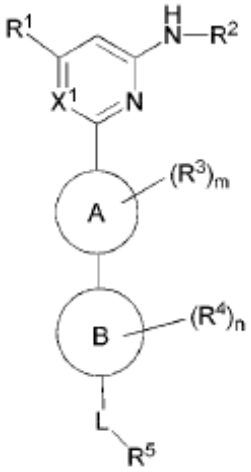
CLAIMS

1. A compound, a stereoisomer, tautomer, or mixture thereof, a N-oxide thereof, a pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or a stable isotope derivative, metabolite, or prodrug thereof, wherein the compound has a structure of formula I:



Formula I

wherein:

ring A is selected from 5-6-membered heteroaromatic ring and C_{6-10} aromatic ring;

ring B is selected from 4-11-membered heterocyclyl and C_{3-8} cycloalkyl;

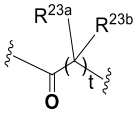
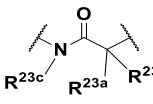
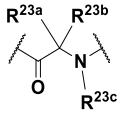
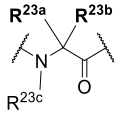
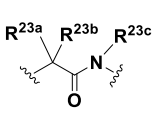
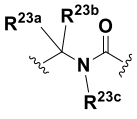
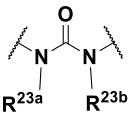
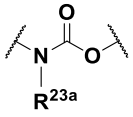
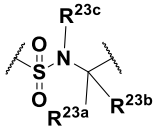
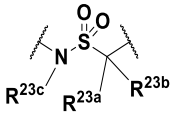
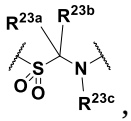
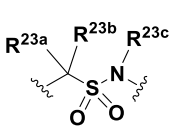
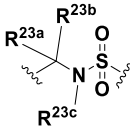
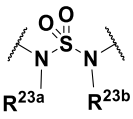
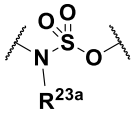
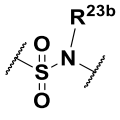
X^1 is selected from N and CH;

R^1 is selected from the group consisting of C_{1-6} alkyl, H, halogen, hydroxy, cyano, C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy), C_{3-8} cycloalkyl, 4-10-membered heterocyclyl, and -$NR^{20a}R^{20b}$, and the alkyl, heteroalkyl (e.g., alkoxy), cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, and C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy);

R^2 is selected from the group consisting of 5-10-membered heteroaryl, C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{3-8} cycloalkyl, 4-10-membered heterocyclyl, and -C(=O)R^{21}, and the alkyl,

heteroalkyl, cycloalkyl, heterocyclyl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: C_{1-4} alkyl, hydroxy, halogen, CN, NO_2, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl, and C_{3-6} cycloalkyl;

R^3 and R^4 are absent or are, at each occurrence, each independently selected from the group consisting of hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy), and C_{3-6} cycloalkyl, the alkyl, heteroalkyl (for example, alkoxy), and cycloalkyl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy; when m is greater than 1, two R^3 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl; and/or when n is greater than 1, two R^4 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl;

L is selected from the group consisting of C_{1-6} alkylene, -O-, -S-, -S(O)-, -$S(O)_2$-, -$N{=}CR^{21}$-, -$N(R^{23a})$-C(O)-, C_{1-6} heteroalkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, , , , , , , , , , , , , , , ,  and , the alkylene, heteroalkylene, alkenylene, and alkynylene are each optionally substituted with one or more substituents selected from the group consisting of:

hydroxy, halogen, CN, NO_2, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkoxy, C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy), and C_{3-8} cycloalkyl; or L is -N(R^{23a})-;

R^5 is selected from the group consisting of 5-10-membered heteroaryl, hydroxy, halogen, CN, NO_2, C_{1-6} alkyl, C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, -$NR^{20a}R^{20b}$, -OR^{21}, -SR^{21}, -$S(=O)R^{22}$, -$S(=O)_2R^{22}$, -$S(=O)NR^{20a}R^{20b}$, -$S(=O)_2NR^{20a}R^{20b}$, -$NR^{20a}S(=O)R^{20b}$, -$NR^{20a}S(=O)_2R^{20b}$, -$C(=O)R^{21}$, -$C(=O)NR^{23a}R^{23b}$, -$NR^{23a}C(=O)R^{23b}$, -$OC(=O)NR^{23a}R^{23b}$, and -$NR^{24a}C(=O)NR^{25a}R^{25b}$, and the alkyl, heteroalkyl (e.g., alkoxy), alkenyl, alkynyl, cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: 5-10-membered heteroaryl, hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, -$NR^{30a}R^{30b}$, -OR^{31}, -SR^{31}, -$S(=O)R^{32}$, -$S(=O)_2R^{32}$, -$S(=O)NR^{30a}R^{30b}$, -$S(=O)_2NR^{30a}R^{30b}$, -$NR^{30a}S(=O)R^{30b}$, -$NR^{30a}S(=O)_2R^{30b}$, -$C(=O)R^{31}$, -$C(=O)NR^{33a}R^{33b}$, -$NR^{33a}C(=O)R^{33b}$, -$OC(=O)NR^{33a}R^{33b}$, and -$NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, hydroxy, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-10-membered heterocyclyl;

R^{20a}, R^{20b}, R^{23a}, R^{23b}, R^{23c}, R^{24a}, R^{25a}, and R^{25b} are each independently selected from the group consisting of H, OH, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{3-8} cycloalkyl; or R^{20a} and R^{20b}, R^{23a} and R^{23b}, or R^{25a} and R^{25b} form, together with an atom to which they are attached, a 3-8-membered cycloalkyl or heterocyclyl, and the alkyl, alkoxy, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting

of: OH, CN, halogen, NO_2, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

R^{30a}, R^{30b}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

R^{21}, R^{22}, R^{31}, and R^{32} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, 4-10-membered heterocyclyl, C_{6-12} aryl, and 5-10-membered heteroaryl, and the alkyl, alkoxy, cycloalkyl, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: OH, halogen, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl;

m is 0, 1, 2, 3, or 4, and is preferably 0;

n is 0, 1, 2, 3, or 4, and is preferably 0, 1, or 2;

t is 0, 1, 2, 3 or 4, and is preferably 0 or 1; and

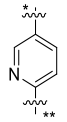
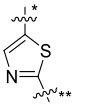
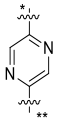
u is 0, 1, 2, 3, or 4, and is preferably 0 or 1;

provided that when ring B is a piperazine ring and X^1 is CH, R^2 is not 4-CF_3-pyridin-2-yl or 4-CN-pyridin-2-yl.

2. The compound according to claim 1, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

the ring A is a benzene ring or a 5-6-membered heteroaromatic ring;

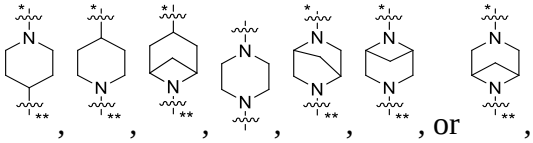
preferably, the ring A is a benzene ring, a thiazole ring, a pyridine ring, a pyrazine ring, or a pyrimidine ring;

more preferably, the ring A is , , or , is linked to the ring where X^1 is located through a position marked with *, and is linked to the ring B through a position marked with **;

and/or

the ring B is C_{3-6} cycloalkyl or 5-7-membered heterocyclyl;

preferably, the ring B is a piperidine ring, a piperazine ring, an azacycloheptane bridged ring, or a diazacycloheptane bridged ring;

more preferably, the ring B is , is linked to the ring A through the position marked with *, and is linked to L through the position marked with **;

and/or

X^1 is CH or N, and is preferably N.

3. The compound according to claim 1 or 2, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

R^1 is selected from the group consisting of H, halogen, hydroxy, cyano, C_{1-4} alkyl, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl, and the alkyl, heteroalkyl (for example, alkoxy), cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, and C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy);

preferably, R^1 is selected from the group consisting of C_{1-4} alkyl, 5-membered nitrogen-containing heterocyclyl, and C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), and the alkyl, heterocyclyl, and heteroalkyl (e.g., alkoxy) are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, and C_{1-3} heteroalkyl (e.g., C_{1-3} alkoxy);

more preferably, R^1 is selected from the group consisting of C_{1-3} alkyl (e.g., methyl), pyrrolidinyl (e.g., pyrrolidin-1-yl), and C_{1-3} alkoxy (e.g., ethoxy);

and/or

R^2 is selected from the group consisting of C_{1-4} alkyl, C_{1-4} heteroalkyl, C_{3-6} cycloalkyl, 4-6-membered heterocyclyl, 5-6-membered heteroaryl, and $-C(=O)R^{21}$, and the alkyl, heteroalkyl, cycloalkyl, heterocyclyl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl, and C_{3-6} cycloalkyl;

preferably, R^2 is selected from the group consisting of C_{1-3} alkyl, 5-6-membered heteroaryl, and $-C(=O)CH_3$, and the alkyl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl, and C_{3-6} cycloalkyl;

more preferably, R^2 is selected from the group consisting of C_{1-3} alkyl (e.g., methyl), $-C(=O)CH_3$, thienyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, thiadiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, isoxazolyl, and pyridyl, and the alkyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, thiadiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, isoxazolyl, and pyridyl are each optionally substituted with one or more substituents selected from the group

consisting of: hydroxy, halogen, CN, C_{1-3} alkyl (e.g., methyl), C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl (e.g., C_{1-3} alkoxy), and C_{3-6} cycloalkyl; and

further preferably, R^2 is a methyl-substituted pyrazolyl (e.g., 5-methyl-1H-pyrazol-3-yl or 1-methyl-1H-pyrazol-4-yl), a cyclopropyl-substituted pyrazolyl (e.g., 5-cyclopropyl-1H-pyrazol-3-yl), or -C(O)CH_3.

4. The compound according to any one of claims 1 to 3, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

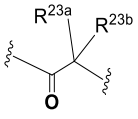
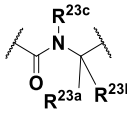
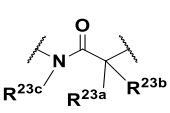
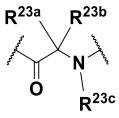
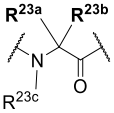
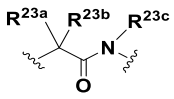
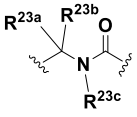
R^3 and R^4 are absent or are, at each occurrence, independently selected from the group consisting of hydroxy, halogen, CN, C_{1-4} alkyl, and C_{1-4} alkoxy, the alkyl and alkoxy are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy; when m is greater than 1, two R^3 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl; and/or when n is greater than 1, two R^4 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl;

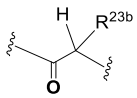
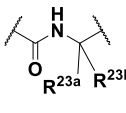
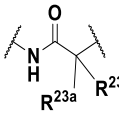
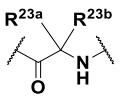
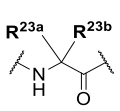
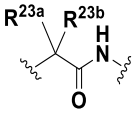
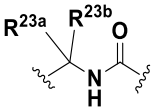
preferably, R^3 and R^4 are absent or are, at each occurrence, independently selected from the group consisting of hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} alkoxy, the alkyl and alkoxy are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, and C_{1-3} alkyl; when m is greater than 1, two R^3 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl; and/or when n is greater than 1, two R^4 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl;

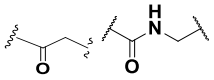
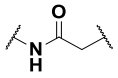
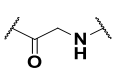
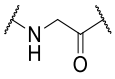
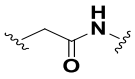
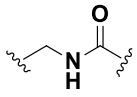
more preferably, R^3 and R^4 are absent or are, at each occurrence, independently selected from the group consisting of: F, Cl, CN, OH, C_{1-3} alkyl, and C_{1-3} alkoxy; and

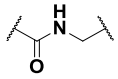
further preferably, R^3 and R^4 are absent.

5. The compound according to any one of claims 1 to 4, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

L is selected from the group consisting of -O-, -S-, -C(O)-, -N(R^{23a})-C(O)-, -C(O)-N(R^{23c})-, C_{1-4} alkylene, C_{1-4} heteroalkylene, , , , , , , and , and the alkylene and heteroalkylene are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), and C_{3-6} cycloalkyl;

preferably, L is selected from the group consisting of -O-, -C(O)-, -NHC(O)-, -C(O)NH-, C_{1-3} alkylene, C_{1-3} heteroalkylene, , , , , , , and , and the alkylene and heteroalkylene are each optionally substituted with one or more substituents selected from the group of: hydroxy, halogen, CN, NO_2, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl(e.g., C_{1-3} alkoxy), and C_{3-6} cycloalkyl, wherein R^{23a} and R^{23b} are preferably H or C_{1-3} alkyl;

more preferably, L is selected from the group consisting of -O-, -C(O)-, -NHC(O)-, -C(O)NH-, C_{1-3} alkylene, , , , , , and , and the alkylene is optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-3} alkyl, and C_{1-3} haloalkyl; and

further preferably, L is -CH_2-, -$CH(CH_3)$-, -O-, -C(O)-, , -C(O)NH-, or .

6. The compound according to any one of claims 1 to 5, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

R^5 is selected from the group consisting of hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, -$NR^{20a}R^{20b}$, -OR^{21}, -SR^{21}, -$S(=O)R^{22}$, -$S(=O)_2R^{22}$, -$S(=O)NR^{20a}R^{20b}$, -$S(=O)_2NR^{20a}R^{20b}$, -$NR^{20a}S(=O)R^{20b}$, -$NR^{20a}S(=O)_2R^{20b}$, -$C(=O)R^{21}$, -$C(=O)NR^{23a}R^{23b}$, -$NR^{23a}C(=O)R^{23b}$, -$OC(=O)NR^{23a}R^{23b}$, and -$NR^{24a}C(=O)NR^{25a}R^{25b}$, and the alkyl, heteroalkyl (e.g., alkoxy), alkenyl, alkynyl, cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, -$NR^{30a}R^{30b}$, -OR^{31}, -SR^{31}, -$S(=O)R^{32}$, -$S(=O)_2R^{32}$, -$S(=O)NR^{30a}R^{30b}$, -$S(=O)_2NR^{30a}R^{30b}$, -$NR^{30a}S(=O)R^{30b}$, -$NR^{30a}S(=O)_2R^{30b}$, -$C(=O)R^{31}$, -$C(=O)NR^{33a}R^{33b}$, -$NR^{33a}C(=O)R^{33b}$, -$OC(=O)NR^{33a}R^{33b}$, and -

$NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-10-membered heterocyclyl;

preferably, R^5 is selected from the group consisting of C_{3-6} cycloalkyl, 4-10-membered heterocyclyl, C_{6-12} aryl, and 5-10-membered heteroaryl, and the cycloalkyl, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-10-membered heterocyclyl;

more preferably, R^5 is selected from the group consisting of C_{6-10} aryl and 5-6-membered heteroaryl, and the aryl and heretoaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl (e.g., C_{1-3} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, and $-NR^{33a}C(=O)R^{33b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted

with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-6-membered heterocyclyl;

further preferably, R^5 is selected from phenyl and 5-6-membered heteroaryl (e.g., pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrazolyl, oxazolyl, imidazolyl, or thiazolyl), and the phenyl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl (e.g., C_{1-3}alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4- 6-membered heterocyclyl, 5-8-membered heteroaryl (e.g., pyridyl, pyrrolyl, pyrazolyl, furyl, oxazolyl, imidazolyl, thiazolyl, or cyclopentyl-pyrazolyl), $-NR^{30a}R^{30b}$, $-OR^{31}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, and $-NR^{33a}C(=O)R^{33b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} heteroalkyl (e.g., C_{1-3}alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-6-membered heterocyclyl;

further more preferably, R^5 is selected from the group consisting of phenyl, pyridyl, pyrazolyl, and thiazolyl, and the phenyl, pyridyl, pyrazolyl, and thiazolyl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-6-membered heterocyclyl, 5-8-membered heteroaryl (e.g., pyridyl, pyrrolyl, pyrazolyl, furyl, oxazolyl, imidazolyl, thiazolyl, or cyclopentyl-pyrazolyl), $-NR^{30a}R^{30b}$, and $-OR^{31}$, wherein the heterocyclyl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} hydroxyalkyl, C_{1-3} haloalkoxy, C_{1-3} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-6-membered heterocyclyl; and

most preferably, R^5 is phenyl, pyridyl, pyrazolyl, or thiazolyl that is optionally substituted with one or more substituents selected from the group consisting of halogen (e.g., fluoro or chloro), CN, C_{1-3} alkyl (e.g., methyl or ethyl), C_{1-3} haloalkyl (e.g., trifluoromethyl), C_{1-3} alkoxy (e.g., methoxy or ethoxy), C_{3-6} cycloalkyl (e.g., cyclopropyl), C_{3-6} cycloalkoxy (e.g., cyclopropoxy), and 5-6-membered heteroaryl (e.g., pyridyl, pyrrolyl, pyrazolyl, furyl, oxazolyl, imidazolyl, or thiazolyl), wherein the 5-6-membered heteroaryl is optionally further substituted with one or more substituents selected from the group consisting of halogen (e.g., fluoro or chloro), C_{1-3} alkyl (e.g., methyl, ethyl, or isopropyl), C_{1-3} haloalkyl (e.g., fluoromethyl), C_{1-3} hydroxyalkyl (e.g., hydroxymethyl or hydroxypropyl), C_{1-3} alkoxy (e.g., methoxy), C_{3-6} cycloalkyl (e.g., cyclopropyl), and C_{3-6} cycloalkoxy (e.g., cyclopropoxy or cyclobutoxy).

7. The compound according to any one of claims 1 to 6, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, wherein:

R^{20a}, R^{20b}, R^{23a}, R^{23b}, R^{23c}, R^{24a}, R^{25a}, and R^{25b} are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{3-8} cycloalkyl; or R^{20a} and R^{20b}, R^{23a} and R^{23b}, or R^{25a} and R^{25b} form, together with an atom to which they are attached, a 3-8-membered cycloalkyl or heterocyclyl, and the alkyl, alkoxy, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: OH, CN, halogen, NO_2, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

preferably, R^{20a}, R^{20b}, R^{23a}, R^{23b}, R^{23c}, R^{24a}, R^{25a}, and R^{25b} are each independently H, C_{1-4} alkyl, or C_{1-4} alkoxy;

In particular, R^{23a} and R^{23b} are each independently selected from the group consisting of H, C_{1-3} alkyl, C_{1-3} alkoxy, and C_{3-6} cycloalkyl; or R^{23a} and R^{23b} form, together with a C atom to which they are attached, a C_{3-6} cycloalkyl or heterocyclyl, and the alkyl, alkoxy, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} hydroxyalkyl, C_{1-3} haloalkyl, and C_{1-3} haloalkoxy;

and/or

R^{21}, R^{22}, R^{31}, and R^{32} are each independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-8} cycloalkyl, and 4-10-membered heterocyclyl, and the alkyl, alkoxy, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: OH, halogen, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl;

preferably, R^{21}, R^{22}, R^{31}, and R^{32} are each independently selected from C_{1-4} alkyl;

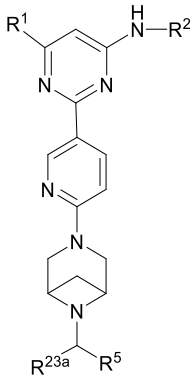
and/or

R^{30a}, R^{30b}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are each independently selected from the group consisting of H, C_{1-4} alkyl,C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy; and

preferably, R^{30a}, R^{30b}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are each independently selected from H and C_{1-4} alkyl.

8. The compound according to claim 1, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof,

wherein the compound has a structure shown in one of formula I-A to formula I-G:



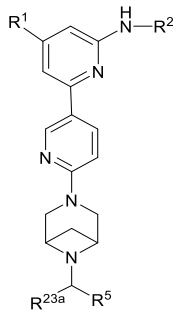
I-A ;

wherein:

R^5 is selected from the group consisting of C_{6-12} aryl and 5-10-membered heteroaryl, wherein (1) the C_{6-12} aryl is optionally substituted with one or more substituents selected from the group consisting of: C_{3-6} cycloalkoxy, C_{6-12} aryl, 5-10-membered heteroaryl, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkoxy, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl, and (2) the 5-10-membered heteroaryl is optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4}

alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, and 4-10-membered heterocyclyl; and

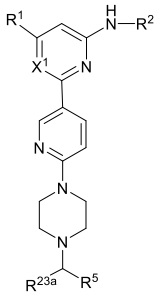
R^1, R^2, R^{23a}, R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7, and R^{23a} is preferably H or C_{1-3} alkyl;



I-B

wherein:

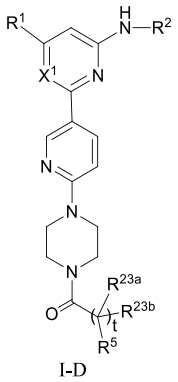
R^1, R^2, R^5, and R^{23a} are as defined in any one of claims 1 to 7, and R^{23a} is preferably H or C_{1-3} alkyl;



I-C

wherein:

when X^1 is CH, R^1, R^2, R^5, and R^{23a} are as defined in any one of claims 1 to 7, R^{23a} is preferably H or C_{1-3} alkyl; and when X^1 is N, R^1, R^2, R^5, and R^{23a} are as defined in the above formula I-A;



I-D

wherein:

R^1, R^2, R^{23a}, R^{23b}, and t are as defined in any one of claims 1 to 7;

when X^1 is CH, R^5 is as defined in any one of claims 1 to 7; and

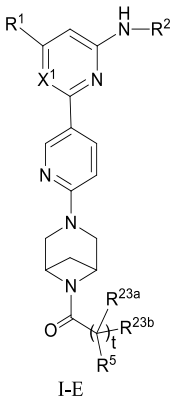
when X^1 is N, R^5 is C_{6-12} aryl or 5-10-membered heteroaryl, wherein

(i) when t is 0, the C_{6-12} aryl and 5-10-membered heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6}cycloalkyl, and 4-10-membered heterocyclyl,

(ii) when t is 1, (1) the C_{6-12} aryl is optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6}

alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4- 10-membered heterocyclyl, and (2) the 5-10-membered heteroaryl is optionally substituted with one or more substituents selected from the group consisting of: NO_2, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkoxy, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the aryl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl; and

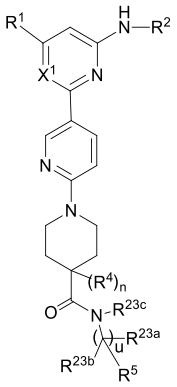
R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7;



I-E

wherein:

R^1, R^2, R^5, R^{23a}, R^{23b}, X^1, and t are as defined in the above formula I-D;



I-F

wherein:

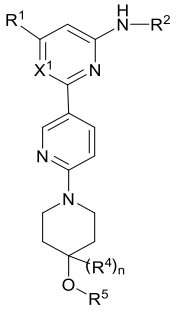
R^1, R^2, R^5, R^{23a}, R^{23b}, and X^1 are as defined in the above formula I-D;

R^4 is as defined in any one of claims 1 to 7, and is preferably C_{1-3} alkyl or C_{1-3} alkoxy;

R^{23c} is H, C_{1-3} alkyl, or C_{1-3} alkoxy, and the alkyl and alkoxy are each optionally substituted with one or more substituents selected from the group consisting of: OH, CN, halogen, C_{1-4} alkoxy, and C_{1-4} hydroxyalkyl;

u is 0 or 1; and

n is 0 or 1;



I-G

wherein:

X^1 is CH or N;

R^1, R^2, and R^4 are as defined in any one of claims 1 to 7, and R^4 is preferably C_{1-3} alkyl or C_{1-3} alkoxy;

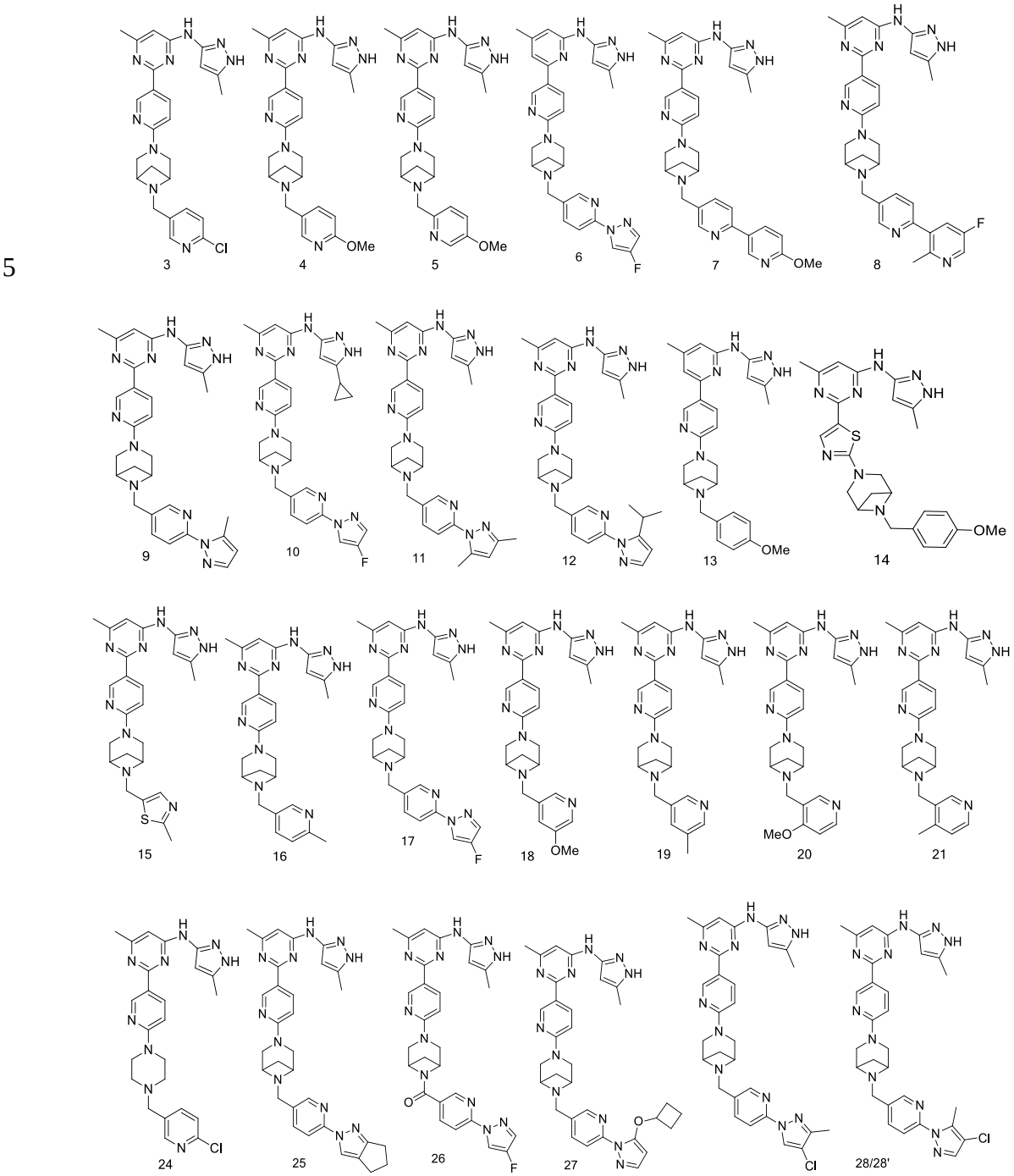
n is 0 or 1;

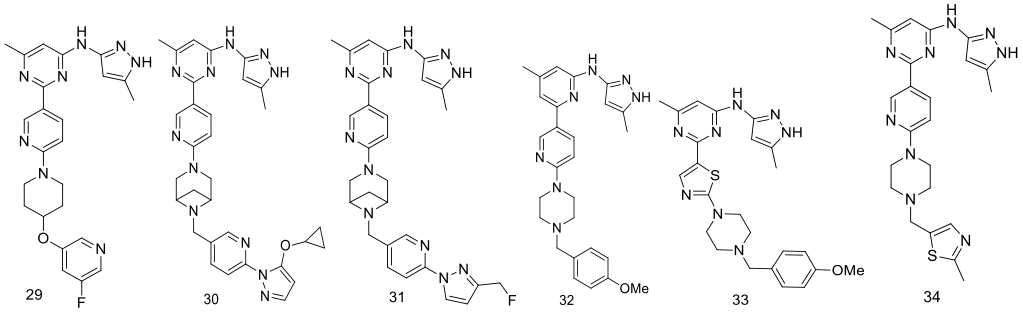
R^5 is selected from C_{6-12} aryl and 5-10-membered heteroaryl, wherein (1) the C_{6-12} aryl is optionally substituted with one or more substituents selected from the group consisting of: C_{3-6} cycloalkoxy, C_{6-12} aryl, 5-10-membered heteroaryl, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkoxy, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl; and (2) the 5-10-membered heteroaryl is optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, 4-10-membered heterocyclyl, C_{6-12} aryl, 5-10-membered heteroaryl, $-NR^{30a}R^{30b}$, $-OR^{31}$, $-SR^{31}$, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, wherein the cycloalkyl, cycloalkoxy, heterocyclyl, aryl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy), C_{3-6} cycloalkyl, and 4-10-membered heterocyclyl; and

R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7.

9. The compound according to claim 1, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof,

wherein the compound is selected from:

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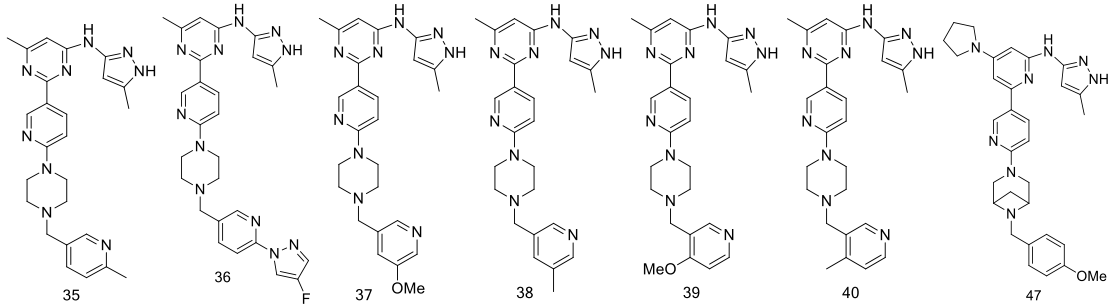
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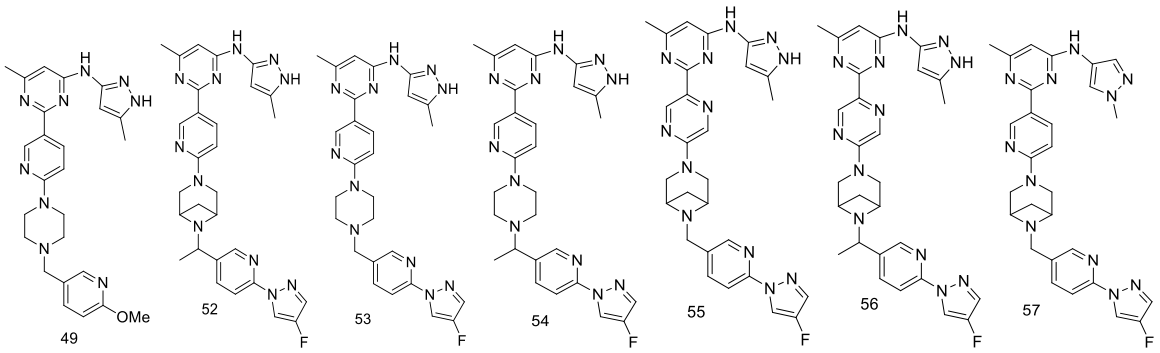
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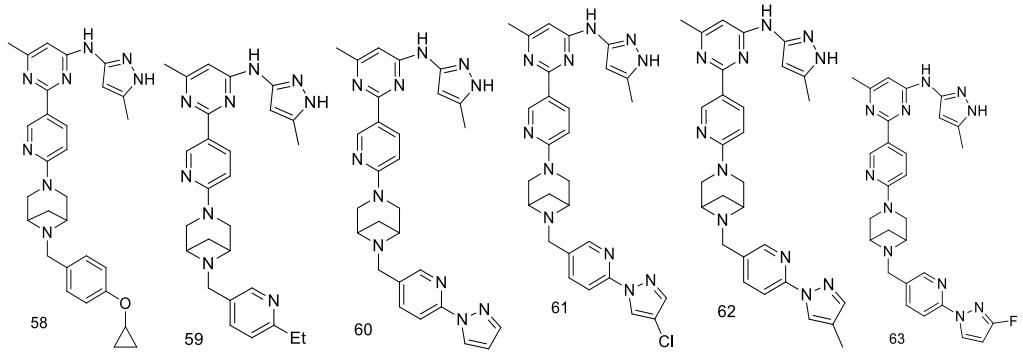
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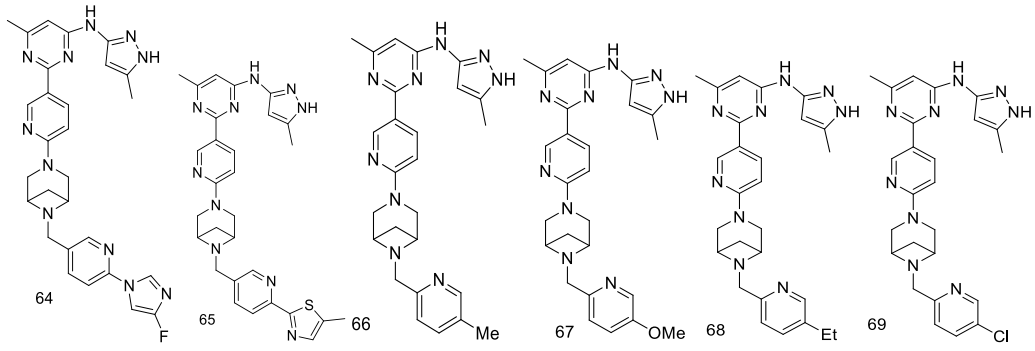
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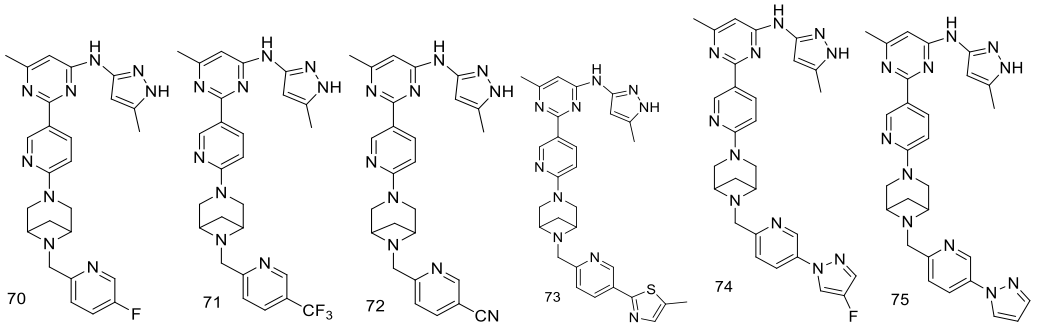
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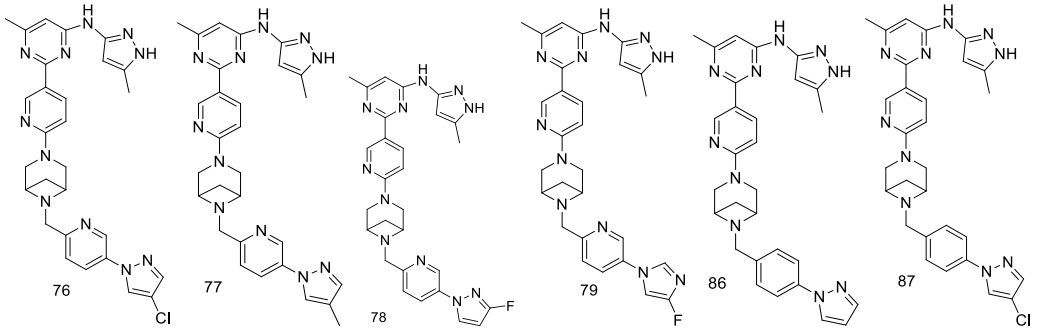
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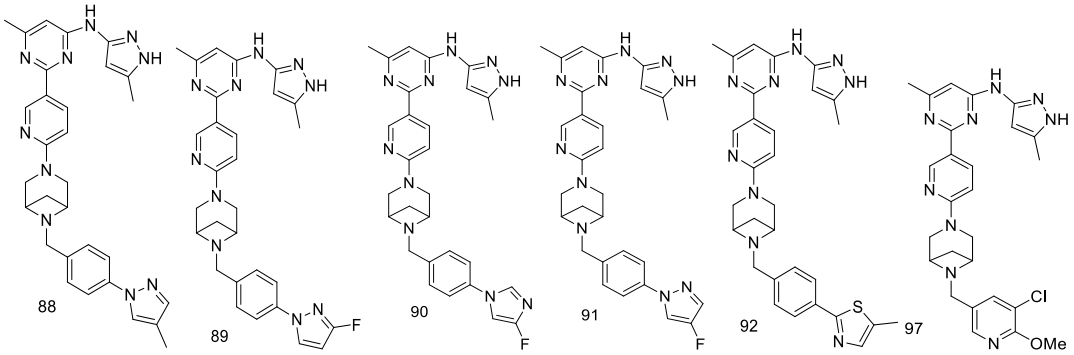
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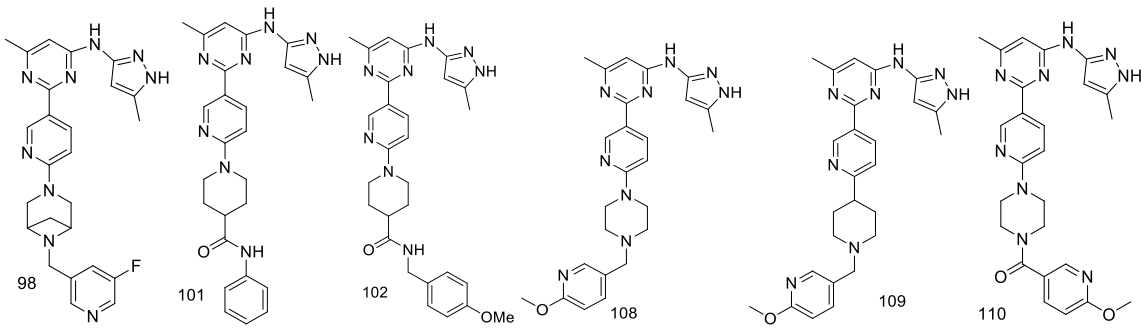
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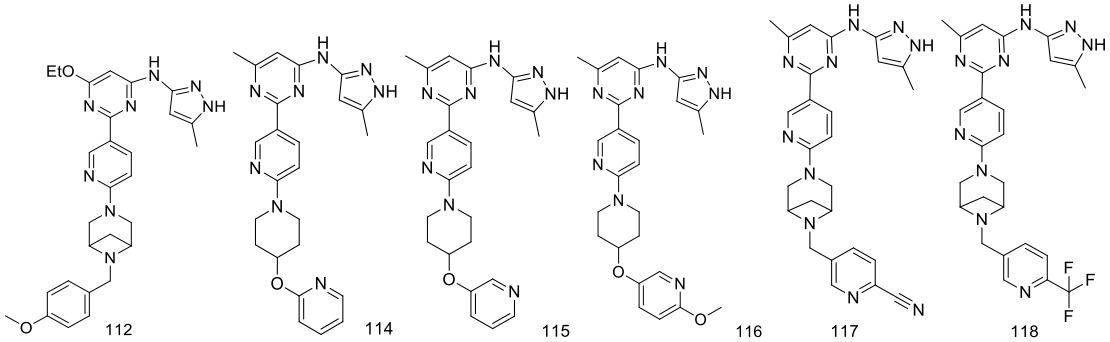
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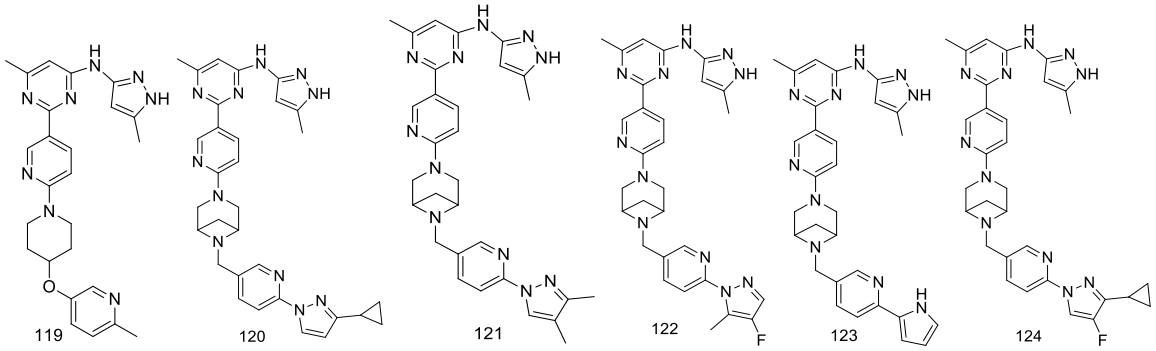
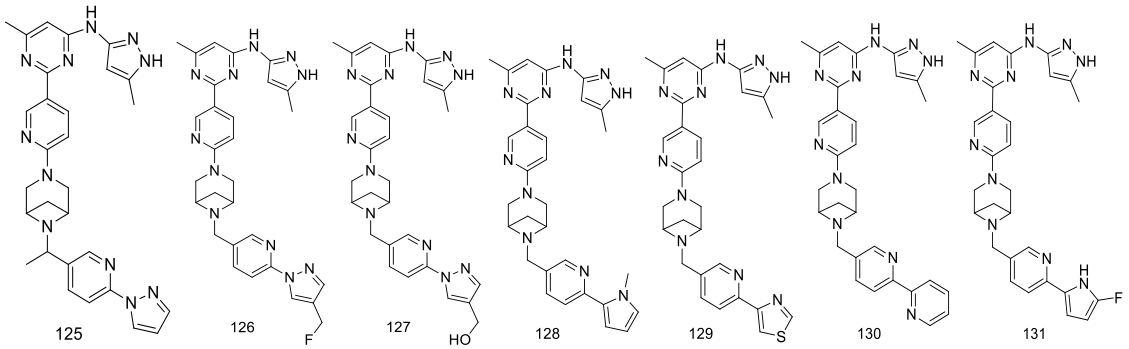
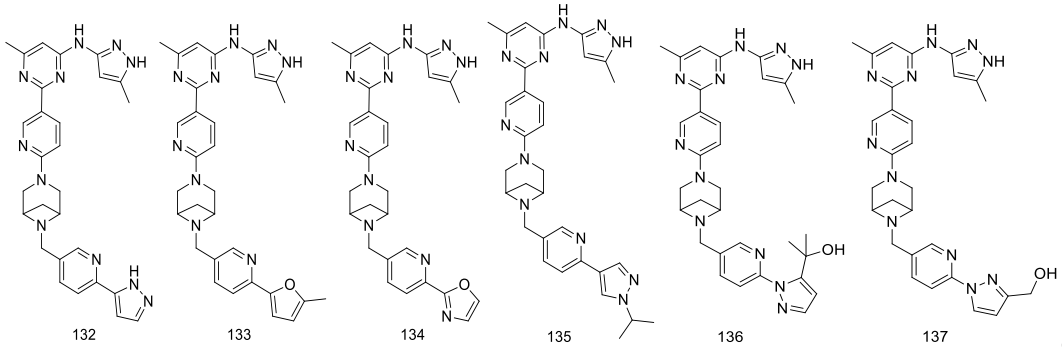
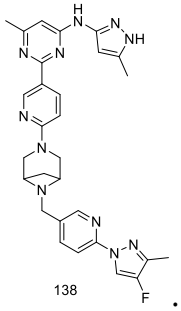






and



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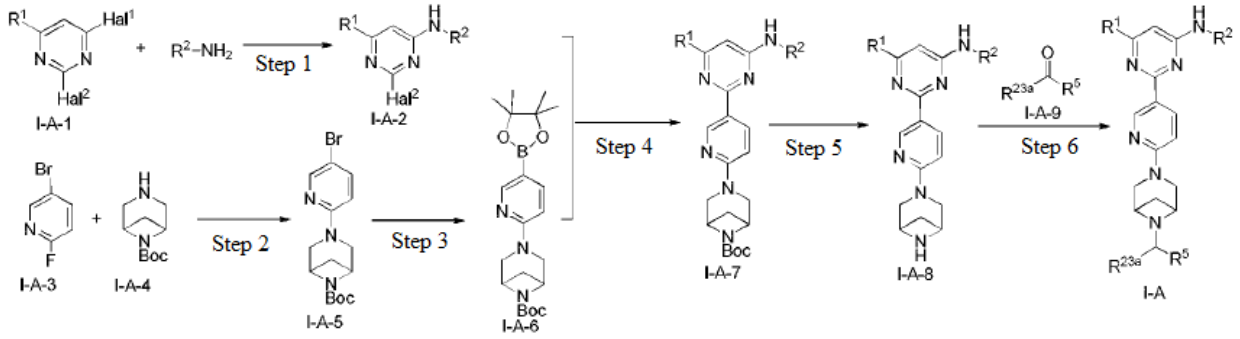
10. A method for preparing the compound according to claim 8, wherein the method comprises following steps:

Route A



wherein:

Hal^1 and Hal^2 are each independently F, Cl, Br, or I; and preferably, Hal^1 is F, Cl, Br, or I, and Hal^2 is Cl, Br, or I;

R^1 is selected from the group consisting of H, cyano, C_{1-6} alkyl, C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy), C_{3-8} cycloalkyl, 4-6-membered heterocyclyl, and $-NR^{20a}R^{20b}$, and the alkyl, heteroalkyl (e.g., alkoxy), cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, and C_{1-4} heteroalkyl (e.g., C_{1-4} alkoxy);

R^2 is selected from the group consisting of C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{3-8} cycloalkyl, 4-6-membered heterocyclyl, and 5-6-membered heteroaryl, and the alkyl, heteroalkyl, cycloalkyl, heterocyclyl, and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of: hydroxy, halogen, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{1-4} heteroalkyl, and C_{3-6} cycloalkyl;

R^{23a} is selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{3-8} cycloalkyl, and the alkyl, alkoxy, and cycloalkyl are each optionally substituted with one or more substituents selected from the group consisting of: OH, CN, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, and C_{1-4}haloalkoxy; and

R^{20a}, R^{20b}, and R^5 are as defined in formula I-A of claim 8;

Step 1: reacting compound I-A-1 with R^2-NH_2 in the presence of a base to generate compound I-A-2;

Step 2: reacting compound I-A-3 with compound I-A-4 in the presence of a base to generate compound I-A-5;

Step 3: reacting the compound I-A-5 with a boron-containing reagent to generate compound I-A-6;

Step 4: reacting the compound I-A-2 with the compound I-A-6 to generate compound I-A-7;

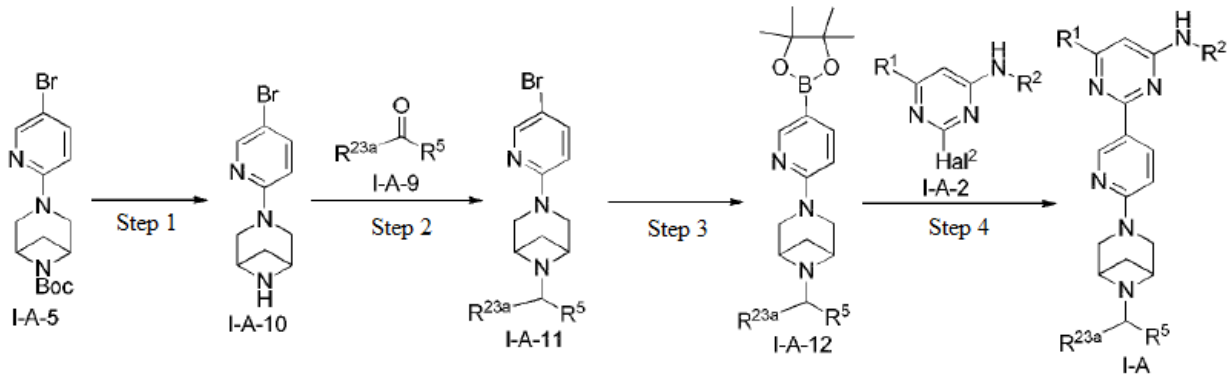
Step 5: deprotecting the compound I-A-7 under an acidic condition to generate compound I-A-8; and

Step 6: reacting the compound I-A-8 with compound I-A-9 to generate compound I-A;

or,

the method comprises following steps:

Route B



wherein:

each group is as defined in the above Route A;

Step 1: deprotecting the compound I-A-5 under an acidic condition to generate compound I-A-10;

Step 2: reacting the compound I-A-10 with the compound I-A-9 to generate compound I-A-11;

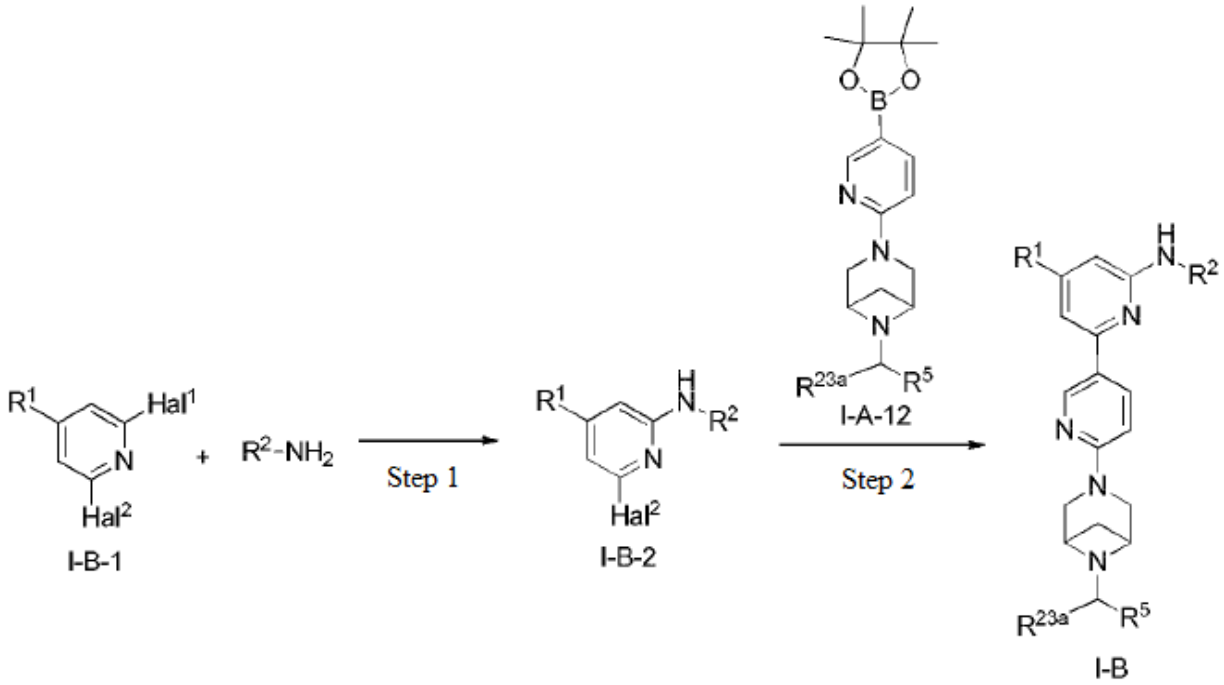
Step 3: reacting the compound I-A-11 with a boron-containing reagent to generate compound I-A-12; and

Step 4: reacting the compound I-A-12 with the compound I-A-2 to generate the compound I-A;

or,

the method comprises following steps:

Route C



wherein:

each group is as defined in the above Route A;

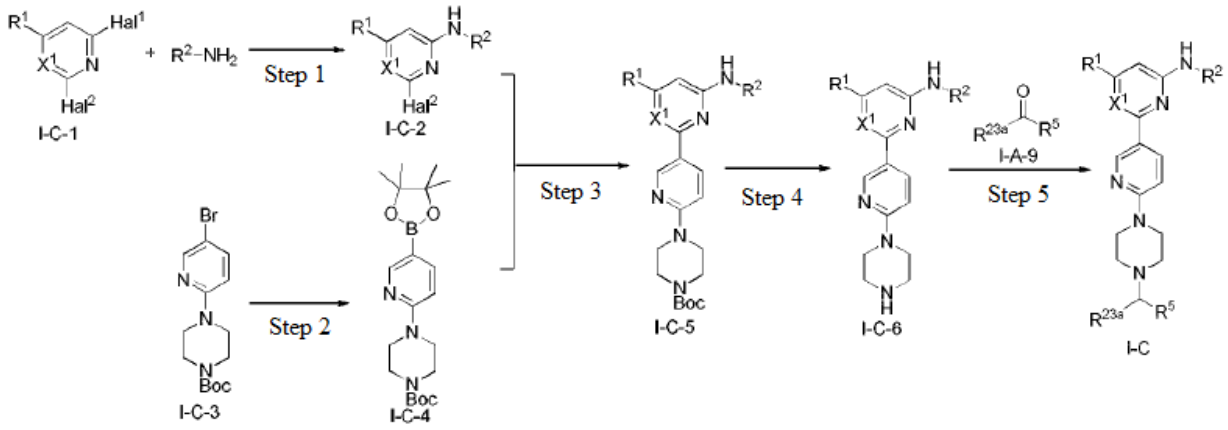
Step 1: reacting compound I-B-1 with R^2-NH_2 in the presence of a base to generate compound I-B-2; and

Step 2: reacting the compound I-B-2 with the compound I-A-12 to generate compound I-B;

or,

the method comprises following steps:

Route D



wherein:

each group is as defined in the above Route A; and X^1 is selected from CH and N;

Step 1: reacting compound I-C-1 with R^2-NH_2 in the presence of a base to generate compound I-C-2;

Step 2: reacting compound I-C-3 with a boron-containing reagent to generate compound I-C-4;

Step 3: reacting the compound I-C-2 with the compound I-C-4 to generate compound I-C-5;

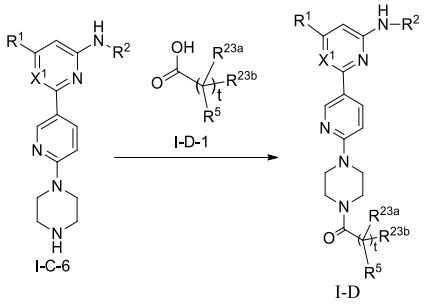
Step 4: deprotecting the compound I-C-5 under an acidic condition to generate compound I-C-6; and

Step 5: reacting the compound I-C-6 with the compound I-A-9 to generate compound I-C;

or,

the method comprises following steps:

Route E



wherein:

R^1 and R^2 are as defined in the Route A;

R^5 is as defined in formula I-D of claim 8;

R^{23a} and R^{23b} are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{3-8} cycloalkyl; or R^{23a} and R^{23b} form, together with a C atom to which they are attached, a 3-8-membered cycloalkyl or heterocyclyl, and the alkyl, alkoxy, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents selected from the group consisting of: CN, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

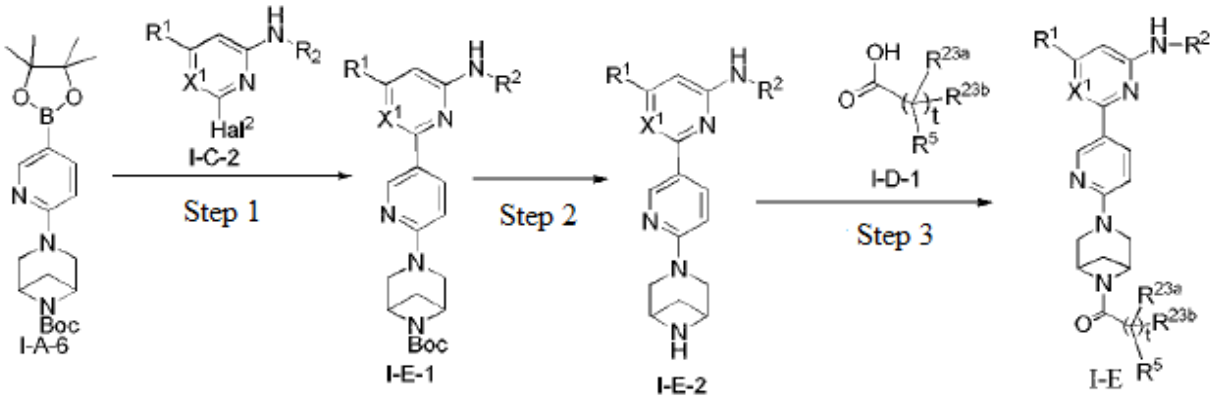
X^1 is selected from CH and N; and

t is 0 or 1;

or,

the method comprises following steps:

Route F



wherein:

R^1, R^2, R^5, R^{23a}, R^{23b}, and t are as defined in the Route E;

X^1 is selected from CH and N; and

Hal^2 is F, Cl, Br, or I; and preferably, Hal^2 is Cl, Br, or I;

Step 1: reacting the compound I-C-2 with the compound I-A-6 to generate compound I-E-1;

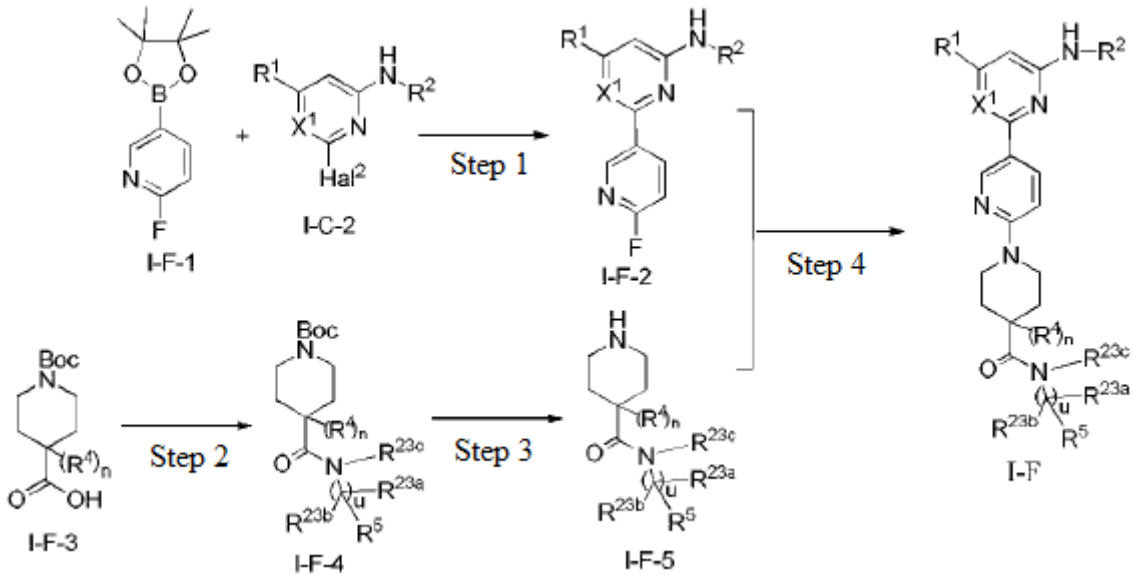
Step 2: deprotecting the compound I-E-1 under an acidic condition to generate compound I-E-2; and

Step 3: reacting the compound I-E-2 with the compound I-D-1 through a condensation reaction to generate compound I-E;

or,

the method comprises following steps:

Route G



wherein:

R^1, R^2, R^{23a}, R^{23b}, and R^5 are as defined in the Route E;

X^1 is selected from CH and N;

R^4 is absent or is selected from the group consisting of hydroxy, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, and C_{1-6} heteroalkyl (e.g., C_{1-6} alkoxy);

R^{23c} is H, C_{1-3} alkyl, or C_{1-3} alkoxy, and the alkyl and alkoxy are each optionally substituted with one or more substituents selected from the group consisting of: OH, CN, halogen, C_{1-4} alkoxy, and C_{1-4} hydroxyalkyl;

Hal^2 is F, Cl, Br, or I; and preferably, Hal^2 is Cl, Br, or I;

u is 0 or 1; and

n is 0 or 1;

Step 1: reacting the compound I-C-2 with compound I-F-1 to generate compound I-F-2;

Step 2: reacting compound I-F-3 with an amine to generate compound I-F-4;

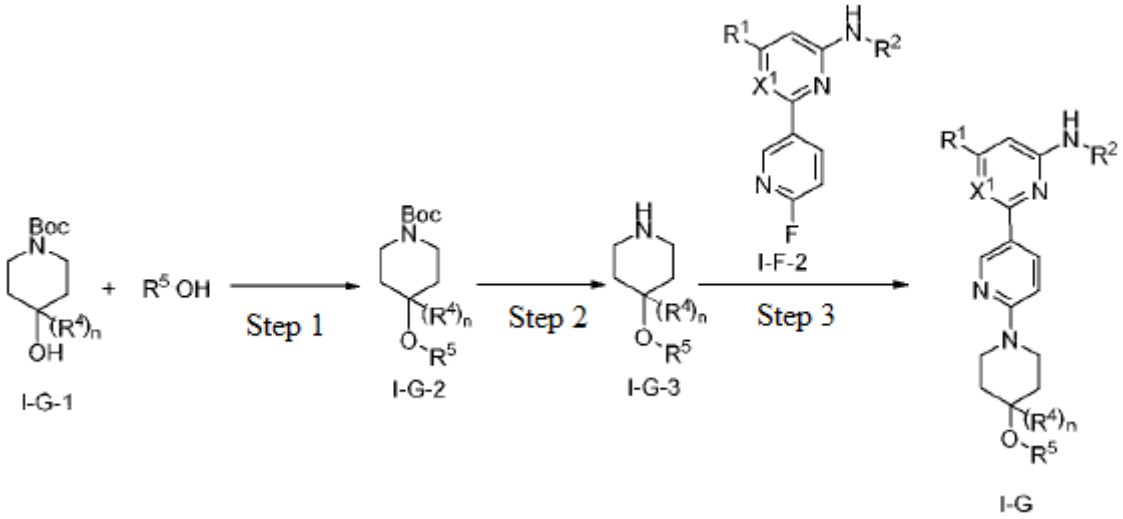
Step 3: deprotecting the compound I-F-4 under an acidic condition to generate compound I-F-5; and

Step 4: reacting the compound I-F-2 with the compound I-F-5 in the presence of a base to generate compound I-F;

or,

the method comprises following steps:

Route H



wherein:

R^1 and R^2 are as defined in the Route A;

X^1 is selected from CH and N;

R^4 is selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} haloalkyl, and C_{1-6} heteroalkyl;

R^5 is as defined in the above formula I-G; and

n is 0 or 1;

Step 1: reacting compound I-G-1 with R^5-OH to generate compound I-G-2;

Step 2: deprotecting the compound I-G-2 under an acidic condition to generate compound I-G-3; and

Step 3: reacting the compound I-F-2 with the compound I-G-3 through a nucleophilic substitution reaction in the presence of a base to generate compound I-G.

11. A pharmaceutical composition, comprising a prophylactically or therapeutically effective amount of the compound according to any one of claims 1 to 9, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof;

optionally, the pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers.

12. Use of the compound according to any one of claims 1 to 9, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative, metabolite, or prodrug thereof, or the pharmaceutical composition according to claim 11 in the preparation of a drug for preventing or treating a disease or condition associated with RET activity;

wherein, preferably the disease or condition associated with RET activity is a cancer or tumor, or an irritable bowel syndrome;

and the cancer or tumor further preferably is lung cancer (such as non-small cell lung cancer), breast cancer, head and neck cancer, rectal cancer, liver cancer, lymphoma, thyroid cancer (such as medullary thyroid cancer or papillary thyroid cancer), colon cancer, multiple myeloma, melanoma, glioma, brain tumor, or sarcoma.