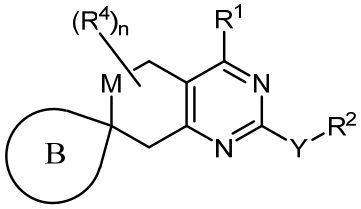
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (II):



Formula (II)

or a pharmaceutically acceptable salt thereof wherein:

M is selected from O, and NR^3;

R^1 is selected from 7- to 10-membered heterocycle, each of which are optionally substituted with one or more substituents independently selected from halogen, $-B(OR^{20})_2$, $-OR^{20}$, $-SR^{20}$, $-S(O)_2(R^{20})$, $-S(O)_2N(R^{20})_2$, $-S(O)N(R^{20})_2$, $-S(O)R^{20}(=NR^{20})$, $-NR^{20}S(O)_2R^{20}$, $-C(O)N(R^{20})_2$, $-C(=NR^{20})N(R^{20})_2$, $-C(O)NR^{20}OR^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-OC(O)N(R^{20})_2$, $-NO_2$, =O, $=N(R^{20})$, $=NO(R^{20})$, -CN, -NHCN, C_{1-6} alkyl-$N(R^{20})_2$, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} cyanoalkyl, C_{1-6} haloalkyl, C_{1-6} alkyl-SO_2R^{20}, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_{12} carbocycle and 5- to 12-membered heterocycle, wherein the C_3-C_{12} carbocycle and 5- to 12-membered heterocycle are each optionally substituted independently with one or more R^{1*};

each R^{1*} is independently selected from halogen, $-B(OR^{20})_2$, $-OR^{20}$, $-SR^{20}$, $-S(O)_2(R^{20})$, $-S(O)_2N(R^{20})_2$, $-S(O)N(R^{20})_2$, $-S(O)R^{20}(=NR^{20})$, $-NR^{20}S(O)_2R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)NR^{20}OR^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-OC(O)N(R^{20})_2$, $-NO_2$, =O, $=N(R^{20})$, $=NO(R^{20})$, -CN, -NHCN, C_{1-6} alkyl-$N(R^{20})_2$, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} cyanoalkyl, C_{1-6} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_3-C_{12} carbocycle;

Y is O;

R^2 is selected from -L-$N(R^{21})_2$ and -L-heterocycle, wherein the heterocycle portion of -L-heterocycle, is optionally substituted with one or more R^6,

each L is independently selected from a C_1-C_4 alkylene optionally substituted with one or more substituents selected from hydroxy, C_1-C_4 hydroxyalkyl, C_1-C_4 alkyl, C_3-C_6 carbocycle, and

3- to 8-membered heterocycle, wherein the C_3-C_6 carbocycle and 3- to 8-membered heterocycle are each optionally substituted with one or more substituents selected from halogen, -OH, -NO_2, =O, =S, -CN, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl; and wherein optionally two substituents on the same carbon atom of L come together to form a C_3-C_6 carbocycle or 3- to 8-membered heterocycle, wherein the C_3-C_6 carbocycle and 3- to 8-membered heterocycle are each optionally substituted with one or more substituents selected from halogen, -OH, -NO_2, =O, =S, -CN, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl;

R^3 is selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl-N(R^{20})$_2$, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} cyanoalkyl, C_{1-6} haloalkyl, C_{1-6} alkoxyalkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, wherein C_{3-12} carbocycle and 3- to 12-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, -OH, -CN, -NO_2, -NH_2, -N(C_{1-6} alkyl)$_2$, C_{1-10} alkyl, -C_{1-10} haloalkyl, -O-C_{1-10} alkyl, oxo, C_{3-12} carbocycle, and 3- to 12-membered heterocycle;

n is selected from 0 to 2;

each R^4 is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, oxo, hydroxyl, halogen, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, wherein the C_1-C_6 alkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle are each optionally substituted with one or more substituents independently selected from cyano, halogen, —OR^5, and —N(R^5)$_2$;

each R^5 is independently selected from hydrogen and C_1-C_6 alkyl;

each R^6 is independently selected from halogen, hydroxy, C_1-C_3 hydroxyalkyl, C_1-C_3 alkyl, oxo, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, =CH_2, =NO-C_1-C_3 alkyl, C_1-C_3 aminoalkyl, -N(R^5)S(O)$_2$(R^5), -Q-phenyl, -Q-phenylSO_2F, -NHC(O)phenyl, - NHC(O)phenylSO_2F, C_1-C_3 alkyl substituted pyrazolyl, tert-butyldimethylsilyloxyCH_2- , -N(R^5)$_2$, (C_1-C_3 alkoxy)C_1-C_3 alkyl-, (C_1-C_3 alkyl)C(=O), oxo, (C_1-C_3 haloalkyl)C(=O)-, -SO_2F, (C_1-C_3 alkoxy)C_1-C_3 alkoxy, -CH_2OC(O)N(R^5)$_2$, -CH_2NHC(O)OC_1-C_6 alkyl, -CH_2NHC(O)N(R^5)$_2$, -CH_2NHC(O)C_1-C_6 alkyl, -CH_2(pyrazolyl), -CH_2NHSO_2C_1-C_6 alkyl, -CH_2OC(O)heterocycle, -OC(O)N(R^5)$_2$, -OC(O)NH(C_1-C_3 alkyl)O(C_1-C_3 alkyl), -OC(O)NH(C_1-C_3 alkyl)O(C_1-C_3 alkyl)phenyl(C_1-C_3 alkyl)N(CH_3)$_2$, -OC(O)NH(C_1-C_3 alkyl)O(C_1-C_3 alkyl)phenyl, - OC(O)heterocycle, -O-C_1-C_3 alkyl, and -CH_2heterocycle, wherein the phenyl of -NHC(O)phenyl and -OC(O)NH(C_1-C_3 alkyl)(C_1-C_3 alkyl)phenyl are each optionally substituted with one or more substituents selected

from -C(O)H and OH, and wherein the alkyl of -O-C_1-C_3 alkyl is optionally substituted with substituents selected from heterocycle, oxo and hydroxy; and wherein the heterocycle of -CH_2heterocyclyl is optionally substituted with oxo;

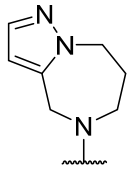
each Q is independently selected from a bond, S, and O;

each R^{20} is independently selected from hydrogen; and C_{1-6} alkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OH, -CN, -NO_2, -NH_2, -N(C_{1-6} alkyl)$_2$, C_{1-10} alkyl, -C_{1-10} haloalkyl, -O-C_{1-10} alkyl, oxo, =NH, C_{3-12} carbocycle, and 3- to 12-membered heterocycle;

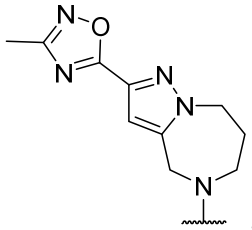
each R^{21} is independently selected from hydrogen; and C_{1-6} alkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OH, -CN, -NO_2, -NH_2, -N(C_{1-6} alkyl)$_2$, C_{1-10} alkyl, -C_{1-10} haloalkyl, -O-C_{1-10} alkyl, oxo, C_{3-12} carbocycle, and 3- to 12-membered heterocycle; and

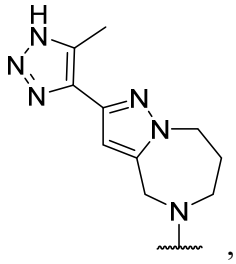
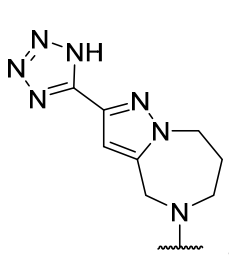
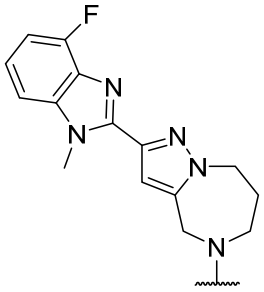
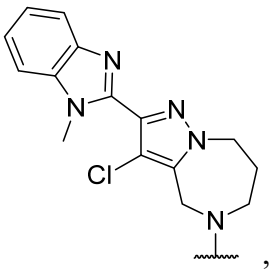
B is selected from a heterocycle and carbocycle, wherein the heterocycle and carbocycle is are each optionally substituted with one or more substituents independently selected from halogen, cyano, hydroxy, =O, -NO_2, C_1-C_4 alkyl, C_{1-6} aminoalkyl, -S-C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_2-C_4 hydroxyalkynyl, C_1-C_3 cyanoalkyl, triazolyl, C_1-C_3 haloalkyl, -O-C_1-C_3 haloalkyl, -S-C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 hydroxyalkyl, -CH_2C(=O)N(R^5)$_2$, -C_3-C_4 alkynyl(NR^5)$_2$, -N(R^5)$_2$, (C_1-C_3 alkoxy)haloC_1-C_3 alkyl-, C_{1-6} alkyl-N(R^{20})$_2$, C_3-C_{12} carbocycle and 5- to 12-membered heterocycle, wherein C_3-C_{12} carbocycle and 5- to 12-membered heterocycle are each optionally substituted with one or more substituents selected from halogen, -OH, -NO_2, -NH_2, =O, =S, -CN, C_{1-6} alkyl-N(R^{20})$_2$, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl.

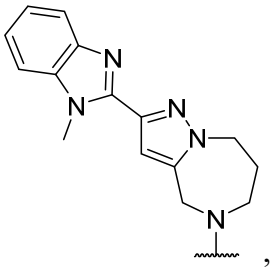
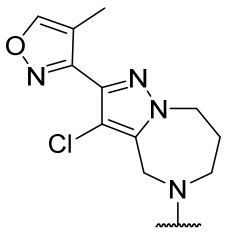
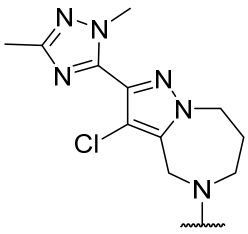
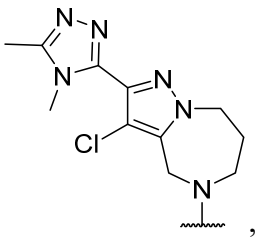
2. The compound or salt of claim 1, wherein R^1 is selected from an optionally substituted 10-membered heterocycle.

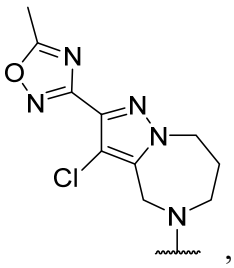
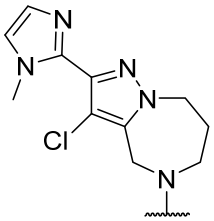
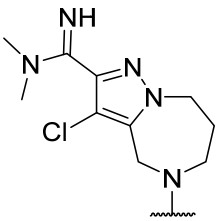
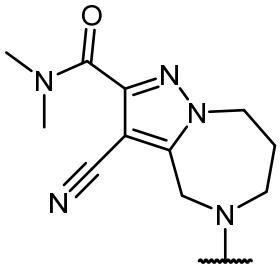
3. The compound or salt of claim 2, wherein R^1 is , which is optionally substituted with one or more substituents independently selected from halogen, -OH, -

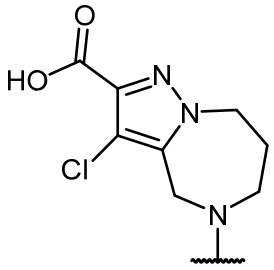
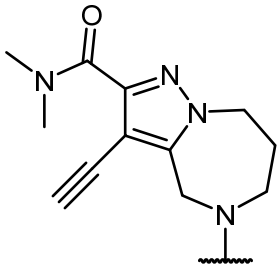
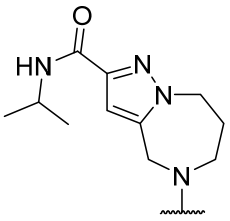
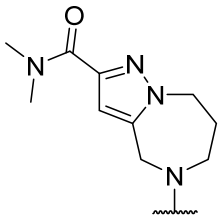
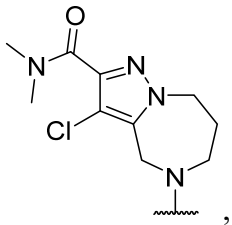
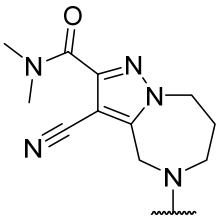
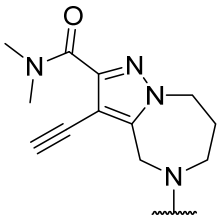
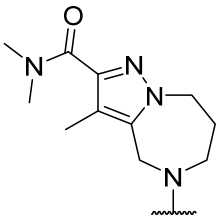
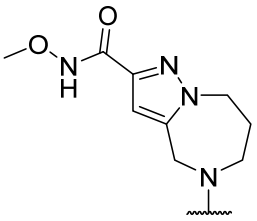
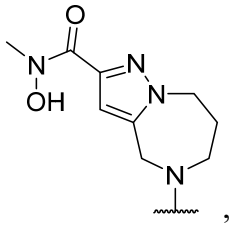
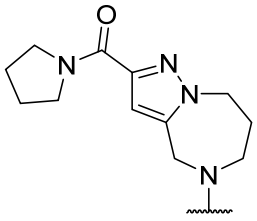
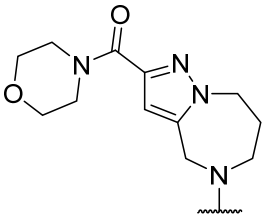
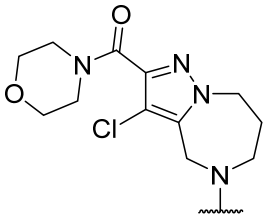
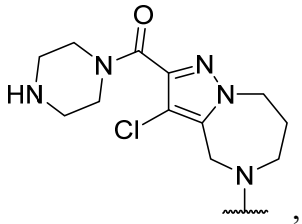
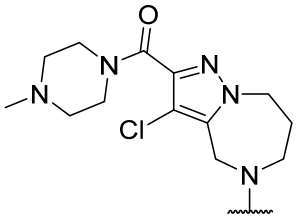
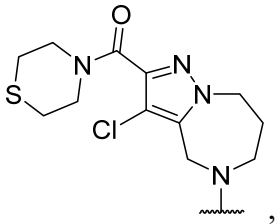
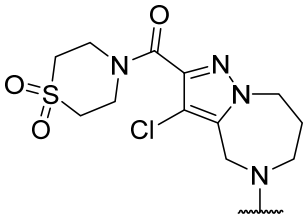
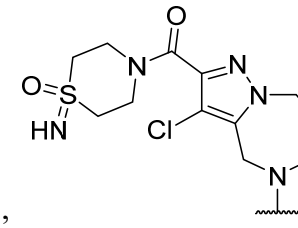
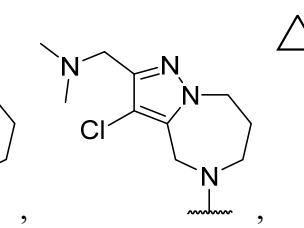
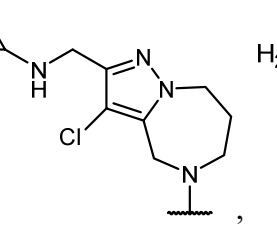
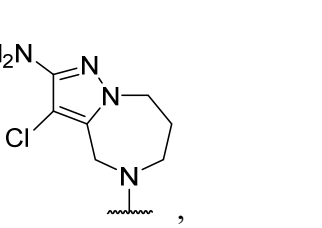
$S(O)_2(R^{20})$, $-S(O)_2N(R^{20})_2$, $-S(O)N(R^{20})_2$, $-S(O)R^{20}(=NR^{20})$, $-C(O)N(R^{20})_2$, $-C(=NR^{20})N(R^{20})_2$, $-C(O)OR^{20}$, $-C(O)NR^{20}OR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-NO_2$, =O, -CN, C_{1-6} alkyl-$N(R^{20})_2$, C_{1-6} aminoalkyl, C_{1-6} alkoxy, C_{1-6} alkoxyalkyl, C_{1-6} hydroxyalkyl, C_{1-6} cyanoalkyl, C_{1-6} haloalkyl, C_{1-6} alkyl, C_{2-6} alkynyl, and 5- to 12-membered heterocycle, wherein the 5- to 12-membered heterocycle is optionally substituted with one or more substituents selected from halogen, $-OR^{20}$, and C_{1-6} alkyl.

4. The compound or salt of claim 3, wherein R^1 is selected from ,

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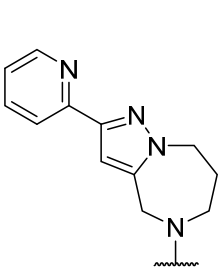
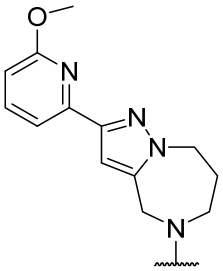
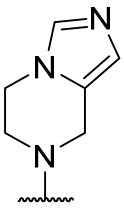
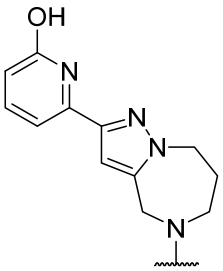
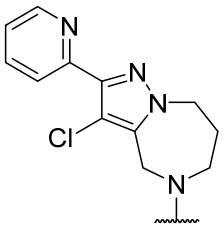
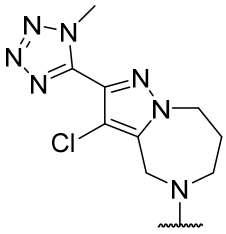
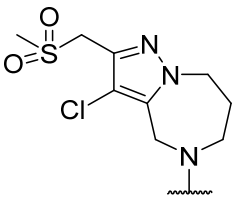
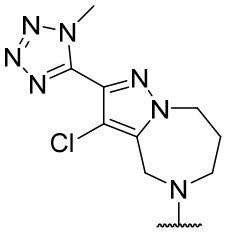
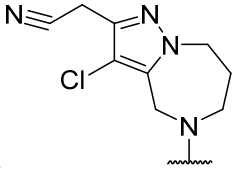

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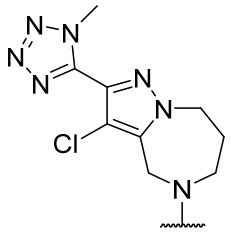
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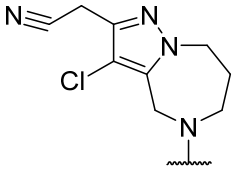
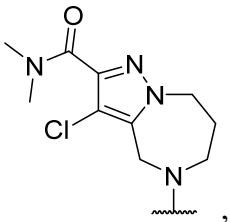
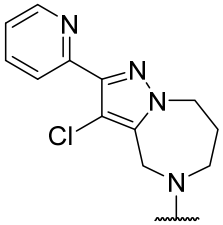
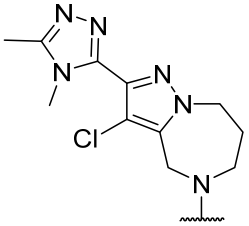
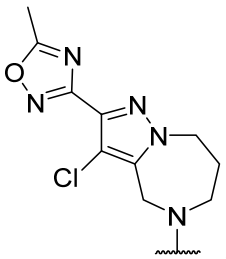
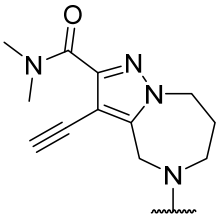
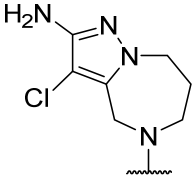
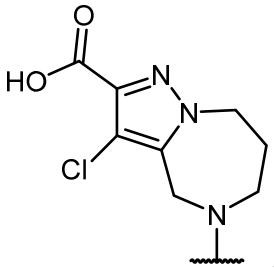
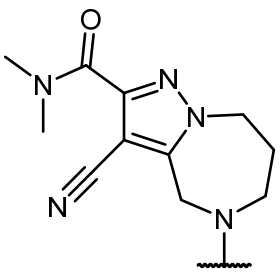
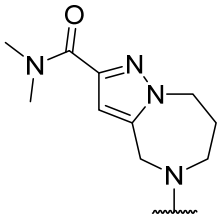
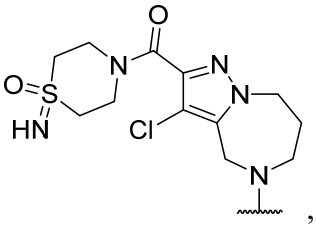
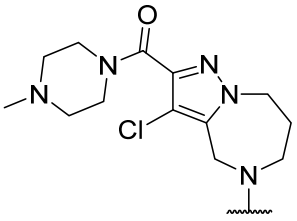
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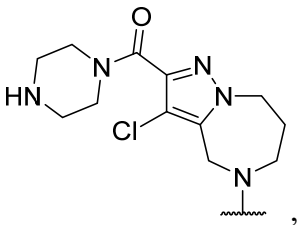
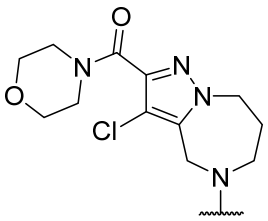
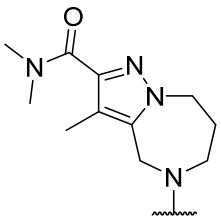
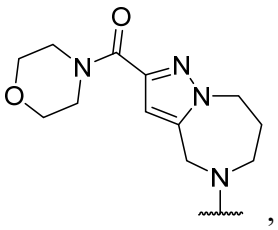
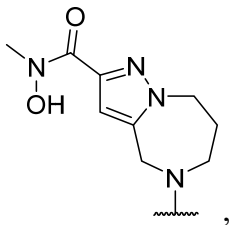
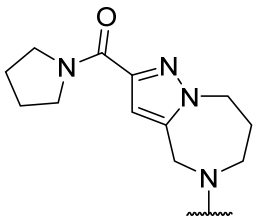
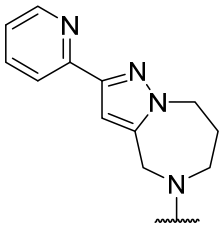
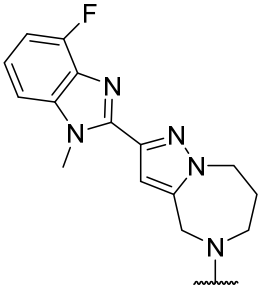
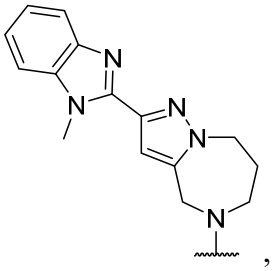
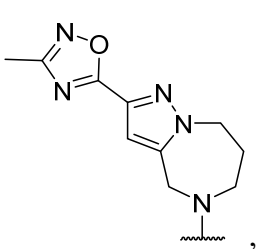
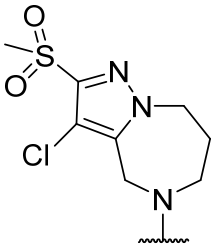
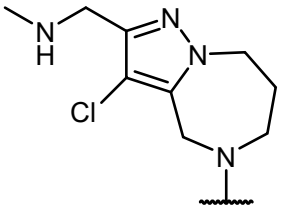
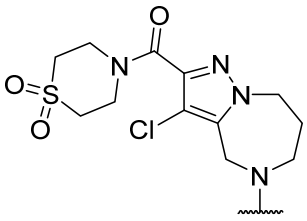
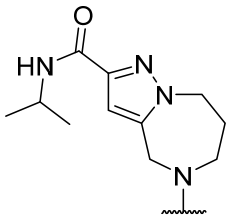
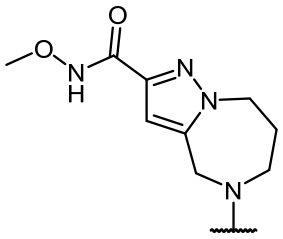
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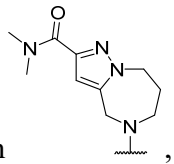
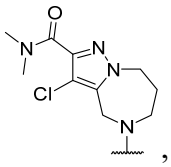
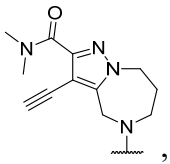
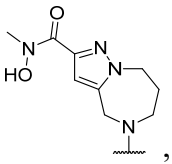
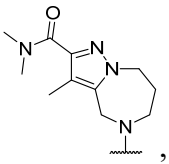
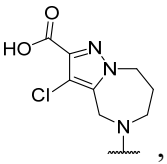
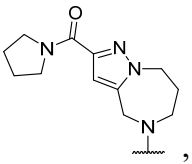
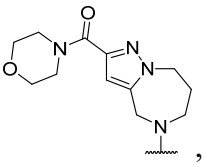
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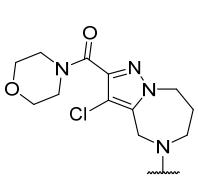
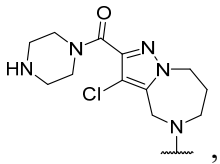
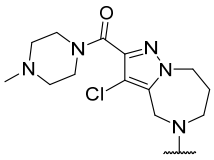
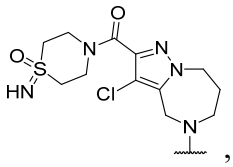
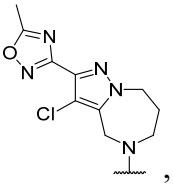

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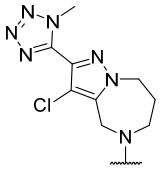
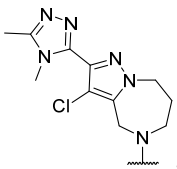
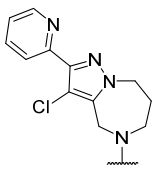
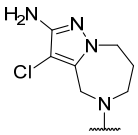
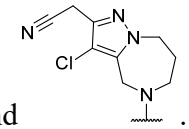
5. The compound or salt of claim 4, wherein R^1 is selected from

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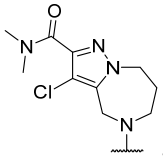

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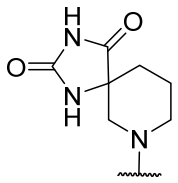

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6. The compound or salt of claim 5, wherein R^1 is selected from

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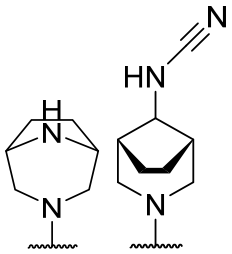
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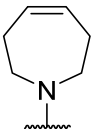
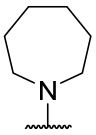
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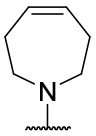
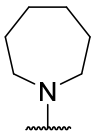
7. The compound or salt of claim 6, wherein R^1 is .

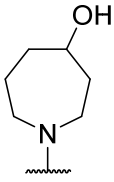
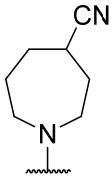
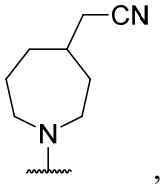
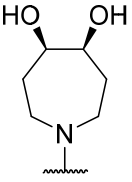
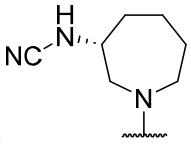
8. The compound or salt of claim 1, wherein R^1 is .

9. The compound or salt of claim 1, wherein R^1 is selected from an optionally substituted 7- to 8-membered bridged heterocycle.

10. The compound or salt of claim 9, wherein R^1 is selected from  and .

11. The compound or salt of claim 1, wherein R^1 is selected from , and , each of which is optionally substituted.

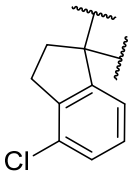
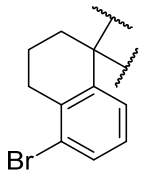
12. The compound or salt of claim 11, wherein R^1 is selected from  ,  ,

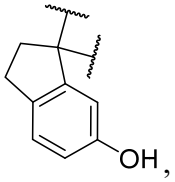
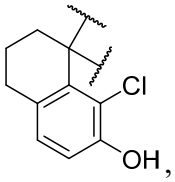
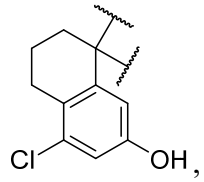
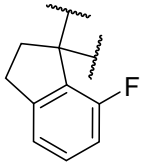
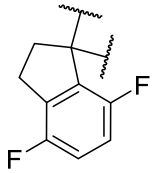
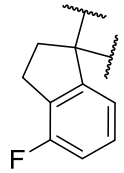
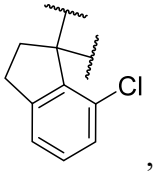
 ,  ,  ,  , and  .

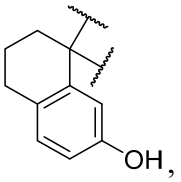
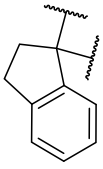
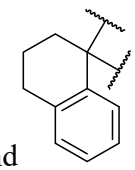
13. The compound or salt of claim 1, wherein M is O.

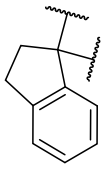
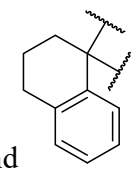
14. The compound or salt of claim 1, wherein M is NMe.

15. The compound or salt of claim 1, wherein B is selected from an optionally substituted 8- to 15-membered fused heterocycle and optionally substituted C_8-C_{15} fused carbocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -NH_2, C_1-C_3 alkyl, hydroxy, =O, cyano, C_1-C_3 alkoxy, C_1-C_3 hydroxyalkyl, and C_2-C_4 alkynyl.

16. The compound or salt of claim 15, wherein B is selected from  ,  ,

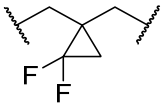
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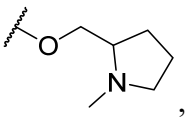
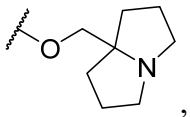
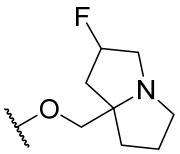
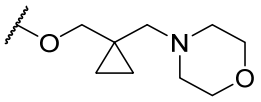
 ,  and  .

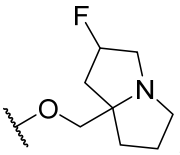
17. The compound or salt of claim 16, wherein B is selected from  and  .

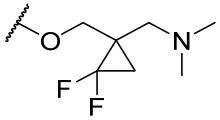
18. The compound or salt of claim 1, wherein R^2 is -L-heterocycle, optionally substituted with one or more R^6, wherein each R^6 is independently selected from halogen, hydroxy, C_1-C_3 alkyl, -$N(R^5)S(O)_2(R^5)$, -$OC(O)N(R^5)_2$, =CH_2, oxo, =NO-C_1-C_3 alkyl, -$CH_2OC(O)$heterocycle, -

CH_2heterocycle, -$CH_2OC(O)N(R^5)_2$, and -O-C_1-C_3 alkyl, wherein the alkyl of -O-C_1-C_3 alkyl is optionally substituted with substituents selected from heterocycle, oxo, and hydroxy.

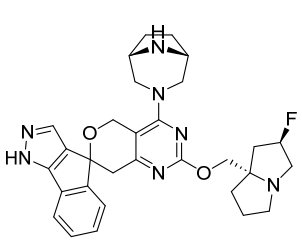
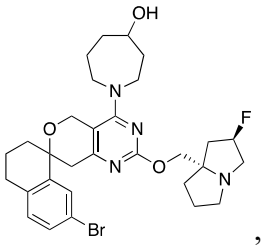
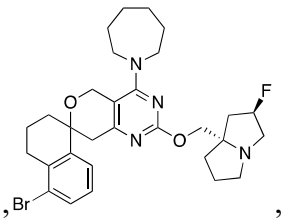
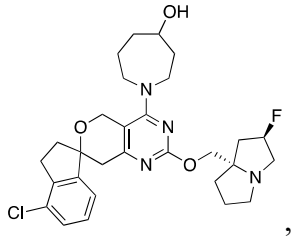
19. The compound or salt of claim 18, wherein each L is independently selected from unsubstituted C_1-C_4 alkylene, , and .

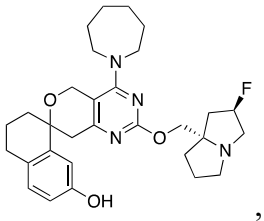
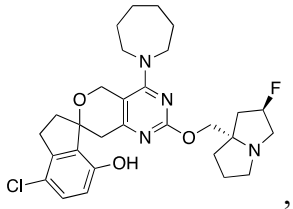
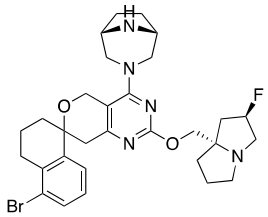
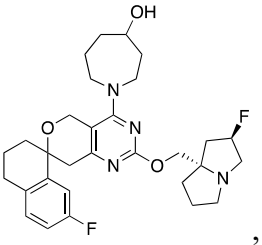
20. The compound or salt of claim 19, wherein Y-R^2 is selected from , , , and .

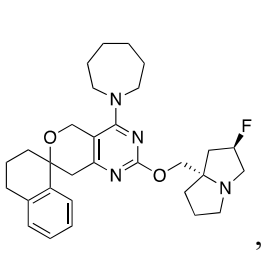
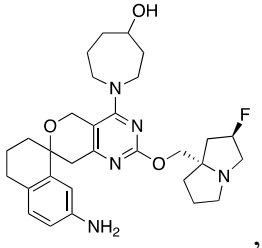
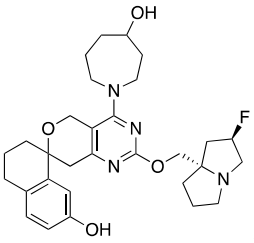
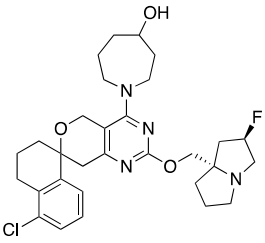
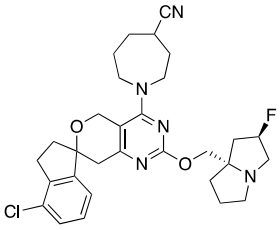
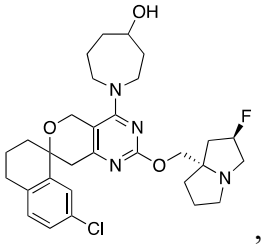
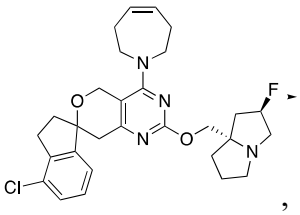
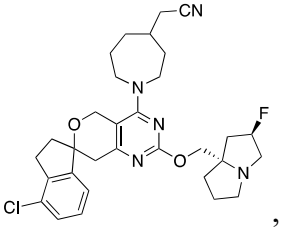
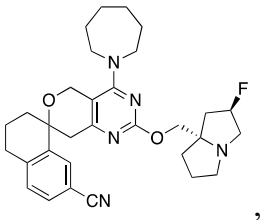
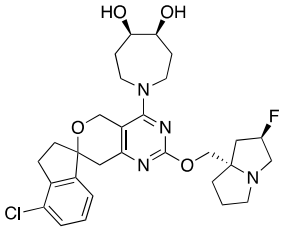
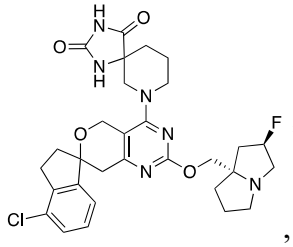
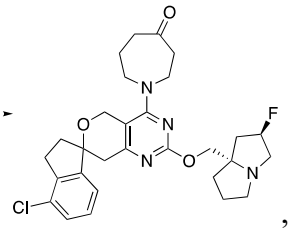
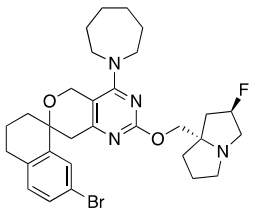
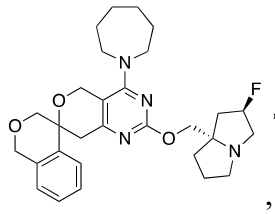
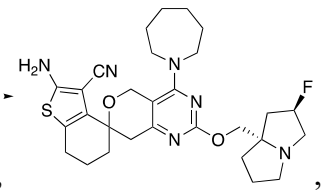
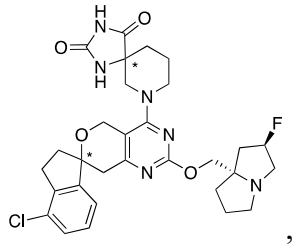
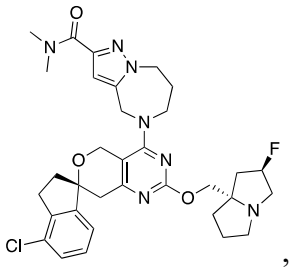
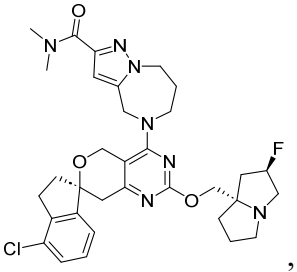
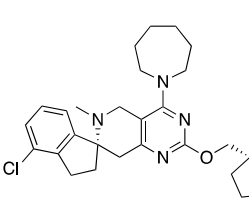
21. The compound or salt of claim 1, wherein Y-R^2 is .

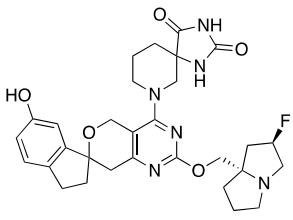
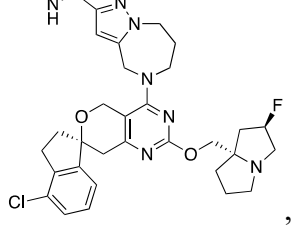
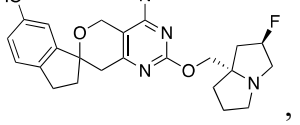
22. The compound or salt of claim 1, wherein Y-R^2 is .

23. The compound or salt of claim 1, wherein the compound is selected from:

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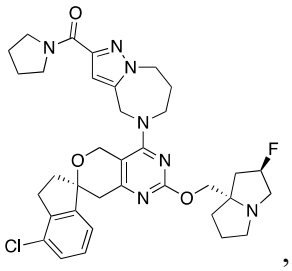
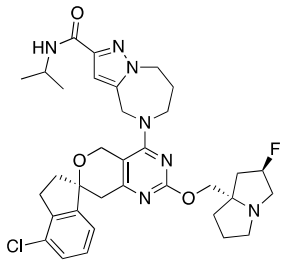
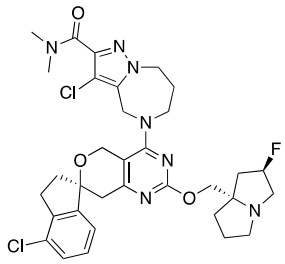
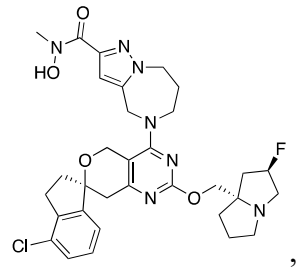
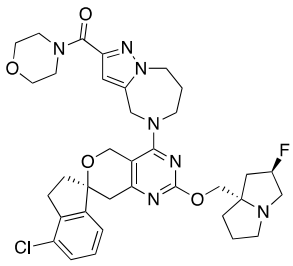
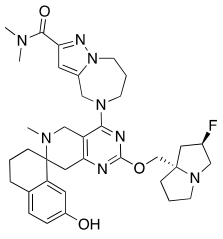
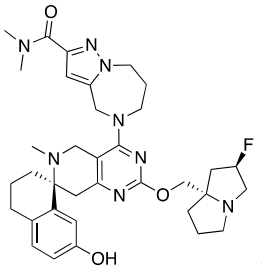
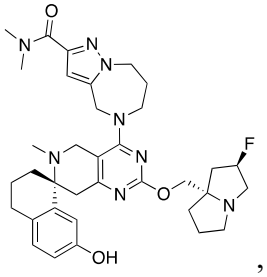
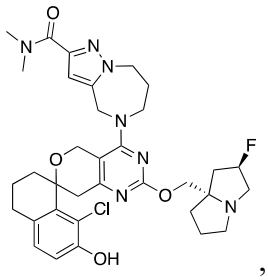
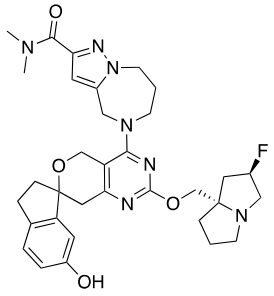
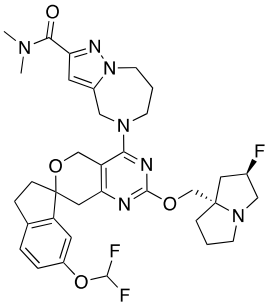
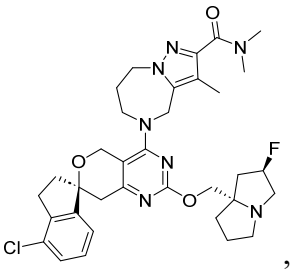
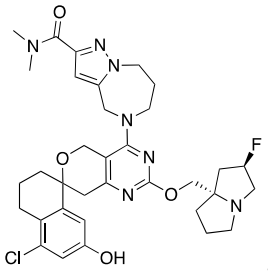
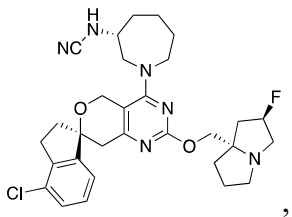
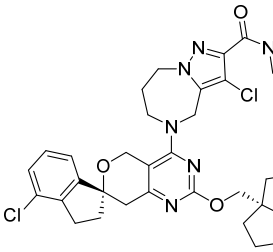
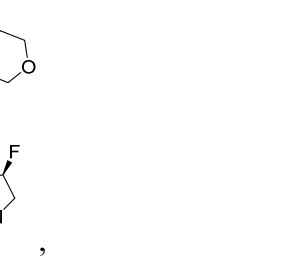
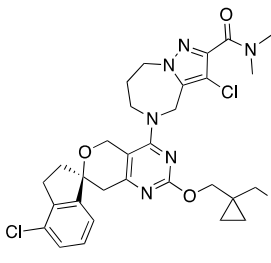
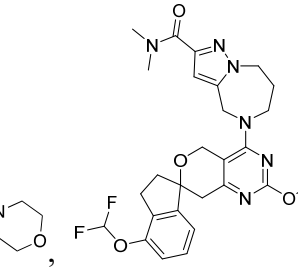
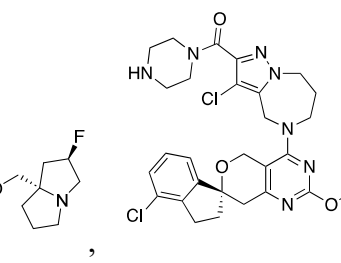
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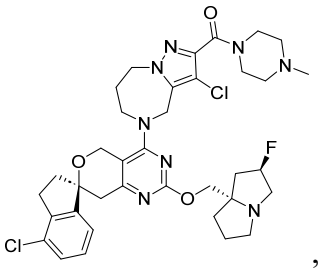
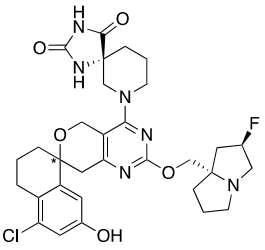
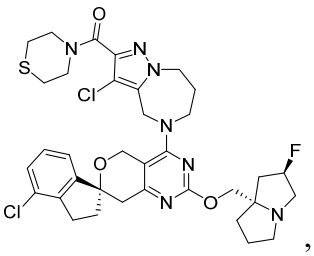
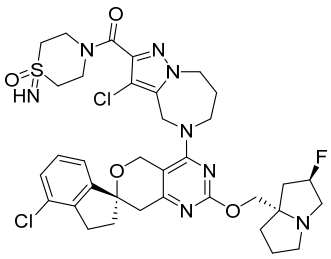
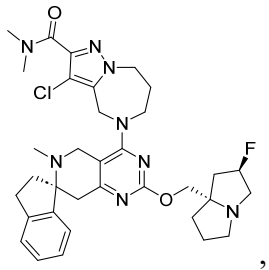
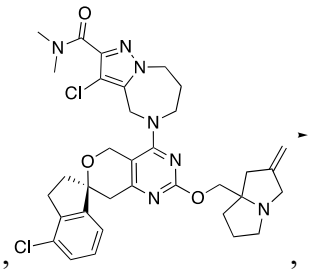
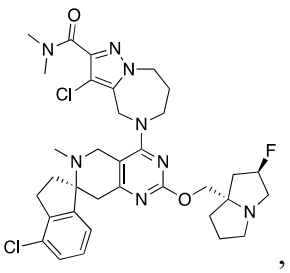
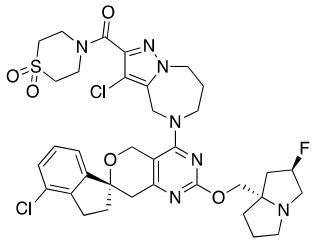
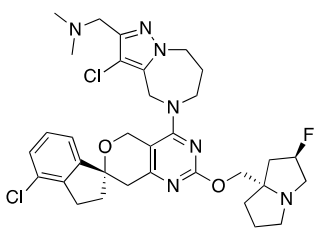
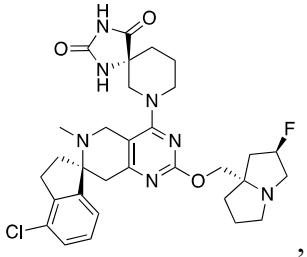
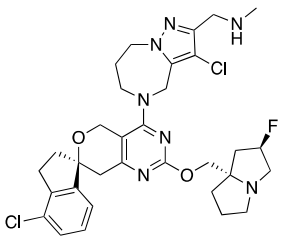
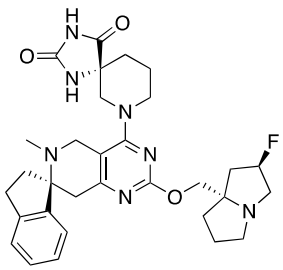
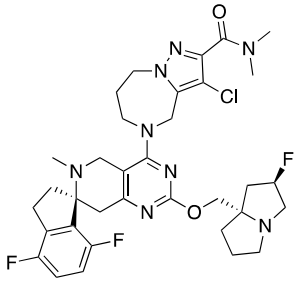
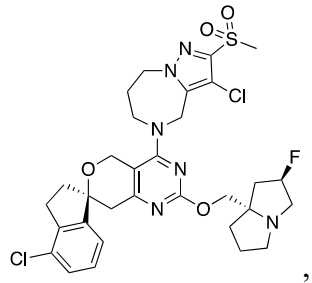
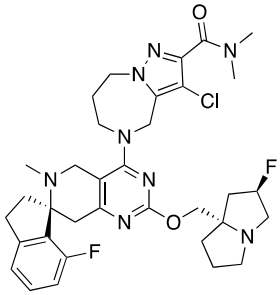
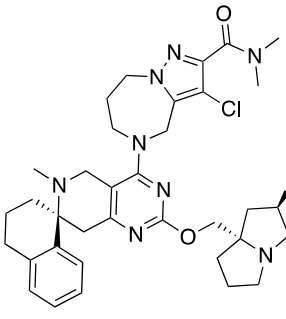
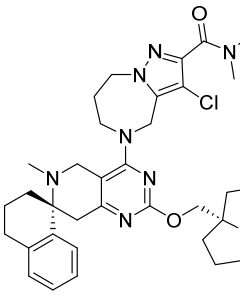
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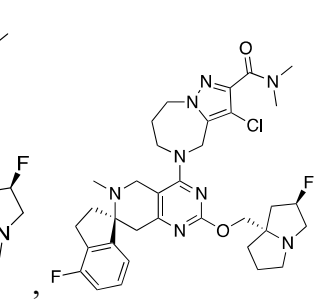

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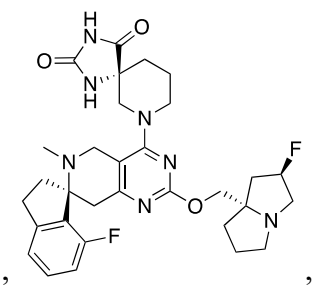
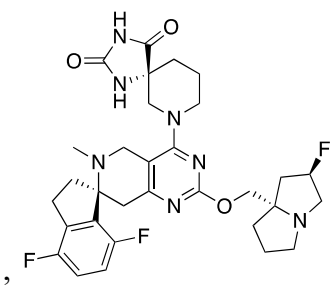
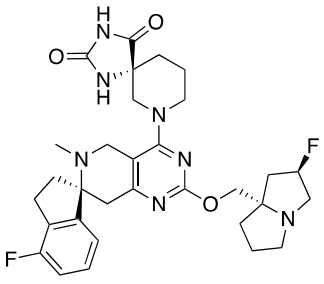
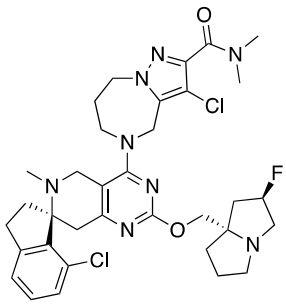
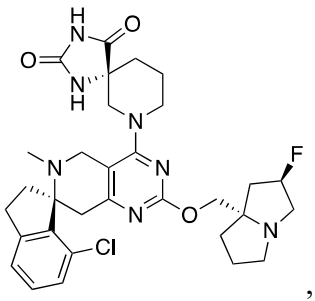
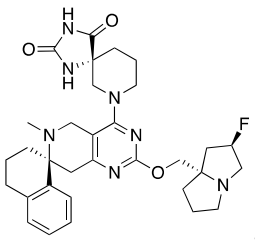
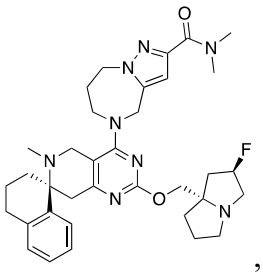
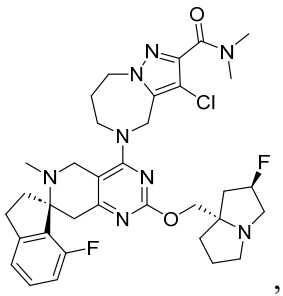
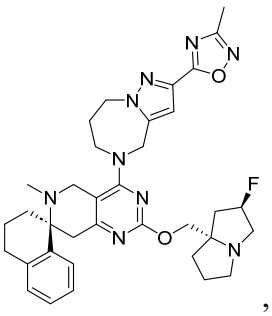
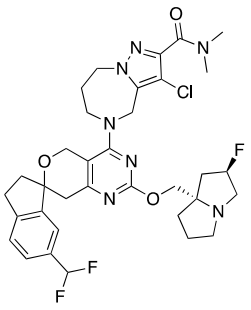
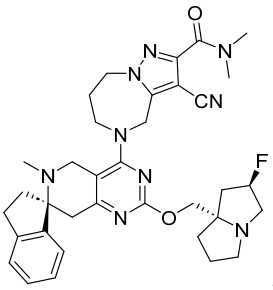
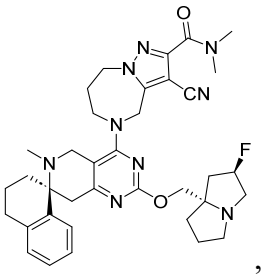
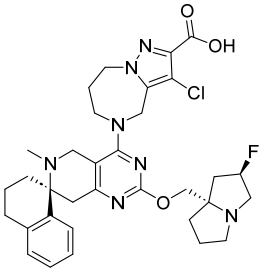
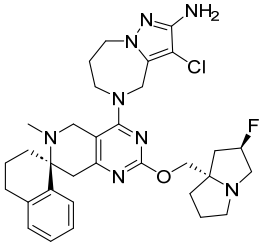
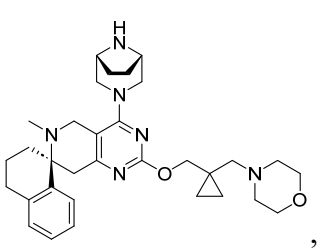
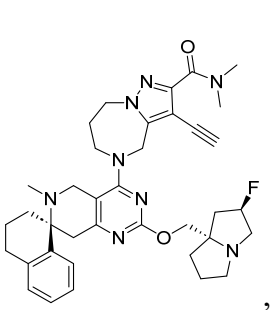
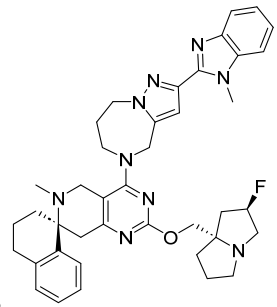
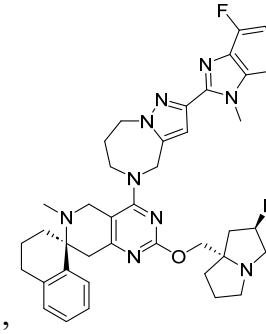
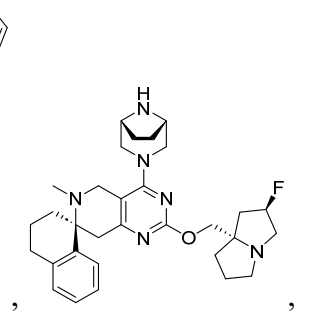
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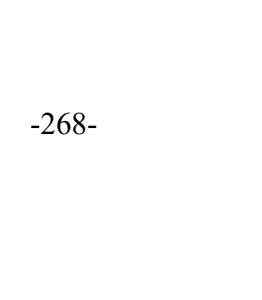
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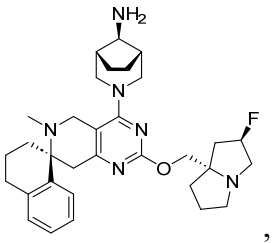
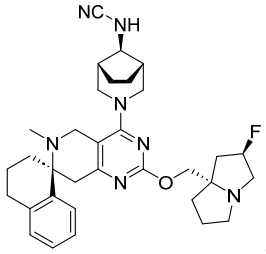
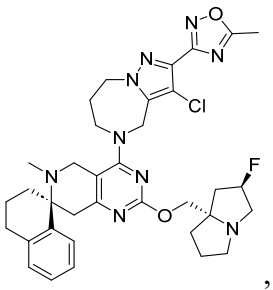
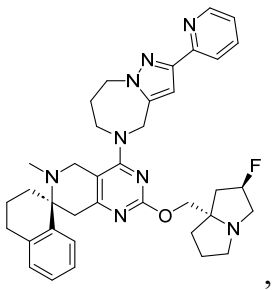
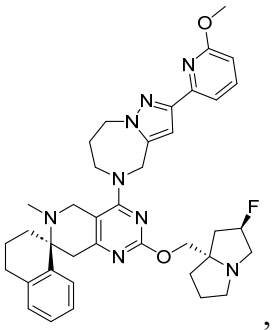
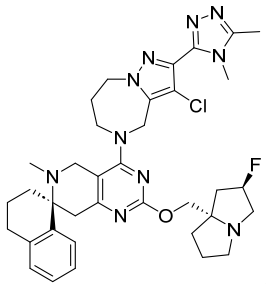
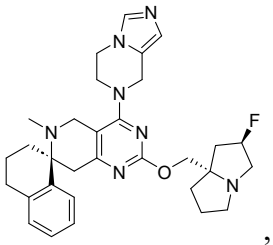
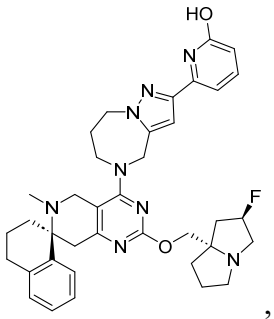
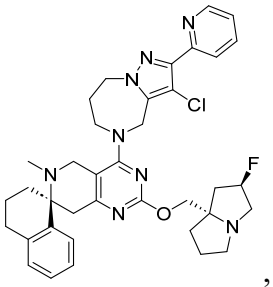
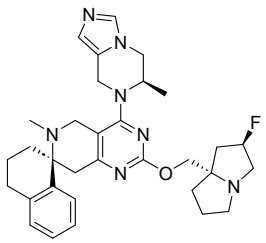
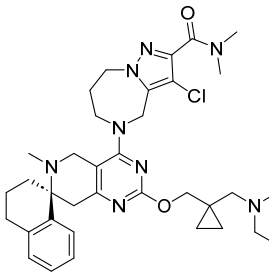
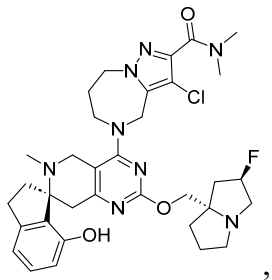
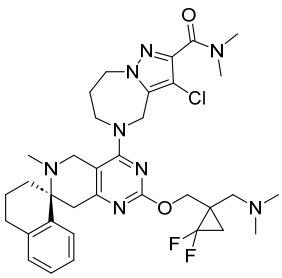
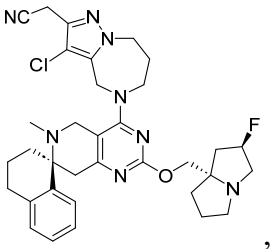
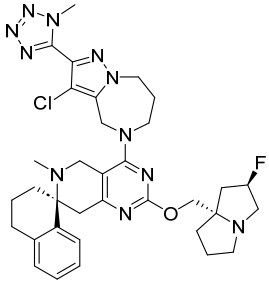
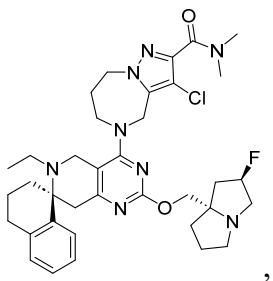
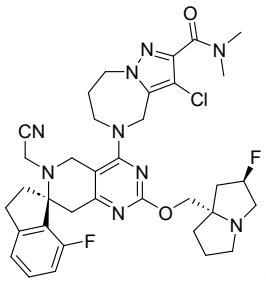
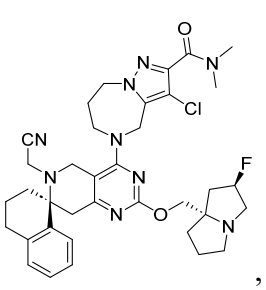
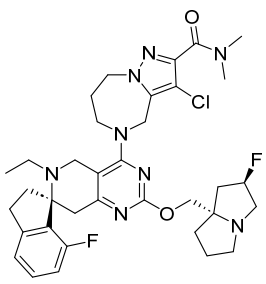
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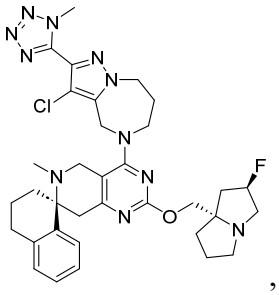
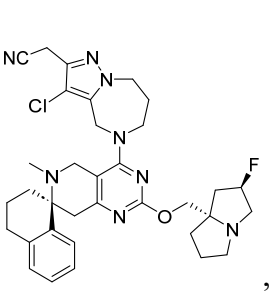
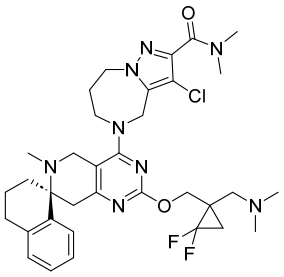
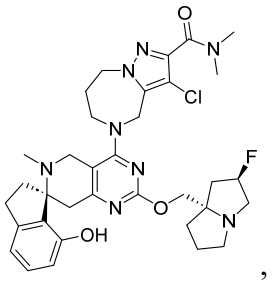
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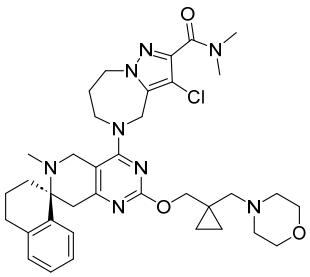
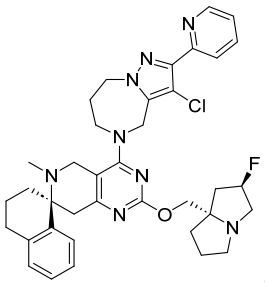
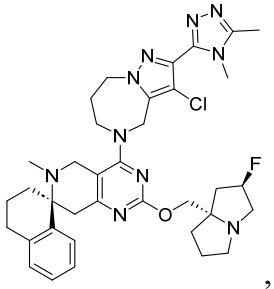
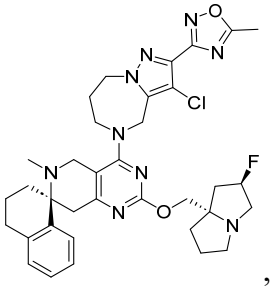
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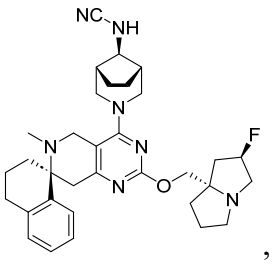
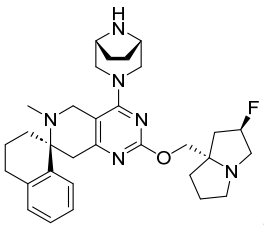
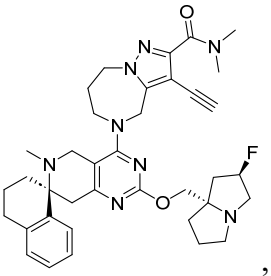
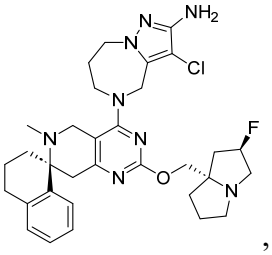
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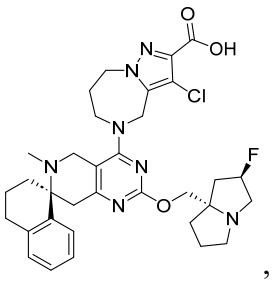
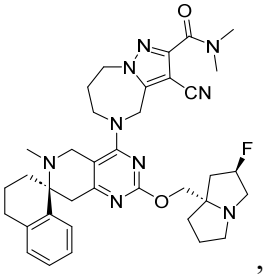
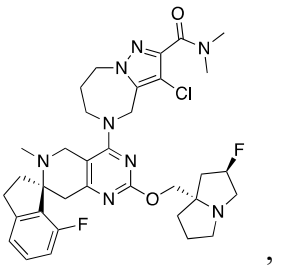
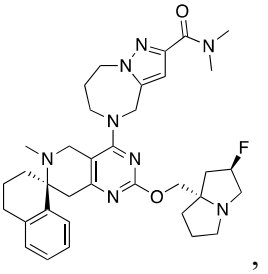

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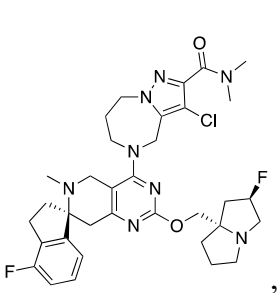
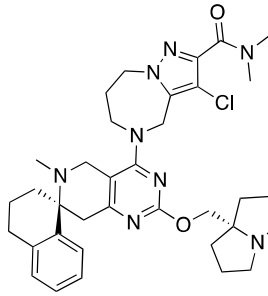
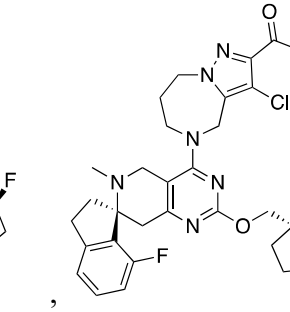
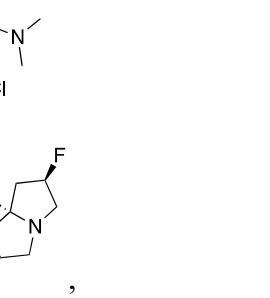
24. The compound or salt of claim 1, wherein the compound is selected from:

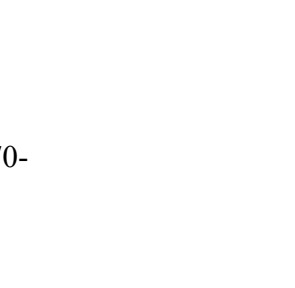
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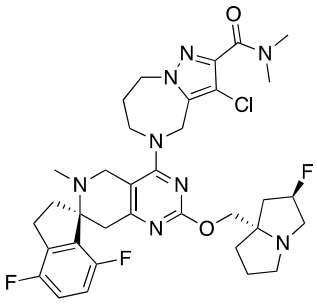
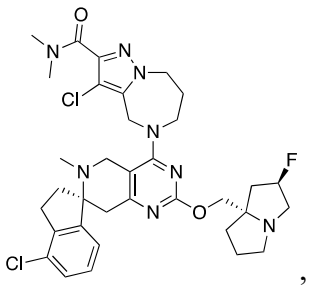
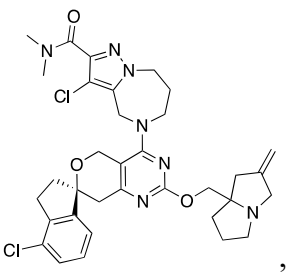
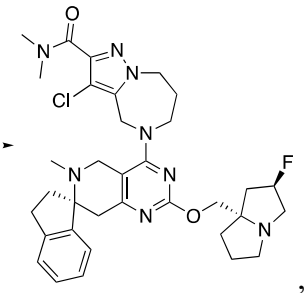
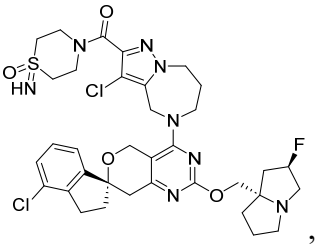
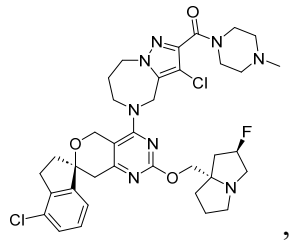
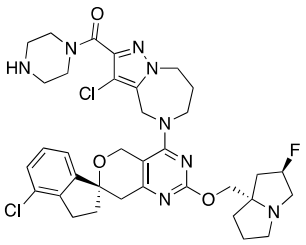
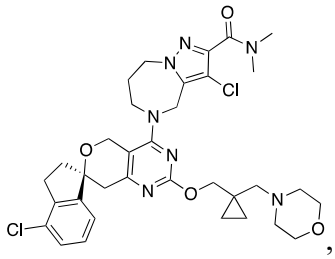
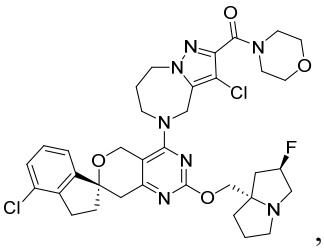
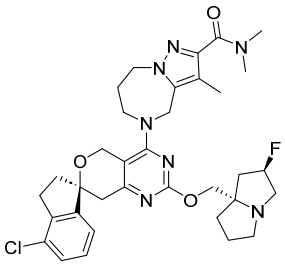
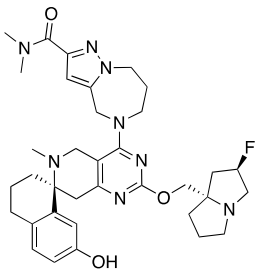
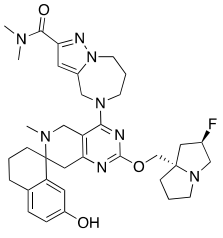
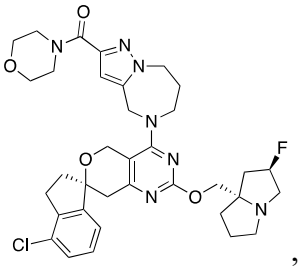
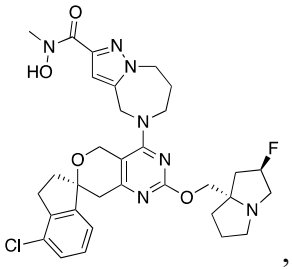
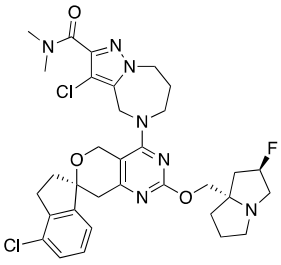
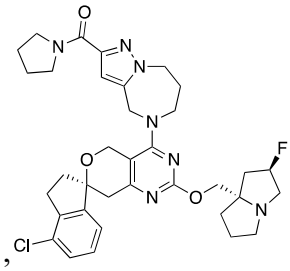
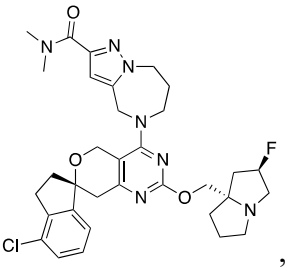
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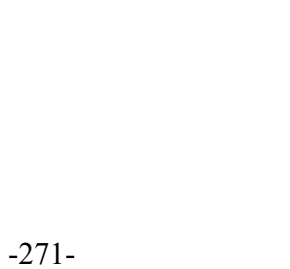
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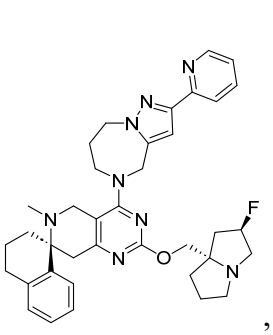
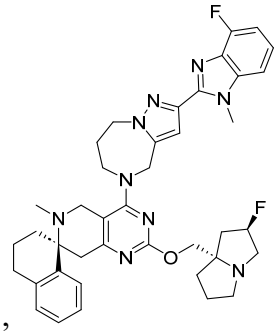
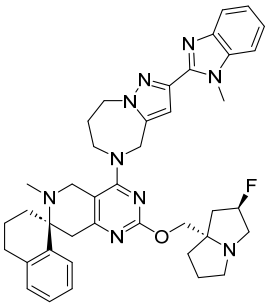
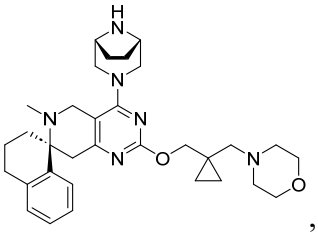
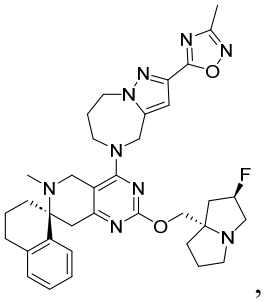
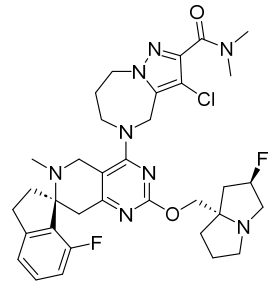
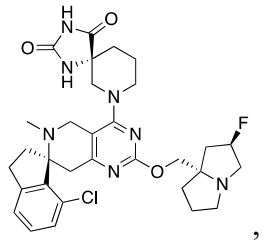
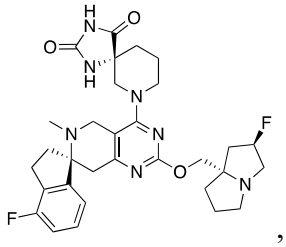
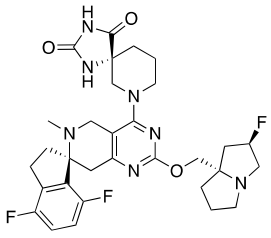
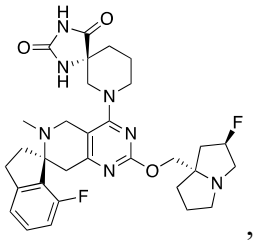
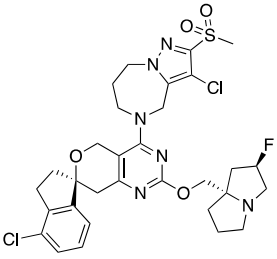
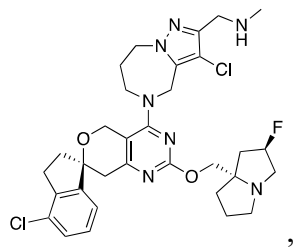
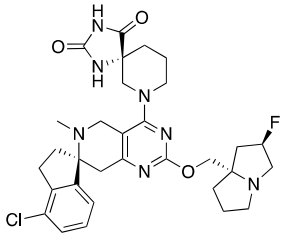
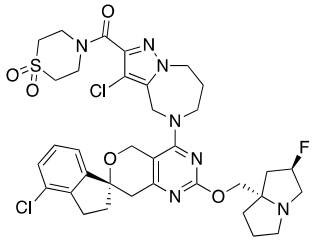
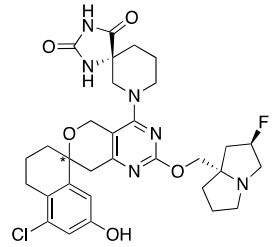
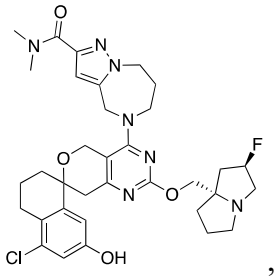
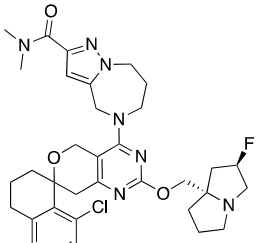
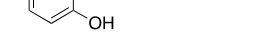
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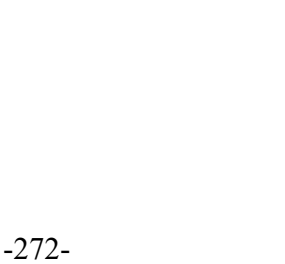

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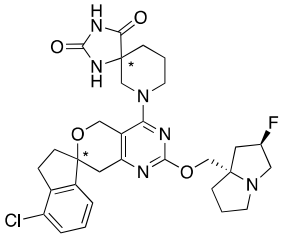
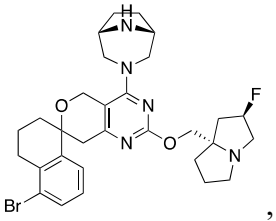
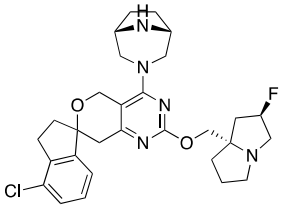
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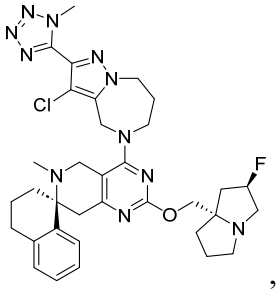
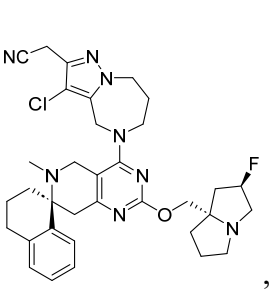
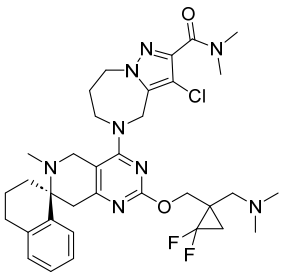
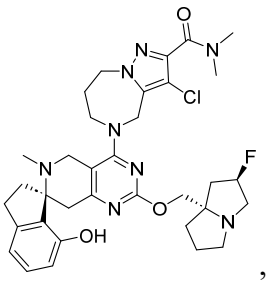
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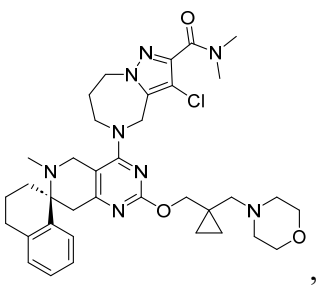
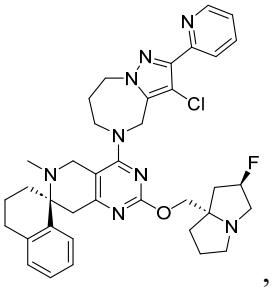
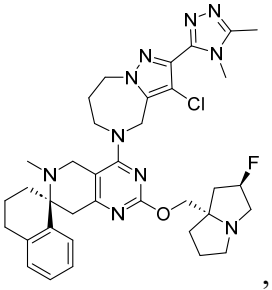
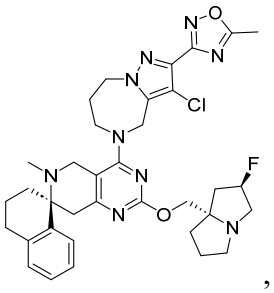
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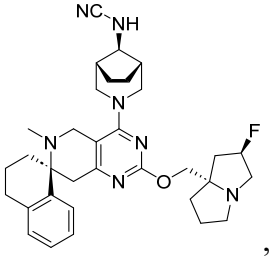
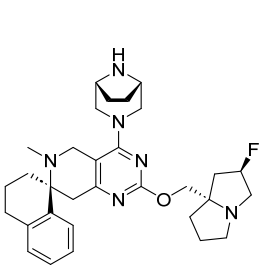
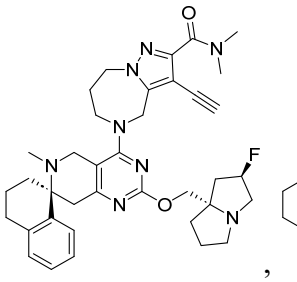
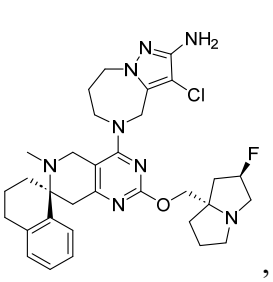
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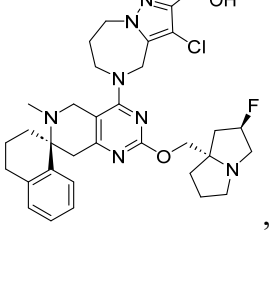
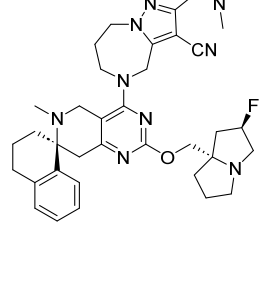
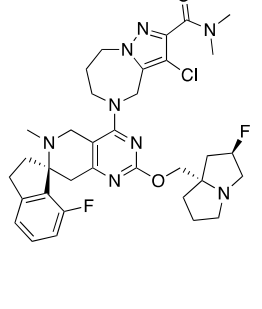
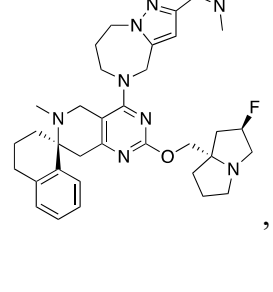

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, or a salt of any one thereof.

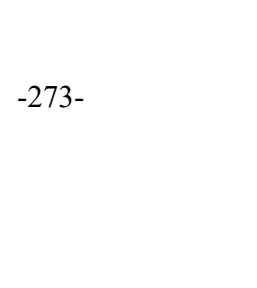
25. The compound or salt of claim 1, wherein the compound is selected from:

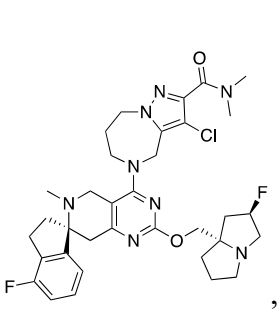
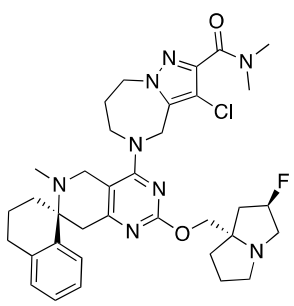
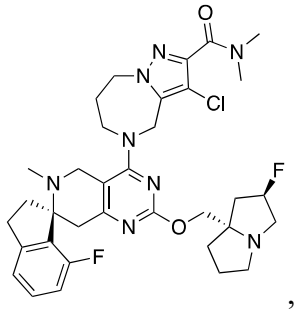
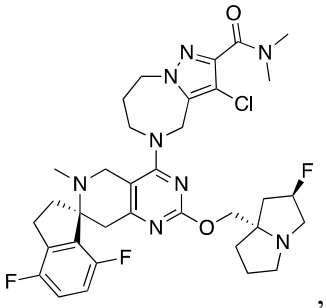
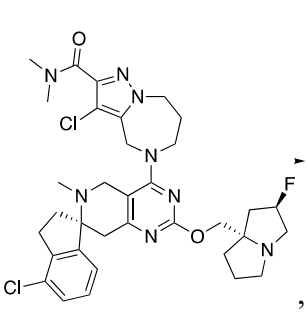
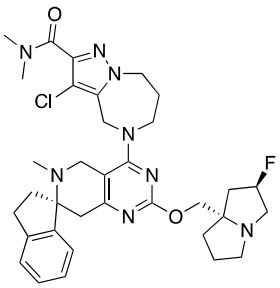
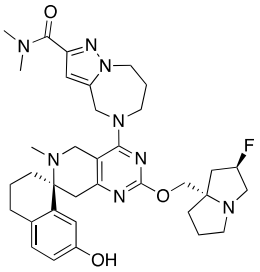
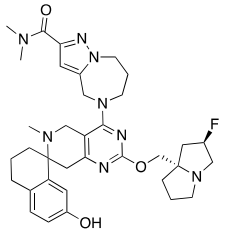
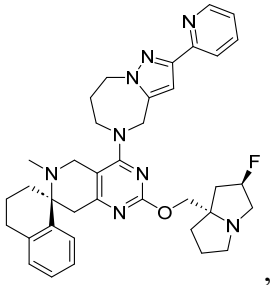
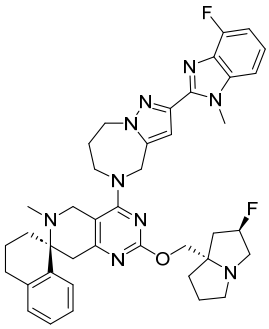
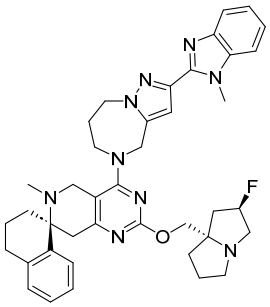
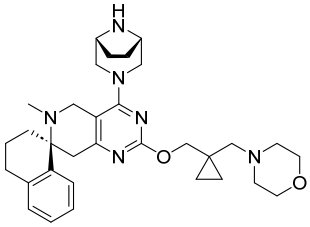
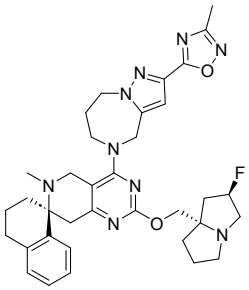
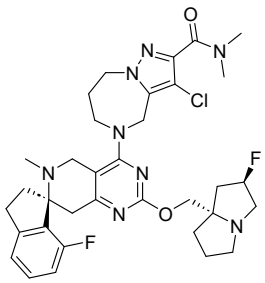
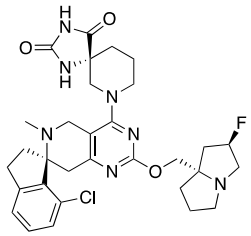
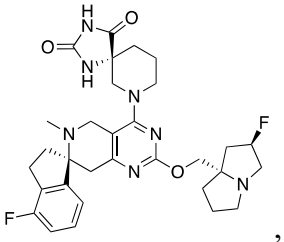
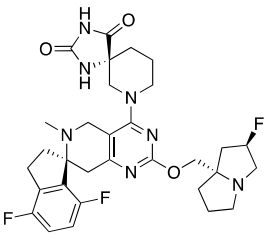
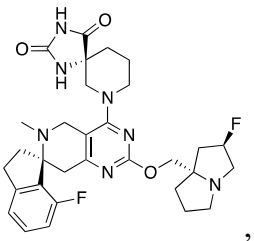
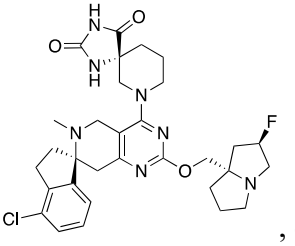

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, or a salt of any one thereof.

26. A pharmaceutical composition comprising a compound or salt of claim 1 and a pharmaceutically acceptable excipient.

27. Use of the pharmaceutical composition of claim 26 in the manufacture of a medicament for the treatment of a disease or disorder, wherein the medicament is to be administered to a patient in need thereof, wherein the disease or disorder is a cancer selected from:

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, osteochronfroma (osteocartilaginous 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);

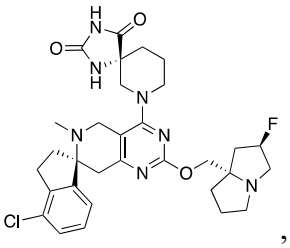
Gynecological: uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma), granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma);

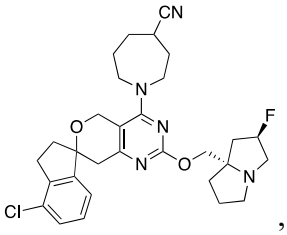
Hematologic: blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma);

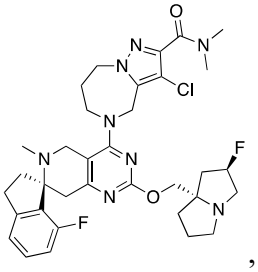
Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and

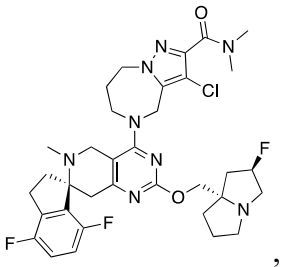
Adrenal glands: neuroblastoma.

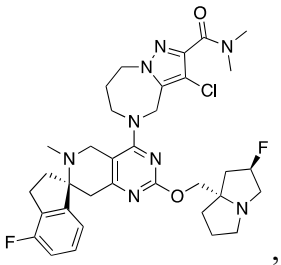
28. The use of claim 27, wherein the disease or disorder is a cancer, wherein the cancer is non-small cell lung cancer, small cell lung cancer, colorectal cancer, rectal cancer or pancreatic cancer; or wherein the cancer is a tumor cancer.

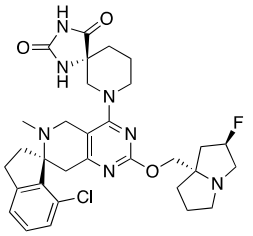
29. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

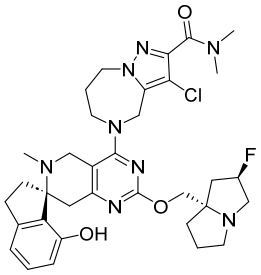
30. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

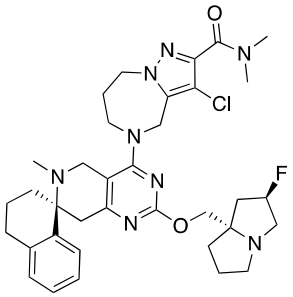
31. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

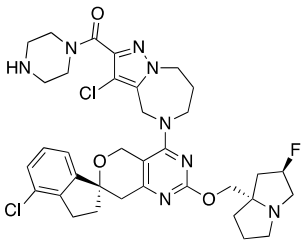
32. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

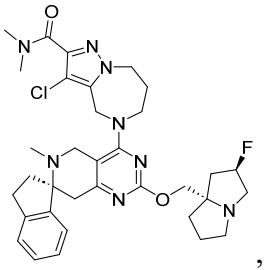
33. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

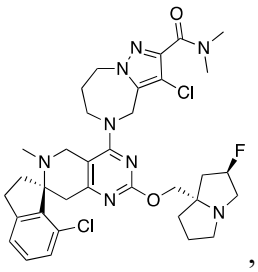
34. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

35. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

36. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

37. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

38. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

39. The compound or salt of claim 1, wherein the compound is , or a salt thereof.

40. The compound or salt of claim 1 for use as a medicament.