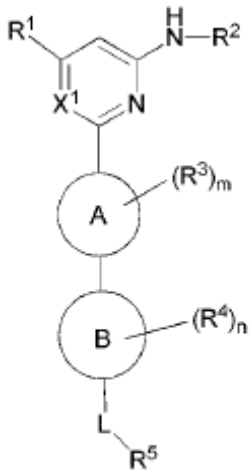
CLAIMS

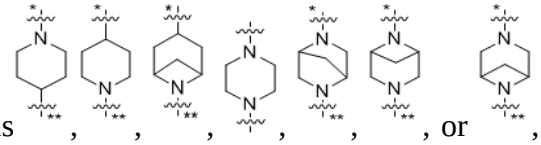
[Claim 1]. A compound, a stereoisomer, tautomer, or mixture thereof, a N-oxide thereof, a pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or a stable isotope derivative, thereof, wherein the compound has a structure of formula I:



Formula I

wherein:

ring A is 5-6-membered nitrogen-containing heteroaromatic ring;

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

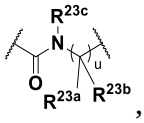
X^1 is selected from N and CH;

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 5membered heteroaryl, and the heteroaryl is 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-, -C(O)-, , the C_{1-6} alkylene is 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;;

R^5 is selected from the group consisting of phenyl and 5-6-membered heteroaryl, and the phenyl and 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}, and R^{23c} 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}, 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;

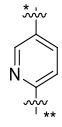
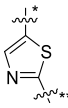
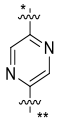
R^{31}, and R^{32} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, 4-10-membered heterocyclyl, C_{6-12} aryl, and 5-10-membered heteroaryl, and the alkyl, alkoxy, cycloalkyl, heterocyclyl, aryl, and heteroaryl are each optionally substituted 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; andu is 0 or 1.

[Claim 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 thereof, wherein:

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

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 **;

X^1 is N.

[Claim 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 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 5-membered heteroaryl, and the heteroaryl is 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;

preferably, R^2 is selected from the group consisting of thienyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, thiadiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, and isoxazolyl, and the thienyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, thiadiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, and isoxazolyl, 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), or a cyclopropyl-substituted pyrazolyl (e.g., 5-cyclopropyl-1H-pyrazol-3-yl),.

[Claim 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 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;

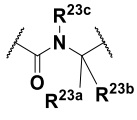
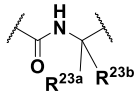
preferably, R^3 and R^4 are absent or are, at each occurrence, independently selected from the group consisting of hydroxy, halogen, CN, C_{1-3} alkyl, C_{1-3} alkoxy, the alkyl and alkoxy are each optionally substituted with one or more substituents selected from the group consisting of: halogen, CN, 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

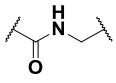
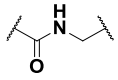
heterocyclyl; and/or when n is greater than 1, two R^4 optionally form, together with an atom to which they are attached, a C_{3-6} cycloalkyl or a 4-10-membered heterocyclyl;

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.

[Claim 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 thereof, wherein:

L is selected from the group consisting of -O-, C(O)-, C(O)-N(R^{23c})-, C_{1-4} alkylene, and  and the C_{1-4} alkylene 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), and C_{3-6} cycloalkyl;preferably, L is selected from the group consisting of -O-, -C(O)-, C(O)NH-, C_{1-3} alkylene and , and the C_{1-3} alkylene is 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)-, C(O)NH-, C_{1-3} alkylene and , and the C_{1-3} 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; andfurther preferably, L is -CH_2-, -$CH(CH_3)$-, -O-, -C(O)-, , -C(O)NH-, or .

[Claim 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 thereof, wherein:

R^5 is selected from phenyl and 5-6-membered heteroaryl, said 5-6-membered heteroaryl is 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;

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

more 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).

[Claim 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 thereof, wherein:

R^{20a}, R^{20b}, R^{23a}, R^{23b} and R^{23c} 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}, or R^{23a} and R^{23b}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} and R^{23c} 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^{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^{31}, and R^{32} are each independently selected from C_{1-4} alkyl;

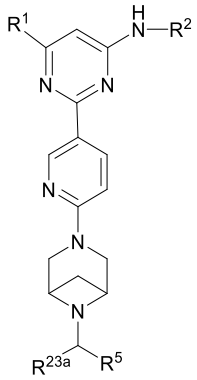
and/or

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.

[Claim 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 thereof,

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

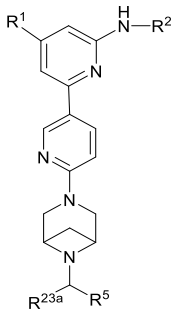


I-A ;

wherein:

R^5 is selected from the group consisting of phenyl and 5-6-membered heteroaryl, wherein (1) the phenyl 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 5-6-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

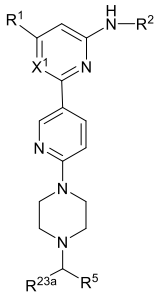
R^1, R^2, R^{23a}, R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7, and R^{23a} is preferably H or C_{1-3} alkyl;



I-B

wherein:

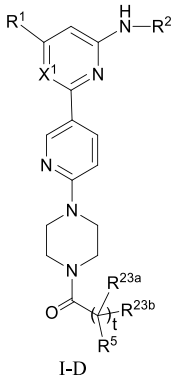
R^1, R^2, R^5, and R^{23a} are as defined in any one of claims 1 to 7, and R^{23a} is preferably H or C_{1-3} alkyl;



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

t is 0;

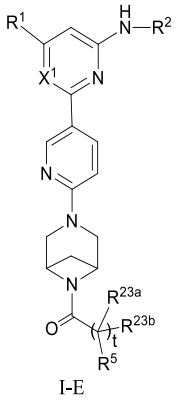
when X^1 is CH, R^5 is as defined in any one of claims 1 to 7; and

when X^1 is N, R^5 is phenyl or 5-6-membered heteroaryl, wherein

the phenyl and 5-6-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,

and

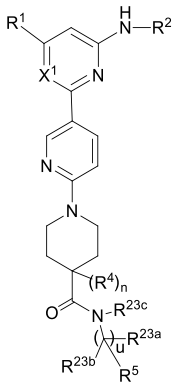
R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7;



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:

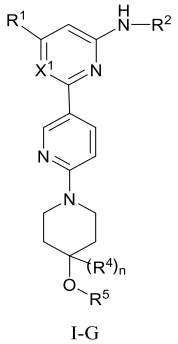
R^1, R^2, R^5, R^{23a}, R^{23b}, and X^1 are as defined in the above formula I-D;

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;

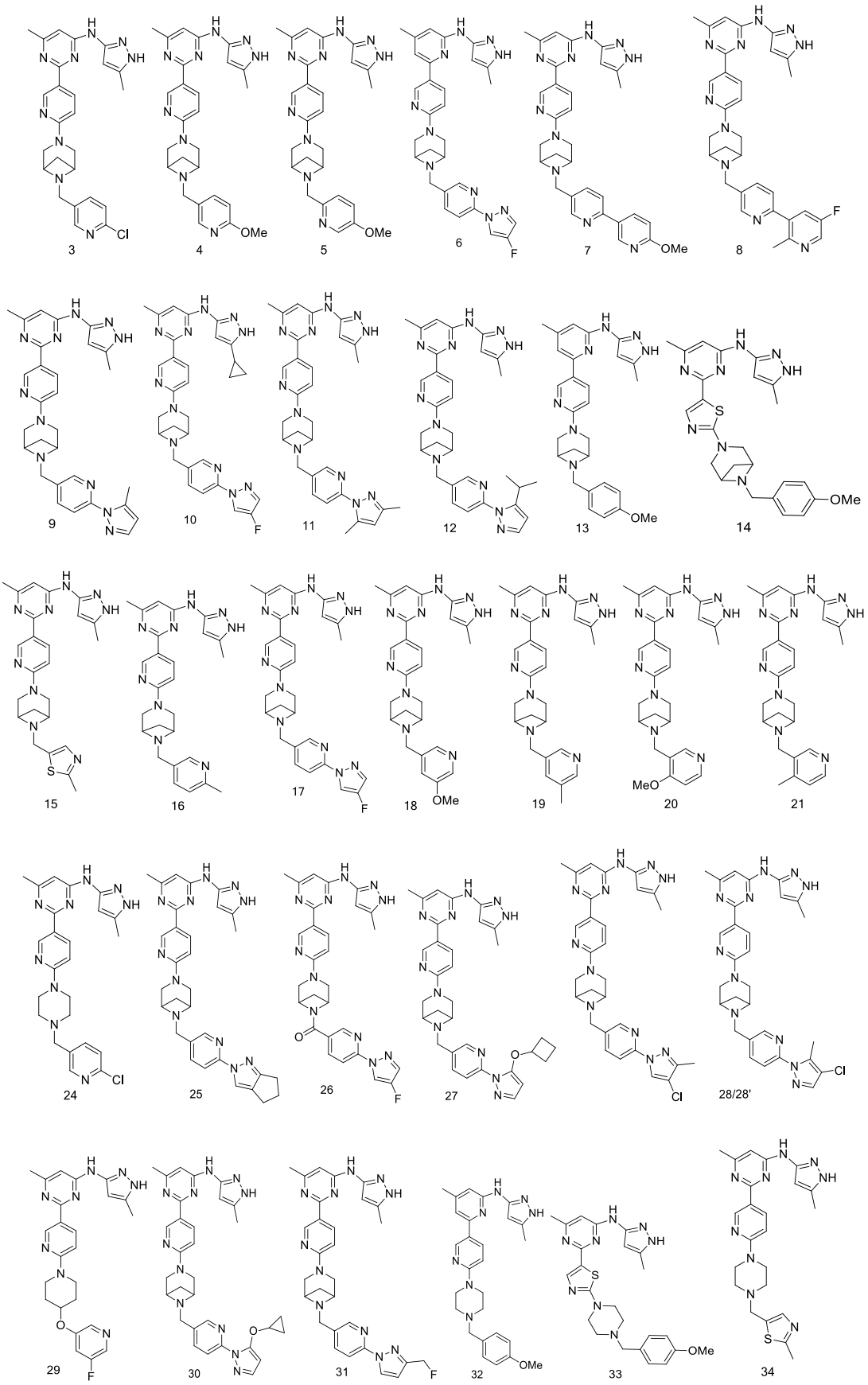
R^5 is selected from phenel and 5-6-membered heteroaryl, wherein (1) the phenyl is optionally substituted with one or more substituents selected from the group consisting of:

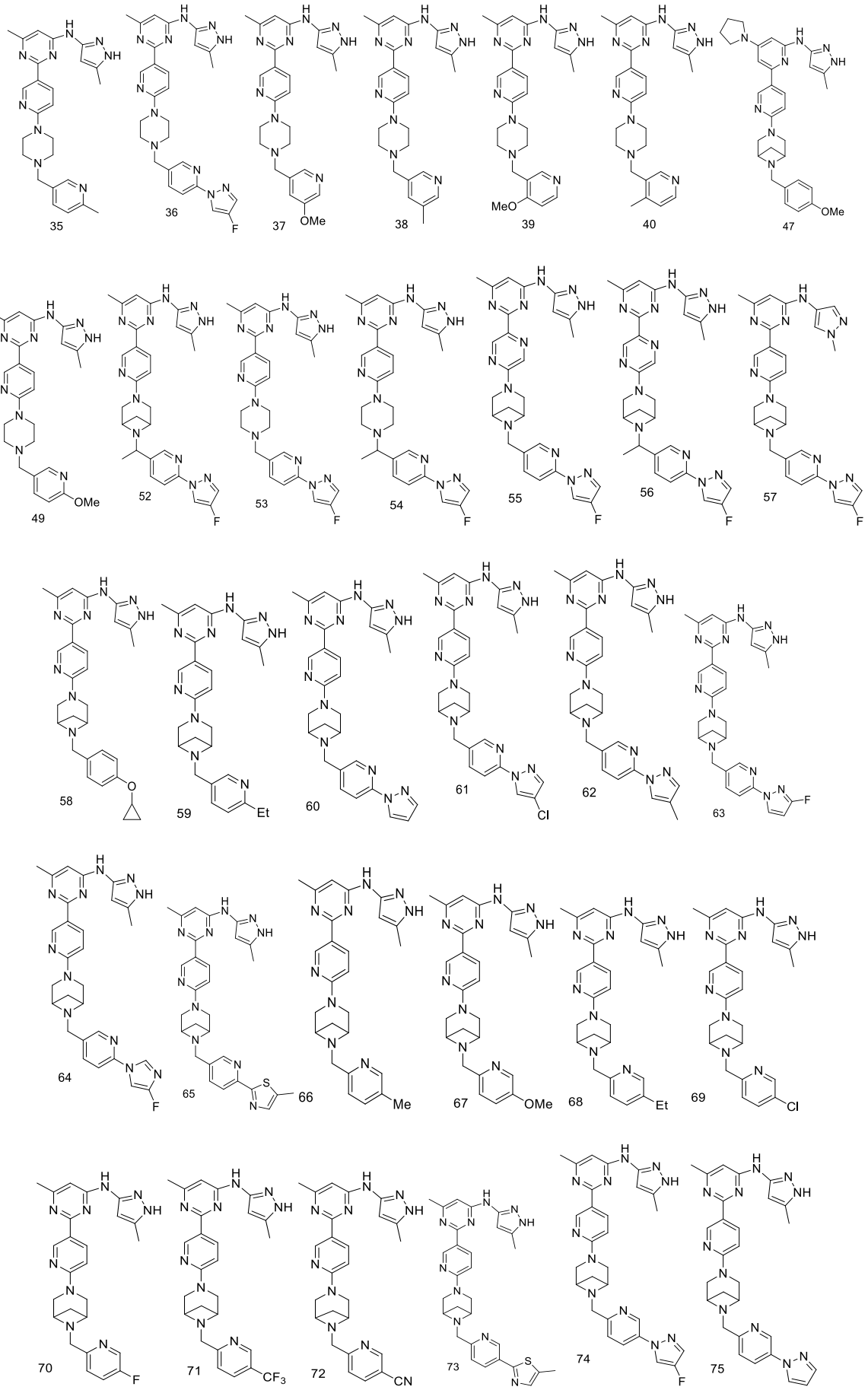
C_{3-6} cycloalkoxy, C_{6-12} aryl, 5-10-membered heteroaryl, $-S(=O)R^{32}$, $-S(=O)_2R^{32}$, $-S(=O)NR^{30a}R^{30b}$, $-S(=O)_2NR^{30a}R^{30b}$, $-NR^{30a}S(=O)R^{30b}$, $-NR^{30a}S(=O)_2R^{30b}$, $-C(=O)R^{31}$, $-C(=O)NR^{33a}R^{33b}$, $-NR^{33a}C(=O)R^{33b}$, $-OC(=O)NR^{33a}R^{33b}$, and $-NR^{34a}C(=O)NR^{35a}R^{35b}$, 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 5-6-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

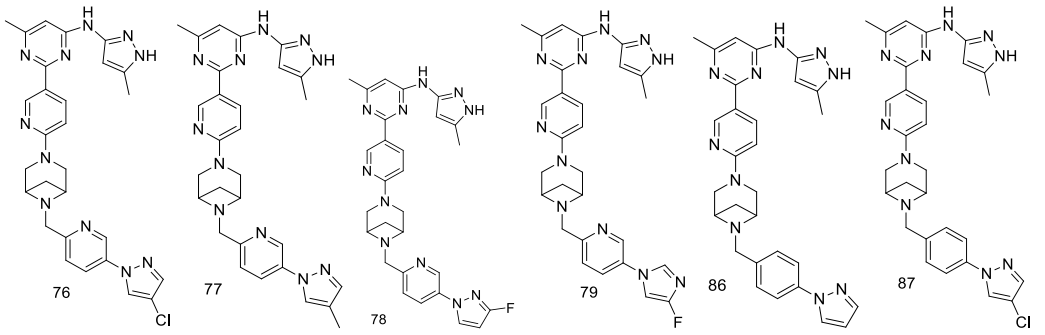
R^{30a}, R^{30b}, R^{31}, R^{32}, R^{33a}, R^{33b}, R^{34a}, R^{35a}, and R^{35b} are as defined in any one of claims 1 to 7.

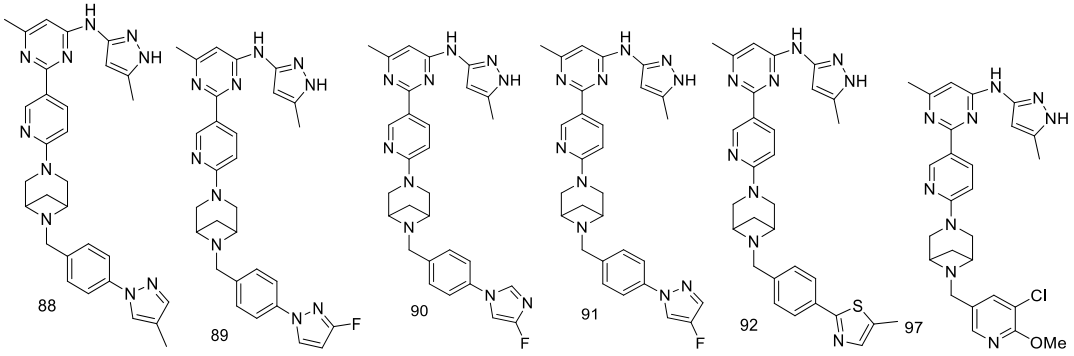
[Claim 9]. A compound a stereoisomer, tautomer, or mixture thereof, a N-oxide thereof, a pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or a stable isotope derivative thereof,

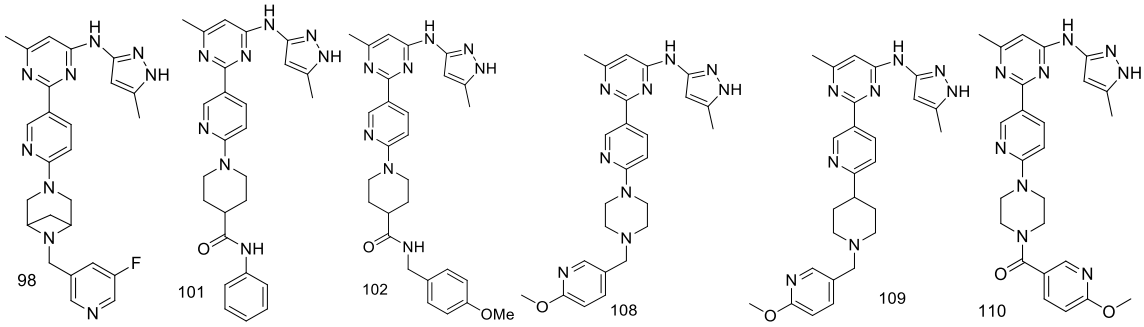
wherein the compound is selected from:

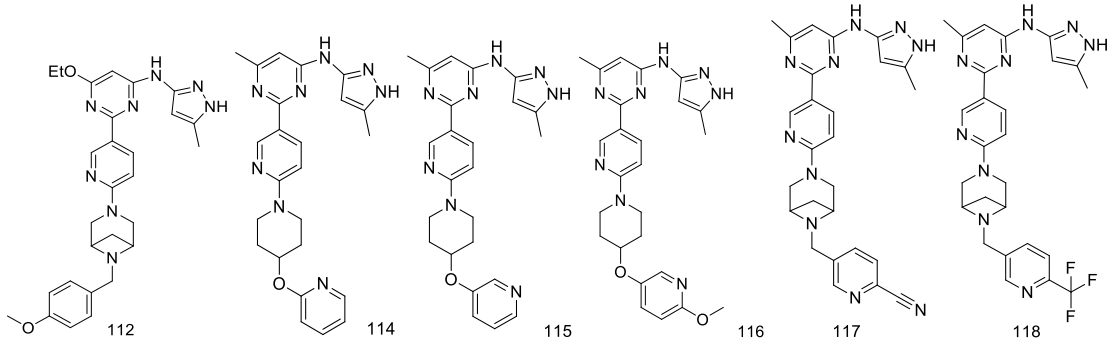

3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
24
25
26
27
28/28'
29
30
31
32
33
34

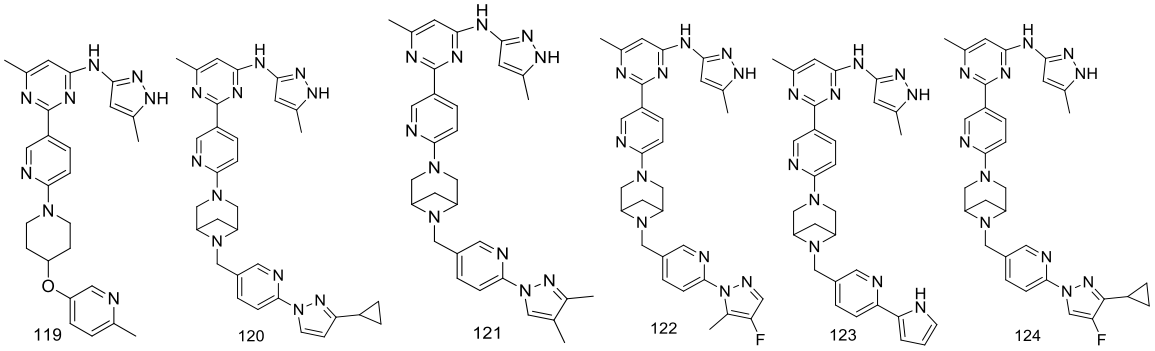

35
36
F
37
OMe
38
39
MeO
40
47
OMe
49
OMe
52
F
53
F
54
F
55
F
56
F
57
F
58
O
59
Et
60
61
Cl
62
63
F
64
F
65
66
Me
67
OMe
68
Et
69
Cl
70
F
71
CF3
72
CN
73
74
F
75

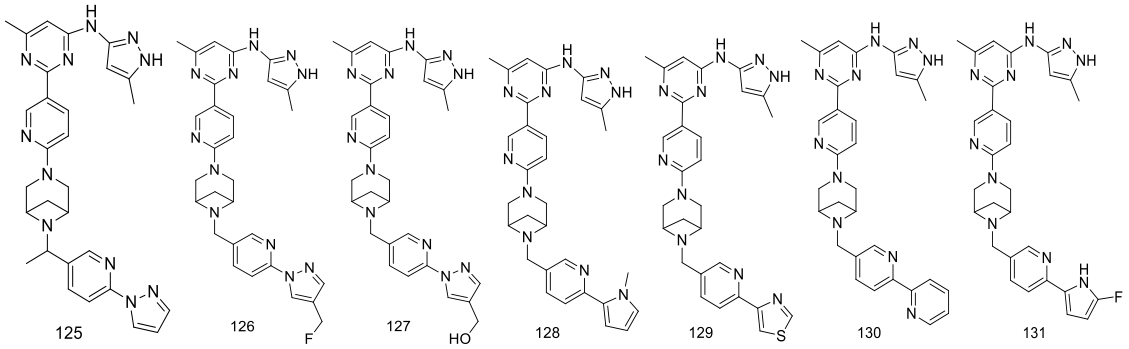

76
77
78
79
86
87

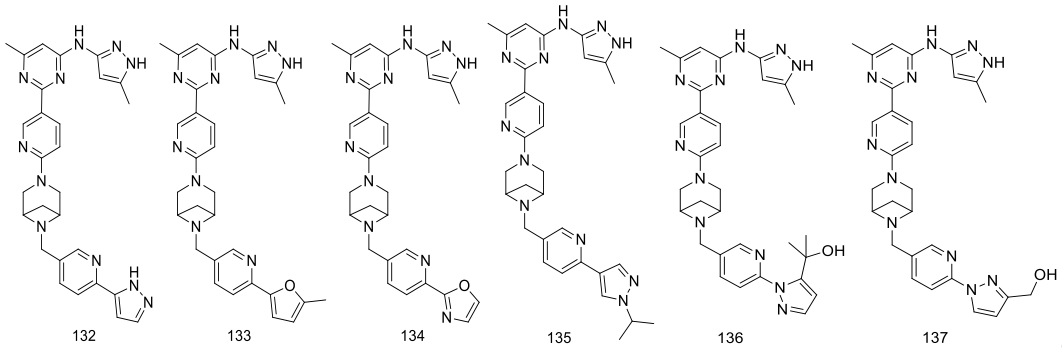

88
89
90
91
92
97


98
101
102
108
109
110

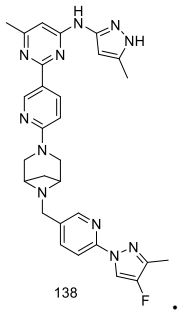

112
114
115
116
117
118


119
120
121
122
123
124





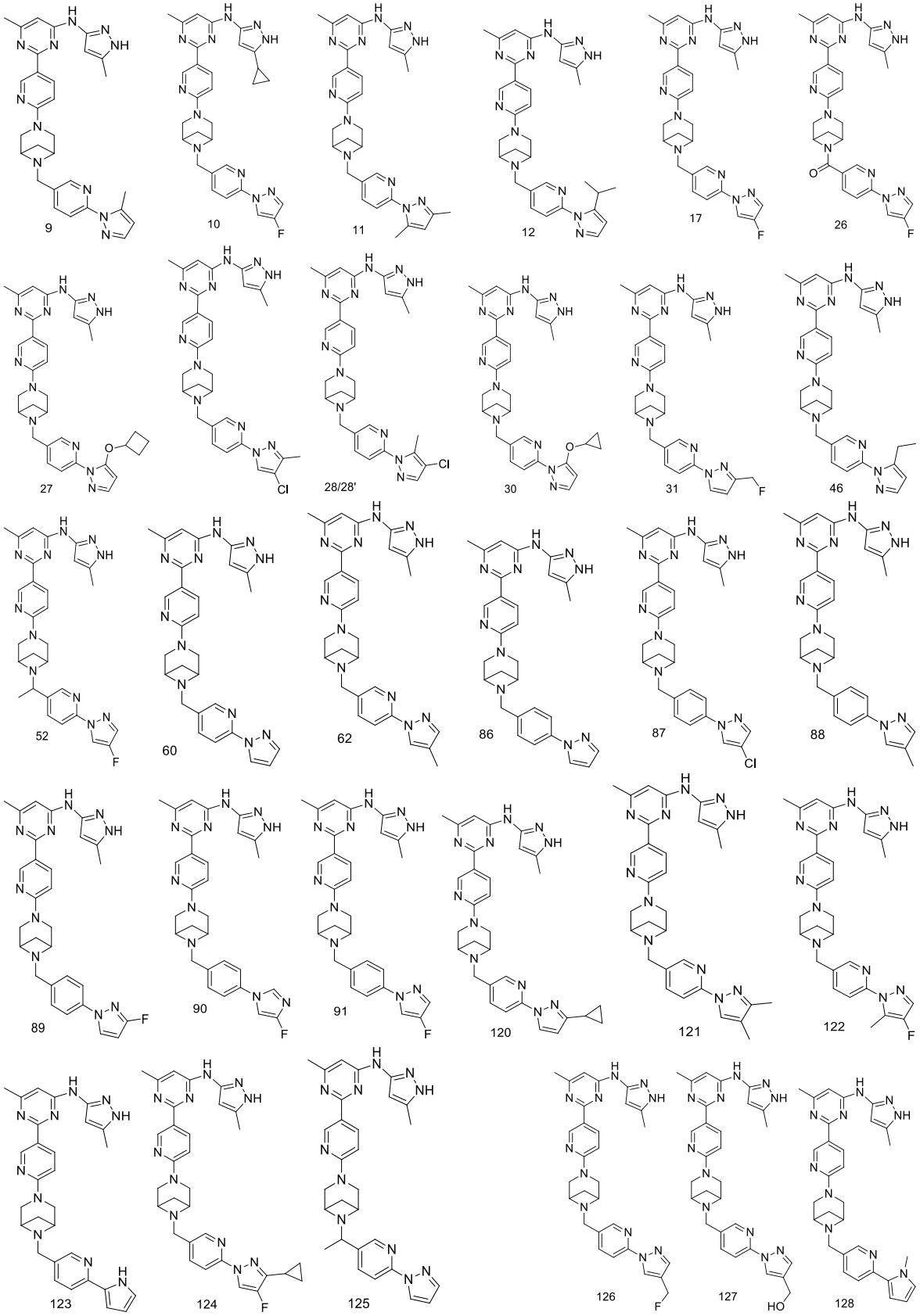
and

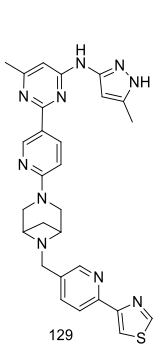


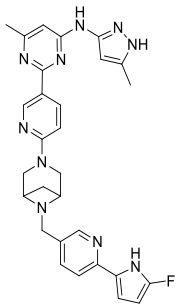
.

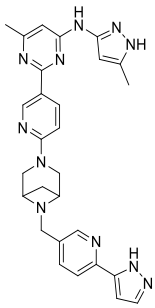
[Claim 10]. A compound, a stereoisomer, tautomer, or mixture thereof, a N-oxide thereof, a pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or a stable isotope derivative thereof,

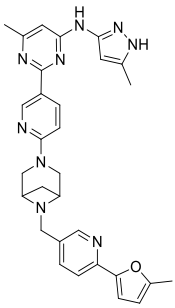
wherein the compound is selected from:

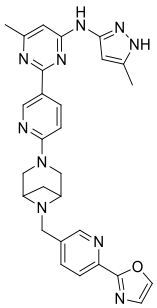

9
10
11
12
17
26
27
28/28'
30
31
46
52
60
62
86
87
88
89
90
91
120
121
122
123
124
125
126
127
128

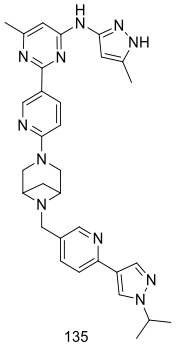

129

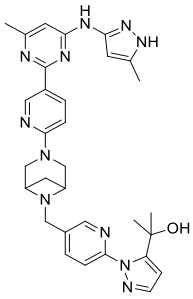

131

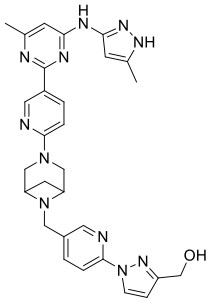

132


133

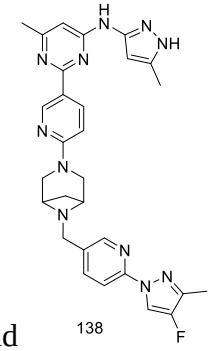

134


135


136


137

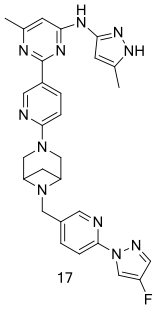
and

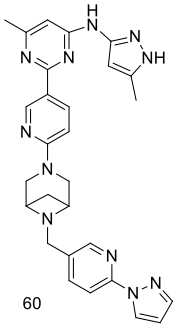

138

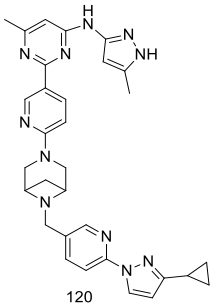
.

[Claim 11]. 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 thereof,

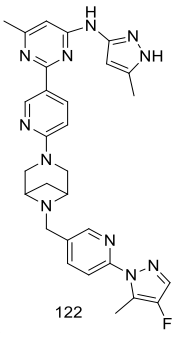
wherein the compound is selected from:


17


60


120

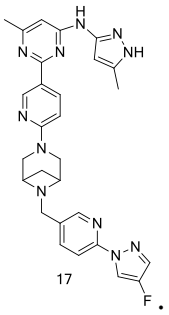
and


122

.

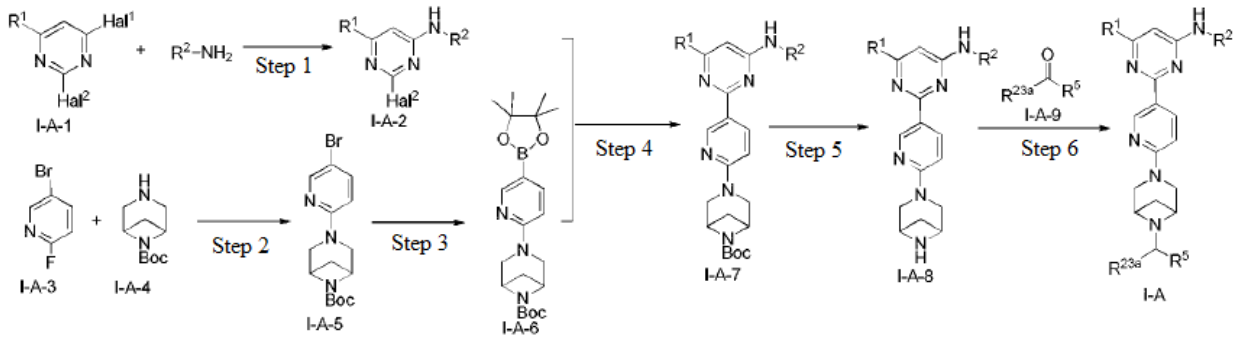
[Claim 12]. A compound, a stereoisomer, tautomer, or mixture thereof, a N-oxide thereof, a pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or a stable isotope derivative thereof,

wherein the compound is:



[Claim 13]. 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 5-membered heteroaryl, and the heteroaryl is 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;

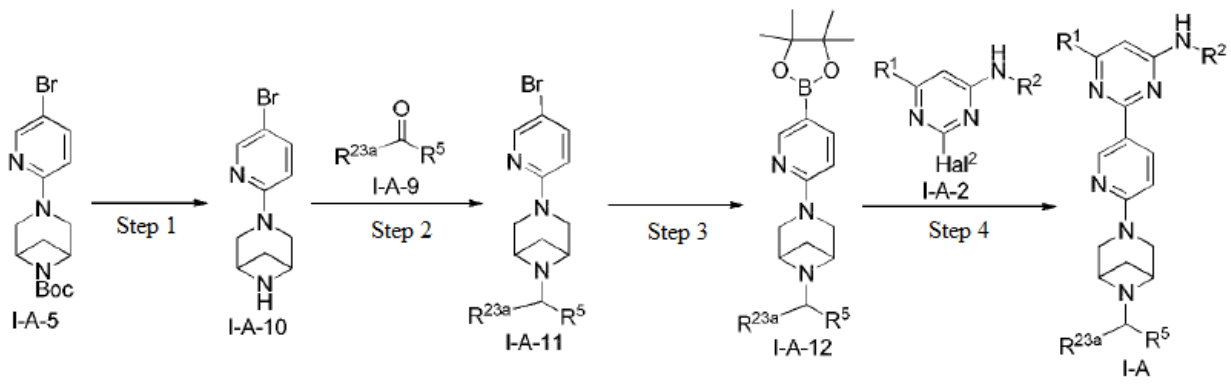
Step 4: reacting the compound I-A-2 with the compound I-A-6 to generate compound I-A-7;

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;

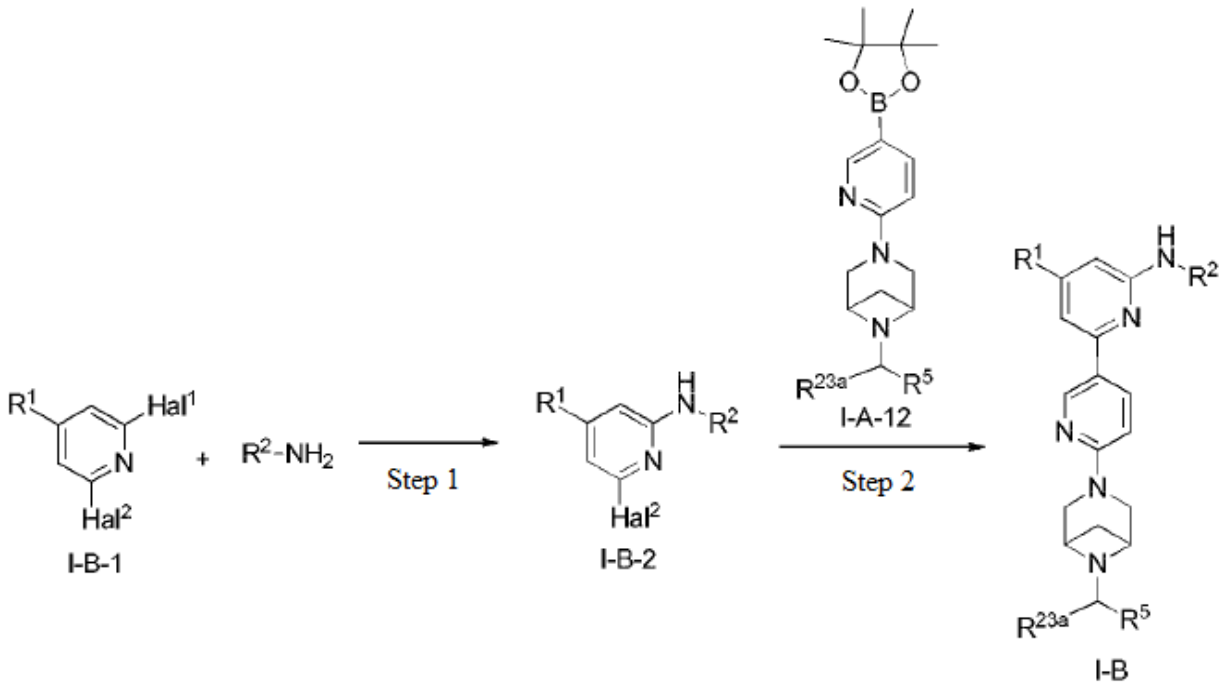
Step 3: reacting the compound I-A-11 with a boron-containing reagent to generate compound I-A-12; and

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;

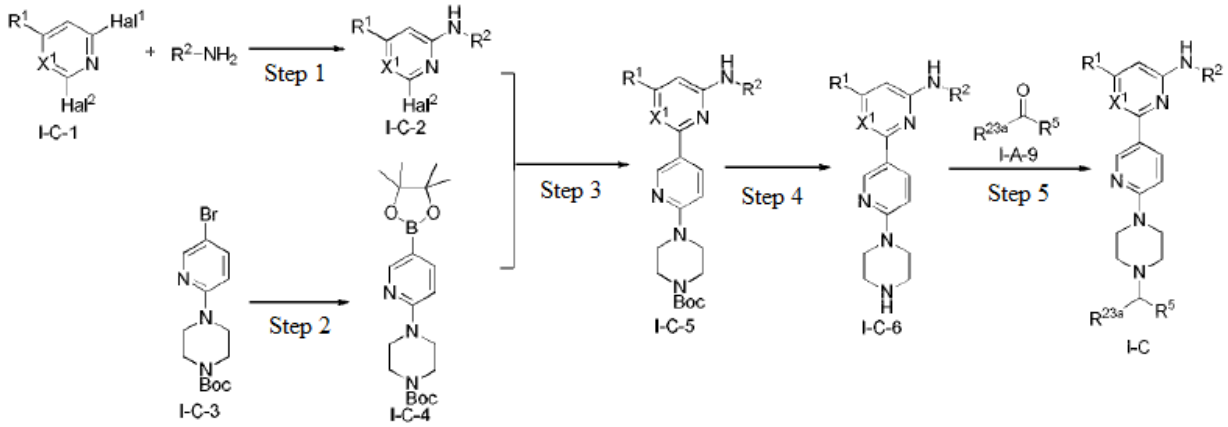
Step 1: reacting compound I-B-1 with R^2-NH_2 in the presence of a base to generate compound I-B-2; and

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;

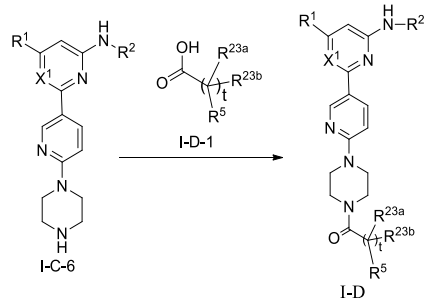
Step 4: deprotecting the compound I-C-5 under an acidic condition to generate compound I-C-6; and

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;

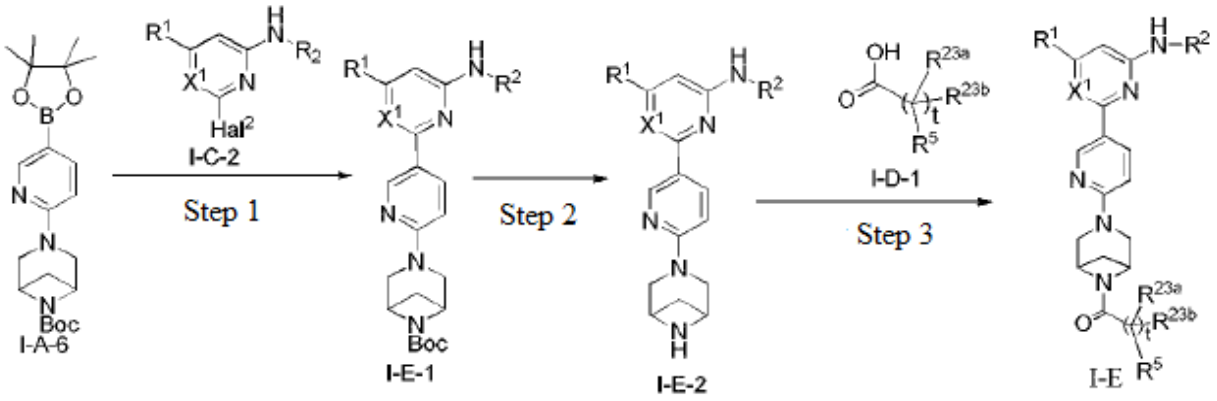
X^1 is selected from CH and N; and

t is 0;

or,

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;

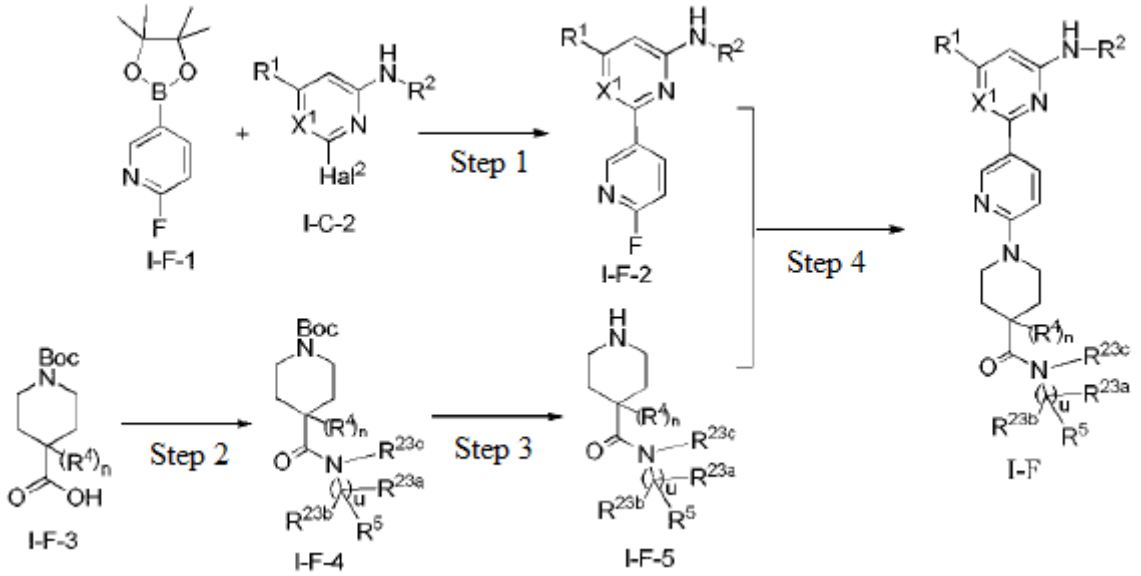
Step 2: deprotecting the compound I-E-1 under an acidic condition to generate compound I-E-2; and

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;

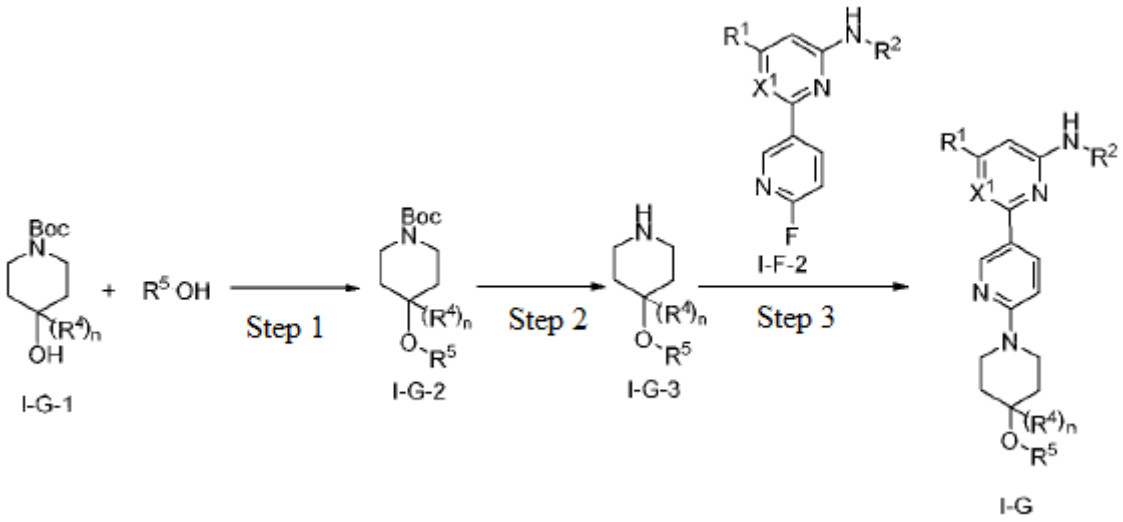
Step 3: deprotecting the compound I-F-4 under an acidic condition to generate compound I-F-5; and

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 formula I-G of claim 8; 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.

[Claim 14]. A pharmaceutical composition, comprising a prophylactically or therapeutically effective amount of the compound according to any one of claims 1 to 12, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative thereof;

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

[Claim 15]. Use of the compound according to any one of claims 1 to 12, the stereoisomer, tautomer, or mixture thereof, the N-oxide thereof, the pharmaceutically acceptable salt, eutecticum, polymorph, or solvate thereof, or the stable isotope derivative thereof, or the pharmaceutical composition according to claim 14 in the preparation of a drug for preventing or treating a disease or condition associated with RET activity;

wherein, 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.