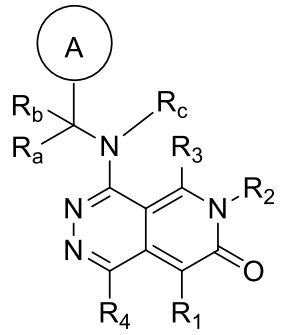
CLAIMS

1. A compound represented by Formula I, or a tautomer, stereoisomer, solvate, metabolite, isotopically labeled compound, pharmaceutically acceptable salt or co-crystal thereof:



Formula I

wherein:

ring A is selected from aryl, heteroaryl, the aryl, heteroaryl are optionally substituted with a substituent selected from halogen, alkyl, alkoxy, -OH, -CN, -NR_5R_6, -SF_5, -SO_2R_{10}, the alkyl, alkoxy are further optionally substituted with a substituent selected from halogen, -NR_5R_6, -OH, wherein, R_5, R_6 are independently selected from H, alkyl, R_{10} is alkyl and optionally substituted with halogen; or, two substituents on the aryl or heteroaryl are connected to form an aliphatic carbocyclic ring, the aliphatic carbocyclic ring is optionally substituted with halogen;

R_a, R_b, R_c are independently selected from H, alkyl;

R_1, R_3 are independently selected from H, halogen, alkyl, alkoxy, -OH, -CN, -NR_7R_8, the alkyl, alkoxy are optionally substituted with a substituent selected from halogen, -NR_7R_8, wherein R_7, R_8 are independently selected from H, alkyl;

R_2 is selected from H, alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl are optionally substituted with a substituent selected from halogen, alkyl, alkoxy, , -C(=O)R_9, R_9 is selected from alkyl, cycloalkyl, heterocycloalkyl;

R_4 is -$NR_{11}R_{12}$, R_{11}, R_{12} are independently selected from H, alkyl, cycloalkyl, heterocycloalkyl, wherein, when R_{11} and/or R_{12} are alkyl, the alkyl is optionally substituted with a substituent selected from -OH, alkenyl, halogen, -$NR_{14}R_{15}$, cycloalkyl, R_{14}, R_{15} are independently selected from H, alkyl; when R_{11} and/or R_{12} are selected from cycloalkyl, heterocycloalkyl, the cycloalkyl, heterocycloalkyl are optionally substituted with alkyl; or,

R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a heterocycloalkyl, the heterocycloalkyl is optionally substituted with a substituent selected from halogen, alkyl, cycloalkyl, -C(=O)R_{13}, , -OH, the alkyl is further optionally substituted with a substituent selected from -OH, cycloalkyl, wherein, R_{13} is alkyl; or,

R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a heteroaryl.

2. The compound according to claim 1, wherein R_4 is -$NR_{11}R_{12}$, R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 3-10 membered heterocycloalkyl, the heterocycloalkyl contains heteroatoms selected from N, O, S, the heterocycloalkyl is optionally substituted with a substituent selected from

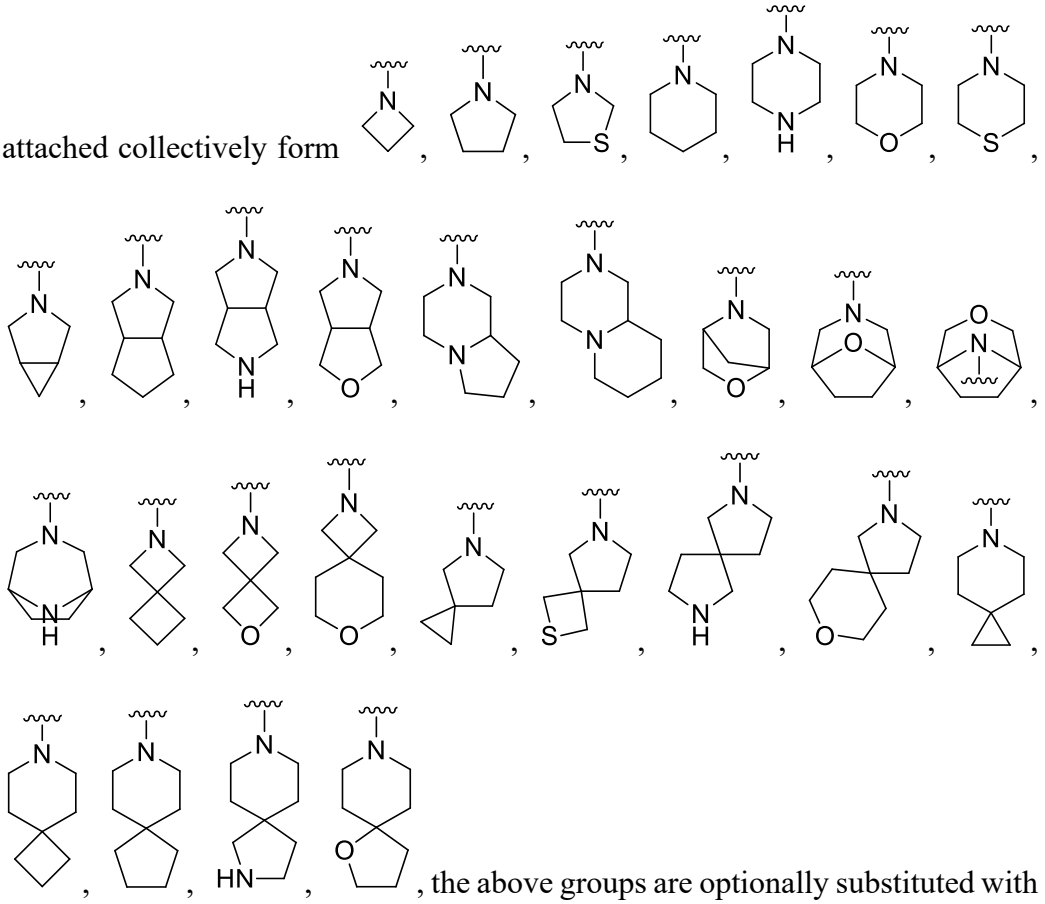
halogen, C1-C6 alkyl, 3-10 membered cycloalkyl, -C(=O)R_{13}, , -OH, the alkyl is further optionally substituted with a substituent selected from -OH, 3-10 membered cycloalkyl, wherein, R_{13} is C1-C6 alkyl;

preferably, R_4 is -$NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 3-10 membered heterocycloalkyl, the heterocycloalkyl contains heteroatoms selected from N, O, S, the heterocycloalkyl is optionally substituted with a substituent selected from halogen, C1-C6 alkyl, 3-10 membered cycloalkyl, -C(=O)R_{13}, , R_{13} is C1-C6 alkyl;

preferably, R_4 is -$NR_{11}R_{12}$, R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 4-10 membered heterocycloalkyl, the heterocycloalkyl contains 1-2 heteroatoms selected from N, O, S, the heterocycloalkyl is optionally substituted with a substituent selected from halogen, C1-C6 alkyl, 3-5 membered cycloalkyl, -C(=O)R_{13}, , -OH, the alkyl is further optionally substituted with a substituent selected from -OH, 3-5 membered cycloalkyl, wherein, R_{13} is C1-C6 alkyl;

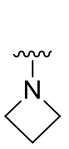
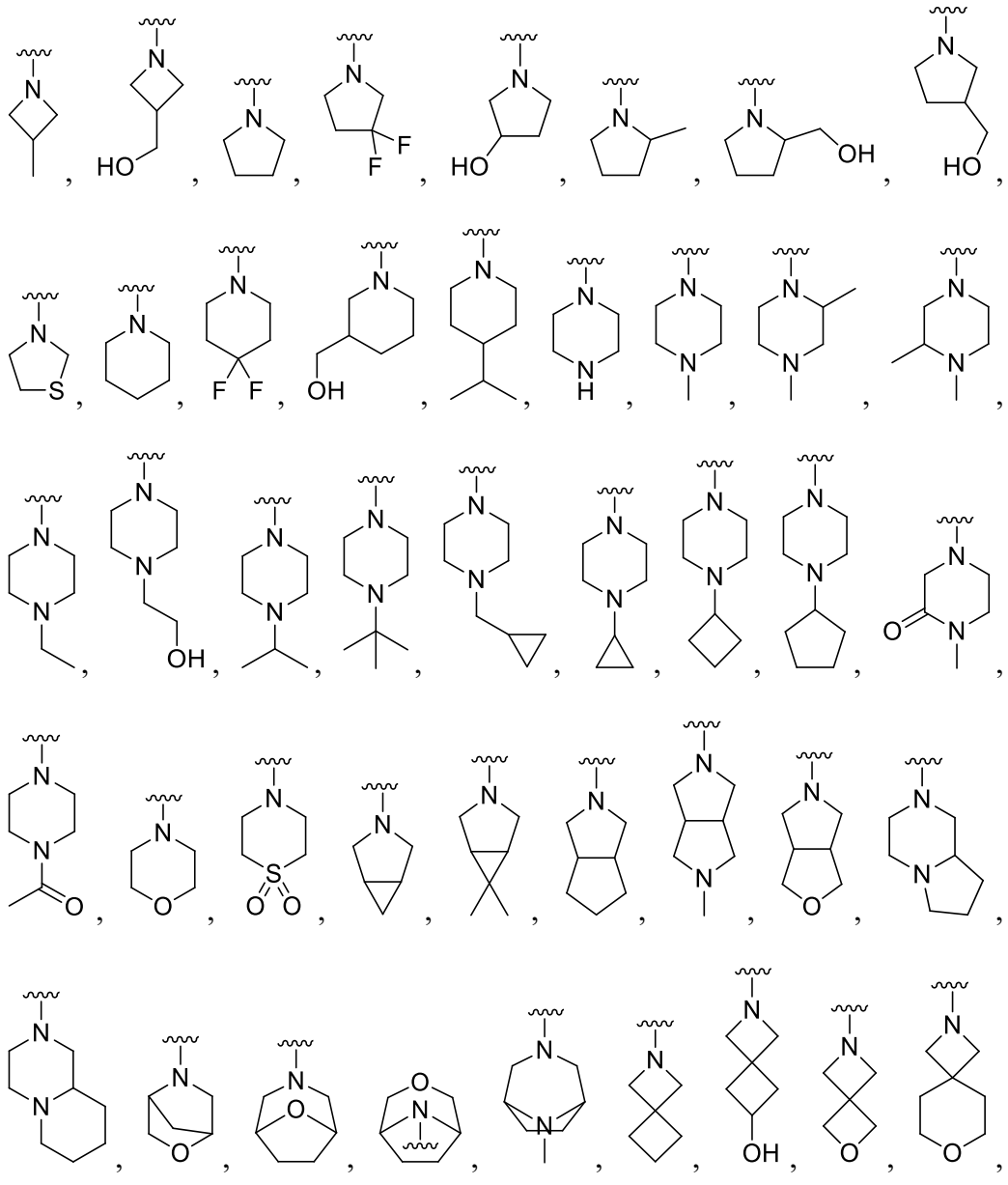
preferably, R_4 is -$NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 4-6 membered heterocycloalkyl, the heterocycloalkyl contains 1-2 heteroatoms selected from N, O, S, the heterocycloalkyl is optionally substituted with a substituent selected from halogen, C1-C6 alkyl, -C(=O)R_{13}, , R_{13} is C1-C6 alkyl;

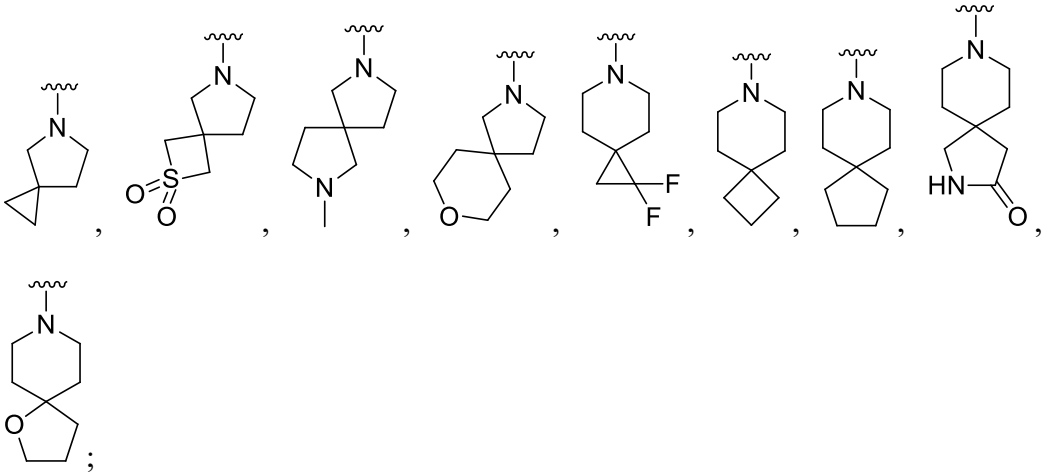
preferably, R_4 is -$NR_{11}R_{12}$, R_{11}, R_{12} and the nitrogen atom to which they are

attached collectively form , the above groups are optionally substituted with a substituent selected from halogen, C1-C6 alkyl, 3-5 membered cycloalkyl, -C(=O)R_{13}, , -OH, the alkyl is further optionally substituted with a substituent selected from -OH, 3-5 membered cycloalkyl, wherein, R_{13} is C1-C6 alkyl;

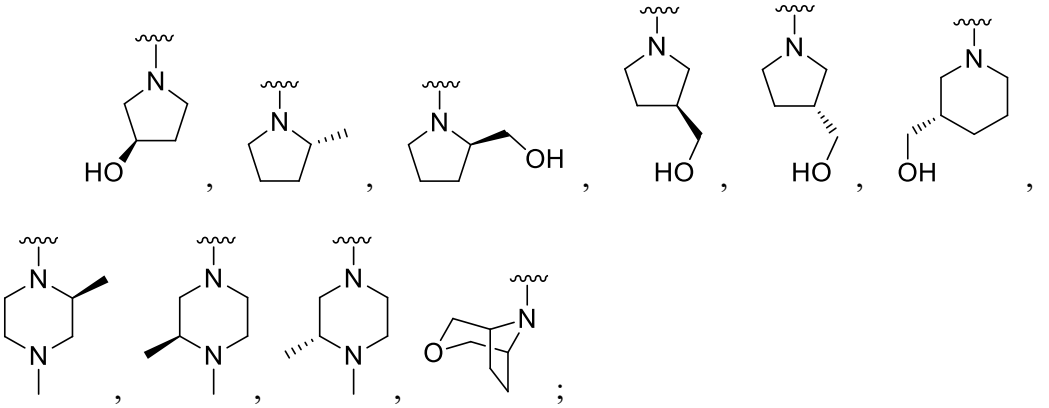
preferably, R_4 is -$NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form azetidinyl, tetrahydropyrrolyl, tetrahydrothiazolyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 3-azabicyclo[3.1.0]hexyl, the above groups are optionally substituted with a substituent selected from fluorine, methyl, -C(=O)R_{13}, , R_{13} is methyl;

preferably, R_4 is -$NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which

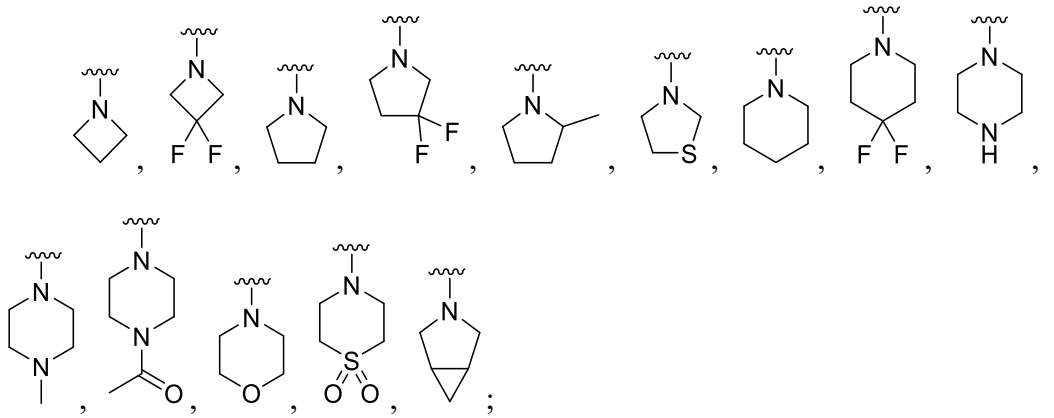
they are attached collectively form azetidinyl, piperazinyl, the above groups are optionally substituted with a substituent selected from fluorine, methyl, -C(=O)R_{13}, , R_{13} is methyl;preferably, R_4 is selected from: , , 

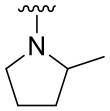
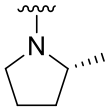


preferably, the configuration of R_4 is selected from at least one of the following:



preferably, R_4 is selected from:

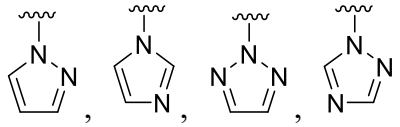


preferably,  is ;

preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 5-10 membered heteroaryl, the heteroaryl contains heteroatoms selected from N, O, S;

preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a 5 membered heteroaryl, the heteroaryl contains 1-3 nitrogen heteroatoms;

preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form pyrazolyl, imidazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl;

preferably, R_4 is selected from: .

3. The compound according to claim 1 or 2, wherein R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} are independently selected from H, alkyl, cycloalkyl, the alkyl is optionally substituted with a substituent selected from -OH, alkenyl, the cycloalkyl is optionally substituted with alkyl; or, R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a heterocycloalkyl, the heterocycloalkyl is optionally substituted with a substituent selected from halogen, alkyl, cycloalkyl, $-C(=O)R_{13}$, , R_{13} is alkyl; or, R_{11}, R_{12} and the nitrogen atom to which they are attached collectively form a heteroaryl;

preferably, R_4 is $-NR_{11}R_{12}$, R_{11}, R_{12} are independently selected from H, C1-

C6 alkyl, 3-10 membered cycloalkyl, 3-10 membered heterocycloalkyl, the heterocycloalkyl contains heteroatoms selected from N, O, S; wherein, when R_{11} and/or R_{12} are C1-C6 alkyl, the alkyl is optionally substituted with a substituent selected from halogen, $-NR_{14}R_{15}$, 3-10 membered cycloalkyl, R_{14}, R_{15} are independently selected from H, C1-C6 alkyl; when R_{11} and/or R_{12} are selected from 3-10 membered cycloalkyl, 3-10 membered heterocycloalkyl, the cycloalkyl, heterocycloalkyl are optionally substituted with C1-C6 alkyl;

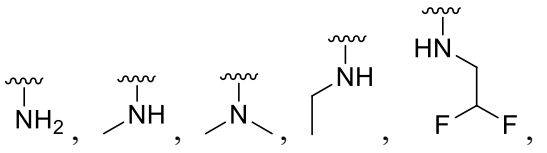
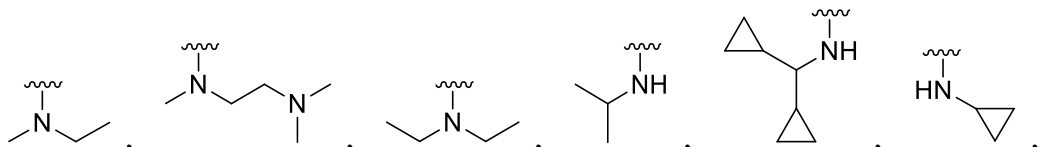
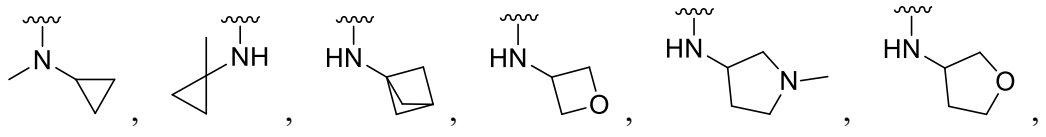
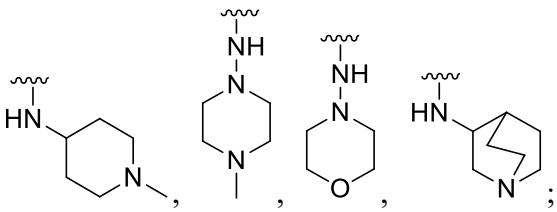
preferably, R_4 is $-NR_{11}R_{12}$, R_{11}, R_{12} are independently selected from H, C1-C6 alkyl, 3~8 membered cycloalkyl, 4-8 membered heterocycloalkyl, the heterocycloalkyl contains 1-2 heteroatoms selected from N, O; wherein, when R_{11} and/or R_{12} are C1-C6 alkyl, the alkyl is optionally substituted with a substituent selected from halogen, $-NR_{14}R_{15}$, 3-8 membered cycloalkyl, R_{14}, R_{15} are independently selected from H, C1-C6 alkyl; when R_{11} and/or R_{12} are selected from 3-8 membered cycloalkyl, 4-8 membered heterocycloalkyl, the cycloalkyl, heterocycloalkyl are optionally substituted with C1-C6 alkyl;

preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} are independently selected from H, C1-C6 alkyl, 3-10 membered cycloalkyl, the C1-C6 alkyl is optionally substituted with a substituent selected from -OH, C2-C6 alkenyl, the 3-10 membered cycloalkyl is optionally substituted with C1-C6 alkyl;

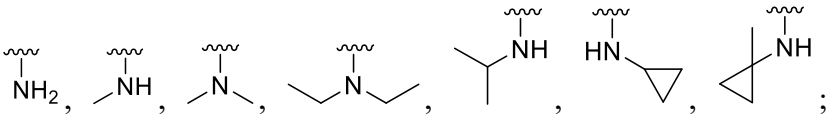
preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} are independently selected from H, C1-C6 alkyl, 3-5 membered cycloalkyl, the C1-C6 alkyl is optionally substituted with a substituent selected from -OH, C2-C6 alkenyl, the 3-5 membered cycloalkyl is optionally substituted with C1-C6 alkyl;

preferably, R_4 is $-NR_{11}R_{12}$, R_{11}, R_{12} are independently selected from H, C1-C6 alkyl, cyclopropyl, bicyclo[1.1.1]pentyl, oxacyclobutyl, tetrahydropyrrolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, 1-azabicyclo[2.2.2]octyl; wherein, when R_{11} and/or R_{12} are C1-C6 alkyl, the alkyl is optionally substituted with a substituent selected from halogen, $-NR_{14}R_{15}$, 3 membered cycloalkyl, R_{14}, R_{15} are independently selected from H, C1-C6 alkyl; when R_{11} and/or R_{12} are selected from cyclopropyl, bicyclo[1.1.1]pentyl, oxacyclobutyl, tetrahydropyrrolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, 1-azabicyclo[2.2.2]octyl, the above groups are optionally substituted with C1-C6 alkyl;

preferably, R_4 is $-NR_{11}R_{12}$, wherein R_{11}, R_{12} are independently selected from H, methyl, ethyl, propyl, cyclopropyl, the cyclopropyl is optionally substituted with methyl;

preferably, R_4 is selected from: 



;

preferably, R_4 is selected from:



preferably, R_4 is .

4. The compound according to any one of claims 1-3, wherein, ring A is selected from aryl, heteroaryl, the aryl, heteroaryl are optionally substituted with a substituent selected from halogen, alkyl, alkoxy, -OH, -CN, $-NR_5R_6$, $-SF_5$, $-SO_2R_{10}$, the alkyl, alkoxy are further optionally substituted with a substituent selected from halogen, $-NR_5R_6$, wherein, R_5, R_6 are independently selected from H, alkyl, R_{10} is alkyl and optionally substituted with halogen;

preferably, ring A is selected from 6-12 membered aryl, 5-12 membered heteroaryl, the heteroaryl contains heteroatoms selected from N, O, S, the substituents of the above groups are as defined in any one of claims 1-3;

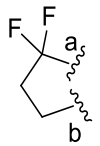
preferably, ring A is phenyl, the substituents thereof are as defined in any one of claims 1-3.

5. The compound according to any one of claims 1-4, wherein, the substituent contained in ring A is selected from halogen, C1-C6 alkyl, C1-C6 alkoxy, -OH, -CN, $-NR_5R_6$, $-SF_5$, $-SO_2R_{10}$, the alkyl, alkoxy are further optionally substituted with a substituent selected from halogen, $-NR_5R_6$, -OH, wherein, R_5, R_6 are independently selected from H, C1-C6 alkyl, R_{10} is C1-C6 alkyl and optionally substituted with halogen; or, two substituents on ring A are connected

to form a 5-6 membered aliphatic carbocyclic ring, the aliphatic carbocyclic ring is optionally substituted with halogen;

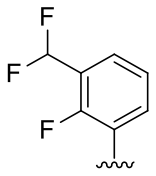
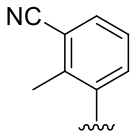
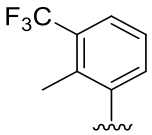
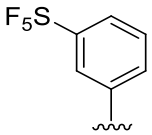
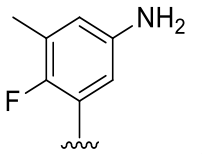
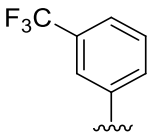
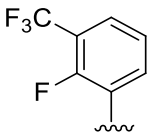
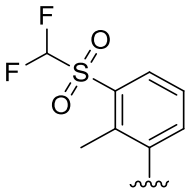
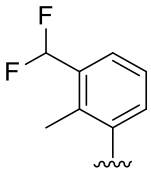
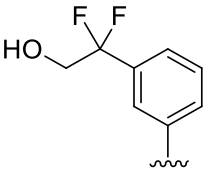
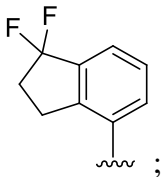
preferably, the substituent contained in ring A is selected from halogen, C1-C6 alkyl, -CN, -NR_5R_6, -SF_5, -SO_2R_{10}, the alkyl is further optionally substituted with a substituent selected from halogen, -OH, wherein, R_5, R_6 are independently selected from H, C1-C6 alkyl, R_{10} is C1-C6 alkyl and optionally substituted with halogen; or, two substituents on ring A are connected to form a 5-6 membered aliphatic carbocyclic ring, the aliphatic carbocyclic ring is optionally substituted with halogen; preferably, the substituent contained in ring A is selected from halogen, C1-C6 alkyl, C1-C6 alkoxy, -OH, -CN, -NR_5R_6, -SF_5, -SO_2R_{10}, the alkyl, alkoxy are further optionally substituted with a substituent selected from halogen, -NR_5R_6, wherein, R_5, R_6 are independently selected from H, C1-C6 alkyl, R_{10} is C1-C6 alkyl and optionally substituted with halogen;

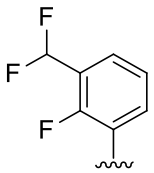
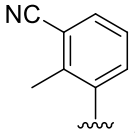
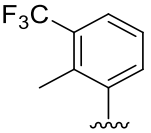
preferably, the substituent contained in ring A is selected from halogen, C1-C6 alkyl, -CN, -NR_5R_6, the alkyl is further optionally substituted with halogen, R_5, R_6 are independently selected from H, C1-C6 alkyl;

preferably, the substituent contained in ring A is selected from -F, -CH_3, -CHF_2, -CF_3, -CN, -NH_2, -SF_5, -SO_2CHF_2, -CF_2CH_2OH; or, two substituents on ring A are connected to form 

, wherein the two ends of a and b are respectively connected to two adjacent ring carbon atoms on ring A;

preferably, the substituent contained in ring A is selected from -F, -CH_3, -CHF_2, -CF_3, -CN, -NH_2.

6. The compound according to any one of claims 1-5, wherein, ring A is selected from: , , , , , , , , , , ;

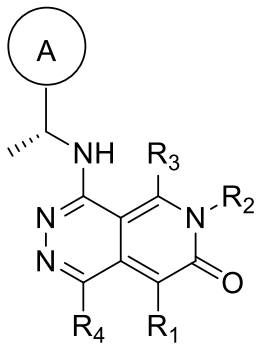
preferably, ring A is selected from: , , .

7. The compound according to any one of claims 1-6, wherein, R_a, R_b, R_c are independently selected from H, C1-C6 alkyl;

preferably, R_a, R_b, R_c are independently selected from H, methyl;

preferably, R_a is methyl, R_b is H, R_c is H.

8. The compound according to any one of claims 1-7, wherein, the structure is represented by Formula II:



Formula II

wherein each group is as defined in any one of claims 1-7.

9. The compound according to any one of claims 1-8, wherein, R_1, R_3 are independently selected from H, halogen, C1-C6 alkyl, C1~C6 alkoxy, -OH, -CN, $-NR_7R_8$, the alkyl, alkoxy are optionally substituted with a substituent selected from halogen, $-NR_7R_8$, wherein R_7, R_8 are independently selected from H, C1-C6 alkyl;

preferably, R_1, R_3 are independently selected from H, C1-C6 alkyl, C1-C6 alkoxy, -OH, -CN, $-NR_7R_8$, the alkyl, alkoxy are optionally substituted with a substituent selected from halogen, $-NR_7R_8$, wherein R_7, R_8 are independently selected from H, alkyl;

preferably, R_1, R_3 are independently selected from H, C1-C6 alkyl, C1-C6 alkoxy, -OH, -CN, $-NR_7R_8$, the alkyl, alkoxy are optionally substituted with a substituent selected from halogen, $-NR_7R_8$, wherein R_7, R_8 are independently selected from H, C1-C6 alkyl;

preferably, both R_1, R_3 are H.

10. The compound according to any one of claims 1-9, wherein, R_2 is

selected from H, C1~C6 alkyl, 3-10 membered cycloalkyl, 3-10 membered heterocycloalkyl, 3-10 membered cycloalkenyl, 3-10 membered heterocycloalkenyl, the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl are optionally substituted with a substituent selected from halogen, C1-C6 alkyl, C1-C6 alkoxy, , -C(=O)R_9, R_9 is selected from C1-C6 alkyl, 3-10 membered cycloalkyl, 3-10 membered heterocycloalkyl, the heterocycloalkyl, heterocycloalkenyl contain heteroatoms selected from N, O, S;

preferably, R_2 is selected from H, C1-C6 alkyl, 3-10 membered cycloalkyl, 3-10 membered heterocycloalkyl, 3-10 membered heterocycloalkenyl, the cycloalkyl, heterocycloalkyl, heterocycloalkenyl are optionally substituted with a substituent selected from C1-C6 alkyl, C1-C6 alkoxy, -C(=O)R_9, R_9 is selected from C1-C6 alkyl, 3-10 membered heterocycloalkyl, the heterocycloalkyl, heterocycloalkenyl contain 1-2 heteroatoms selected from N, O, S;

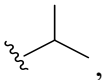
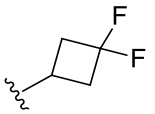
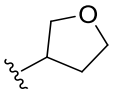
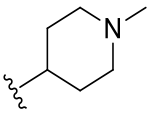
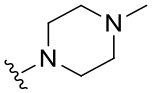
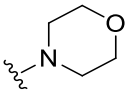
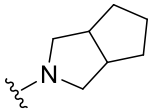
preferably, R_2 is selected from H, C1-C6 alkyl, 3 membered cycloalkyl, 5-6 membered heterocycloalkyl, 6 membered heterocycloalkenyl, the cycloalkyl, heterocycloalkyl, heterocycloalkenyl are optionally substituted with a substituent selected from C1-C6 alkyl, C1-C6 alkoxy, -C(=O)R_9, R_9 is selected from C1-C6 alkyl, 6 membered heterocycloalkyl, the heterocycloalkyl, heterocycloalkenyl contain 1-2 heteroatoms selected from N, O;

preferably, R_2 is selected from C1-C6 alkyl, 3-8 membered cycloalkyl, 5-8 membered heterocycloalkyl, the cycloalkyl, heterocycloalkyl are optionally substituted with a substituent selected from halogen, C1-C6 alkyl, the heterocycloalkyl contains 1-2 heteroatoms selected from N, O;

preferably, R_2 is C1-C6 alkyl; or,

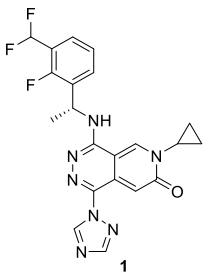
R_2 is selected from cyclopropyl, cyclobutyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, 3-azabicyclo[3.3.0]octy, the above groups are optionally substituted with a substituent selected from halogen, C1-C6 alkyl;

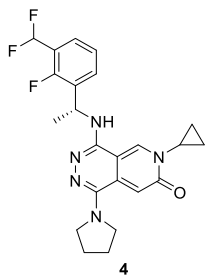
preferably, R_2 is cyclopropyl, the cyclopropyl is optionally substituted with C1-C6 alkyl;

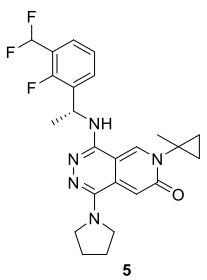
preferably, R_2 is selected from: methyl, ethyl, , , , , , , , , , ;

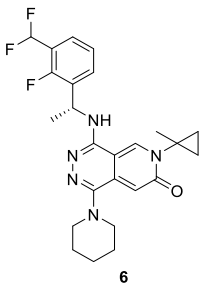
preferably, R_2 is selected from: , .

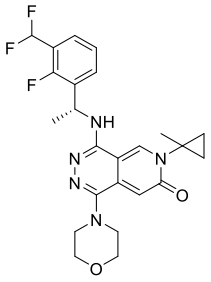
11. The compound according to any one of claims 1-10, wherein, the compound is selected from one of the following:


1

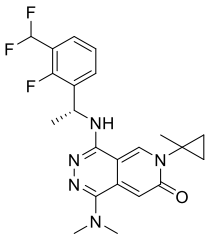

4


5

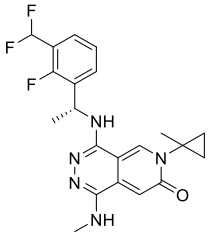

6



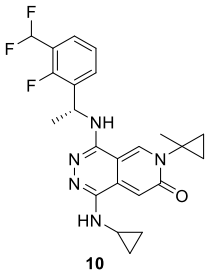
7



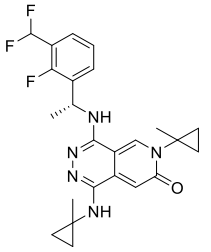
8



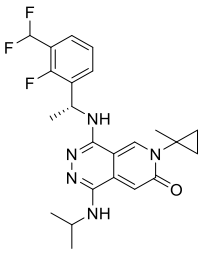
9



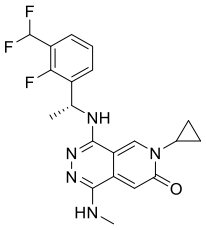
10



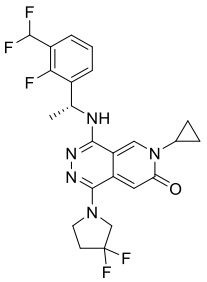
11



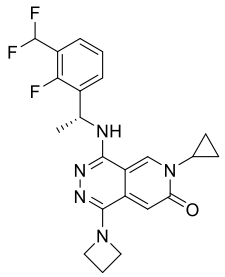
12



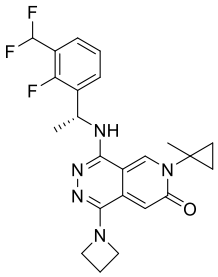
13



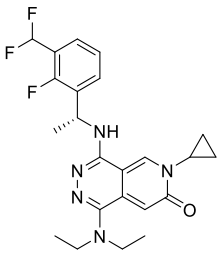
14



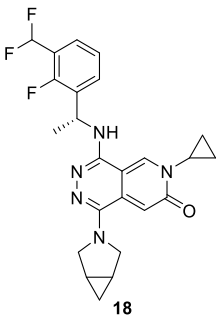
15



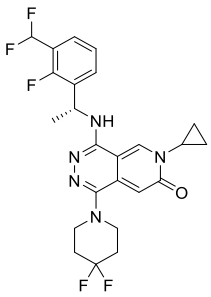
16



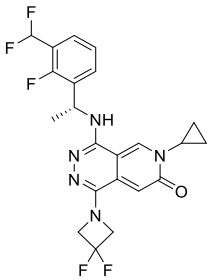
17



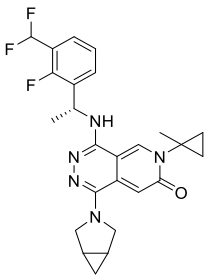
18



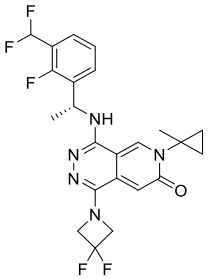
19



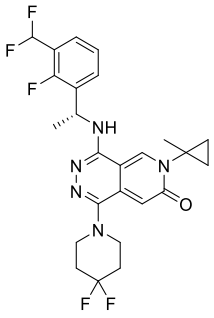
20



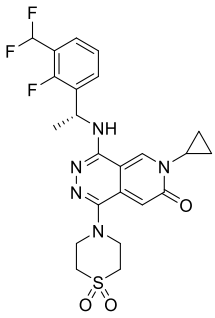
21



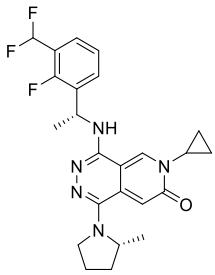
22



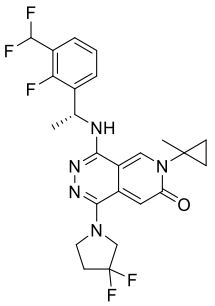
23



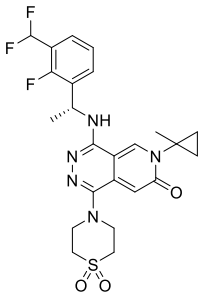
24



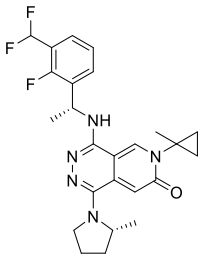
25



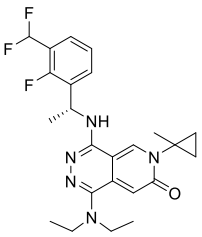
26



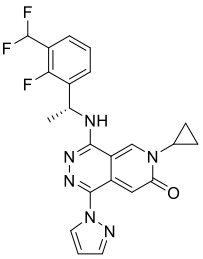
27



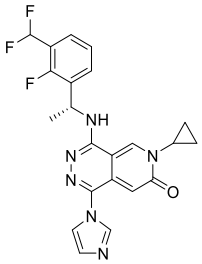
28



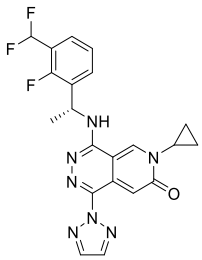
29



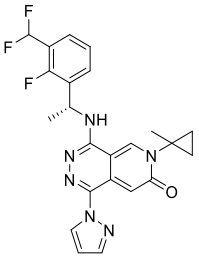
30



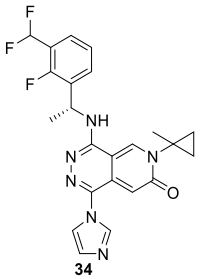
31



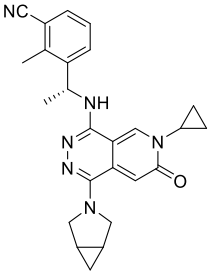
32



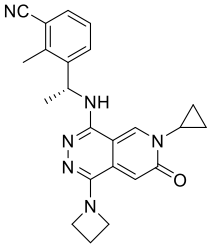
33



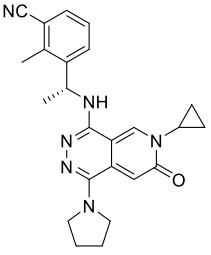
34



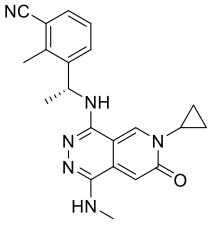
35



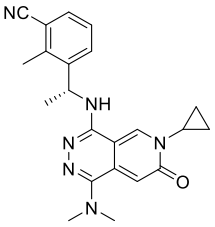
36

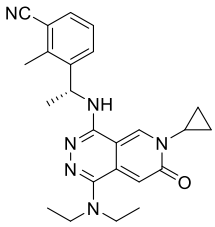


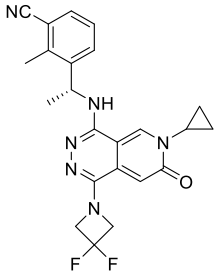
37

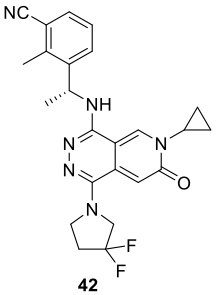


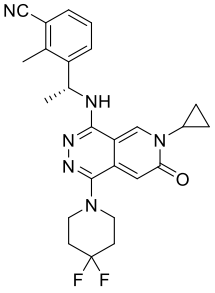
38

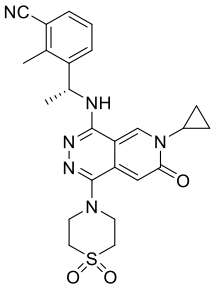

39

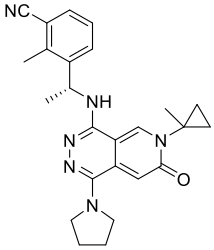

40

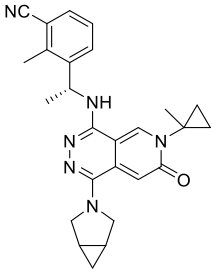

41

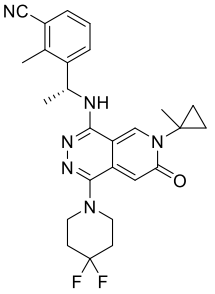

42

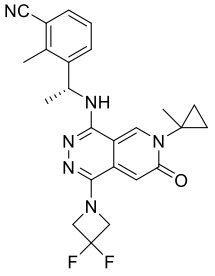

43

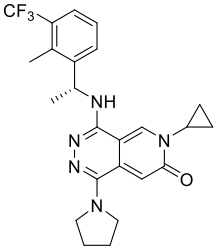

44

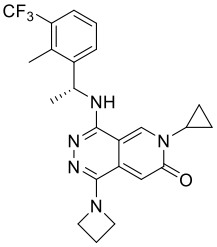

45

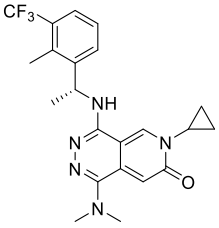

46

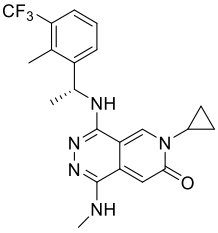

47

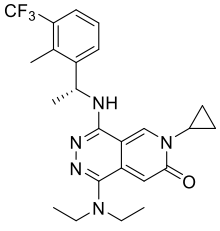

48

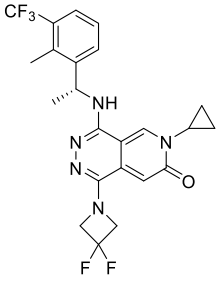

49

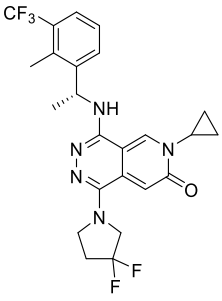

50


51

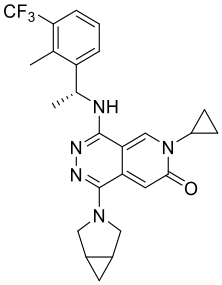

52


53

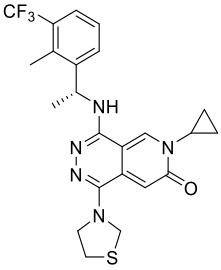

54



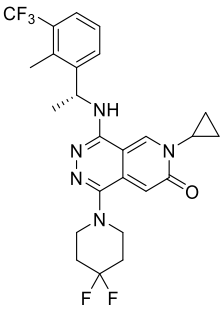
55



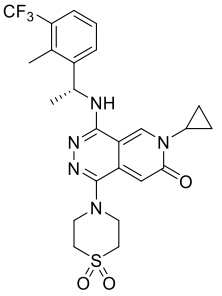
56



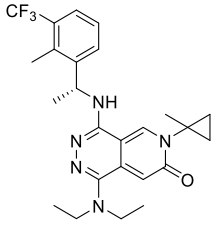
57



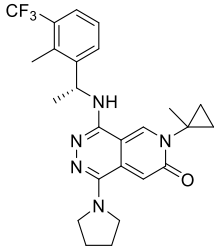
58



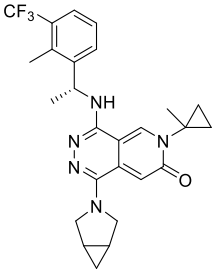
59



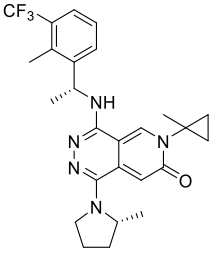
60



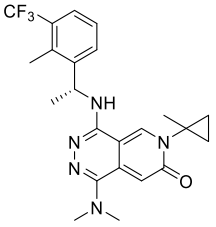
61



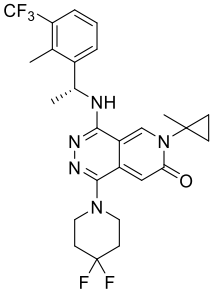
62



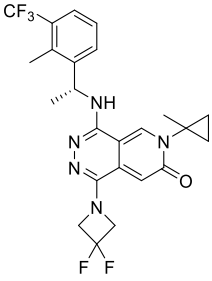
63



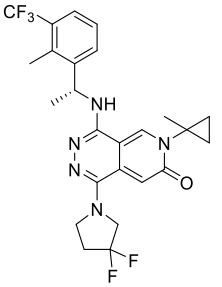
64



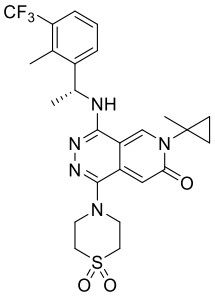
65



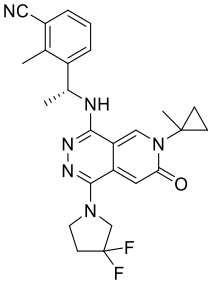
66



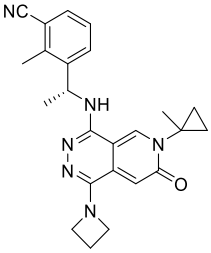
67



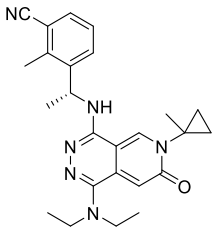
68



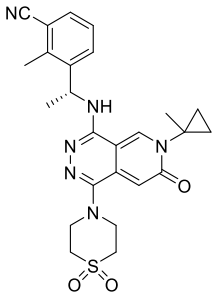
69



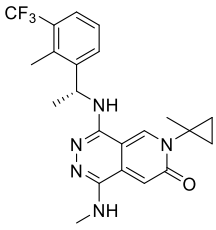
70



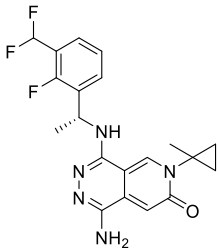
71



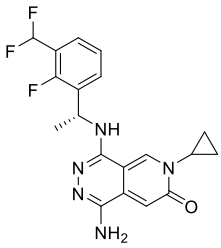
72



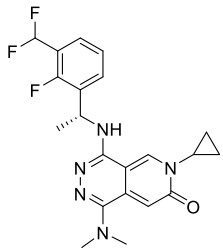
73



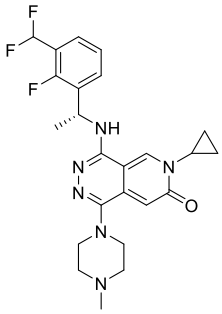
74



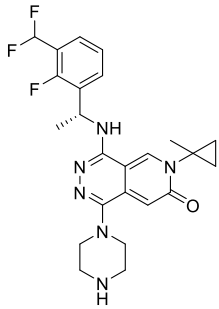
75



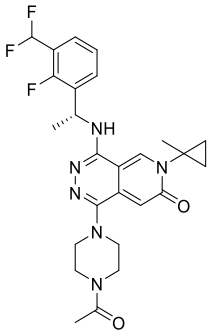
76



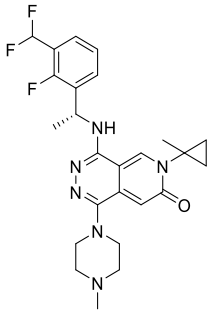
77



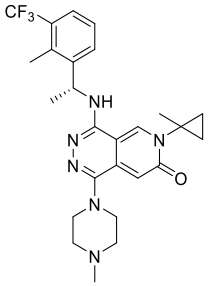
78



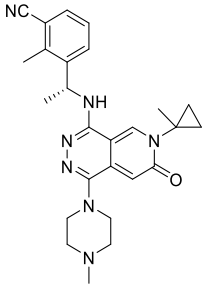
79



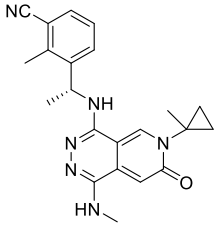
80



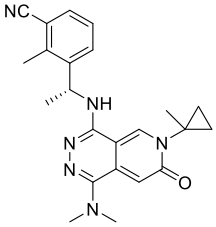
81



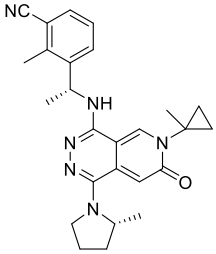
82



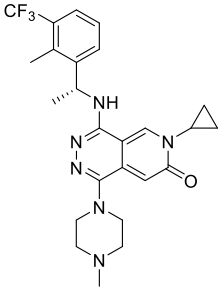
83



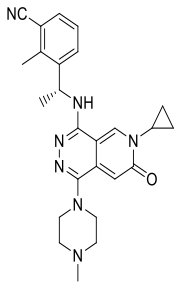
84



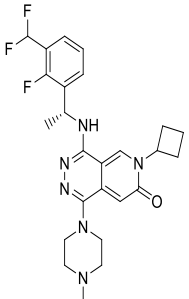
85



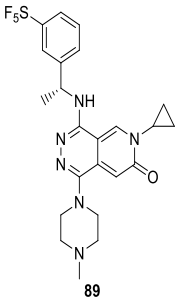
86



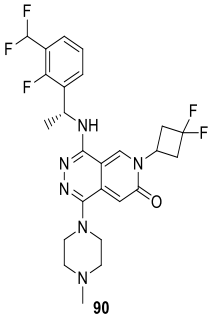
87



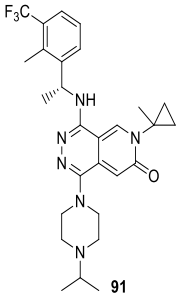
88



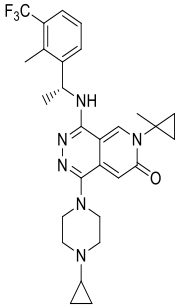
89



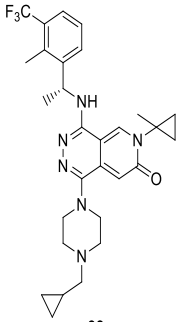
90



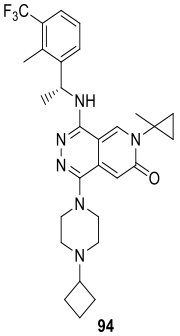
91



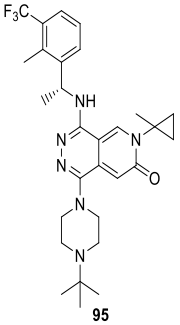
92



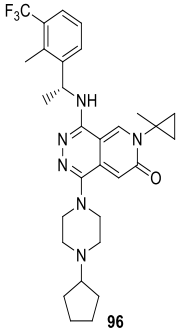
93



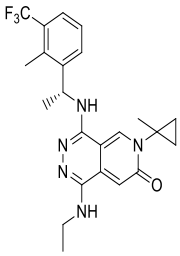
94



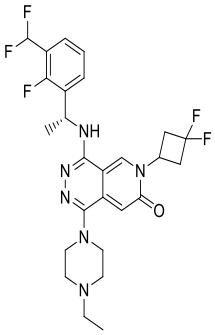
95



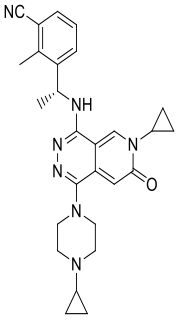
96



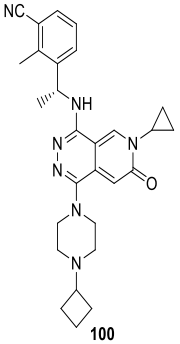
97



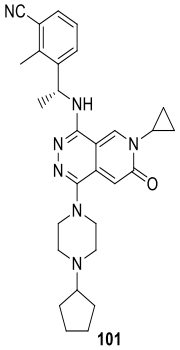
98



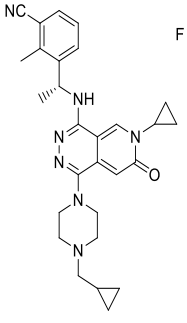
99



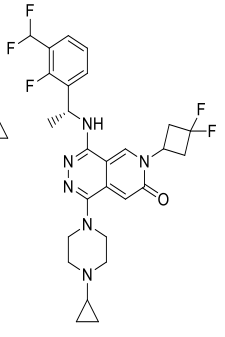
100



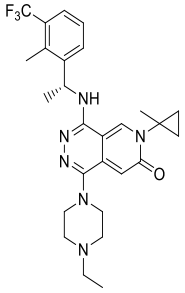
101



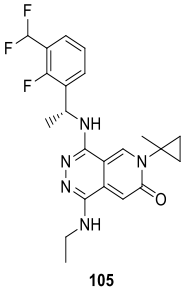
102



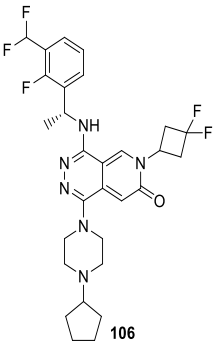
103



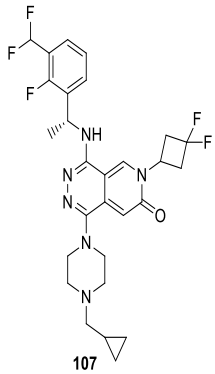
104



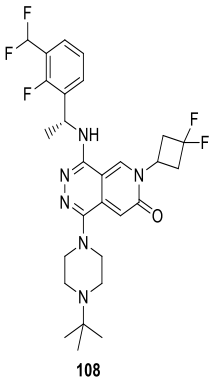
105



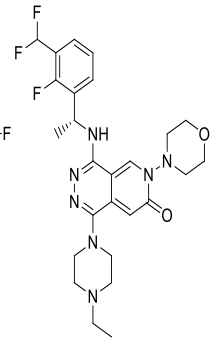
106



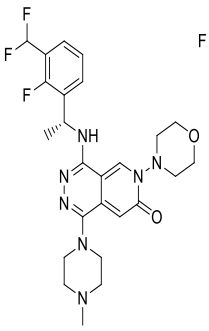
107



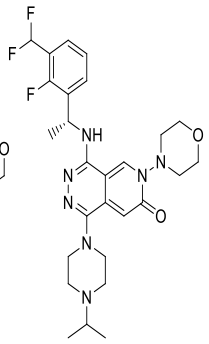
108



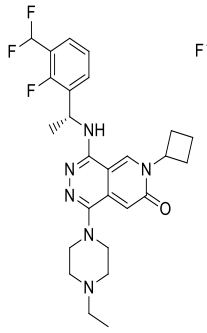
109



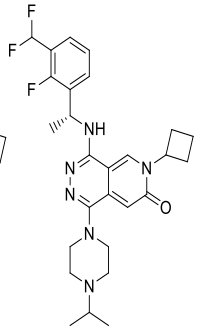
110



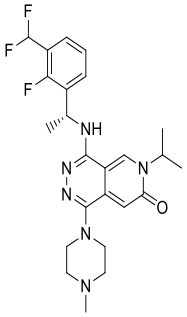
111



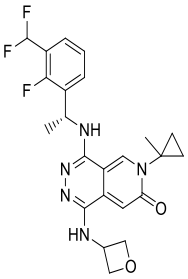
112



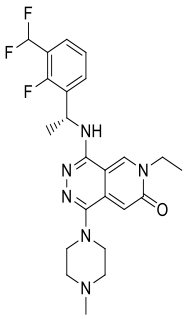
113



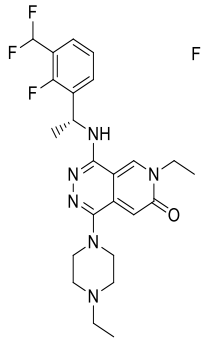
114



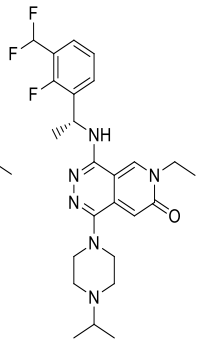
115



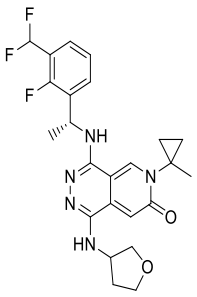
116



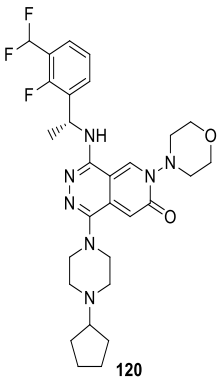
117



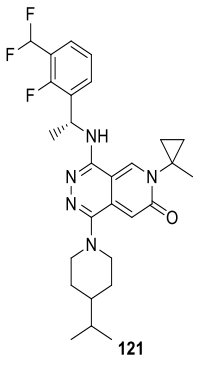
118



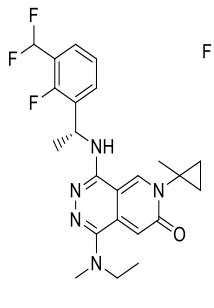
119



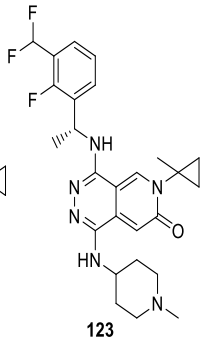
120



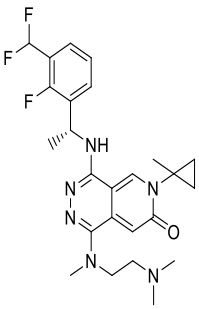
121



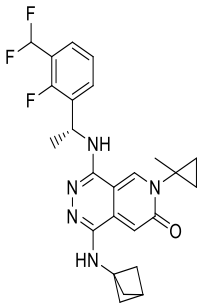
122



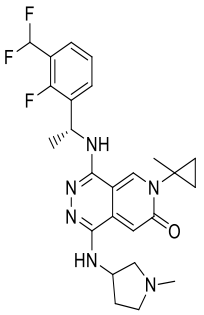
123



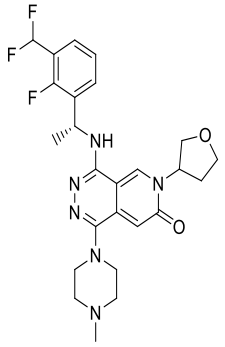
124



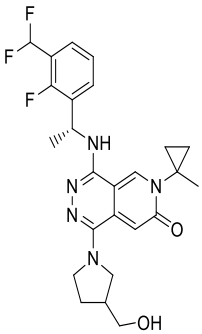
125



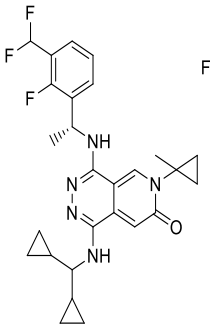
126



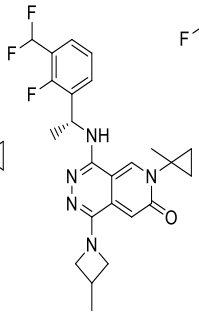
127



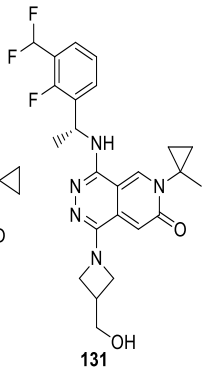
128



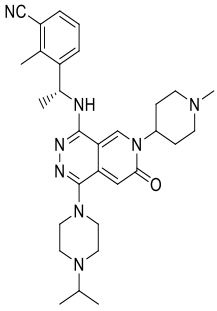
129



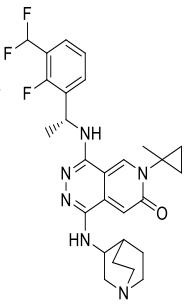
130



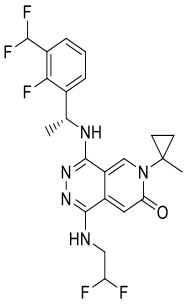
131



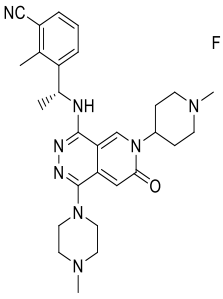
132



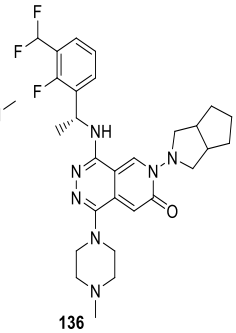
133



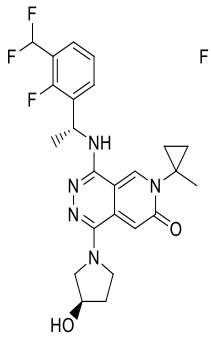
134



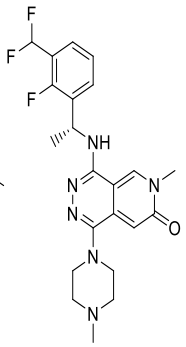
135



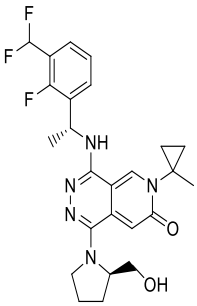
136



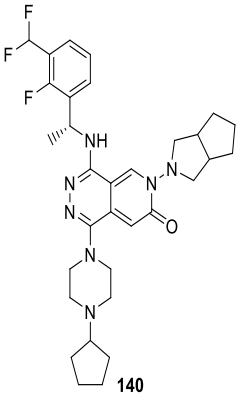
137



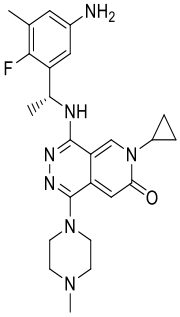
138



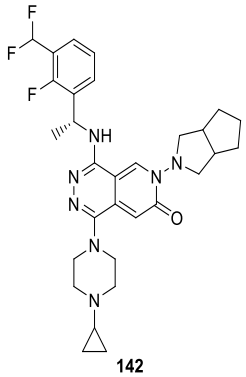
139



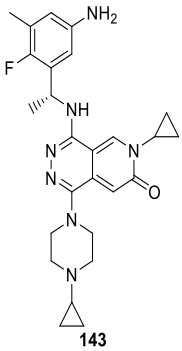
140



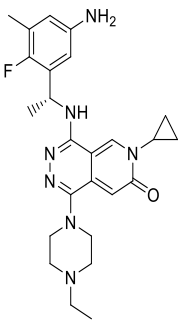
141



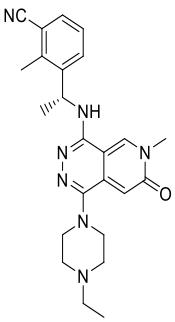
142



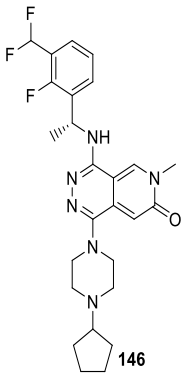
143



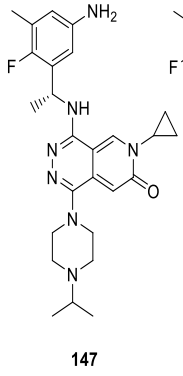
144



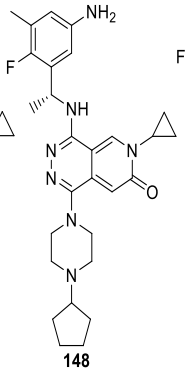
145



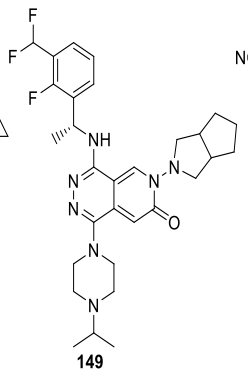
146



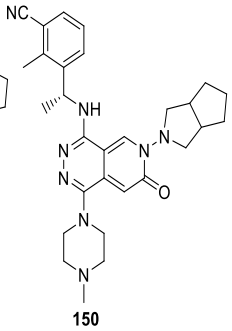
147



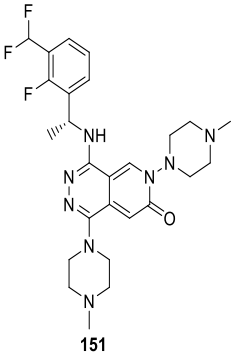
148



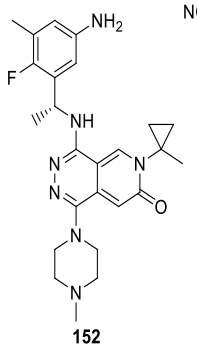
149



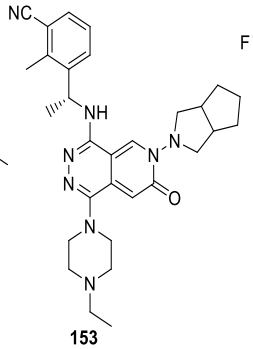
150



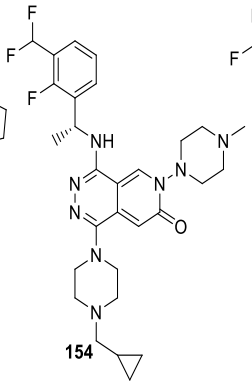
151



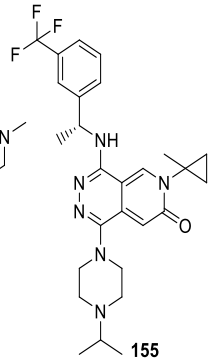
152



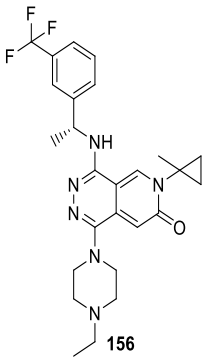
153



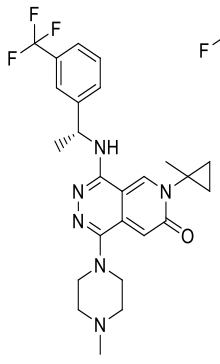
154



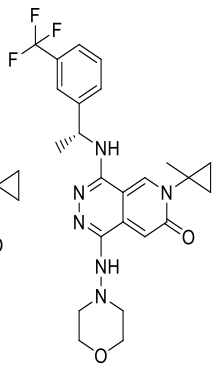
155



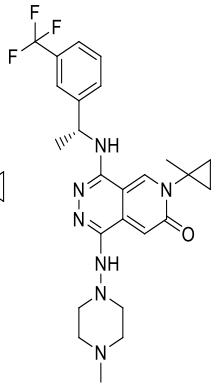
156



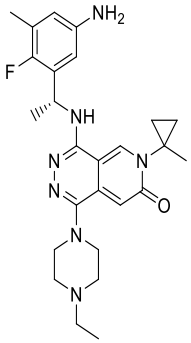
157



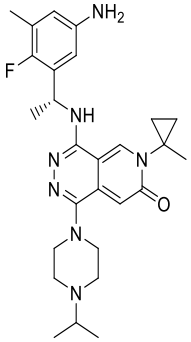
158



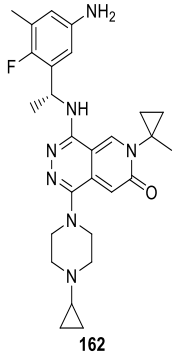
159



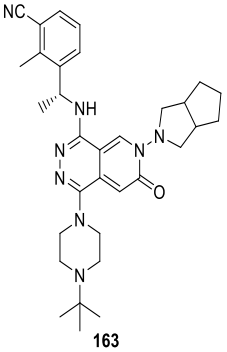
160



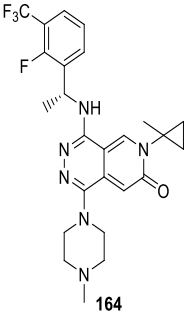
161



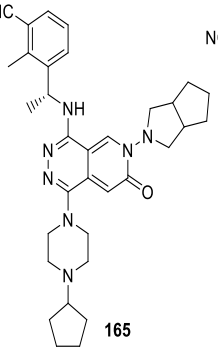
162



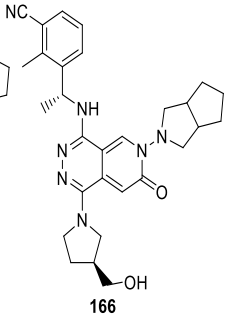
163



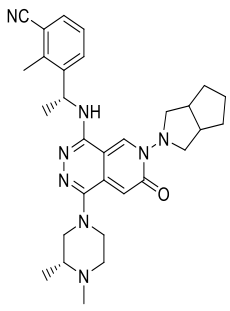
164



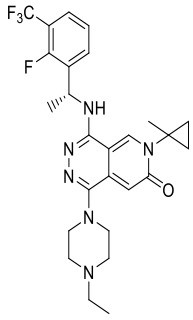
165



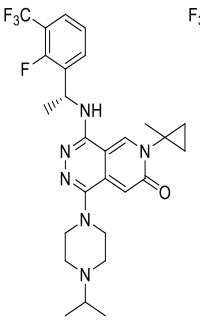
166



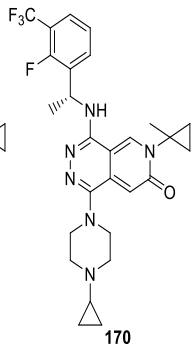
167



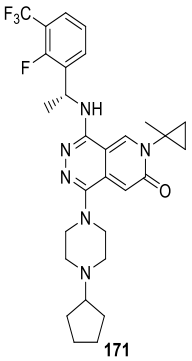
168



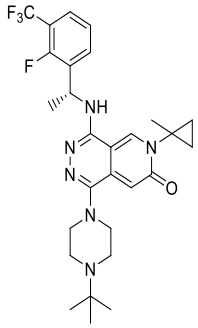
169



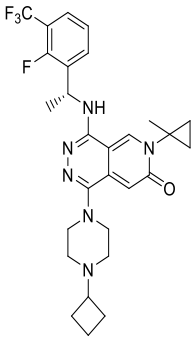
170



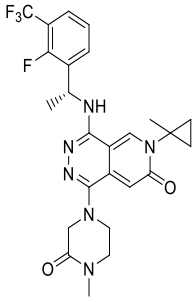
171



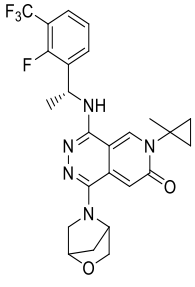
172



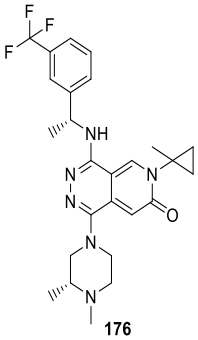
173



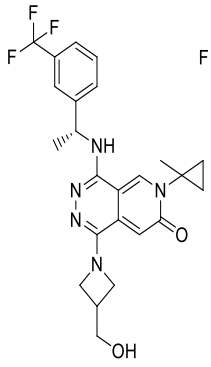
174



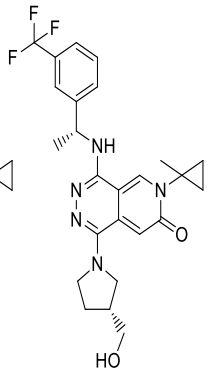
175



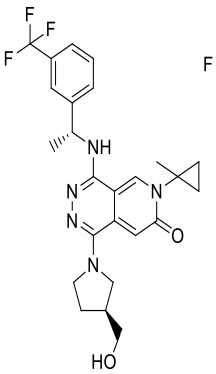
176



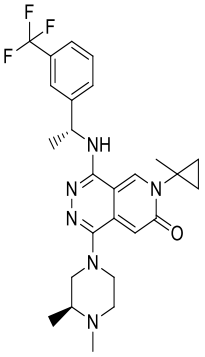
177



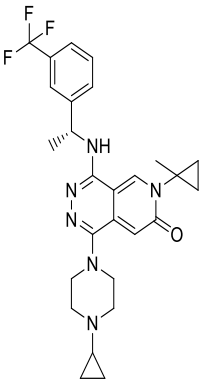
178



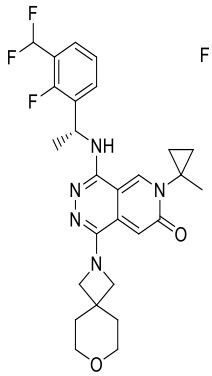
179



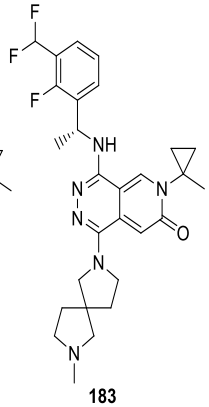
180



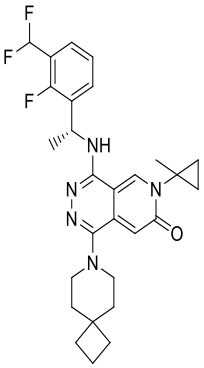
181



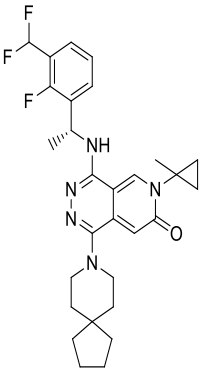
182



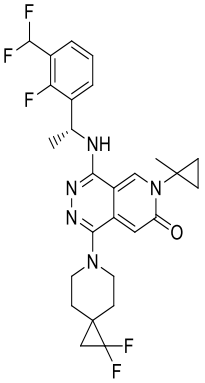
183



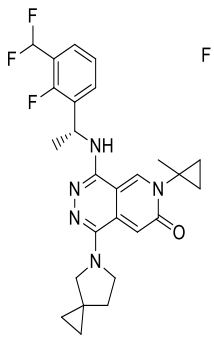
184

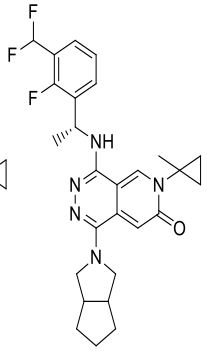


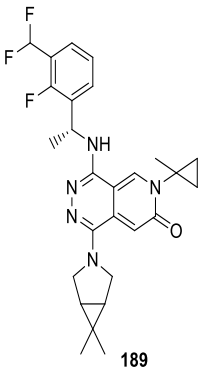
185

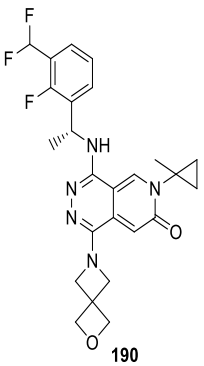


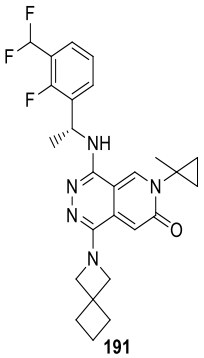
186

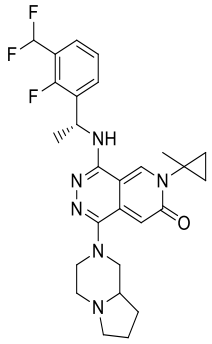

187

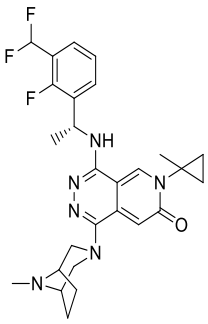

188

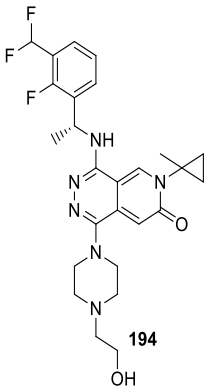

189

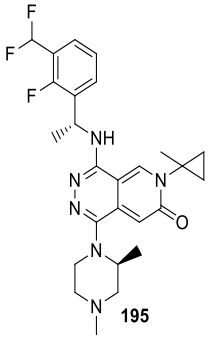

190

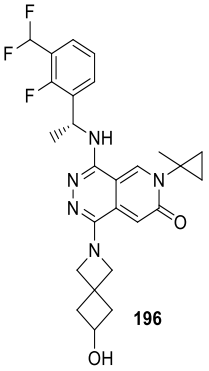

191

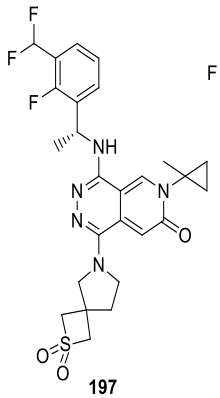

192

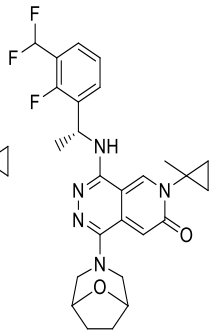

193

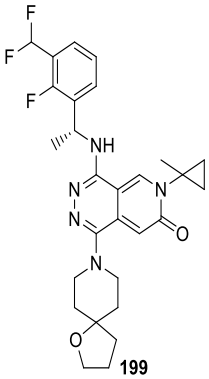

194

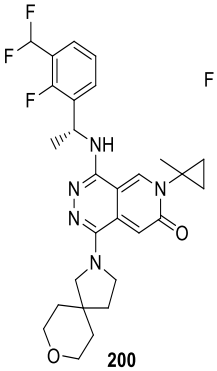

195

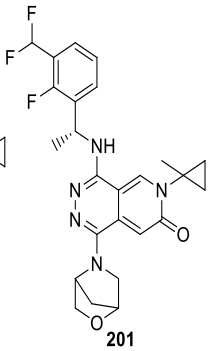

196

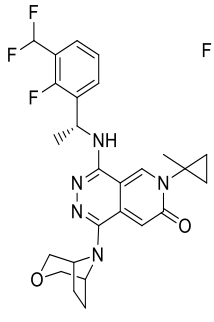

197

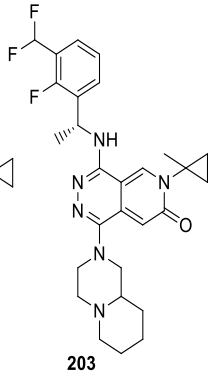

198

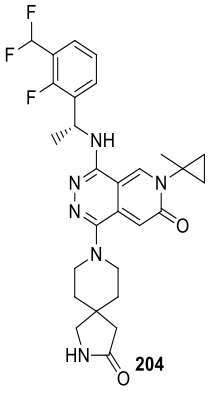

199

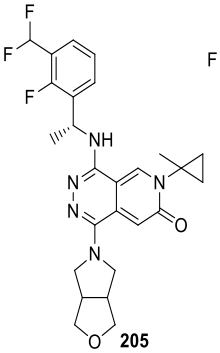

200

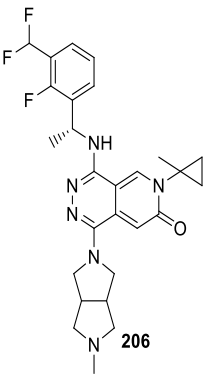

201

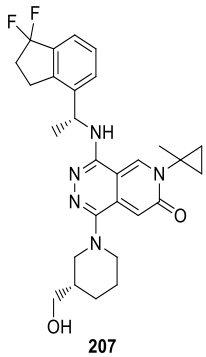

202

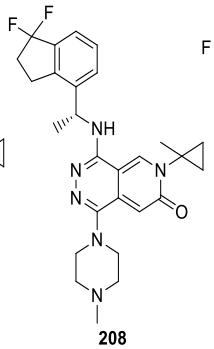

203

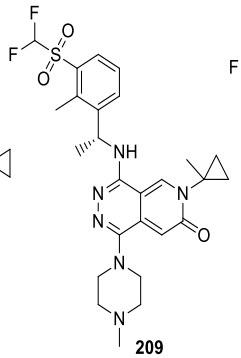

204

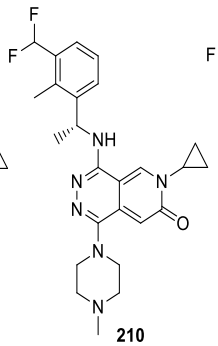

205

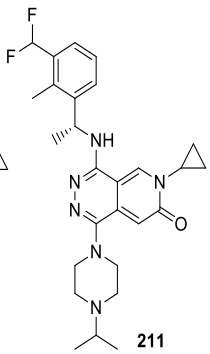

206

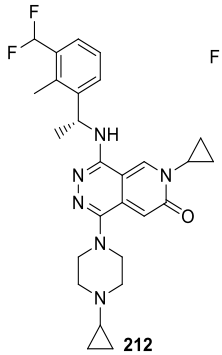

207

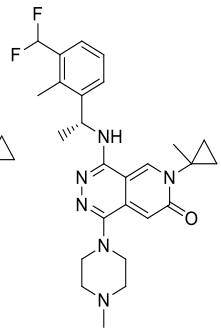

208

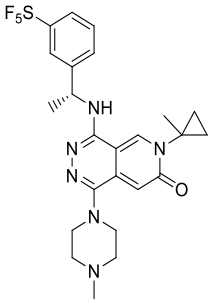

209

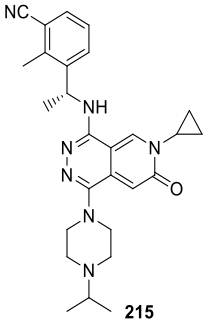

210

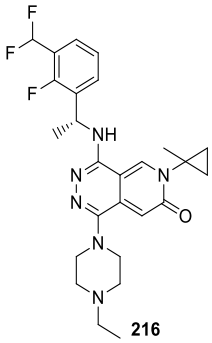

211

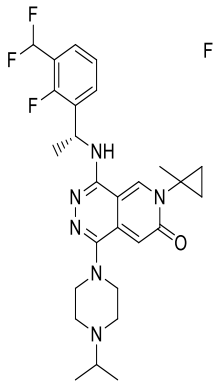

212

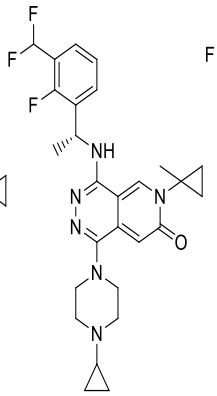

213

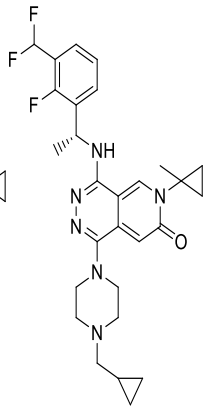

214

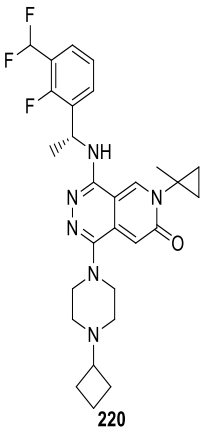

215

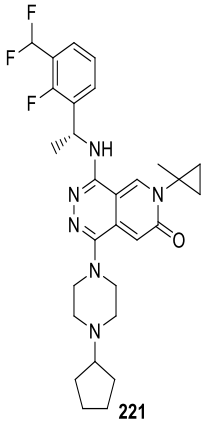

216

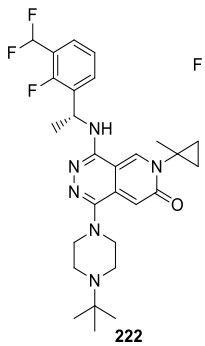

217

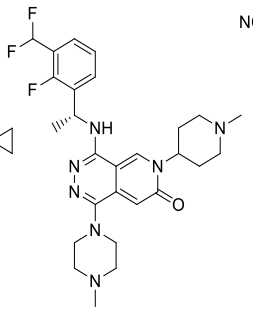

218

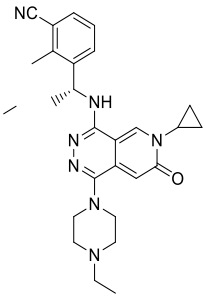

219

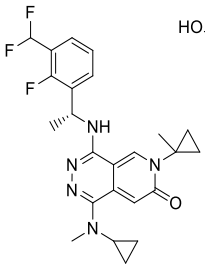

220

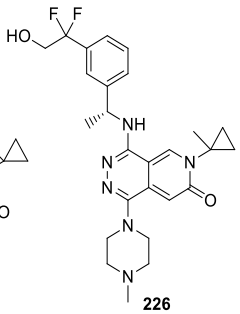

221

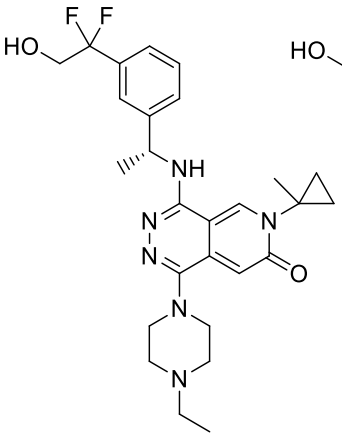

222


223

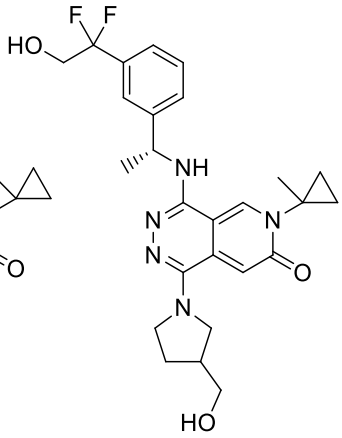

224


225

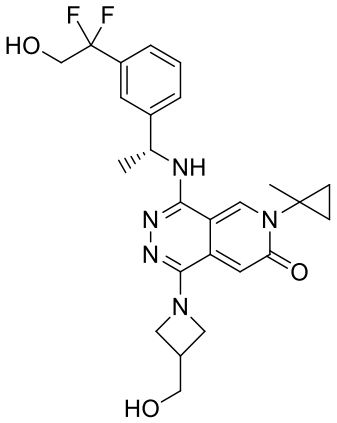

226



227



228



229

12. A pharmaceutical composition, wherein, the pharmaceutical composition comprises the compound according to any one of claims 1-11, or tautomer, stereoisomer, solvate, metabolite, isotopically labeled compound, pharmaceutically acceptable salt or co-crystal thereof, and a pharmaceutically acceptable excipient or an accessory ingredient.

13. Use of the compound according to any one of claims 1-11, or tautomer, stereoisomer, solvate, metabolite, isotopically labeled compound, pharmaceutically acceptable salt or co-crystal thereof, or the pharmaceutical composition according to claim 12 in the manufacture of a medicament for treating a disease mediated by SOS1;

preferably, the disease is selected from: cancer, pathogenic skin rash disease;

preferably, the cancer is selected from: non-small cell lung cancer, lung cancer, pancreatic cancer, ovarian cancer, bladder cancer, prostate cancer, chronic granulocytic leukemia, colorectal cancer, brain cancer, liver cancer, kidney cancer, gastric cancer, and breast cancer;

the pathogenic skin rash disease is selected from: Noonan syndrome, cardiofaciocutaneous syndrome, hereditary gingival fibromatosis type I.

14. The compound according to any one of claims 1-11, or tautomer, stereoisomer, solvate, metabolite, isotopically labeled compound, pharmaceutically acceptable salt or co-crystal thereof, or the pharmaceutical composition according to claim 12, for use in treating a disease mediated by SOS1;

preferably, the disease is selected from: cancer, pathogenic skin rash disease;

preferably, the cancer is selected from: non-small cell lung cancer, lung cancer, pancreatic cancer, ovarian cancer, bladder cancer, prostate cancer, chronic granulocytic leukemia, colorectal cancer, brain cancer, liver cancer, kidney cancer, gastric cancer, and breast cancer;

the pathogenic skin rash disease is selected from: Noonan syndrome, cardiofaciocutaneous syndrome, hereditary gingival fibromatosis type I.