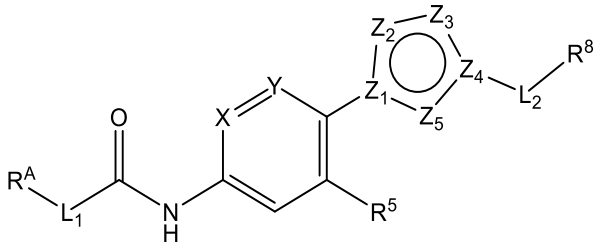
Claims

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof,



(I)

wherein:

-X=Y- is $-CR^x=CR^y-$, $-CR^x=N-$ or $-N=CR^y-$;

R^x is H, D, halogen or C_1-C_4alkyl;

R^y is H, D, halogen, -CN, C_1-C_4alkyl, C_1-C_4fluoroalkyl or C_1-C_4alkoxy;

R^5 is H, halogen, -CN, C_1-C_4alkyl, C_1-C_4fluoroalkyl or C_1-C_4alkoxy;

R^A is:

(i) phenyl which is unsubstituted or is substituted with 1, 2, 3 or 4 R^1 groups;

(ii) a partially saturated 9-, 10-, 11- or 12-membered bicyclic carbocyclyl which is unsubstituted or is substituted with 1 to 4 R^1 groups;

(iii) a 5- or 6- membered monocyclic heteroaryl having 1, 2, 3 or 4 ring members independently selected from N, NR^4, O and S, wherein the monocyclic heteroaryl is unsubstituted or is substituted with 1, 2, 3 or 4 R^1 groups;

or

(iv) a partially saturated 8-, 9-, 10-, 11- or 12-membered fused bicyclic heterocyclyl having 1, 2, 3 or 4 ring members independently selected from N, NR^4, O and S, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with 1, 2, 3 or 4 R^1 groups;

each R^1 is independently selected from the group consisting of halogen, C_1-C_4alkyl, C_2-C_4alkenyl, C_2-C_4alkynyl, C_1-C_4alkoxy, C_1-C_4alkoxycarbonyl, C_3-C_6cycloalkyl, C_1-C_4fluoroalkyl, C_1-C_4fluoroalkoxy, pentafluorosulfanyl, C_1-C_4hydroxyalkyl, C_1-C_4thioalkyl, azido, diC_1-C_4alkylamino, diC_1-C4alkylaminocarbonyl, D, CD_3, cyano, formyl, phenyl and a 5- to 6-membered heterocycloalkyl comprising 1 or 2 ring members independently selected from N, NR^4, O and S;

L_1 is a bond, $-(CR^2R^3)_p-$, $-(CR^2R^3)_p-NR^4-$, $-(CR^2R^3)_p-O-$, $-NR^4(CR^2R^3)_q-$, $-(CR^2R^3)_qNR^4-$, $-O-(CR^2R^3)_p-$ or $-S-(CR^2R^3)_p-$;

R^2 is H, D, halogen or C_1-C_4alkyl;

R^3 is H, D, halogen, C_1-C_4alkyl C_1-C_4alkoxy, OH, amino or *t*-Boc-amino;

or R^2 and R^3, together with the C atom to which they are attached, are linked to form C_3-C_4cycloalkyl which is unsubstituted or is substituted with a single substituent selected from C_1-C_4alkyl and oxo;

each R^4 is independently selected from the group consisting of H and C_1-C_4alkyl;

p is 1, 2 or 3;

q is 0, 1 or 2;

Z_1 is N or C; Z_2 is N or CR^z; Z_3 is N or CR^z; Z_4 is N or C; Z_5 is N or CR^z;

wherein each R^z is independently selected from the group consisting of H, halogen, C_1-C_4alkyl and C_1-C_4fluoroalkyl; and provided that at least two, and not more than four, of Z_1, Z_2, Z_3, Z_4 and Z_5 are N;

L_2 is a bond, $-(CR^6R^7)_n-$ or $-(CR^6R^7)_nO-*$, where the * indicates the point of attachment to R^8;

each R^6 is independently selected from the group consisting of H, C_1-C_4alkyl, C_1-C_4fluoroalkyl and C_1-C_4hydroxyalkyl;

each R^7 is independently selected from the group consisting of H, C_1-C_4alkyl, C_1-C_4fluoroalkyl and C_1-C_4hydroxyalkyl;

or R^6 and R^7, together with the C atom to which they are attached, are linked to form C_3-C_6cycloalkyl, oxetanyl, tetrahydrofuranyl or tetrahydropyranyl;

n is 1, 2 or 3;

R^8 is:

(i) 4-, 5- or 6-membered heterocycloalkyl having 1, 2 or 3 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents each independently selected from -OH, -CN, $-N(R^{10})_2$, halogen, C_1-C_4fluoroalkyl, C_1-C_4alkyl, C_1-C_4alkoxy, oxo and a 5- or 6-membered monocyclic heteroaryl having 1, 2, 3 or 4 ring members independently selected from N, NR^9, O and S, wherein the monocyclic heteroaryl is unsubstituted;

(ii) 4-, 5- or 6-membered heterocycloalkyl wherein one ring member is $S(=O)_2$, S(=O) or S(=O)(=NH), and wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents, each independently selected from -OH, C_1-C_4alkyl and oxo;

(iii) 4-, 5- or 6-membered heterocycloalkyl wherein one ring member is $S(=O)_2$ or S(=O), and 1, 2 or 3 other ring members are independently selected from N, NR^9 and O, and wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents each independently selected from C_1-C_4alkyl and oxo;

(iv) a partially saturated 5- or 6-membered heterocyclyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the partially saturated

heterocyclyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents independently selected from -OH, C_1-C_4alkyl, and oxo;

(v) a partially saturated 5- or 6-membered heterocyclyl wherein one ring member is $S(=O)_2$ and 1, 2 or 3 other ring members are independently selected from N, NR^9, O and S, wherein the partially saturated heterocyclyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents independently selected from -OH, C_1-C_4alkyl, and oxo;

(vi) a 5- or 6- membered monocyclic heteroaryl having 1, 2, 3 or 4 ring members independently selected from N, NR^9, O and S, wherein the monocyclic heteroaryl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents each independently selected from -OH, C_1-C_4alkoxy and C_1-C_4alkyl;

(vii) a 6- or 7-membered fused bicyclic heterocyclyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents, each independently selected from -OH, $-N(R^{10})_2$, C_1-C_4alkyl-NH_2, halogen, C_1-C_4alkyl, and oxo;

(viii) a partially saturated 8-, 9-, 10-, 11- or 12-membered fused bicyclic heterocyclyl having 1, 2, 3 or 4 ring members independently selected from N, NR^9, O and S, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents, each independently selected from -OH, $-N(R^{10})_2$, C_1-C_4alkyl-NH_2, halogen, C_1-C_4alkyl, and oxo;

(ix) a 6-, 7-, 8-, 9- or 10- membered spiro bicyclic heterocycloakyl having 1, 2 or 3 ring members independently selected from N, NR^9, O and S, wherein the spiro bicyclic heterocycloakyl is unsubstituted or is substituted with 1, 2, 3 or 4 substituents, each independently selected from -OH, $-N(R^{10})_2$, C_1-C_4alkyl-NH_2, halogen, C_1-C_4alkyl, and oxo;

(x) a 6- membered heterocycloalkyl having 1 to 2 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl has a C_1-C_3alkyl bridge or a $-CH_2OCH_2-$ bridge;

(xi) phenyl which is unsubstituted or is substituted with 1, 2, 3 or 4 substituents, each independently selected from $-S(=O)_2N(R^{10})_2$, -OH, $-N(R^{10})_2$, C_1-C_4alkyl-NH_2, halogen and C_1-C_4alkyl;

or

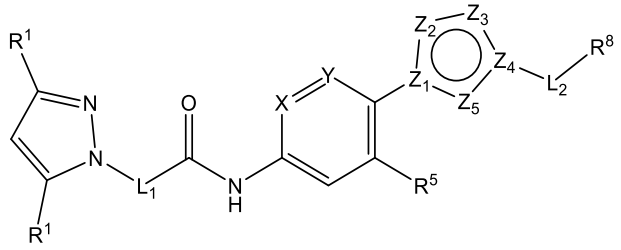
(xii) C_4-C_8cycloalkyl which is unsubstituted or is substituted with 1, 2, 3 or 4 substituents independently selected from -OH, $-N(R^{10})_2$, $-S(=O)_2R^{10}$, C1-C_4alkyl-NH_2, halogen, C_1-C_4alkoxy, C_1-C_4alkyl, and oxo;

R^9 is H, C_1-C_4alkyl, benzyl, C_1-C_4alkyl-OR^{10}, -C(=O)OR^{10} or -C(=O)R^{10},

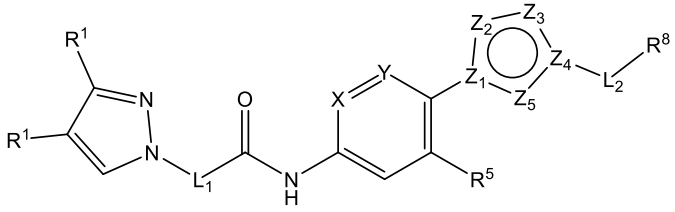
and

R^{10} is H or C_1-C_4alkyl.

2. The compound of Formula (I) of claim 1 having the structure if Formula (I-a) or Formula (I-b), or a pharmaceutically acceptable salt thereof,

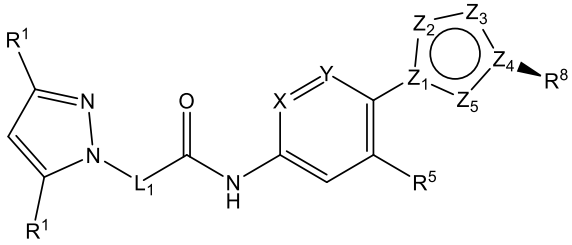


(I-a)

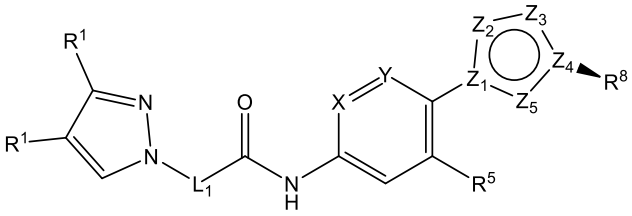


(I-b).

3. The compound of Formula (I) of claim 1 having the structure if Formula (I-c) or Formula (I-d), or a pharmaceutically acceptable salt thereof,



(I-c)



(I-d).

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is -CR^x=CR^y-, -CR^x=N- or -N=CR^y-;

R^x is H, D, or halogen;

R^y is H, D, halogen or -CN;

R^5 is halogen or -CN;

each R^1 is independently selected from the group consisting of halogen, D, CD_3, C_1-C_4alkyl, C_1-C_4fluoroalkyl, C_1-C_4fluorolkoxy, C_3-C_6cycloalkyl and pentafluorosulfanyl;

L_1 is $-(CR^2R^3)_p-$, $-NR^4(CR^2R^3)_q-$ or $-O-(CR^2R^3)_p-$;

R^2 is H, D or halogen;

R^3 is H, D, halogen, OH or C_1-C_4alkyl;

or R^2 and R^3, together with the C atom to which they are attached, are linked to form C_3-C_4cycloalkyl which is unsubstituted

R^4 is H or C_1-C_4alkyl;

p is 1;

q is 0;

Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

or Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is CR^z;

or Z_1 is C, Z_2 is CR^z, Z_3 is N, Z_4 is N and Z_5 is CR^z;

or Z_1 is C, Z_2 is N, Z_3 is N, Z_4 is N and Z_5 is CR^z;

each R^z is H;

L_2 is a bond, $-(CR^6R^7)_n-$ or $-(CR^6R^7)_nO-*$, where the * indicates the point of attachment to R^8;

each R^6 is independently selected from the group consisting of H, C_1-C_4alkyl, C_1-C_4fluoroalkyl and C_1-C_4hydroxyalkyl;

each R^7 is independently selected from the group consisting of H, C_1-C_4alkyl, C_1-C_4fluoroalkyl and C_1-C_4hydroxyalkyl;

or R^6 and R^7, together with the C atom to which they are attached, are linked to form tetrahydropyranyl;

n is 1 or 2;

R^8 is:

(i) 4-, 5- or 6-membered heterocycloalkyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2 or 3 substituents each independently selected from -OH, -CN, $-N(R^{10})_2$, halogen, C_1-C_4fluoroalkyl, C_1-C_4alkyl, C_1-C_4alkoxy, oxo and a 5- or 6-membered monocyclic heteroaryl having 1or 2 ring members independently selected from N and NR^9, wherein the monocyclic heteroaryl is unsubstituted;

(ii) 5- membered heterocycloalkyl wherein one ring member is $S(=O)_2$, S(=O) or S(=O)(=NH), and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from -OH and C_1-C_4alkyl;

(iii) 6-membered heterocycloalkyl wherein one ring member is $S(=O)_2$ or S(=O), and one other ring member is selected from N, NR^9 and O, and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from C_1-C_4alkyl;

(iv) a partially saturated 6-membered heterocyclyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the partially saturated heterocyclyl is unsubstituted or is substituted with an oxo;

(v) a partially saturated 6-membered heterocyclyl wherein one ring member is $S(=O)_2$ and one other ring member is selected from N, NR^4, and O, wherein the partially saturated heterocyclyl is unsubstituted or is substituted with an oxo;

(vi) a 5- or 6- membered monocyclic heteroaryl having 1, 2, 3 or 4 ring members independently selected from N, NR^9 and O, wherein the monocyclic heteroaryl is unsubstituted or is substituted with a substituent selected from -OH, C_1-C_4alkoxy and C_1-C_4alkyl;

(vii) a 6- membered fused bicyclic heterocyclyl having 1 ring member selected from N and NR^9, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with an oxo;

(viii) a partially saturated 10- membered fused bicyclic heterocyclyl having 1, 2, or 3 ring members independently selected from N, NR^9, and O, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with an oxo;

(ix) a 7- membered spiro bicyclic heterocycloakyl having 1 ring member selected from N, NR^9, and O, wherein the spiro bicyclic heterocycloakyl is unsubstituted;

(x) a 6- membered heterocycloalkyl having 1 to 2 ring members independently selected from N, NR^9 and O, wherein the heterocycloalkyl has a C_1-C_3alkyl bridge or a -CH_2OCH_2- bridge;

(xi) phenyl which is substituted with $-S(=O)_2N(R^{10})_2$;

or

(xii) C_4-C_8cycloalkyl which is substituted with 1, 2 or 3 substituents independently selected from -OH, $-N(R^{10})_2$, $-S(=O)_2R^{10}$, C_1-C_4alkyl-NH_2, halogen and C_1-C_4alkoxy;

R^9 is H, C_1-C_4alkyl, benzyl, C_1-C_4alkyl-OR^{10}, $-C(=O)OR^{10}$ or $-C(=O)R^{10}$,

and

R^{10} is H or C_1-C_4alkyl.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is $-CR^x=CR^y-$ or $-CR^x=N-$;

R^x is H;

R^y is H, halogen or -CN;

R^5 is halogen or -CN;

each R^1 is independently selected from the group consisting of halogen, C_1-C_4alkyl, C_1-C_4fluoroalkyl and pentafluorosulfanyl;

L_1 is $-(CR^2R^3)_p-$, $-NR^4(CR^2R^3)_q-$ or $-O-(CR^2R^3)_p-$;

R^2 is H;

R^3 is H, OH or C_1-C_4alkyl;

R^4 is H or C_1-C_4alkyl;

p is 1;

q is 0;

Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

or Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is CR^z;

or Z_1 is C, Z_2 is CR^z, Z_3 is N, Z_4 is N and Z_5 is CR^z;

or Z_1 is C, Z_2 is N, Z_3 is N, Z_4 is N and Z_5 is CR^z;

each R^z is H;

L_2 is a bond, $-(CR^6R^7)_n-$ or $-(CR^6R^7)_nO-*$, where the * indicates the point of attachment to R^8;

each R^6 is independently selected from the group consisting of H, C_1-C_4alkyl, and C_1-C_4hydroxyalkyl;

each R^7 is independently selected from the group consisting of H, C_1-C_4alkyl, and C_1-C_4hydroxyalkyl;

n is 1 or 2;

R^8 is:

(i) 4-, 5- or 6-membered heterocycloalkyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2 or 3 substituents each independently selected from -OH, -CN, $-N(R^{10})_2$, halogen, C_1-C_4fluoroalkyl, C_1-C_4alkyl, C_1-C_4alkoxy, oxo and a 5- or 6-membered monocyclic heteroaryl having 1or 2 ring members independently selected from N and NR^9, wherein the monocyclic heteroaryl is unsubstituted;

(ii) 5- membered heterocycloalkyl wherein one ring member is $S(=O)_2$, S(=O) or S(=O)(=NH), and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from -OH and C_1-C_4alkyl;

(iii) 6-membered heterocycloalkyl wherein one ring member is $S(=O)_2$ or S(=O), and one other ring member is selected from N, NR^9 and O, and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from C_1-C_4alkyl;

(iv) a partially saturated 6-membered heterocyclyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the partially saturated heterocyclyl is unsubstituted or is substituted with an oxo;

(v) a partially saturated 6-membered heterocyclyl wherein one ring member is $S(=O)_2$ and one other ring member is selected from N, NR^4, and O, wherein the partially saturated heterocyclyl is unsubstituted or is substituted with an oxo;

(vi) a 5- or 6- membered monocyclic heteroaryl having 1, 2, 3 or 4 ring members independently selected from N, NR^9 and O, wherein the monocyclic heteroaryl is unsubstituted or is substituted with a substituent selected from -OH, C_1-C_4alkoxy and C_1-C_4alkyl;

(vii) a 6- membered fused bicyclic heterocyclyl having 1 ring member selected from N and NR^9, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with an oxo;

(viii) a partially saturated 10- membered fused bicyclic heterocyclyl having 1, 2, or 3 ring members independently selected from N, NR^9, and O, wherein the fused bicyclic heterocyclyl is unsubstituted or is substituted with an oxo;

(ix) a 7- membered spiro bicyclic heterocycloakyl having 1 ring member selected from N, NR^9, and O, wherein the spiro bicyclic heterocycloakyl is unsubstituted;

(x) a 6- membered heterocycloalkyl having 1 to 2 ring members independently selected from N, NR^9 and O, wherein the heterocycloalkyl has a C_1-C_3alkyl bridge or a $-CH_2OCH_2-$ bridge;

(xi) phenyl which is substituted with $-S(=O)_2N(R^{10})_2$;

or

(xii) C_4-C_8cycloalkyl which is substituted with 1, 2 or 3 substituents independently selected from -OH, $-N(R^{10})_2$, $-S(=O)_2R^{10}$, C_1-C_4alkyl-NH_2, halogen and C_1-C_4alkoxy;

R^9 is H, C_1-C_4alkyl, benzyl, C_1-C_4alkyl-OR^{10}, $-C(=O)OR^{10}$ or $-C(=O)R^{10}$,

and

R^{10} is H or C_1-C_4alkyl.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is $-CR^x=N-$;

R^x is H;

R^5 is halogen;

each R^1 is independently selected from the group consisting of halogen, C_1-C_4alkyl and C_1-C_4fluoroalkyl

L_1 is $-(CR^2R^3)_p-$;

R^2 is H;

R^3 is H, or C_1-C_4alkyl;

p is 1;

Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

or Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is CR^z;

or Z_1 is C, Z_2 is CR^z, Z_3 is N, Z_4 is N and Z_5 is CR^z;

or Z_1 is C, Z_2 is N, Z_3 is N, Z_4 is N and Z_5 is CR^z;

each R^z is H;

L_2 is a bond or $-(CR^6R^7)_n-$;

each R^6 is independently selected from the group consisting of H and C_1-C_4alkyl;

each R^7 is independently selected from the group consisting of H and C_1-C_4alkyl;

n is 1 or 2;

R^8 is:

(i) 4-, 5- or 6-membered heterocycloalkyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2 or 3 substituents each independently selected from -OH, halogen, C_1-C_4fluoroalkyl, C_1-C_4alkyl, and oxo;

(ii) 5- membered heterocycloalkyl wherein one ring member is $S(=O)_2$, or S(=O)(=NH), and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from C_1-C_4alkyl;

(iii) 6-membered heterocycloalkyl wherein one ring member is $S(=O)_2$ or S(=O), and one other ring member is selected from N, NR^9 and O, and wherein the heterocycloalkyl is unsubstituted or is substituted with a substituent selected from C_1-C_4alkyl;

(iv) a partially saturated 6-membered heterocyclyl having 1 or 2 ring members independently selected from O and S, wherein the partially saturated heterocyclyl is unsubstituted;

(v) a partially saturated 6-membered heterocyclyl wherein one ring member is $S(=O)_2$ and one other ring member is O, wherein the partially saturated heterocyclyl is unsubstituted;

(vi) a 5- membered monocyclic heteroaryl having 3 ring members independently selected from N, and O, wherein the monocyclic heteroaryl is unsubstituted;

(vii) a 6- membered fused bicyclic heterocyclyl having 1 ring member selected from NR^9, wherein the fused bicyclic heterocyclyl is unsubstituted;

(viii) a 7- membered spiro bicyclic heterocycloakyl having 1 ring member selected from N, NR^9, and O, wherein the spiro bicyclic heterocycloakyl is unsubstituted;

(ix) a 6- membered heterocycloalkyl having 1 ring members selected from NR^9, wherein the heterocycloalkyl has a C_1-C_3alkyl bridge;

or

(x) C_4-C_8cycloalkyl which is substituted with 1, 2 or 3 substituents independently selected from -OH, -N(R^{10})$_2$, C_1-C_4alkyl-NH_2 and halogen;

R^9 is H, C_1-C_4alkyl, or -C(=O)R^{10},

and

R^{10} is H or C_1-C_4alkyl.

7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is -CRx=N-;

R^x is H;

R^5 is F;

each R^1 is independently selected from the group consisting of F, Cl, methyl and -CF_3;

L_1 is -(CR^2R^3)$_p$-,

R^2 is H;

R^3 is H or methyl;

p is 1;

Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

or Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is CR^z;

each R^z is H;

L_2 is a bond or -(CR^6R^7)$_n$-;

each R^6 is independently selected from the group consisting of H and methyl;

each R^7 is independently selected from the group consisting of H and methyl;

n is 1 or 2;

R^8 is:

(i) 4-, 5- or 6-membered heterocycloalkyl having 1 or 2 ring members independently selected from N, NR^9, O and S, wherein the heterocycloalkyl is unsubstituted or is substituted with 1, 2 or 3 substituents each independently selected from -OH, F, CF_3, methyl and oxo;

(ii) 5- membered heterocycloalkyl wherein one ring member is S(=O)$_2$ or S(=O)(=NH), and wherein the heterocycloalkyl is unsubstituted or is substituted with a methyl;

(iii) 6-membered heterocycloalkyl wherein one ring member is S(=O)$_2$ or S(=O), and one other ring member is selected from N, NR^9 and O, and wherein the heterocycloalkyl is unsubstituted or is substituted with a methyl,

(iv) a partially saturated 6-membered heterocyclyl having 1 or 2 ring members independently selected from O and S, wherein the partially saturated heterocyclyl is unsubstituted;

(v) a partially saturated 6-membered heterocyclyl wherein one ring member is $S(=O)_2$ and one other ring member is and O, wherein the partially saturated heterocyclyl is unsubstituted;

(vi) a 5- membered monocyclic heteroaryl having 3 ring members independently selected from N and O, wherein the monocyclic heteroaryl is unsubstituted;

(vii) a 6- membered fused bicyclic heterocyclyl having 1 ring member selected from NR^9, wherein the fused bicyclic heterocyclyl is unsubstituted;

(viii) a 7- membered spiro bicyclic heterocycloakyl having 1 ring member selected from NR^9, and O, wherein the spiro bicyclic heterocycloakyl is unsubstituted;

(ix) a 6- membered heterocycloalkyl having 1 ring members selected from NR^9, wherein the heterocycloalkyl has a C_1-C_3alkyl bridge;

or

(x) cyclobutyl, cyclopentyl,or cyclohexyl which is substituted with 1, 2 or 3 substituents independently selected from -OH, $-NH_2$, $-CH_2NH_2$, and F;

and

R^9 is H, methyl or $-C(=O)CH_3$.

8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is $-CR^x=N-$;

R^x is H;

R^5 is halogen;

each R^1 is independently selected from the group consisting of halogen, C_1-C_4alkyl and C_1-C_4fluoroalkyl;

L_1 is $-(CR^2R^3)_p-$;

R^2 is H;

R^3 is H;

p is 1;

Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

each R^z is H;

L_2 is a bond;

R^8 is pyrrolidinyl which is substituted with 1 or 2 substituents, each independently selected from halogen and C_1-C_4fluoroalkyl.

9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein:

-X=Y- is -CR^x=N-;

R^x is H;

R^5 is F;

each R^1 is independently selected from the group consisting of F, Cl, methyl, and CF_3;

L_1 is -$(CR^2R^3)_p$-;

R^2 is H;

R^3 is H;

p is 1;

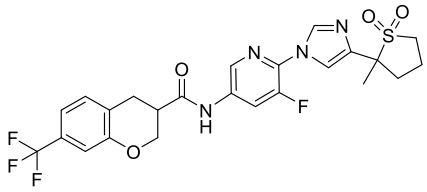
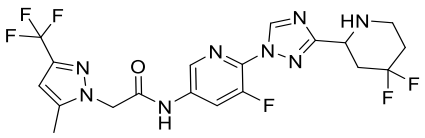
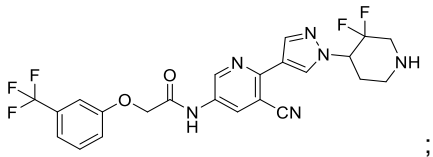
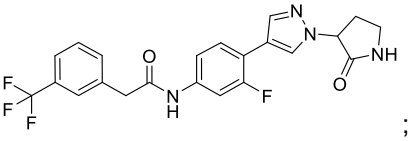
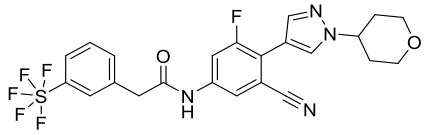
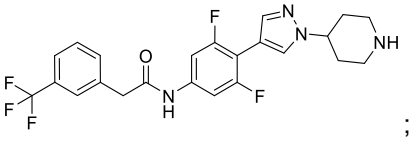
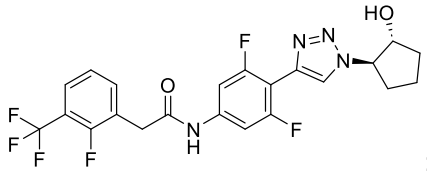
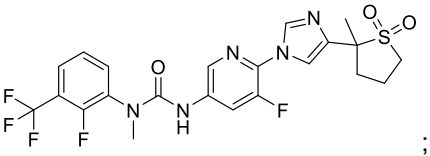
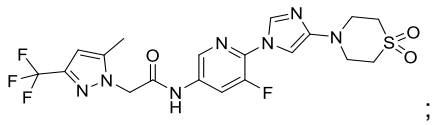
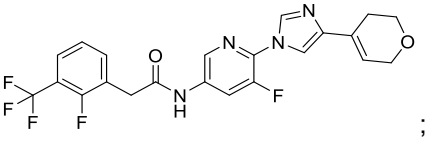
Z_1 is N, Z_2 is CR^z, Z_3 is N, Z_4 is C and Z_5 is N;

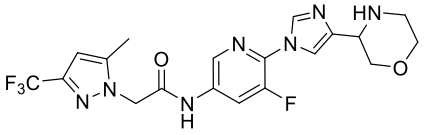
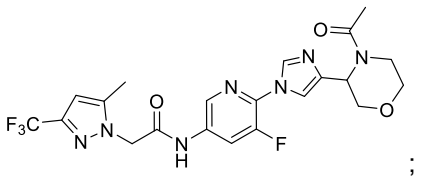
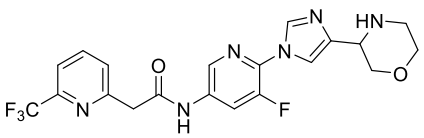
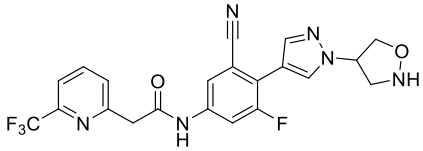
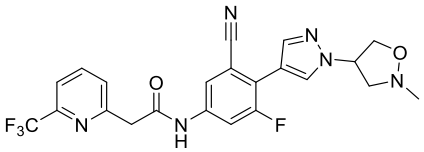
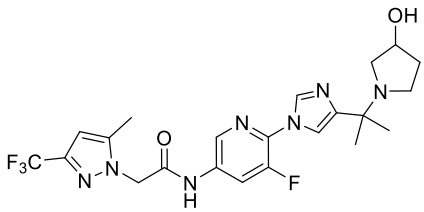
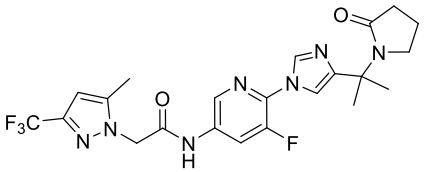
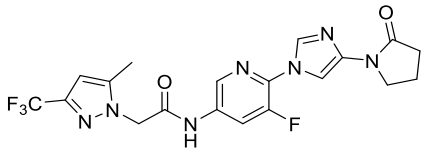
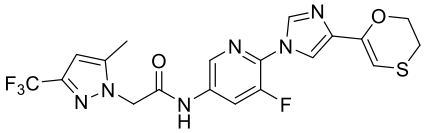
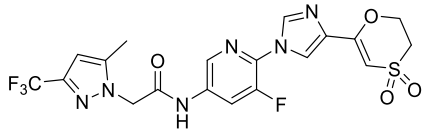
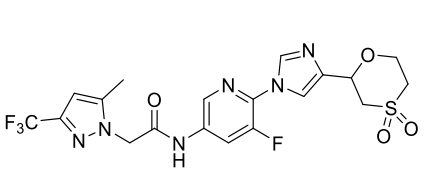
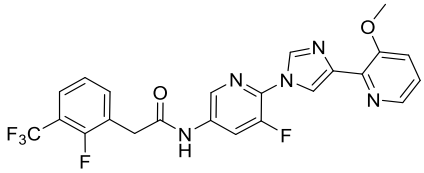
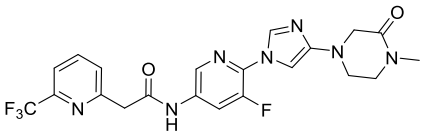
each R^z is H;

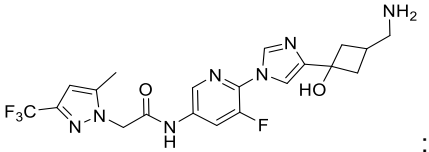
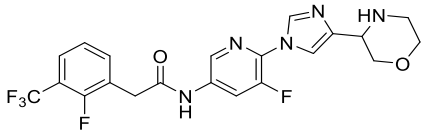
L_2 is a bond;

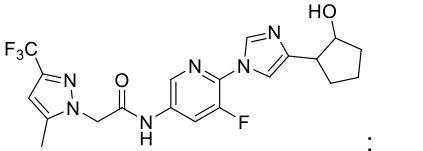
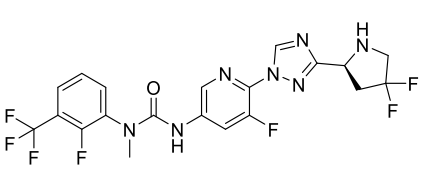
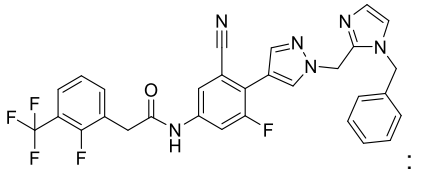
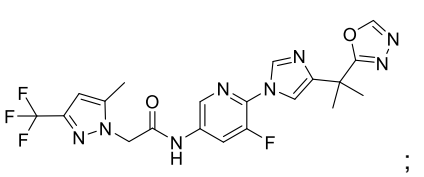
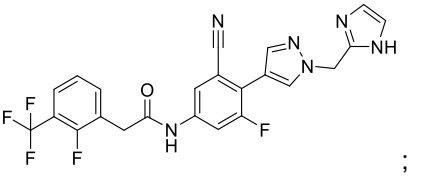
R^8 is pyrrolidinyl which is substituted with 1 or 2 substituents, each independently selected from F and CF_3.

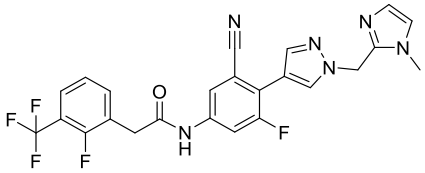
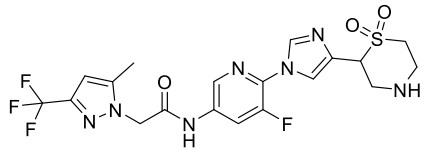
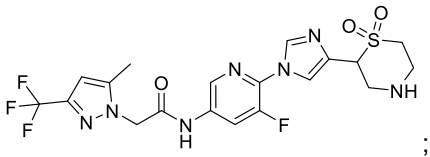
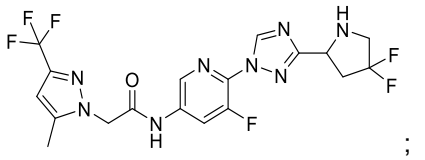
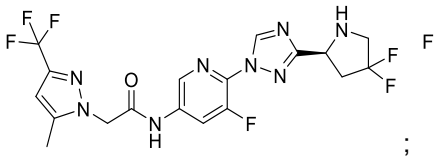
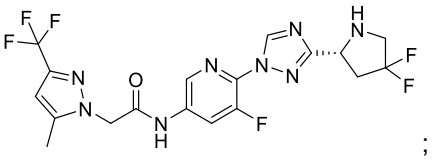
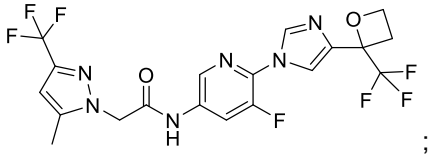
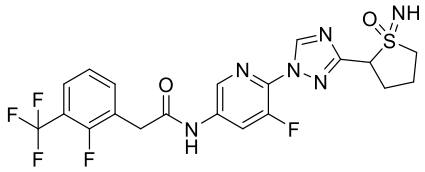
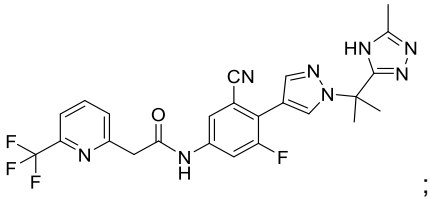
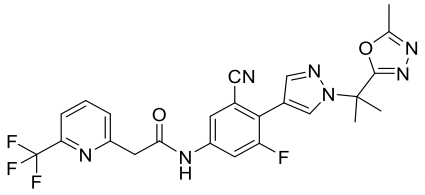
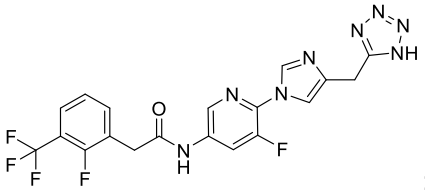
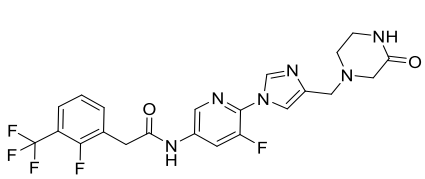
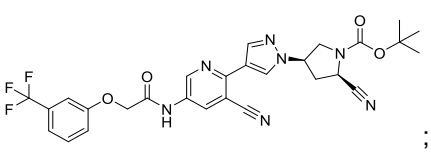
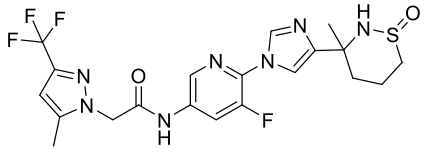
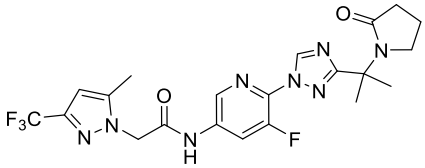
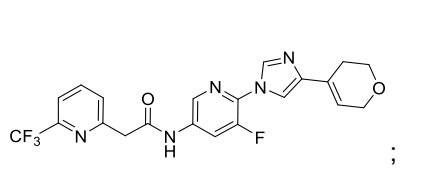
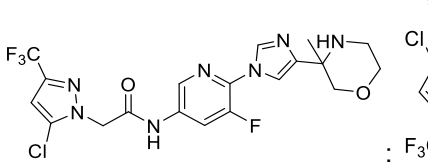
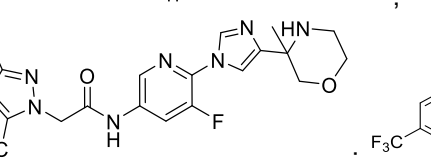
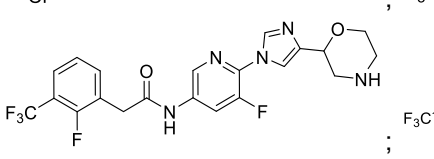
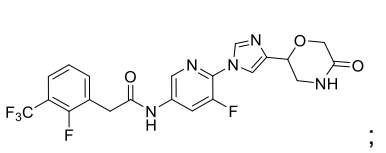
10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from:


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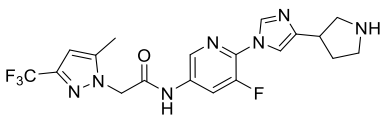
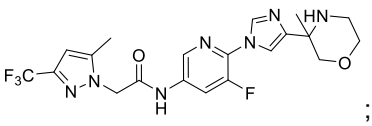
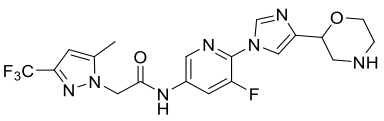
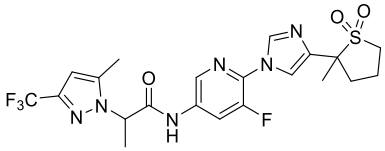
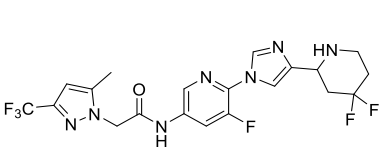
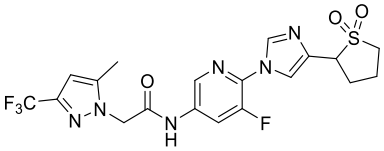
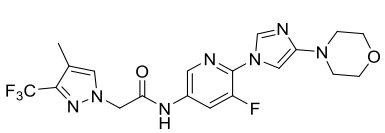
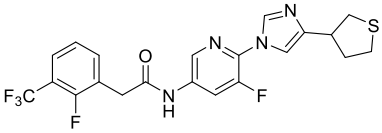
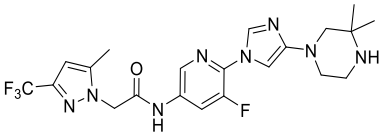
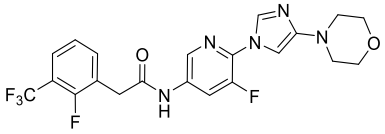
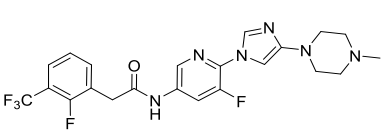
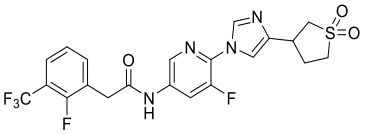
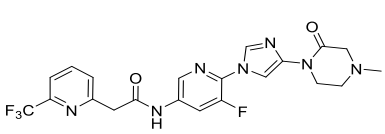
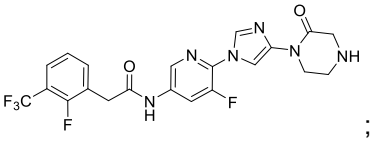
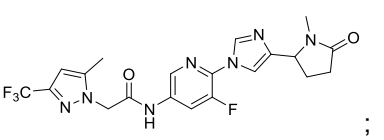
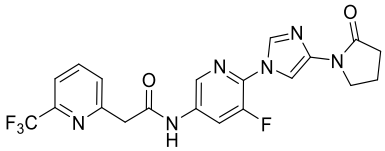
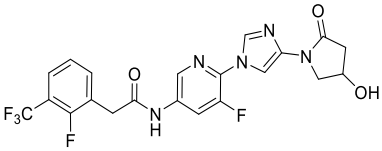
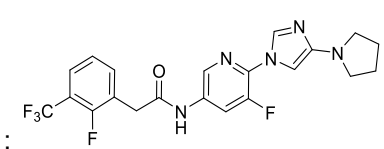
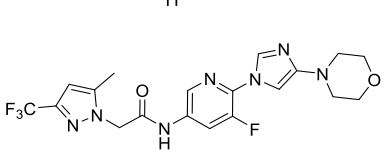
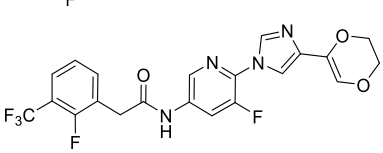
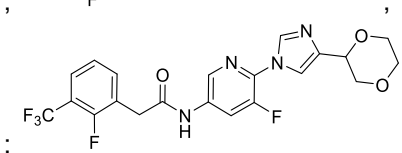
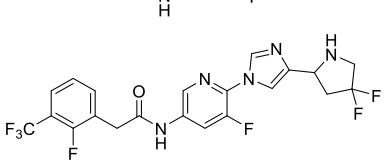
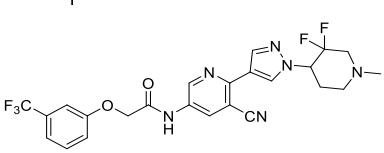
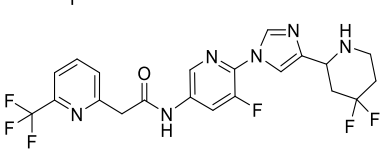
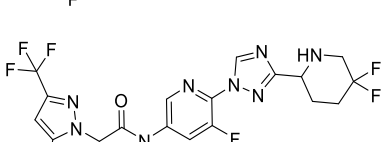
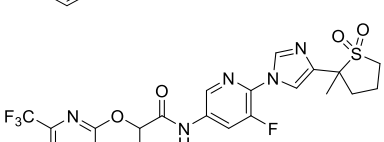
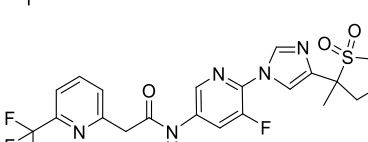
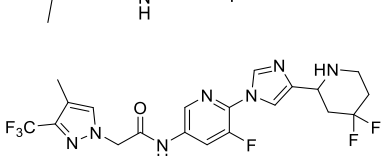
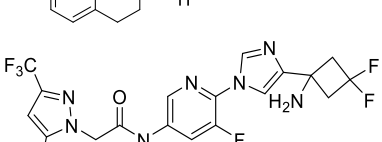
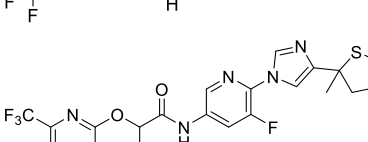
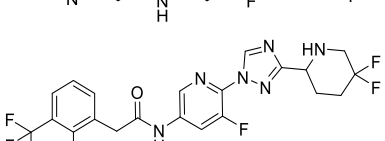
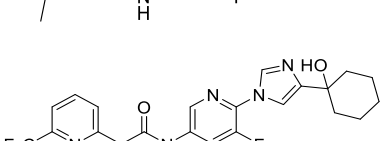
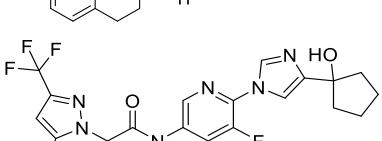
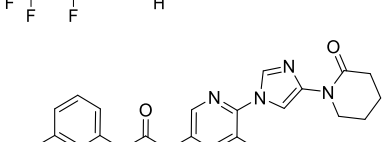
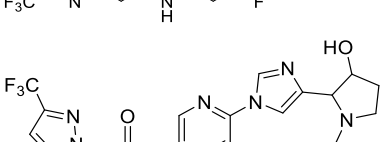
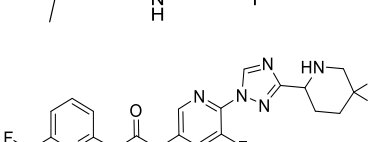
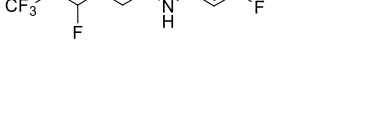
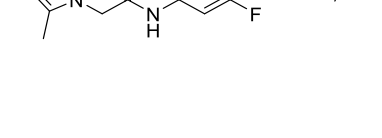
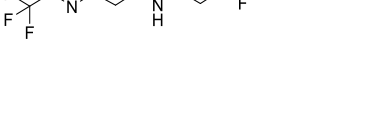
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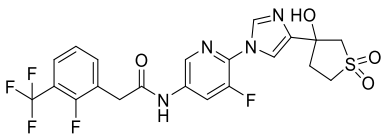
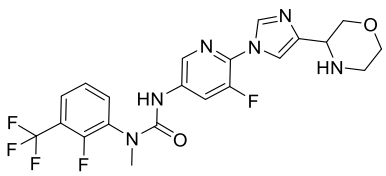
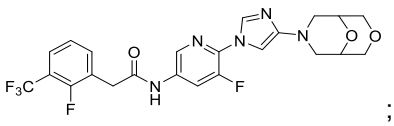
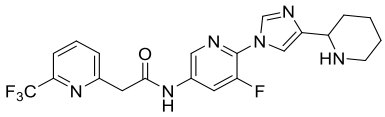
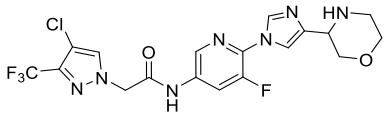
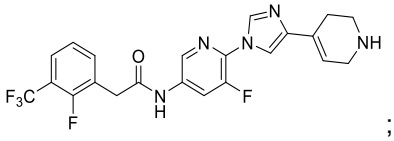
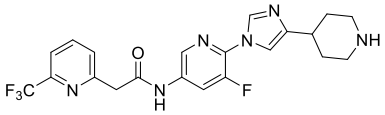
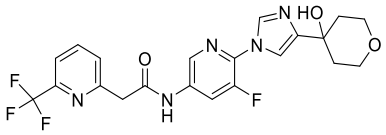
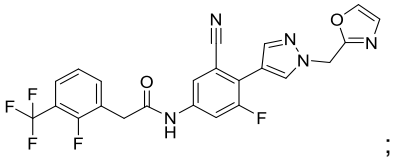
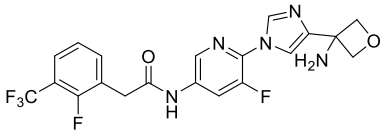
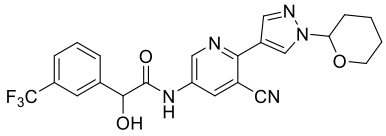
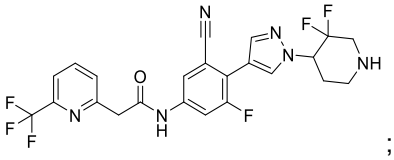
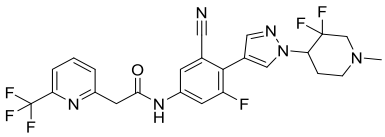
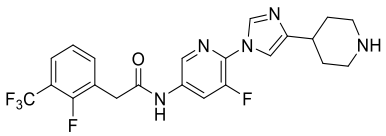
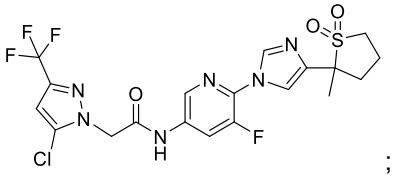
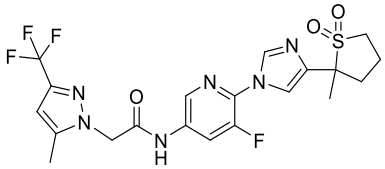
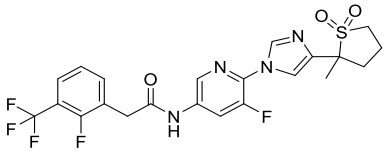
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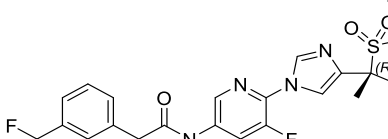
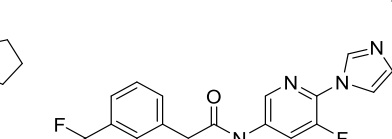
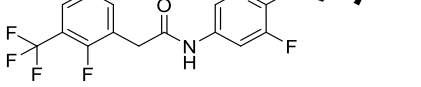
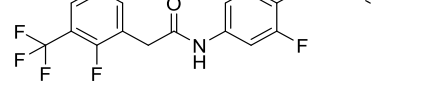
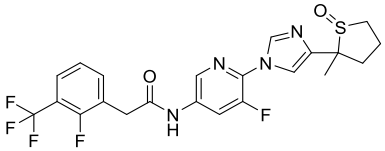
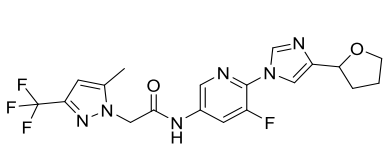
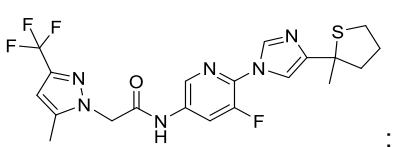
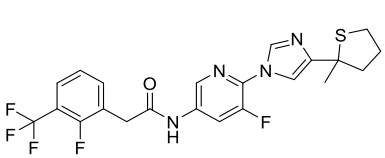
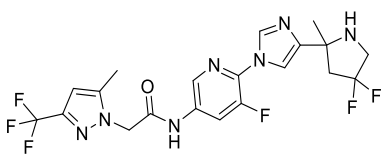
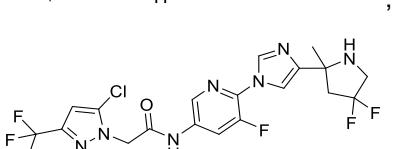
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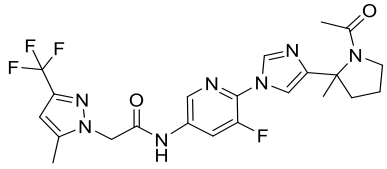
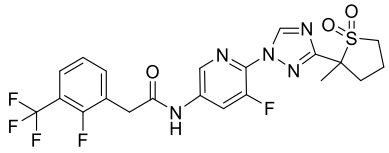
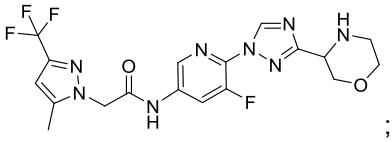
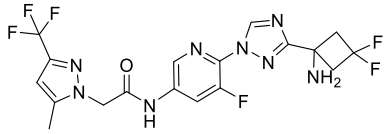
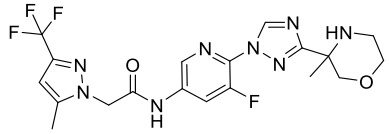
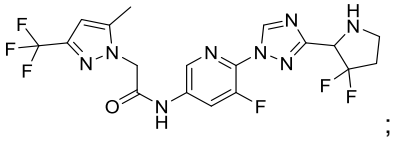
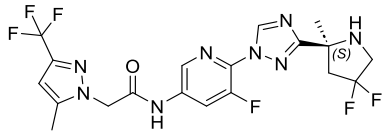
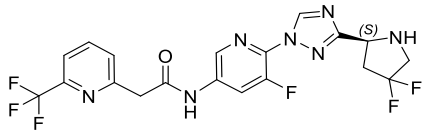
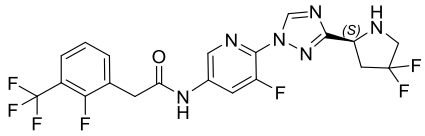
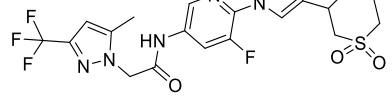
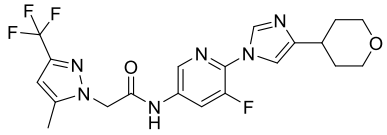
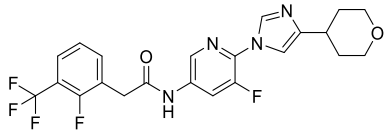
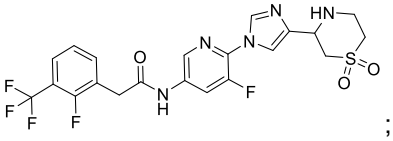
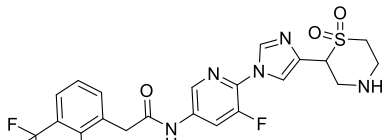
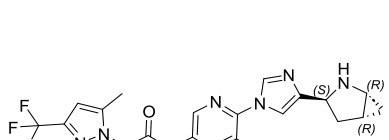
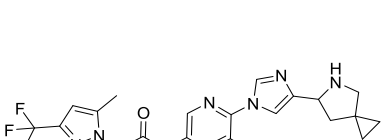
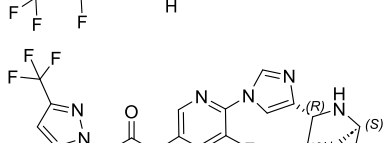
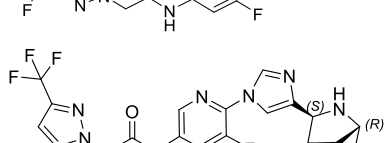
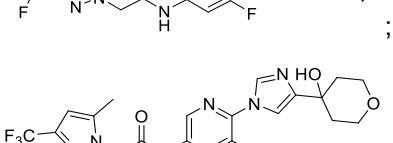
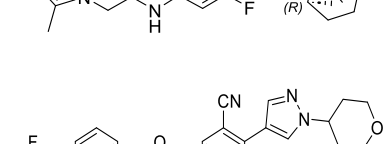
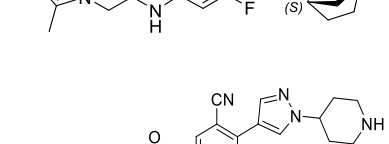
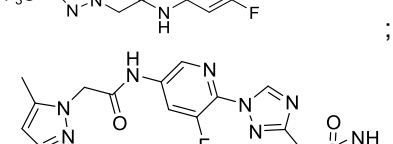
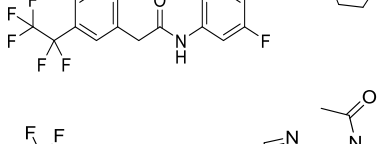
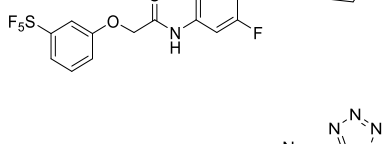
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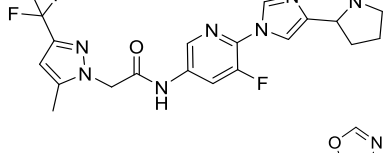
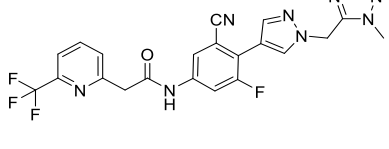
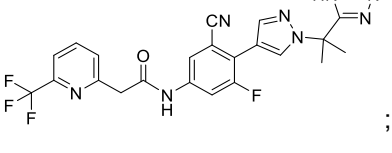
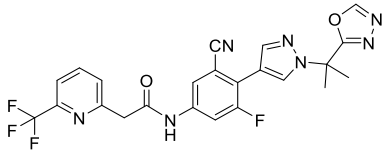
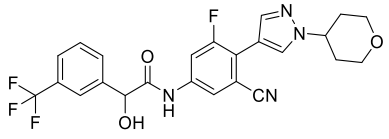
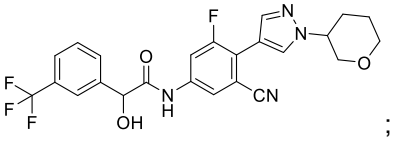
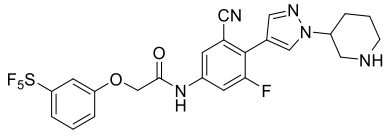
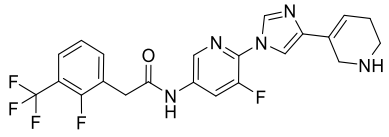
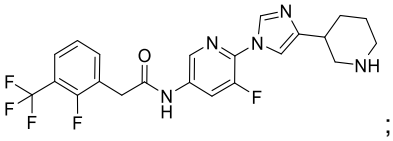
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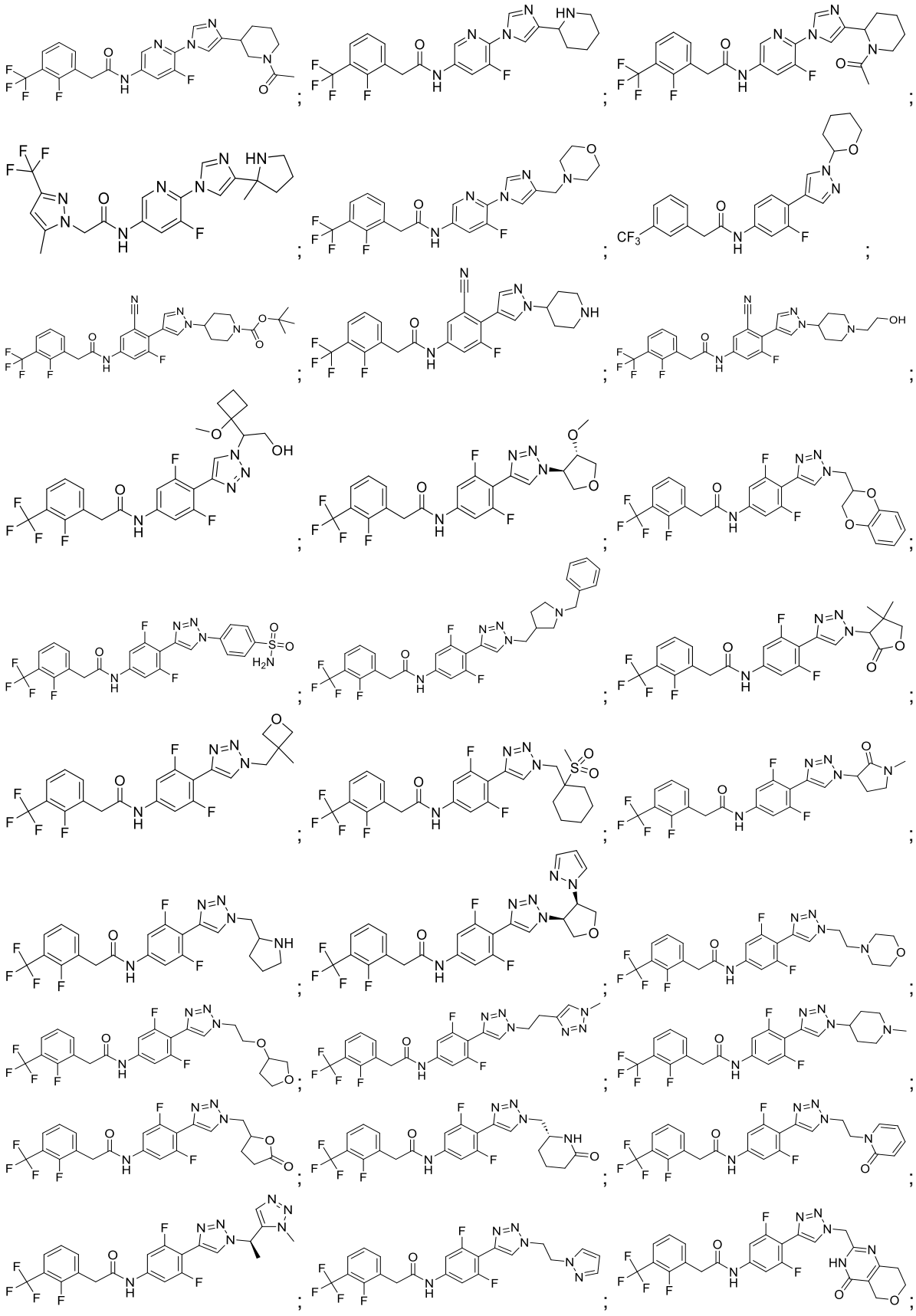

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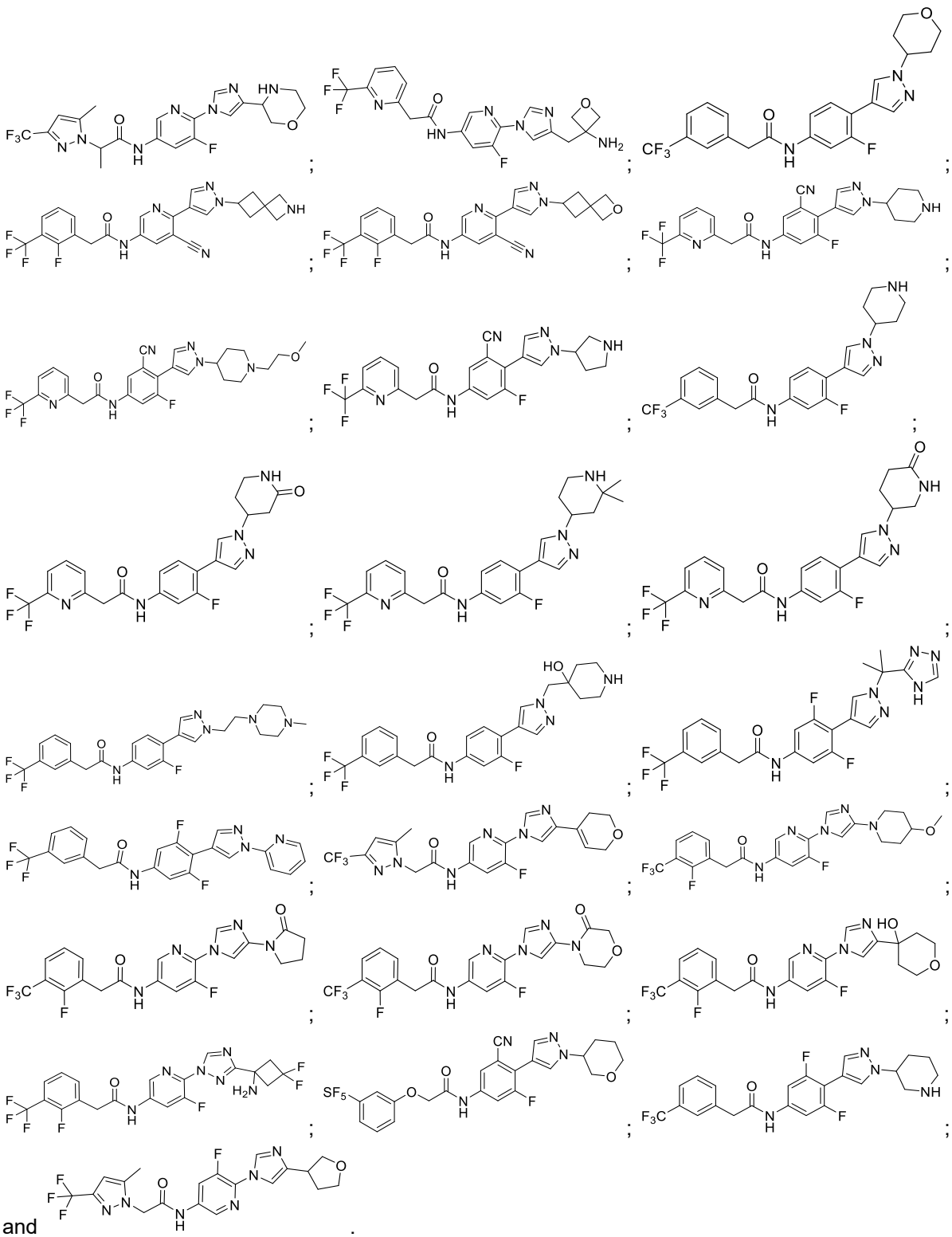

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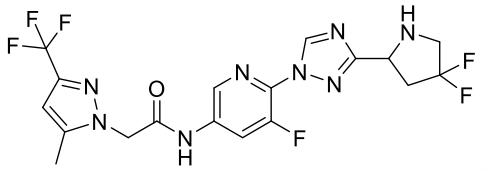
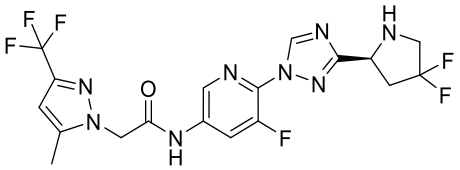
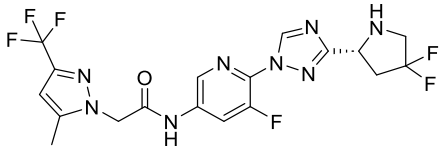
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and .

11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from:


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and

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12. A pharmaceutical composition comprising a compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers.

13. A pharmaceutical composition comprising a compound of any one of claims 1 to 11, or a pharmaceutically acceptable acid addition salt thereof, and one or more pharmaceutically acceptable carriers.

14. A compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, for use in the treatment of a PNPLA3I148M associated disease.

15. Use of a compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a PNPLA3I148M associated disease.

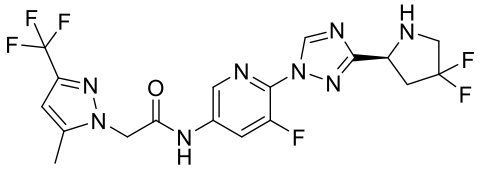
16. The use of claim 15, wherein the PNPLA3I148M associated disease is a liver disease.

17. The use of claim 15, wherein the PNPLA3I148M associated disease is a metabolic dysfunction-associated steatotic liver disease (MASLD) or a nonalcoholic fatty liver disease (NAFLD).

18. The use of claim 15, wherein the PNPLA3I148M associated disease is metabolic dysfunction–associated steatohepatitis (MASH), nonalcoholic steatohepatitis (NASH), alcoholic steatohepatitis (ASH), cirrhosis with liver fibrosis or hepatocellular carcinoma (HCC).

19. The use of claim 15, wherein the PNPLA3I148M associated disease is metabolic dysfunction–associated steatohepatitis (MASH).

20. The compound of Formula (I) of claim 1, wherein the compound is (S)-N-(6-(3-(4,4-difluoropyrrolidin-2-yl)-1H-1,2,4-triazol-1-yl)-5-fluoropyridin-3-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)acetamide and has the structure


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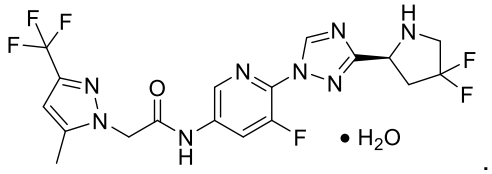
21. The compound of claim 20, which is crystalline (S)-N-(6-(3-(4,4-difluoropyrrolidin-2-yl)-1H-1,2,4-triazol-1-yl)-5-fluoropyridin-3-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)acetamide.

22. The compound of claim 21, which is characterized by having a powder X-ray diffractogram comprising at least four reflections at 2-Theta angles selected from the group consisting of (12.36 ± 0.2)°, (16.90 ± 0.2)°, (17.49 ± 0.2)°, (19.21 ± 0.2)°, (20.15 ± 0.2)°, (21.77 ± 0.2)°, (23.01 ± 0.2)°, (23.47 ± 0.2)°, (25.91 ± 0.2)° and **(**29.88 ± 0.2)°, when measured at a temperature in the range of from 20 to 40 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

23. The compound of claim 21, which is characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of (16.90 ± 0.2)°, (17.49 ± 0.2)°, (23.01 ± 0.2)°, (25.91 ± 0.2)° and **(**29.88 ± 0.2)°, when measured at a temperature in the range of from 20 to 40 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

24. The compound of any one of claims 21 to 23, which is characterized by having a differential scanning calorimetry curve comprising an endothermic peak having a peak temperature of (176.8 °C ±0.5) °C, when measured at a heating rate of 10°C/min.

25. The compound of any one of claims 21 to 24, which is characterized by having a thermogravimetric analysis curve showing a mass loss of not more than 3.56 weight%, based on the weight of the (S)-N-(6-(3-(4,4-difluoropyrrolidin-2-yl)-1H-1,2,4-triazol-1-yl)-5-fluoropyridin-3-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)acetamide monohydrate, when heated from 20°C to 350°C at a rate of 10°C/min.

26. The compound of any one of claims 21 to 25, which is (S)-N-(6-(3-(4,4-difluoropyrrolidin-2-yl)-1H-1,2,4-triazol-1-yl)-5-fluoropyridin-3-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)acetamide monohydrate and has the structure 

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