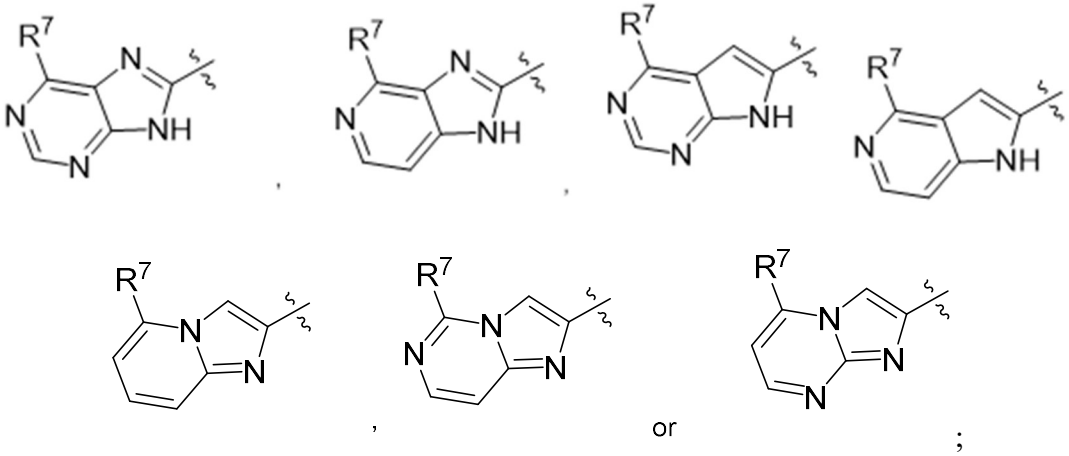
or a pharmaceutically acceptable salt or a stereoisomer thereof,

wherein:

A is N;

Cy is



wherein

X is $–NR^{3a}$-, $–C(R^{3b})_2$-, or –O-;

Y is a single bond, $–NR^{3a}$-, $–C(R^{3b})_2$-, or –O-;

W is -C(O)-, -S(O)-, or $-S(O)_2$-;

(i) R^1 is H, halo, CN, C_{1-6} alkyl, or C_{1-6} haloalkyl; and

R^2 is CH_2-Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$ or Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$; or

(ii) R^1 is CH_2-Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$ or Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$; and

R^2 is H, halo, CN, C_{1-6} alkyl, or C_{1-6} haloalkyl;

Cy^2 is an optionally substituted 4-7 membered heterocycloalkyl ring, phenyl, or pyridyl, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from group consisting of nitrogen, oxygen, and sulfur;

each R^{3a} is independently H or C_{1-6} alkyl;

each R^{3b} is independently H or C_{1-6} alkyl;

each R^{4a} is independently H, halo, CN, C_{1-6} alkyl, C(O)R, $C(O)N(R)_2$, C(O)OR, $N(R)_2$, NRC(O)R, OR, $S(O)_2R$, C_{3-7} cycloalkyl, a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4

heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

each R^{4b} is independently H, halo, CN, C_{1-6} alkyl, C(O)R, $C(O)N(R)_2$, C(O)OR, $N(R)_2$, NRC(O)R, OR, $S(O)_2R$, C_{3-7} cycloalkyl, a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

each R is independently H, C_{1-6} aliphatic, a saturated or partially unsaturated 4- to 7-membered heterocyclic ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the saturated or partially unsaturated 4- to 7-membered heterocyclic has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur; and the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

or:

two geminal R groups together with the nitrogen atom to which they are attached form a saturated, or partially unsaturated 4- to 7-membered heterocyclic ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocyclic ring or the 5- or 6-membered heteroaryl has 0, 1, 2, or 3 additional heteroatoms, independently selected from the group consisting of nitrogen, oxygen, and sulfur;

R^{6a} is H or C_{1-6} alkyl;

R^{6b} is H or C_{1-6} alkyl; or

R^{6a} and R^{6b}, joined together, form a single bond;

R^{6c} is H or unsubstituted C_{1-6} alkyl; or each of R^{6a}, and R^{6b} is H, and R^{6c} is C_1-C_6 alkyl, wherein the C_{1-6} alkyl is optionally substituted with $N(CH_3)_2$;

R^7 is

(i) independently a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to -10-membered bicyclic aryl ring, or 5- or 6-membered heteroaryl ring, wherein the 4- to 7- membered heterocycloalkyl independently has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

(ii) a 4- to 7-membered heterocycloalkyl ring having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, and substituted with Me, Et, or i-Pr;

(iii) pyridyl substituted with halo, hydroxyl, CN, substituted or unsubstituted $C_{1\text{-}6}$alkyl, amino, or alkoxy;

(iv) pyridyl substituted with Me, Et, i-Pr, OH, Cl, F, CF_3, CN, or NH_2; or

(v) imidazoyl substituted with Me, Et, i-Pr, Cl, F, CF_3, or CN;

m is 1, 2, or 3; and

n is 1, 2, 3, or 4.

[0012] In some examples, the present disclosure provides a compound according to Formula (XXI):

herein can be selected by one of ordinary skill in the art to provide compounds that are chemically stable and that can be synthesized by techniques known in the art, as well as those set forth herein.

[0029] In some examples, the present disclosure provides pharmaceutical compositions, which include a therapeutically effective amount of at least one of any of the compounds herein, or a pharmaceutically acceptable salt, pharmaceutically active metabolite, pharmaceutically acceptable prodrug, or pharmaceutically acceptable solvate. In certain examples, compositions provided herein further include a pharmaceutically acceptable diluent, excipient and/or binder.

[0030] Pharmaceutical compositions formulated for administration by an appropriate route and means containing effective concentrations of one or more of the compounds provided herein, or pharmaceutically effective derivatives thereof, that deliver amounts effective for the treatment, prevention, or amelioration of one or more symptoms of dieases, disorders or conditions that are modulated or otherwise affected by Menin-MLL activity, or in which Menin-MLL activity is implicated, are provided. The effective amounts and concentrations are effective for ameliorating any of the symptoms of any of the diseases, disorders or conditions disclosed herein.

[0031] In certain examples, provided herein is a pharmaceutical composition containing: i) a physiologically acceptable carrier, diluent, and/or excipient; and ii) one or more compounds provided herein.

[0032] In some examples, provided herein are methods for treating a patient by administering a compound provided herein. In some examples, provided herein is a method of inhibiting the activity of Menin-MLL, or of treating a disease, disorder, or condition, which would benefit from inhibition of Menin-MLL activity, in a patient, which includes administering to the patient a therapeutically effective amount of at least one of any of the compounds herein, or pharmaceutically acceptable salt, pharmaceutically active metabolite, pharmaceutically acceptable prodrug, or pharmaceutically acceptable solvate.

[0033] In some examples, provided herein is the use of a compound disclosed herein for inhibiting Menin-MLL activity or for the treatment of a disease, disorder, or condition, which would benefit from inhibition of Menin-MLL activity.

[0033a] In another aspect, the present disclosure refers to use of any one of the compounds provided herein, or a pharmaceutical composition provided herein, in the manufacture of a medicament for inhibiting menin-MLL activity in a patient in need thereof, wherein the patient has an autoimmune disease or an autoimmune condition.

[0033b] In another aspect, the present disclosure refers to use of any one of the compounds provided herein, or a pharmaceutical composition provided herein, in the manufacture of a medicament for the treatment of cancer.

[0033c] In another aspect, the present disclosure refers to any one of the compounds provided herein, or a pharmaceutical composition provided herein, for use in treating an autoimmune disease or an autoimmune condition.

[0033d] In another aspect, the present disclosure refers to any one of the compounds provided herein, or a pharmaceutical composition provided herein, for use in treating cancer.

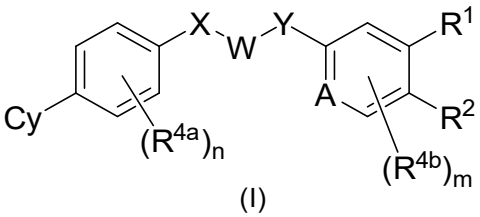
[0033e] In another aspect, the present disclosure refers to any one of the compounds provided herein, or a pharmaceutical composition provided herein, for use in inhibiting menin-MLL activity in a patient in need thereof.

[0033f] In another aspect, the present disclosure refers to any one of the compounds provided herein, or a pharmaceutical composition provided herein, for use in inhibiting menin activity in a patient in need thereof.

[0034] In some examples, compounds provided herein are administered to a human.

WHAT IS CLAIMED IS:

1. A compound according to formula (I):



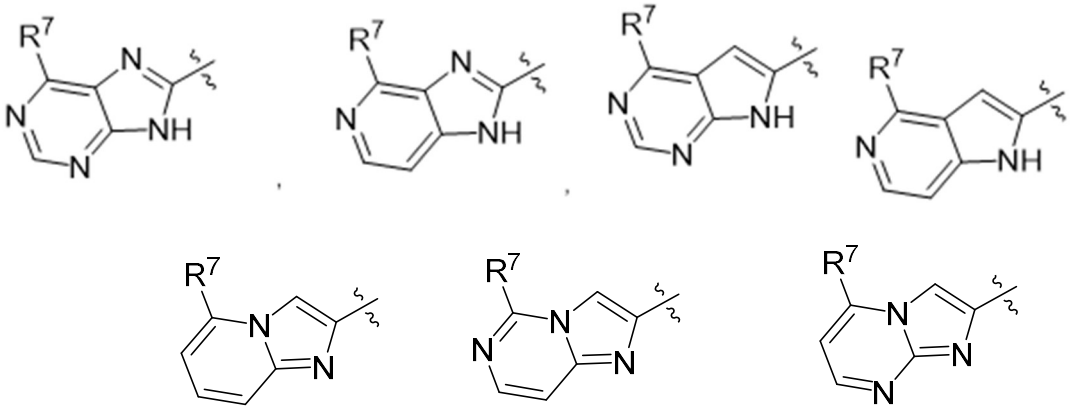
(I)

or a pharmaceutically acceptable salt or a stereoisomer thereof,

wherein:

A is N;

Cy is



wherein

X is $–NR^{3a}$-, $–C(R^{3b})_2$-, or –O-;

Y is a single bond, $–NR^{3a}$-, $–C(R^{3b})_2$-, or –O-;

W is -C(O)-, -S(O)-, or $-S(O)_2$-;

(i) R^1 is H, halo, CN, C_{1-6} alkyl, or C_{1-6} haloalkyl; and

R^2 is CH_2-Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$ or Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$; or

(ii) R^1 is CH_2-Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$ or Cy^2-NHC(O)-$C(R^{6a})$=$C(R^{6b})(R^{6c})$; and

R^2 is H, halo, CN, C_{1-6} alkyl, or C_{1-6} haloalkyl;

Cy^2 is an optionally substituted 4-7 membered heterocycloalkyl ring, phenyl, or pyridyl, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from group consisting of nitrogen, oxygen, and sulfur;

each R^{3a} is independently H or C_{1-6} alkyl;

each R^{3b} is independently H or C_{1-6} alkyl;

each R^{4a} is independently H, halo, CN, C_{1-6} alkyl, C(O)R, $C(O)N(R)_2$, C(O)OR, $N(R)_2$, NRC(O)R, OR, $S(O)_2R$, C_{3-7} cycloalkyl, a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

each R^{4b} is independently H, halo, CN, C_{1-6} alkyl, C(O)R, $C(O)N(R)_2$, C(O)OR, $N(R)_2$, NRC(O)R, OR, $S(O)_2R$, C_{3-7} cycloalkyl, a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocycloalkyl ring has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

each R is independently H, C_{1-6} aliphatic, a saturated or partially unsaturated 4- to 7-membered heterocyclic ring, phenyl, an 8- to 10-membered bicyclic aryl ring, or a 5- or 6-membered heteroaryl ring, wherein the saturated or partially unsaturated 4- to 7-membered heterocyclic has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur; and the 5- or 6-membered heteroaryl ring has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;
or:

two geminal R groups together with the nitrogen atom to which they are attached form a saturated, or partially unsaturated 4- to 7-membered heterocyclic ring, or a 5- or 6-membered heteroaryl ring, wherein the 4- to 7-membered heterocyclic ring or the 5- or 6-membered heteroaryl has 0, 1, 2, or 3 additional heteroatoms, independently selected from the group consisting of nitrogen, oxygen, and sulfur;

R^{6a} is H or C_{1-6} alkyl;

R^{6b} is H or C_{1-6} alkyl; or

R^{6a} and R^{6b}, joined together, form a single bond;

R^{6c} is H or unsubstituted C_{1-6} alkyl; or each of R^{6a}, and R^{6b} is H, and R^{6c} is C_1-C_6 alkyl, wherein the C_{1-6} alkyl is optionally substituted with $N(CH_3)_2$;

R^7 is

(i) independently a 4- to 7-membered heterocycloalkyl ring, phenyl, an 8- to -10-membered bicyclic aryl ring, or 5- or 6-membered heteroaryl ring, wherein the 4- to 7- membered

heterocycloalkyl independently has 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, and each 5- or 6-membered heteroaryl ring independently has 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

(ii) a 4- to 7-membered heterocycloalkyl ring having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, and substituted with Me, Et, or i-Pr;

(iii) pyridyl substituted with halo, hydroxyl, CN, substituted or unsubstituted C_{1-6}alkyl, amino, or alkoxy;

(iv) pyridyl substituted with Me, Et, i-Pr, OH, Cl, F, CF_3, CN, or NH_2; or

(v) imidazoyl substituted with Me, Et, i-Pr, Cl, F, CF_3, or CN;

m is 1, 2, or 3; and

n is 1, 2, 3, or 4.

2. The compound according to claim 1, wherein —XWY- is -CH_2C(O)NH-, -CH_2S(O)NH-, -$CH_2S(O)_2$NH-, -NHC(O)-, -NHC(O)CH_2-, -NHC(O)NH-, -NHS(O)CH_2-, -NHS(O)NH-, -$NHS(O)_2CH_2$-, or -$NHS(O)_2$NH-.

3. The compound according to any one of claims 1-2 or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

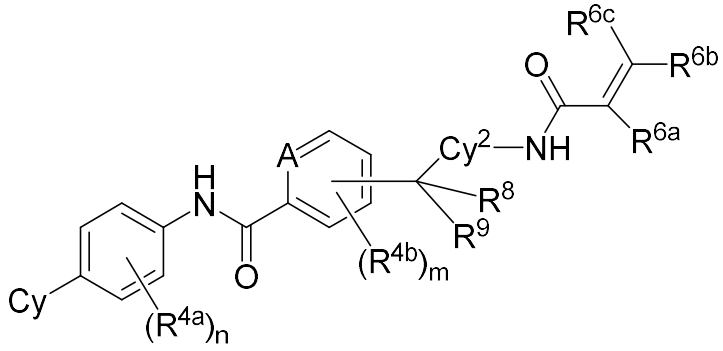
R^7 is pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, imidazoyl, pyridyl, pyrimidinyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, triazolyl, thiazolyl, oxadiazolyl, or thiadiazolyl;

wherein the imidazoyl is optionally substituted with one or more substituents independently selected from the group consisting of F, Cl, CN, CH_3, CF_3, CH_2CH_3, and $CH(CH_3)_2$; and

wherein the pyridyl is optionally substituted with one or more substituents independently selected from the group consisting of F, Cl, CN, CH_3, CF_3, CH_2CH_3, $CH(CH_3)_2$, NH_2, and OH.

4. The compound according to any one of claims 1-3, or a pharmaceutically acceptable salt, or stereoisomer thereof, wherein Cy^2 is optionally substituted azetidinyl, pyrrolidinyl, piperidinyl, azepinyl, phenyl, or pyridyl.

5. The compound according to claim 1, wherein when R^1 or R^2 is CH_2-Cy^2-NHC(O)-$C(R^{6a})=C(R^{6b})(R^{6c})$, the compound of formula (I) is of formula (XXI):



(XXI)

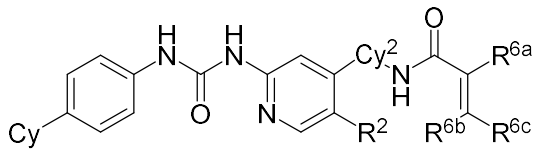
or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

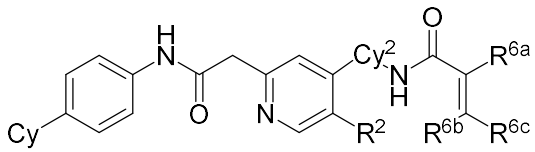
R^8 is H; and

R^9 is H.

6. The compound according to claim 1, wherein the compound is according to formula (IIc) or formula (IId):



(IIc), or

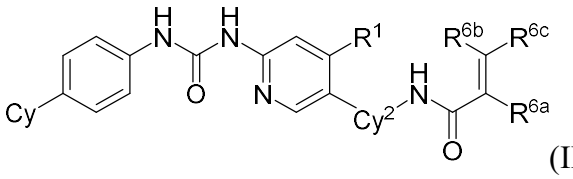


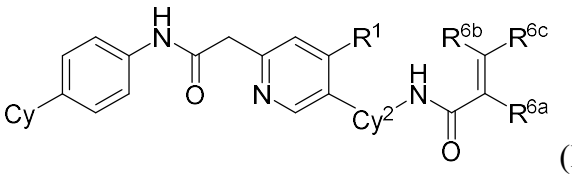
(IId);

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein R^2 is H, F, Cl, CN, CH_3, CH_2CH_3, $CH(CH_3)_2$, or CF_3.

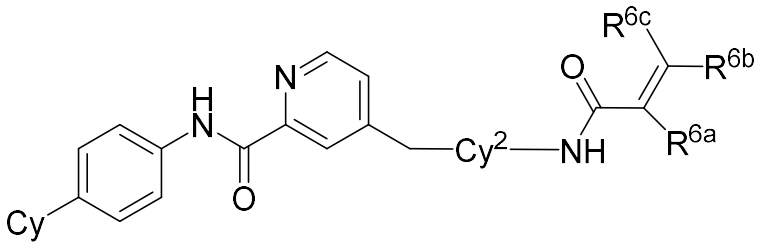
7. The compound according to claim 1, wherein the compound is according to formula (IIIc) or formula (IIId):


(IIIc),

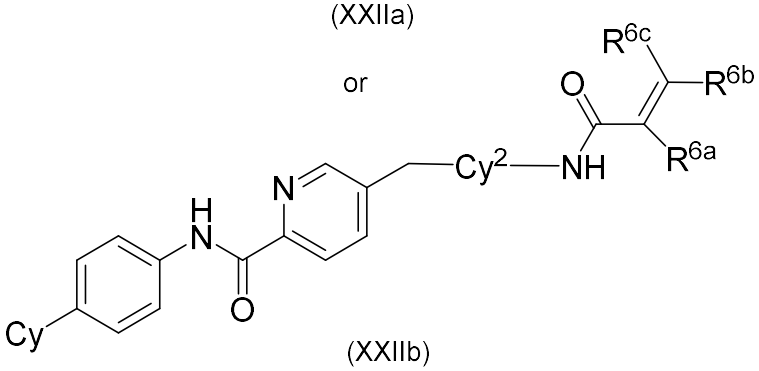

(IIId),

or a pharmaceutically acceptable salt or stereoisomer thereof.

8. The compound according to claim 1, wherein the compound is according to formula (XXIIa) or formula (XXIIb):

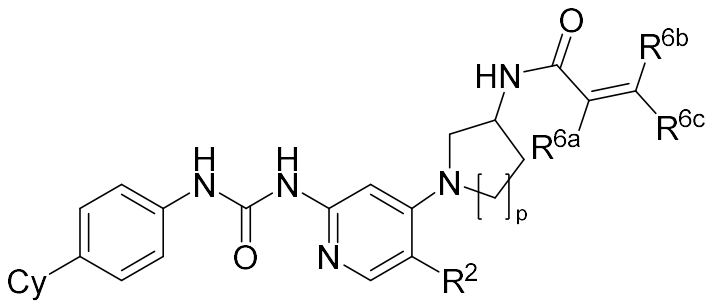

(XXIIa)

or

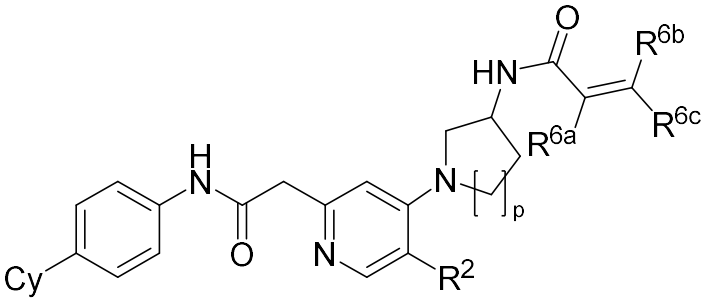

(XXIIb)

or a pharmaceutically acceptable salt or stereoisomer thereof.

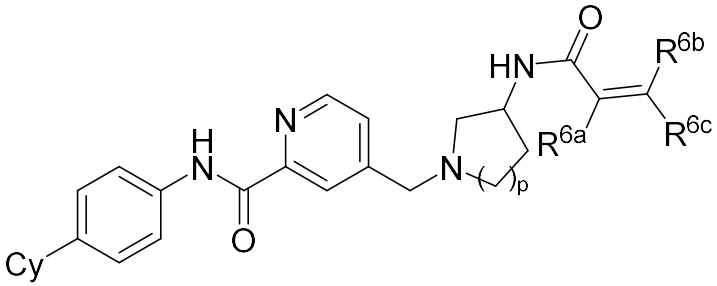
9. The compound according to claim 1, wherein the compound is according to formula (IVa), formula (IVb), formula (XXIIIa), or formula (XXIIIb):



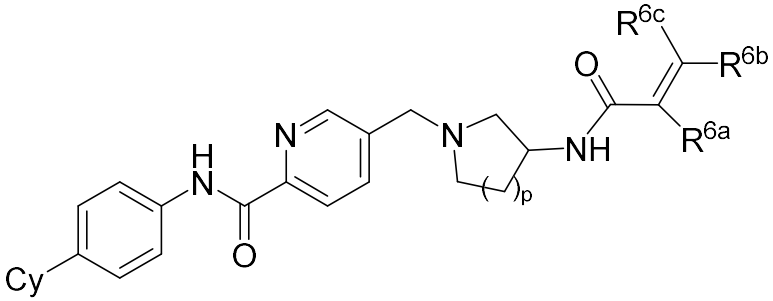
(IVa);



(IVb);



(XXIIIa); or

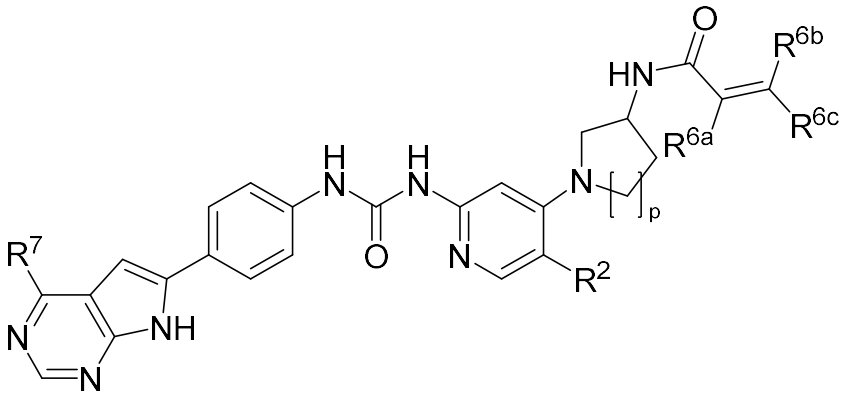


(XXIIIb),

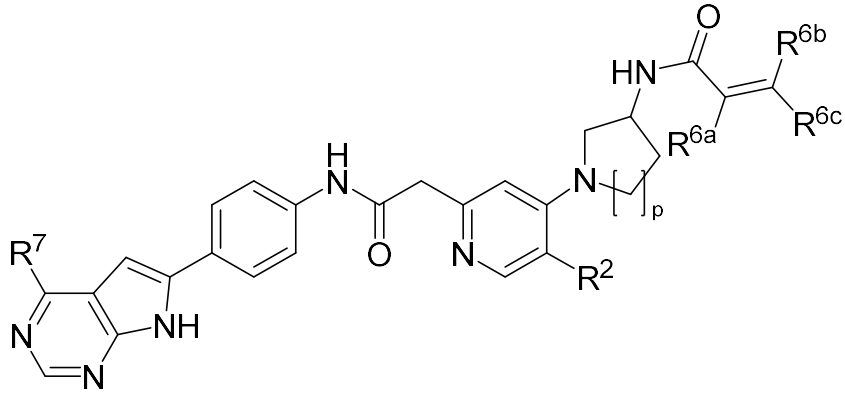
or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein p is 0, 1, 2, or 3.

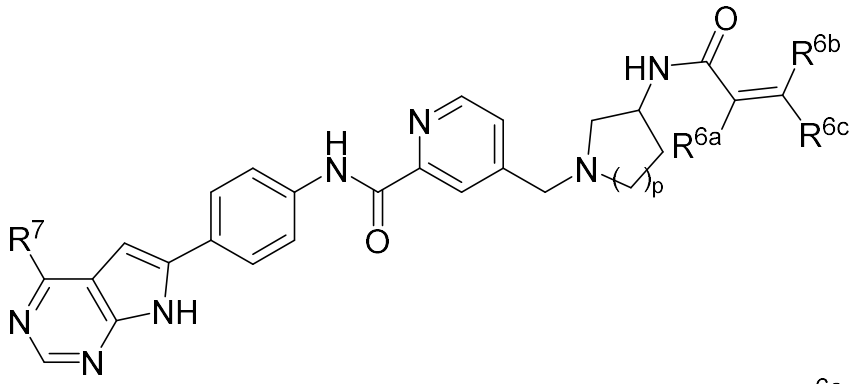
10. The compound according to claim 1, wherein the compound is according to formula (Va), formula (Vb), formula (XXIVa), or formula (XXIVb):



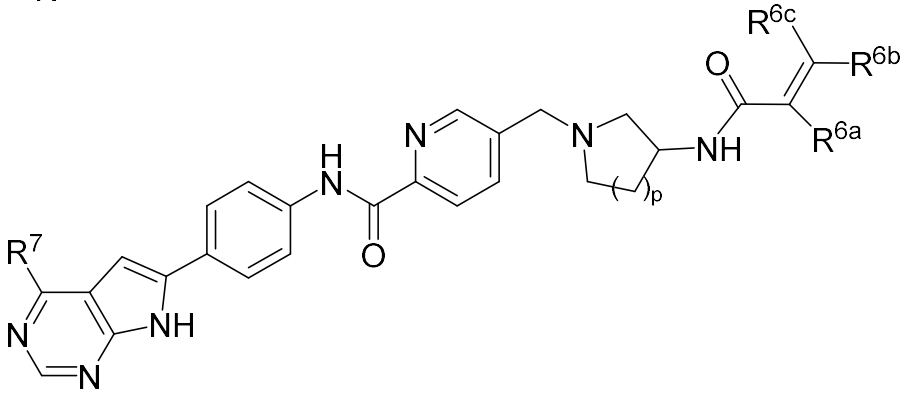
(Va);



(Vb);



(XXIVa); or



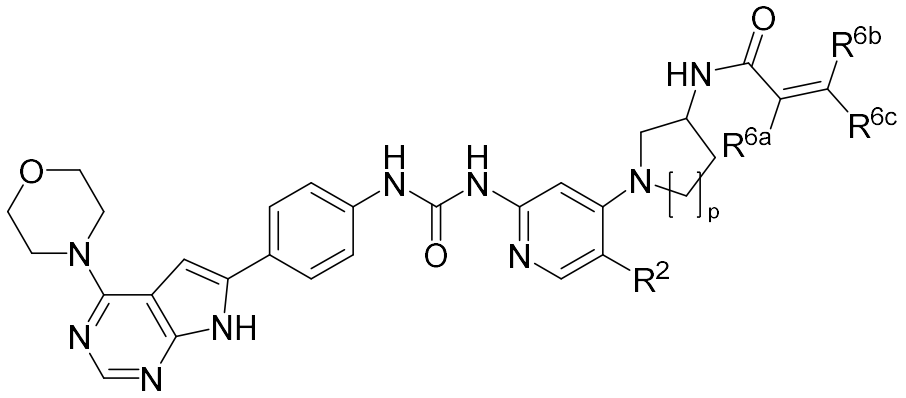
(XXIVb),

or a pharmaceutically acceptable salt or stereoisomer thereof,

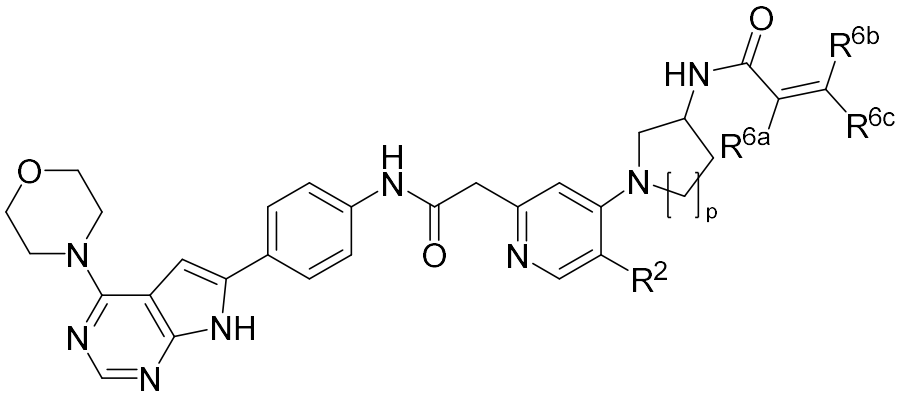
wherein p is 0, 1, 2, or 3.

11. The compound according to any one of claims 1-10, wherein R^7 is pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, triazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, pyridyl, or pyrimidinyl.

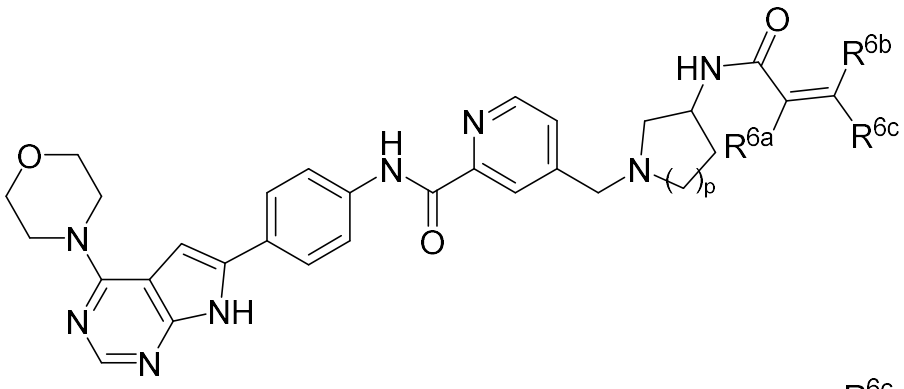
12. The compound according to claim 1, wherein the compound is according to formula (VIa), formula (VIb), formula (XXVa), or formula (XXVb):



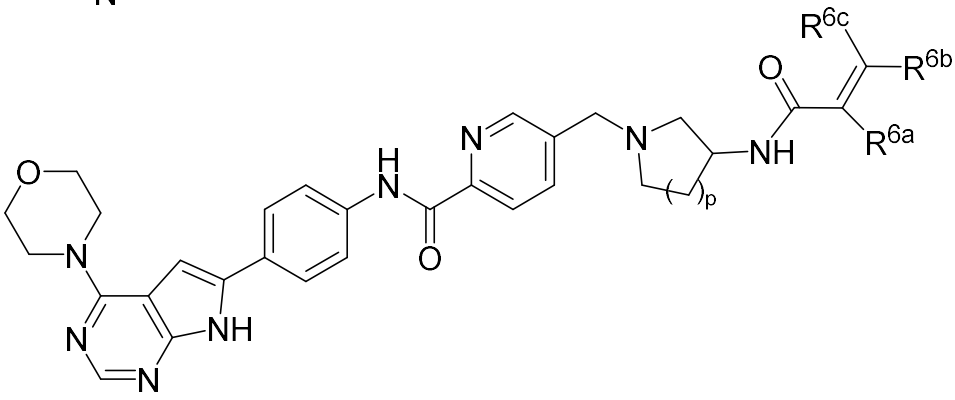
(VIa);



(VIb);



(XXVa); or

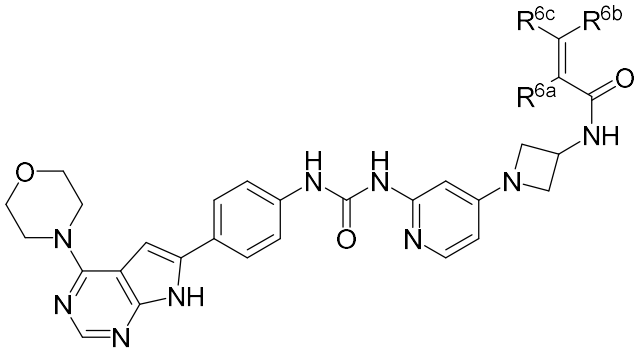


(XXVb),

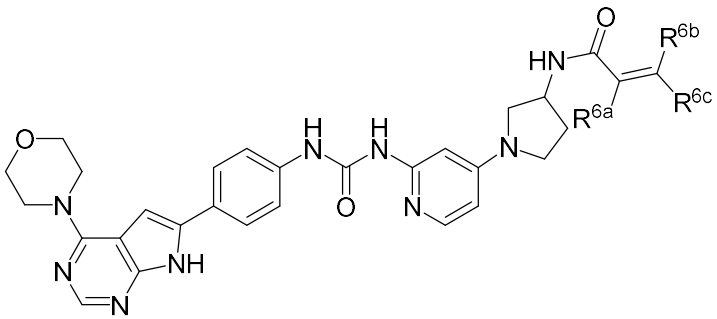
or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein p is 0, 1, 2, or 3.

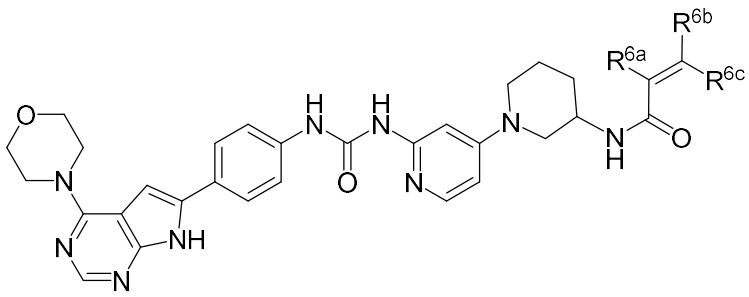
13. The compound according to claim 1, wherein the compound is according to formula (VIIa), formula (VIIb), formula (VIIc), formula (VIIIa), formula (VIIIb), formula (VIIIc), formula (XXVIa), formula (XXVIb), or formula (XXVIc):



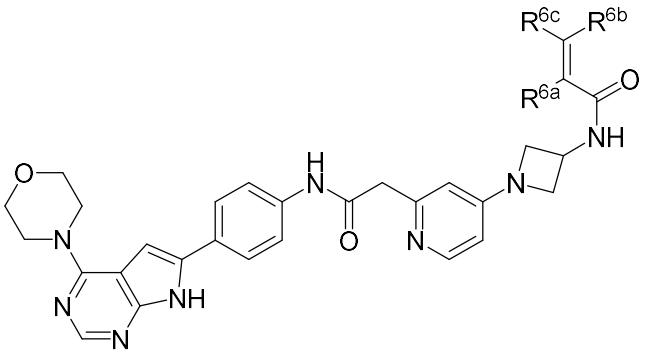
(VIIa);



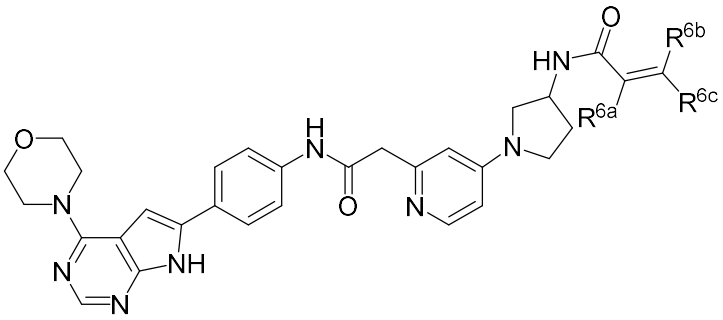
(VIIb);



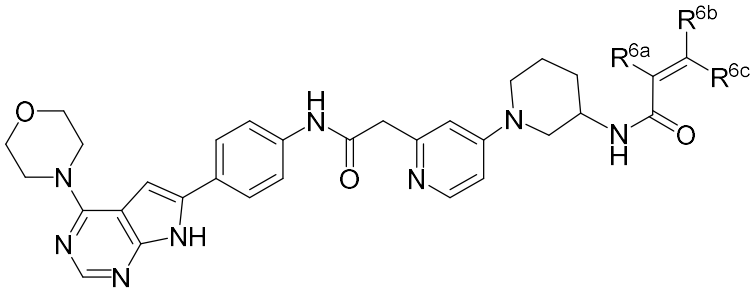
(VIIc);



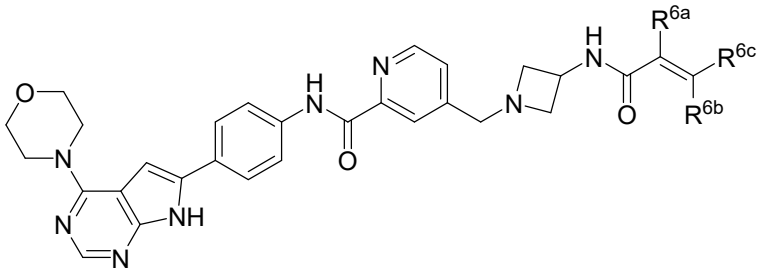
(VIIIa);



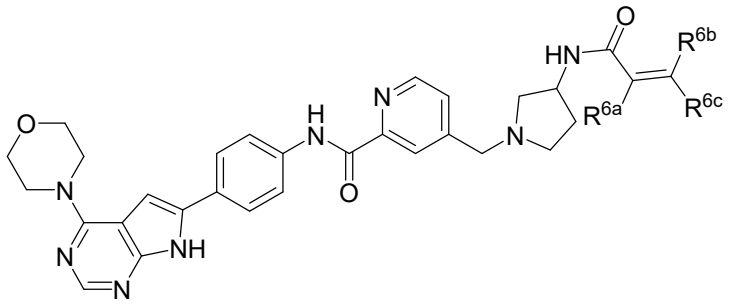
(VIIIb);



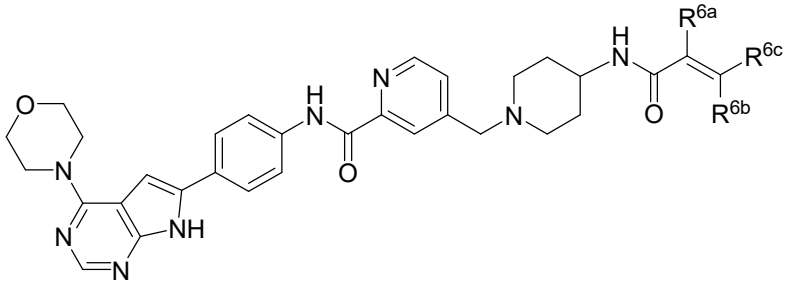
(VIIIc);



(XXVIa);



(XXVIb); or



(XXVIc),

or a pharmaceutically acceptable salt or stereoisomer thereof.

14. The compound according to any one of claims 1-13, or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

i) R^{6a} is H;

R^{6b} is H; and

R^{6c} is H; or

ii) R^{6a} is H;

R^{6b} is H; and

R^{6c} is CH_3 or CH_2CH_3; or

iii) R^{6a} is H;

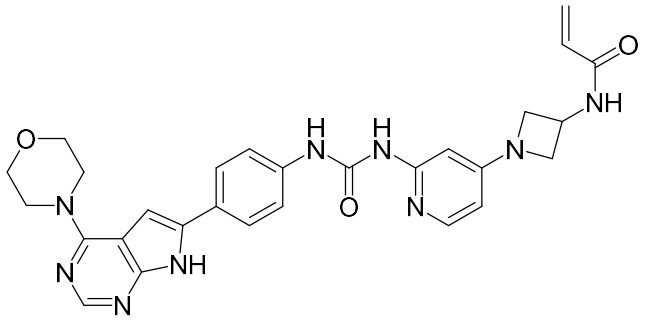
R^{6b} is H; and

R^{6c} is $CH_2N(CH_3)_2$; or

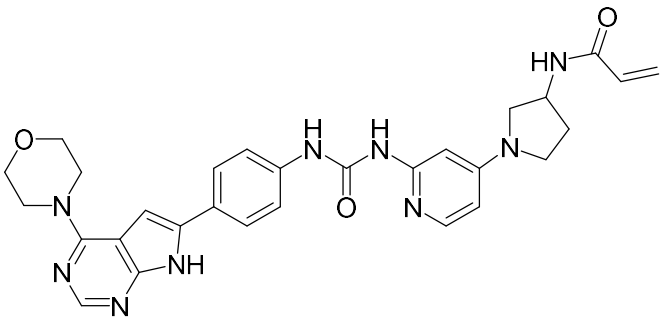
iv) R^{6a}, and R^{6b}, joined together, form a single bond; and

R^{6c} is CH_3.

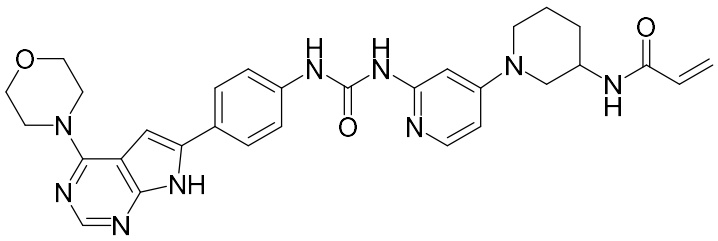
15. The compound according to claim 1, wherein the compound is according to formula (IXa), formula (IXb), formula (IXc), formula (Xa), formula (Xb), formula (Xc), formula (XIa), formula (XIb), formula (XIc), formula (XIIa), formula (XIIb), or formula (XIIc):



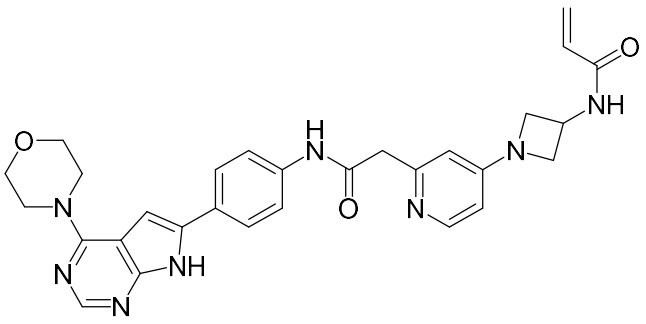
(IXa);



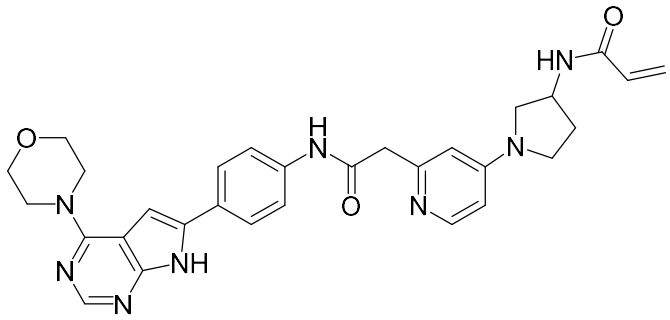
(IXb);



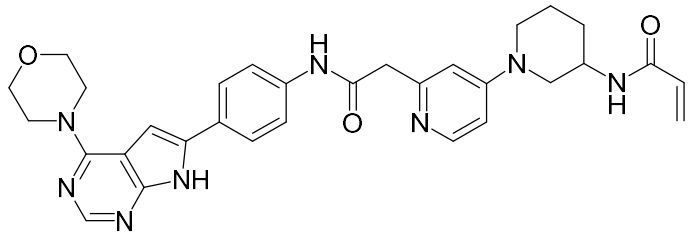
(IXc);



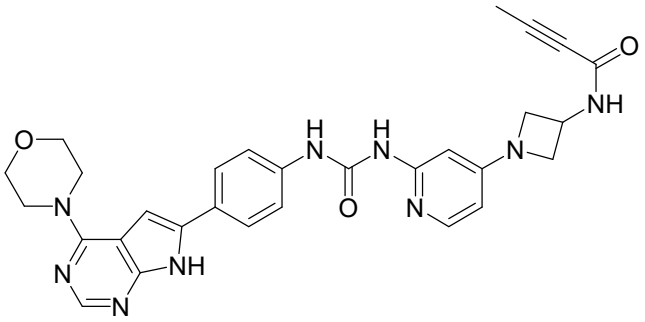
(Xa);



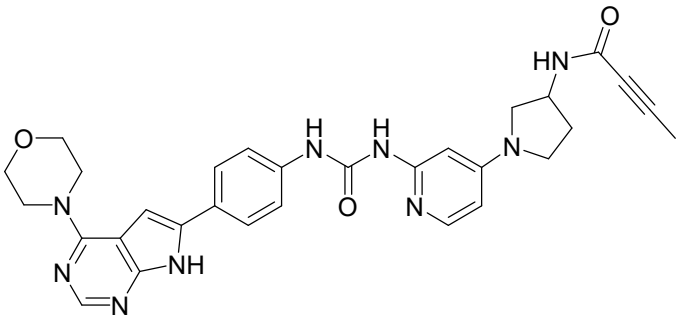
(Xb);



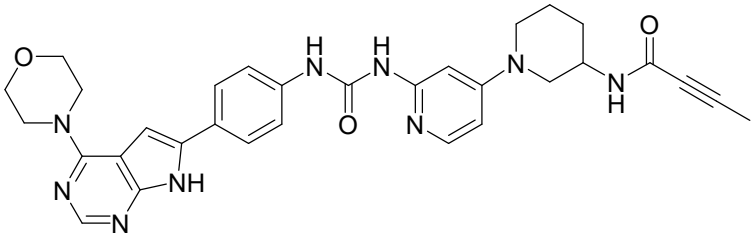
(Xc);



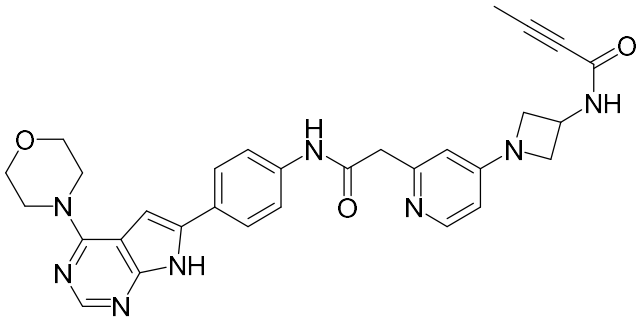
(XIa);



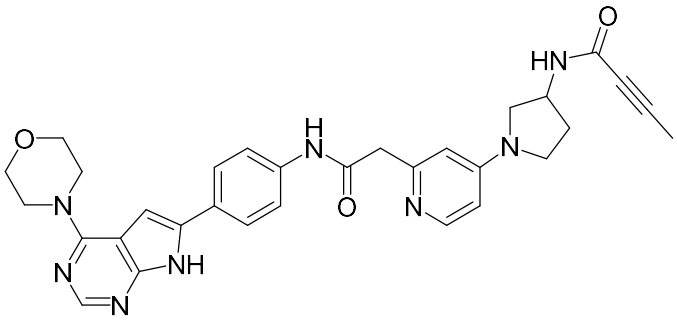
(XIb);



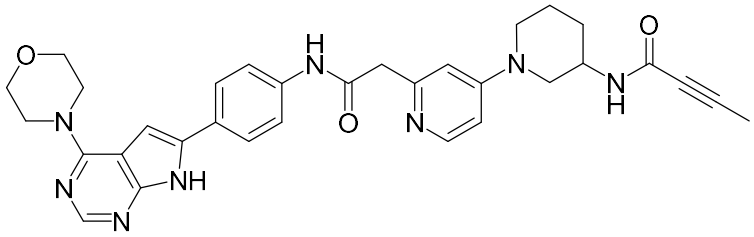
(XIc);



(XIIa);



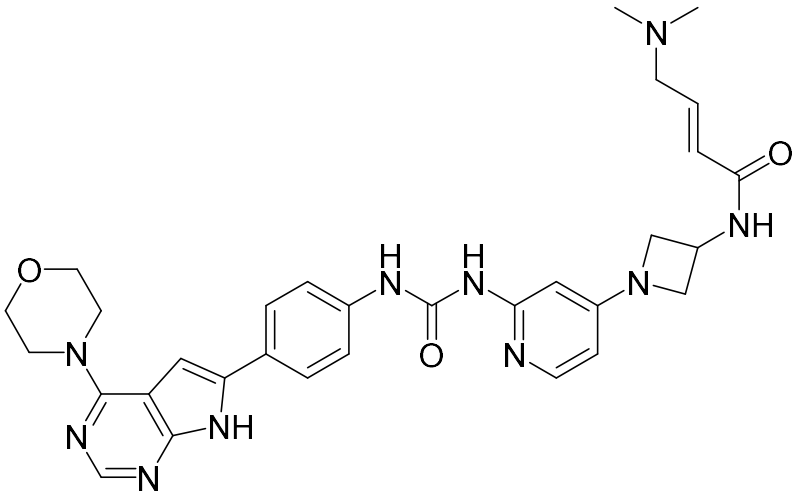
(XIIb); or



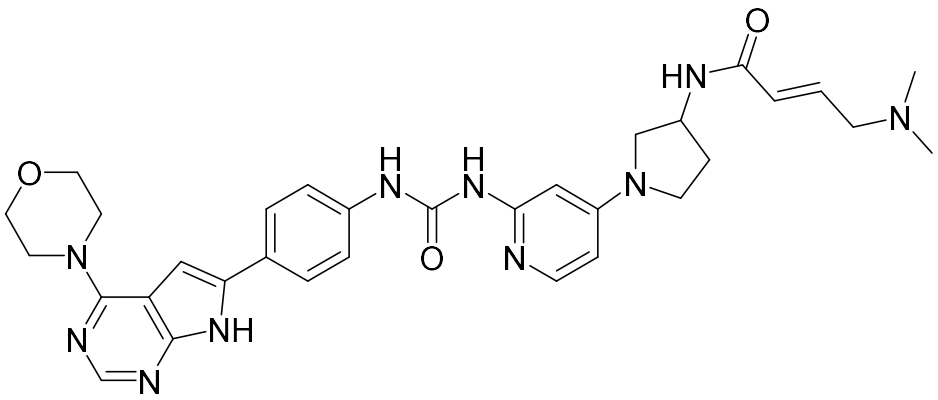
(XIIc),

or a pharmaceutically acceptable salt or stereoisomer thereof.

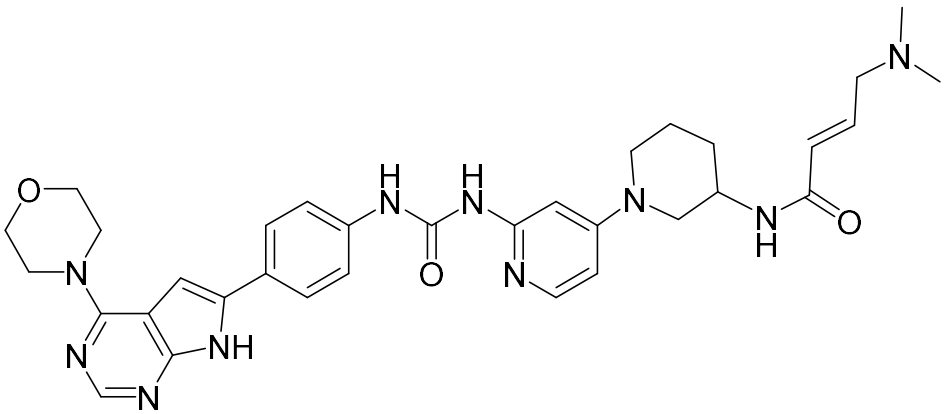
16. The compound according to claim 1, wherein the compound is according to formula (XIIIa), formula (XIIIb), formula (XIIIc), formula (XIVa), formula (XIVb), or formula (XIVc):



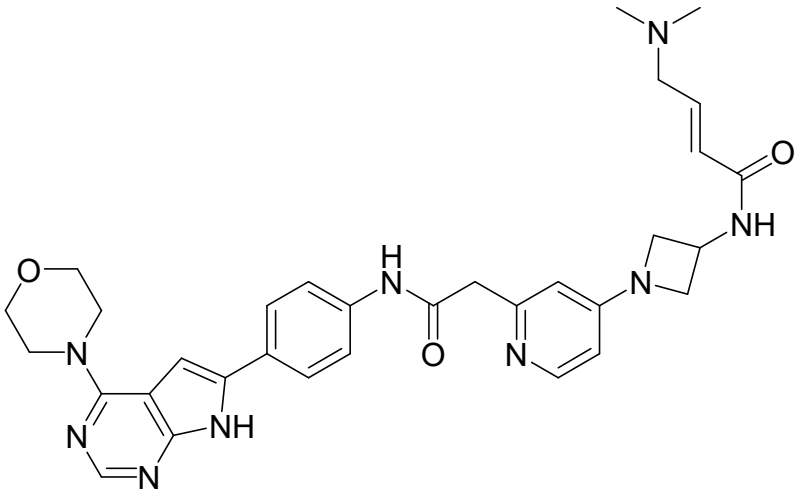
(XIIIa);



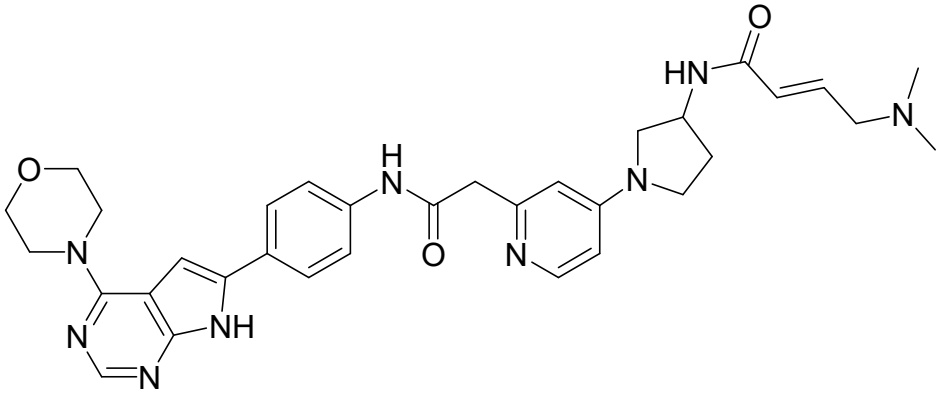
(XIIIb);



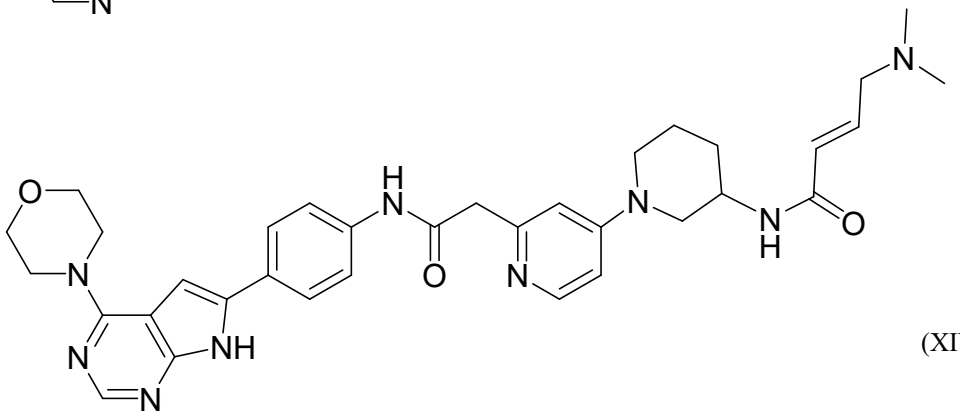
(XIIIc);



(XIVa);



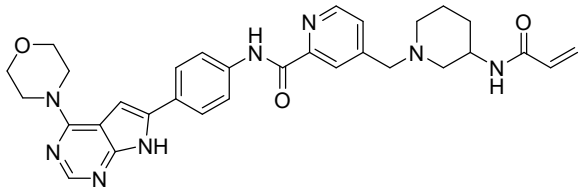
(XIVb); or



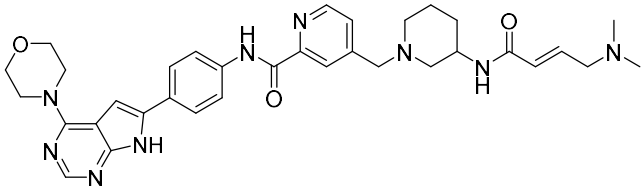
(XIVc),

or a pharmaceutically acceptable salt or stereoisomer thereof.

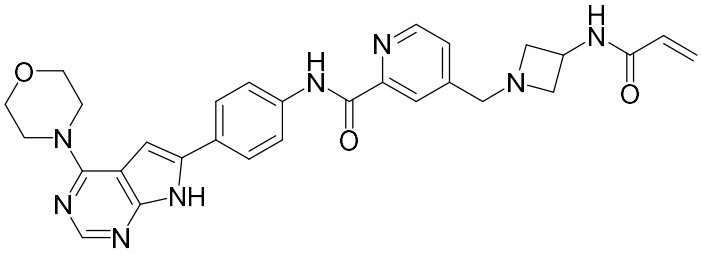
17. The compound according to claim 1, wherein the compound is according to formula (XVI), formula (XVII), formula (XXVIIa), formula (XXVIIb), formula (XXVIIc), formula (XXVIIIa), formula (XXVIIIb), or formula (XXVIIIc):



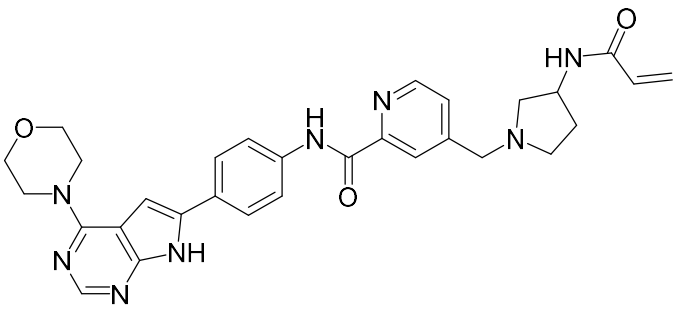
(XVI);



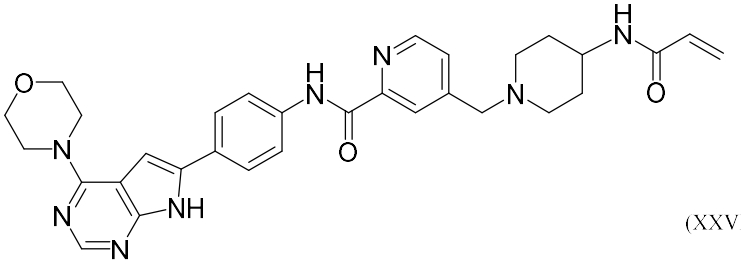
(XVII);



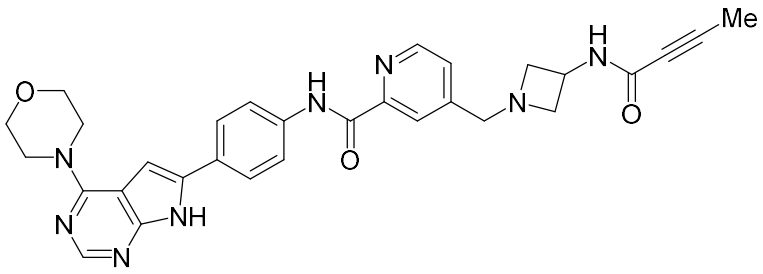
(XXVIIa);



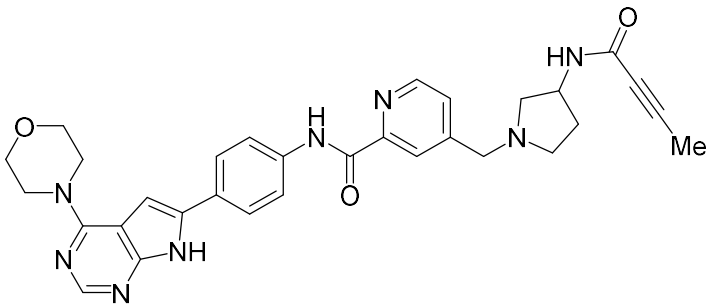
(XXVIIb);



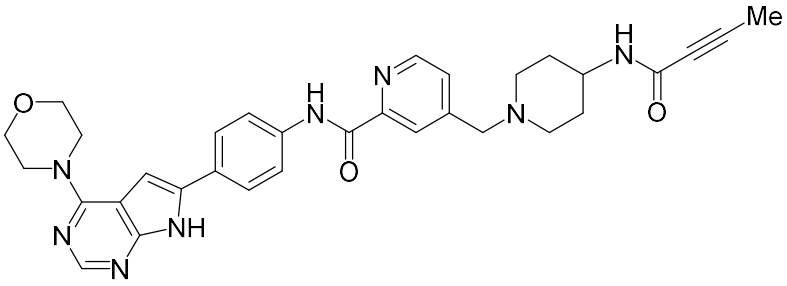
(XXVIIc);



(XXVIIIa);



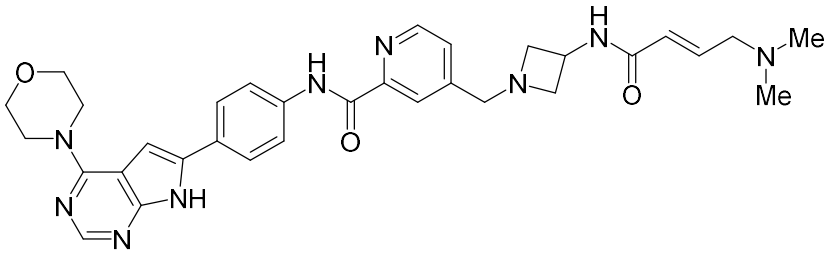
(XXVIIIb); or



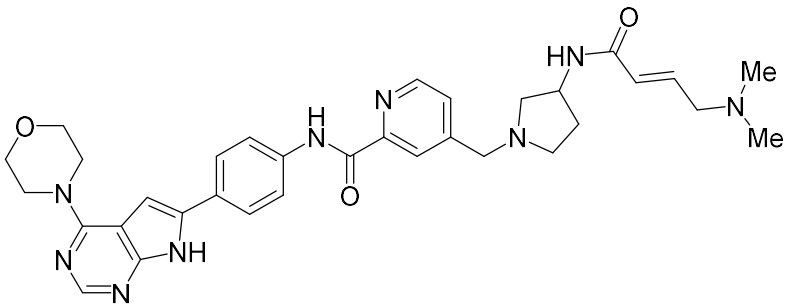
(XXVIIIc),

or a pharmaceutically acceptable salt or stereoisomer thereof.

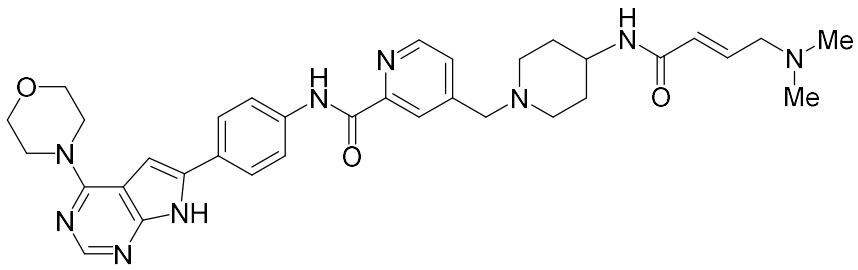
18. The compound according to claim 1, wherein the compound is according to formula (XXIXa), formula (XXIXb), or formula (XXIXc):



(XXIXa);



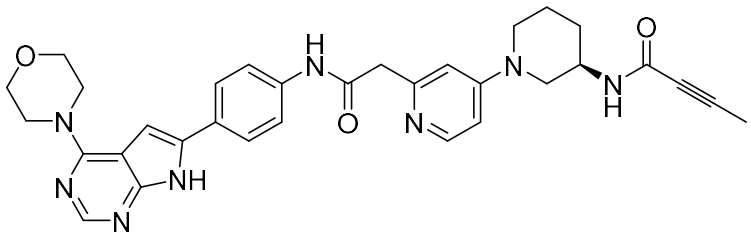
(XXIXb); or



(XXIXc),

or a pharmaceutically acceptable salt or stereoisomer thereof.

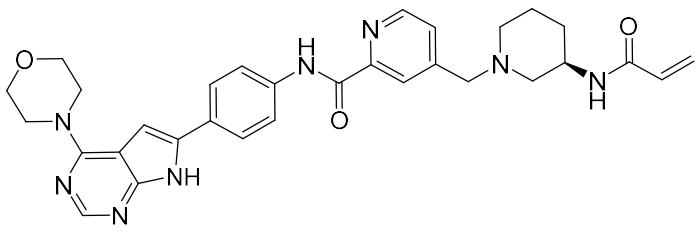
19. The compound according to claim 1, wherein the compound is:



Compound 3

or a pharmaceutically acceptable salt thereof.

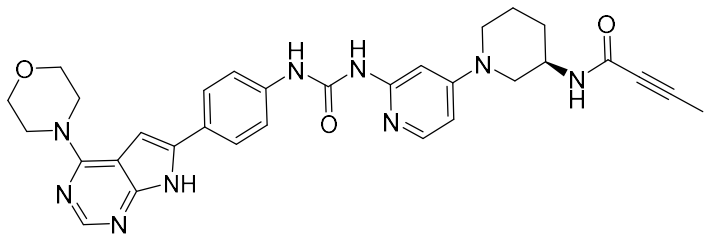
20. The compound according to claim 1, wherein the compound is:



Compound 10

or a pharmaceutically acceptable salt thereof.

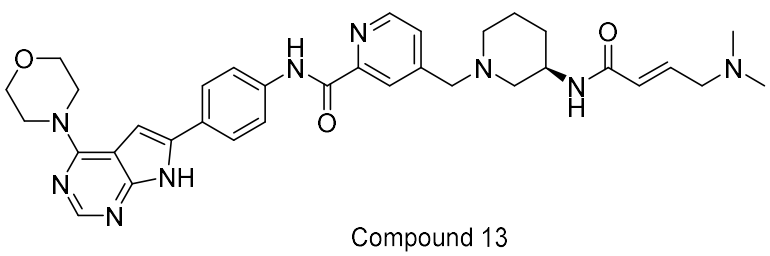
21. The compound according to claim 1, wherein the compound is:



Compound 6

or a pharmaceutically acceptable salt thereof.

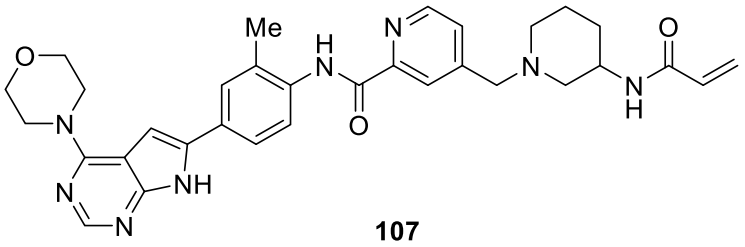
22. The compound according to claim 1, wherein the compound is:



Compound 13

or a pharmaceutically acceptable salt thereof.

23. The compound according to claim 1, wherein the compound is:



107

or a pharmaceutically acceptable salt or stereoisomer thereof.

24. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-23 or a pharmaceutically acceptable salt or stereoisomer thereof.

25. The pharmaceutical composition of claim 24 that is formulated for a route of administration selected from oral administration, parenteral administration, buccal administration, nasal administration, topical administration, or rectal administration.

26. Use of any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, in the manufacture of a medicament for inhibiting menin-MLL activity in a patient in need thereof, wherein the patient has an autoimmune disease or an autoimmune condition.

27. Use of any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, in the manufacture of a medicament for the treatment of cancer.

28. The use of claim 27, wherein the cancer is a B-cell proliferative disorder.

29. The use of claim 28, wherein the B-cell proliferative disorder is diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic leukemia, lymphoid leukemia, ALL, soft tissue tumor, Glioblastoma, pancreatic tumor or renal cell cancer.

30. Any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, for use in treating an autoimmune disease or an autoimmune condition.

31. Any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, for use in treating cancer.

32. Any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, for use in inhibiting menin-MLL activity in a patient in need thereof.

33. Any one of the compounds according to claims 1-23, or a pharmaceutical composition thereof of claim 24 or 25, for use in inhibiting menin activity in a patient in need thereof.