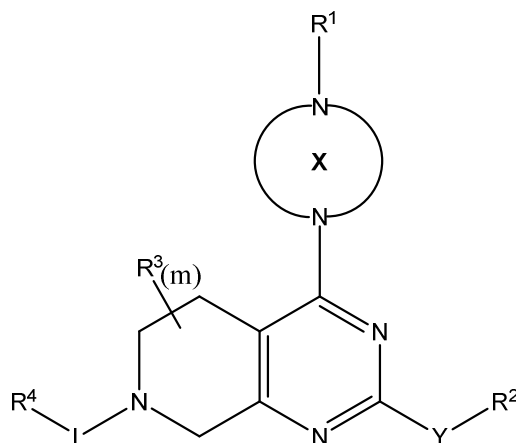


CLAIMS

WE CLAIM:

1. A compound of formula (II):



Formula (II)

or a pharmaceutically acceptable salt thereof:

wherein:

X is a 4-12 membered saturated or partially saturated monocyclic, bridged or spirocyclic ring, wherein the saturated or partially saturated monocyclic ring is optionally substituted with one or more R^8 ;

Y is a bond, O, S or NR^5 ;

R^1 is $-C(O)C(R^A) \equiv C(R^B)_p$ or $-SO_2C(R^A) \equiv C(R^B)_p$;

R^2 is hydrogen, alkyl, hydroxyalkyl, dihydroxyalkyl, alkylaminylalkyl, dialkylaminylalkyl, $-Z-NR^5R^{10}$, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, or heteroarylalkyl, wherein each of the Z, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, and heteroarylalkyl may be optionally substituted with one or more R^9 ;

each Z is C1 – C4 alkylene;

each R^3 is independently C1 – C3 alkyl, oxo, haloalkyl, hydroxyl or halogen;

L is a bond, $-C(O)-$, or C1 – C3 alkylene;

R^4 is hydrogen, cycloalkyl, heterocyclyl, aryl, aralkyl or heteroaryl, wherein each of the cycloalkyl, heterocyclyl, aryl, aralkyl and heteroaryl may be optionally substituted with one or more R^6 , R^7 or R^8 ;

5 each R^5 is independently hydrogen or C1 – C3 alkyl;

R^6 is cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, or heteroaryl, wherein each of the cycloalkyl, heterocyclyl, aryl, or heteroaryl may be optionally substituted with one or more R^7 ;

10 each R^7 is independently halogen, hydroxyl, C1 – C6 alkyl, cycloalkyl, alkoxy, haloalkyl, amino, cyano, heteroalkyl, hydroxyalkyl or Q-haloalkyl, wherein Q is O or S;

R^8 is oxo, C1 – C3 alkyl, C2 – C4 alkynyl, heteroalkyl, cyano, $-C(O)OR^5$, $-C(O)N(R^5)_2$, $-N(R^5)_2$, wherein the C1 – C3 alkyl may be optionally substituted with cyano, halogen, $-OR^5$, $-N(R^5)_2$, or
15 heteroaryl;

each R^9 is independently hydrogen, oxo, acyl, hydroxyl, hydroxyalkyl, cyano, halogen, C1 – C6 alkyl, aralkyl, haloalkyl, heteroalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, alkoxy, dialkylaminyl, dialkylamidoalkyl, or dialkylaminylalkyl, wherein the C1 – C6 alkyl may be
20 optionally substituted with cycloalkyl;

each R^{10} is independently hydrogen, acyl, C1 – C3 alkyl, heteroalkyl or hydroxyalkyl;

R^{11} is haloalkyl;

25 R^A is absent, hydrogen, deuterium, cyano, halogen, C1 - C-3 alkyl, haloalkyl, heteroalkyl, $-C(O)N(R^5)_2$, or hydroxyalkyl;

each R^B is independently hydrogen, deuterium, cyano, C1 – C3 alkyl, hydroxyalkyl, heteroalkyl, C1 – C3 alkoxy, halogen, haloalkyl, $-ZNR^5R^{11}$, $-C(O)N(R^5)_2$, $-NHC(O)C1 – C3$ alkyl, $-CH_2NHC(O)C1 – C3$ alkyl, heteroaryl, heteroarylalkyl, dialkylaminylalkyl, or heterocyclylalkyl wherein the heterocyclyl portion is substituted with one or more substituents independently selected from halogen, hydroxyl, alkoxy and C1 – C3 alkyl, wherein the heteroaryl or the heteroaryl portion of the heteroarylalkyl is optionally substituted with one or more R^7 ;

35 or when $\overset{\text{-----}}{\text{=====}}$ is a double bond and p is two, one R^B is hydrogen and R^A and one R^B and the carbon atoms to which they are attached form a 4-8 membered partially saturated cycloalkyl substituted with oxo;

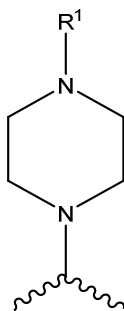
40 m is zero or an integer between 1 and 2;

p is one or two; and wherein,

when $\text{---}\text{---}\text{---}$ is a triple bond then R^A is absent, p equals one and R^B is hydroxyalkyl,

or when $\text{---}\text{---}\text{---}$ is a double bond then R^A is present, R^B is present and p equals two, wherein when R^A is hydrogen or C1 – C3 alkyl, at least one R^B is deuterium, cyano, halogen, haloalkyl, hydroxyalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, $-\text{ZNR}^5\text{R}^{11}$, $-\text{C}(\text{O})\text{N}(\text{R}^5)_2$, $-\text{NHC}(\text{O})\text{C1} - \text{C3}$ alkyl, $-\text{CH}_2\text{NHC}(\text{O})\text{C1} - \text{C3}$ alkyl, or heterocyclalkyl, wherein the heterocycl portion is substituted with one or more substituents independently selected from halogen, hydroxyl, alkoxy and C1 – C3 alkyl; or when each R^B is hydrogen, then R^A is deuterium, cyano, halogen, haloalkyl, $-\text{C}(\text{O})\text{N}(\text{R}^5)_2$, hydroxyalkyl or heteroalkyl.

2. The compound of claim 1, wherein $R^1\text{-X}$ is:



wherein the piperazinyl ring is optionally substituted with R^8 .

3. The compound of claim 2, wherein R^1 is $-\text{C}(\text{O})\text{C}(\text{R}^A)\text{---}\text{---}\text{---}\text{C}(\text{R}^B)_p$.

4. The compound of claim 3, wherein $\text{---}\text{---}\text{---}$ is a double bond and p is two, each R^B is hydrogen, and R^A is deuterium, cyano, halogen, haloalkyl, heteroalkyl, $-\text{C}(\text{O})\text{N}(\text{R}^5)_2$, or hydroxyalkyl.

5. The compound of claim 4, wherein R^A is halogen.

6. The compound of claim 2, wherein Y is O.

7. The compound of claim 2, wherein R^2 is selected from the group consisting of hydroxyalkyl, alkylaminylalkyl, dialkylaminylalkyl, $-\text{ZNR}^5\text{R}^{10}$, heterocycl and heterocyclalkyl, wherein each of the Z, heterocycl or heterocyclalkyl are independently optionally substituted with R^9 .

8. The compound of claim 7, wherein the heterocyclyl of the heterocyclalkyl is independently azetidiny, methylazetidiny, N-ethylazetidiny, N-isopropylazetidiny, N-tert-butylazetidiny, fluoroazetidiny, difluoroazetidiny, cyclopropylazetidiny, cyclopentylazetidiny, tetrahydropyranylazetidiny, tetrahydropyranyl, pyrrolidiny, methylpyrrolidiny, dimethylpyrrolidiny, (N-methyl)-2-methylpyrrolidiny, (N-methyl)-2-ethylpyrrolidiny, (N-methyl)-3,3-dimethylpyrrolidiny, isopropylpyrrolidiny, N-tert-butylpyrrolidiny, cycloalkylalkylpyrrolidiny, hydroxypyrrolidiny, hydroxyethylpyrrolidiny, fluoropyrrolidiny, difluoropyrrolidiny, (N-methyl)fluoropyrrolidiny, (N-methyl)difluoropyrrolidiny, fluoroethylpyrrolidiny, methoxyethylpyrrolidiny, (N-methyl)methoxypyrrolidiny, piperaziny, dimethylaminylpyrrolidiny, morpholiny, methylmorpholiny, N-ethylmorpholiny, N-isopropylmorpholiny, oxetany, 1,4-oxazepany, piperdiny, methylpiperidiny acylpiperdiny, cyanopiperdiny, cycloalkylpiperdiny, halopiperdiny, dihalopiperdiny, fluoropiperdiny, difluoropiperdiny, alkoxypiperdiny, pyrrolidony, methylpyrrolidony, (N-methyl)-2-pyrrolidin-2-one, (N-ethyl)-2-pyrrolidony, (N-benzyl)-2-pyrrolidony, hydroxy-substituted-(N-methyl)pyrrolidony, piperidinony, hexahydropyrroliziny, thiomorpholiny-1,1-dioxide, 3-azabicyclo[3.1.0]hexany, oxa-5-azabicyclo[2.2.1]heptan-5-yl, or azabicyclo[2.2.1]heptan-2-yl.
9. The compound of claim 10, wherein the (N-methyl)difluoropyrrolidiny is 3,3-difluoro-1-methylpyrrolidiny.
10. The compound of claim 10, wherein the heterocyclyl is N-methylpyrrolidiny.
11. The compound of claim 8, wherein R^2 is dialkylaminylalkyl optionally substituted with one or more R^9 .
12. The compound of claim 2, wherein R^4 is aryl optionally substituted with one or more R^7 .
13. The compound of claim 12, wherein the aryl is selected from the group consisting of phenyl and naphthyl optionally substituted with one or more R^7 .
14. The compound of claim 13, wherein the phenyl and the naphthyl are each optionally substituted with one or more R^7 selected from the group consisting of cyano, halogen, hydroxyl, C1- C6 alkyl, hydroxyalkyl, Q-haloalkyl, cycloalkyl, and alkoxy.
15. The compound of claim 14, wherein R^7 is selected from the group consisting of chloro, fluoro, bromo, hydroxymethyl, methyl, ethyl, isopropyl, methoxy, trifluoromethyl, hydroxyl, cyclopropyl and cyano.

16. The compound of claim 2, wherein m is zero.

17. The compound of claim 2, wherein L is a bond.

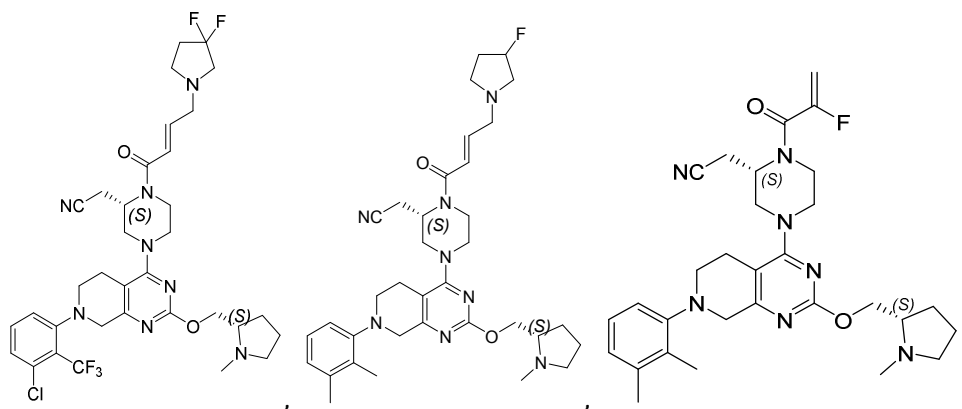
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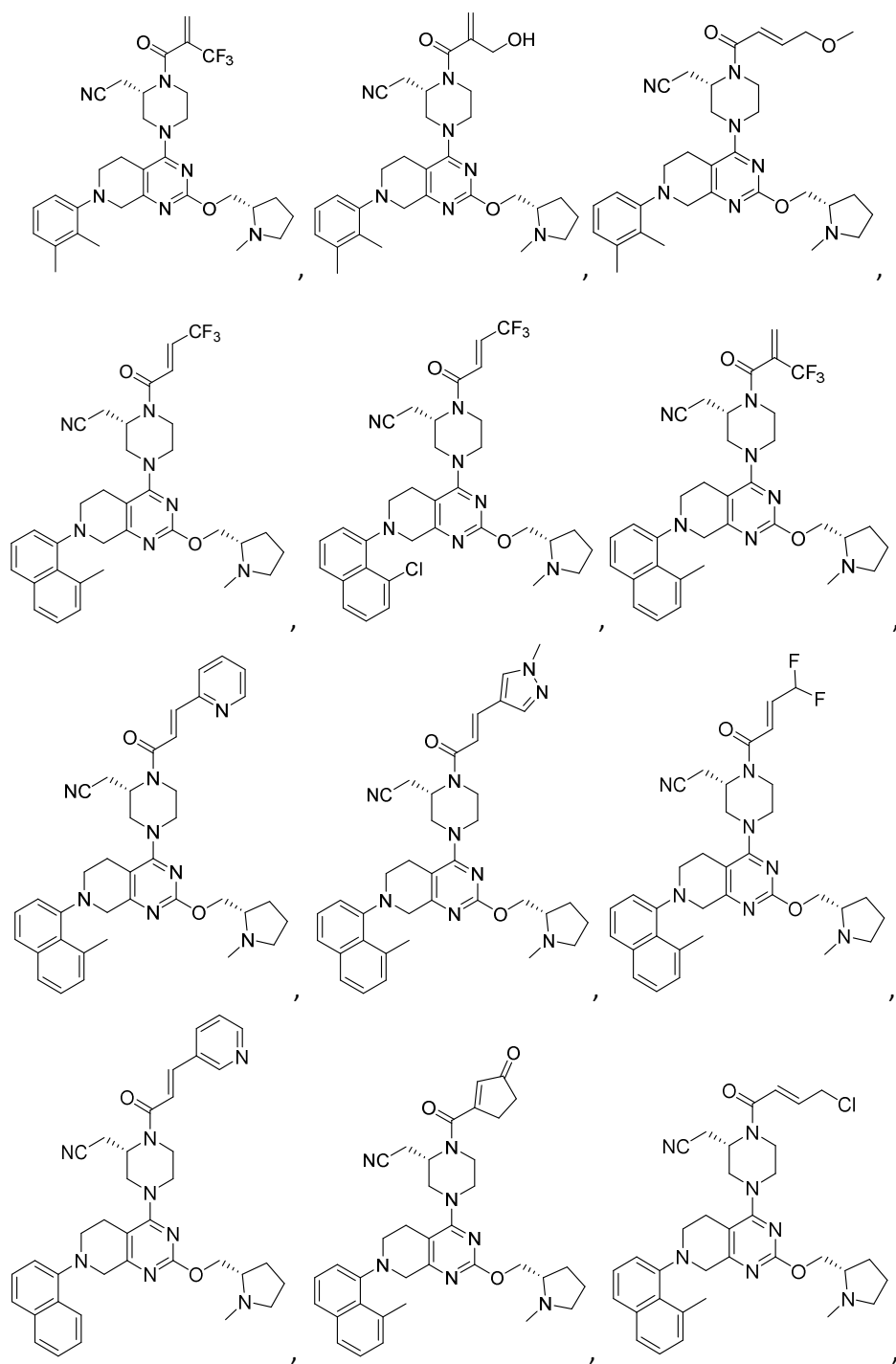
18. The compound of claim 2, wherein R⁸ is heteroalkyl, C2-C4 alkynyl, or C1 – C3alkyl optionally substituted with halogen, -OR⁵, cyano or heteroaryl.

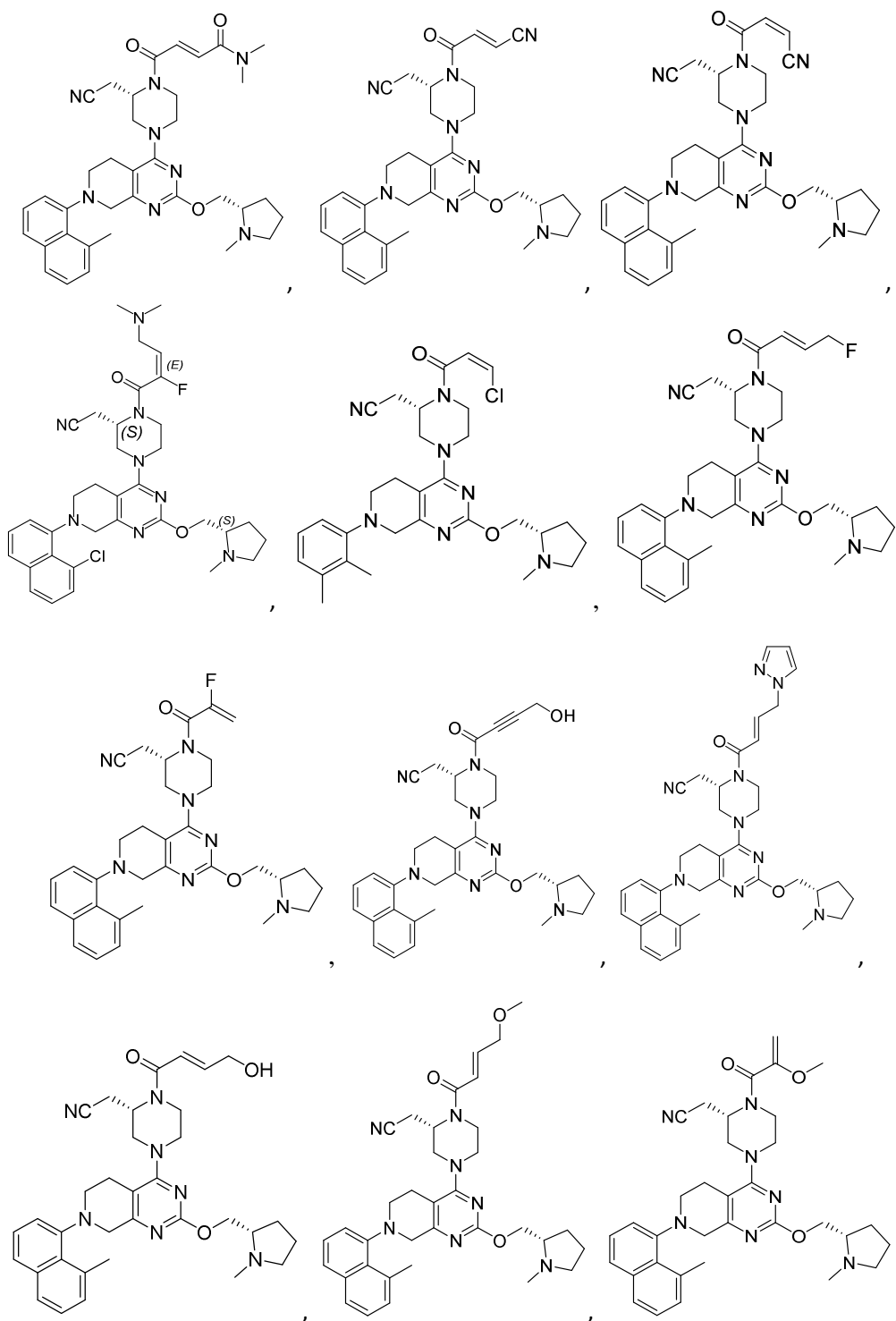
10 19. The compound of claim 18, wherein R⁸ is C1 – C3 alkyl optionally substituted with cyano.

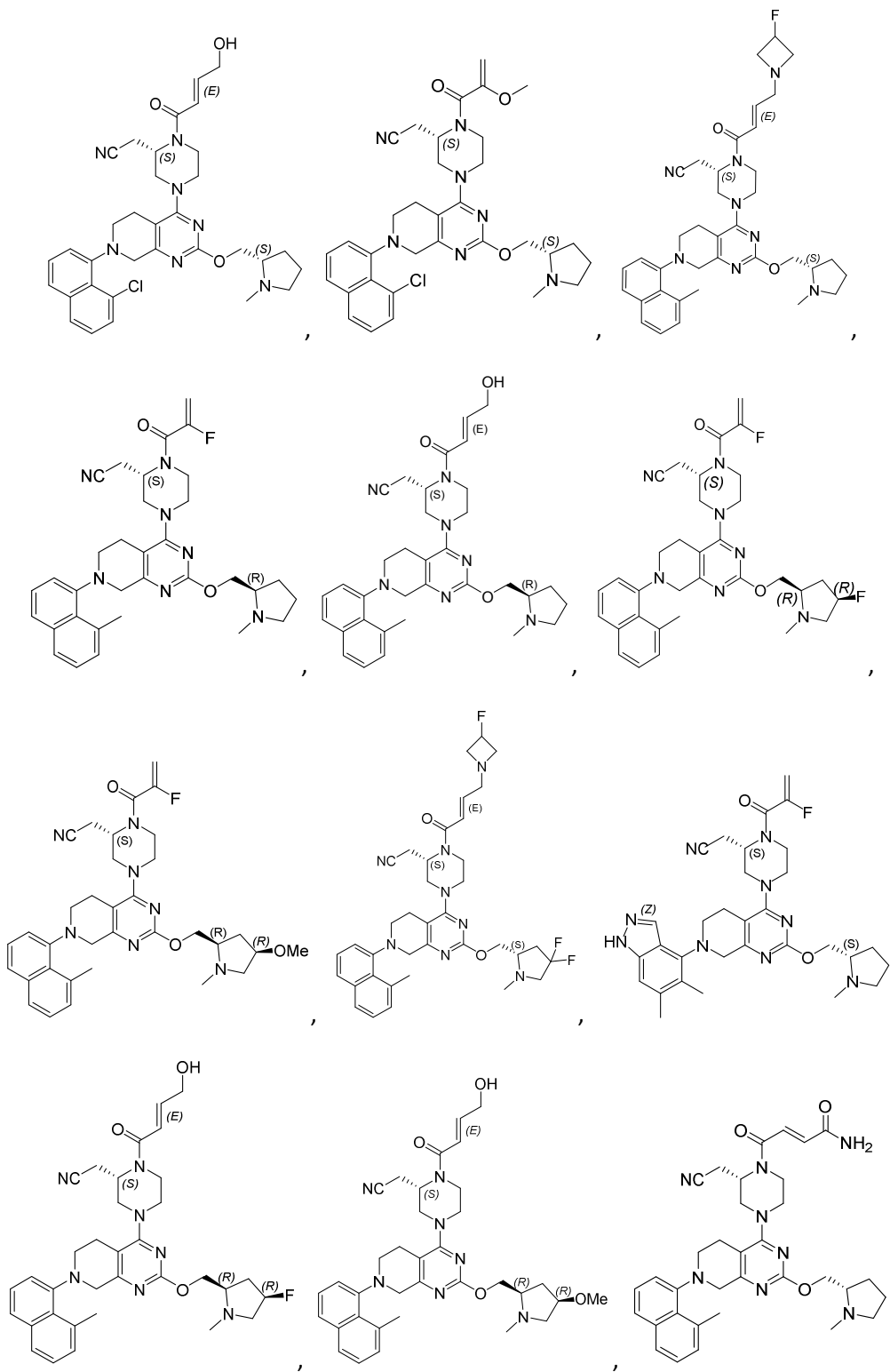
20. The compound of claim 18, wherein R⁸ is cyanomethyl.

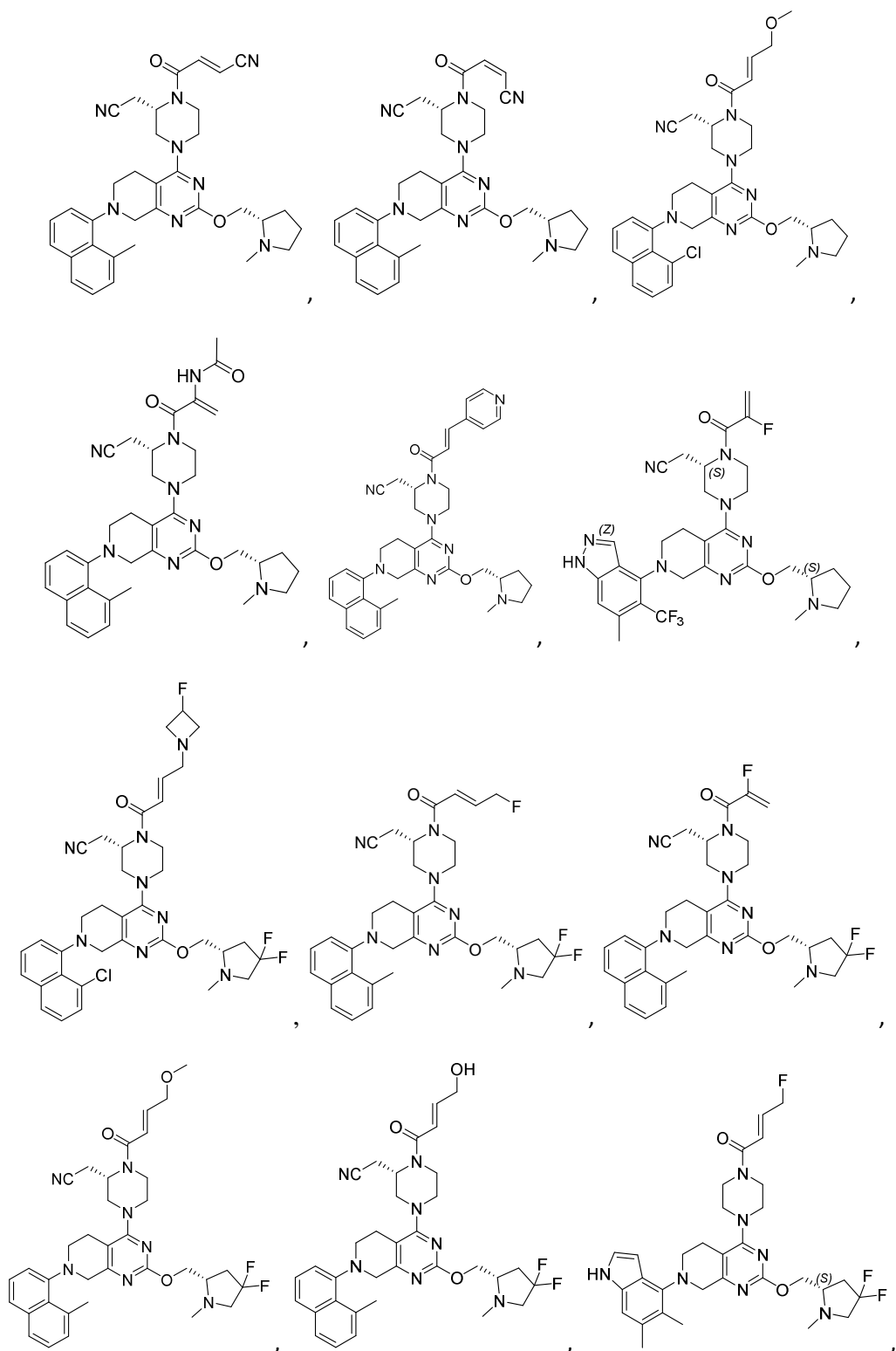
15 21. The compound of claim 1, wherein the compound is:

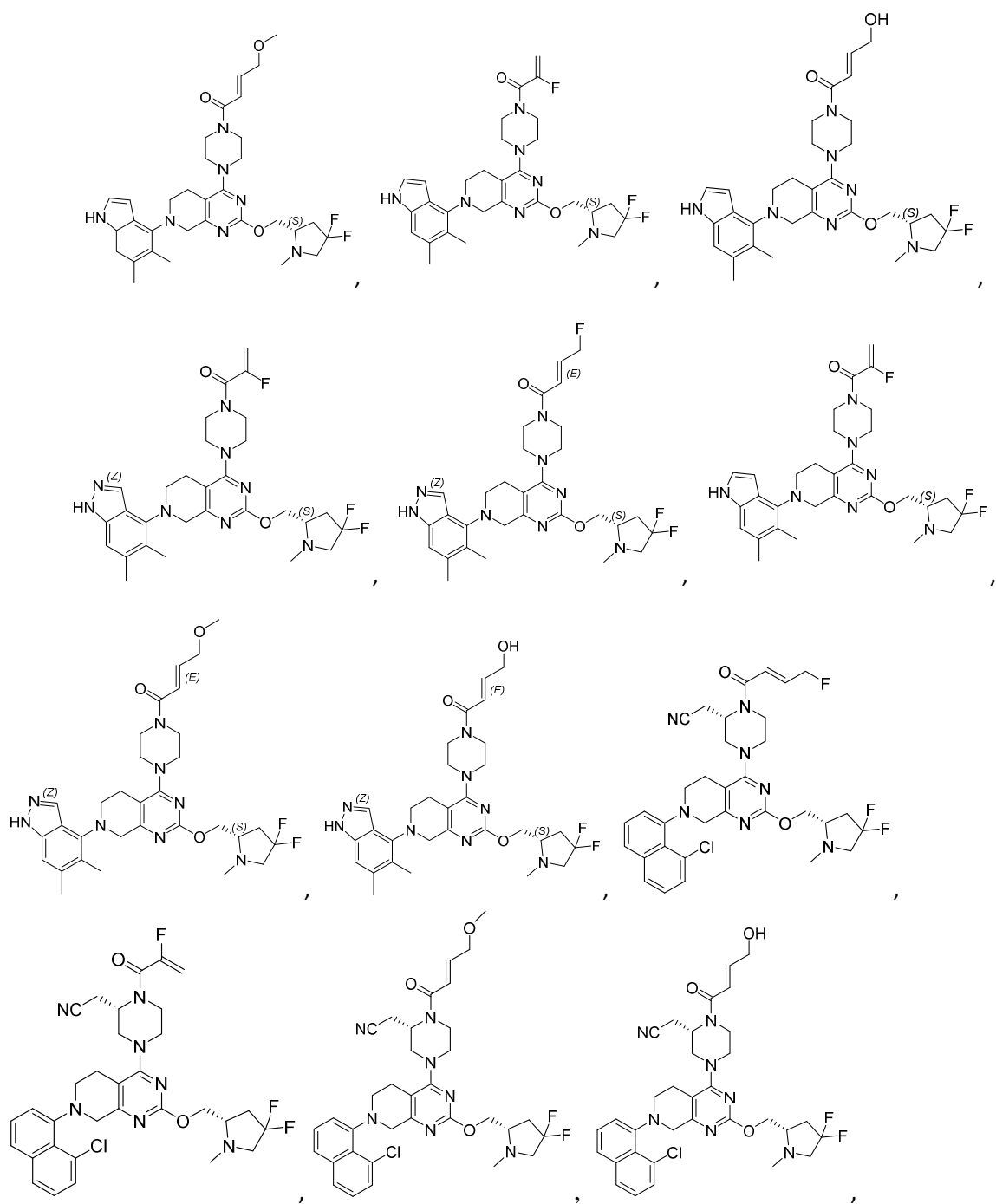


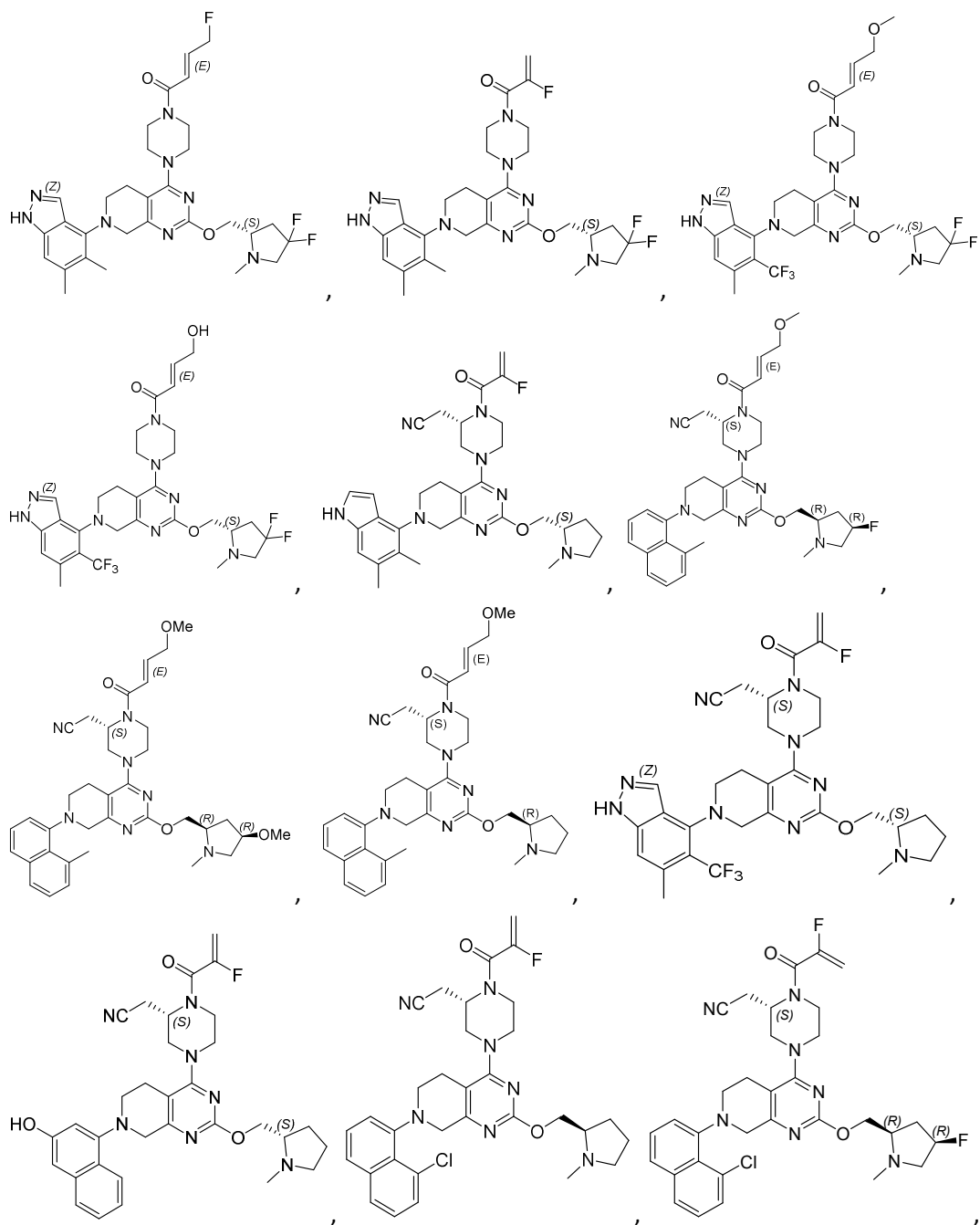


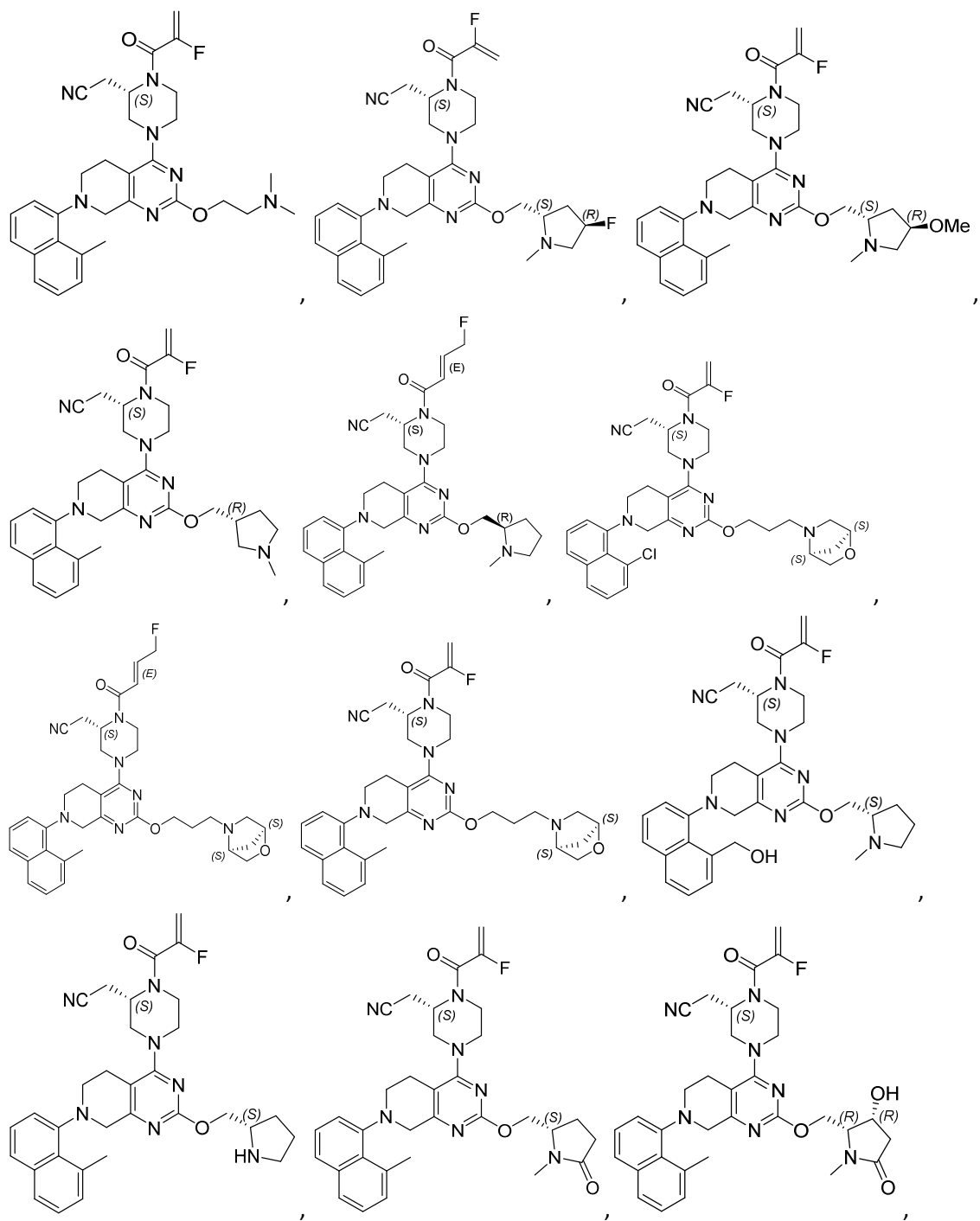


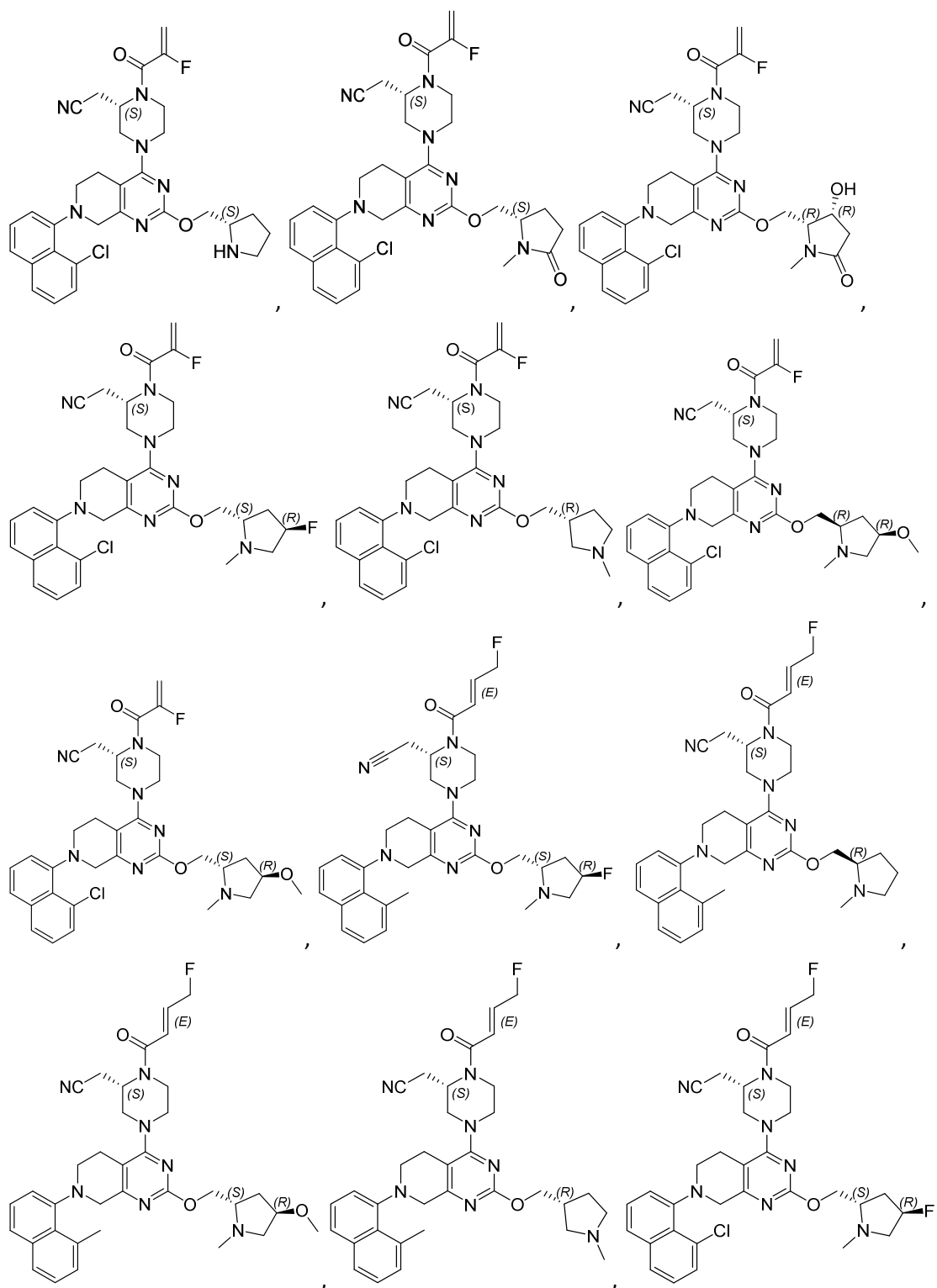


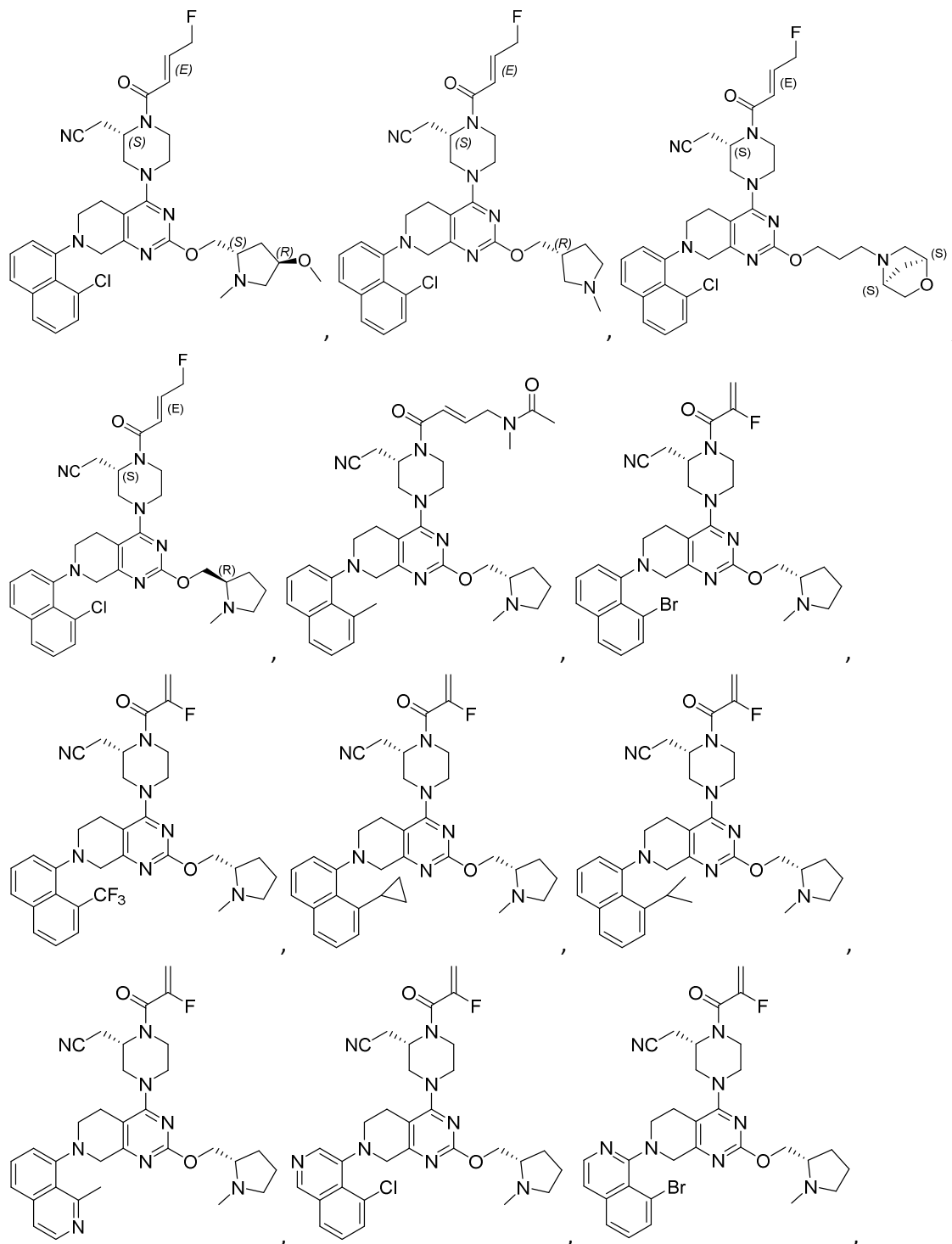


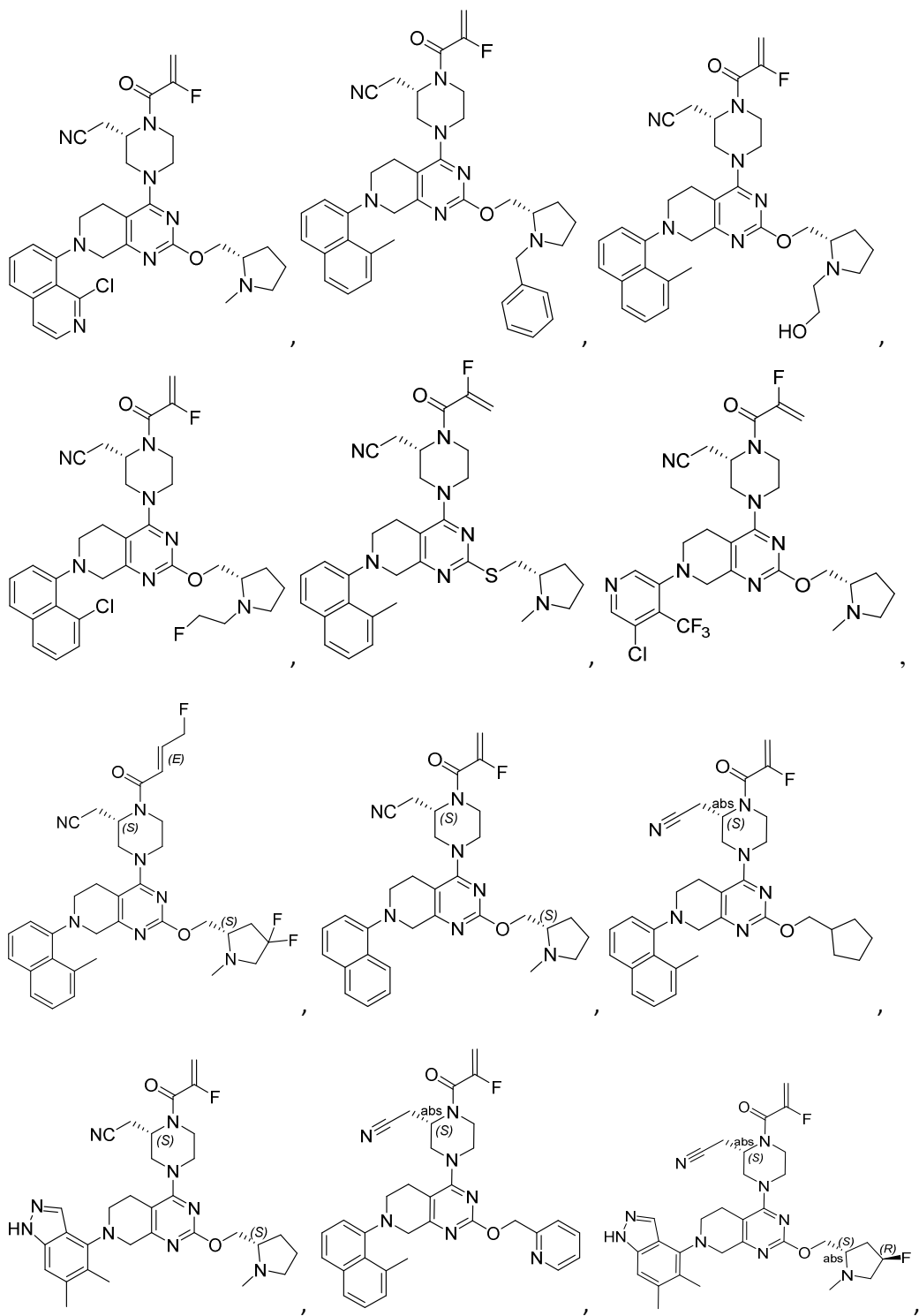


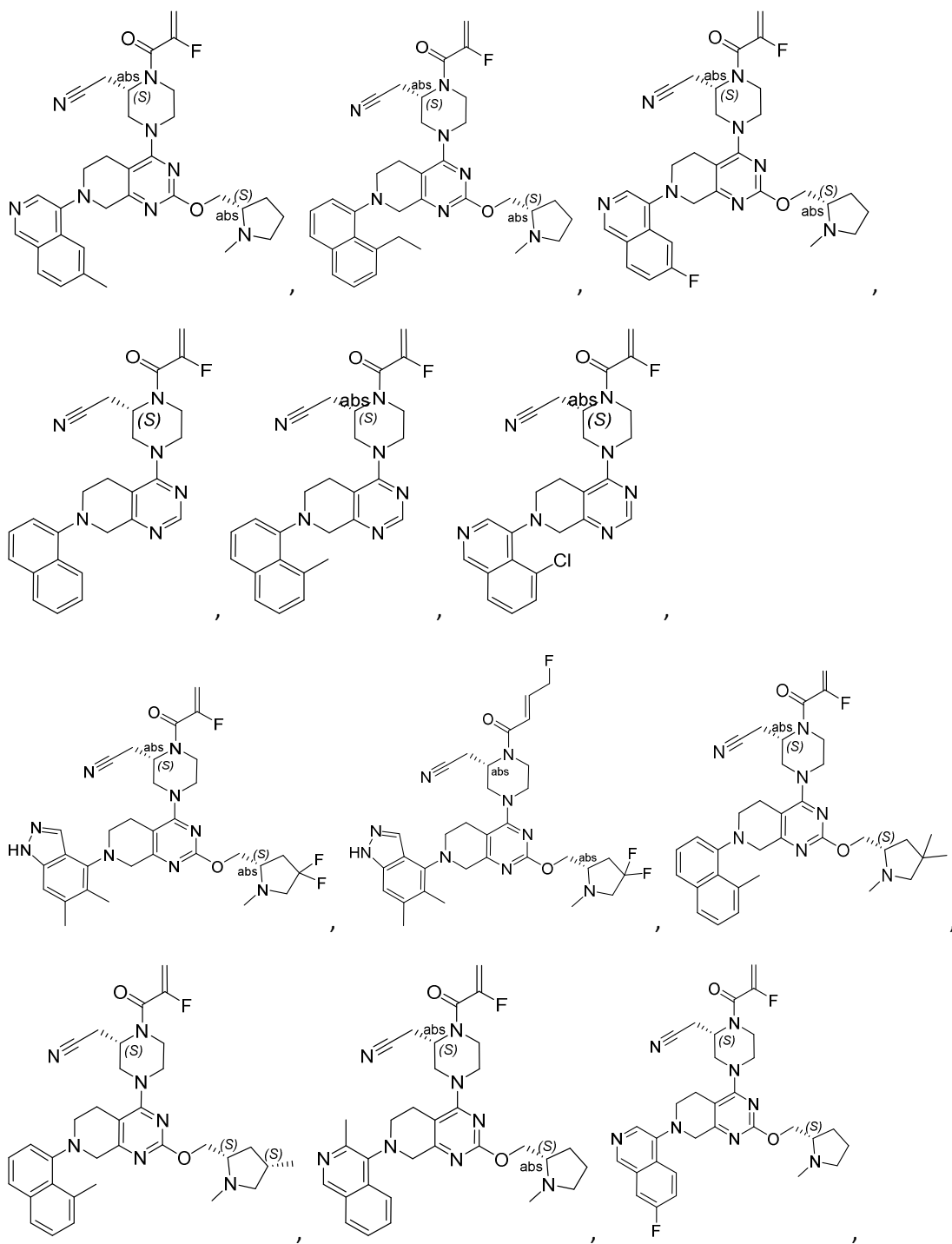


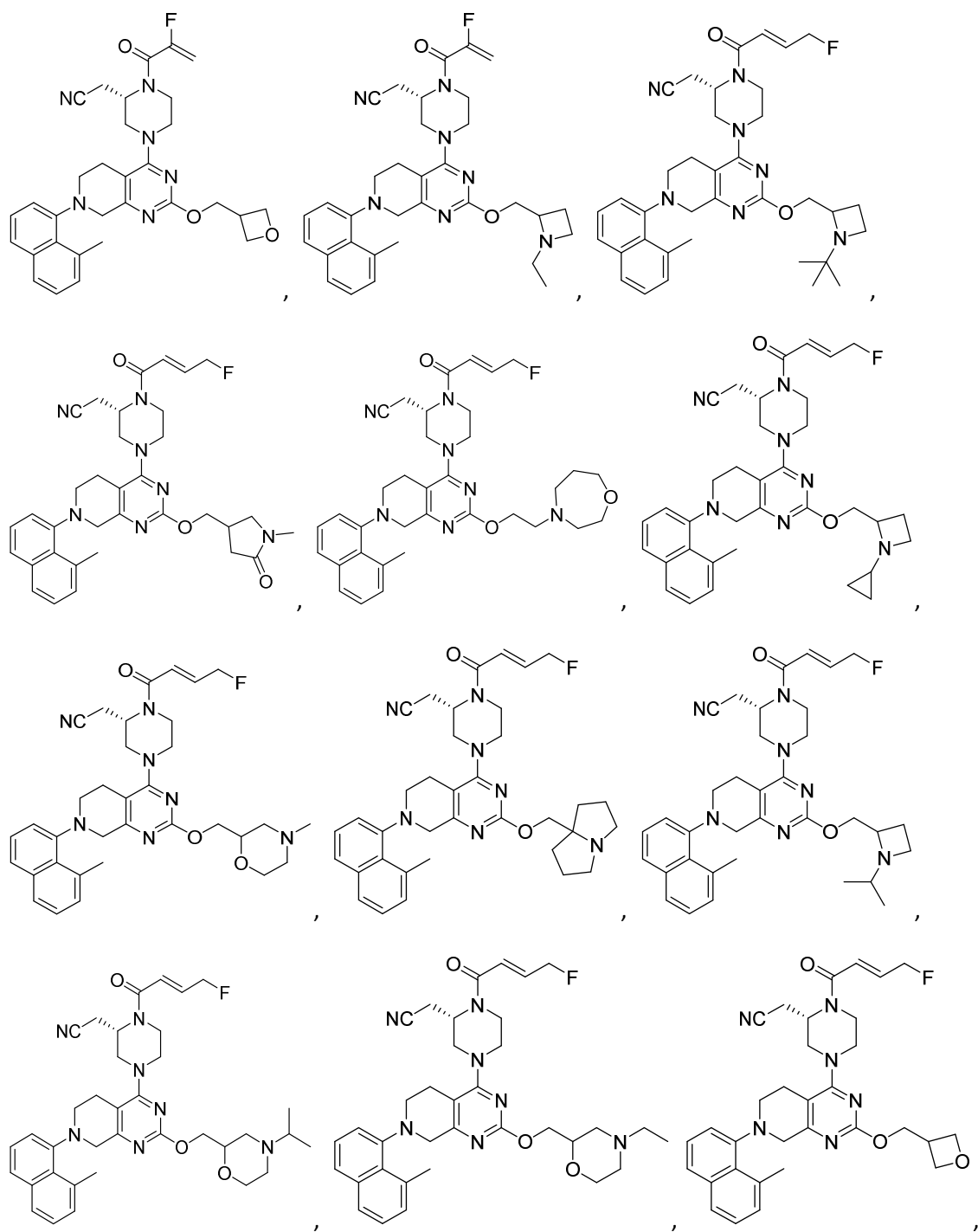


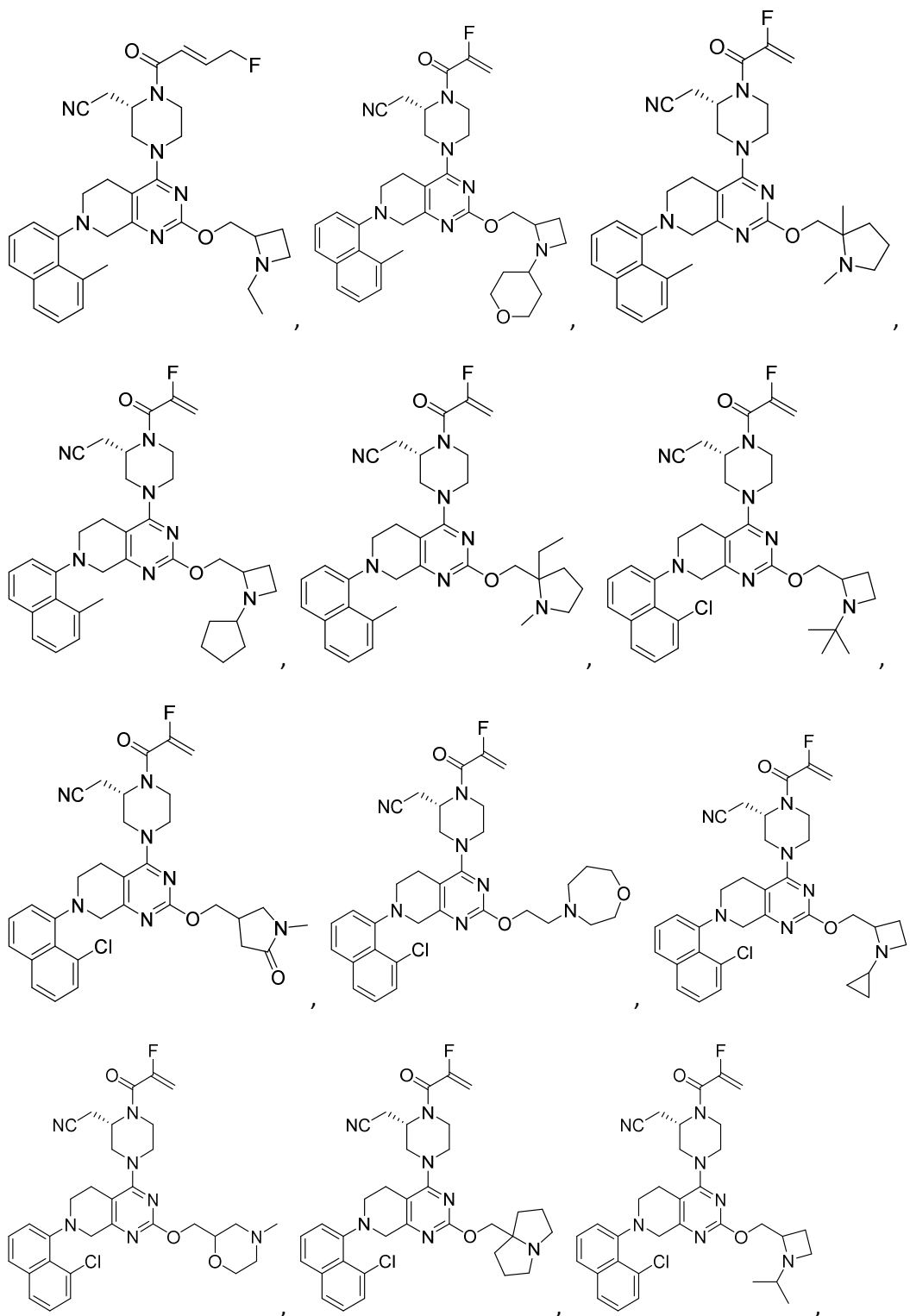


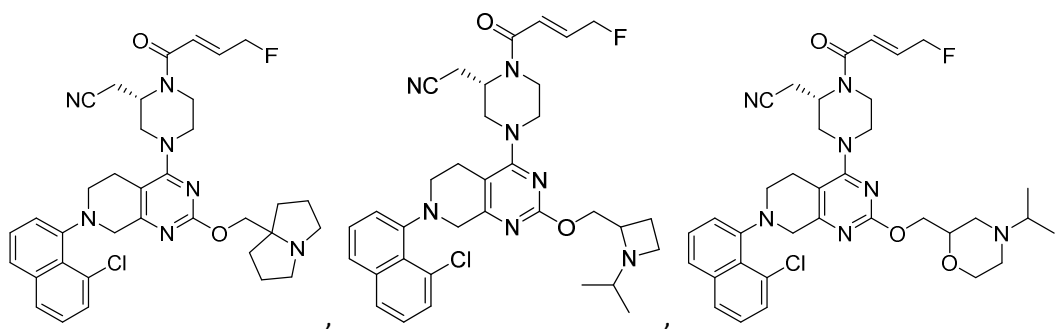
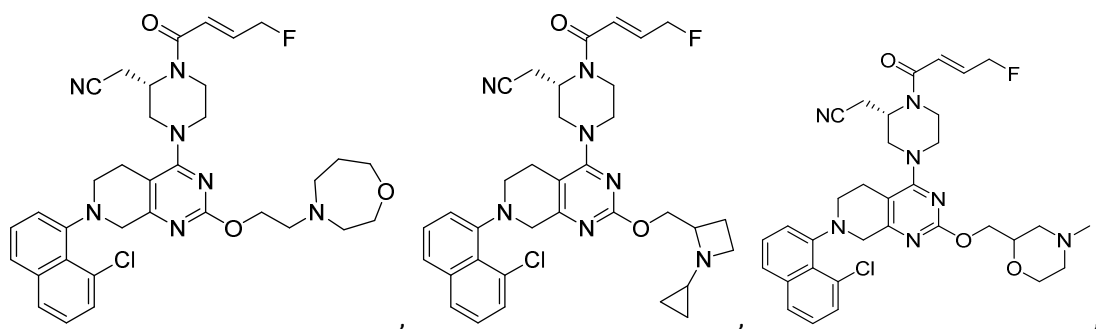
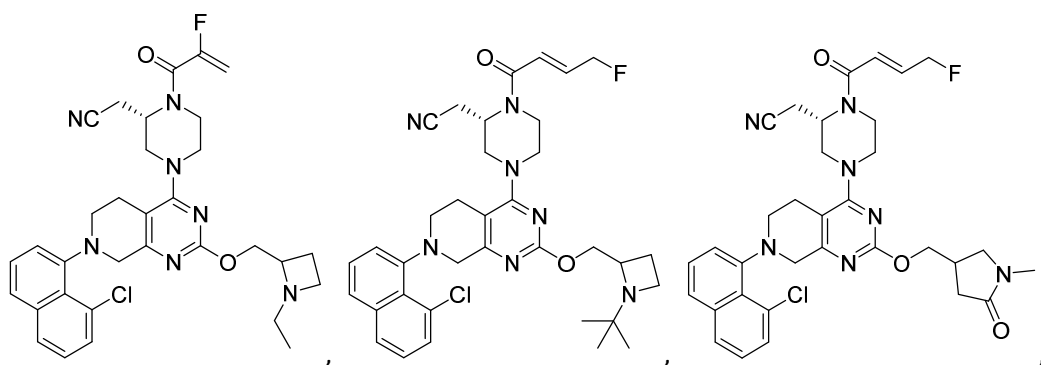
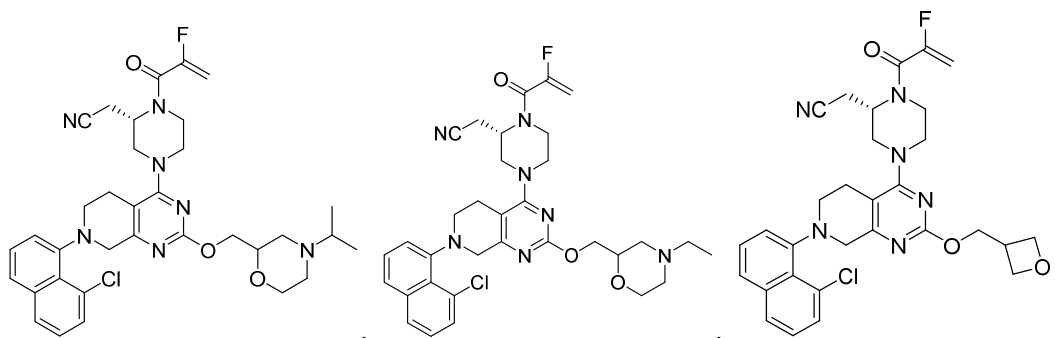


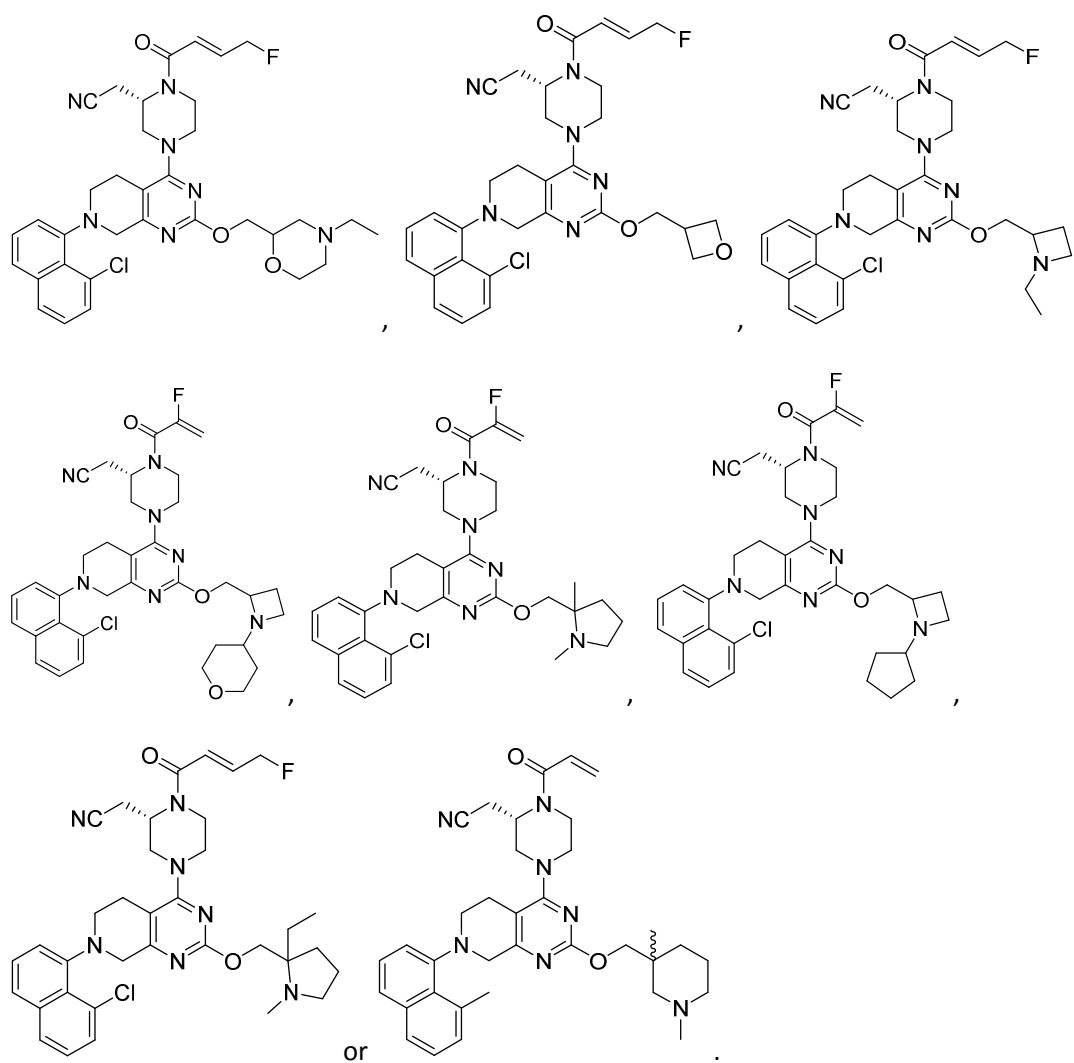






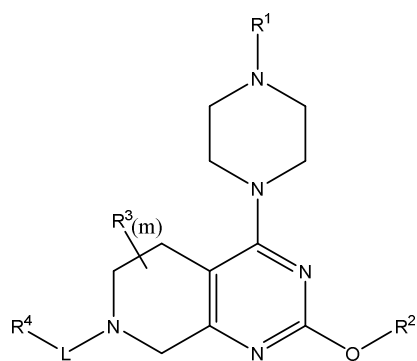






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22. The compound of claim 1, wherein the compound is of Formula II-B:



Formula II-B

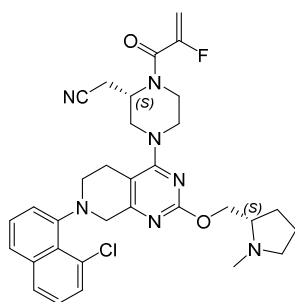
where the piperazinyl ring is optionally substituted with R^8 , and R^1 , R^3 , R^4 , R^8 , L and m are as defined in claim 1.

5

23. The compound of claim 22, wherein R^1 is $-C(O)C(R^A) \text{---} C(R^B)_p$ and --- is a double bond, each R^B is hydrogen, and R^A is deuterium, cyano, halogen, C1 - C-3 alkyl, haloalkyl, heteroalkyl, $-C(O)N(R^5)_2$, or hydroxyalkyl.

10

24. A compound of the following structure:



15 25. A pharmaceutical composition, comprising a therapeutically effective amount of a compound of Formula (II) according to claim 1, and a pharmaceutically acceptable excipient.

20 26. A method for inhibiting KRas G12C activity in a cell, comprising contacting the cell in which inhibition of KRas G12C activity is desired with an effective amount of a compound of Formula (II) according to claim 1, pharmaceutically acceptable salts thereof or pharmaceutical compositions containing the compound of Formula (II), or pharmaceutically acceptable salt thereof.

25 27. Use of a therapeutically effective amount of a compound of Formula (II) or a pharmaceutically acceptable salt thereof according to claim 1, alone or combined with a pharmaceutically acceptable carrier, excipient or diluents in the manufacture of a medicament for treating a KRas G12C-associated cancer in a patient having cancer.

28. The use of claim 27, wherein the therapeutically effective amount of the compound is between about 0.01 to 100 mg/kg per day.

29. The use of claim 27, wherein the cancer is selected from the group consisting of Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Biliary tract: gall bladder carcinoma, ampullary carcinoma, cholangiocarcinoma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochondroma (osteochondrogenous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial carcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma), granulosa-thecal cell tumors, Sertoli-Leydig cell

tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma); Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal glands: neuroblastoma.

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30. The use of claim 29, wherein the cancer is non-small cell lung cancer.

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