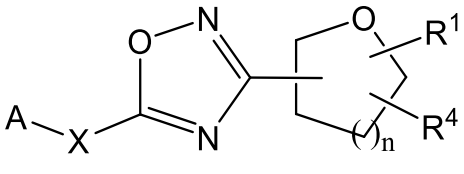
SUMMARY

[0005] There is provided a compound of formula (I), stereoisomers thereof, tautomers thereof, and salts thereof:


(I);

wherein:

A is: substituted or unsubstituted 6-6 fused bicyclic heteroaryl;substituted or unsubstituted 5-6 fused bicyclic heteroaryl; or substituted and unsubstituted 6-5 fused bicyclic heteroaryl;

X is; a bond; C_{1-4} alkylene; -O-; -S-; $-SO_2-$; or $-N(R^a)-$;

n is: 0, 1, 2 or 3;

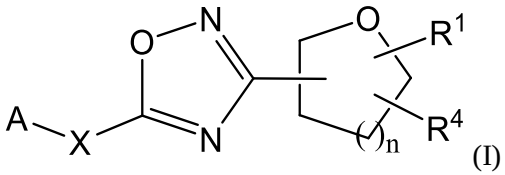
R^a is H or C_{1-6} alkyl which may be unsubstituted or substituted one or more times with halo;

R^1 is: H; or C_{1-6}alkyl; and

R^4 is: substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl;

or R^1 and R^4 may together form an unsubstituted or substituted C_{3-6}cylcoalkyl fused to a substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl.

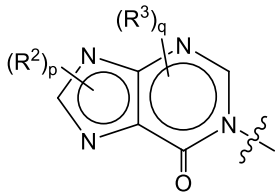
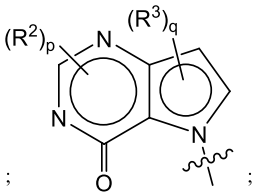
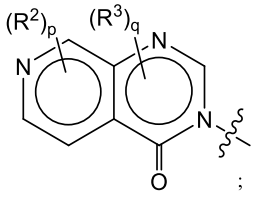
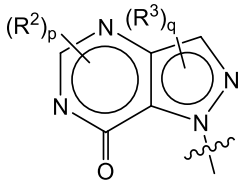
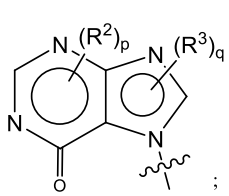
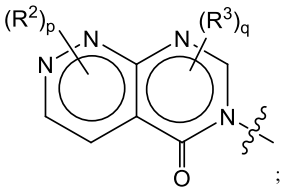
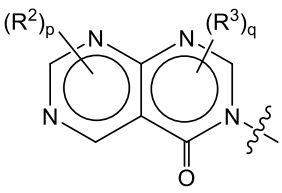
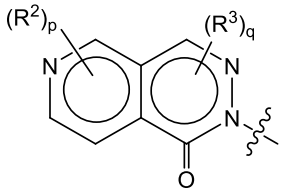
[0005a] In one aspect, there is provded a compound of formula I,

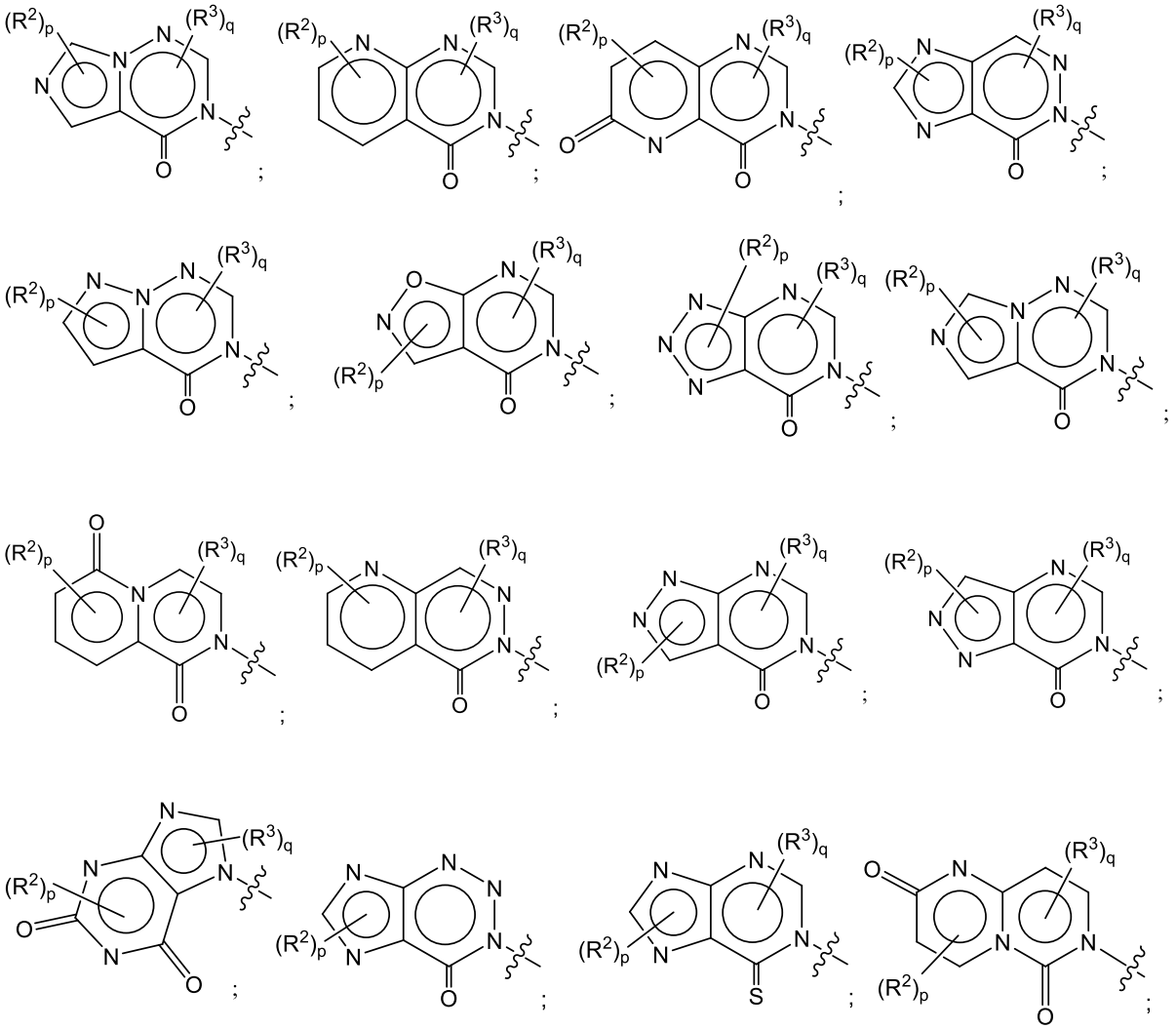

(I)

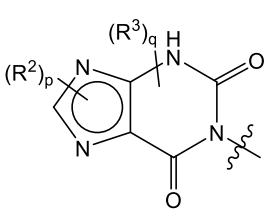
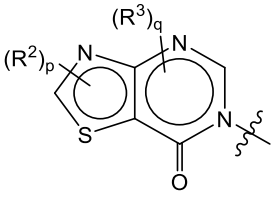
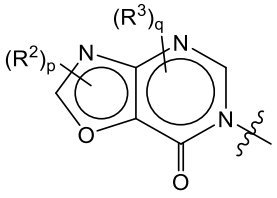
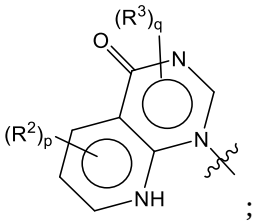
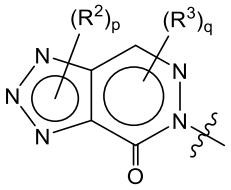
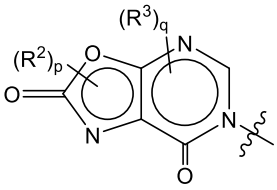
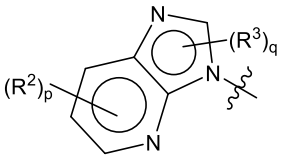
or a pharmaceutically acceptable salt thereof,

wherein:

A is selected from:


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; and

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X is: a bond; C_{1-4} alkylene; -O-; -S-; -SO_2-; or -N(R^a)-;

n is: 0, 1, 2 or 3;

R^a is H or C_{1-6} alkyl which may be unsubstituted or substituted one or more times with halo;

R^1 is: H; or C_{1-6}alkyl;

each R^2 is independently: H; D; -C_{1-4} alkyl; -C_{1-4} haloalkyl; C_{1-4} alkoxy; -CN, halo; halo-C_{1-4}alkoxy; -OH; -SO_2-C_{1-4}alkyl; -C_{1-4}CN, C_{1-4} aldehyde; C_{1-4} ketone; benzylamino; or $NR^{14}R^{15}$;

each R^3 is independently: H; D: -C_{1-4} alkyl; -C_{1-4} haloalkyl; -CN; $NR^{14}R^{15}$; or halo;

R^4 is: substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl;

or R^1 and R^4 may together form an unsubstituted or substituted C_{3-6}cylcoalkyl fused to a substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl.

p is 0, 1 or 2;

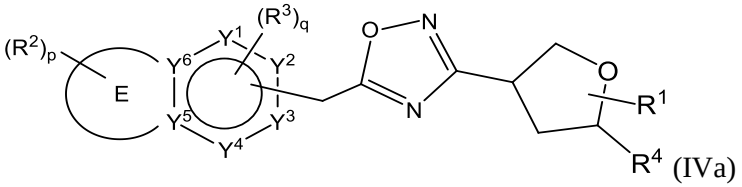
q is 0 or 1;

R^{14} and R^{15} are each independently: H; substituted or unsubstituted -C_{1-4} alkyl; substituted or unsubstituted -C(O)-C_{1-4} alkyl; substituted or unsubstituted C_{3-6} cycloalkyl; substituted or unsubstituted 3- to 6-membered heterocycloalkyl; substituted or unsubstituted -C_{1-4} heteroalkyl; -C(O)$NR^{16}R^{17}$; substituted or unsubstituted -C_{1-4} alkyl-C(O)$NR^{16}R^{17}$; substituted or unsubstituted phenyl; or substituted or unsubstituted benzyl;

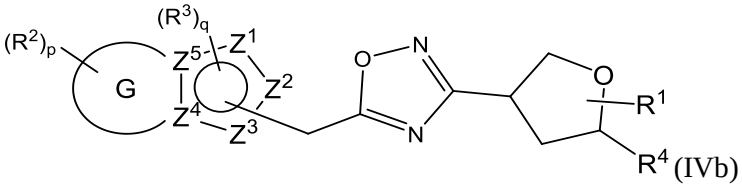
or R^{14} and R^{15} together with the atoms to which they are attached may form a 4-, 5-, 6- or 7-membered ring that optionally includes one additional heteroatom selected from O, N and S; and

R^{16} and R^{17} each are independently H and C_{1-4} alkyl.

[0005b] In another aspect, there is provided a compound of formula (IVa) or formula (IVb), or a pharmaceutically acceptable salt thereof,



(IVa)



(IVb)

wherein:

E is a five membered or a six membered heteroaryl ring wherein one ring carbon atom is optionally substituted with oxo;

G is a six membered heteroaryl ring having one ring carbon atom substituted with oxo;

one to three of Y^1, Y^2, Y^3, Y^4, Y^5 and Y^6 are nitrogen, and the other of Y^1, Y^2, Y^3, Y^4, Y^5 and Y^6 are carbon, and one of Y^1, Y^2, Y^3 and Y^4 may be –C(O)- or -C(S)-;

one or two of Z^1, Z^2, Z^3, Z^4 and Z^5 are nitrogen and the other of Z^1, Z^2, Z^3, Z^4 and Z^5 are carbon;

R^1 is: H; or C_{1-6}alkyl;

each R^2 is independently; H; D; -C_{1-4} alkyl; -C_{1-4} haloalkyl; -CN; halo; haloC_{1-4}alkoxy; C_{1-4} alkoxy; -OH; -SO_2-C_{1-4}alkyl; -C_{1-4}CN, C_{1-4} aldehyde; C_{1-4} ketone; benzylamino; or $NR^{14}R^{15}$;

each R^3 is independently: H; D; -C_{1-4} alkyl; -C_{1-4} haloalkyl; -CN; halo; or $NR^{14}R^{15}$;

R^4 is: substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl;

or R^1 and R^4 may together form an unsubstituted or substituted C_{3-6}cylcoalkyl fused to a substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl.

p is 0, 1 or 2;

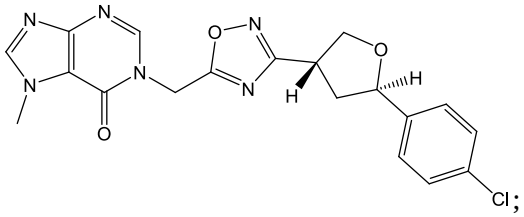
q is 0 or 1;

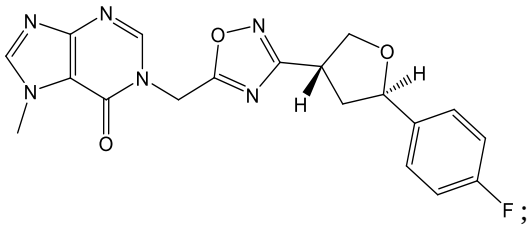
R^{14} and R^{15} are each independently: H; substituted or unsubstituted -C_{1-4} alkyl; substituted or unsubstituted -C(O)-C_{1-4} alkyl; substituted or unsubstituted C_{3-6} cycloalkyl; substituted or unsubstituted 3- to 6-membered heterocycloalkyl; substituted or unsubstituted -C_{1-4} heteroalkyl; -C(O)$NR^{16}R^{17}$; substituted or unsubstituted -C_{1-4} alkyl-C(O)$NR^{16}R^{17}$; substituted or unsubstituted phenyl; or substituted or unsubstituted benzyl;

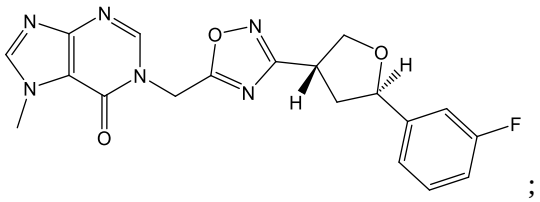
or R^{14} and R^{15} together with the atoms to which they are attached may form a 4-, 5-, 6- or 7-membered ring that optionally includes one additional heteroatom selected from O, N and S; and

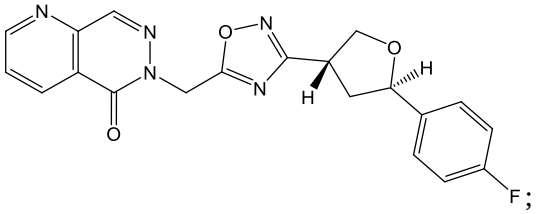
R^{16} and R^{17} each are independently H and C_{1-4} alkyl.

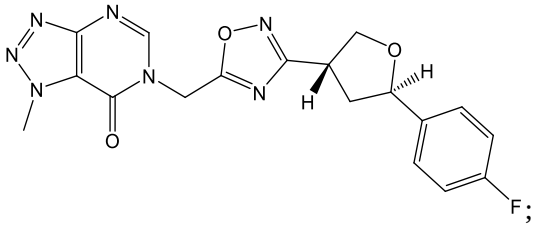
[0005c] In another aspect, there is provided a compound selected from:

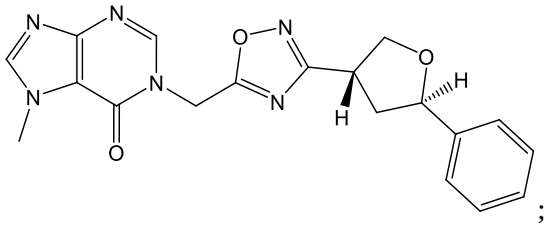

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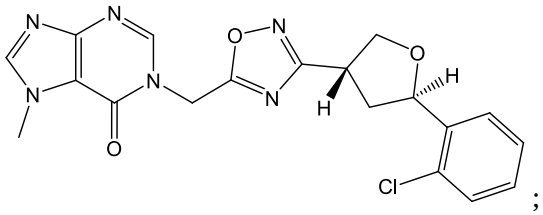

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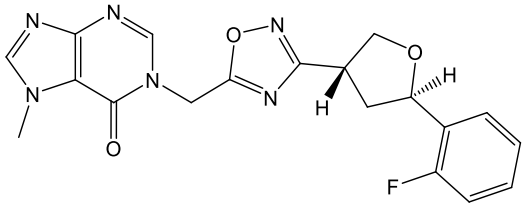

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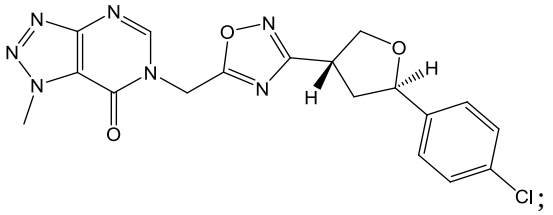

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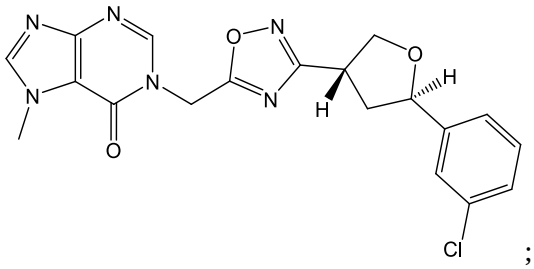

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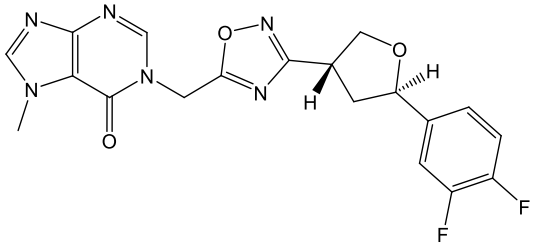

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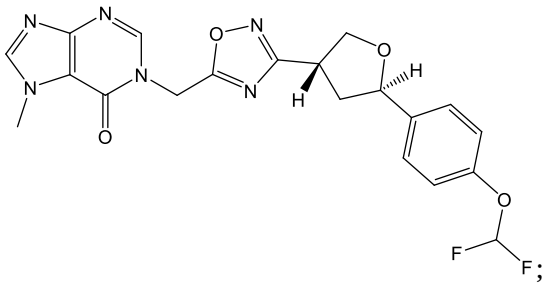

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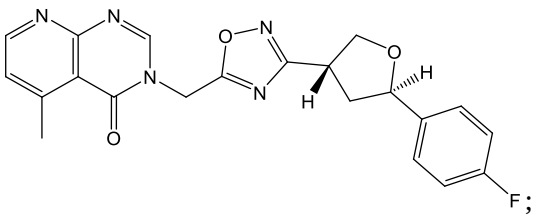

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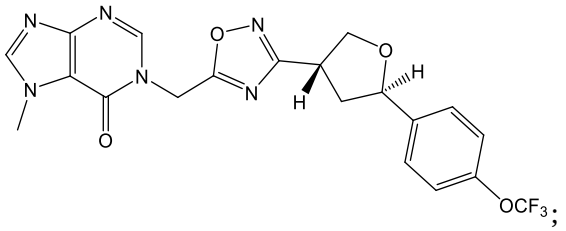

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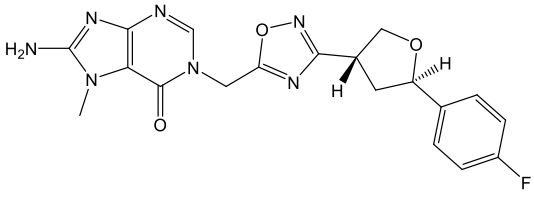

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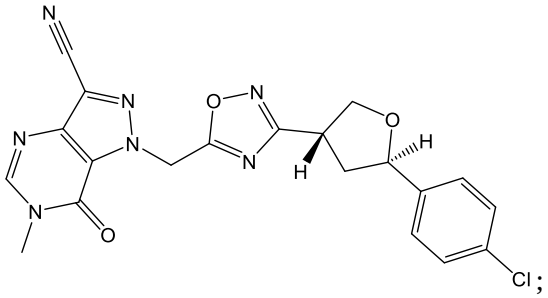

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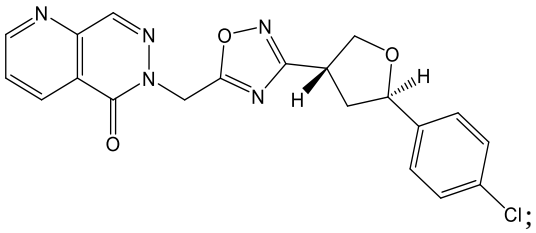

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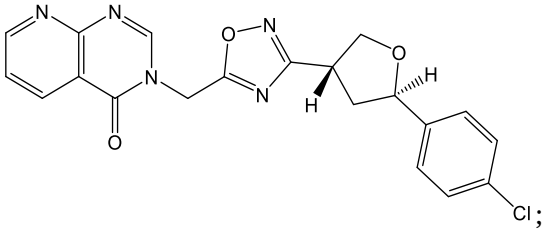

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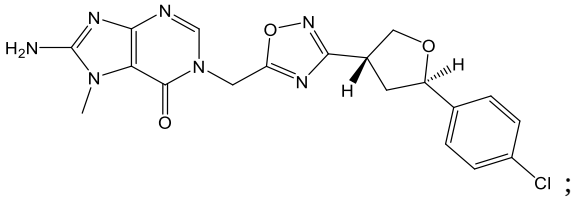

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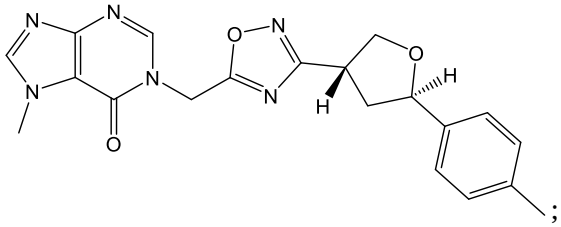

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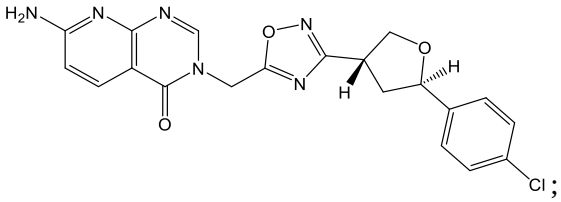


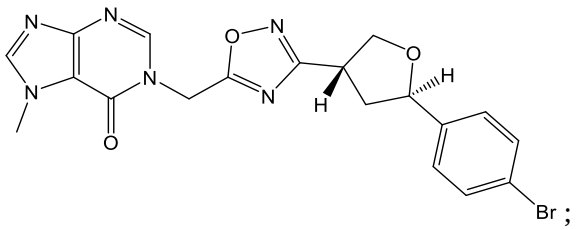


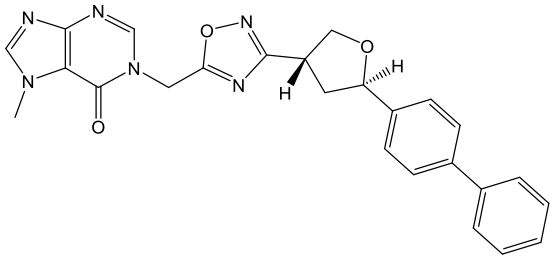


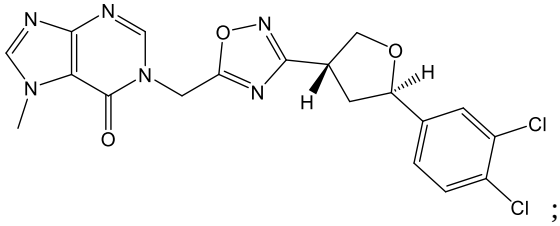


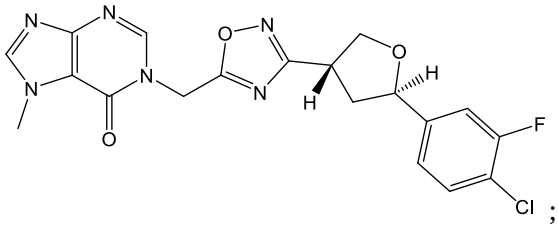


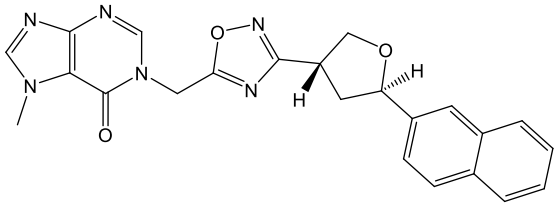


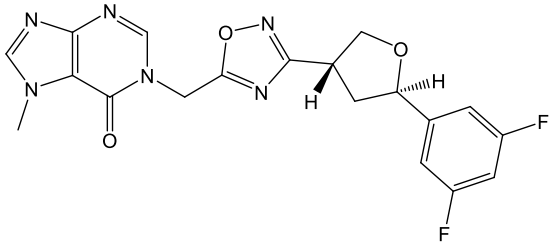


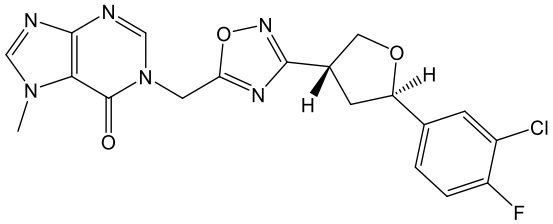

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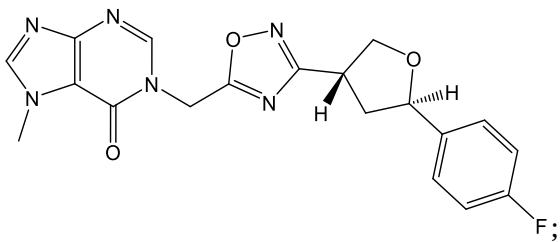

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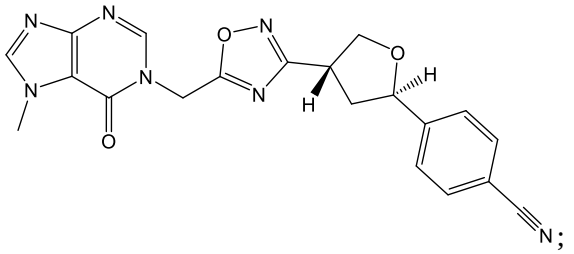

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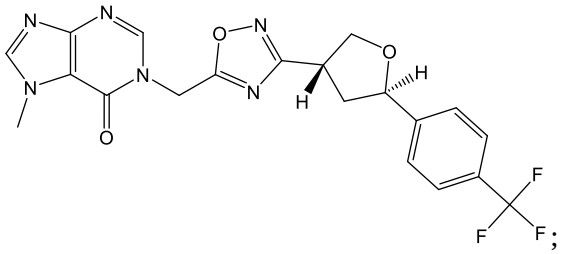

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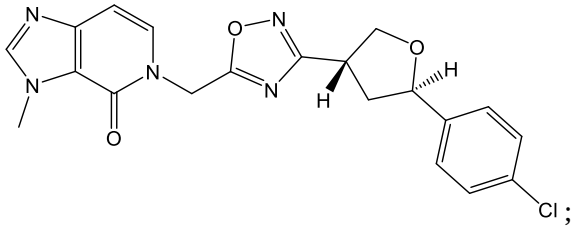

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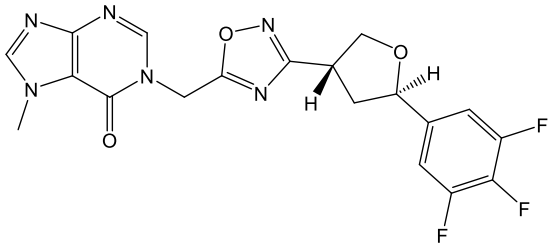

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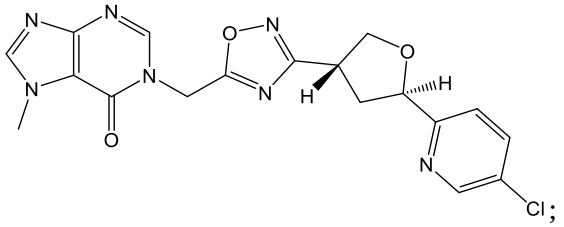

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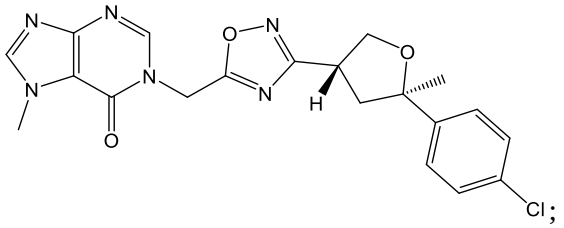


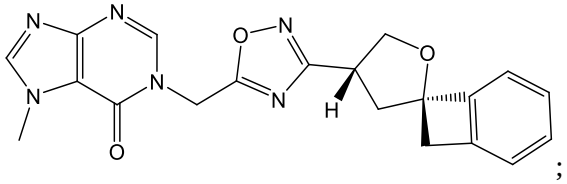


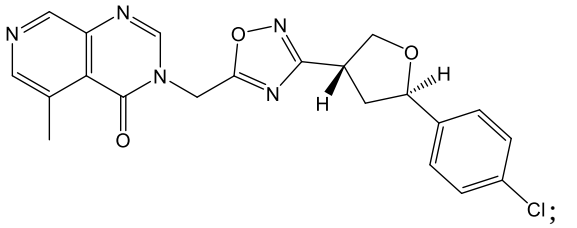


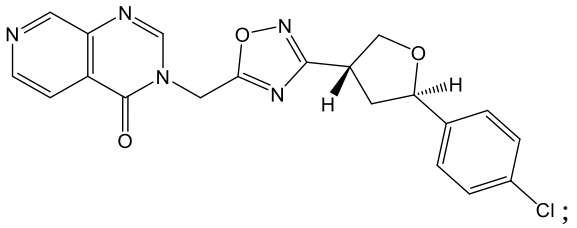


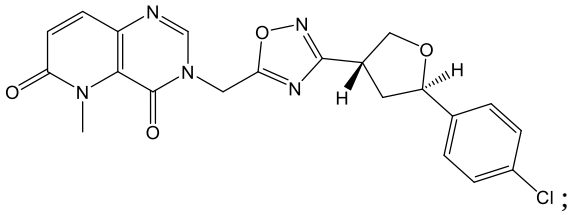


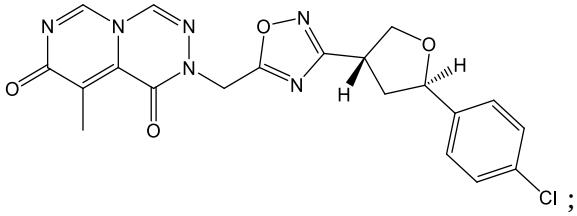


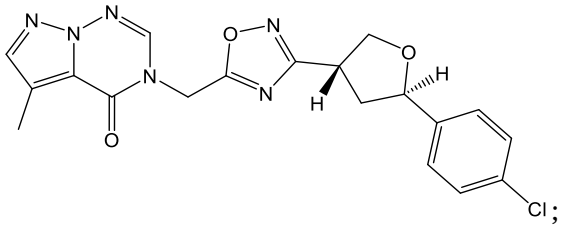


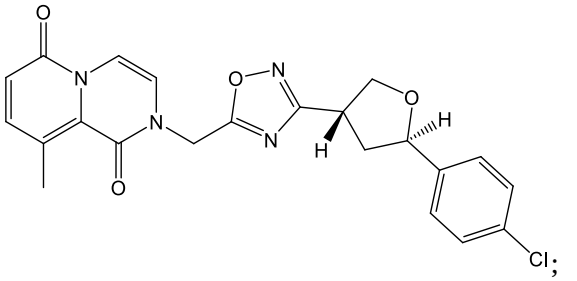


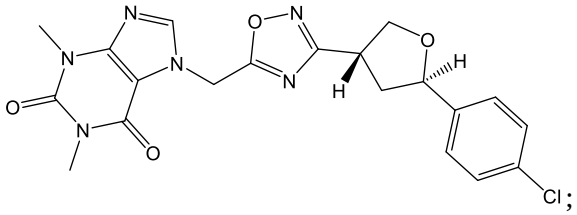




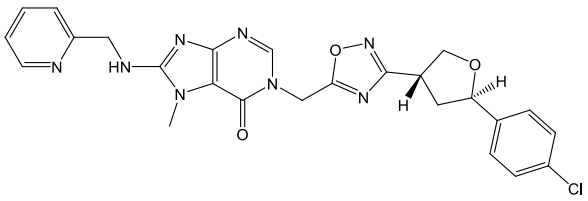


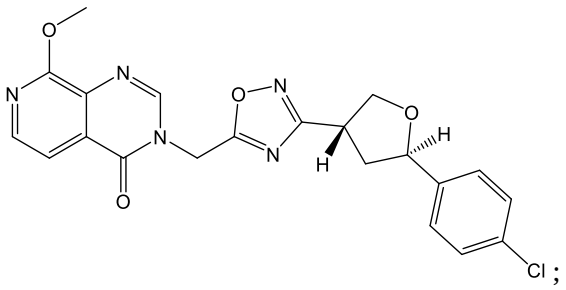


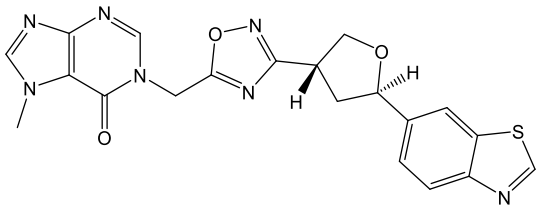


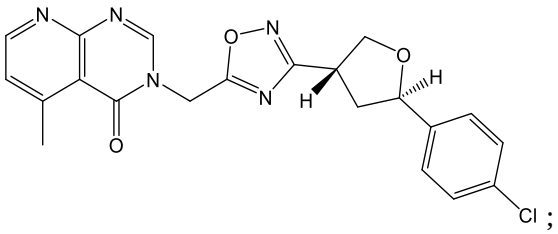


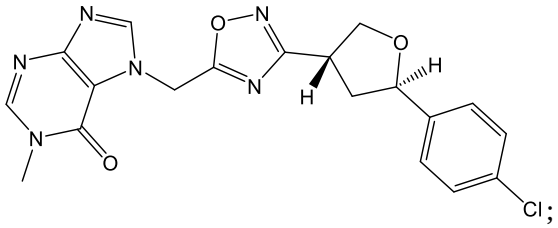
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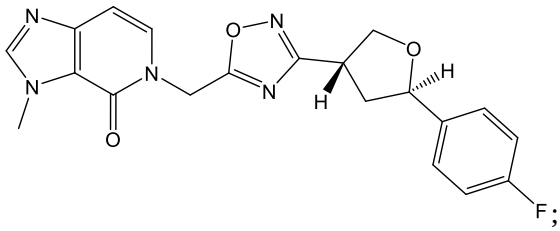

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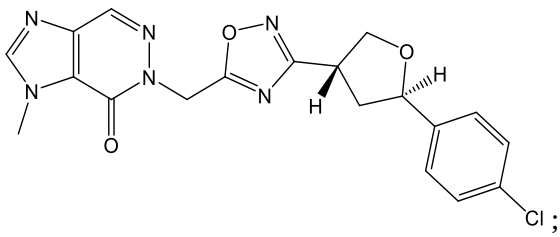

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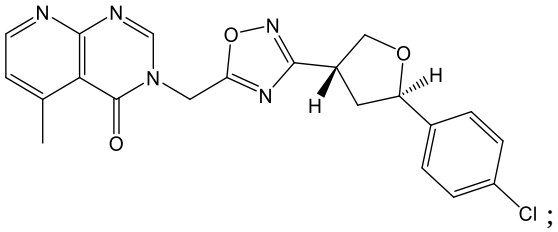

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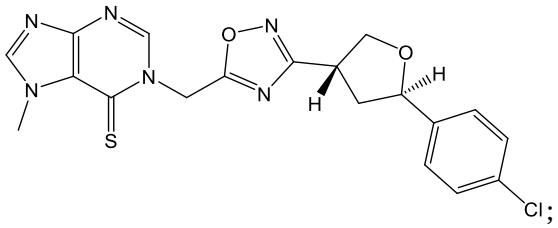

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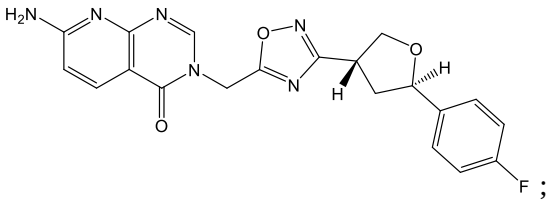

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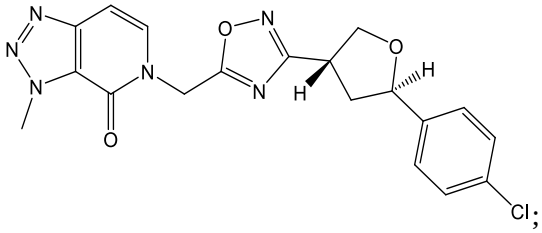

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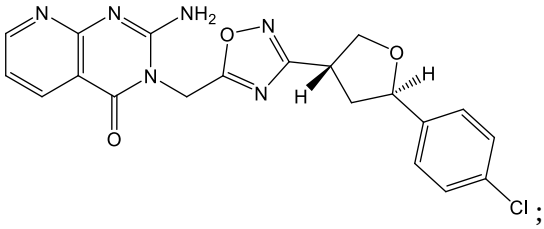

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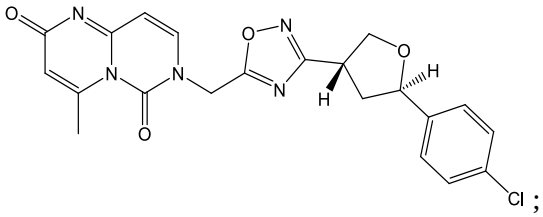


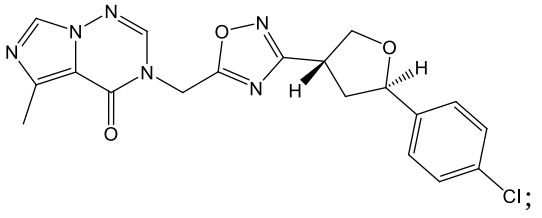


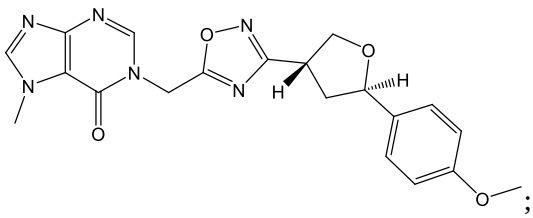


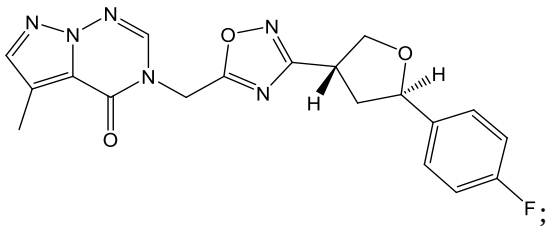


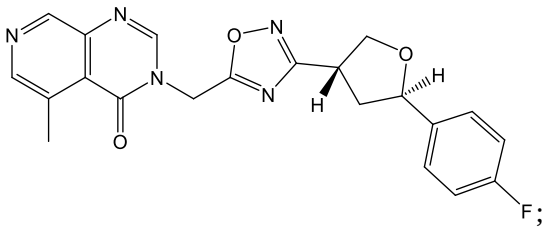


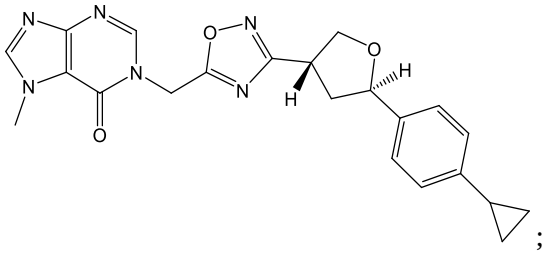




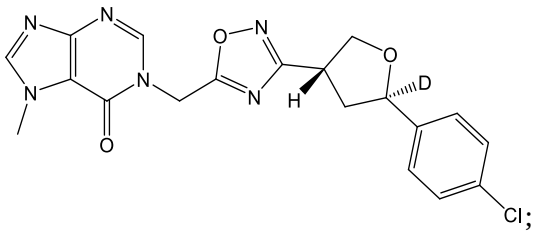

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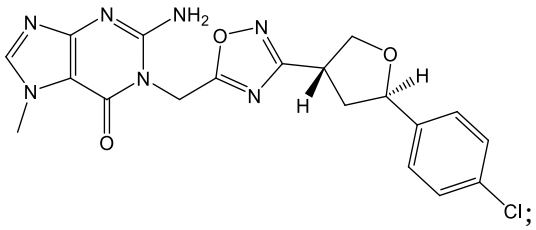

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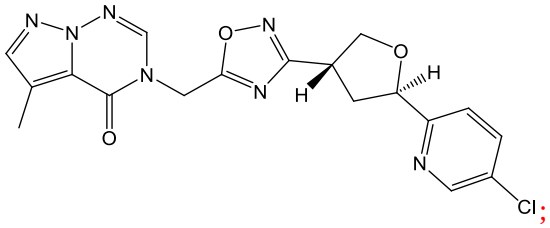

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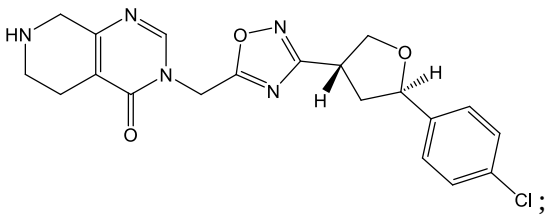

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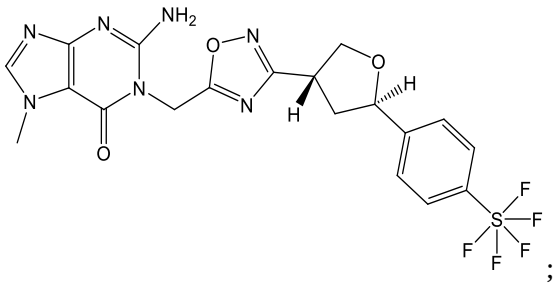

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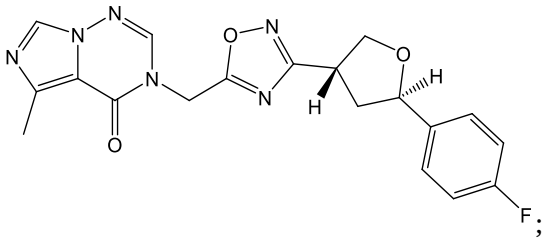

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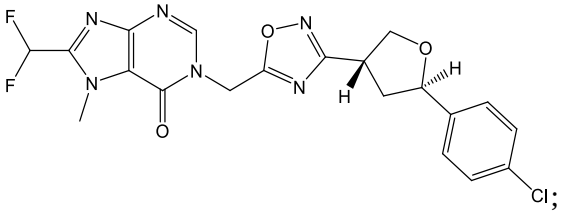
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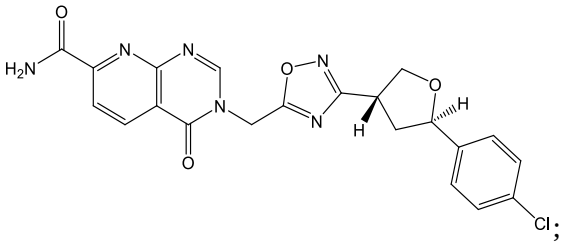
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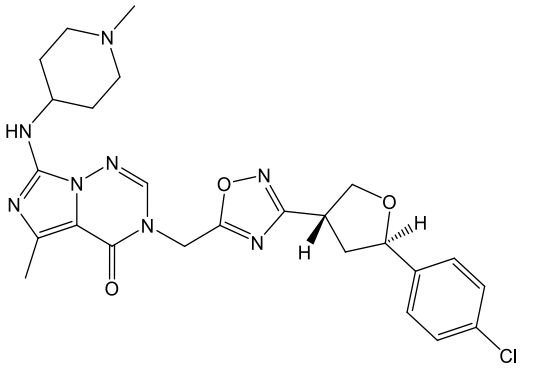
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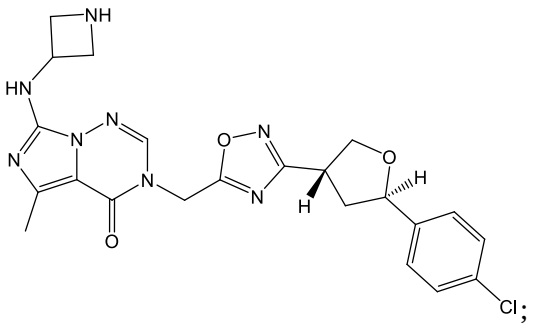


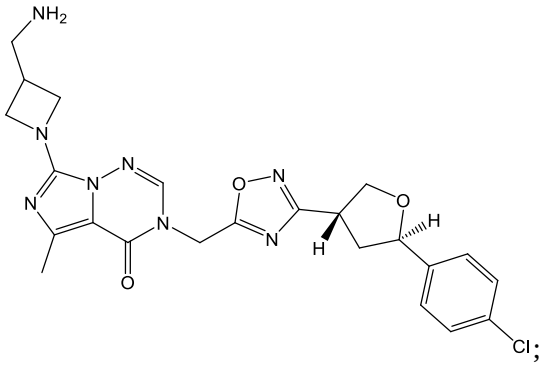
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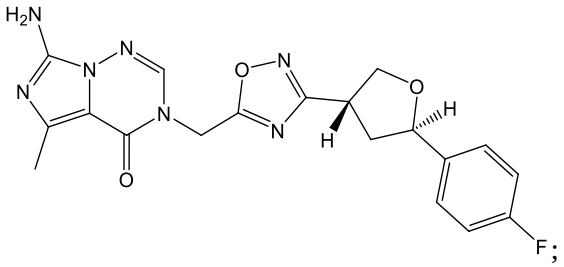


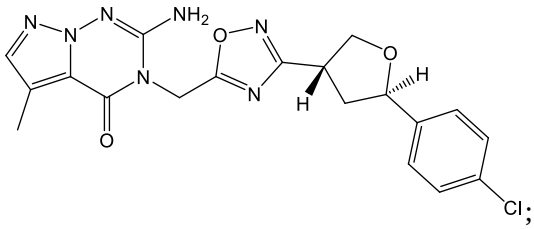
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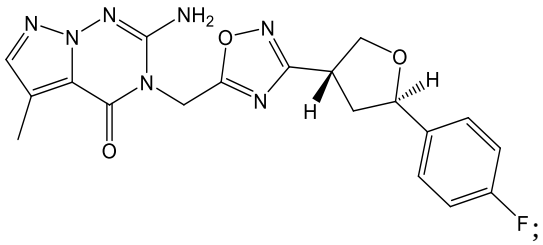


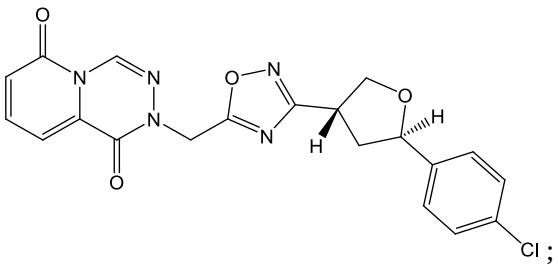


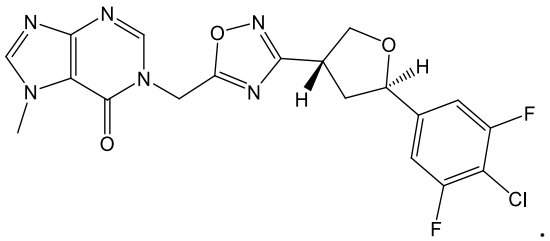


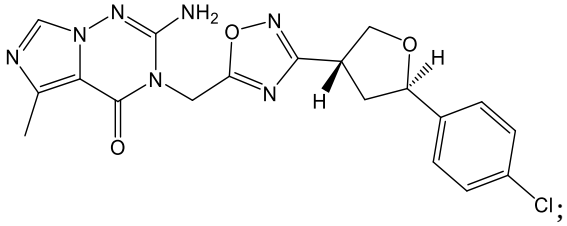


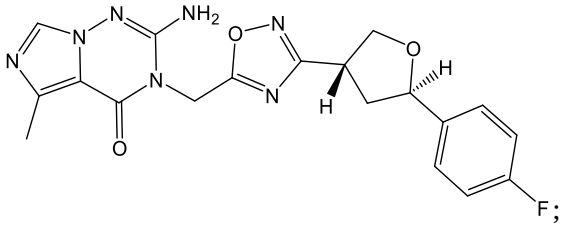


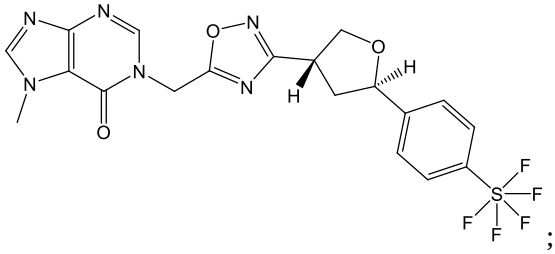


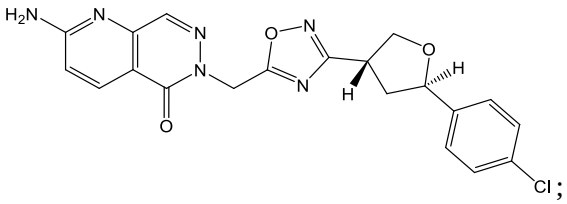


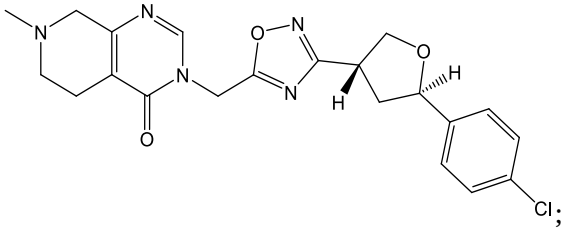

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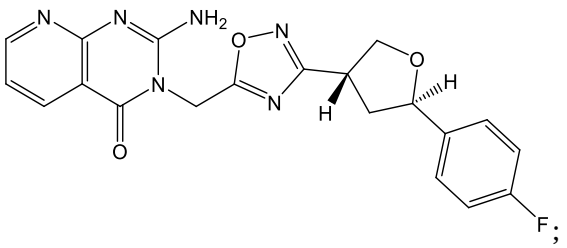

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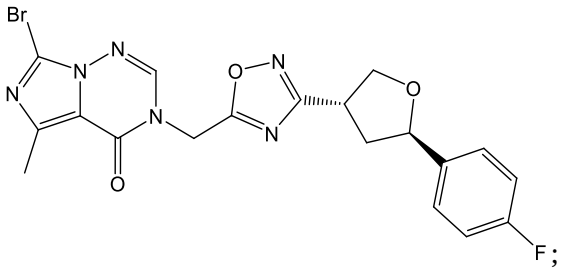

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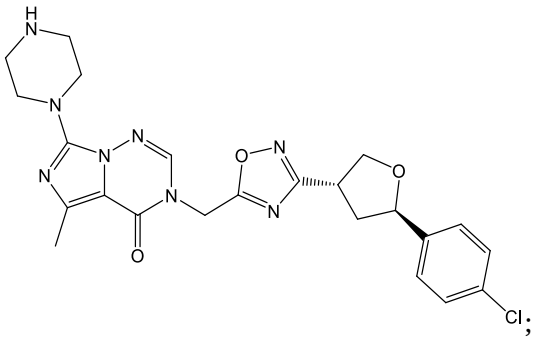

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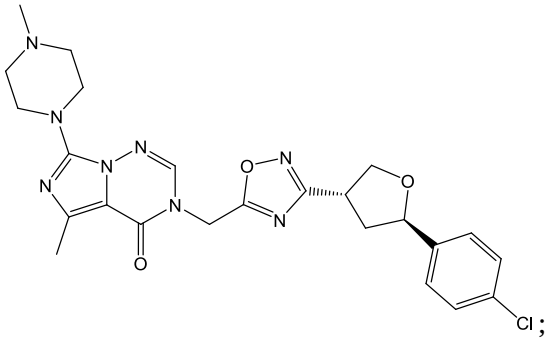

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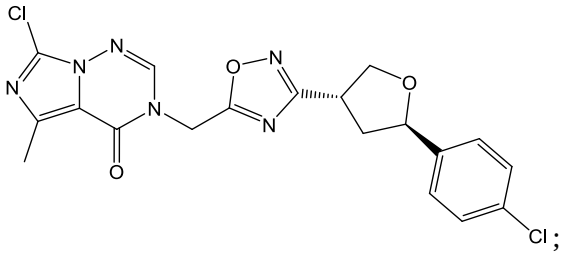

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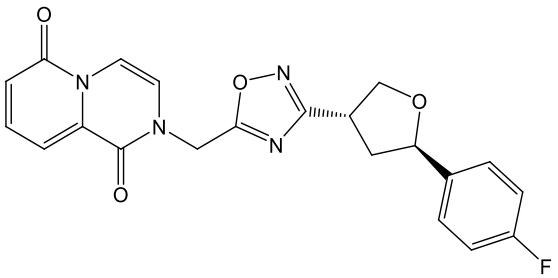

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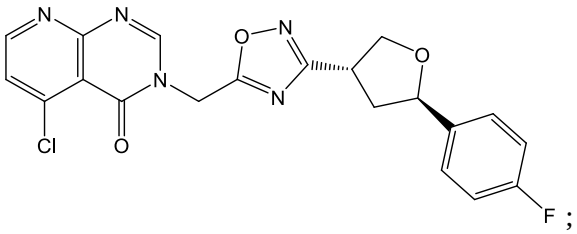


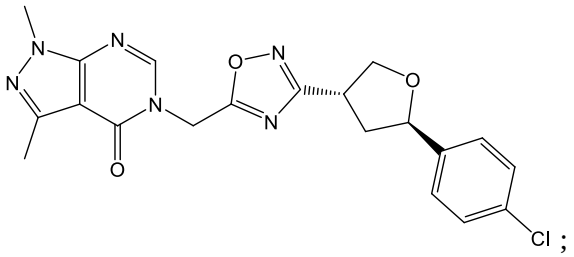


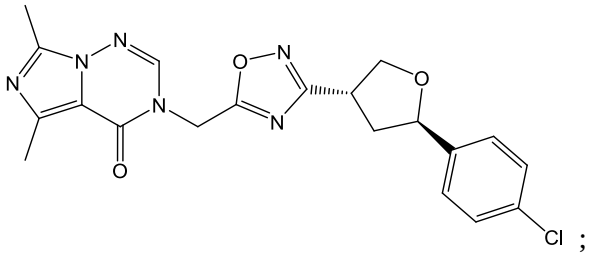


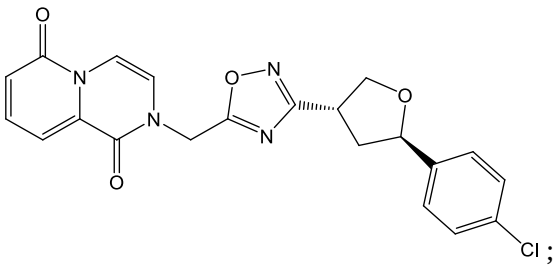


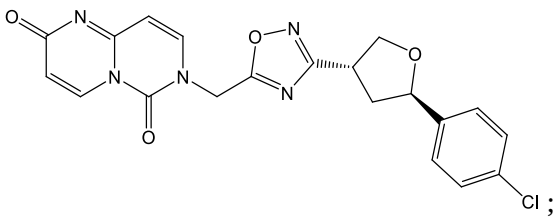


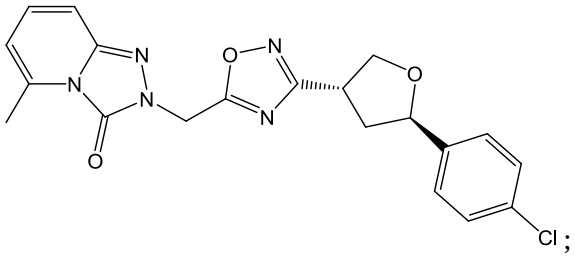


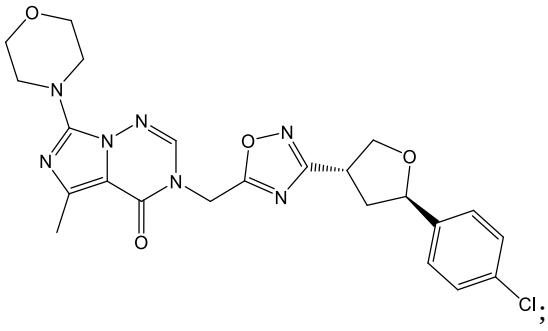


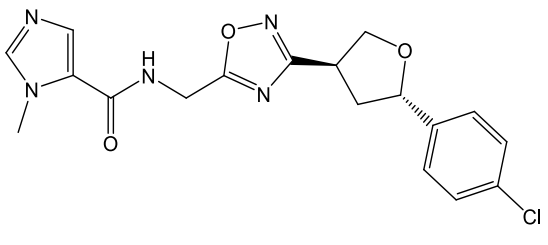




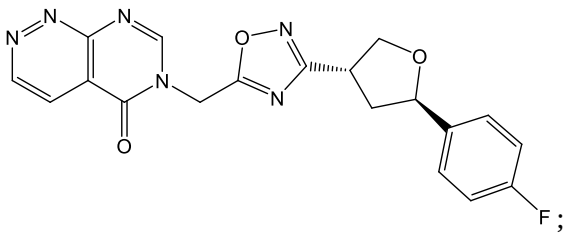


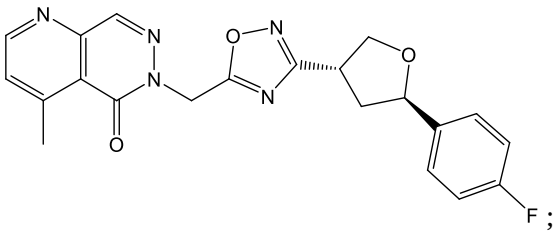


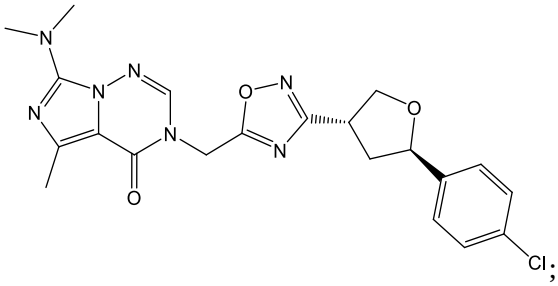


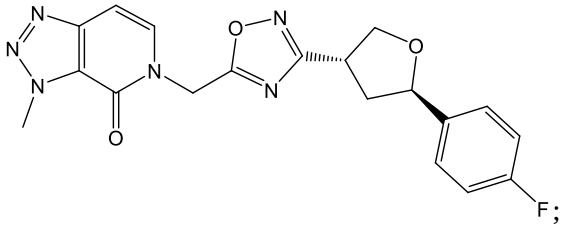


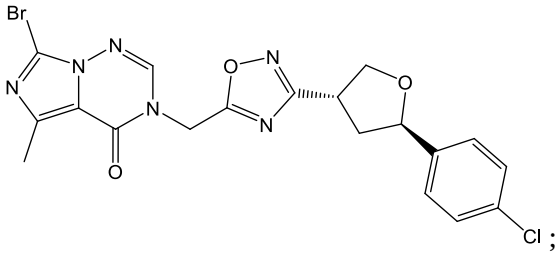
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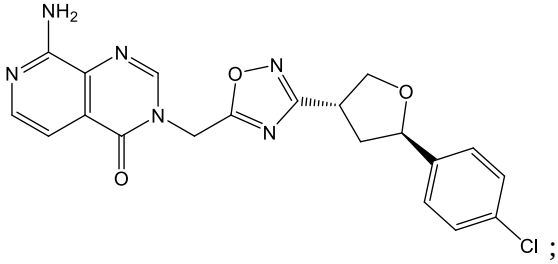


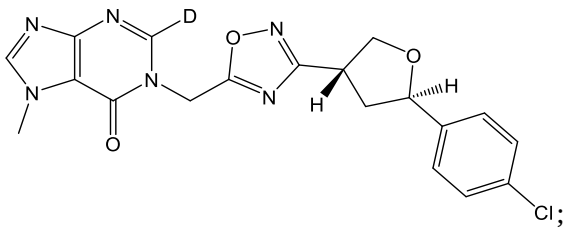


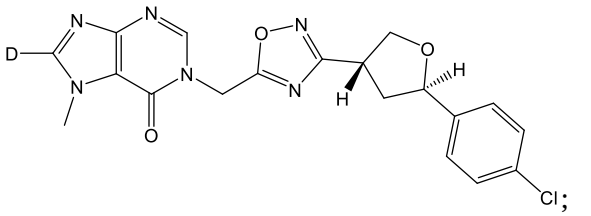


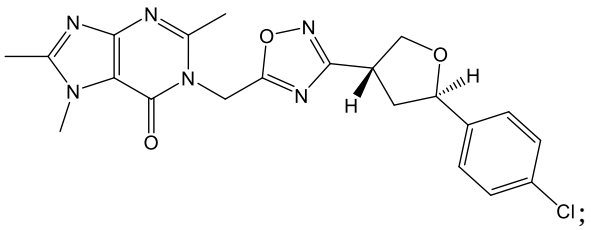


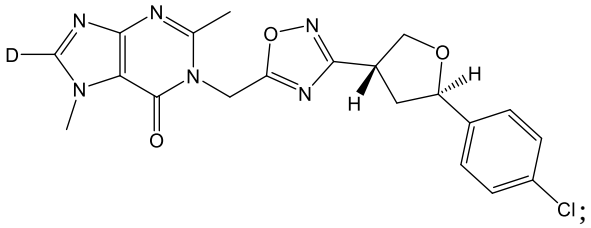


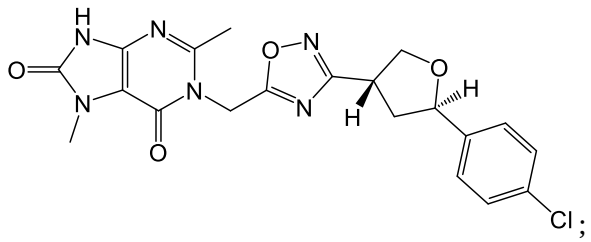


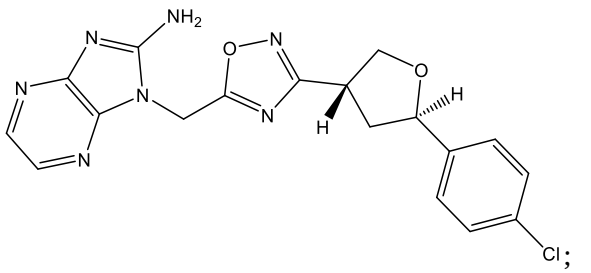


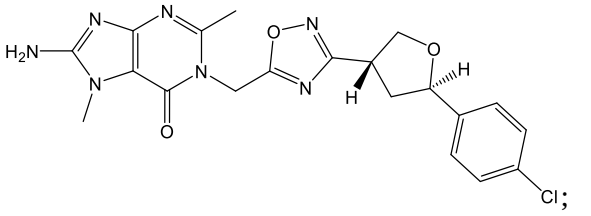


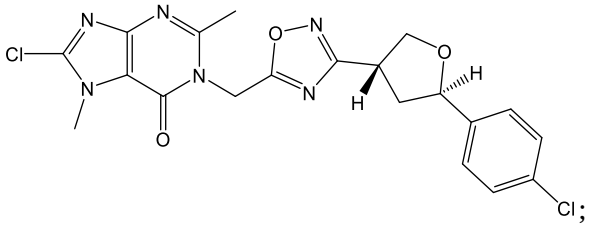




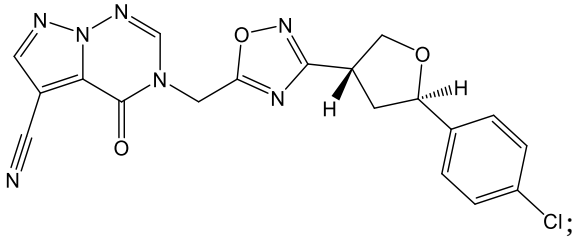


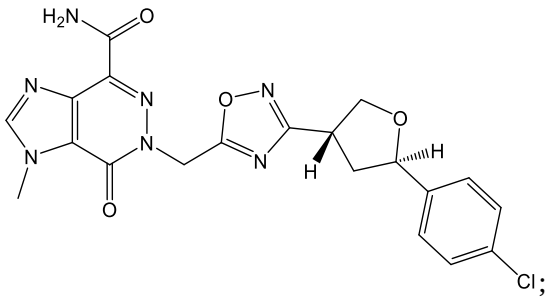


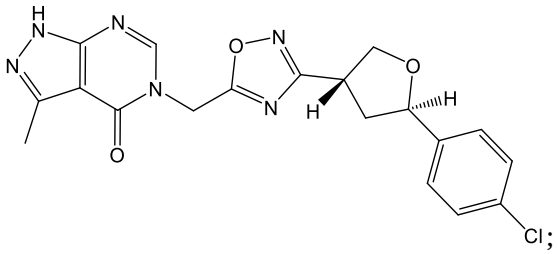


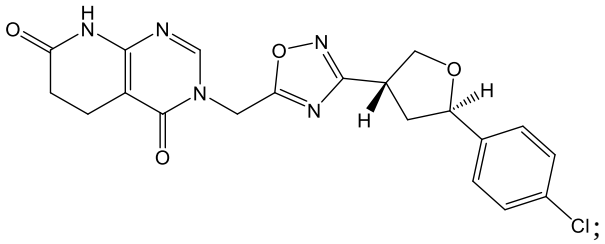


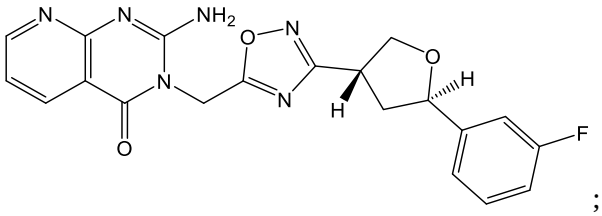
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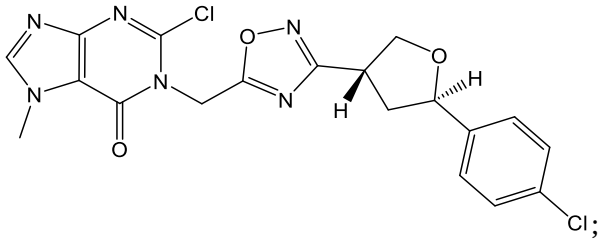


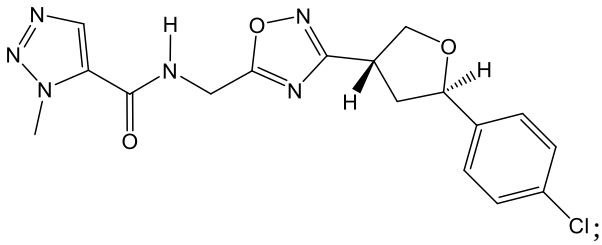


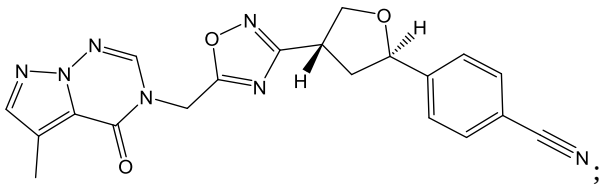


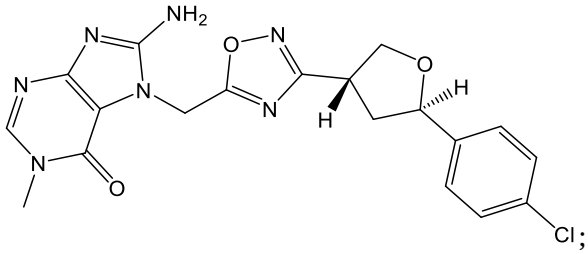


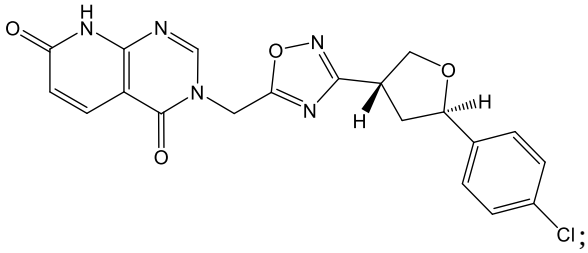

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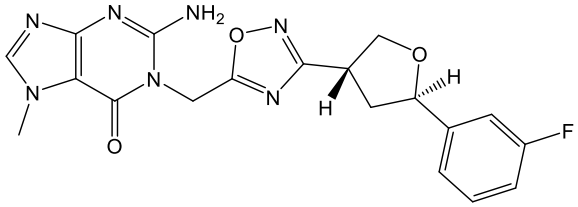


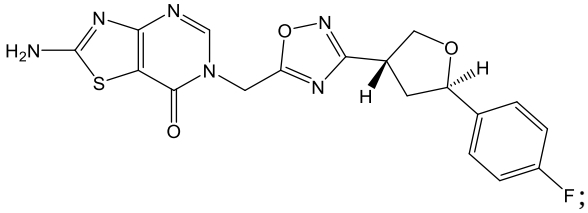


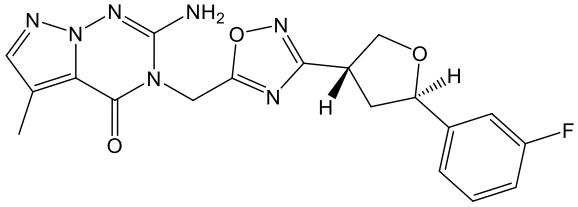
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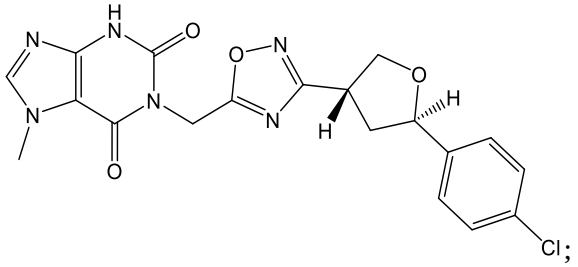
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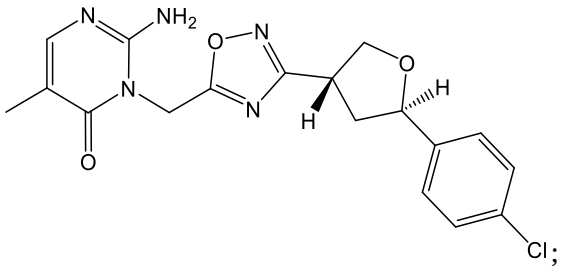
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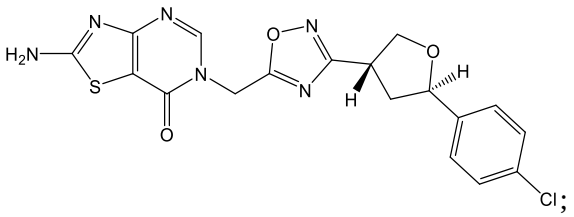
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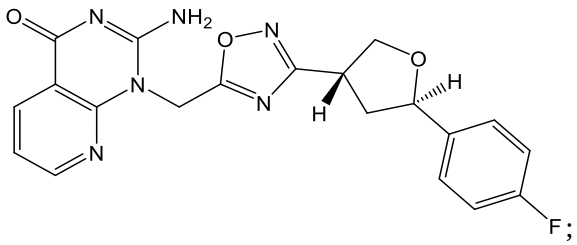
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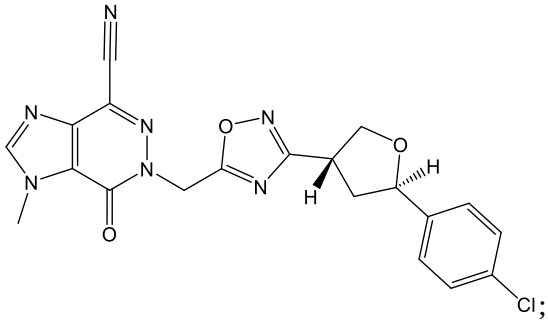
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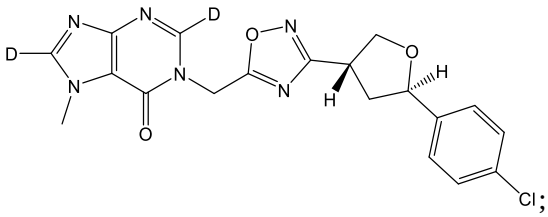
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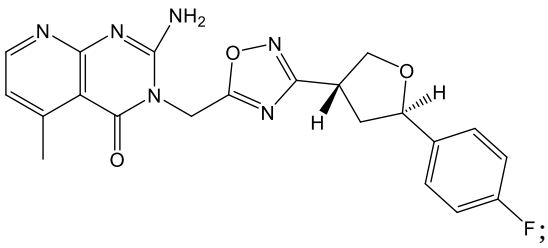


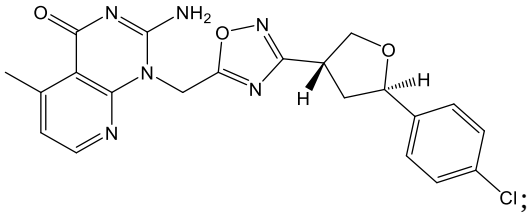


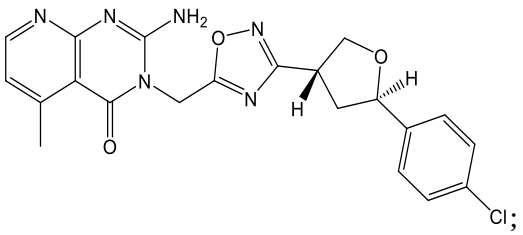


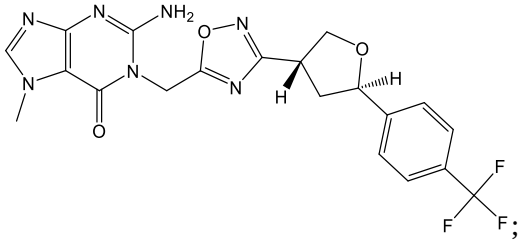


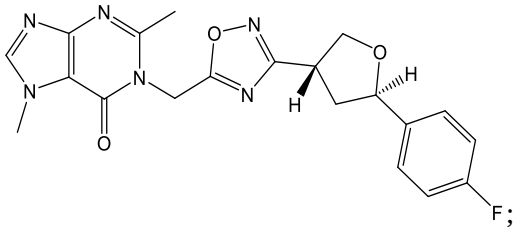


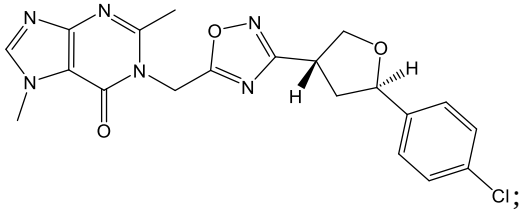


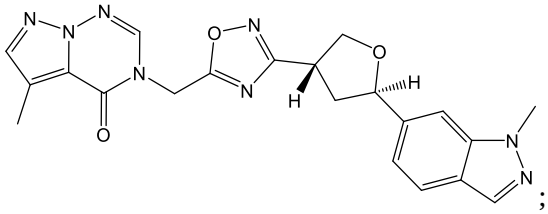


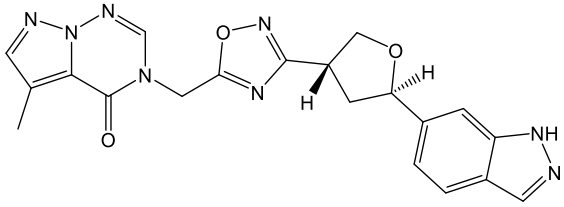


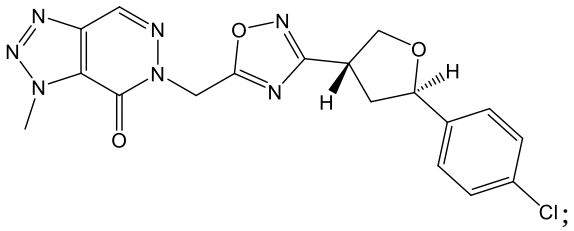




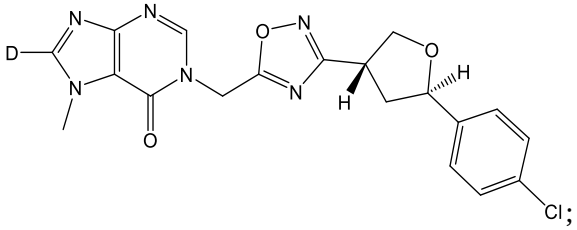


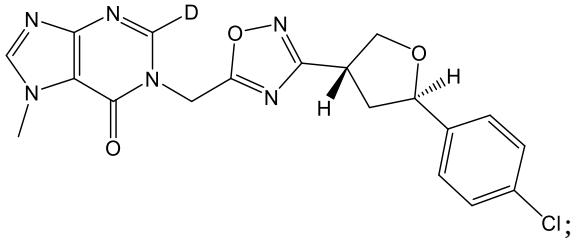


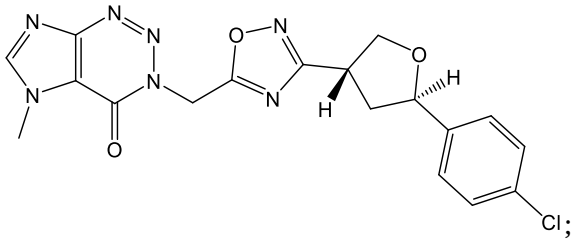


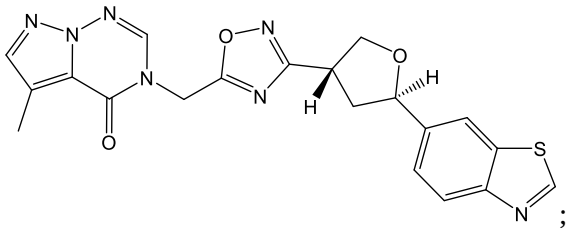


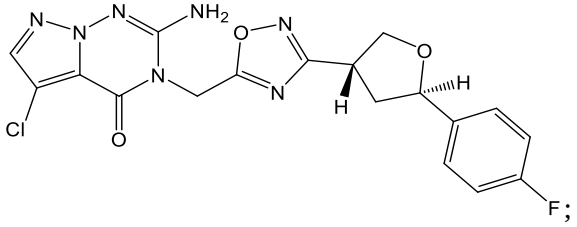
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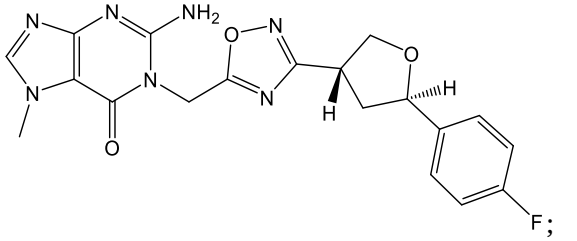


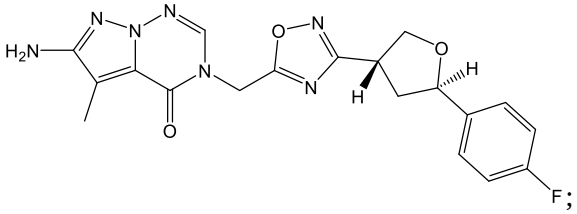




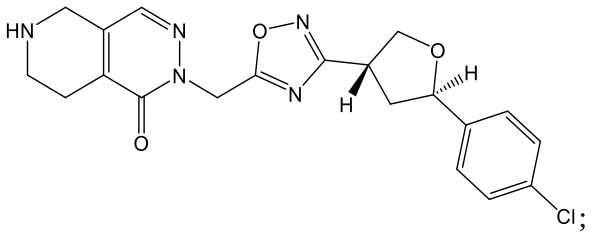


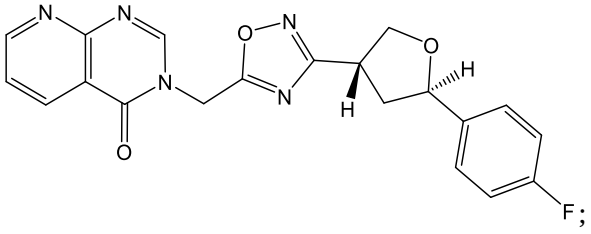


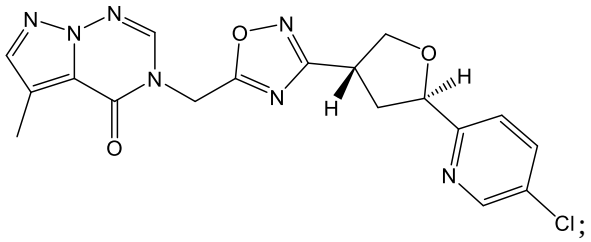


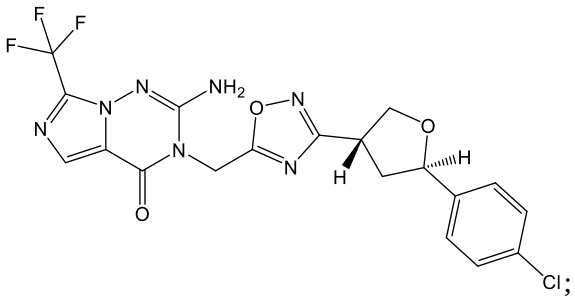


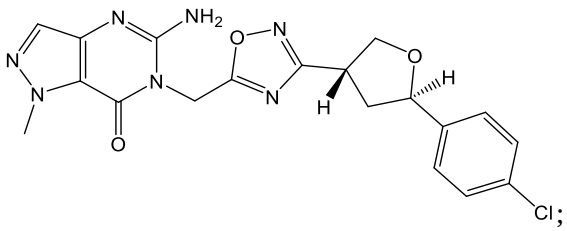
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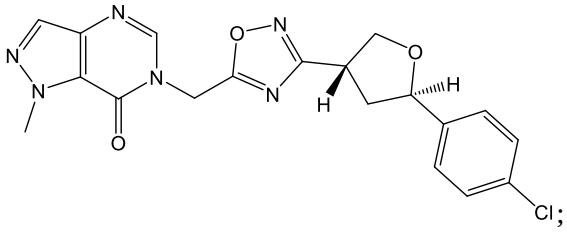


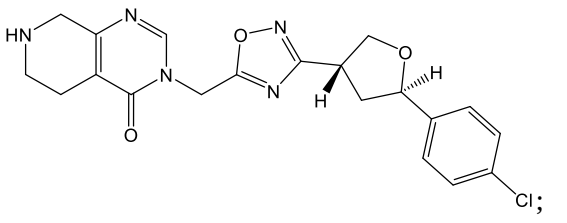




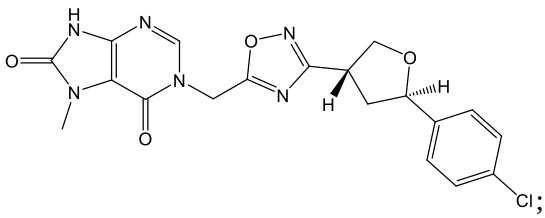


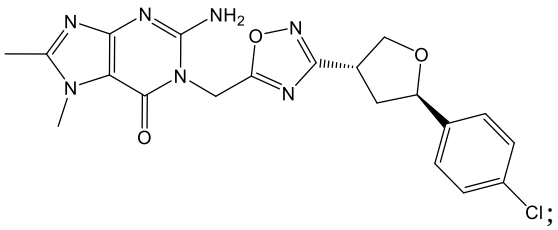


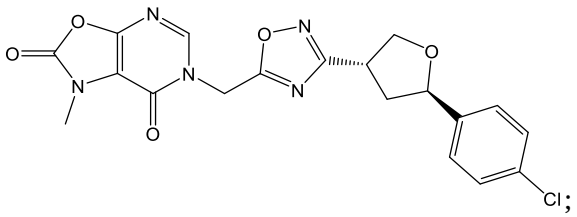


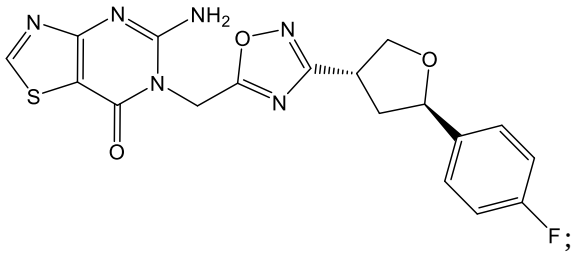


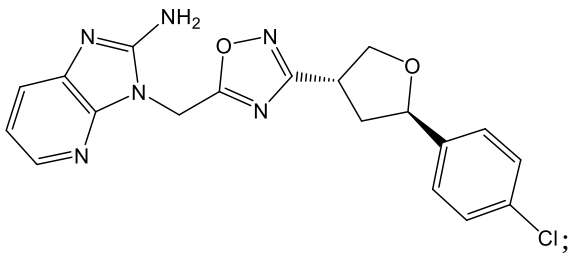
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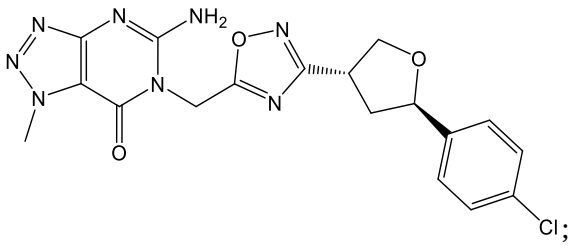


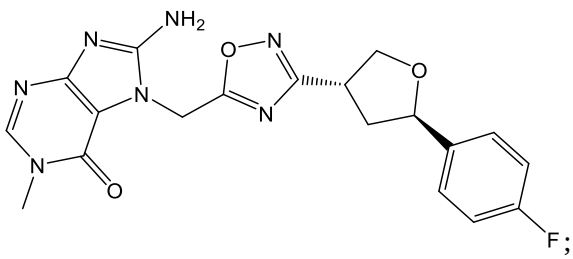


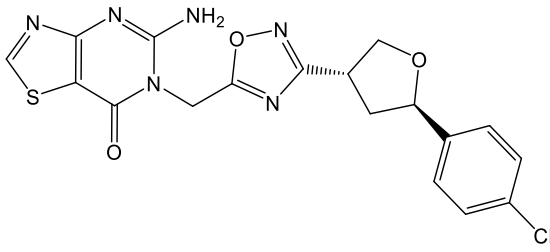


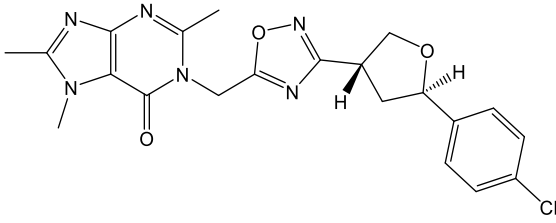




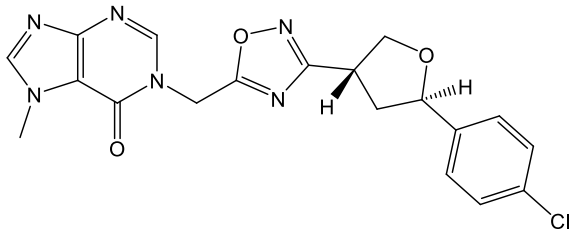





; and

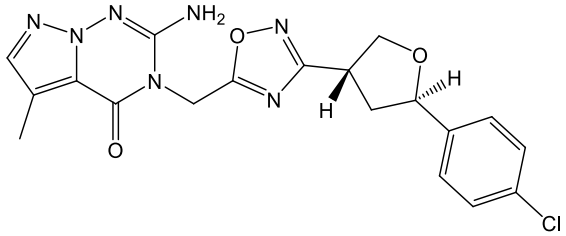

; or a pharmaceutically acceptable salt thereof.

[0005d] In another aspect, there is provided the compound



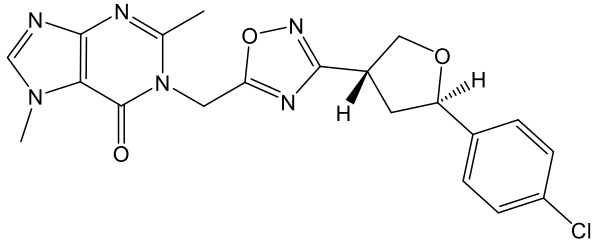
or a pharmaceutically acceptable salt thereof.

[0005e] In another aspect, there is provided the compound



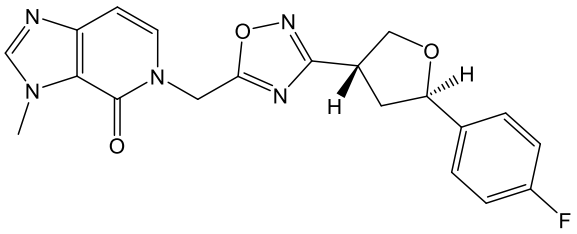
or a pharmaceutically acceptable salt thereof.

[0005f] In another aspect, there is provided the compound



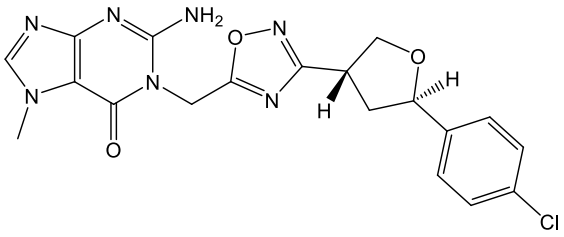
or a pharmaceutically acceptable salt thereof.

[0005g] In another aspect, there is provided the compound



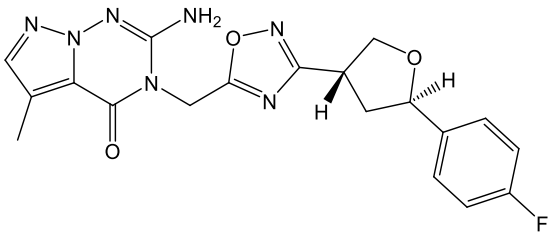
or a pharmaceutically acceptable salt thereof.

[0005h] In another aspect, there is provided the compound



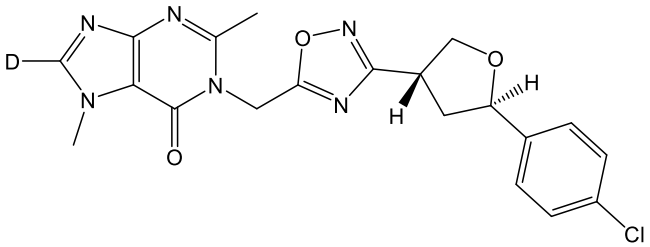
or a pharmaceutically acceptable salt thereof.

[0005i] In another aspect, there is provided the compound



or a pharmaceutically acceptable salt thereof.

[0005j] In another aspect, there is provided the compound



[0006] or a pharmaceutically acceptable salt thereof.In other examples, the following compounds, stereoisomers thereof, and pharmaceutically acceptable salts thereof are provided.

[0007] In another aspect, there is provided a pharmaceutical composition, comprising a compound described above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

[0008] In another aspect, there is provided a compound as described above, or a pharmaceutically acceptable salt thereof, for use in medical therapy.

[0009] Some other examples provide a compound as described above, or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a respiratory disorder. In another aspect, there

is provided a compound as described above or a pharmaceutically acceptable salt thereof for use in the treatment or prophylaxis of a respiratory disorder.

[0010] Some other examples provide a compound as described above, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment or prophylaxis of a respiratory disorder. In another aspect, there is provided use of a compound as described above or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment or prophylaxis of a respiratory disorder.

[0011] Some other examples provide a method for treating a respiratory disorder in a mammal comprising, administering a therapeutically effective amount of a compound as described above, or a pharmaceutically acceptable salt thereof, to the mammal.

[0012] Some other examples provide a compound as described above, or a pharmaceutically acceptable salt thereof, for modulating TRPA1 activity. In another aspect, there is provided a compound as described above or a pharmaceutically acceptable salt thereof for use in modulating TRPA1 activity.

[0013] Some other examples provide a compound as described above, or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a disease or condition mediated by TRPA1 activity. In another aspect, there is provided a compound as described above or a pharmaceutically acceptable salt thereof for use in the treatment or prophylaxis of a disease or condition mediated by TRPA1 activity.

[0014] Some other examples provide a use of a compound as described above, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment or prophylaxis of a disease or condition that is mediated by TRPA1 activity. In another aspect, there is provided use of a compound as described above or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment or prophylaxis of a disease or condition selected from pain, itch, an inflammatory disorder, an inner ear disorder, fever or another disorder of thermoregulation, tracheobronchial or diaphragmatic dysfunction, a gastrointestinal or urinary tract disorder, chronic obstructive pulmonary disease, incontinence, or a disorder associated with reduced blood flow to the CNS or CNS hypoxia.

[0015] Some other examples provide a method for modulating TRPA1 activity, comprising contacting TRPA1 with a compound as described above, or a pharmaceutically acceptable salt thereof.

[0016] Some other examples provide a method for treating a disease or condition mediated by TRPA1 activity in a mammal, comprising administering a therapeutically effective amount of a compound as described above, or a pharmaceutically acceptable salt thereof, to the mammal.

DETAILED DESCRIPTION OF THE INVENTION

[0017] **Definitions**

[0018] Unless otherwise indicated, the following specific terms and phrases used in the description and claims are defined as follows:

[0019] The terms “moiety” and “substituent” refer to an atom or group of chemically bonded atoms that is attached to another atom or molecule by one or more chemical bonds thereby forming part of a molecule.

[0020] The term “substituted” refers to the replacement of at least one of hydrogen atom of a compound or moiety with another substituent or moiety. Examples of such substituents include, without limitation, halogen, -OH, -CN, oxo, alkoxy, alkyl, alkylene, aryl, heteroaryl, haloalkyl, haloalkoxy, cycloalkyl and heterocycle. For example, the term “alkyl substituted by halogen” refers to the fact that one or more hydrogen atoms of a alkyl (as defined below) is replaced by one or more halogen atoms (e.g., trifluoromethyl, difluoromethyl, fluoromethyl, chloromethyl, etc.).

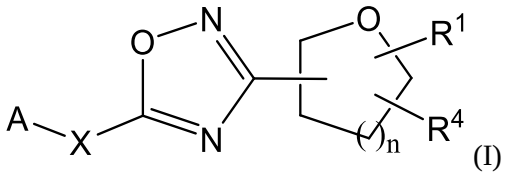
[0021] The term “alkyl” refers to an aliphatic straight-chain or branched-chain saturated hydrocarbon moiety having 1 to 20 carbon atoms. In particular embodiments the alkyl has 1 to 10 carbon atoms. In particular embodiments the alkyl has 1 to 6 carbon atoms. Alkyl groups may be optionally substituted independently with one or more substituents described herein.

[0022] The term "alkylene" as used herein refers to a linear or branched saturated divalent hydrocarbon radical of one to twelve carbon atoms, and in another embodiment one to six carbon atoms, wherein the alkylene radical may be optionally substituted independently with one or more substituents described herein. Examples include, but are not limited to, methylene, ethylene, propylene, 2-methylpropylene, pentylene, and the like.

[0023] The term "alkenylene" refers to linear or branched-chain divalent hydrocarbon radical of two to eight carbon atoms (C_{2-8}) with at least one site of unsaturation, i.e., a carbon-carbon double bond, wherein the alkenylene radical may be optionally substituted. Examples include, but are not limited to, ethylenylene or vinylene (-CH=CH-), allyl (-CH_2CH=CH-), and the like.

WHAT IS CLAIMED IS:

1. A compound of formula I,

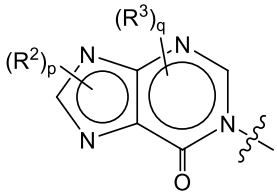
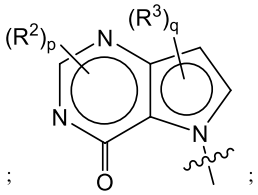
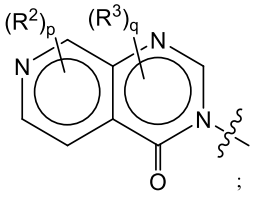
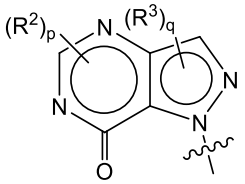
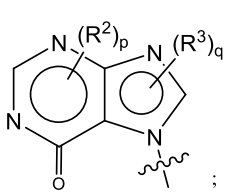
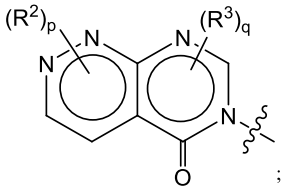
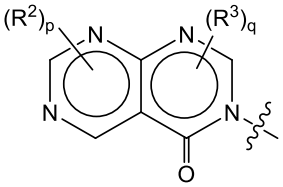
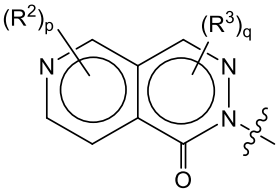
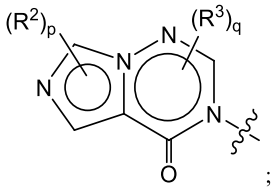
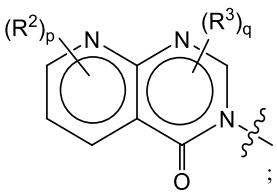
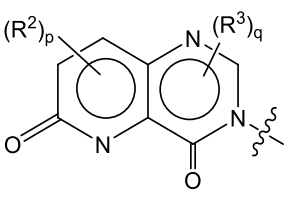
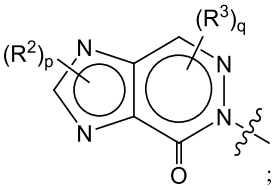
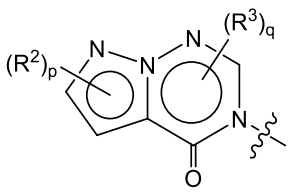
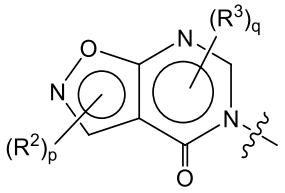
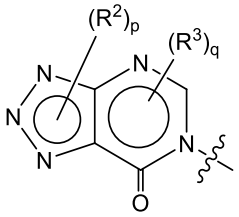
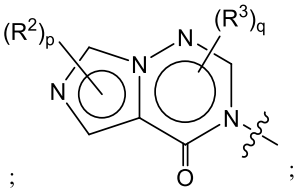
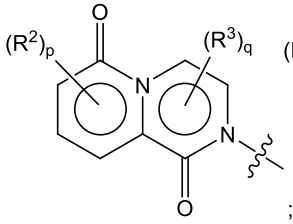
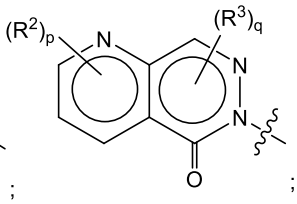
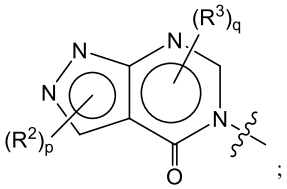
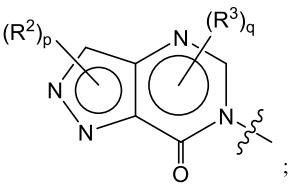
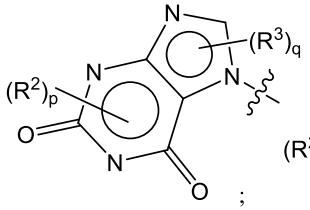
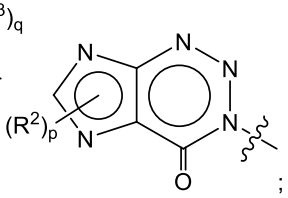
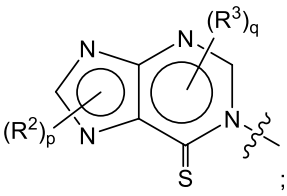
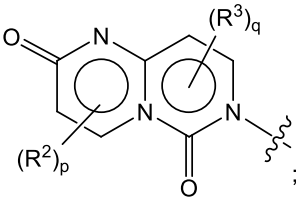


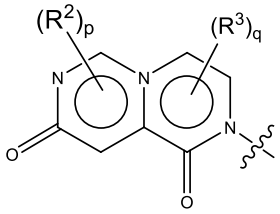
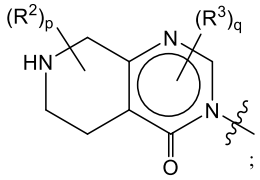
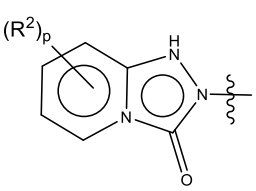
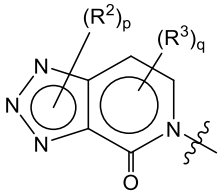
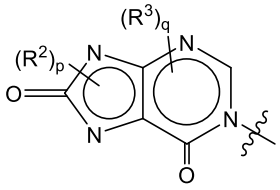
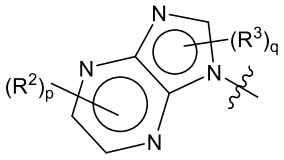
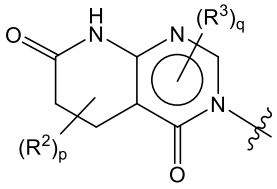
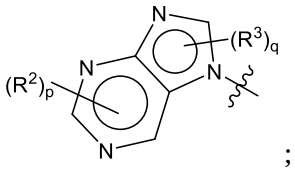
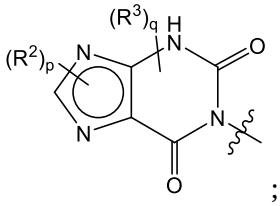
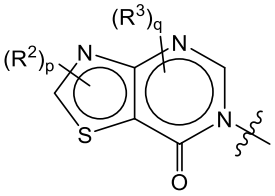
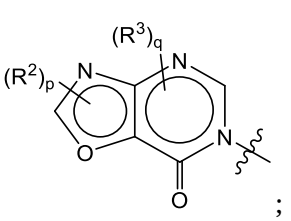
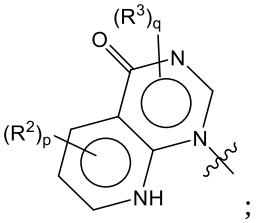
(I)

or a pharmaceutically acceptable salt thereof,

wherein:

A is selected from:


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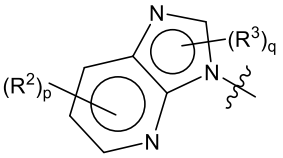
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X is: a bond; C_{1-4} alkylene; -O-; -S-; -SO_2-; or -N(R^a)-;

n is: 0, 1, 2 or 3;

R^a is H or C_{1-6} alkyl which may be unsubstituted or substituted one or more times with halo;

R^1 is: H; or C_{1-6}alkyl;

each R^2 is independently: H; D; -C_{1-4} alkyl; -C_{1-4} haloalkyl; C_{1-4} alkoxy; -CN, halo; halo-C_{1-4}alkoxy; -OH; -SO_2-C_{1-4}alkyl; -C_{1-4}CN, C_{1-4} aldehyde; C_{1-4} ketone; benzylamino; or $NR^{14}R^{15}$;

each R^3 is independently: H; D: -C_{1-4} alkyl; -C_{1-4} haloalkyl; -CN; $NR^{14}R^{15}$; or halo;

R^4 is: substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl;

or R^1 and R^4 may together form an unsubstituted or substituted C_{3-6}cylcoalkyl fused to a substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl.

p is 0, 1 or 2;

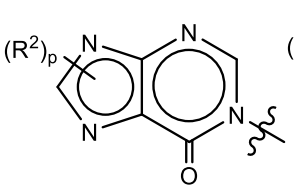
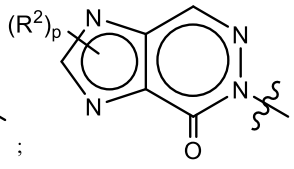
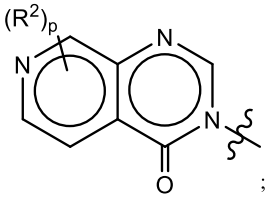
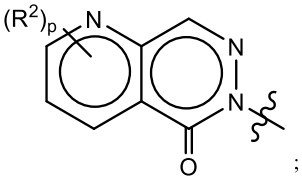
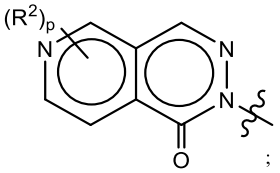
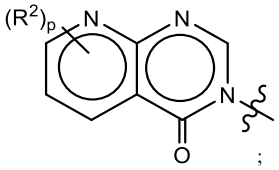
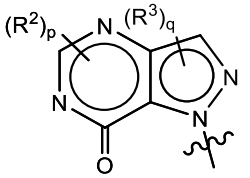
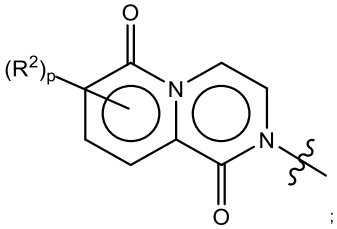
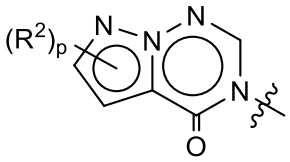
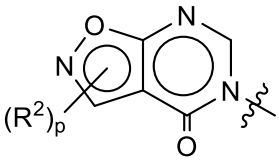
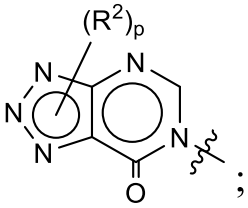
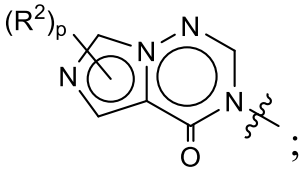
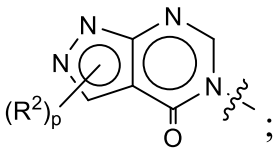
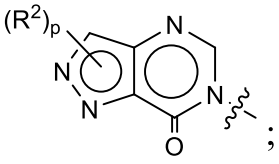
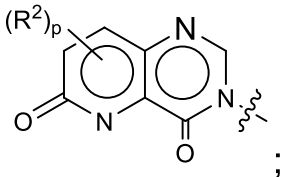
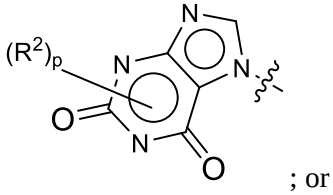
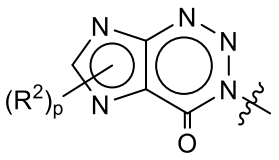
q is 0 or 1;

R^{14} and R^{15} are each independently: H; substituted or unsubstituted -C_{1-4} alkyl; substituted or unsubstituted -C(O)-C_{1-4} alkyl; substituted or unsubstituted C_{3-6} cycloalkyl; substituted or unsubstituted 3- to 6-membered heterocycloalkyl; substituted or unsubstituted -C_{1-4} heteroalkyl; -C(O)$NR^{16}R^{17}$; substituted or unsubstituted -C_{1-4} alkyl-C(O)$NR^{16}R^{17}$; substituted or unsubstituted phenyl; or substituted or unsubstituted benzyl;

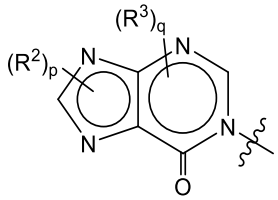
or R^{14} and R^{15} together with the atoms to which they are attached may form a 4-, 5-, 6- or 7-membered ring that optionally includes one additional heteroatom selected from O, N and S; and

R^{16} and R^{17} each are independently H and C_{1-4} alkyl.

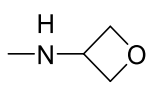
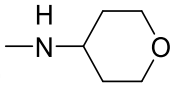
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:


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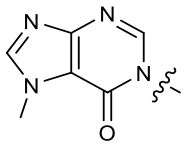
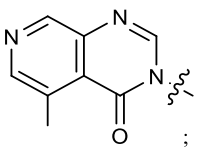
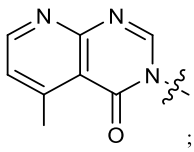
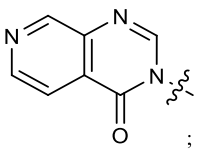
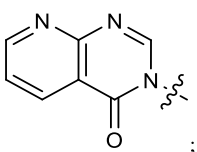
3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:

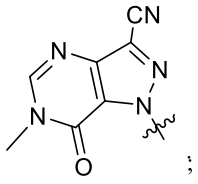
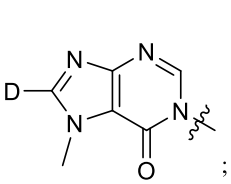
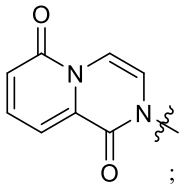
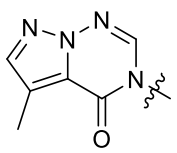
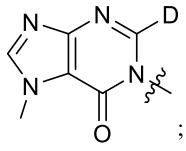


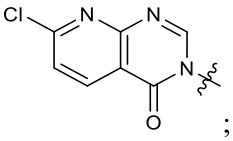
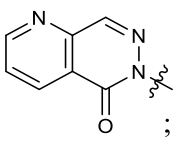
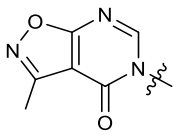
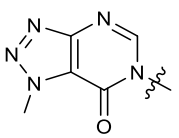
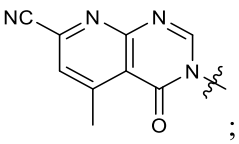
4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently; H;, $-CH_3$; –CN; -halo; $-NH_2$; $-NHCH_3$; $NHCH_2CH_3$; $-NHCH_2CH_2CH_2OH$; -

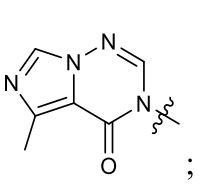
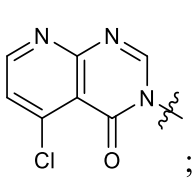
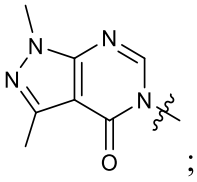
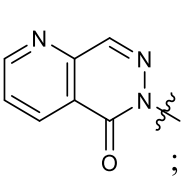
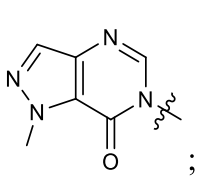
$NHCH_2CH_2OCH_3$; $-NHC(O)CH_3$; $-NHCH_2C(O)N(CH_3)_2$; , or ; and p is 0 or 1.

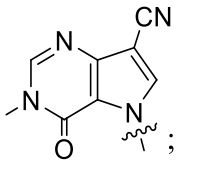
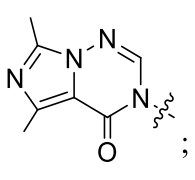
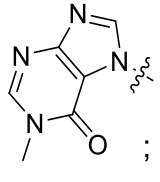
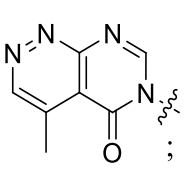
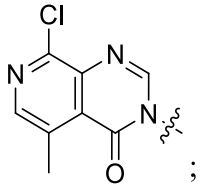
5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:

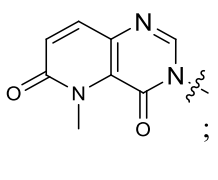
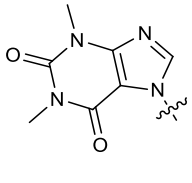
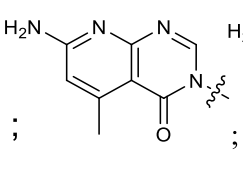
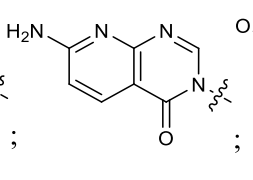
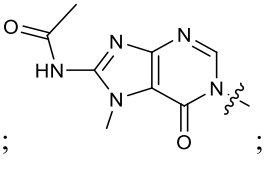
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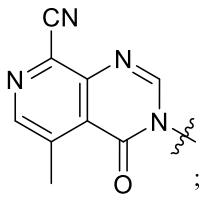
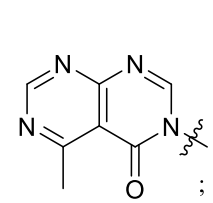
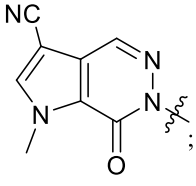
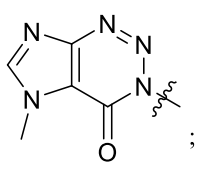
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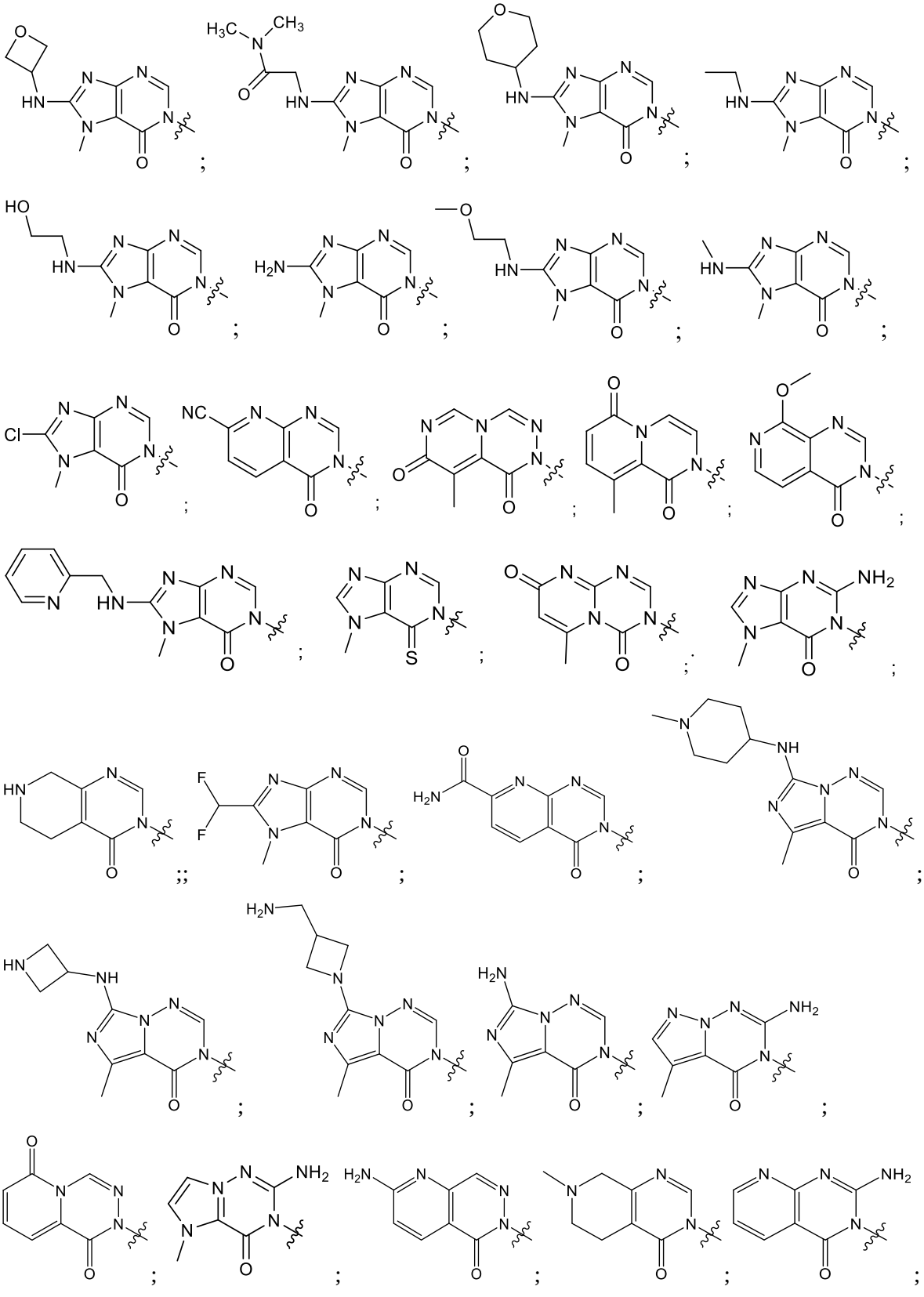
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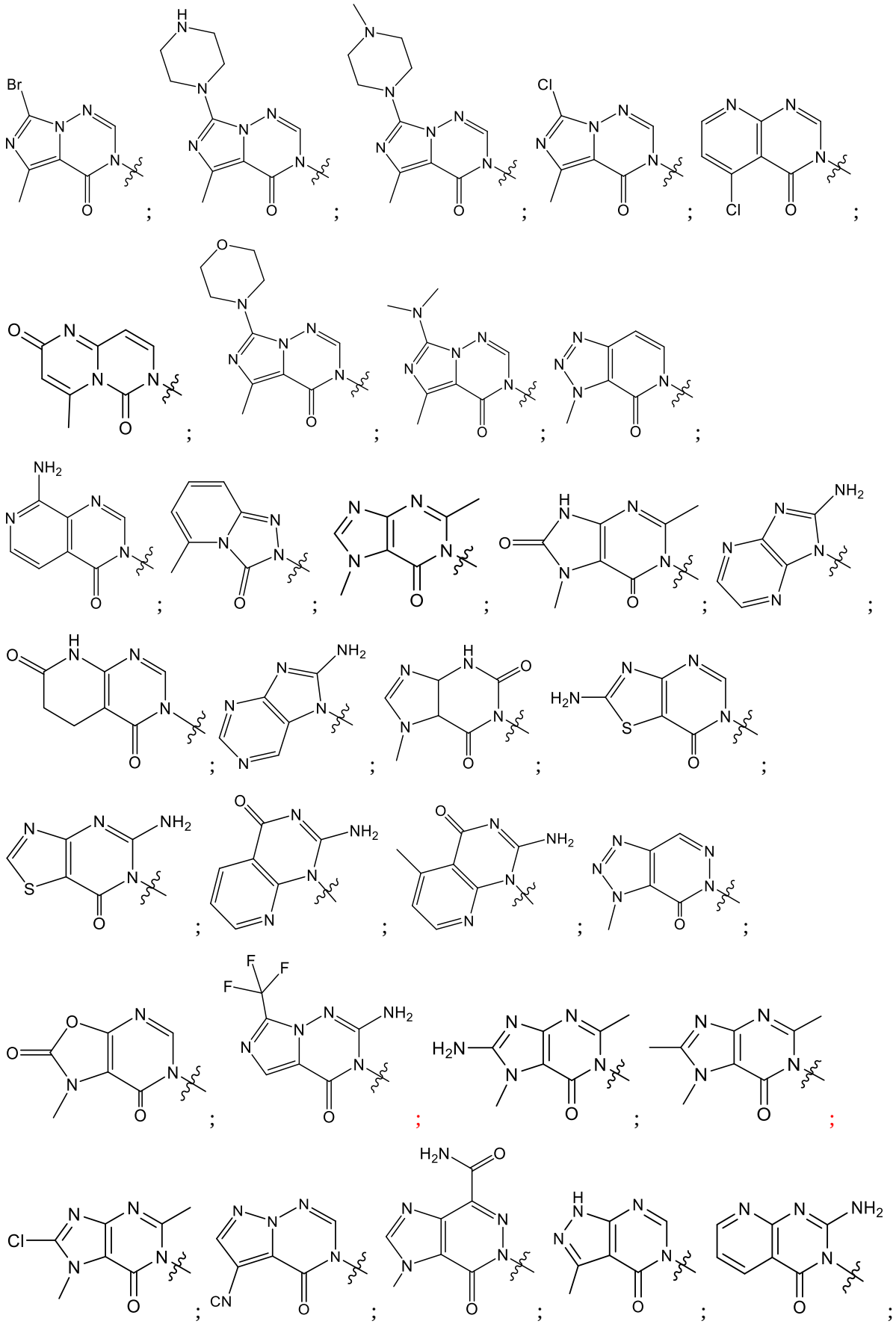
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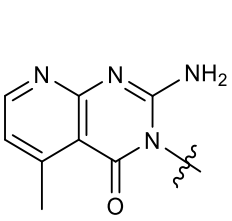
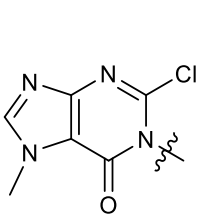
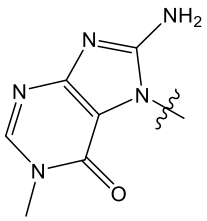
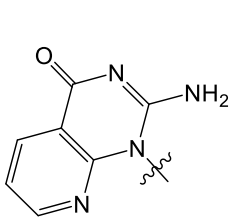
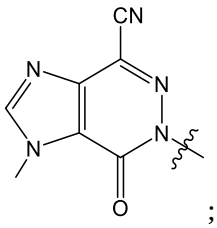
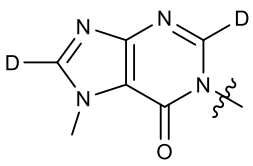
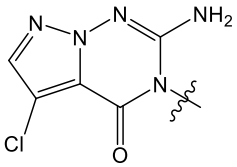
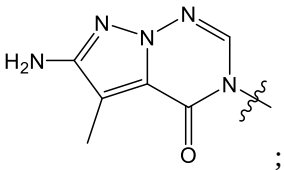
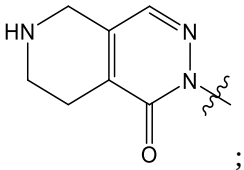
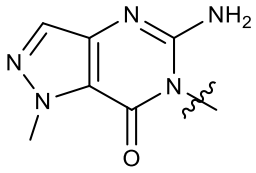
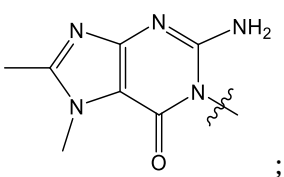
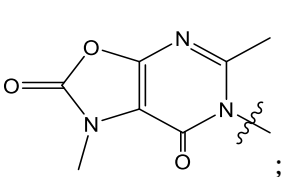
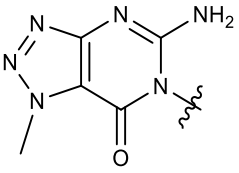
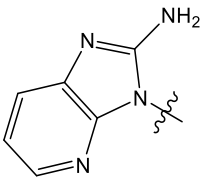
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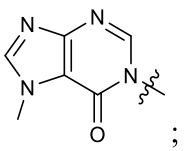
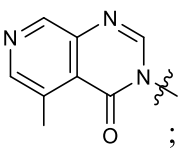
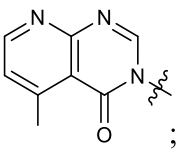
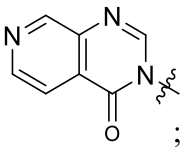
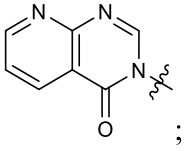
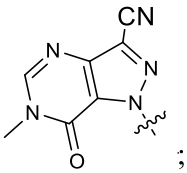
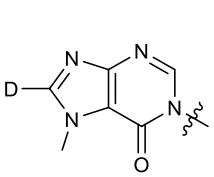
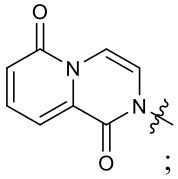
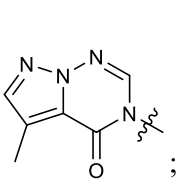
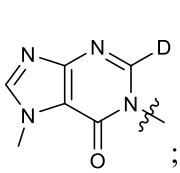
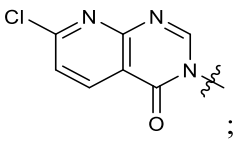
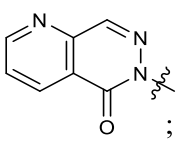
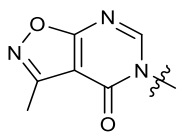
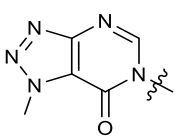
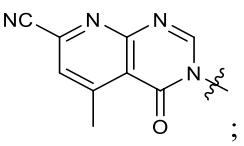
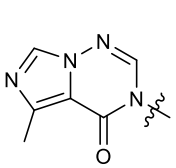
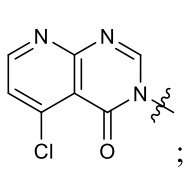
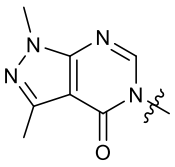
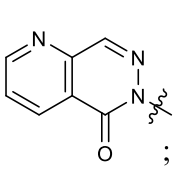
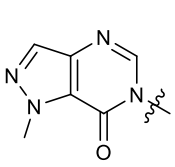
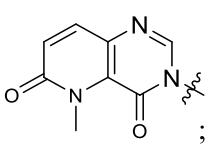
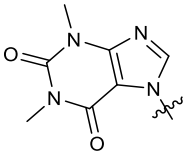
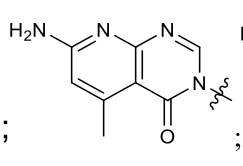
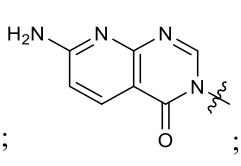
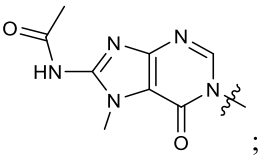
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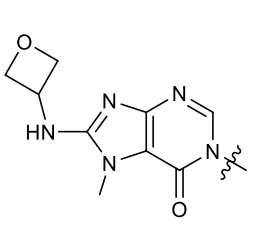
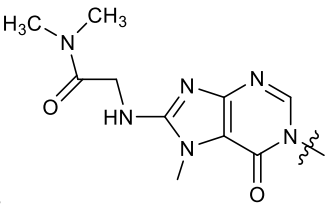
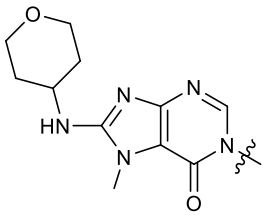
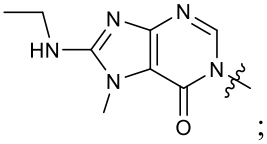
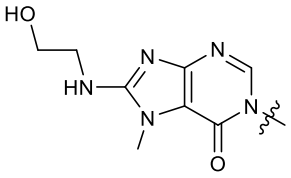
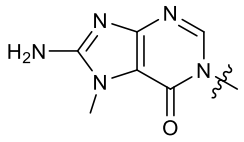
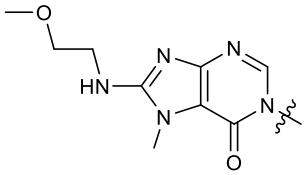
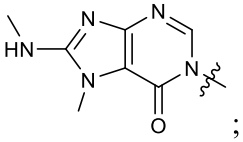
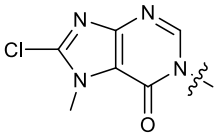
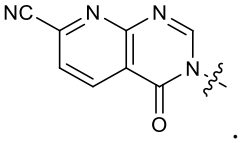




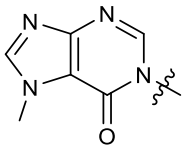
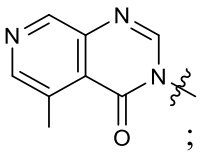
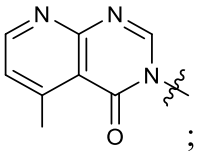
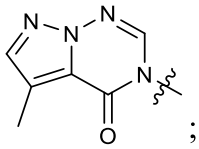
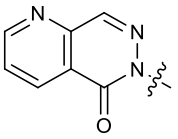
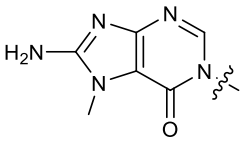

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6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:

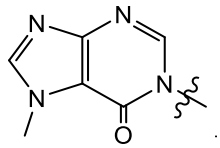

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; or .

7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:

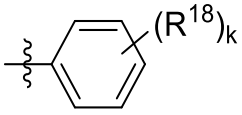

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or

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8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein A is:


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9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is methylene.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



wherein:

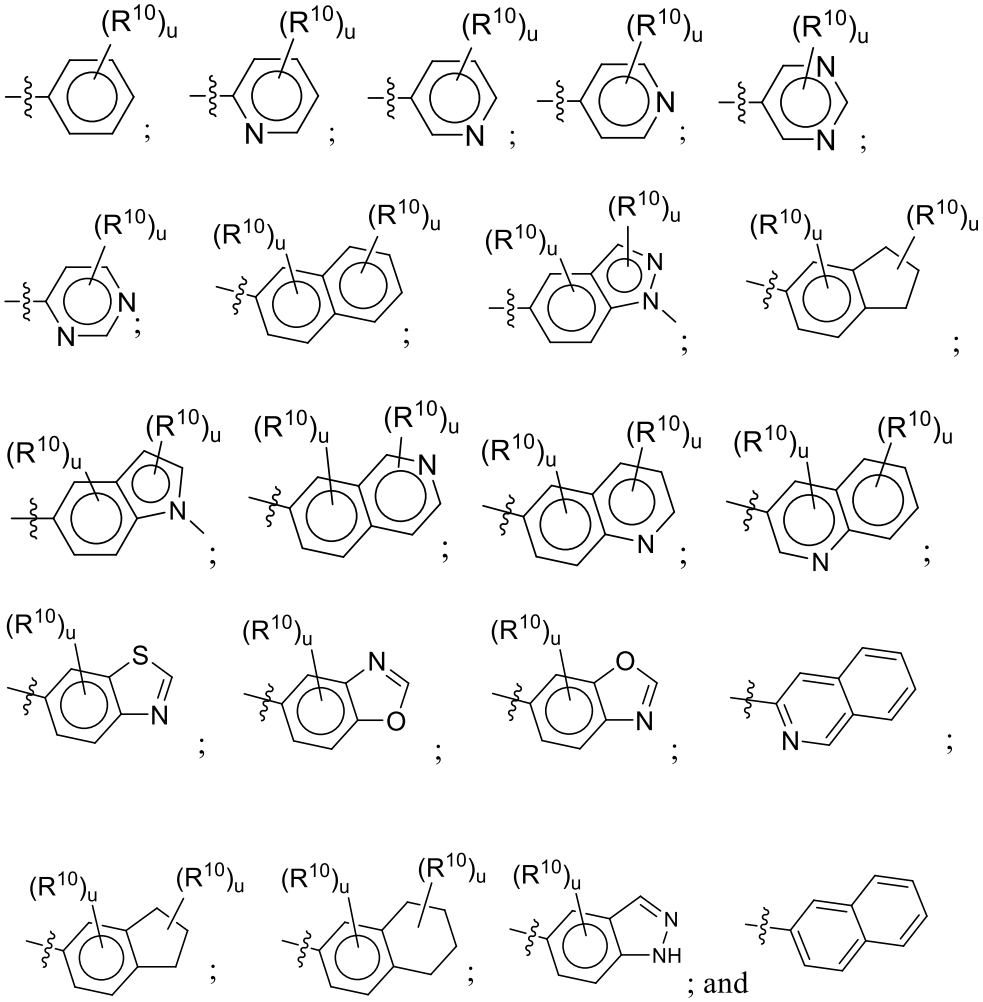
each R^{18} is independently selected from H, halogen, -OH, -C_{1-4} alkyl, -C_{1-4} haloalkyl, -CN, halo, C_{1-4} haloalkoxy, C_{1-4} alkoxy, -SO_2-C_{1-4}alkyl, -C_{1-4}CN, C_{1-4} aldehyde, -SF_5, C_{1-4} ketone, unsubstituted or substituted C_{3-6}cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted heteroaryl, fused aryl, and fused heteroaryl; and

k is from 0 to 3.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein each R^{18} is independently: H; Cl; -$OCHF_2$; -OCF_3; -OCH_3; or -CN.

12. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein each R^{18} is independently fluoro or chloro.

13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



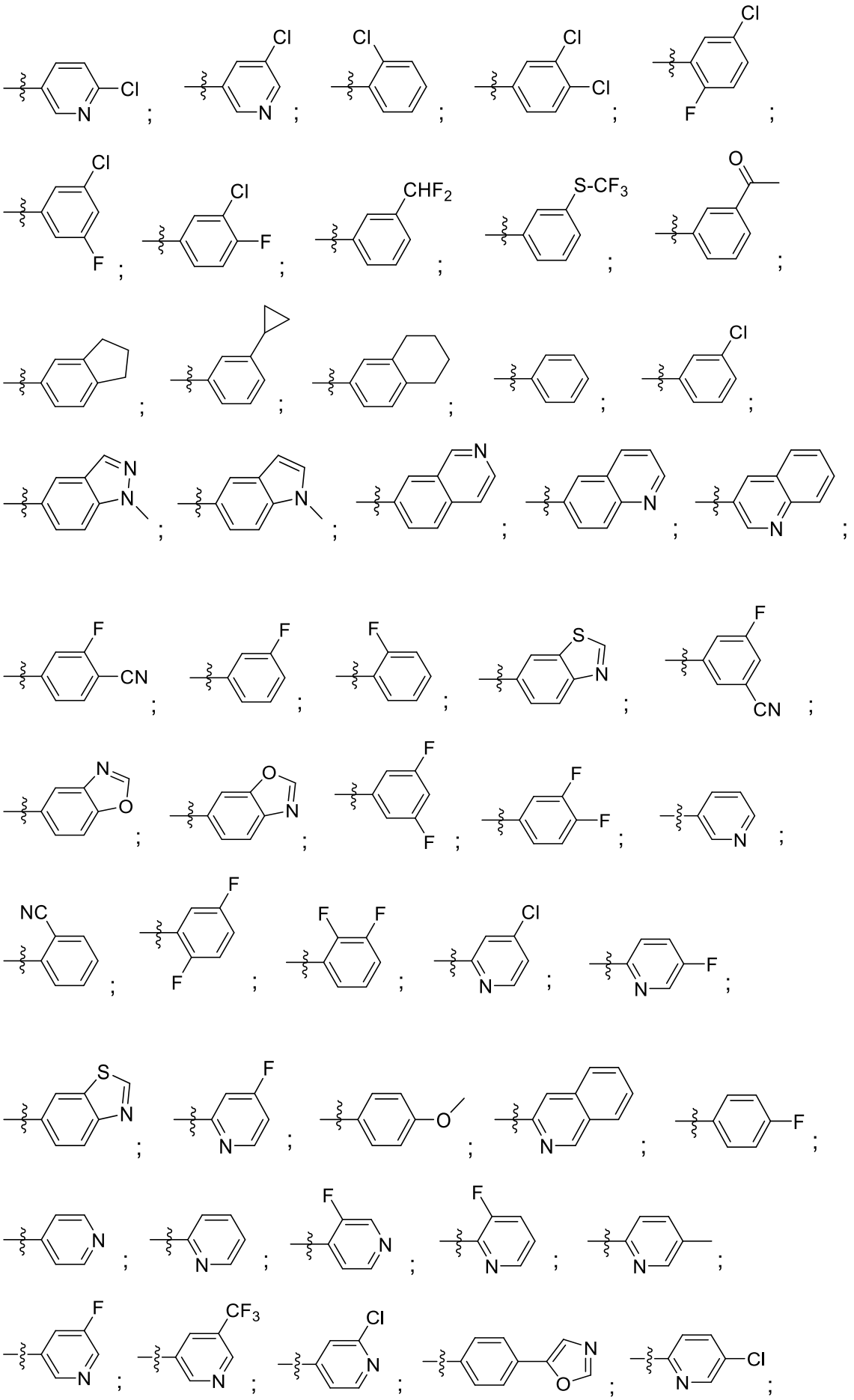
; and

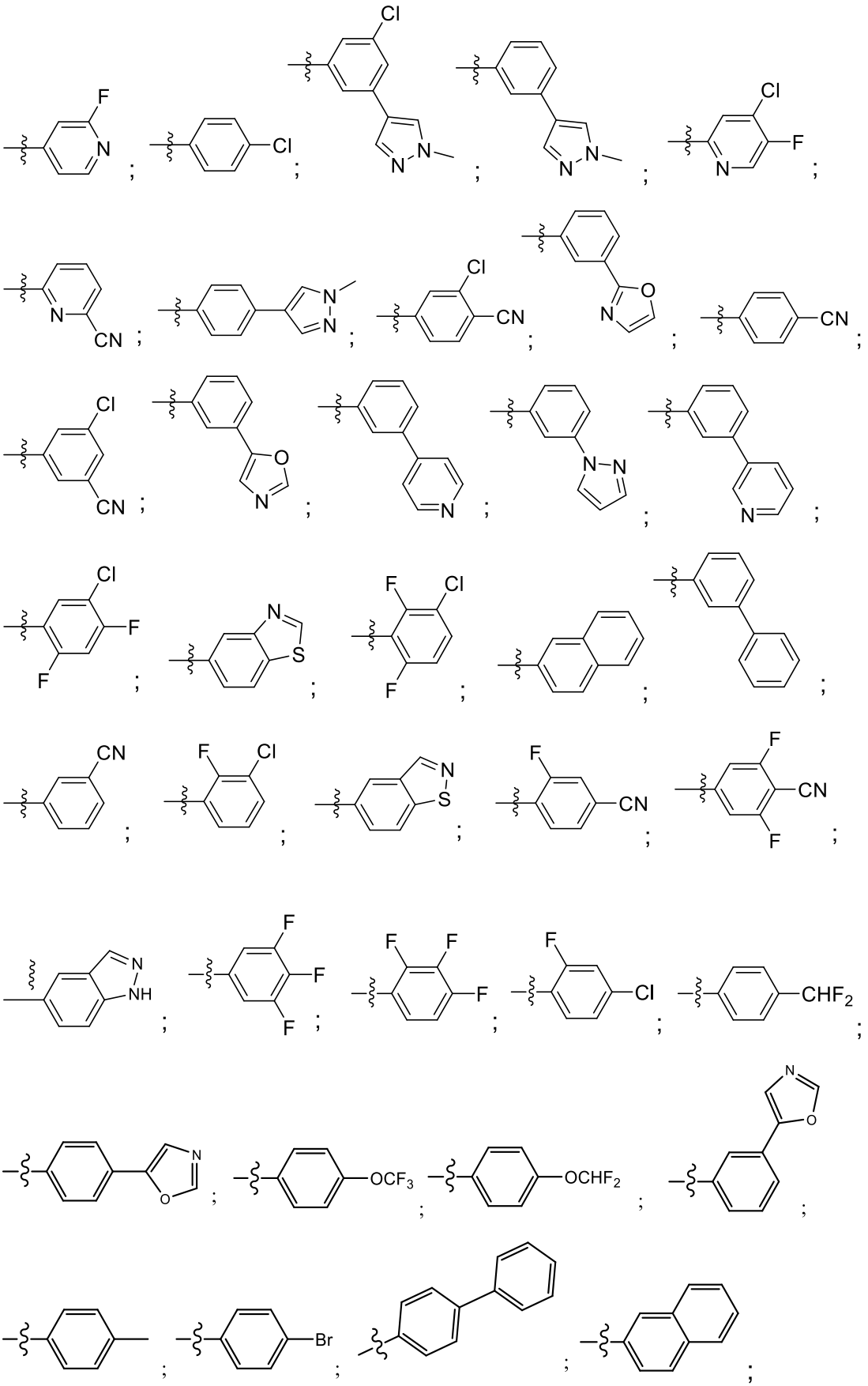
wherein:

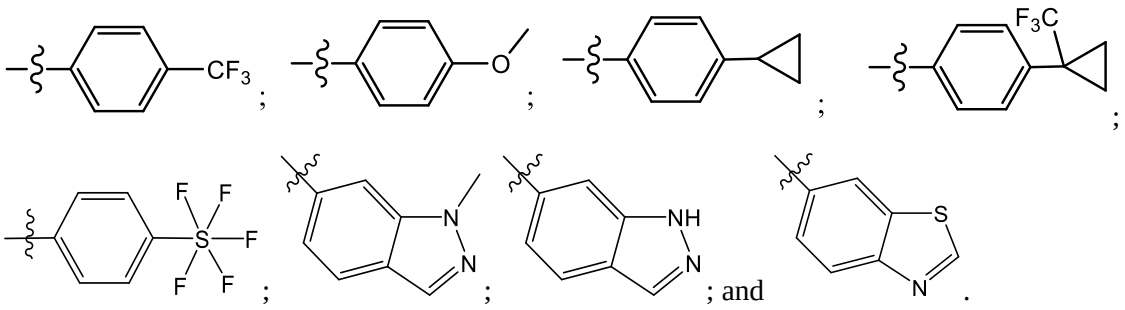
each R^{10} is independently: H; halogen; -CN; -OH; C_{1-4} alkyl; substituted or unsubstituted C_{3-6} cycloalkyl; C_{1-4} haloalkyl; C_{1-4} haloalkoxy; C_{1-4} alkoxy; -SO_2-C_{1-4} alkyl; C_{1-4} CN;C_{1-4} aldehyde; C_{1-4} ketone; -S-C_{1-4} haloalkyl; substituted or unsubstituted 5- to 6-membered heteroaryl; substituted or unsubstituted 4- to 6-membered hetercycloalkyl; or substituted or unsubstituted C_{5-6} aryl; and

each u is independently 0, 1, 2 or 3.

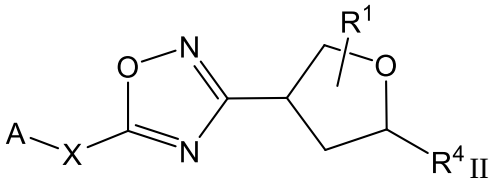
14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 is:





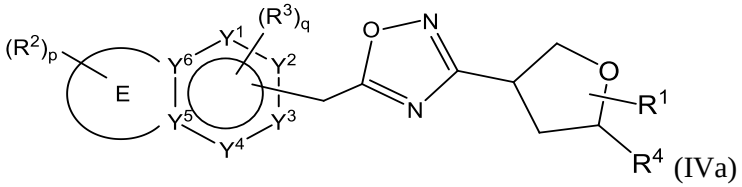


15. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (II)

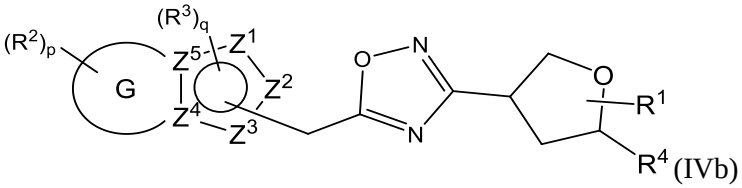


II

16. A compound of formula (IVa) or formula (IVb), or a pharmaceutically acceptable salt thereof,



(IVa)



(IVb)

wherein:

E is a five membered or a six membered heteroaryl ring wherein one ring carbon atom is optionally substituted with oxo;

G is a six membered heteroaryl ring having one ring carbon atom substituted with oxo;

one to three of Y^1, Y^2, Y^3, Y^4, Y^5 and Y^6 are nitrogen, and the other of Y^1, Y^2, Y^3, Y^4, Y^5 and Y^6 are carbon, and one of Y^1, Y^2, Y^3 and Y^4 may be –C(O)- or -C(S)-;

one or two of Z^1, Z^2, Z^3, Z^4 and Z^5 are nitrogen and the other of Z^1, Z^2, Z^3, Z^4 and Z^5 are carbon;

R^1 is: H; or $C_{1\text{-}6}$alkyl;

each R^2 is independently; H; D; -$C_{1\text{-}4}$ alkyl; -$C_{1\text{-}4}$ haloalkyl; -CN; halo; halo$C_{1\text{-}4}$alkoxy; $C_{1\text{-}4}$ alkoxy; -OH; -SO_2-$C_{1\text{-}4}$alkyl; -$C_{1\text{-}4}$CN, $C_{1\text{-}4}$ aldehyde; $C_{1\text{-}4}$ ketone; benzylamino; or $NR^{14}R^{15}$;

each R^3 is independently: H; D; -$C_{1\text{-}4}$ alkyl; -$C_{1\text{-}4}$ haloalkyl; -CN; halo; or $NR^{14}R^{15}$;

R^4 is: substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl;

or R^1 and R^4 may together form an unsubstituted or substituted C_{3-6}cylcoalkyl fused to a substituted or unsubstituted phenyl; substituted or unsubstituted heteroaryl; or substituted or unsubstituted naphthyl.

p is 0, 1 or 2;

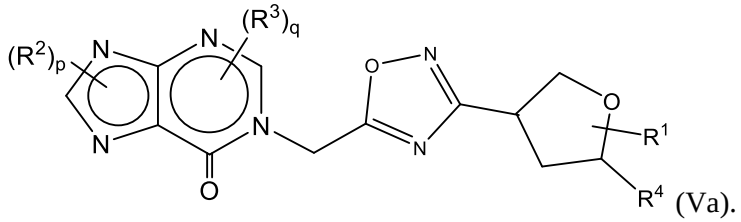
q is 0 or 1;

R^{14} and R^{15} are each independently: H; substituted or unsubstituted -C_{1-4} alkyl; substituted or unsubstituted -C(O)-C_{1-4} alkyl; substituted or unsubstituted C_{3-6} cycloalkyl; substituted or unsubstituted 3- to 6-membered heterocycloalkyl; substituted or unsubstituted -C_{1-4} heteroalkyl; -$C(O)NR^{16}R^{17}$; substituted or unsubstituted -C_{1-4} alkyl-$C(O)NR^{16}R^{17}$; substituted or unsubstituted phenyl; or substituted or unsubstituted benzyl;

or R^{14} and R^{15} together with the atoms to which they are attached may form a 4-, 5-, 6- or 7-membered ring that optionally includes one additional heteroatom selected from O, N and S; and

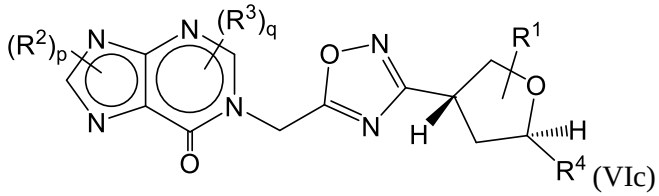
R^{16} and R^{17} each are independently H and C_{1-4} alkyl.

17. The compound of claim 16, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (Va)

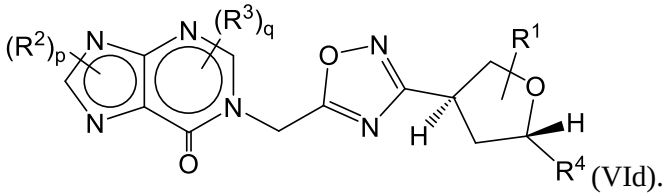


(Va).

18. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of formula (VIc) or formula (VId)

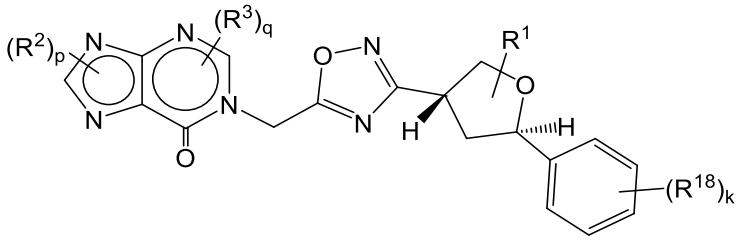


(VIc)

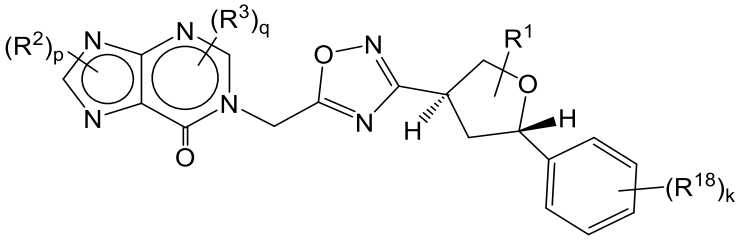


(VId).

19. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of formula (VIIc) or formula (VIId)



(VIIc)



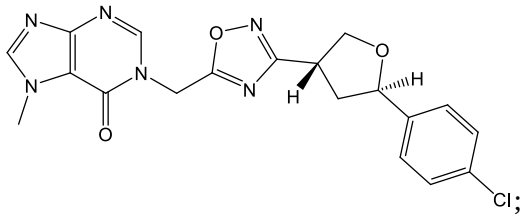
(VIId)

wherein:

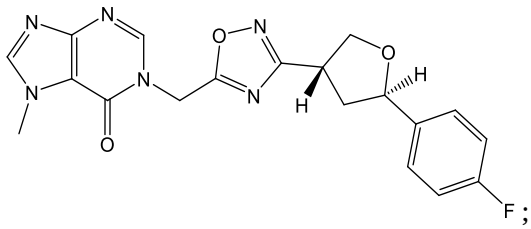
each R^{18} is independently selected from H, halogen, -OH, -C_{1-4} alkyl, -C_{1-4} haloalkyl, -CN, halo, C_{1-4} haloalkoxy, C_{1-4} alkoxy, -SO_2-C_{1-4}alkyl, -C_{1-4}CN, C_{1-4} aldehyde, -SF_5, C_{1-4} ketone, unsubstituted or substituted C_{3-6}cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted heteroaryl, fused aryl, and fused heteroaryl; and

k is from 0 to 3

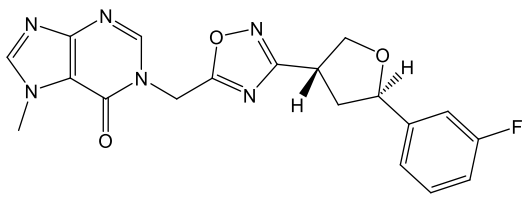
20. A compound selected from:



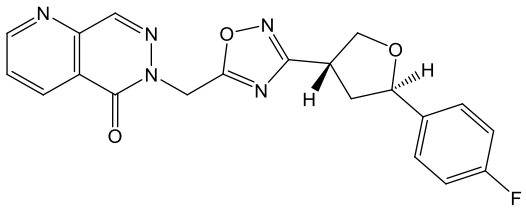
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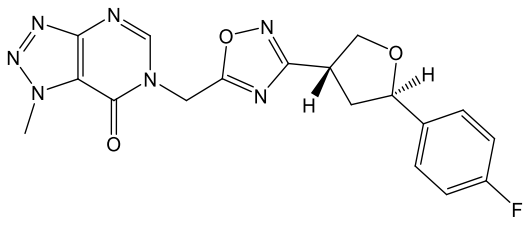
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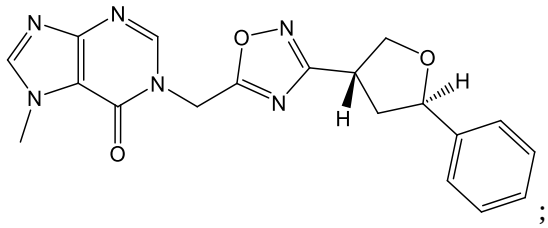


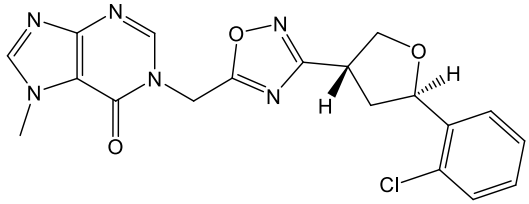
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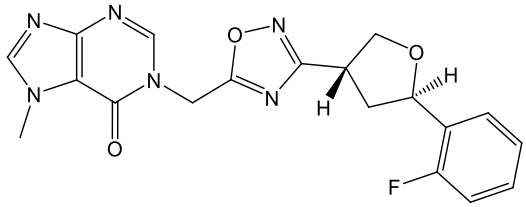


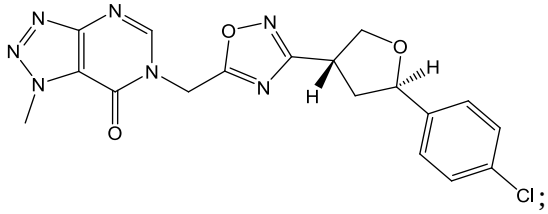
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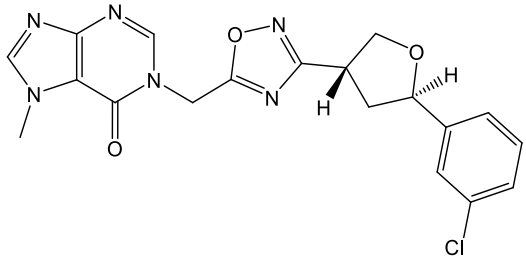

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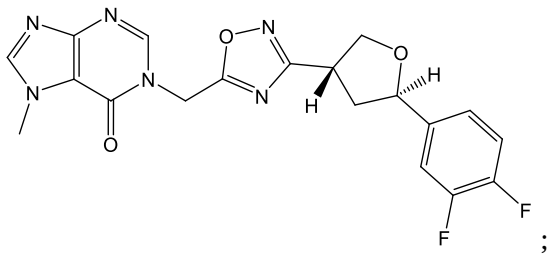

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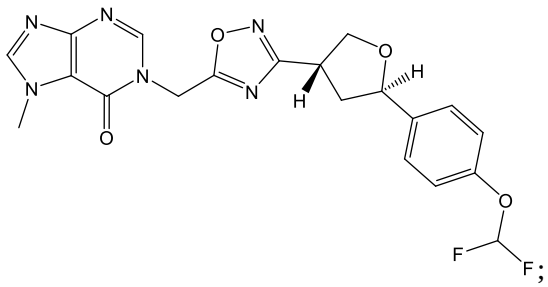

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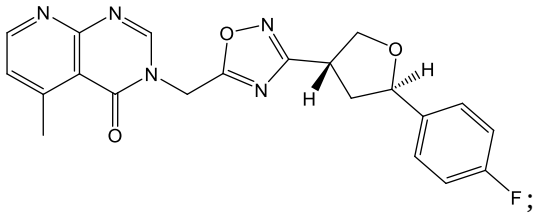

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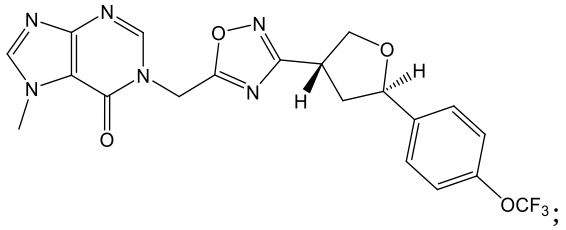

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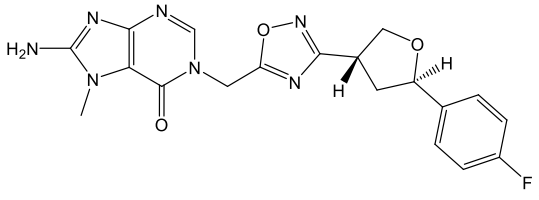

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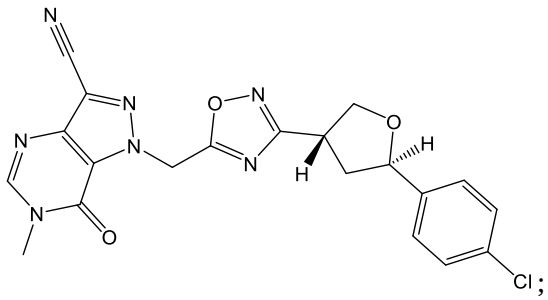

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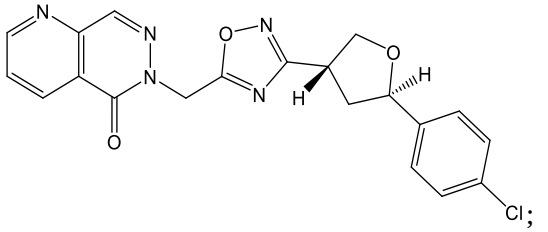


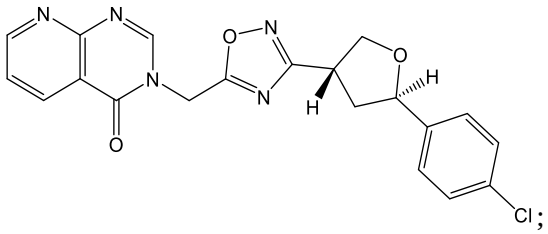


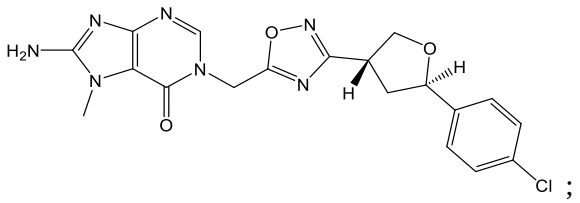


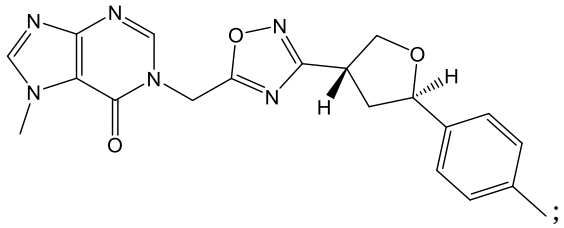


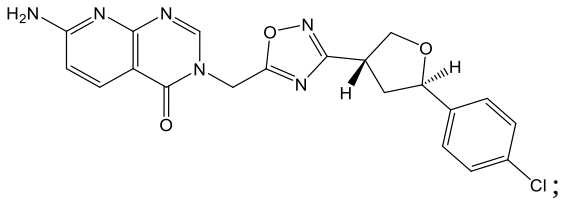


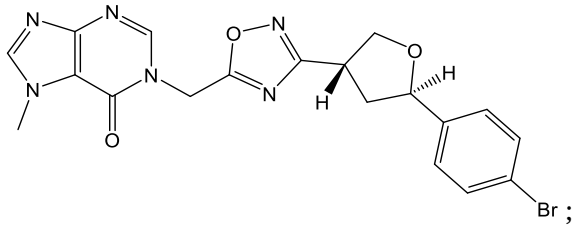


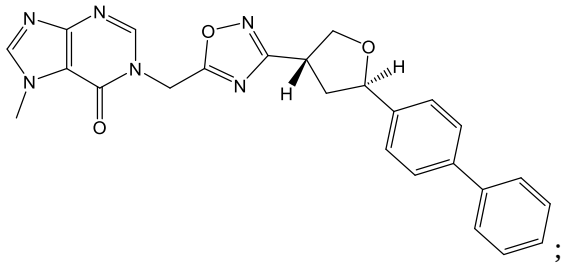


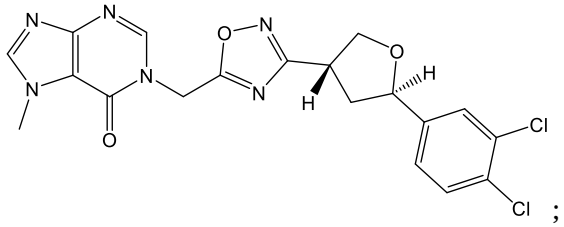

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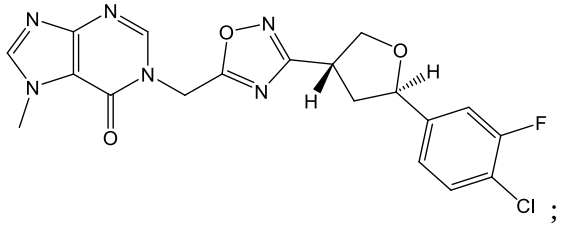

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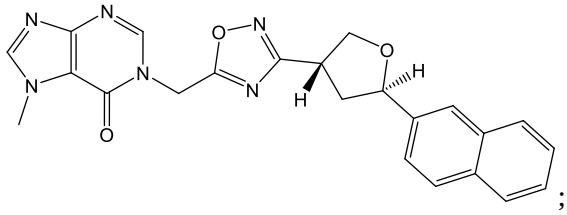

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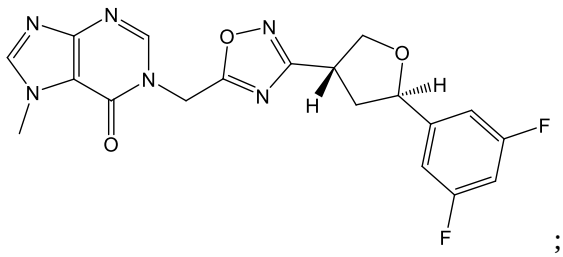

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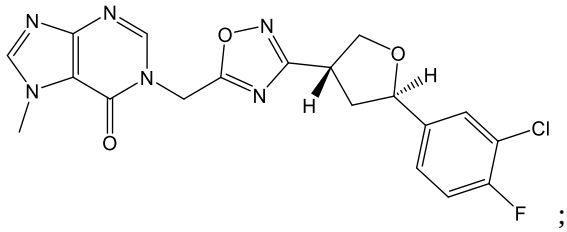

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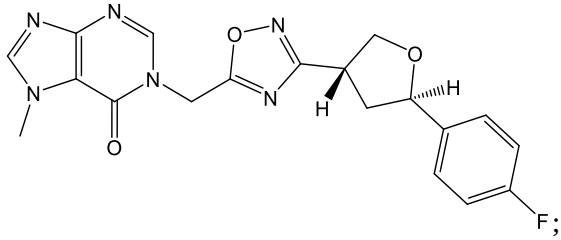

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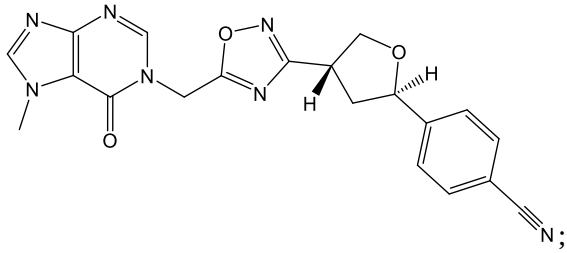

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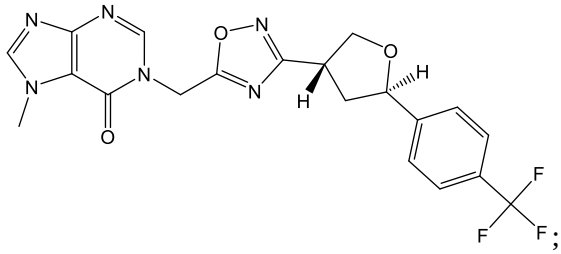

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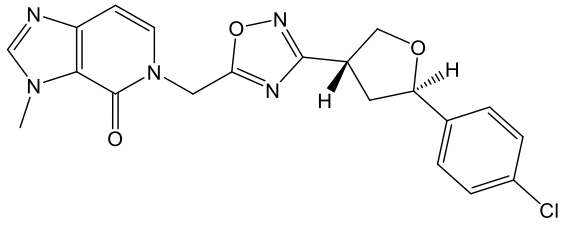

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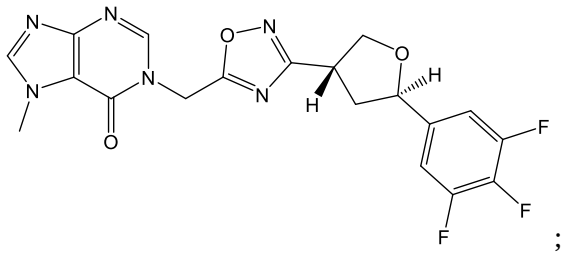

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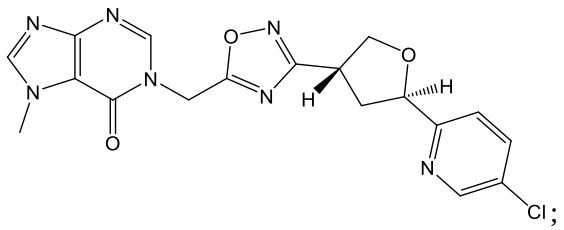

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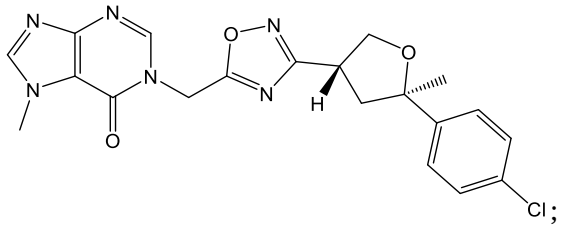

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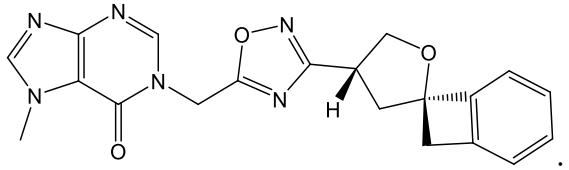

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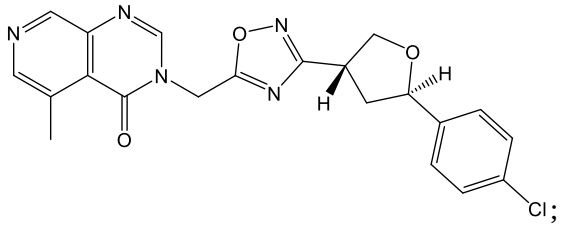

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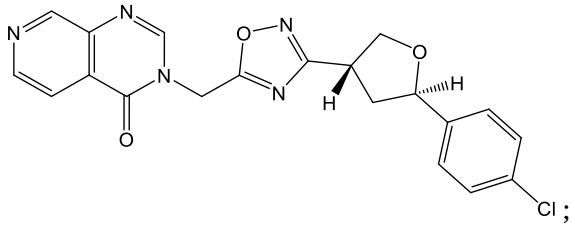

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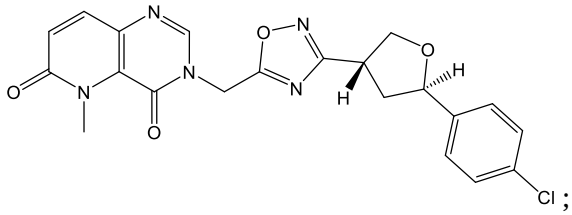


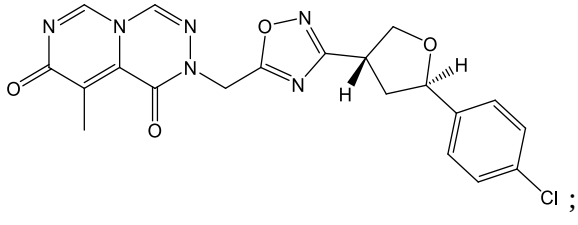


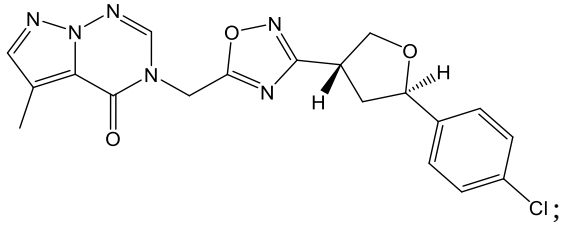


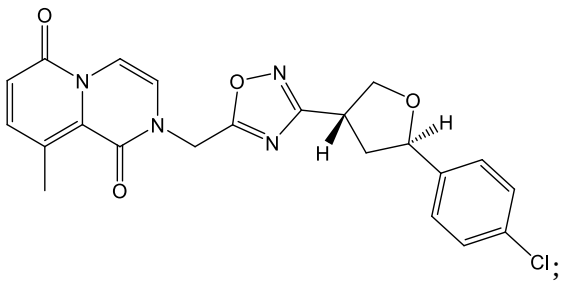


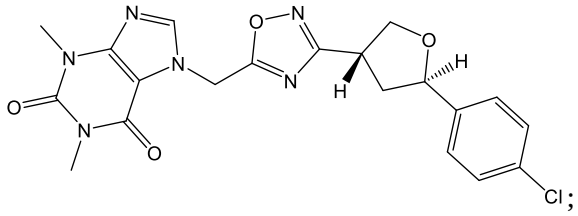


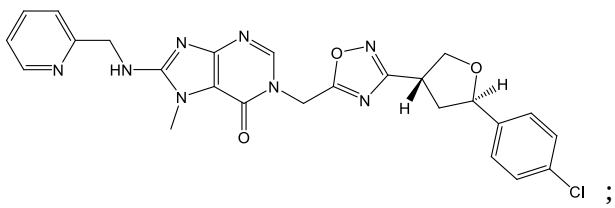


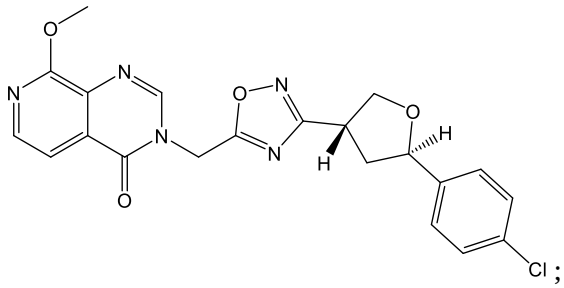


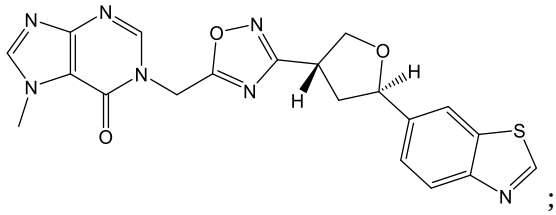


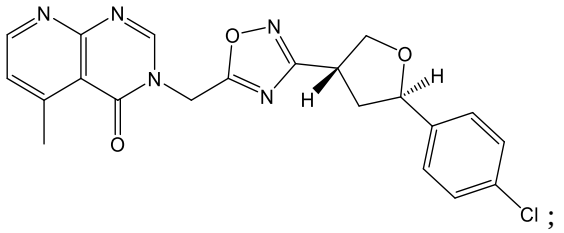


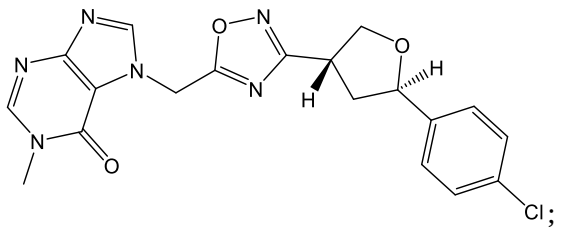


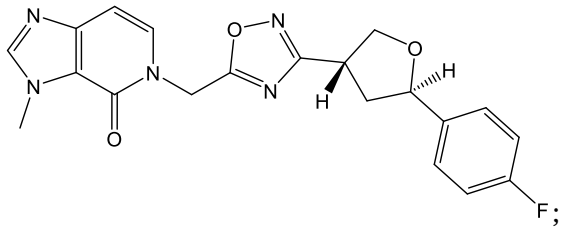


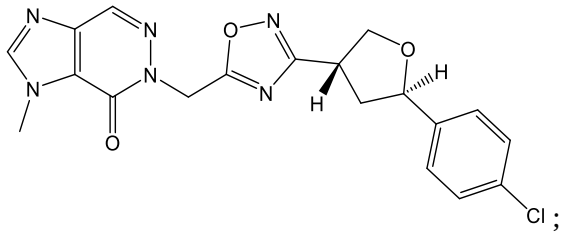


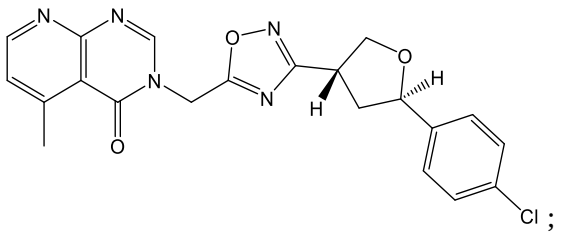


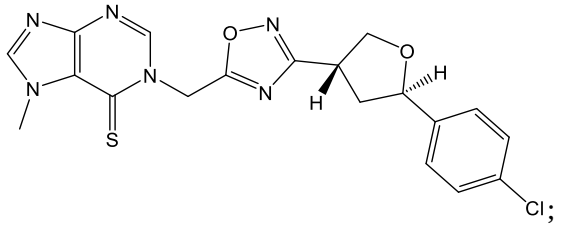


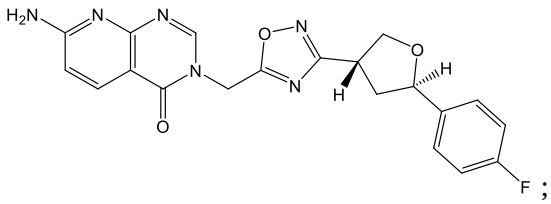


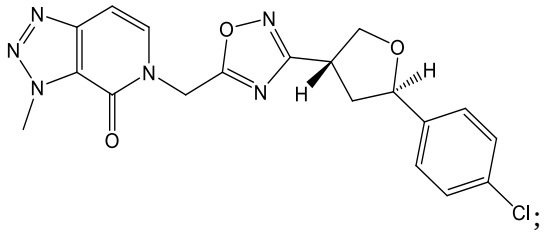


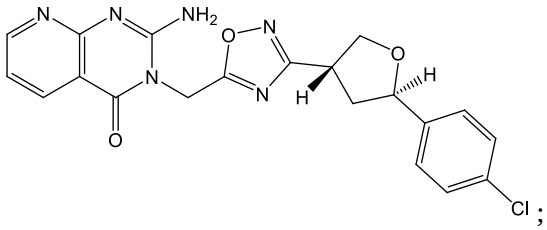


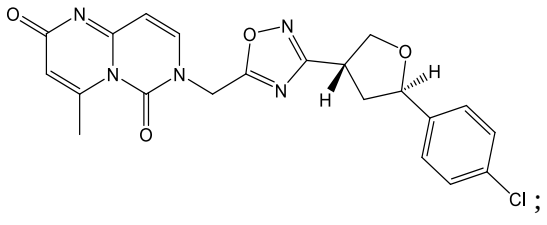


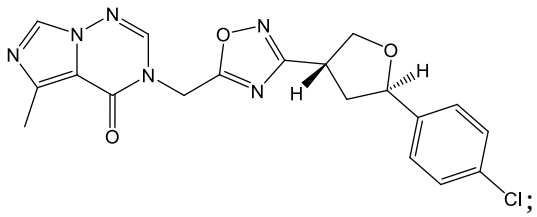


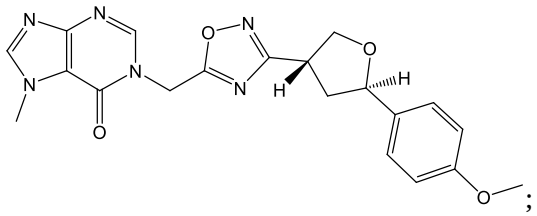


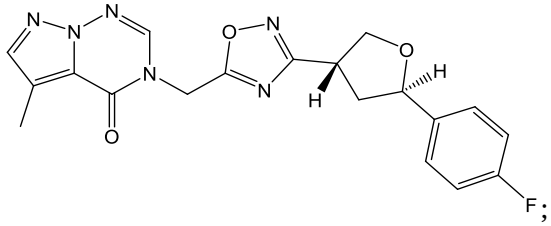


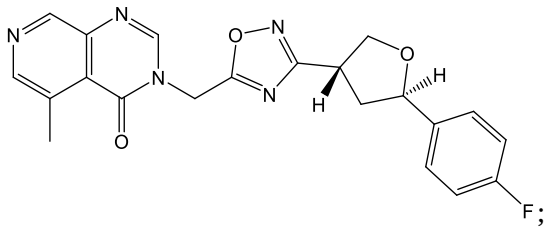


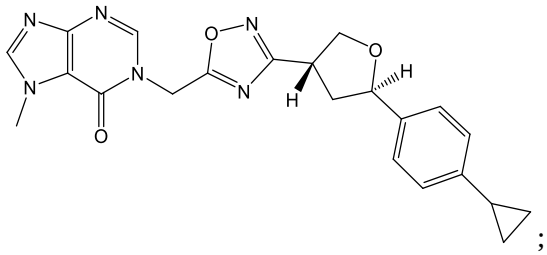






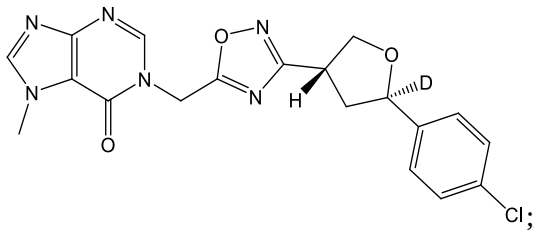


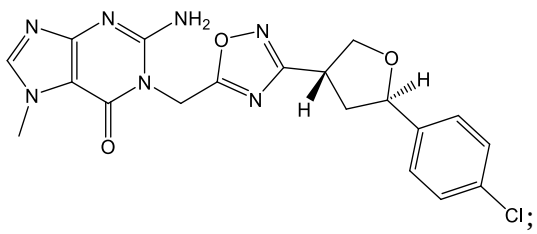


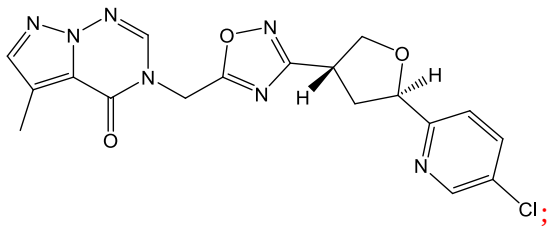


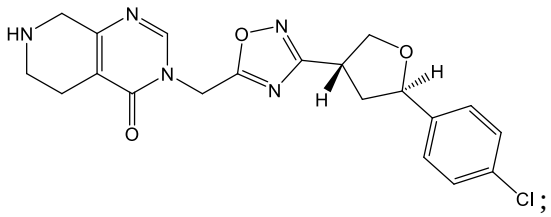
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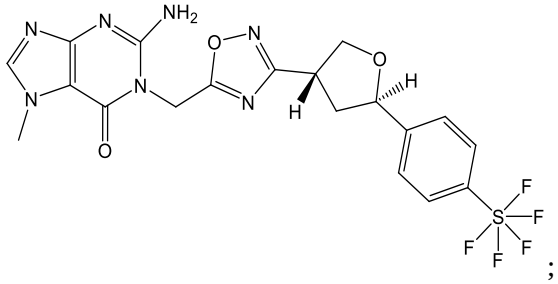
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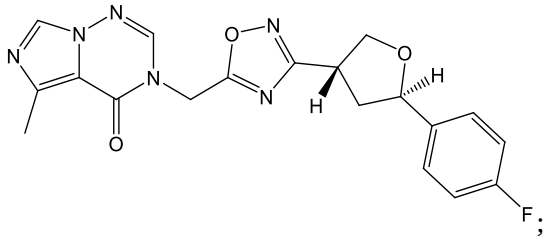


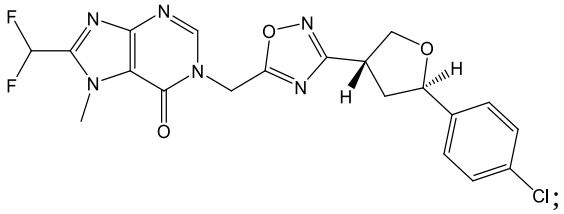


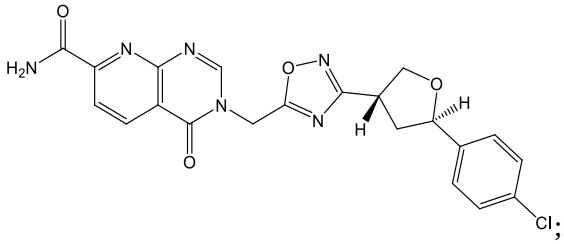


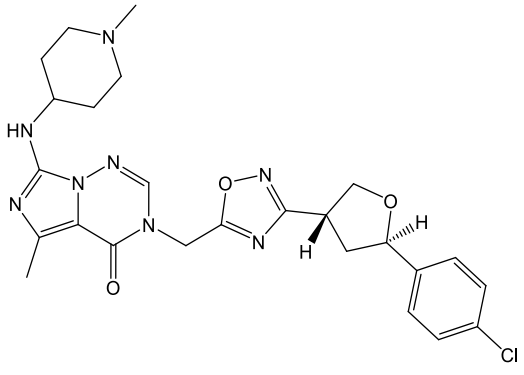


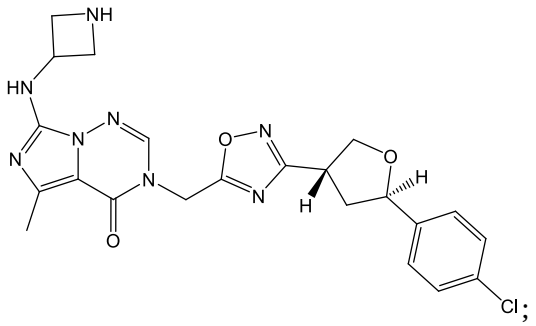


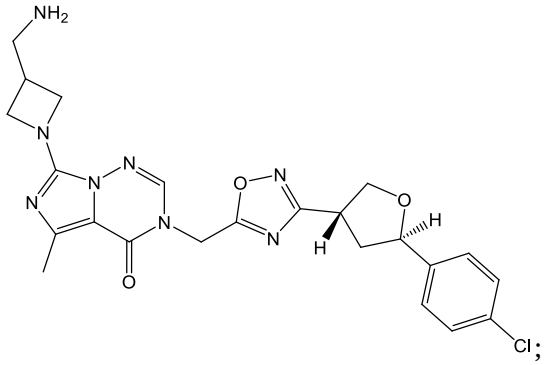


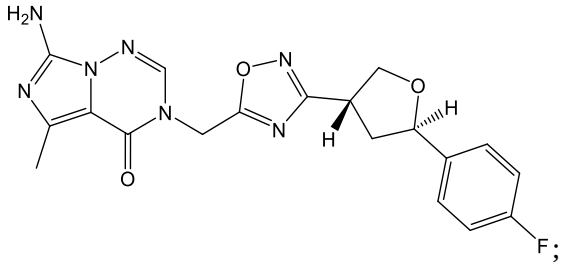


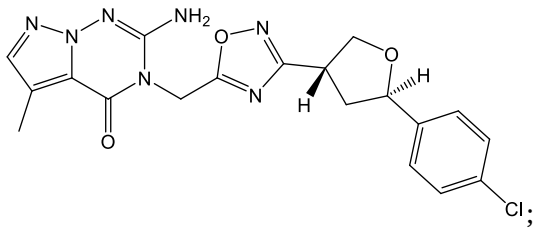


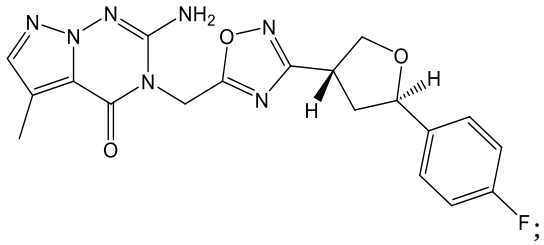


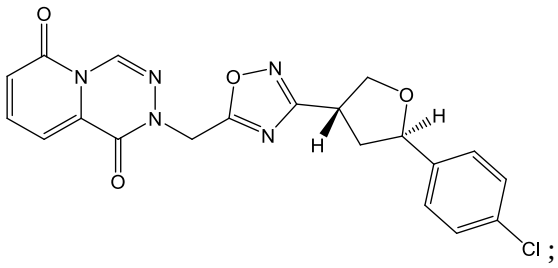


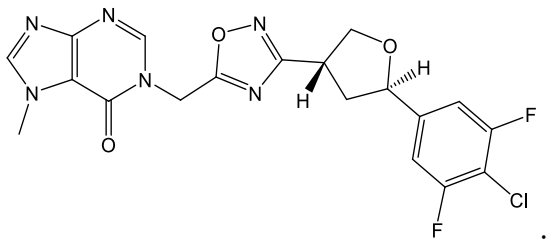


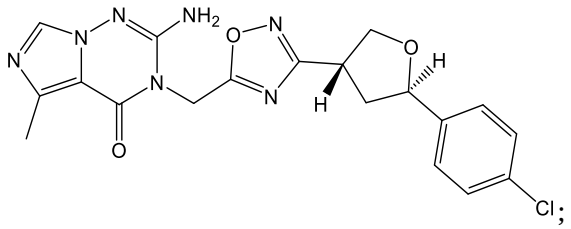


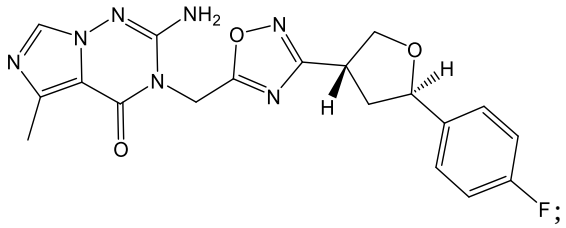


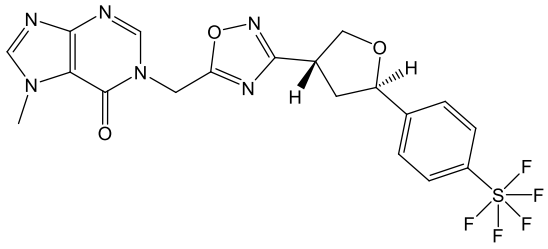


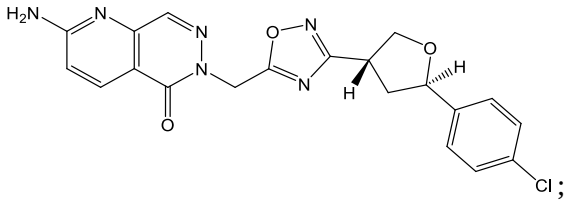


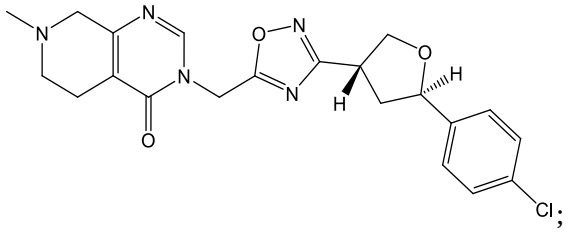

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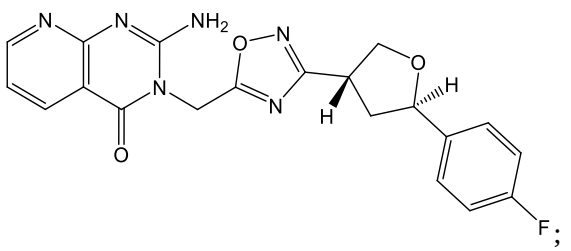

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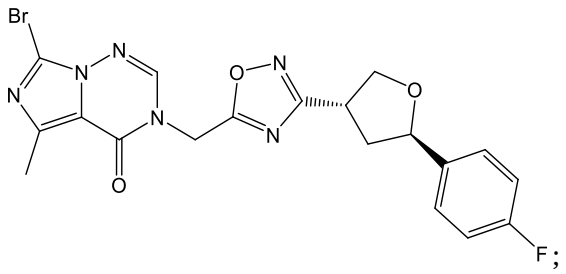

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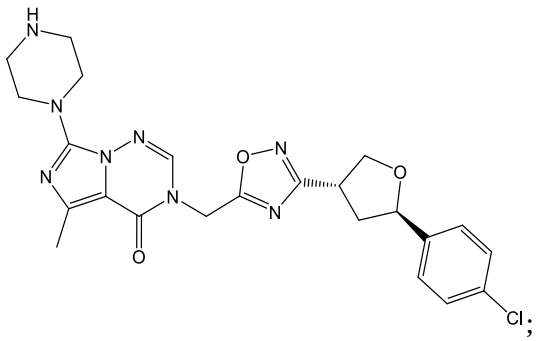

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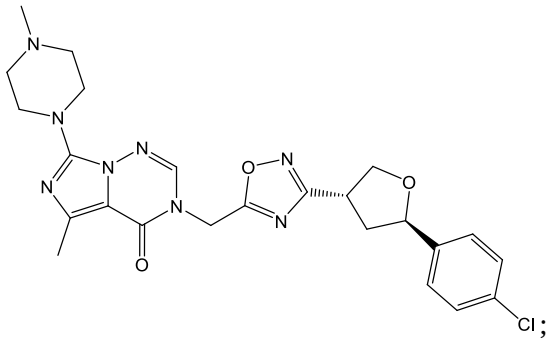

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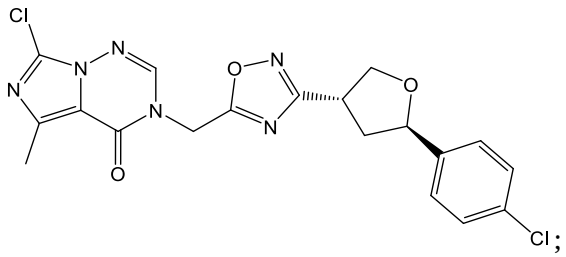

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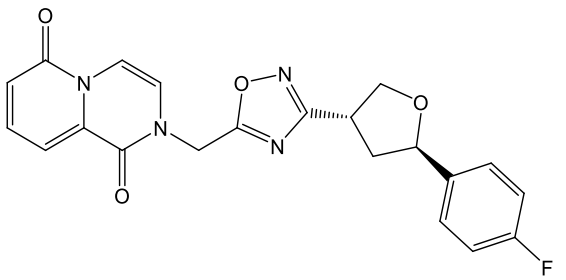

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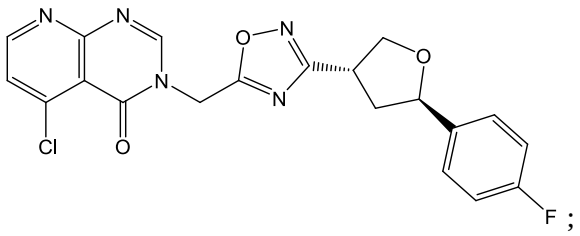


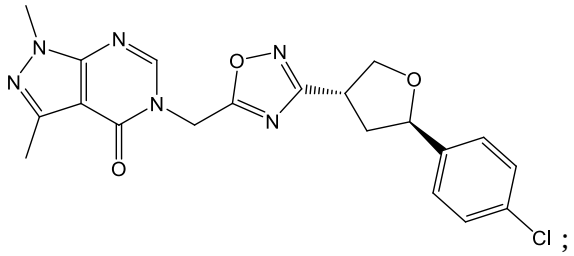


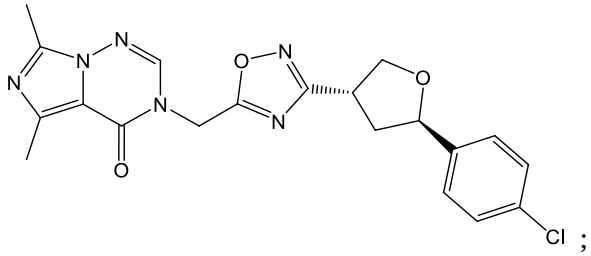


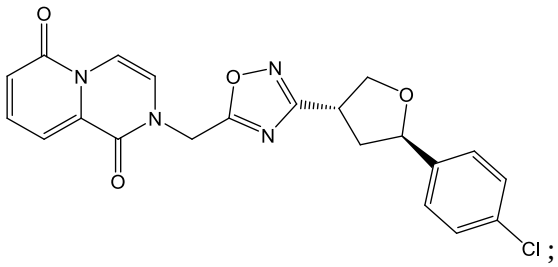


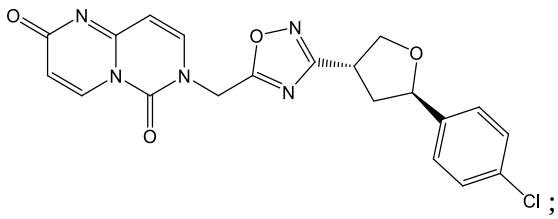


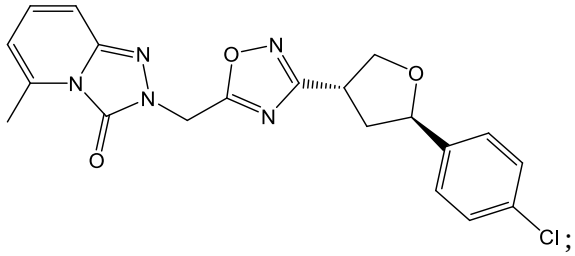


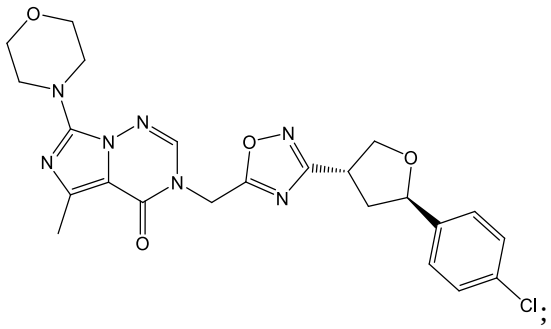


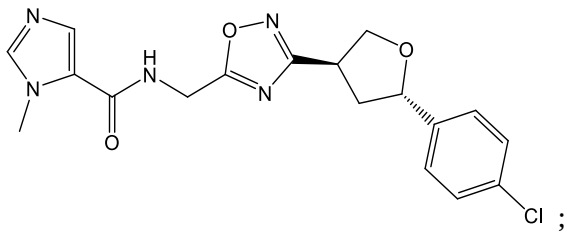


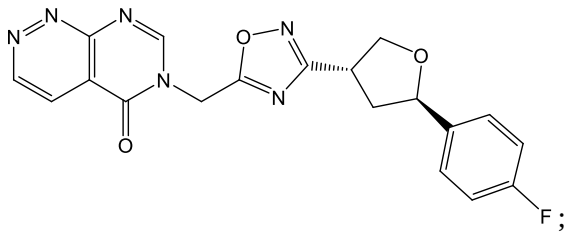


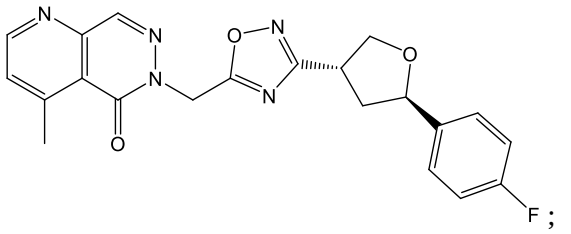


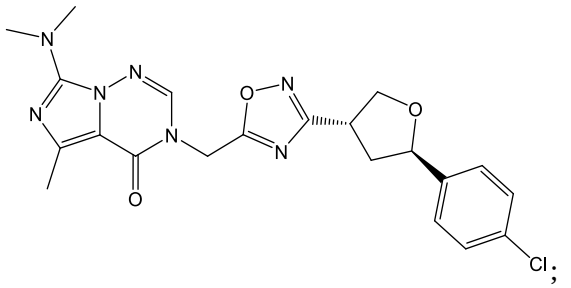


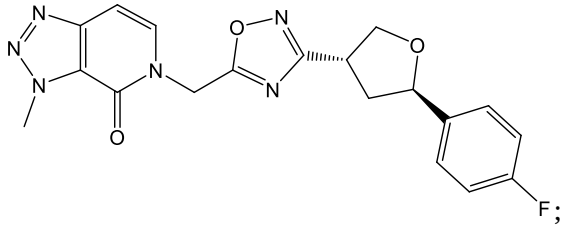


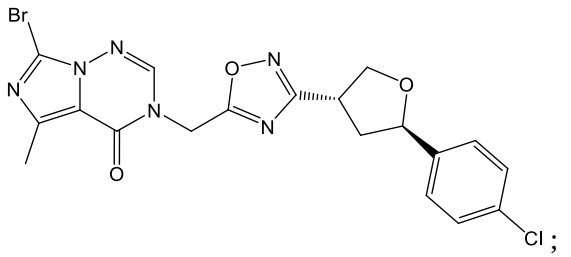


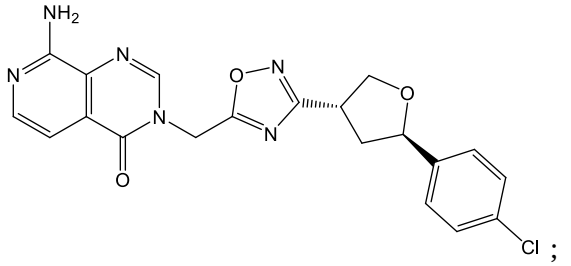


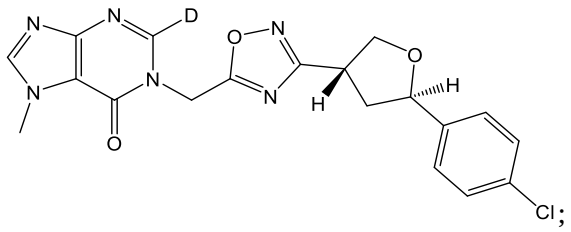


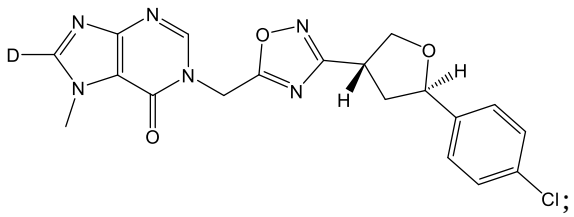


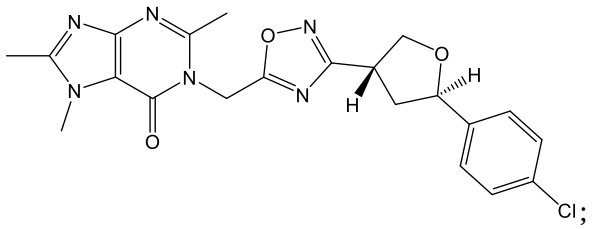


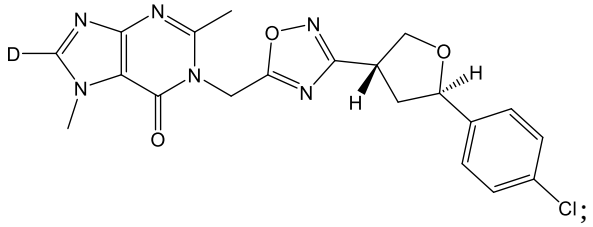


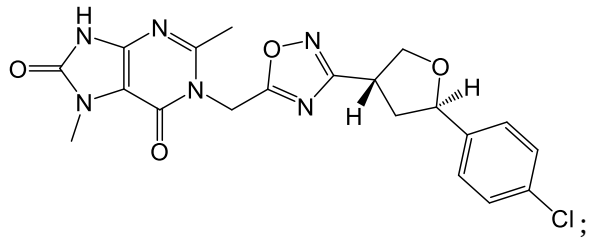


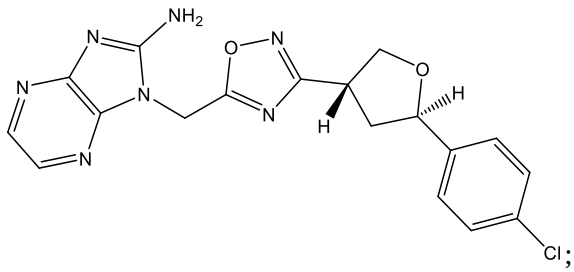


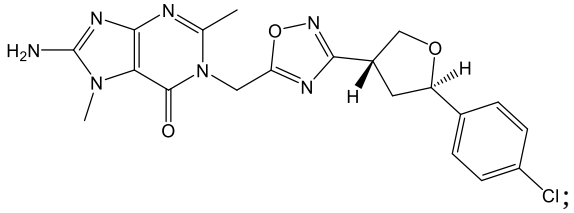


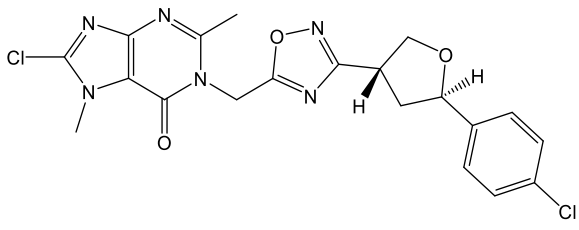


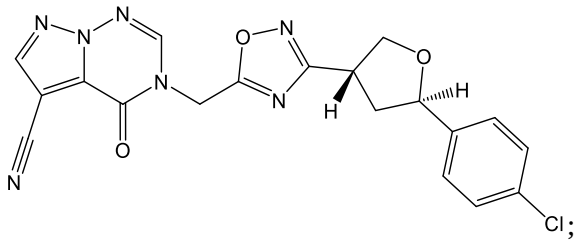


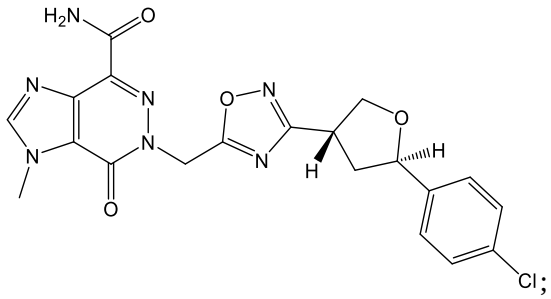


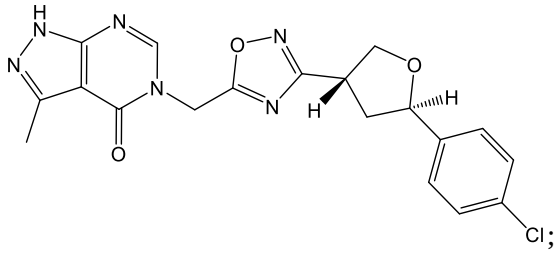


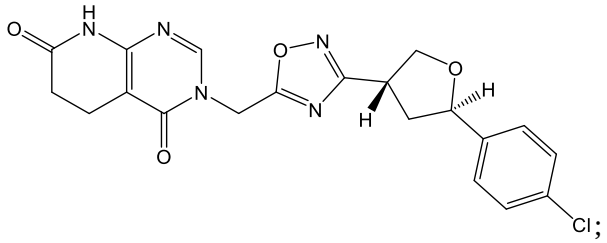


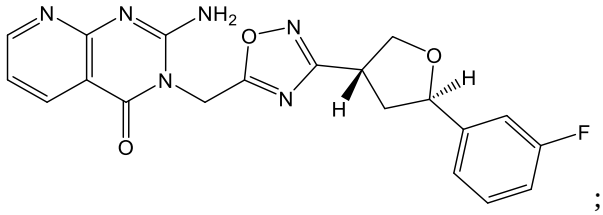


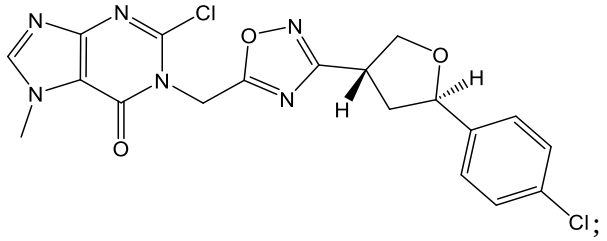


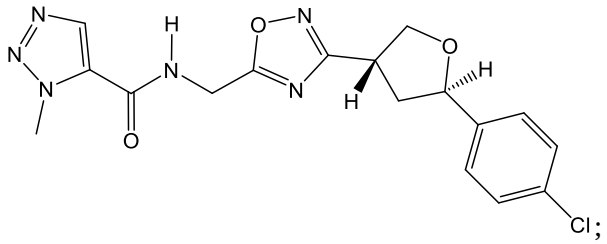


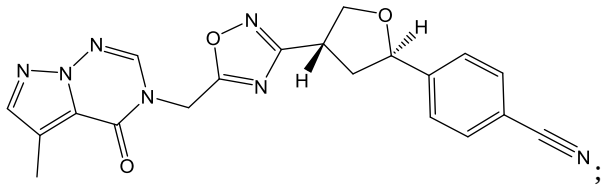


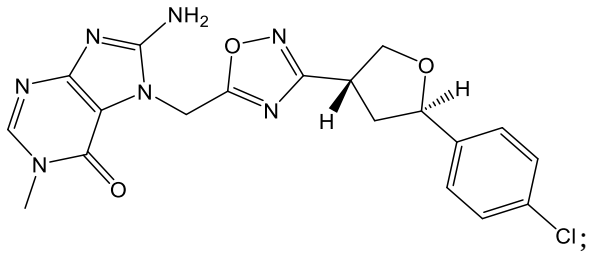


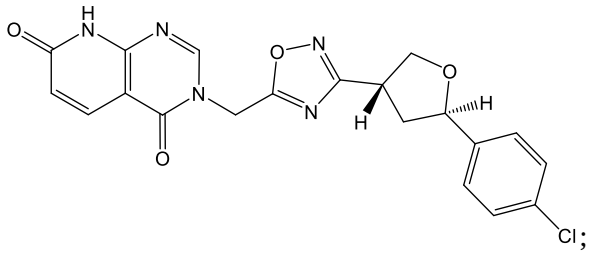

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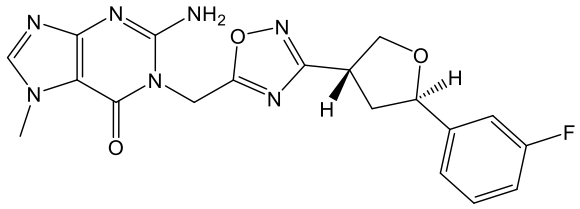


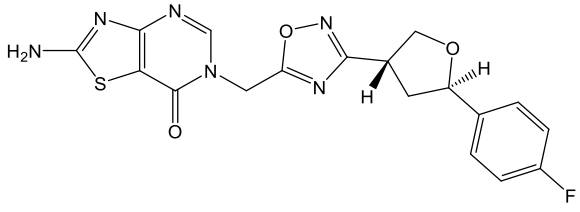


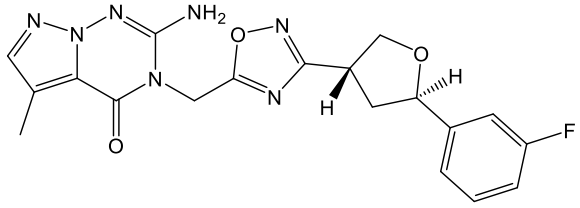

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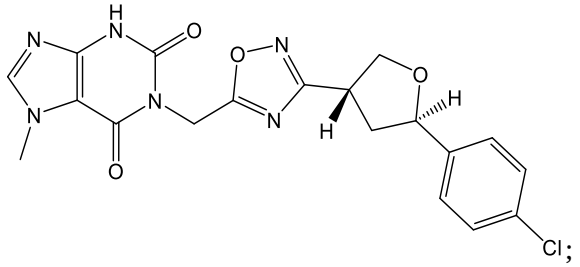

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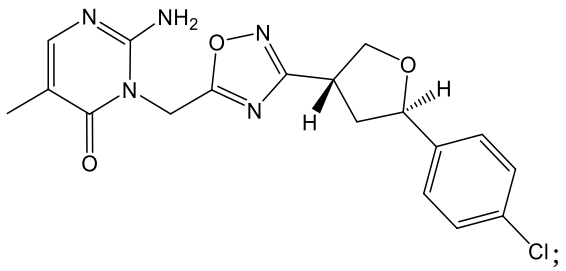

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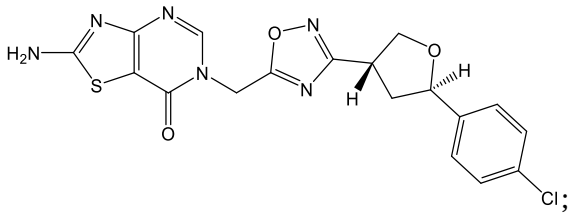

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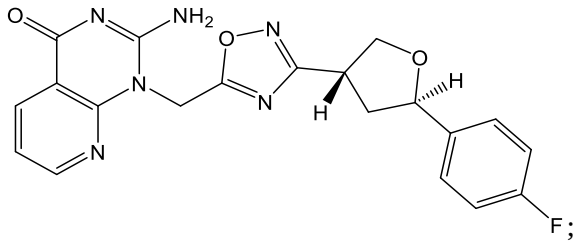

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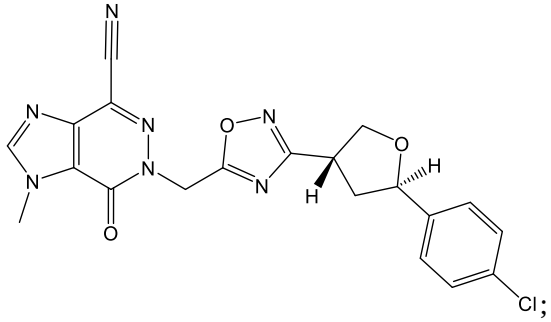

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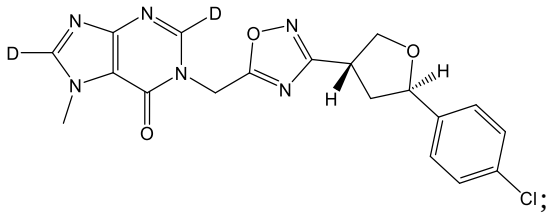

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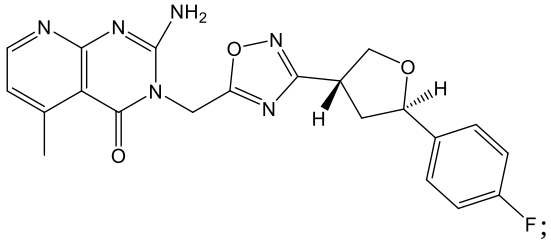


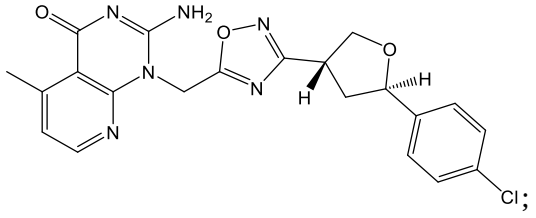


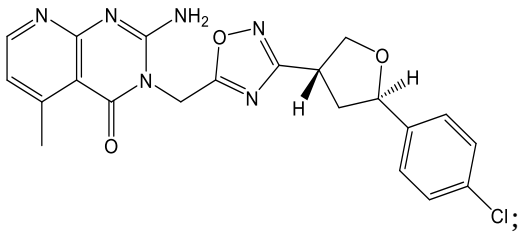


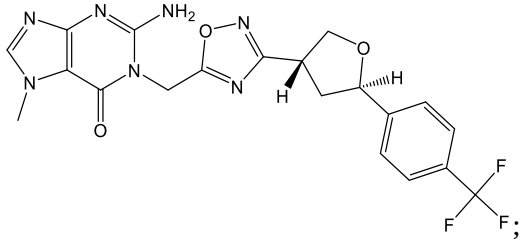


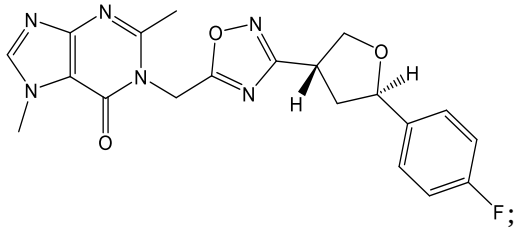


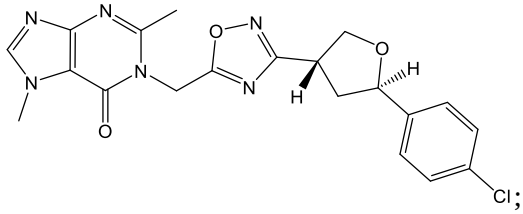


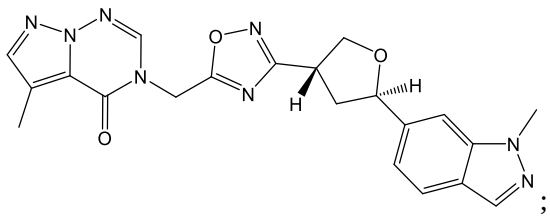


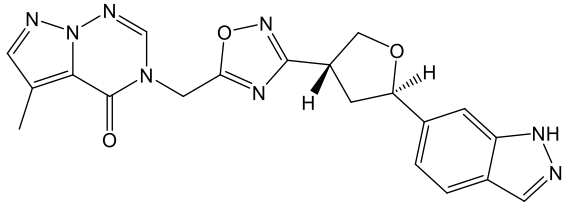


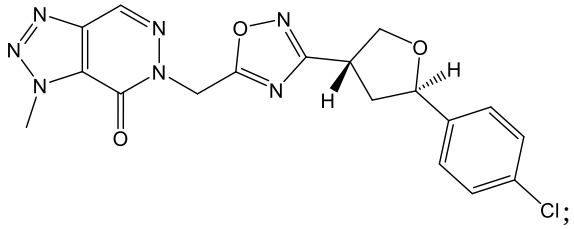


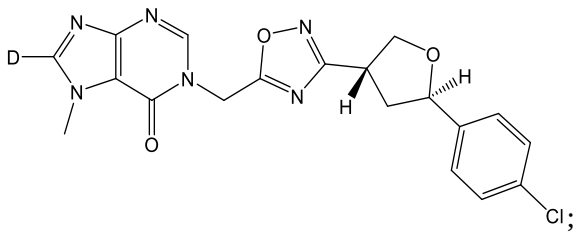


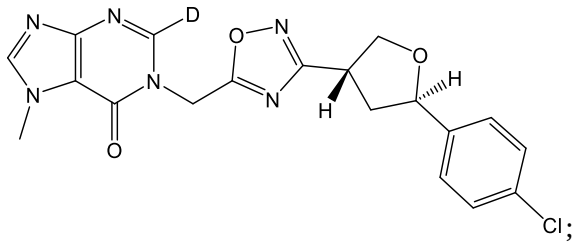


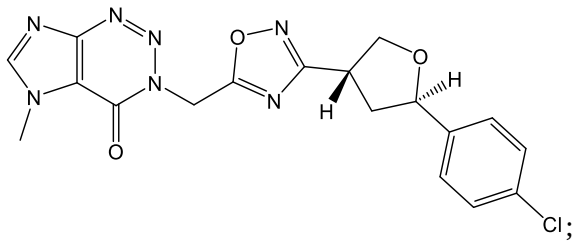


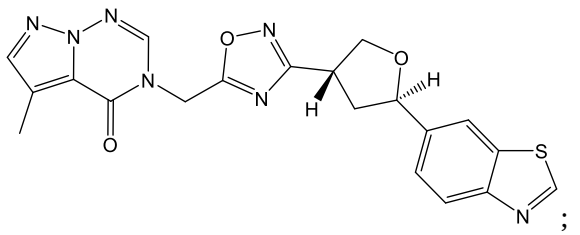


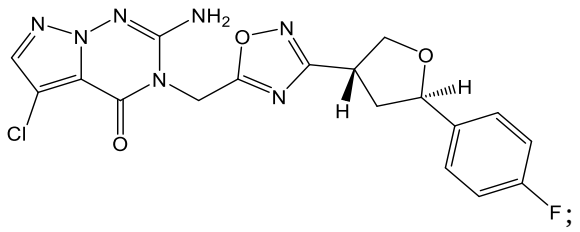


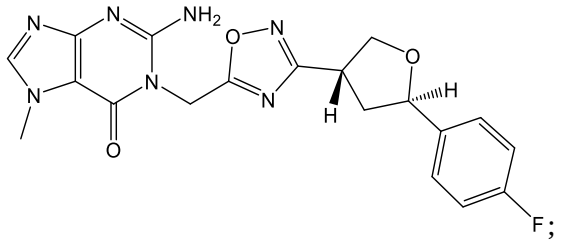


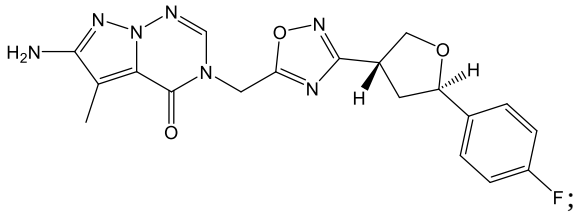


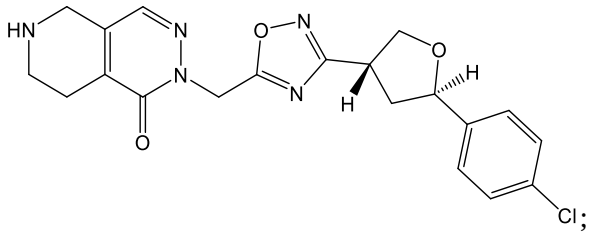


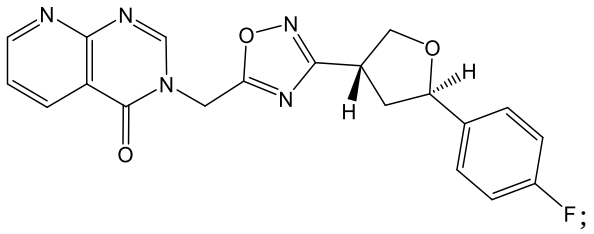


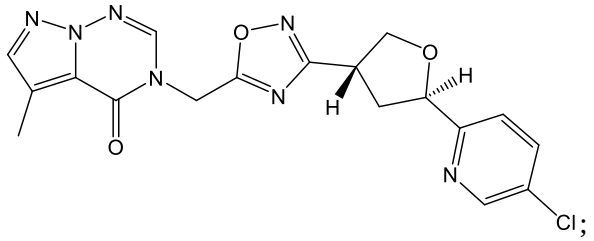


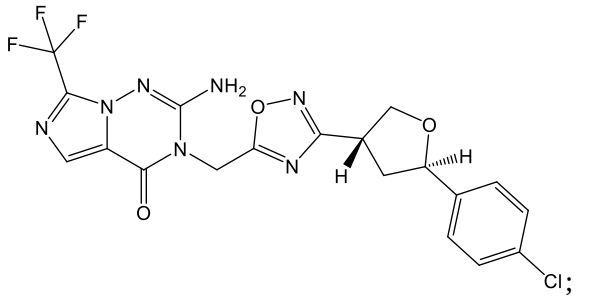


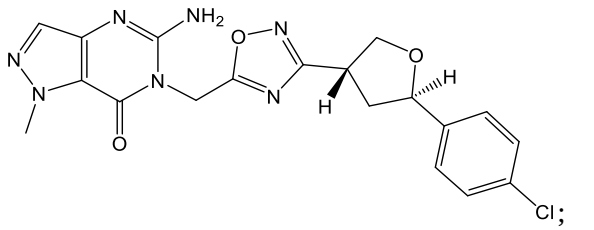


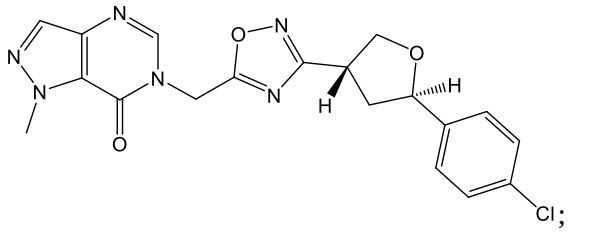


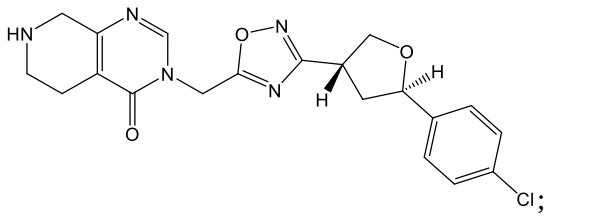


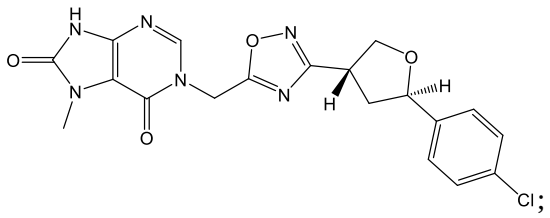


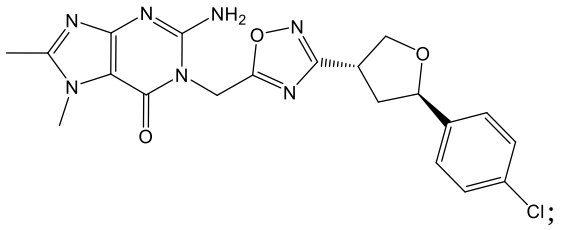


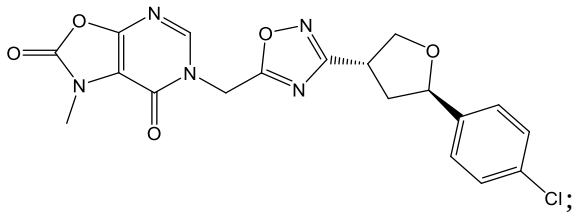


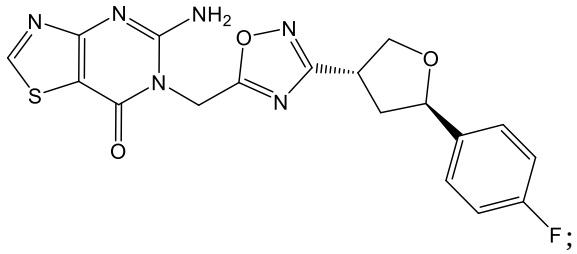


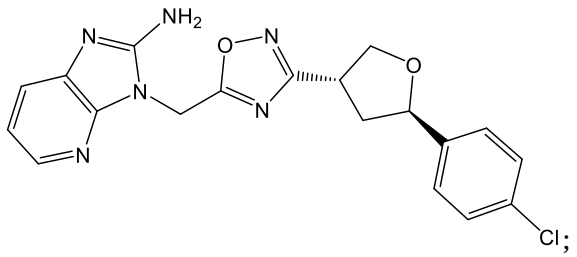


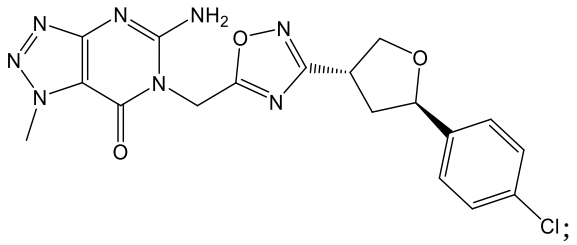


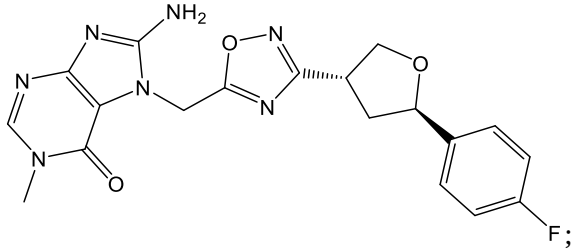


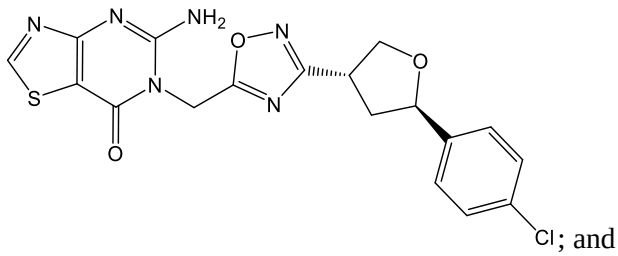


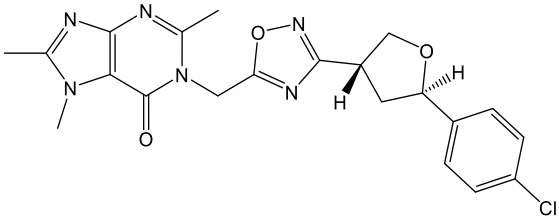






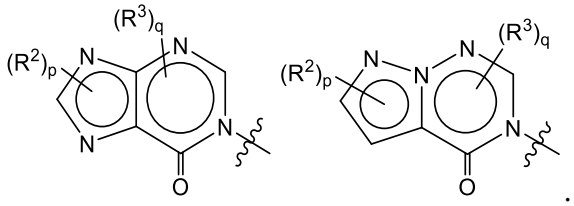



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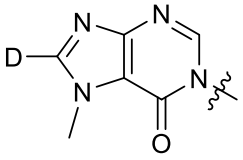

; or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition, comprising a compound as described in claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

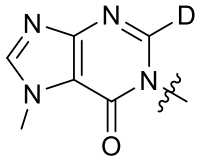
22. The compound of claim 1, or a pharmaceutical salt thereof, wherein A is:


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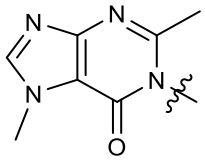
23. The compound of claim 3, or a pharmaceutical salt thereof, wherein A is:


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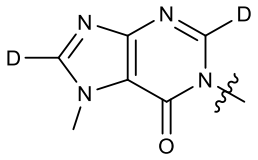
24. The compound of claim 3, or a pharmaceutical salt thereof, wherein A is:


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25. The compound of claim 3, or a pharmaceutical salt thereof, wherein A is:

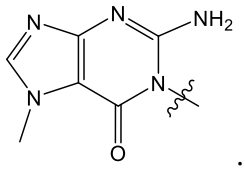

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26. The compound of claim 3, or a pharmaceutical salt thereof, wherein A is:



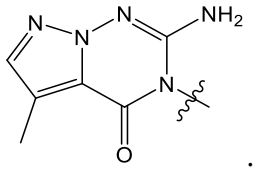
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27. The compound of claim 3, or a pharmaceutical salt thereof, wherein A is:



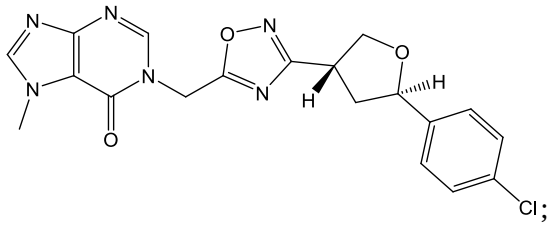
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28. The compound of claim 22, or a pharmaceutical salt thereof, wherein A is:

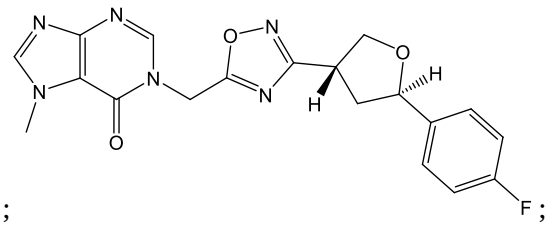


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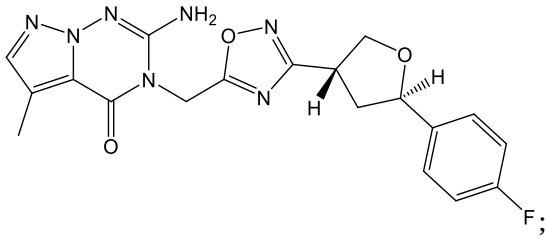
29. The compound of claim 20, wherein the compound is selected from:



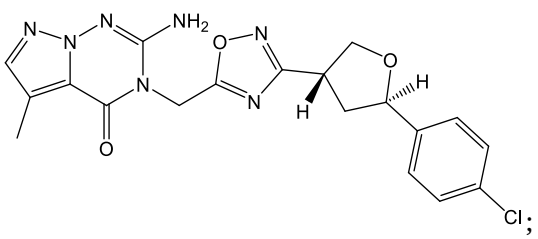
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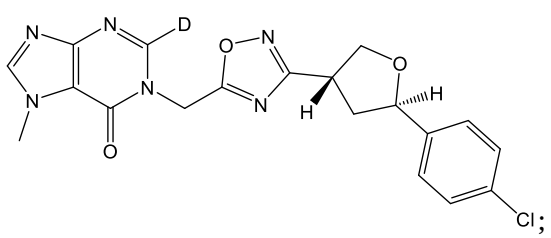
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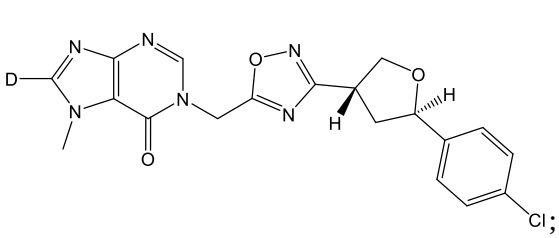
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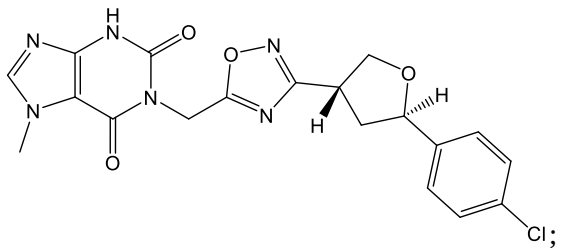
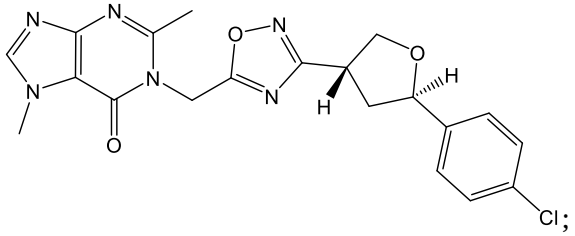
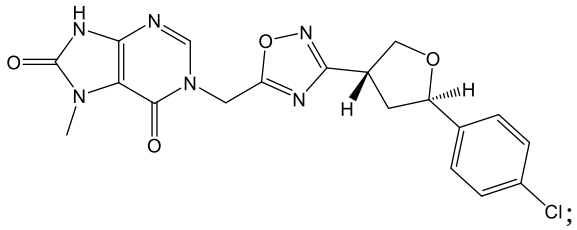
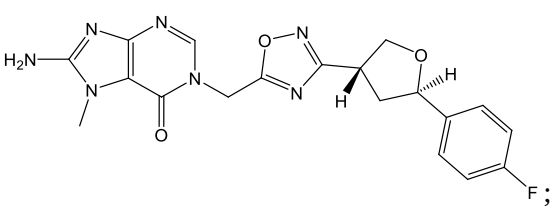
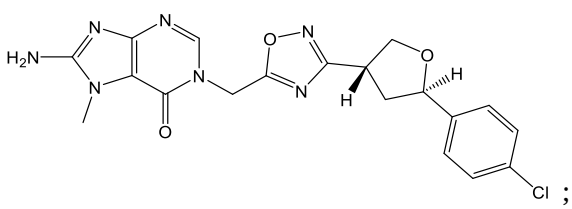
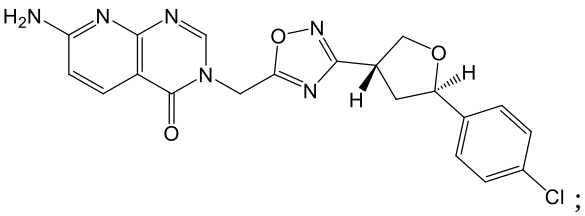
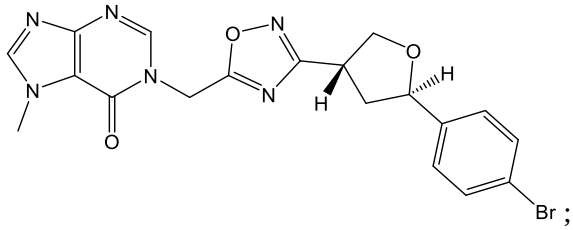
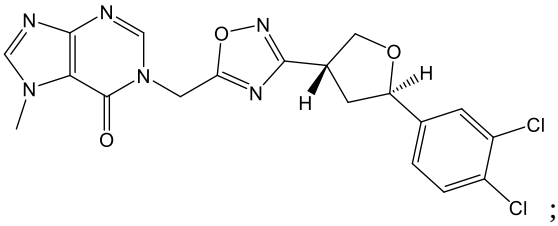
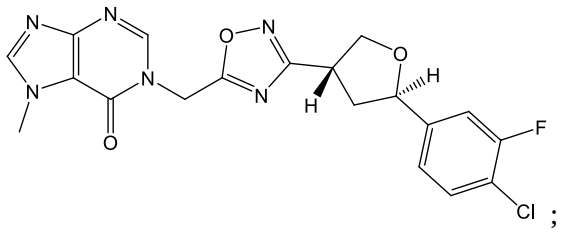
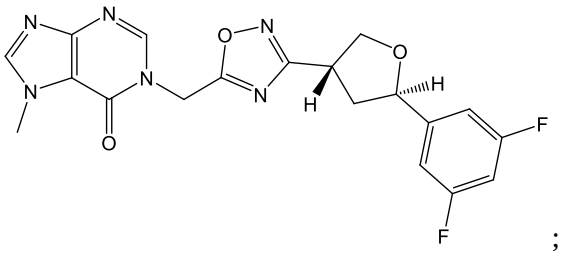
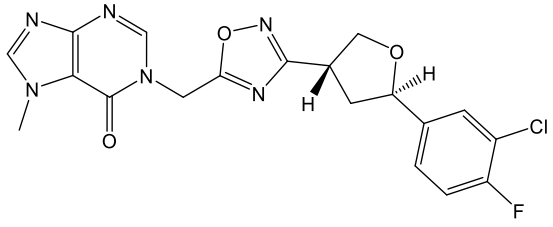
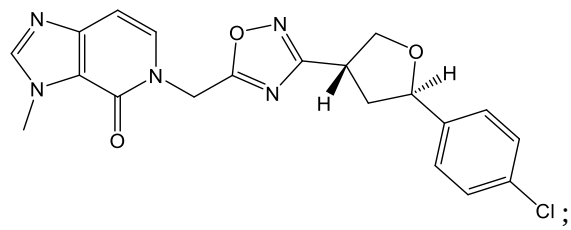
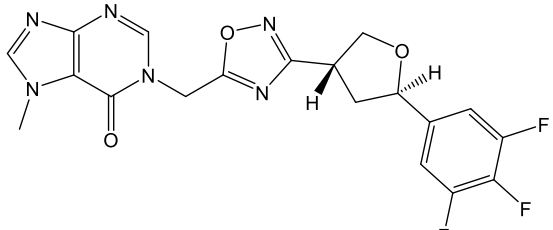
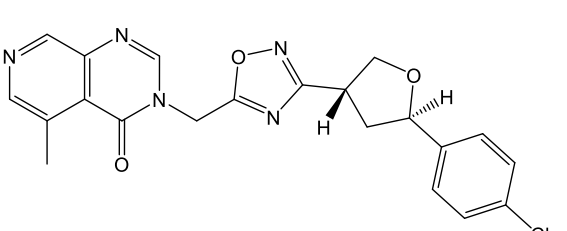
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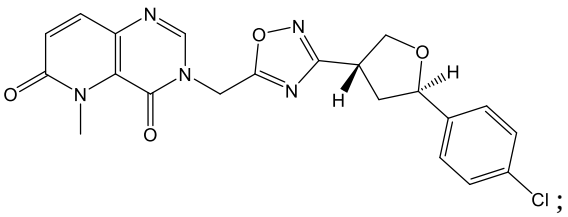


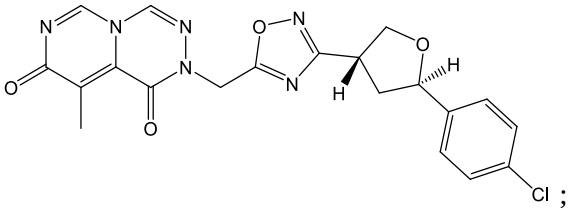
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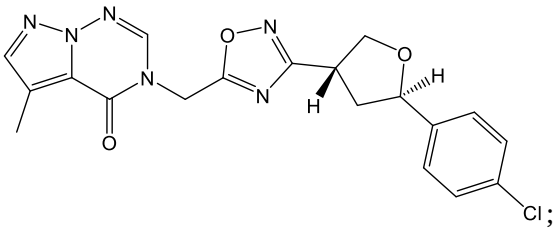

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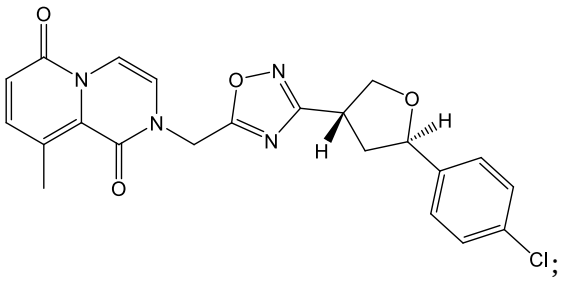
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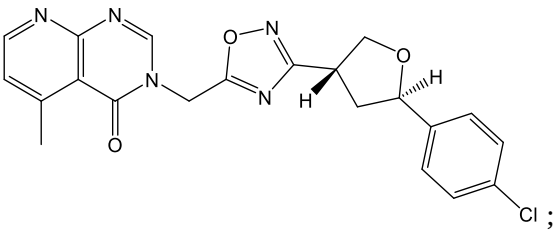
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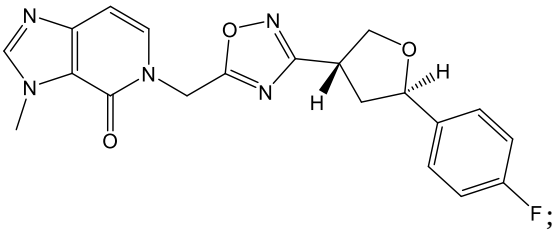


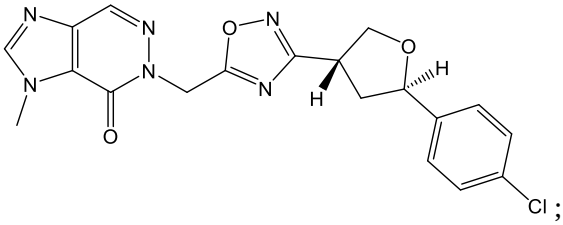


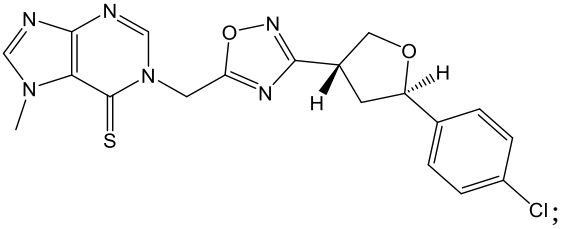


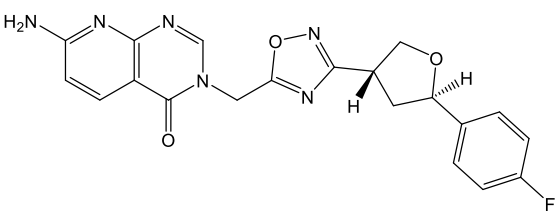


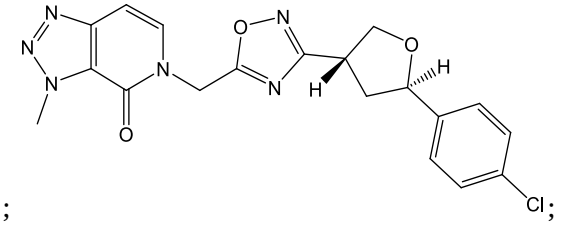


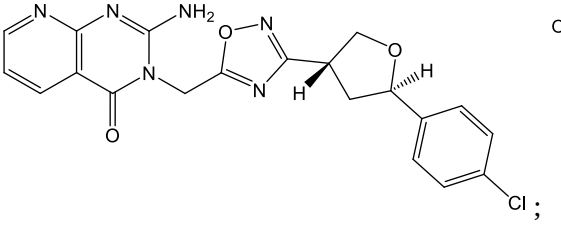


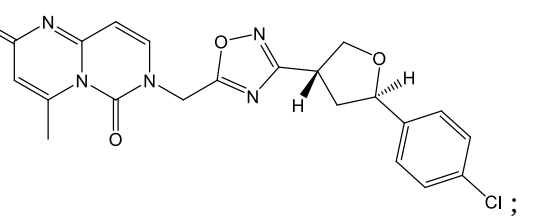


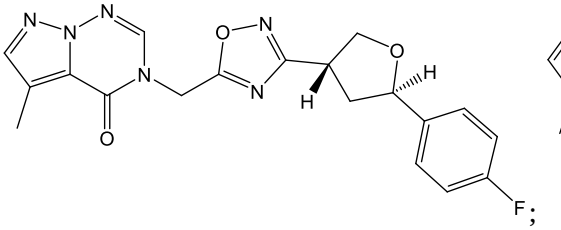


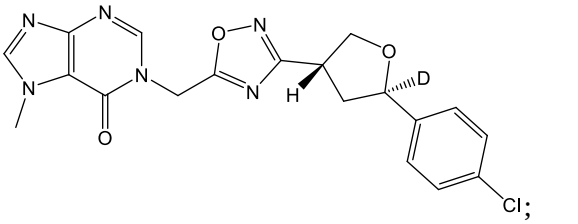




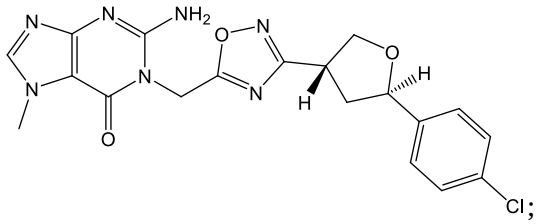


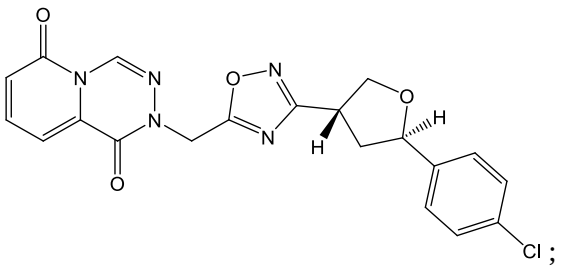


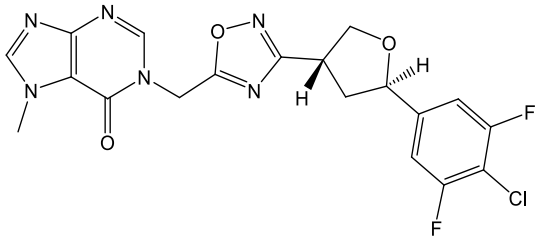


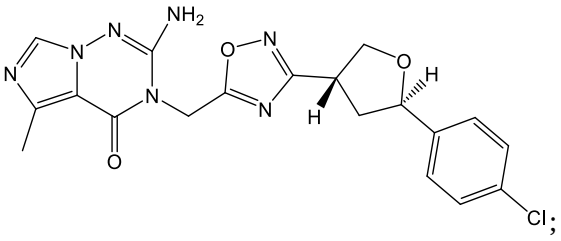


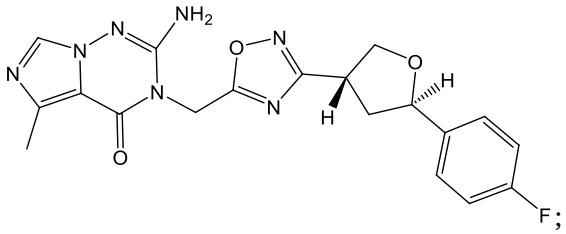


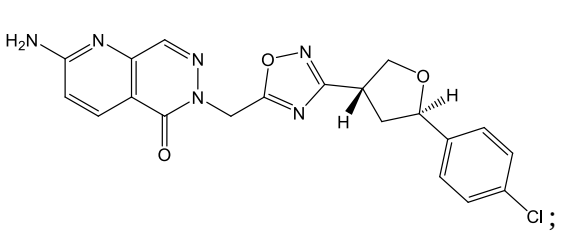

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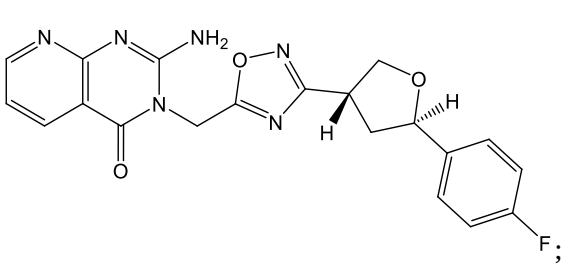

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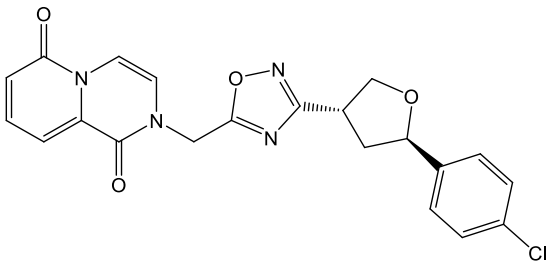

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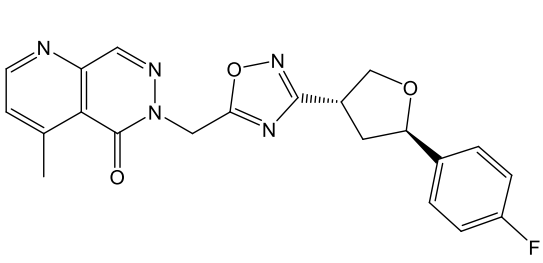

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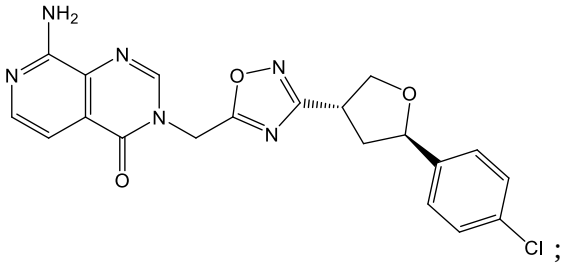

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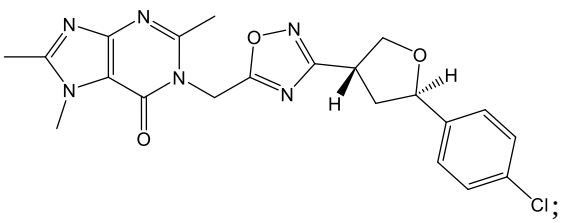

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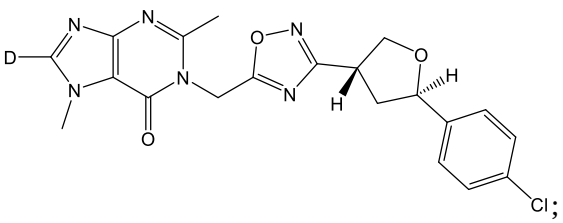

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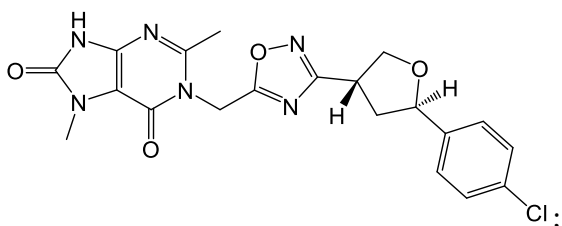

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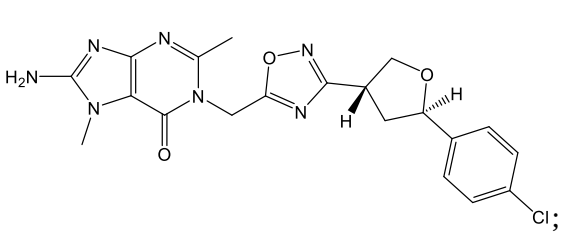

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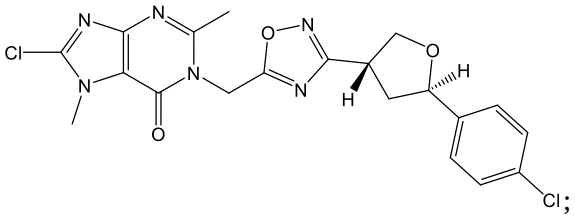
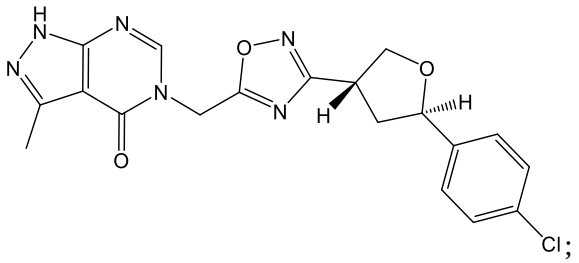
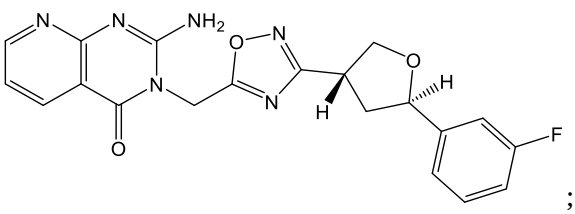
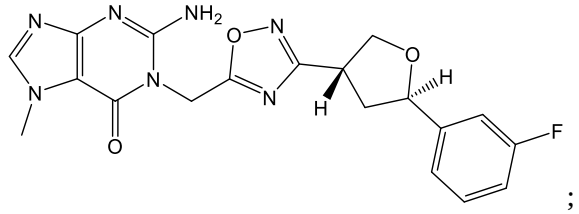
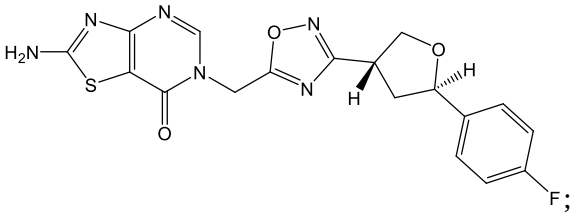
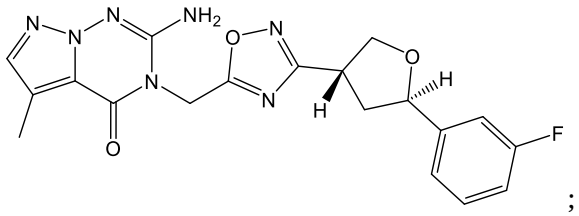
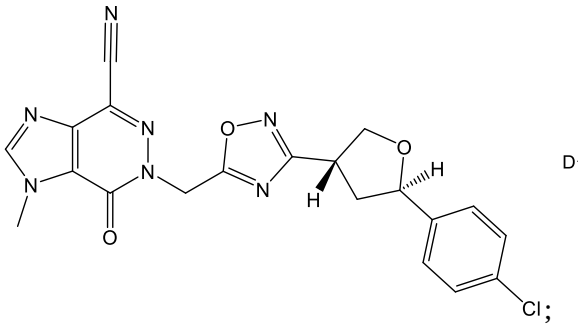
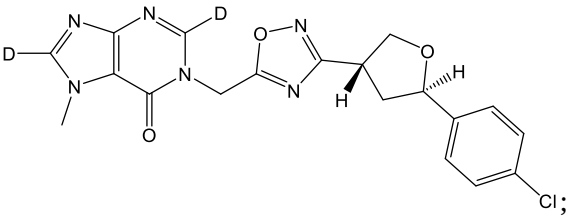
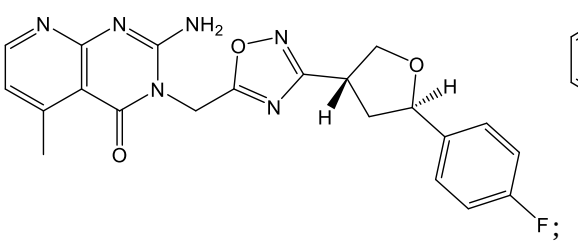
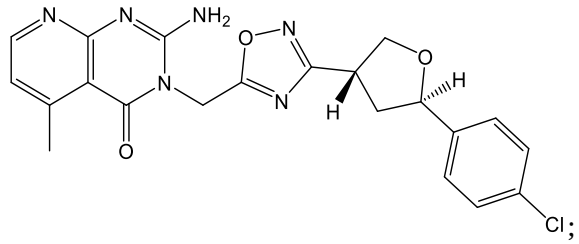

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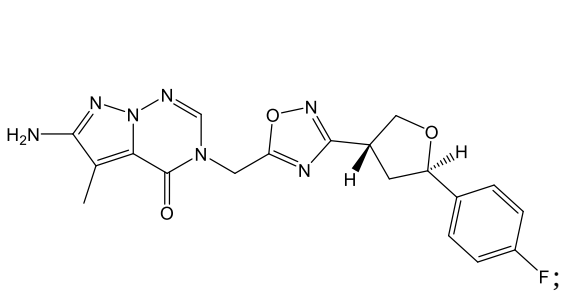
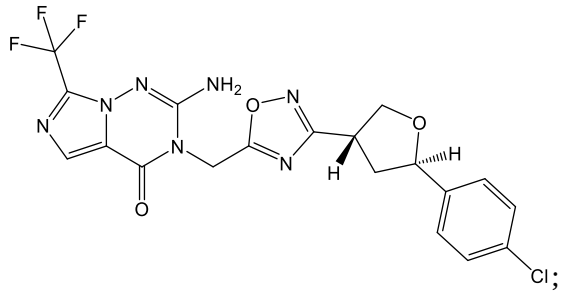
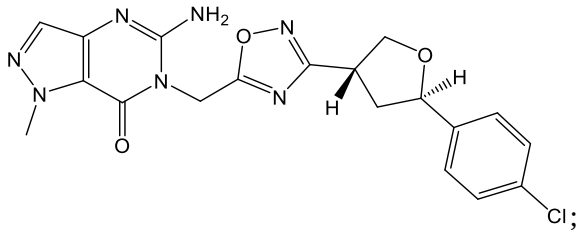
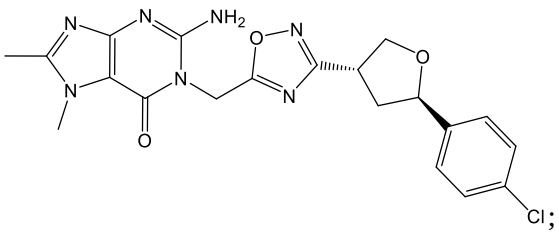
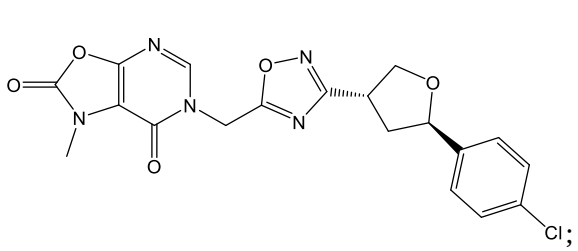
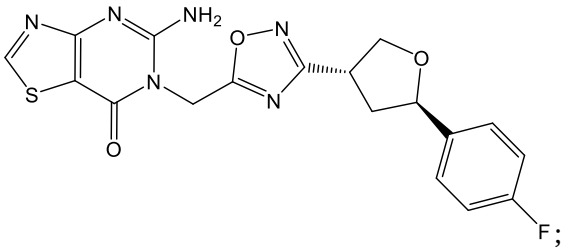
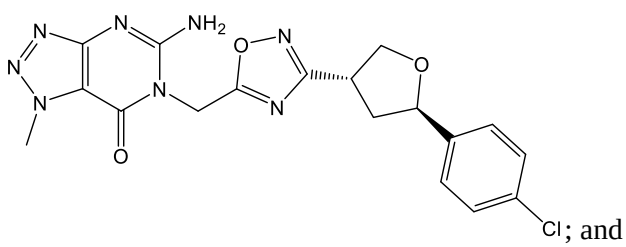
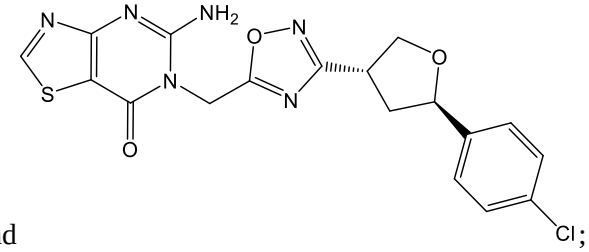

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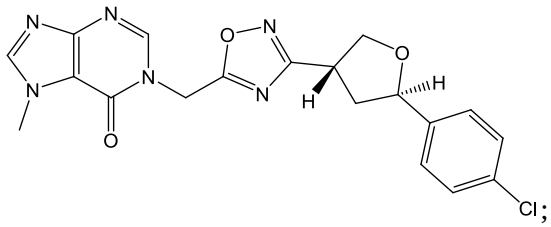
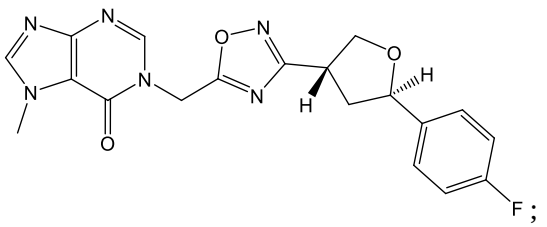
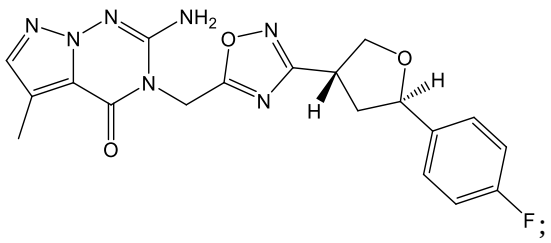
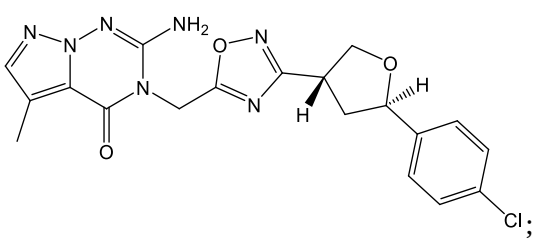

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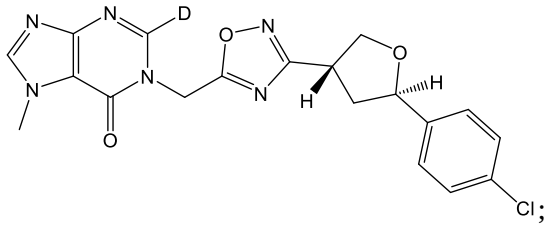
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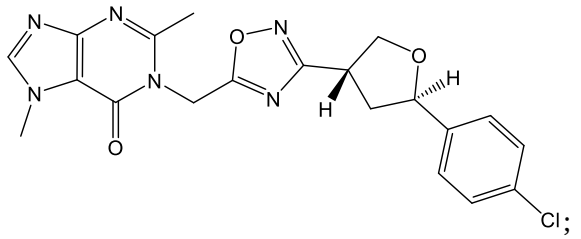








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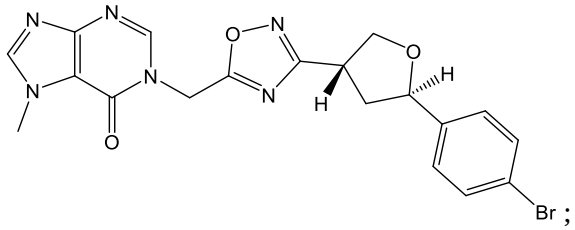
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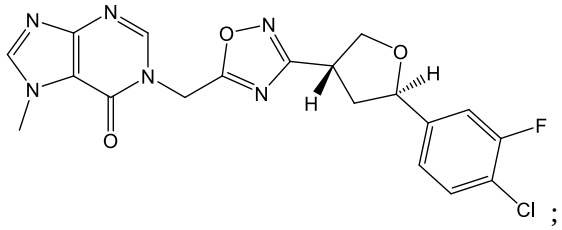
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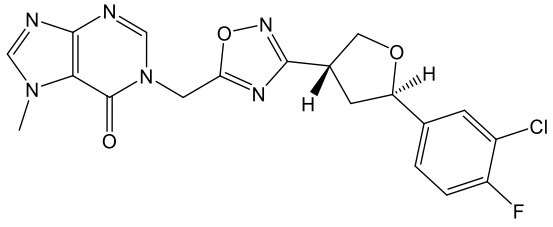





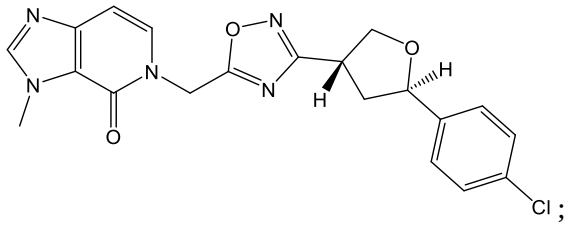


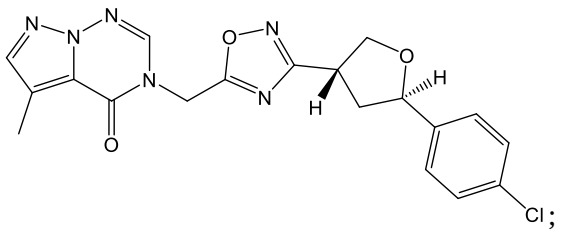


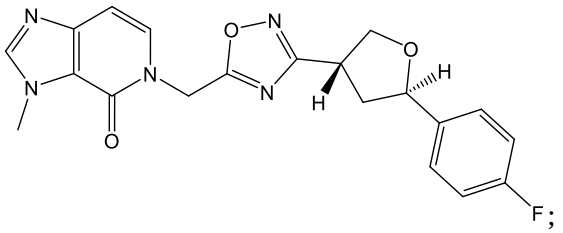


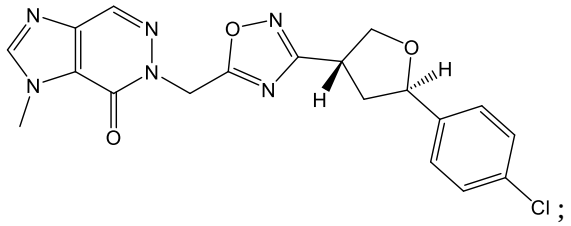


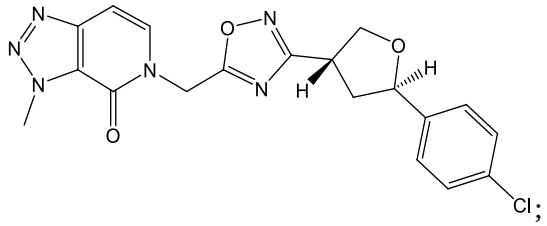


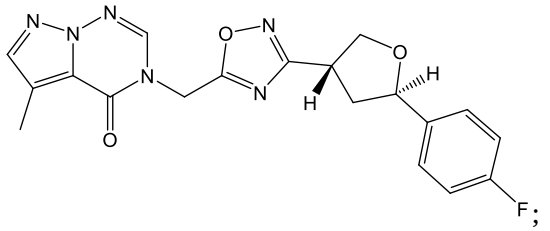


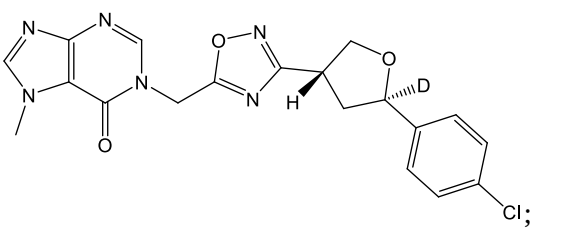


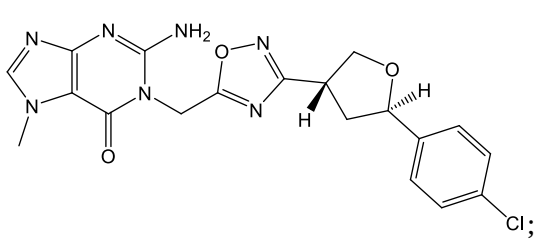


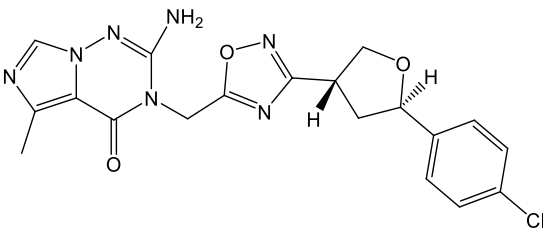




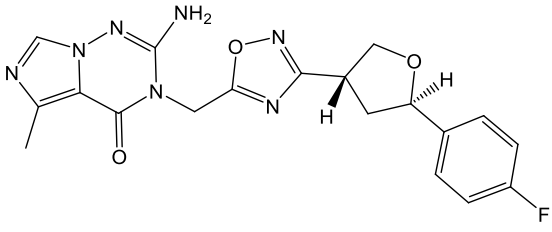


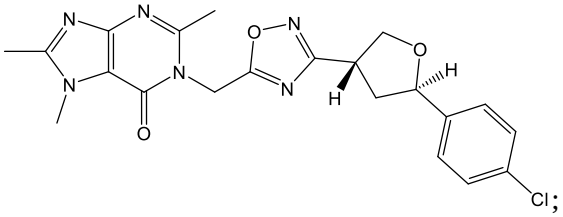


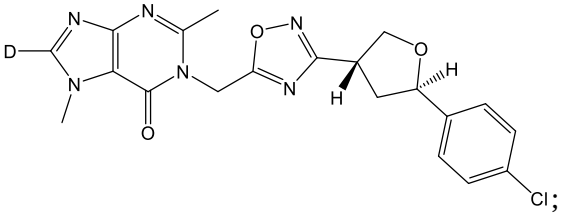


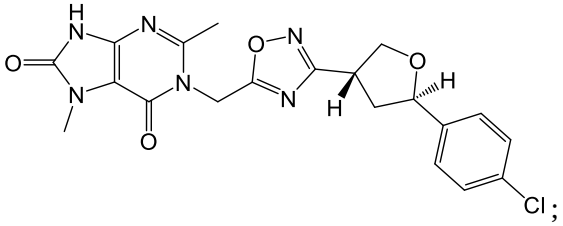


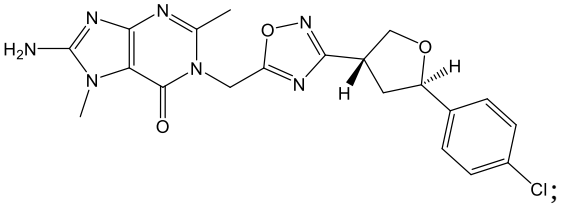


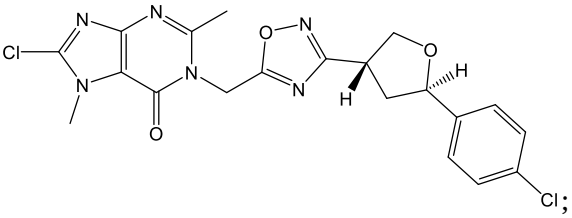


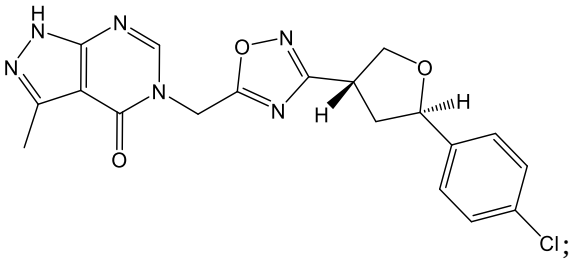


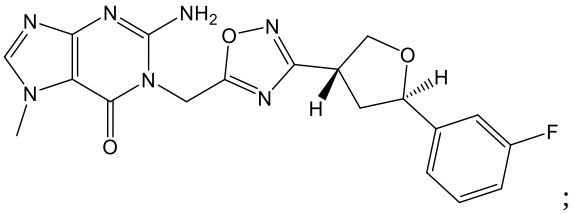


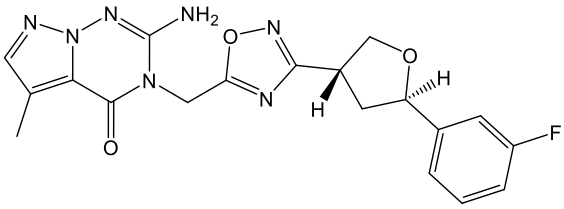


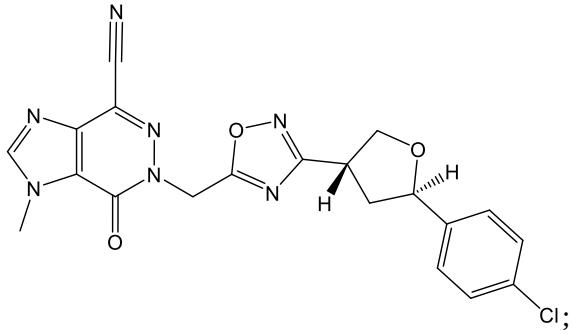


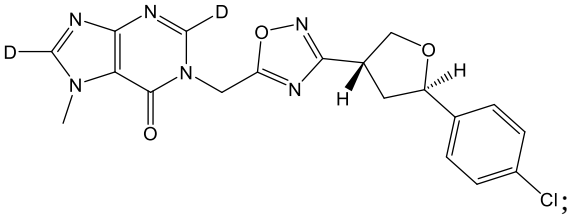


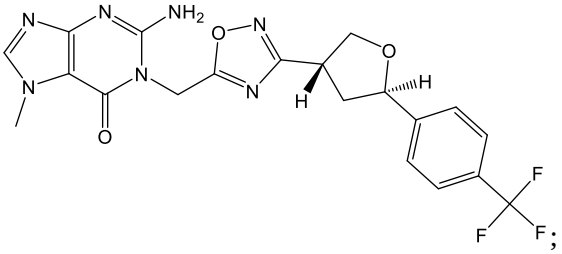


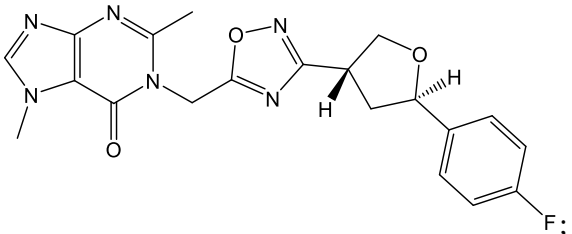


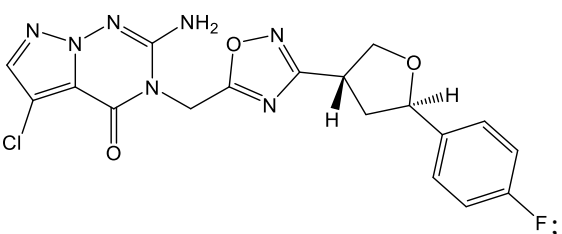


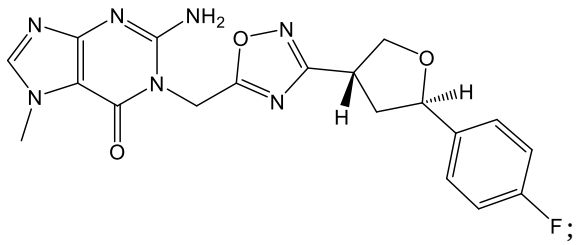
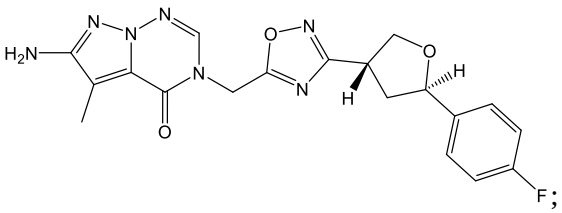
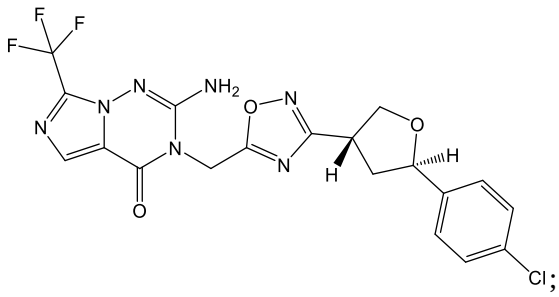
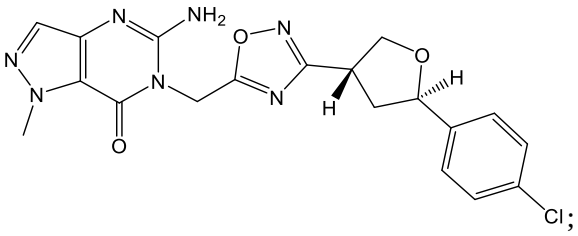
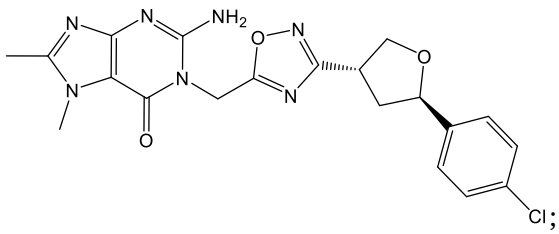
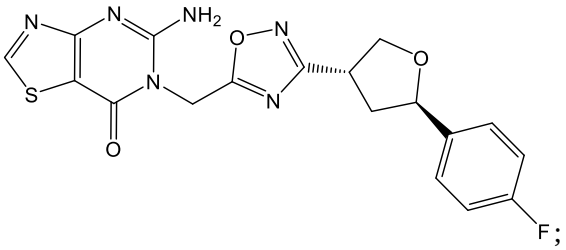
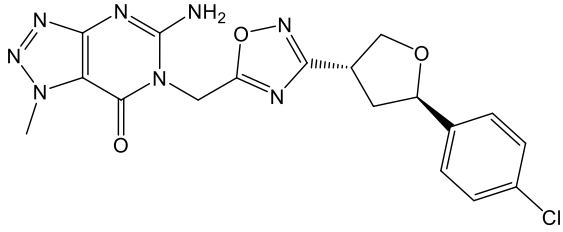
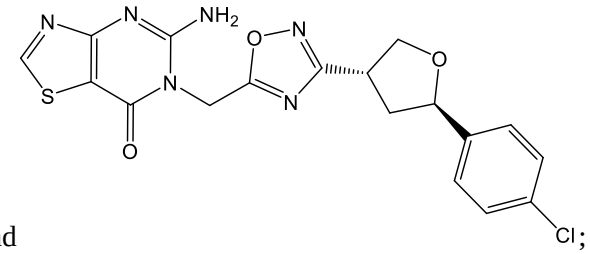






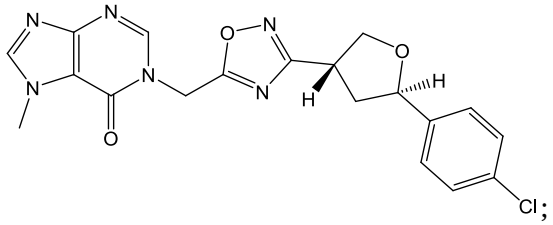
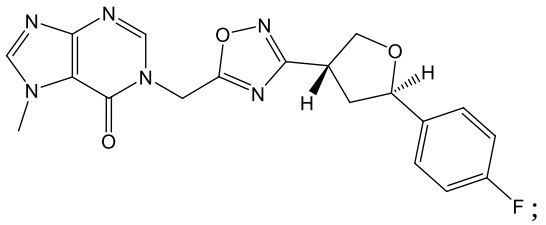
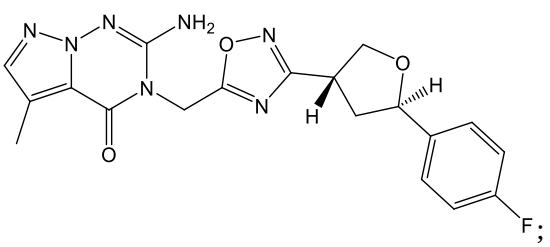
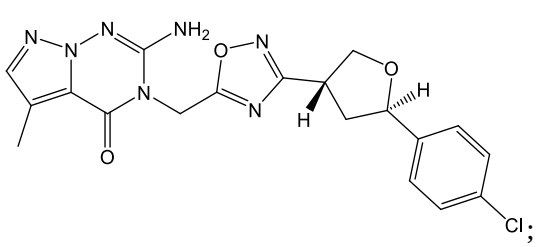


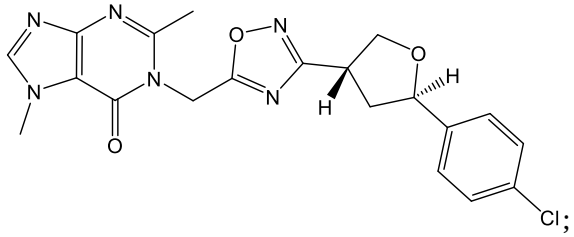


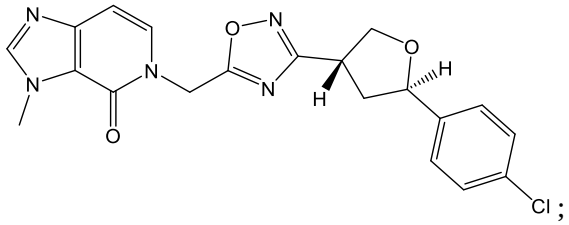








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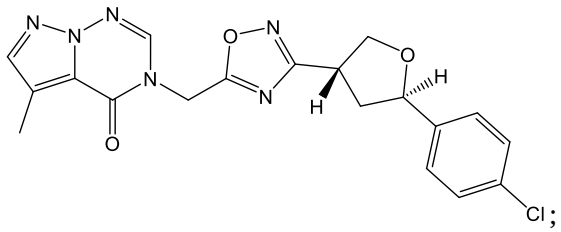
or a pharmaceutically acceptable salt thereof.

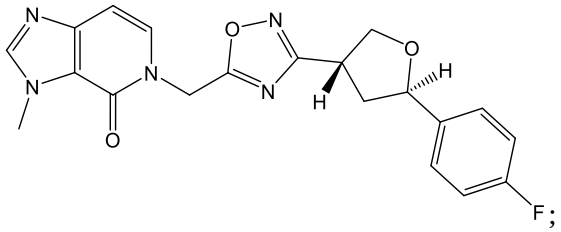
31. The compound of claim 20, wherein the compound is selected from:

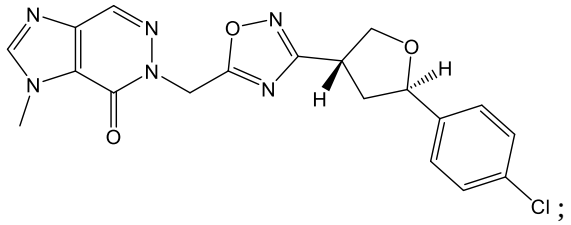





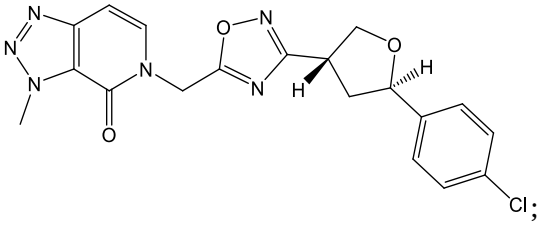


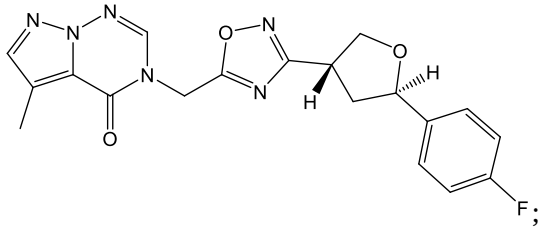


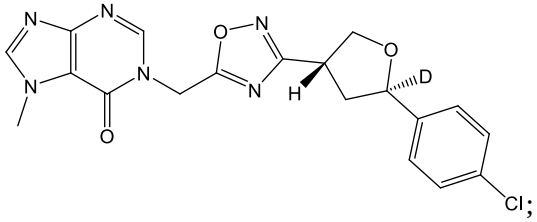


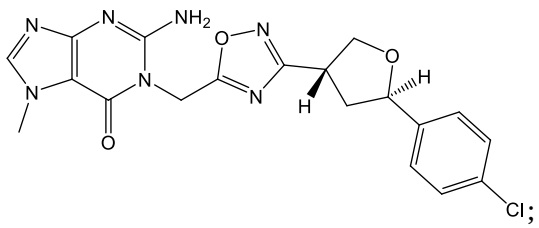


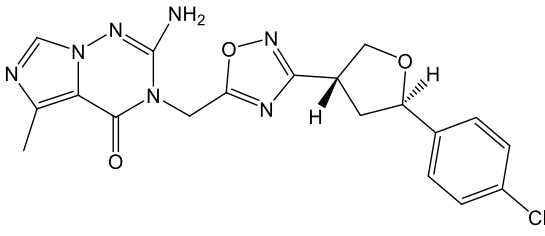


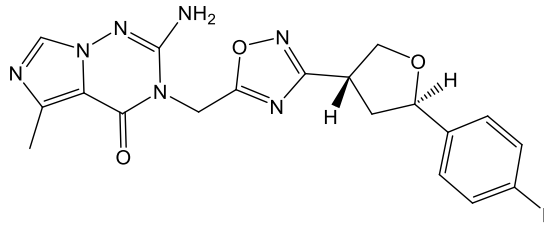


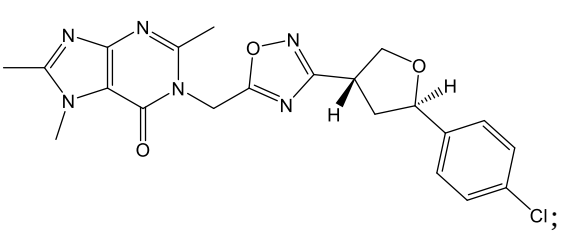


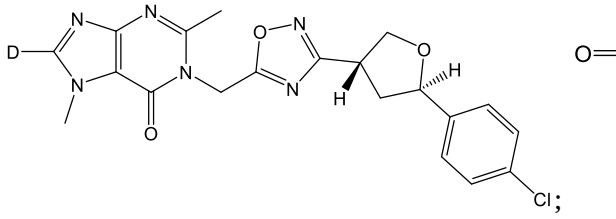


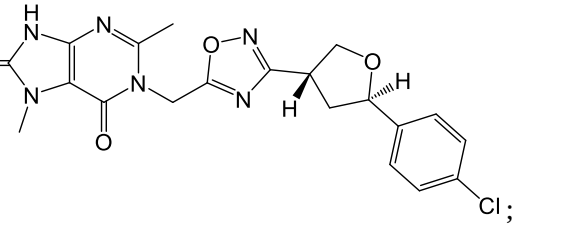




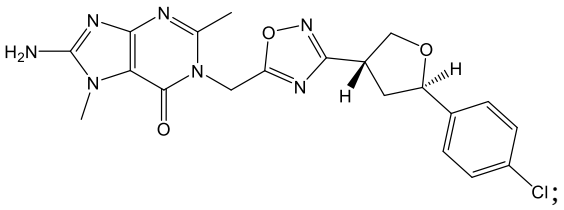
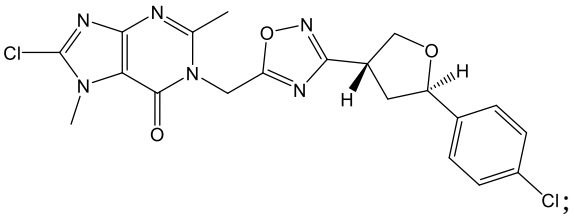


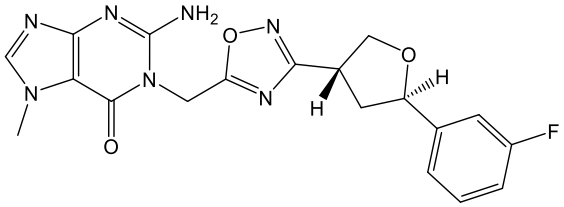
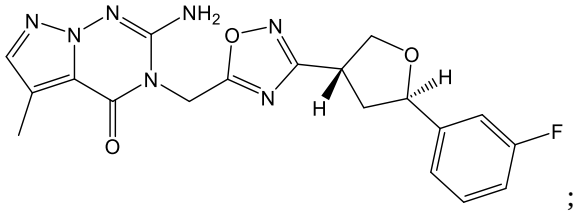


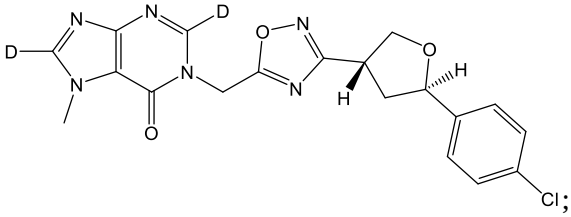
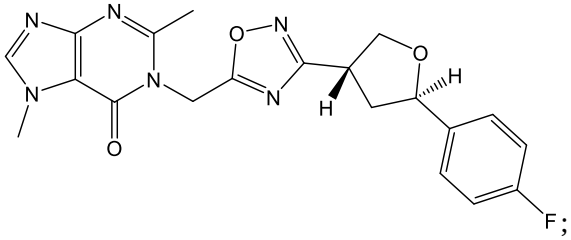


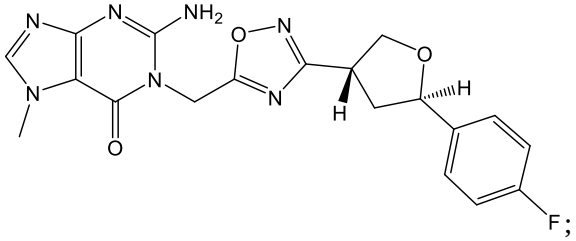
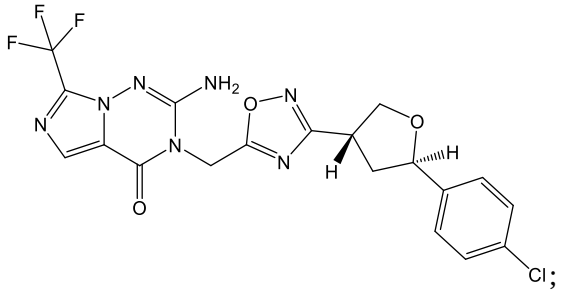


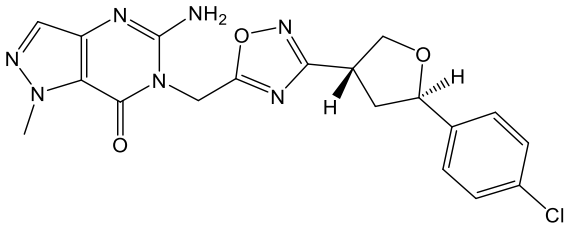
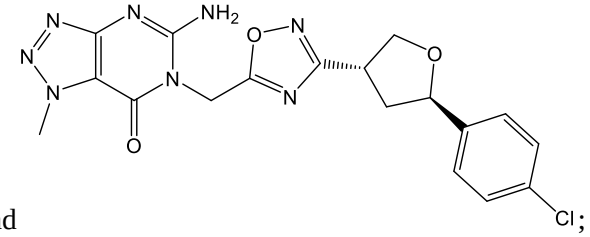


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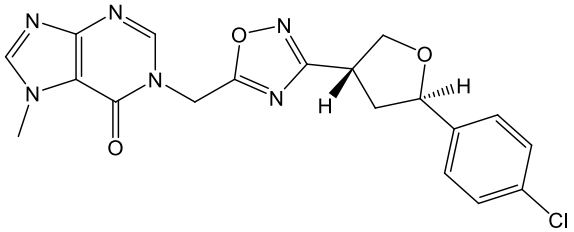
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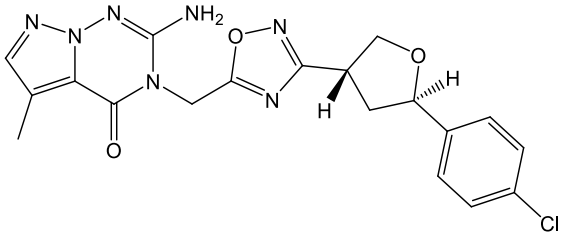
or a pharmaceutically acceptable salt thereof.

32. The compound



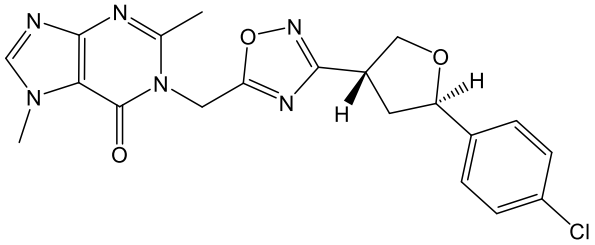
or a pharmaceutically acceptable salt thereof.

33. The compound



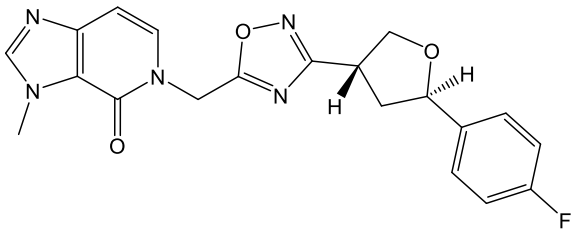
or a pharmaceutically acceptable salt thereof.

34. The compound



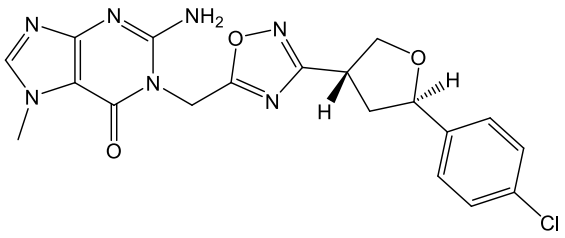
or a pharmaceutically acceptable salt thereof.

35. The compound



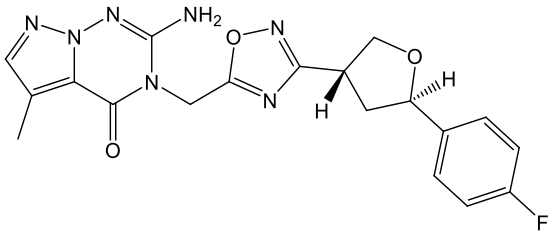
or a pharmaceutically acceptable salt thereof.

36. The compound



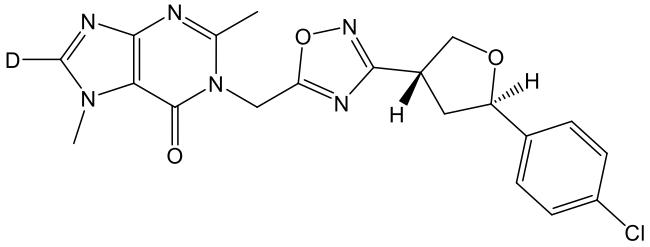
or a pharmaceutically acceptable salt thereof.

37. The compound



or a pharmaceutically acceptable salt thereof.

38. The compound



or a pharmaceutically acceptable salt thereof.

39. A compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof for use in medical therapy.

40. A compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof for use in the treatment or prophylaxis of a respiratory disorder.

41. Use of a compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment or prophylaxis of a respiratory disorder.

42. A compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof for use in modulating TRPA1 activity.

43. A compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof for use in the treatment or prophylaxis of a disease or condition mediated by TRPA1 activity.

44. The compound of claim 43 wherein the disease or condition is pain, itch, an inflammatory disorder, an inner ear disorder, fever or another disorder of thermoregulation, tracheobronchial or diaphragmatic dysfunction, a gastrointestinal or urinary tract disorder, chronic obstructive pulmonary disease, incontinence, or a disorder associated with reduced blood flow to the CNS or CNS hypoxia.

45. The compound of claim 44 wherein the disease or condition is pain, arthritis, itch, cough, asthma, inflammatory bowel disease, or an inner ear disorder.

46. Use of a compound as described in any one of claims 1 to 20 or 22 to 38 or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment or prophylaxis of a disease or condition selected from pain, itch, an inflammatory disorder, an inner ear disorder, fever or another disorder of thermoregulation, tracheobronchial or diaphragmatic dysfunction, a

gastrointestinal or urinary tract disorder, chronic obstructive pulmonary disease, incontinence, or a disorder associated with reduced blood flow to the CNS or CNS hypoxia.

47. The use of claim 46 wherein the disease or condition is pain, arthritis, itch, cough, asthma, inflammatory bowel disease, or an inner ear disorder.