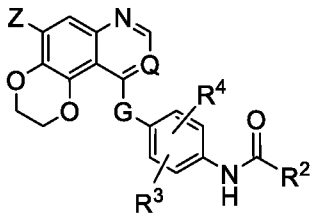
CLAIMS

WHAT IS CLAIMED IS:

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



Formula (I)

wherein

Q is N or CH;

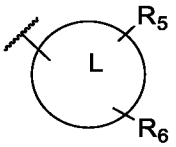
G is O, S or NH;

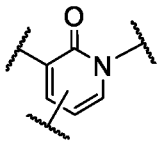
Z is $-OR^1$;

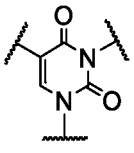
R^1 is -H, C_3-C_8 cycloalkyl, C_1-C_{10} alkyl, or $-(CH_2)_n-R^8$, wherein the C_3-C_8 cycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_3 acyl, hydroxyl, halogen, trifluoromethyl, cyano, $-CONH_2$, oxo (=O) and $-NR^aR^b$; the C_1-C_{10} alkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_3 acyl, hydroxyl, halogen, trifluoromethyl, cyano, $-CONH_2$, C_3-C_7 cycloalkyl, and $-NR^aR^b$; and R^8 is a substituted or unsubstituted 4- to 8-membered heteroalicyclic group containing 1 to 2 atoms selected from the group consisting of N, O, and S as a ring atom, and the substituted 4- to 8-membered heteroalicyclic group is substituted with 1 to 3 substituents selected from the group consisting of halogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 alkylthio, hydroxyl, $-NR^aR^b$, C_1-C_3 acyl, trifluoromethyl, cyano, and oxo, and n is an integer from 0 to 10,

R^a and R^b are each independently -H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkyl substituted with C_1-C_3 alkoxy, C_1-C_6 alkyl substituted with C_1-C_3 alkylthio, or C_1-C_6 alkyl substituted with unsubstituted or mono- or di-C_1-C_3 alkyl-substituted amino;

R^3 and R^4 are each independently -H, $-CF_3$, halogen, C_1-C_3 alkyl, or C_1-C_3 alkoxy;

R^2 is 

, wherein L is an aryl group, a 5- to 6-membered unsaturated heterocyclyl or heteroaryl group containing 1 to 3 heteroatoms selected from the group consisting of N, O, and S, 

, or 

,

R_5 is -H, C_1-C_6 alkyl, C_1-C_3 alkoxy, or C_1-C_3 alkyl, wherein the C_1-C_3 alkyl is substituted with 1 to 3 substituents selected from the group consisting of C_3-C_6 cycloalkyl, hydroxyl, C_1-C_3 alkoxy, halogen, carboxyl, tert-butoxycarbonyl, alkenyl, morpholinyl, piperazinyl, 4-methylpiperazinyl, pyrrolyl, piperidinyl, 4,4-dimethylpiperidinyl, 4-methyl-4-hydroxy-piperidinyl, and 4-methyl-4-aminopiperidinyl,

R_6 is $-(CH_2)_t-R^7$, where t is an integer from 0 to 3, and R^7 is an aryl or heteroaryl group, or C_3-C_6 cycloalkyl, wherein the aryl or heteroaryl group is unsubstituted or substituted with one or more of trifluoromethyl, halogen, C_1-C_3 alkyl, and C_1-C_3 alkoxy, and the C_3-C_6 cycloalkyl is unsubstituted or substituted with one or more of trifluoromethyl, halogen, C_1-C_3 alkyl, and C_1-C_3 alkoxy.

2. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 1, wherein R^1 is -H, unsubstituted C_3-C_8 cycloalkyl, C_1-C_8 alkyl, or $-(CH_2)_n-R^8$, wherein the C_1-C_8 alkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_3 acyl, hydroxyl, -F, trifluoromethyl, cyano, $-CONH_2$, C_3-C_6 cycloalkyl, and $-NR^aR^b$,

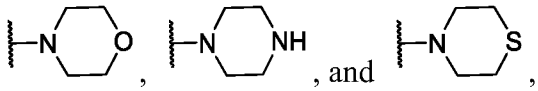
wherein R^8 is a substituted or unsubstituted 4- to 8-membered heteroalicyclic group containing 1 to 2 atoms selected from the group consisting of N, O, and S as a ring atom, and the substituted 4- to 8-membered heteroalicyclic group is substituted with 1 to 3 substituents selected from the group consisting of -F, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxy, $-NR^aR^b$, trifluoromethyl, cyano, C_1-C_3 acyl, and oxo, and n is an integer from 0 to 8,

R^a and R^b are each independently -H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or C_1-C_6 alkyl

substituted with C_1-C_3 alkoxy.

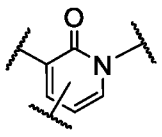
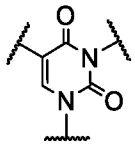
3. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 2, wherein R^1 is -H, unsubstituted C_3-C_6 cycloalkyl, C_1-C_6 alkyl, or -$(CH_2)_n$-R^8, wherein the C_1-C_6 alkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_3 alkoxy, C_1-C_3 alkylthio, C_1-C_3 acyl, hydroxyl, -F, trifluoromethyl, cyano, -$CONH_2$, C_3-C_5 cycloalkyl, and -NR^aR^b,
wherein R^8 is a substituted or unsubstituted 4- to 6-membered heteroalicyclic group containing 1-2 atoms selected from the group consisting of N, O, and S as a ring atom, and the substituted 4- to 6-membered heteroalicyclic group is substituted with 1 to 3 substituents selected from the group consisting of -F, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl, -NR^aR^b, trifluoromethyl, cyano, C_1-C_3 acyl, and oxo, and n is an integer from 0 to 6,
R^a and R^b are each independently -H, C_1-C_3 alkyl, C_3-C_6 cycloalkyl, or C_1-C_3 alkyl substituted with C_1-C_3 alkoxy.

4. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 2, wherein R^1 is -H, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, C_1-C_6 alkyl, or -$(CH_2)_n$-R^8, wherein the C_1-C_6 alkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of methoxy, ethoxy, propoxy, isopropoxy, methylthio, ethylthio, formyl, acetyl, hydroxyl, -F, trifluoromethyl, cyano, -$CONH_2$, cyclopropyl, cyclobutyl, cyclopentyl, and -NR^aR^b; wherein R^8 is a substituted or unsubstituted 4- to 6-membered heteroalicyclic group containing 1 to 2 atoms selected from the group consisting of N, O, and S as a ring atom, and the substituted 4- to 6-membered heteroalicyclic group is substituted with 1 to 3 substituents selected from the group consisting of -F, methyl, ethyl, hydroxy, amino, acetyl, formyl, trifluoromethyl, cyano, and oxo, and n is from 0 to 6,
the 4- to 6-membered heteroalicyclic group is selected from the group consisting of a 4- to 6-membered oxacycloalkyl group, a 4- to 6-membered azacycloalkyl group, a 4- to 6-membered thiacycloalkyl group, and the following groups:

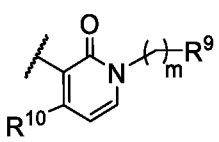
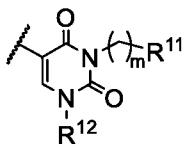
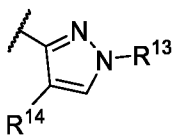


R^a and R^b are each independently -H, methyl, ethyl, methoxymethyl, methoxyethyl, methoxypropyl, cyclopropyl, or cyclobutyl.

5. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 1, wherein R^3 and R^4 are each independently -H, $-CF_3$, -F, -Cl, methyl, ethyl, propyl, or isopropyl.

6. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 1, wherein in R^2, L is phenyl, pyridyl, pyrimidinyl, naphthyl, imidazolyl, pyrazolyl, thiazolyl, oxazolyl, pyrrolyl, pyranyl,  , or  .

7. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 6, wherein R^2 is

 ,  , or  ,

wherein R^{10} and R^{14} are each independently H, C_1-C_3 alkyl, or C_1-C_3 alkoxy,

R^9 and R^{11} are each independently a phenyl, pyridyl, or pyrimidinyl group, or a C_3-C_6 cycloalkyl, wherein the phenyl, pyridyl, or pyrimidinyl group is unsubstituted or substituted with one or more of trifluoromethyl, halogen, C_1-C_3 alkyl, and C_1-C_3 alkoxy, and the C_3-C_6 cycloalkyl group is unsubstituted or substituted with one or more of trifluoromethyl, halogen, C_1-C_3 alkyl, and C_1-C_3 alkoxy,

R^{12} is H, C_1-C_6 alkyl, or C_1-C_3 alkyl, wherein the C_1-C_3 alkyl is substituted with 1 to 3 substituents selected from the group consisting of C_3-C_6 cycloalkyl, hydroxyl, C_1-C_3 alkoxy, halogen, carboxy, tert-butoxycarbonyl, alkenyl, and morpholinyl,

R^{13} is a phenyl, pyridyl, or pyrimidinyl group, wherein the phenyl, pyridyl, or pyrimidinyl group is unsubstituted or substituted with one or more of trifluoromethyl, halogen, C_1-C_3 alkyl, and C_1-C_3 alkoxy,

m is an integer from 0 to 3.

8. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 7, wherein

R^{10} and R^{14} are each independently H, methoxy, or ethoxy,

R^9 and R^{11} are each independently C_3-C_6 cycloalkyl, or a phenyl, pyridyl, or pyrimidinyl group, wherein the phenyl, pyridyl, or pyrimidinyl group is substituted with at least one substituent selected from the group consisting of methyl, ethyl, -F, and -Cl,

R^{12} is methyl, ethyl, propyl, isopropyl, isobutyl, cyclopropylmethyl, hydroxyethyl, hydroxypropyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, fluoroethyl, morpholinopropyl, a hydroxylcarbonylmethyl group, tert-butoxycarbonylmethyl, or allyl,

R^{13} is a methylphenyl, pyridyl, or pyrimidinyl group, wherein the methylphenyl, pyridyl, or pyrimidinyl group is substituted with at least one substituent selected from the group consisting of -F and -Cl.

9. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 1, wherein Q is CH;

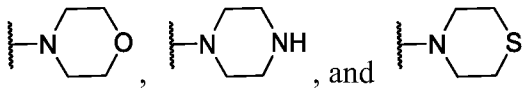
G is O;

Z is $-OR^1$;

R^1 is C_1-C_6 alkyl, or $-(CH_2)_n$-R^8, wherein the C_1-C_6 alkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of methoxy, ethoxy, propoxy, isopropoxy, methylthio, ethylthio, formyl, acetyl, hydroxyl, -F, trifluoromethyl, cyano, $-CONH_2$, cyclopropyl, cyclobutyl, cyclopentyl, and $-NR^aR^b$, wherein R^8 is substituted or unsubstituted 4- to 6-membered heteroalicyclic group containing 1 to 2 atoms selected from the group consisting of N, O, and S as a ring atom, and the substituted 4- to 6-membered heteroalicyclic group is substituted with 1 to 3 substituents selected from the group consisting

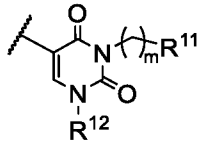
of -F, methyl, ethyl, hydroxyl, amino, acetyl, formyl, trifluoromethyl, cyano, and oxo, and n is 0 to 6,

the 4- to 6-membered heteroalicyclic group is selected from the group consisting of a 4- to 6-membered oxacycloalkyl group, a 4- to 6-membered azacycloalkyl group, a 4- to 6-membered thiacycloalkyl group, and the following groups:



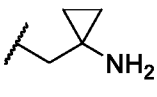
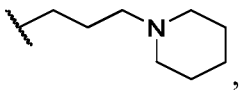
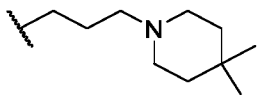
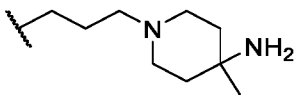
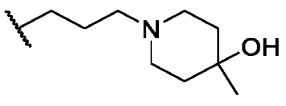
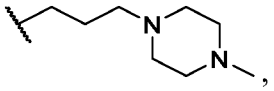
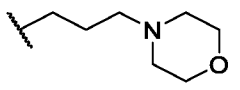
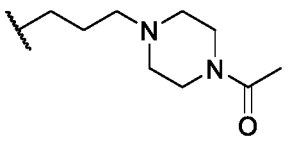
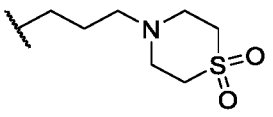
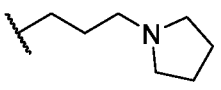
R^a and R^b are each independently -H, methyl, ethyl, methoxymethyl, methoxyethyl, methoxypropyl, cyclopropyl, or cyclobutyl;

R^3 and R^4 are each independently -H, -F, -Cl, methyl, or ethyl;

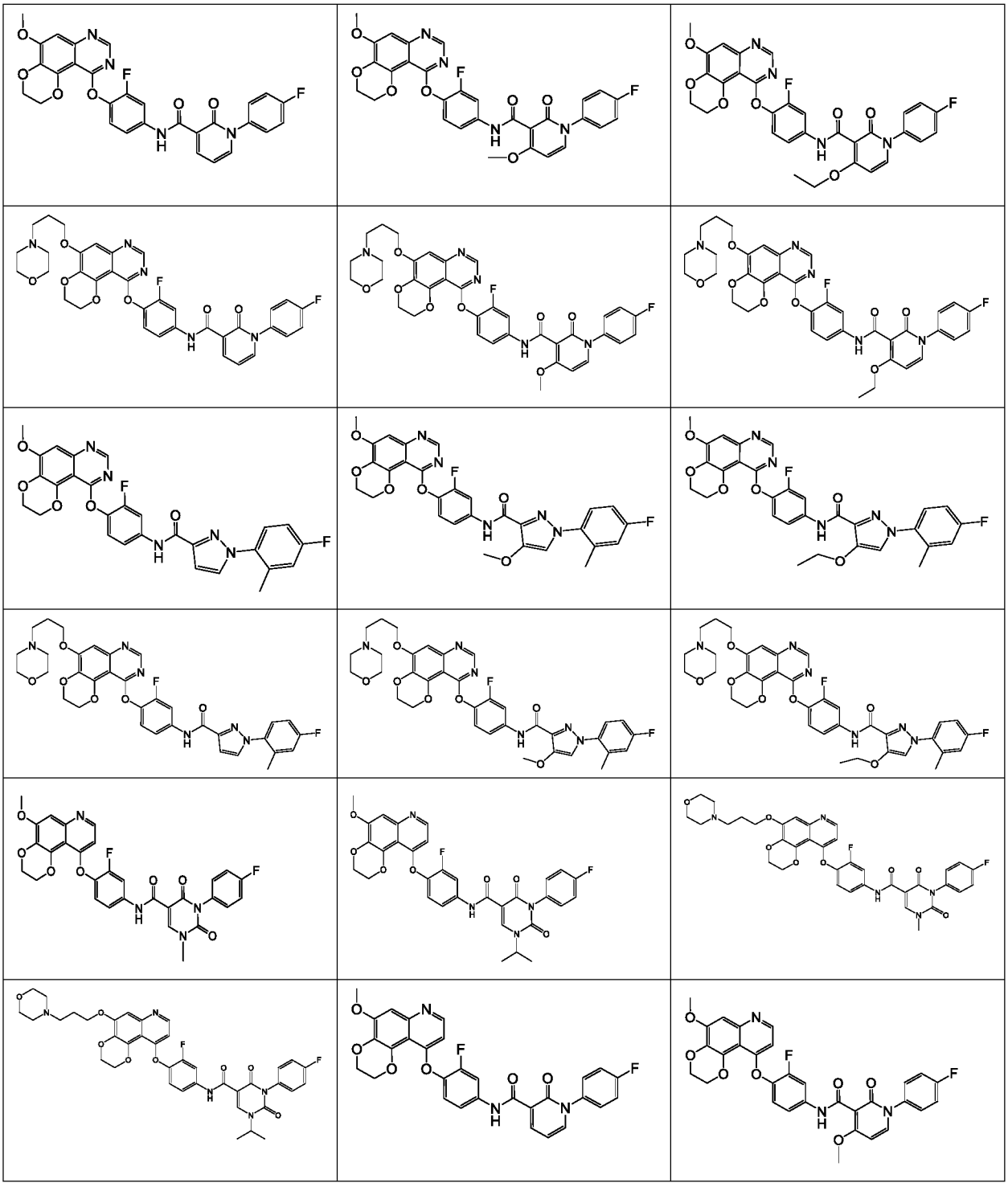
R^2 is , wherein m is an integer from 0 to 3,

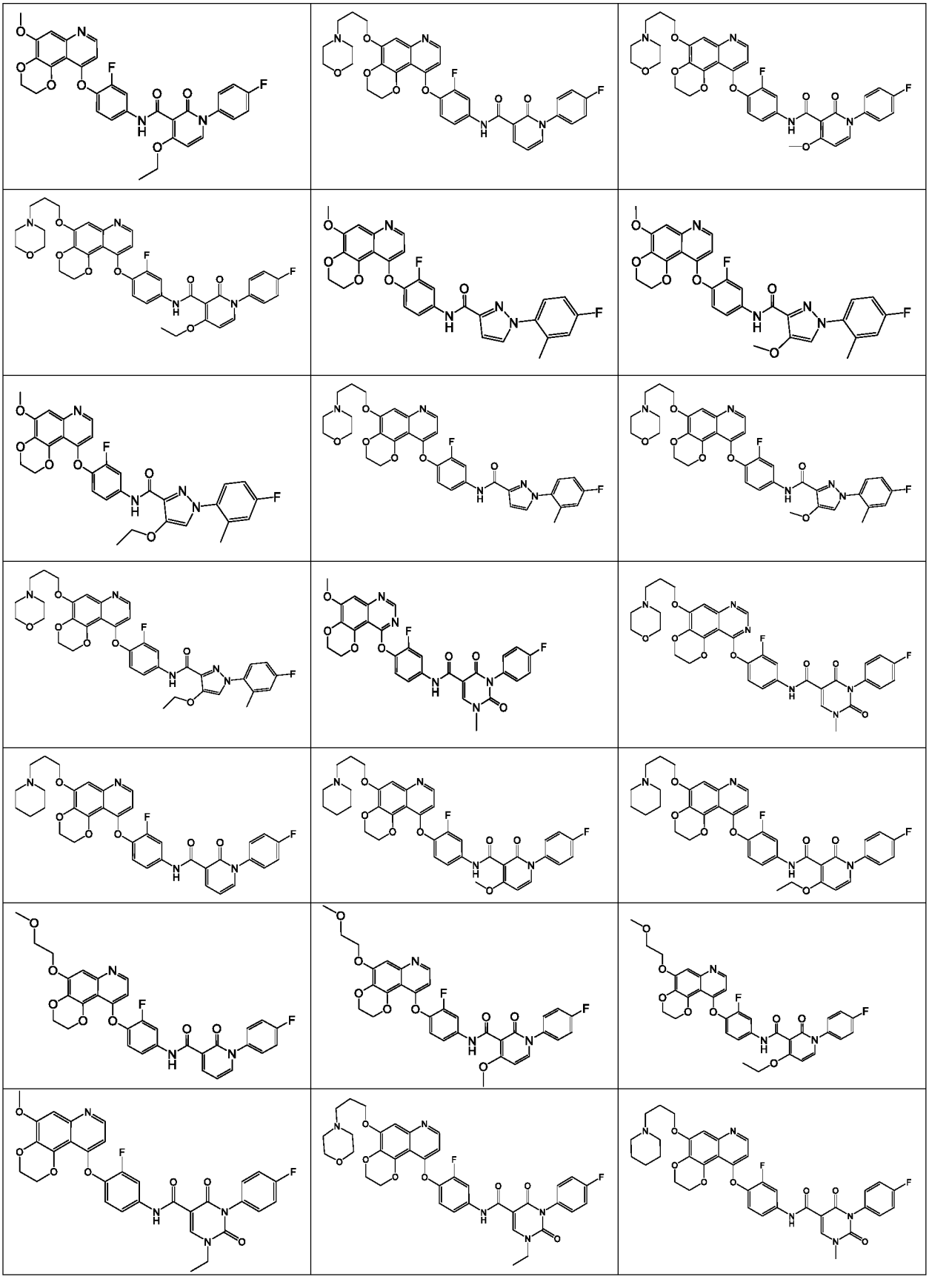
R^{11} is phenyl unsubstituted or substituted with one or more of trifluoromethyl, F, Cl, methyl, ethyl, methoxy, and ethoxy,

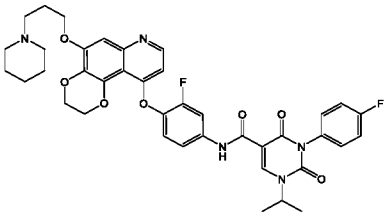
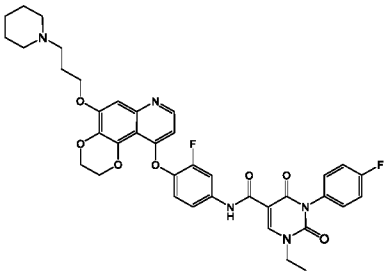
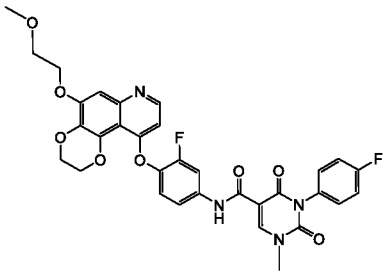
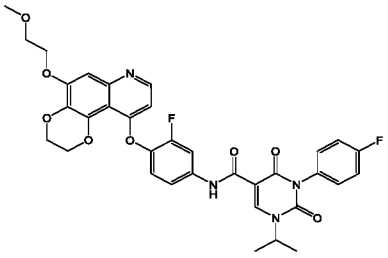
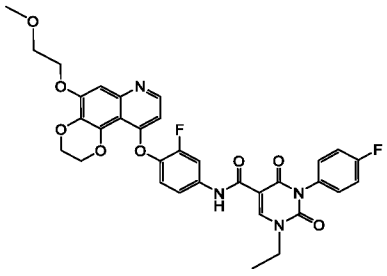
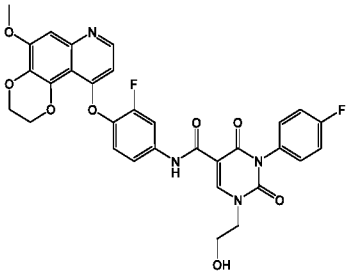
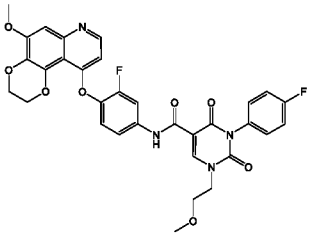
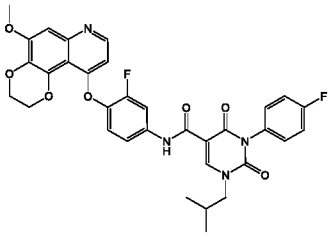
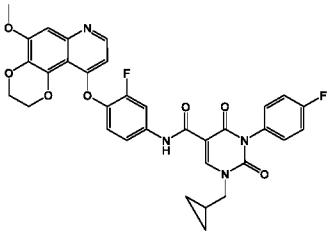
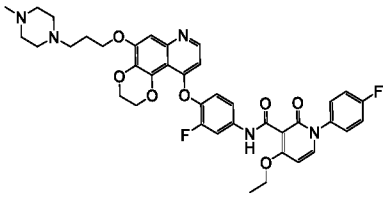
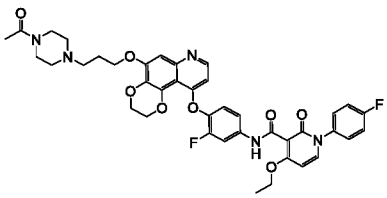
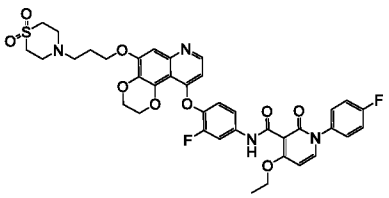
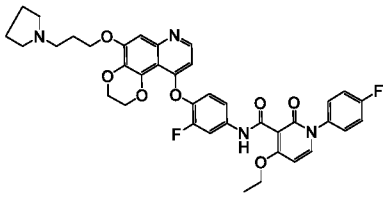
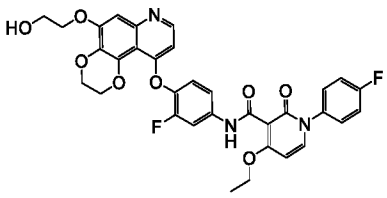
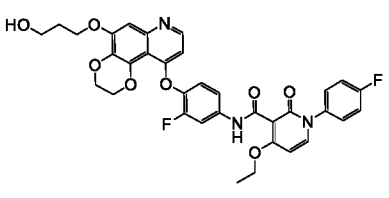
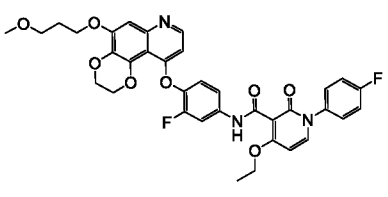
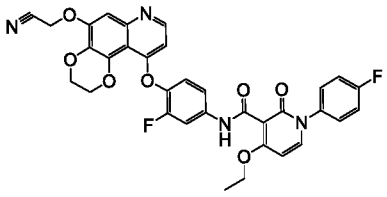
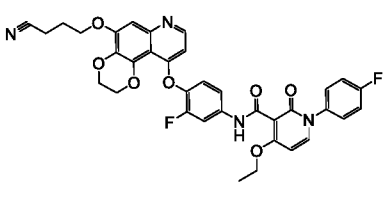
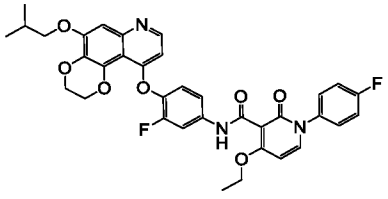
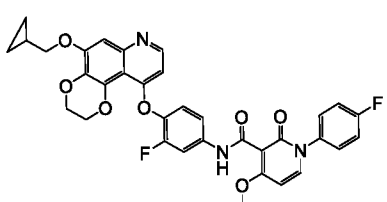
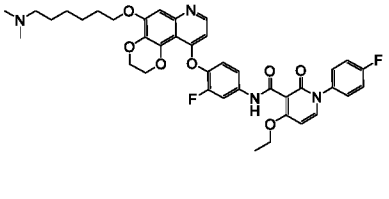
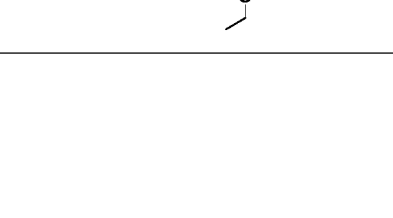
R^{12} is H, methyl, ethyl, propyl, or isopropyl.

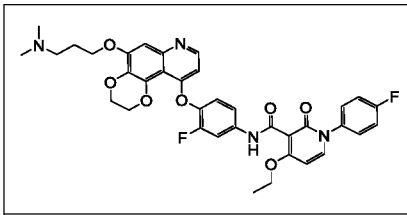
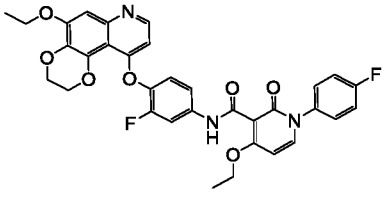
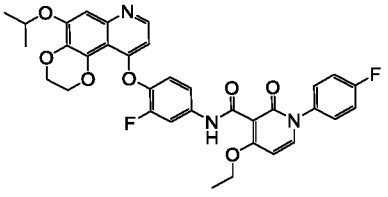
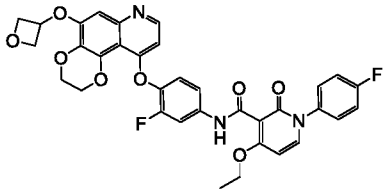
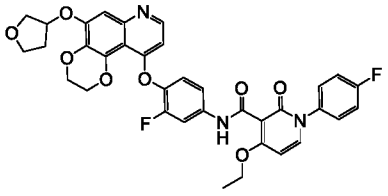
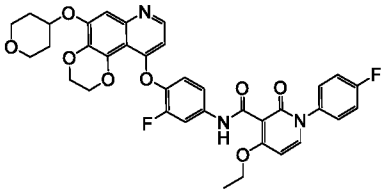
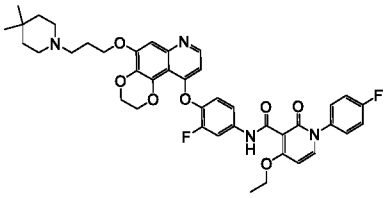
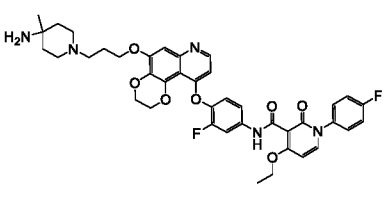
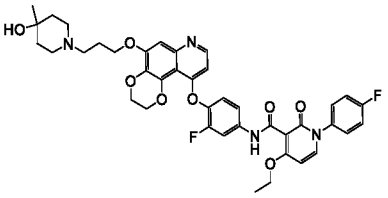
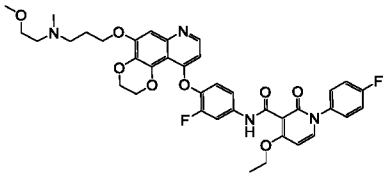
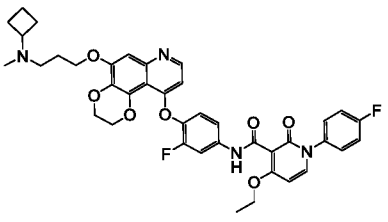
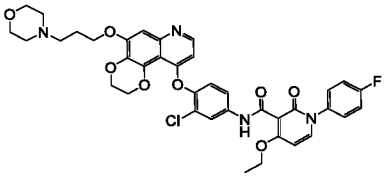
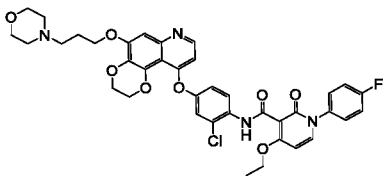
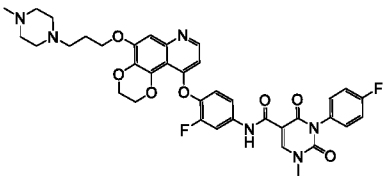
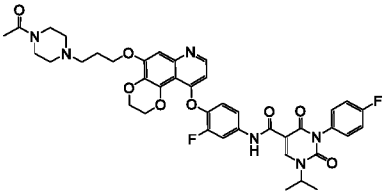
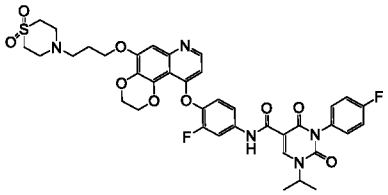
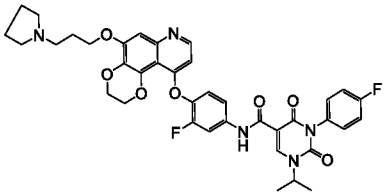
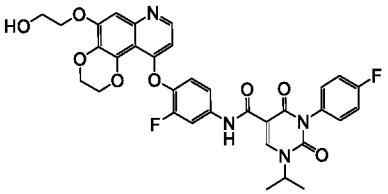
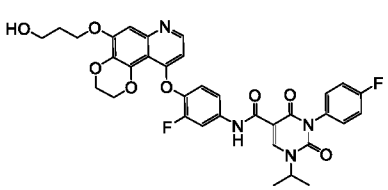
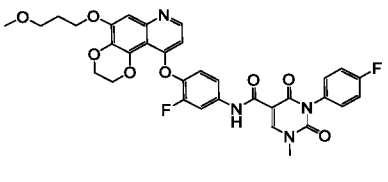
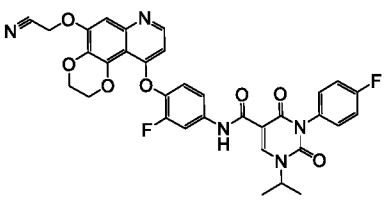
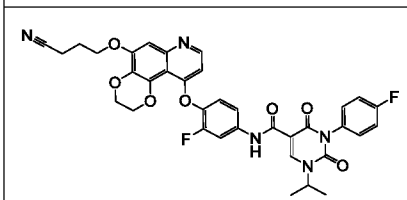
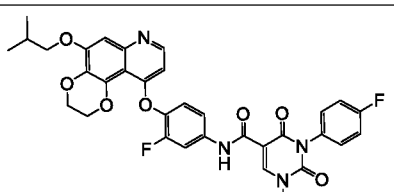
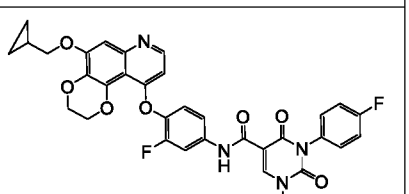
10. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 9, wherein R^1 is C_1-C_4 alkyl, oxetan-3-yl, tetrahydrofuran-3-yl, tetrahydropyran-4-yl, tetrahydropyran-3-yl, hydroxyethyl, hydroxypropyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, cyanomethyl, cyanoethyl, cyanopropyl, cyclopropylmethyl, , , , , , , , , , , or $-(CH_2)_n-NR^aR^b$, wherein R^a and R^b are each independently H, methyl, ethyl, hydroxy, methoxymethyl, methoxyethyl, cyclopropyl, or cyclobutyl, and n is an integer of 1 to 6.

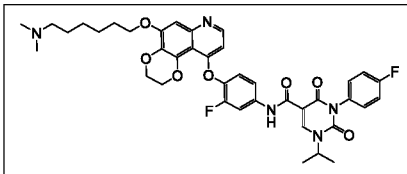
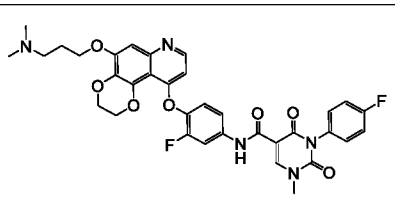
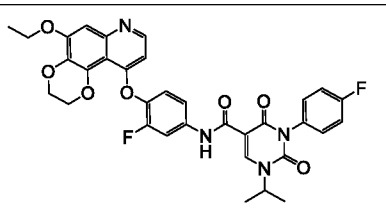
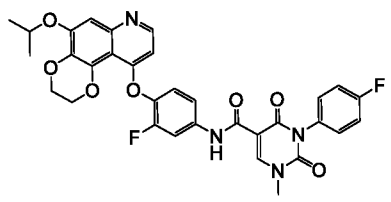
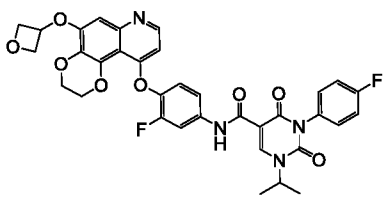
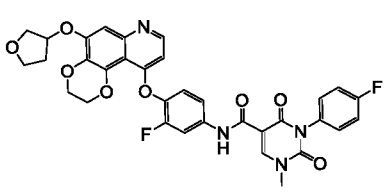
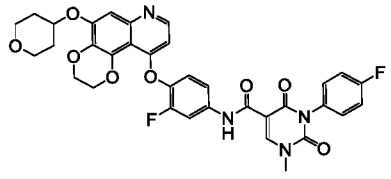
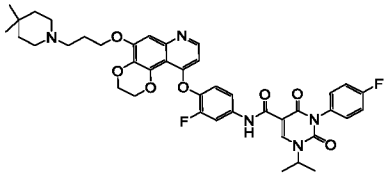
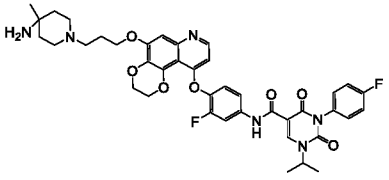
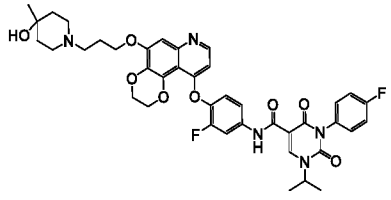
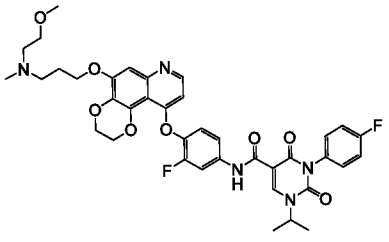
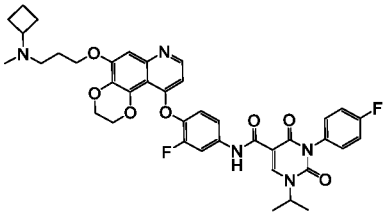
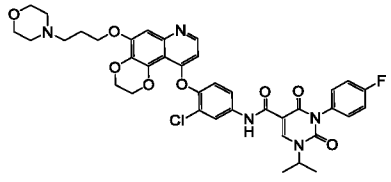
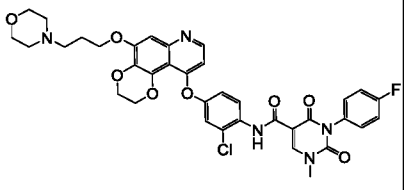
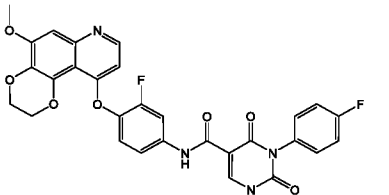
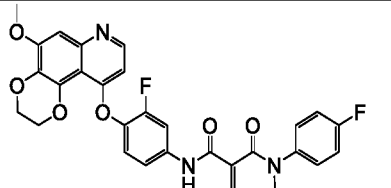
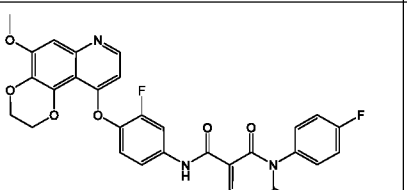
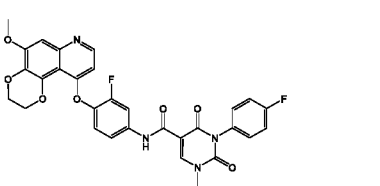
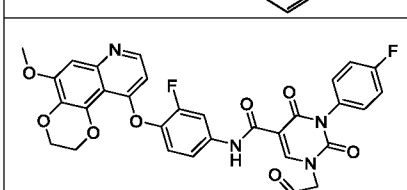
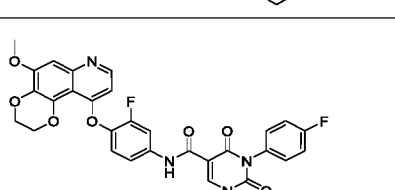
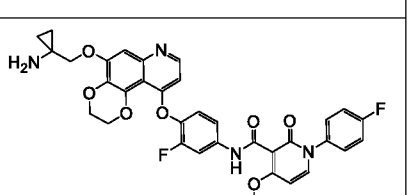
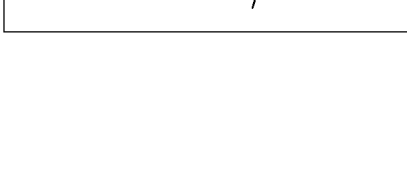
11. The compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to claim 1, wherein the compound is selected from the group consisting of:

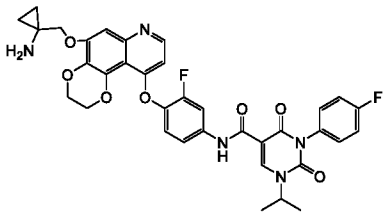
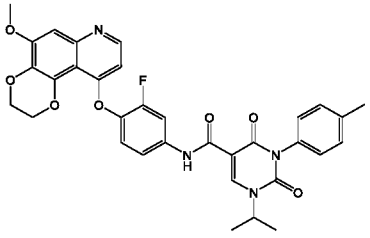
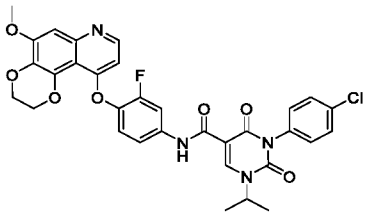
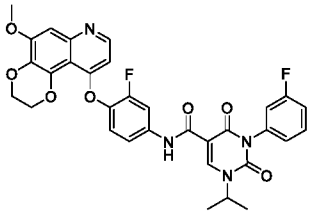
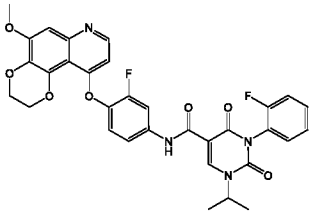
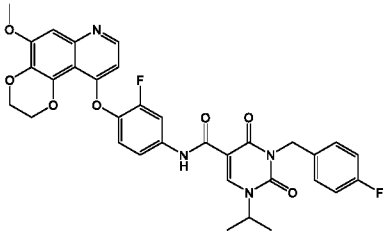
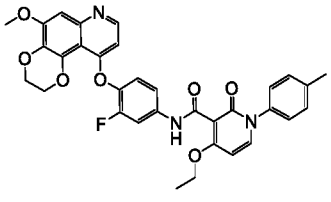
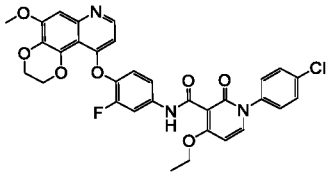
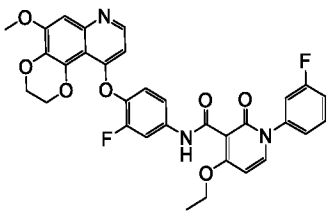
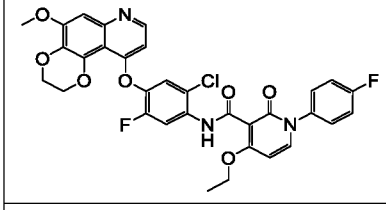
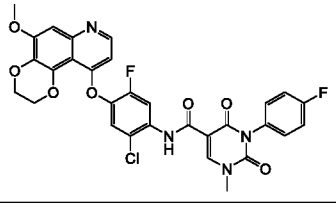
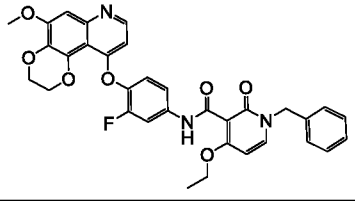
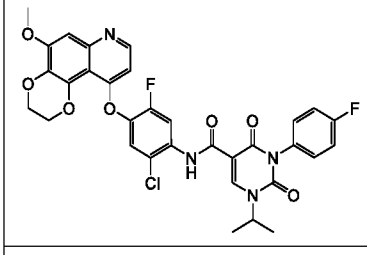
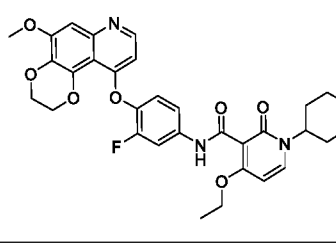
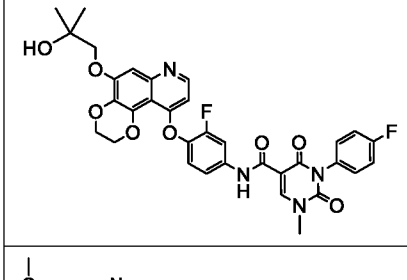
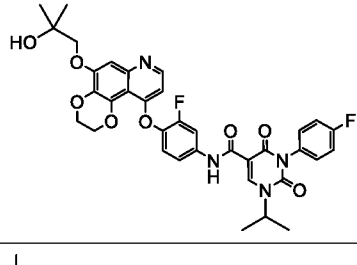
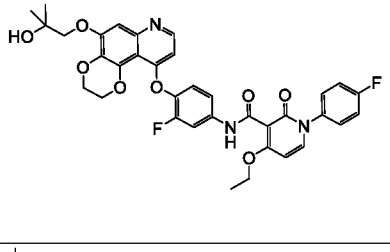
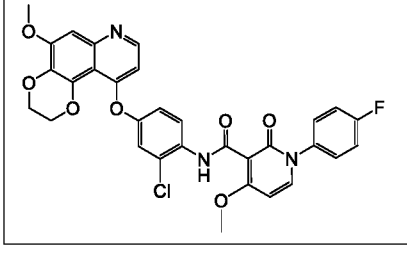
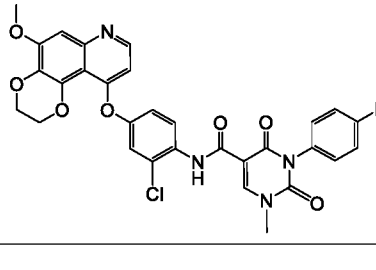
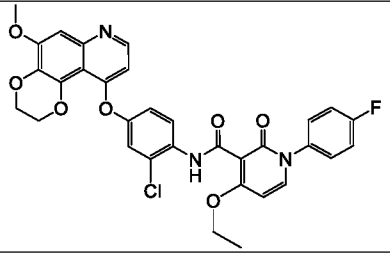
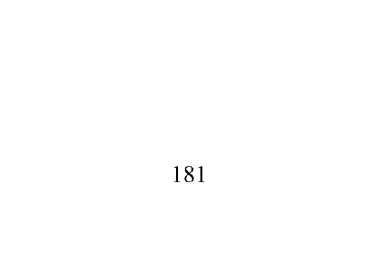


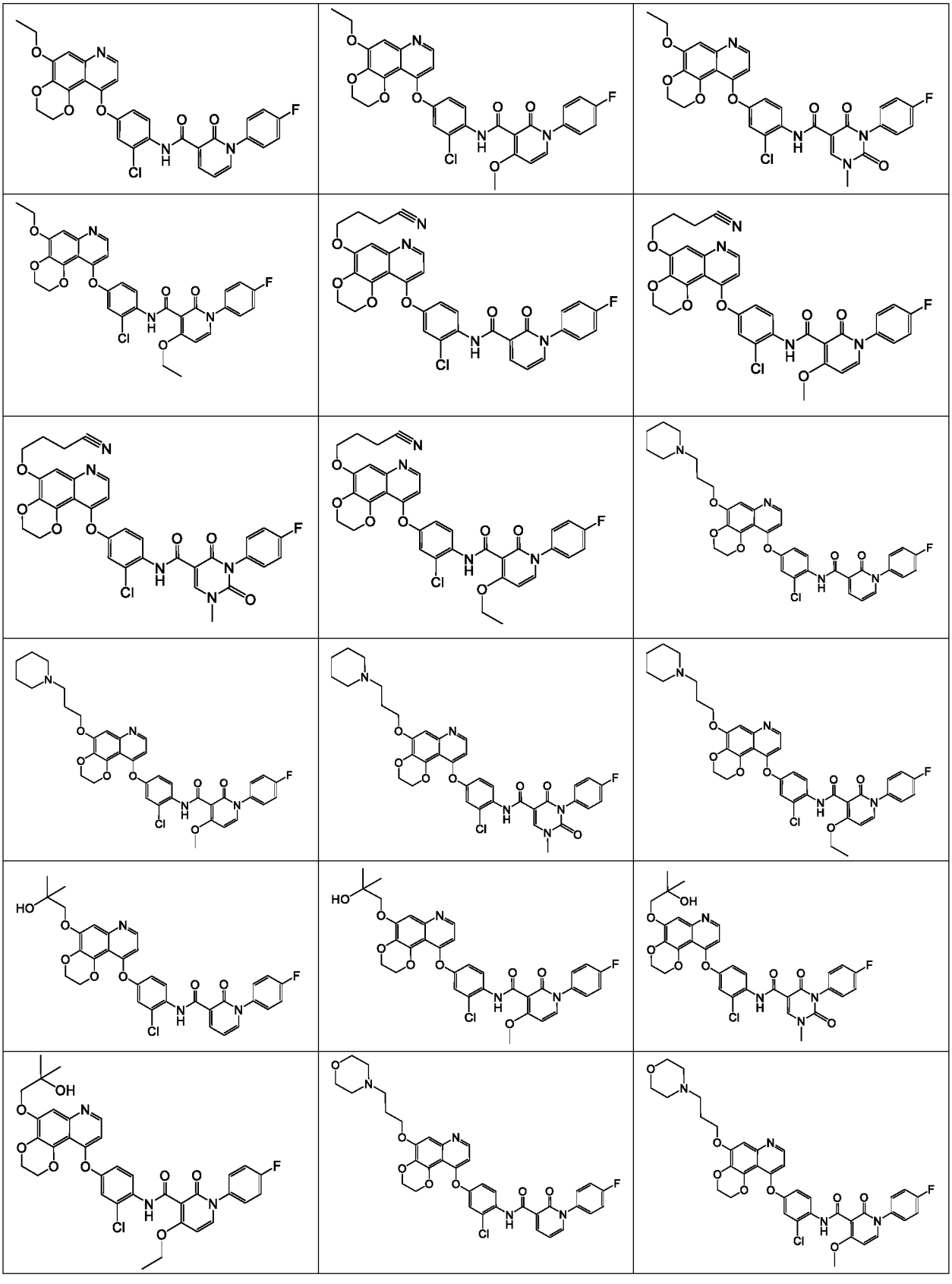


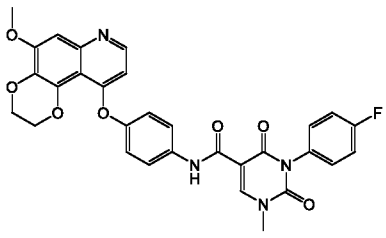
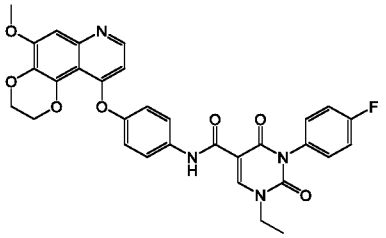
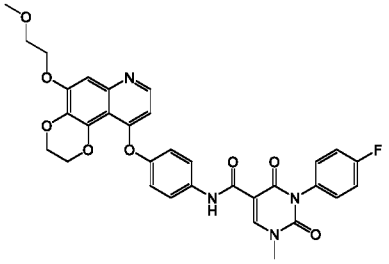
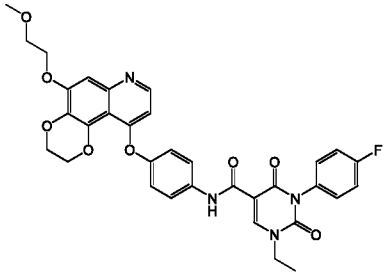
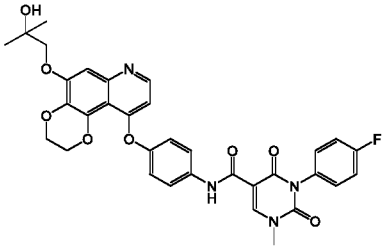
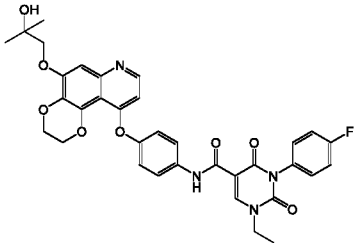
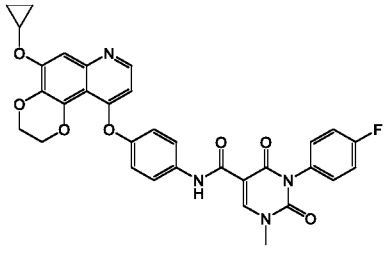
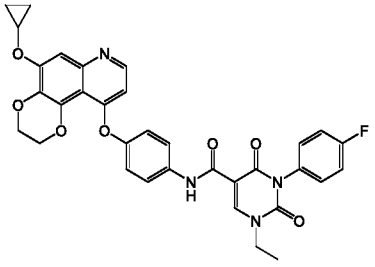
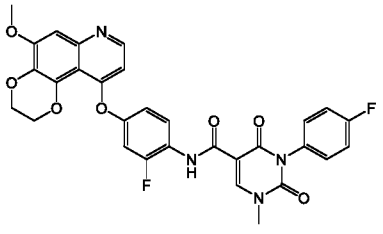
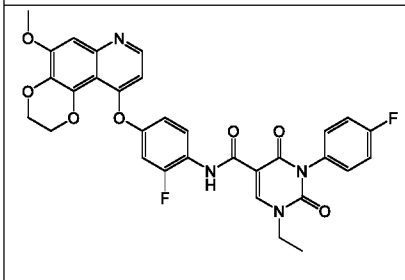
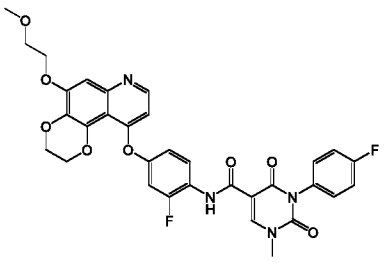
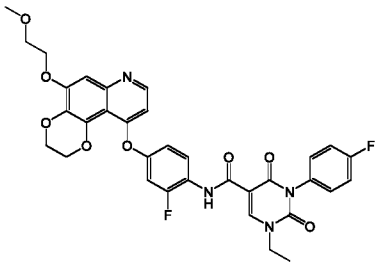
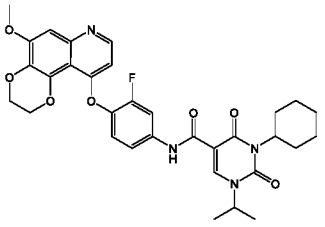
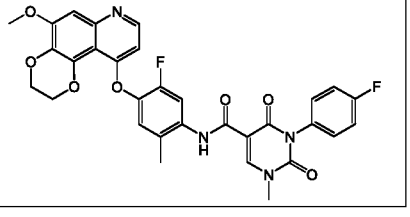
		
		
		
		
		
		
		
		

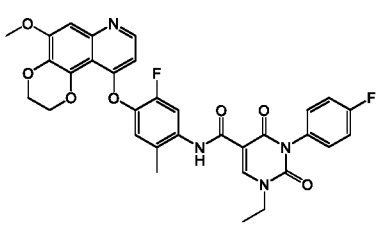
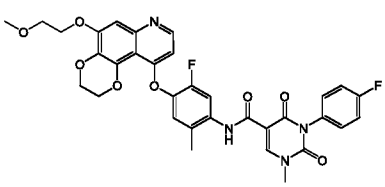
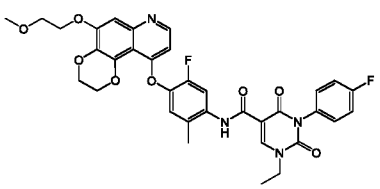
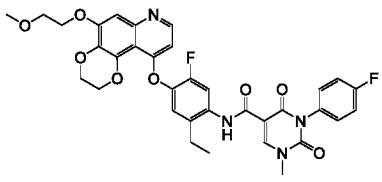
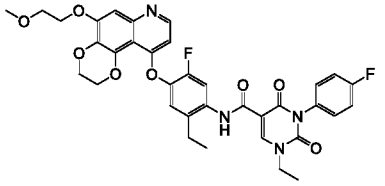
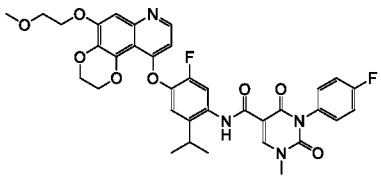
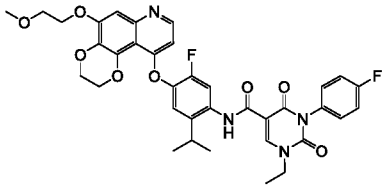
		
		
		
		
		
		
		
		

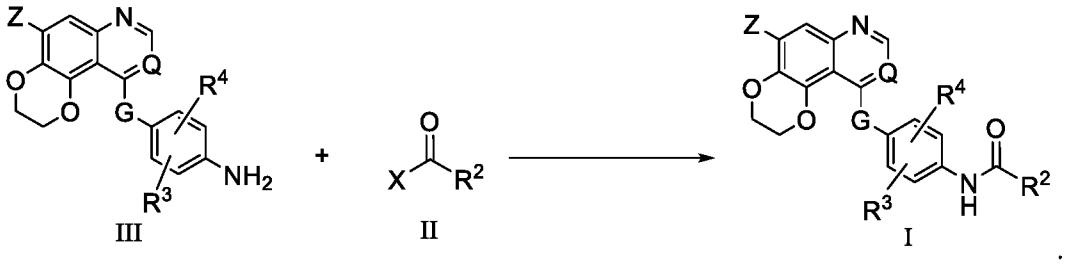
		
		
		
		
		
		
		
		



		
		
and		.

12. A method for preparing the compound according to claims 1 to 11, or a pharmaceutically acceptable salt, a stereoisomer, a tautomer, a hydrate, a solvate, or a prodrug thereof, characterized in that the method comprises the step of reacting the compound represented by formula (III) with the compound represented by formula (II) to afford the compound of formula (I), wherein Q, G, Z, R^1, R^2, R^3 and R^4 are as defined in claims 1 to 11, and X is hydroxy, or halogen,



13. Use of the compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to any one of claims 1 to 11, in the manufacture of a medicament for treating diseases related to tyrosine kinase TRK, c-MET, AXL, MER and/or VEGFR2, wherein the diseases related to tyrosine kinase TRK, c-MET, AXL, MER and/or VEGFR2 include fundus oculi disease, xerophthalmia, psoriasis, vitiligo, dermatitis, alopecia areata, rheumatoid arthritis, colitis, multiple sclerosis, systemic

lupus erythematosus, Crohn's disease, atherosclerosis, pulmonary fibrosis, liver fibrosis, bone marrow fibrosis, non-small cell lung cancer, small cell lung cancer, breast cancer, pancreatic cancer, glioma, glioblastoma, ovarian cancer, cervical cancer, colorectal cancer, melanoma, endometrial cancer, prostate cancer, bladder cancer, leukemia, gastric cancer, liver cancer, gastrointestinal stromal tumor, thyroid cancer, chronic granulocytic leukemia, acute myelocytic leukemia, non-Hodgkin's lymphoma, nasopharyngeal cancer, esophageal cancer, brain tumor, B-cell and T-cell lymphoma, lymphoma, multiple myeloma, biliary tract cancerous sarcoma, and bile duct cancer.

14. A pharmaceutical composition, comprising the compound, or the stereoisomer, the tautomer, the hydrate, the solvate, the pharmaceutically acceptable salt, or the prodrug thereof according to any one of claims 1 to 11, and one or more pharmaceutically acceptable carriers or excipients.