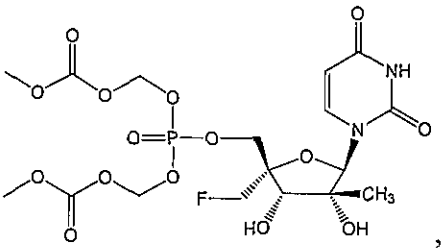

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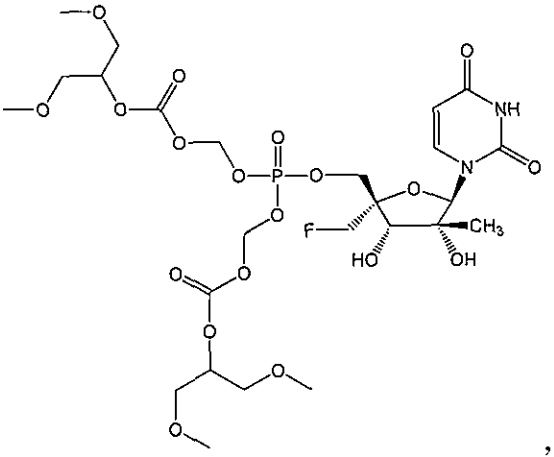

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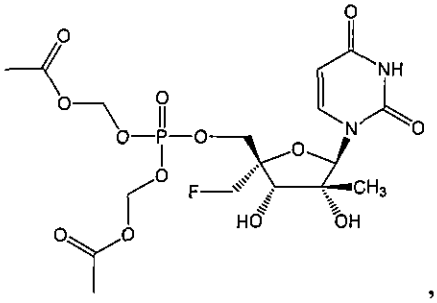

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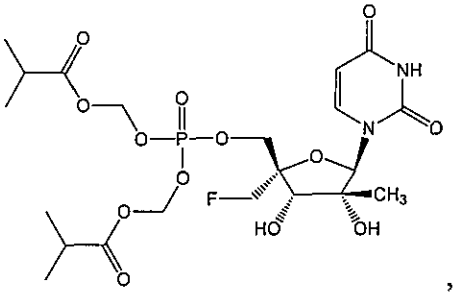

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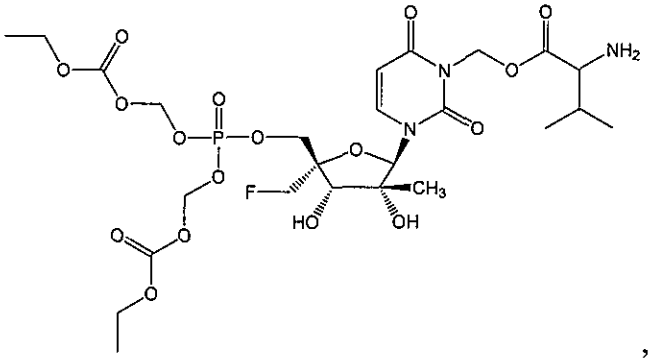

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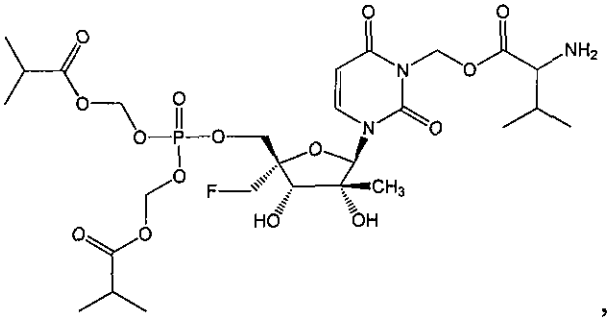

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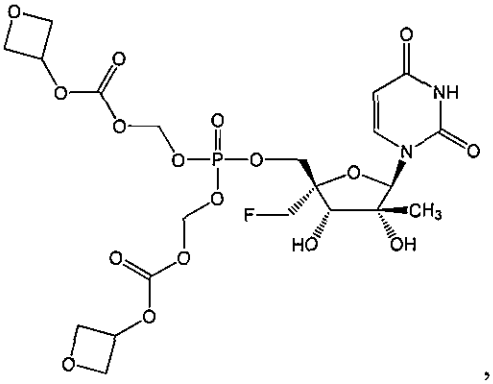

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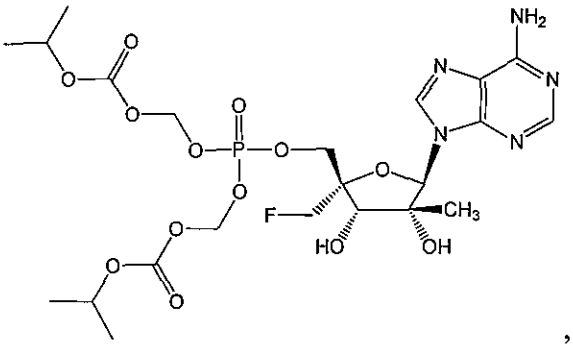
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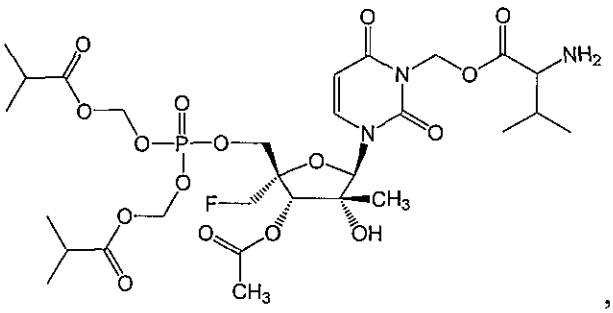
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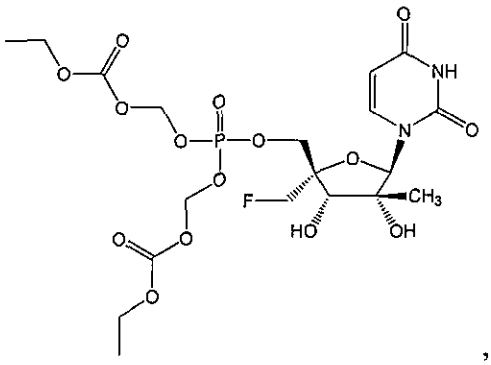
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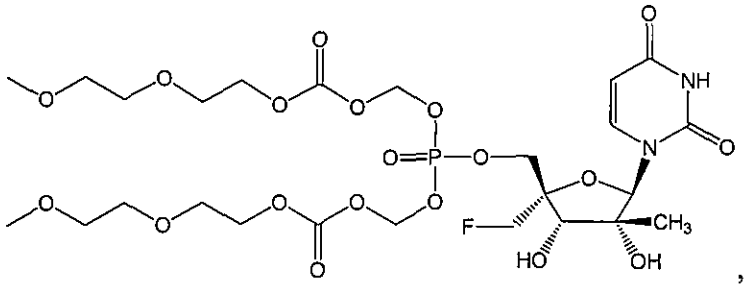
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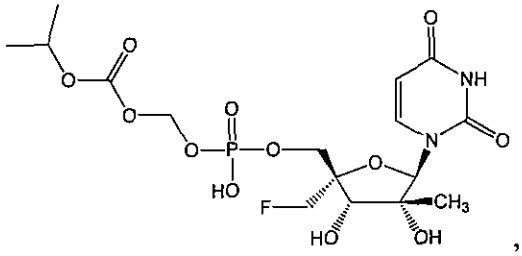
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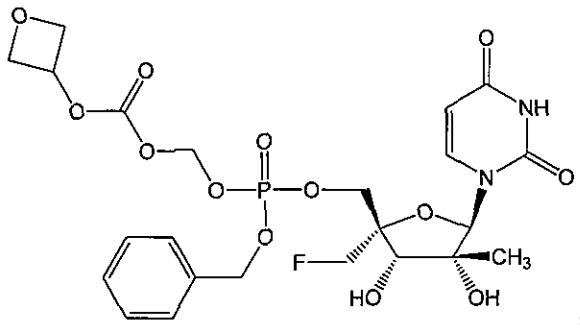
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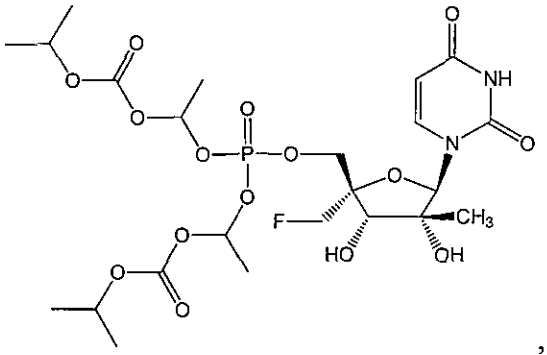
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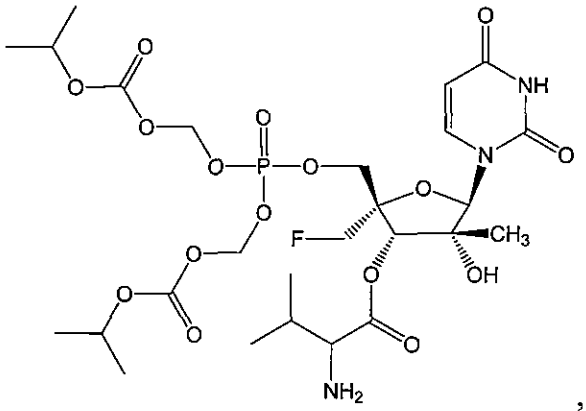
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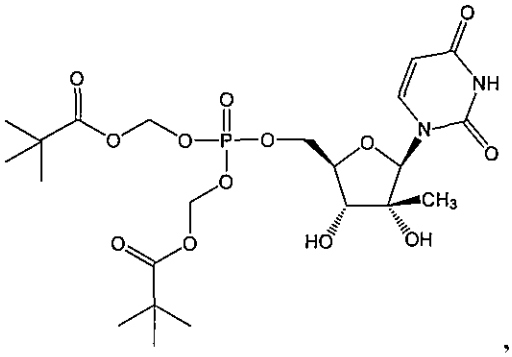
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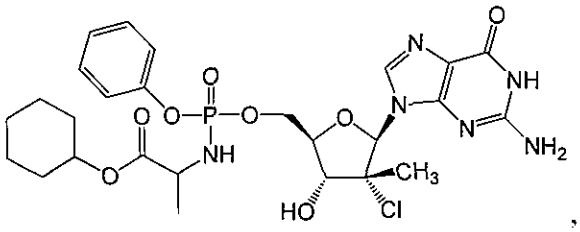
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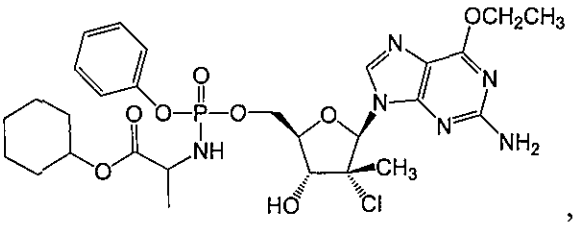
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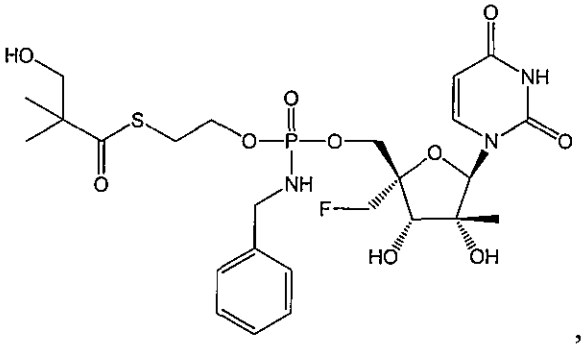
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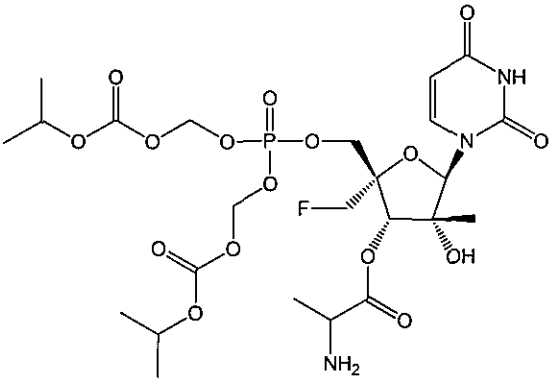
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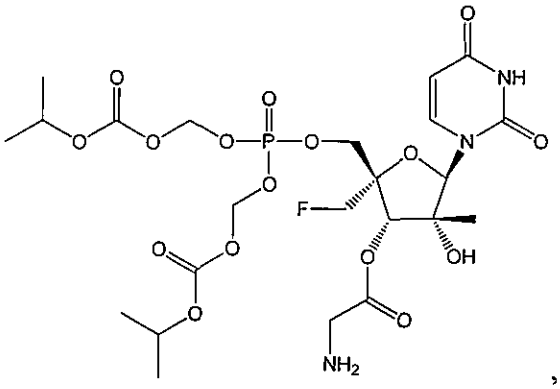
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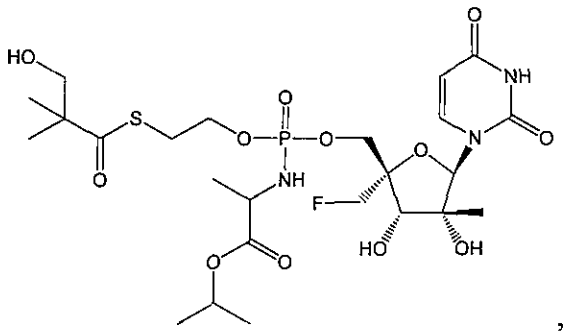
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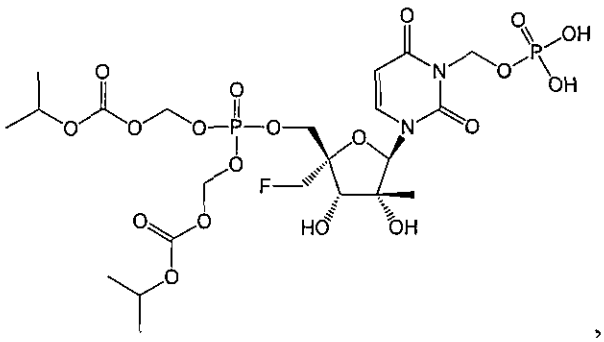
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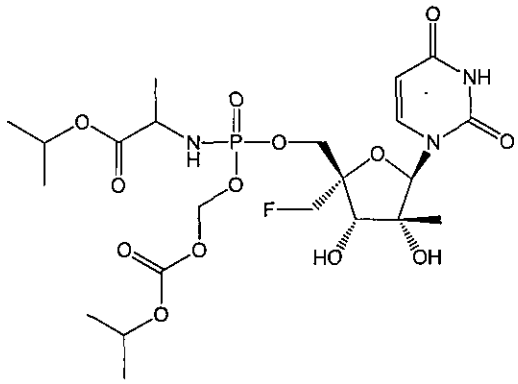
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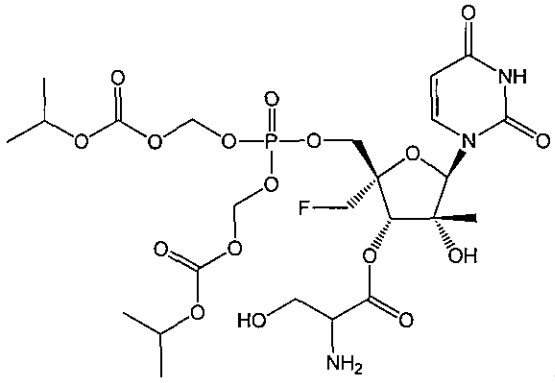
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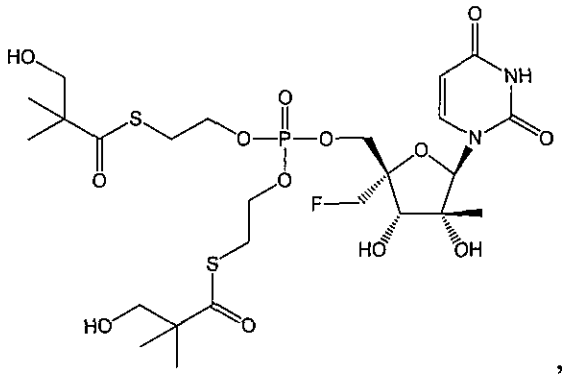
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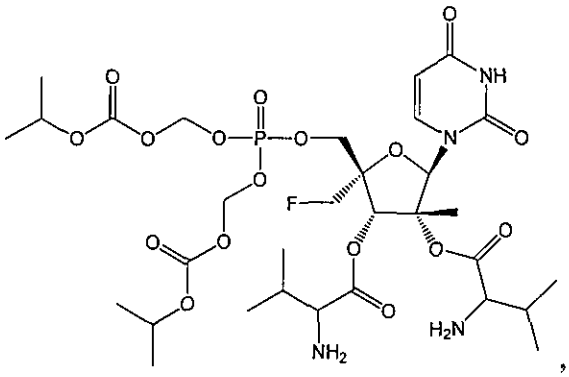
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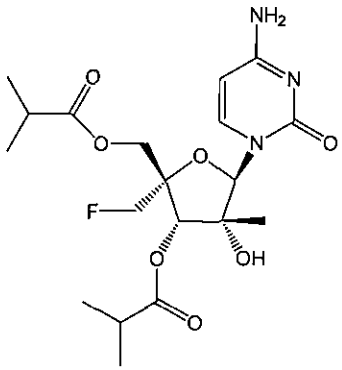
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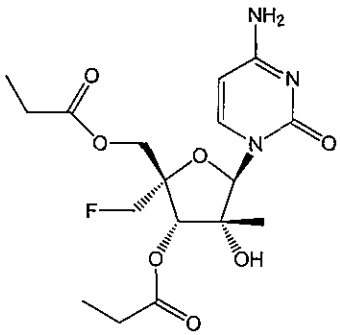
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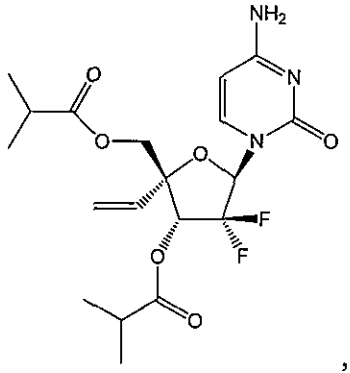
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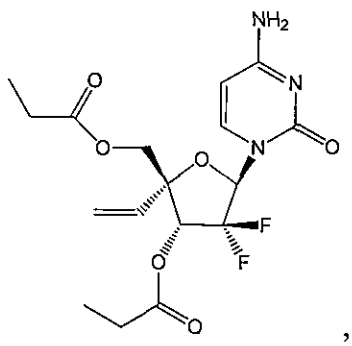
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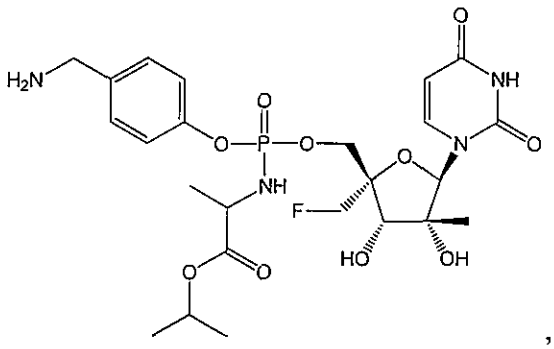
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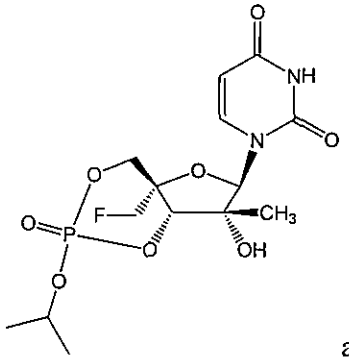
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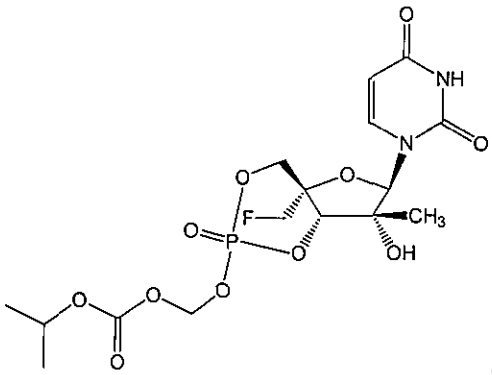

, or a pharmaceutically acceptable salt of the foregoing.

136. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 91-135, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

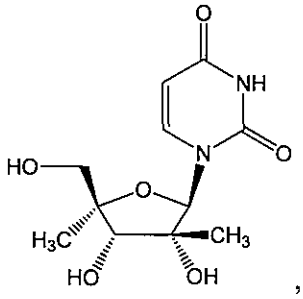
137. Use of a compound of any one of Claims 91-135 in the preparation of a medicament for ameliorating or treating a HCV infection, wherein the medicament is manufactured for use in combination with one or more agents selected from the group consisting of an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA), a compound of Formula (BB) and a compound of Formula (CC), or a pharmaceutically acceptable salt any of the aforementioned compounds.

138. Use of a compound of any one of Claims 91-135 in the preparation of a medicament for contacting a cell infected with a hepatitis C virus, wherein the medicament is manufactured for use in combination with one or more agents selected from the group consisting of an interferon, ribavirin, a HCV protease inhibitor, a HCV polymerase inhibitor, a NS5A inhibitor, an antiviral compound, a compound of Formula (AA) , a compound of Formula (BB)

and a compound of Formula (CC), or a pharmaceutically acceptable salt any of the aforementioned compounds.

139. The use of any one of Claim 136-138, wherein the one or more agents are selected from the group consisting of Compounds 1001-1016, 2001-2012, 3001-3014, 4001-4012, 5001-5011, 6001-6078, 7000-7027 and 8000-8016, or a pharmaceutically acceptable salt of any of the aforementioned compounds.

140. Use of a compound selected from the group consisting of: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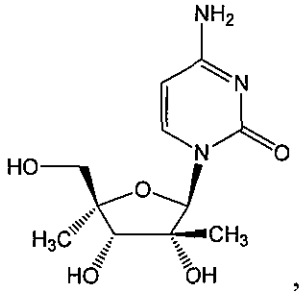
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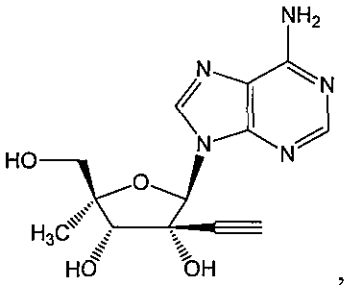
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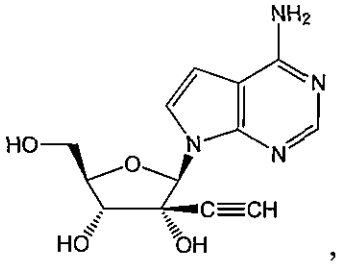
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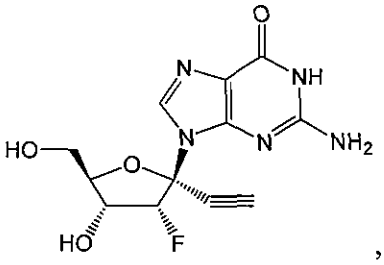
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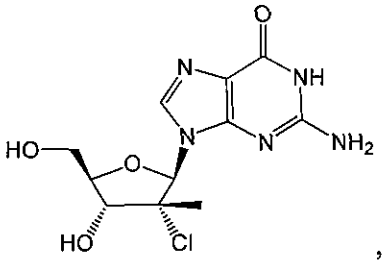
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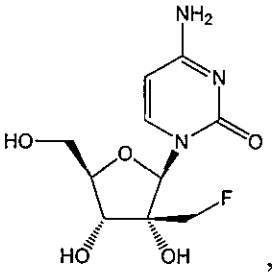
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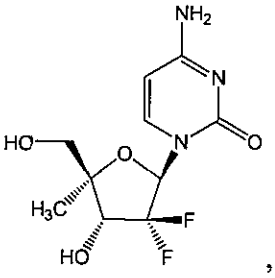
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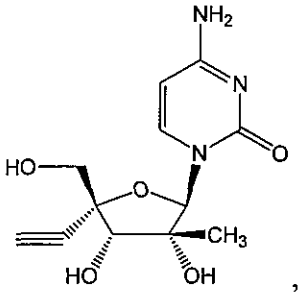
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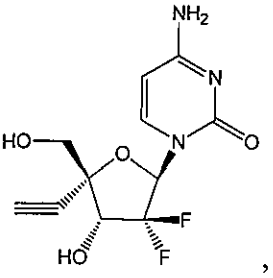
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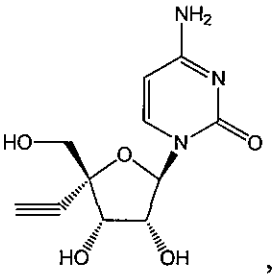
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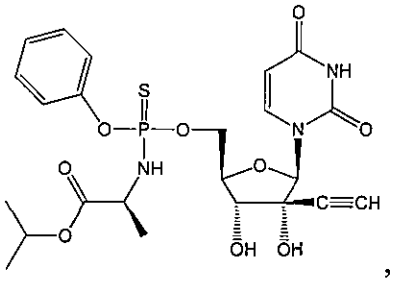
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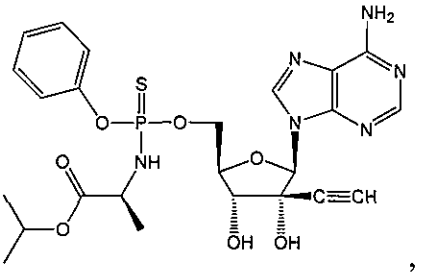
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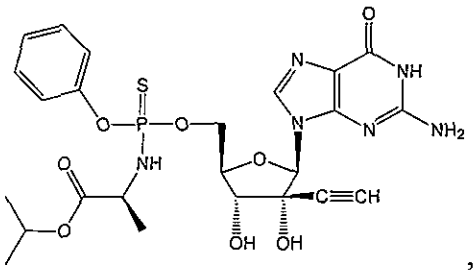
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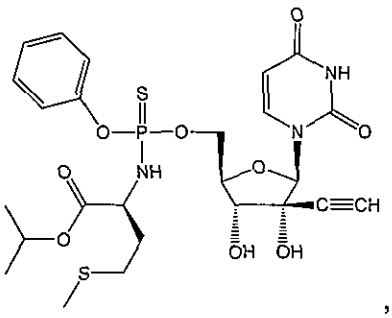
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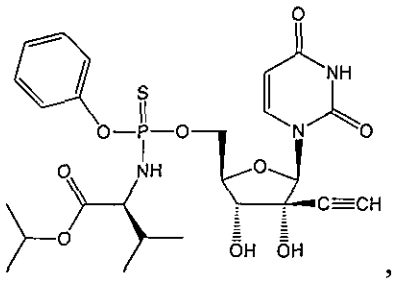
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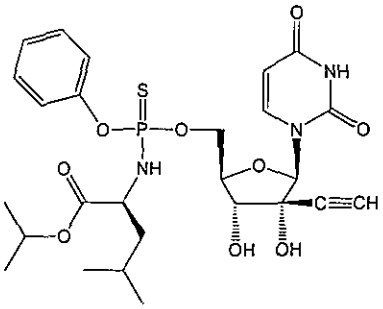
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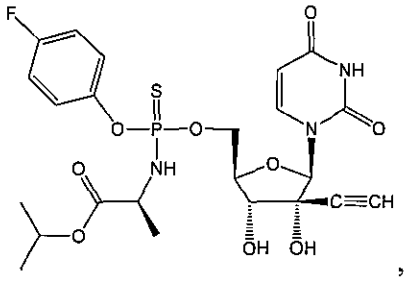
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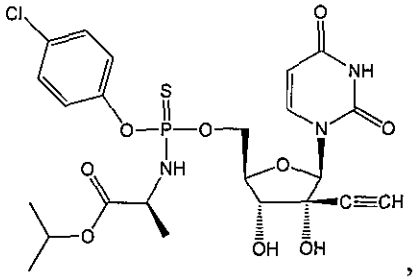
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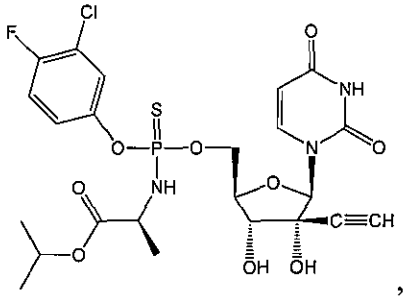
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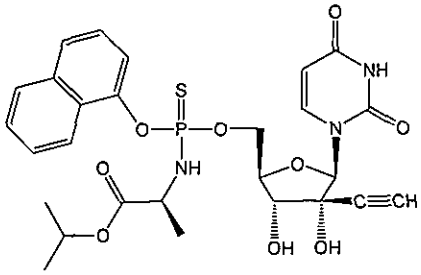
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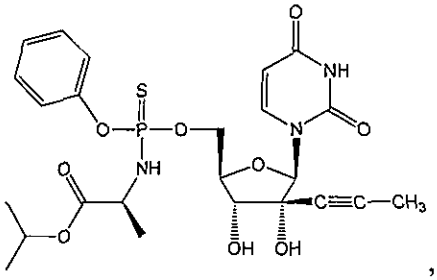
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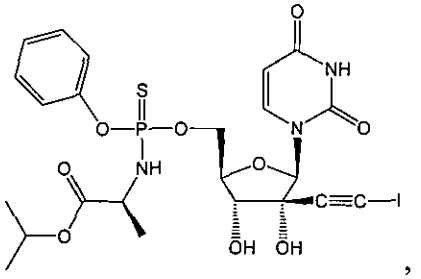
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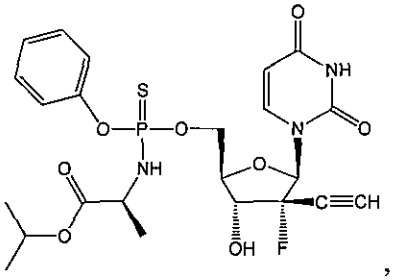
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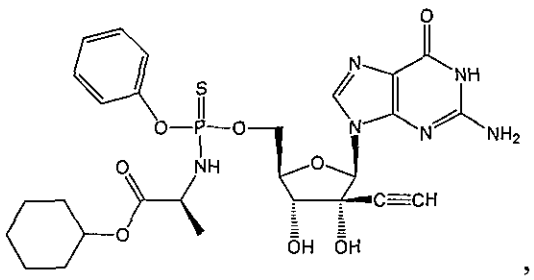

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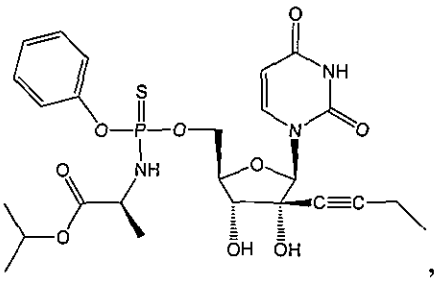

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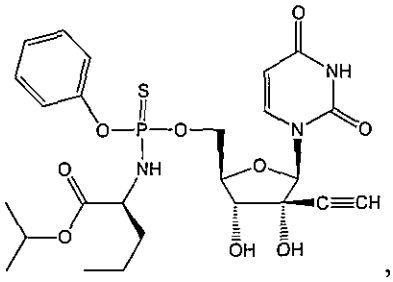

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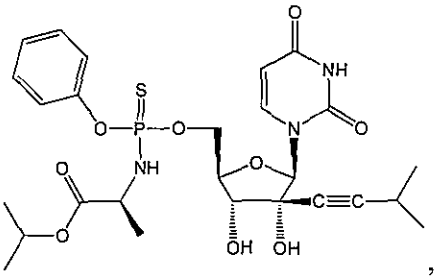

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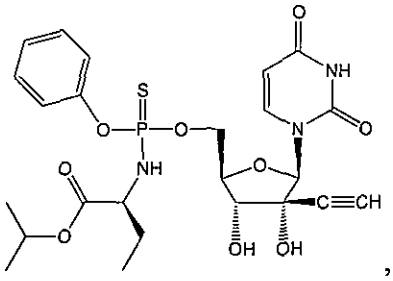

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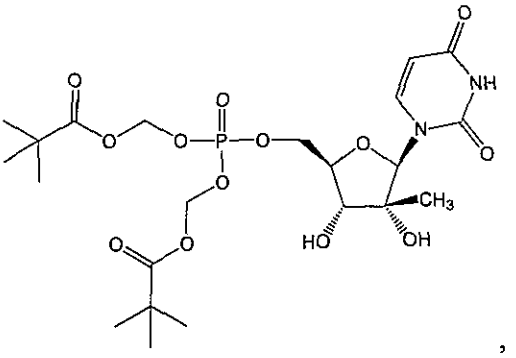

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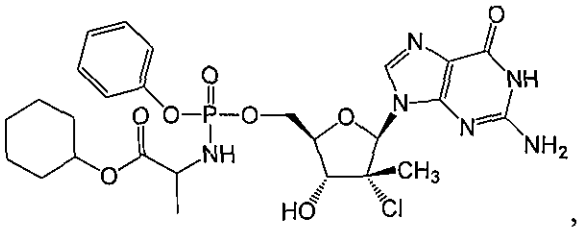

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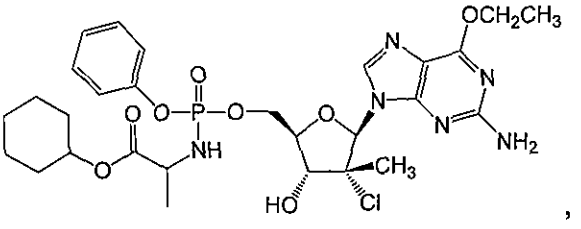

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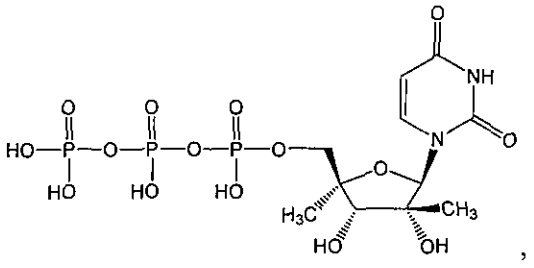

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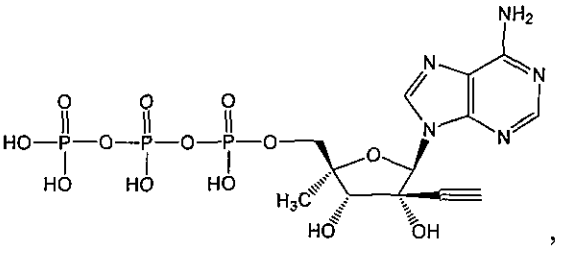

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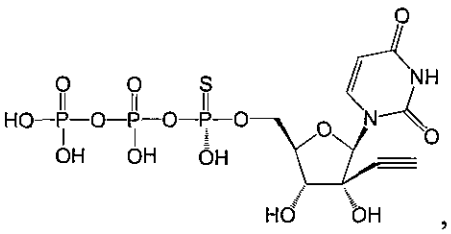
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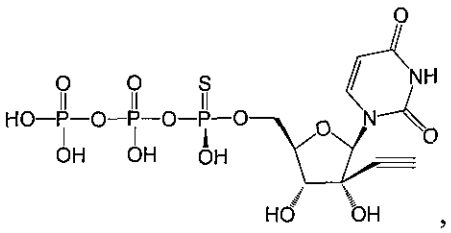
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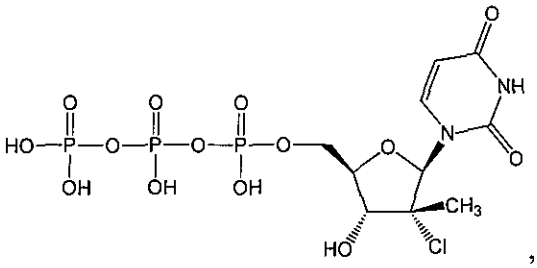
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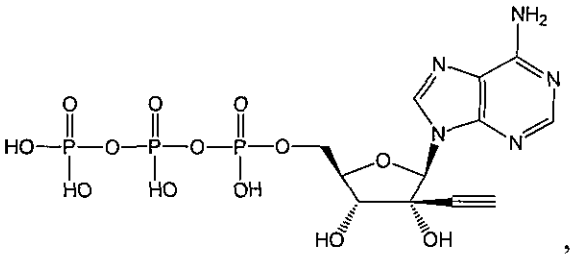
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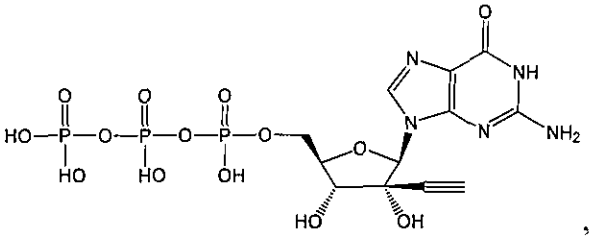
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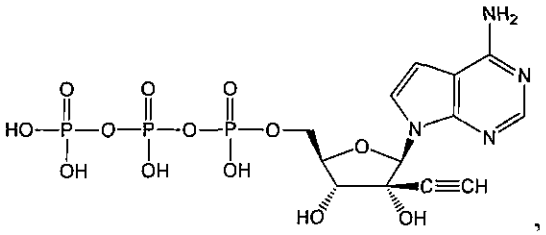
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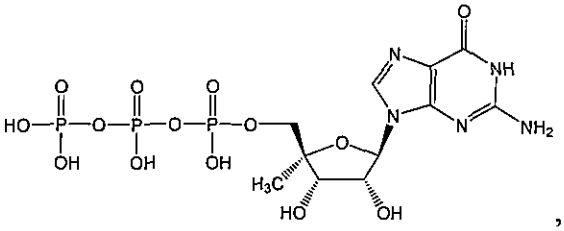
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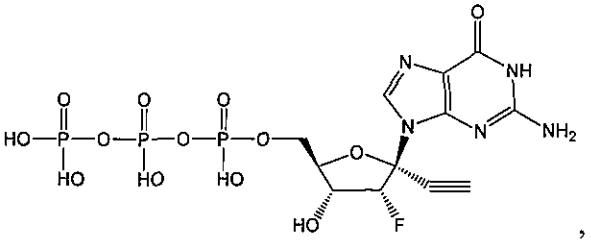
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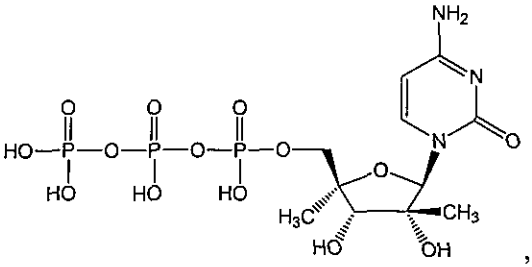
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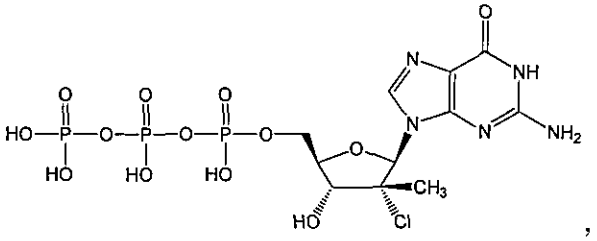
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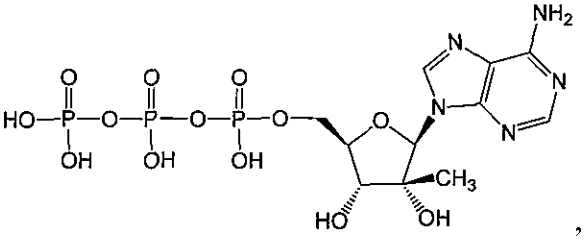
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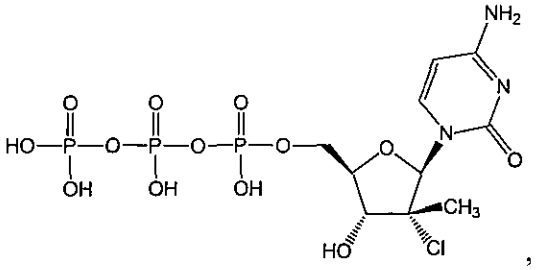
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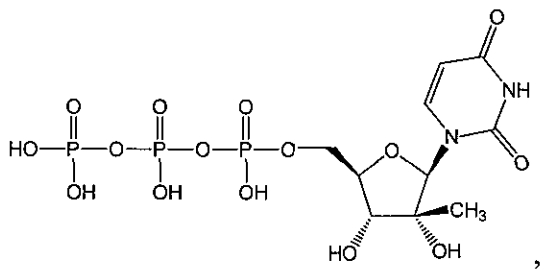
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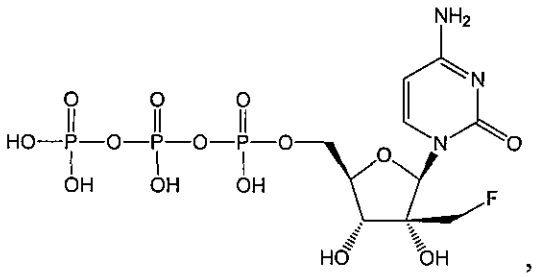
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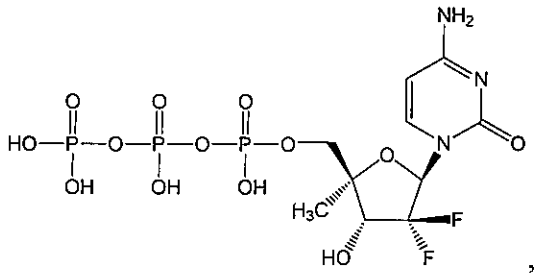
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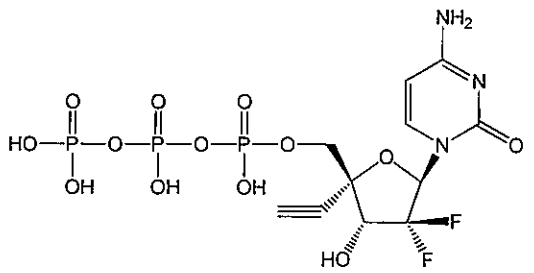
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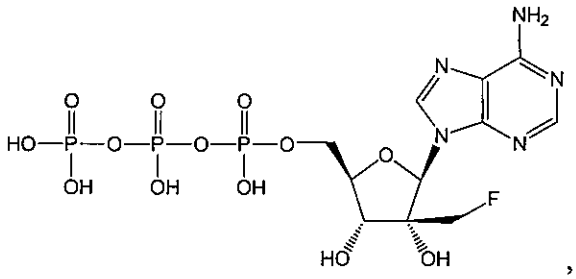
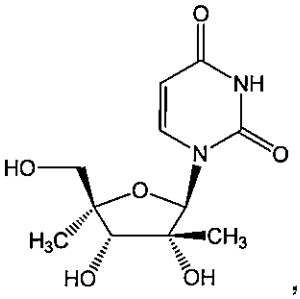

, or a pharmaceutically acceptable salt of the foregoing, in the preparation of a medicament for ameliorating or treating a *Picornaviridae* viral infection.

141. Use of a compound selected from the group consisting of: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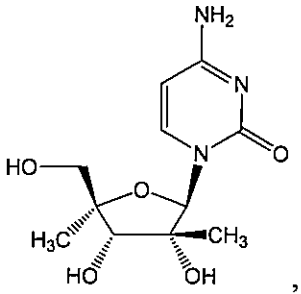
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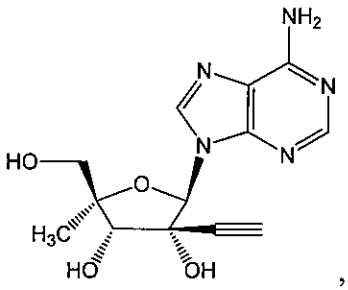
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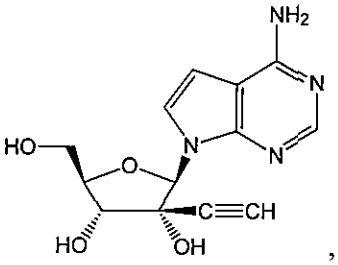
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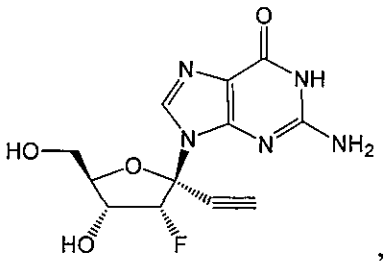
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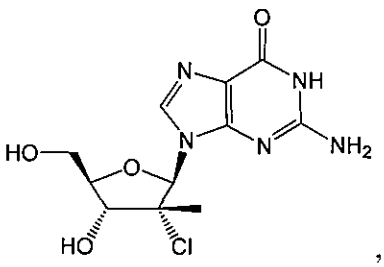
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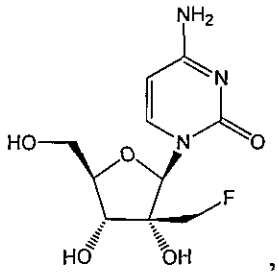
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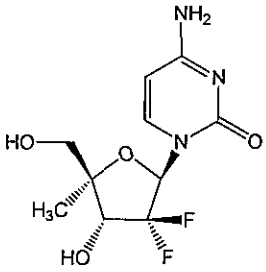
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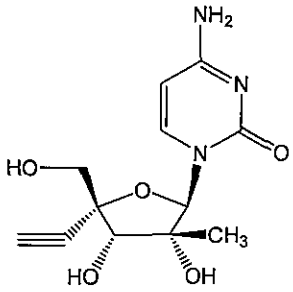
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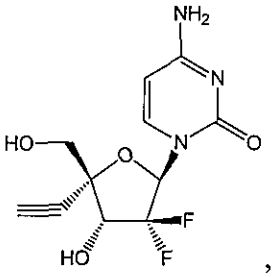
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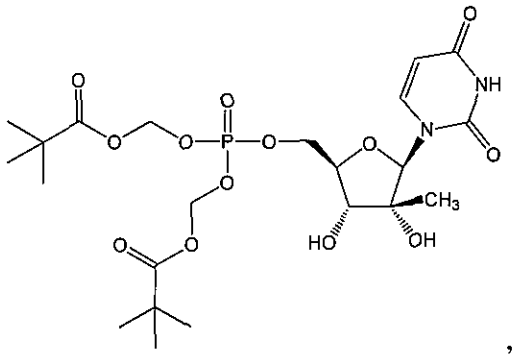
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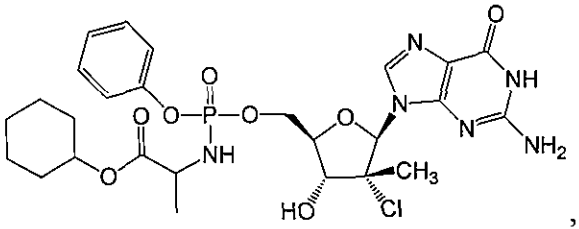
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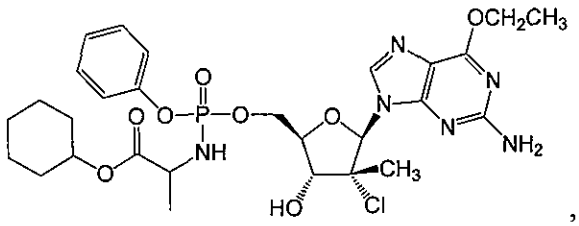
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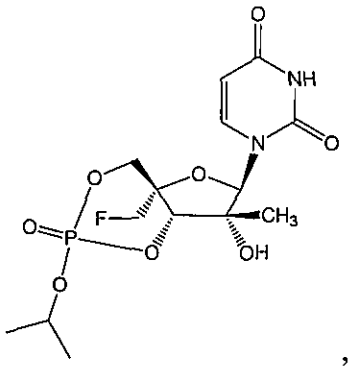
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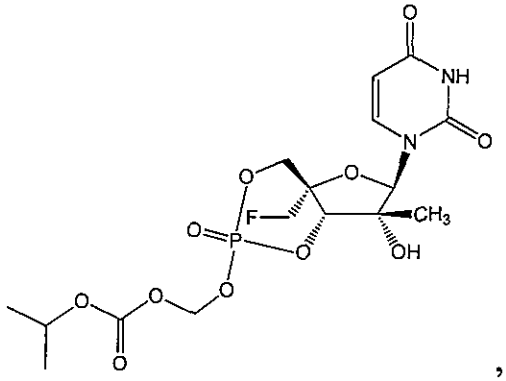
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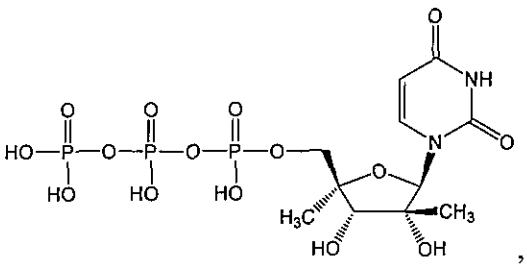
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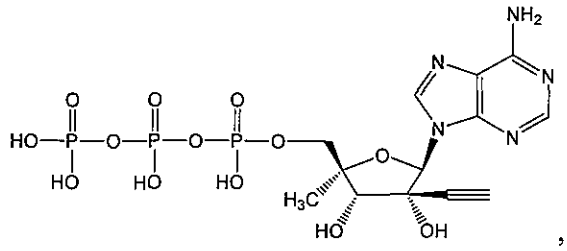
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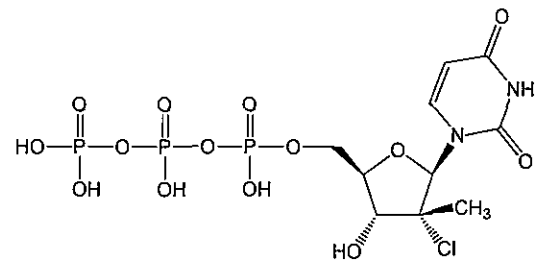
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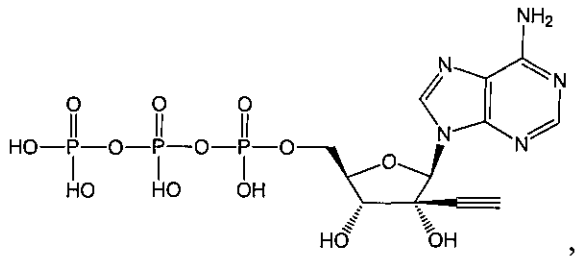
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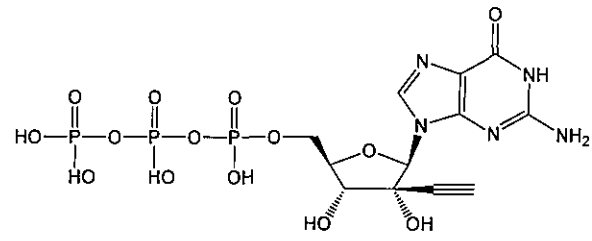
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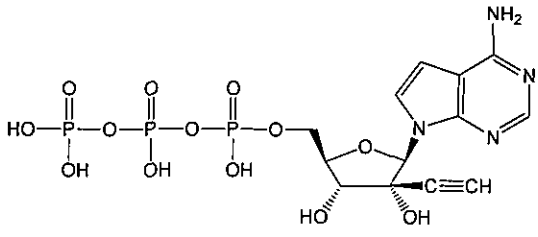
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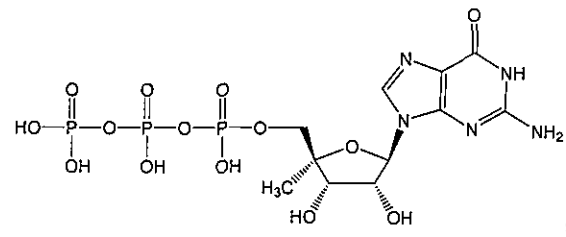
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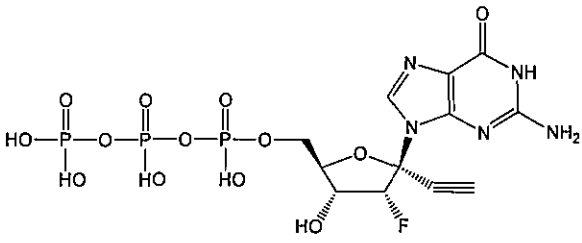
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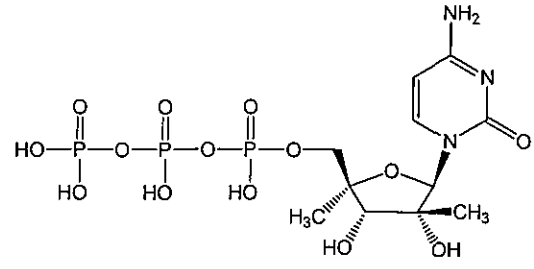
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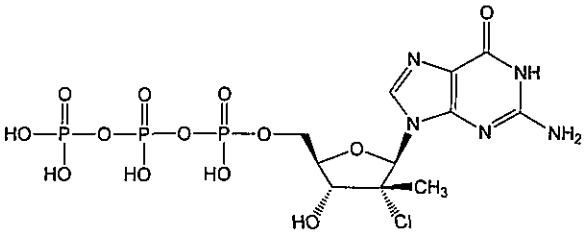
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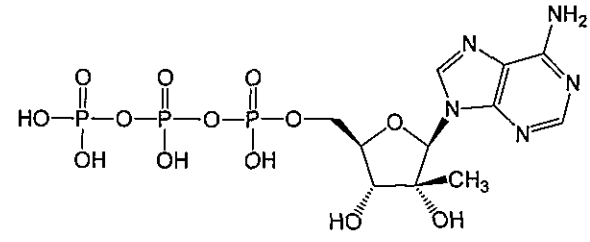
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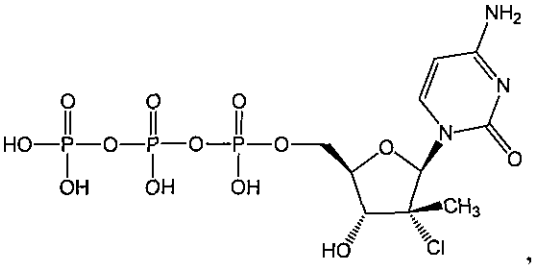
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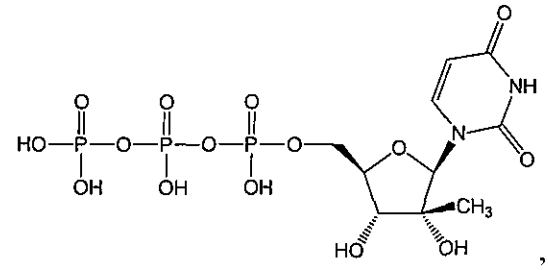
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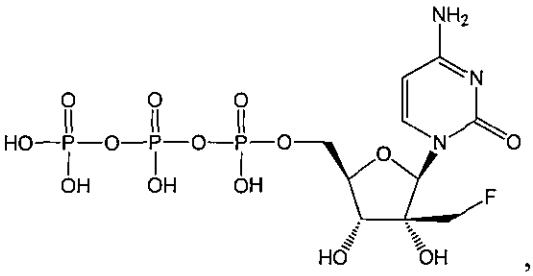
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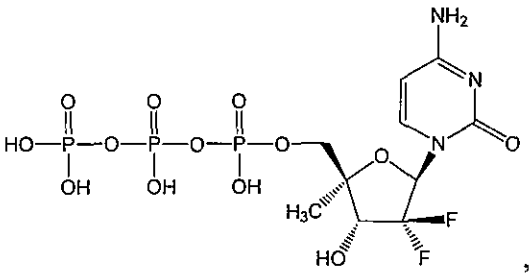
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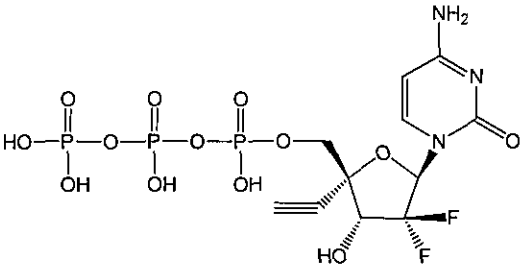
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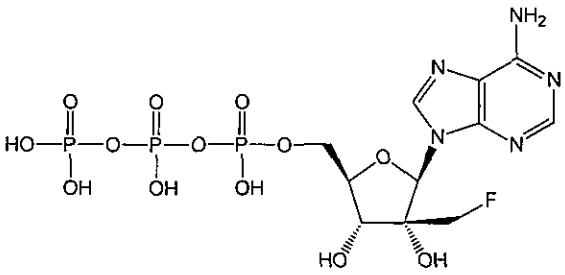
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