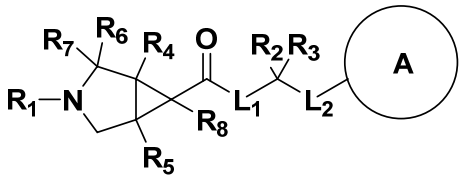
CLAIMS

1. A compound of Formula (I), or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof:



(I)

wherein R_1 is selected from -H and a C_{1-6} alkyl;

L_1 is selected from -NH- and -O-;

R_2 and R_3 are each independently selected from -H, a C_{1-6} alkyl, and a C_{3-6} cycloalkyl, wherein R_2 and R_3 are not both -H; or R_2 and R_3 together form a 3- to 6-membered saturated cyclic group comprising 0 to 1 group selected from -O-, -NR_9-, -SO-, and -SO_2-;

R_4, R_5, R_6, R_7, and R_8 are each independently selected from -H, a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{1-6} alkoxy C_{1-6} alkyl, a -$(CH_2)_m$-C_{3-10} carbocyclyl, a -$(CH_2)_m$-(3- to 10-membered heterocyclyl), a -$(CH_2)_m$-O-C_{3-10} carbocyclyl, a -$(CH_2)_m$-O-(3- to 10-membered heterocyclyl), phenyl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the carbocyclyl, the phenyl, the heteroaryl, or the heterocyclyl in R_4, R_5, R_6, R_7, and R_8 is each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_9 is selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a halogen, hydroxy, cyano, and a C_{3-6} cycloalkyl;

A is selected from a C_{6-14} aryl, a 5- to 14-membered heteroaryl, a 5- to 14-membered heterocyclyl, and a 5- to 14-membered cycloalkyl, and the aryl, the heteroaryl, the heterocyclyl, and the cycloalkyl in A are optionally further substituted with 1 to 4 R_{10}, wherein the heteroaryl or the heterocyclyl contains 1 to 4 heteroatoms selected from N, O, and S;

when L_2 is selected from a single bond, -$(CR_aR_b)_n$-, and -$(CR_aR_b)_nO$-, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a C_{3-6} cycloalkyl, and -SR_{11}, and at least one R_{10} is -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl and the heteroaryl contain 1 to 4 heteroatoms selected from N, O, and S, the alkyl, and the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

when L_2 is selected from -$(CR_aR_b)_nS$-, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -O-$(CH_2)_n$-C_{3-10} carbocyclyl or -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), and -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

m is independently selected from 0, 1, 2, and 3 at each occurrence;

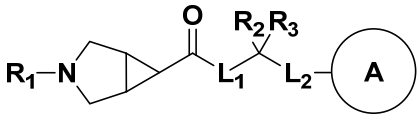
n is independently selected from 0, 1, 2, and 3 at each occurrence;

preferably, wherein:

L_1 is -NH-;

R_1 is -H;

preferably, wherein the Formula (I) compound has structural features of Formula (VI):



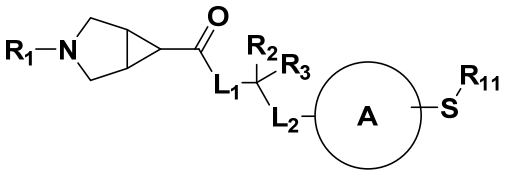
(VI)

L_1 is selected from -NH- and -O-;

L_2 is selected from a single bond and -$(CR_aR_b)_n$- or -$(CR_aR_b)_nO$-, wherein R_a and R_b are independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence.

2. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (II):



(II)

L_1 is selected from -NH- and -O-;

L_2 is selected from a single bond, -$(CR_aR_b)_n$-, and -$(CR_aR_b)_nO$-, wherein R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence;

preferably, in Formula (II):

R_1 is -H;

L_1 is -NH-;

L_2 is selected from a single bond, -CH_2-, -CH_2CH_2-, -$CH_2CH_2CH_2$-, -CH_2O-, and -CH_2CH_2O-;

preferably, in Formula (II):

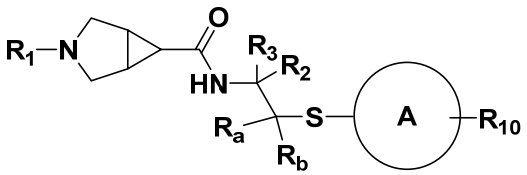
R_2 and R_3 are each independently selected from a C_{1-6} alkyl and a C_{3-6} cycloalkyl; or

R_2 and R_3 together form a 3- to 6-membered saturated cyclic group comprising 0 to 1 group selected from -O-, -SO-, and -SO_2-;

preferably, in Formula (II):

R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy; preferably, R_{11} is each independently selected from methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, imidazolyl, pyrrolyl, furyl, thiophenyl, and pyridyl.

3. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (III):



(III)

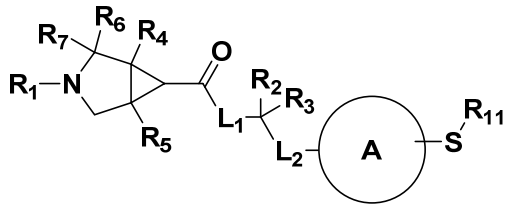
R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -O-$(CH_2)_n$-C_{3-10} carbocyclyl, a -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -O-$(CH_2)_n$-C_{3-10} carbocyclyl, a -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), and -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from

N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

preferably, in Formula (III):wherein R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclobutoxy, tetrahydrofuranyl, and $-SR_{11}$, wherein R_{11} is each independently selected from methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, imidazolyl, pyrrolyl, furyl, thienyl, and pyridyl; R_a and R_b are each independently selected from -H, methyl, ethyl, and isopropyl.

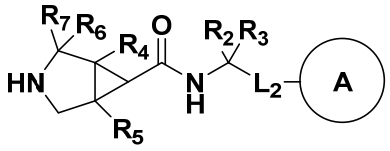
4. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (IV):



(IV)

R_4 is selected from a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{1-6} alkoxy C_{1-6} alkyl, a $-(CH_2)_m-C_{3-10}$ carbocyclyl, a $-(CH_2)_m-$(3- to 10-membered heterocyclyl), a $-(CH_2)_m-O-C_{3-10}$ carbocyclyl, a $-(CH_2)_m-O-$(3- to 10-membered heterocyclyl), phenyl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the carbocyclyl, the phenyl, the heteroaryl, or the heterocyclyl in R_4 is each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy.

5. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (V):



(V)

R_2 and R_3 are each independently selected from a C_{1-6} alkyl and a C_{3-6} cycloalkyl, wherein R_2 and R_3 are not both -H; or R_2 and R_3 together form a 3- to 6-membered saturated cycloalkyl;

R_4, R_5, R_6, and R_7 are each independently selected from -H, a C_{1-6} alkyl, a C_{1-6} alkoxy, and a C_{1-6} alkoxy C_{1-6} alkyl, and the alkyl and the alkoxy in R_4, R_5, R_6, and R_7 are each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

A is selected from a C_{6-14} aryl, a 5- to 14-membered heteroaryl, a 5- to 14-membered heterocyclyl, and a 5- to 14-membered cycloalkyl, and the aryl, the heteroaryl, the heterocyclyl, and the cycloalkyl in A are optionally further substituted with 1 to 4 R_{10}, wherein the heteroaryl or the heterocyclyl contains 1 to 4 N atoms;

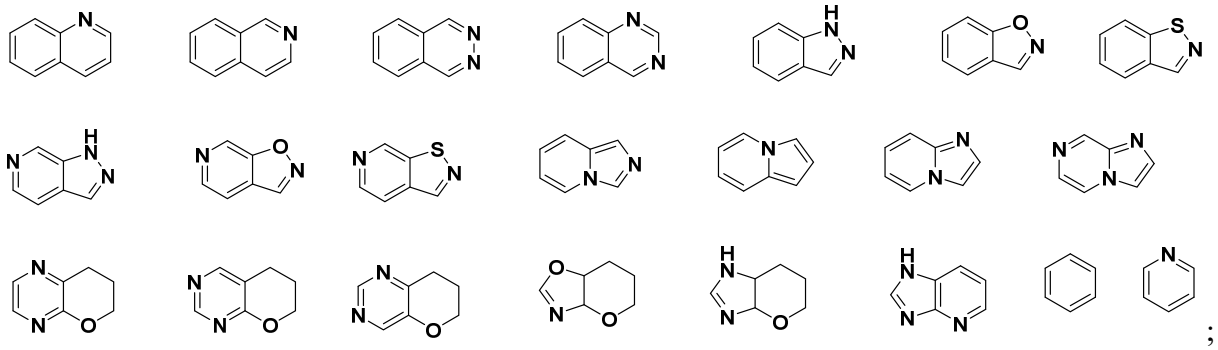
when L_2 is selected from a single bond, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a C_{3-6} cycloalkyl, and $-SR_{11}$, and at least one R_{10} is $-SR_{11}$, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a $-(CH_2)_n$-C_{3-10} carbocyclyl, a $-(CH_2)_n$-(3- to 10-membered heterocyclyl), and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from O, S, and N, and the alkyl, the alkoxy, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

when L_2 is selected from $-(CR_aR_b)_nS-$, R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, and a C_{1-4} alkoxy C_{1-6} alkyl, the alkyl and the alkoxy are each independently optionally further substituted with 0 to 4 substituents selected from H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

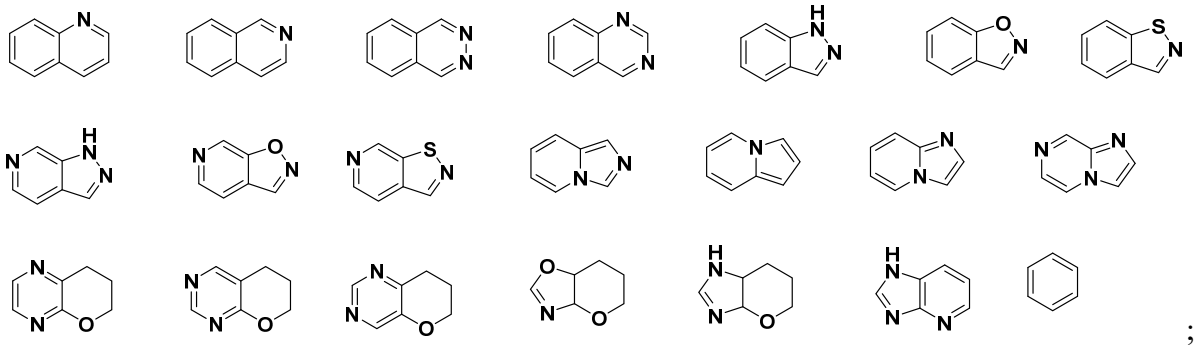
R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence;

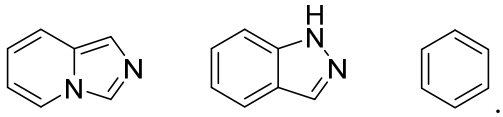
preferably, wherein A is selected from the following structures:


;

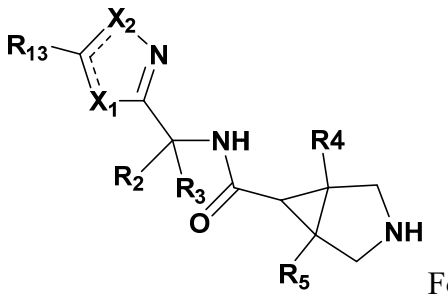
preferably, wherein A is selected from one of the following structures:


;

preferably, wherein A is selected from the following structures:


.

6. A compound of Formula (a) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (a)

wherein

--- represents a single or double bond, provided that one and only one of two --- represents a double bond;

X_1 is CR_{13} or NR_{12};

X_2 is CR_{13} or NR_{12};

alternatively, X_1 and a substituent thereof together with an adjacent carbon atom and a substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is optionally substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, a halogen, cyano, $-(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n$-OR, a $-(CH_2)_n$-C_{2-6} alkenyl, a $-(CH_2)_n$-C_{2-6} alkynyl, a $-(CH_2)_n$-C_{3-10} carbocyclyl, a $-(CH_2)_n$-(3- to 10-membered heterocyclyl), a $-(CH_2)_n$-C_{6-10} aryl, a $-(CH_2)_n$-5- to 6-membered heteroaryl, and $-SR_{11}$;

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n$-C_{2-6} alkenyl, a $-(CH_2)_n$-C_{2-6} alkynyl, a $-(CH_2)_n$-C_{3-10} carbocyclyl, a $-(CH_2)_n$-(3- to 10-membered heterocyclyl), a $-(CH_2)_n$-C_{6-10} aryl, and a $-(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n$-OR;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n-OR$;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is an $-SR_{11}$ substituent;

preferably, wherein

X_2 is CR_{13};

X_1 and the substituent thereof together with the adjacent carbon atom and the substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, halogen, cyano, $-(CH_2)_n-NR'R''$, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n-OR$, a $-(CH_2)_n-C_{2-6}$ alkenyl, a $-(CH_2)_n-C_{2-6}$ alkynyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, a $-(CH_2)_n-$(3- to 10-membered heterocyclyl), a $-(CH_2)_n-C_{6-10}$ aryl, a $-(CH_2)_n-$5- to 6-membered heteroaryl, and $-SR_{11}$;

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{2-6}$ alkenyl, a $-(CH_2)_n-C_{2-6}$ alkynyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, a $-(CH_2)_n-$(3- to 10-membered heterocyclyl), a $-(CH_2)_n-C_{6-10}$ aryl, and a $-(CH_2)_n-$5- to 6-membered heteroaryl;

R' and R'' are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R'' together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n-OR$;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n-OR$;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is an $-SR_{11}$ substituent;

preferably, wherein:

X_2 is NR_{12};

X_1 and the substituent thereof together with the adjacent carbon atom and the substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, a halogen, cyano, $-(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n$-OR, a $-(CH_2)_n$-C_{2-6} alkenyl, a $-(CH_2)_n$-C_{2-6} alkynyl, a $-(CH_2)_n$-C_{3-10} carbocyclyl, a $-(CH_2)_n$-(3- to 10-membered heterocyclyl), a $-(CH_2)_n$-C_{6-10} aryl, a $-(CH_2)_n$-5- to 6-membered heteroaryl, and $-SR_{11}$;

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n$-C_{2-6} alkenyl, a $-(CH_2)_n$-C_{2-6} alkynyl, a $-(CH_2)_n$-C_{3-10} carbocyclyl, a $-(CH_2)_n$-(3- to 10-membered heterocyclyl), a $-(CH_2)_n$-C_{6-10} aryl, and a $-(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

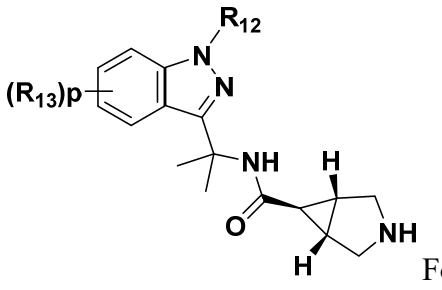
R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n$-OR;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-(CH_2)_n$-OR;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is $-SR_{11}$.

7. A compound of Formula (b) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (b)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

n is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;

preferably, wherein

p is 1, 2, or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_{12} is selected from H, a C_{1-6} alkyl, or a halogenated C_{1-6} alkyl;

n is 0 or 1;

preferably, wherein:

p is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-SR_{11}$, and at least one R_{13} is $-SR_{11}$;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{12} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

n is 0 or 1;

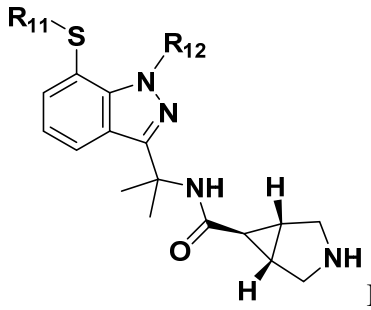
preferably, wherein:

P is 1;

R_{13} is -SMe;

R_{12} is H or a C_{1-4} alkyl.

8. A compound of Formula (b-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (b-1)

wherein:

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n-C_{2-6}$ alkenyl, a $-(CH_2)_n-C_{2-6}$ alkynyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, a $-(CH_2)_n-$(3- to 10-membered heterocyclyl), a $-(CH_2)_n-C_{6-10}$ aryl, and a $-(CH_2)_n-$5- to 6-membered heteroaryl;

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl; and

n is 0, 1, 2, or 3;

preferably, wherein:

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl; and

n is 0 or 1;

preferably, wherein:

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{12} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

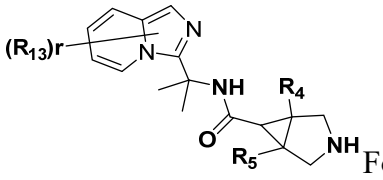
n is 0 or 1;

preferably, wherein:

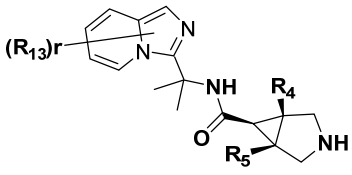
R_{11} is methyl;

R_{12} is H or a C_{1-4} alkyl.

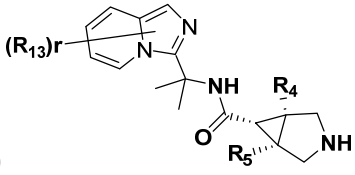
9. A compound of Formula (c) or a stereoisomer thereof of Formula (c-1) or Formula (c-2), an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (c)



Formula (c-1)



Formula (c-2)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

r is 1, 2, 3, 4, or 5;

preferably, wherein

r is 1, 2 or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_4 and R_5 are each independently selected from H and a C_{1-6} alkyl;

n is 0 or 1;

preferably, wherein

r is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-4} alkyl and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

R_4 and R_5 are each independently selected from H and a C_{1-6} alkyl;

n is 0 or 1;

preferably, wherein

r is 2;

one of R_{13} is -SMe, and another one is selected from H and a C_{1-4} alkyl;

R_4 and R_5 are each independently selected from H and a C_{1-4} alkyl;

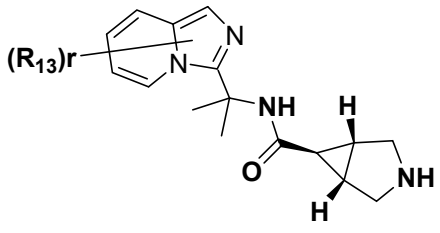
preferably, wherein

r is 1;

R_{13} is -SMe;

R_4 and R_5 are each independently selected from H and a C_{1-4} alkyl.

10. A compound of Formula (d) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

r is 1, 2, 3, 4, or 5;

preferably, wherein

r is 1, 2 or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

n is 0 or 1;

preferably, wherein

r is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-4} alkyl and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

n is 0 or 1;

preferably, wherein

r is 2;

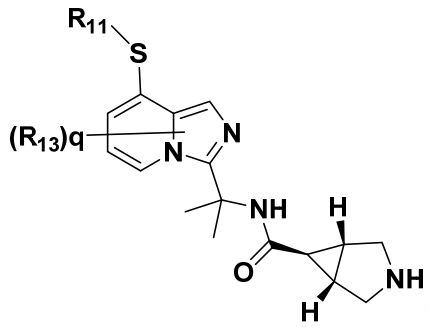
one of R_{13} is -SMe and another one is selected from H and a C_{1-4} alkyl;

preferably, wherein

r is 1;

R_{13} is -SMe.

11. A compound of Formula (d-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-1)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

q is 0, 1, 2, 3, or 4;

preferably, wherein

q is 0, 1 or 2;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

n is 0 or 1;

preferably, wherein

q is 0 or 1;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{13} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

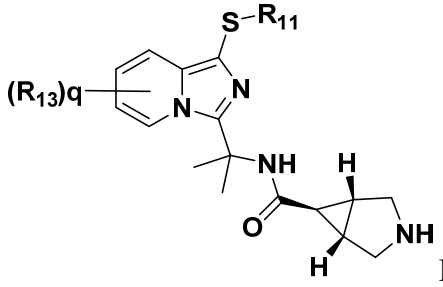
n is 0 or 1;

preferably, wherein

q is 0;

R_{11} is a C_{1-4} alkyl.

12. A compound of Formula (d-2) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-2)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

q is 0, 1, 2, 3, or 4;

preferably, wherein

q is 0, 1, or 2;

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11};

n is 0 or 1;

preferably, wherein

q is 0 or 1;

R_{11} is selected from a C_{1-4} alkyl, a halogenated C_{1-4} alkyl, and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

R_{13} is each independently selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0 or 1;

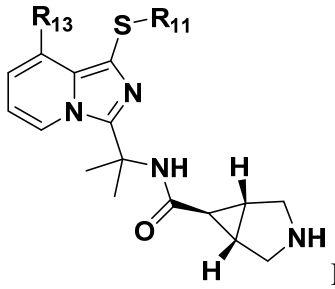
preferably, wherein

q is 1;

R_{11} is methyl;

R_{13} is H or a C_{1-4} alkyl.

13. A compound of Formula (d-3) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-3)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

preferably, wherein

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

n is 0 or 1;

preferably, wherein

R_{11} is selected from a C_{1-4} alkyl, a halogenated C_{1-4} alkyl, and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{13} is each independently selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

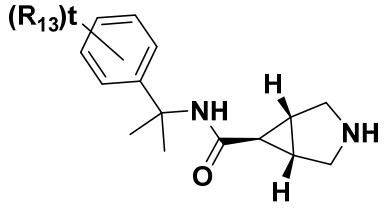
n is 0 or 1;

preferably, wherein

R_{11} is methyl;

R_{13} is H or a C_{1-4} alkyl.

14. A compound of Formula (e) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (e)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{3-10} cycloaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

t is 1, 2, 3, 4, or 5;

preferably, wherein

t is 1, 2, or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

n is 0 or 1;

preferably, wherein

t is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-4} alkyl and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

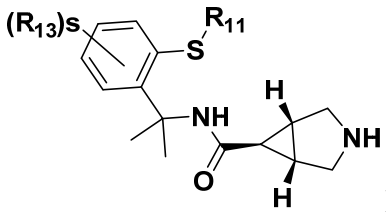
n is 0 or 1;

preferably, wherein

t is 1;

R_{11} is a C_{1-4} alkyl.

15. A compound of Formula (e-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (e-1)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{3-10} cycloaryl, and -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

s is 0, 1, 2, 3, or 4;

preferably, wherein

s is 0, 1, or 2;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

n is 0 or 1;

preferably, wherein

s is 0 or 1;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

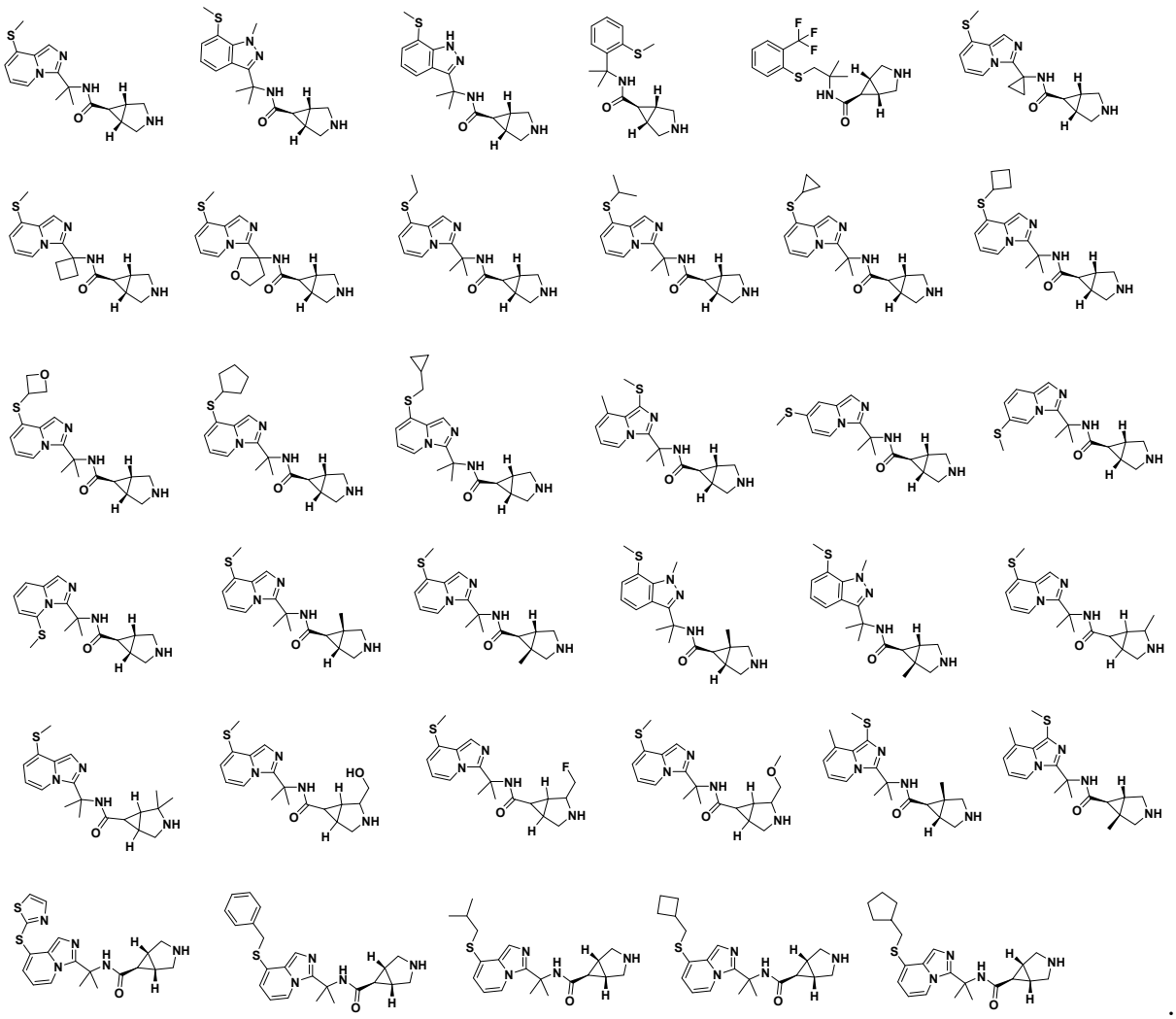
n is 0 or 1;

preferably, wherein

s is 0;

R_{11} is a C_{1-4} alkyl.

16. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, selected from the following structures:



17. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 16, wherein the pharmaceutically acceptable salt is selected from a hydrochloride, a hydrobromide, a sulfate, a nitrate, a phosphate, an acetate, a maleate, a succinate, a mandelate, a fumarate, a malonate, a malate, a 2-hydroxypropionate, an oxalate, a glycolate, a salicylate, a glucuronate, a galacturonate, a citrate, a tartrate, an aspartate, a glutamate, a benzoate, a cinnamate, a *p*-toluenesulfonate, a benzenesulfonate, a mesylate, an ethanesulfonate, and a trifluoromethanesulfonate, or combinations thereof.

18. A pharmaceutical composition, characterized by containing a therapeutically effective dose of the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the

pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 17, and a pharmaceutically acceptable carrier or excipient.

19. Use of the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 17 or the pharmaceutical composition according to claim 18 in the preparation of a drug for treatment and/or prevention of a disease or a symptom affected by SSTR4 activation; preferably, for treatment and/or prevention of pain; preferably, the pain is neuralgia; preferably, the pain is back pain, chronic back pain, trigeminal neuralgia, type I complex regional pain syndrome, type II complex regional pain syndrome, irritable bowel syndrome symptoms, diabetic neuropathy, osteoarthritis-caused pain, tumor pain, or fibromyalgia.