The term "n-membered azaalkylene" refers to a divalent group formed by replacing one or more carbon atoms in the main chain of an n-membered alkylene with nitrogen atom(s), and the two valences described may be on the same atom of the rest of the compound, or on two separate atoms of the rest of the compound. For example, 2-aza-1,3-propylene (-CH2NHCH2-) is an example of 3-membered azaalkylene, and aza-1,2-ethylene (-CH2NH-) is an example of a 2-membered azaalkylene, and the like. An alkylene group in which only branched-chain carbon atom(s) is substituted with nitrogen atom(s) should not be considered "azaalkylene"; for example, in 2-methyl-1,3-propylene, when the branched-chain methyl is replaced by nitrogen, and the resulted group (-CH2CH(NH2)CH2-) should be regarded as 2-amino substituted 1,3-propylene.

The term "isomer" refers to isomers that result from different spatial arrangements of atoms in a molecule. "Stereoisomers" of the compounds described herein refers to all stereoisomers. For example, when the compound has asymmetric carbon atoms, enantiomers and diastereomers are produced; when the compound has carbon-carbon double bonds, carbon-nitrogen double bonds, or ring structures, cis- or trans- isomers are produced. Unless otherwise indicated, the compounds described herein include all isomers thereof, such as optical isomers, geometric isomers, rotational isomers, tautomers, stably existing conformational isomers, and the like; and the compounds may exist as a mixture of isomers or as isolated isomers.

Methods for preparing optically active products from optically inactive starting materials are known in the art, e.g., by resolution of racemic mixtures or by stereoselective synthesis.

Resolution of racemic mixtures of compounds may be carried out by any of a number of methods known in the art. One method involves fractional recrystallization using a chiral resolving acid that is an optically active salt-forming organic acid. Suitable resolving agents for fractional recrystallization may be optically active acids such as D-tartaric acid, L-tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid, camphorsulfonic acid, etc. Other suitable resolving agents for fractional recrystallization include, for example, α-methylbenzylamine, 2-phenylglycinol, cyclohexylethylamine and the like in stereoisomerically pure form.

Methods for resolution of racemic mixtures also include, for example, the separation of diastereomers obtained by reaction with appropriate optically active species such as chiral alcohols or Mosher's acid chlorides, and then conversion (such as hydrolysis) to the corresponding single optical isomer. For example, it may be performed by elution on a chromatographic column packed with an optically active resolving agent. Suitable chromatographic column and elution solvents may be determined by those skilled in the art.

The term "isotope labeled compounds" refers to a compound of the present application in which one or more atoms are replaced by a particular isotopic atom thereof. For example, the isotopic atom in the compound of the present application may include various isotopes of elements H, C, N, O, F, P, S, Cl and I, such as ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{17}O, ^{18}O, ^{18}F, ^{30}P, ^{32}P, ^{35}S, ^{36}S, ^{123}I, ^{124}I and ^{125}I, etc. This application includes various isotope labeled compounds as defined. For example, they may be those compounds in which radioactive isotopes such as ^{3}H and ^{14}C are present, or those in which non-radioactive isotopes such as ^{2}H and ^{13}C are present. Such isotope labeled compounds are suitable for metabolic studies (using ^{14}C), reaction kinetic studies (using e.g, ^{2}H or ^{3}H), detection or imaging techniques such as positron emission tomography (PET) or single photon emission computed tomography (SPECT), including drug or substrate tissue distribution analysis; or radiotherapy for patients, etc.

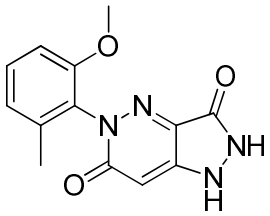
In particular, ^{18}F compounds may be particularly desirable for PET or SPECT studies. Isotope labeled compounds of formula (I) may generally be prepared by conventional techniques known to those skilled in the art or by methods analogous to those described in the accompanying examples and preparations using an appropriate isotope labeled reagent in place of the unlabeled reagents.

Furthermore, substitution with heavier isotopes, especially deuterium (i.e, ^{2}H or D), may

(about 0°C) and dried in vacuo to give 4-hydrazino-1-(2-methoxy-6-methylphenyl)-6-oxo-1,6-dihydropyridazine-3-carbohydrazide (2.06 g, 6.77 mmol) as a yellow solid. Yield: 88%.

ESI-MS: m/z = 305.2 ([M+H]$^+$).

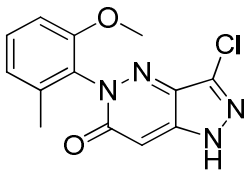
Step 5: Preparation of 5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-3,6(2*H*,5*H*)-dione



4-hydrazino-1-(2-methoxy-6-methylphenyl)-6-oxo-1,6-dihydropyridazine-3-carbohydrazide ~~Methyl 4-hydrazino-1-(2-methoxy-6-methylphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate~~ (2.06 g, 6.78 mmol), glacial acetic acid (2.33 mL, 40.7 mmol) and DIPEA (5.60 mL, 33.9 mmol) were added into n-butanol (20 mL), and heated to 120 °C under nitrogen for 15 hours. The reaction was complete. The reaction mixture was cooled to room temperature and concentrated to dryness. The residue was purified by column chromatography (dichloromethane/methanol: 40/1 to 8/1) to give 5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-3,6(2*H*,5*H*)-dione (1.67 g, 6.14 mmol) as a reddish-brown solid. Yield: 90%.

ESI-MS: m/z = 273.1 ([M+H]$^+$).

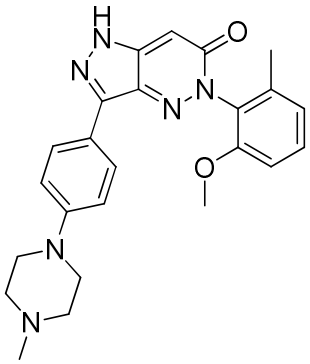
Step 6: Preparation of 3-chloro-5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-6(5*H*)-one



To a solution of 5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-3,6(2*H*,5*H*)-dione ~~5-(2-methoxy-6-methylphenyl)-1,2-dihydro-3*H*-pyrazolo[4,3-c]pyridazine-3,6(5*H*)-dione~~ (200 mg, 0.74 mmol) in acetonitrile (100 mL) was added phosphorus oxychloride (334 uL, 3.67 mmol) and benzyltrimethylammonium chloride (136 mg, 0.74 mmol). The mixture was heated to 70 °C under nitrogen, and stirred for 18 hours. The reaction mixture was cooled to room temperature, and concentrated to dryness. The residue was purified by thin layer chromatography (dichloromethane/methanol: 20/1) to give 3-chloro-5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-6(5*H*)-one (95 mg, 0.33 mmol) as a yellow solid. Yield: 44%.

ESI-MS: m/z = 291.2 ([M+H]$^+$).

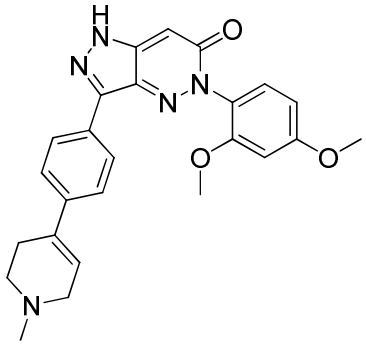
Step 7: Preparation of Compound 2



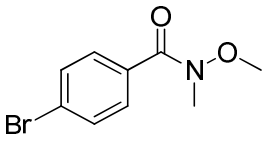
3-Chloro-5-(2-methoxy-6-methylphenyl)-1*H*-pyrazolo[4,3-c]pyridazin-6(5*H*)-one ~~3-Chloro-5-(2-methoxy-6-methylphenyl)-1,5-dihydro-6H-pyrazolo[4,3-c]pyridazin-6-one~~ (50 mg, 0.17 mmol), 4-(4-methyl-1-piperazinyl)phenylboronic acid (76 mg, 0.34 mmol), SPhos-Pd-G2 (10 mg, 0.014 mmol) and potassium phosphate (110 mg, 0.52 mmol) were added to a mixture of 1,4-dioxane (4 mL) and water (1 mL). The mixture was heated to 100° C under nitrogen for 14 hours to complete the reaction. The reaction mixture was cooled to room temperature and concentrated to dryness. The residue was purified by thin layer chromatography (dichloromethane/methanol: 20/1) to give a crude product, which was slurried with methanol (1 mL) in ice-water bath to give compound 2 (61 mg, 0.14 mmol) as a yellow solid. Yield: 82%.

Example 4

Compound 4: 5-(2,4-dimethoxyphenyl)-3-(4-(1-methyl-1,2,3,6-tetrahydropyridin- 4-yl)phenyl)-1*H*-pyrazolo[4,3-c]pyridazin-6(5*H*)-one (Scheme 3A)



Step 1: Preparation of 4-bromo-*N*-methoxy-*N*-methylbenzamide



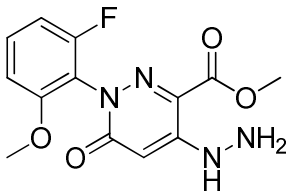
To a solution of 4-bromobenzoyl chloride (5.0 g, 22.8 mmol) in dichloromethane (50 mL) cooled in ice-water bath under nitrogen Was added *N*,*O*-dimethylhydroxylamine hydrochloride (2.667 g, 27.34 mmol) and triethylamine (6.32 mL, 45.6 mmol) successively. The mixture was warmed to room temperature gradually and further stirred for 2 hours. Dilute hydrochloric acid (0.1M, 100 mL) was added to quench the reaction. The reaction mixture was extracted with dichloromethane for three times (100 mL×3). The combined organic phase was washed with brine, dried and filtered. The filtrate was concentrated to dryness under reduced pressure to give 4-bromo-*N*-methoxy-*N*-methylbenzamide (5.46 g, 22.4 mmol) as a yellow oil. Yield: 98%.

ESI-MS: m/z = 244.0 ($[M+H]^+$).

This compound was prepared according to the procedure described in Example 2 (step 3) using methyl 4-hydroxy-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate instead of methyl 4-hydroxy-1-(2-methoxy-6-methylphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate as starting material. Yield: 84%.

ESI-MS: m/z = 313.2 ($[M+H]^+$).

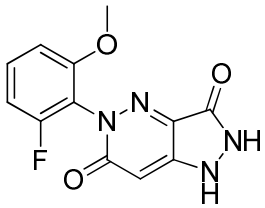
Step 4: Preparation of methyl 4-hydrazino-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate



To a suspension of methyl 4-chloro-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate (4.0 g, 12.8 mmol, 1.0 eq) and DIPEA (8.4 mL, 51.3 mmol, 4.0 eq) in ethanol (40 mL)was added a solution of 98% hydrazine hydrate (785 mg, 15.4 mmol, 1.2 eq) in ethanol (40 mL) at room temperature. After the addition, the mixture was stirred at room temperature for 4 hours. The reaction mixture was diluted with water (150 mL) and extracted with ethyl acetate for three times. The organic phases were combined, washed with brine, dried, filtered and concentrated to dryness. The residue was purified by column chromatography (dichloromethane/methanol: 100/1) to give methyl 4-hydrazino-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate (2.3 g) as a yellow solid. Yield: 59%.

ESI-MS: m/z = 309.1 ($[M+H]^+$).

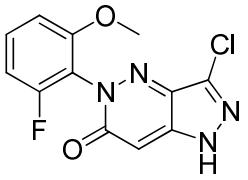
Step 5: Preparation of 5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazine-3,6(2H,5H)-dione



To a solution of methyl 4-hydrazino-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate (1.6 g, 5.19 mmol, 1.0 eq) in a solvent mixture of methanol (15 mL) and tetrahydrofuran (15 mL) was added aqueous solution (15 mL) of lithium hydroxide monohydrate (436 mg, 10.38 mmol, 2.0 eq), and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (dichloromethane/methanol: 15/1) to give –5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazine-3,6(2H,5H)-dione~~methyl 4-hydrazino-1-(2-fluoro-6-methoxyphenyl)-6-oxo-1,6-dihydropyridazine-3-carboxylate~~ (1.4 g) as a brown-red solid. Yield: 99%.

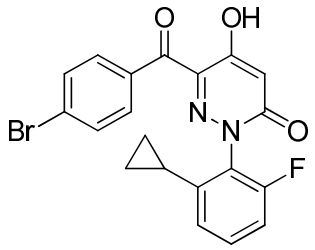
ESI-MS: m/z = 277.2 ($[M+H]^+$).

Step 6: Preparation of 3-chloro-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one



ESI-MS: m/z = 461.0 ([M+H]$^+$).

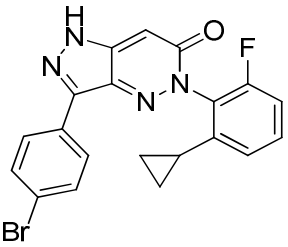
Step 5: Preparation of 6-(4-bromobenzoyl)-2-(2-fluoro-6-cyclopropylphenyl)-5-hydroxypyridazin-3(2H)-one



This compound was prepared according to the procedure described in Example 4 (step 4) using methyl 5-(4-bromophenyl)-4-(2-(2-fluoro-6-cyclopropylphenyl)hydrazinomethylene)-3,5-dioxopentanoate instead of methyl 5-(4-bromophenyl)-4-(2-(2,4-dimethoxyphenyl)hydrazinomethylene)-3,5-dioxopentanoate as the starting material. Yield: 38%.

ESI-MS: m/z = 429.0 ([M+H]$^+$).

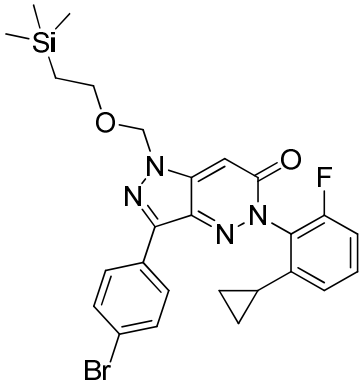
Step 6: Preparation of 3-(4-bromophenyl)-5-(2-fluoro-6-cyclopropylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one



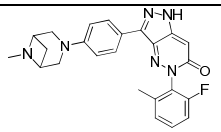
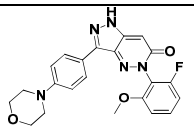
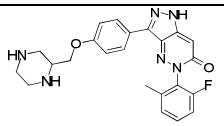
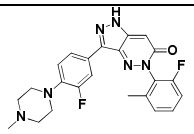
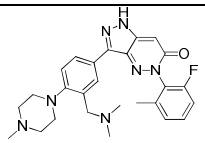
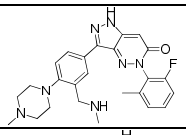
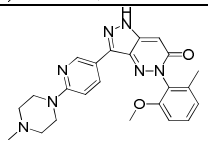
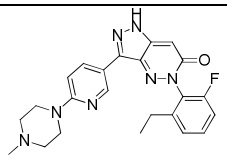
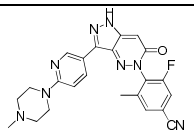
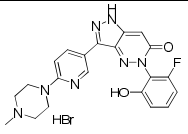
This compound was prepared according to the procedure described in Example 4 (step 5) using 6-(4-bromobenzoyl)-2-(2-fluoro-6-cyclopropylphenyl)-5-hydroxypyridazine-3(2H)-one instead of 6-(4-bromobenzoyl)-2-(2,4-dimethoxyphenyl)-5-hydroxypyridazin-3(2H)-one as starting material. Yield: 71%.

ESI-MS: m/z = 425.1 ([M+H]$^+$).

Step 7: Preparation of 3-(4-bromophenyl)-5-(2-cyclopropyl-6-fluorophenyl)-1-(2-(trimethylsilyl)ethoxymethyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one



To a solution of 3-(4-bromophenyl)-5-(2-fluoro-6-cyclopropylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one (92 mg, 0.22 mmol) in dry N,N-dimethylformamide (5 mL) at 0 °C was added sodium hydride (26 mg, 0.65 mmol) under nitrogen, and the mixture was stirred at 0°C for 20 min. 2-(Trimethylsilyl)ethoxymethyl chloride (111 mg, 0.67 mmol) was then added dropwise,

Example 58	Compound 91		ESI-MS: 431.2 $[M+H]^+$ ^{1}H NMR (400MHz, DMSO-d_6) δ 12.74 (br, 1H), 7.99 (d, J = 9.0 Hz, 2H), 7.52-7.46 (m, 1H), 7.32-7.26 (m, 2H), 6.84 (d, J = 9.0 Hz, 2H), 6.64 (s, 1H), 3.56 (d, J = 5.8 Hz, 2H), 3.47 (d, J = 11.2 Hz, 2H), 3.30-3.27 (m, 2H), 2.42 (q, J = 6.7 Hz, 1H), 2.10 (s, 3H), 1.99 (s, 3H), 1.50 (d, J = 8.2 Hz, 1H).	4
Example 59	Compound 92		ESI-MS: 422.2 $[M+H]^+$ ^{1}H NMR (400MHz, DMSO-d_6) δ 12.81 (s,1H), 7.97 (d, J = 8.8 Hz, H), 7.59-7.53 (m, 1H), 7.12 (d, J = 8.4 Hz, 1H), 7.09-7.04 (m, 3H), 6.63 (s, 1H), 3.78 (s, 3H), 3.73 (t, J = 4.8 Hz, 4H), 3.18 (t, J = 4.8 Hz, 4H).	2A
Example 60	Compound 93		ESI-MS: 435.2 $[M+H]^+$ ^{1}H NMR (400MHz, DMSO-d_6) δ 13.05 (s, 1H), 9.79 (br, 3H), 8.10 (d, J = 8.5 Hz, 2H), 7.54-7.45 (m, 1H), 7.34-7.26 (m, 2H), 7.17 (d, J = 8.6 Hz, 2H), 6.74 (s, 1H), 4.38-4.28 (m, 2H), 4.01-3.92 (m, 1H), 3.66-3.17 (m, 4H), 2.10 (s, 3H).	4
Example 61	Compound 94		ESI-MS: 437.2 $[M+H]^+$ ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.89 (br, 1H), 7.87 (dd, J = 8.4, 2.0 Hz, 1H), 7.75 (dd, J = 14.2, 2.0 Hz, 1H), 7.55 – 7.46 (m, 1H), 7.33 – 7.27 (m, 2H), 7.15 (t, J = 8.9 Hz, 1H), 6.72 (s, 1H), 3.10-3.04 (m, 4H), 2.48-2.43 (m, 4H), 2.21 (s, 3H), 2.10 (s, 3H).	2A
Example 62	Compound 95		ESI-MS: 476.4 $[M+H]^+$ ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.04 (s, 1H), 8.18 (s, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.49 (q, J = 7.0 Hz, 1H), 7.35-7.19 (m, 3H), 6.74 (s, 1H), 3.59 (br, 2H), 3.00 (s, 4H), 2.70 (br, 4H), 2.39 (s, 3H), 2.27 (s, 6H), 2.12 (s, 3H).	2A
Example 63	Compound 96		ESI-MS: 462.4 $[M+H]^+$	2A
Example 64	Compound 97		ESI-MS: 432.2 $[M+H]^+$ 1HNMR (~~DMSO-d6,~~ 400MHz, DMSO-d_6), δ 12.79 (s, 1H), 8.82 (d, J = 2.2 Hz, 1H), 8.12 (dd, J = 9.0, 2.4 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.06 (d, J = 8.2 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H), 6.95 (d, J = 9.0 Hz, 1H), 6.62 (s, 1H), 3.70 (s, 3H), 3.60 – 3.50 (m, 4H), 2.42 – 2.32 (m, 4H), 2.20 (s, 3H), 2.00 (s, 3H).	2A
Example 65	Compound 98		ESI-MS: 434.2 $[M+H]^+$ ^{1}HNMR (400MHz, DMSO-d_6) δ 12.92 (s, 1H), 8.83 (d, J = 2.4 Hz, 1H), 8.14 (dd, J = 9.2, 2.4 Hz, 1H), 7.57-7.51 (m, 1H), 7.33-7.28 (m, 2H), 6.97 (d, J = 9.2 Hz, 1H), 6.71 (s, 1H), 3.59-3.52 (m, 4H), 2.47-2.34 (m, 6H), 2.22 (s, 3H), 1.06 (t, J = 7.6 Hz, 3H).	2A
Example 66	Compound 99		ESI-MS: 445.2 $[M+H]^+$ ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.99 (br, 1H), 8.82 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 9.2 Hz, 1H), 7.89 (s, 1H), 6.96 (d, J = 9.2 Hz, 1H), 6.74 (s, 1H), 3.56 (s, 4H), 2.38 (s, 4H), 2.21 (s, 3H), 2.17 (s, 3H).	2A
Example 67	Compound 100		ESI-MS: 422.1 $[M+H]^+$ ^{1}H NMR (400MHz, DMSO-d_6) δ 12.82 (s,1H), 10.37 (s, 1H), 8.85 (d, J = 2.4 Hz, 1H), 8.14 (dd, J = 8.8, 2.4 Hz, 1H), 7.40-7.33 (m, 1H), 6.97 (d, J = 9.2 Hz, 1H), 6.83-6.89 (m, 2H), 6.64 (s, 1H), 3.60-3.54 (m, 4H),	2A

HPK1	4878 nM	1μL	10 nM	5 nM
1× kinase reaction buffer solution		487μL		

Prepare 4×ATP mixture:

Material	ATP Km	Concentration of Stock Solution	Volume	4×Final Concentration	Final Concentration
ATP	1.669μM	1 mM (125×)	3μL	8μM	2μM
4×kinase reaction buffer solution			372μL		

Procedures:

Dilute the stock solution of the compound to be tested by 5 times with 100% DMSO, make a 4-fold equal dilution in a 96-well dilution plate, add 1 μL of the compound to 49 μL of kinase reaction buffer, and shake on a microplate shaker for 20 minutes. Transfer 2 μL of 2×HPK1 kinase solution to 384 reaction plate, add 1 μL of the test compound ~~(prepared in step (1))~~ to the 384 reaction plate (Greiner, 784075), centrifuge for 1 minute (1000rpm/min), incubate at 25℃ for 10 minutes. Transfer 1 μL of the 4×ATP mixture to a 384 reaction plate, centrifuge for 1 minute (1000 rpm/min), and incubate at 25°C for 60 minutes. In the reaction system, the final concentration of DMSO was 0.5%. Transfer 4 μL of ADP-Glo to a 384 reaction plate, centrifuge for 1 minute (1000 rpm/min), and incubate at 25°C for 40 minutes. Transfer 8 μL detection solution to a 384 reaction plate, centrifuge for 1 minute (1000 rpm/min), and incubate at 25°C for 40 minutes. The fluorescence signal was read using a Biotek multi-function plate reader, and the IC50 (half inhibitory concentration) of the compound was obtained using a four-coefficient nonlinear fitting formula.

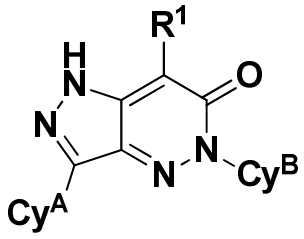
Compounds as shown in the Examples exhibited IC50 values in the following ranges: +++ = IC50 ≤ 50 nM,++ = 50 nM < IC50 ≤ 500 nM,+ = 500 nM < IC50 < 2000 nM.

Table 1 Inhibitory effects of compounds on HPK1 kinase activity

Compound	IC50	Compound	IC50
Compound 1	+++	Compound 123	+++
Compound 2	++	Compound 124	+++
Compound 3	+++	Compound 125	+++
Compound 4	+++	Compound 126	+++
Compound 5	++	Compound 127	+++
Compound 6	+++	Compound 128	+++
Compound 7	++	Compound 129	+++
Compound 8	+++	Compound 130	+++
Compound 9	+++	Compound 131	++
Compound 10	+++	Compound 132	+++
Compound 11	++	Compound 133	+++
Compound 12	+	Compound 134	+++
Compound 13	++	Compound 135	+++
Compound 14	++	Compound 136	+++
Compound 15	+	Compound 137	+++
Compound 16	+	Compound 138	+++
Compound 17	+	Compound 139	+++
Compound 19	+	Compound 140	+++
Compound 20	++	Compound 141	+++
Compound 21	++	Compound 142	+++
Compound 23	+++	Compound 143	+++
Compound 24	+++	Compound 144	+++
Compound 25	++	Compound 145	+++
Compound 26	+	Compound 146	+++

Claims

1. A compound of formula (I) or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof,



(I)

wherein, R^1 is selected from the group consisting of:

1) hydrogen, halogen, cyano, -C(=O)NR^aR^b, -OR^a and -NR^aR^b;

2) C_{1-6} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-8} cycloalkyl and 3- to 8-membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{11};

R^a and R^b are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-6} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} monocyclic cycloalkyl, and 3- to 6-membered aliphatic monocyclic heterocyclyl, unsubstituted or optionally substituted with 1, 2, or 3 substituents independently selected from R^{11}; or

R^a and R^b attached to the same nitrogen atom, together with the nitrogen atom, form a 3-6 membered aliphatic monocyclic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{11};

R^{11} is selected from the group consisting of fluorine, chlorine, cyano, C_{1-3} alkyl and hydroxyl;

Cy^A is selected from 6- to 10-membered aryl or 5- to 10-membered heteroaryl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{12};

R^{12} is selected from the group consisting of:

1) oxo, halogen, cyano, -C(=O)R^{a2}, -C(=O)OR^{a2}, -C(=O)$NR^{a2}R^{b2}$, -C(=NR^{d2})$NR^{a2}R^{b2}$, -OR^{a2}, -OC(=O)R^{a2}, -OC(=O)OR^{c2}, -OC(=O)$NR^{a2}R^{b2}$, -SR^{a2}, -S(=O)R^{c2}, -$S(=O)_2R^{c2}$, sulfonic acid group, -S(=O)$NR^{a2}R^{b2}$, -$S(=O)_2NR^{a2}R^{b2}$, -S(=O)(=NR^{d2})R^{c2}, -$NR^{a2}R^{b2}$, -NR^{a2}C(=O)R^{b2}, -NR^{a2}C(=O)OR^{c2}, -NR^{e2}C(=O)$NR^{a2}R^{b2}$, -NR^{e2}C(=NR^{d2})$NR^{a2}R^{b2}$, -$NR^{a2}S(=O)_2R^{c2}$, -$NR^{e2}S(=O)_2NR^{a2}R^{b2}$, nitro, -$PR^{c2}R^{f2}$, -P(=O)$R^{c2}R^{f2}$ and phosphonic acid group;

2) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, C_{3-12} cycloalkyl and 3- to 12-membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4, 5 or 6 substituents independently selected from R^{22};

3) the two R^{12} substituents attached to two adjacent ring-forming atoms on the aryl or heteroaryl group of Cy^A, respectively, together with the two said ring-forming atoms, form a C_{5-12} alicyclyl or a 5- to 12-membered aliphatic heterocyclyl, unsubstituted or optionally substituted by 1, 2, 3, 4, 5 or 6 substituents independently selected from R^{22};

R^{a2}, R^{b2} and R^{e2} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4, 5 or 6 substituents independently selected from R^{22};

or,

R^{a2} and R^{b2} attached to the same nitrogen atom, together with the nitrogen, form a 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5

substituents independently selected from R^{22};

R^{c2} and R^{f2} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{22};

or,

R^{c2} and R^{f2} attached to the same phosphorous atom, together with the phosphorous, form a 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{22};

R^{d2} is selected from the group consisting of:

1) hydrogen, cyano, nitro and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{22};

R^{22} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a4}$, $-C(=O)OR^{a4}$, $-C(=O)NR^{a4}R^{b4}$, $-C(=NR^{d4})NR^{a4}R^{b4}$, $-OR^{a4}$, $-OC(=O)R^{a4}$, $-OC(=O)OR^{c4}$, $-OC(=O)NR^{a4}R^{b4}$, $-SR^{a4}$, $-S(=O)R^{c4}$, $-S(=O)_2R^{c4}$, sulphonic acid group, $-S(=O)NR^{a4}R^{b4}$, $-S(=O)_2NR^{a4}R^{b4}$, $-S(=O)(=NR^{d4})R^{c4}$, $-NR^{a4}R^{b4}$, $-NR^{a4}C(=O)R^{b4}$, $-NR^{a4}C(=O)OR^{c4}$, $-NR^{e4}C(=O)NR^{a4}R^{b4}$, $-NR^{e4}C(=NR^{d4})NR^{a4}R^{b4}$, $-NR^{a4}S(=O)_2R^{c4}$, $-NR^{e4}S(=O)_2NR^{a4}R^{b4}$, nitro, $-PR^{c4}R^{f4}$, $-P(=O)R^{c4}R^{f4}$, phosphonic acid group, and $=N-R^{d4}$;

2) C_{1-6} alkyl, C_{1-6} alkylene, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

R^{a4}, R^{b4} and R^{e4} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

or,

R^{a4} and R^{b4} attached to the same nitrogen atom, together with the nitrogen, form a 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

R^{c4} and R^{f4} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

or,

R^{c4} and R^{f4} attached to the same phosphorous atom, together with the phosphorous, form a 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

R^{d4} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{32};

R^{32} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a6}$, $-C(=O)OR^{a6}$, $-C(=O)NR^{a6}R^{b6}$, $-C(=NR^{d6})NR^{a6}R^{b6}$, $-OR^{a6}$, $-OC(=O)R^{a6}$, $-OC(=O)OR^{c6}$, $-OC(=O)NR^{a6}R^{b6}$, $-SR^{a6}$, $-S(=O)R^{c6}$, $-S(=O)_2R^{c6}$, sulphonic acid group, $-S(=O)NR^{a6}R^{b6}$, $-S(=O)_2NR^{a6}R^{b6}$, $-S(=O)(=NR^{d6})R^{c6}$, $-NR^{a6}R^{b6}$, $-NR^{a6}C(=O)R^{b6}$, $-NR^{a6}C(=O)OR^{c6}$, $-NR^{e6}C(=O)NR^{a6}R^{b6}$, $-NR^{e6}C(=NR^{d6})NR^{a6}R^{b6}$, $-NR^{a6}S(=O)_2R^{c6}$, -

$NR^{e6}S(=O)_2NR^{a6}R^{b6}$, nitro, $-PR^{c6}R^{f6}$, $-P(=O)R^{c6}R^{f6}$, phosphonic acid group, and $=N-R^{d6}$;

2) C_{1-4} alkyl, C_{1-4} alkylene, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{a6}, R^{b6} and R^{e6} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

or,

R^{a6} and R^{b6} attached to the same nitrogen atom, together with the nitrogen, form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{c6} and R^{f6} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

or,

R^{c6} and R^{f6} attached to the same phosphorous atom, together with the phosphorous, form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{d6} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

Cy^B is selected from the group consisting of 6-10 membered aryl and 5-10 membered heteroaryl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{13};

R^{13} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a3}$, $-C(=O)OR^{a3}$, $-C(=O)NR^{a3}R^{b3}$, $-C(=NR^{d3})NR^{a3}R^{b3}$, $-OR^{a3}$, $-OC(=O)R^{a3}$, $-OC(=O)OR^{c3}$, $-OC(=O)NR^{a3}R^{b3}$, $-SR^{a3}$, $-S(=O)R^{c3}$, $-S(=O)_2R^{c3}$, sulphonic acid group, $-S(=O)NR^{a3}R^{b3}$, $-S(=O)_2NR^{a3}R^{b3}$, $-S(=O)(=NR^{d3})R^{c3}$, $-NR^{a3}R^{b3}$, $-NR^{a3}C(=O)R^{b3}$, $-NR^{a3}C(=O)OR^{c3}$, $-NR^{e3}C(=O)NR^{a3}R^{b3}$, $-NR^{e3}C(=NR^{d3})NR^{a3}R^{b3}$, $-NR^{a3}S(=O)_2R^{c3}$, $-NR^{e3}S(=O)_2NR^{a3}R^{b3}$, nitro, $-PR^{c3}R^{f3}$, $-P(=O)R^{c3}R^{f3}$, and phosphonic acid group ;

2) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, 6-10 membered aryl, 5-10 membered heteroaryl, C_{3-12} cycloalkyl, and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4, 5 or 6 substituents independently selected from R^{23};

3) two R^{13} substituents attached to two adjacent ring-forming atoms of the aryl or heteroaryl of Cy^B respectively, together with the two said ring-forming atoms, form a C_{5-12} aliphatic cyclyl or a 5-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{23};

R^{a3}, R^{b3} and R^{e3} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl, and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4, 5 or 6 substituents independently selected from R^{23};

or,

R^{a3} and R^{b3} attached to the same nitrogen atom, together with the nitrogen, form a 3-12

membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{23};

R^{c3} and R^{f3} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl, and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{23};

or,

R^{c3} and R^{f3} attached to the same phosphorous atom, together with the phosphorous atom, form a 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{23};

R^{d3} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-12} cycloalkyl, and 3-12 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{23};

R^{23} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a5}$, $-C(=O)OR^{a5}$, $-C(=O)NR^{a5}R^{b5}$, $-C(=NR^{d5})NR^{a5}R^{b5}$, $-OR^{a5}$, $-OC(=O)R^{a5}$, $-OC(=O)OR^{c5}$, $-OC(=O)NR^{a5}R^{b5}$, $-SR^{a5}$, $-S(=O)R^{c5}$, $-S(=O)_2R^{c5}$, sulphonic acid group, $-S(=O)NR^{a5}R^{b5}$, $-S(=O)_2NR^{a5}R^{b5}$, $-S(=O)(=NR^{d5})R^{c5}$, $-NR^{a5}R^{b5}$, $-NR^{a5}C(=O)R^{b5}$, $-NR^{a5}C(=O)OR^{c5}$, $-NR^{e5}C(=O)NR^{a5}R^{b5}$, $-NR^{e5}C(=NR^{d5})NR^{a5}R^{b5}$, $-NR^{a5}S(=O)_2R^{c5}$, $-NR^{e5}S(=O)_2NR^{a5}R^{b5}$, nitro, $-PR^{c5}R^{f5}$, $-P(=O)R^{c5}R^{f5}$, phosphonic acid group, and $=N-R^{d5}$;

2) C_{1-6} alkyl, C_{1-6} alkylene, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

R^{a5}, R^{b5} and R^{e5} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

or,

R^{a5} and R^{b5} attached to the same nitrogen atom, together with the nitrogen atom, form a 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

R^{c5} and R^{f5} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

or,

R^{c5} and R^{f5} attached to the same phosphorous atom, together with the phosphorous atom, form a 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

R^{d5} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from R^{33};

R^{33} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a7}$, $-C(=O)OR^{a7}$, $-C(=O)NR^{a7}R^{b7}$, $-C(=NR^{d7})NR^{a7}R^{b7}$, $-OR^{a7}$, $-OC(=O)R^{a7}$, $-OC(=O)OR^{c7}$, $-OC(=O)NR^{a7}R^{b7}$, $-SR^{a7}$, $-S(=O)R^{c7}$, $-S(=O)_2R^{c7}$, sulphonic acid group, $-S(=O)NR^{a7}R^{b7}$, $-S(=O)_2NR^{a7}R^{b7}$, $-S(=O)(=NR^{d7})R^{c7}$, $-NR^{a7}R^{b7}$, $-NR^{a7}C(=O)R^{b7}$, -

$NR^{a7}C(=O)OR^{c7}$, $-NR^{e7}C(=O)NR^{a7}R^{b7}$, $-NR^{e7}C(=NR^{d7})NR^{a7}R^{b7}$, $-NR^{a7}S(=O)_2R^{c7}$, $-NR^{e7}S(=O)_2NR^{a7}R^{b7}$, nitro, $-PR^{c7}R^{f7}$, $-P(=O)R^{c7}R^{f7}$, phosphonic acid group, and $=N-R^{d7}$;

2) C_{1-4} alkyl, C_{1-4} alkylene, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{a7}, R^{b7} and R^{e7} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

or,

R^{a7} and R^{b7} attached to the same nitrogen atom, together with the nitrogen atom, form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{c7} and R^{f7} are each independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

or,

R^{c7} and R^{f7} attached to the same phosphorous atom, together with the phosphorous atom, form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{d7} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl, and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^G is selected from the group consisting of:

1) halogen, oxo, cyano, carboxyl, hydroxyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, nitro, C_{1-4} alkylthio, sulphonic acid group, C_{1-4} alkyl sulfinyl, C_{1-4} alkyl sulfonyl, C_{1-4} alkylaminosulfinyl, and C_{1-4} alkylaminosulfonyl;

2) C_{1-4} alkyl, C_{1-4} alkylene, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from the group consisting of oxo, halogen, hydroxyl, hydroxymethyl, carboxyl, cyano, C_{1-3} alkoxy, amino, C_{1-4} alkylamino, nitro, and sulphonic acid group.

2. The compound according to claim 1, wherein,

R^1 is selected from the group consisting of hydrogen, fluorine, cyano, methyl, ethyl, 1-propyl, isopropyl, cyclopropyl, methoxy, ethoxy and cyclopropyloxy;

Cy^A is selected from the group consisting of phenyl, naphthyl and 5-10 membered heteroaryl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{12}; wherein 5-10 membered heteroaryl contains at least two ring-forming carbon atoms and 1, 2, or 3 ring-forming heteroatoms independently selected from the group consisting of N, O and S;

R^{12} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a2}$, $-C(=O)OR^{a2}$, $-C(=O)NR^{a2}R^{b2}$, $-C(=NR^{d2})NR^{a2}R^{b2}$, $-OR^{a2}$, $-NR^{a2}R^{b2}$, $-NR^{a2}C(=O)R^{b2}$, $-NR^{a2}C(=O)OR^{c2}$, $-NR^{e2}C(=O)NR^{a2}R^{b2}$, $-NR^{e2}C(=NR^{d2})NR^{a2}R^{b2}$, $-NR^{a2}S(=O)_2R^{c2}$ and $-NR^{e2}S(=O)_2NR^{a2}R^{b2}$;

2) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, 6-10 membered aryl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl, 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with

1, 2, 3 or 4 substituents independently selected from R^{22};

3) two R^{12}, together with two adjacent ring-forming atoms of the aryl or heteroaryl in Cy^A to which they are attached respectively, form a C_{4-8} aliphatic cyclyl or 4-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituens independently selected from R^{22};

R^{a2}, R^{b2} and R^{e2} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 subsituents independently selected from R^{22};

or,

R^{a2} and R^{b2}, togehter with the same N atom to which they are attached, form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{22};

R^{c2} is selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{22};

R^{d2} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{22};

R^{22} is selected from the group consisting of:

1) oxo, halogen, cyano, carboxyl, $-C(=O)R^{a4}$, $-C(=O)OR^{a4}$, $-C(=O)NR^{a4}R^{b4}$, $-C(=NR^{d4})NR^{a4}R^{b4}$, $-OR^{a4}$, $-S(=O)_2R^{c4}$, sulphonic acid group, $-S(=O)_2NR^{a4}R^{b4}$, $-S(=O)(=NR^{d4})R^{c4}$, $-NR^{a4}R^{b4}$, $-NR^{a4}C(=O)R^{b4}$, $-NR^{e4}C(=O)NR^{a4}R^{b4}$, $-NR^{e4}C(=NR^{d4})NR^{a4}R^{b4}$, $-NR^{a4}S(=O)_2R^{c4}$, $-NR^{e4}S(=O)_2NR^{a4}R^{b4}$ and $=N-R^{d4}$;

2) C_{1-4} alkyl, C_{1-4} alkylene, phenyl, 5-6 membered heteroaryl, C_{3-7} cycloalkyl and 3-7 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{32};

R^{a4}, R^{b4} and R^{e4} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, phenyl, 5-6 membered heteraryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{32};

or,

R^{a4} and R^{b4}, together with the same N atom to which they are attached, form a 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{32};

R^{c4} is selected from the group consisting of C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{32};

R^{d4} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{32};

R^{32} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a6}$, $-C(=O)OR^{a6}$, $C(=O)NR^{a6}R^{b6}$, $-C(=NR^{d6})NR^{a6}R^{b6}$, $-OR^{a6}$, $-S(=O)_2R^{c6}$, $-S(=O)_2NR^{a6}R^{b6}$, $-S(=O)(=NR^{d6})R^{c6}$, $-NR^{a6}R^{b6}$, $-NR^{a6}C(=O)R^{b6}$, -

$NR^{e6}C(=O)NR^{a6}R^{b6}$, $-NR^{e6}C(=NR^{d6})NR^{a6}R^{b6}$, $-NR^{a6}S(=O)_2R^{c6}$, $-NR^{e6}S(=O)_2NR^{a6}R^{b6}$, and $=N-R^{d6}$;

2) C_{1-4} alkyl, C_{1-4} alkylene, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^G;

R^{a6}, R^{b6} and R^{e6} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, or 3 substituents independently selected from R^G;

or,

R^{a6} and R^{b6} attached to the same nitrogen atom, together with the nitrogen, form a 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, or 3 substituents independently selected from R^G;

R^{c6} is independently selected from the group consisting of C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, or 3 substituents independently selected from R^G;

R^{d6} is selected from the group consisting of:

1) hydrogen, cyano, nitro, and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

Cy^B is selected from the group consisting of phenyl, naphthyl and 5-10 membered heteroaryl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{12}; wherein the 5-10 membered heteroaryl contains at least one ring-forming carbon atom and 1, 2, or 3 ring-forming heteroatoms independently selected from the group consisting of N, O and S;

R^{13} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a3}$, $-C(=O)OR^{a3}$, $-C(=O)NR^{a3}R^{b3}$, $-C(=NR^{d3})NR^{a3}R^{b3}$, $-OR^{a3}$, $-NR^{a3}R^{b3}$, $-NR^{a3}C(=O)R^{b3}$, $-NR^{e3}C(=O)NR^{a3}R^{b3}$, $-NR^{e3}C(=NR^{d3})NR^{a3}R^{b3}$, $-NR^{a3}S(=O)_2R^{c3}$ and $-NR^{e3}S(=O)_2NR^{a3}R^{b3}$;

2) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, 6-10 membered aryl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl, and 3-10 membered aliphatic heterocyclyl;

3) two R^{13}, together with two adjacent ring-forming atoms of the aryl or heteroaryl of Cy^B to which they are attached respectively, form a C_{4-8} aliphatic cyclyl or 4-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{23};

R^{a3}, R^{b3} and R^{e3} are each independently selected from the group consisting of:

1) hydrogen;

2) C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{23};

or,

R^{a3} and R^{b3} together with the same N atom to which they are attached form a 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{23};

R^{c3} is selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{23};

R^{d3} is selected from the group consisting of:

1) hydrogen, cyano, nitro and -S(=O)$_2$R^G;

2) C$_{1-4}$ alkyl, C$_{2-4}$ alkenyl, C$_{2-4}$ alkynyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{23};

R^{23} is selected from the group consisting of:

1) oxo, halogen, cyano, carboxyl, -C(=O)R^{a5}, -C(=O)OR^{a5}, -C(=O)NR^{a5}R^{b5}, -C(=NR^{d5})NR^{a5}R^{b5}, -OR^{a5}, -S(=O)$_2$R^{c5}, sulphonic acid group, -S(=O)$_2$NR^{a5}R^{b5}, -S(=O)(=NR^{d5})R^{c5}, -NR^{a5}R^{b5}, -NR^{a5}C(=O)R^{b5}, -NR^{e5}C(=O)NR^{a5}R^{b5}, -NR^{e5}C(=NR^{d5})NR^{a5}R^{b5}, -NR^{a5}S(=O)$_2$R^{c5}, -NR^{e5}S(=O)$_2$NR^{a5}R^{b5} and =N-R^{d5};

2) C$_{1-6}$ alkyl, C$_{1-6}$ alkylene, phenyl, 5-6 membered heteroaryl, C$_{3-7}$ cycloalkyl and 3-7 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituens independently selected from R^{33};

R^{a5}, R^{b5} and R^{e5} are each independently selected from the group consisting of:

1) hydrogen;

2) C$_{1-4}$ alkyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{33};

or,

R^{a5} and R^{b5} together with the same N atom to which they are linked form a 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substitents independently selected from R^{33};

R^{e5} is selected from the group consisting of C$_{1-4}$ alkyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{33};

R^{d5} is selected from the group consisting of:

1) hydrogen, cyano, nitro and -S(=O)$_2$R^G;

2) C$_{1-4}$ alkyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{33};

R^{33} is selected from the group consisting of:

1) oxo, halogen, cyano, -C(=O)R^{a7}, -C(=O)OR^{a7}, -C(=O)NR^{a7}R^{b7}, -C(=NR^{d7})NR^{a7}R^{b7}, -OR^{a7}, -S(=O)$_2$R^{c7}, -S(=O)$_2$NR^{a7}R^{b7}, -S(=O)(=NR^{d7})R^{c7}, -NR^{a7}R^{b7}, -NR^{a7}C(=O)R^{b7}, -NR^{e7}C(=O)NR^{a7}R^{b7}, -NR^{e7}C(=NR^{d7})NR^{a7}R^{b7}, -NR^{a7}S(=O)$_2$R^{c7}, -NR^{e7}S(=O)$_2$NR^{a7}R^{b7} and =N-R^{d7};

2) C$_{1-4}$ alkyl, C$_{1-4}$ alkylene, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

R^{a7}, R^{b7} and R^{e7} are each independently selected from the group consisting of:

1) hydrogen;

2) C$_{1-4}$ alkyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

or,

R^{a7} and R^{b7} together with the same N atom to which they are attahced form a 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

R^{c7} is selected from the group consisting of C$_{1-4}$ alkyl, C$_{2-4}$ alkenyl, C$_{2-4}$ alkynyl, phenyl, 5-6 membered heteroaryl, C$_{3-6}$ cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

R^{d7} is selected from the group consisting of:

1) hydrogen, cyano, nitro and $-S(=O)_2R^G$;

2) C_{1-4} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl and 3-6 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^G;

R^G is selected from the group consisting of:

1) halogen, oxo, cyano, carboxyl, hydroxyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, sulfonic acid group, C_{1-4} alkylsulfonyl and C_{1-4} alkylaminosulfonyl;

2) C_{1-4} alkyl, C_{1-4} alkylene, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl and 3-8 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, halogen, hydroxyl, hydroxymethyl, carboxyl, cyano, C_{1-3} alkoxy, amino, and C_{1-3} alkylamino;

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

3. The compound according to claim 2, wherein,

R^1 is selected from the group consisting of hydrogen, fluorine, cyano, methyl and methoxy;

Cy^A is selected from phenyl and 5 or 6 membered heteroaryl, unsubstituted or optionally substituted with 1 or 2, or 3 substituents independently selected from R^{12}; wherein 5 or 6 membered heteroaryl contains 1 or 2 heteroatom(s) independently selected from the group consisting of N and S;

Cy^B is selected from phenyl and 5 or 6 membered heteroaryl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{13}; wherein the 5 or 6 membered heteroaryl contains 1, 2, or 3 ring-forming heteroatoms independently selected from the group consisting of N and S;

R^{12} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a2}$, $-C(=O)NR^{a2}R^{b2}$, $-C(=NR^{d2})NR^{a2}R^{b2}$, $-OR^{a2}$, $-NR^{a2}R^{b2}$, $-NR^{a2}C(=O)R^{b2}$, $-NR^{a2}C(=O)OR^{c2}$, $-NR^{e2}C(=O)NR^{a2}R^{b2}$, $-NR^{e2}C(=NR^{d2})NR^{a2}R^{b2}$, $-NR^{a2}S(=O)_2R^{c2}$, and $-NR^{e2}S(=O)_2NR^{a2}R^{b2}$;

2) C_{1-6} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{22};

3) two R^{12}, together with two adjacent ring-forming atoms of the aryl or heteroaryl of Cy^A to which they are connected respectively, form a C_5, C_6, C_7 aliphatic monocyclyl or 5-, 6-, 7-membered aliphatic monoheterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituens independently selected from R^{22};

R^{13} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a3}$, $-C(=O)NR^{a3}R^{b3}$, $-C(=NR^{d3})NR^{a3}R^{b3}$, $-OR^{a3}$, $-NR^{a3}R^{b3}$, $-NR^{a3}C(=O)R^{b3}$, $-NR^{e3}C(=O)NR^{a3}R^{b3}$, $-NR^{e3}C(=NR^{d3})NR^{a3}R^{b3}$, $-NR^{a3}S(=O)_2R^{c3}$, and $-NR^{e3}S(=O)_2NR^{a3}R^{b3}$;

2) C_{1-6} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl and 3-10 membered aliphatic heterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{23};

3) two R^{13}, together with two adjacent ring-forming atoms of the aryl or heteroaryl of Cy^B to which they are connected respectively, form a C_5, C_6, C_7 aliphatic monocyclyl or 5-, 6-, 7-membered aliphatic monoheterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituens independently selected from R^{23};

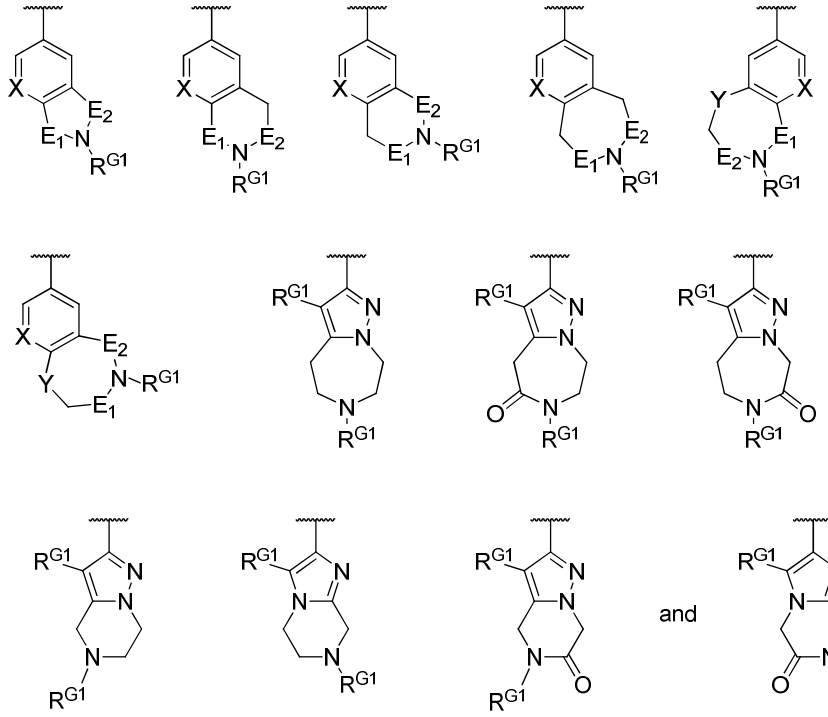
or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

4. The compound according to claim 2, wherein,

R^1 is selected from the group consisting of hydrogen, fluorine, cyano, methyl and methoxy;

Cy^A is selected from the group consisting of:

1) the following structures, wherein the "~~" at the end of the chemical bond in each structure means that the structures is connected to the rest of formula (I) through the bond:



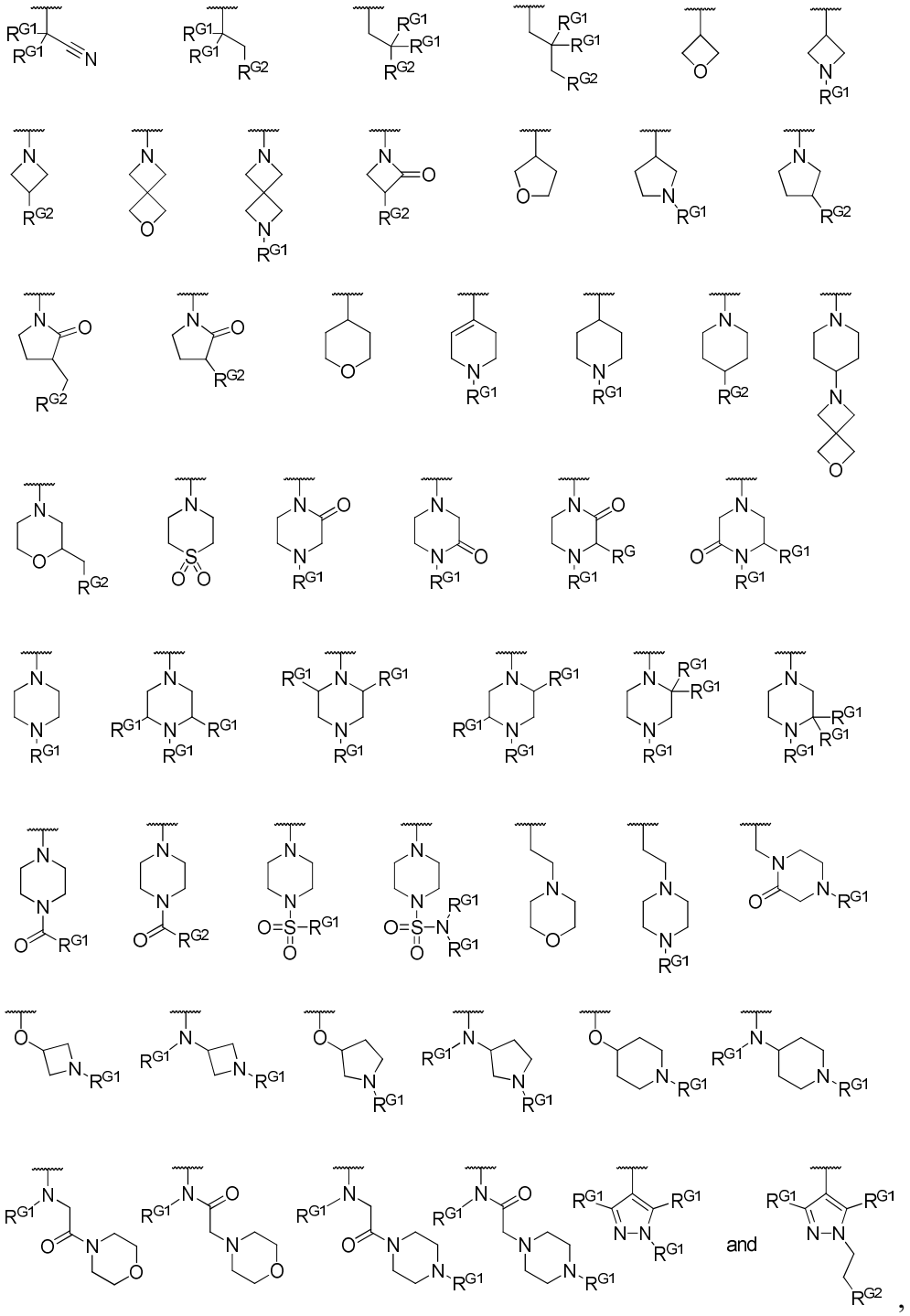
;

2) phenyl, pyridyl, pyrimidyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isoxazolyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{12}; wherein,

(a) each R^{12} is independently selected from the group consisting of fluorine and chlorine; non-hydrogen R^{G1}, and OR^{G1};

or,

(b) Cy^A contains one R^{12}, and the R^{12} is selected from one of the following structures, wherein the "~~" at the end of the chemical bond in each structure means that the structure is connected to the rest of formula (I) through the bond:



or,

Cy^A contains two or three R^{12}, wherein one of R^{12} is selected from the group consisting of the above structures and the others of $R^{12}$are each independently selected from the group consisting of fluorine, chlorine, non-hydrogen R^{G1}, and -OR^{G1};

wherein

X is selected from the group consisting of CH and N;

Y is selected from the group consisting of -CH_2-, NH and O;

E_1 and E_2 are each independently selected from the group consisting of -CH_2- and carbonyl, provided that E_1 and E_2 are not carbonyl simultaneously;

R^{G2} is selected from the group consisting of hydrogen, -OR^{G1} and -$N(R^{G1})_2$;

each R^{G1} is independently selected from the group consisting of:

1) hydrogen, methyl, ethyl, isopropyl, cyclopropyl, 3-oxetanyl and 3-methyl-3-azetidinyl;

2) two R^{G1} attached to the same atom, together with said atom, form a C_{3-6} monocyclyl or 3-6 membered aliphatic monoheterocyclyl;

3) two R^{G1} attached to two different ring-forming atoms of the same monocycle are connected to form a ring structure together with part of the ring-forming atoms of said monocycle, wherein the two connected R^{G1} form a C2, C3 or C4 alkylene;

Cy^B is phenyl, pyridyl, pyrimidyl, pyridazinyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, thienyl, optionally substituted with 1, 2 or 3 substituents independently selected from R^{13};

R^{13} is selected from the group consisting of:

1) oxo, halogen, cyano, $-C(=O)R^{a3}$, $-C(=O)NR^{a3}R^{b3}$, $-C(=NR^{d3})NR^{a3}R^{b3}$, $-OR^{a3}$, $-NR^{a3}R^{b3}$, $-NR^{a3}C(=O)R^{b3}$, $-NR^{e3}C(=O)NR^{a3}R^{b3}$, $-NR^{e3}C(=NR^{d3})NR^{a3}R^{b3}$, $-NR^{a3}S(=O)_2R^{c3}$, and $-NR^{e3}S(=O)_2NR^{a3}R^{b3}$;

2) C_{1-6} alkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} monocyclic cycloalkyl and 3-6 membered aliphatic monoheterocyclyl, unsubstituted or optionally substituted with 1, 2, 3 or 4 substituents independently selected from R^{23};

3) two R^{13}, together with two adjacent ring-forming atoms of the aryl or heteroaryl of Cy^B to which they are connected respectively, form a C_5, C_6, C_7 aliphatic monocyclyl or 5-, 6-, 7-membered aliphatic monocyclic heterocyclyl, unsubstituted or optionally substituted with 1, 2 or 3 substituens independently selected from R^{23};

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

5. The compound according to claim 1, wherein,

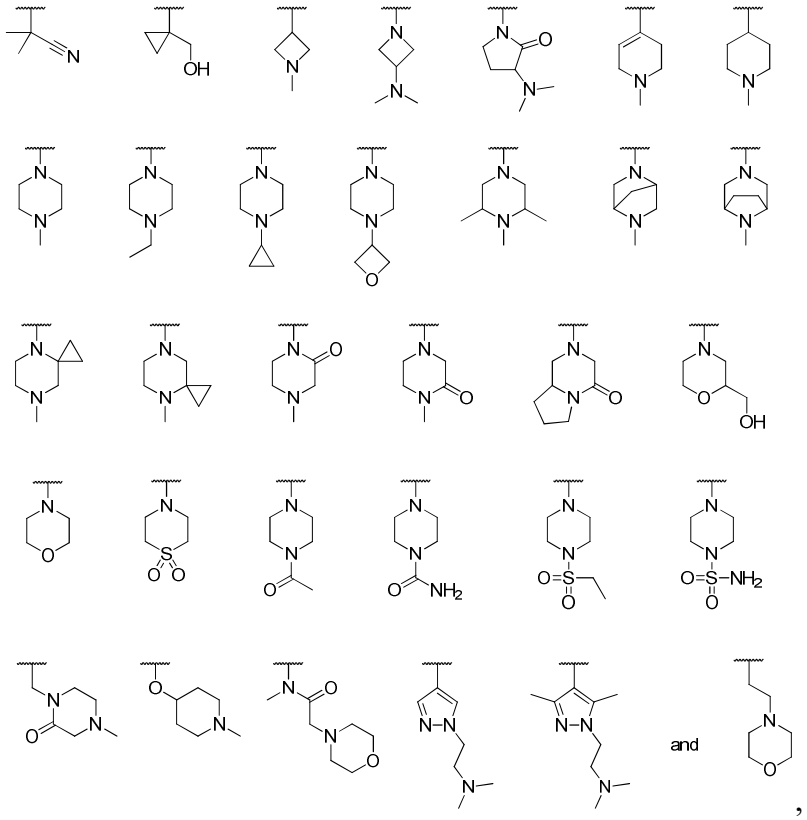
R^1 is selected from the group consisting of hydrogen, fluorine, cyano, methyl and methoxy;

Cy^A is phenyl, pyridyl, pyrimidyl, pyrazolyl, imidazolyl, thiazolyl or isothiazolyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{12}, wherein

1) each R^{12} is independently selected from the group consisting of: fluorine, chlorine; non-hydrogen R^{G1}, and OR^{G1};

or,

2) Cy^A contains one R^{12}, and the R^{12} is selected from one of the following strucutres:



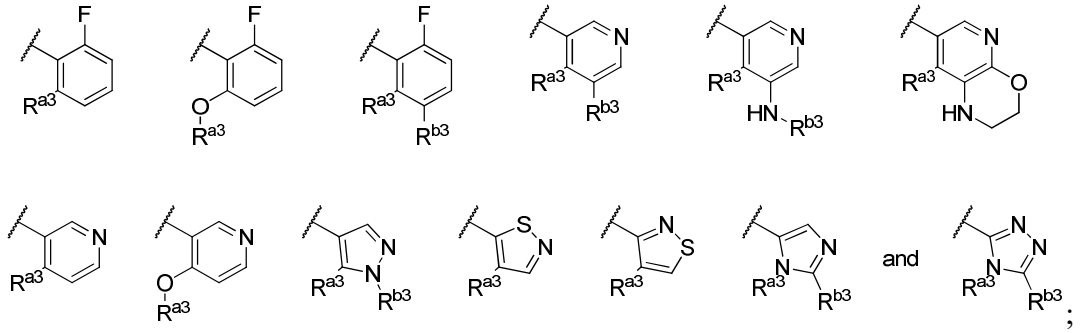
or,

Cy^A contains two or three R^{12}, wherein one of R^{12} is selected from the group consisting of the above structures and others of R^{12} are each independently selected from the group consisting of fluorine, chlorine, non-hydrogen R^{G1}, and $-OR^{G1}$;

each R^{G1} is independently selected from the group consisting of:

1) hydrogen,
2) methyl, ethyl, isopropyl, cyclopropyl, 3-oxetanyl and 3-methyl-3-azetidinyl; optionally substituted with hydroxyl, C_{1-6} alkoxy or amino;

Cy^B is selected from one of the following structures:

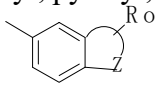
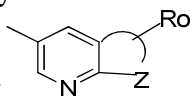


R^{a3} and R^{b3} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{1-6} cycloalkyl, or, two R^{a3} and R^{b3} attached to two adjacent ring-forming atoms respectively, together with said two ring-forming atoms form unsubstituted 5-6 membered aliphatic cyclyl or unsubstituted 5-6 membered aliphatic heterocyclyl;

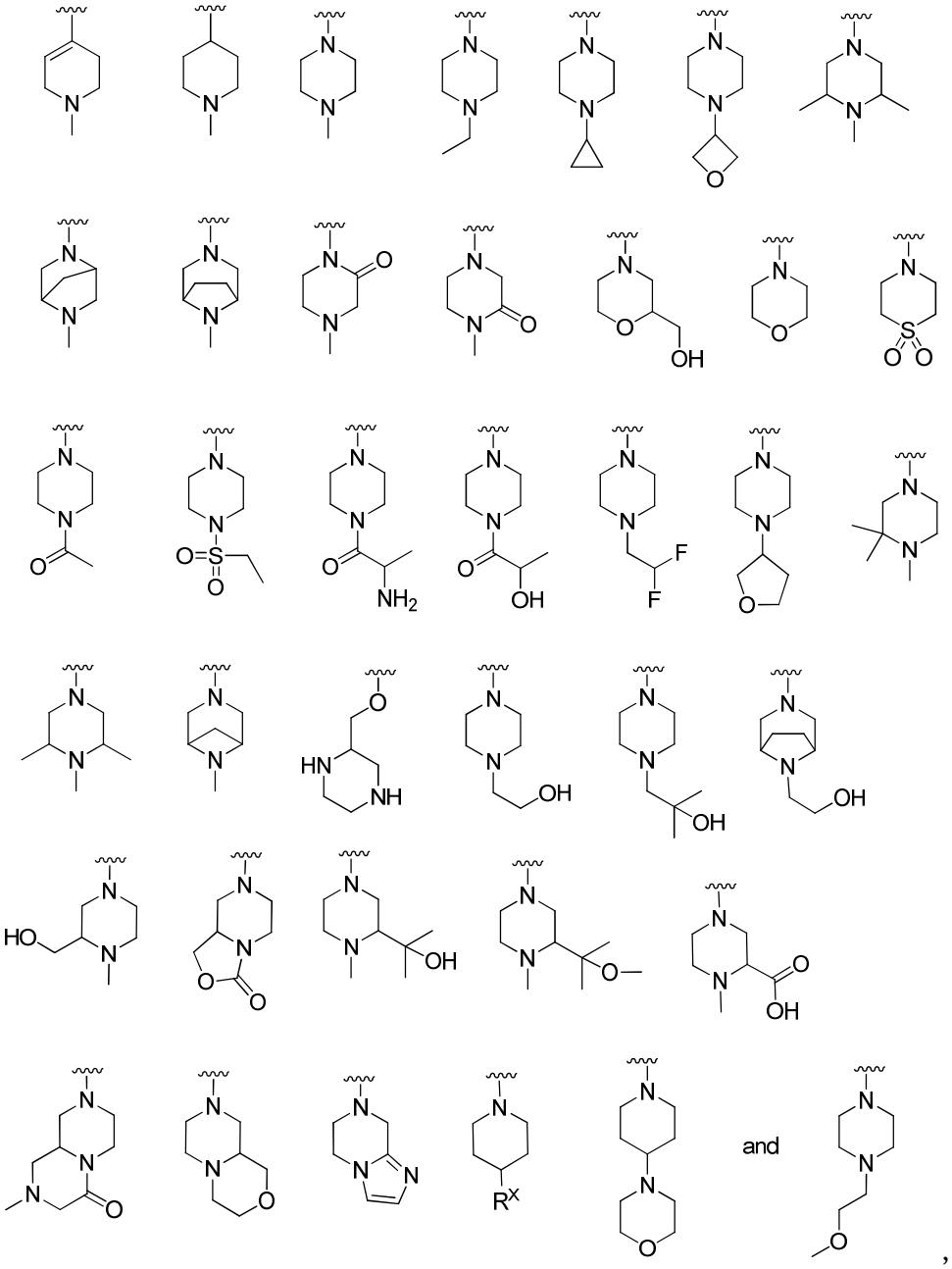
or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

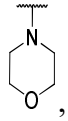
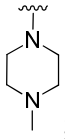
6. The compound according to claim 1, wherein,

R^1 is selected from the group consisting of hydrogen, fluorine, cyano, methyl and methoxy;

Cy^A is phenyl, pyridyl, pyrimidyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl or a bicyclyl represented by  where a phenyl is fused with a 5-7 membered saturated aliphatic heterocyclyl, or a bicyclyl represented by  where a pyridyl is fused with a 5-7 membered saturated aliphatic heterocyclyl; wherein Z represents 1-3 heteroatoms selected from the group consisting of nitrogen and oxygen; when Z=N, N is optionally linked to Ry; Ro is selected from the group consisting of oxo, F, amino, and optionally substituted C_{1-3} alkyl; wherein said aliphatic heterocyclyl may be fused with another 5-6 membered nitrogen-containing saturated aliphatic heterocyclyl to form a fused ring; said phenyl, pyridyl, pyrimidyl, pyrazolyl, imidazolyl, thiazolyl, and isothiazolyl is unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{12}, wherein,

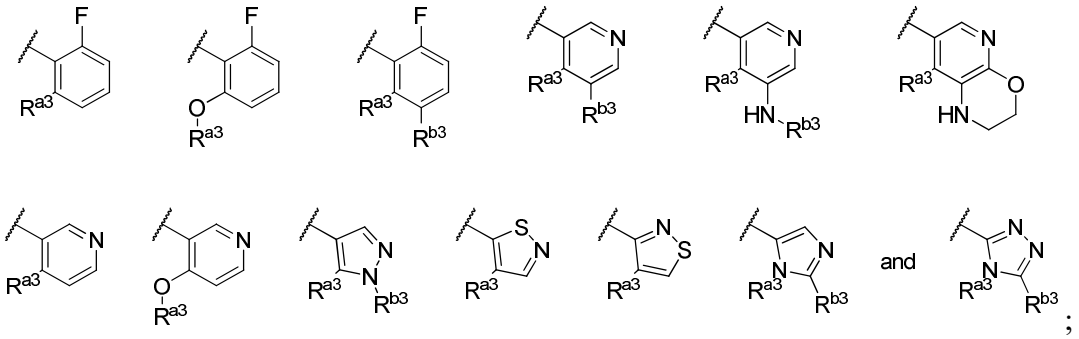
1) when Cy^A contains one R^{12}, the R^{12} is selected from one of the followings:



wherein R^x is selected from the group consisting of -OH, C_{1-6} alkyl, C1-6 alkoxy, $-NH_2$, C_{1-6} alkylamino, , and ;

2) when Cy^A contains more than one R^{12}, the others of R^{12} are each independently selected from the group consisting of fluorine, C_{1-6} alkyl, C_{1-6} alkoxy, and (C_{1-6} alkylamino)methyl;

Cy^B is selected from one of the following structures:



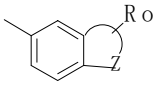
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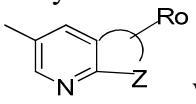
R^{a3} and R^{b3} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{3-6} cycloalkyl, or R^{a3} and R^{b3} together with N atom to which they are attached form a 4-6 membered saturated aliphatic heterocyclyl; said C_{1-6} alkyl, C_{3-6} cycloalkyl, and 4-6 membered saturated aliphatic heterocyclyl is unsubstituted or optionally substituted with substituent(s) selected from the group consisting of fluorine, hydroxyl, C_{1-6} alkyl, and fluoro-substituted C_{1-6} alkyl;

R^y is selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} alkyl substituted with a substituent selected from the group consisting of hydroxyl and halogen, C_{3-6} cycloalkyl, nitrogen-containing 4-6 membered saturated aliphatic heterocyclyl, oxygen-containing 5-6 membered saturated aliphatic heterocyclyl, and -C(=O)Rs; Rs is selected from C_{1-6} alkyl optionally substituted with substituents selected from the group consisting of hydroxyl, amino, and nitrogen-containing aliphatic heterocyclyl;

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

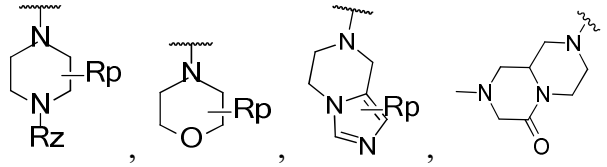
7. The compound according to any of claims 1-6, wherein,

Cy^A is phenyl, pyridyl, pyrimidyl, thiazolyl or a bicyclyl represented by 

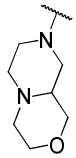
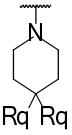
where a phenyl is fused with a 5-7 membered saturated aliphatic heterocyclyl, or a bicyclyl represented by 

where a pyridyl is fused with a 5-7 membered saturated aliphatic heterocyclyl, wherein Z represents 1-3 heteroatoms selected from the group consisting of nitrogen and oxygen; when Z=N, N is optionally linked to Ry; Ro is selected from the group consisting of oxo, F, amino, optionally substituted C1-3 alkyl; wherein said saturated aliphatic heterocyclyl may be fused with another 5-6 membered nitrogen-containing saturated aliphatic heterocyclyl form a fused ring, wherein,

R^y is selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} alkyl substituted with the substituent consisting of hydroxyl and halogen, C_{3-6} cycloalkyl, 4-6 membered N-containing saturated aliphatic heterocyclyl, 5-6 membered O-containing saturated aliphatic heterocyclyl, and -C(=O)Rs, Rs is selected from C_{1-6} alkyl optionally substituted with the group consisting of hydroxyl, amino, and N-containing aliphatic heterocyclyl;

when Cy^A is selected from the group consisting of phenyl, pyridyl, pyrimidyl, and thiazolyl, R^{12} is selected from the group consisting of 

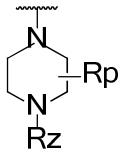
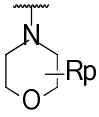
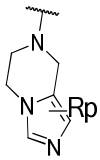
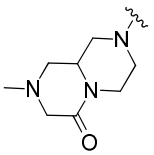
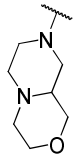
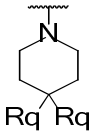
,


, and , wherein Rz is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, 4-6 membered O-containing aliphatic heterocyclyl, and $-S(=O)_2-C_{1-6}$ alkyl; Rp, single or multiple substituent(s), are each optionally selected from the group consisting of hydrogen, and optionally substituted C_{1-6} alkyl; Rq is selected from the group consisting of hydroxyl, amino, optionally substituted C_{1-3} alkyl, spiro heterocyclyl composed of two 4-5 membered nitrogen- and/or oxygen-containing rings, and 5-6 membered aliphatic heterocyclyl containing one or two heteroatoms selected from the group consisting of nitrogen and oxygen, said aliphatic heterocyclyl is optionally substituted with F, and C_{1-3} alkyl;

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

8. The compound according to claim 7, wherein,

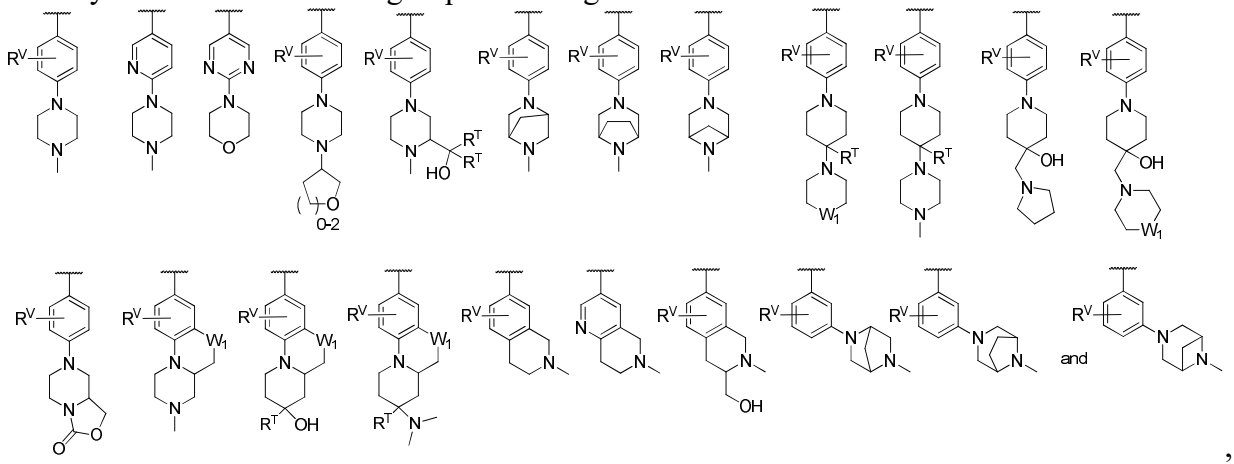
Cy^A is selected from phenyl,

R^{12} is selected from the group consisting of , , , ,

, and , wherein Rz is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, 4-6 membered O-containing aliphatic heterocyclyl, and $-S(=O)_2-C_{1-6}$ alkyl; Rp, single or multiple substituent(s), are each optionally selected from the group consisting of hydrogen, and optionally substituted C_{1-6} alkyl; Rq is selected from the group consisting of hydroxyl, amino, optionally substituted C_{1-3} alkyl, spiro heterocyclyl composed of two 4-5 membered nitrogen and/or oxygen containing rings, and 5-6 membered aliphatic heterocyclyl containing one or two heteroatoms selected from the group consisting of nitrogen and oxygen, said aliphatic heterocyclyl is optionally substituted with F, and C_{1-3} alkyl;

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

9. The compound according to any of claims 1-8, wherein,

Cy^A is selected from the group consisting of:


and ,

wherein, W_1 is selected from CH_2 or oxygen;

R^T is selected from hydrogen or methyl;

R^V is selected from fluorine or methyl, the number of R^V is 0, 1 or 2;

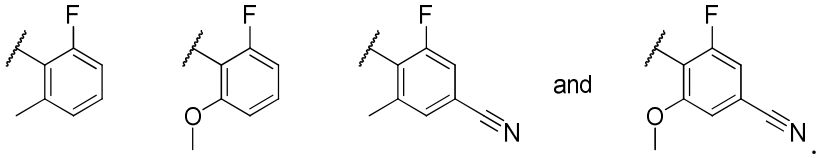
or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

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

Cy^B is selected from phenyl optionally substituted with a group selected from the group consisting of H, F, -CN, optionally substituted C_{1-3} alkyl, optionally substituted C_{1-3} alkoxy, optionally substituted C_{3-6} cycloalkoxy and $C(=O)NR^{a3}R^{b3}$, wherein R^{a3} and R^{b3} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and optionally substituted C_{3-6} cycloalkyl, or R^{a3} and R^{b3} together with the N atom to which whihch they attached form an optionally substituted 4-5 membered alicyclic heterocyclyl;

or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

11. The compound according to any of claims 1-10, wherein, Cy^B is selected from the group consisting of:



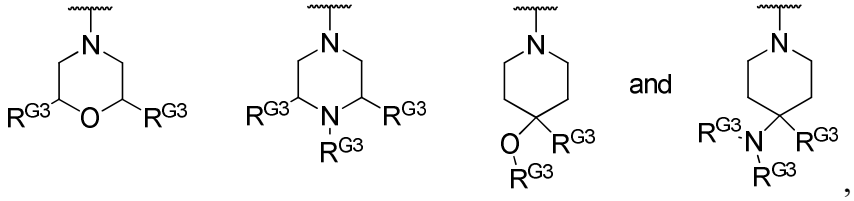
12. The compound according to claim 1, wherein,

R^1 is H;

Cy^A is selected from the group consisting of:

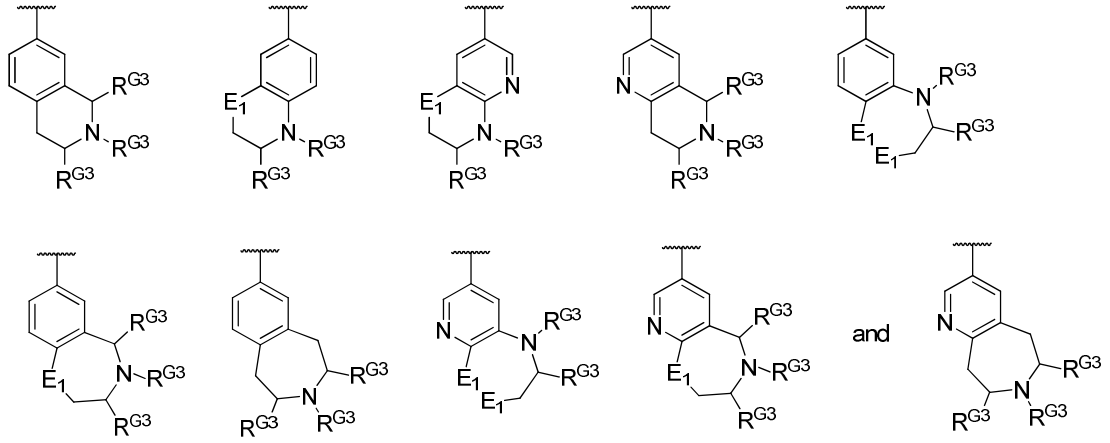
1) phenyl, pyridyl, and pyrimidyl, unsubstituted or optionally substituted with 1, 2 or 3 substituents independently selected from R^{12}; each R^{12} is independently selected from the group consisting of fluorine, chlorine, non-hydrogen R^{G1}, and OR^{G1};

2) phenyl, pyridyl, and pyrimidyl, optionally substituted with 1, 2 or 3 substituents independently selected from R^{12}; one of R^{12} is selected from the group consisting of:



and other R^{12} are each independently selected from the group consisting of: fluorine, chlorine; non-hydrogen R^{G1}, and OR^{G1};

3) the following structure:



wherein the phenyl or pyridyl is unsubstituted or optionally substituted with 1 or 2 substituents independently selected from R^{12};

Cy^B is selected from



wherein

R^{a3} is selected from the group consisting of methyl, ethyl, difluoromethyl, trifluoromethyl, isopropyl and cyclopropyl; preferably selected from methyl, or ethyl;

E^1 is independently selected from the group consisting of $-CH_2-$ and oxygen;

~~R^{G3}~~-R^{G1} is selected from the group consisting of hydrogen, oxo, methyl, ethyl, isopropyl, cyclopropyl, 3-oxetanyl and 3-methyl-3-azetidinyl;

R^{13} is selected from the group consisting of hydrogen, fluorine, cyano and $-C(=O)-N(R^{G3})_2$; preferably selected from the group consisting of hydrogen and cyano;

each R^{G3} is independently selected from the group consisting of:

1) hydrogen, methyl, ethyl, isopropyl, cyclopropyl, oxetanyl, oxacyclopentyl, azetidinyl, and azacyclopentyl;

2) two R^{G3} connected to the same atom, together with said atom, form a C_{3-6} monocyclyl or a 3-6 membered aliphatic monoheterocyclyl;

3) two R^{G3} respectively connected to two different ring-forming atoms on the same single ring are connected to form a ring structure together with part of the ring-forming atoms of said single ring, and the two connected R^{G3} form a C_2, C_3 or C_4 alkylene, or a 2-, 3- or 4-membered oxaalkylene, or a 2-, 3- or 4-membered azaalkylene;

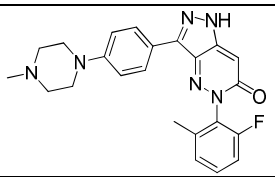
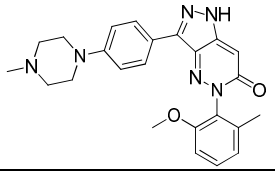
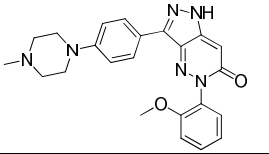
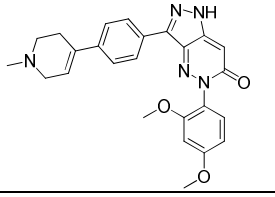
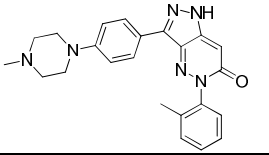
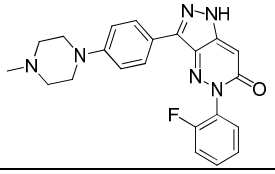
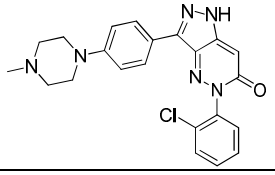
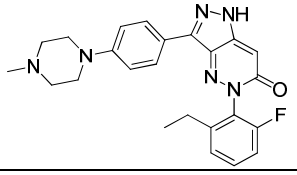
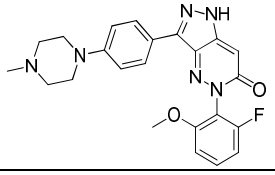
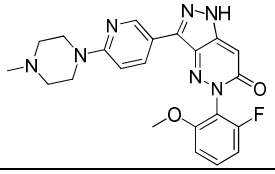
and, when R^{G3} is not hydrogen, R^{G3} is unsubstituted or independently substituted with 1, 2 or 3 substituents optionally selected from the group consisting of oxo, fluorine, hydroxyl, methoxy, amino, methylamino, dimethylamino, methyl, ethyl, and cyano;

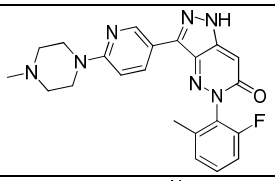
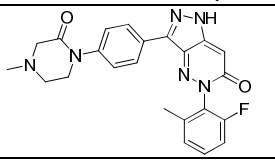
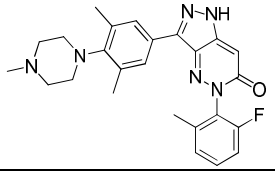
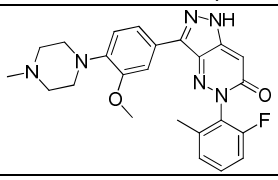
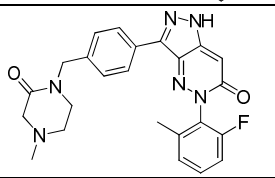
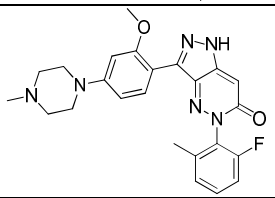
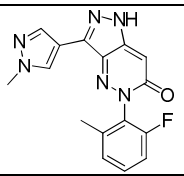
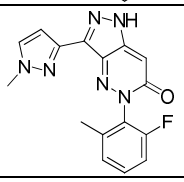
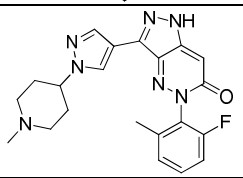
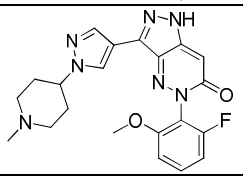
or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

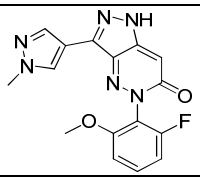
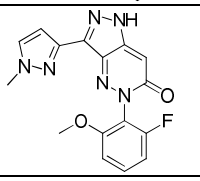
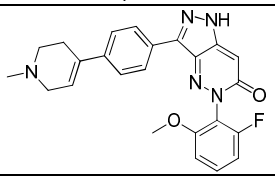
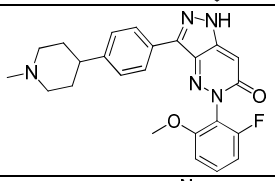
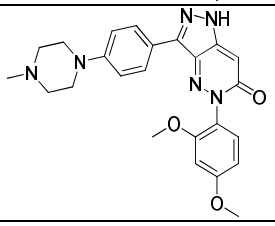
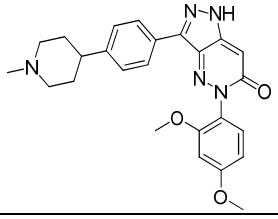
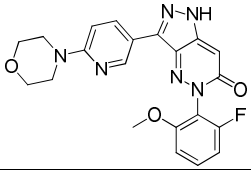
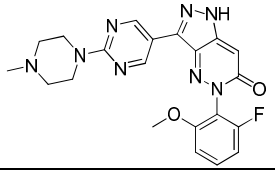
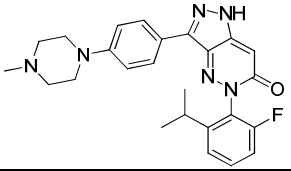
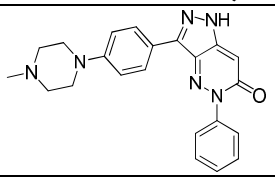
13. The compound according to any of claims 1-12, wherein, when Cy^A is phenyl, and R^{12} is heterocyclyl, R^{12} is attached to para- or meta- position of the phenyl; or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof.

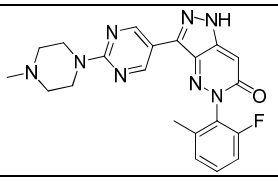
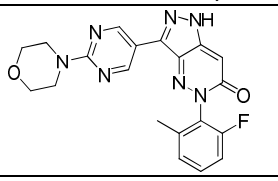
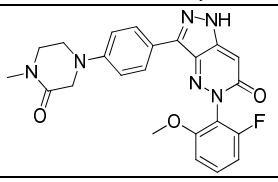
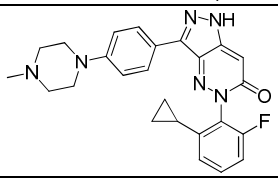
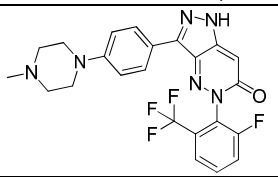
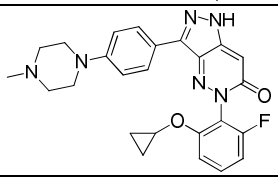
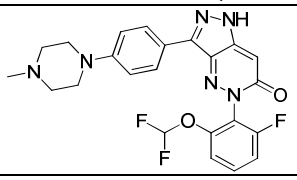
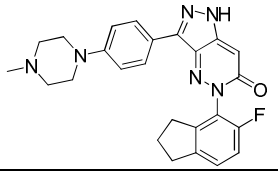
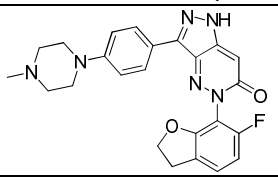
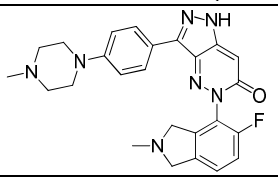
14. The compound according to claim 1, wherein the compound is selected from:

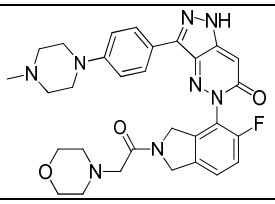
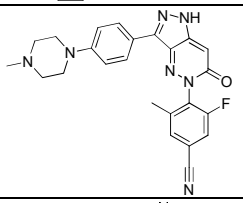
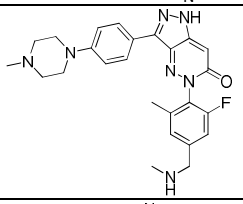
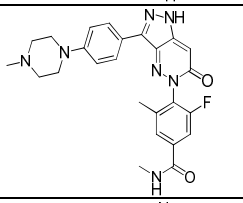
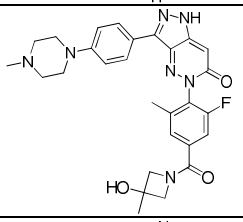
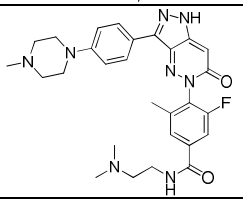
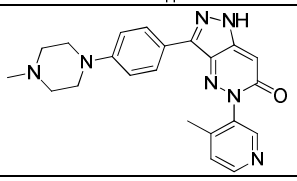
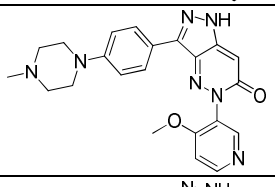
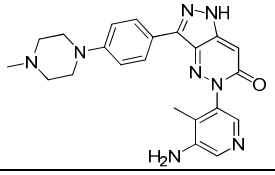
Compound	Structural Formula	Name of Compound

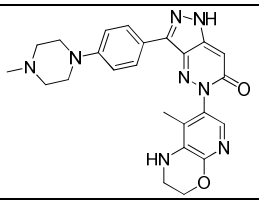
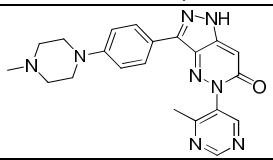
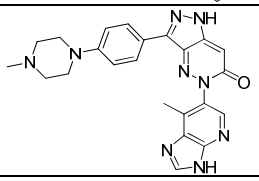
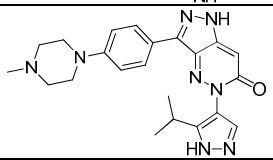
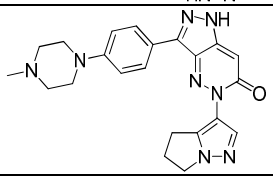
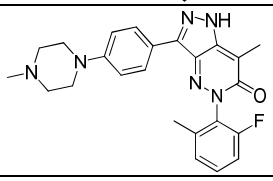
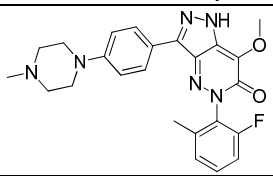
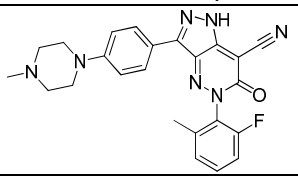
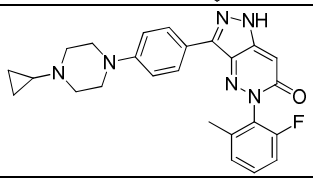
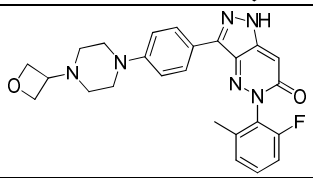
Compound 1		5-(2-fluoro-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 2		5-(2-methoxy-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 3		5-(2-methoxyphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 4		5-(2,4-dimethoxyphenyl)-3-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 5		5-(2-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 6		5-(2-fluorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 7		5-(2-chlorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 8		5-(2-ethyl-6-fluorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 9		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 10		5-(2-fluoro-6-methoxyphenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

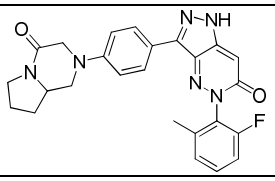
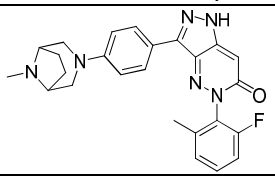
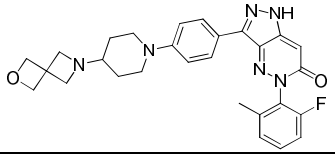
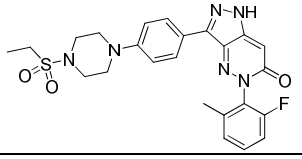
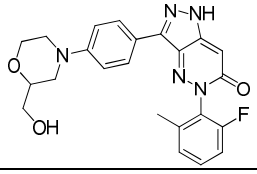
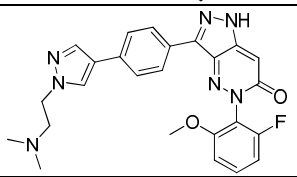
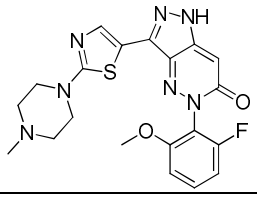
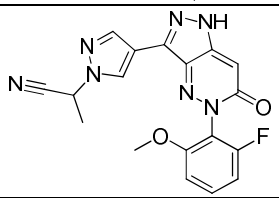
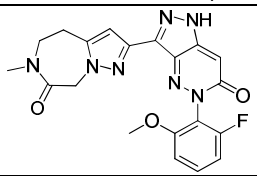
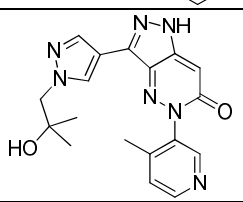
Compound 11		5-(2-fluoro-6-methylphenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 12		5-(2-fluoro-6-methylphenyl)-3-(4-(4-methyl-2-oxopiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 13		3-(3,5-dimethyl-4-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 14		5-(2-fluoro-6-methylphenyl)-3-(3-methoxy-4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 15		5-(2-fluoro-6-methylphenyl)-3-(4-((4-methyl-2-oxo-piperazin-1-yl)methyl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 16		5-(2-fluoro-6-methylphenyl)-3-(2-methoxy-4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 17		5-(2-fluoro-6-methylphenyl)-3-(1-methyl-*1H*-pyrazol-4-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 18		5-(2-fluoro-6-methylphenyl)-3-(1-methyl-*1H*-pyrazol-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 19		5-(2-fluoro-6-methylphenyl)-3-(1-(1-methylpiperidin-4-yl)-*1H*-pyrazol-4-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 20		5-(2-fluoro-6-methoxyphenyl)-3-(1-(1-methylpiperidin-4-yl)-*1H*-pyrazol-4-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

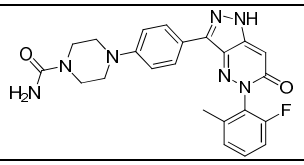
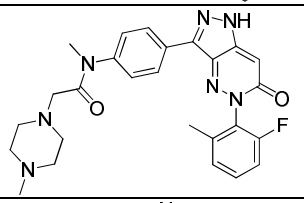
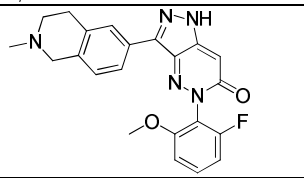
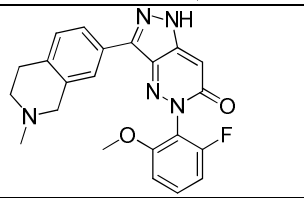
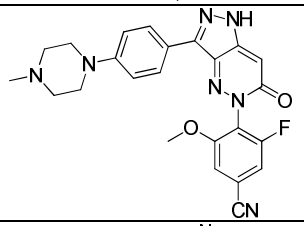
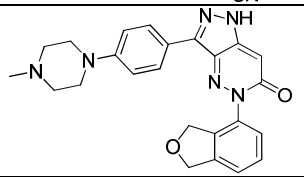
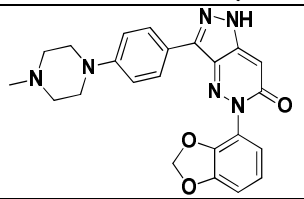
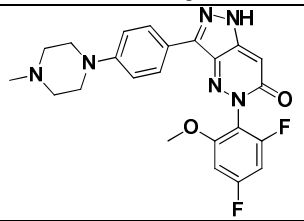
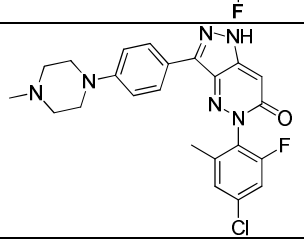
Compound 21		5-(2-fluoro-6-methoxyphenyl)-3-(1-methyl-*1H*-pyrazol-4-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 22		5-(2-fluoro-6-methoxyphenyl)-3-(1-methyl-*1H*-pyrazol-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 23		5-(2-fluoro-6-methoxyphenyl)-3-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 24		5-(2-fluoro-6-methoxyphenyl)-3-(4-(1-methylpiperidin-4-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 25		5-(2,4-dimethoxyphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 26		5-(2,4-dimethoxyphenyl)-3-(4-(1-methylpiperidin-4-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 27		5-(2-fluoro-6-methoxyphenyl)-3-(6-morpholinopyrid-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 28		5-(2-fluoro-6-methoxyphenyl)-3-(2-(4-methylpiperazin-1-yl)pyrimidin-5-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 29		5-(2-fluoro-6-isopropylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 30		3-(4-(4-methylpiperazin-1-yl)phenyl)-5-phenyl-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

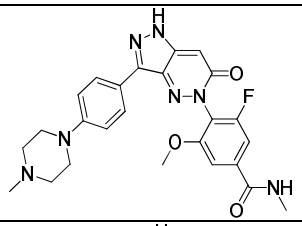
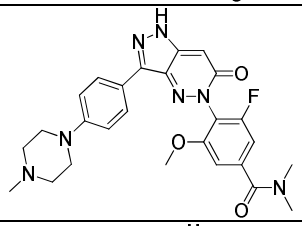
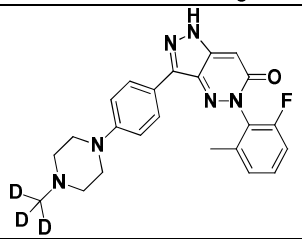
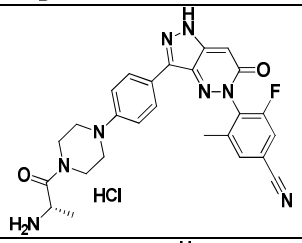
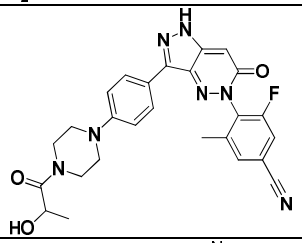
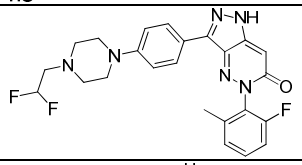
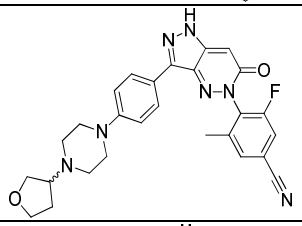
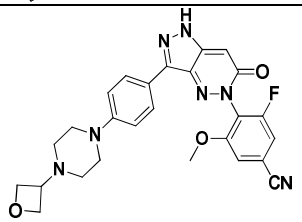
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Compound 32		5-(2-fluoro-6-methylphenyl)-3-(2-morpholinyl pyrimidin-5-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 33		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-methyl-3-oxopiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 34		5-(2-cyclopropyl-6-fluorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 35		5-(2-fluoro-6-(trifluoromethyl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 36		5-(2-cyclopropoxy-6-fluorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 37		5-(2-(difluoromethoxy)-6-fluorophenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 38		5-(5-fluoro-2,3-dihydro-*1H*-indan-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 39		5-(6-fluoro-2,3-dihydrobenzofuran-7-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 40		5-(5-fluoro-2-methylisoindolin-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

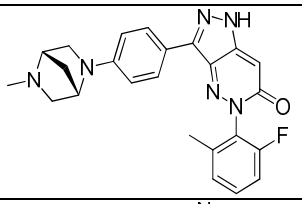
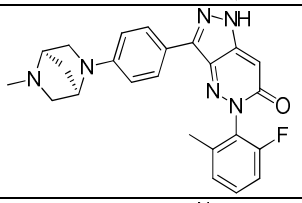
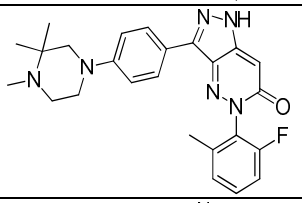
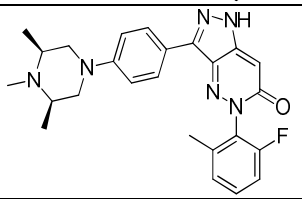
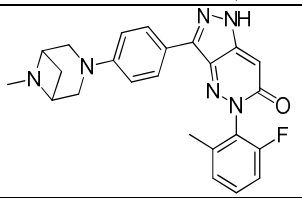
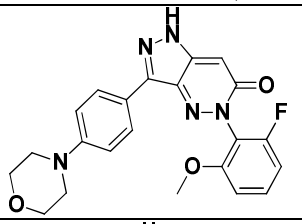
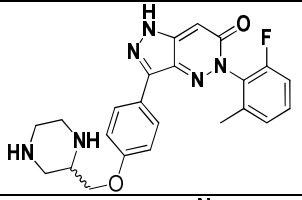
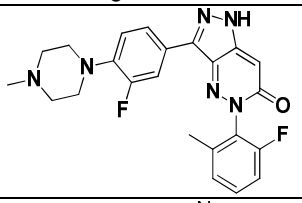
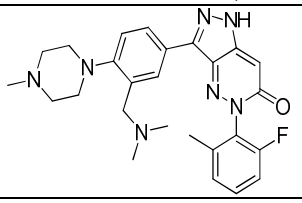
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Compound 42		3-fluoro-5-methyl-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-*1H*-pyrazolo[4,3-c]pyridazin-5(*6H*)-yl)benzonitrile
Compound 43		5-(2-fluoro-6-methyl-4-((methylamino)methyl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1*H*-pyrazolo[4,3-c]pyridazin-6(5*H*)-one
Compound 44		3-fluoro-*N*,5-dimethyl-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-*1H*-pyrazolo[4,3-c]pyridazin-5(*6H*)-yl)benzamide
Compound 45		5-(2-fluoro-4-(3-hydroxyl-3-methylazetidine-1-carbonyl)-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 46		*N*-(2-(dimethylamino)ethyl)-3-fluoro-5-methyl-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-*1H*-pyrazolo[4,3-c]pyridazin-5(*6H*)-yl)benzamide
Compound 47		3-(4-(4-methylpiperazin-1-yl)phenyl)-5-(4-methylpyrid-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 48		5-(4-methoxypyrid-3-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 49		5-(5-amino-4-methylpyrid-3-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

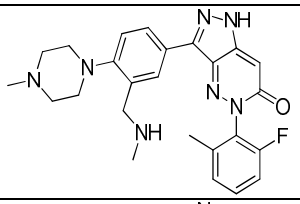
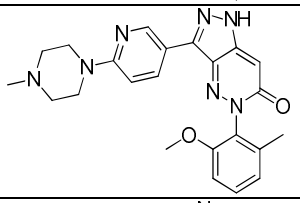
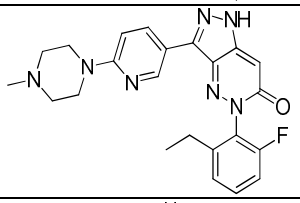
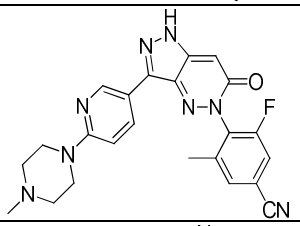
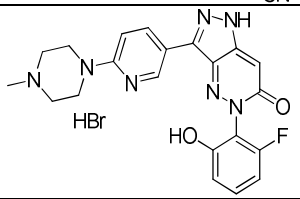
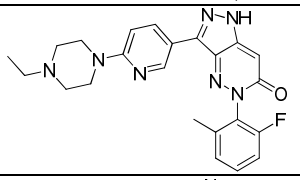
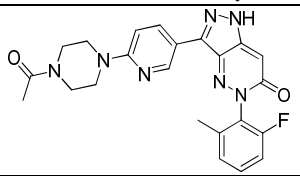
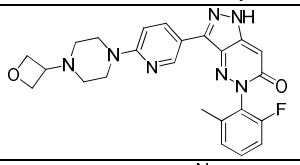
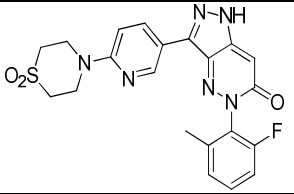
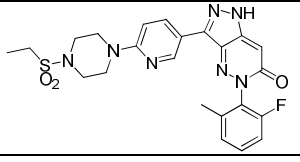
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Compound 51		3-(4-(4-methylpiperazin-1-yl)phenyl)-5-(4-methylpyrimidin-5-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 52		5-(7-methyl-3*H*-imidazolo[4,5-b]pyrid-6-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 53		5-(5-isopropyl-*1H*-pyrazol-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 54		5-(5,6-dihydro-4*H*-pyrrolo[1,2-b]pyrazol-3-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 55		5-(2-fluoro-6-methylphenyl)-7-methyl-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 56		5-(2-fluoro-6-methylphenyl)-7-methoxy-3-(4-(4-methylpiperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 57		5-(2-fluoro-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-5,6-dihydro-*1H*-pyrazolo[4,3-c]pyridazin-7-carbonitrile
Compound 58		3-(4-(4-cyclopropylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 59		5-(2-fluoro-6-methylphenyl)-3-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

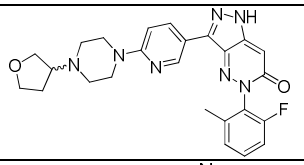
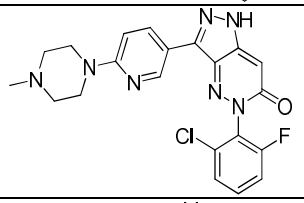
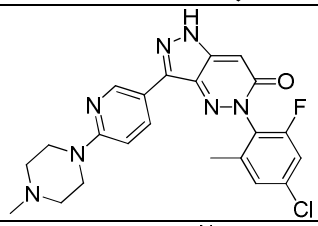
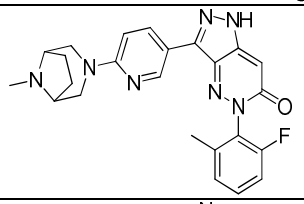
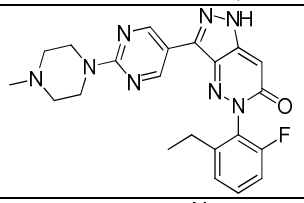
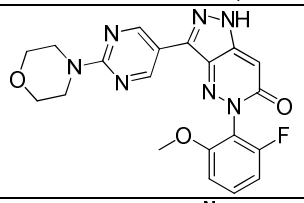
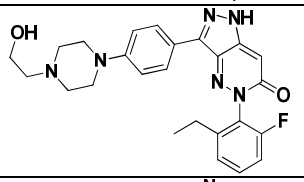
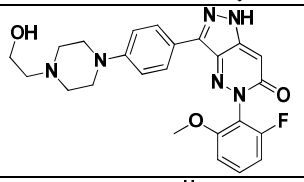
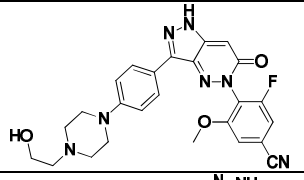
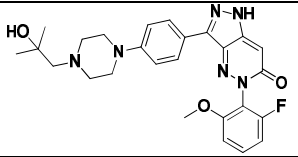
Compound 60		5-(2-fluoro-6-methylphenyl)-3-(4-(4-oxohexahydropyrrolo[1,2-a]pyrazin-2(*1H*)-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 61		5-(2-fluoro-6-methylphenyl)-3-(4-(8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 62		3-(4-(4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)piperidin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 63		3-(4-(4-(ethylsulfonyl)piperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 64		5-(2-fluoro-6-methylphenyl)-3-(4-(2-(hydroxymethyl)morpholino)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 65		3-(4-(1-(2-(dimethylamino)ethyl)-*1H*-pyrazol-4-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 66		5-(2-fluoro-6-methoxyphenyl)-3-(2-(4-methylpiperazin-1-yl)thiazol-5-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one
Compound 67		2-(4-(5-(2-fluoro-6-methoxyphenyl)-6-oxo-5,6-dihydro-*1H*-pyrazolo[4,3-c]pyridazin-3-yl)-*1H*-pyrazol-1-yl)propionitrile
Compound 68		2-(5-(2-fluoro-6-methoxyphenyl)-6-oxo-5,6-dihydro-*1H*-pyrazolo[4,3-c]pyridazin-3-yl)-6-methyl-5,6-dihydro-4*H*-pyrazolo[1,5-d][1,4]diazepin-7(*8H*)-one
Compound 69		3-(1-(2-hydroxyl-2-methylpropyl)-*1H*-pyrazol-4-yl)-5-(4-methylpyrid-3-yl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one

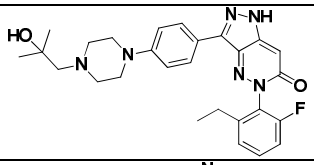
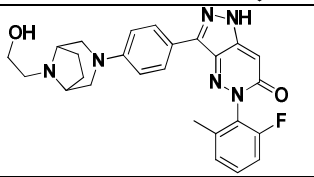
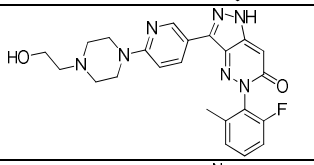
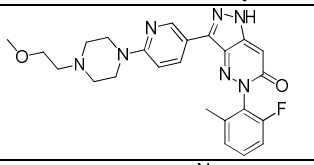
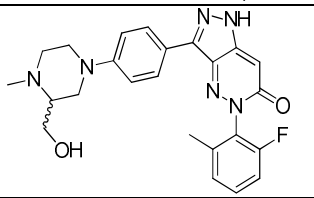
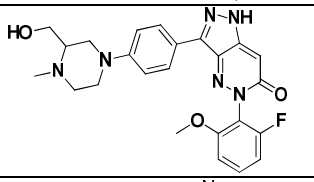
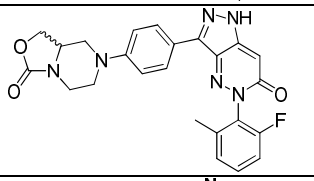
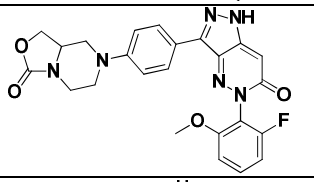
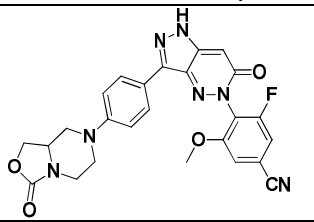
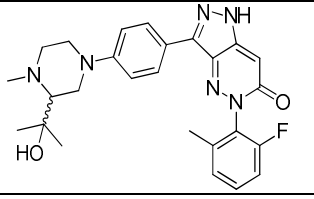
Compound 70		4-(4-(5-(2-fluoro-6-methylphenyl)-6-oxo-5,6-dihydro-*1H*-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)piperazinyl-1-carbonamide
Compound 71		*N*-(4-(5-(2-fluoro-6-methylphenyl)-6-oxo-5,6-dihydro-*1H*-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)-*N*-methyl-2-(4-methylpiperazin-1-yl)acetamide
Compound 72		5-(2-fluoro-6-methoxyphenyl)-3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 73		5-(2-fluoro-6-methoxyphenyl)-3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 74		3-fluoro-5-methoxy-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 75		5-(1,3-dihydroisobenzofuran-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 76		5-(benzo[d][1,3]dioxacyclopent-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 77		5-(2,4-difluoro-6-methoxyphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 78		5-(4-chloro-2-fluoro-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

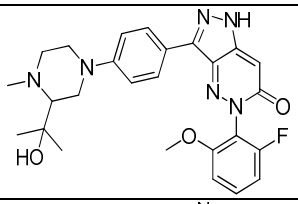
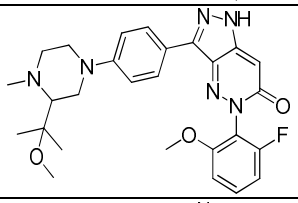
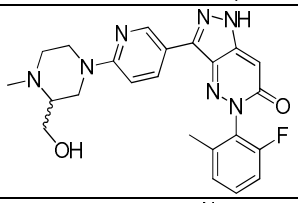
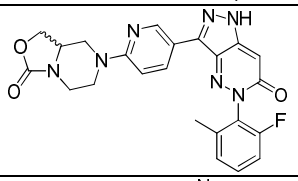
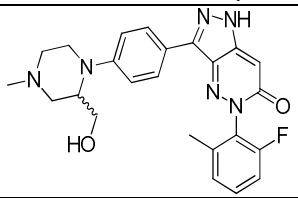
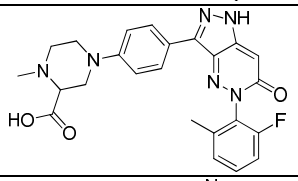
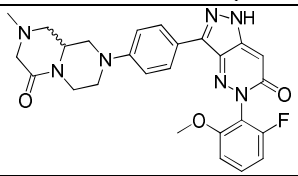
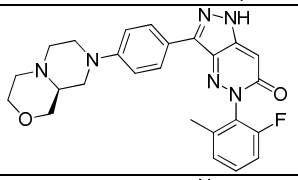
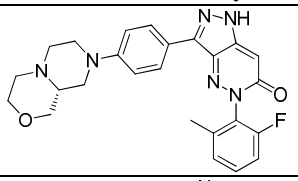
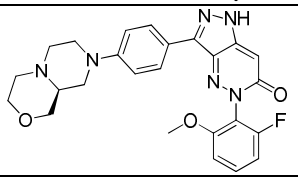
Compound 79		3-fluoro-5-methoxy-*N*-methyl-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzamide
Compound 80		3-fluoro-5-methoxy-*N*,*N*-dimethyl-4-(3-(4-(4-methylpiperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzamide
Compound 81		5-(2-fluoro-6-~~(~~methyl-~~d_3)~~phenyl)-3-(4-(4-(methyl-d_3)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 82		(*S*)-4-(3-(4-(4-(2-aminopropionyl)piperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-3-fluoro-5-methylbenzonitrile hydrochloride
Compound 83		4-(3-(4-(4-(2-hydroxylpropionyl)piperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-3-fluoro-5-methylbenzonitrile
Compound 84		3-(4-(4-(2,2-difluoroethyl)piperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 85		3-fluoro-5-methyl-4-(6-oxo~~oxa~~-3-(4-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 86		3-fluoro-5-methoxy-4-(3-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile ~~5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)-*1H*-pyrazolo[4,3-c]pyridazin-6(*5H*)-one~~

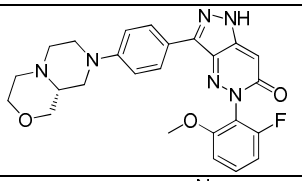
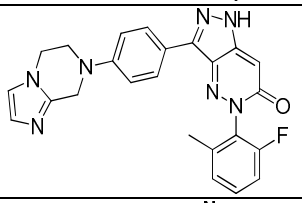
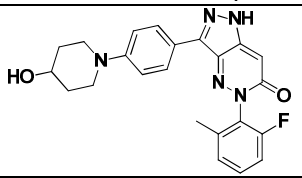
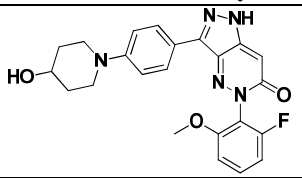
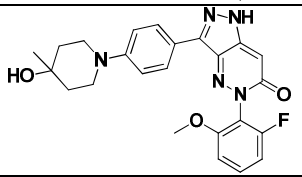
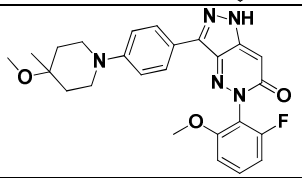
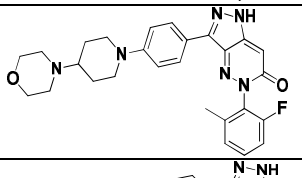
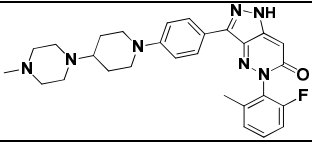
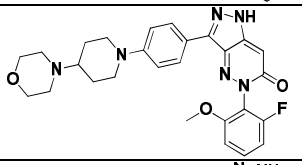
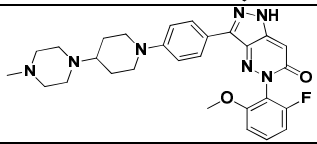
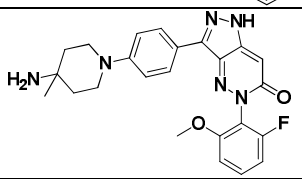
Compound 87		5-(2-fluoro-6-methylphenyl)-3-(4-((1*S*,4*S*)-5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 88		5-(2-fluoro-6-methylphenyl)-3-(4-((1*R*,4*R*)-5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 89		5-(2-fluoro-6-methylphenyl)-3-(4-(3,3,4-trimethylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 90		5-(2-fluoro-6-methylphenyl)-3-(4-((3*S*,5*R*)-3,4,5-trimethylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 91		5-(2-fluoro-6-methylphenyl)-3-(4-(6-methyl-3,6-diazabicyclo[3.1.1]heptan-3-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 92		5-(2-fluoro-6-methoxyphenyl)-3-(4-morpholinophenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 93		5-(2-fluoro-6-methylphenyl)-3-(4-(piperazin-2-ylmethoxy)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 94		3-(3-fluoro-4-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 95		3-(3-((dimethylamino)methyl)-4-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

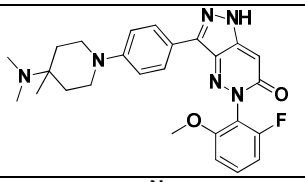
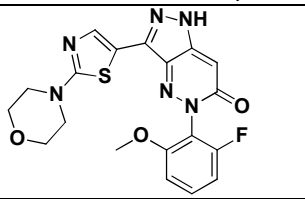
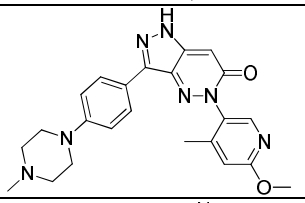
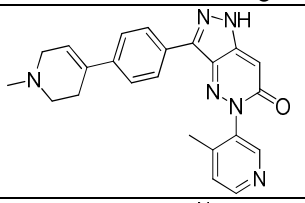
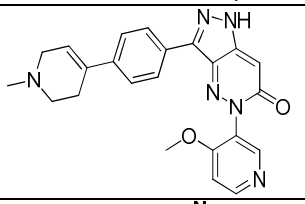
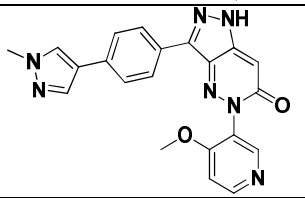
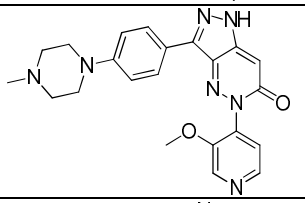
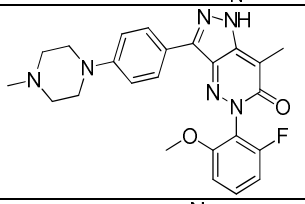
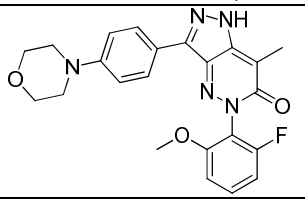
Compound 96		3-(3-((methylamino)methyl)-4-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 97		5-(2-methoxy-6-methylphenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 98		5-(2-ethyl-6-fluorophenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 99		3-fluoro-5-methyl-4-(3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 100		5-(2-fluoro-6-hydroxylphenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrobromide
Compound 101		3-(6-(4-ethylpiperazin-1-yl)pyrid-3-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 102		3-(6-(4-acetylpiperazin-1-yl)pyrid-3-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 103		5-(2-fluoro-6-methylphenyl)-3-(6-(4-(oxetan-3-yl))piperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 104		3-(6-(1,1-dioxidothiomorpholino)pyrid-3-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 105		3-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyrid-3-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

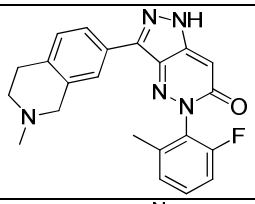
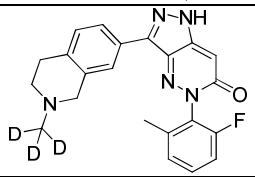
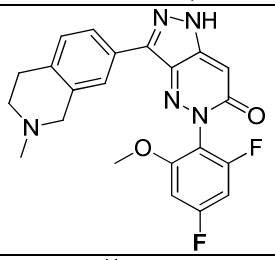
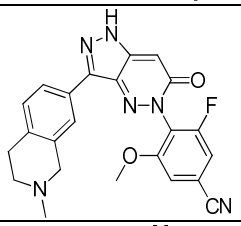
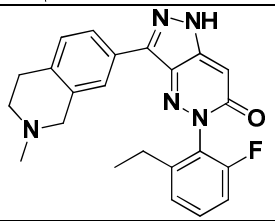
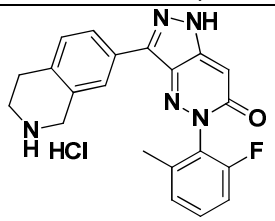
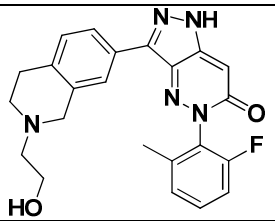
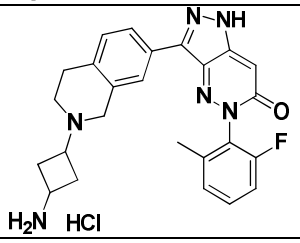
Compound 106		5-(2-fluoro-6-methylphenyl)-3-(6-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c] pyridazin-6(5H)-one
Compound 107		5-(2-chloro-6-fluorophenyl)-3-(6-(4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 108		5-(4-chloro-2-fluoro-6-methylphenyl)-3-(4-(4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 109		5-(2-fluoro-6-methylphenyl)-3-(6-(8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 110		5-(2-ethyl-6-fluorophenyl)-3-(2-(4-methylpiperazin-1-yl)pyrimidin-5-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 111		5-(2-fluoro-6-methoxyphenyl)-3-(2-morpholinyl-pyrimidin-5-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 112		5-(2-ethyl-6-fluorophenyl)-3-(4-(4-(2-hydroxyethyl)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 113		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-(2-hydroxyethyl)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)–one
Compound 114		3-fluoro-4-(3-(4-(4-(2-hydroxyethyl)piperazin-1-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-5-methoxybenzonitrile
Compound 115		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-(2-hydroxyl-2-methylpropyl)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

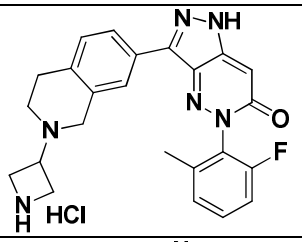
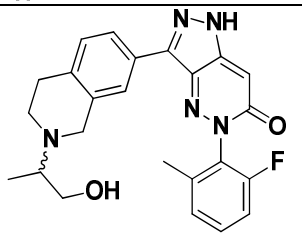
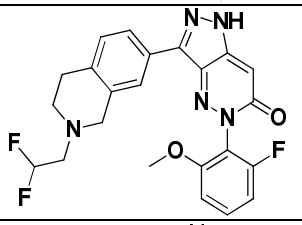
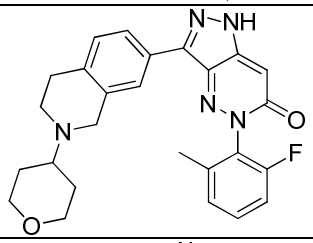
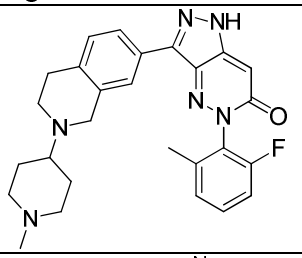
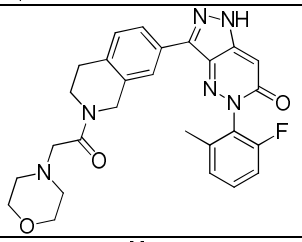
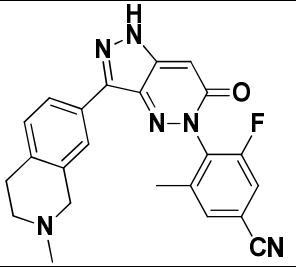
Compound 116		5-(2-ethyl-6-fluorophenyl)-3-(4-(4-(2-hydroxyl-2-methylpropyl)piperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 117		5-(2-fluoro-6-methylphenyl)-3-(4-(8-(2-hydroxyethyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 118		5-(2-fluoro-6-methylphenyl)-3-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 119		5-(2-fluoro-6-methylphenyl)-3-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 120		5-(2-fluoro-6-methylphenyl)-3-(4-(3-(hydroxymethyl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 121		5-(2-fluoro-6-methoxyphenyl)-3-(4-(3-(hydroxymethyl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 122		7-(4-(5-(2-fluoro-6-methylphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)tetrahydro-1H-oxazolo[3,4-a]pyrazin-3(5H)-one
Compound 123		7-(4-(5-(2-fluoro-6-methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)tetrahydro-1H-oxazolo[3,4-a]pyrazin-3(5H)-one
Compound 124		3-fluoro-5-methoxy-4-(6-oxo-3-(4-(3-oxotetrahydro-1H-oxazolo[3,4-a]pyrazin-7(3H)-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 125		5-(2-fluoro-6-methylphenyl)-3-(4-(3-(2-hydroxylprop-2-yl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

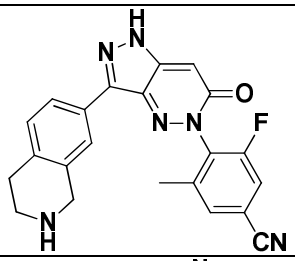
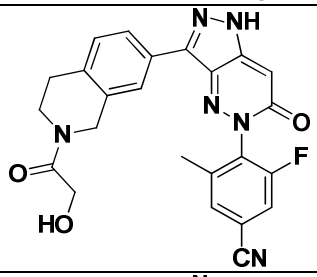
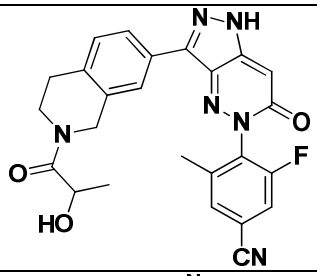
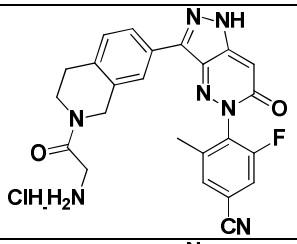
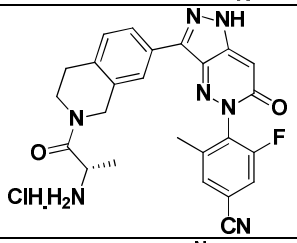
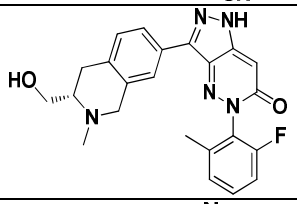
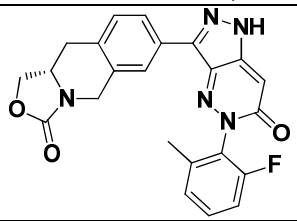
Compound 126		5-(2-fluoro-6-methoxyphenyl)-3-(4-(3-(2-hydroxylprop-2-yl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 127		5-(2-fluoro-6-methoxyphenyl)-3-(4-(3-(2-methoxyprop-2-yl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 128		5-(2-fluoro-6-methylphenyl)-3-(6-(3-(hydroxymethyl)-4-methylpiperazin-1-yl)pyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 129		7-(5-(5-(2-fluoro-6-methylphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)pyridin-2-yl)tetrahydro-1H-oxazolo[3,4-a]pyrazin-3(5H)-one
Compound 130		5-(2-fluoro-6-methylphenyl)-3-(4-(2-(hydroxymethyl)-4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 131		4-(4-(5-(2-fluoro-6-methylphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)-1-methylpiperazin-2-carboxylic acid
Compound 132		8-(4-(5-(2-fluoro-6-methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)phenyl)-2-methylhexahydro-1H-pyrazino[1,2-a]pyrazin-4(6H)-one
Compound 133		(S)-5-(2-fluoro-6-methylphenyl)-3-(4-(hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 134		(R)-5-(2-fluoro-6-methylphenyl)-3-(4-(hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 135		(S)-5-(2-fluoro-6-methoxyphenyl)-3-(4-(hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

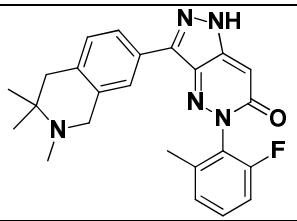
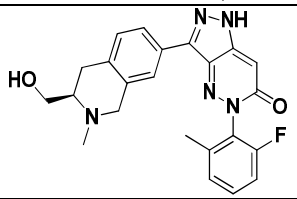
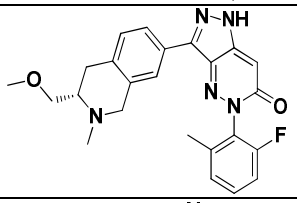
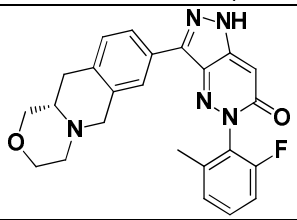
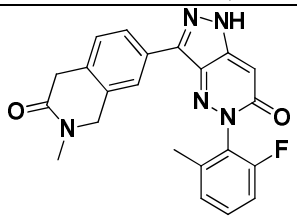
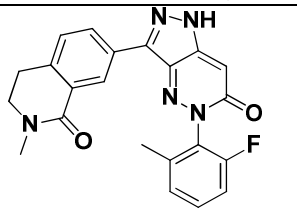
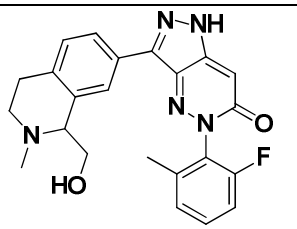
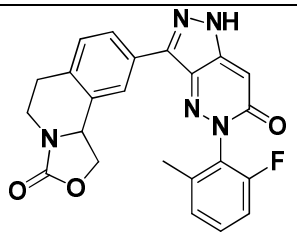
Compound 136		(R)-5-(2-fluoro-6-methoxyphenyl)-3-(4-(hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 137		3-(4-(5,6-dihydroimidazolo[1,2-a]pyrazin-7(8H)-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 138		5-(2-fluoro-6-methylphenyl)-3-(4-(4-hydroxylpiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 139		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-hydroxylpiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 140		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-hydroxyl-4-methylpiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 141		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-methoxy-4-methylpiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 142		5-(2-fluoro-6-methylphenyl)-3-(4-(4-morpholinopiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 143		5-(2-fluoro-6-methylphenyl)-3-(4-(4-(4-methylpiperazin-1-yl)piperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 144		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-morpholinopiperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 145		5-(2-fluoro-6-methoxyphenyl)-3-(4-(4-(4-methylpiperazin-1-yl)piperidin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 146		3-(4-(4-amino-4-methylpiperidin-1-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

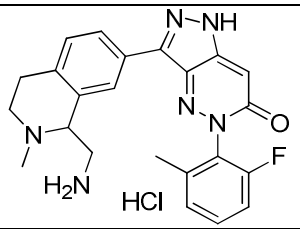
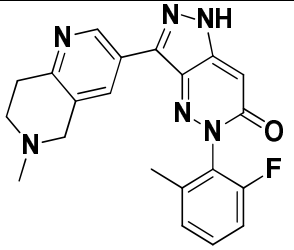
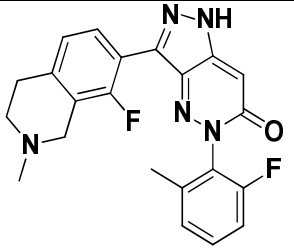
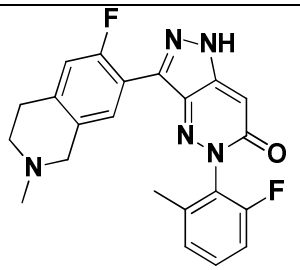
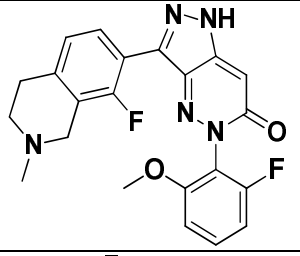
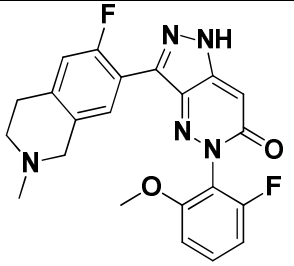
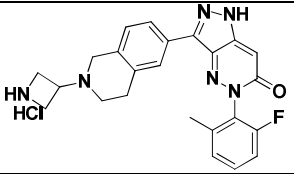
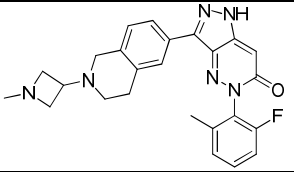
Compound 147		3-(4-(4-(dimethylamino)-4-methylpiperidin-1-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 148		5-(2-fluoro-6-methoxyphenyl)-3-(2-morpholinothiazol-5-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 149		5-(6-methoxy-4-methylpyrid-3-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 150		3-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-5-(4-methylpyrid-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 151		5-(4-methoxypyrid-3-yl)-3-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 152		5-(4-methoxypyrid-3-yl)-3-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 153		5-(3-methoxypyrid-4-yl)-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 154		5-(2-fluoro-6-methoxyphenyl)-7-methyl-3-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 155		5-(2-fluoro-6-methoxyphenyl)-7-methyl-3-(4-morpholinophenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

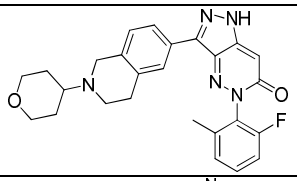
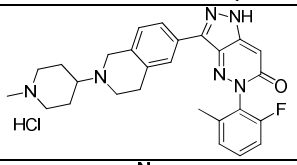
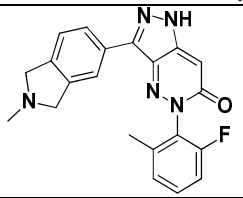
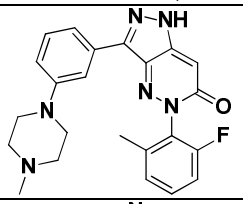
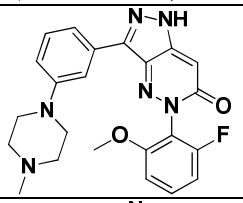
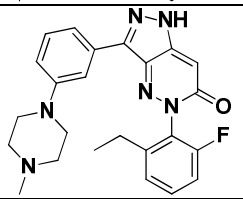
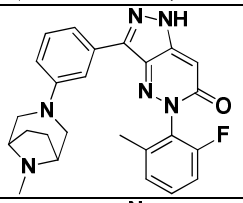
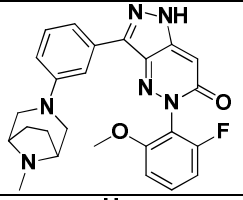
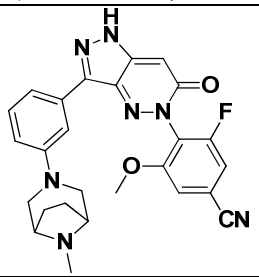
Compound 156		5-(2-fluoro-6-methylphenyl)-3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 157		5-(2-fluoro-6-methylphenyl)-3-(2-(methyl-d_3) -1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 158		5-(2,4-difluoro-6-methoxyphenyl)-3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 159		3-fluoro-5-methoxy-4-(3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 160		5-(2-ethyl-6-fluorophenyl)-3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 161		5-(2-fluoro-6-methylphenyl)-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride
Compound 162		5-(2-fluoro-6-methylphenyl)-3-(2-(2-hydroxyethyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 163		3-(2-(3-aminocyclobutyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride

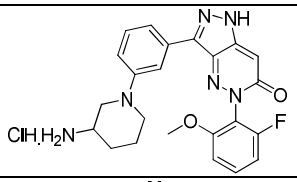
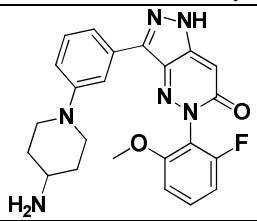
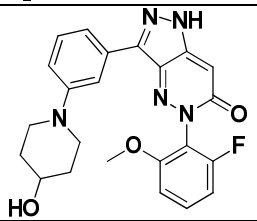
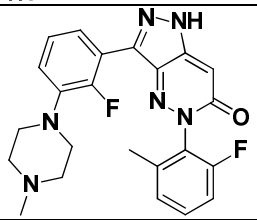
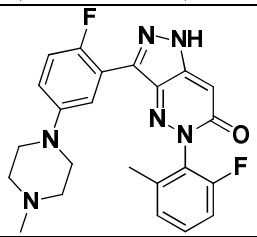
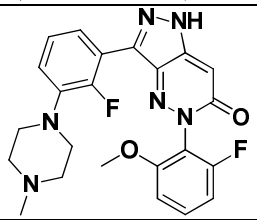
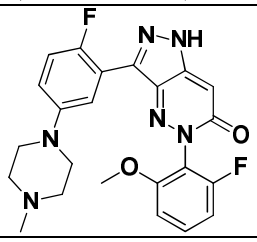
Compound 164		3-(2-(azetidin-3-yl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride
Compound 165		5-(2-fluoro-6-methylphenyl)-3-(2-(1-hydroxylprop-2-yl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 166		3-(2-(2,2-difluoroethyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 167		5-(2-fluoro-6-methylphenyl)-3-(2-(tetrahydro-2H-pyran-4-yl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 168		5-(2-fluoro-6-methylphenyl)-3-(2-(1-methylpiperidin-4-yl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 169		5-(2-fluoro-6-methylphenyl)-3-(2-(2-morpholinoacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 170		3-fluoro-5-methyl-4-(3-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile

Compound 171		3-fluoro-5-methyl-4-(3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile
Compound 172		3-fluoro-4-(3-(2-(2-hydroxylacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-5-methylbenzonitrile
Compound 173		3-fluoro-4-(3-(2-(2-hydroxylpropionyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-5-methylbenzonitrile
Compound 174		3-fluoro-4-(3-(2-(2-aminoacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-5-methylbenzonitrile hydrochloride
Compound 175		(*S*)-3-fluoro-4-(3-(2-(2-aminopropionyl)-1,2,3,4-tetrahydroisoquinolin-7-yl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)-5-methylbenzonitrile hydrochloride
Compound 176		(S)-5-(2-fluoro-6-methylphenyl)-3-(3-(hydroxymethyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 177		(S)-7-(5-(2-fluoro-6-methylphenyl)-6-oxo~~oxa~~-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-10,10a-dihydro-1H-oxazolo[3,4-b]isoquinolin-3(5H)-one

Compound 178		5-(2-fluoro-6-methylphenyl)-3-(2,3,3-trimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 179		(R)-5-(2-fluoro-6-methylphenyl)-3-(3-(hydroxymethyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 180		(S)-5-(2-fluoro-6-methylphenyl)-3-(3-(methoxymethyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 181		(S)-5-(2-fluoro-6-methylphenyl)-3-(1,3,4,6,11,11a-hexahydro-[1,4]oxazino[4,3-b]isoquinolin-8-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 182		7-(5-(2-fluoro-6-methylphenyl)-6-oxo~~oxa~~-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-2-methyl-1,2-dihydroisoquinolin-3(4H)-one
Compound 183		7-(5-(2-fluoro-6-methylphenyl)-6-oxo~~oxa~~-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-2-methyl-3,4-dihydroisoquinolin-1(2H)-one
Compound 184		5-(2-fluoro-6-methylphenyl)-3-(1-(hydroxymethyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazolo[4,3-c] pyridazin-6(5H)-one
Compound 185		9-(5-(2-fluoro-6-methylphenyl)-6-oxo~~oxa~~-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-5,6-dihydro-1H-oxazolo[4,3-a]isoquinolin-3(10bH)-one

Compound 186		3-(1-(aminomethyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride
Compound 187		5-(2-fluoro-6-methylphenyl)-3-(6-methyl-5,6,7,8-tetrahydro-1,6-naphthyridin-3-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 188		3-(8-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 189		3-(6-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 190		3-(8-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 191		3-(6-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 193		3-(2-(azetidin-3-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c] pyridazin-6(5H)-one hydrochloride
Compound 194		5-(2-fluoro-6-methylphenyl)-3-(2-(1-methylazetidin-3-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

Compound 195		5-(2-fluoro-6-methylphenyl)-3-(2-(tetrahydro-2H-pyran-4-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 196		5-(2-fluoro-6-methylphenyl)-3-(2-(1-methylpiperidin-4-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride
Compound 197		5-(2-fluoro-6-methylphenyl)-3-(2-methylisoindolin-5-yl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 198		5-(2-fluoro-6-methylphenyl)-3-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 199		5-(2-fluoro-6-methoxyphenyl)-3-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 200		5-(2-ethyl-6-fluorophenyl)-3-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 201		5-(2-fluoro-6-methylphenyl)-3-(3-(8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 202		5-(2-fluoro-6-methoxyphenyl)-3-(3-(8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 203		3-fluoro-5-methoxy-4-(3-(3-(8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-6-oxo-1H-pyrazolo[4,3-c]pyridazin-5(6H)-yl)benzonitrile

Compound 204		3-(3-(3-aminopiperidin-1-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one hydrochloride
Compound 205		3-(3-(4-aminopiperidin-1-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 206		3-(3-(4-hydroxylpiperidin-1-yl)phenyl)-5-(2-fluoro-6-methoxyphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 207		3-(2-fluoro-3-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 208		3-(2-fluoro-5-(4-methylpiperazin-1-yl)phenyl)-5-(2-fluoro-6-methylphenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 209		3-(2-fluoro-3-(4-methyl~~oxy~~piperazin-1-yl)phenyl)-5-(2-fluoro-6-methoxy~~yl~~phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one
Compound 210		3-(2-fluoro-5-(4-methyl~~oxy~~piperazin-1-yl)phenyl)-5-(2-fluoro-6-methoxy~~yl~~phenyl)-1H-pyrazolo[4,3-c]pyridazin-6(5H)-one

15. A pharmaceutical composition comprising the compound or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof according to any of claims 1-14 and a pharmaceutically acceptable carrier.

16. Use of the compound or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof, or a pharmaceutical composition thereof according to any of claims 1-14, or the pharmaceutical composition of claim 15 in the preparation of a medicament for the prevention or treatment of a

disease mediated with HPK1.

17. Use of the compound or a pharmaceutically acceptable salt, hydrate, solvate, active metabolite, polymorph, isotope labeled compound, isomer or prodrug thereof, or a pharmaceutical composition thereof according to any of claims 1-14, or the pharmaceutical composition of claim 15 in the preparation of a medicament for the prevention or treatment of benign or malignant tumors, myelodysplastic syndromes and diseases caused by viruses.

18. The use according to claim 17, wherein the benign or malignant tumor is selected from the group consisting of leukemia, lymphoma, multiple myeloma, lung cancer, hepatocellular carcinoma, cholangiocarcinoma, gallbladder cancer, gastric cancer, colorectal cancer, intestinal leiomyosarcoma, breast cancer, ovarian cancer, cervical cancer, endometrial cancer, vaginal cancer, malignant teratoma, pancreatic cancer, pancreatic ductal adenocarcinoma, nasopharyngeal cancer, oral cancer, laryngeal cancer, esophageal squamous cell carcinoma, thyroid cancer, kidney cancer, bladder cancer, malignant brain tumor, rhabdomyosarcoma, osteosarcoma, chondrosarcoma, osteofibrosarcoma, malignant thymoma, malignant peripheral nerve sheath tumor, prostate cancer, testicular cancer, penile cancer and other malignant tumors, as well as benign and malignant tumors of the skin.

19. The use according to claim 17, wherein the virus is selected from the group consisting of hepatitis virus, human immunodeficiency virus, human papillomavirus, herpes simplex virus, measles virus, norovirus, Boca virus, Coxsackie virus, Ebola virus, enterovirus, lymphocytic meningitis virus, influenza virus, SARS virus and COVID-19 virus.