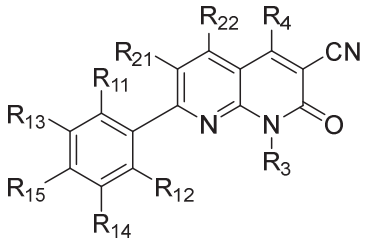
NRAS and HRAS family members was much lower (8% and 3%, respectively). The most common KRAS mutations were found at residues G12 and G13 in the P-loop as well as at residue Q61.

G12C is a frequently occurring KRAS gene mutation (glycine-12 is mutated to cysteine). This mutation has been found in about 13% of cancers, about 43% in lung cancer, and almost 100% in MYH-associated polyposis (familial colon cancer syndrome). However, targeting this gene with small molecules is a challenge.

Thus, despite advances in this field, there remains a need in the art for improved compounds and methods for treating cancer, such as by inhibiting KRAS, HRAS or NRAS. The present invention fulfills this need and provides other related advantages.

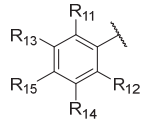
Summary

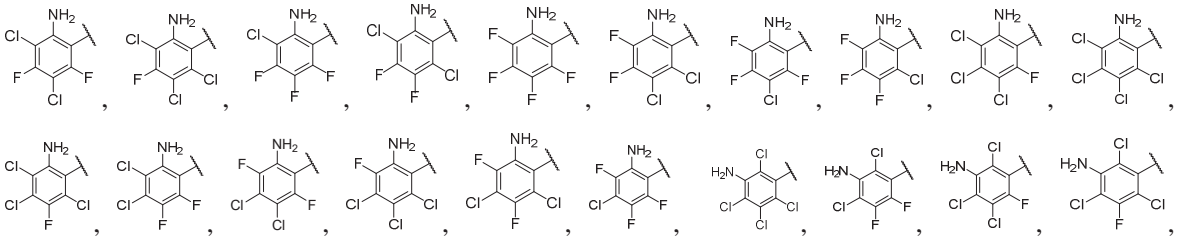
In one aspect, the present disclosure refers to a compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof:

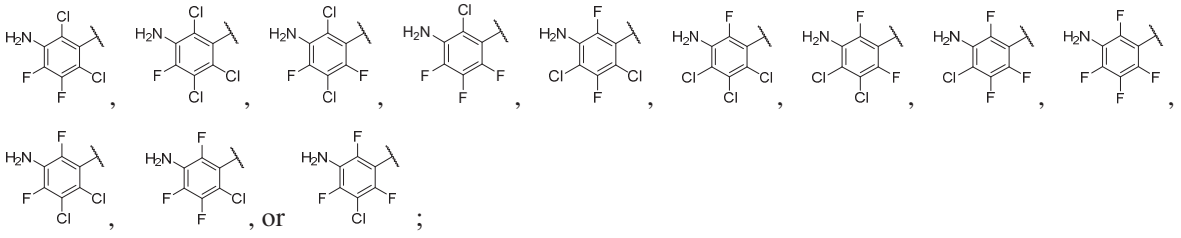


(I)

Wherein:

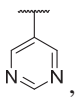
the  in the formula (I) is selected from:



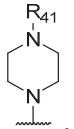
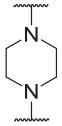


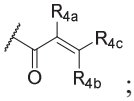
R_{21} is selected from halogen;

R_{22} is selected from hydrogen;

R_3 is selected from ,  or , each hydrogen in the R_3 at each occurrence is independently optionally substituted by 1 R_{31} or 2 R_{31};

Each R_{31} at each occurrence is independently selected from -C_{1-6}alkyl;

R_4 is selected from , each hydrogen in the  is independently optionally substituted with 1 R_{42} or 2 R_{42};

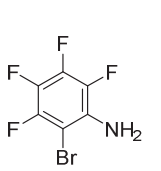
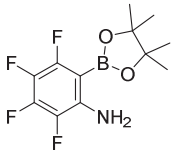
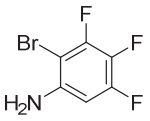
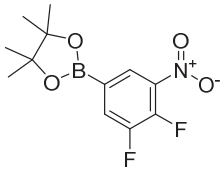
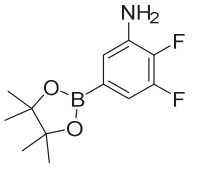
R_{41} is selected from ;

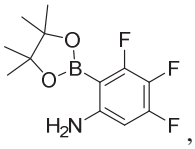
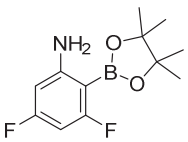
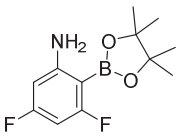
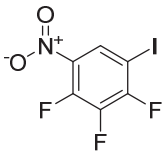
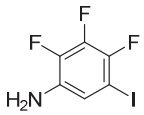
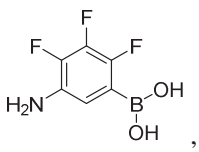
R_{4a}, R_{4b} or R_{4c} is independently selected from hydrogen or halogen;

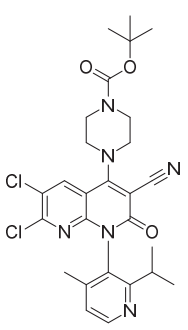
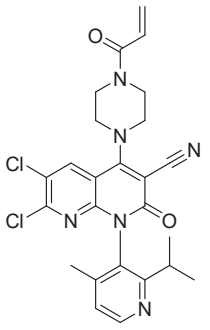
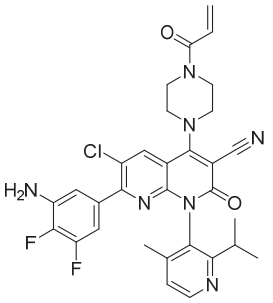
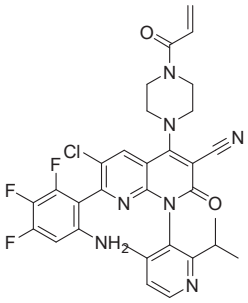
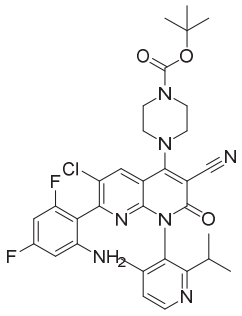
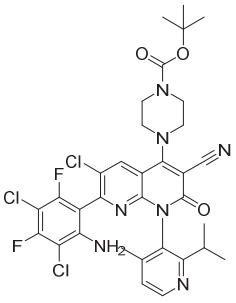
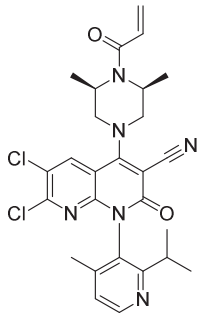
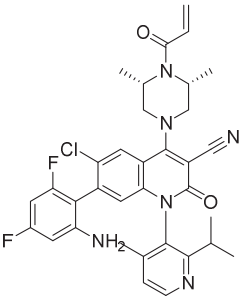
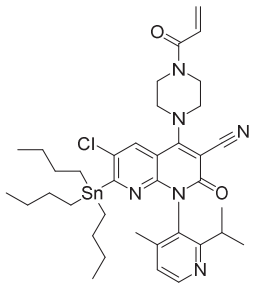
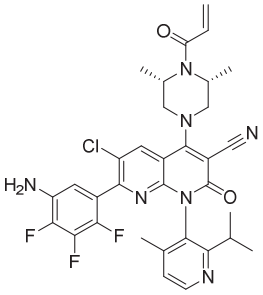
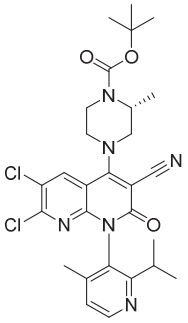
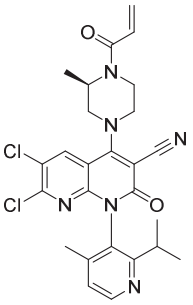
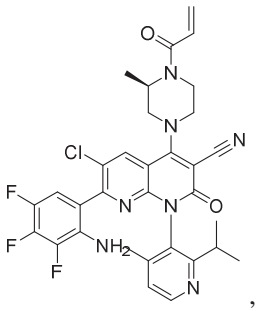
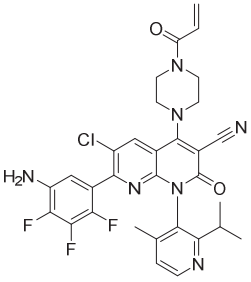
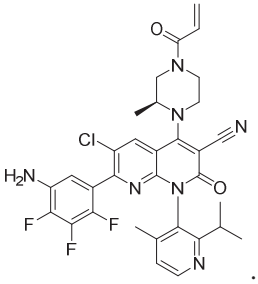
Each R_{42} at each occurrence is independently selected from -C_{1-6}alkyl or -C_{1-6}alkylene-CN.

In another aspect, the present disclosure refers to a pharmaceutical composition comprising the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof as described herein, and at least one pharmaceutically acceptable excipient. In another aspect, the present disclosure refers to use of the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof as described herein; or the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment of cancer related to KRAS G12C mutant protein.

In yet another aspect, the present disclosure refers to an intermediate selected from:

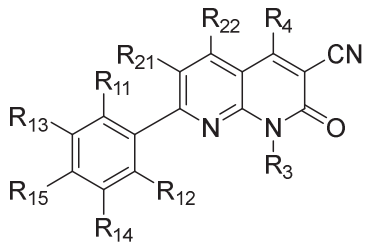
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or

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In a further aspect, the present disclosure refers to a compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof as described herein; or the pharmaceutical composition as described herein for use in therapy.

In one example, provided herein is A compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof:



(I)

Wherein:

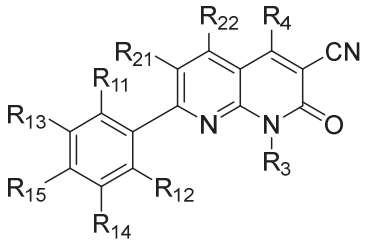
R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently selected from halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_5R_6, -C(=O)R_5, -C(=O)OR_5, -OC(=O)R_5, -C(=O)NR_5R_6, -NR_5C(=O)R_6, -$NR_5SO_2R_6$, -SO_2R_5, -S(=O)$_2NR_5R_6$, -POR_5R_6, -C_{3-6}carbocyclic, 3-6 membered heterocyclic, -C_{6-10}aryl, or 5-10 membered heteroaryl, each hydrogen in R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently optionally substituted with 1, 2, 3, 4, 5 or 6 substituent(s) selected from halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, oxo, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_5R_6, -C(=O)R_5, -C(=O)OR_5, -OC(=O)R_5, -C(=O)NR_5R_6, -NR_5C(=O)R_6, -$NR_5SO_2R_6$, -SO_2R_5, -S(=O)$_2NR_5R_6$, -POR_5R_6, -C_{3-6}carbocyclic, 3-6 membered heterocyclic, -C_{6-10}aryl, or 5-10 membered heteroaryl; each heterocyclic or heteroaryl at each occurrence independently contains 1, 2, 3 or 4 heteroatom(s) selected from N, O, S, S=O or S(=O)$_2$;

R_{21} or R_{22} is independently selected from hydrogen, halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_5R_6, -C(=O)R_5, -C(=O)OR_5, -OC(=O)R_5, -C(=O)NR_5R_6, -NR_5C(=O)R_6, -$NR_5SO_2R_6$, -SO_2R_5, -S(=O)$_2NR_5R_6$, -POR_5R_6, -C_{3-6}carbocyclic, 3-6 membered heterocyclic, -C_{6-10}aryl, or 5-10 membered heteroaryl, each hydrogen in R_{21} or R_{22} is independently optionally substituted with 1, 2, 3, 4, 5 or 6 substituent(s) selected from halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, oxo, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_5R_6, -C(=O)R_5, -C(=O)OR_5, -OC(=O)R_5, -C(=O)NR_5R_6, -NR_5C(=O)R_6, -S(=O)$_2NR_5R_6$, -POR_5R_6, -C_{3-6}carbocyclic, 3-6

Each R_{51} is selected from halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_7R_8, -C(=O)R_7, -C(=O)OR_7, -OC(=O)R_7, -C(=O)NR_7R_8, -NR_7C(=O)R_8, -$NR_7SO_2R_8$, -SO_2R_7, -S(=O)$_2NR_7R_8$, -POR_7R_8, -C_{3-6}carbocyclic, 3-6 membered heterocyclic, -C_{6-10}aryl, or 5-10 membered heteroaryl, each hydrogen in R_{51} is independently optionally substituted with 1, 2, 3, 4, 5 or 6 substituent(s) selected from halogen, -C_{1-6}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, heteroC_{2-6}alkyl, -CN, oxo, -OC_{1-6}alkyl, -SC_{1-6}alkyl, -NR_7R_8, -C(=O)R_7, -C(=O)OR_7, -OC(=O)R_7, -C(=O)NR_7R_8, -NR_7C(=O)R_8, -$NR_7SO_2R_8$, -SO_2R_7, -S(=O)$_2NR_7R_8$, -POR_7R_8, -C_{3-6}carbocyclic, 3-6 membered heterocyclic, -C_{6-10}aryl, or 5-10 membered heteroaryl; each heterocyclic or heteroaryl at each occurrence independently contains 1, 2, 3 or 4 heteroatom(s) selected from N, O, S, S=O or S(=O)$_2$;

Each R_7 and R_8 at each occurrence is independently selected from hydrogen or -C_{1-6}alkyl.

In some examples, there is provided a compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof:



(I)

Wherein:

R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently selected from -OH; halogen; -NR_aR_b; -C_{1-6}alkyl; -OC_{1-6}alkyl; -C_{1-6}alkylene-OH; -C_{1-6}alkylene-O-C_{1-6}alkyl; -C_{1-6}alkyl substituted with halogen, -NH_2, -CN or -OH; -O-C_{1-6}alkyl substituted with halogen, -NH_2, -CN or -OH; -O-C_{1-6}alkyl; -SO_2R_a; -CN; -C(=O)NR_aR_b; -C(=O)R_a; -OC(=O)R_a; -C(=O)OR_a; or -C_{3-6}carbocyclic;

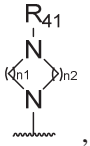
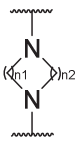
R_a or R_b is independently selected from hydrogen or -C_{1-6}alkyl;

R_{21} is selected from hydrogen; halogen; -C_{1-6}alkyl; -C_{1-6}alkyl substituted with halogen, -NH_2, -CN or -OH; -C_{2-6}alkenyl; or -C_{3-6}carbocyclic;

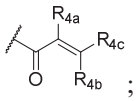
R_{22} is selected from hydrogen; halogen; -C_{1-6}alkyl; -C_{1-6}alkyl substituted with halogen, -NH_2, -CN or -OH; -C_{2-6}alkenyl; or -C_{3-6}carbocyclic;

R_3 is selected from -C_{6-10}aryl or 5-10 membered heteroaryl, each of 5-10 membered heteroaryl at each occurrence independently contains 1, 2, 3 or 4 heteroatoms selected from N, O or S, each hydrogen in the -C_{6-10}aryl or 5-10 membered heteroaryl at each occurrence is independently optionally substituted with 1R_{31}, 2R_{31}, 3R_{31}, 4R_{31}, 5R_{31} or 6 R_{31};

Each R_{31} at each occurrence is independently selected from halogen, -C_{1-6}alkyl, -CN, -OH, -O-C_{1-6}alkyl, -NH_2, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)$_2$ or -C_{3-6}carbocyclic;

R_4 is  , each hydrogen in the  is independently optionally substituted with $1R_{42}$, $2R_{42}$, $3R_{42}$, $4R_{42}$, $5R_{42}$ or 6 R_{42};

n1 or n2 is independently selected from 1, 2, 3, 4, 5 or 6;

R_{41} is  ;

R_{4a}, R_{4b} or R_{4c} is independently selected from hydrogen, halogen, -C_{1-6}alkyl or -C_{1-6}alkylene-N(C_{1-6}alkyl)$_2$;

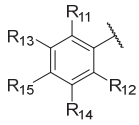
Each R_{42} at each occurrence is independently selected from -C_{1-6}alkyl; -C_{1-6}alkylene-CN or -C_{1-6}alkyl substituted with halogen.

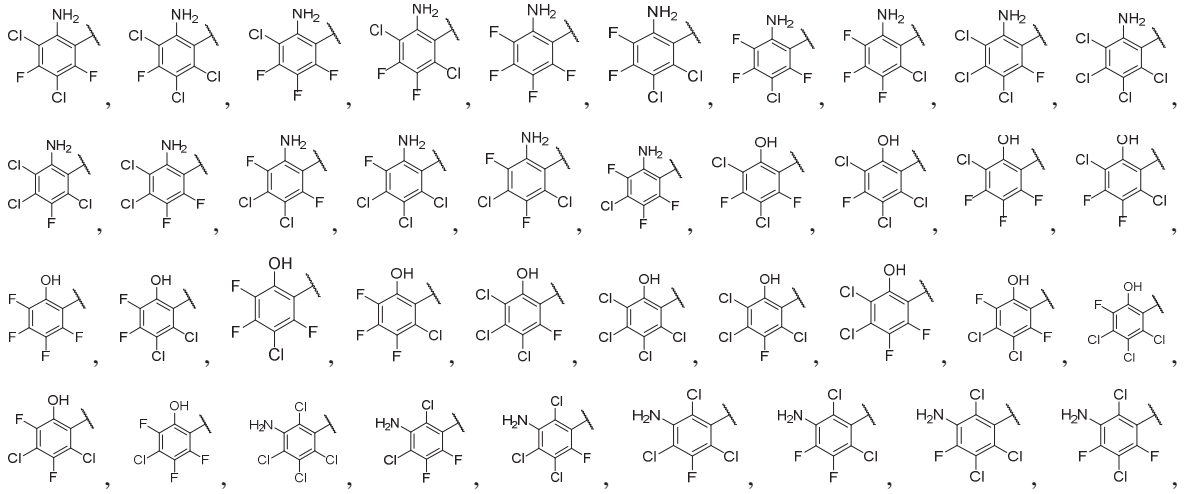
In some examples, R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently selected from -OH; -F; -Cl; -Br; -NR_aR_b; -C_{1-3}alkyl; -OC_{1-3}alkyl; -C_{1-3}alkylene-OH; -C_{1-3}alkylene-O-C_{1-3}alkyl; -C_{1-3}alkyl substituted with -F or -Cl; -O-C_{1-3}alkyl substituted with -F or -Cl; -SO_2R_a; -CN; -C(=O)NR_aR_b; -C(=O)R_a; -OC(=O)R_a; -C(=O)OR_a; 3-membered carbocyclic; 4-membered carbocyclic; 5-membered carbocyclic or 6-membered carbocyclic;

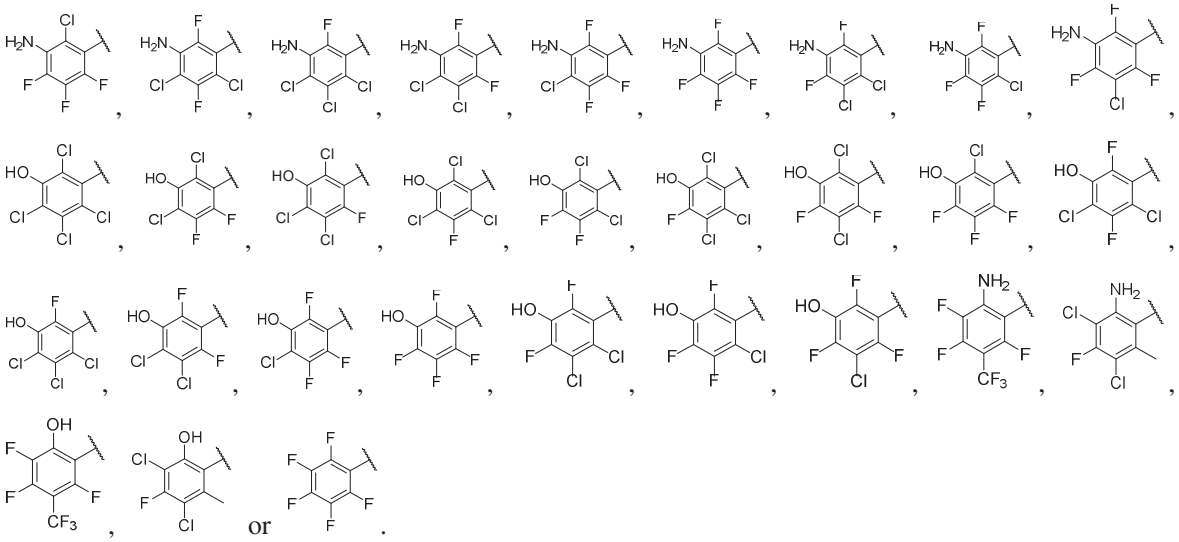
R_a or R_b is independently selected from hydrogen or -C_{1-3}alkyl.

In some examples, R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently selected from -OH, -F, -Cl, -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH(CH_3)_2$, -OCH_3, -OCH_2CH_3, -$OCH_2CH_2CH_3$, -$OCH(CH_3)_2$, -CH_2OH, -CH_2CH_2OH, -CH_2OCH_3, -CHF_2, -CH_2F, -CF_3, -OCH_2F, -$OCHF_2$, -OCF_3, -SO_2CH_3, -CN, -C(=O)NH_2, -C(=O)CH_3, -OC(=O)CH_3, -C(=O)OCH_3 or 3-membered carbocyclic.

In some examples, R_{11}, R_{12}, R_{13}, R_{14} or R_{15} is independently selected from -OH, -F, -Cl, -NH_2, -CH_3 or -CF_3.

In some examples, the  in the formula (I) is selected from:





In some examples, R_{21} is selected from hydrogen; -F; -Cl; -Br; -C_{1-3}alkyl; -C_{1-3}alkyl substituted with -F or -Cl; -C_{2-3}alkenyl; or -C_{3-6}carbocyclic.

In some examples, R_{21} is selected from hydrogen; -F; -Cl; methyl; ethyl; propyl; isopropyl; methyl substituted with -F; ethyl substituted with -F; propyl substituted with -F; isopropyl substituted with -F; ethenyl; propenyl; 3 membered carbocyclic; 4 membered carbocyclic; 5 membered carbocyclic; or 6 membered carbocyclic.

In some examples, R_{21} is -Cl.

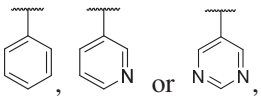
In some examples, R_{22} is selected from hydrogen; -F; -Cl; -Br; -C_{1-3}alkyl; -C_{1-3}alkyl substituted with -F or -Cl; -C_{2-3}alkenyl; or -C_{3-6}carbocyclic.

In some examples, R_{22} is selected from hydrogen; -F; -Cl; methyl; ethyl; propyl; isopropyl; methyl substituted with -F; ethyl substituted with -F; propyl substituted with -F; isopropyl substituted with -F; ethenyl; propenyl; 3 membered carbocyclic; 4 membered carbocyclic; 5 membered carbocyclic; or 6 membered carbocyclic.

In some examples, R_{22} is hydrogen.

In some examples, R_3 is selected from phenyl, naphthyl, 5 membered heteroaryl, 6 membered heteroaryl, 7 membered heteroaryl, 8 membered heteroaryl, 9 membered heteroaryl or 10 membered heteroaryl, each heteroaryl at each occurrence independently contains 1, 2 or 3 heteroatoms selected from N or O, each hydrogen in R_3 at each occurrence is independently optionally substituted with $1R_{31}$, $2R_{31}$, $3R_{31}$, $4R_{31}$ or $5R_{31}$.

In some examples, R_3 is selected from phenyl or 6 membered heteroaryl, the heteroaryl contains 1 or 2 heteroatoms selected from N, each hydrogen in the phenyl or 6 membered heteroaryl at each occurrence is independently optionally substituted by $1R_{31}$, $2R_{31}$, $3R_{31}$ or $4R_{31}$.

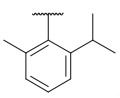
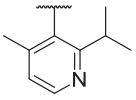
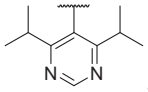
In some examples, R_3 is selected from , each hydrogen in the R_3 at each occurrence is independently optionally substituted by $1R_{31}$, $2R_{31}$, $3R_{31}$ or $4R_{31}$.

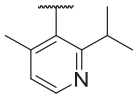
In some examples, each R_{31} at each occurrence is independently selected from -F, -Cl, -Br,

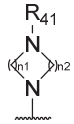
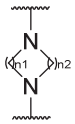
-C_{1-3}alkyl, -CN, -OH, -O-C_{1-3}alkyl, -NH_2, -NH(C_{1-3}alkyl), -N(C_{1-3}alkyl)$_2$ or -C_{3-6}carbocyclic.

In some examples, each R_{31} at each occurrence is independently selected from -F, -Cl, methyl, ethyl, propyl, isopropyl, -CN, -OH, methoxy, ethoxy, propoxy, isopropoxy, -NH_2, -$NHCH_3$, -$NHCH_2CH_3$, -$NH(CH_2CH_2CH_3)$, -$NH(CH(CH_3)_2)$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, -$N(CH_3)(CH_2CH_3)$, 3 membered carbocyclic, 4 membered carbocyclic, 5 membered carbocyclic or 6 membered carbocyclic.

In some examples, each R_{31} at each occurrence is independently selected from methyl or isopropyl.

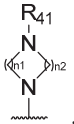
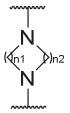
In some examples, R_3 is selected from  ,  or  .

In some examples, R_3 is  .

In some examples, R_4 is  , each hydrogen in the  is independently optionally substituted with $1R_{42}$, $2R_{42}$, $3R_{42}$ or $4R_{42}$;

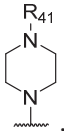
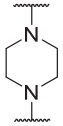
n1 is selected from 1, 2 or 3;

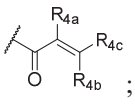
n2 is selected from 1, 2 or 3.

In some examples, R_4 is selected from  , each hydrogen in the  is independently optionally substituted with $1R_{42}$ or $2R_{42}$;

n1 is selected from 1 or 2;

n2 is selected from 1 or 2.

In some examples, R_4 is  , each hydrogen in the  is independently optionally substituted with $1R_{42}$ or $2R_{42}$.

In some examples, R_{41} is  ;

R_{4a}, R_{4b}, or R_{4c} is independently selected from hydrogen, -F, -Cl, -Br, -C_{1-3}alkyl or -C_{1-3}alkylene-N(C_{1-3}alkyl)$_2$.

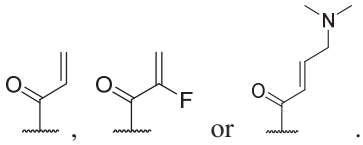
In some examples, R_{4a}, R_{4b} or R_{4c} is independently selected from hydrogen, -F, -Cl, methyl, ethyl, propyl, isopropyl, -CH_2-N(CH_3)$_2$, -CH_2-N(CH_2CH_3)$_2$ or -CH_2-N(CH_3)(CH_2CH_3).

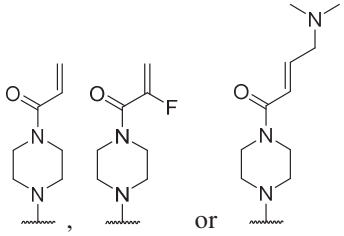
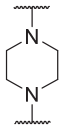
In some examples, R_{4a}, R_{4b} or R_{4c} is independently selected from hydrogen, -F, methyl or -CH_2-N(CH_3)$_2$.

In some examples, R_{4a} is selected from hydrogen or -F; R_{4b} is hydrogen; R_{4c} is selected from

hydrogen or -CH_2-$N(CH_3)_2$.

In some examples, R_{41} is selected from:



In some examples, R_4 is selected from , each hydrogen in the  at each occurrence is independently optionally substituted with $1R_{42}$ or $2R_{42}$.

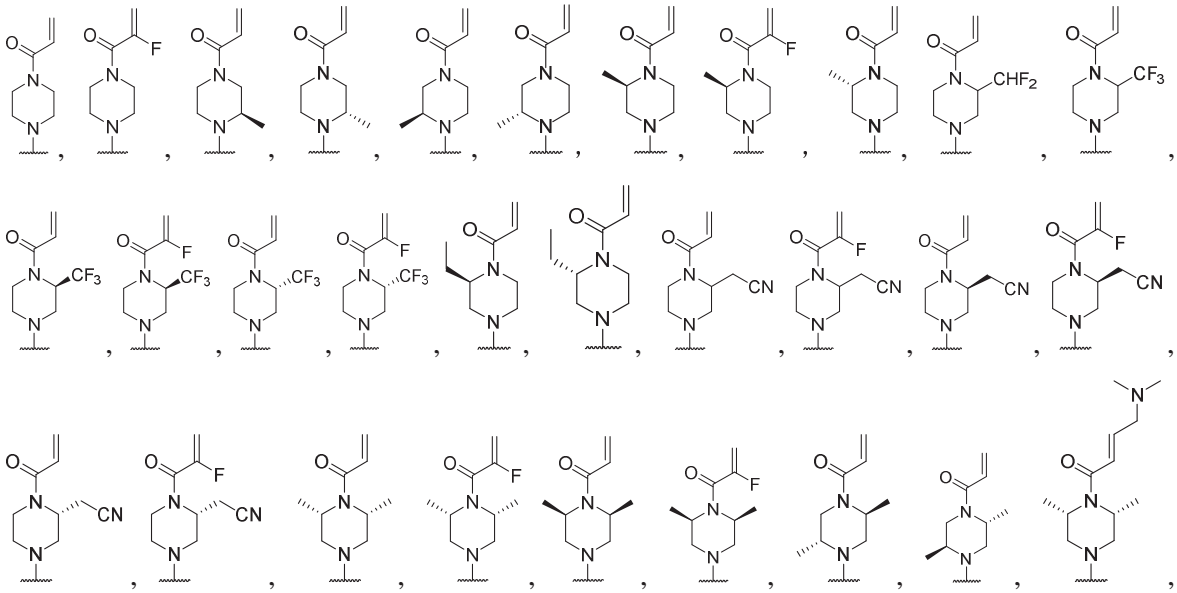
In some examples, each R_{42} at each occurrence is independently selected from -$C_{1\text{-}3}$alkyl; -$C_{1\text{-}3}$alkylene-CN; or -$C_{1\text{-}3}$alkyl substituted with -F or -Cl.

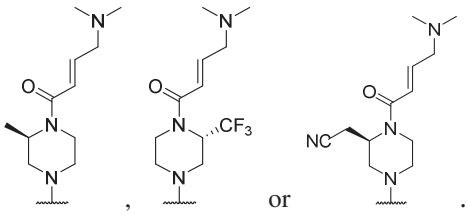
In some examples, each R_{42} at each occurrence is independently selected from methyl; ethyl; propyl; isopropyl; -methylene-CN; -ethylene-CN; -propylene-CN; methyl substituted with -F; ethyl substituted with -F; propyl substituted with -F; or isopropyl substituted with -F.

In some examples, each R_{42} at each occurrence is independently selected from methyl; ethyl; -methylene-CN or methyl substituted with -F.

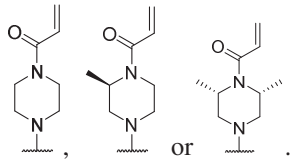
In some examples, each R_{42} at each occurrence is independently selected from -CH_3, -CH_2CH_3, -CH_2CN, -CHF_2 or -CF_3.

In some examples, R_4 is selected from:

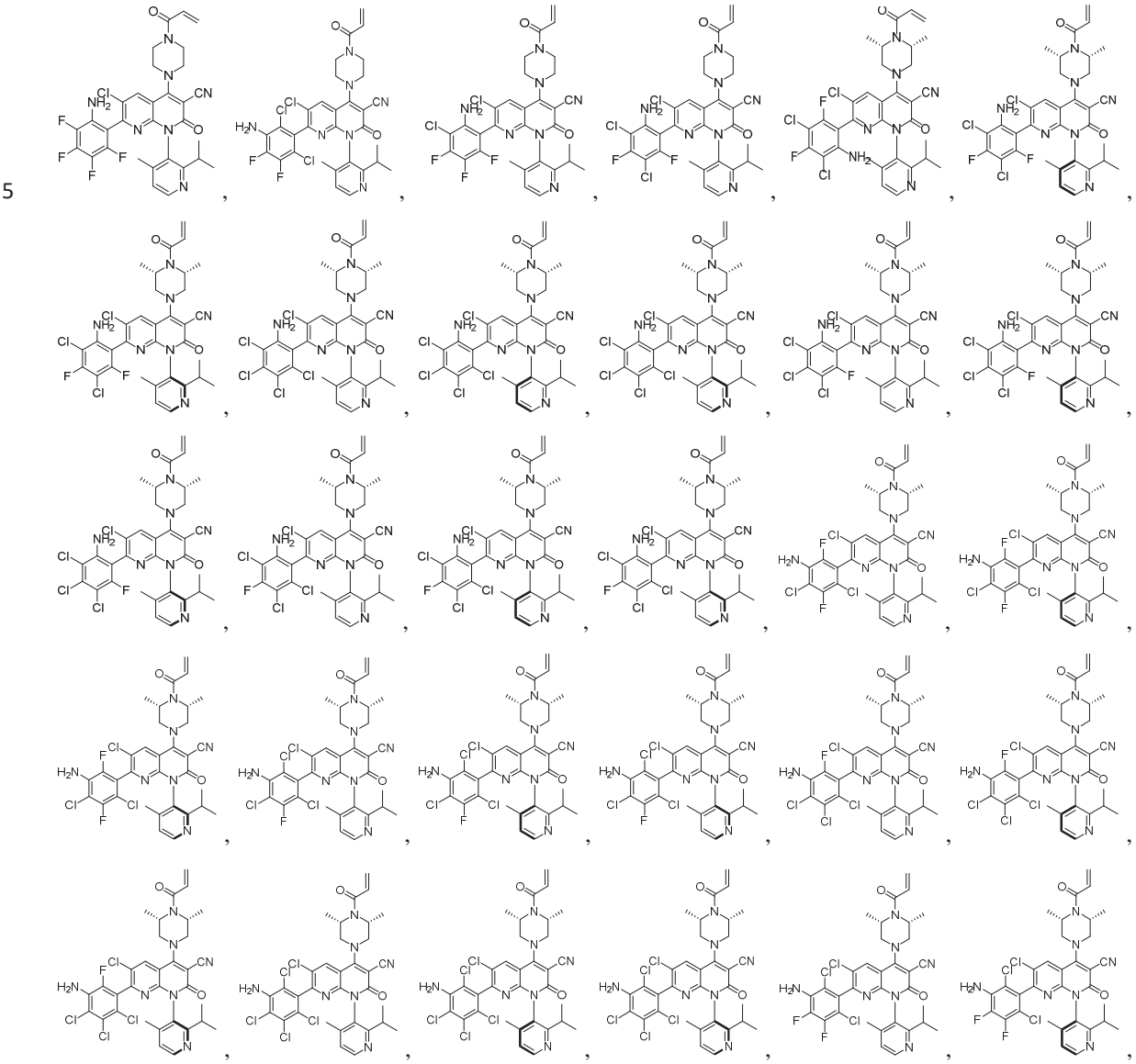


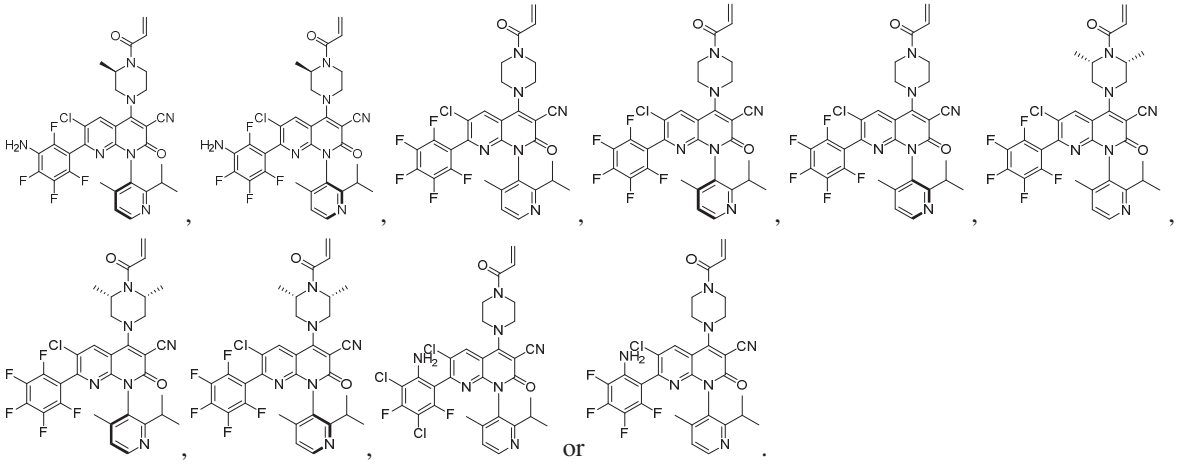


In some examples, R_4 is selected from:



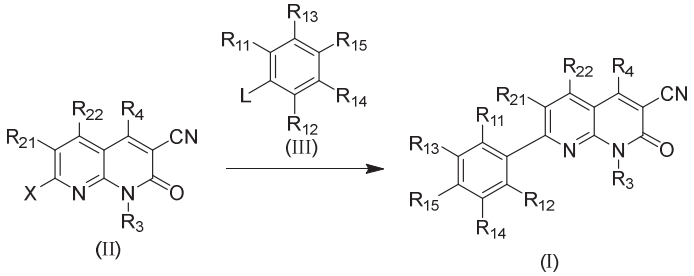
In some examples, the compound is selected from:



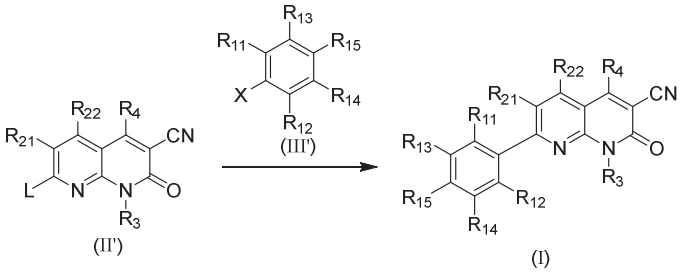


In another examples, provided herein is a method for preparing the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof, the method comprises a coupling reaction between a compound of formula (II) and a compound of formula(III) according to the following reaction Scheme 1 or between a compound of formula (II') and a compound of formula(III') according to the following reaction Scheme 2 catalyzed by a transition metal palladium or nickel reagent:

Scheme 1:

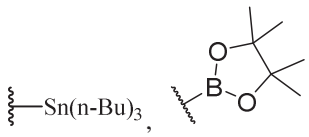


Scheme 2:



Wherein

the L in the compound of formula(III) or formula(II') is a leaving group; preferably, the leaving group is selected from halogen, $-OS(O)_2CF_3$ or -OTs; more preferably, the halogen is selected from -F, -Cl, -Br, or -I; more preferably, the leaving group is -Cl or -Br;

the X in the compound of formula (II) or formula(III') is selected from boronic acid, borate ester or organotin; more preferably, the X is selected from ; preferably, the coupling reaction is Suzuki coupling reaction or Stille coupling reaction;

preferably, the coupling reaction is catalyzed by the transition metal palladium reagent; more preferably, the transition metal palladium reagent is $Pd(PPh_3)_4$.

In another example, provided herein is a pharmaceutical composition comprising the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof of the present disclosure, and at least one pharmaceutically acceptable excipient. In some examples, the said compound in a weight ratio to the said excipient within the range from about 0.0001 to about 10.

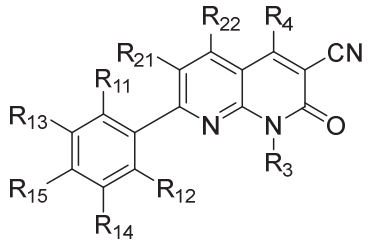
In another example, provided herein is use of the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof of the present disclosure; or the pharmaceutical composition of the present disclosure for the manufacture of a medicament for the treatment of diseases or conditions related to KRAS mutant protein. In some examples, the diseases or conditions related to KRAS mutant protein is the diseases or conditions related to KRAS G12C mutant protein. In some examples, the diseases or conditions related to KRAS G12C mutant protein is cancer related to KRAS G12C mutant protein. In some examples, the cancer is selected from blood cancer, pancreatic cancer, colon cancer, rectal cancer, colorectal cancer or lung cancer. In some examples, the blood cancer is selected from acute myeloid leukemia or acute lymphocytic leukemia; the lung cancer is selected from non-small cell lung cancer or small cell lung cancer.

In another example, provided herein is a method of treating a subject having a diseases or conditions related to KRAS mutant protein, said method comprising administering to the subject a therapeutically effective amount of the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof of the present disclosure; or the pharmaceutical composition of the present disclosure. In some examples, the diseases or conditions related to KRAS mutant protein is the diseases or conditions related to KRAS G12C mutant protein. In some examples, the diseases or conditions related to KRAS G12C mutant protein is cancer related to KRAS G12C mutant protein. In some examples, the cancer is selected from blood cancer, pancreatic cancer, colon cancer, rectal cancer, colorectal cancer or lung cancer. In some examples, the blood cancer is selected from acute myeloid leukemia or acute lymphocytic leukemia; the lung cancer is selected from non-small cell lung cancer or small cell lung cancer.

Definition

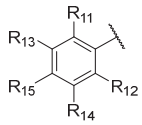
What is claimed is:

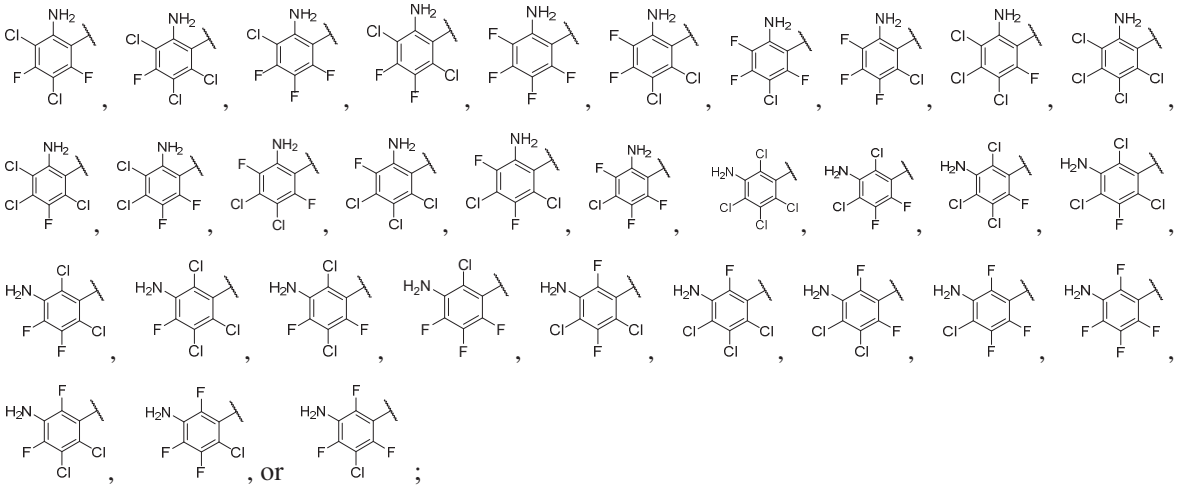
1. A compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof:



(I)

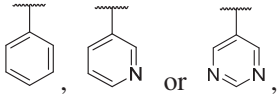
Wherein:

the  in the formula (I) is selected from:

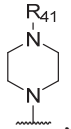
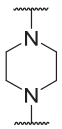


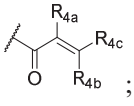
R_{21} is selected from halogen;

R_{22} is selected from hydrogen;

R_3 is selected from , each hydrogen in the R_3 at each occurrence is independently optionally substituted by 1 R_{31} or 2 R_{31};

Each R_{31} at each occurrence is independently selected from -C_{1-6}alkyl;

R_4 is selected from , each hydrogen in the  is independently optionally substituted with 1 R_{42} or 2 R_{42};

R_{41} is selected from ;

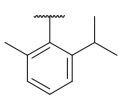
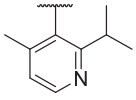
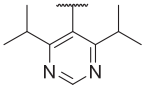
R_{4a}, R_{4b} or R_{4c} is independently selected from hydrogen or halogen;

Each R_{42} at each occurrence is independently selected from -C_{1-6}alkyl or -C_{1-6}alkylene-CN.

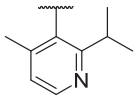
2. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to claim 1, wherein:

R_{21} is selected from -Cl.

3. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to claim 1 or 2, wherein:

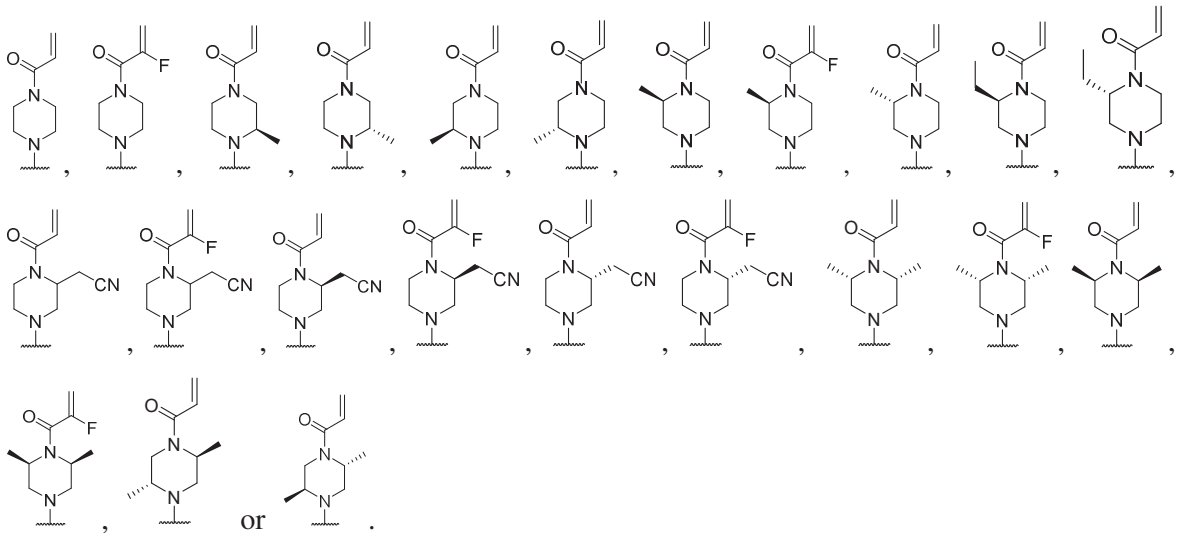
R_3 is selected from ,  or .

4. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 3, wherein:

R_3 is selected from .

5. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 4, wherein:

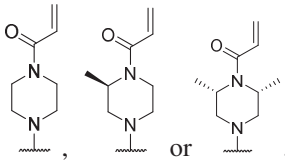
R_4 is selected from:



6. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 5,

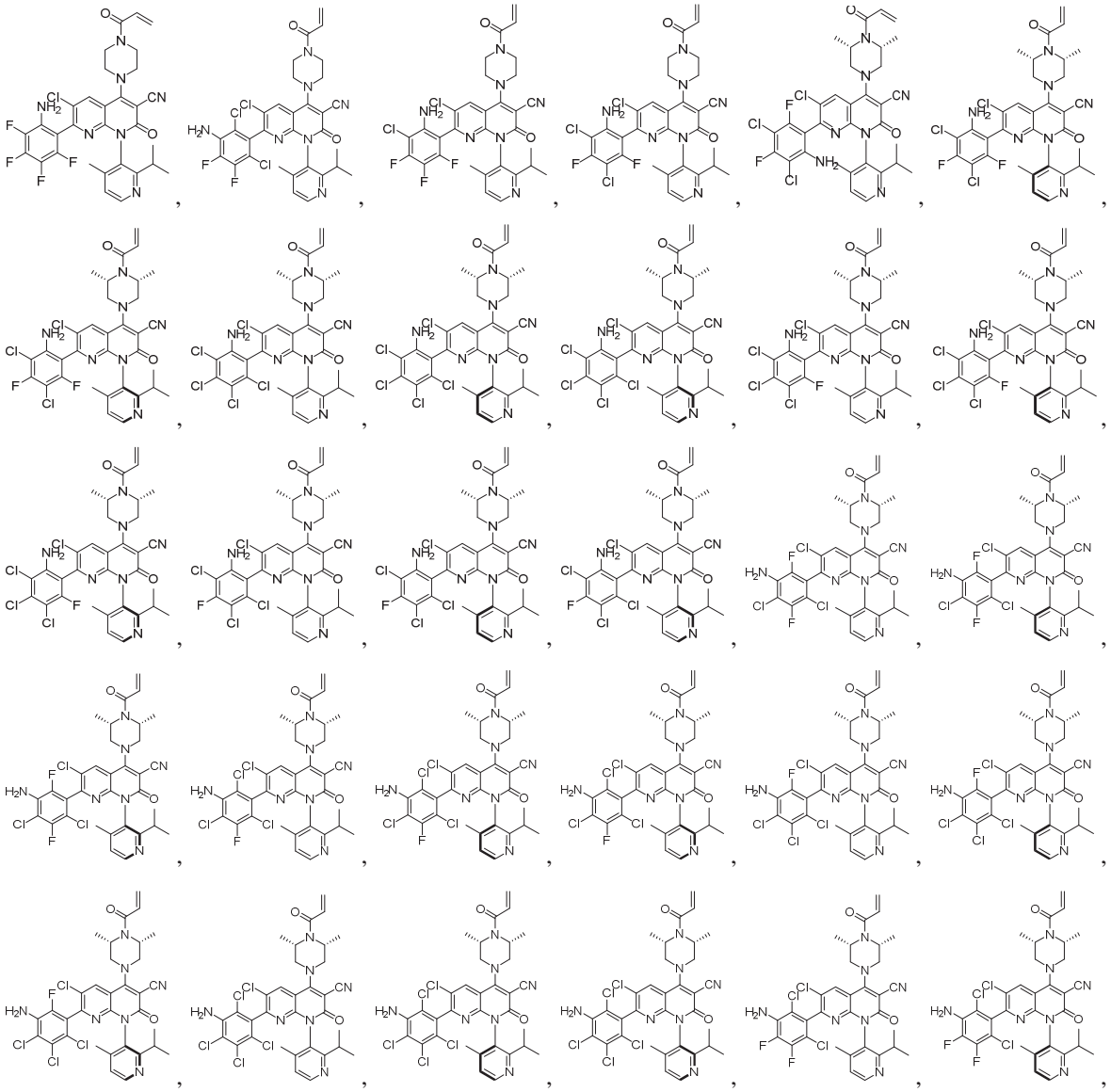
wherein:

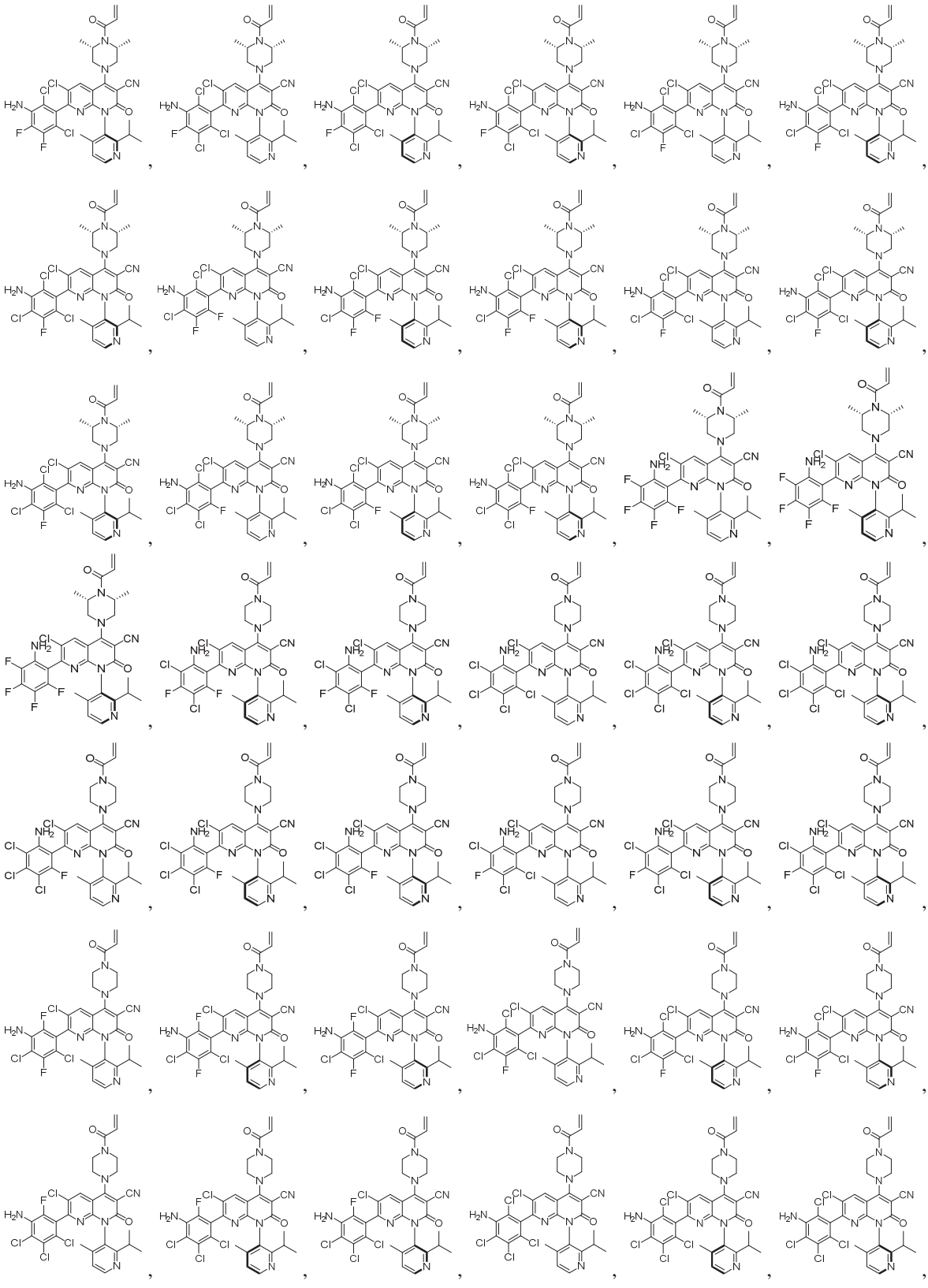
R_4 is selected from:

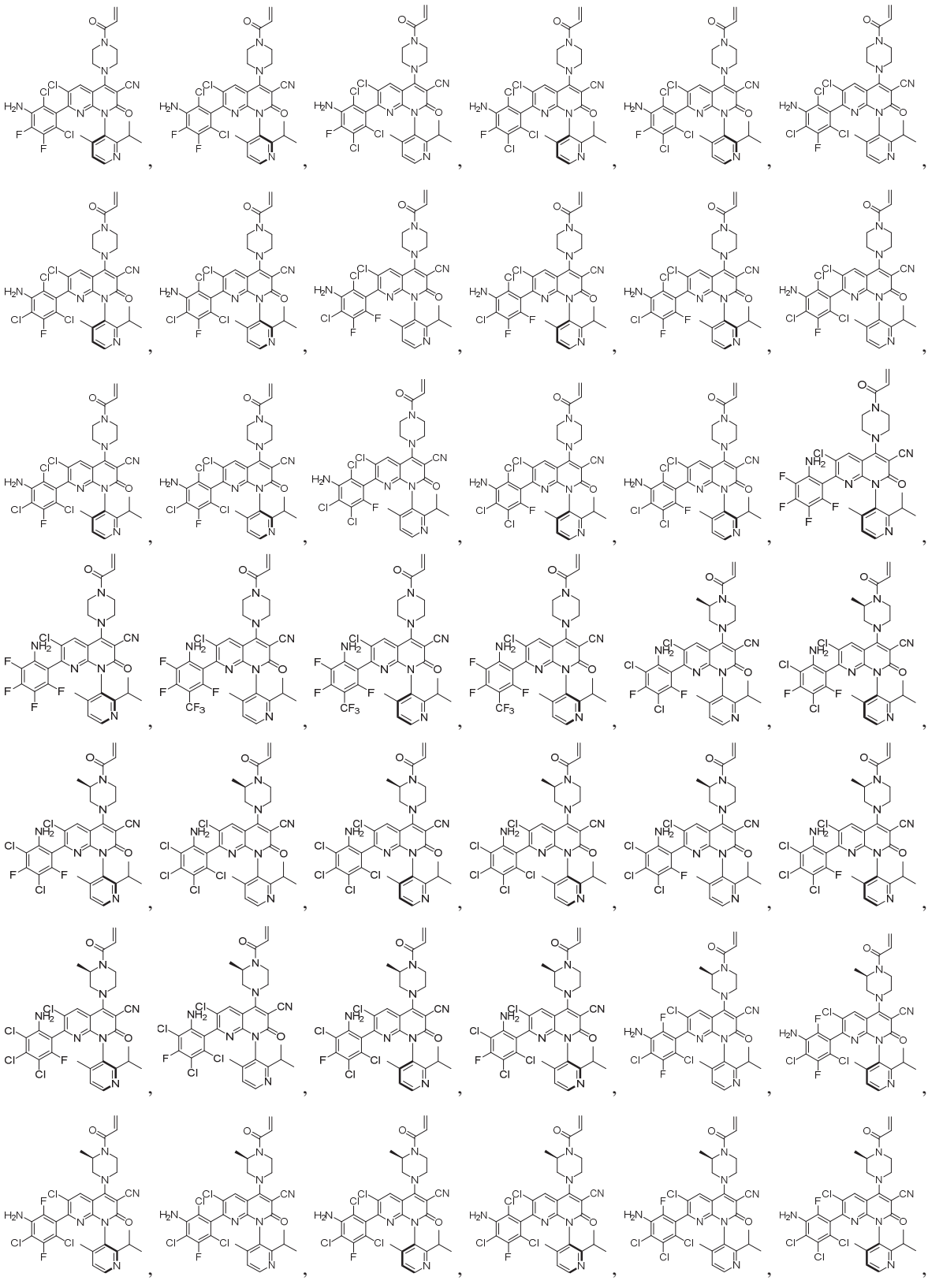


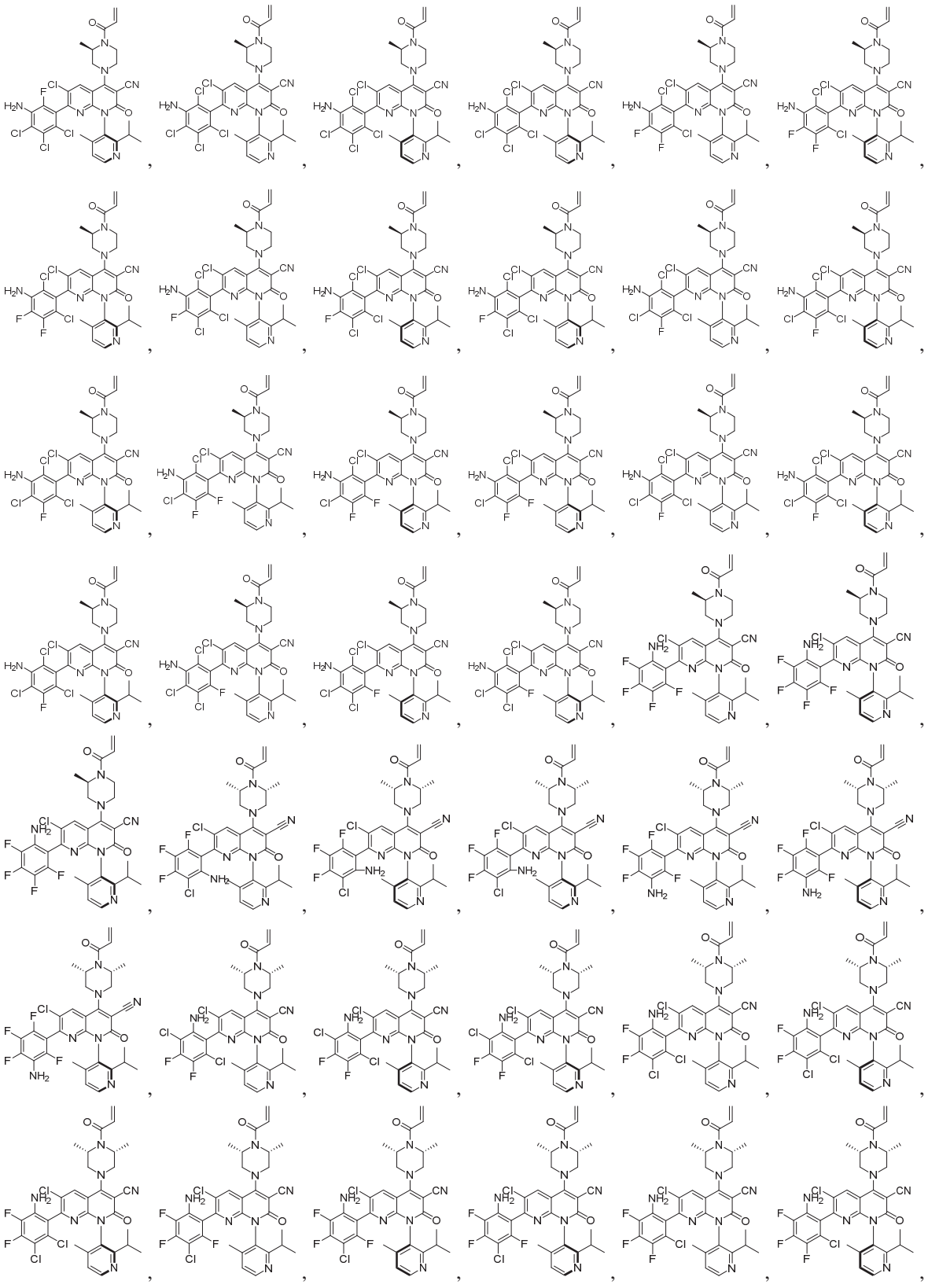
7. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 6, wherein:

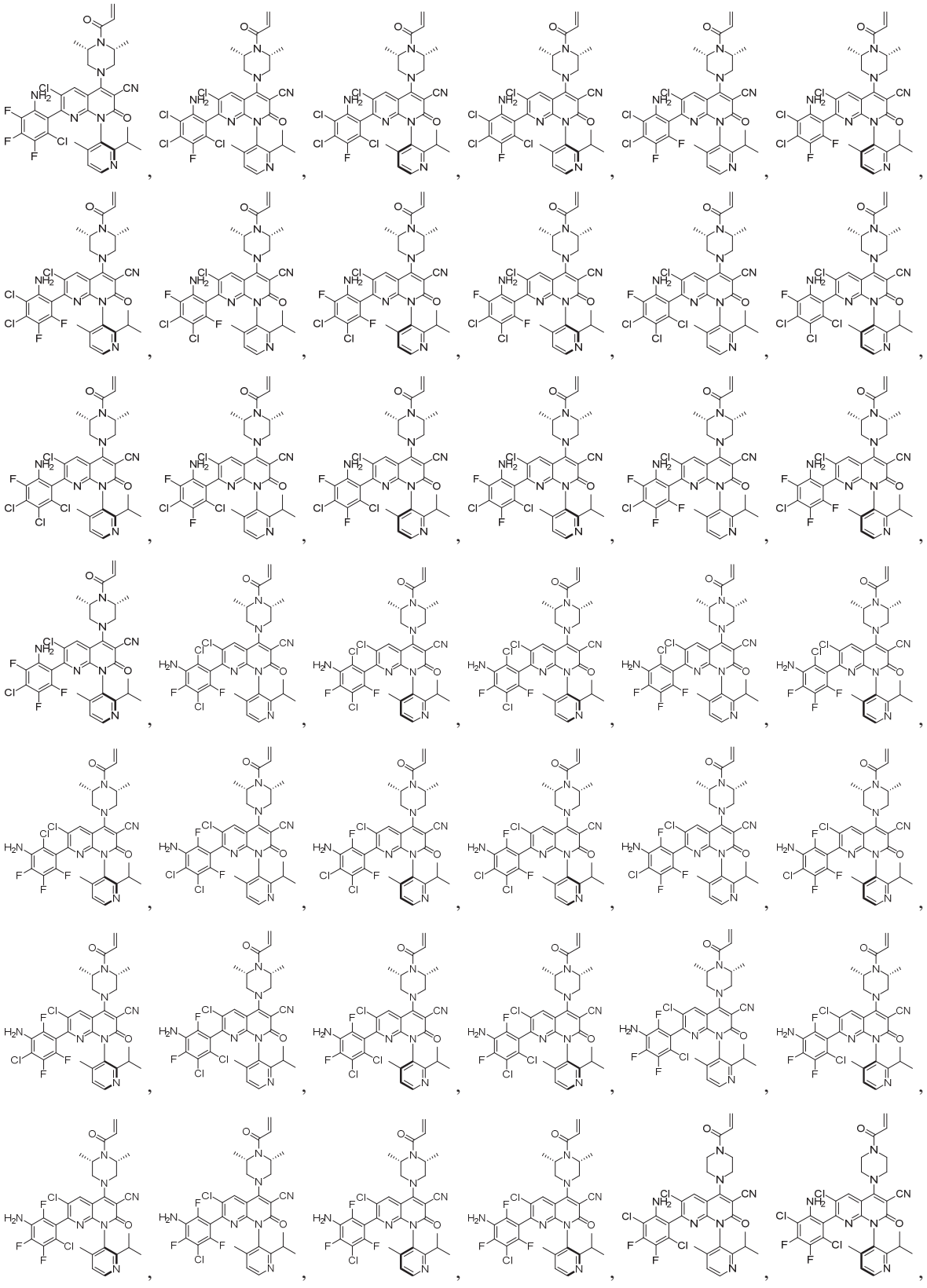
the compound is selected from:

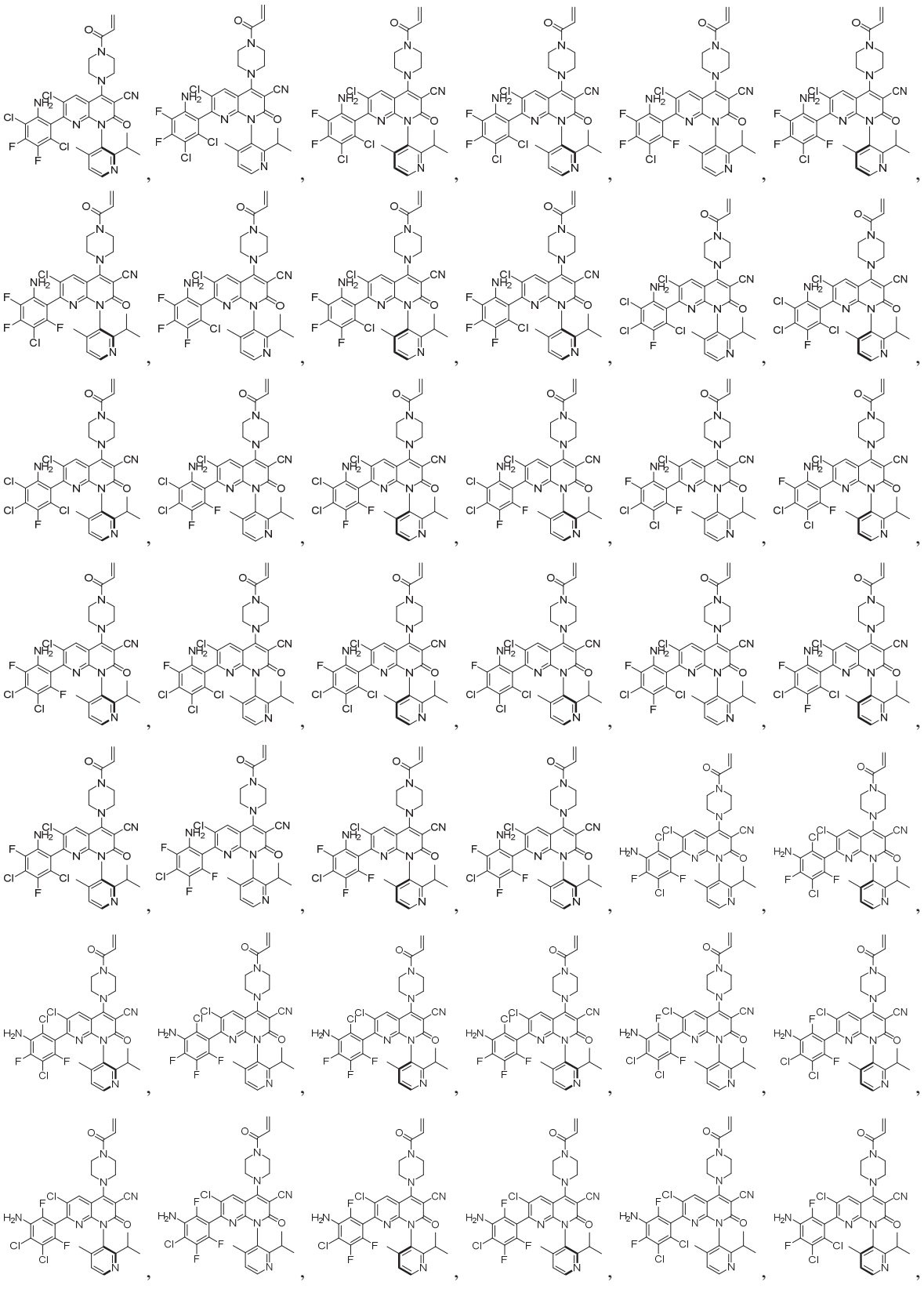


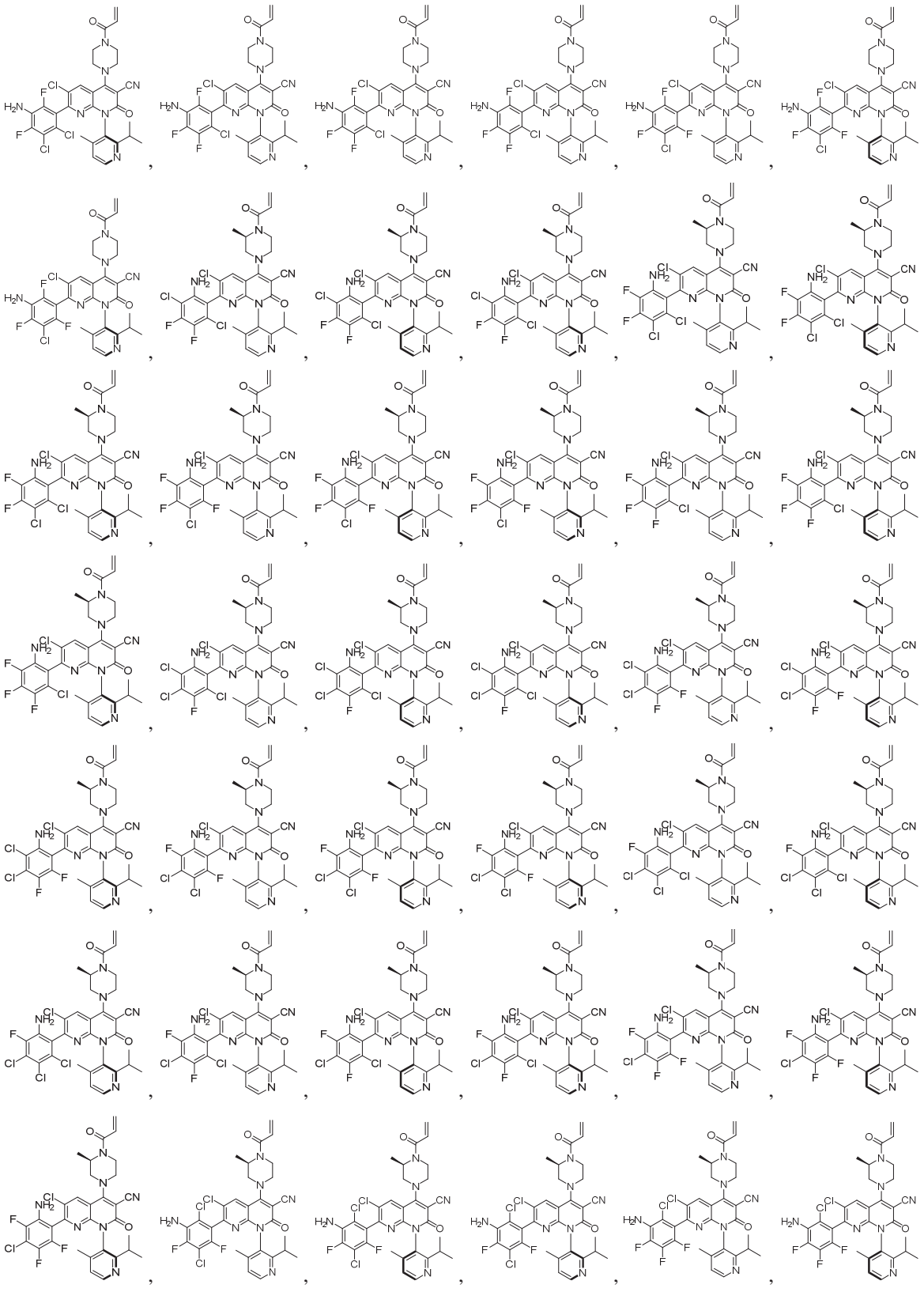


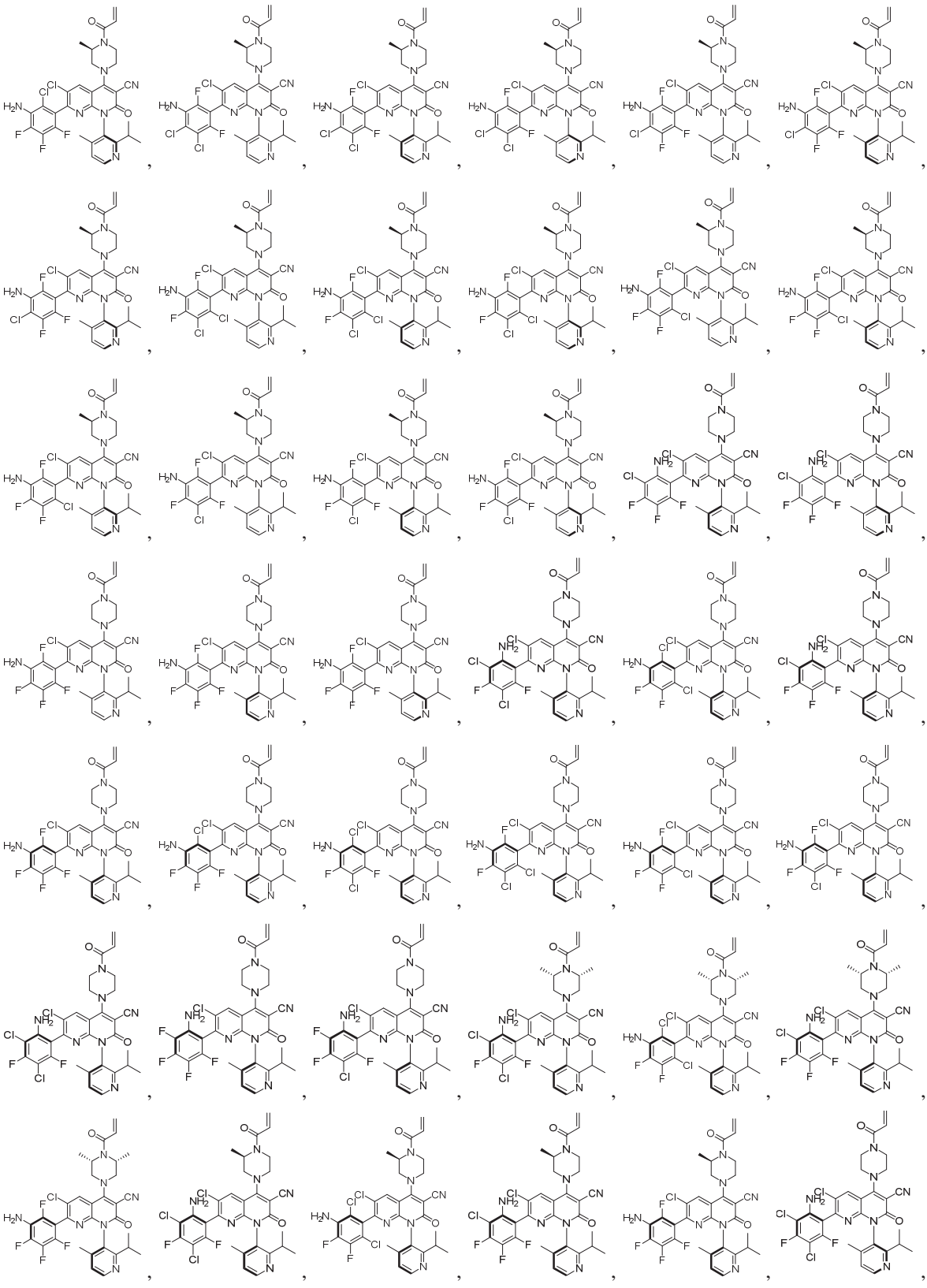


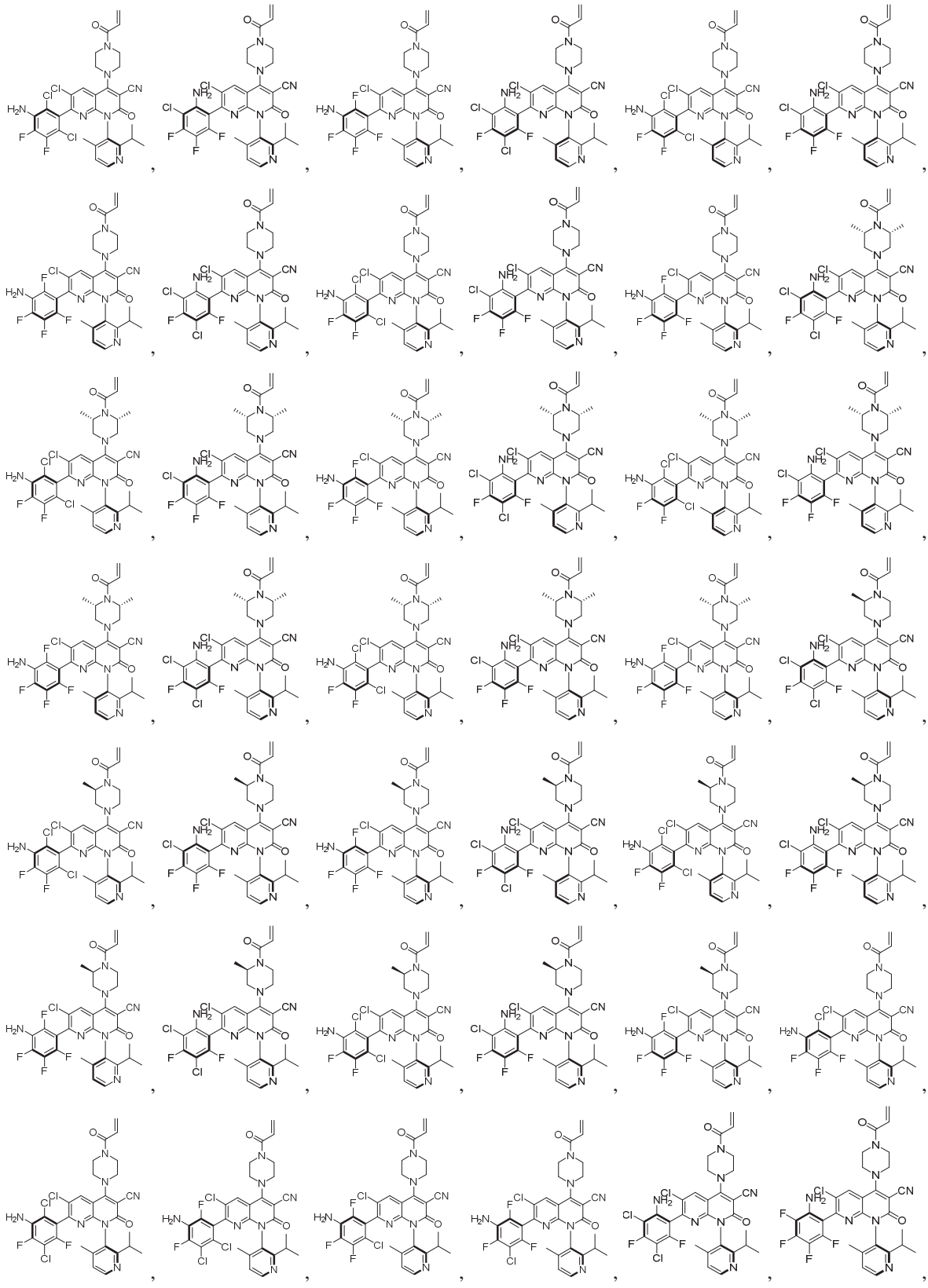


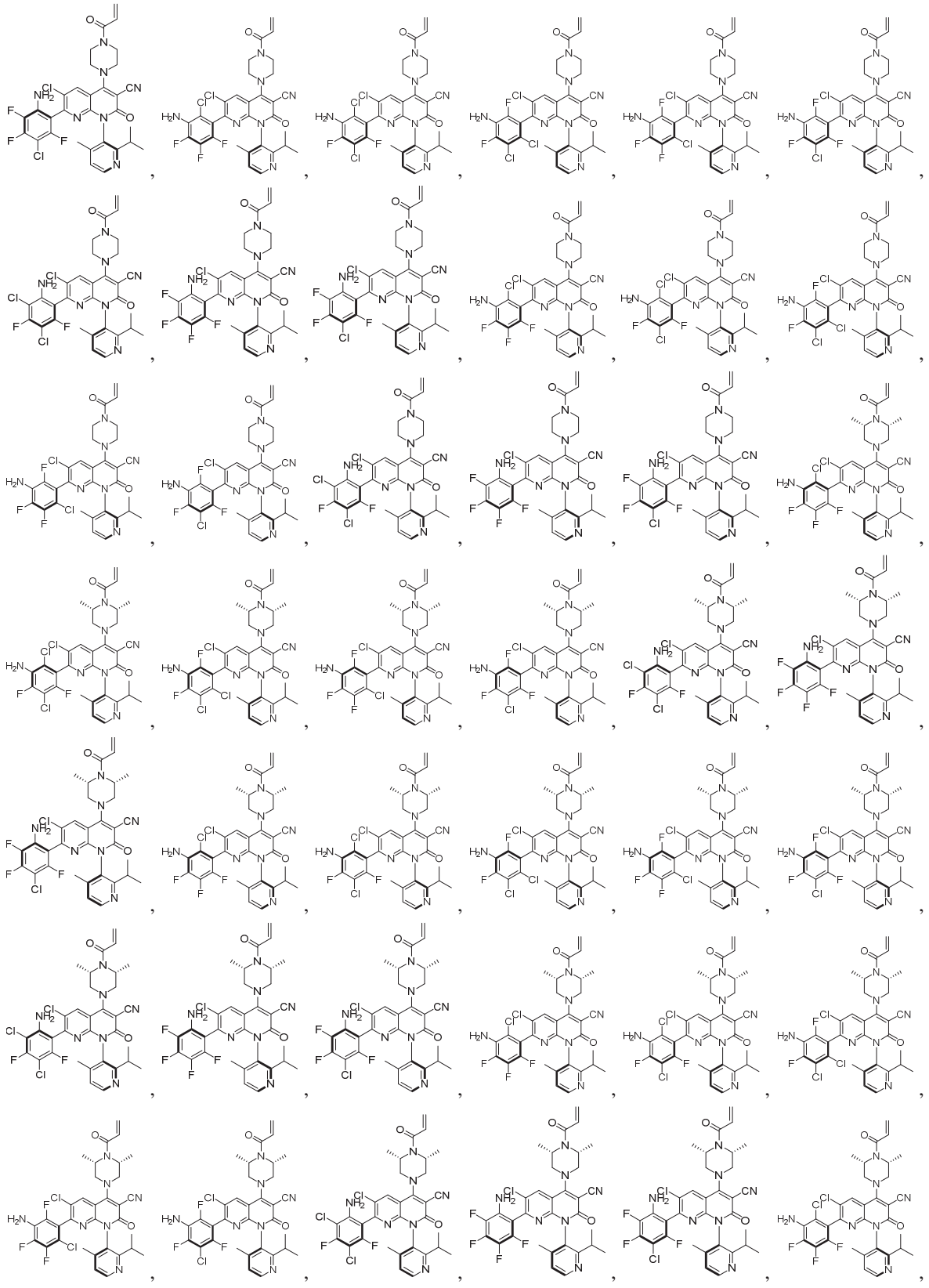


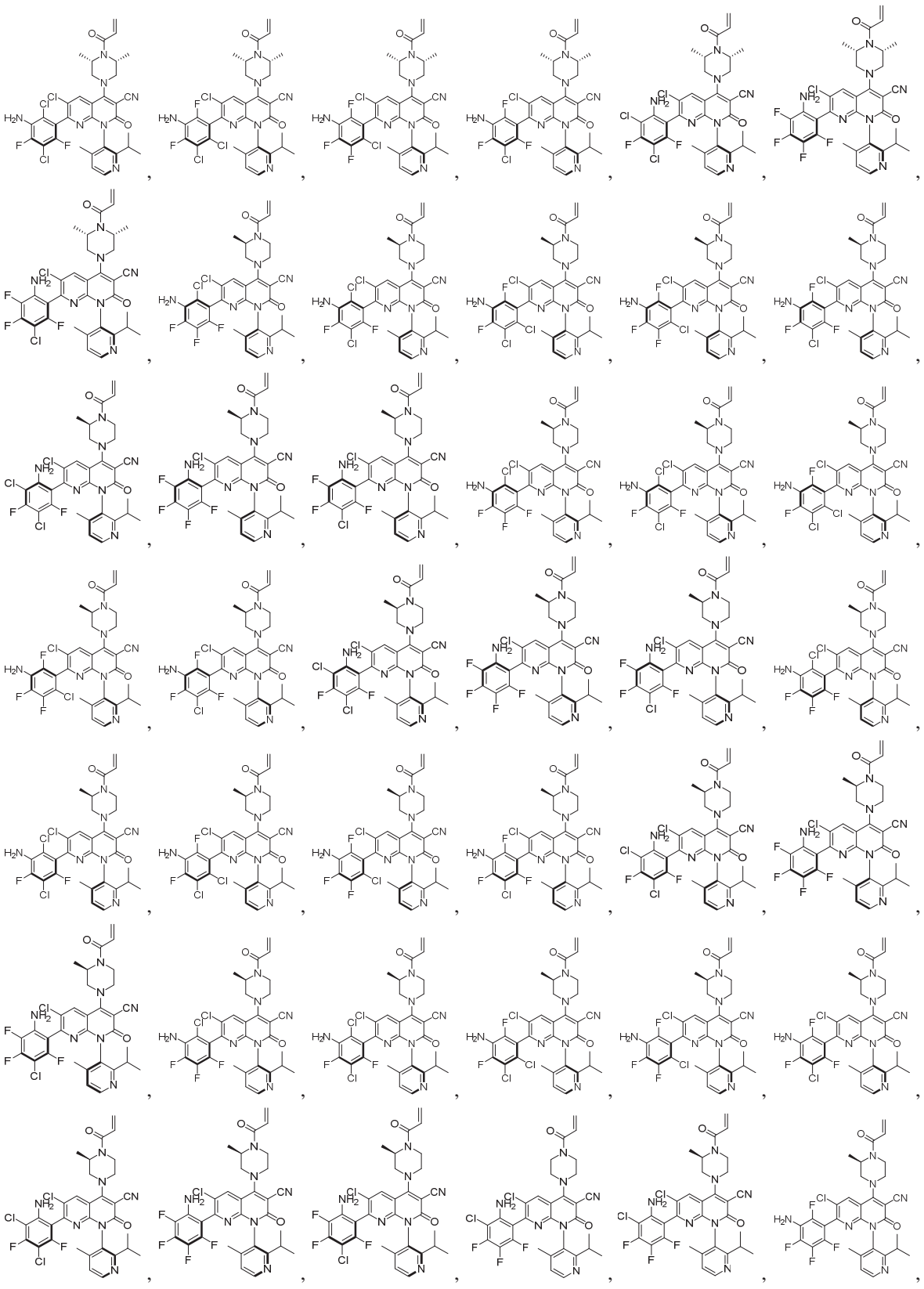


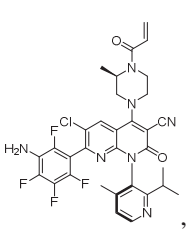
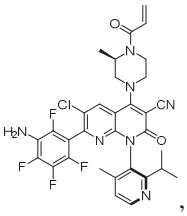
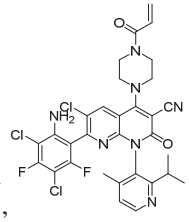
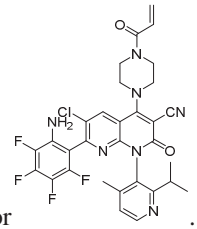






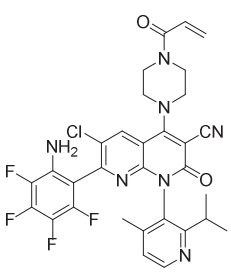
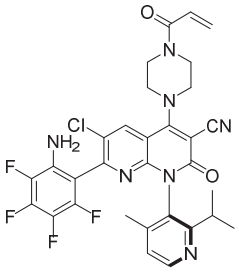
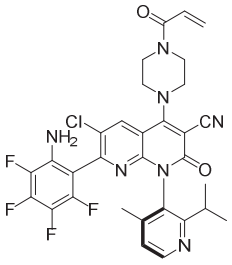




, ,  or .

8. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 7, wherein:

the compound is selected from:

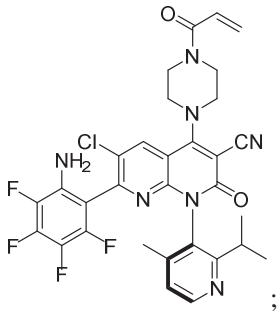
  or .

9. A pharmaceutical composition comprising the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 8, and at least one pharmaceutically acceptable excipient.

10. Use of the compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 8; or the pharmaceutical composition according to claim 9 in the manufacture of a medicament for the treatment of cancer related to KRAS G12C mutant protein.

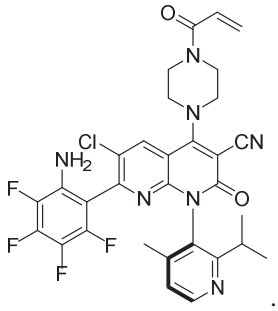
11. The use according to claim 10, wherein,

the compound of formula (I) has the following formula:

;

the pharmaceutical composition comprises the compound of formula (I), the stereoisomer thereof, the atropisomer thereof, the pharmaceutically acceptable salt thereof, the pharmaceutically acceptable salt

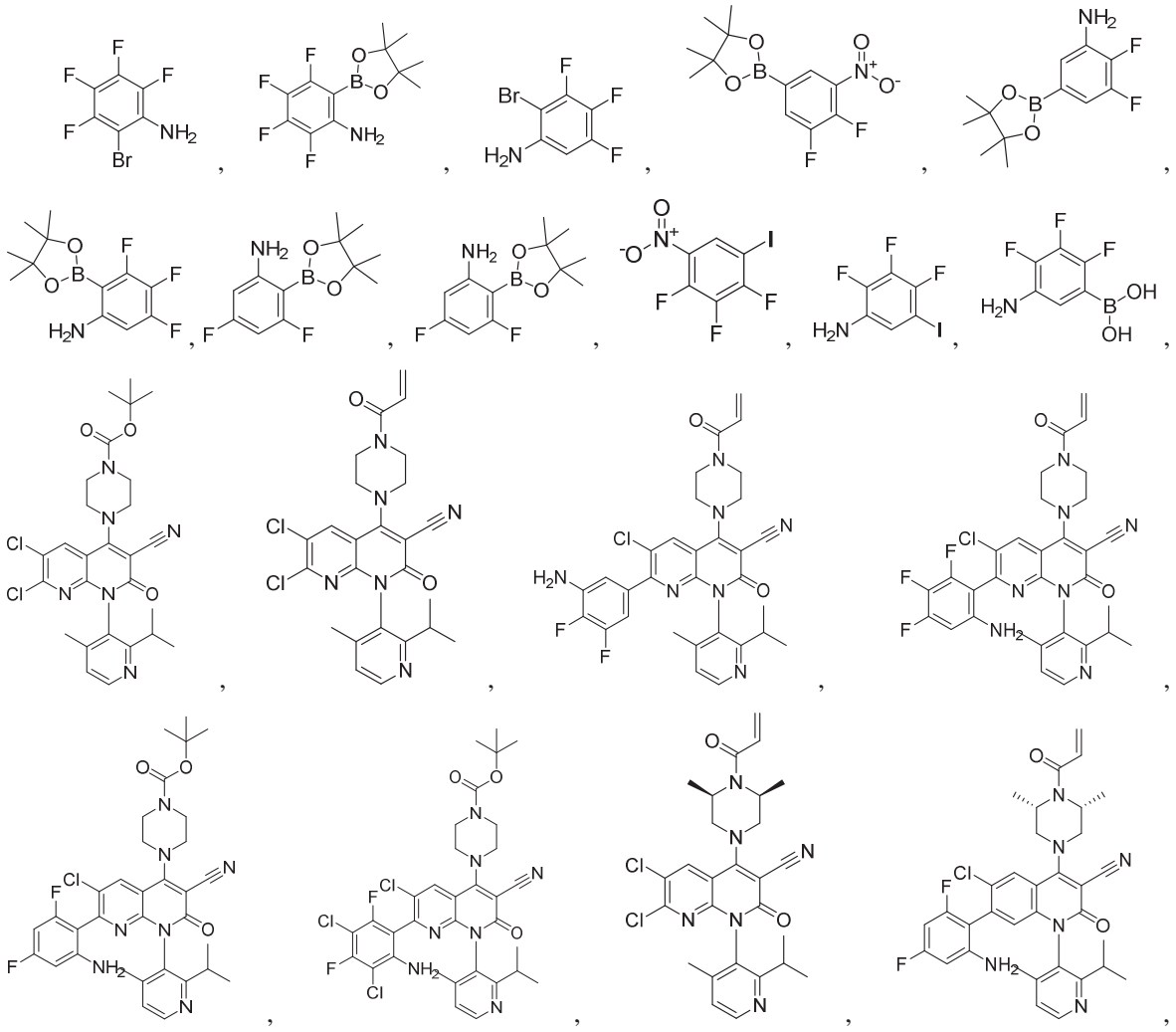
of the stereoisomer thereof or the pharmaceutically acceptable salt of the atropisomer thereof, and at least one pharmaceutically acceptable excipient, wherein the compound has the following structure:

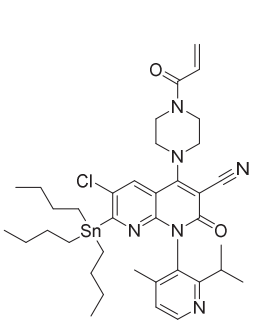
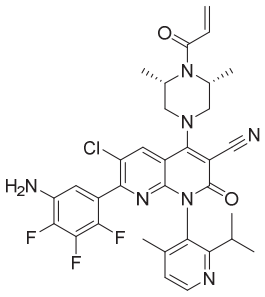
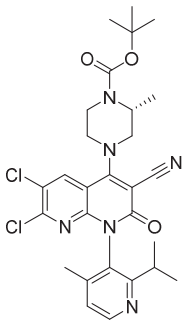
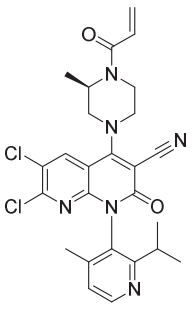
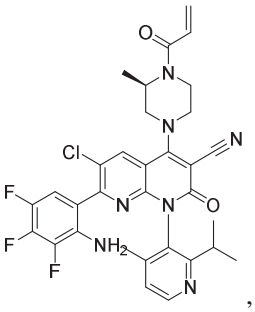
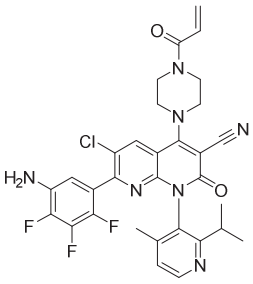
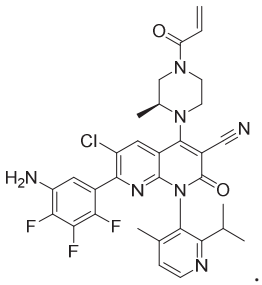


12. The use according to claim 10 or 11, wherein the cancer is selected from blood cancer, pancreatic cancer, colon cancer, rectal cancer, colorectal cancer or lung cancer,

wherein the blood cancer is selected from acute myeloid leukemia or acute lymphocytic leukemia; the lung cancer is selected from non-small cell lung cancer or small cell lung cancer.

13. An intermediate selected from:




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or

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14. The compound of formula (I), a stereoisomer thereof, an atropisomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable salt of the stereoisomer thereof or a pharmaceutically acceptable salt of the atropisomer thereof according to any one of claims 1 to 8; or the pharmaceutical composition according to claim 9 for use in therapy.