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(54) Title **4'-FLUORO-NUCLEOSIDES, 4'-FLUORO-NUCLEOTIDES AND ANALOGS THEREOF FOR THE TREATMENT OF HCV**

(56) References
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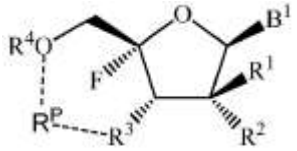
US-A1- 2005 009 737

Patentkrav

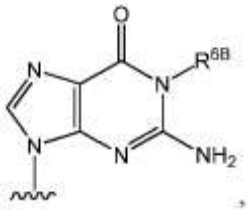
1. En forbindelse med formel (I), eller et farmasøytisk akseptabelt salt derav, som har strukturen:



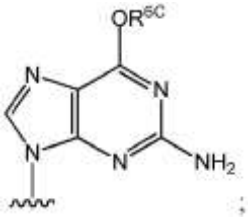
(I)

hvor:

B^1 er valgt fra gruppen bestående av en eventuelt substituert



og en eventuelt substituert



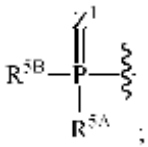
R^1 er valgt fra gruppen bestående av et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl og et eventuelt substituert C_{3-6} sykloalkyl;

hver -------- er fraværende og R^p er fraværende;

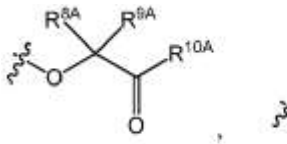
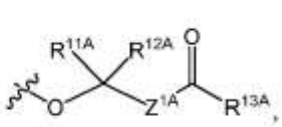
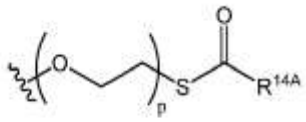
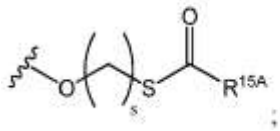
R^2 er halo, N_3, $-OR^{7A}$ eller $-N(R^{7B}R^{7C})$;

R^3 er -OH eller $-OC(=O)R^8$; eller R^2 og R^3 er hver et oksygenatom som er bundet sammen av en karbonylgruppe;

R^4 er hydrogen eller

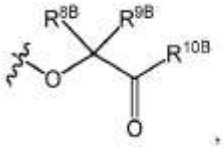
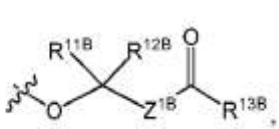
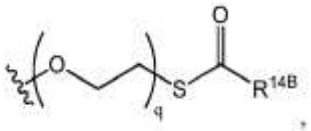
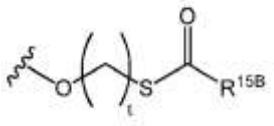


R^{5A} er valgt fra gruppen bestående av O^-, OH, en eventuelt substituert N-koblet aminosyre, en eventuelt substituert N-koblet aminosyreester,

og

R^{5B} er valgt fra gruppen bestående av O^-, OH, en -O-eventuelt substituert aryl, en -O-eventuelt substituert heteroaryl, en -O-eventuelt substituert heterosyklyl, en eventuelt substituert N-koblet aminosyre, en eventuelt substituert N-koblet aminosyreester,

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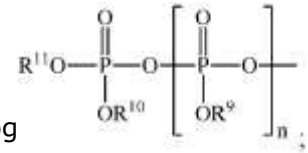


R^{6B} og R^{6C} er uavhengig valgt fra gruppen bestående av hydrogen, et usubstituert C_{1-6} alkyl, et usubstituert C_{3-6} alkenyl, et usubstituert C_{3-6} alkynyl og et usubstituert C_{3-6} sykloalkyl;

R^{7A} er hydrogen eller -C(=O)R^{12};

R^{7B} og R^{7C} er uavhengig hydrogen eller et eventuelt substituert C_{1-6} alkyl;

R^8 og R^{12} er uavhengig et eventuelt substituert C_{1-6} alkyl eller et eventuelt substituert C_{3-6} sykloalkyl;

R^9, R^{10} og R^{11} er uavhengig fraværende eller hydrogen;

R^{8A}, R^{9A}, R^{11A}, R^{12A}, R^{8B}, R^{9B}, R^{11B} og R^{12B} er uavhengig valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-24} alkyl og en eventuelt substituert aryl;

R^{10A}, R^{10B}, R^{13A} og R^{13B} er uavhengig valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-24} alkyl, en eventuelt substituert aryl, et eventuelt substituert -O-C_{1-24} alkyl, en eventuelt substituert -O-aryl, en eventuelt substituert -O-heteroaryl og en eventuelt substituert -O-monosyklisk heterosyklyl;

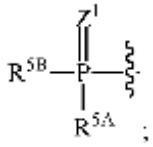
R^{14A}, R^{14B}, R^{15A} og R^{15B} er uavhengig valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-24} alkyl og en eventuelt substituert aryl;

n er 0 eller 1;

p og q er uavhengig 1 eller 2;

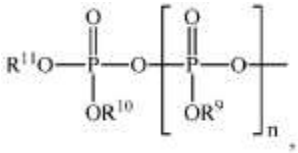
s og t er uavhengig 3, 4 eller 5;

Z^1, Z^{1A} og Z^{1B} er uavhengig O eller S; og forutsatt at når R^4 er



;

og R^{5A} er O^- eller OH, så er R^{5B} O^-, OH, eller



en eventuelt substituert N-koblet aminosyre eller en eventuelt substituert N-koblet aminosyreester, eller et farmasøytisk akseptabelt salt av det foregående.

2. Forbindelsen ifølge krav 1, hvor R^2 er halo.

3. Forbindelsen ifølge krav 2, hvor R^2 er fluor.

4. Forbindelsen ifølge krav 1, hvor R^2 er $-OR^{7A}$.

5. Forbindelsen ifølge krav 4, hvor R^{7A} er hydrogen.

6. Forbindelsen ifølge krav 1, hvor R^2 er valgt fra gruppen bestående av N_3, $-N(R^{7B}R^{7C})$ og $-NH_2$.

7. Forbindelsen ifølge et hvilket som helst av kravene 1-6, hvor R^1 er et eventuelt substituert C_{1-6} alkyl.

8. Forbindelsen ifølge et hvilket som helst av kravene 1-7, hvor R^1 er usubstituert metyl.

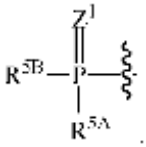
9. Forbindelsen ifølge et hvilket som helst av kravene 1-6, hvor R^1 er valgt fra gruppen bestående av et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl og et eventuelt substituert C_{3-6} sykloalkyl.

10. Forbindelsen ifølge et hvilket som helst av kravene 1-9, hvor R^3 er -OH.

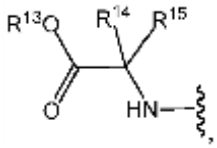
11. Forbindelsen ifølge et hvilket som helst av kravene 1-9, hvor R^3 er -OC(=O)R^8.

12. Forbindelsen ifølge et hvilket som helst av kravene 1-11, hvor R^4 er hydrogen.

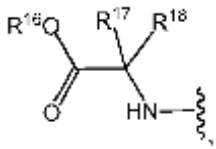
13. Forbindelsen ifølge et hvilket som helst av kravene 1-11, hvor R^4 er



14. Forbindelsen ifølge krav 13, hvor R^{5A} er en eventuelt substituert N-koblet aminosyre eller er en eventuelt substituert N-koblet aminosyreester; og R^{5B} er en eventuelt substituert N-koblet aminosyre eller er en eventuelt substituert N-koblet aminosyreester; eller R^{5A} er valgt fra gruppen bestående av alaninisopropylester, alaninsykloheksylester, alaninneopentylester, valinisopropylester, isoleucinisopropylester, metioninisopropylester og leucinisopropylester; og R^{5B} er valgt fra gruppen bestående av alaninisopropylester, alaninsykloheksylester, alaninneopentylester, valinisopropylester, isoleucinisopropylester, metioninisopropylester og leucinisopropylester; eller R^{5A} har strukturen



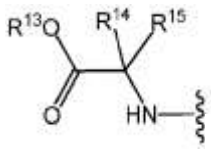
hvor R^{13} er valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-6}-alkyl, et eventuelt substituert C_{3-6} sykloalkyl, en eventuelt substituert aryl, en eventuelt substituert aryl(C_{1-6} alkyl) og et eventuelt substituert haloalkyl; R^{14} er valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{1-6} haloalkyl, et eventuelt substituert C_{3-6} sykloalkyl, en eventuelt substituert C_6 aryl, en eventuelt substituert C_{10} aryl og en eventuelt substituert aryl(C_{1-6} alkyl); og R^{15} er hydrogen eller et eventuelt substituert C_{1-4}-alkyl; eller R^{14} og R^{15} blir tatt sammen for å danne et eventuelt substituert C_{3-6} sykloalkyl; og R^{5B} har strukturen



hvor R^{16} er valgt fra gruppen bestående av hydrogen, et eventuelt substituert C_{1-6}-alkyl, et eventuelt substituert C_{3-6} sykloalkyl, en eventuelt substituert aryl, en eventuelt substituert aryl(C_{1-6} alkyl) og et eventuelt substituert haloalkyl; R^{17} er valgt fra gruppen

bestående av hydrogen, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{1-6} haloalkyl, et eventuelt substituert C_{3-6} sykloalkyl, en eventuelt substituert C_6 aryl, en eventuell C_{10} aryl og en eventuelt substituert aryl(C_{1-6} alkyl); og R^{18} er hydrogen eller et eventuelt substituert C_{1-4}-alkyl; eller R^{17} og R^{18} blir tatt sammen for å danne et eventuelt substituert C_{3-6} sykloalkyl; fortrinnsvis R^{14}, R^{15}, R^{17} og R^{18} er uavhengig hydrogen eller et eventuelt substituert C_{1-6}-alkyl; fortrinnsvis R^{13} er et eventuelt substituert C_{1-6} alkyl eller et eventuelt substituert C_{3-6} sykloalkyl.

15. Forbindelsen ifølge krav 14, hvor



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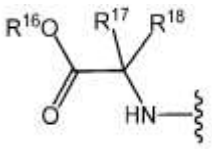
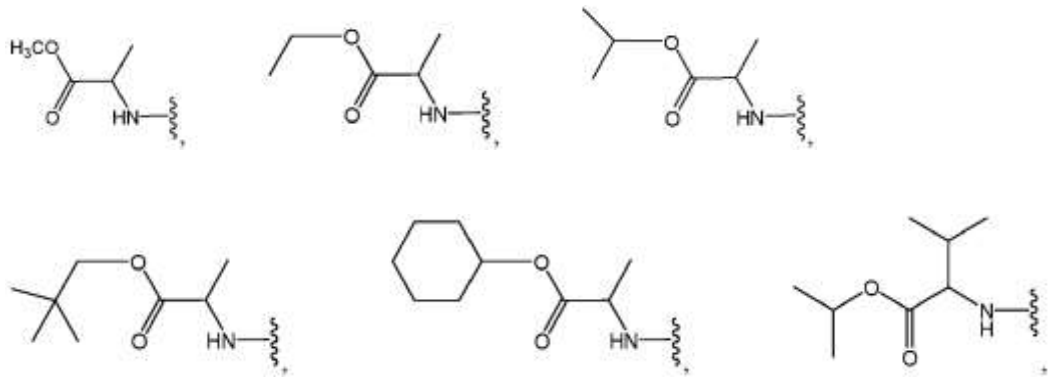
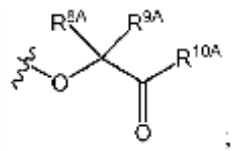


er uavhengig

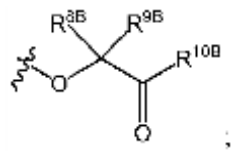


eller

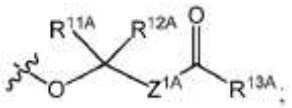
16. Forbindelsen ifølge krav 13, hvor R^{5A} er



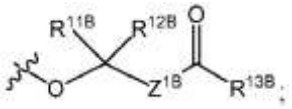
og R^{5B} er



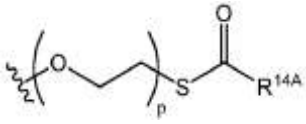
eller hvor R^{5A} er



og R^{5B} er



eller hvor R^{5A} er



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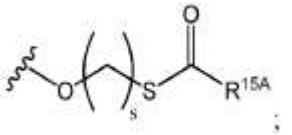
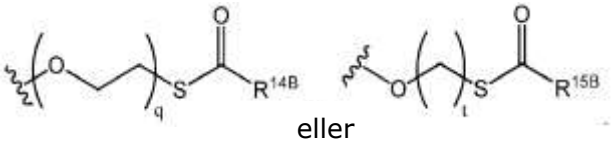


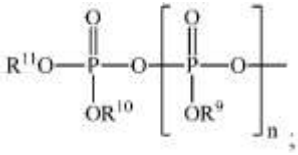
og R^{5B} er



eller

17. Forbindelsen ifølge krav 13, hvor R^{5A} er en eventuelt substituert N-koblet aminosyreester; og R^{5B} er valgt fra gruppen bestående av en -O-eventuelt substituert aryl, en -O-eventuelt substituert heteroaryl og en -O-eventuelt substituert heterosyklyl.

18. Forbindelsen ifølge krav 13, hvor R^{5A} er O^- eller OH; R^{5B} er O^-, OH eller

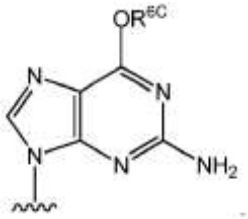


og n er 0 eller 1.

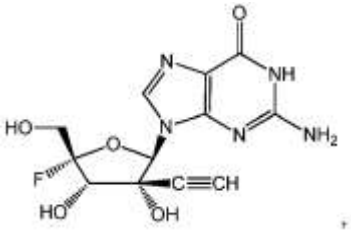
19. Forbindelsen ifølge et hvilket som helst av kravene 1-18, hvor Z^1 er O.

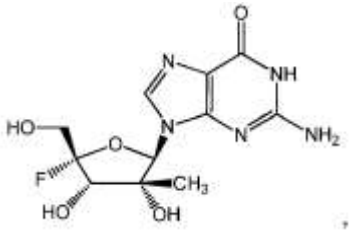
20. Forbindelsen ifølge et hvilket som helst av kravene 1-18, hvor Z^1 er S.

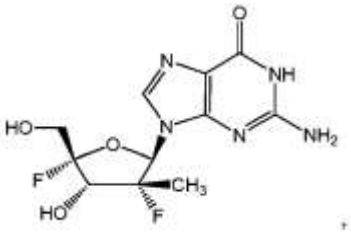
21. Forbindelsen ifølge et hvilket som helst av kravene 1-20, hvor B^1 er en eventuelt substituert

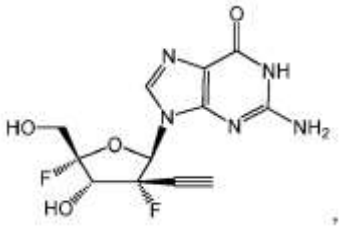


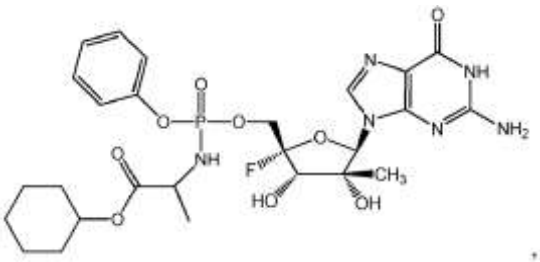
22. Forbindelsen ifølge krav 1 valgt fra gruppen bestående av:

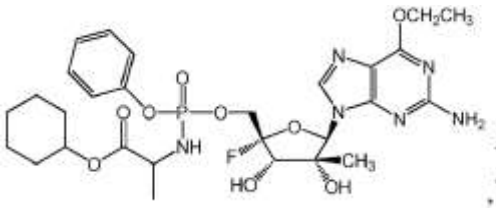


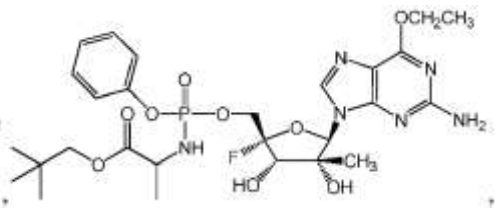


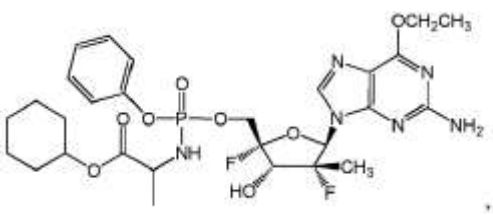


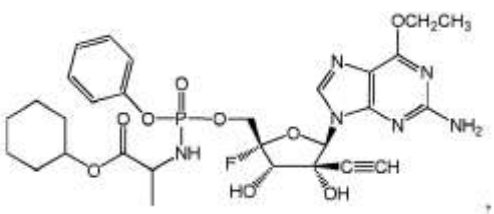


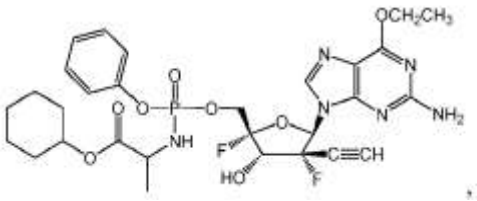


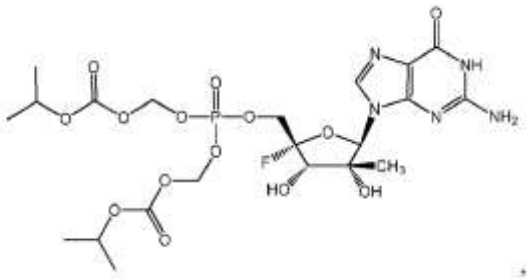


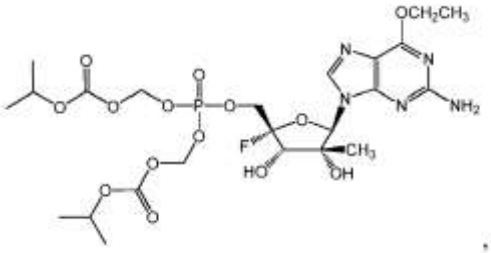


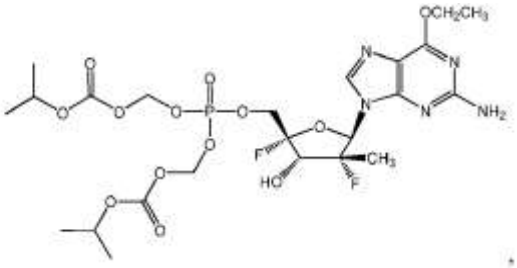


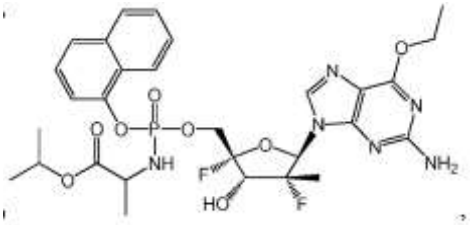


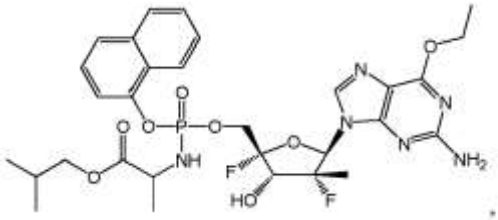


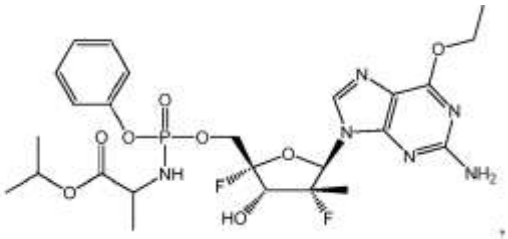


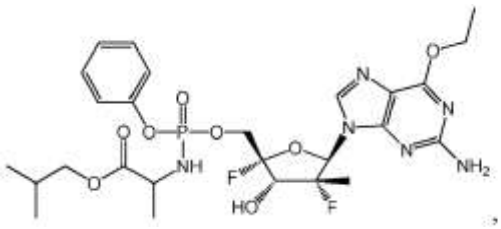


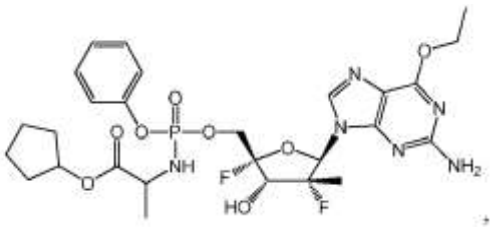


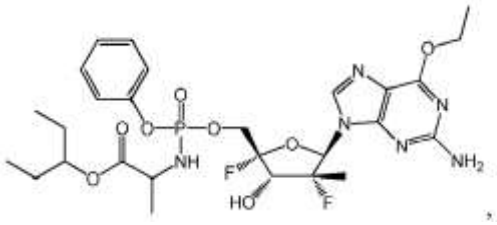


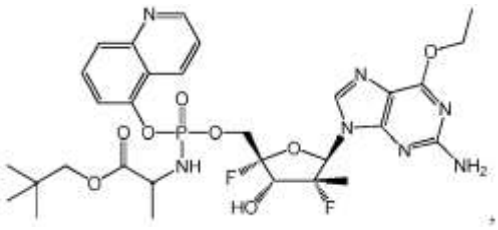


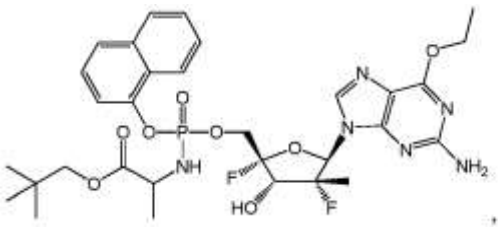


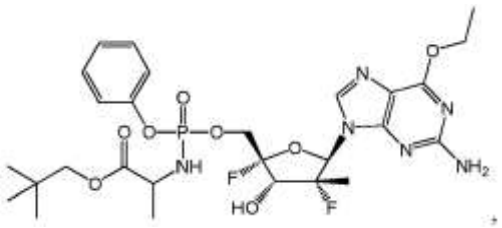


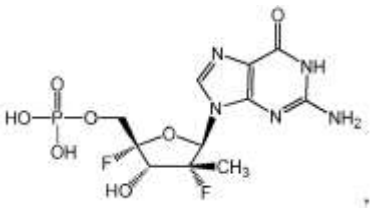


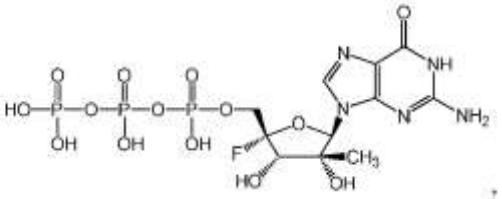


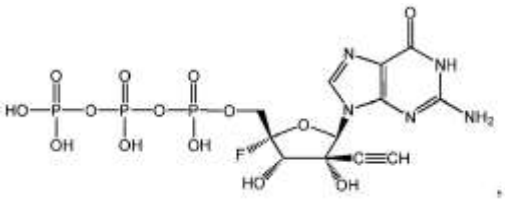


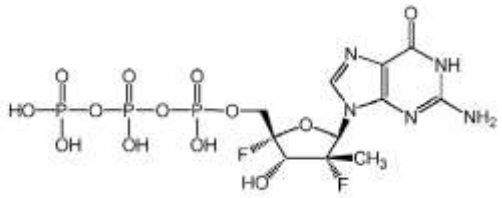




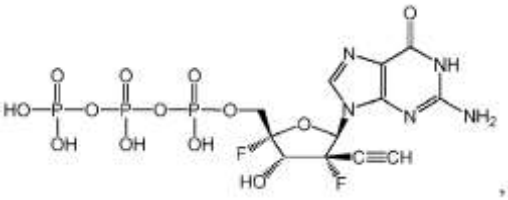






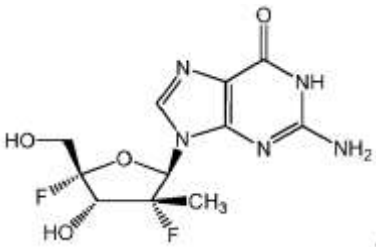


og



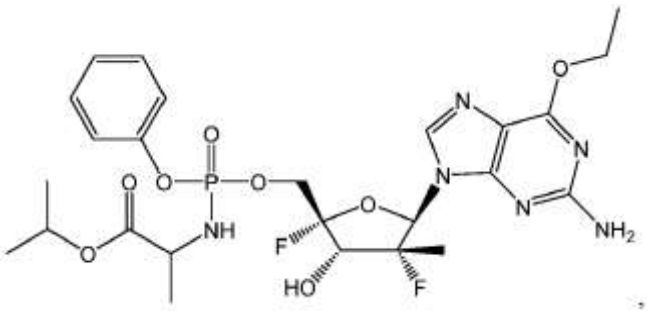
eller et farmasøytisk akseptabelt salt av det foregående.

23. Forbindelsen ifølge krav 1, hvor forbindelsen er



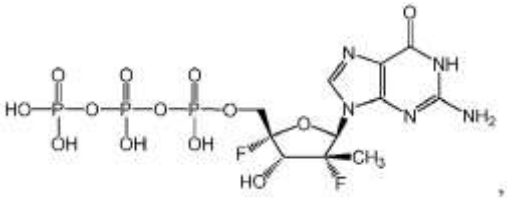
eller et farmasøytisk akseptabelt salt derav.

24. Forbindelsen ifølge krav 1, hvor forbindelsen er



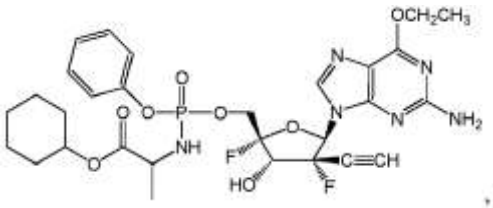
eller et farmasøytisk akseptabelt salt derav.

25. Forbindelsen ifølge krav 1, hvor forbindelsen er



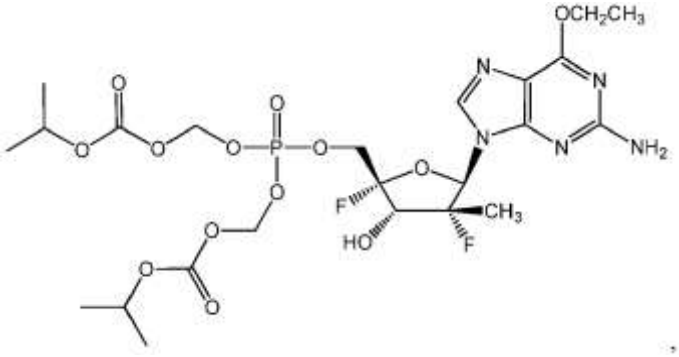
eller et farmasøytisk akseptabelt salt derav.

26. Forbindelsen ifølge krav 1, hvor forbindelsen er



eller et farmasøytisk akseptabelt salt derav.

27. Forbindelsen ifølge krav 1, hvor forbindelsen er



eller et farmasøytisk akseptabelt salt derav.

28. En farmasøytisk sammensetning som omfatter en effektiv mengde av en forbindelse ifølge et hvilket som helst av kravene 1-27, eller et farmasøytisk akseptabelt salt derav, og en farmasøytisk akseptabel bærer, fortynningsmiddel, eksipiens eller kombinasjon derav.

29. En forbindelse ifølge et hvilket som helst av kravene 1-27, eller et farmasøytisk akseptabelt salt derav, for anvendelse ved lindring eller behandling av en HCV infeksjon.

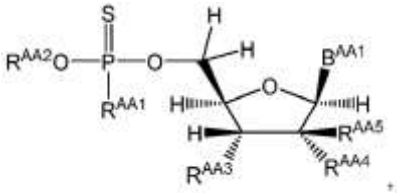
30. En forbindelse ifølge et hvilket som helst av kravene 1-27, eller et farmasøytisk akseptabelt salt derav, for anvendelse ved inhibering av NS5B polymerase aktivitet av et hepatitt C virus.

31. En forbindelse ifølge et hvilket som helst av kravene 1-27, eller et farmasøytisk akseptabelt salt derav, for anvendelse ved inhibering av replikasjon av et hepatitt C virus.

32. Forbindelsen for anvendelse ifølge et hvilket som helst av kravene 29-31, som videre omfatter anvendelsen av ett eller flere midler valgt fra gruppen bestående av et interferon, ribavirin, en HCV proteaseinhibitor, en HCV polymeraseinhibitor, en NS5A-inhibitor, en antivirus-forbindelse, en forbindelse med formel (AA), en forbindelse med formel (BB) og en forbindelse med formel (CC), eller et farmasøytisk akseptabelt salt av noen av de ovennevnte,

hvor:

Formel (AA) har strukturen:

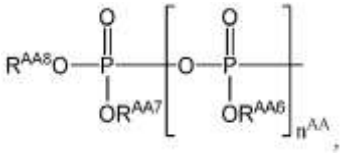


hvor:

B^{AA1} er en eventuelt substituert heterosyklisk base eller en eventuelt substituert heterosyklisk base med en beskyttet aminogruppe;

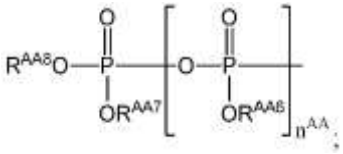
R^{AA1} er valgt fra O^-, OH, en eventuelt substituert N-koblet aminosyre og en eventuelt substituert N-koblet aminosyreester;

R^{AA2} er fraværende eller valgt fra hydrogen, en eventuelt substituert aryl, en eventuelt substituert heteroaryl, en eventuelt substituert heterosyklyl og



hvor R^{AA6}, R^{AA7} og R^{AA8} er uavhengig fraværende eller hydrogen, og n^{AA} er 0 eller 1;

forutsatt at når R^{AA1} er O^- eller OH, så er R^{AA2} fraværende, hydrogen eller



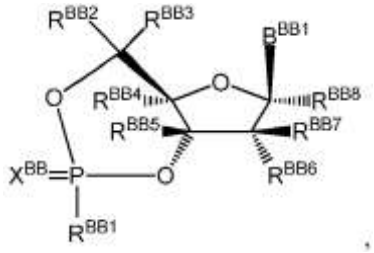
R^{AA3} er valgt fra hydrogen, halogen, $-OR^{AA9}$ og $-OC(=O)R^{AA10}$;

R^{AA4} er valgt fra halogen, $-OR^{AA11}$ og $-OC(=O)R^{AA12}$; eller R^{AA3} og R^{AA4} er begge et oksygenatom som er bundet sammen av en karbonylgruppe;

R^{AA5} er valgt fra et eventuelt substituert C_{2-6} alkyl, et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl og et eventuelt substituert C_{3-6} sykloalkyl; eller R^{AA4} og R^{AA5} danner sammen -(C_{1-6} alkyl)-O- eller -O-(C_{1-6} alkyl)-;

R^{AA9} og R^{AA11} er uavhengig hydrogen eller et eventuelt substituert C_{1-6} alkyl; og R^{AA10} og R^{AA12} er uavhengig et eventuelt substituert C_{1-6} alkyl eller en eventuelt substituert C_{3-6} sykloalkyl;

Formel (BB) har strukturen:



hvor:

B^{BB1} er en eventuelt substituert heterosyklisk base eller en eventuelt substituert heterosyklisk base med en beskyttet aminogruppe;

X^{BB} er O (oksygen) eller S (svovel);

R^{BB1} er valgt fra -Z^{BB}-R^{BB9}, en eventuelt substituert N-koblet aminosyre og en eventuelt substituert N-koblet aminosyreester;

Z^{BB} er valgt fra O (oksygen), S (svovel) og N(R^{BB10});

R^{BB2} og R^{BB3} er uavhengig valgt fra hydrogen, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl, et eventuelt substituert C_{1-6} haloalkyl og en eventuelt substituert aryl(C_{1-6} alkyl); eller R^{BB2} og R^{BB3} blir tatt sammen for å danne en gruppe valgt fra et eventuelt substituert C_{3-6} sykloalkyl, et eventuelt substituert C_{3-6} sykloalkenyl, en eventuelt substituert C_{3-6} aryl og en eventuelt substituert C_{3-6} heteroaryl;

R^{BB4} er valgt fra hydrogen, halogen, azido, cyano, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl og et eventuelt substituert allenyl;

R^{BB5} er hydrogen eller et eventuelt substituert C_{1-6} alkyl;

R^{BB6} er valgt fra hydrogen, halogen, azido, amino, cyano, et eventuelt substituert C_{1-6} alkyl, -OR^{BB11} og -OC(=O)R^{BB12};

R^{BB7} er valgt fra hydrogen, halogen, azido, cyano, et eventuelt substituert C_{1-6} alkyl, -OR^{BB13} og -OC(=O)R^{BB14};

R^{BB8} er valgt fra hydrogen, halogen, azido, cyano, et eventuelt substituert C_{1-6} alkyl, $-OR^{BB15}$ og $-OC(=O)R^{BB16}$;

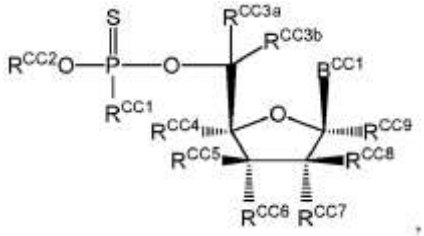
R^{BB9} er valgt fra et eventuelt substituert alkyl, et eventuelt substituert alkenyl, et eventuelt substituert alkynyl, et eventuelt substituert sykloalkyl, et eventuelt substituert sykloalkenyl, en eventuelt substituert aryl, en eventuelt substituert heteroaryl, et eventuelt substituert heterosyklyl, en eventuelt substituert aryl(C_{1-6} alkyl), en eventuelt substituert heteroaryl(C_{1-6}alkyl) og et eventuelt substituert heterosyklyl(C_{1-6}alkyl);

R^{BB10} er valgt fra hydrogen, et eventuelt substituert alkyl, et eventuelt substituert alkenyl, et eventuelt substituert alkynyl, et eventuelt substituert sykloalkyl, et eventuelt substituert sykloalkenyl, en eventuelt substituert aryl, en eventuelt substituert heteroaryl, en eventuelt substituert heterosyklyl, en eventuelt substituert aryl(C_{1-6}alkyl), en eventuelt substituert heteroaryl(C_{1-6}alkyl) og et eventuelt substituert heterosyklyl(C_{1-6}alkyl);

R^{BB11}, R^{BB13} og R^{BB15} er uavhengig hydrogen eller et eventuelt substituert C_{1-6} alkyl; og

R^{BB12}, R^{BB14} og R^{BB16} er uavhengig et eventuelt substituert C_{1-6} alkyl eller et eventuelt substituert C_{3-6} sykloalkyl; og

Formel (CC) har strukturen:

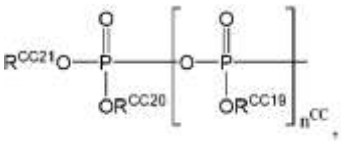


hvor:

B^{CC1} er en eventuelt substituert heterosyklisk base eller en eventuelt substituert heterosyklisk base med en beskyttet aminogruppe;

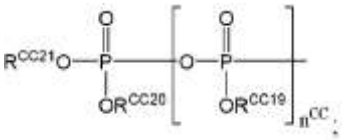
R^{CC1} er valgt fra O^-, OH, en eventuelt substituert N-koblet aminosyre og en eventuelt substituert N-koblet aminosyreester;

R^{CC2} er valgt fra en eventuelt substituert aryl, en eventuelt substituert heteroaryl, et eventuelt substituert heterosyklyl og



hvor R^{CC19}, R^{CC20} og R^{CC21} er uavhengig fraværende eller hydrogen, og n^{CC} er 0 eller

1; forutsatt at når R^{CC1} er O^- eller OH, så er R^{CC2}



R^{CC3a} og R^{CC3b} er uavhengig valgt fra hydrogen, deuterium, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{2-6} alkenyl, et eventuelt substituert C_{2-6} alkynyl, en eventuelt substituert C_{1-6} haloalkyl og aryl(C_{1-6} alkyl); eller R^{CC3a} og R^{CC3b} blir tatt sammen for å danne en eventuelt substituert C_{3-6} sykloalkyl;

R^{CC4} er valgt fra hydrogen, azido, et eventuelt substituert C_{1-6} alkyl, et eventuelt substituert C_{2-6} alkenyl og et eventuelt substituert C_{2-6} alkynyl;

R^{CC5} er valgt fra hydrogen, halogen, azido, cyano, et eventuelt substituert C_{1-6} alkyl, $-OR^{CC10}$ og $-OC(=O)R^{CC11}$;

R^{CC6} er valgt fra hydrogen, halogen, azido, cyano, en eventuelt substituert C_{1-6} alkyl, $-ORCC^{12}$ og $-OC(=O)R^{CC13}$;

R^{CC7} er valgt fra hydrogen, halogen, azido, cyano, en eventuelt substituert C_{1-6} alkyl, $-OR^{CC14}$ og $-OC(=O)R^{CC15}$; eller R^{CC6} og R^{CC7} er begge oksygenatomer og bundet sammen av en karbonylgruppe;

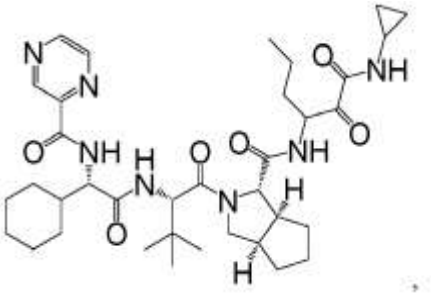
R^{CC8} er valgt fra hydrogen, halogen, azido, cyano, et eventuelt substituert C_{1-6} alkyl, $-ORCC^{16}$ og $-OC(=O)R^{CC17}$;

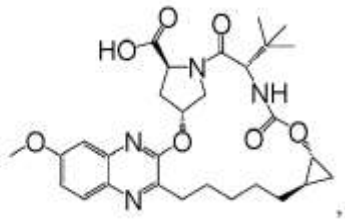
R^{CC9} er valgt fra hydrogen, azido, cyano, en eventuelt substituert C_{1-6} alkyl og $-OR^{CC18}$;

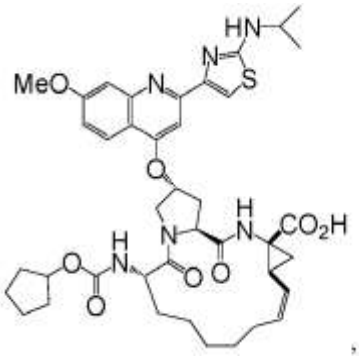
R^{CC10}, R^{CC12}, R^{CC14}, R^{CC16} og R^{CC18} er uavhengig valgt fra hydrogen og en eventuelt substituert C_{1-6} alkyl; og

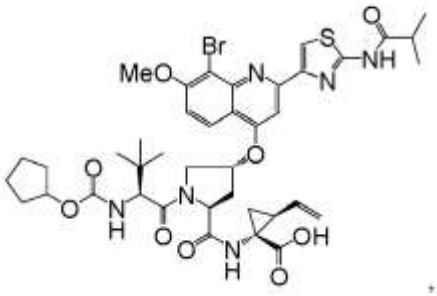
R^{CC11}, R^{CC13}, R^{CC15} og R^{CC17} er uavhengig valgt fra en eventuelt substituert C_{1-6} alkyl og en eventuelt substituert C_{3-6} sykloalkyl;

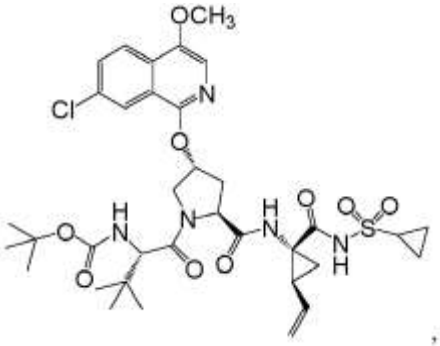
fortrinnsvis de ett eller flere midler er valgt fra gruppen bestående av:
ABT-450, GS-9256, GS-9451, IDX-320, ACH-1625, ACH-2684, PHX1766, PSI-661, GS-6620, TMC649128, NM283, BCX5191, IDX19368, IDX19370, ABT-333, BI-207127, ABT-072, MK-3281, TMC647055, BMS-791325, PPI-383, GS9669, PPI-461, ACH-2928, GS-5885, BMS-824393, ABT 267, ACH-3102, AZD-7295, IDX719, PPI-668, MK8742, GSK805, alisporivir, MIR-122, clemizole, ITX 5061, BIT225, NIM811, SCY-635, miravirsen, GS9620,

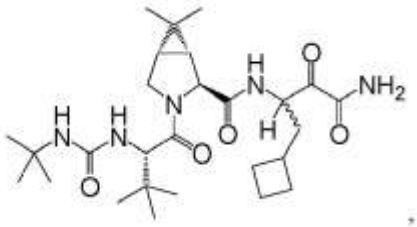


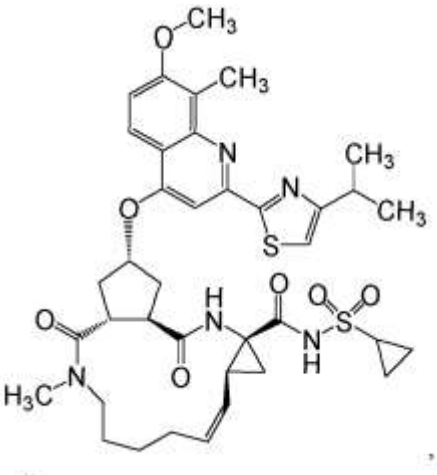


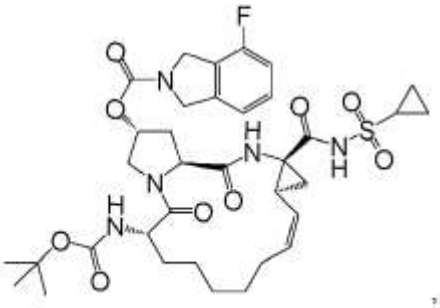


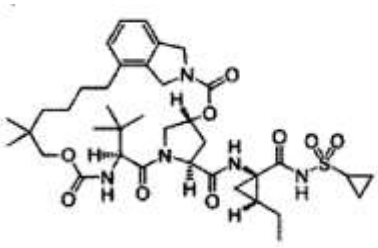


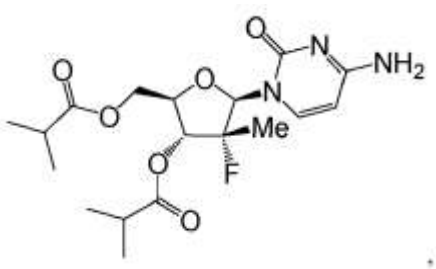


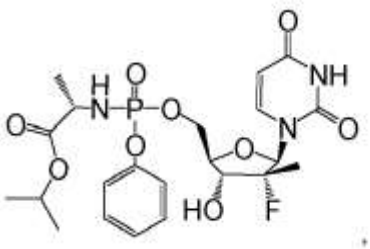


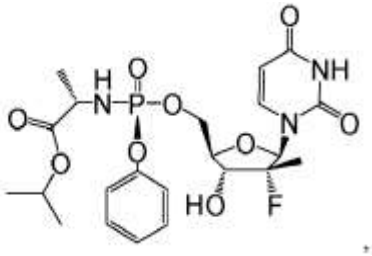


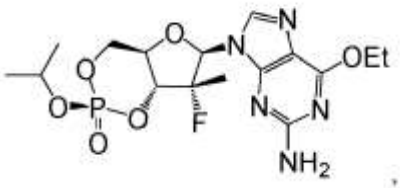


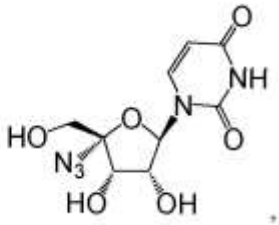


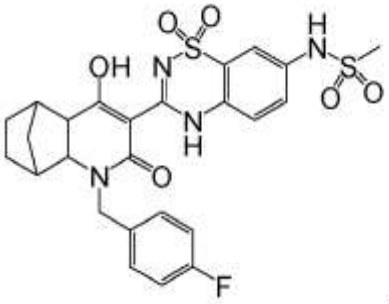


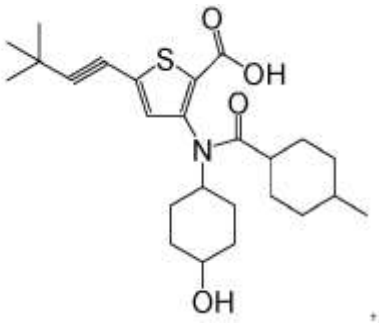


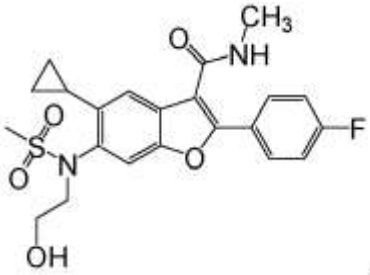


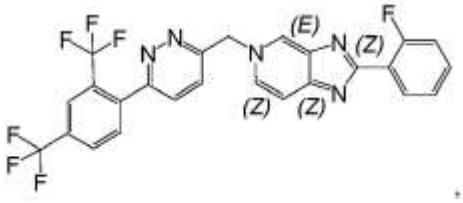


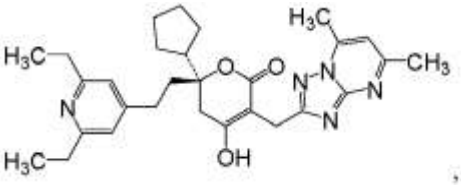


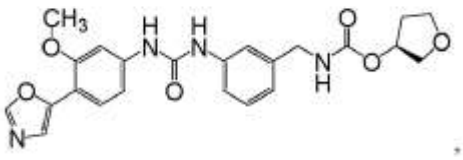


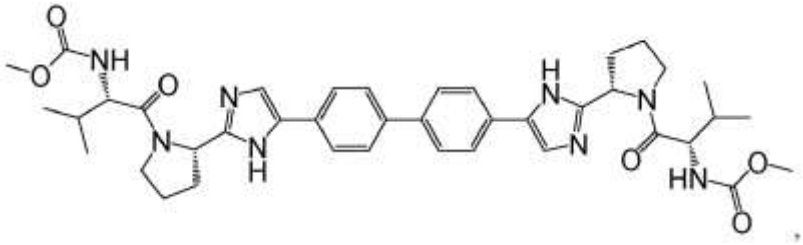


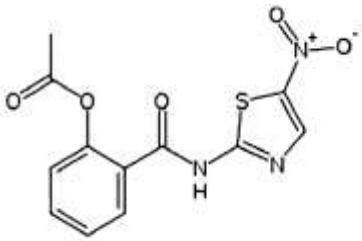


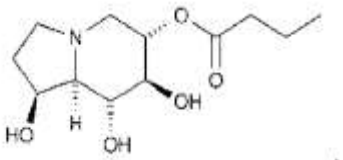


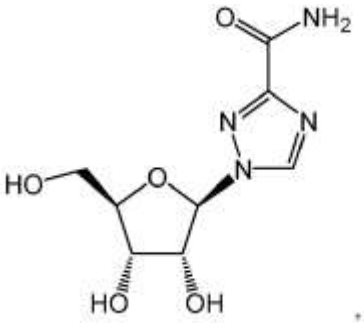


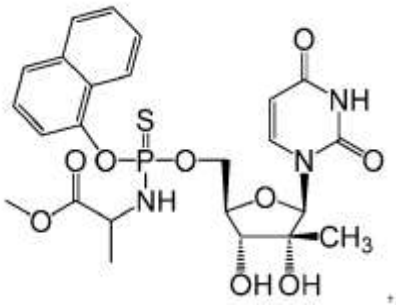


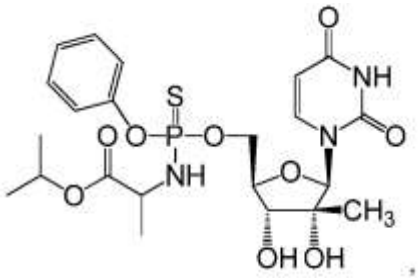


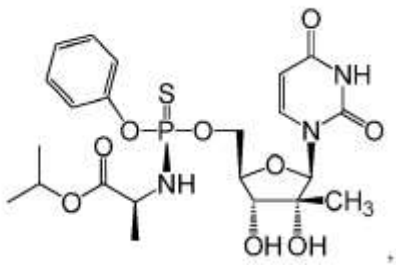


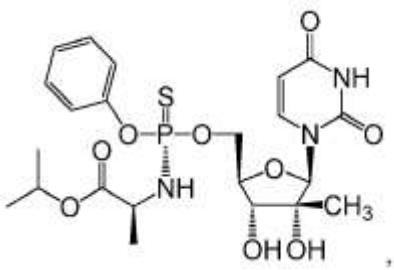


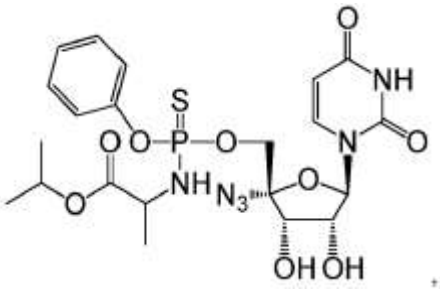


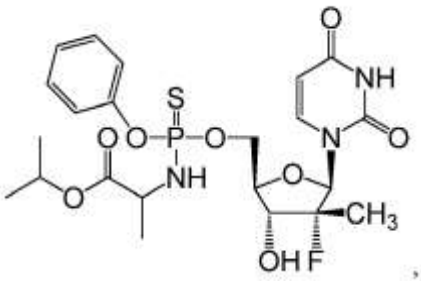


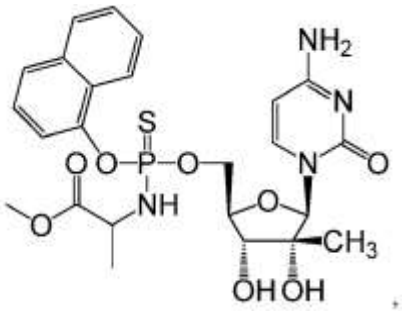


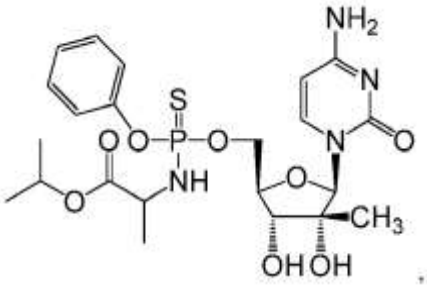


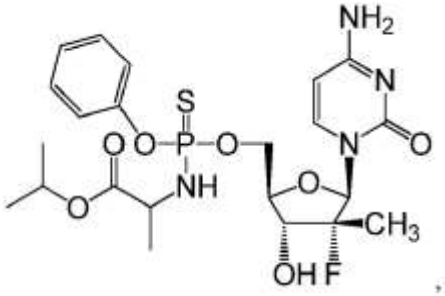


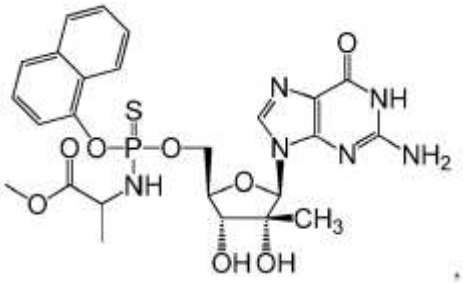


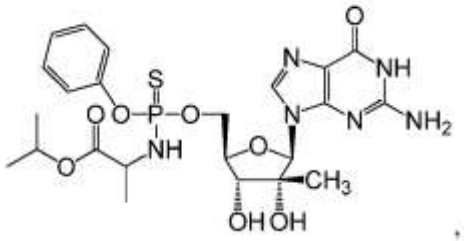


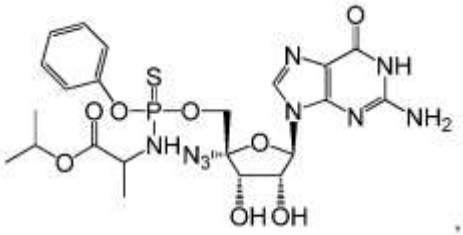


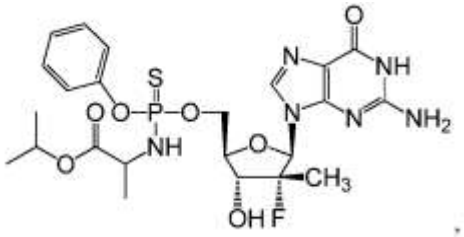


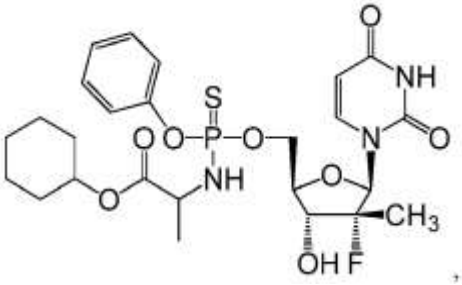


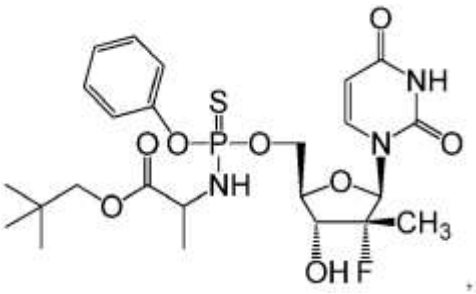


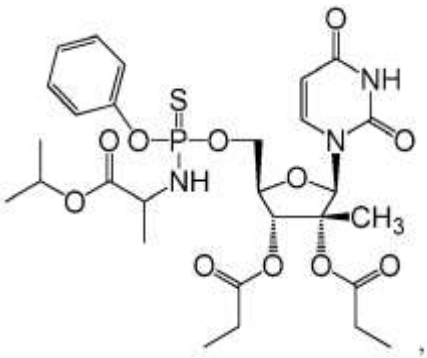


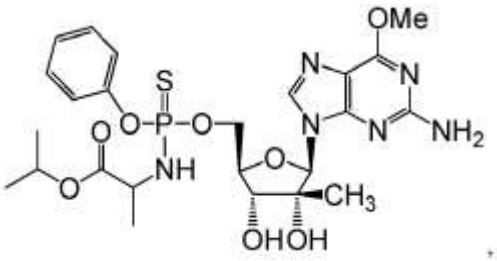


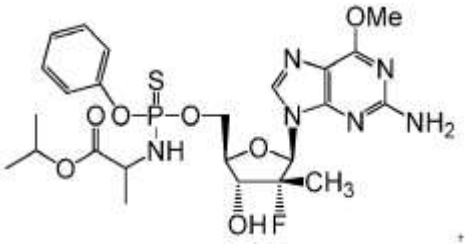


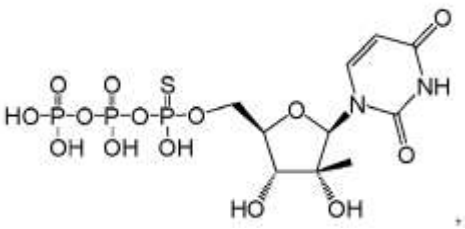


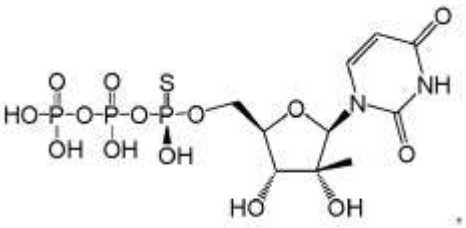


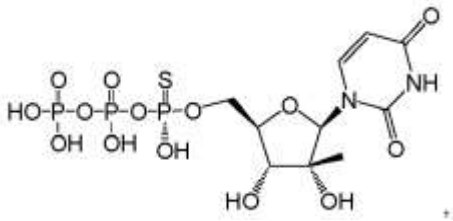


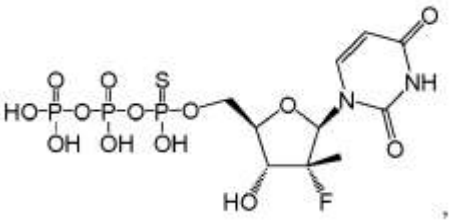


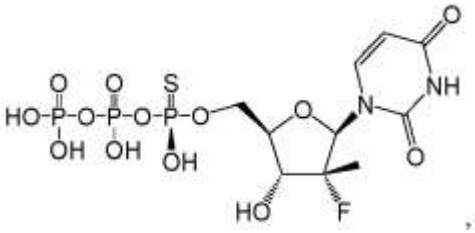


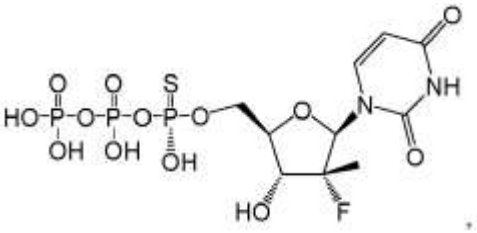


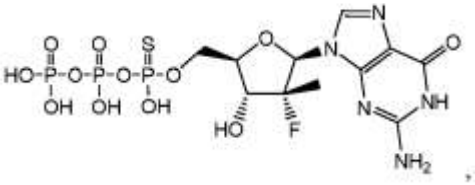


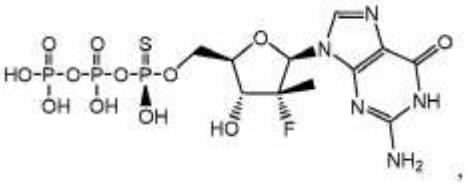


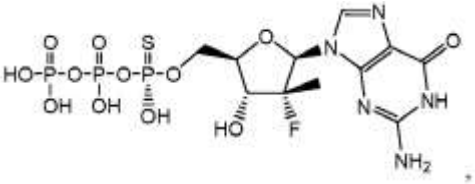


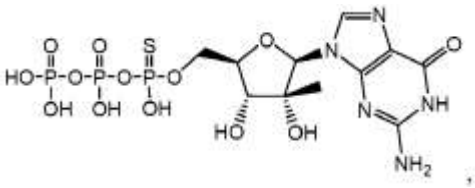


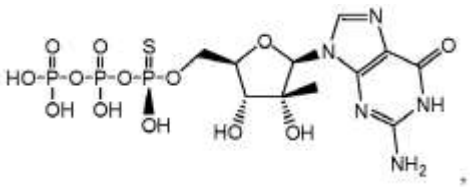


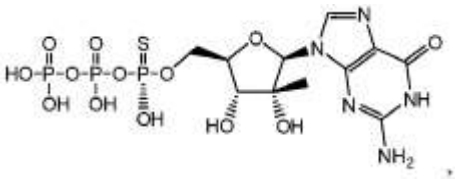


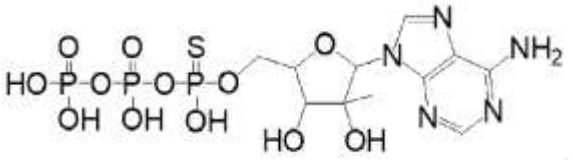


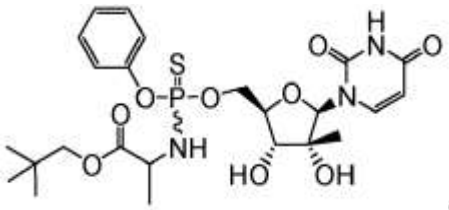


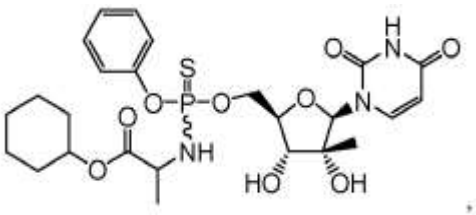


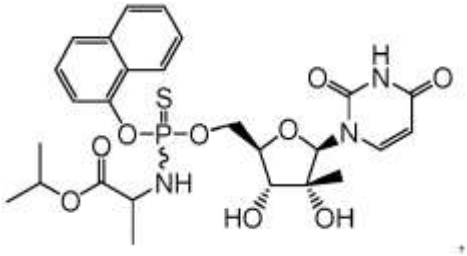


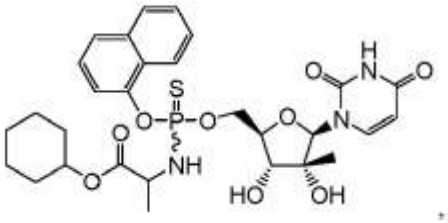


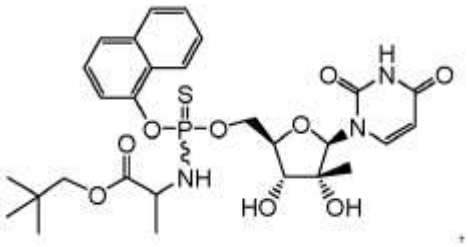


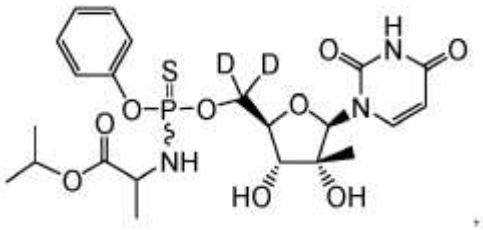


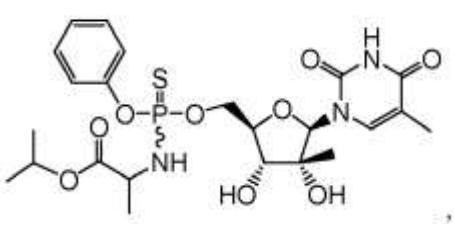


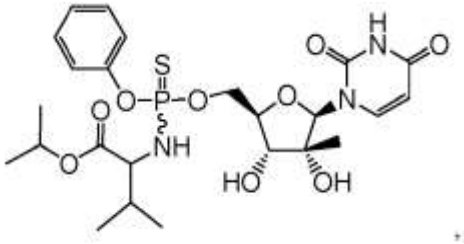


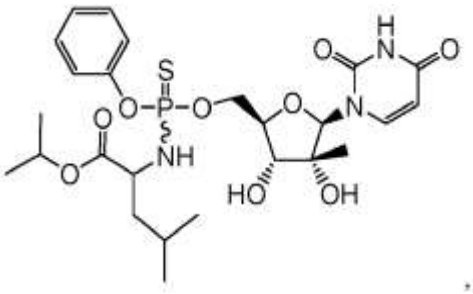


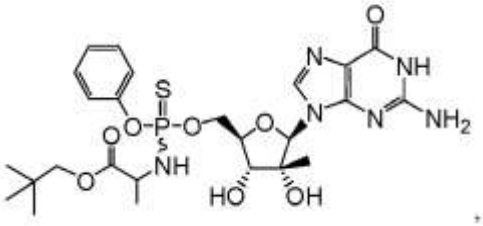


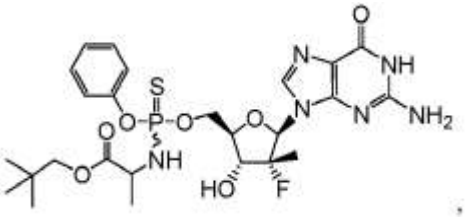


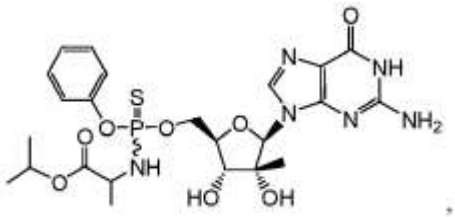


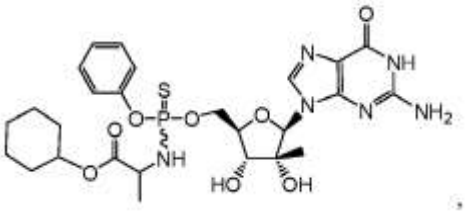


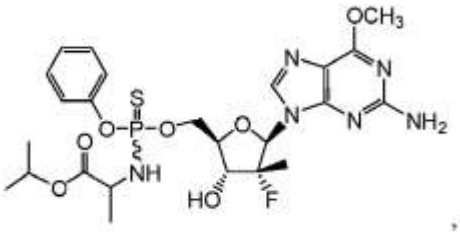


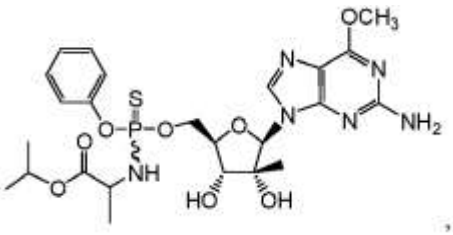


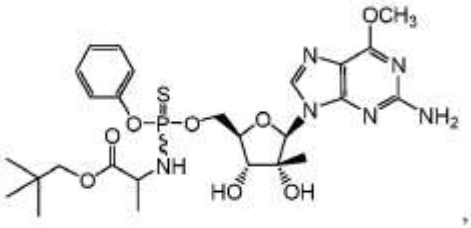


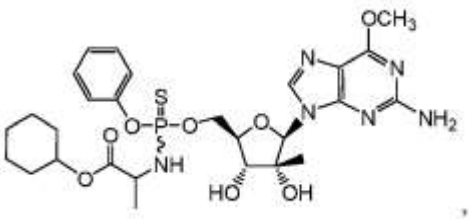


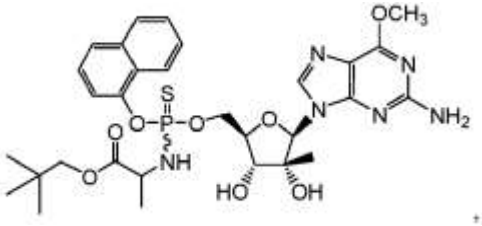


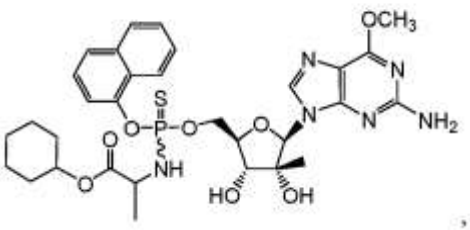


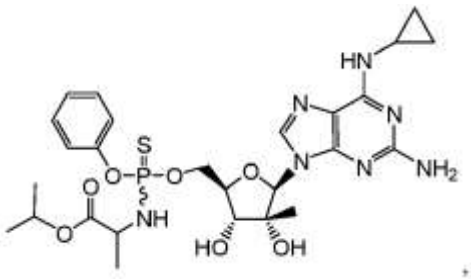


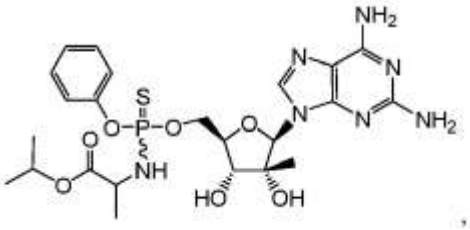


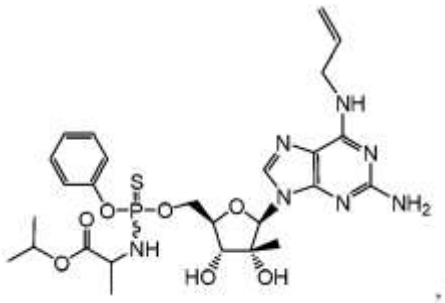


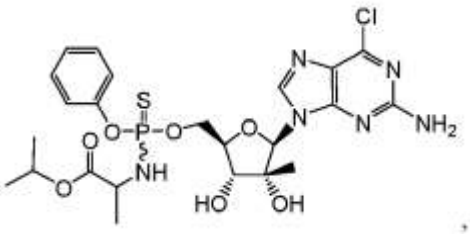


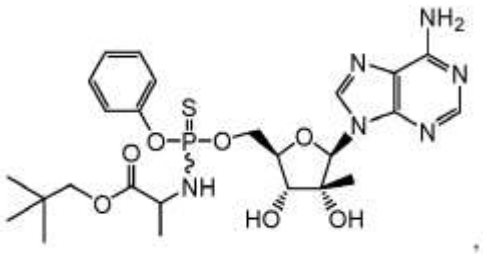


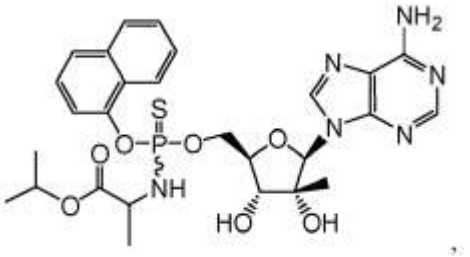


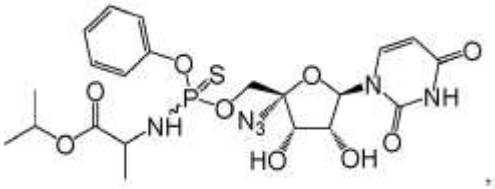


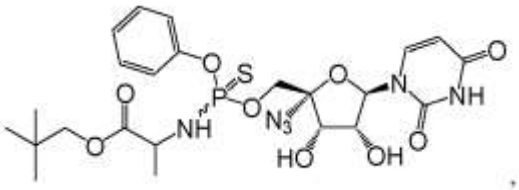


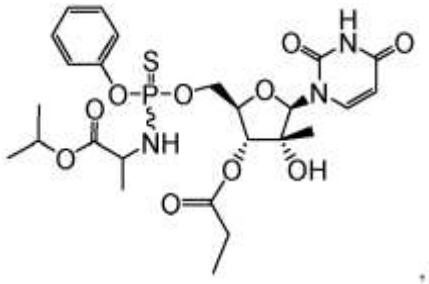


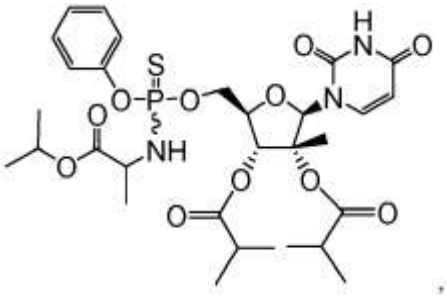


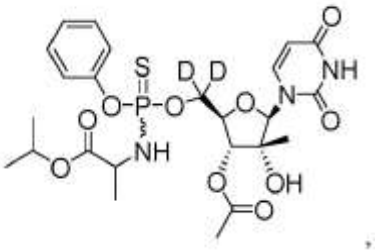


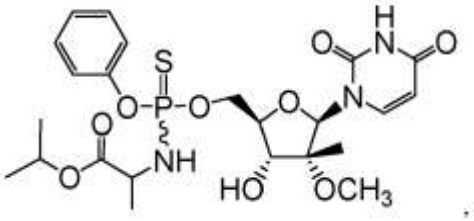


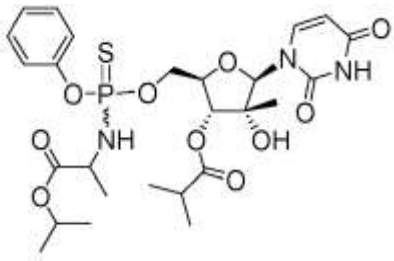


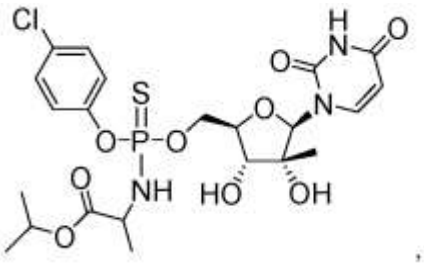


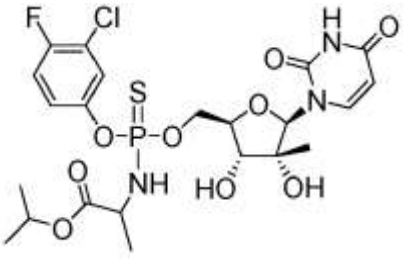


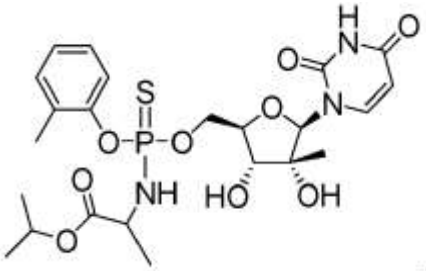


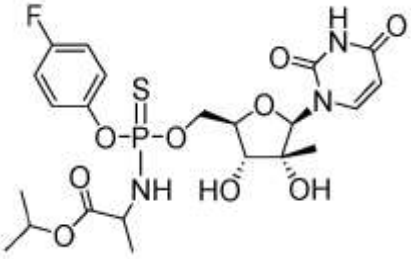


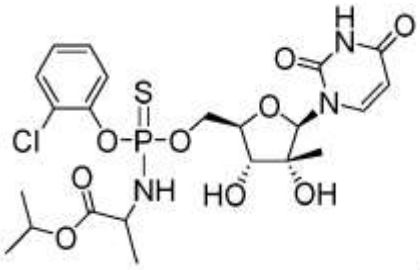


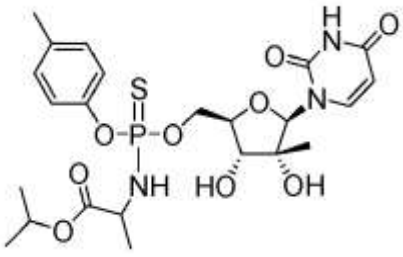


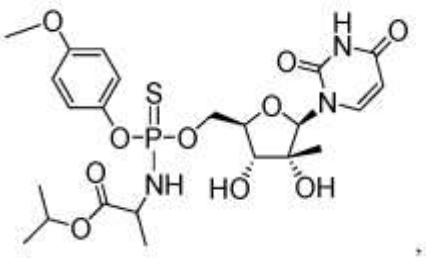


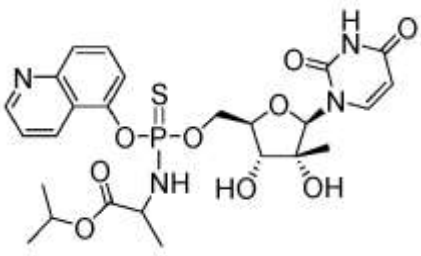


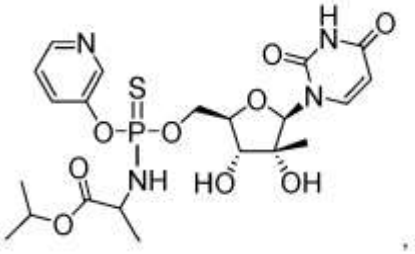


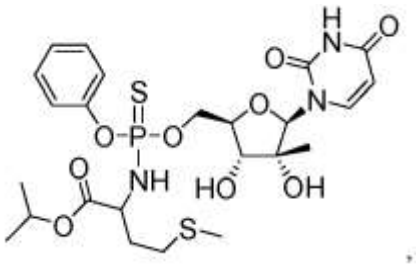


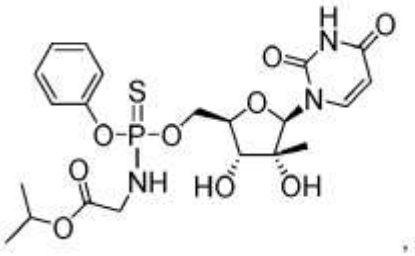


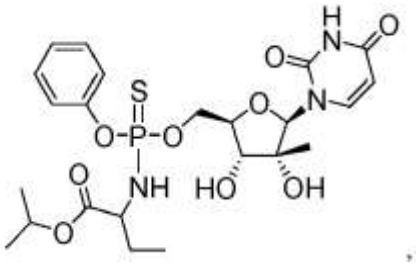


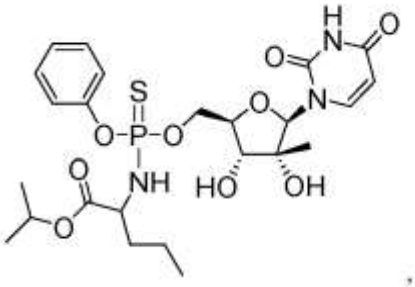


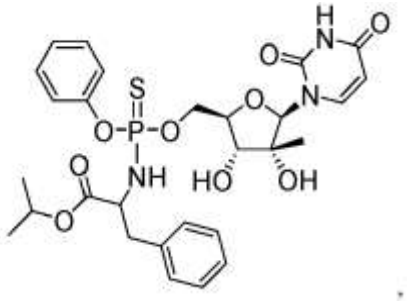


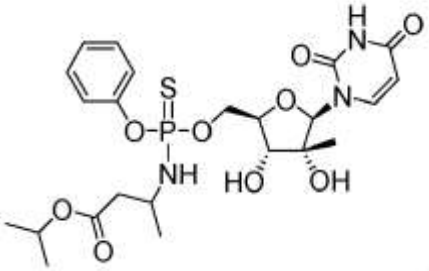


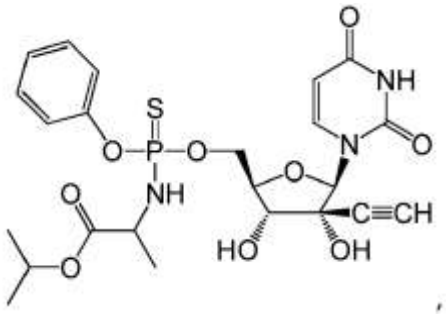


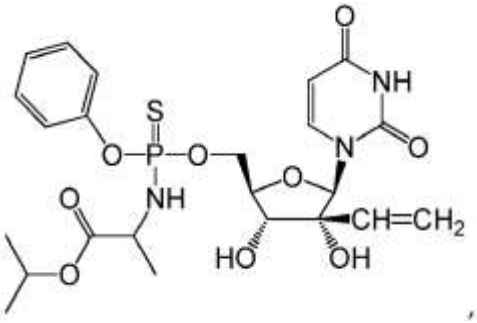


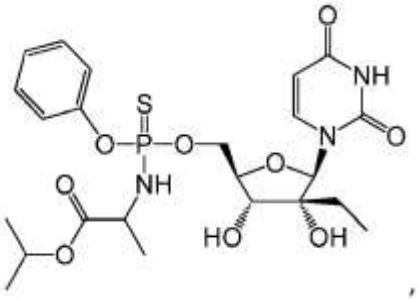


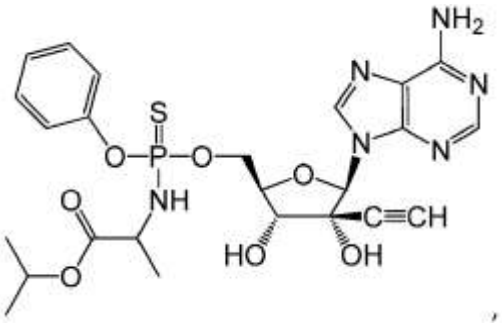


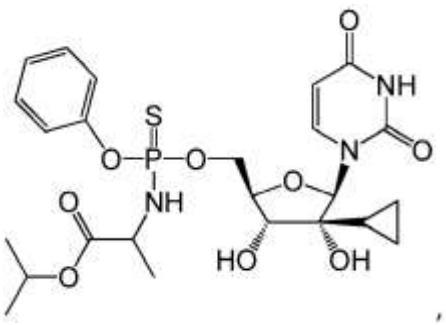


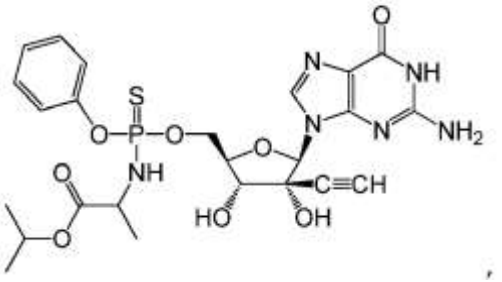


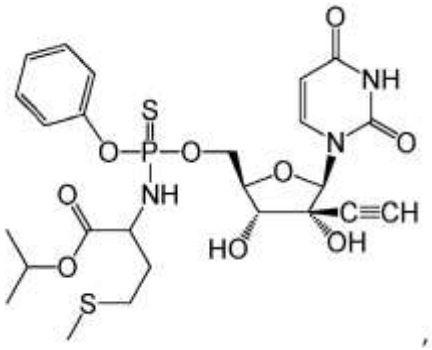


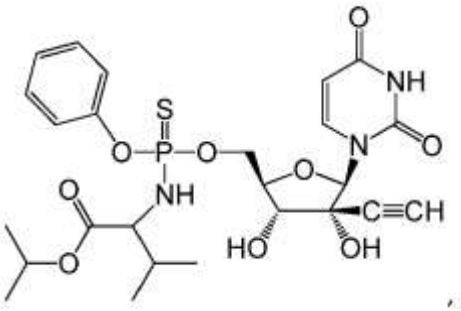


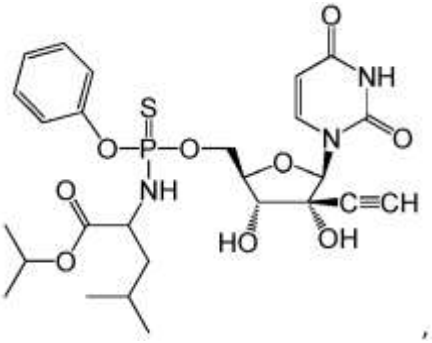


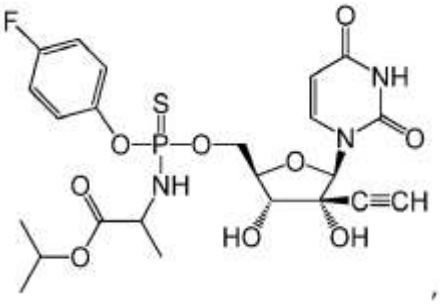


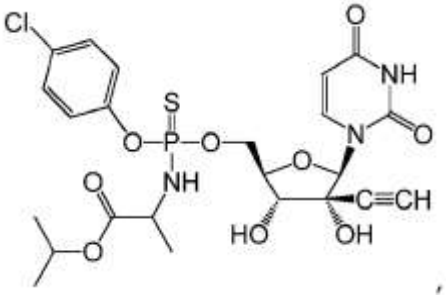


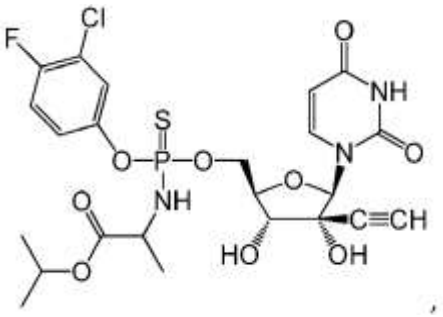












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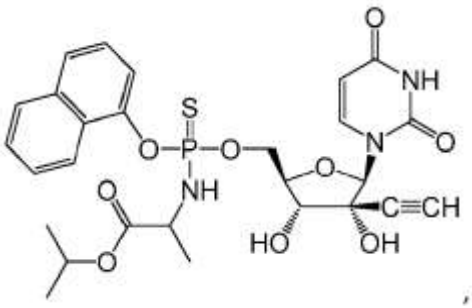

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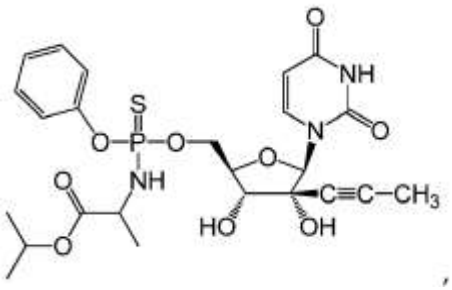

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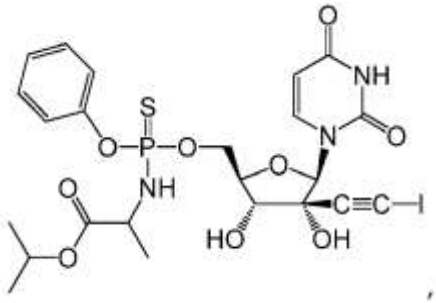

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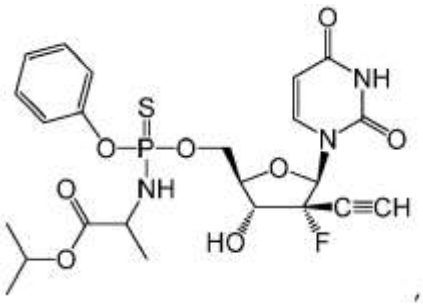

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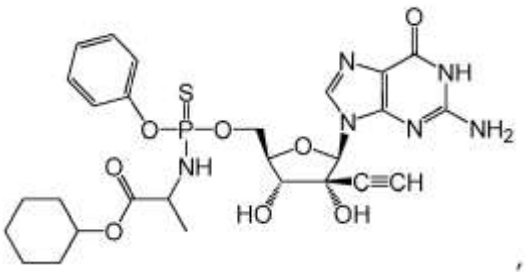

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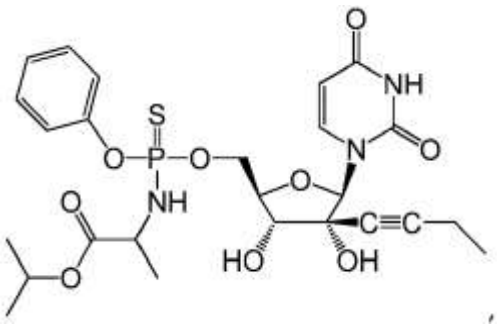

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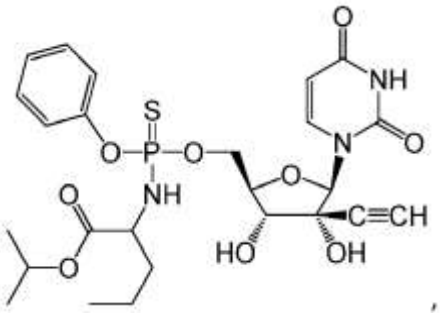

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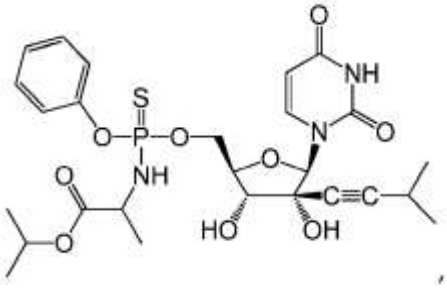

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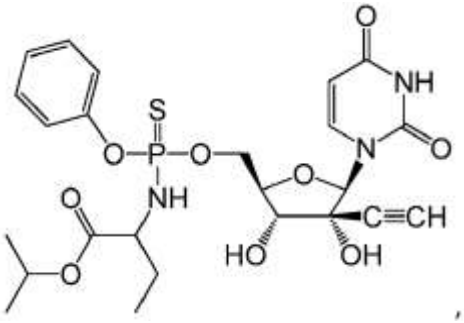

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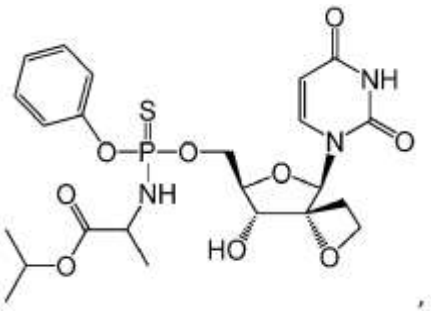

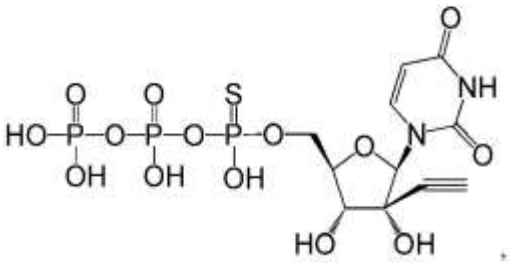

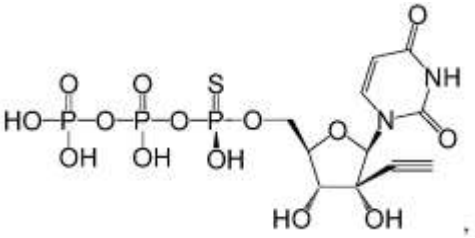

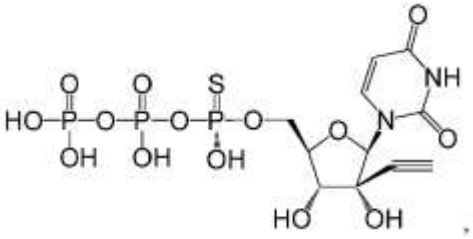

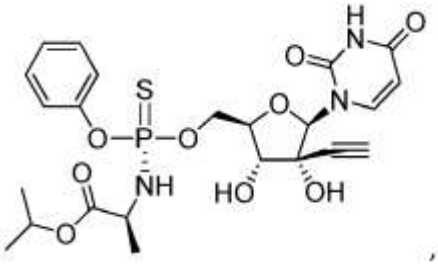

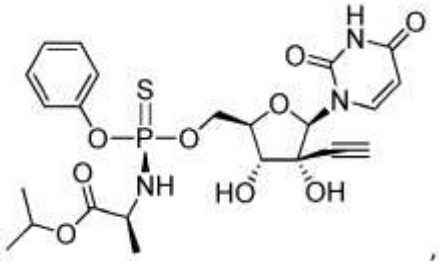

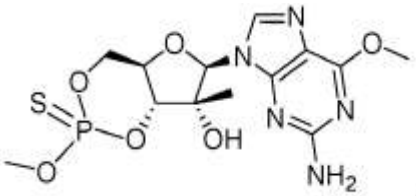

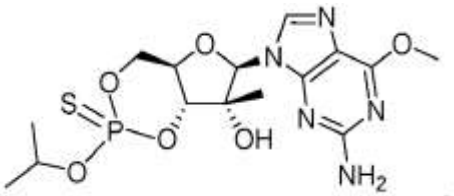

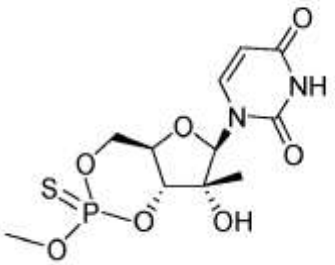

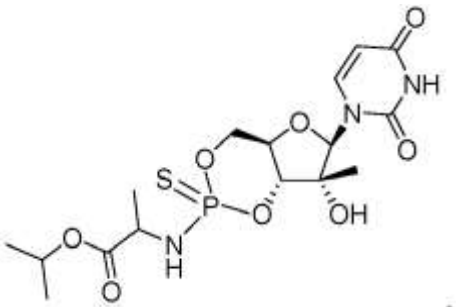

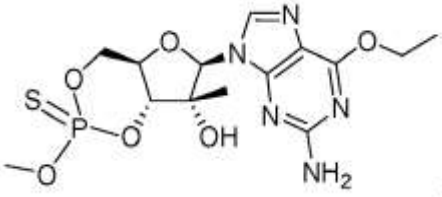

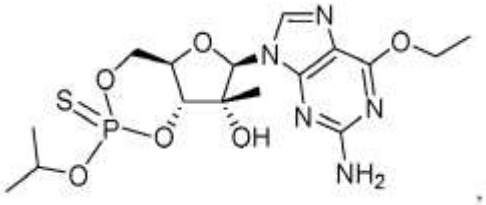

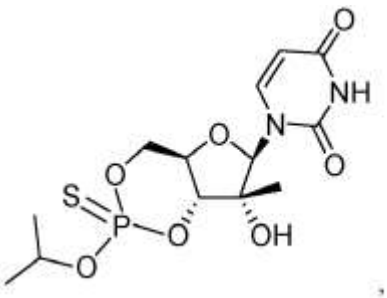

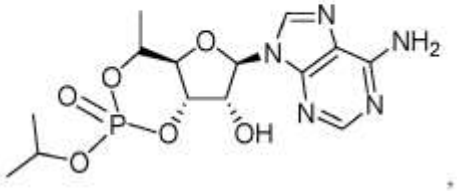

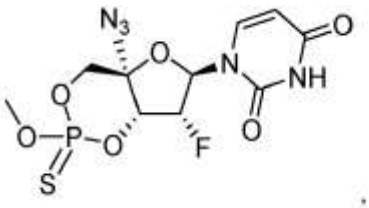

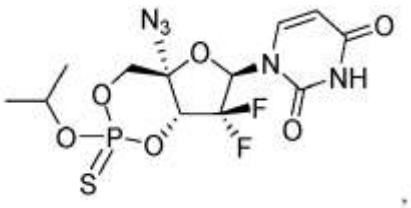

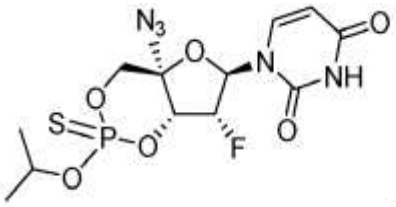

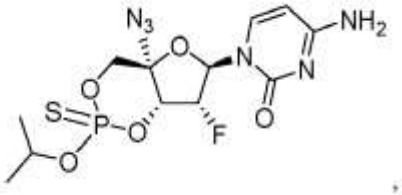

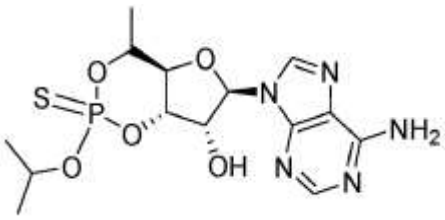

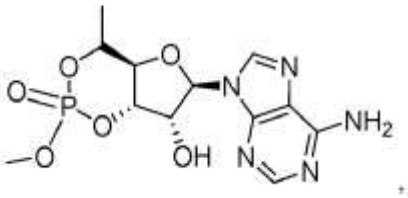

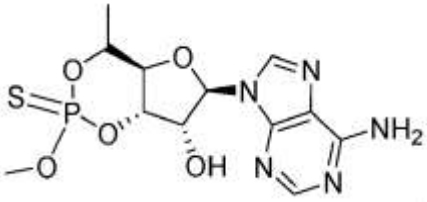

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