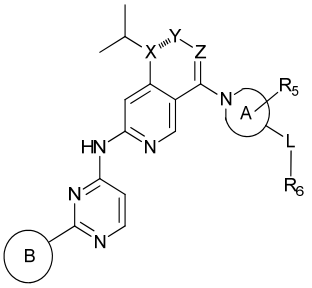
CLAIMS

1. A compound of formula (I), or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof:



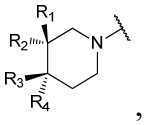
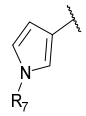
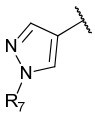
(I)

wherein:

 represents  or ; wherein when is , X is selected from CH and N, and Y is selected from CH_2, C=O and C=S; and when is , X is C, and Y is CH;

Z is selected from CH and N;

ring A is 4- to 8-membered heterocyclyl;

ring B is selected from ,  and ;

L is selected from a chemical bond, -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)-, -C(=O)-CH(R_N)-, -CH(R_N)-S(=O)(=M)- and -S(=O)(=M)-CH(R_N)-;

R_1 and R_2 are independently selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_3 and R_4 are independently selected from H, OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from -C_{0-6} alkylene-OR_a, -C_{0-6} alkylene-NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_7 is selected from H, -C_{1-6} alkylene-CN, -C_{1-6} alkylene-OR_a, -C_{1-6} alkylene-NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

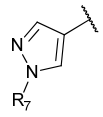
R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from -C_{0-6} alkylene-OR_a, -C_{0-6} alkylene-NR_bR_c, C_{1-6} alkyl, -C_{1-6} alkylene-C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl, which are optionally substituted with one or more R_a;

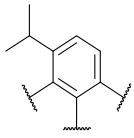
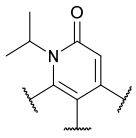
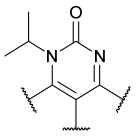
R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl;

each group in X, Y, Z, ring A, ring B, L, R_1-R_8, R_N, R_a, R_b and R_c may be substituted by one or more deuterium atoms, up to full deuteration;

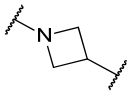
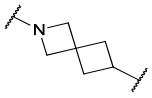
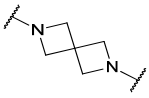
provided that, when L is -CH(R_N)-S(=O)(=M)-, and the ring where X, Y and Z are located is a benzene ring, B is .

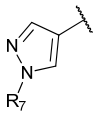
2. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, wherein the compound has one or more of the following definitions:

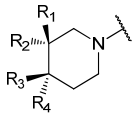
i) wherein the ring where X, Y and Z are located is selected from:

,  and ;

ii) wherein ring A is selected from:

,  and ;

iii) wherein ring B is ;

iv) wherein ring B is ;

v) wherein L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -N(R_N)-C(=O)-, -CH(R_N)-C(=O)- and -CH(R_N)-S(=O)(=M)-; alternatively, L is -N(R_N)-S(=O)(=M)- or -CH(R_N)-S(=O)(=M)-;

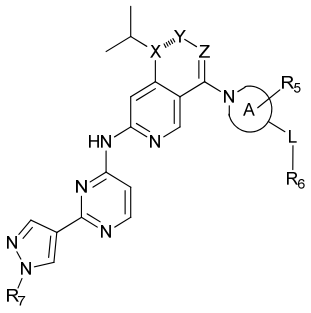
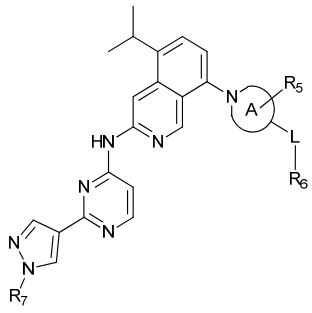
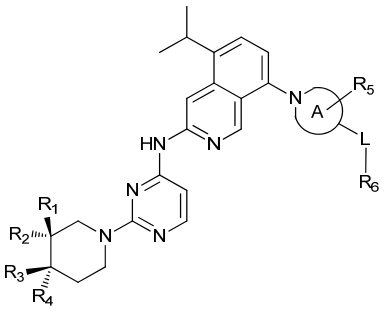
vi) wherein one of R_1 and R_2 is halogen, and the other is selected from H, halogen and C_{1-6} alkyl;

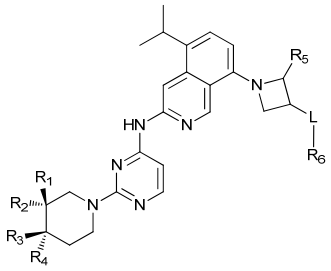
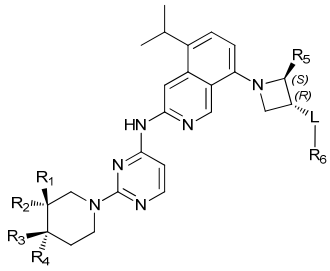
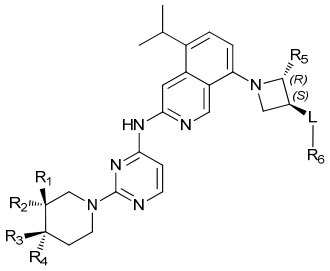
alternatively, one of R_1 and R_2 is F, and the other is selected from H, F and Me; alternatively, one of R_1 and R_2 is F, and the other is H;

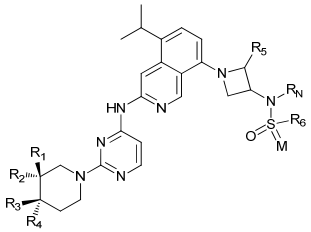
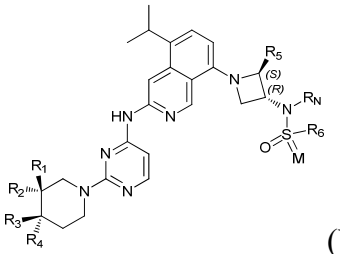
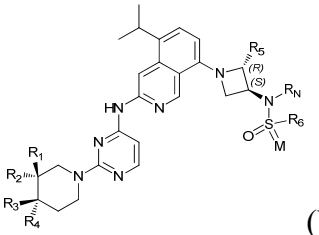
vii) wherein one of R_3 and R_4 is OR_a, and the other is selected from H and C_{1-6} alkyl; alternatively, one of R_3 and R_4 is OH or OMe, and the other is selected from H and Me;

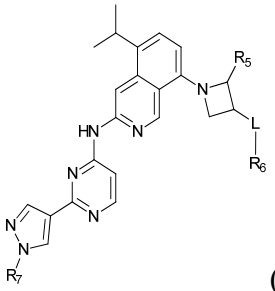
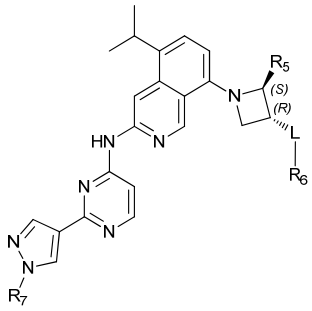
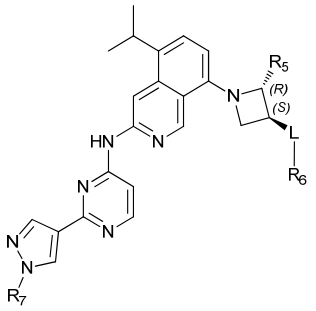
viii) wherein R_5 is selected from H and Me.

3. The compound of formula (I) according to claim 1 or 2, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, having the following structures:


(II),

(III),

(IV),

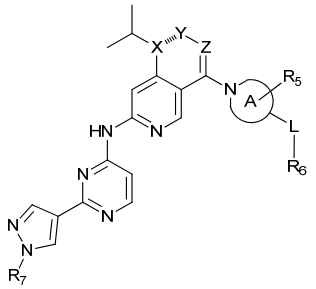

(V),

(V-1),

(V-2),


(VI),

(VI-1),

(VI-2),


(VII),

(VII-1) or

(VII-2),

wherein each group is as defined in claim 1 or 2.

4. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula (II):



(II)

wherein:

 represents  or ; wherein when is , X is selected from CH and N, and Y is selected from CH_2, C=O and C=S; and when is , X is C, and Y is CH;

Z is selected from CH and N;

ring A is 4- to 8-membered heterocyclyl;

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)-, -C(=O)-CH(R_N)-, -CH(R_N)-S(=O)(=M)- and -S(=O)(=M)-CH(R_N)-;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_7 is selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

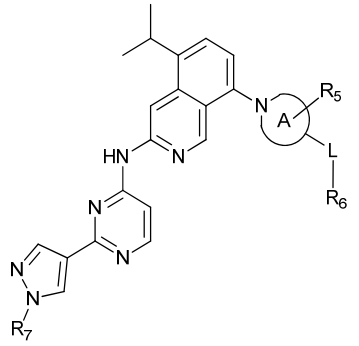
or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, -CH_2-C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl, which are optionally substituted with one or more R_a;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

5. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula

(III):



(III)

wherein:

ring A is 4- to 8-membered heterocyclyl;

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)-, -C(=O)-CH(R_N)-, -CH(R_N)-S(=O)(=M)- and -S(=O)(=M)-CH(R_N)-;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_7 is selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

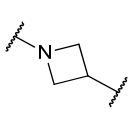
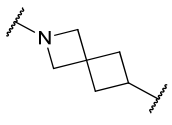
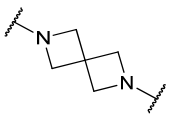
or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl, which are optionally substituted with one or more R_a;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

6. The compound of claim 5, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof,

- wherein:

ring A is selected from ,  and ;

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -

C(=O)-N(R_N)-, -CH(R_N)-C(=O)-, -C(=O)-CH(R_N)-, -CH(R_N)-S(=O)(=M)- and -S(=O)(=M)-CH(R_N)-;

R_5 is selected from H and Me;

R_6 is selected from Me, Et, Pr, CH_2CF_3, cyclopropyl, OH, NH_2, NHMe, NMe_2, furan-2-yl and pyridin-4-yl;

R_7 is selected from H, trifluoroethyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from Me, Et, Pr, CH_2CF_3, cyclopropyl, OH, NH_2, NHMe, NMe_2, pyran-4-yl, furan-2-yl and pyridin-4-yl;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl;

- alternatively, wherein:

ring A is 4- to 8-membered heterocyclyl;

L is selected from -S(=O)(=M)-, -CH(R_N)-C(=O)- and -CH(R_N)-S(=O)(=M)-;

R_5 is H, C_{1-6} alkyl or C_{1-6} haloalkyl;

R_6 is selected from OR_a, N$R_b$$R_c$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl;

R_7 is selected from H, trifluoroethyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from OR_a, N$R_b$$R_c$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl;

- alternatively, wherein:

ring A is 4- to 8-membered heterocyclyl;

L is selected from -S(=O)(=M)-, -CH(R_N)-C(=O)- and -CH(R_N)-S(=O)(=M)-;

R_5 is selected from H and C_{1-6} alkyl;

R_6 is selected from NR_bR_c, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_7 is selected from H, trifluoroethyl and -S(=O)(=M)-R_8;

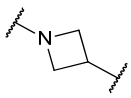
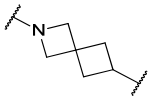
wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_8 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and pyran-4-yl;

R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

- alternatively, wherein:

ring A is selected from  and ;

L is selected from -S(=O)(=M)-, -CH(R_N)-C(=O)- and -CH(R_N)-S(=O)(=M)-;

R_5 is H;

R_6 is selected from Me and NH_2;

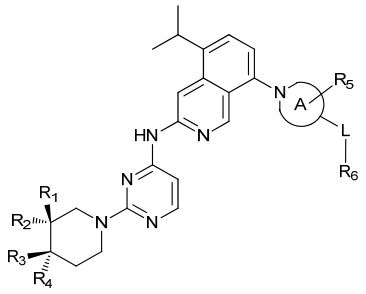
R_7 is selected from H and -S(=O)(=M)-R_8;

wherein M is O;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_8 is selected from Me, Et, Pr, cyclopropyl and pyran-4-yl.

7. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula (IV):



(IV)

- wherein:

ring A is 4- to 8-membered heterocyclyl;

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)- and -C(=O)-CH(R_N)-;

R_1 and R_2 are independently selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_3 and R_4 are independently selected from H, OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

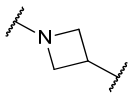
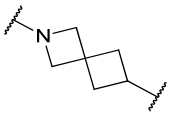
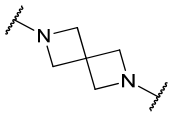
wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl

- alternatively, wherein:

ring A is selected from ,  and ;

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)- and -C(=O)-CH(R_N)-;

R_1 and R_2 are independently selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_3 and R_4 are independently selected from H, OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_5 is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

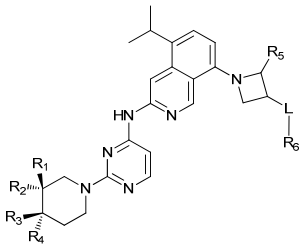
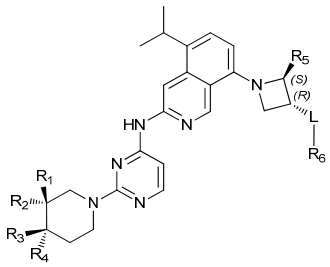
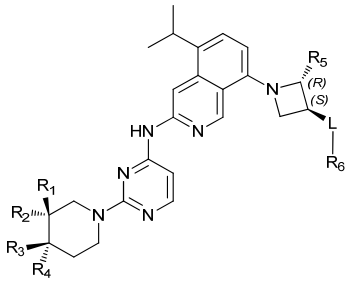
wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

8. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula (V), (V-1) or (V-2):


(V),

(V-1) or

(V-2)

- wherein:

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)- and -C(=O)-CH(R_N)-;

R_1 and R_2 are independently selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_3 and R_4 are independently selected from H, OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl

- alternatively, wherein:

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -N(R_N)-C(=O)- and -CH(R_N)-C(=O)-;

one of R_1 and R_2 is halogen, and the other is selected from H, halogen and C_{1-6} alkyl;

one of R_3 and R_4 is OR_a, and the other is selected from H and C_{1-6} alkyl;

R_5 is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 5- to 6-membered heteroaryl;

wherein M is O or NH;

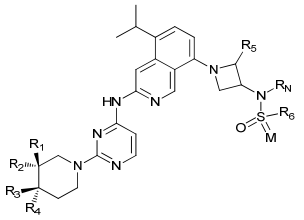
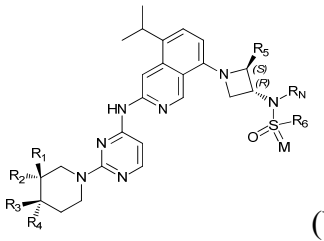
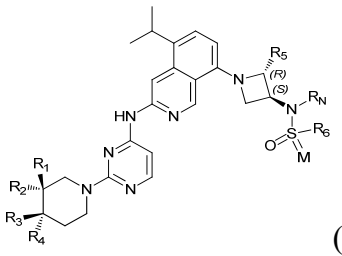
R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

9. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer,

stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula (VI), (VI-1) or (VI-2):


(VI),

(VI-1) or

(VI-2)

wherein:

M is O or NH;

R_1 and R_2 are independently selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_3 and R_4 are independently selected from H, OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

wherein R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

10. The compound of claim 9, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof,

- wherein:

M is O or NH;

one of R_1 and R_2 is halogen, and the other is selected from H, halogen and C_{1-6} alkyl;

one of R_3 and R_4 is OR_a, and the other is selected from H and C_{1-6} alkyl;

R_5 is selected from H and C_{1-6} alkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 5- to 6-membered heteroaryl;

R_N is selected from H and C_{1-6} alkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene;

wherein R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl

- alternatively, wherein:

M is O;

one of R_1 and R_2 is F, and the other is selected from H, F and Me;

one of R_3 and R_4 is OH or OMe, and the other is selected from H and Me;

R_5 is selected from H and Me;

R_6 is selected from Me, Et, Pr, CH_2CF_3, cyclopropyl, NMe_2, furan-2-yl and pyridin-4-yl;

R_N is selected from H and Me;

or R_N and R_6 are linked to form C_{1-4} alkylene;

- alternatively, wherein:

M is O or NH;

one of R_1 and R_2 is selected from halogen, C_{1-6} alkyl and C_{1-6} haloalkyl, and the other is H;

one of R_3 and R_4 is selected from OR_a, C_{1-6} alkyl and C_{1-6} haloalkyl, and the other is H;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

wherein R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl;

- alternatively, wherein:

M is O or NH;

one of R_1 and R_2 is selected from halogen and C_{1-6} alkyl, and the other is H;

one of R_3 and R_4 is OR_a, and the other is H;

R_5 is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

wherein R_a is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

- alternatively, wherein:

M is O;

one of R_1 and R_2 is halogen (alternatively F), and the other is H;

one of R_3 and R_4 is OR_a, and the other is H;

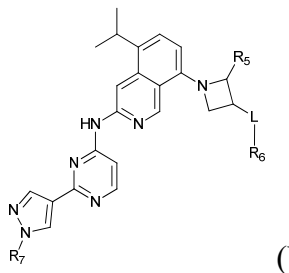
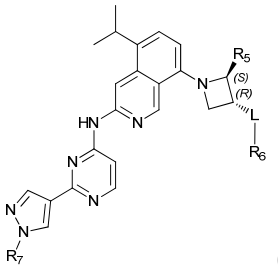
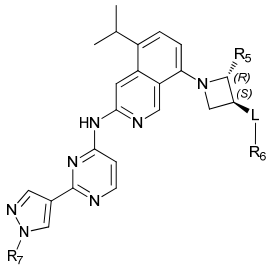
R_5 is selected from H and C_{1-4} alkyl;

R_6 is selected from C_{1-4} alkyl and C_{1-4} haloalkyl;

R_N is selected from H, C_{1-4} alkyl and C_{1-4} haloalkyl; alternatively C_{1-4} alkyl;

wherein R_a is selected from H and C_{1-4} alkyl.

11. The compound of claim 3, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, which is a compound of formula (VII), (VII-1) or (VII-2):


(VII),

(VII-1) or

(VII-2)

wherein:

L is selected from -S(=O)(=M)-, -N(R_N)-S(=O)(=M)-, -S(=O)(=M)-N(R_N)-, -N(R_N)-C(=O)-, -C(=O)-N(R_N)-, -CH(R_N)-C(=O)-, -C(=O)-CH(R_N)-, -CH(R_N)-S(=O)(=M)- and -S(=O)(=M)-CH(R_N)-;

R_5 is selected from H, halogen, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl;

R_7 is selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl and -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

or R_N and R_6 are linked to form C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene;

R_8 is selected from OR_a, NR_bR_c, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4- to 6-membered heterocyclyl, C_{6-10} aryl and 5- to 6-membered heteroaryl, which are optionally substituted with one or more R_a;

R_a, R_b and R_c are independently selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl; or R_b and R_c together with the nitrogen atom to which they are attached form 4- to 7-membered heterocyclyl.

12. The compound of claim 11, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof,

- wherein:

L is selected from -N(R_N)-S(=O)(=M)- and -CH(R_N)-S(=O)(=M)-;

R_5 is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl;

R_7 is -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R_8 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl, which are optionally substituted with one or more R_a;

R_a is selected from H, C_{1-6} alkyl and C_{1-6} haloalkyl

- alternatively, wherein:

L is selected from -N(R_N)-S(=O)(=M)- and -CH_2-S(=O)(=M)-;

R_5 is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_7 is -S(=O)(=M)-R_8;

wherein M is O or NH;

R_N is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_8 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} cycloalkyl and 4- to 6-membered heterocyclyl;

- alternatively, wherein:

L is selected from -N(R_N)-S(=O)$_2$- and -CH_2-S(=O)$_2$-;

R_5 is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_6 is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_7 is -S(=O)$_2$-R_8;

wherein R_N is selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

R_8 is selected from C_{1-6} alkyl, C_{1-6} haloalkyl and C_{3-6} cycloalkyl;

- alternatively, wherein:

L is selected from -N(R_N)-S(=O)$_2$- and -CH_2-S(=O)$_2$-;

R_5 is C_{1-4} alkyl;

R_6 is C_{1-4} alkyl;

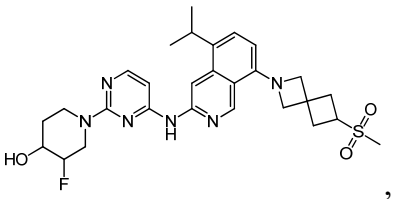
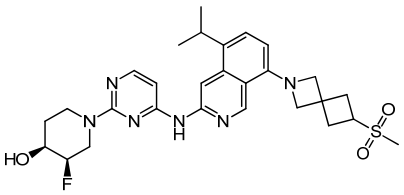
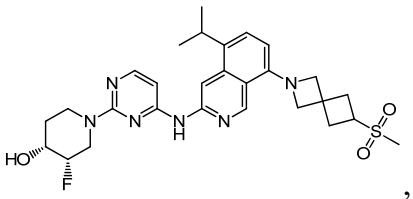
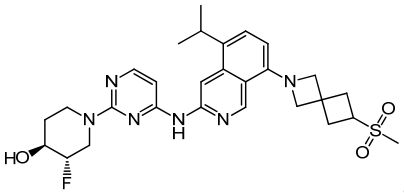
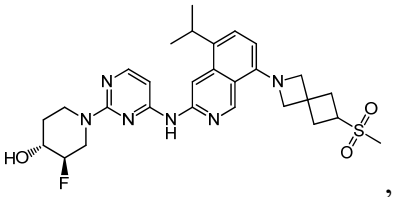
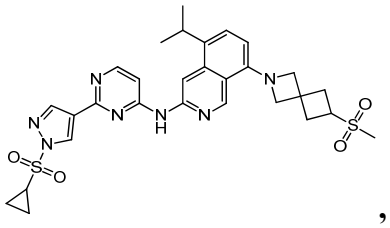
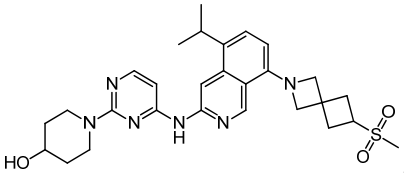
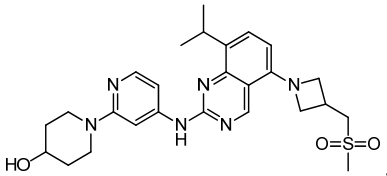
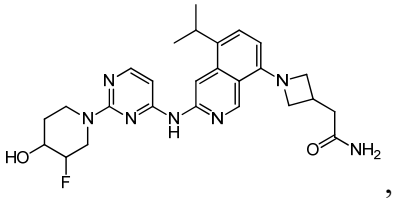
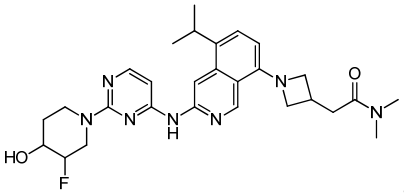
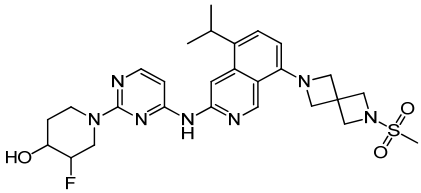
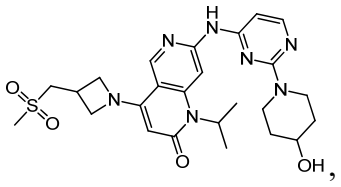
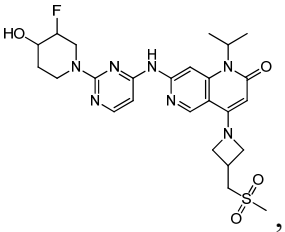
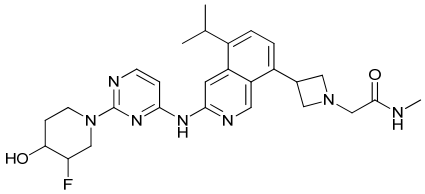
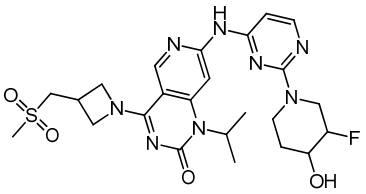
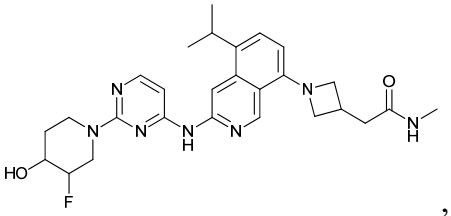
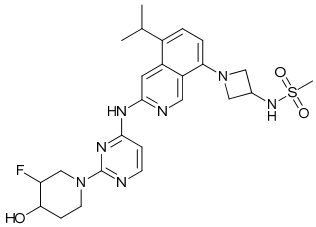
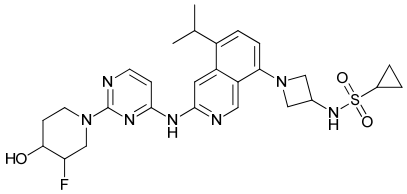
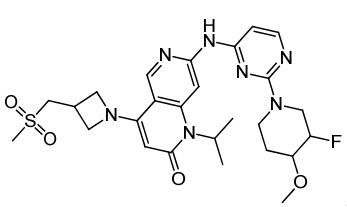
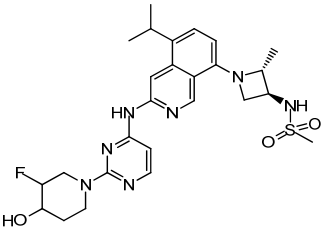
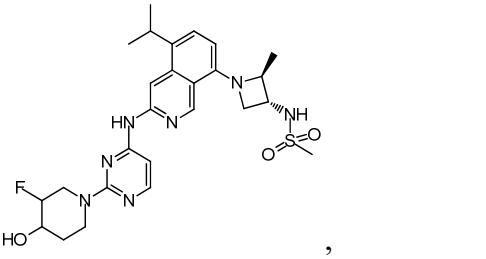
R_7 is -S(=O)$_2$-R_8;

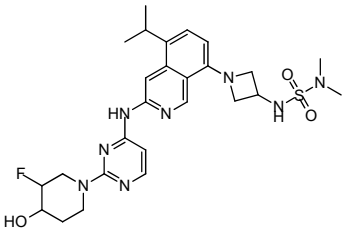
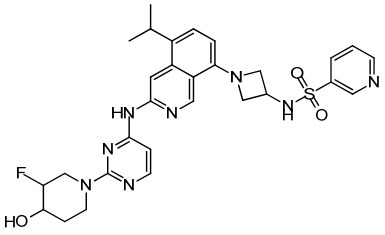
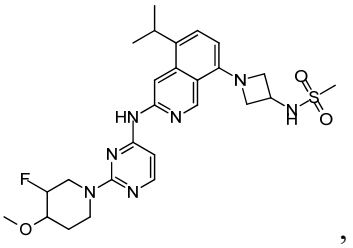
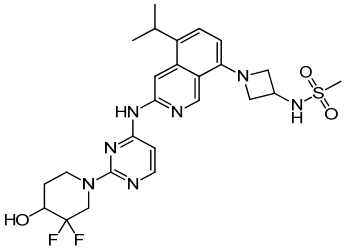
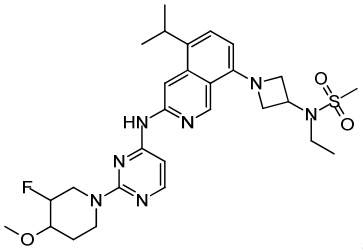
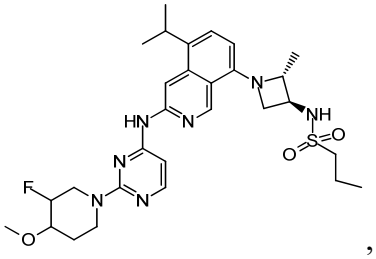
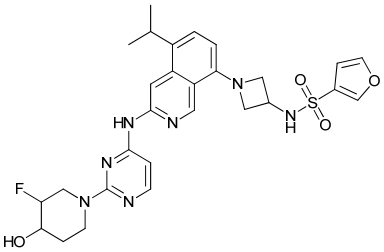
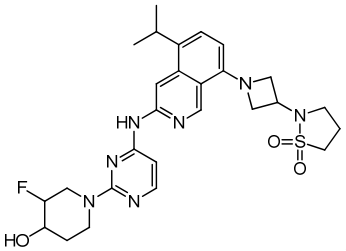
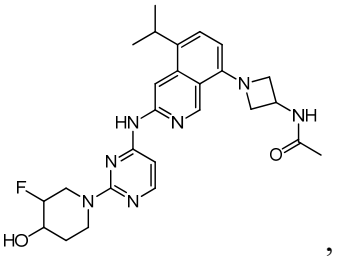
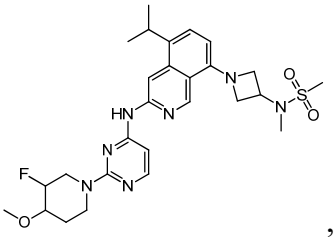
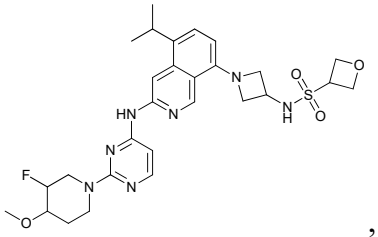
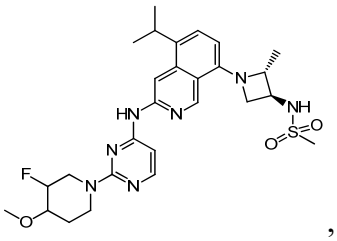
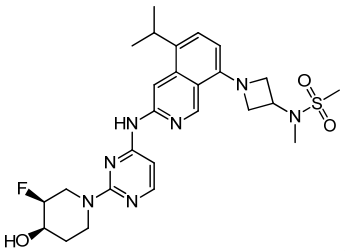
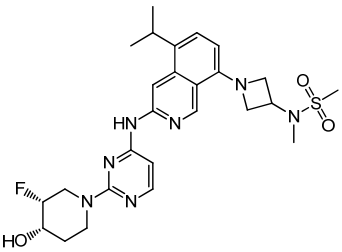
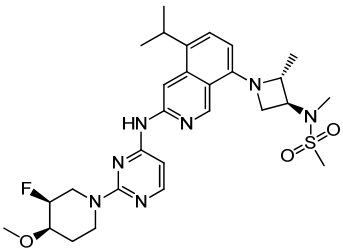
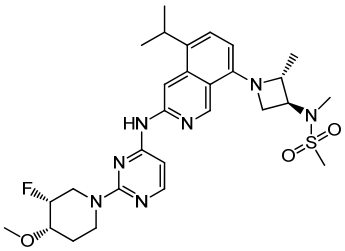
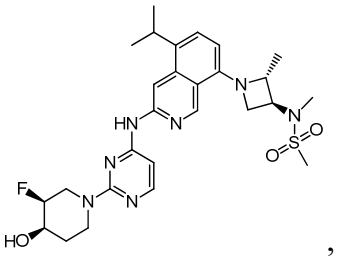
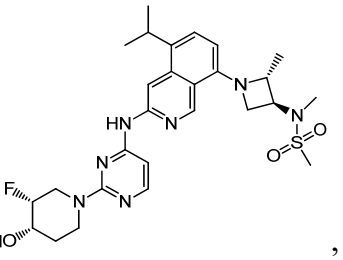
wherein R_N is C_{1-4} alkyl;

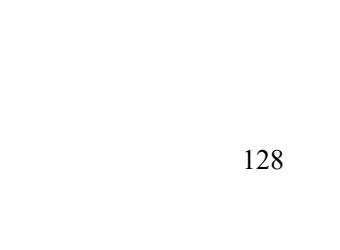
R_8 is selected from C_{1-4} alkyl and C_{3-6} cycloalkyl.

13. A compound, or a tautomer, stereoisomer, prodrug, crystalline form, pharmaceutically

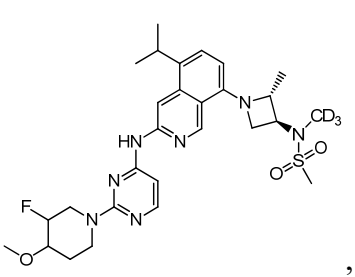
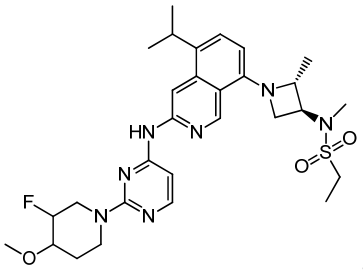
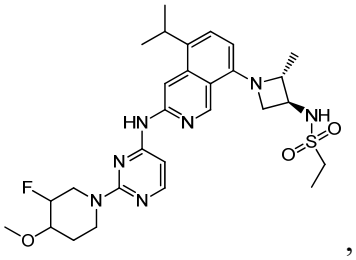
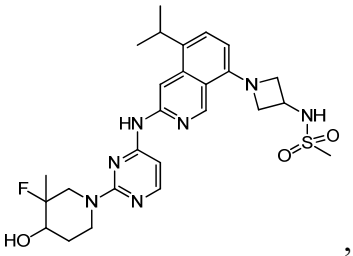
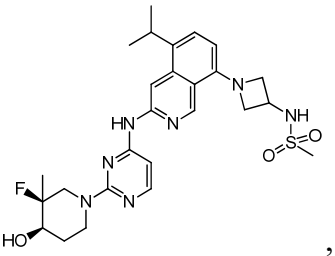
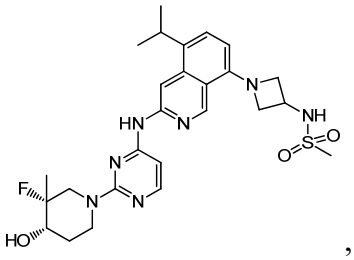
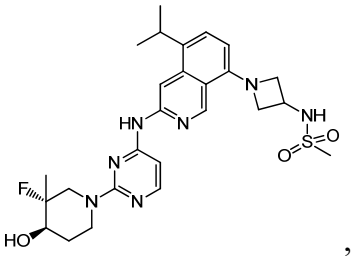
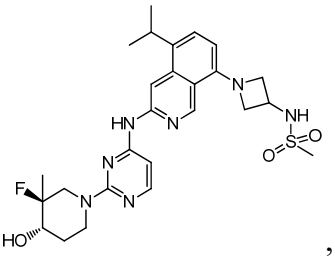
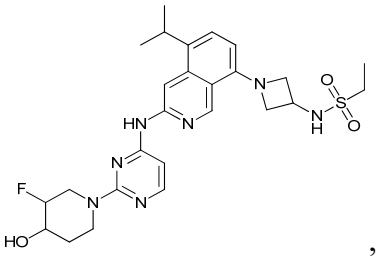
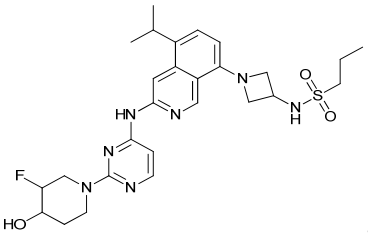
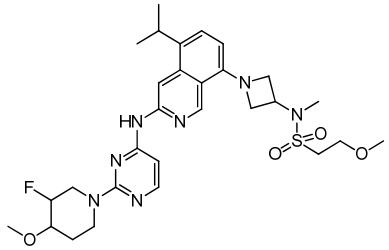
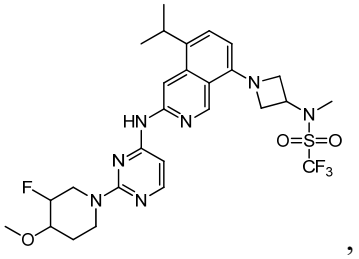
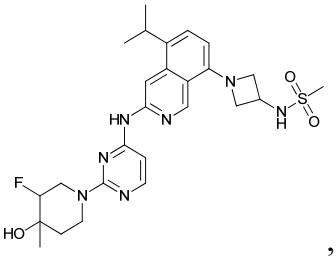
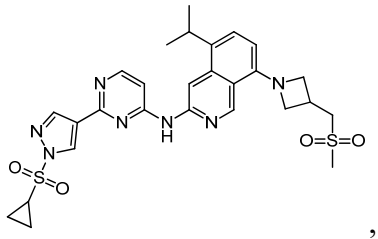
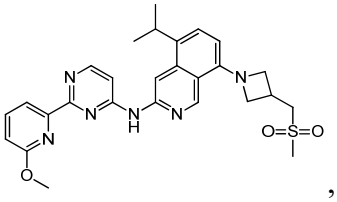
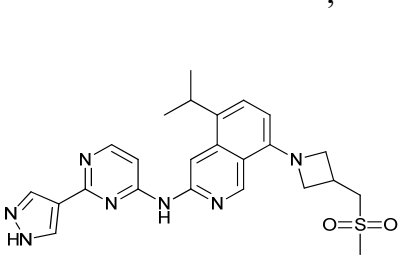
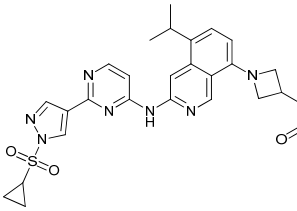
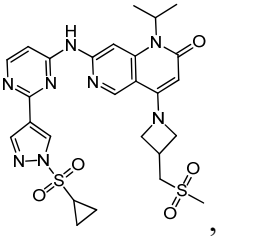
acceptable salt, hydrate or solvate thereof, wherein the compound is selected from:

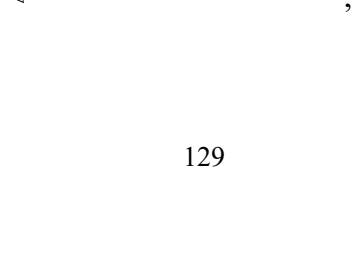

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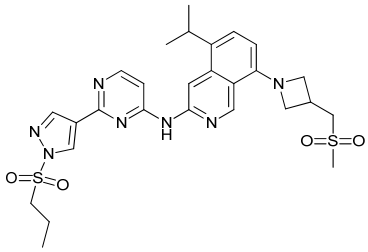
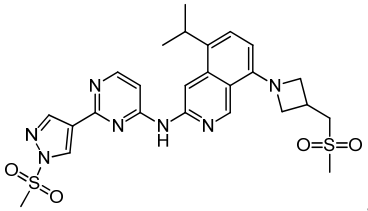
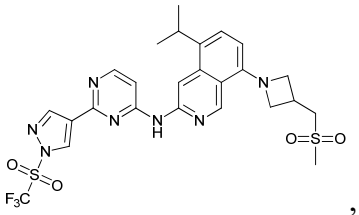
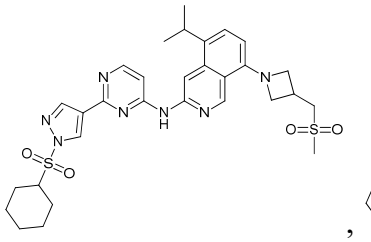
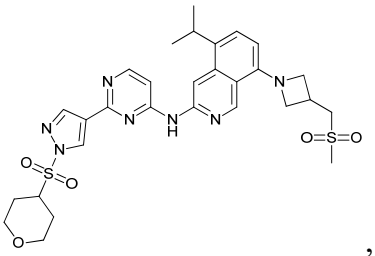
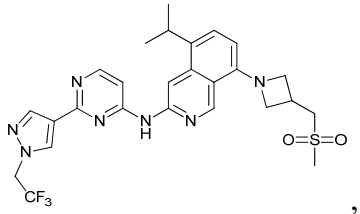
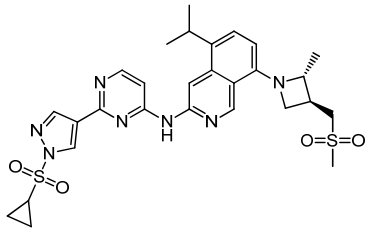
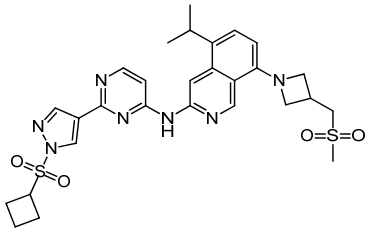
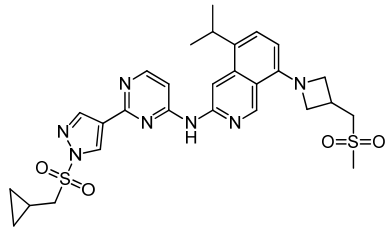
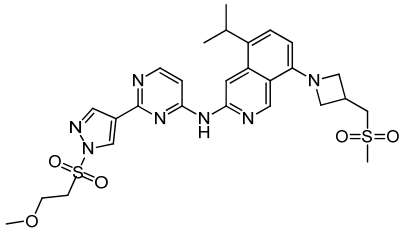
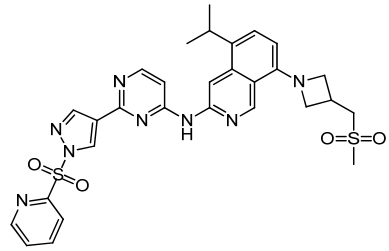
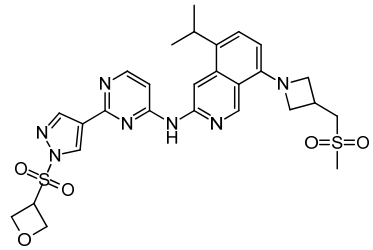
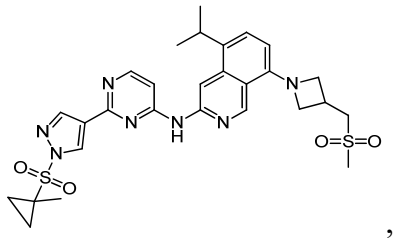
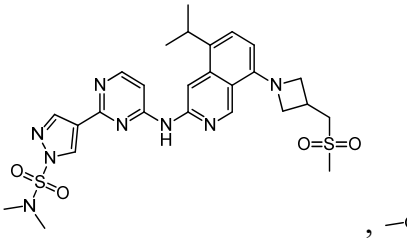
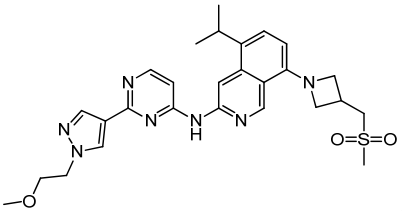
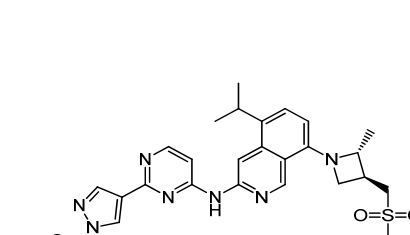
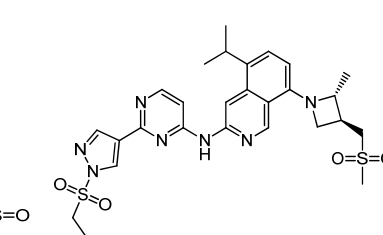
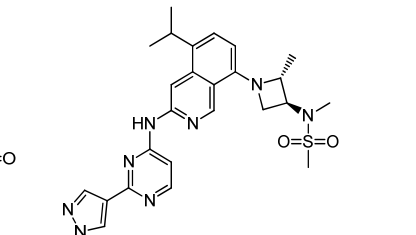
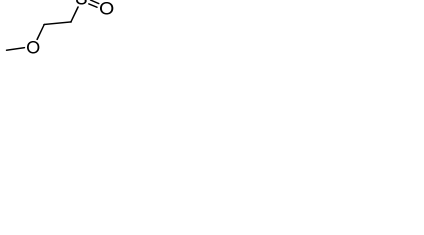
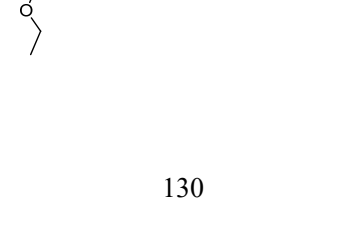
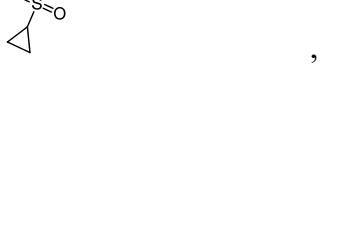
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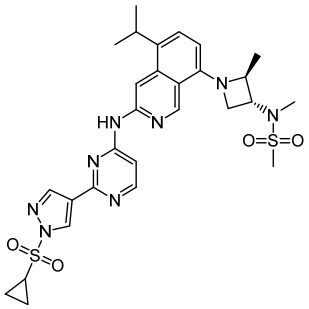
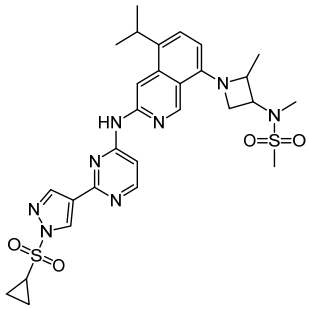
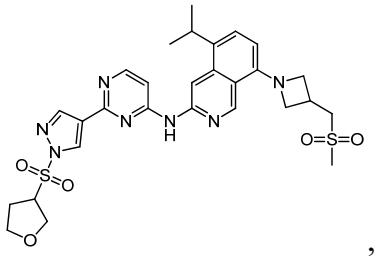
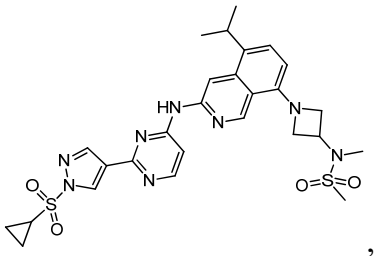
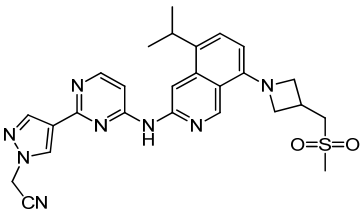
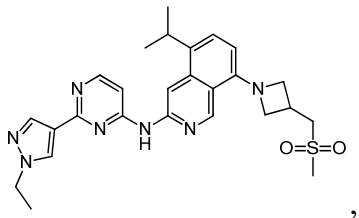
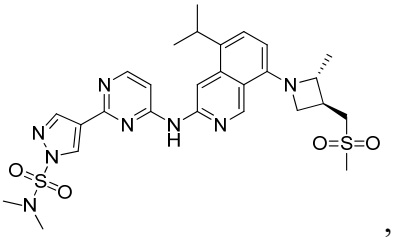
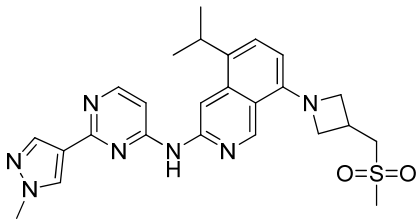
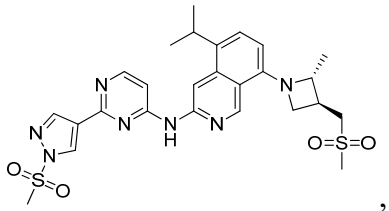
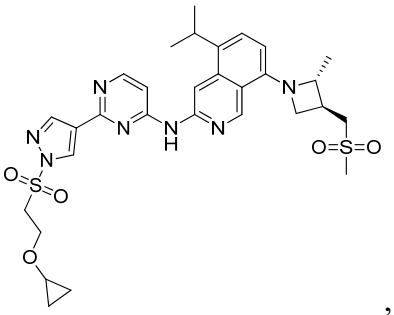
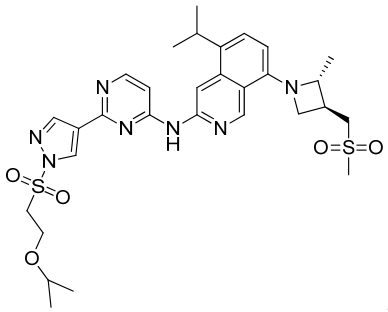
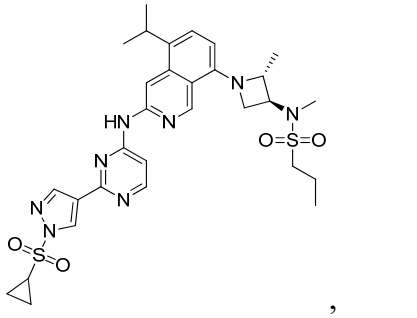
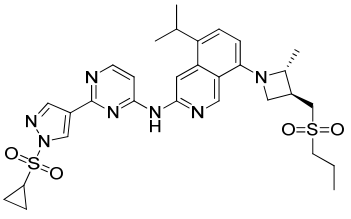
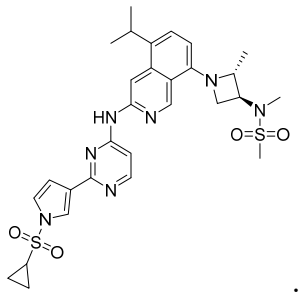
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and

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14. A pharmaceutical composition comprising the compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, and a pharmaceutically acceptable excipient; alternatively, further comprising other therapeutic agent.

15. Use of the compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, or the pharmaceutical composition according to claim 14, in the manufacture of a medicament for treating and/or preventing a disease mediated by EGFR protein and mutants thereof.

16. The compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt, isotopic variant, tautomer, stereoisomer, prodrug, polymorph, hydrate or solvate thereof, or the pharmaceutical composition according to claim 14, for use in treating and/or preventing a disease mediated by EGFR protein and mutants thereof.

17. The use according to claim 15, wherein the EGFR mutant is selected from one or more of L858R mutant, del19 mutant, T790M mutant, and C797S mutant; optionally, the disease is selected from lung cancer, colon cancer, urothelial carcinoma, breast cancer, prostate cancer, brain cancer, ovarian cancer, gastric cancer, pancreatic cancer, head and neck cancer, bladder cancer and mesothelioma, alternatively non-small cell lung cancer.