

the clinical potential of non-conjugated BH3 mimetics combinations is still to be demonstrated. Therefore, there is need to find disease-modifying agents therapeutically targeting Bcl-2 family proteins (*e.g.*, Bcl-2, Bcl-xL, Mcl-1) or upstream and/or downstream proteins in an apoptotic signaling pathway in oncology and in the field of immune and autoimmune diseases.

SUMMARY

[9a] In one aspect, the present disclosure provides an antibody-drug conjugate comprising an antibody or an antigen-binding fragment thereof covalently linked to two antineoplastic payloads through a dual linker, wherein at least one antineoplastic payload is a BH3 mimetic, and wherein the dual linker has one attachment point connected to the antibody and two attachment points to the two antineoplastic payloads and wherein the two antineoplastic payloads can be the same or different.

[9b] In another aspect, the present disclosure provides a composition comprising multiple copies of the antibody-drug conjugate as described herein, wherein the average *a* of the antibody-drug conjugates in the composition is from about 1 to about 8, *e.g.*, about 1 to about 6, about 1 to about 4, or about 1 to about 2,

[9c] In yet another aspect, the present disclosure provides a pharmaceutical composition comprising the antibody-drug conjugate as described herein or the composition as described herein, and a pharmaceutically acceptable carrier.

[9d] In yet another aspect, the present disclosure provides the antibody-drug conjugate as described herein, the composition as described herein, or the pharmaceutical composition as described herein, for use in:

- (i) treating a subject having or suspected of having a cancer,
 - (ii) reducing or inhibiting the growth of a tumor in a subject;
 - (iii) reducing or inhibiting a hematological cancer in a subject; or
 - (iv) reducing or slowing the expansion of a cancer cell population in a subject,
- optionally wherein

(a) the cancer is a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(b) the tumor is a breast cancer, gastric cancer, bladder cancer, brain cancer, cervical cancer, colorectal cancer, esophageal cancer, hepatocellular cancer, melanoma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(c) the hematological cancer is chronic lymphocytic leukemia (CLL), follicular lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphoma or myelodysplasia syndrome (MDS); or

(d) the cancer cell population is from a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer.

[9e] In yet another aspect, the present disclosure provides use of the antibody-drug conjugate as described herein, the composition as described herein, or the pharmaceutical composition as described herein, in the manufacture of a medicament for:

- (i) treating a subject having or suspected of having a cancer,
- (ii) reducing or inhibiting the growth of a tumor in a subject;
- (iii) reducing or inhibiting a hematological cancer in a subject; or
- (iv) reducing or slowing the expansion of a cancer cell population in a subject, optionally wherein

(a) the cancer is a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(b) the tumor is a breast cancer, gastric cancer, bladder cancer, brain cancer, cervical cancer, colorectal cancer, esophageal cancer, hepatocellular cancer, melanoma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(c) the hematological cancer is chronic lymphocytic leukemia (CLL), follicular lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphoma or myelodysplasia syndrome (MDS); or

(d) the cancer cell population is from a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer.

[10] In a first embodiment, the present disclosure provides an antibody-drug conjugate comprising an antibody or an antigen-binding fragment thereof covalently linked to two antineoplastic payloads through a dual linker, wherein at least one antineoplastic payload is a BH3 mimetic, and wherein the dual linker has one attachment point connected to the antibody and two attachment points to the two antineoplastic payloads and wherein the two antineoplastic payloads can be the same or different. In some embodiments, one antineoplastic payload is a BH3 mimetic and the other antineoplastic payload is an antineoplastic non-BH3 mimetic. In some embodiments, the antineoplastic non-BH3 mimetic is a topoisomerase 1 inhibitor or an anti-mitotic drug. In some embodiments, the topoisomerase 1 inhibitor is selected from topotecan, exatecan, deruxtecan and SN-38. In some embodiments, the anti-mitotic drug is monomethyl auristatin E (MMAE) or a taxane. In some embodiments, the taxane is selected from docetaxel, paclitaxel, or cabazitaxel. In some embodiments, said two antineoplastic payloads are two BH3 mimetics. In some embodiments, the BH3 mimetic is selected from a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor. In some embodiments, the BH3 mimetic of said two antineoplastic payloads are the same. In some embodiments, the BH3 mimetic of said two antineoplastic payloads are different. In some embodiments, the antineoplastic payloads in the antibody-drug conjugate of the present disclosure are defined as: (i) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a Bcl-2 inhibitor; (ii) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a Bcl-xL inhibitor; or (iii) one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is a Bcl-xL inhibitor. In some embodiments, one antineoplastic payload is a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor, and the other antineoplastic payload is a topoisomerase 1 inhibitor or an anti-mitotic drug. In some embodiments, one antineoplastic payload is a Bcl-xL inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor. In some embodiments, one antineoplastic payload is a Bcl-xL inhibitor and the other antineoplastic payload is an anti-mitotic drug. In some embodiments, one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor. In some embodiments, one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is an anti-mitotic drug. In some embodiments, one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor. In some

embodiments, one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is an anti-mitotic drug.

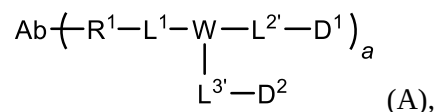
[11] In a second embodiment, the present disclosure provides antibody-drug conjugate of the first

CLAIMS

1. An antibody-drug conjugate comprising an antibody or an antigen-binding fragment thereof covalently linked to two antineoplastic payloads through a dual linker, wherein at least one antineoplastic payload is a BH3 mimetic, and wherein the dual linker has one attachment point connected to the antibody and two attachment points to the two antineoplastic payloads and wherein the two antineoplastic payloads can be the same or different.
2. The antibody-drug conjugate of claim 1, wherein one antineoplastic payload is a BH3 mimetic and the other antineoplastic payload is an antineoplastic non-BH3 mimetic.
3. The antibody-drug conjugate of claim 2, wherein the antineoplastic non-BH3 mimetic is a topoisomerase 1 inhibitor or an anti-mitotic drug; optionally wherein:
 - (i) the topoisomerase 1 inhibitor is selected from topotecan, exatecan, deruxtecan and SN-38; or
 - (ii) the anti-mitotic drug is monomethyl auristatin E (MMAE) or a taxane; preferably wherein the taxane is docetaxel, paclitaxel, or cabazitaxel.
4. The antibody-drug conjugate of claim 1, wherein:
 - (i) said two antineoplastic payloads are two BH3 mimetics;
 - (ii) the BH3 mimetic is selected from a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor;
 - (iii) the BH3 mimetics of said two antineoplastic payloads are the same;
 - (iv) the BH3 mimetics of said two antineoplastic payloads are different;
 - (v) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a Bcl-2 inhibitor;
 - (vi) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a Bcl-xL inhibitor; or
 - (vii) one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is a Bcl-xL inhibitor.

5. The antibody-drug conjugate of any one of claims 1 to 3, wherein:
- (i) one antineoplastic payload is a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor, and the other antineoplastic payload is a topoisomerase 1 inhibitor or an anti-mitotic drug;
 - (ii) one antineoplastic payload is a Bcl-xL inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor;
 - (iii) one antineoplastic payload is a Bcl-xL inhibitor and the other antineoplastic payload is an anti-mitotic drug;
 - (iv) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor;
 - (v) one antineoplastic payload is a Mcl-1 inhibitor and the other antineoplastic payload is an anti-mitotic drug;
 - (vi) one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is a topoisomerase 1 inhibitor; or
 - (vii) one antineoplastic payload is a Bcl-2 inhibitor and the other antineoplastic payload is an anti-mitotic drug.

6. The antibody-drug conjugate of claim 1, wherein the antibody-drug conjugate is represented by Formula (A):



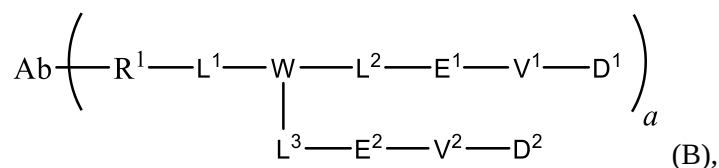
wherein:

- Ab is an antibody or an antigen-binding fragment thereof;
- R¹ is an attachment group;
- L¹ is a bridging spacer;
- W is branching moiety;
- L^{2'} and L^{3'}, are each independently a linker;
- D¹ and D² are each independently an antineoplastic payload, wherein at least one of D¹ and D² is a BH3 mimetic; and
- a* is an integer from 1 to 16.

7. The antibody-drug conjugate of claim 6, wherein:
- (i) D¹ and D² are each independently a BH3 mimetic; and/or
 - (ii) *a* is an integer from 1 to 6 or from 1 to 4 or *a* is 1 or 2 or *a* is determined by liquid chromatography-mass spectrometry (LC-MS); and/or

- (iii) each of $L^{2'}$ and $L^{3'}$ comprises a cleavable group, optionally wherein:
- (a) at least one cleavable group comprises a glucuronide group, pyrophosphate group, a peptide group, and/or a self-immolative group; or
 - (b) at least one cleavable group comprises a pyrophosphate group, a peptide group, and/or a self-immolative group.

8. The antibody-drug conjugate of claim 1 or 6, wherein the antibody-drug conjugate is represented by Formula (B):



wherein:

- Ab is an antibody or an antigen-binding fragment thereof;
- R^1 is an attachment group;
- L^1 is a bridging spacer;
- W is N or CR^w ; wherein R^w is H or C_{1-6} alkyl;
- L^2 and L^3 are each independently a connecting spacer;
- E^1 and E^2 are each independently an enzyme cleavage element or a hydrophilic moiety;
- V^1 and V^2 each independently comprise i) a self immolative group, ii) an enzyme cleavage element, or iii) a self immolative group and an enzyme cleavage element;
- D^1 and D^2 are each independently an antineoplastic payload, wherein at least one of D^1 and D^2 is a BH3 mimetic; and
- a is an integer from 1 to 16.

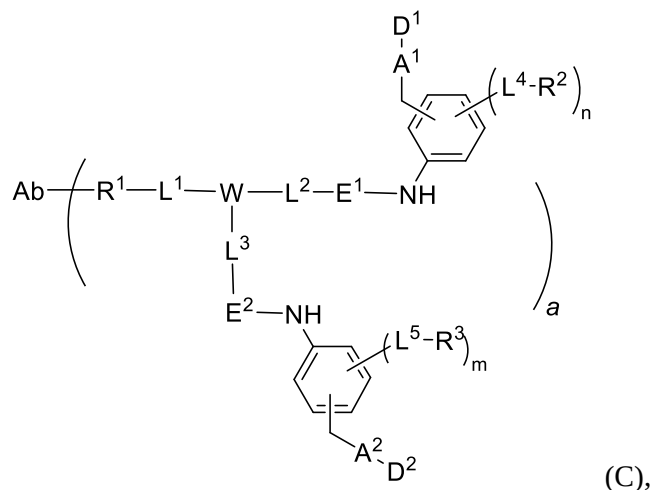
9. The antibody-drug conjugate of claim 8, wherein:

- (i) V^1 and V^2 are each independently (a) a self immolative group or (b) an enzyme cleavage element; and D^1 and D^2 are each independently a BH3 mimetic;
- (ii) V^1 and V^2 each independently comprises a phosphate, a pyrophosphate and/or a self-immolative group;
- (iii) V^1 and V^2 each independently comprises a self-immolative group;
- (iv) V^1 and V^2 each independently comprises a self-immolative group comprising $-\text{CH}_2\text{O}-$, $-\text{OC}(=\text{O})-$, $-\text{NH}-\text{CH}_2-$, para-aminobenzyl-carbamate, para-aminobenzyl-ammonium, para-amino-(sulfo)benzyl-ammonium, para-amino-(sulfo)benzyl-carbamate, para-amino-(alkoxy-PEG-alkyl)benzyl-

carbamate, para-amino-(polyhydroxycarboxytetrahydropyranyl)alkyl-benzyl-carbamate, or para-amino-(polyhydroxycarboxytetrahydropyranyl)alkyl-benzyl-ammonium; or

(v) V¹ and V² each independently comprises a group comprising para-aminobenzyl-phosphate or para-aminobenzyl-pyrophosphate.

10. The antibody-drug conjugate of any one of claims 1, 6, and 8, wherein the antibody-drug conjugate is represented by Formula (C):



or pharmaceutically acceptable salt thereof, wherein

Ab is an antibody or an antigen-binding fragment thereof;

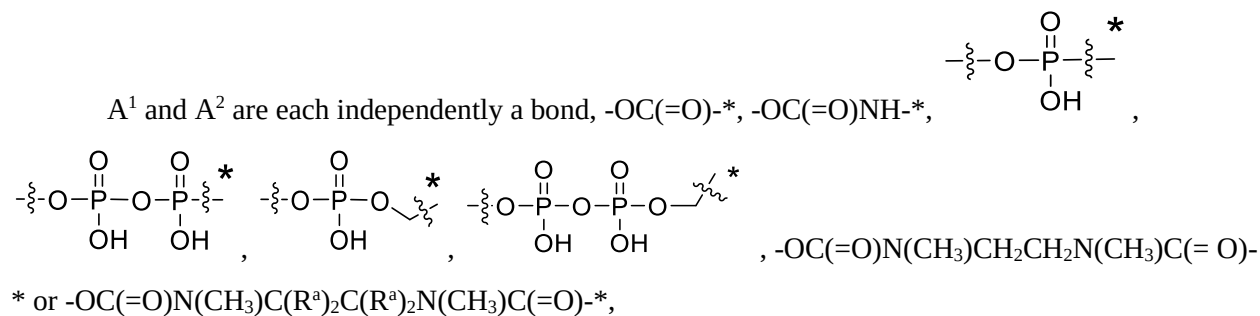
R¹ is an attachment group;

L¹ is a bridging spacer;

W is N or CR^w; wherein R^w is H or C₁₋₆alkyl;

L² and L³ are each independently a connecting spacer;

E¹ and E² are each independently a peptide group comprising 1 to 6 amino acids, wherein said peptide group is optionally substituted by a hydrophilic group;



wherein each R^a is independently selected from H, C₁-C₆ alkyl, and C₃-C₈ cycloalkyl and the * of A¹ or A² indicates the point of attachment to D¹ or D²;

D¹ and D² are each independently an antineoplastic payload, wherein at least one of D¹ and D² is a BH3 mimetic; preferably wherein D¹ and D² are each independently a BH3 mimetic;

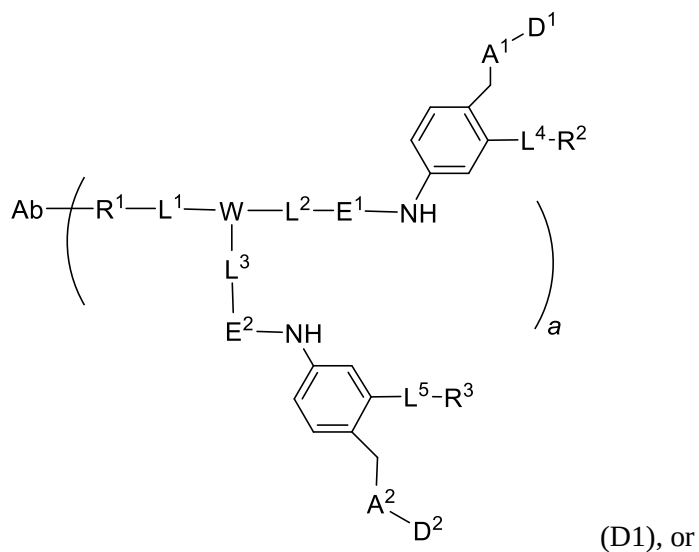
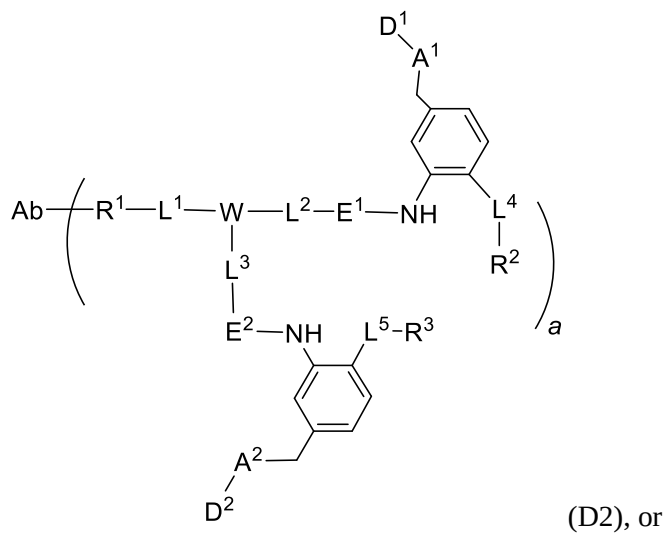
L⁴ and L⁵ are each independently a spacer moiety;

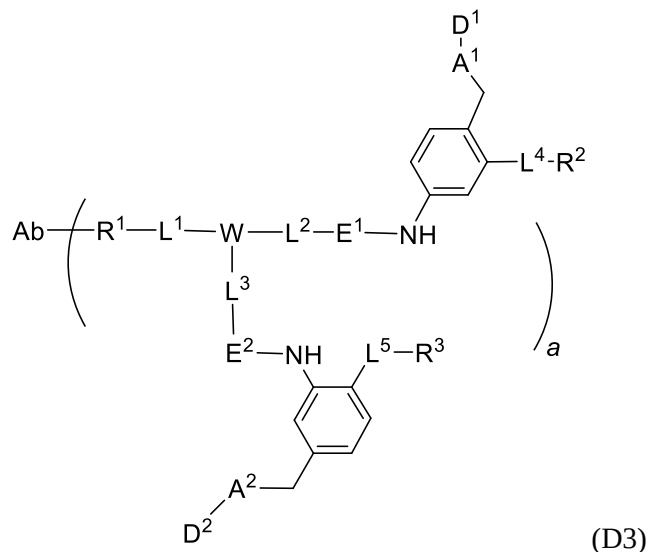
R² and R³ are each independently a hydrophilic group or an enzyme cleavage element;

m and n are each independently 0 or 1; and

a is an integer from 1 to 16.

11. The antibody-drug conjugate of any one of claims 1, 6, 8, and 10, wherein the antibody-drug conjugate is represented by Formula (D1), (D2), or (D3):





or pharmaceutically acceptable salt thereof, wherein D^1 and D^2 are each independently an antineoplastic payload, wherein at least one of D^1 and D^2 is a BH3 mimetic; for Formula (D2), R^2 and R^3 are each independently an enzyme cleavage element; and for Formula (D3), R^2 is a hydrophilic group and R^3 is an enzyme cleavage element; preferably wherein D^1 and D^2 are each independently a BH3 mimetic; optionally wherein for Formula (D1), R^2 and R^3 are each independently a hydrophilic group.

12. The antibody-drug conjugate of any one of claims 6 to 11, wherein:

(i) a is an integer from 1 to 8, 1 to 6, 1 to 4, or a is 1 or 2, optionally wherein a is determined by liquid chromatography-mass spectrometry (LC-MS);

(ii) the attachment group is formed by a reaction comprising at least one reactive group;

(iii) the attachment group is formed by reacting:

a first reactive group that is attached to the linker, and

a second reactive group that is attached to the antibody or is an amino acid residue of the antibody, wherein optionally,

(a) at least one of the reactive groups comprises:

a thiol,

a maleimide,

a haloacetamide,

an azide,

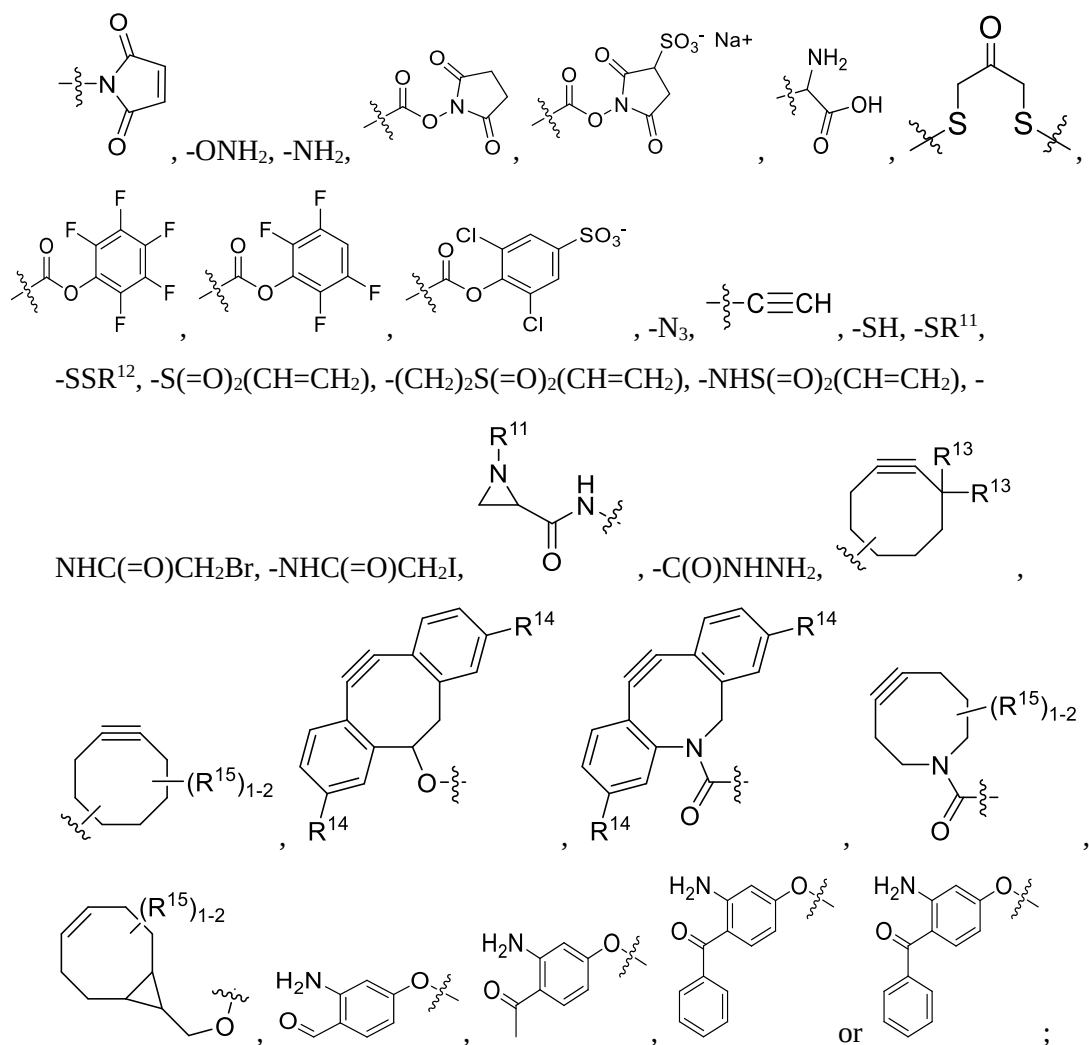
an alkyne,

a cyclooctene,

a triaryl phosphine,

an oxanorbornadiene,

a cyclooctyne,
 a diaryl tetrazine,
 a monoaryl tetrazine,
 a norbornene,
 an aldehyde,
 a hydroxylamine,
 a hydrazine,
 $\text{NH}_2\text{-NH-C(=O)-}$,
 a ketone,
 a vinyl sulfone,
 an aziridine,
 an amino acid residue,



wherein:

each R^{11} is independently selected from H and C_1 - C_6 alkyl;

each R^{12} is 2-pyridyl or 4-pyridyl;

each R^{13} is independently selected from H, C_1 - C_6 alkyl, F, Cl, and $-OH$;

each R^{14} is independently selected from H, C_1 - C_6 alkyl, F, Cl, $-NH_2$, $-OCH_3$, $-OCH_2CH_3$, $-N(CH_3)_2$, $-CN$, $-NO_2$ and $-OH$;

each R^{15} is independently selected from H, C_{1-6} alkyl, fluoro, benzyloxy substituted with $-C(=O)OH$, benzyl substituted with $-C(=O)OH$, C_{1-4} alkoxy substituted with $-C(=O)OH$ and C_{1-4} alkyl substituted with $-C(=O)OH$; and/or

(b) the first reactive group and second reactive group comprise:

a thiol and a maleimide,

a thiol and a haloacetamide,

a thiol and a vinyl sulfone,

a thiol and an aziridine,

an azide and an alkyne,

an azide and a cyclooctyne,

an azide and a cyclooctene,

an azide and a triaryl phosphine,

an azide and an oxanorbornadiene,

a diaryl tetrazine and a cyclooctene,

a monoaryl tetrazine and a norbornene,

an aldehyde and a hydroxylamine,

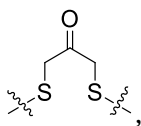
an aldehyde and a hydrazine,

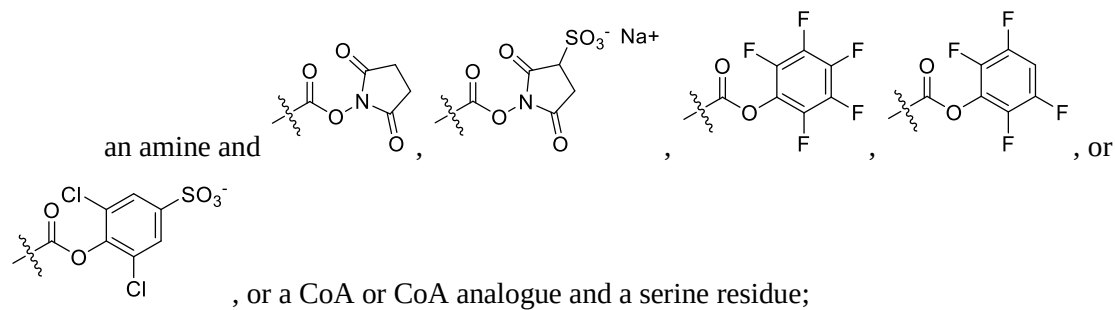
an aldehyde and $NH_2-NH-C(=O)-$,

a ketone and a hydroxylamine,

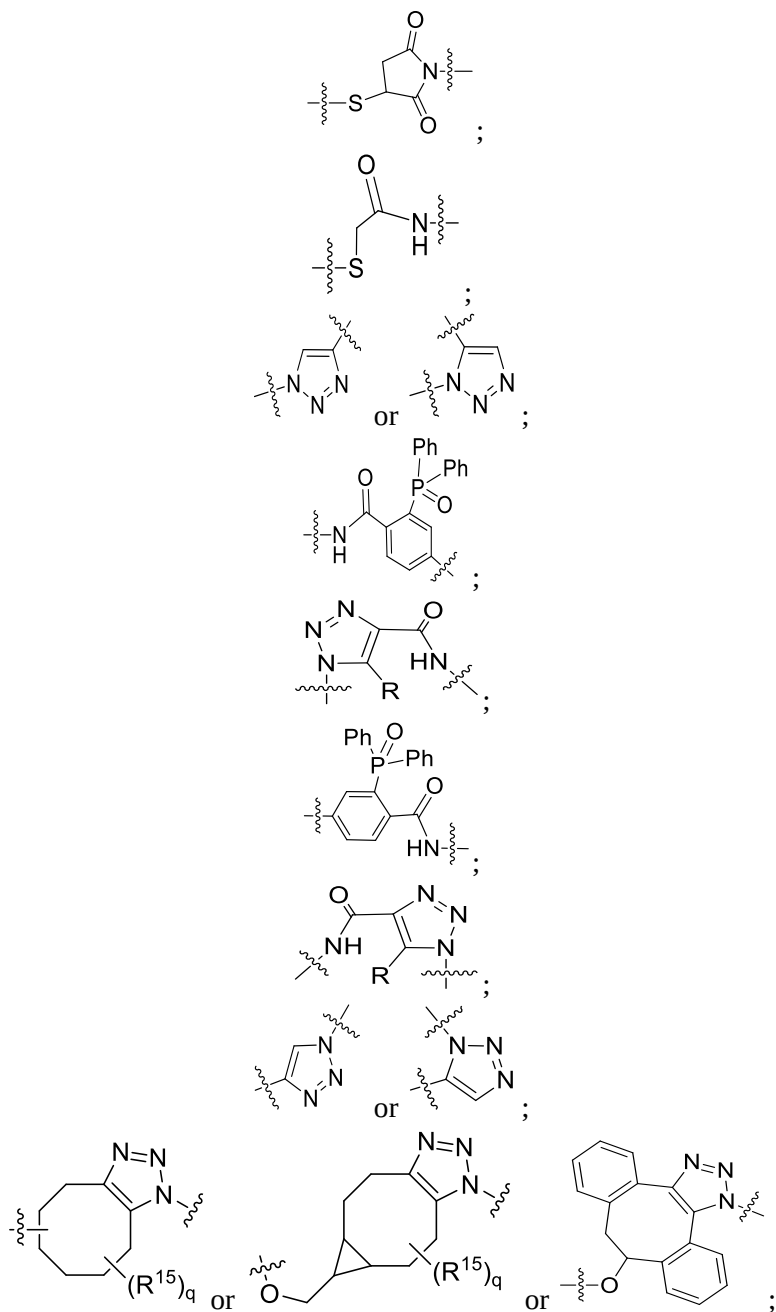
a ketone and a hydrazine,

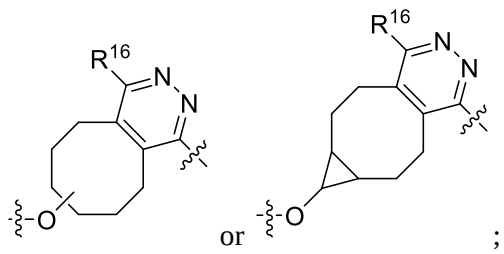
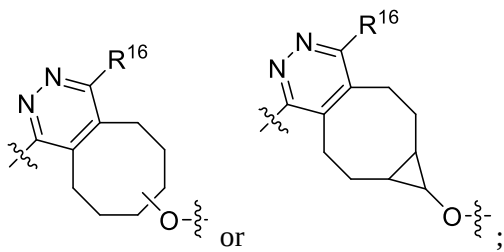
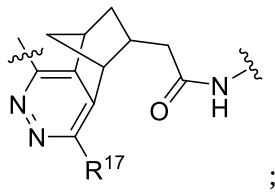
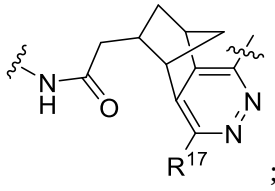
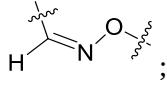
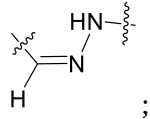
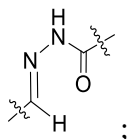
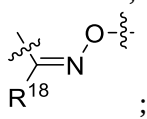
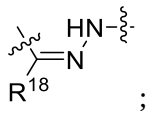
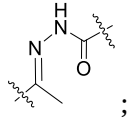
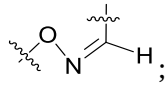
a ketone and $NH_2-NH-C(=O)-$,

a hydroxylamine and ,

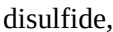


(iv) the attachment group is selected from:







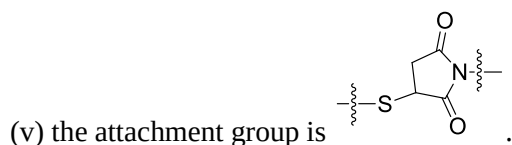


R¹⁷ is independently selected from H, phenyl and pyridine;

q is 0, 1, 2 or 3;

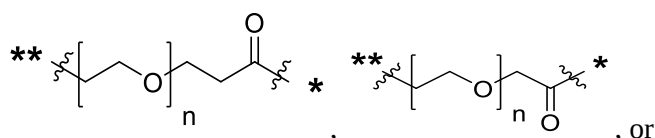
R¹⁹ is H or methyl; and

R²⁰ is H, -CH₃ or phenyl; or



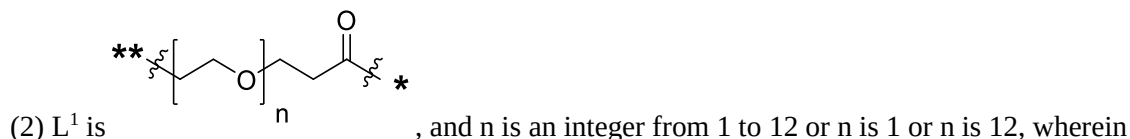
13. The antibody-drug conjugate of any one of claims 6 to 12, wherein:

(1) L¹ comprises:

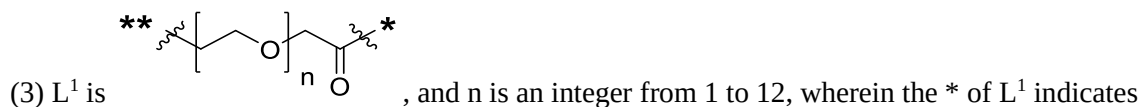


*-CH(OH)CH(OH)CH(OH)CH(OH)-**,

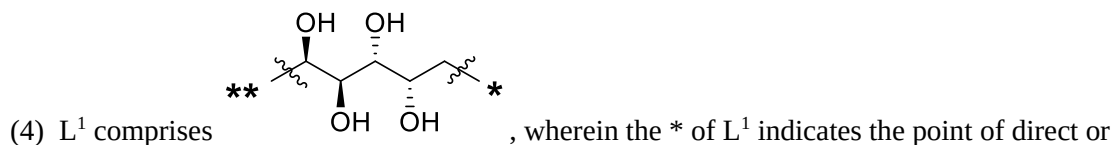
wherein each n is an integer from 1 to 12, wherein the * of L¹ indicates the point of direct or indirect attachment to W, and the ** of L¹ indicates the point of direct or indirect attachment to R¹;



the * of L¹ indicates the point of direct or indirect attachment to W, and the ** of L¹ indicates the point of direct or indirect attachment to R¹;



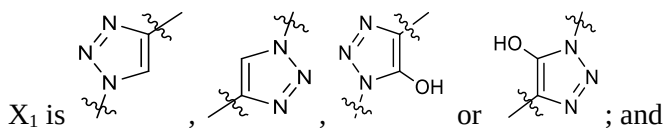
the point of direct or indirect attachment to W, and the ** of L₁ indicates the point of direct or indirect attachment to R¹;



indirect attachment to W, and the ** of L¹ indicates the point of direct or indirect attachment to R¹;

(5) L¹ is a bridging spacer comprising:

*-C(=O)(CH₂)_mO(CH₂)_m-**, *-C(=O)((CH₂)_mO)_t(CH₂)_n-**, *-C(=O)(CH₂)_m-**,
 *-C(=O)NH((CH₂)_mO)_t(CH₂)_n-**,
 *-C(=O)O(CH₂)_mSSC(R^{L1})₂(CH₂)_mC(=O)NR^{L1}(CH₂)_mNR^{L1}C(=O)(CH₂)_m-**,
 *-C(=O)O(CH₂)_mC(=O)NH(CH₂)_m-**, *-C(=O)(CH₂)_mNH(CH₂)_m-**,
 *-C(=O)(CH₂)_mNH(CH₂)_nC(=O)-**, *-C(=O)(CH₂)_mX₁(CH₂)_m-**,
 *-C(=O)((CH₂)_mO)_t(CH₂)_nX₁(CH₂)_n-**, *-C(=O)(CH₂)_mNHC(=O)(CH₂)_n-**,
 *-C(=O)((CH₂)_mO)_t(CH₂)_nNHC(=O)(CH₂)_n-**,
 *-C(=O)(CH₂)_mNHC(=O)(CH₂)_nX₁(CH₂)_n-**,
 *-C(=O)((CH₂)_mO)_t(CH₂)_nNHC(=O)(CH₂)_nX₁(CH₂)_n-**,
 *-C(=O)((CH₂)_mO)_t(CH₂)_nC(=O)NH(CH₂)_m-**, *-C(=O)(CH₂)_mC(R^{L1})₂-** or
 *-C(=O)(CH₂)_mC(=O)NH(CH₂)_m-**, wherein the * of L¹ indicates the point of direct or indirect attachment to W, and the ** of L¹ indicates the point of direct or indirect attachment to R¹;



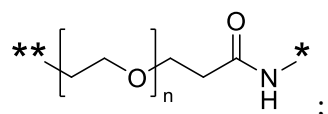
each m is independently selected from 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

each n is independently selected from 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10; and

each t is independently selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 and 30; and

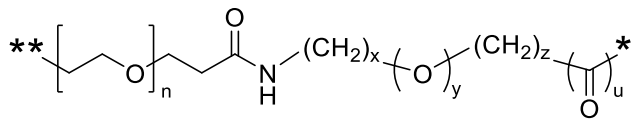
each R^{L1} is independently selected from H and C₁-C₆alkyl;

(6) L¹ comprises a moiety represented by



wherein n is an integer from 1 to 12, wherein the * of L¹ indicates the point of direct or indirect attachment to W, and the ** of L¹ indicates the point of direct or indirect attachment to R¹;

(7) L¹ is represented by a formula



wherein

n is an integer from 1 to 12;

x is an integer from 0 to 6;

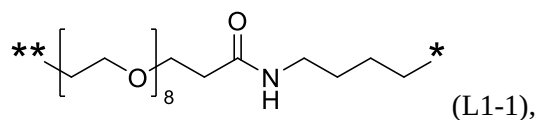
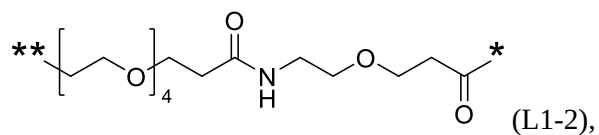
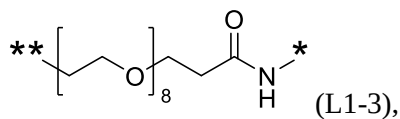
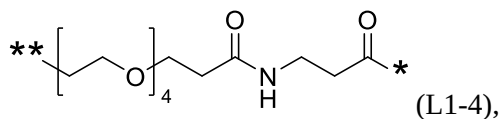
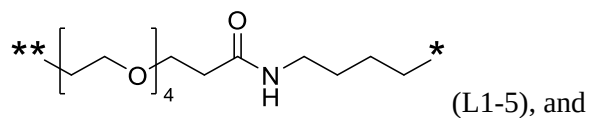
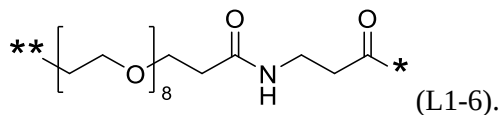
y is 0 or 1;

z is an integer from 0 to 6;

u is 0 or 1; and

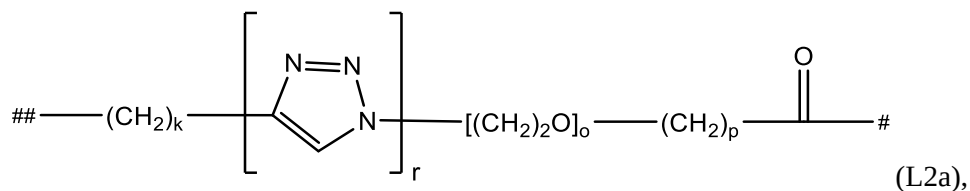
wherein the * of L¹ indicates the point of direct attachment to W, and the ** of L¹ indicates the point of direct attachment to R¹; or

(8) L¹ is selected from the group consisting of :



14. The antibody-drug conjugate of any one of claims 8 to 13, wherein:

(i) L² and L³ are each independently a connecting spacer comprising a moiety represented by:



wherein

k is an integer from 0 to 6;

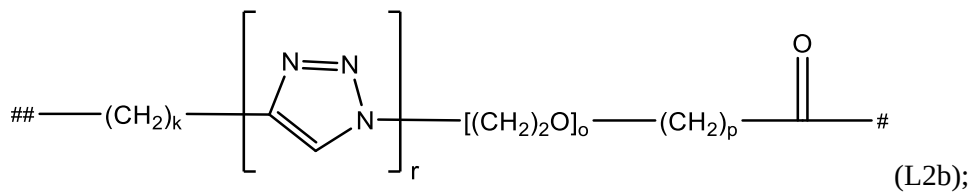
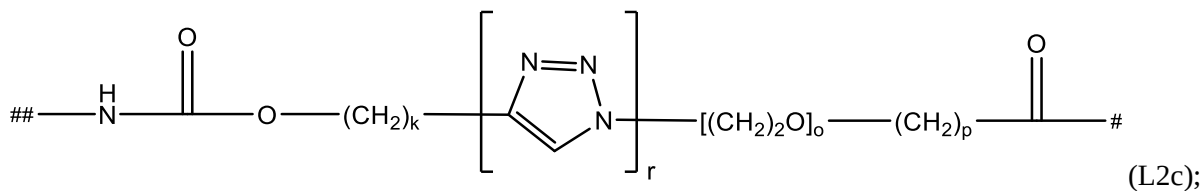
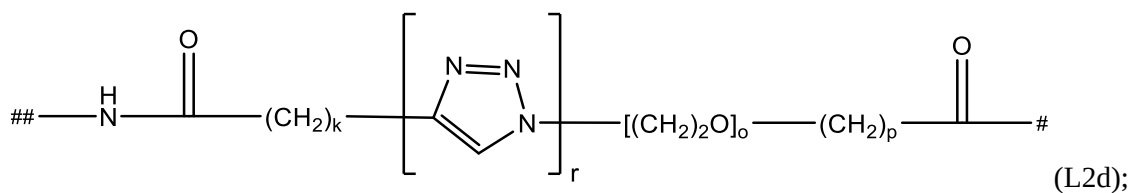
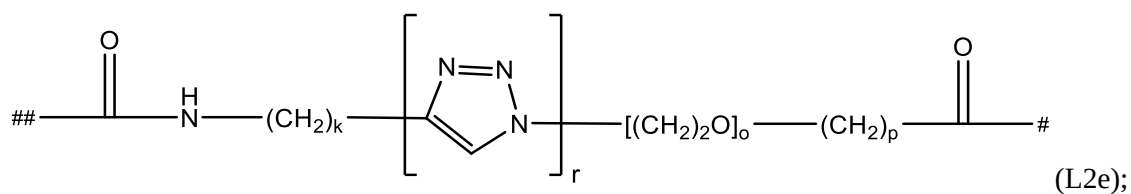
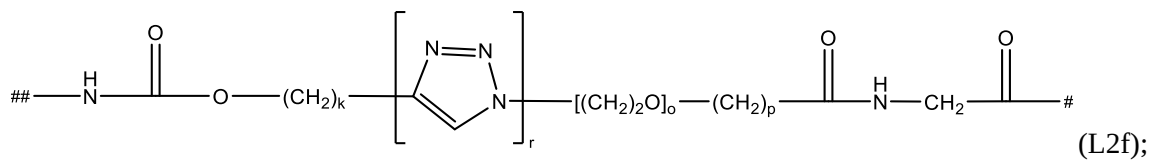
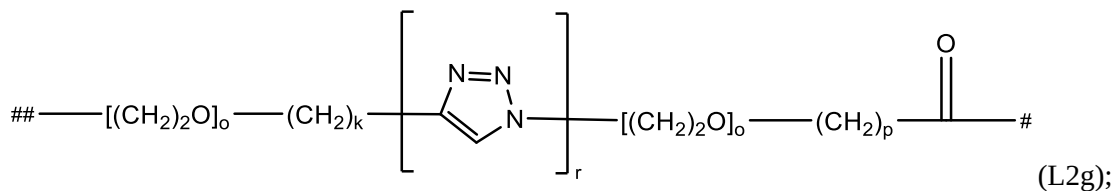
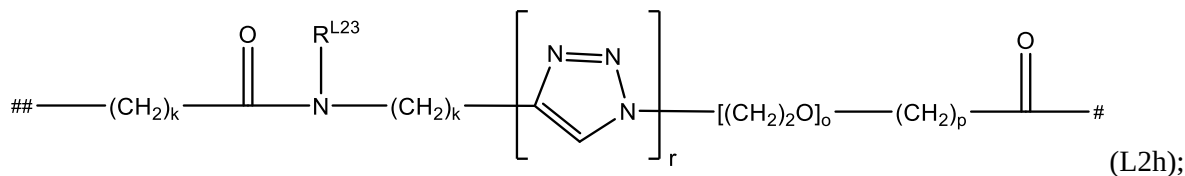
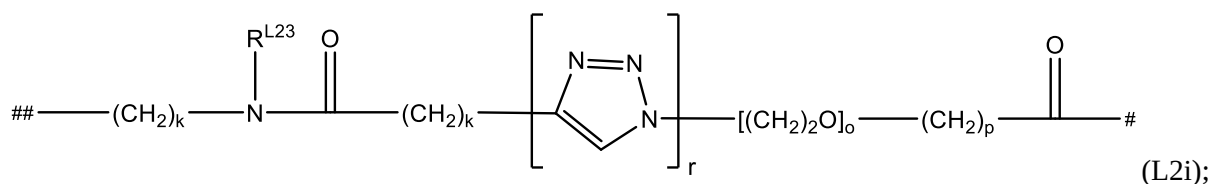
r is 0 or 1;

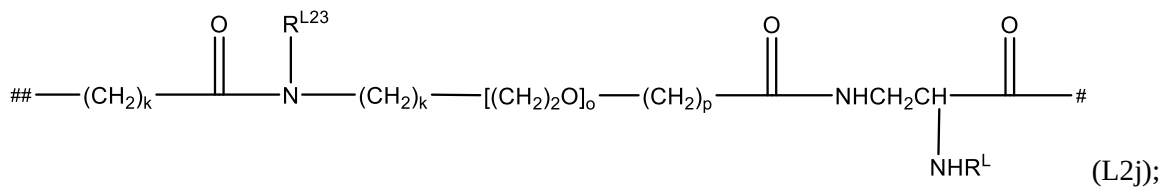
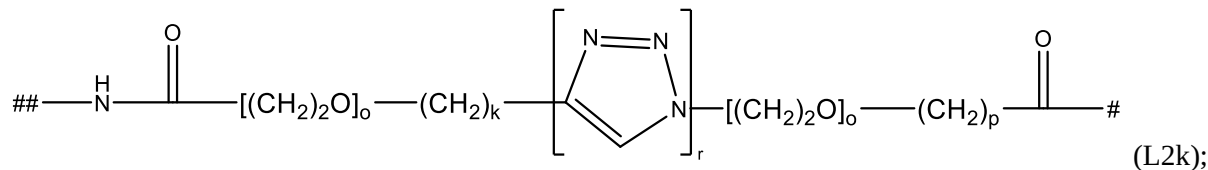
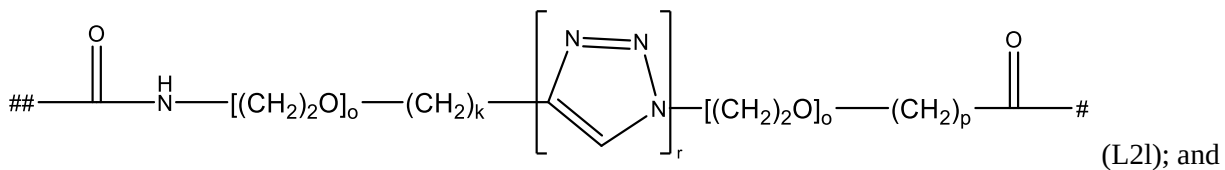
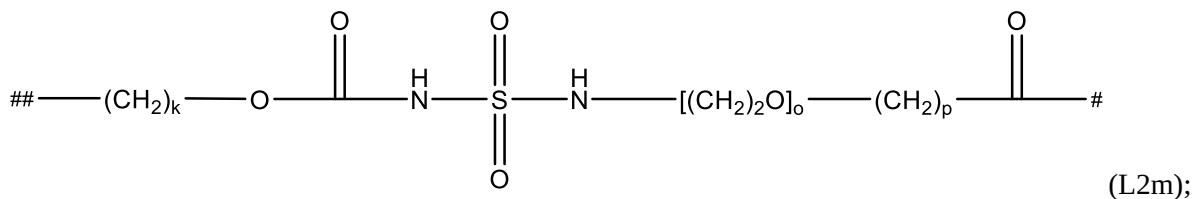
o is an integer from 0 to 12;

p is an integer from 0 to 6; and

wherein the # of L² or L³ indicates the point of direct or indirect attachment to E¹ or E², respectively, and the ## of L² or L³ indicates the point of direct or indirect attachment to W;

(ii) L² and L³ are each independently a connecting spacer selected from a group consisting of





wherein

k, in each occurrence, is independently an integer from 0 to 4;

r, in each occurrence, is independently 0 or 1;

o, in each occurrence, is independently an integer from 0 to 10;

p, in each occurrence, is independently an integer from 0 to 4;

R^{L23} is hydrogen or C₁₋₆alkyl;

R^L is hydrogen or -C(O)-R^H;

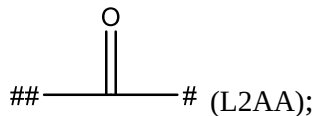
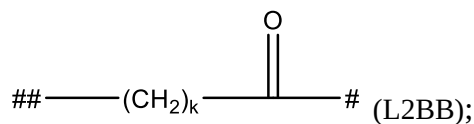
R^H is a hydrophilic group; and

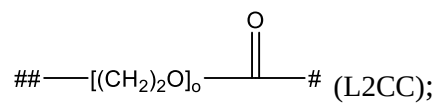
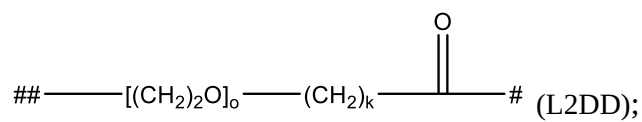
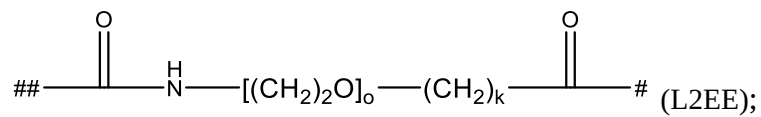
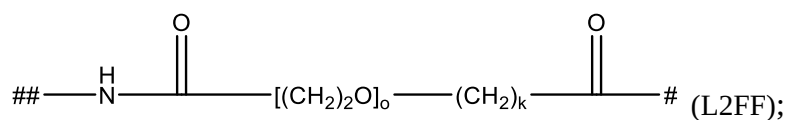
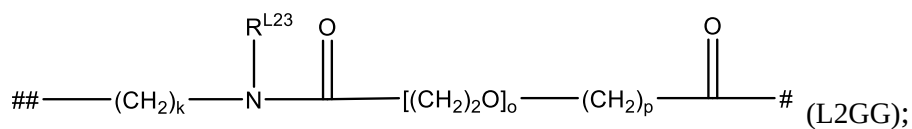
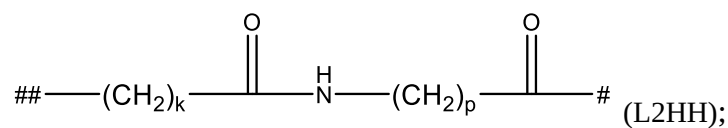
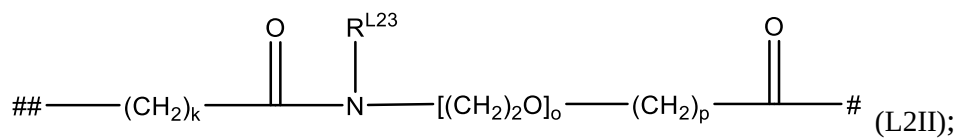
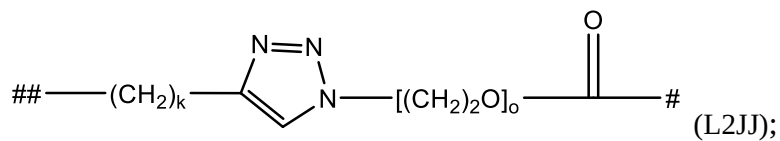
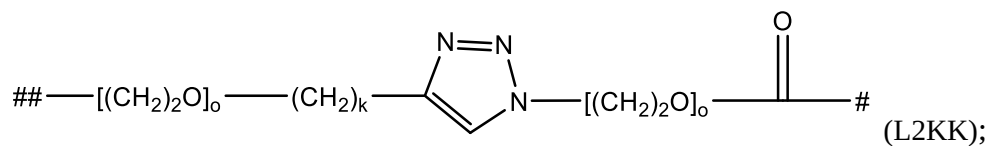
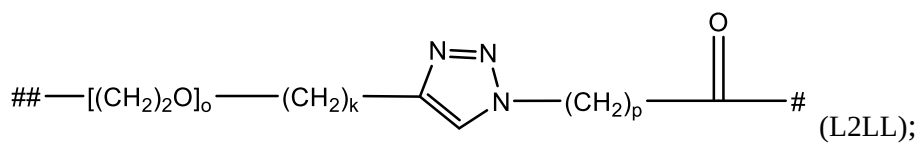
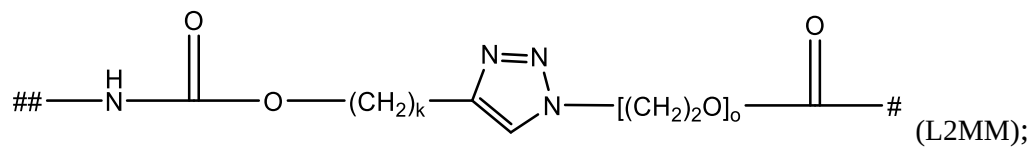
the # of L² or L³ indicates the point of direct attachment to E¹ or E², respectively, and the

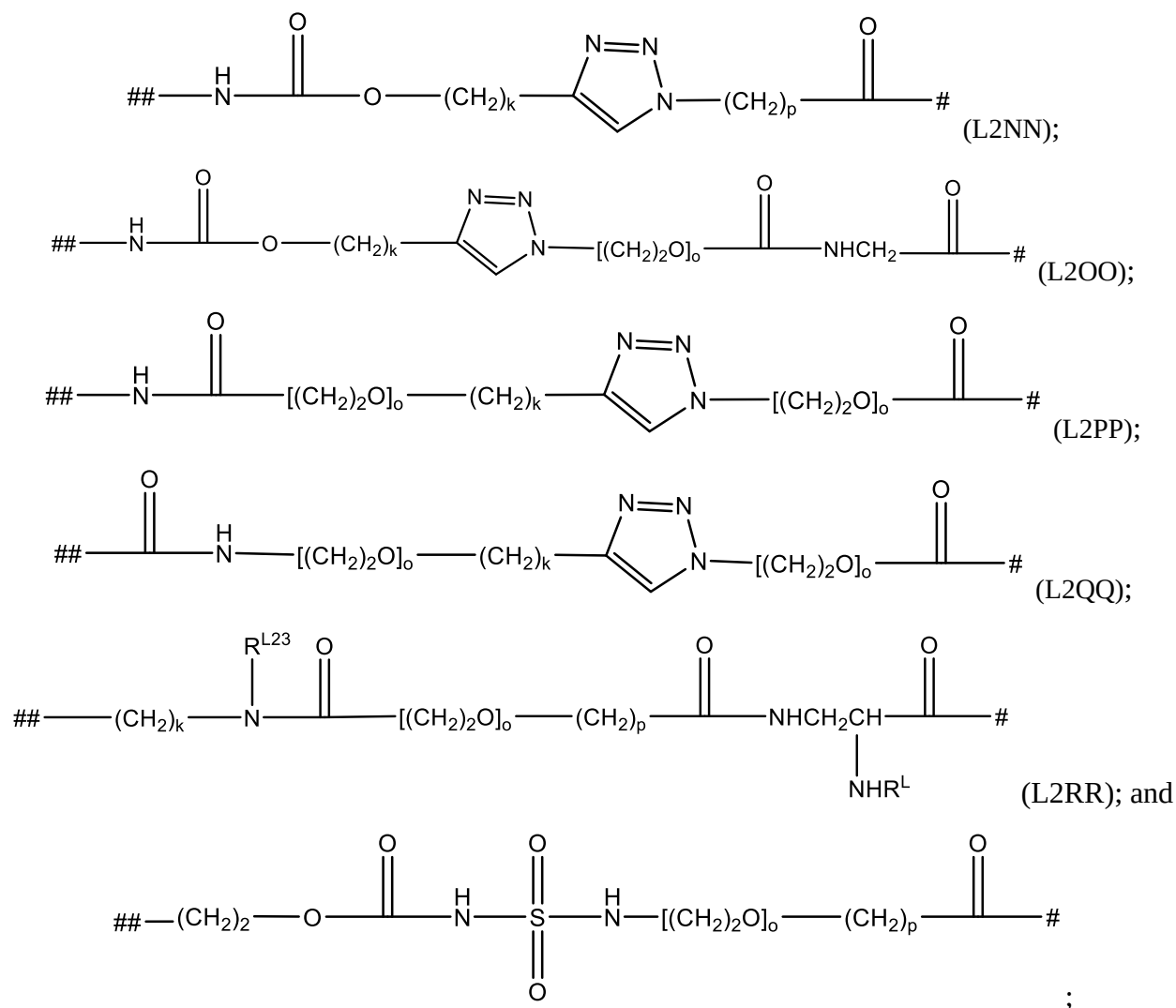
of L² or L³ indicates the point of direct attachment to W;

provided that when W is N, L² and L³ are not (L2c), (L2d), (L2f), or (L2k);

(iii) L² and L³ are each independently a connecting spacer selected from a group consisting of







wherein

k, in each occurrence, is independently an integer from 1 to 3;

o, in each occurrence, is independently an integer from 1 to 9;

p, in each occurrence, is independently an integer from 1 to 3;

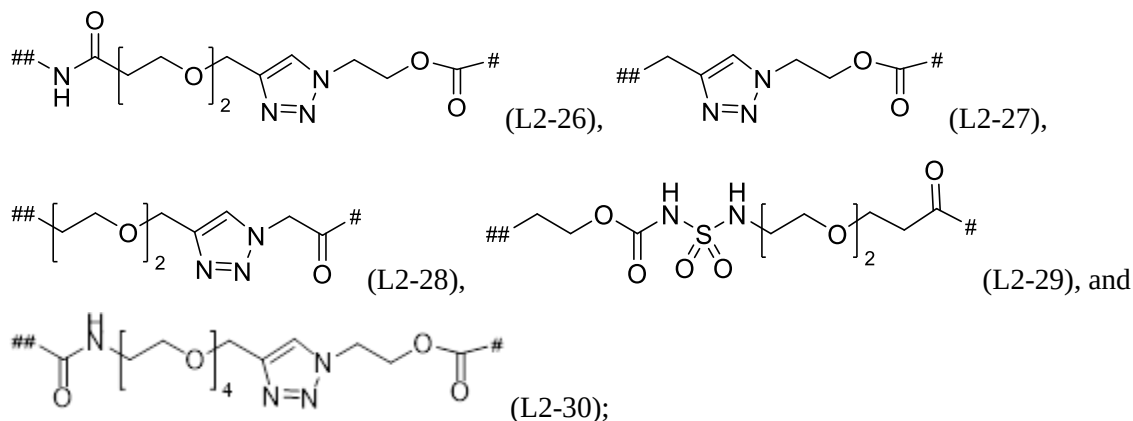
R^{L23} is hydrogen or C₁₋₃alkyl;

R^L is hydrogen or -C(O)-R^H;

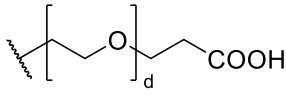
R^H is a hydrophilic group; and

the # of L² or L³ indicates the point of direct attachment to E¹ or E², respectively, and the ## of L² or L³ indicates the point of direct attachment to W; provided that when W is N, L² and L³ are not (L2FF), (L2MM), (L2NN), (L2OO), or (L2PP); or

(iv) L² and L³, independently, are a connecting spacer selected from a group consisting of



wherein the # of L² or L³ indicates the point of direct attachment to E¹ or E², respectively, the ## of L² or L³ indicates the point of direct attachment to W; R^L is hydrogen or –C(O)-R^H; and

R^H is , and d is an integer from 20 to 30 (*e.g.*, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30); optionally wherein d is 25.

15. The antibody-drug conjugate of any one of claims 10 to 14, wherein:

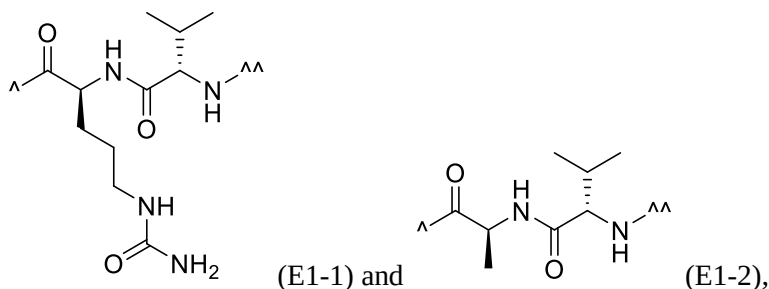
(i) the peptide group comprises 1 to 4, 1 to 3, or 1 to 2 amino acid residues; optionally wherein the amino acid residues are selected from glycine (Gly), L-valine (Val), L-citrulline (Cit), L-cysteic acid (sulfo-Ala), L-lysine (Lys), L-isoleucine (Ile), L-phenylalanine (Phe), L-methionine (Met), L-asparagine (Asn), L-proline (Pro), L-alanine (Ala), L-leucine (Leu), L-tryptophan (Trp), L-tyrosine (Tyr) and β -alanine (β -Ala);

(ii) the peptide group comprises Val-Cit, Phe-Lys, Val-Ala, Val-Lys, Leu-Cit, Cit-(β -Ala), Gly-Gly-Gly, Gly-Gly-Phe-Gly, and/or sulfo-Ala-Val-Ala;

(iii) the peptide group represented by E¹ or E² is an enzyme cleavage element; or

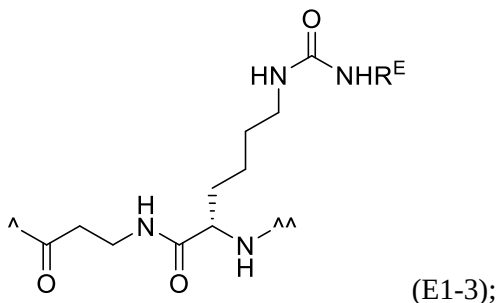
(iv) the peptide group represented by E¹ or E² is a hydrophilic moiety; optionally wherein

(a) E¹ or E², independently, is an enzyme cleavage element selected from a group consisting of

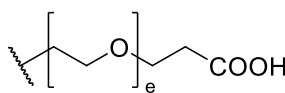


wherein $\wedge$ of E^1 or E^2 indicates the point of direct attachment to V^1 or V^2 in Formula (B) or direct attachment to the $-\text{NH}-$ group in Formula (C) and (D); and $\wedge\wedge$ of E^1 or E^2 indicates the point of direct attachment to L^2 or L^3 , respectively; or

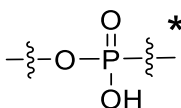
(b) E^1 or E^2 , independently, is a hydrophilic moiety represented by

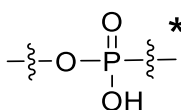


wherein R^E is a hydrophilic group R^H ; preferably wherein each hydrophilic group R^H in

E^1 or E^2 is independently ; wherein e is an integer between 20 and 30 (e.g., 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30); preferably wherein e is 24.

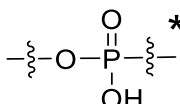
16. The antibody-drug conjugate of any one of claims 10 to 15, or pharmaceutically acceptable salt thereof, wherein:

(i) A^1 and A^2 independently are a bond, $-\text{OC}(=\text{O})-\ast$, or , wherein $\ast$ indicates the point of attachment to D^1 or D^2 ;

(ii) A^1 and A^2 independently are a bond or , wherein $\ast$ indicates the point of attachment to D^1 or D^2 ;

(iii) A^1 and A^2 independently are a bond or $-\text{OC}(=\text{O})-\ast$, wherein $\ast$ indicates the point of attachment to D^1 or D^2 ;

(iv) A^1 and A^2 are $-\text{OC}(=\text{O})-\ast$;

(v) A^1 and A^2 are ;

(vi) A^1 is $-\text{OC}(=\text{O})-\ast$ and A^2 is a bond;

(vii) A¹ is -OC(=O)-* and A² is $\begin{array}{c} \text{O} \\ \parallel \\ -\text{O}-\text{P}-\text{O}- \\ | \\ \text{OH} \end{array}$;

(viii) A¹ is a bond and A² is $\begin{array}{c} \text{O} \\ \parallel \\ -\text{O}-\text{P}-\text{O}- \\ | \\ \text{OH} \end{array}$;

(ix) A¹ is a bond and A² is -OC(=O)-*; or

(x) A¹ and A² are a bond,

wherein * indicates the point of attachment to D¹ or D².

17. The antibody-drug conjugate of any one of claims 10 to 16, wherein

i) L⁴ and L⁵ are each independently a spacer moiety having the structure $\text{---} \text{Z} \text{---} \text{X} \text{---}$,

wherein:

Z is -O-, -CH₂-, -CH₂O-, -CH₂N(R^{L45})C(=O)O-, -NHC(=O)C(R^{L45})₂NHC(=O)O-, -NHC(=O)C(R^{L45})₂NH-, -NHC(=O)C(R^{L45})₂NHC(=O)-, -C(=O)NR^{L45}-, -C(=O)NH-, -CH₂NR^{L45}C(=O)-, -CH₂NR^{L45}C(=O)NH-, -CH₂NR^{L45}C(=O)NR^{L45}-, -NHC(=O)-, -NHC(=O)O-, -NHC(=O)NH-, -OC(=O)NH-, -S(O)₂NH-, -NHS(O)₂-, -C(=O)-, -C(=O)O- or -NH-, wherein each R^{L45} is independently selected from H, C₁-C₆alkyl, and C₃-C₈ cycloalkyl; and

X is a bond, triazolyl, or -CH₂-triazolyl-,

wherein X is connected to R² or R³;

(ii) L⁴ and L⁵, independently, are a spacer moiety having the structure $\text{---} \text{Z} \text{---} \text{X} \text{---}$,

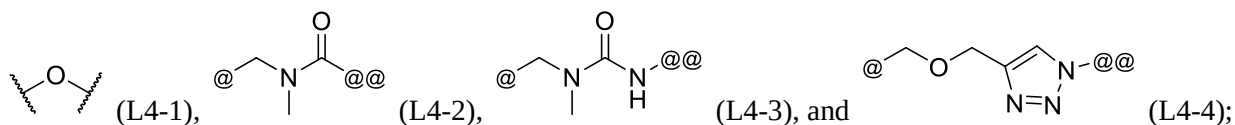
wherein:

Z is -CH₂-, -CH₂O-, -CH₂N(R^{L45})C(=O)O-, -NHC(=O)C(R^{L45})₂NHC(=O)O-, -NHC(=O)C(R^{L45})₂NH-, -NHC(=O)C(R^{L45})₂NHC(=O)-, -C(=O)NR^b-, -C(=O)NH-, -CH₂NR^{L45}C(=O)-, -CH₂NR^{L45}C(=O)NH-, -CH₂NR^{L45}C(=O)NR^{L45}-, -NHC(=O)-, -NHC(=O)O-, -NHC(=O)NH-, -OC(=O)NH-, -S(O)₂NH-, -NHS(O)₂-, -C(=O)-, -C(=O)O- or -NH-, wherein each R^{L45} is independently selected from H, C₁-C₆alkyl, and C₃-C₈ cycloalkyl; and

X is -CH₂-triazolyl-C₁₋₄ alkylene-OC(O)NHS(O)₂NH-, -C₄₋₆ cycloalkylene-OC(O)NHS(O)₂NH-, -(CH₂CH₂O)_n-C(O)NHS(O)₂NH-, -(CH₂CH₂O)_n-C(O)NHS(O)₂NH-(CH₂CH₂O)_n-, -CH₂-triazolyl-C₁₋₄ alkylene-OC(O)NHS(O)₂NH-(CH₂CH₂O)_n-, -C₄₋₆cycloalkylene-OC(O)NHS(O)₂NH-(CH₂CH₂O)_n-, wherein each n independently is 1, 2, or 3,

wherein X is connected to R² or R³; preferably wherein Z is -O-, -CH₂NR^{L45}C(=O)-, -CH₂NR^{L45}C(=O)NH- or -CH₂O-; X is a bond, triazolyl, or -CH₂-triazolyl-; and R^{L45}, in each occurrence, is independently H or C₁₋₃alkyl; or

(iii) L⁴ and L⁵ are each independently a spacer moiety selected from a group consisting of



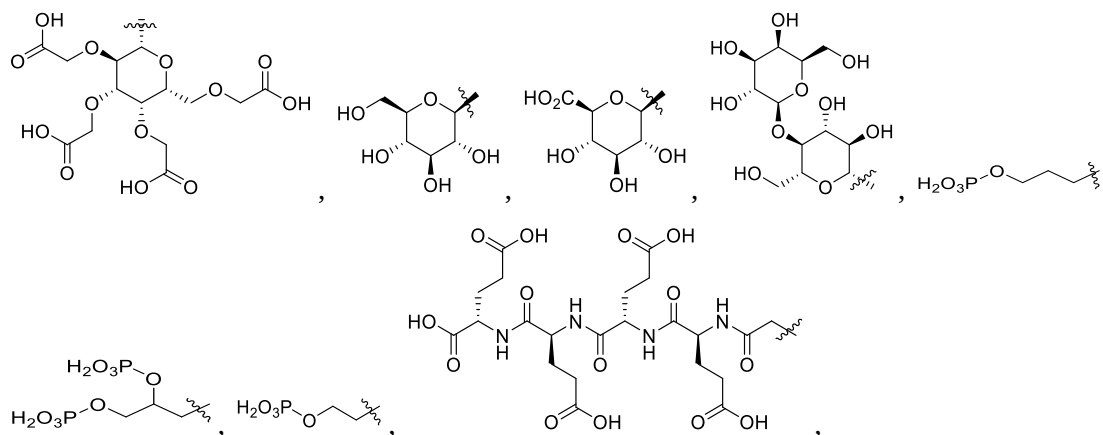
wherein the @ of L⁴ or L⁵ indicates the point of direct attachment to the phenyl group, and the @@ of L⁴ or L⁵ indicates the point of direct attachment to R² or R³.

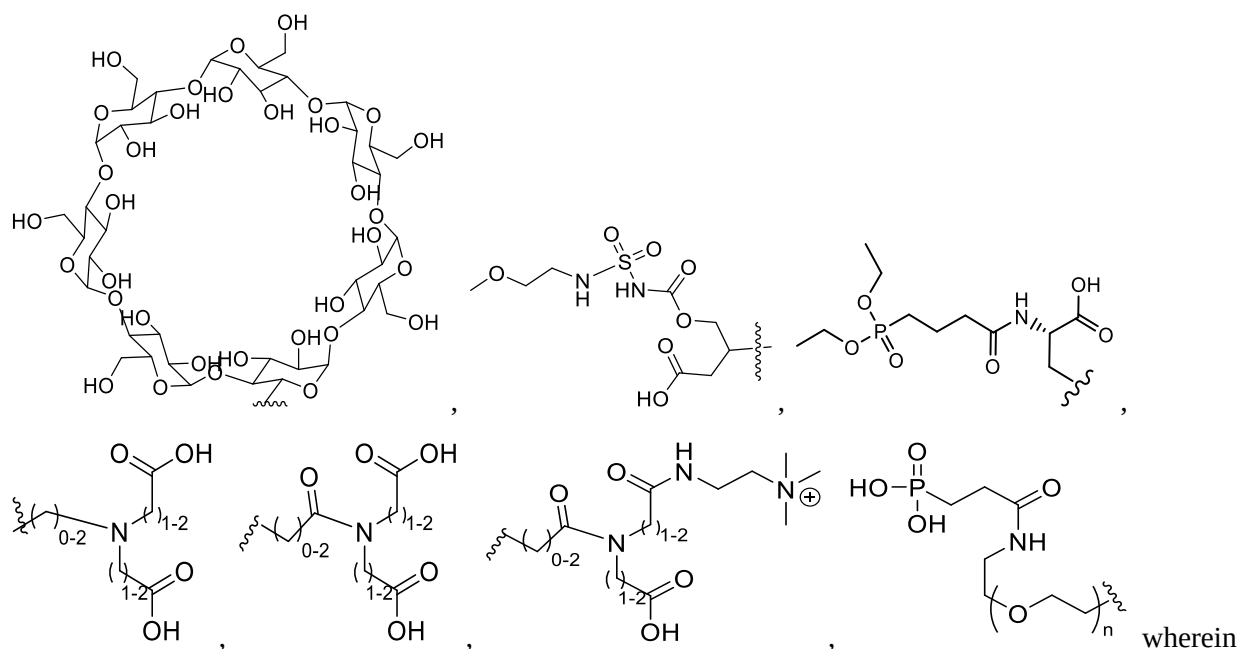
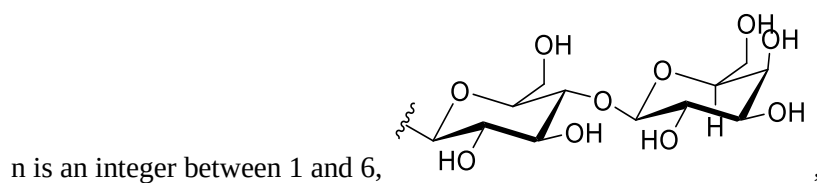
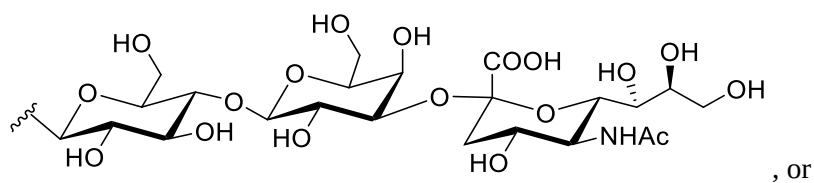
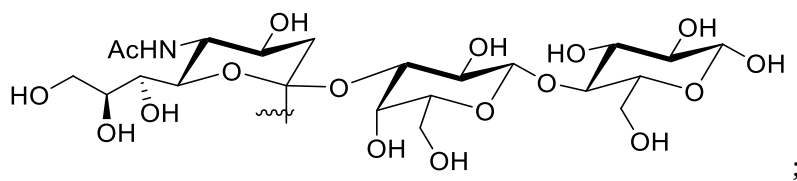
18. The antibody-drug conjugate of any one of claims 10 to 17, wherein:

(i) the hydrophilic groups represented by R² and R³ each independently comprises polyethylene glycol, polyalkylene glycol, a polyol, a polysarcosine, a sugar, an oligosaccharide, a polypeptide, C₂-C₆

alkyl substituted with 1 to 3 or , or C₂-C₆alkyl substituted with 1 to 2 substituents independently selected from -OC(=O)NHS(O)₂NHCH₂CH₂OCH₃, -NHC(=O)C₁₋₄alkylene-P(O)(OCH₂CH₃)₂ and -COOH groups;

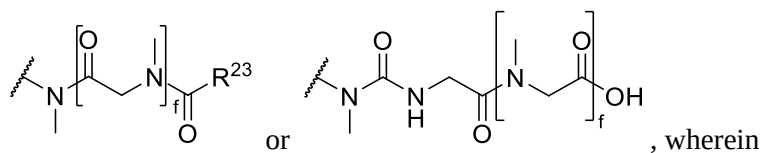
(ii) R² or R³ independently is





(iii) the hydrophilic group represented by R^2 or R^3 each independently comprises:

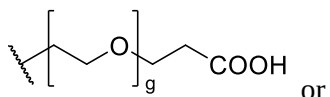
(a) a polysarcosine with the following moiety:



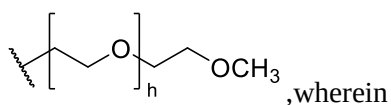
f is an integer between 3 and 25; and

R^{23} is H, $-\text{CH}_3$ or $-\text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{OH}$; or

(b) a polyethylene glycol of formula:



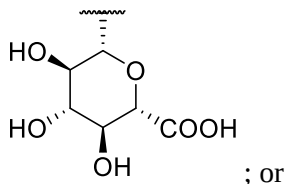
or



, wherein

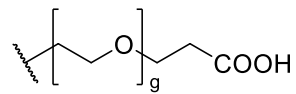
g and h are independently an integer between 2 and 30;

(iv) the enzyme cleavage element represented by R² or R³ each independently comprises:

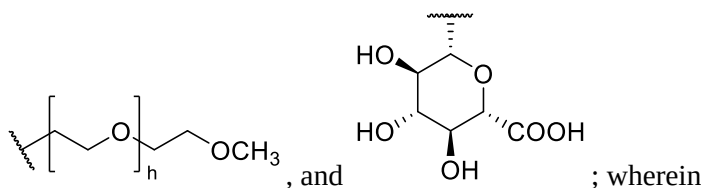


; or

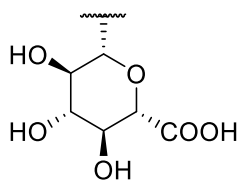
(v) R² or R³, independently, is selected from a group consisting of



,



, and



; wherein

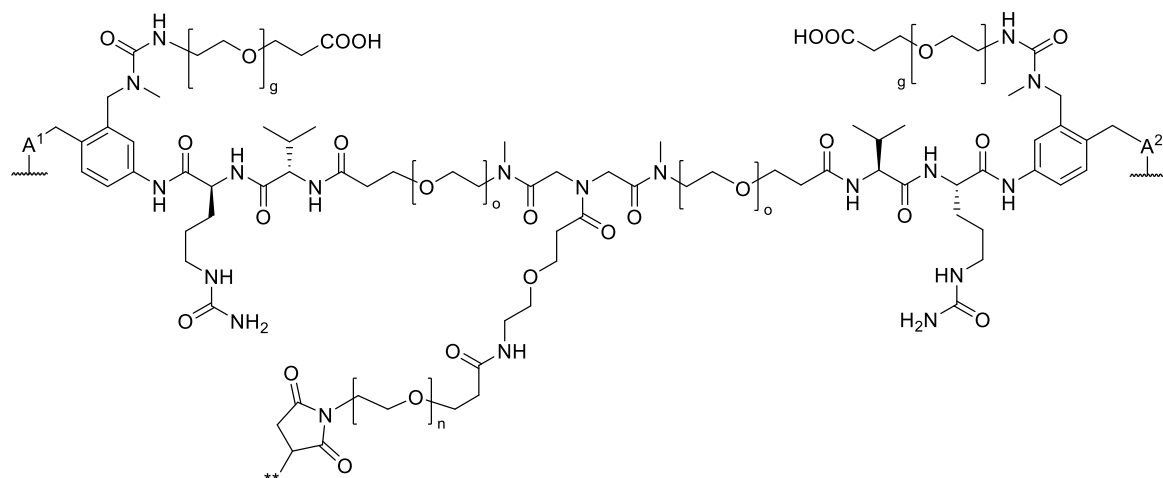
g and h are independently an integer between 20 and 30; preferably wherein

g is 23, 24, or 25; and

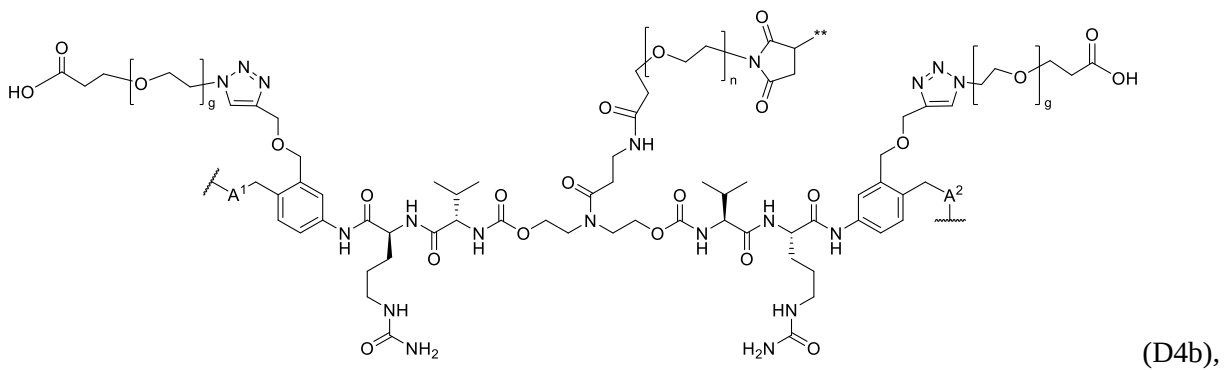
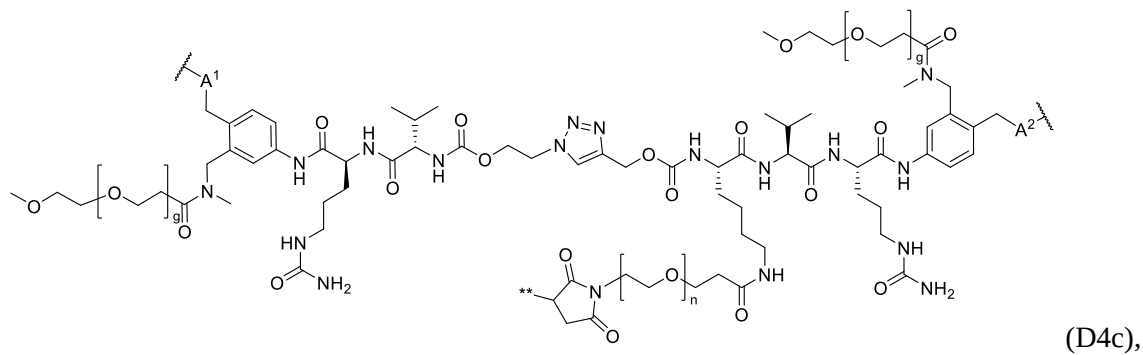
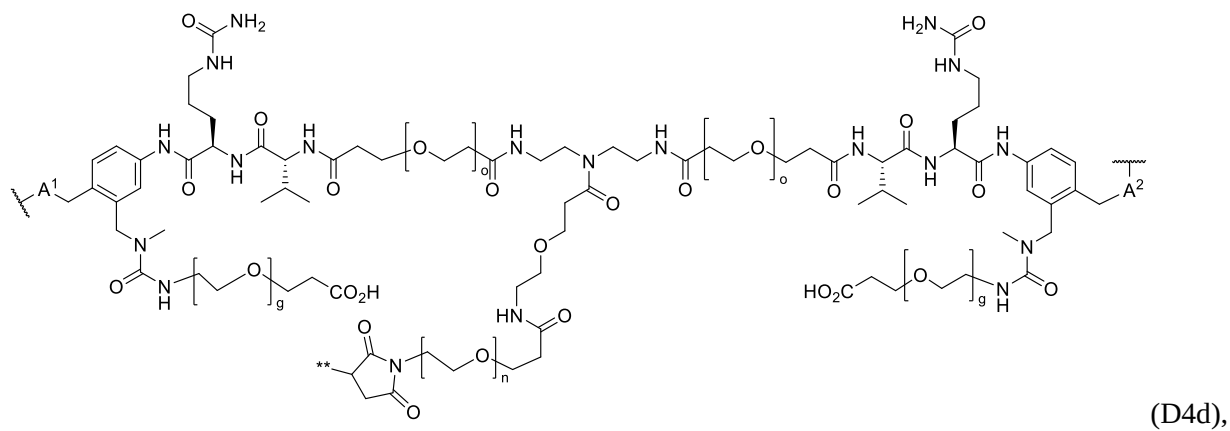
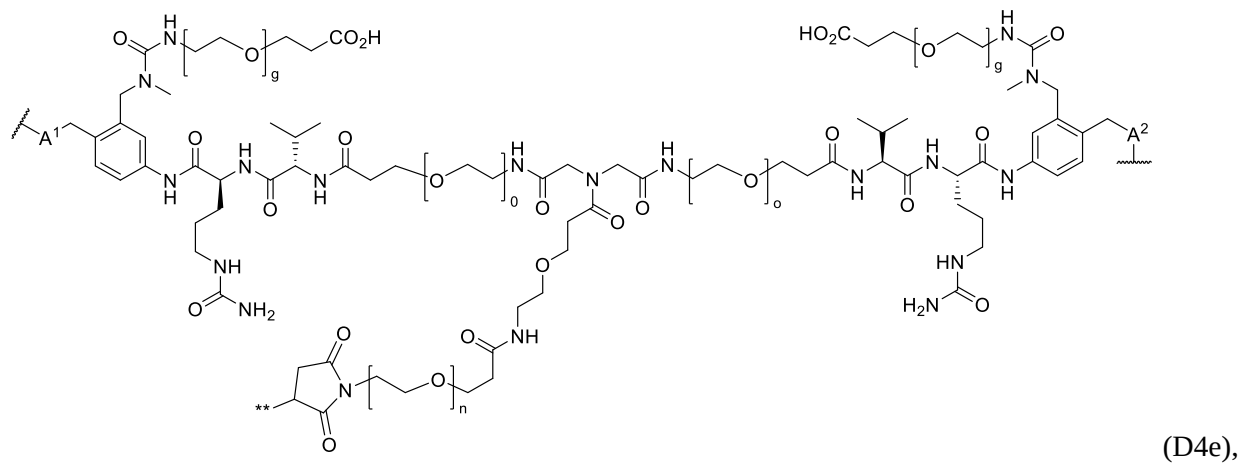
h is 23, 24, or 25.

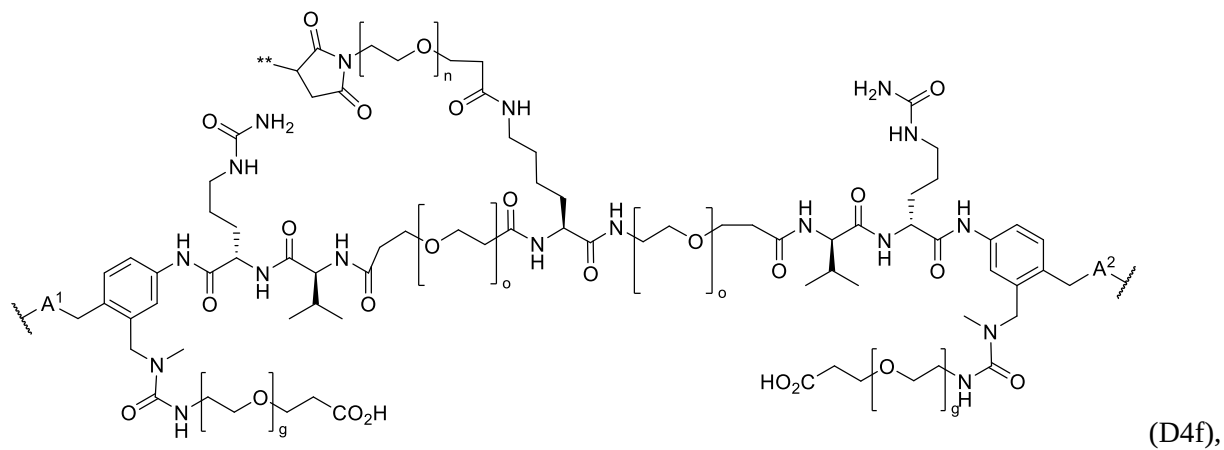
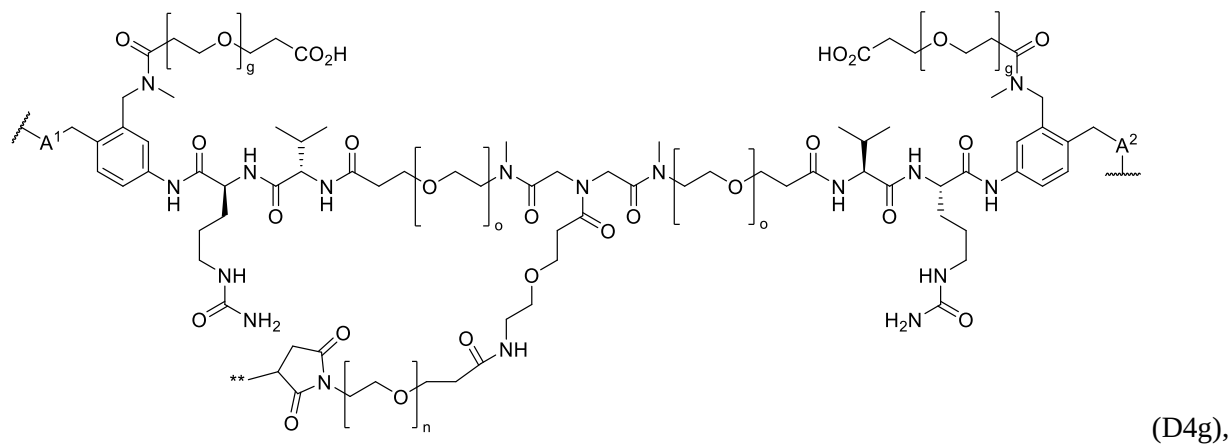
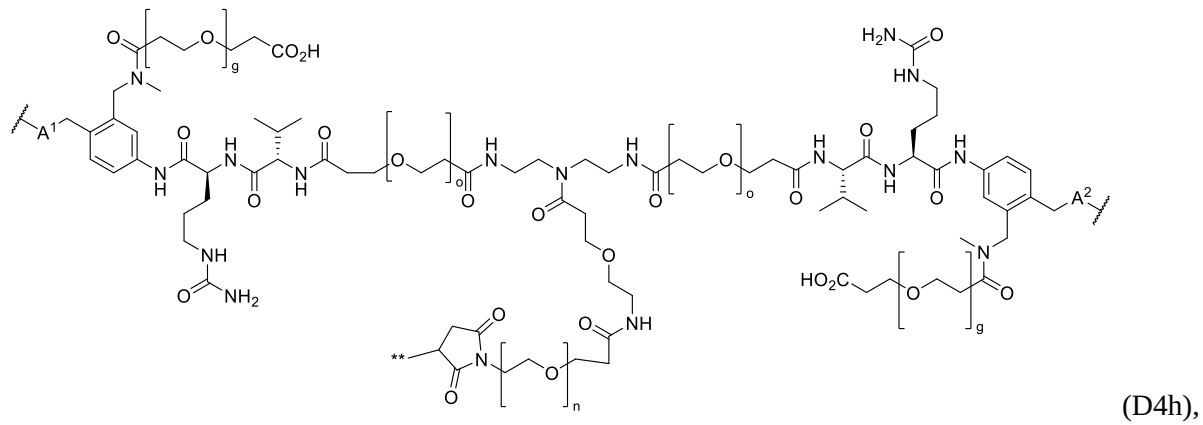
19. The antibody-drug conjugate of claim 10, wherein:

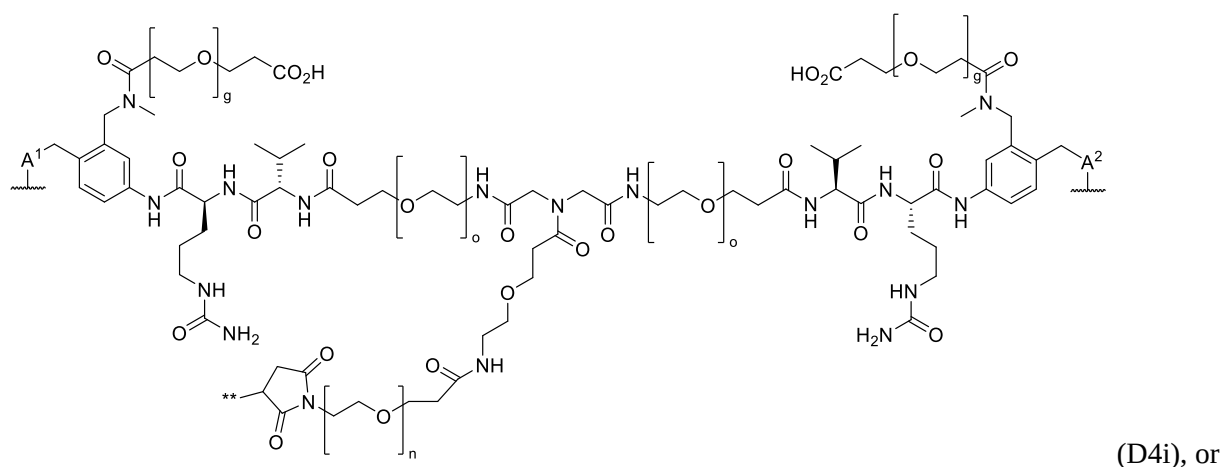
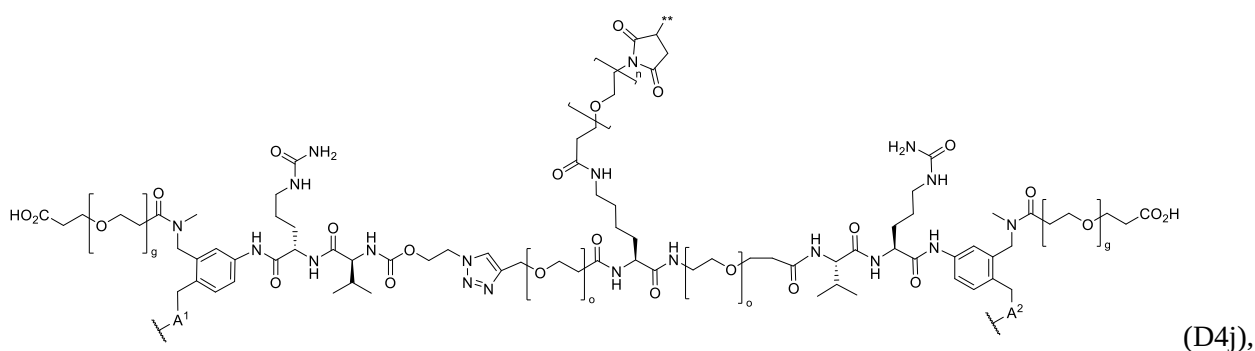
(i) the dual linker is represented by the following formula:



(D4a),







wherein:

A^1 and A^2 are each independent a bond, $-O-C(=O)-*$, or $\begin{array}{c} \text{O} \\ \parallel \\ -\text{O}-\text{P}-\text{O}- \\ | \\ \text{OH} \end{array} *$, preferably A^1 and A^2 are each independent a bond or $-O-C(=O)-*$, wherein * in A^1 and A^2 indicates the point of attachment to D^1 or D^2 ;

g for each occurrence is independently an integer between 20 and 30 (*e.g.*, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30);

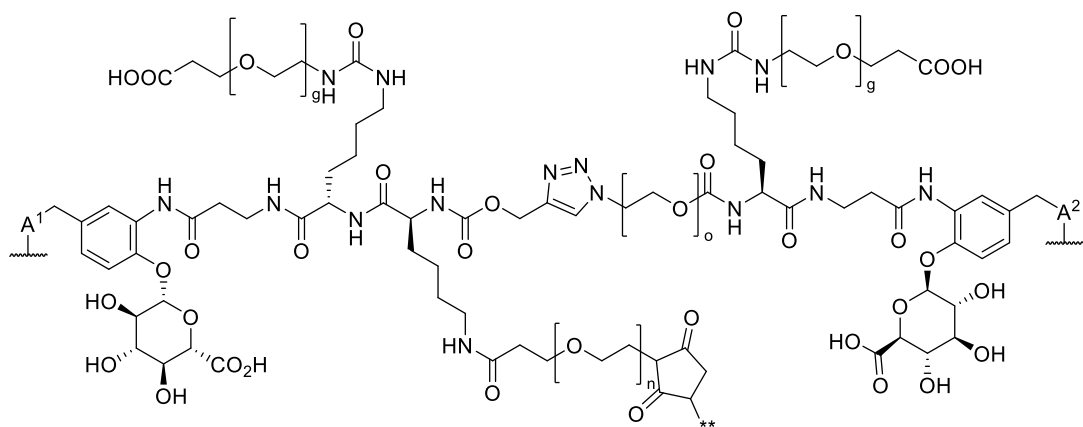
o for each occurrence is independently an integer between 1 and 9 (*e.g.*, between 2 and 5);

n is an integer between 1 and 12 (*e.g.*, between 2 and 5);

**— indicates the point of attachment to the Ab ; and

 indicates the point of direct attachment to D^1 or D^2 ;

(ii) the dual linker is represented by Formula (D5):



(D5),

wherein:

A^1 and A^2 are each independent a bond, $-O-C(=O)-*$, or $-O-C(=O)-P(=O)(OH)-*$, preferably wherein A^1 and A^2 are each independent a bond or $-O-C(=O)-*$, wherein * in A^1 and A^2 indicates the point of attachment to D^1 or D^2 ;

g for each occurrence is independently an integer between 20 and 30 (*e.g.*, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30);

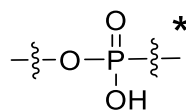
o for each occurrence is independently an integer between 1 and 9 (*e.g.*, between 1 and 3);

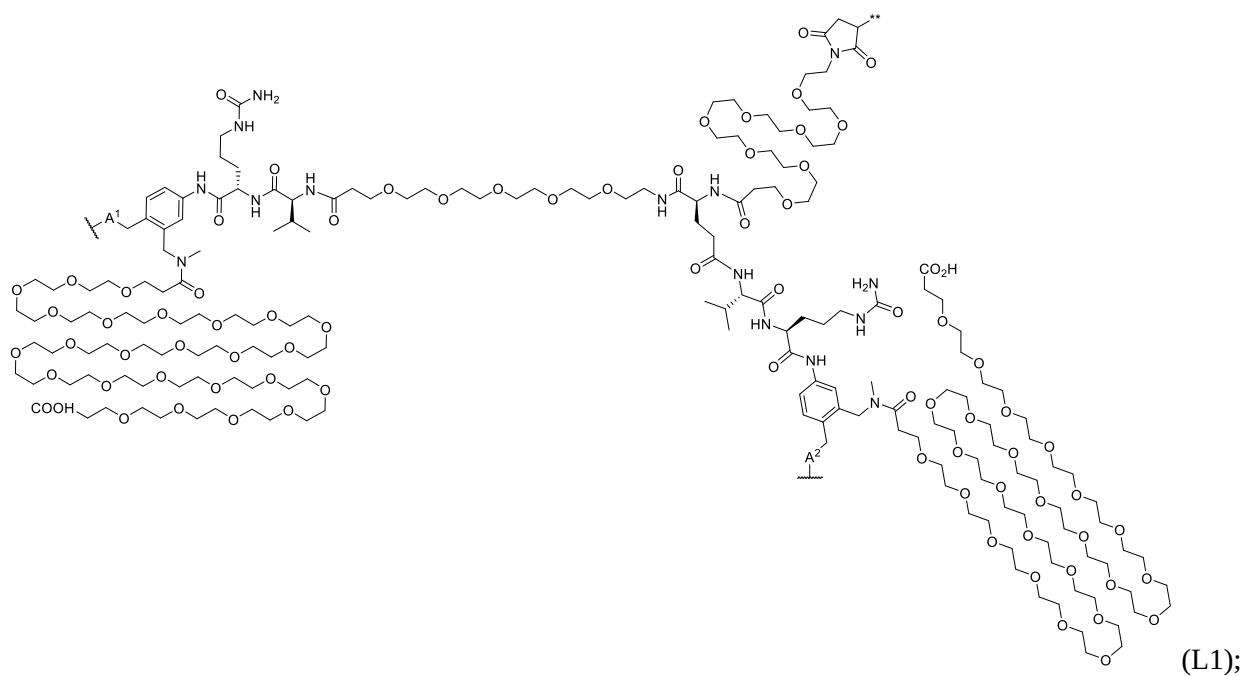
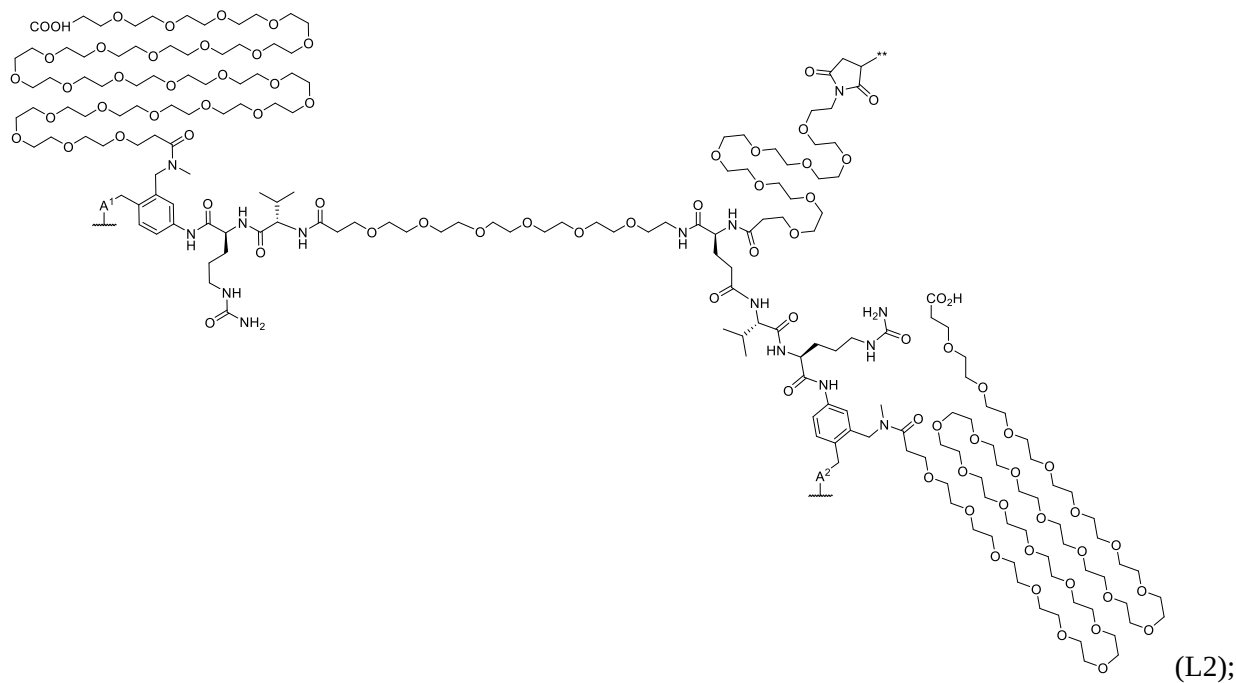
n is an integer between 1 and 12 (*e.g.*, between 5 and 10);

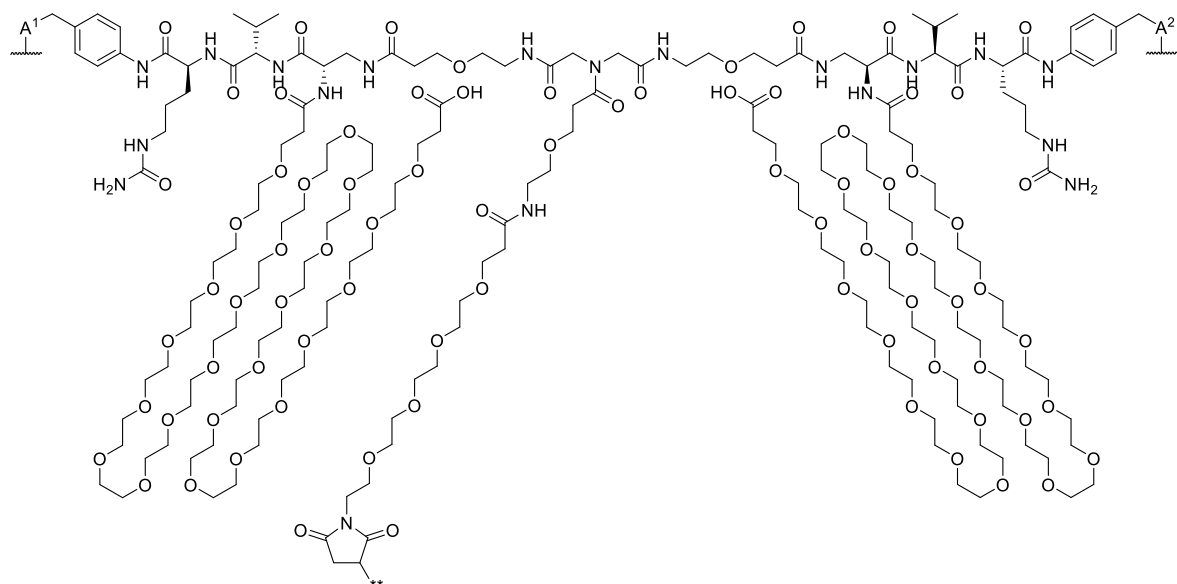
**— indicates the point of attachment to the Ab; and

 indicates the point of direct attachment to D^1 or D^2 ; or

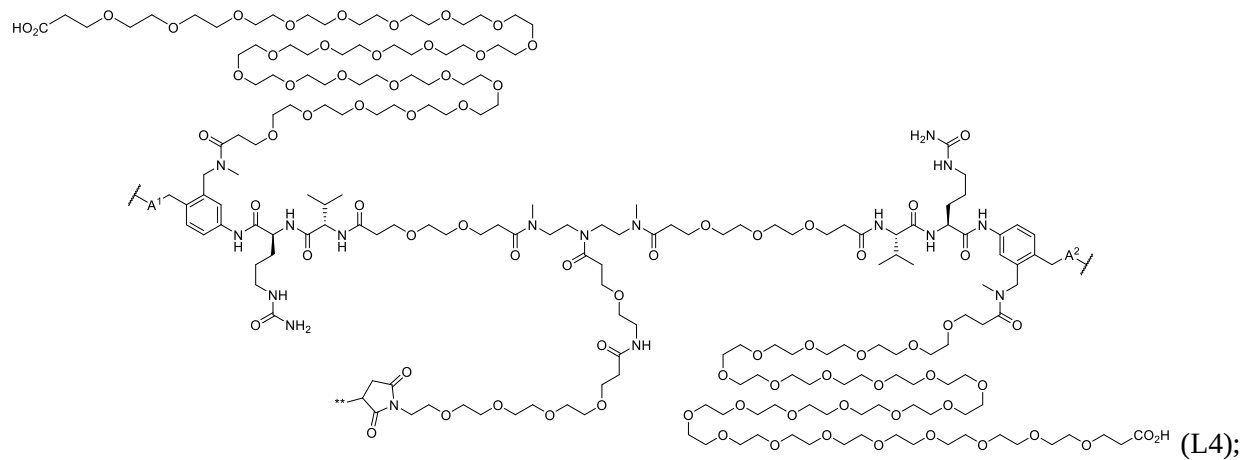
(iii) the dual linker is represented by the following formula:



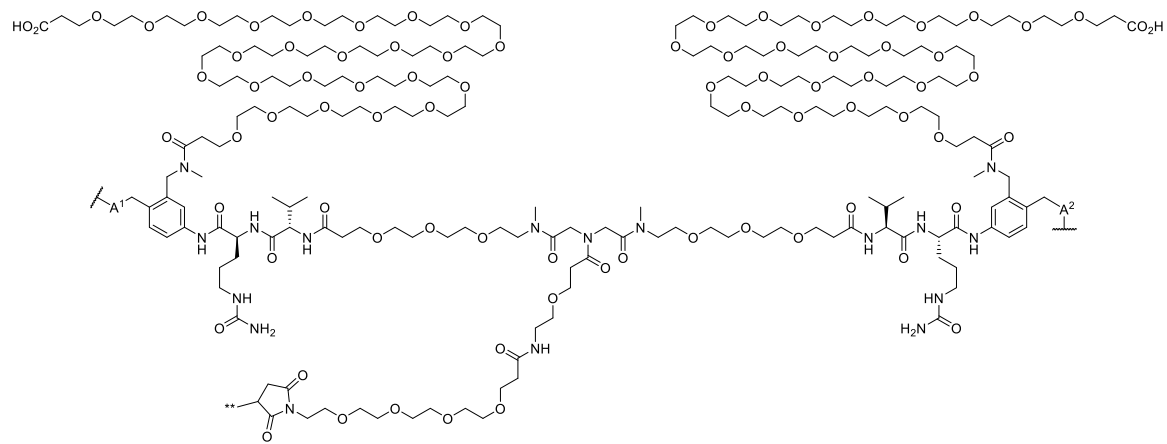




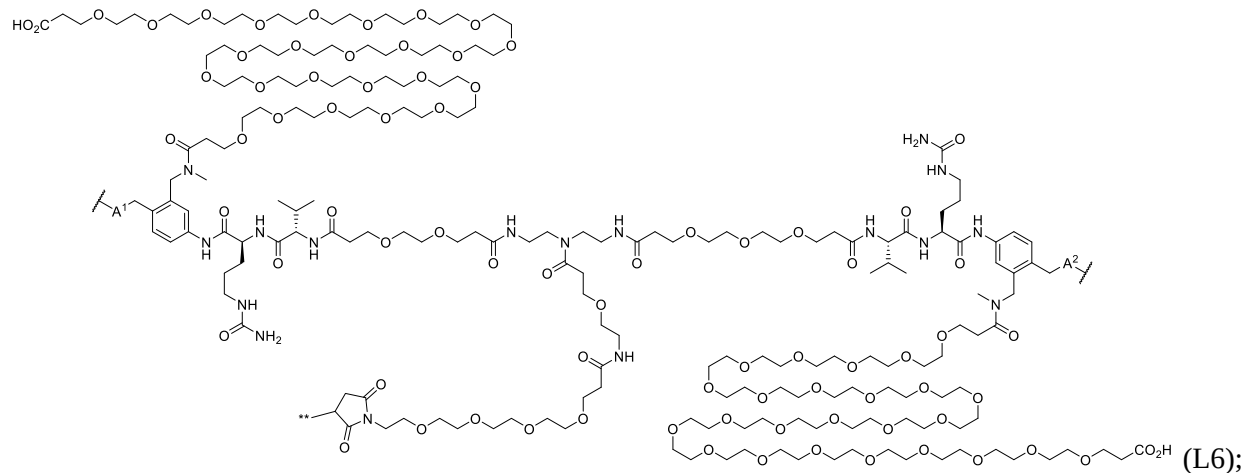
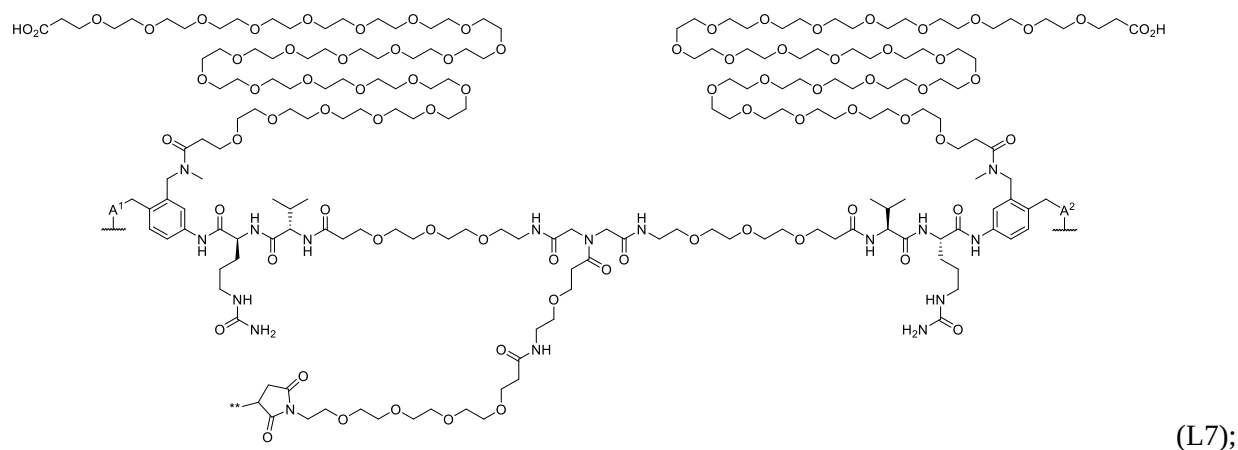
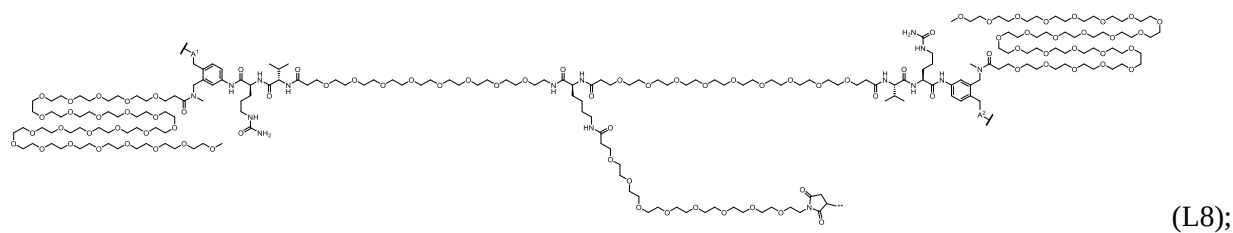
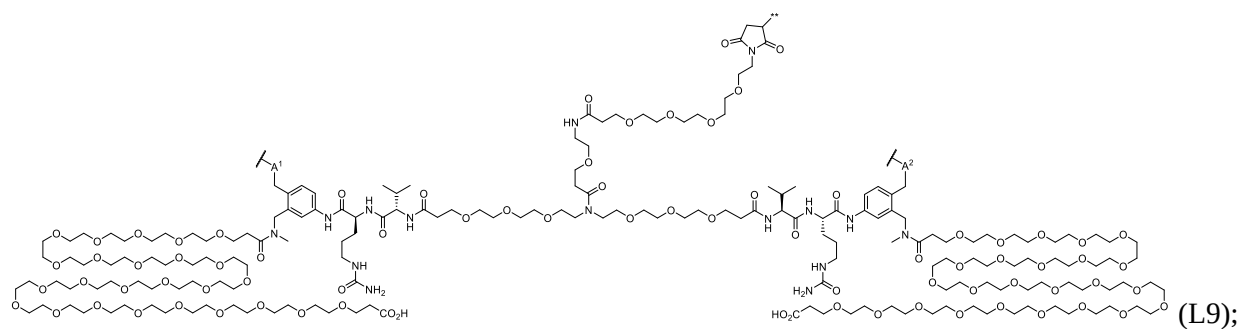
(L3);

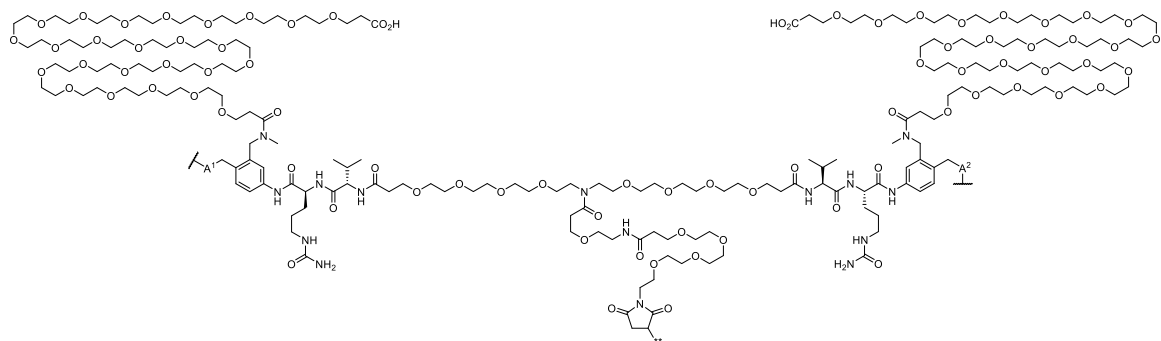


(L4);

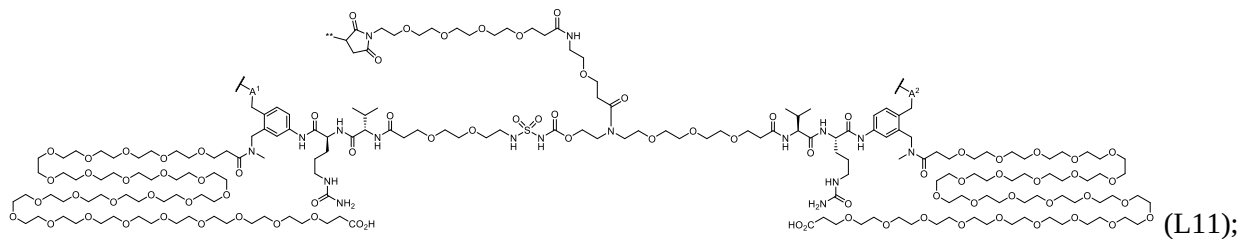


(L5);

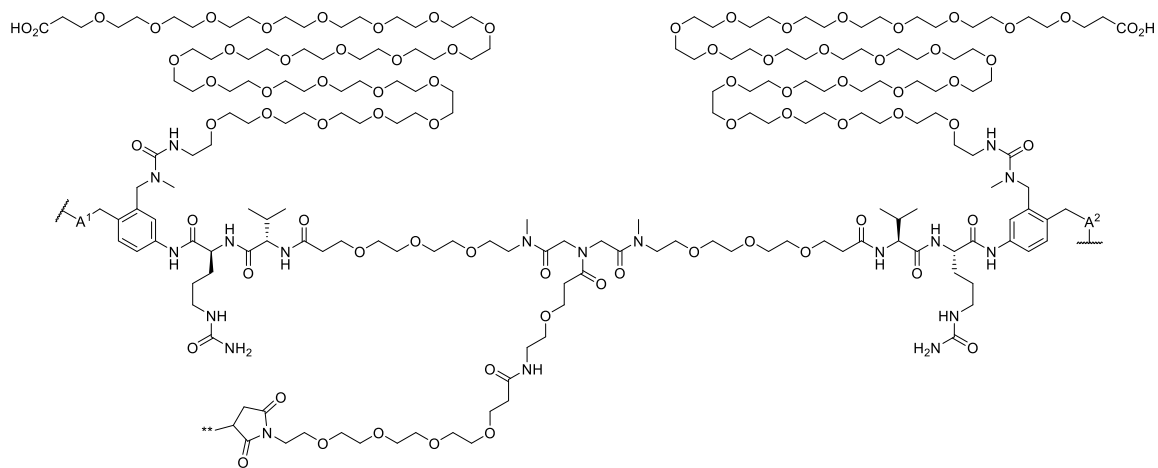




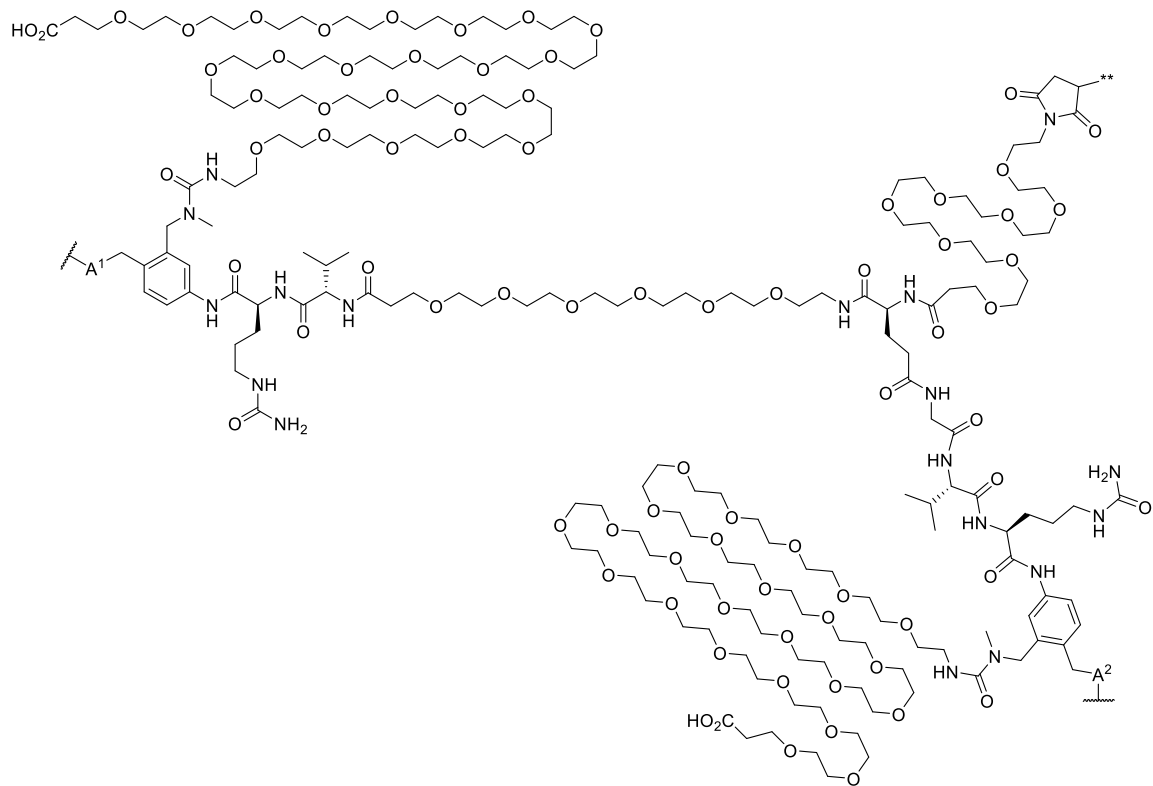
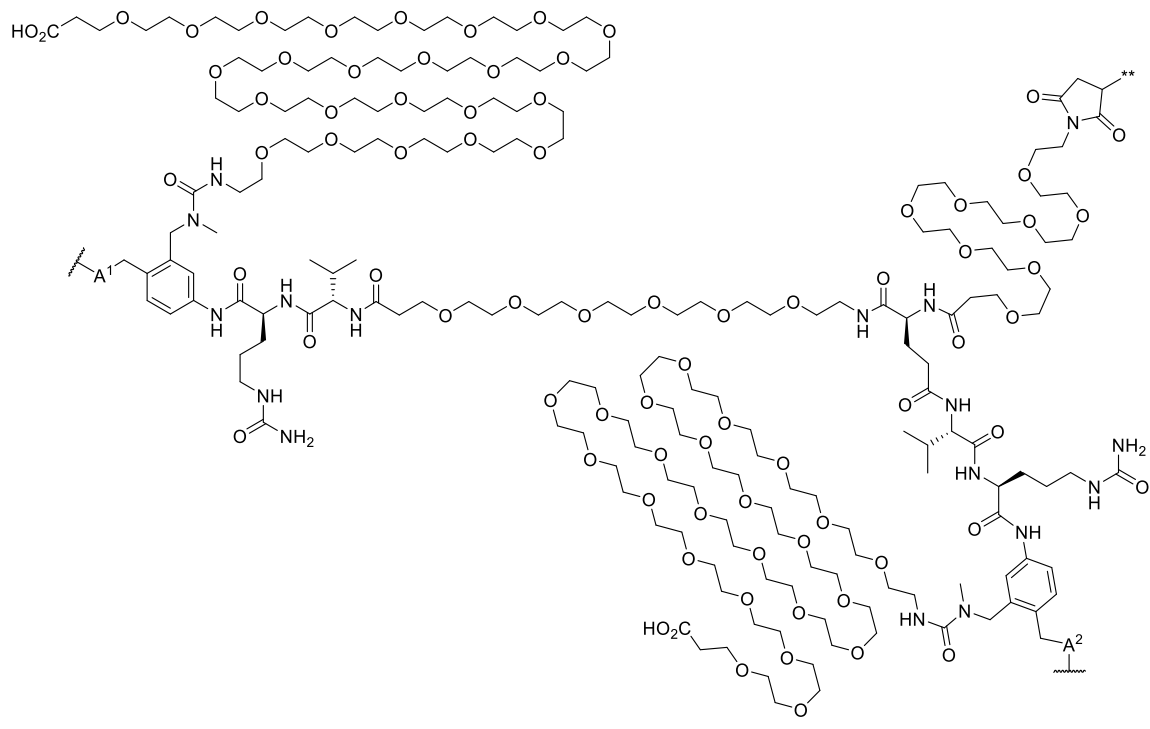
(L10);

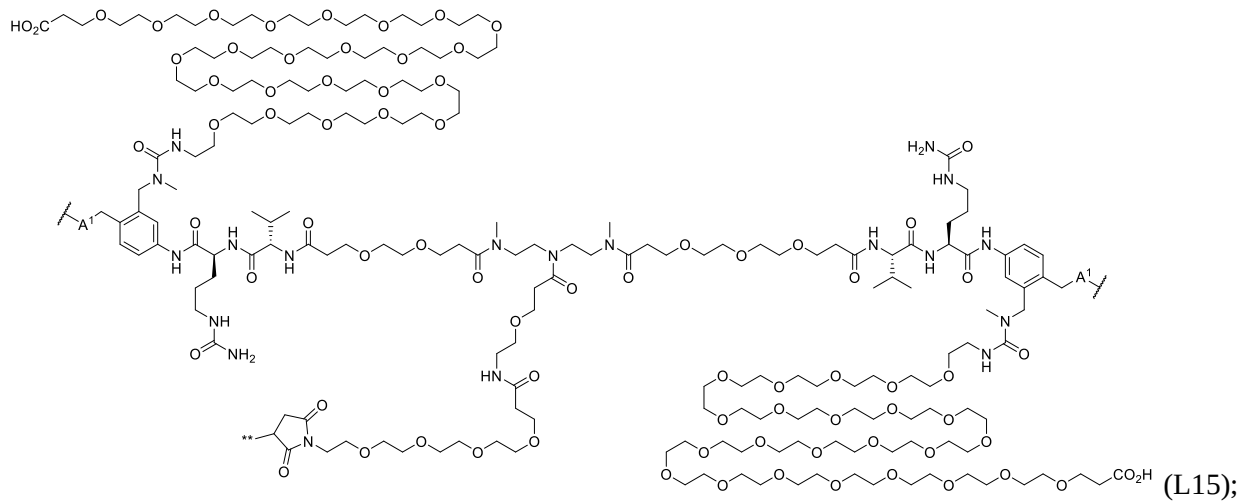
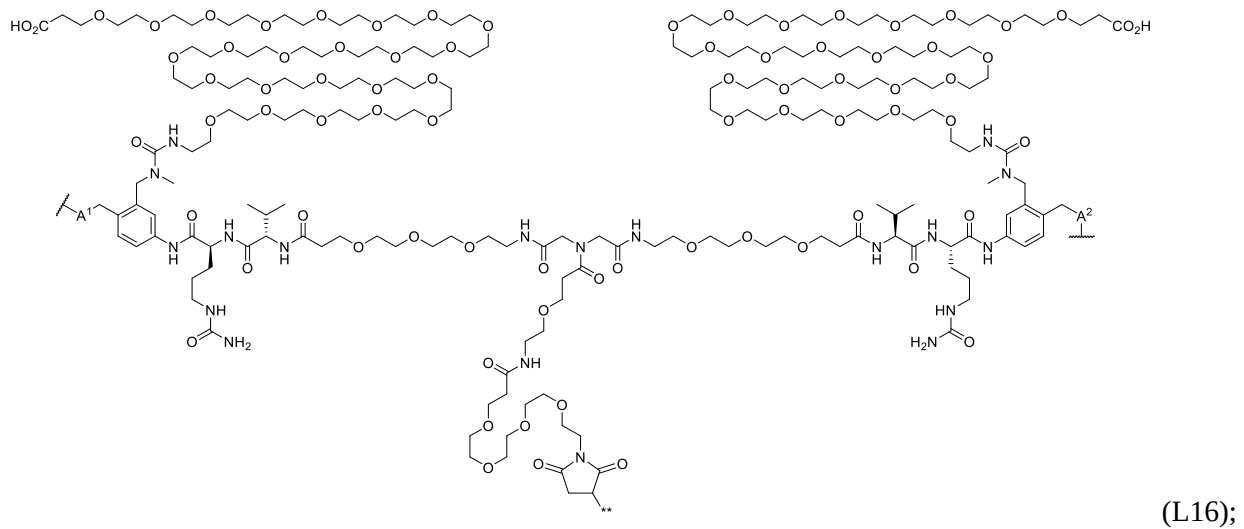
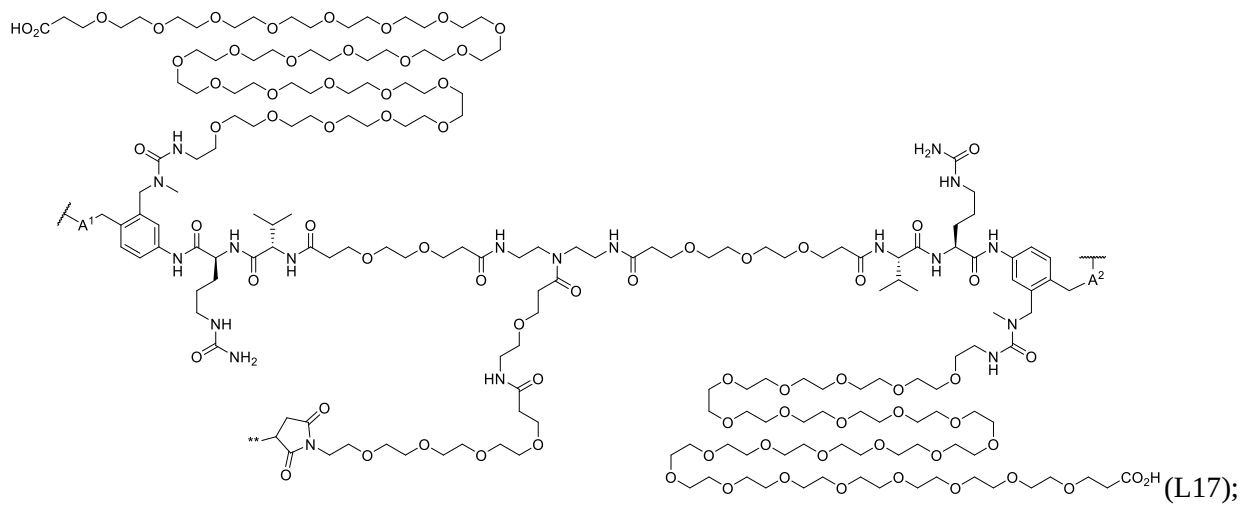


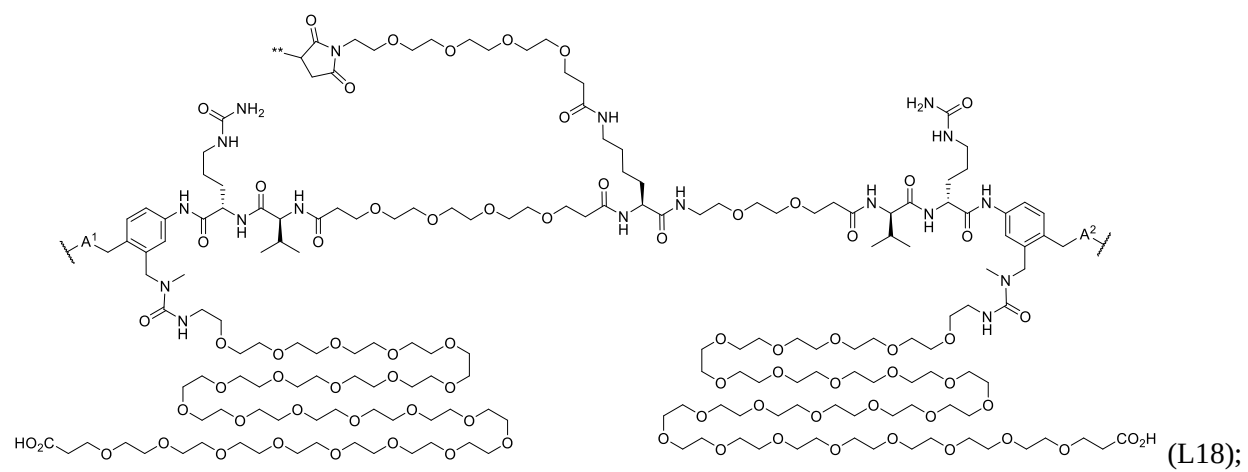
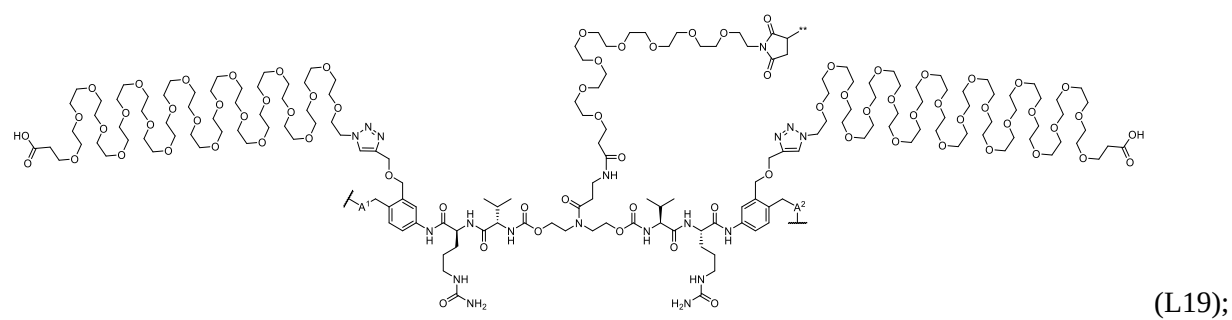
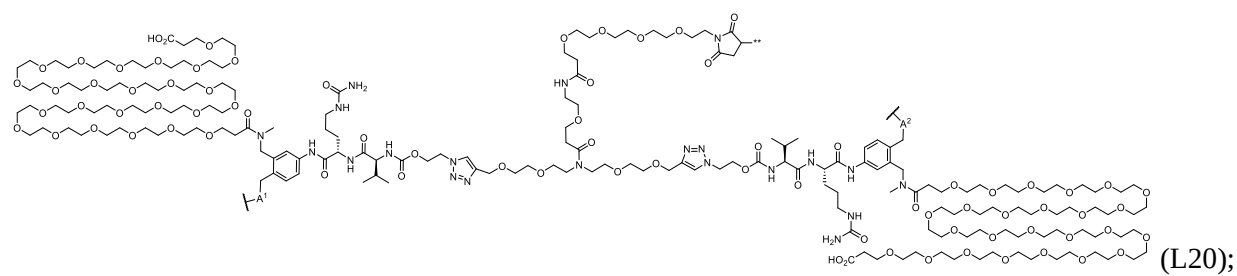
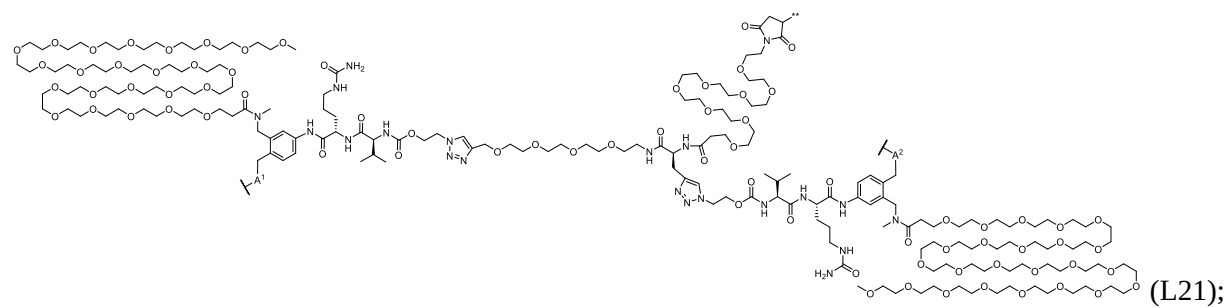
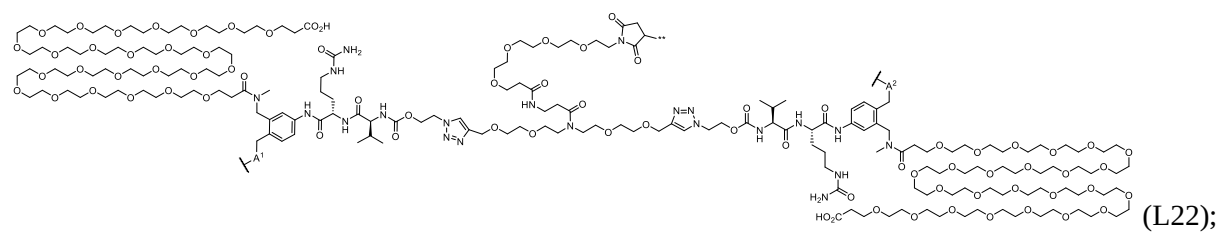
(L11);

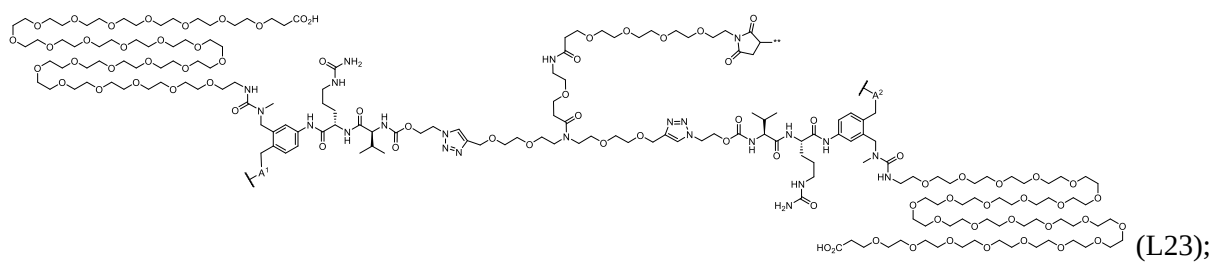
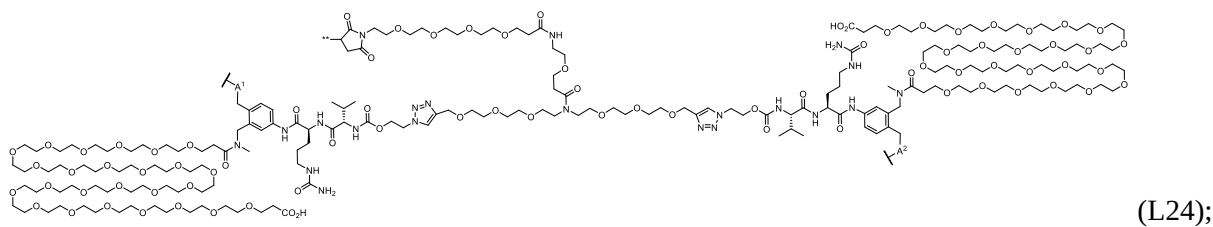
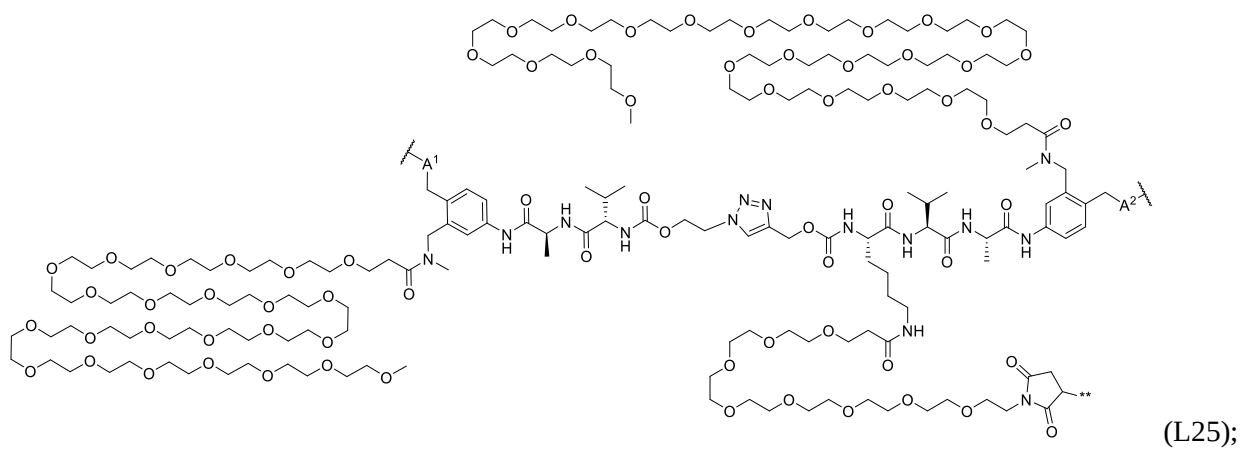
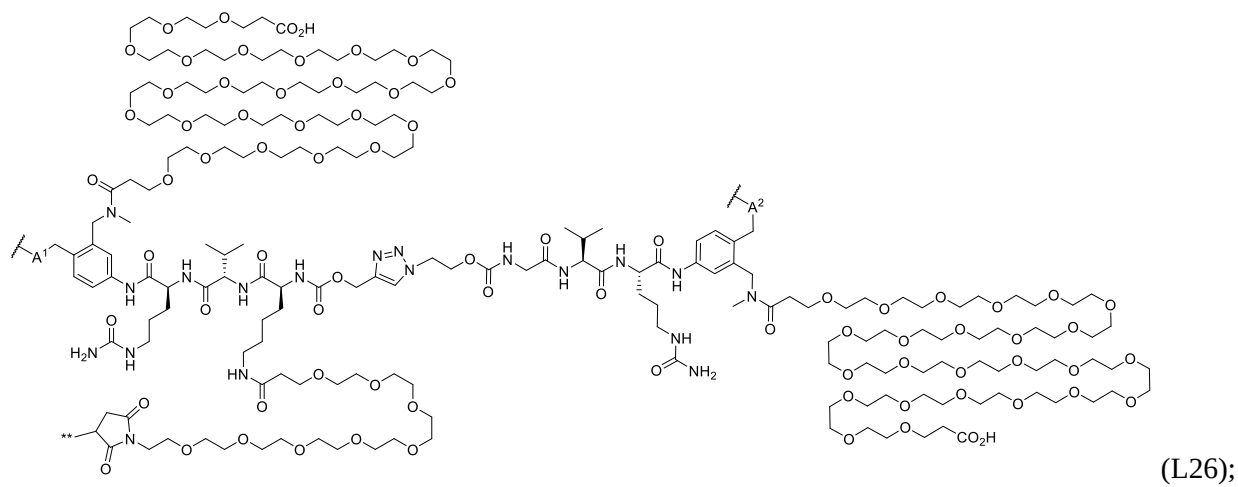


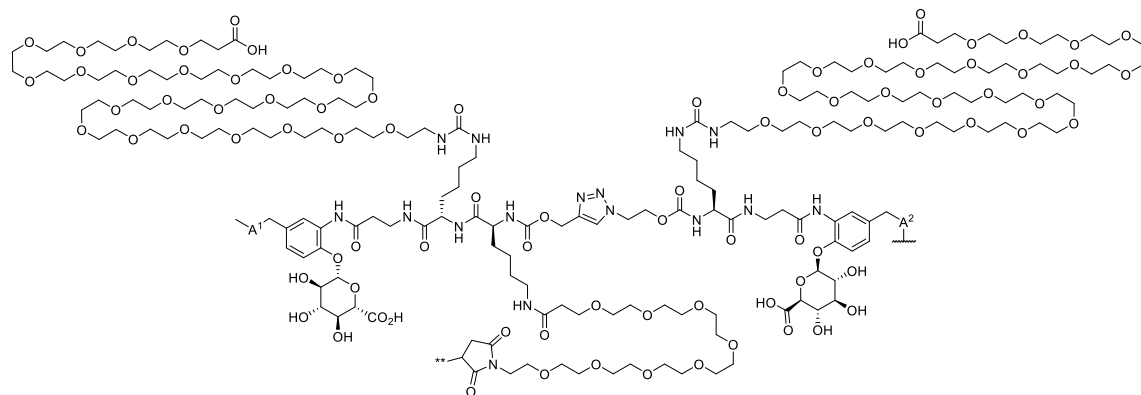
(L12);



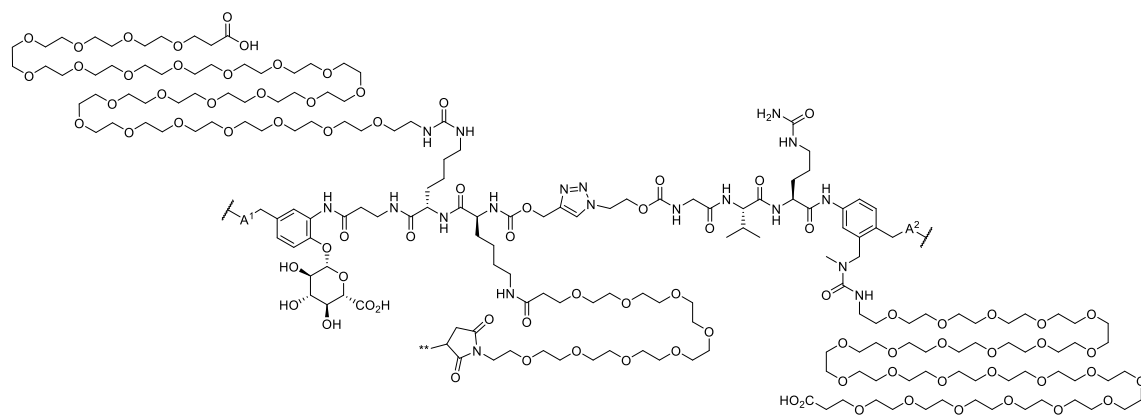




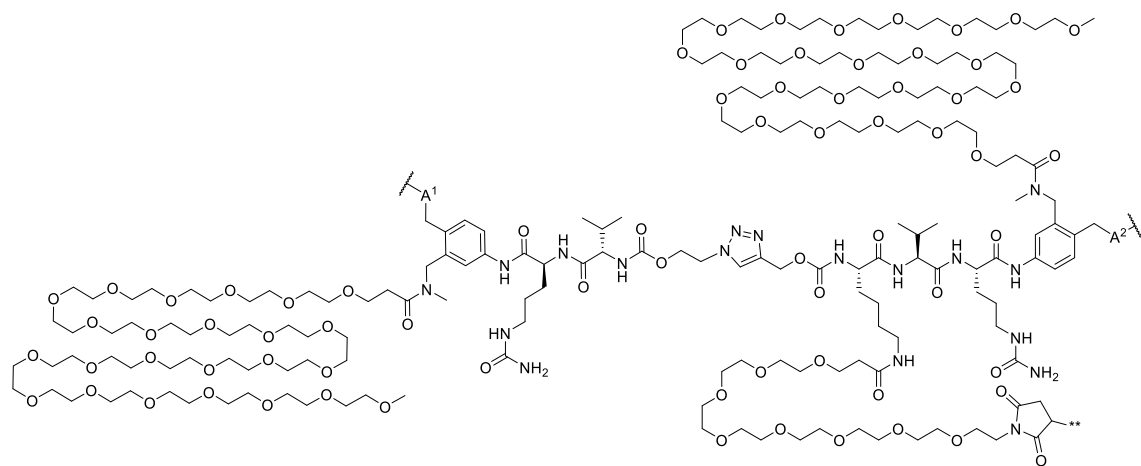




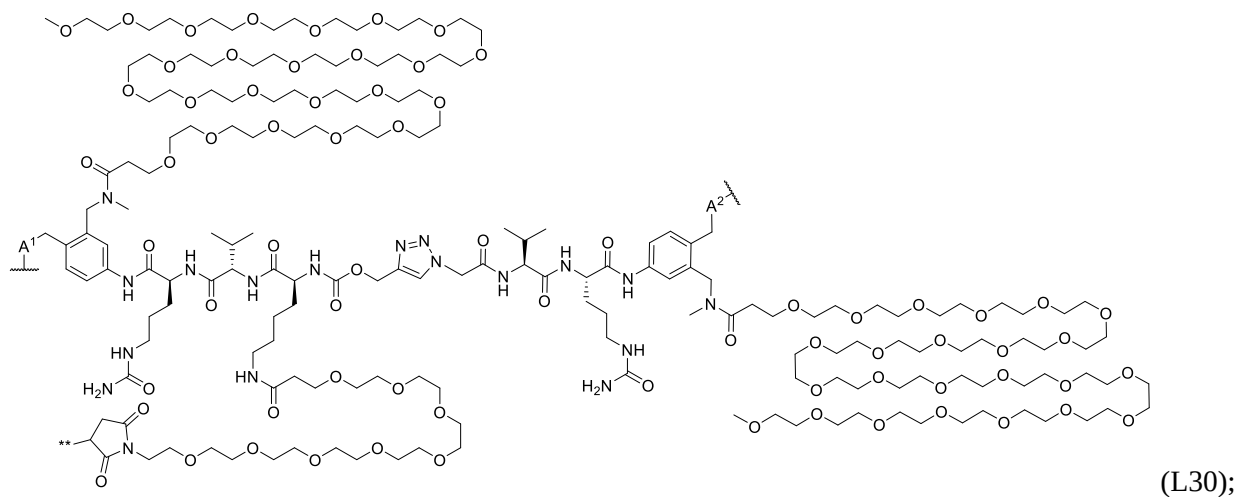
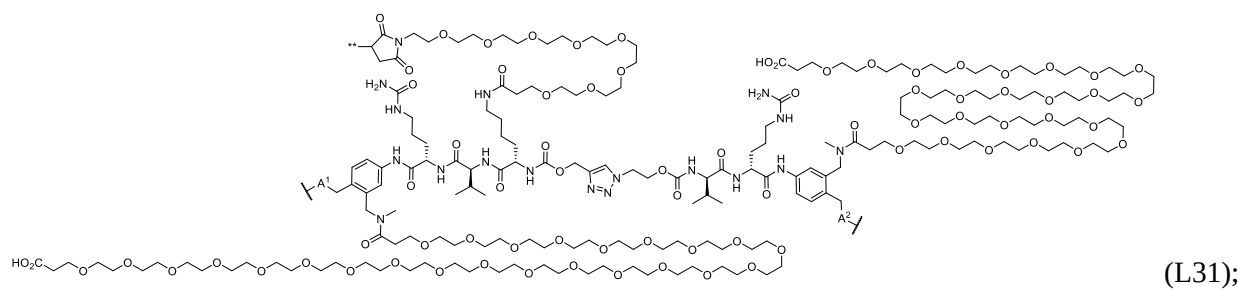
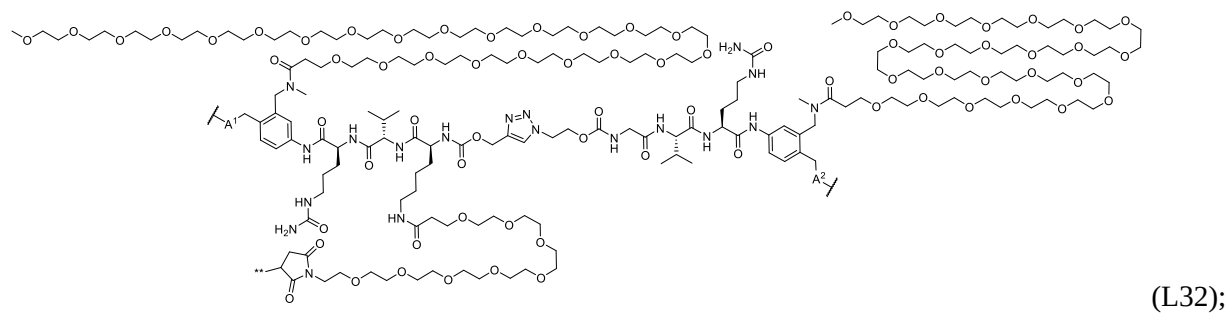
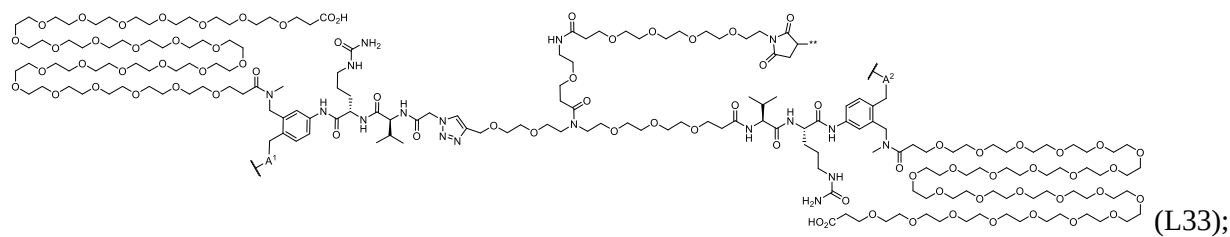
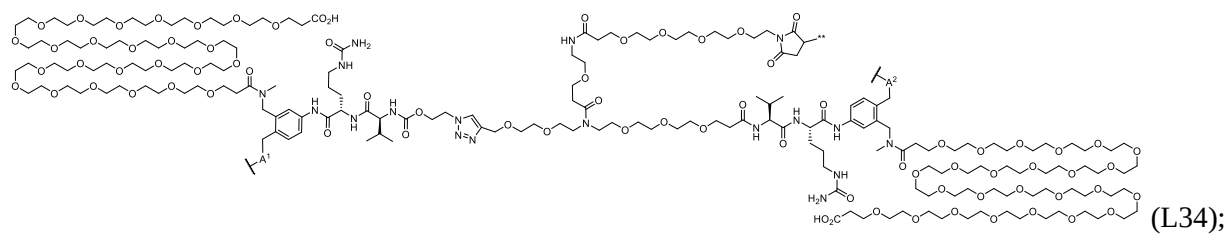
(L27);

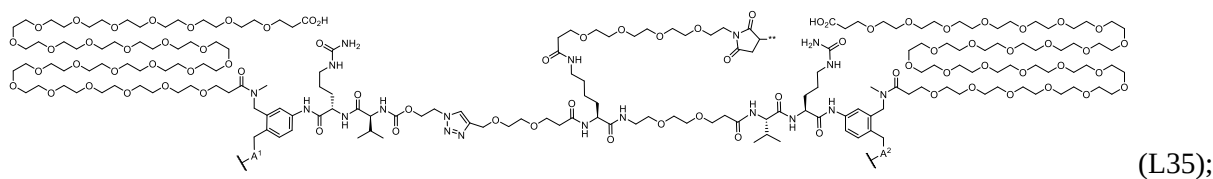
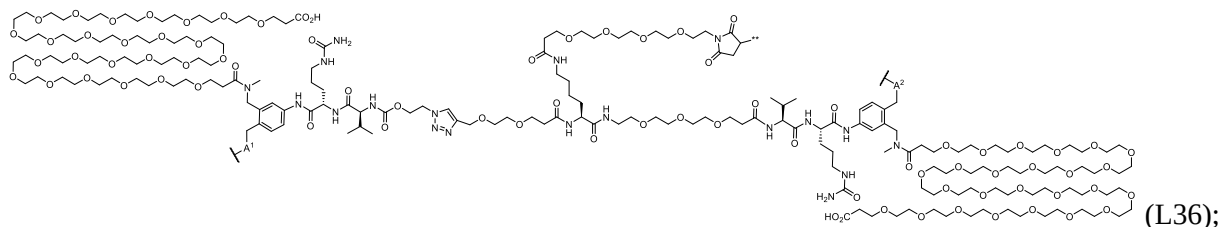


(L28);

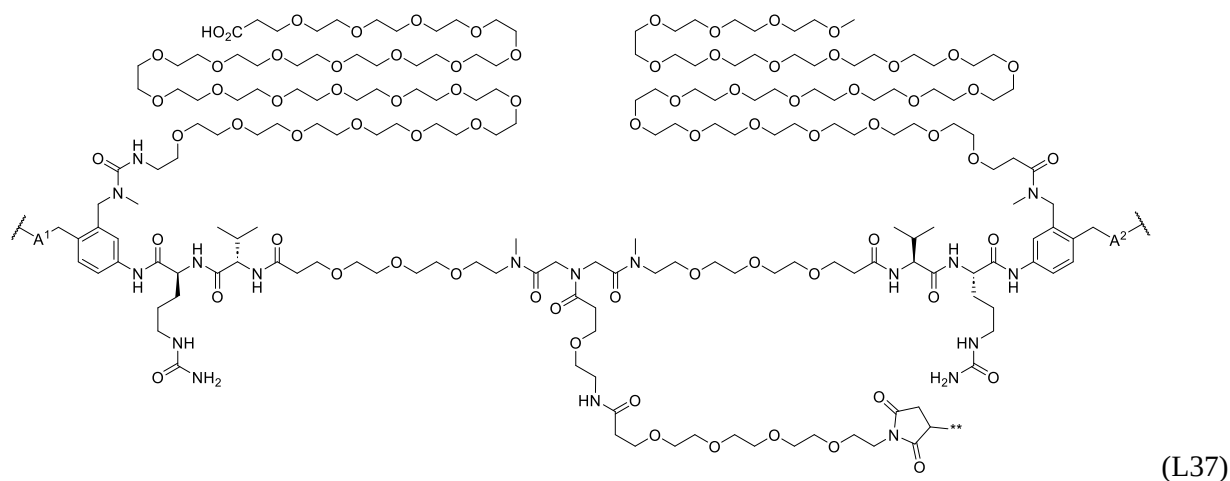
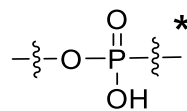


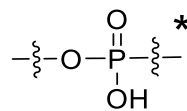
(L29);





and



wherein each A¹ or A² independently is a bond, -OC(=O)-*, or , preferably wherein A¹ and A² are each independent a bond or -O-C(=O)-*, wherein * indicates the point of attachment to the antineoplastic payload; **— indicates the point of attachment to the Ab; and  indicates the point of direct attachment to the antineoplastic payload, wherein at least one antineoplastic payload is a BH3 mimetic; preferably wherein D¹ and D² are each independently a BH3 mimetic.

20. The antibody-drug conjugate of any one of claims 6 to 19, wherein:

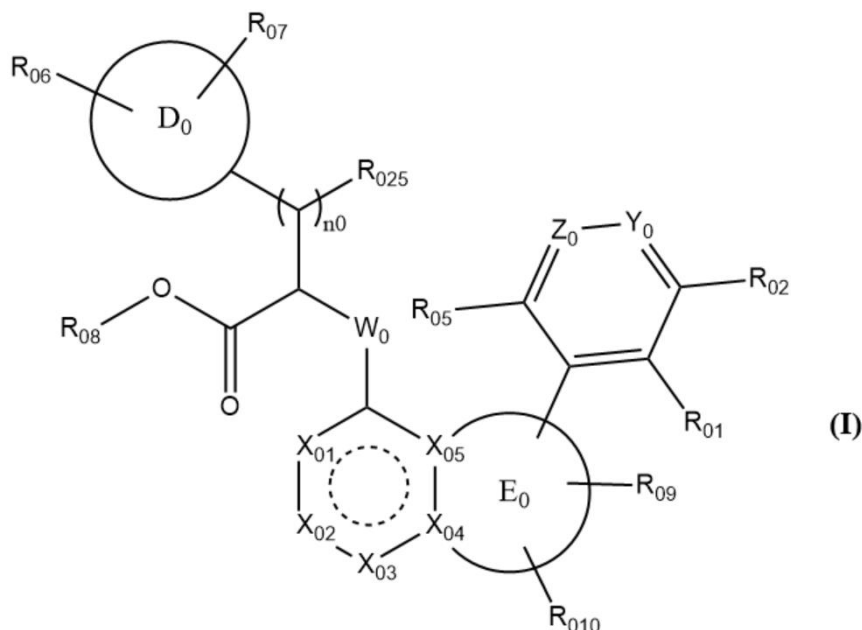
(i) one of D¹ and D² is a BH3 mimetic selected from a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor, and the other is an antineoplastic non-BH3 mimetic selected from topoisomerase 1 inhibitor or an anti-mitotic drug;

(ii) D¹ and/or D² are each independently selected from a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor;

- (iii) both D¹ and D² are (a) a Mcl-1 inhibitor; (b) a Bcl-2 inhibitor; or (c) a Bcl-xL inhibitor;
- (iv) D¹ and D² are the same;
- (v) D¹ and D² are different;
- (vi) one of D¹ and D² is a Mcl-1 inhibitor and the other is a Bcl-2 inhibitor;
- (vii) one of D¹ and D² is a Mcl-1 inhibitor and the other is a Bcl-xL inhibitor;
- (viii) one of D¹ and D² is a Bcl-2 inhibitor and the other is a Bcl-xL inhibitor;
- (ix) D¹ is a Mcl-1 inhibitor and D² is a Mcl-1 inhibitor;
- (x) D¹ is a Mcl-1 inhibitor and D² is a Bcl-2 inhibitor;
- (xi) D¹ is a Bcl-xL inhibitor and D² is a Bcl-xL inhibitor;
- (xii) D¹ is a Bcl-xL inhibitor and D² is a Bcl-2 inhibitor;
- (xiii) D¹ is a Bcl-2 inhibitor and D² is a Mcl-1 inhibitor;
- (xiv) D¹ is a Mcl-1 inhibitor and D² is a Bcl-xL inhibitor;
- (xv) D¹ is a BH3 mimetic and D² is an antineoplastic non-BH3 mimetic;
- (xvi) D¹ is selected from a Mcl-1 inhibitor, a Bcl-2 inhibitor, and a Bcl-xL inhibitor, and D² is a topoisomerase 1 inhibitor or an anti-mitotic drug;
- (xvii) D¹ is a Bcl-xL inhibitor and D² is a topoisomerase 1 inhibitor; or
- (xviii) D¹ is a Bcl-xL inhibitor and D² is an anti-mitotic drug.

21. The antibody-drug conjugate of any one of claims 19-20, or pharmaceutically acceptable salt thereof, the Mcl-1 inhibitor is represented by:

- (i) Formula (I):



or an enantiomer, diastereoisomer, atropisomer, deuterated derivative, and/or pharmaceutically acceptable salt of any of the foregoing,

wherein:

Ring D₀ is a cycloalkyl group, a heterocycloalkyl group, an aryl group or a heteroaryl group,

Ring E₀ is a furyl, thienyl or pyrrolyl ring,

X₀₁, X₀₃, X₀₄ and X₀₅, independently of one another, are a carbon atom or a nitrogen atom,

X₀₂ is a C-R₀₂₆ group or a nitrogen atom,

 means that the ring is aromatic,

Y₀ is a nitrogen atom or a C-R₀₃ group,

Z₀ is a nitrogen atom or a C-R₀₄ group,

R₀₁ is a halogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a linear or branched (C₁-C₆)haloalkyl group, a hydroxy group, a hydroxy(C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, -S-(C₁-C₆)alkyl group, a cyano group, a nitro group, -Cy₀₈, -(C₀-C₆)alkyl-NR₀₁₁R₀₁₁', -O-(C₁-C₆)alkyl-NR₀₁₁R₀₁₁', -O-(C₁-C₆)alkyl-R₀₁₂, -C(O)-OR₀₁₁, -O-C(O)-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁', -NR₀₁₁-C(O)-R₀₁₁', -NR₀₁₁-C(O)-OR₀₁₁', -(C₁-C₆)alkyl-NR₀₁₁-C(O)-R₀₁₁', -SO₂-NR₀₁₁R₀₁₁', or -SO₂-(C₁-C₆)alkyl,

R₀₂, R₀₃, R₀₄ and R₀₅, independently of one another, are a hydrogen atom, a halogen atom,

a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a linear or branched (C₁-C₆)haloalkyl, a hydroxy group, a hydroxy(C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, a -S-(C₁-C₆)alkyl group, a cyano group, a nitro group, -(C₀-C₆)alkyl-NR₀₁₁R₀₁₁', -O-Cy₀₁, -(C₀-C₆)alkyl-Cy₀₁, -(C₂-C₆)alkenyl-Cy₀₁, -(C₂-C₆)alkynyl-Cy₀₁, -O-(C₁-C₆)alkyl-NR₀₁₁R₀₁₁', -O-(C₁-C₆)alkyl-R₀₃₁, -O-(C₁-C₆)alkyl-R₀₁₂, -C(O)-OR₀₁₁, -O-C(O)-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁', -NR₀₁₁-C(O)-R₀₁₁', -NR₀₁₁-C(O)-OR₀₁₁', -(C₁-C₆)alkyl-NR₀₁₁-C(O)-R₀₁₁', -SO₂-NR₀₁₁R₀₁₁', or -SO₂-(C₁-C₆)alkyl, or the pair (R₀₁, R₀₂), (R₀₂, R₀₃), (R₀₃, R₀₄), or (R₀₄, R₀₅) together with the carbon atoms to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains 1 to 3 heteroatoms selected from O, S and N, wherein the resulting ring is optionally substituted by 1 or 2 groups selected from halogen, linear or branched (C₁-C₆)alkyl, (C₀-C₆)alkyl-NR₀₁₁R₀₁₁', -NR₀₁₃R₀₁₃', -(C₀-C₆)alkyl-Cy₀₁ or oxo,

R₀₆ and R₀₇, independently of one another, are a hydrogen atom, a halogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a linear or branched (C₁-C₆)haloalkyl, a hydroxy group, a linear or branched (C₁-C₆)alkoxy group, a -S-(C₁-C₆)alkyl group, a cyano group, a nitro group, -(C₀-C₆)alkyl-NR₀₁₁R₀₁₁', -O-(C₁-C₆)alkyl-NR₀₁₁R₀₁₁', -O-Cy₀₁, -(C₀-C₆)alkyl-Cy₀₁, -(C₂-C₆)alkenyl-Cy₀₁, -(C₂-C₆)alkynyl-Cy₀₁, -O-(C₁-C₆)alkyl-R₀₁₂, -C(O)-OR₀₁₁, -O-C(O)-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁', -NR₀₁₁-C(O)-R₀₁₁', -NR₀₁₁-C(O)-OR₀₁₁', -(C₁-C₆)alkyl-NR₀₁₁-C(O)-R₀₁₁', -SO₂-NR₀₁₁R₀₁₁', or -SO₂-(C₁-C₆)alkyl, or the pair (R₀₆, R₀₇), when fused with the two adjacent carbon atoms, together with the carbon atoms to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains 1 to 3 heteroatoms selected from O, S and N, wherein the resulting ring is optionally substituted by a linear or branched (C₁-C₆)alkyl group,

-NR₀₁₃R₀₁₃', -(C₀-C₆)alkyl-Cy₀₁ or an oxo,

W₀ is a -CH₂- group, a -NH- group or an oxygen atom,

R₀₈ is a hydrogen atom, a linear or branched (C₁-C₈)alkyl group, a -CHR_{0a}R_{0b} group, an aryl group, a heteroaryl group, an aryl(C₁-C₆)alkyl group, or a heteroaryl(C₁-C₆)alkyl group,

R₀₉ is a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, -Cy₀₂, -(C₁-C₆)alkyl-Cy₀₂, -(C₂-C₆)alkenyl-Cy₀₂, -(C₂-C₆)alkynyl-Cy₀₂, -Cy₀₂-Cy₀₃, -(C₂-C₆)alkynyl-O-Cy₀₂, -Cy₀₂-(C₀-C₆)alkyl-O-(C₀-C₆)alkyl-Cy₀₃, a halogen atom, a cyano group, -C(O)-R₀₁₄, or -C(O)-NR₀₁₄R₀₁₄',

R₀₁₀ is a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, an aryl(C₁-C₆)alkyl group, a

(C₁-C₆)cycloalkylalkyl group, a linear or branched (C₁-C₆)haloalkyl, or -(C₁-C₆)alkyl-O-Cy₀₄, or the pair (R₀₉, R₀₁₀), when fused with the two adjacent carbon atoms, together with the carbon atoms to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains 1 to 3 heteroatoms selected from O, S and N,

R₀₁₁ and R₀₁₁', independently of one another, are a hydrogen atom, an optionally substituted linear or branched (C₁-C₆)alkyl group, or -(C₀-C₆)alkyl-Cy₀₁, or the pair (R₀₁₁, R₀₁₁') together with the nitrogen atom to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains, in addition to the nitrogen atom, 1 to 3 heteroatoms selected from O, S, and N, wherein the N atom may be substituted by 1 or 2 groups selected from a linear or branched (C₁-C₆)alkyl group, and wherein one or more of the carbon atoms of the linear or branched (C₁-C₆)alkyl group is optionally deuterated,

R₀₁₂ is -Cy₀₅, -Cy₀₅-(C₀-C₆)alkyl-O-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-(C₀-C₆)alkyl-NR₀₁₁-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-Cy₀₆-O-(C₀-C₆)alkyl-Cy₀₇, -Cy₀₅-(C₀-C₆)alkyl-O-(C₀-C₆)alkyl-Cy₀₉, -Cy₀₅-(C₀-C₆)alkyl-Cy₀₉, -NH-C(O)-NH-R₀₁₁, -Cy₀₅-(C₀-C₆)alkyl-NR₀₁₁-(C₀-C₆)alkyl-Cy₀₉, -C(O)-NR₀₁₁R₀₁₁', -NR₀₁₁R₀₁₁', -OR₀₁₁, -NR₀₁₁-C(O)-R₀₁₁', -O-(C₁-C₆)alkyl-OR₀₁₁, -SO₂-R₀₁₁, -C(O)-OR₀₁₁,

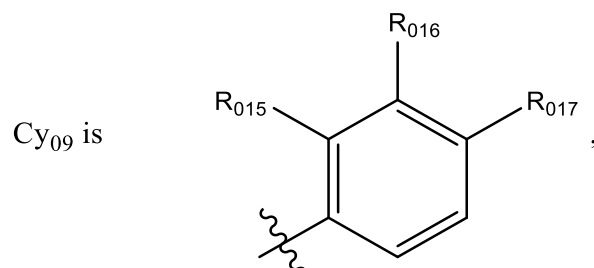
R₀₁₃, R₀₁₃', R₀₁₄ and R₀₁₄', independently of one another, are a hydrogen atom, or an optionally substituted linear or branched (C₁-C₆)alkyl group,

R_{0a} is a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

R_{0b} is a -O-C(O)-O-R_{0c} group, a -O-C(O)-NR_{0c}R_{0c}' group, or a -O-P(O)(OR_{0c})₂ group,

R_{0c} and R_{0c}', independently of one another, are a hydrogen atom, a linear or branched (C₁-C₈)alkyl group, a cycloalkyl group, a (C₁-C₆)alkoxy(C₁-C₆)alkyl group, or a (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl group, or the pair (R_{0c}, R_{0c}') together with the nitrogen atom to which they are attached form a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen atom from 1 to 3 heteroatoms selected from oxygen and nitrogen, wherein the nitrogen is optionally substituted by a linear or branched (C₁-C₆)alkyl group,

Cy₀₁, Cy₀₂, Cy₀₃, Cy₀₄, Cy₀₅, Cy₀₆, Cy₀₇, Cy₀₈ and Cy₀₁₀, independently of one another, are a cycloalkyl group, a heterocycloalkyl group, an aryl group or a heteroaryl group, each of which is optionally substituted,



or Cy₀₉ is a heteroaryl group which is substituted by a group selected from -O-P(O)(OR₀₂₀)₂; -O-P(O)(O⁻M⁺)₂; -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀; hydroxy; hydroxy(C₁-C₆)alkyl; -(CH₂)_{r0}-U₀-(CH₂)_{s0}-heterocycloalkyl; and -U₀-(CH₂)_{q0}-NR₀₂₁R₀₂₁' ,

R₀₁₅ is a hydrogen atom; a -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀ group; a linear or branched (C₁-C₆)alkoxy(C₁-C₆)alkyl group; a -U₀-(CH₂)_{q0}-NR₀₂₁R₀₂₁' group; or a -(CH₂)_{r0}-U₀-(CH₂)_{s0}-heterocycloalkyl group,

R₀₁₆ is a hydrogen atom; a hydroxy group; a hydroxy(C₁-C₆)alkyl group; a -(CH₂)_{r0}-U₀-(CH₂)_{s0}-heterocycloalkyl group; a (CH₂)_{r0}-U₀-V₀-O-P(O)(OR₀₂₀)₂ group; a -O-P(O)(O⁻M⁺)₂ group; a -O-S(O)₂OR₀₂₀ group; a -S(O)₂OR₀₂₀ group; a -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀ group; a -(CH₂)_{p0}-O-C(O)-NR₀₂₂R₀₂₃ group; or a -U₀-(CH₂)_{q0}-NR₀₂₁R₀₂₁' group,

R₀₁₇ is a hydrogen atom; a -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀ group; a -CH₂-P(O)(OR₀₂₀)₂ group, a -O-P(O)(OR₀₂₀)₂ group; a -O-P(O)(O⁻M⁺)₂ group; a hydroxy group; a hydroxy(C₁-C₆)alkyl group; a -(CH₂)_{r0}-U₀-(CH₂)_{s0}-heterocycloalkyl group; a -U₀-(CH₂)_{q0}-NR₀₂₁R₀₂₁' group; or an aldonic acid,

M⁺ is a pharmaceutically acceptable monovalent cation,

U₀ is a bond or an oxygen atom,

V₀ is a -(CH₂)_{s0}- group or a -C(O)- group,

R₀₁₈ is a hydrogen atom or a (C₁-C₆)alkoxy(C₁-C₆)alkyl group,

R₀₁₉ is a hydrogen atom or a hydroxy(C₁-C₆)alkyl group,

R₀₂₀ is a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

R₀₂₁ and R₀₂₁' independently of one are a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or a hydroxy(C₁-C₆)alkyl group, or the pair (R₀₂₁, R₀₂₁') together with the nitrogen atom to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains, in addition to the nitrogen atom, 1 to 3 heteroatoms selected from O, S and N, wherein the resulting ring is optionally substituted by a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

R₀₂₂ is a (C₁-C₆)alkoxy(C₁-C₆)alkyl group, a -(CH₂)_{p0}-NR₀₂₄R₀₂₄' group, or a -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀ group,

R₀₂₃ is a hydrogen atom or a (C₁-C₆)alkoxy(C₁-C₆)alkyl group, or the pair (R₀₂₂, R₀₂₃) together with the nitrogen atom to which they are attached form an aromatic or non-aromatic ring containing 5 to 18 ring members, which optionally contains, in addition to the nitrogen atom, 1 to 5 heteroatoms selected from O, S and N, wherein the resulting ring is optionally substituted by a hydrogen atom, a linear or branched (C₁-C₆)alkyl group or a heterocycloalkyl group,

R₀₂₄ and R_{024'}, independently of one another, are a hydrogen atom or a linear or branched (C₁-C₆)alkyl group, or the pair (R₀₂₄, R_{024'}) together with the nitrogen atom to which they are attached form an aromatic or non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen atom from 1 to 3 heteroatoms selected from O, S and N, and wherein the resulting ring is optionally substituted by a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

R₀₂₅ is a hydrogen atom, a hydroxy group, or a hydroxy(C₁-C₆)alkyl group,

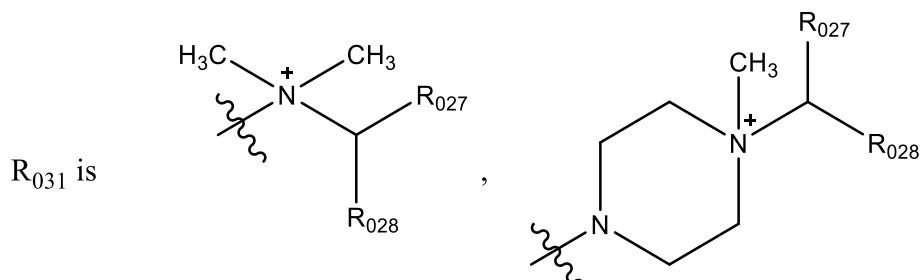
R₀₂₆ is a hydrogen atom, a halogen atom, a linear or branched (C₁-C₆)alkyl group, or a cyano group,

R₀₂₇ is a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

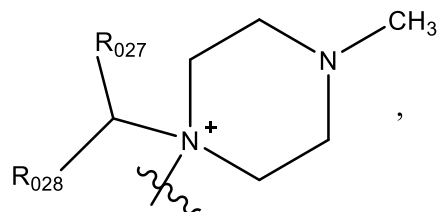
R₀₂₈ is a -O-P(O)(O⁻)(O⁻) group, a -O-P(O)(O⁻)(OR₀₃₀) group, a -O-P(O)(OR₀₃₀)(OR_{030'}) group, a -(CH₂)_{p0}-O-SO₂-O⁻ group, a -(CH₂)_{p0}-SO₂-O⁻ group, a -(CH₂)_{p0}-O-SO₂-OR₀₃₀ group, -Cy₀₁₀, a -(CH₂)_{p0}-SO₂-OR₀₃₀ group, a -O-C(O)-R₀₂₉ group, a -O-C(O)-OR₀₂₉ group or a -O-C(O)-NR₀₂₉R_{029'} group;

R₀₂₉ and R_{029'}, independently of one another, are a hydrogen atom, a linear or branched (C₁-C₆)alkyl group or a linear or branched amino(C₁-C₆)alkyl group,

R₀₃₀ and R_{030'}, independently of one another, are a hydrogen atom, a linear or branched (C₁-C₆)alkyl group or an aryl(C₁-C₆)alkyl group,



or



wherein the ammonium optionally exists as a zwitterionic form or has a monovalent anionic counterion,

n_0 is an integer equal to 0 or 1,

p_0 is an integer equal to 0, 1, 2, or 3,

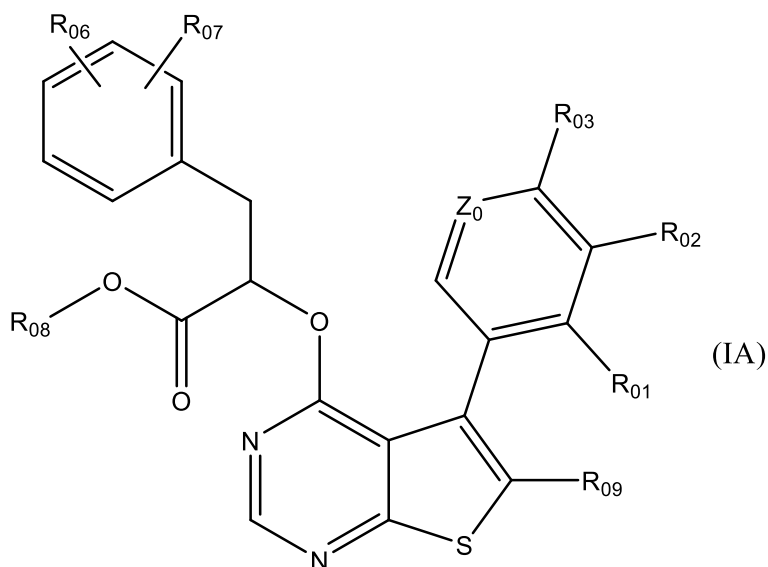
q_0 is an integer equal to 1, 2, 3 or 4,

r_0 and s_0 are independently an integer equal to 0 or 1;

wherein, at most, one of the R_{03} , R_{09} , or R_{012} groups, if present, is covalently attached to the linker, and

wherein the valency of an atom is not exceeded by virtue of one or more substituents bonded thereto;

(ii) Formula (IA):



or an enantiomer, diastereoisomer, atropisomer, deuterated derivative, and/or pharmaceutically acceptable salt of any of the foregoing,

wherein:

Z_0 is a nitrogen atom or a $C-R_{04}$ group,

R_{01} is a halogen atom, a linear or branched (C_1-C_6) alkyl group, a linear or branched (C_2-C_6) alkenyl group, a linear or branched (C_2-C_6) alkynyl group, a linear or branched (C_1-C_6) haloalkyl group, a hydroxy group, a linear or branched (C_1-C_6) alkoxy group, a $-S-(C_1-C_6)$ alkyl

group, a cyano group, -Cy₀₈, -NR₀₁₁R₀₁₁' ,

R₀₂, R₀₃ and R₀₄, independently of one another, are a hydrogen atom, a halogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a linear or branched (C₁-C₆)haloalkyl, a hydroxy group, a linear or branched (C₁-C₆)alkoxy group, a -S-(C₁-C₆)alkyl group, a cyano group, a nitro group, -(C₀-C₆)alkyl-NR₀₁₁R₀₁₁' , -O-Cy₀₁, -(C₀-C₆)alkyl-Cy₀₁, -(C₂-C₆)alkenyl-Cy₀₁, -(C₂-C₆)alkynyl-Cy₀₁, -O-(C₁-C₆)alkyl-NR₀₁₁R₀₁₁' , -O-(C₁-C₆)alkyl-R₀₃₁, -C(O)-OR₀₁₁, -O-C(O)-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁' , -NR₀₁₁-C(O)-R₀₁₁' , -NR₀₁₁-C(O)-OR₀₁₁' , -(C₁-C₆)alkyl-NR₀₁₁-C(O)-R₀₁₁' , -SO₂-NR₀₁₁R₀₁₁' , or -SO₂-(C₁-C₆)alkyl, or the pair (R₀₂, R₀₃) or (R₀₃, R₀₄) together with the carbon atoms to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains 1 to 3 heteroatoms selected from O, S and N, wherein the ring is optionally substituted by a group selected from a linear or branched (C₁-C₆)alkyl, -NR₀₁₃R₀₁₃' , -(C₀-C₆)alkyl-Cy₀₁ and oxo,

R₀₆ and R₀₇, independently of one another, are a hydrogen atom, a halogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a linear or branched (C₁-C₆)haloalkyl, a hydroxy group, a linear or branched (C₁-C₆)alkoxy group, a -S-(C₁-C₆)alkyl group, a cyano group, a nitro group, -(C₀-C₆)alkyl-NR₀₁₁R₀₁₁' , -O-Cy₀₁, -(C₀-C₆)alkyl-Cy₀₁, -(C₂-C₆)alkenyl-Cy₀₁, -(C₂-C₆)alkynyl-Cy₀₁, -O-(C₁-C₆)alkyl-R₀₁₂, -C(O)-OR₀₁₁, -O-C(O)-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁' , -NR₀₁₁-C(O)-R₀₁₁' , -NR₀₁₁-C(O)-OR₀₁₁' , -(C₁-C₆)alkyl-NR₀₁₁-C(O)-R₀₁₁' , -SO₂-NR₀₁₁R₀₁₁' , or -SO₂-(C₁-C₆)alkyl, or the pair (R₀₆, R₀₇), when fused with two adjacent carbon atoms, together with the carbon atoms to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains 1 to 3 heteroatoms selected from O, S and N, and wherein the resulting ring is optionally substituted by a group selected from a linear or branched (C₁-C₆)alkyl group, -NR₀₁₃R₀₁₃' , -(C₀-C₆)alkyl-Cy₀₁ and an oxo,

R₀₈ is a hydrogen atom, a linear or branched (C₁-C₈)alkyl group, an aryl group, a heteroaryl group, an aryl-(C₁-C₆)alkyl group, or a heteroaryl(C₁-C₆)alkyl group,

R₀₉ is a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, -Cy₀₂, -(C₁-C₆)alkyl-Cy₀₂, -(C₂-C₆)alkenyl-Cy₀₂, -(C₂-C₆)alkynyl-Cy₀₂, -Cy₀₂-Cy₀₃, -(C₂-C₆)alkynyl-O-Cy₀₂, -Cy₀₂-(C₀-C₆)alkyl-O-(C₀-C₆)alkyl-Cy₀₃, a halogen atom, a cyano group, -C(O)-R₀₁₄, -C(O)-NR₀₁₄R₀₁₄' ,

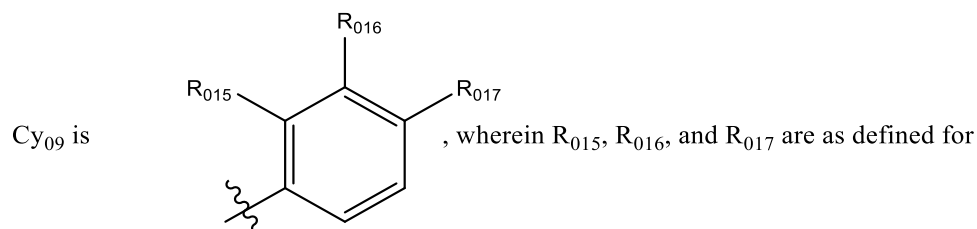
R₀₁₁ and R₀₁₁' , independently of one another, are a hydrogen atom, an optionally substituted linear or branched (C₁-C₆)alkyl group, or -(C₀-C₆)alkyl-Cy₀₁, or the pair (R₀₁₁, R₀₁₁') together with

the nitrogen atom to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains, in addition to the nitrogen atom, 1 to 3 heteroatoms selected from O, S and N, wherein the N atom is optionally substituted by a linear or branched (C₁-C₆)alkyl group, and wherein one or more of the carbon atoms of the linear or branched (C₁-C₆)alkyl group is optionally deuterated,

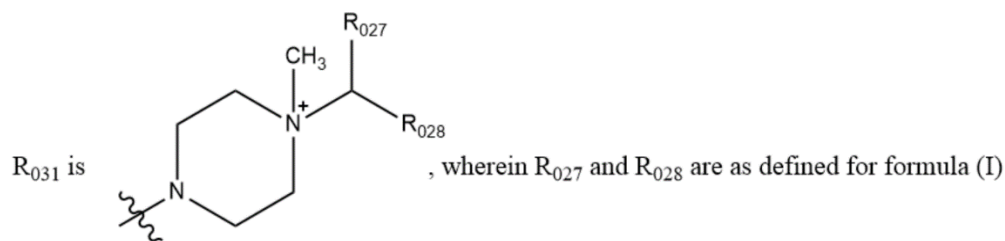
R₀₁₂ is -Cy₀₅, -Cy₀₅-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-(C₀-C₆)alkyl-O-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-(C₀-C₆)alkyl-NR₀₁₁-(C₀-C₆)alkyl-Cy₀₆, -Cy₀₅-Cy₀₆-O-(C₀-C₆)alkyl-Cy₀₇, -Cy₀₅-(C₀-C₆)alkyl-Cy₀₉, -NH-C(O)-NH-R₀₁₁, -C(O)-NR₀₁₁R₀₁₁', -NR₀₁₁R₀₁₁', -OR₀₁₁, -NR₀₁₁-C(O)-R₀₁₁', -O-(C₁-C₆)alkyl-OR₀₁₁, -SO₂-R₀₁₁, or -C(O)-OR₀₁₁,

R₀₁₃, R₀₁₃', R₀₁₄ and R₀₁₄', independently of one another, are a hydrogen atom, or an optionally substituted linear or branched (C₁-C₆)alkyl group,

Cy₀₁, Cy₀₂, Cy₀₃, Cy₀₅, Cy₀₆, Cy₀₇ and Cy₀₈, independently of one another, are a cycloalkyl group, a heterocycloalkyl group, an aryl group or a heteroaryl group, each of which is optionally substituted,

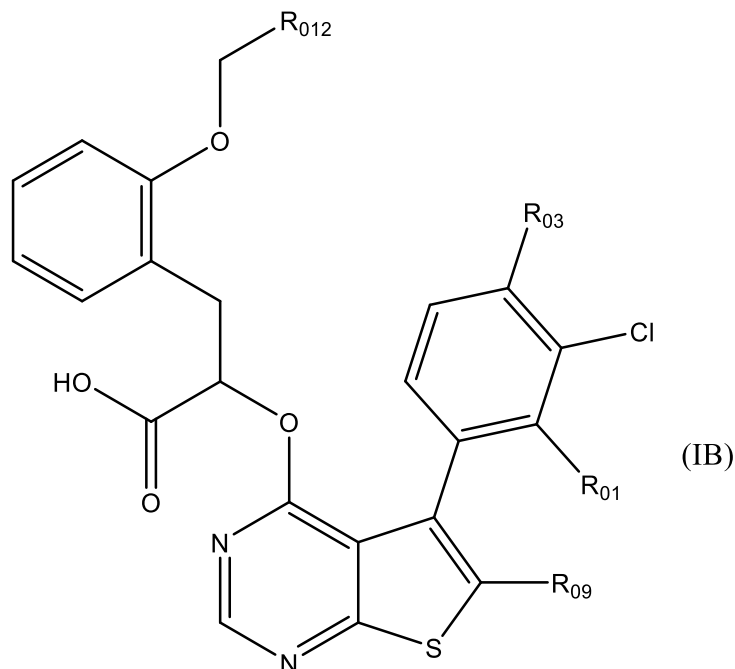


formula (I),



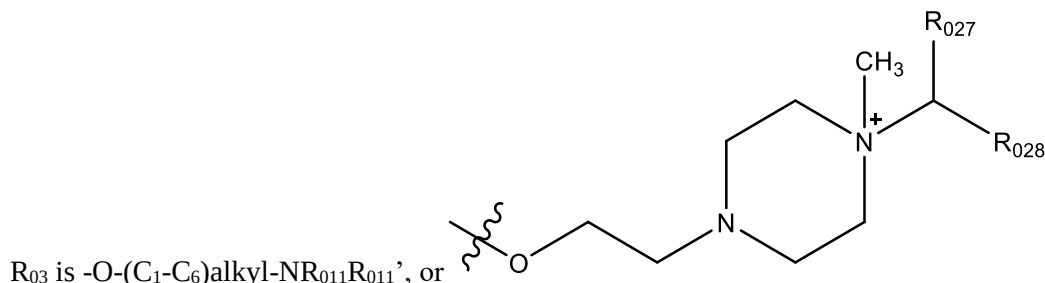
wherein, at most, one of the R₀₃, R₀₉, or R₀₁₂ groups, if present, is covalently attached to the linker; or

(iii) Formula (IB):



or the enantiomer, diastereoisomer, atropisomer, deuterated derivative, and/or pharmaceutically acceptable salt of any of the foregoing wherein:

R_{01} is a linear or branched (C_1-C_6) alkyl group,



wherein R_{011} and R_{011}' , independently of one another, are a hydrogen atom, an optionally substituted linear or branched (C_1-C_6) alkyl group, or $-(C_0-C_6)alkyl-Cy_{01}$;

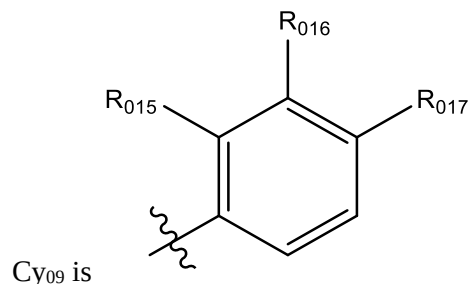
or the pair (R_{011}, R_{011}') together with the nitrogen atom to which they are attached form an aromatic or non-aromatic ring containing 5 to 7 ring members, which optionally contains, in addition to the nitrogen atom, 1 to 3 heteroatoms selected from O, S and N, wherein the N atom may be substituted by 1 or 2 groups selected from a hydrogen atom or a linear or branched (C_1-C_6) alkyl group,

and wherein R_{027} is a hydrogen atom and R_{028} is a $-(CH_2)_{p0}-O-SO_2-O^-$ group or a $-(CH_2)_{p0}-SO_2-OR_{030}$ group;

R_{09} is a linear or branched (C_2-C_6) alkynyl group or $-Cy_{02}$,

R₀₁₂ is -Cy₀₅, -Cy₀₅-(C₀-C₆)alkyl-Cy₀₆, or -Cy₀₅-(C₀-C₆)alkyl-Cy₀₉,

Cy₀₁, Cy₀₂, Cy₀₅ and Cy₀₆ independently of one another, are a cycloalkyl group, a heterocycloalkyl group, an aryl group or a heteroaryl group, each of which is optionally substituted,



R₀₁₅, R₀₁₆, and R₀₁₇ are as defined for formula (I),

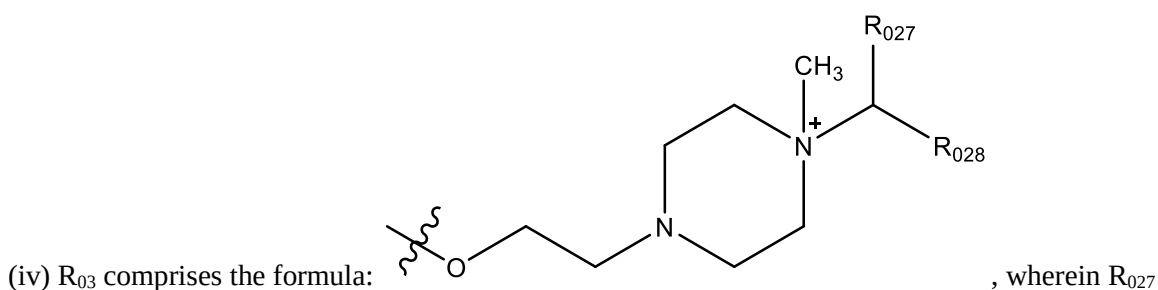
wherein, at most, one of the R₀₃, R₀₉, or R₀₁₂ groups, if present, is covalently attached to the linker.

22. The antibody-drug conjugate of claim 21, wherein:

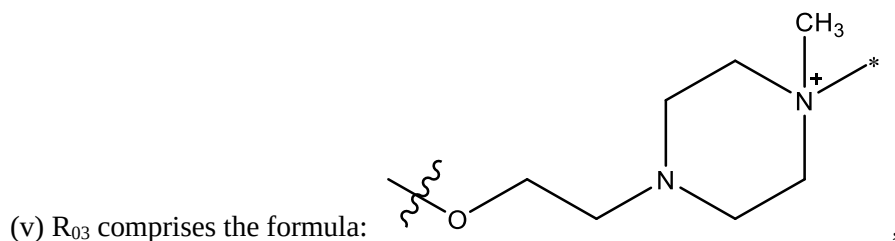
(i) Cy₀₁, Cy₀₂, Cy₀₃, Cy₀₄, Cy₀₅, Cy₀₆, Cy₀₇, Cy₀₈ and Cy₀₁₀, independently of one another, is a cycloalkyl group, a heterocycloalkyl group, an aryl group or a heteroaryl group, each of which is optionally substituted by one or more groups selected from halo; -(C₁-C₆)alkoxy; -(C₁-C₆)haloalkyl; -(C₁-C₆)haloalkoxy; -(CH₂)_{p0}-O-SO₂-OR₀₃₀; -(CH₂)_{p0}-SO₂-OR₀₃₀; -O-P(O)(OR₀₂₀)₂; -O-P(O)(O⁻M⁺)₂; -CH₂-P(O)(OR₀₂₀)₂; -(CH₂)_{p0}-O-(CHR₀₁₈-CHR₀₁₉-O)_{q0}-R₀₂₀; hydroxy; hydroxy(C₁-C₆)alkyl; -(CH₂)_{r0}-U₀-(CH₂)_{s0}-heterocycloalkyl; or -U₀-(CH₂)_{q0}-NR₀₂₁R₀₂₁';

(ii) R₀₁ is methyl or ethyl;

(iii) R₀₃ is -O-CH₂-CH₂-NR₀₁₁R₀₁₁' in which R₀₁₁ and R₀₁₁' form, together with the nitrogen atom carrying them, a piperazinyl group which may be substituted by a group being a hydrogen atom or a linear or branched (C₁-C₆)alkyl group;



is a hydrogen atom and R₀₂₈ is a -(CH₂)_{p0}-SO₂-OR₀₃₀ group;



wherein —* is a bond to the linker;

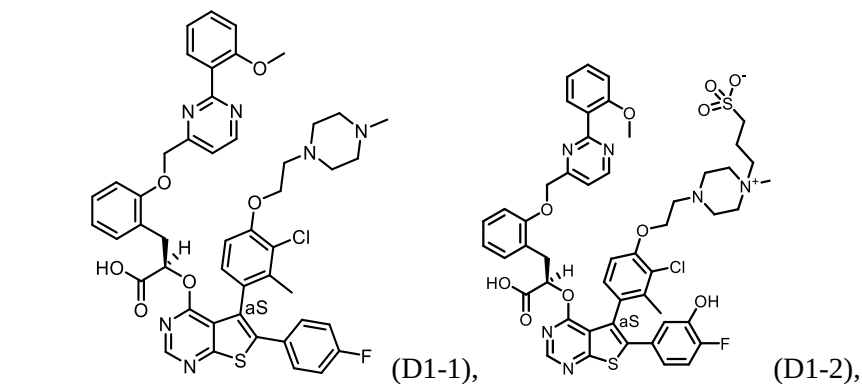
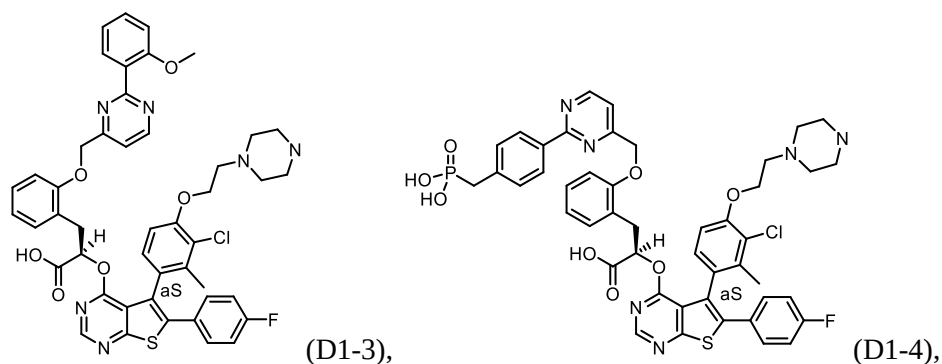
(vi) R₀₉ is Cy₀₂; optionally wherein Cy₀₂ is an optionally substituted aryl group;

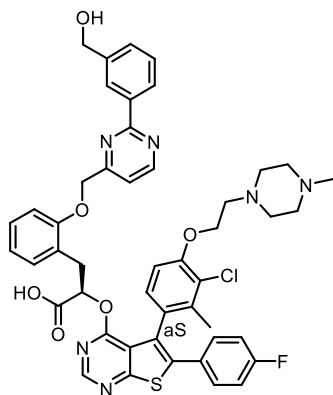
(vii) Cy₀₅ comprises a heteroaryl group selected from a pyrazolyl group and a pyrimidinyl group;

(viii) Cy₀₅ is a pyrimidinyl group; and/or

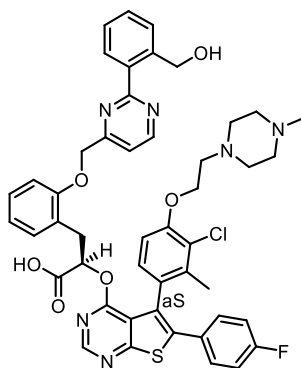
(ix) the Mcl-1 inhibitor is attached by a covalent bond to R₀₃ of formula (I), (IA), or (IB); or is attached by a covalent bond to R₀₉ of formula (I), (IA), or (IB).

23. The antibody-drug conjugate of any one of claims 21 to 22, wherein the Mcl-1 inhibitor is represented by any one of the following formulas:

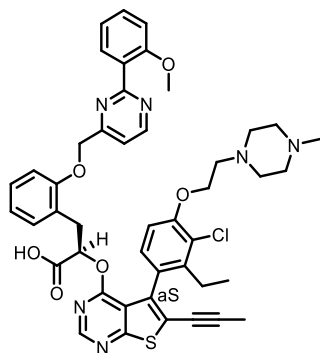




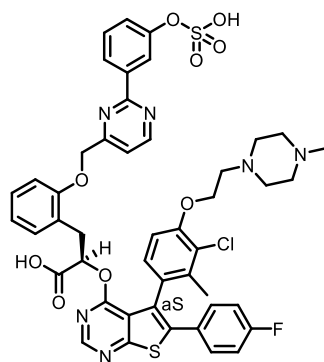
(D1-5),



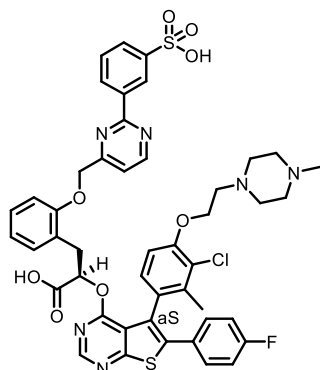
(D1-6),



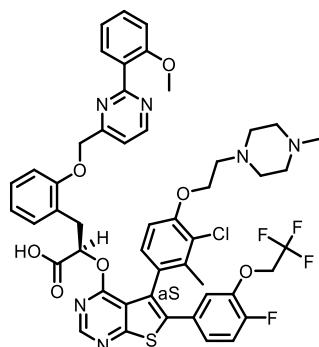
(D1-7),



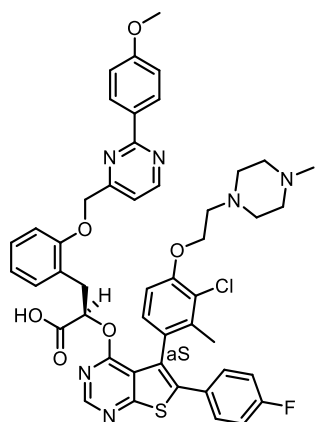
(D1-8),



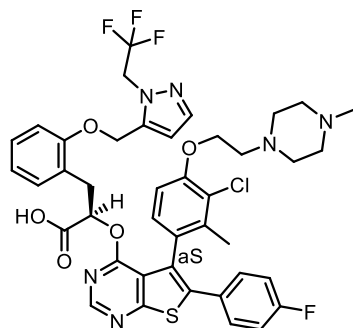
(D1-9),



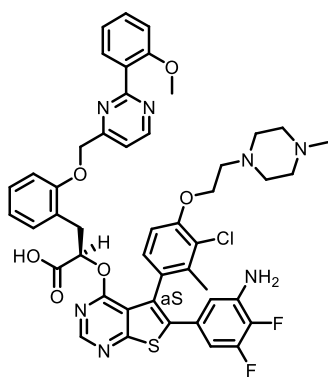
(D1-10),



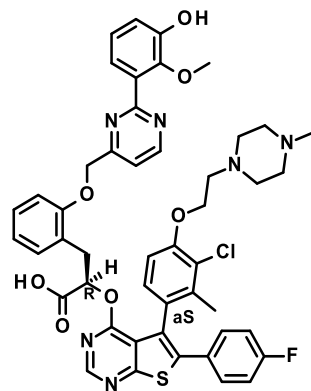
(D1-11),



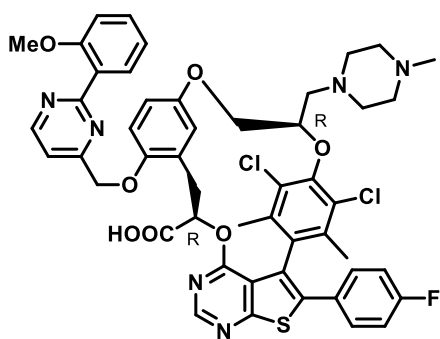
(D1-12),



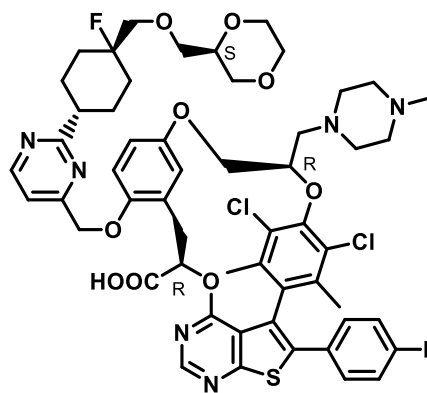
(D1-13),



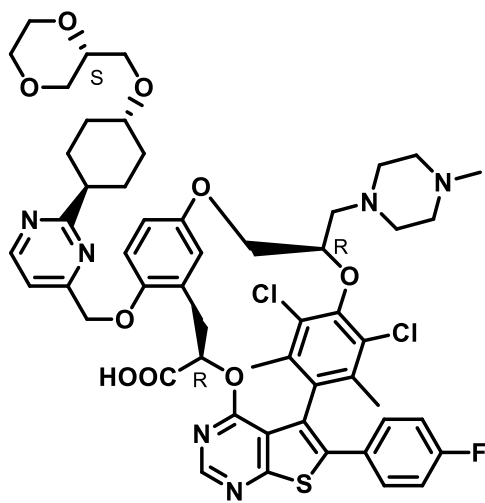
(D1-14),



(D1-15),



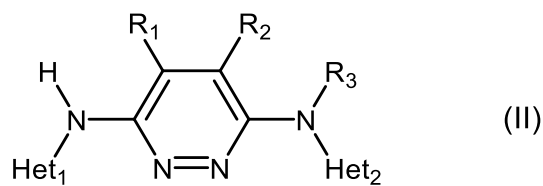
(D1-16), or



(D1-17),

or an enantiomer, diastereoisomer, atropisomer, deuterated derivative, and/or pharmaceutically acceptable salt of any of the foregoing.

24. The antibody-drug conjugate of any one of claims 19-20, wherein
(i) the Bcl-xL inhibitor is represented by Formula (II) or Formula (III):

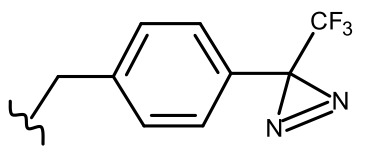


or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

R_1 and R_2 , independently of one another, represent a group selected from the group consisting of: hydrogen; a linear or branched C_1 - C_6 alkyl optionally substituted by a hydroxyl or a C_1 - C_6 alkoxy group; a C_3 - C_6 cycloalkyl; a trifluoromethyl; and a linear or branched C_1 - C_6 alkylene-heterocycloalkyl wherein the heterocycloalkyl group is optionally substituted by a linear or branched C_1 - C_6 alkyl group; or R_1 and R_2 form with the carbon atoms carrying them a C_3 - C_6 cycloalkylene group,

R_3 represents a group selected from the group consisting of: hydrogen; a C_3 - C_6 cycloalkyl; a linear or branched C_1 - C_6 alkyl; $-X_1-NR_aR_b$; $-X_1-N^+R_aR_bR_c$; $-X_1-O-R_c$; $-X_1-COOR_c$; $-X_1-PO(OH)_2$; $-X_1-SO_2(OH)$; $-X_1-N_3$ and: $-X_1-C\equiv CH$,

R_a and R_b , independently of one another, represent a group selected from the group consisting of: hydrogen; a heterocycloalkyl; $-SO_2$ -phenyl wherein the phenyl may be substituted by a linear or branched C_1 - C_6 alkyl; a linear or branched C_1 - C_6 alkyl optionally substituted by one or two hydroxyl groups; a C_1 - C_6 alkylene- SO_2OH ; a C_1 - C_6 alkylene- SO_2O^- ; a C_1 - C_6 alkylene- $COOH$; a C_1 - C_6 alkylene- $PO(OH)_2$; a C_1 - C_6 alkylene- NR_dR_e ; a C_1 - C_6 alkylene- $N^+R_dR_eR_f$; a C_1 - C_6 alkylene-phenyl wherein the phenyl may be substituted by a C_1 - C_6 alkoxy group; and the group:



or R_a and R_b form with the nitrogen atom carrying them a cycle B_1 ;

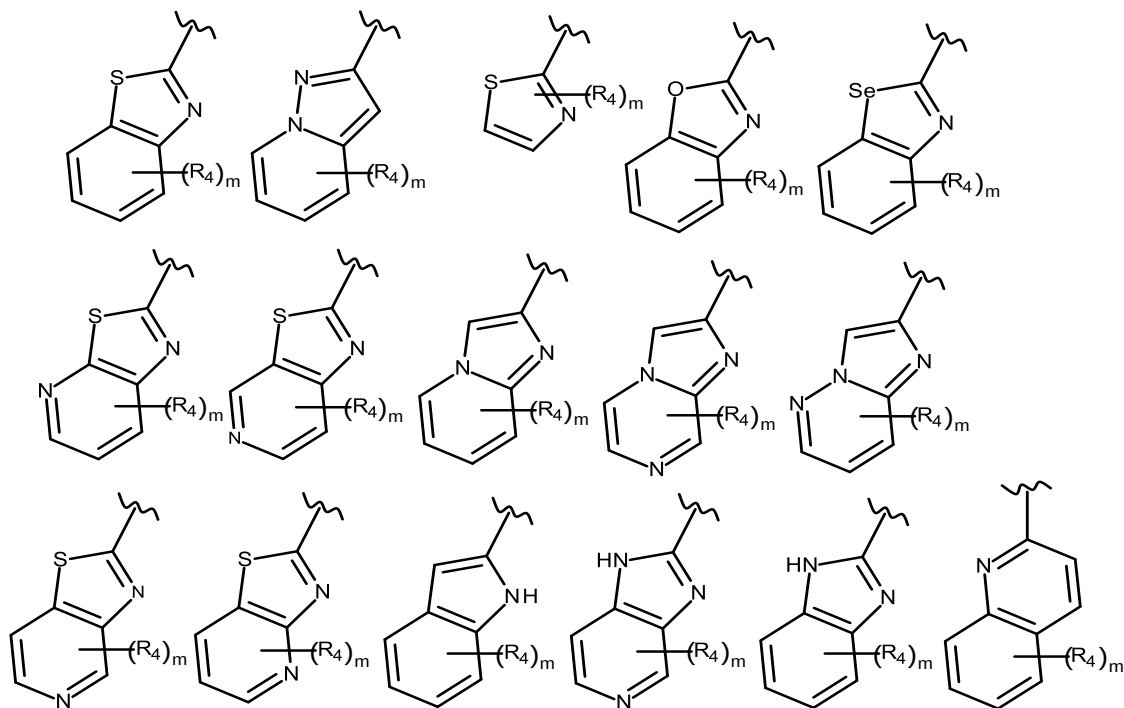
or R_a , R_b and R_c form with the nitrogen atom carrying them a bridged C_3 - C_8 heterocycloalkyl,

R_c , R_d , R_e , R_f , independently of one another, represents a hydrogen or a linear or branched C_1 - C_6 alkyl group,

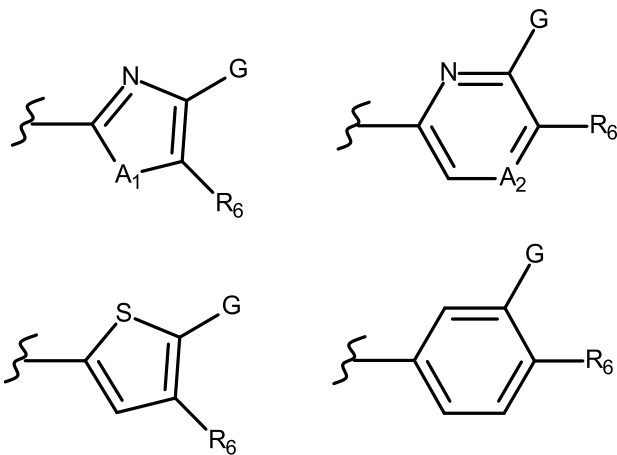
or R_d and R_e form with the nitrogen atom carrying them a cycle B_2 ,

or R_d , R_e and R_f form with the nitrogen atom carrying them a bridged C_3 - C_8 heterocycloalkyl,

Het₁ represents a group selected from the group consisting of:



Het₂ represents a group selected from the group consisting of:



A₁ is -NH-, -N(C₁-C₃alkyl), O, S or Se,

A₂ is N, CH or C(R₅),

G is selected from the group consisting of:

-C(O)OR_{G3}, -C(O)NR_{G1}R_{G2}, -C(O)R_{G2}, -NR_{G1}C(O)R_{G2}, -NR_{G1}C(O)NR_{G1}R_{G2},

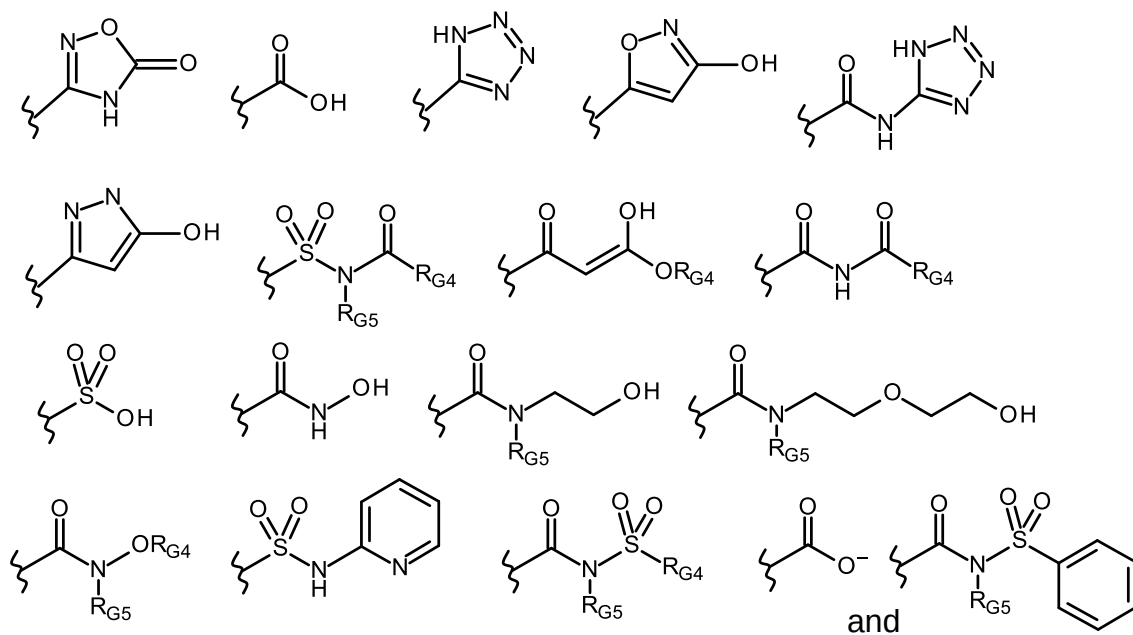
-OC(O)NR_{G1}R_{G2}, -NR_{G1}C(O)OR_{G3}, -C(=NOR_{G1})NR_{G1}R_{G2},

-NR_{G1}C(=NCN)NR_{G1}R_{G2}, -NR_{G1}S(O)₂NR_{G1}R_{G2}, -S(O)₂R_{G3}, -S(O)₂NR_{G1}R_{G2},

$-\text{NR}_{\text{G1}}\text{S}(\text{O})_2\text{R}_{\text{G2}}$, $-\text{NR}_{\text{G1}}\text{C}(=\text{NR}_{\text{G2}})\text{NR}_{\text{G1}}\text{R}_{\text{G2}}$, $-\text{C}(=\text{S})\text{NR}_{\text{G1}}\text{R}_{\text{G2}}$, $-\text{C}(=\text{NR}_{\text{G1}})\text{NR}_{\text{G1}}\text{R}_{\text{G2}}$, $-\text{C}_1\text{-C}_6\text{alkyl}$ optionally substituted by a hydroxyl group, a halogen, $-\text{NO}_2$, and $-\text{CN}$, in which:

- R_{G1} and R_{G2} at each occurrence are each independently selected from the group consisting of hydrogen, a $\text{C}_1\text{-C}_6\text{alkyl}$ optionally substituted by 1 to 3 halogen atoms, a $\text{C}_1\text{-C}_6\text{alkyl}$ substituted by a hydroxyl, a $\text{C}_1\text{-C}_6\text{alkyl}$ substituted by a $\text{C}_1\text{-C}_6\text{alkoxy}$ group, a $\text{C}_2\text{-C}_6\text{alkenyl}$, a $\text{C}_2\text{-C}_6\text{alkynyl}$, a $\text{C}_3\text{-C}_6\text{cycloalkyl}$, phenyl and $-(\text{CH}_2)_{1-4}\text{-phenyl}$;

- R_{G3} is selected from the group consisting of a $\text{C}_1\text{-C}_6\text{alkyl}$ optionally substituted by 1 to 3 halogen atoms, a $\text{C}_2\text{-C}_6\text{alkenyl}$, a $\text{C}_2\text{-C}_6\text{alkynyl}$, a $\text{C}_3\text{-C}_6\text{cycloalkyl}$, phenyl and $-(\text{CH}_2)_{1-4}\text{-phenyl}$; or R_{G1} and R_{G2} , together with the atom to which each is attached are combined to form a $\text{C}_3\text{-C}_8\text{heterocycloalkyl}$; or in the alternative, G is selected from the group consisting of:



wherein R_{G4} is selected from the group consisting of hydrogen, a $\text{C}_1\text{-C}_6\text{alkyl}$ optionally substituted by 1 to 3 halogen atoms, a $\text{C}_1\text{-C}_6\text{alkyl}$ substituted by a hydroxyl, a $\text{C}_1\text{-C}_6\text{alkyl}$ substituted by a $\text{C}_1\text{-C}_6\text{alkoxy}$ group, a $\text{C}_2\text{-C}_6\text{alkenyl}$, a $\text{C}_2\text{-C}_6\text{alkynyl}$ and a $\text{C}_3\text{-C}_6\text{cycloalkyl}$,

and R_{G5} represents a hydrogen atom or a $\text{C}_1\text{-C}_6\text{alkyl}$ group optionally substituted by 1 to 3 halogen atoms,

R_4 represents a hydrogen, fluorine, chlorine or bromine atom, a methyl, a hydroxyl or a methoxy group,

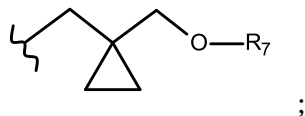
R_5 represents a group selected from the group consisting of: a $\text{C}_1\text{-C}_6\text{alkyl}$ optionally substituted by 1 to 3 halogen atoms; a $\text{C}_2\text{-C}_6\text{alkenyl}$; a $\text{C}_2\text{-C}_6\text{alkynyl}$; a halogen; and $-\text{CN}$,

R_6 represents a group selected from the group consisting of:
hydrogen;

a linear or branched $-C_1-C_6$ alkylene- R_8 group;

a $-C_2-C_6$ alkenyl;

$-X_2-O-R_7$;



$-X_2-NSO_2-R_7$;

$-C=C(R_9)-Y_1-O-R_7$;

a C_3-C_6 cycloalkyl;

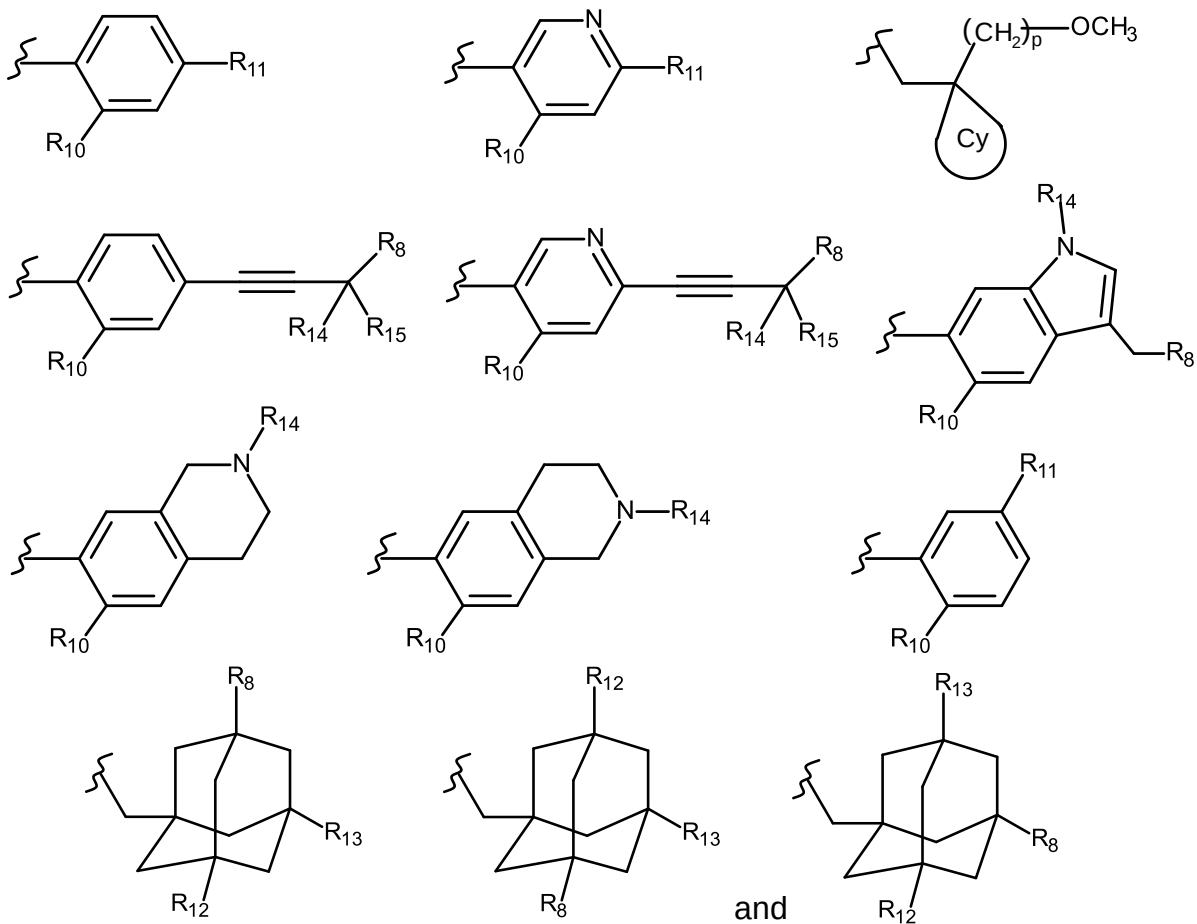
a C_3-C_6 heterocycloalkyl optionally substituted by a hydroxyl group;

a C_3-C_6 cycloalkylene- Y_2-R_7 ;

a C_3-C_6 heterocycloalkylene- Y_2-R_7 group, and

a heteroarylene- R_7 group optionally substituted by a linear or branched C_1-C_6 alkyl group,

R_7 represents a group selected from the group consisting of: a linear or branched C_1-C_6 alkyl group; a (C_3-C_6) cycloalkylene- R_8 ;



wherein Cy represents a C₃-C₈cycloalkyl,

R₈ represents a group selected from the group consisting of: hydrogen; a linear or branched C₁-C₆alkyl, -NR'_aR'_b; -NR'_a-CO-OR'_c; -NR'_a-CO-R'_c; -N⁺R'_aR'_bR'_c; -O-R'_c; -NH-X'₂-N⁺R'_aR'_bR'_c; -O-X'₂-NR'_aR'_b; -X'₂-NR'_aR'_b; -NR'_c-X'₂-N₃ and $\text{---NR}'_c\text{---X}'_2\text{---}\equiv\text{CH}$,

R₉ represents a group selected from the group consisting of a linear or branched C₁-C₆alkyl, trifluoromethyl, hydroxyl, halogen, and a C₁-C₆alkoxy,

R₁₀ represents a group selected from the group consisting of hydrogen, fluorine, chlorine, bromine, -CF₃ and methyl,

R₁₁ represents a group selected from the group consisting of hydrogen, a C₁-C₃alkylene-R₈, a -O-C₁-C₃alkylene-R₈, -CO-NR_hR_i and a -CH=CH-C₁-C₄alkylene-NR_hR_i, -CH=CH-CHO, a C₃-C₈cycloalkylene-CH₂-R₈, and a C₃-C₈heterocycloalkylene-CH₂-R₈,

R₁₂ and R₁₃, independently of one another, represent a hydrogen atom or a methyl group,

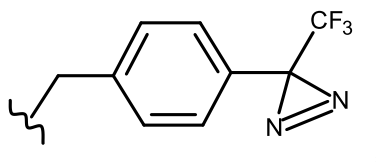
R₁₄ and R₁₅, independently of one another, represent a hydrogen or a methyl group, or R₁₄ and R₁₅ form with the carbon atom carrying them a cyclohexyl,

R_h and R_i, independently of one another, represent a hydrogen or a linear or branched C₁-C₆alkyl group,

X₁ and X₂, independently of one another, represent a linear or branched C₁-C₆alkylene group optionally substituted by one or two groups selected from the group consisting of trifluoromethyl, hydroxyl, a halogen, and a C₁-C₆alkoxy,

X'₂ represents a linear or branched C₁-C₆alkylene,

R'_a and R'_b, independently of one another, represent a group selected from the group consisting of: hydrogen; a heterocycloalkyl; -SO₂-phenyl wherein the phenyl may be substituted by a linear or branched C₁-C₆alkyl; a linear or branched C₁-C₆alkyl optionally substituted by one or two hydroxyl or C₁-C₆alkoxy groups; a C₁-C₆alkylene-SO₂OH; a C₁-C₆alkylene-SO₂O⁻; a C₁-C₆alkylene-COOH; a C₁-C₆alkylene-PO(OH)₂; a C₁-C₆alkylene-NR'_dR'_e; a C₁-C₆alkylene-N⁺R'_dR'_eR'_f; a C₁-C₆alkylene-O-C₁-C₆alkylene-OH; a C₁-C₆alkylene-phenyl wherein the phenyl may be substituted by a hydroxyl or a C₁-C₆alkoxy group; and the group:



or R'_a and R'_b form with the nitrogen atom carrying them a cycle B₃,

or R'_a, R'_b and R'_c form with the nitrogen atom carrying them a bridged C₃-C₈hetero cycloalkyl,

R'_c, R'_d, R'_e, R'_f , independently of one another, represents a hydrogen or a linear or branched C_1 - C_6 alkyl group,

or R'_d and R'_e form with the nitrogen atom carrying them a cycle B_4 ,

or R'_d, R'_e and R'_f form with the nitrogen atom carrying them a bridged C_3 - C_8 heterocycloalkyl,

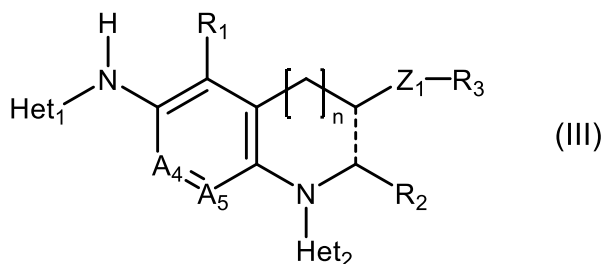
Y_1 represents a linear or branched C_1 - C_4 alkylene,

Y_2 represents a bond, -O-, -O-CH₂-, -O-CO-, -O-SO₂-, -CH₂-, -CH₂-O-, -CH₂-CO-, -CH₂-SO₂-, -C₂H₅-, -CO-, -CO-O-, -CO-CH₂-, -CO-NH-CH₂-, -SO₂-, -SO₂-CH₂-, -NH-CO-, or -NH-SO₂-,

$m=0, 1$ or 2 ,

B_1, B_2, B_3 and B_4 , independently of one another, represents a C_3 - C_8 heterocycloalkyl group, which group can: (i) be a mono- or bi-cyclic group, wherein bicyclic group includes fused, bridged or spiro ring system, (ii) can contain, in addition to the nitrogen atom, one or two hetero atoms selected independently from oxygen, sulphur and nitrogen, (iii) be substituted by one or two groups selected from the group consisting of: fluorine, bromine, chlorine, a linear or branched C_1 - C_6 alkyl, hydroxyl, -NH₂, oxo and piperidinyl,

wherein one of the R_3 and R_8 groups, if present, is covalently attached to the linker, and wherein the valency of an atom is not exceeded by virtue of one or more substituents bonded thereto; or



or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

$n=0, 1$ or 2 ,

----- represents a single or a double bond,

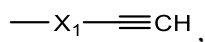
A_4 and A_5 , independently of one another, represent a carbon or a nitrogen atom,

Z_1 represents a bond, -N(R)-, or -O-, wherein R represents a hydrogen or a linear or branched C_1 - C_6 alkyl,

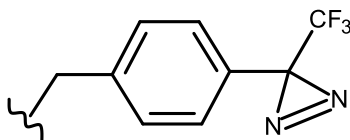
R_1 represents a group selected from the group consisting of: hydrogen; a linear or branched C_1 - C_6 alkyl optionally substituted by a hydroxyl or a C_1 - C_6 alkoxy group; a C_3 - C_6 cycloalkyl; trifluoromethyl; and a linear or branched C_1 - C_6 alkylene-heterocycloalkyl wherein the heterocycloalkyl group is optionally substituted by a linear or branched C_1 - C_6 alkyl group;

R_2 represents a hydrogen or a methyl;

R₃ represents a group selected from the group consisting of: hydrogen; a linear or branched C₁-C₄alkyl; -X₁-NR_aR_b; -X₁-N⁺R_aR_bR_c; -X₁-O-R_c; -X₁-COOR_c; -X₁-PO(OH)₂; -X₁-SO₂(OH); -X₁-N₃ and :



R_a and R_b, independently of one another, represent a group selected from the group consisting of: hydrogen; a heterocycloalkyl; -SO₂-phenyl wherein the phenyl may be substituted by a linear or branched C₁-C₆alkyl; a linear or branched C₁-C₆alkyl optionally substituted by one or two hydroxyl groups; a C₁-C₆alkylene-SO₂OH; a C₁-C₆alkylene-SO₂O⁻; a C₁-C₆alkylene-COOH; a C₁-C₆alkylene-PO(OH)₂; a C₁-C₆alkylene-NR_dR_e; a C₁-C₆alkylene-N⁺R_dR_eR_f; a C₁-C₆alkylene-phenyl wherein the phenyl may be substituted by a C₁-C₆alkoxy group; and the group:



or R_a and R_b form with the nitrogen atom carrying them a cycle B₁;

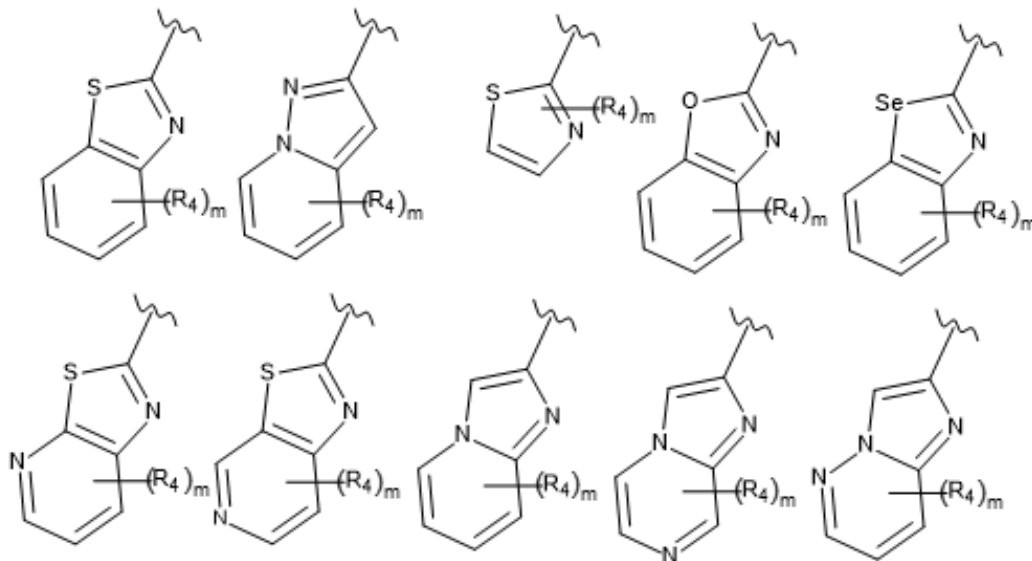
or R_a, R_b and R_c form with the nitrogen atom carrying them a bridged C₃-C₈ heterocycloalkyl,

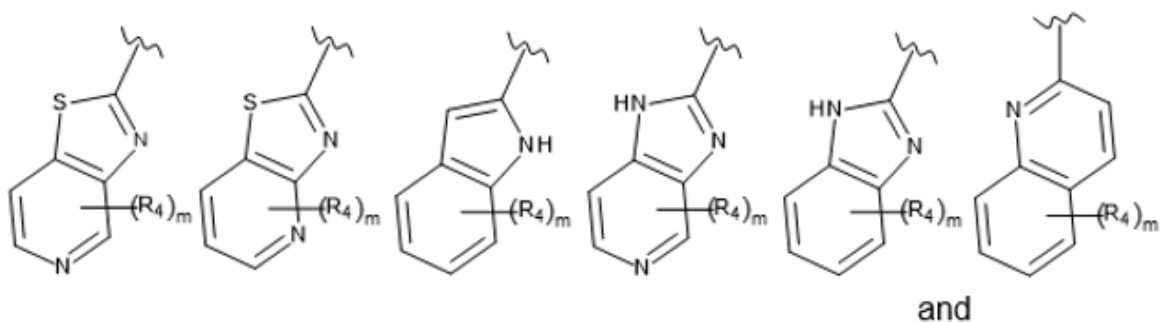
R_c, R_d, R_e, R_f, independently of one another, represents a hydrogen or a linear or branched C₁-C₆alkyl group,

or R_d and R_e form with the nitrogen atom carrying them a cycle B₂,

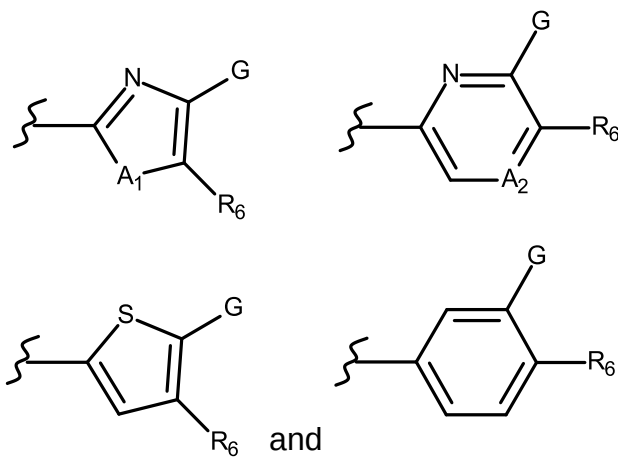
or R_d, R_e and R_f form with the nitrogen atom carrying them a bridged C₃-C₈ heterocycloalkyl,

Het₁ represents a group selected from the group consisting of:





Het₂ represents a group selected from the group consisting of:



A₁ is -NH-, -N(C₁-C₃alkyl), O, S or Se,

A₂ is N, CH or C(R₅),

G is selected from the group consisting of:

-C(O)OR_{G3}, -C(O)NR_{G1}R_{G2}, -C(O)R_{G2}, -NR_{G1}C(O)R_{G2}, -NR_{G1}C(O)NR_{G1}R_{G2},

-OC(O)NR_{G1}R_{G2}, -NR_{G1}C(O)OR_{G3}, -C(=NOR_{G1})NR_{G1}R_{G2},

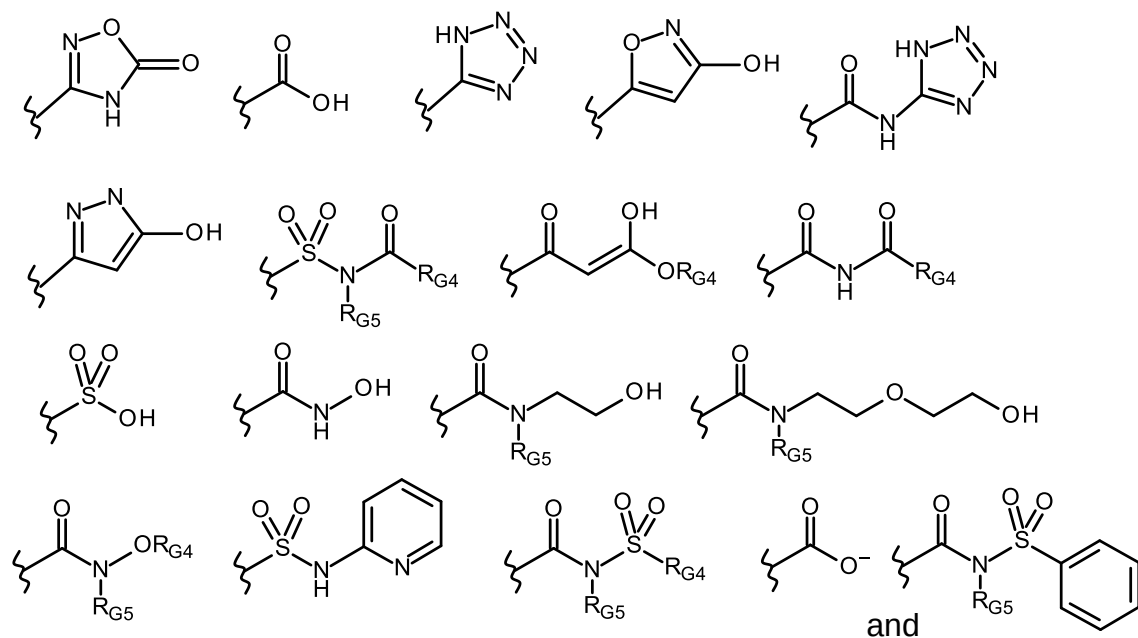
-NR_{G1}C(=NCN)NR_{G1}R_{G2}, -NR_{G1}S(O)₂NR_{G1}R_{G2}, -S(O)₂R_{G3}, -S(O)₂NR_{G1}R_{G2},

-NR_{G1}S(O)₂R_{G2}, -NR_{G1}C(=NR_{G2})NR_{G1}R_{G2}, -C(=S)NR_{G1}R_{G2}, -C(=NR_{G1})NR_{G1}R_{G2}, -C₁-C₆alkyl

optionally substituted by a hydroxyl group, halogen, -NO₂, and -CN, in which:

- R_{G1} and R_{G2} at each occurrence are each independently selected from the group consisting of hydrogen, a C₁-C₆alkyl optionally substituted by 1 to 3 halogen atoms, a C₁-C₆alkyl substituted by a hydroxyl, a C₁-C₆alkyl substituted by a C₁-C₆alkoxy group, a C₂-C₆alkenyl, a C₂-C₆alkynyl, a C₃-C₆cycloalkyl, phenyl and -(CH₂)₁₋₄-phenyl;

- R_{G3} is selected from the group consisting of a C₁-C₆alkyl optionally substituted by 1 to 3 halogen atoms, a C₂-C₆alkenyl, a C₂-C₆alkynyl, a C₃-C₆cycloalkyl, phenyl and -(CH₂)₁₋₄-phenyl; or R_{G1} and R_{G2}, together with the atom to which each is attached are combined to form a C₃-C₈heterocycloalkyl ; or in the alternative, G is selected from the group consisting of:



wherein R_{G4} is selected from the group consisting of hydrogen, a C_1 - C_6 alkyl optionally substituted by 1 to 3 halogen atoms, a C_1 - C_6 alkyl substituted by a hydroxyl, a C_1 - C_6 alkyl substituted by a C_1 - C_6 alkoxy group, a C_2 - C_6 alkenyl, a C_2 - C_6 alkynyl and a C_3 - C_6 cycloalkyl,

and R_{G5} represents a hydrogen atom or a C_1 - C_6 alkyl group optionally substituted by 1 to 3 halogen atoms,

R_4 represents a hydrogen, fluorine, chlorine or bromine atom, a methyl, a hydroxyl or a methoxy group,

R_5 represents a group selected from the group consisting of: a C_1 - C_6 alkyl optionally substituted by 1 to 3 halogen atoms; a C_2 - C_6 alkenyl; a C_2 - C_6 alkynyl; a halogen; and $-CN$,

R_6 represents a group selected from the group consisting of:

hydrogen;

a linear or branched $-C_1$ - C_6 alkylene- R_8 group;

a $-C_2$ - C_6 alkenyl;

$-X_2-O-R_7$;



;

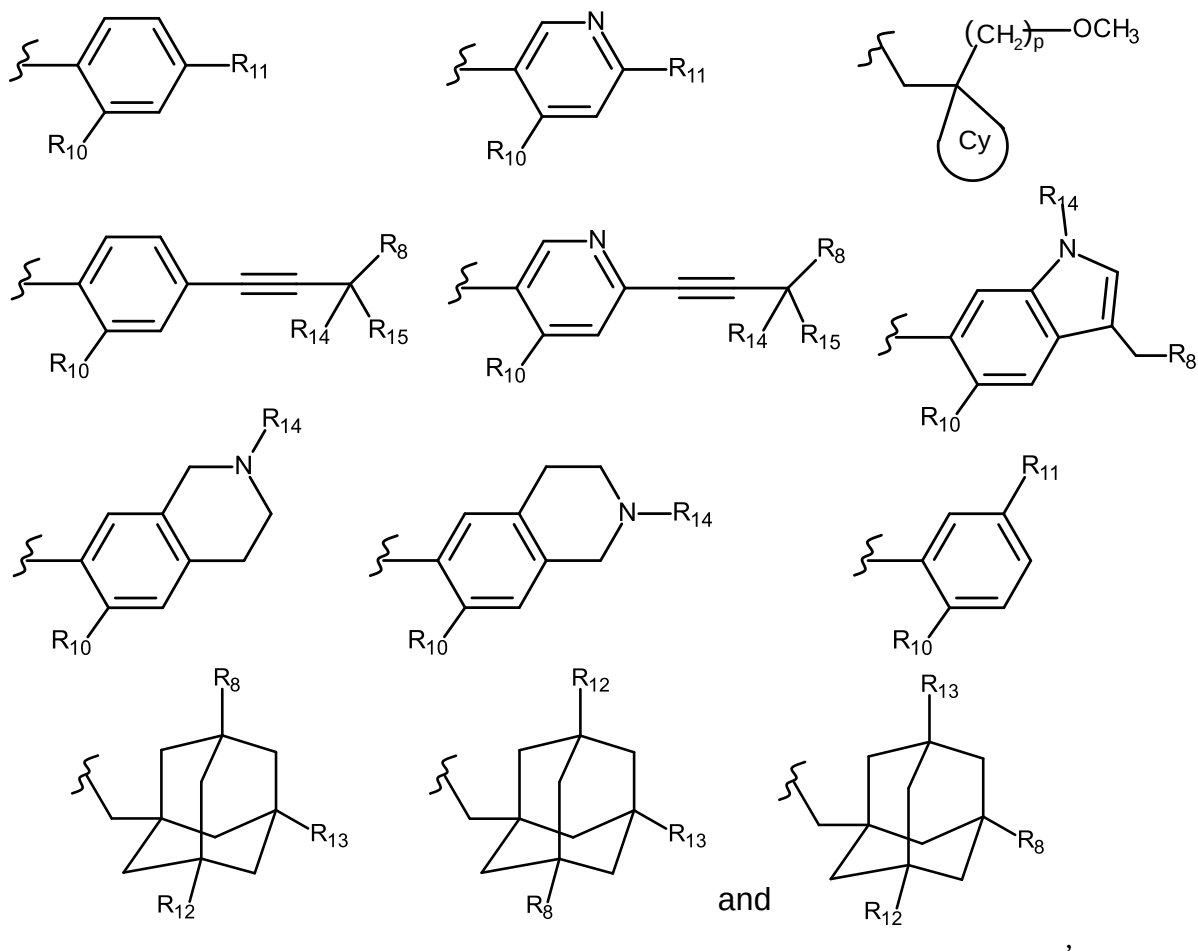
$-X_2-NSO_2-R_7$;

$-C=C(R_9)-Y_1-O-R_7$;

a C_3 - C_6 cycloalkyl;

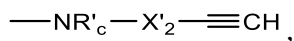
a C_3 - C_6 heterocycloalkyl optionally substituted by a hydroxyl group;

a C₃-C₆cycloalkylene-Y₂-R₇;
 a C₃-C₆heterocycloalkylene-Y₂-R₇ group, and
 a heteroarylene-R₇ group optionally substituted by a linear or branched C₁-C₆alkyl group,
 R₇ represents a group selected from the group consisting of: a linear or branched C₁-C₆alkyl group; a (C₃-C₆)cycloalkylene-R₈;



wherein Cy represents a C₃-C₈cycloalkyl,

R₈ represents a group selected from the group consisting of: hydrogen; a linear or branched C₁-C₆alkyl, -NR'_aR'_b; -NR'_a-CO-OR'_c; -NR'_a-CO-R'_c; -N⁺R'_aR'_bR'_c; -O-R'_c; -NH-X'₂-N⁺R'_aR'_bR'_c; -O-X'₂-NR'_aR'_b, -X'₂-NR'_aR'_b, -NR'_c-X'₂-N₃ and:



R₉ represents a group selected from the group consisting of a linear or branched C₁-C₆alkyl, trifluoromethyl, hydroxyl, a halogen, and a C₁-C₆alkoxy,

R₁₀ represents a group selected from the group consisting of hydrogen, fluorine, chlorine, bromine, -CF₃ and methyl,

R₁₁ represents a group selected from the group consisting of hydrogen, a halogen, a C₁-C₃alkylene-R₈, a -O-C₁-C₃alkylene-R₈, -CO-NR_hR_i and a -CH=CH-C₁-C₄alkylene-NR_hR_i, -CH=CH-CHO, a C₃-C₈cycloalkylene-CH₂-R₈, and a C₃-C₈heterocycloalkylene-CH₂-R₈,

R₁₂ and R₁₃, independently of one another, represent a hydrogen atom or a methyl group,

R₁₄ and R₁₅, independently of one another, represent a hydrogen or a methyl group, or R₁₄ and R₁₅ form with the carbon atom carrying them a cyclohexyl,

R_h and R_i, independently of one another, represent a hydrogen or a linear or branched C₁-C₆alkyl group,

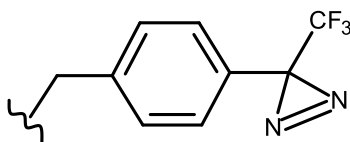
X₁ represents a linear or branched C₁-C₄alkylene group optionally substituted by one or two groups selected from the group consisting of trifluoromethyl, hydroxyl, a halogen, and a C₁-C₆alkoxy,

X₂ represents a linear or branched C₁-C₆alkylene group optionally substituted by one or two groups selected from the group consisting of trifluoromethyl, hydroxyl, a halogen, and a C₁-C₆alkoxy,

X'₂ represents a linear or branched C₁-C₆alkylene,

R'_a and R'_b, independently of one another, represent a group selected from the group consisting of: hydrogen; a heterocycloalkyl; -SO₂-phenyl wherein the phenyl may be substituted by a linear or branched C₁-C₆alkyl; a linear or branched C₁-C₆alkyl optionally substituted by one or two hydroxyl or C₁-C₆alkoxy groups; a C₁-C₆alkylene-SO₂OH; a C₁-C₆alkylene-SO₂O⁻; a C₁-C₆alkylene-COOH; a C₁-C₆alkylene-PO(OH)₂; a C₁-C₆alkylene-NR'_dR'_e; a C₁-C₆alkylene-N⁺R'_dR'_eR'_f; a C₁-C₆alkylene-O-C₁-C₆alkylene-OH; a C₁-C₆alkylene-phenyl wherein the phenyl may be substituted by a hydroxyl or a C₁-C₆alkoxy

group; and the group:



or R'_a and R'_b form with the nitrogen atom carrying them a cycle B₃,

or R'_a, R'_b and R'_c form with the nitrogen atom carrying them a bridged C₃-C₈ heterocycloalkyl,

R'_c, R'_d, R'_e, R'_f, independently of one another, represents a hydrogen or a linear or branched C₁-C₆alkyl group,

or R'_d and R'_e form with the nitrogen atom carrying them a cycle B₄,

or R'_d, R'_e and R'_f form with the nitrogen atom carrying them a bridged C₃-C₈ heterocycloalkyl,

Y₁ represents a linear or branched C₁-C₄alkylene,

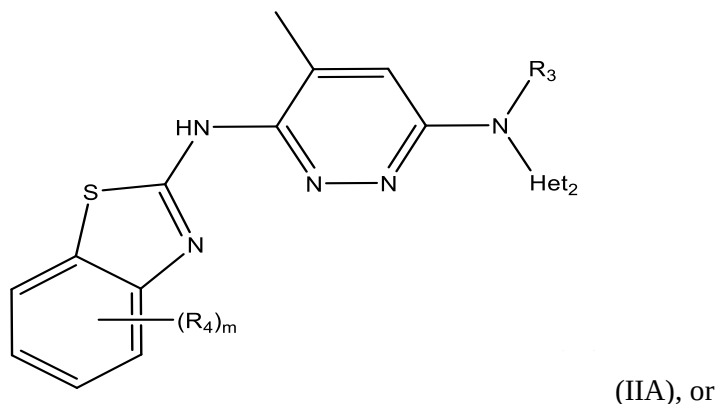
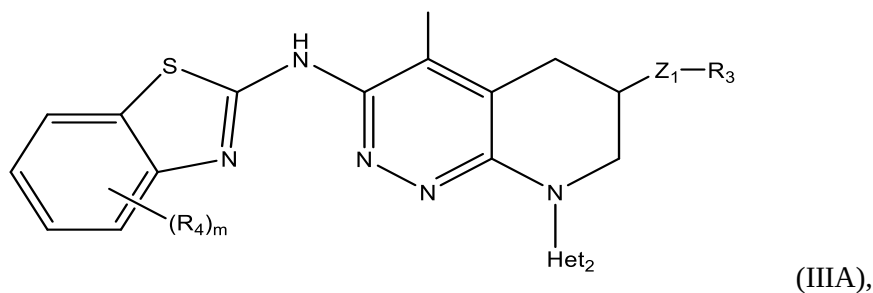
Y_2 represents a bond, -O-, -O-CH₂-, -O-CO-, -O-SO₂-, -CH₂-, -CH₂-O-, -CH₂-CO-, -CH₂-SO₂-, -C₂H₅-, -CO-, -CO-O-, -CO-CH₂-, -CO-NH-CH₂-, -SO₂-, -SO₂-CH₂-, -NH-CO-, or -NH-SO₂-,

$m=0, 1$ or 2 ,

B_1, B_2, B_3 and B_4 , independently of one another, represents a C₃-C₈heterocycloalkyl group, which group can: (i) be a mono- or bi-cyclic group, wherein bicyclic group includes fused, bridged or spiro ring system, (ii) can contain, in addition to the nitrogen atom, one or two hetero atoms selected independently from oxygen, sulphur and nitrogen, (iii) be substituted by one or two groups selected from the group consisting of: fluorine, bromine, chlorine, a linear or branched C₁-C₆alkyl, hydroxyl, -NH₂, oxo and piperidinyl,

wherein one of the R_3, R_8 and G groups, if present, is covalently attached to the linker, and wherein the valency of an atom is not exceeded by virtue of one or more substituents bonded thereto;

(ii) the Bcl-xL inhibitor is represented by formula (IIA) or (IIIA):



or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

Z_1 represents a bond or -O-,

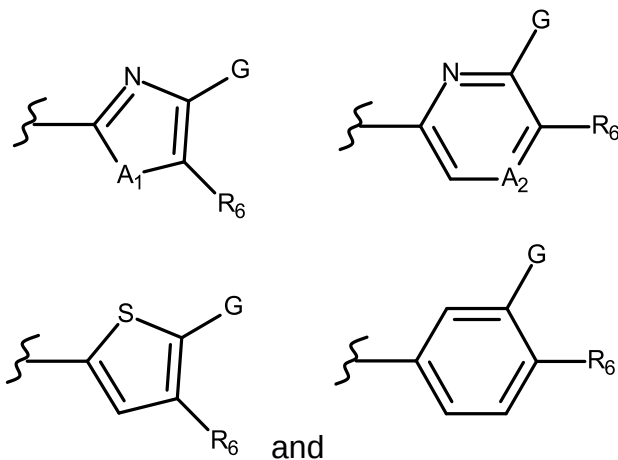
R_3 represents a group selected from the group consisting of: hydrogen; a C₃-C₆cycloalkyl; a linear

or branched C₁-C₆alkyl; -X₁-NR_aR_b; -X₁-N⁺R_aR_bR_c; -X₁-O-R_c; -X₁-N₃ and $-X_1-C\equiv CH$,

R_a and R_b, independently of one another, represent a group selected from the group consisting of: hydrogen; a linear or branched C₁-C₆alkyl optionally substituted by one or two hydroxyl groups; and a C₁-C₆alkylene-SO₂O⁻,

R_c represents a hydrogen or a linear or branched C₁-C₆alkyl group,

Het₂ represents a group selected from the group consisting of:



A₁ is -NH-, -N(C₁-C₃alkyl), O, S or Se,

A₂ is N, CH or C(R₅),

G is selected from the group consisting of:

-C(O)OH, -C(O)OR_{G3}, -C(O)NR_{G1}R_{G2}, -C(O)R_{G2}, -NR_{G1}C(O)R_{G2}, -NR_{G1}C(O)NR_{G1}R_{G2},
 -OC(O)NR_{G1}R_{G2}, -NR_{G1}C(O)OR_{G3}, -C(=NOR_{G1})NR_{G1}R_{G2},
 -NR_{G1}C(=NCN)NR_{G1}R_{G2}, -NR_{G1}S(O)₂NR_{G1}R_{G2}, -S(O)₂R_{G3}, -S(O)₂NR_{G1}R_{G2},
 -NR_{G1}S(O)₂R_{G2}, -NR_{G1}C(=NR_{G2})NR_{G1}R_{G2}, -C(=S)NR_{G1}R_{G2}, -C(=NR_{G1})NR_{G1}R_{G2}, -C₁-C₆alkyl
 optionally substituted by a hydroxyl group, -C(O)NR_{G5}S(O)₂R_{G4}, halogen, -NO₂, and -CN, in
 which:

- R_{G1}, R_{G2}, R_{G4} and R_{G5} at each occurrence are each independently selected from the group consisting of hydrogen, and a C₁-C₆alkyl optionally substituted by 1 to 3 halogen atoms;

- R_{G3} is a C₁-C₆alkyl optionally substituted by 1 to 3 halogen atoms; or

R_{G1} and R_{G2}, together with the atom to which each is attached are combined to form a C₃-C₈heterocycloalkyl;

R₄ represents a hydrogen, fluorine, chlorine or bromine atom, a methyl, a hydroxyl or a methoxy group,

R₅ represents a group selected from the group consisting of: a C₁-C₆alkyl optionally substituted by 1 to 3 halogen atoms; a halogen and -CN,

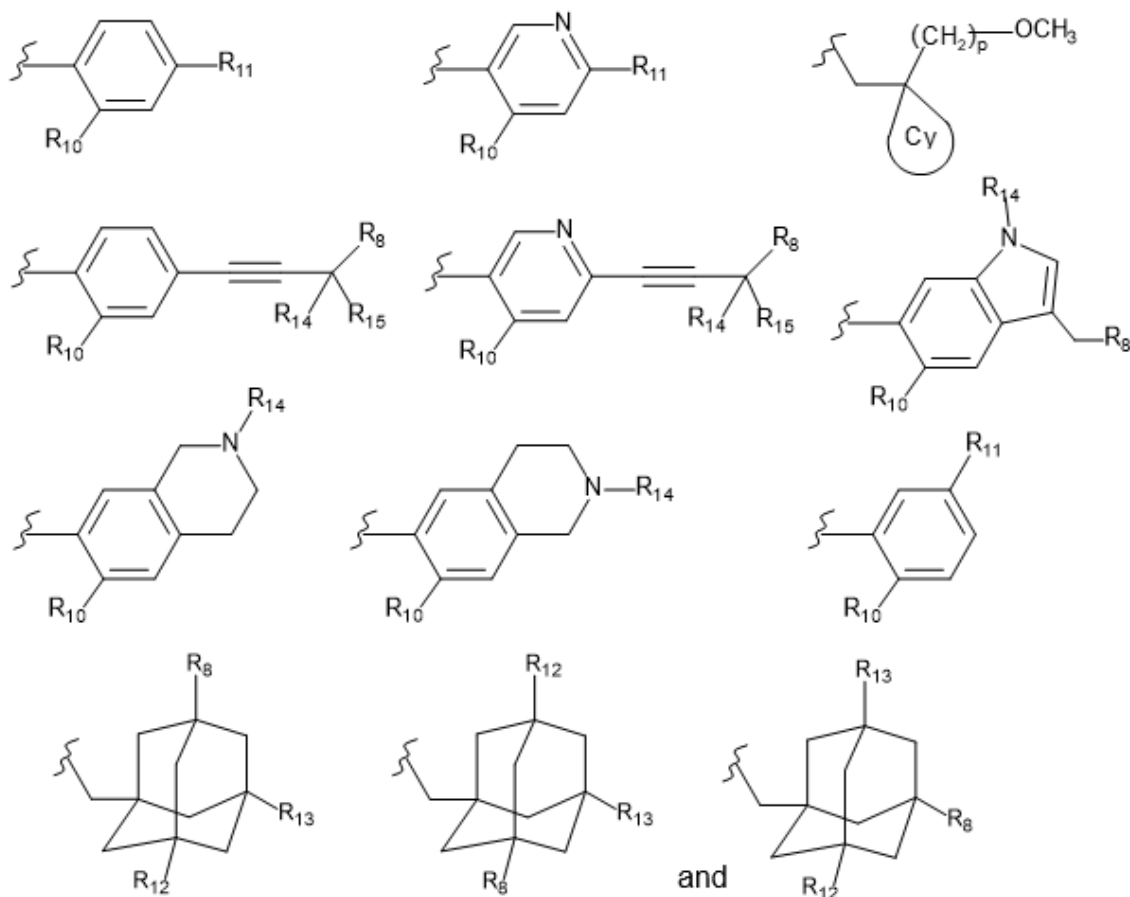
R₆ represents a group selected from the group consisting of:

a linear or branched $-C_1-C_6$ alkylene- R_8 group;

$-X_2-O-R_7$; and

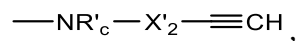
a heteroarylene- R_7 group optionally substituted by a linear or branched C_1-C_6 alkyl group,

R_7 represents a group selected from the group consisting of: a linear or branched C_1-C_6 alkyl group; (C_3-C_6) cycloalkylene- R_8 ;



wherein Cy represents a C_3-C_8 cycloalkyl,

R_8 represents a group selected from the group consisting of: hydrogen; a linear or branched C_1-C_6 alkyl, $-NR'_aR'_b$; $-NR'_a-CO-OR'_c$; $-NR'_a-CO-R'_c$; $-N^+R'_aR'_bR'_c$; $-O-R'_c$; $-NH-X'_2-N^+R'_aR'_bR'_c$; $-O-X'_2-NR'_aR'_b$; $-X'_2-NR'_aR'_b$; $-NR'_c-X'_2-N_3$ and:



R_{10} represents a group selected from the group consisting of hydrogen, fluorine, chlorine, bromine, $-CF_3$ and methyl,

R_{11} represents a group selected from the group consisting of hydrogen, a C_1-C_3 alkylene- R_8 , $-O-C_1-C_3$ alkylene- R_8 , $-CO-NR_hR_i$, $-CH=CH-C_1-C_4$ alkylene- NR_hR_i , $-CH=CH-CHO$, a C_3-C_8 cycloalkylene- CH_2-R_8 , and a C_3-C_8 heterocycloalkylene- CH_2-R_8 ,

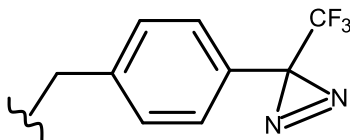
R₁₂ and R₁₃, independently of one another, represent a hydrogen atom or a methyl group,
 R₁₄ and R₁₅, independently of one another, represent a hydrogen or a methyl group, or R₁₄ and R₁₅
 form with the carbon atom carrying them a
 a cyclohexyl,

R_h and R_i, independently of one another, represent a hydrogen or a linear or branched C₁-C₆alkyl
 group,

X₁ and X₂, independently of one another, represent a linear or branched
 C₁-C₆alkylene group optionally substituted by one or two groups selected from the group
 consisting of trifluoromethyl, hydroxyl, a halogen, and C₁-C₆alkoxy,

X'₂ represents a linear or branched C₁-C₆alkylene,

R'_a and R'_b, independently of one another, represent a group selected from the group consisting
 of: hydrogen; a heterocycloalkyl; -SO₂-phenyl wherein the phenyl may be substituted by a linear
 or branched C₁-C₆alkyl; a linear or branched C₁-C₆alkyl optionally substituted by one or two
 hydroxyl or C₁-C₆alkoxy groups; a C₁-C₆alkylene-SO₂OH; a C₁-C₆alkylene-SO₂O⁻; a C₁-
 C₆alkylene-COOH; a C₁-C₆alkylene-PO(OH)₂; a C₁-C₆alkylene-NR'_dR'_e; a C₁-C₆alkylene-
 N⁺R'_dR'_eR'_f; a C₁-C₆alkylene-O-C₁-C₆alkylene-OH; a C₁-C₆alkylene-phenyl wherein the phenyl
 may be substituted by a hydroxyl or a C₁-C₆alkoxy group; and the group:



or R'_a and R'_b form with the nitrogen atom carrying them a
 cycle B₃,

or R'_a, R'_b and R'_c form with the nitrogen atom carrying them a bridged
 C₃-C₈heterocycloalkyl,

R'_c, R'_d, R'_e, R'_f, independently of one another, represents a hydrogen or a linear or branched C₁-
 C₆alkyl group,

or R'_d and R'_e form with the nitrogen atom carrying them a cycle B₄,

or R'_d, R'_e and R'_f form with the nitrogen atom carrying them a
 bridged C₃-C₈heterocycloalkyl,

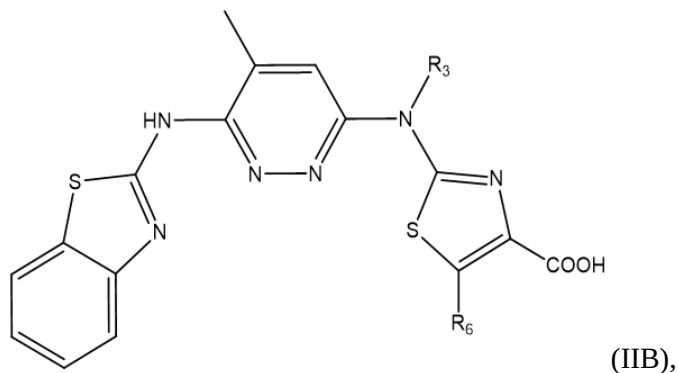
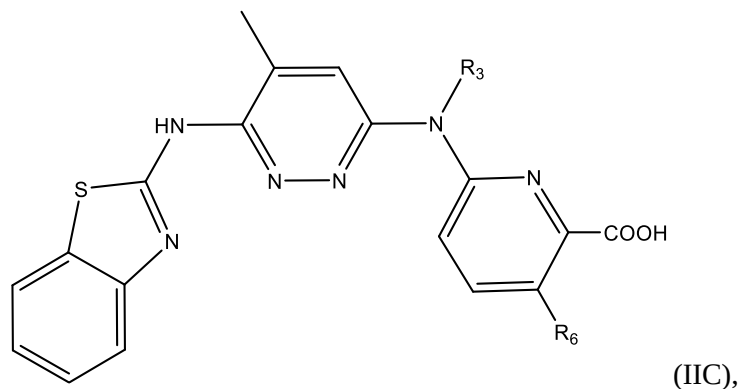
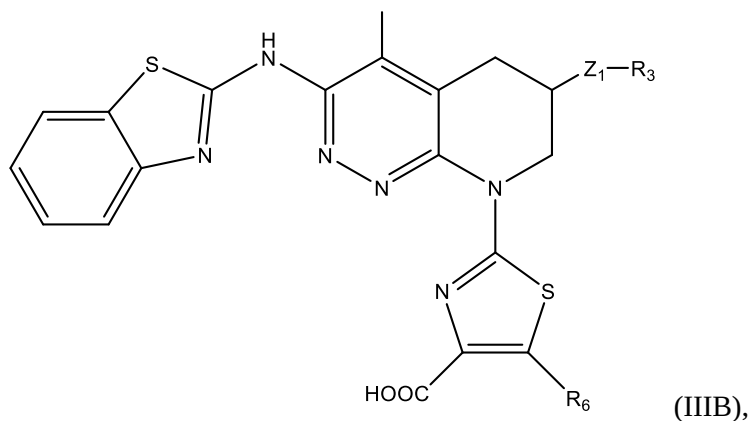
m=0, 1 or 2,

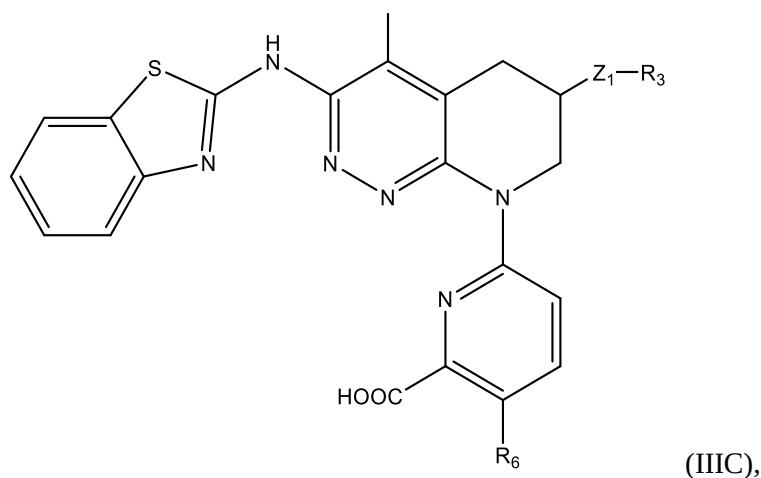
p=1, 2, 3 or 4,

B₃ and B₄, independently of one another, represents a C₃-C₈heterocycloalkyl group, which group
 can: (i) be a mono- or bi-cyclic group, wherein bicyclic group includes fused, bridged or spiro

ring system, (ii) can contain, in addition to the nitrogen atom, one or two hetero atoms selected independently from oxygen, sulphur and nitrogen, (iii) be substituted by one or two groups selected from the group consisting of: fluorine, bromine, chlorine, a linear or branched C₁-C₆alkyl, hydroxyl, -NH₂, oxo and piperidiny; or

(iii) the Bcl-xL inhibitor is represented by formula (IIB), (IIC), (IIB) or (IIIC):





or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

for formula (IIB) or (IIC), R_3 represents a group selected from: hydrogen; linear or branched C_1 - C_6 alkyl; $-X_1-NR_aR_b$; $-X_1-N^+R_aR_bR_c$; and $-X_1-O-R_c$;

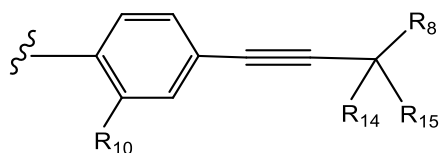
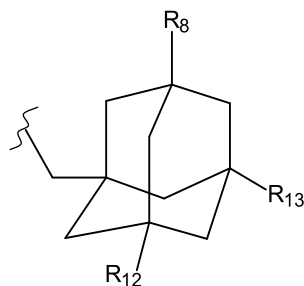
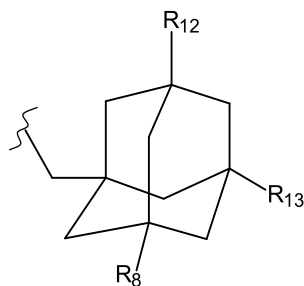
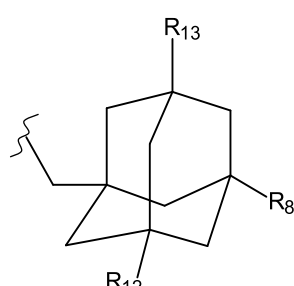
for formula (IIIB) or (IIIC), Z_1 represents a bond, and R_3 represents hydrogen; or Z_1 represents $-O-$, and R_3 represents $-X_1-NR_aR_b$,

R_a and R_b , independently of one another, represent a group selected from: hydrogen; linear or branched C_1 - C_6 alkyl optionally substituted by one or two hydroxyl groups; and C_1 - C_6 alkylene- SO_2O^- ;

R_c represents a hydrogen or a linear or branched C_1 - C_6 alkyl group

R_6 represents $-X_2-O-R_7$ or an heteroarylene- R_7 group optionally substituted by a linear or branched C_1 - C_6 alkyl group,

R_7 represents a group selected from:



R_8 represents a group selected from: $-NR'_aR'_b$; $-O-X'_2-NR'_aR'_b$; and $-X'_2-NR'_aR'_b$,

R₁₀ represents fluorine,

R₁₂ and R₁₃, independently of one another, represent a hydrogen atom or a methyl group,

R₁₄ and R₁₅, independently of one another, represent a hydrogen or a methyl group,

X₁ and X₂, independently of one another, represent a linear or branched

C₁-C₆alkylene group optionally substituted by one or two groups selected from trifluoromethyl, hydroxyl, halogen, C₁-C₆alkoxy,

X'₂ represents a linear or branched C₁-C₆alkylene,

R'_a and R'_b independently of one another, represent a group selected from: hydrogen; linear or branched C₁-C₆alkyl optionally substituted by one or two hydroxyl or C₁-C₆alkoxy groups; C₁-C₆alkylene-NR'_dR'_e;

or R'_a and R'_b form with the nitrogen atom carrying them a cycle B₃,

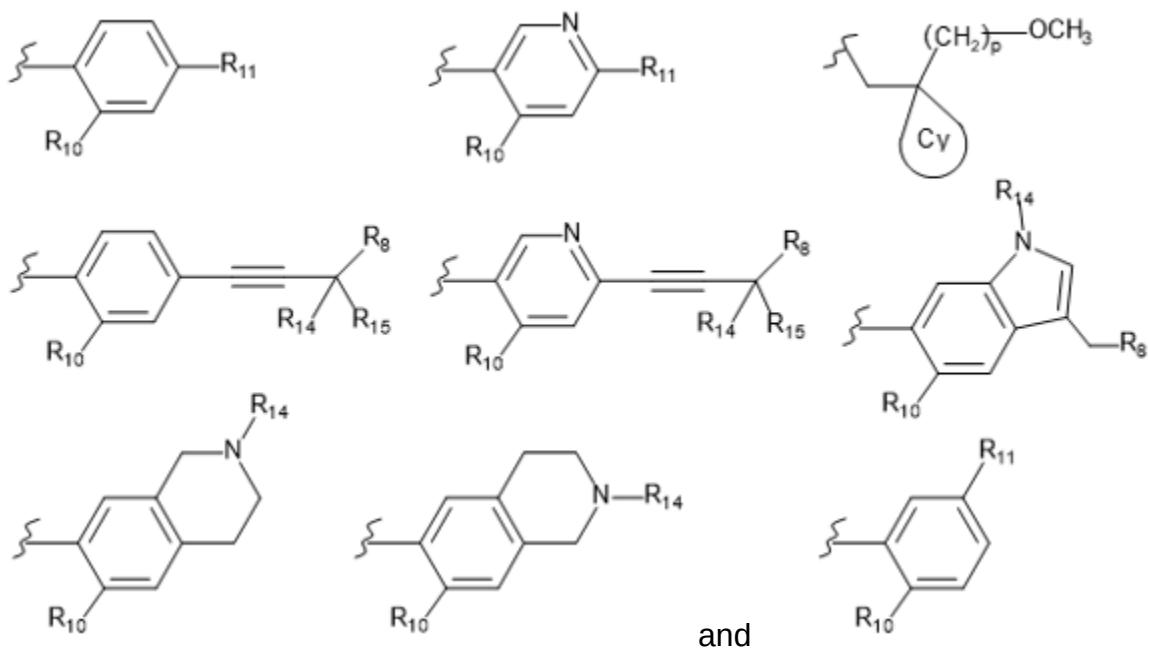
R'_d, R'_e, independently of one another, represents a hydrogen or a linear or branched C₁-C₆alkyl group,

B₃ represents a C₃-C₈heterocycloalkyl group, which group can: (i) be a mono- or bi-cyclic group, wherein bicyclic group includes fused, bridged or spiro ring system, (ii) can contain, in addition to the nitrogen atom, one or two hetero atoms selected independently from oxygen and nitrogen, (iii) be substituted by one or two groups selected from: fluorine, bromine, chlorine, linear or branched C₁-C₆alkyl, hydroxyl, and oxo.

25. The antibody-drug conjugate of claim 24, wherein:

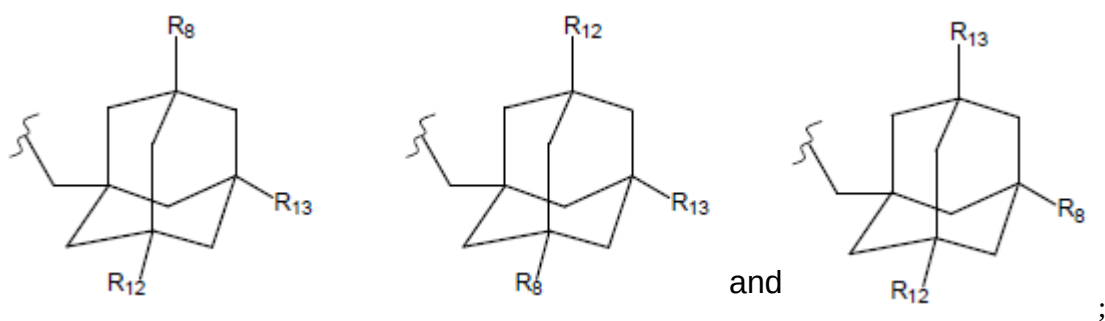
(i) G is selected from the group consisting of: -C(O)OH, -C(O)OR_{G3}, -C(O)NR_{G1}R_{G2}, -C(O)R_{G2}, -NR_{G1}C(O)R_{G2}, -NR_{G1}C(O)NR_{G1}R_{G2}, -OC(O)NR_{G1}R_{G2}, -NR_{G1}C(O)OR_{G3}, -C(=NR_{G1})NR_{G1}R_{G2}, -NR_{G1}C(=NCN)NR_{G1}R_{G2}, -NR_{G1}S(O)₂NR_{G1}R_{G2}, -S(O)₂R_{G3}, -S(O)₂NR_{G1}R_{G2}, -NR_{G1}S(O)₂R_{G2}, -NR_{G1}C(=NR_{G2})NR_{G1}R_{G2}, -C(=S)NR_{G1}R_{G2}, -C(=NR_{G1})NR_{G1}R_{G2}, halogen, -NO₂, and -CN;

(ii) R₇ represents a group selected from the group consisting of: a linear or branched C₁-C₆alkyl group; a (C₃-C₆)cycloalkylene-R₈;

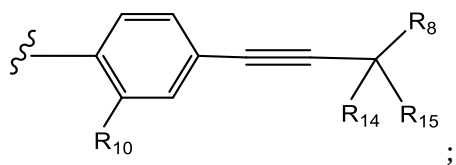


wherein Cy represents a C₃-C₈cycloalkyl;

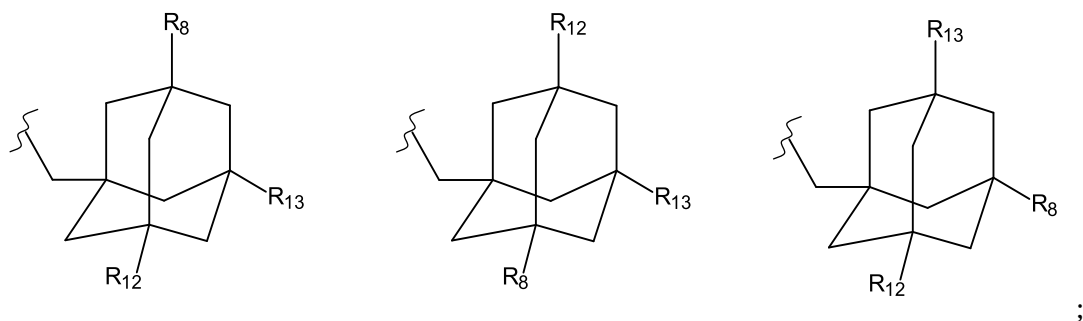
(iii) R₇ represents a group selected from the group consisting of:



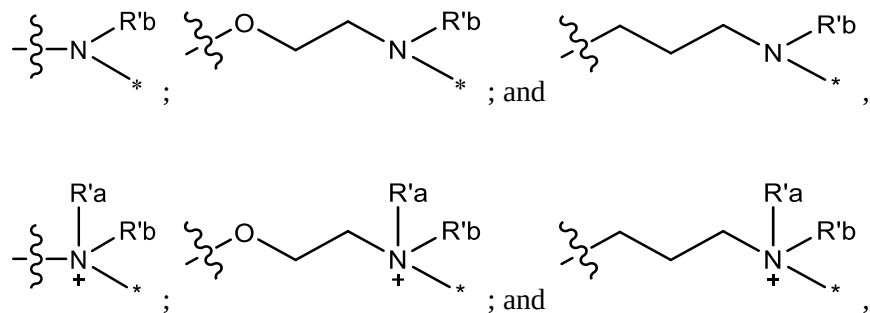
(iv) R₇ represents the following group:



(v) R₇ represents a group selected from:



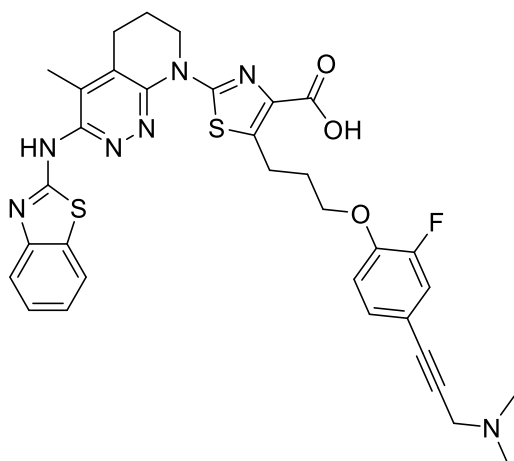
(vi) R_8 represents a group selected from:



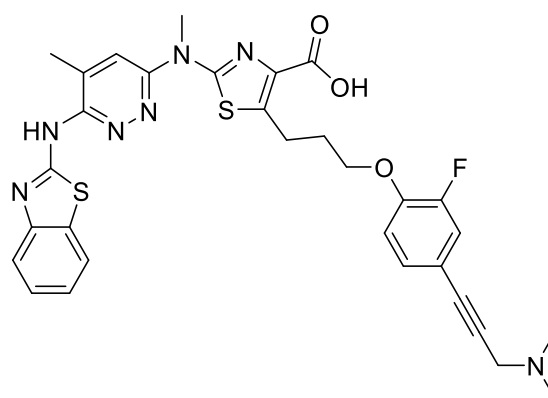
wherein ---^* represents a bond to the linker; and/or

(vii) B_3 represents a C_3 - C_8 heterocycloalkyl group selected from a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, a morpholinyl group, an azepanyl group, and a 4,4-difluoropiperidin-1-yl group.

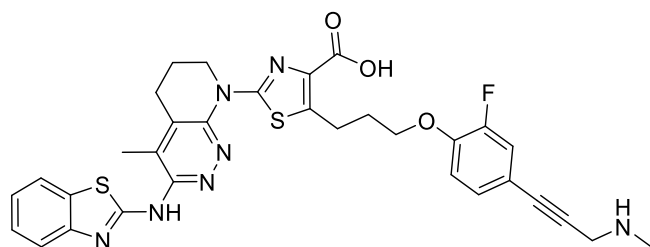
26. The antibody-drug conjugate of any one of claims 24-25, wherein the Bcl-xL inhibitor is represented by any one of the following:



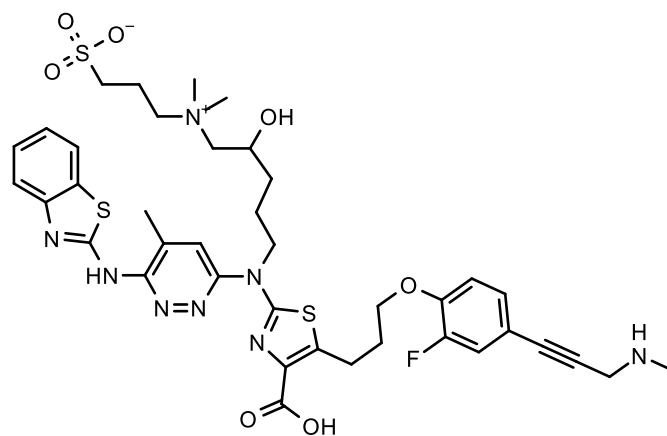
D2-1



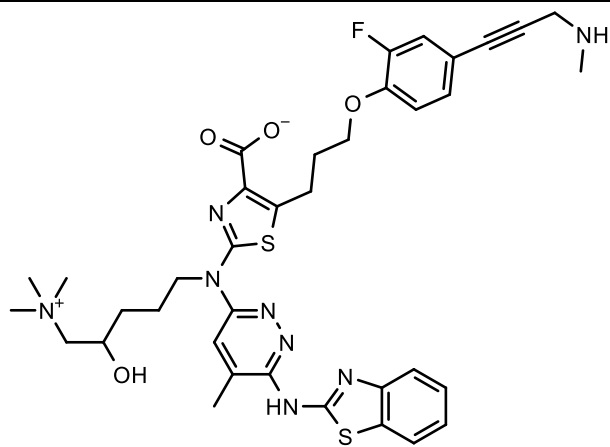
D2-2



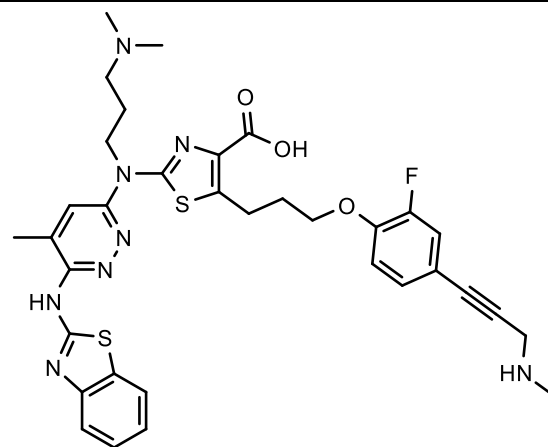
D2-3



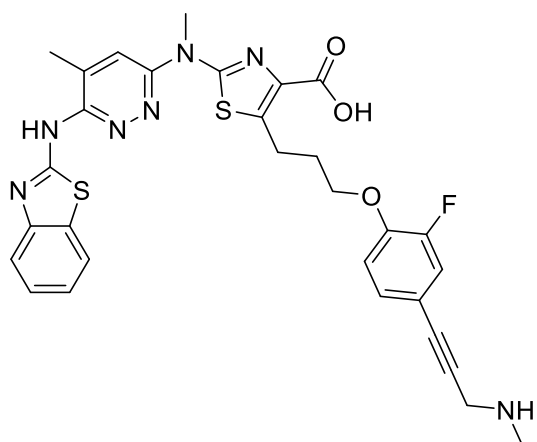
D2-4



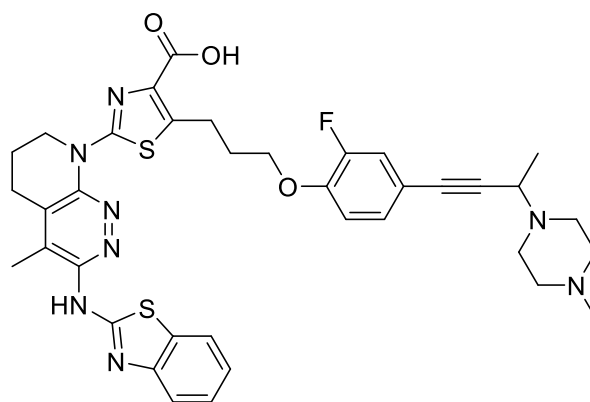
D2-5



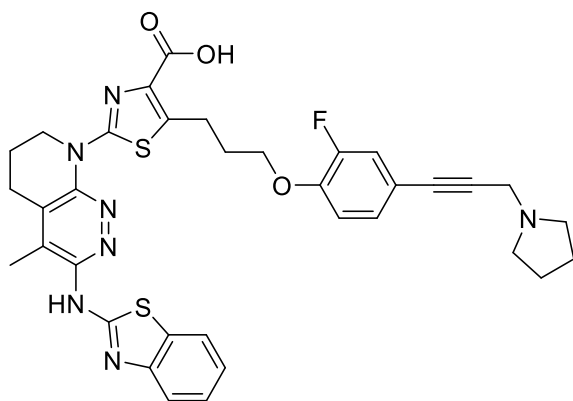
D2-6



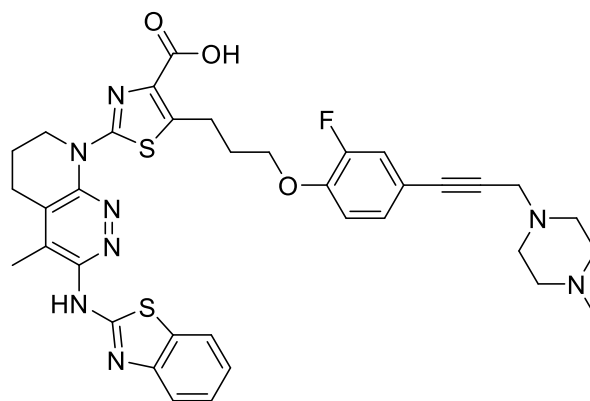
D2-7



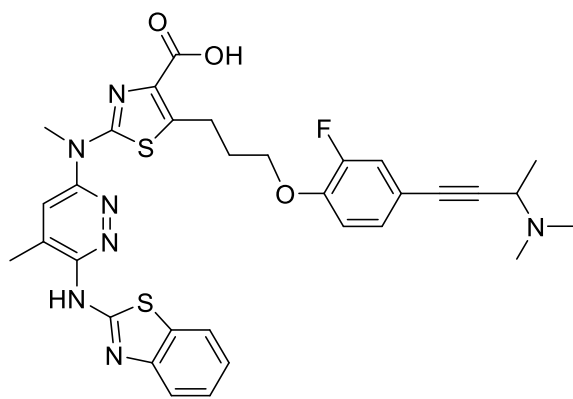
D2-8



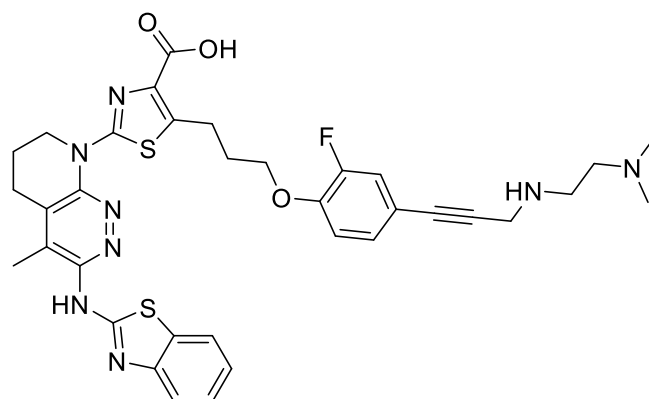
D2-9



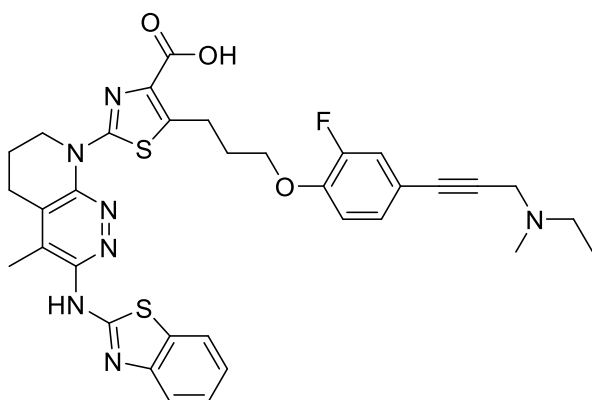
D2-10



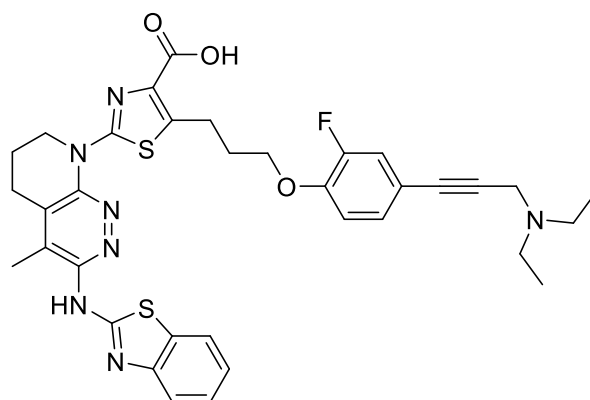
D2-11



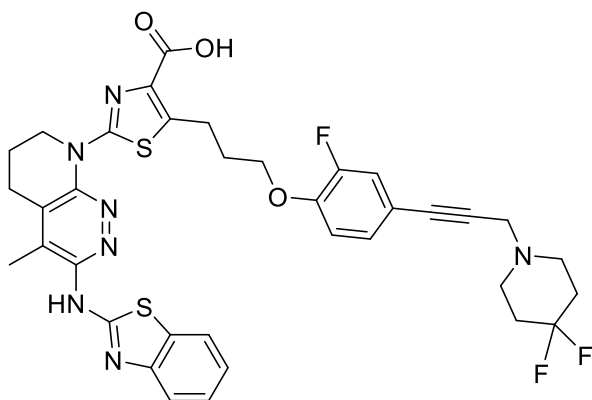
D2-12



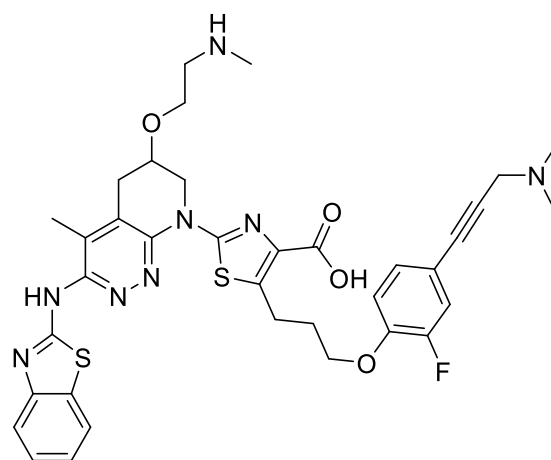
D2-13



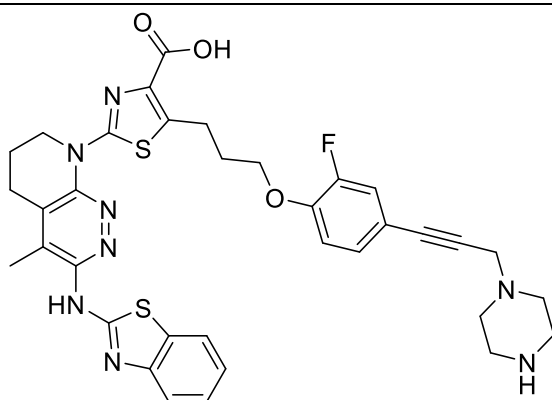
D2-14



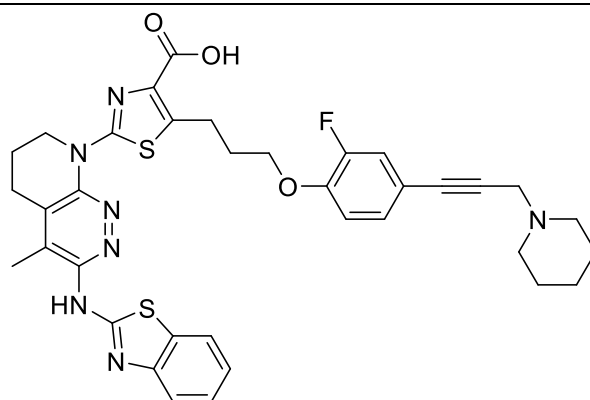
D2-15



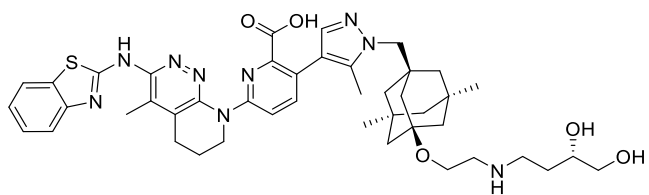
D2-16



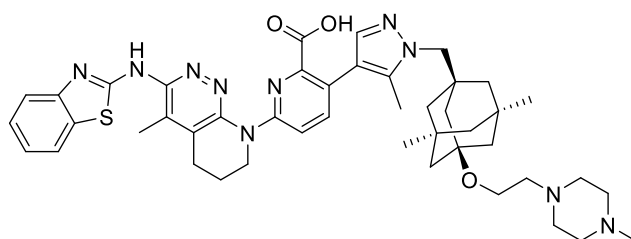
D2-17



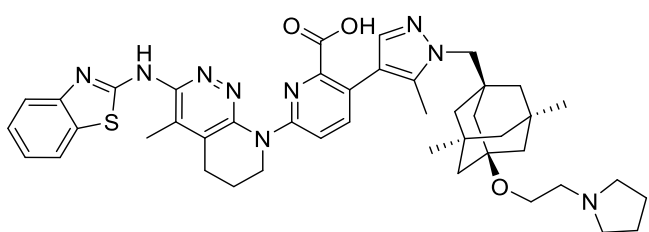
D2-18



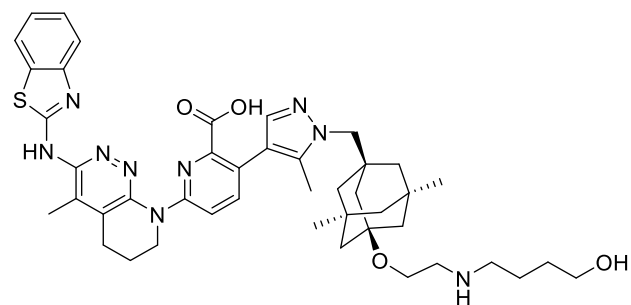
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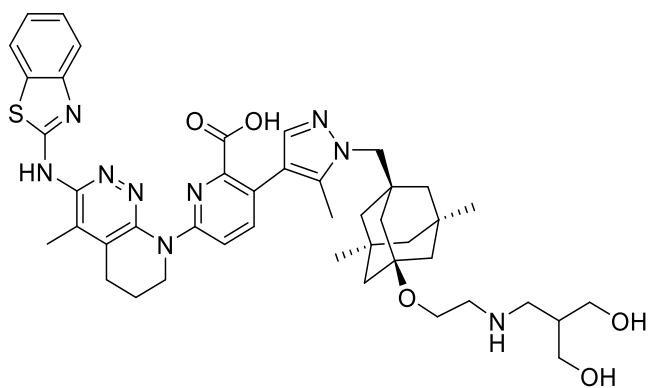
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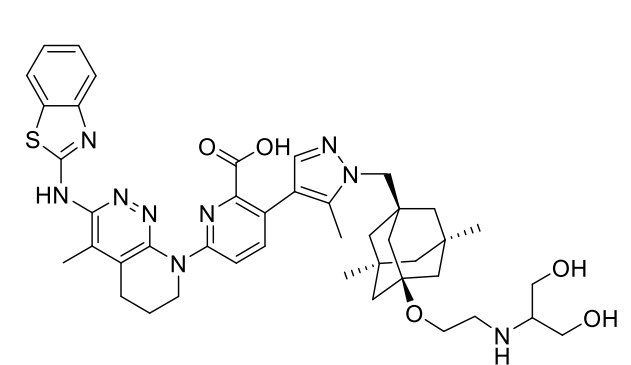
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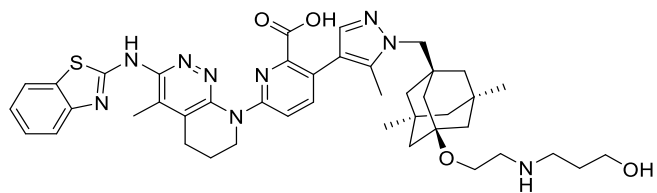
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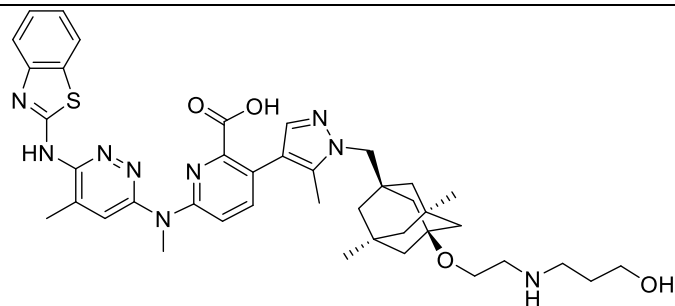
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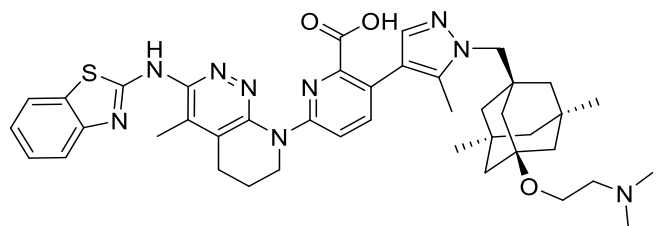
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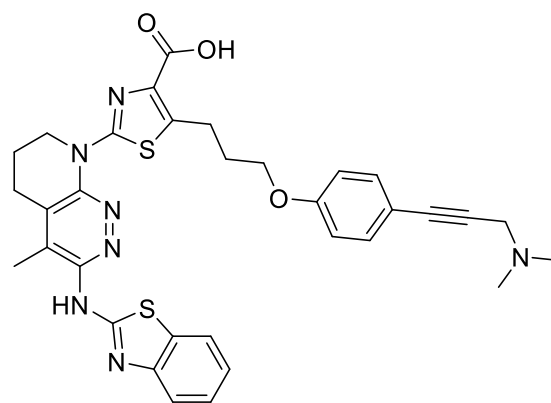
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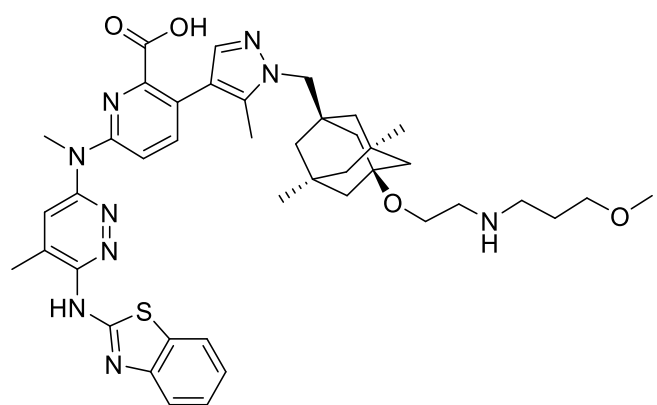
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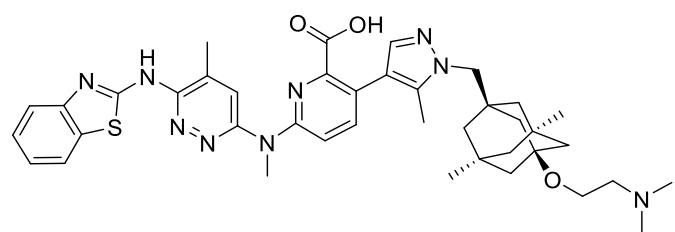
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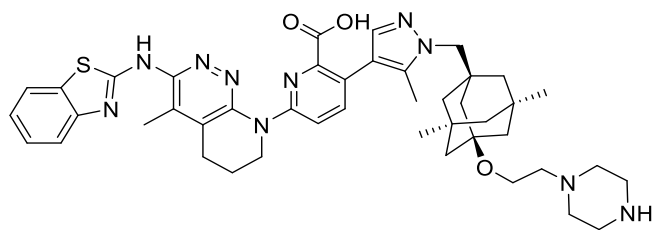
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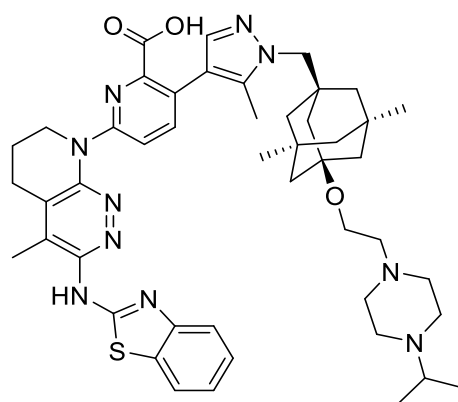
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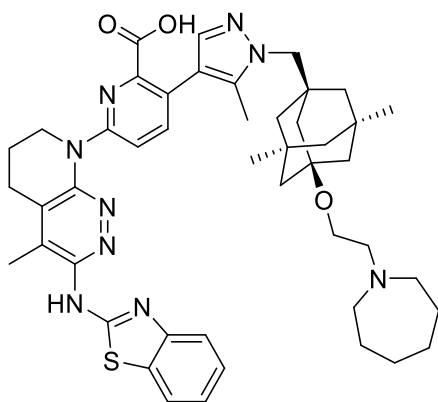
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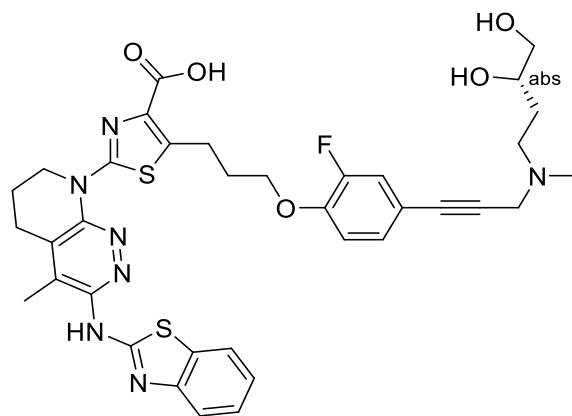
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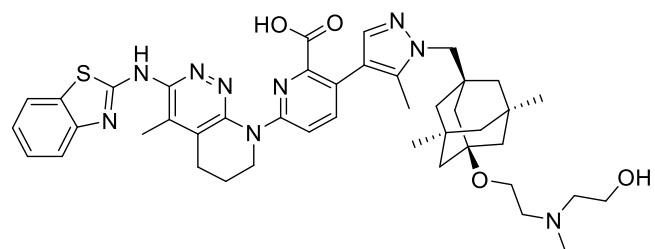
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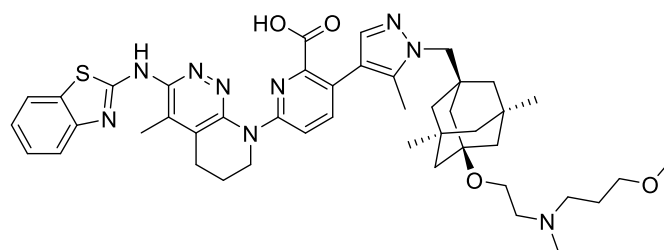
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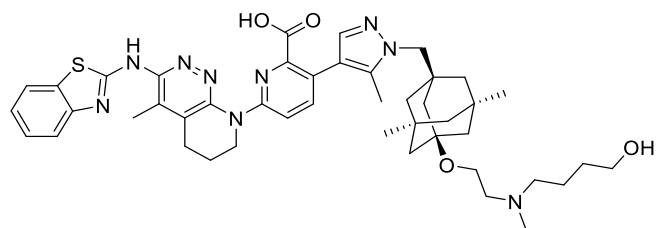
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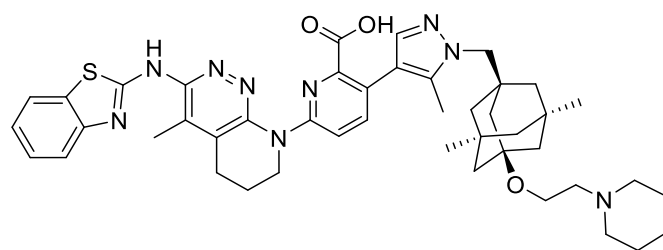
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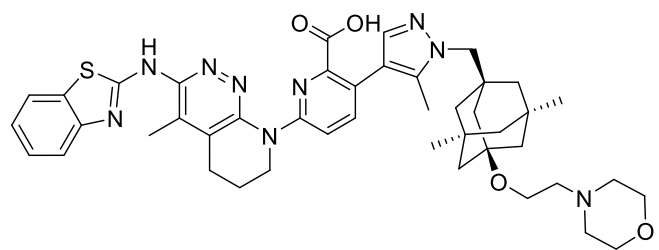
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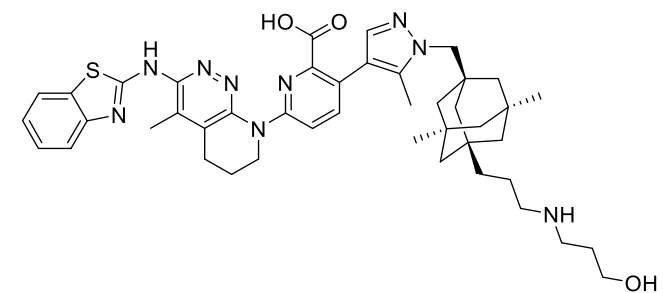
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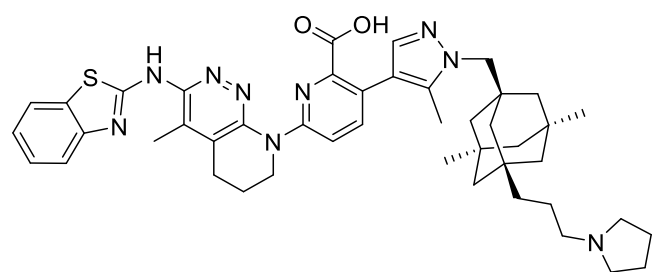
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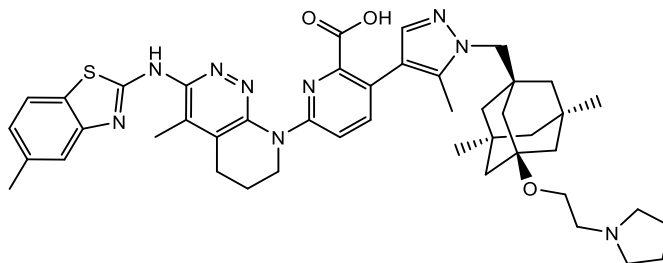
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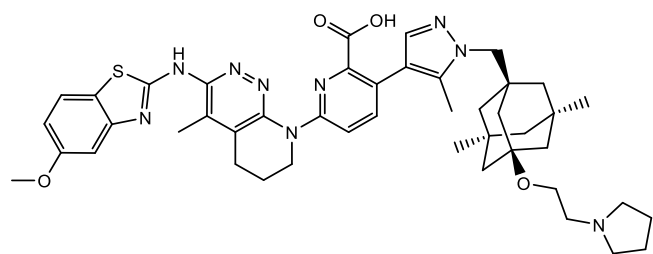
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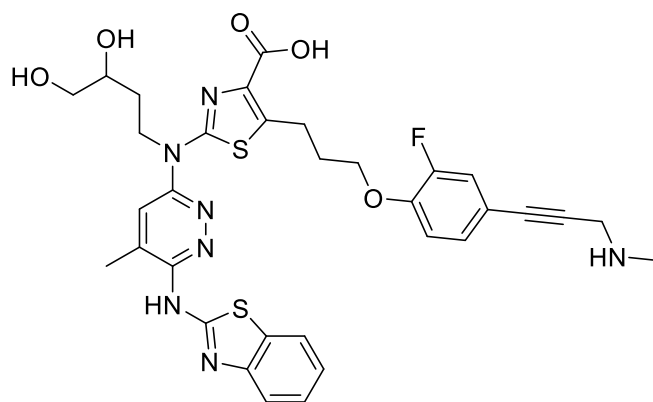
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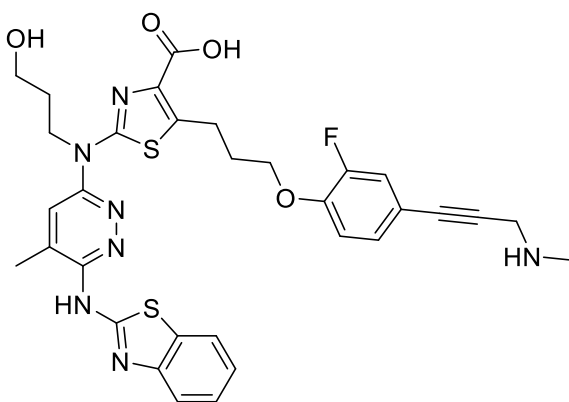
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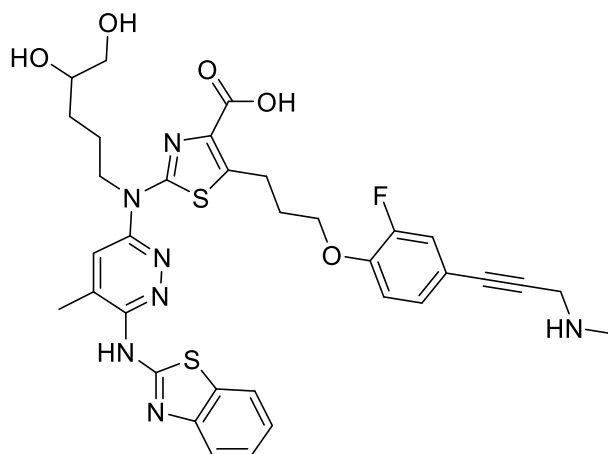
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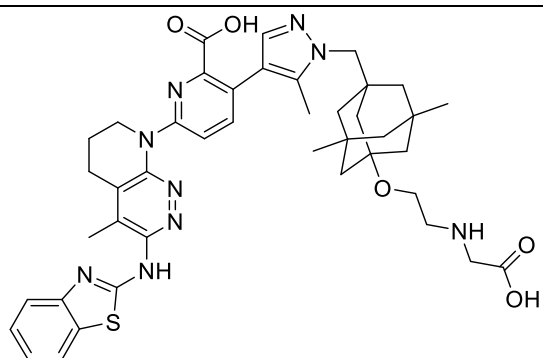
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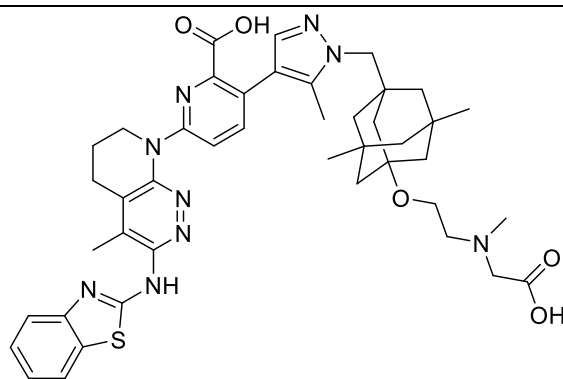
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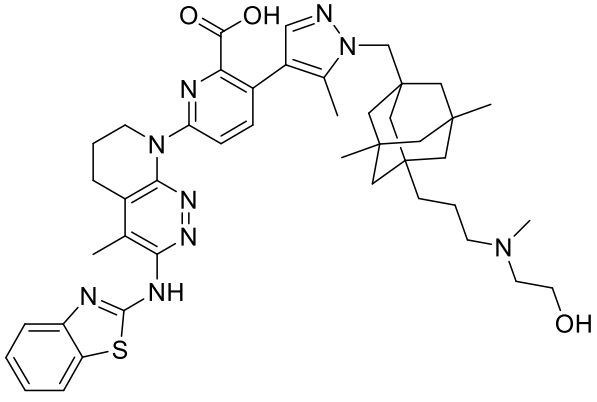
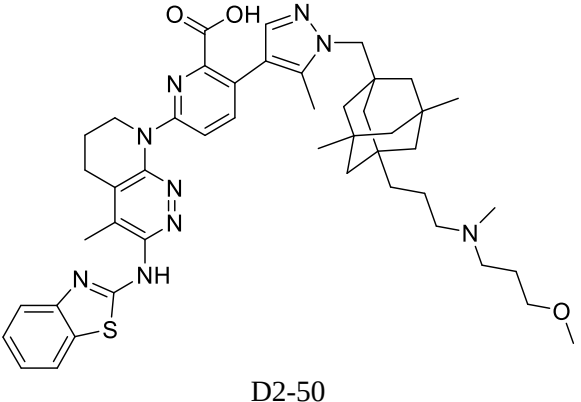
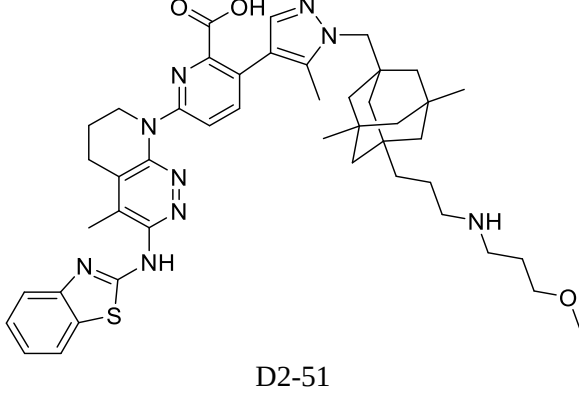
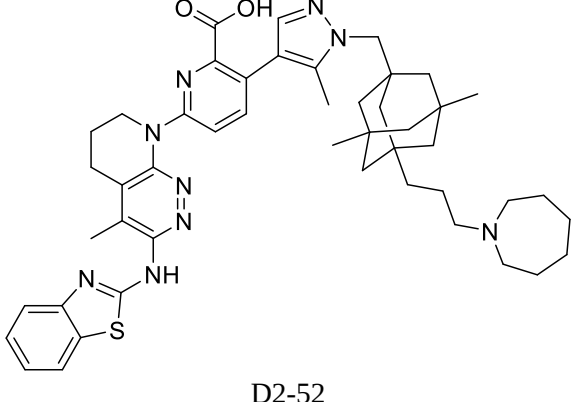
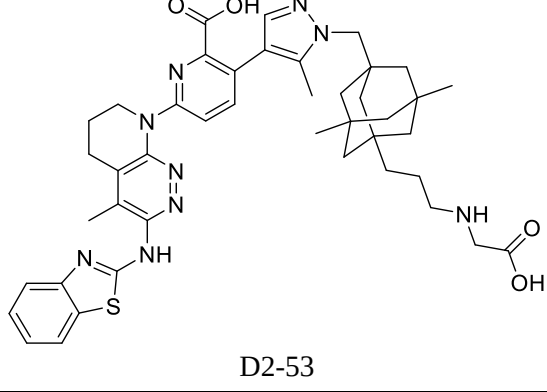
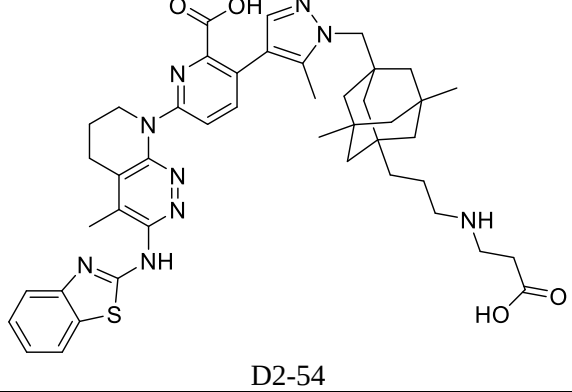
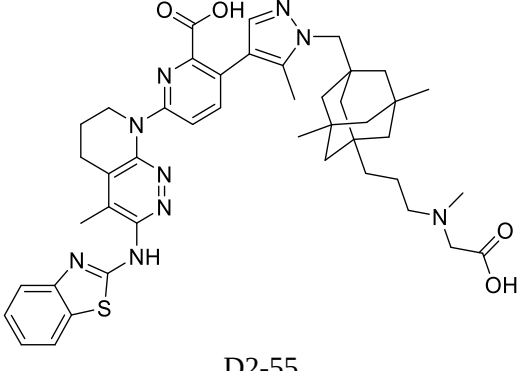
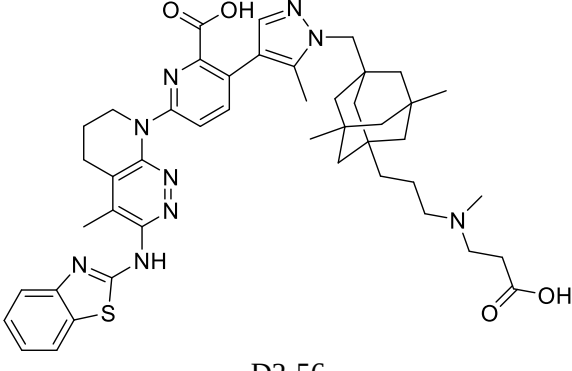
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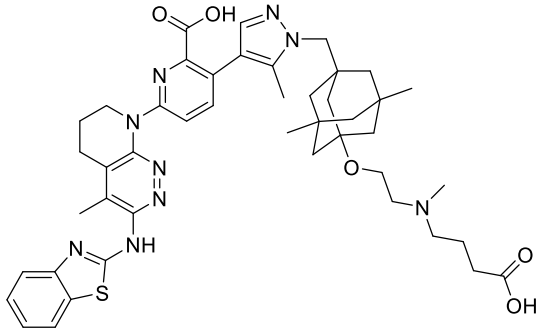
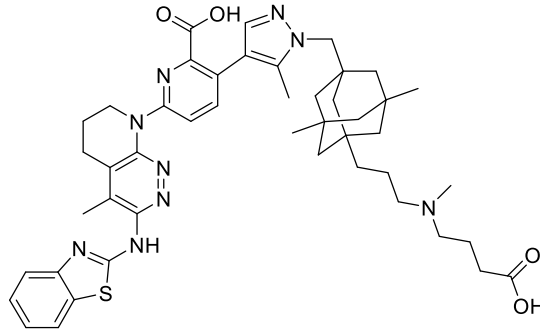
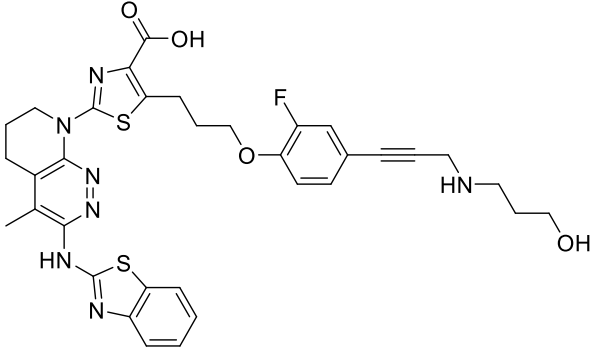
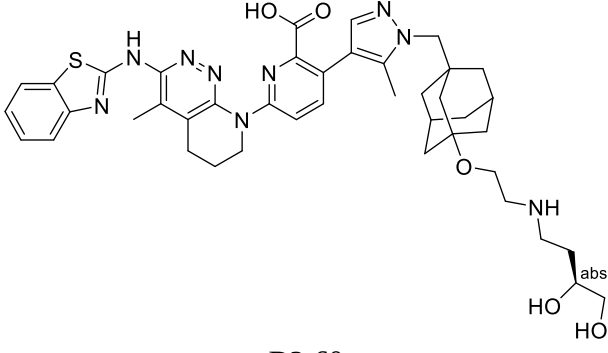
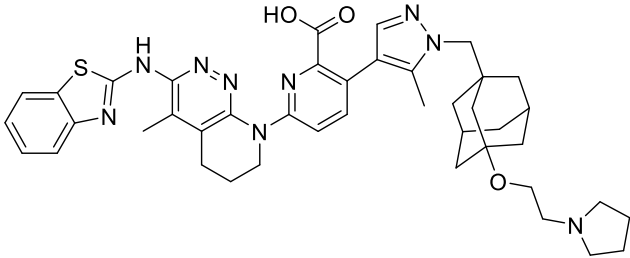
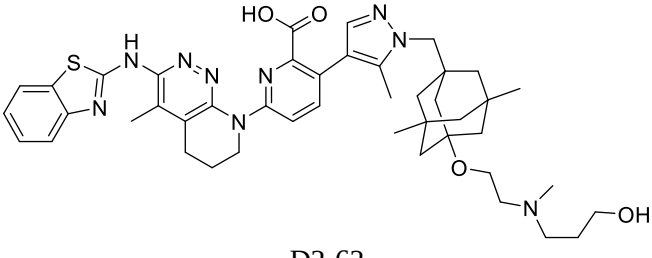
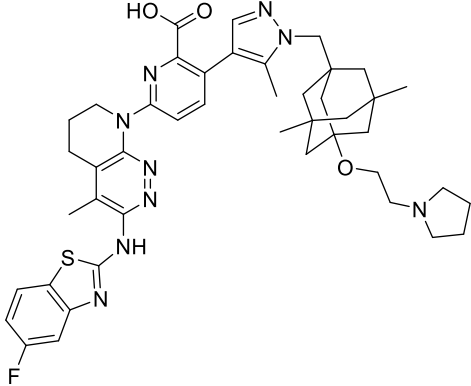
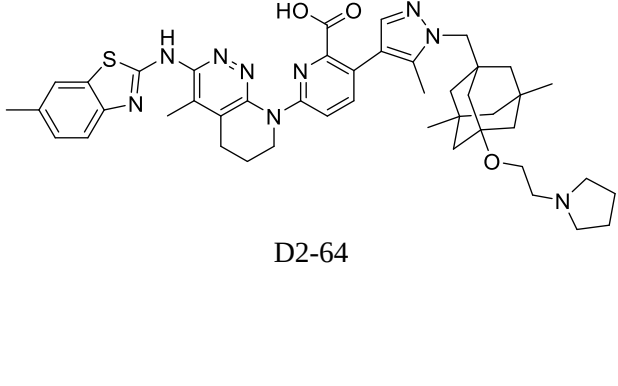


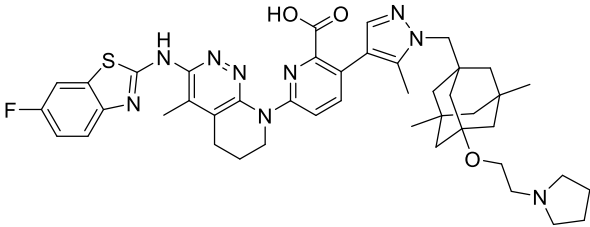
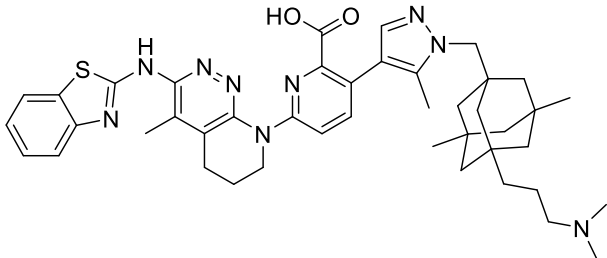
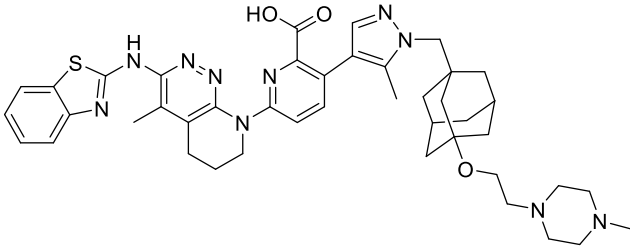
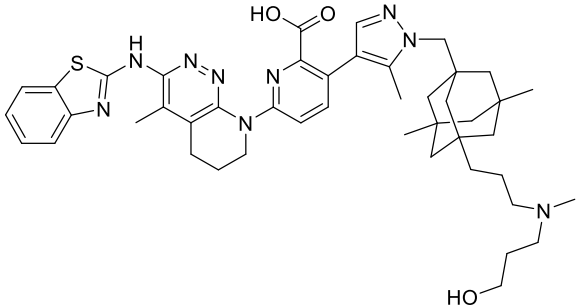
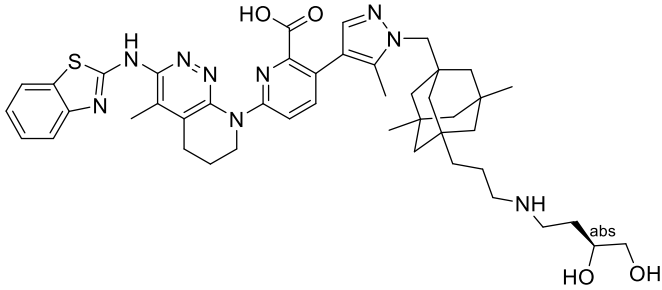
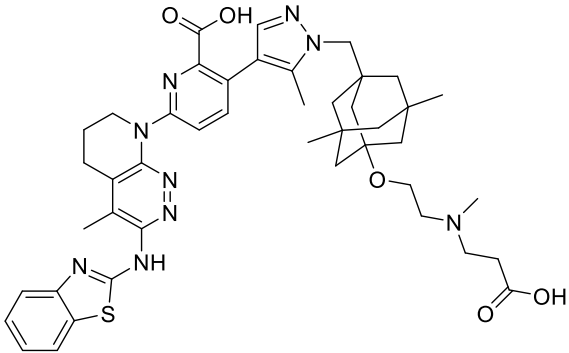
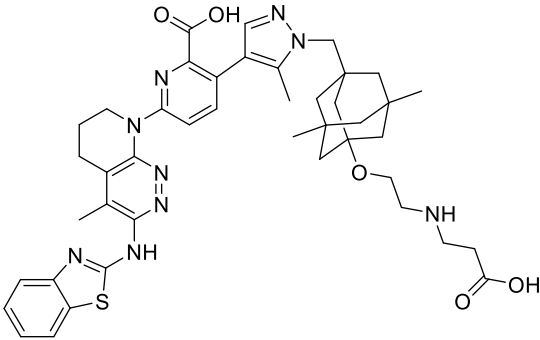
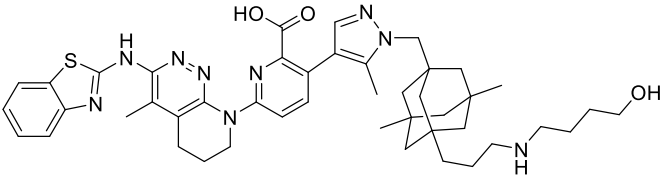
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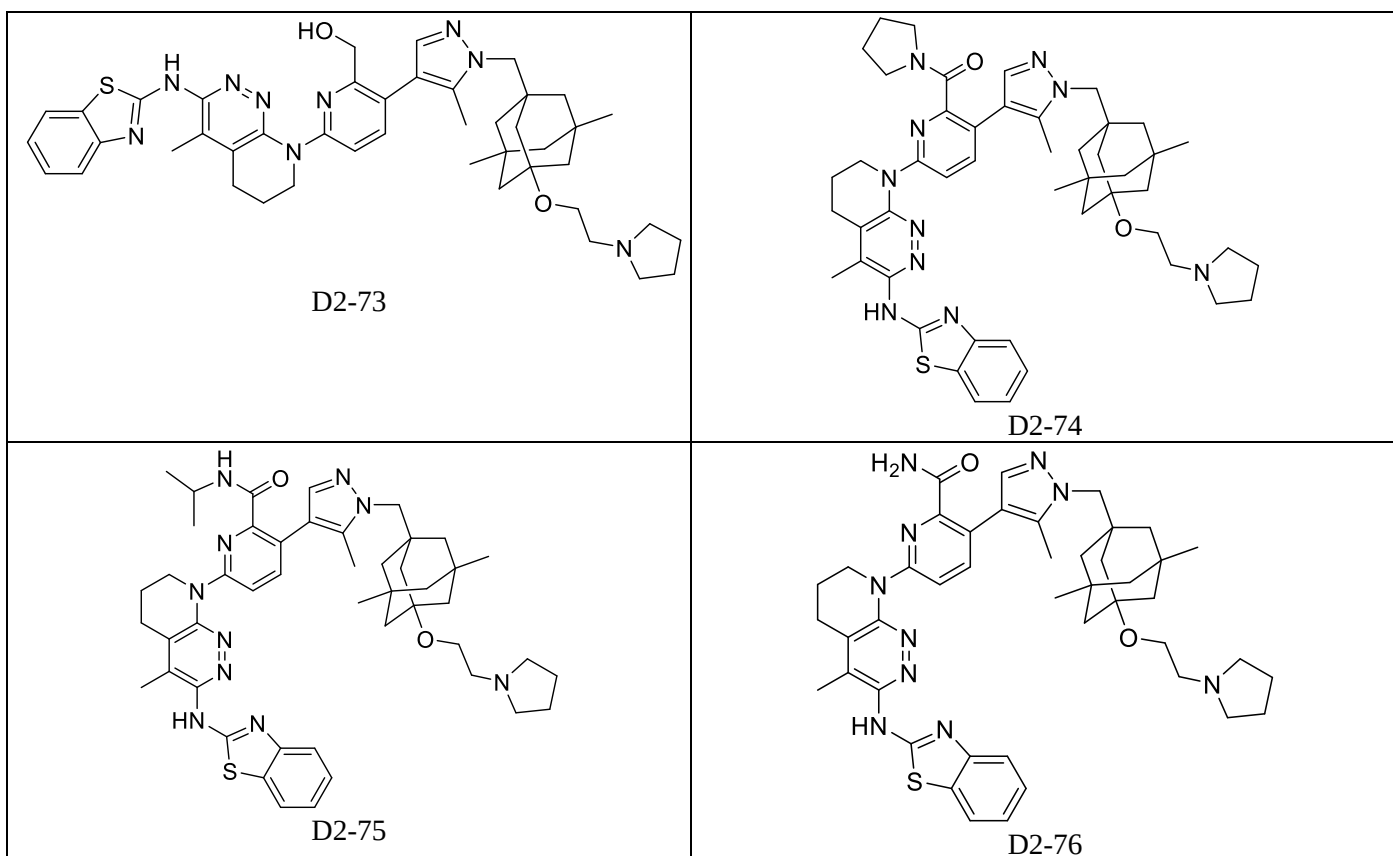


D2-48

 <p>D2-49</p>	 <p>D2-50</p>
 <p>D2-51</p>	 <p>D2-52</p>
 <p>D2-53</p>	 <p>D2-54</p>
 <p>D2-55</p>	 <p>D2-56</p>

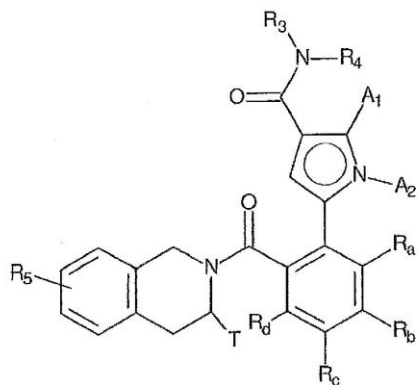
 <p>D2-57</p>	 <p>D2-58</p>
 <p>D2-59</p>	 <p>D2-60</p>
 <p>D2-61</p>	 <p>D2-62</p>
 <p>D2-63</p>	 <p>D2-64</p>

 <p>D2-65</p>	 <p>D2-66</p>
 <p>D2-67</p>	 <p>D2-68</p>
 <p>D2-69</p>	 <p>D2-70</p>
 <p>D2-71</p>	 <p>D2-72</p>



or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing.

27. The antibody-drug conjugate of any one of claims 19-20, or pharmaceutically acceptable salt thereof, wherein the Bcl-2 inhibitor is represented by Formula (IV) or Formula (V):



(IV),

or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

A₁ represents a hydrogen or halogen atom, a linear or branched (C₁-C₆)polyhaloalkyl group, a linear or branched (C₁-C₆)alkyl group or a cycloalkyl group,

A₂ represents a linear or branched (C₁-C₆)alkyl group optionally substituted by a group selected from halogen, hydroxy, linear or branched (C₁-C₆)alkoxy, NR'R'' and morpholine, or A₂ represents a linear or branched (C₁-C₆)polyhaloalkyl group or a cyclopropyl group,

it being understood that R' and R'', each independently of the other, represent a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

T represents a hydrogen atom, a linear or branched (C₁-C₆)alkyl group optionally substituted by from one to three halogen atoms, a group (C₁-C₄)alkyl-NR₁R₂, or a group (C₁-C₄)alkyl-OR₆,

R₁ and R₂, each independently of the other, represent a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

or R₁ and R₂ form with the nitrogen atom carrying them a heterocycloalkyl,

R₃ represents an aryl or heteroaryl group, it being understood that one or more carbon atoms of the preceding groups, or of their possible substituents, may be deuterated,

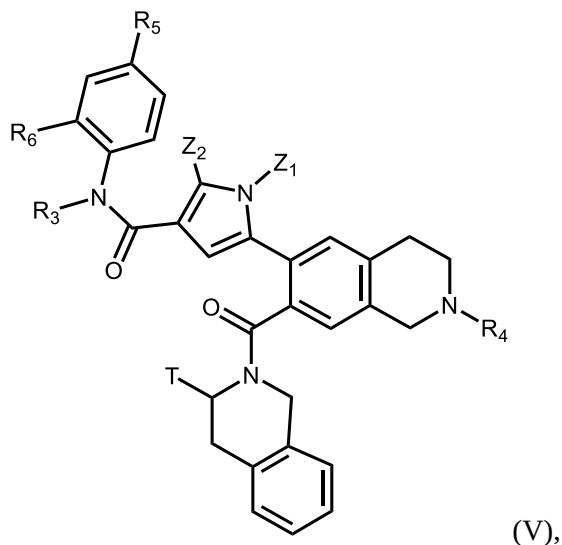
R₄ represents a phenyl group, a 4-hydroxyphenyl group, a 3-fluoro-4-hydroxyphenyl group, a 2-hydroxypyrimidine group or a 3-hydroxypyridine group, it being understood that one or more carbon atoms of the preceding groups, or of their possible substituents, may be deuterated,

R₅ represents a hydrogen or halogen atom, a linear or branched (C₁-C₆)alkyl group, or a linear or branched (C₁-C₆)alkoxy group,

R₆ represents a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

R_a and R_d each represent a hydrogen atom and (R_b,R_c) form together with the carbon atoms carrying them a 1,3-dioxolane group or a 1,4-dioxane group, or R_a, R_c and R_d each represent a hydrogen atom and R_b represents a hydrogen or halogen atom or a methoxy group,

or R_a and R_d each represent a hydrogen atom, R_b represents a hydrogen or halogen atom and R_c represents a hydroxy or methoxy group, or: R_a and R_d each represent a hydrogen atom, R_b represents a hydroxy or methoxy group and R_c represents a halogen atom, or



(V),

or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing, wherein:

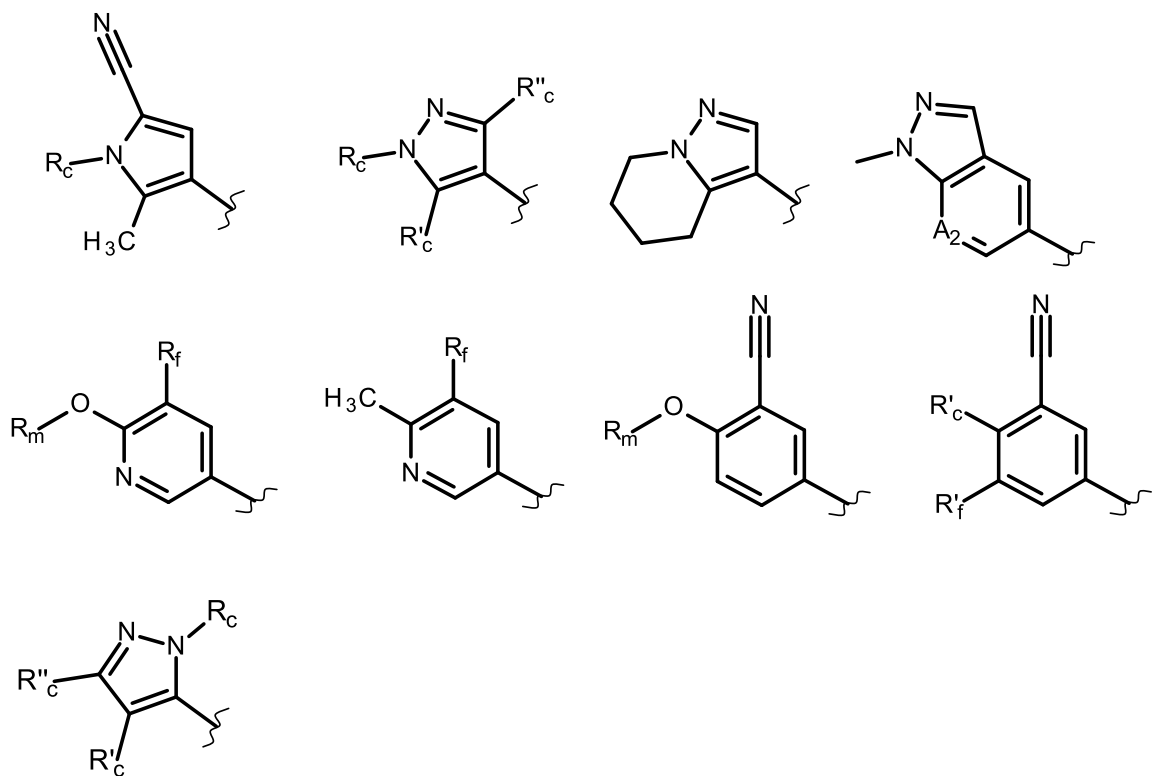
Z₁ and Z₂ represent both a methyl group or they form together with the atoms carrying them a fused piperidine group,

T represents a hydrogen atom, a linear or branched (C₁-C₆)alkyl group optionally substituted by one to three halogen atoms, a (C₁-C₄)alkylene-NR₁R₂ group, a (C₁-C₄)alkylene-OR_i group,

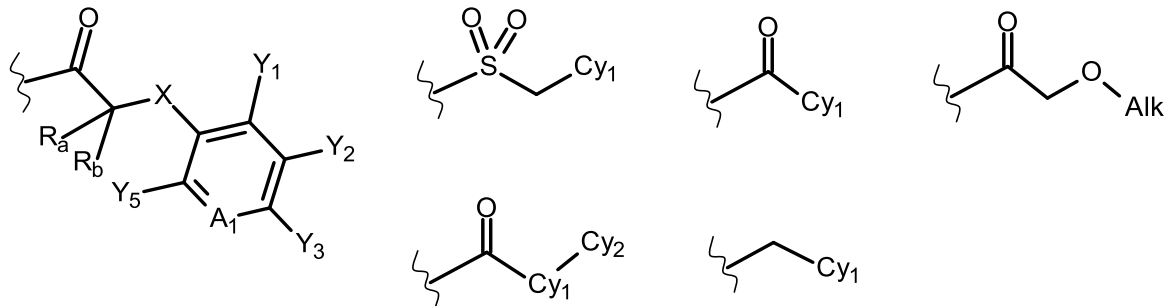
R₁ and R₂, independently of one another, represent a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,

or R₁ and R₂ form with the nitrogen atom carrying them a heterocycloalkyl group, which heterocycloalkyl is optionally substituted by one to three groups selected from: (C₁-C₆)alkyl group and halogen atom,

R₃ represents a group selected from:



R₄ represents a group selected from:



R₅ represents a hydrogen atom, a halogen atom or a hydroxy group,

R₆ represents a hydrogen, a linear or branched (C₁-C₆)alkyl group, or a halogen atom,

Alk represents a linear or branched (C₁-C₆)alkyl group,

A₁ represents a C-Y₄ or a nitrogen atom,

A₂ represents a C-H or a nitrogen atom,

Cy₁ represents a phenyl, a heteroaryl, a cycloalkyl or a heterocycloalkyl group, wherein the phenyl, the heteroaryl, the cycloalkyl and the heterocycloalkyl groups are optionally substituted by one to three groups selected from: linear or branched (C₁-C₆)alkyl group optionally substituted by 1 to 3 halogen atoms, hydroxy group, cycloalkyl group, and halogen atom and the heterocycloalkyl group is optionally further substituted by an oxo group,

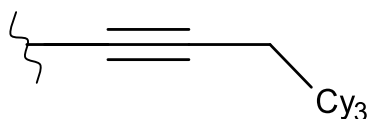
Cy₂ represent a phenyl or a heteroaryl group, wherein the phenyl and the heteroaryl groups are optionally substituted by one to three groups selected from: linear or branched (C₁-C₆)alkyl group optionally substituted by 1 to 3 halogen atoms, hydroxy group, and halogen atom

X represents a bond, -O-, -S- or NR_k,

Y₁ and Y₅, independently of one another, represent a group selected from: hydrogen atom, halogen atom, cyano, linear or branched (C₁-C₆)alkyl group, and linear or branched (C₁-C₆)alkoxy group,

Y₂ and Y₄, independently of one another, represent a group selected from: hydrogen atom, halogen atom, linear or branched (C₁-C₆)alkyl group, linear or branched (C₁-C₆)alkoxy group, and heterocycloalkyl group optionally substituted by a linear or branched (C₁-C₆)alkyl group,

Y₃ represents a group selected from: hydrogen atom, halogen atom, linear or branched (C₁-C₆)alkyl, linear or branched (C₁-C₆)alkynyl, -(C₁-C₄)alkylene-OR_i, linear or branched (C₁-C₆)alkoxy group, -O-phenyl, -S-phenyl, -O-(C₁-C₄)alkylene-Cy₃, -O-(C₁-C₄)alkylene-Cy₄, -O-Cy₃, -O-(C₁-C₄)alkylene-NR_gR_h, -(C₁-C₄)alkylene-Cy₃, -(C₁-C₄)alkylene-Cy₄, Cy₃, Cy₄, and:



wherein the alkylene moiety of the preceding groups may be linear or branched,

Cy₃ represents a heterocycloalkyl optionally substituted by one to three groups selected from: linear or branched (C₁-C₆)alkyl group optionally substituted by 1 to 3 halogen atoms, hydroxy group, cycloalkyl group, heterocycloalkyl group, and halogen atom,

Cy₄ represents a cycloalkyl optionally substituted by one to three groups selected from: linear or branched (C₁-C₆)alkyl group optionally substituted by 1 to 3 halogen atoms, hydroxy group, cycloalkyl group, heterocycloalkyl group, and halogen atom,

R_a and R_b, independently of one another, represent a hydrogen atom or a halogen atom,

R_c represents a group selected from: hydrogen, linear or branched (C₁-C₆)alkyl group optionally substituted by 1 to 3 halogen atoms, (C₁-C₆)alkylene-NR_dR_e, (C₁-C₆)alkylene-OR_j, cycloalkyl, heterocycloalkyl, and (C₁-C₆)alkylene-heterocycloalkyl group,

R'_c and R''_c, independently of one another, represent a hydrogen atom or a linear or branched (C₁-C₆)alkyl,

R_d and R_e, independently of one another, represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a cycloalkyl group or a heterocycloalkyl group,

R_f represents a hydrogen atom, a halogen atom or a cyano group,

R'_f represents a hydrogen atom or a halogen atom,

R_g and R_h, independently of one another, represent a hydrogen atom, a linear or branched (C₁-

C₆)alkyl group optionally substituted by one to three halogen atoms, a cycloalkyl group, a heterocycloalkyl group, or a -(C₁-C₆)alkylene-heterocycloalkyl,

R_i, R_j, and R_k, independently of one another, represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or a -(C₁-C₆)alkylene-cycloalkyl group,

R_l represents a hydrogen atom, a linear or branched (C₁-C₆)alkyl group or a linear or branched (C₁-C₆)alkylene-heterocycloalkyl group,

R_m represents a hydrogen or a linear or branched (C₁-C₆)alkyl group.

28. The antibody-drug conjugate of claim 27, or a pharmaceutically acceptable salt thereof, wherein:
(i) the Bcl-2 inhibitor is represented by Formula (IV) or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing;

(ii) in Formula (IV), (a) A₁ represents a hydrogen atom or a methyl group; or (b) A₁ and A₂ both represent a methyl group;

(iii) in Formula (IV), T represents a methyl, aminomethyl, (morpholin-4-yl)methyl, (4-methylpiperazin-1-yl)methyl, 2-(morpholin-4-yl)ethyl, [2-(morpholin-4-yl)ethoxy]methyl, hydroxymethyl, [2-(dimethylamino)ethoxy]methyl, hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-ylmethyl, 1-oxa-6-azaspiro[3.3]hept-6-ylmethyl, 3-(morpholin-4-yl)propyl or trifluoromethyl group; or

(iv) in Formula (IV), R₃ represents a group selected from phenyl, 1*H*-pyrazole, 1*H*-indole, 1*H*-indazole, pyridine, pyrimidine, 1*H*-pyrrolo[2,3-*b*]pyridine, 2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine, 1*H*-benzimidazole, 1*H*-pyrrole, 1*H*-pyrrolo[2,3-*c*]pyridine, 1*H*-pyrrolo[3,2-*b*]pyridine, 5*H*-pyrrolo[3,2-*d*]pyrimidine, thiophene, pyrazine, 1*H*-pyrazolo[3,4-*b*]pyridine, 1,2-oxazole, and pyrazolo[1,5-*a*]pyrimidine, those groups optionally having one or more substituents selected from halogen, linear or branched (C₁-C₆)alkyl, linear or branched (C₁-C₆)alkoxy, cyano, cyclopropyl, oxetane, tetrahydrofuran, -CO-O-CH₃, trideuteriomethyl, 2-(morpholin-4-yl)ethyl and 2-(morpholin-4-yl)ethoxy.

29. The antibody-drug conjugate of claim 27, wherein:

(i) the Bcl-2 inhibitor is represented by Formula (V) or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing; or

(ii) the Bcl-2 inhibitor is represented by Formula (Va):



optionally wherein:

Cc1cc(C#N)c(Rc)n1

(b) R_c represents a methyl group; and/or

(Vb):

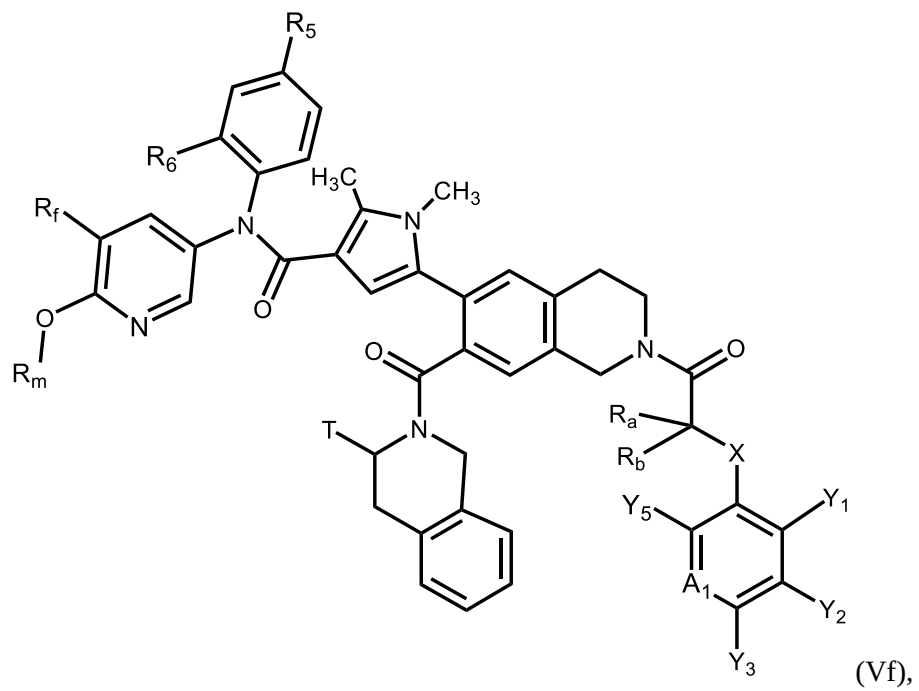
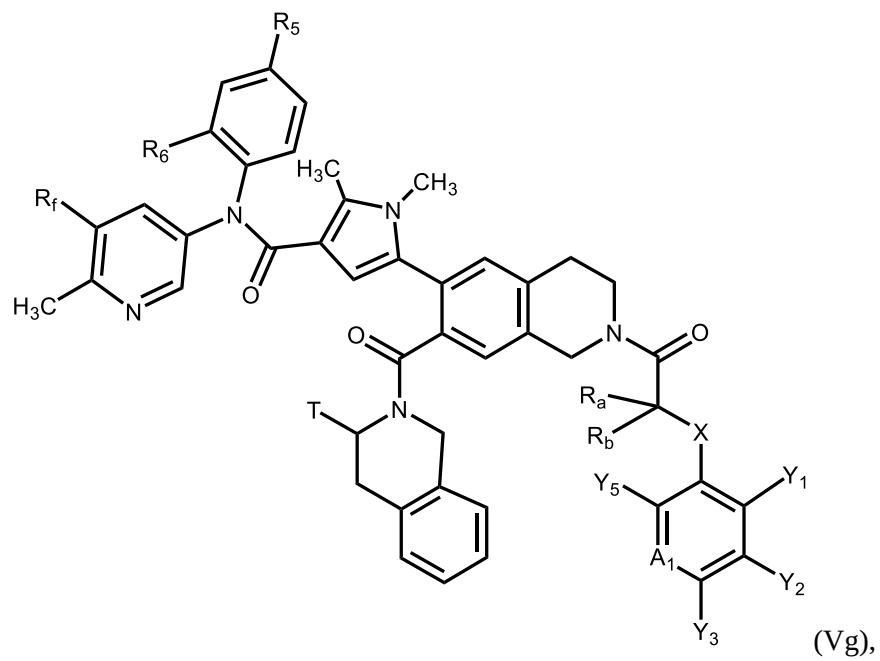


foregoing; optionally wherein R_c in Formula (Vb) represents a methyl group.

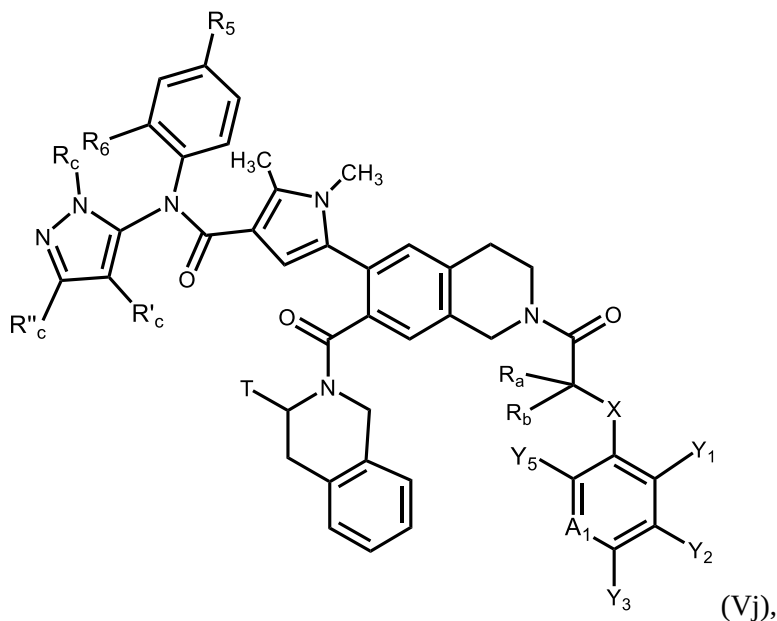
(Vc), (Vd), (Ve), (Vf), (Vg), (Vh), (Vi) or (Vj):











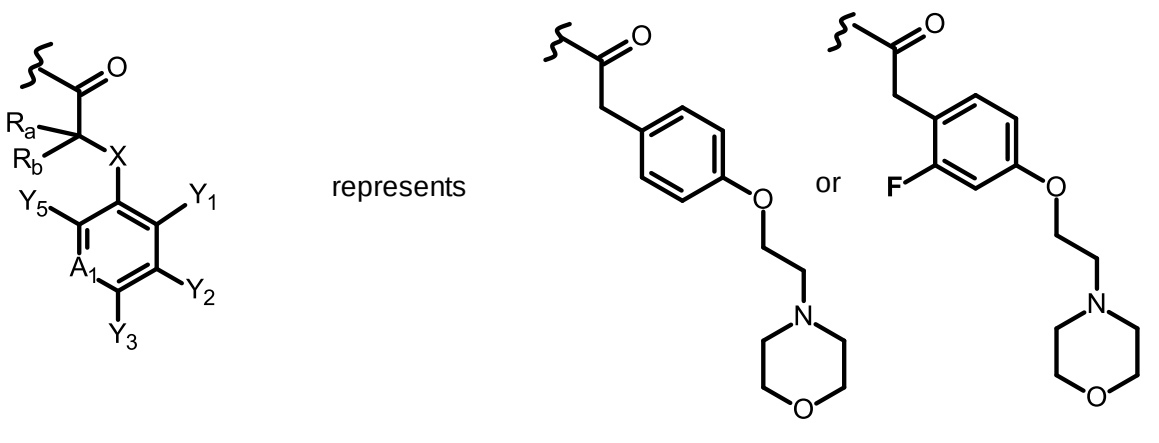
or an enantiomer, a diastereoisomer, and/or a pharmaceutically acceptable salt of any one of the foregoing.

32. The antibody-drug conjugate of any one of claims 29 to 31, wherein in Formula (V), (Va), (Vb), (Vc), (Vd), (Ve), (Vf), (Vg), (Vh), (Vi) or (Vj) :

- (i) X represents a bond;
- (ii) A₁ represents C-Y₄;
- (iii) R_a and R_b both represent a hydrogen atom;
- (iv) R₅ represents a hydrogen atom, a hydroxy group or a fluorine atom, preferably a hydroxy group;
- (v) R₆ represents a hydrogen atom, or a fluorine atom, preferably a hydrogen atom;
- (vi) A₁ represents C-H and Y₂ represents a hydrogen atom;
- (vii) Y₁ and Y₅ represent both a hydrogen atom, or: Y₁ and Y₅ represent a fluoro atom and a hydrogen atom, respectively;
- (viii) Y₃ represents a -O-(C₁-C₆)alkylene-heterocycloalkyl group or a -O-(C₁-C₄)alkylene-Cy₃ group;
- (ix) Y₃ represents a group selected from: 2-(morpholin-4-yl)ethoxy, 2-(oxan-4-yl)ethoxy, 2-(4-hydroxypiperidin-1-yl)ethoxy, 2-(4-cyclopropylpiperazin-1-yl)ethoxy, 2-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]ethoxy, 2-[(9aS)-octahydropyrazino[2,1-c][1,4]oxazin-8-yl]ethoxy, 2-{2-[4-(2-{1,1-dioxo-1λ⁶-thia-6-azaspiro[3.3]heptan-6-yl})ethoxy, 2-[2,6-dimethylmorpholin-4-yl]ethoxy, 2-[4-(2,2-difluoroethyl)piperazin-1-yl]ethoxy, 2-(3-fluoroazetidin-1-yl)ethoxy, 2-(3,3-difluoropyrrolidin-1-yl)ethoxy, 2-(4-fluoropiperidin-1-yl)ethoxy, 2-(thiomorpholin-4-yl)ethoxy, 2-(2-methylmorpholin-4-

yl)ethoxy, 2-{6-oxa-9-azaspiro[4.5]decan-9-yl}ethoxy, 2-{4-oxa-7-azaspiro[2.5]octan-7-yl}ethoxy, 2-[4-(2-fluoroethyl)piperazin-1-yl]ethoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 2-(2,2-dimethylmorpholin-4-yl)ethoxy, 2-(morpholin-4-yl)propoxy, [2-methyl-1-(morpholin-4-yl)propan-2-yl]oxy, 2-(3,3-dimethylmorpholin-4-yl)ethoxy, 2-(3-methylmorpholin-4-yl)ethoxy, 2-(1,4-dioxan-2-yl)ethoxy; preferably Y₃ represents a -O-(C₁-C₄)alkylene-Cy₃ group;

(x) the group:

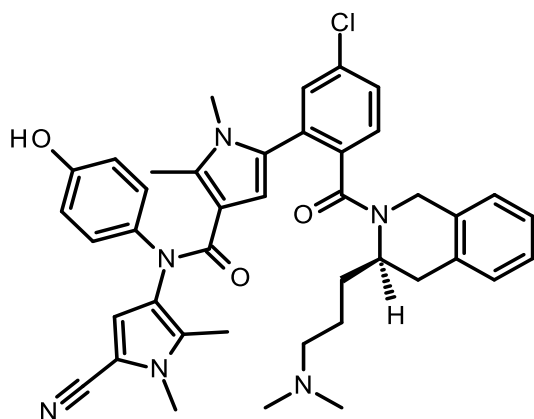


(xi) T represents a linear or branched (C₁-C₆)alkyl group or a (C₁-C₄)alkylene-NR₁R₂ group; and/or

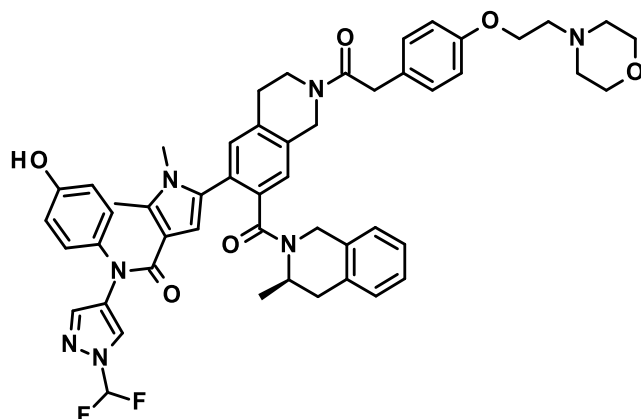
(xii) T represents a group selected from: methyl group, (piperidin-1-yl)methyl, (morpholin-4-yl)methyl, (piperidin-1-yl)ethyl, [(3R)-3-fluoropyrrolidin-1-yl]methyl, (4-fluoropiperidin-1-yl)methyl, [methyl(propan-2-yl)amino]methyl, (azepan-1-yl)methyl, (pyrrolidin-1-yl)methyl, [(3S)-3-methylpiperidin-1-yl]methyl, [(3R)-3-methylpiperidin-1-yl]methyl, [(1RS,5SR)-3-azabicyclo[3.1.0]hexan-3-yl]methyl, [(2S)-2-methylpiperidin-1-yl]methyl, {6-azaspiro[2.5]octan-6-yl}methyl, (4,4-difluoropiperidin-1-yl)methyl, (diethylamino)methyl, (4-methylpiperidin-1-yl)methyl, [ethyl(propan-2-yl)amino]methyl, {5-azaspiro[2.3]hexan-5-yl}methyl, (3,3-dimethylpyrrolidin-1-yl)methyl, (diisopropylamino)methyl, [ethyl(isopropyl) amino]methyl, [(3R)-3-methylpyrrolidin-1-yl]methyl, [(3S)-3-methylpyrrolidin-1-yl]methyl, [(2S)-2-methylpyrrolidin-1-yl]methyl, 5-azaspiro[2.4]heptan-5-ylmethyl, 2-azaspiro[3.3]heptan-2-ylmethyl, and aminomethyl.

33. The antibody-drug conjugate of any one of claims 27-32, wherein the Bcl-2 inhibitor is represented by any one of the following:

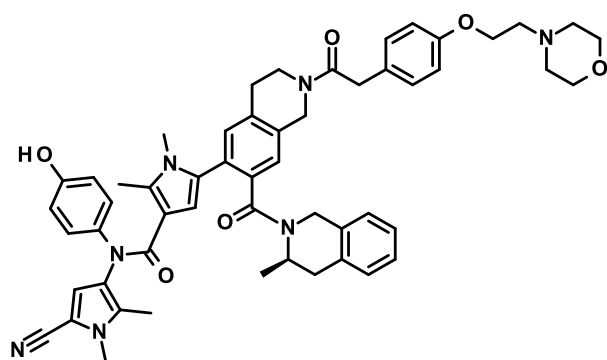
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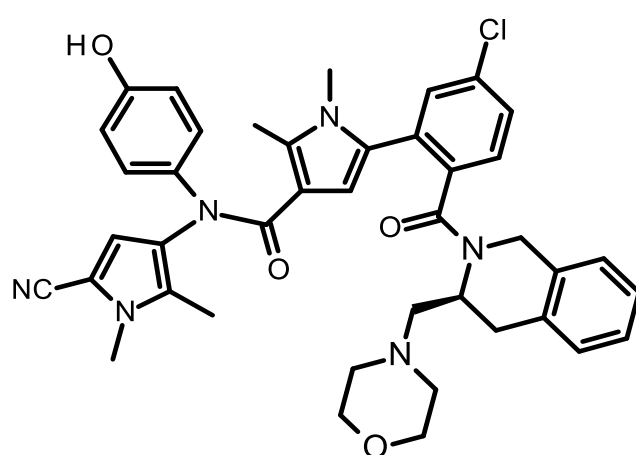
D3-1



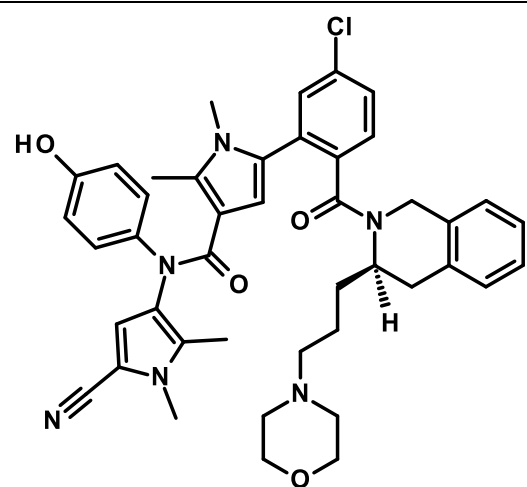
D3-2



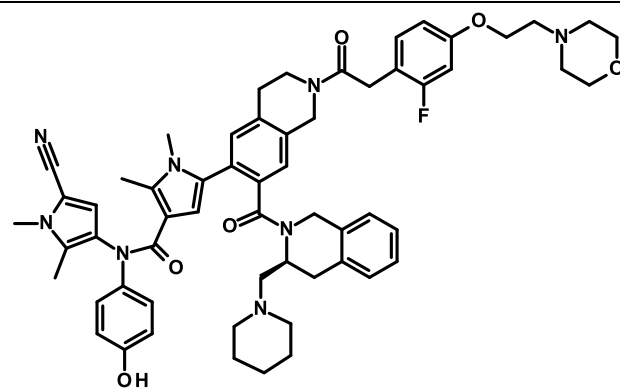
D3-3



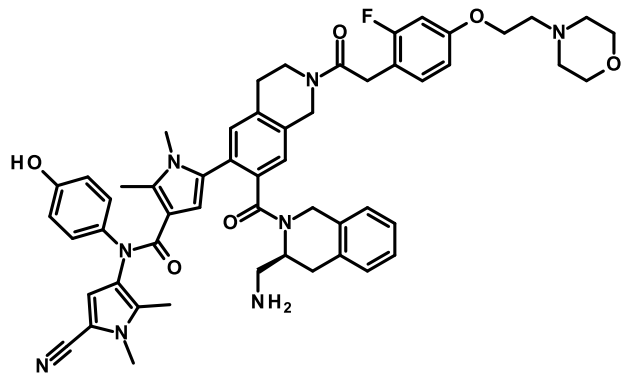
D3-4



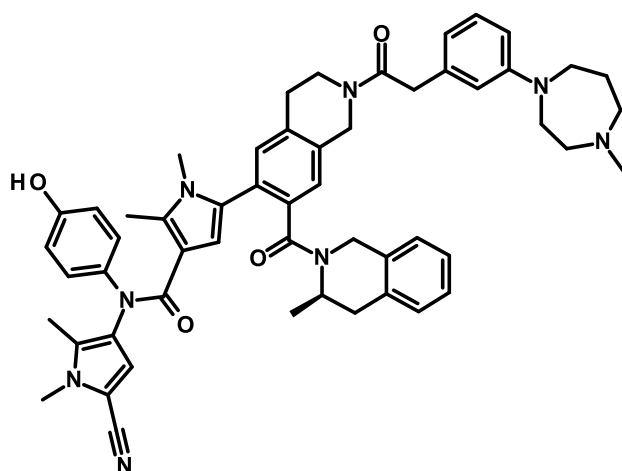
D3-5



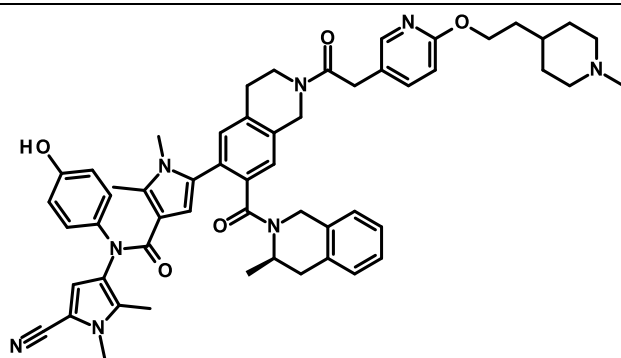
D3-6



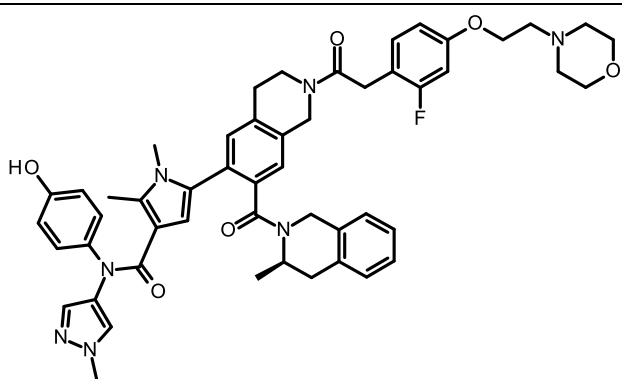
D3-7



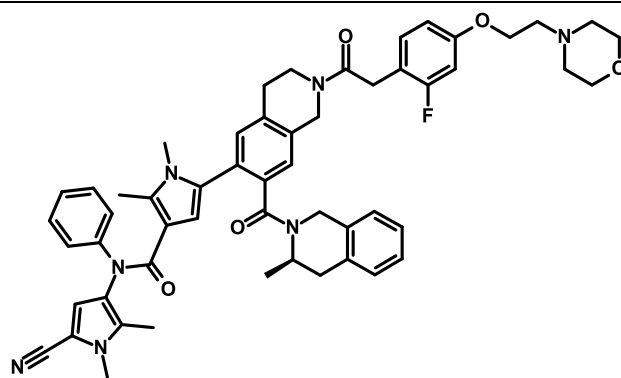
D3-8



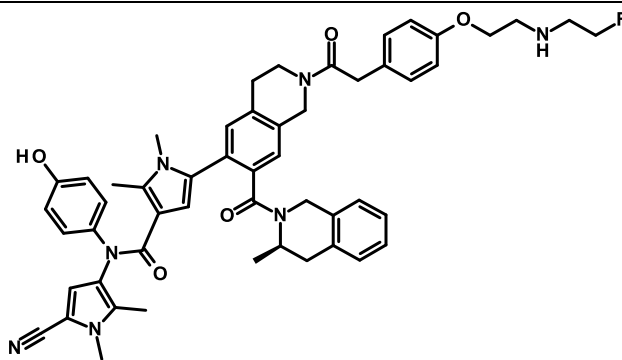
D3-9



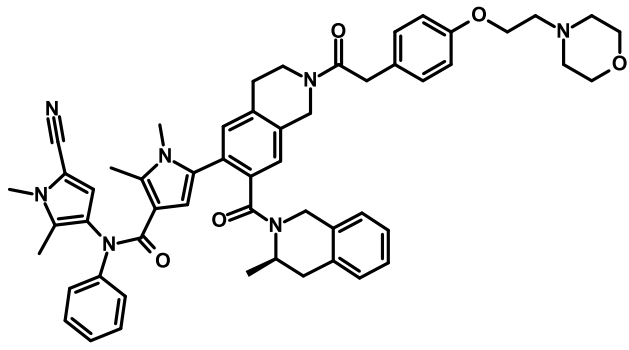
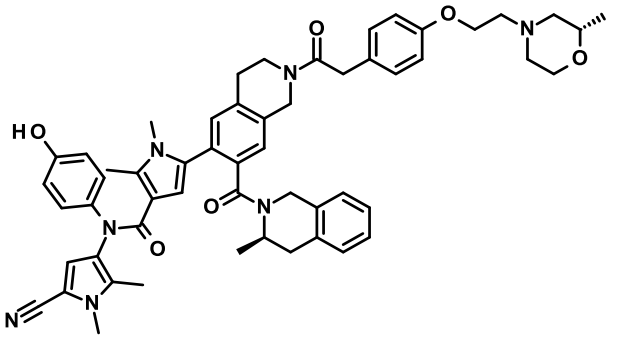
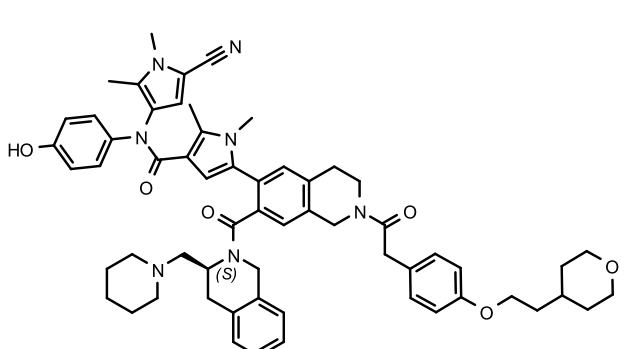
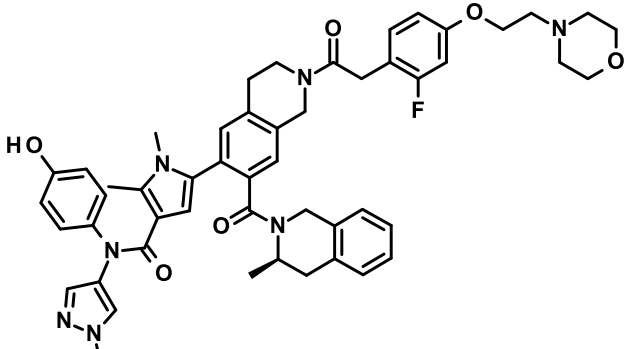
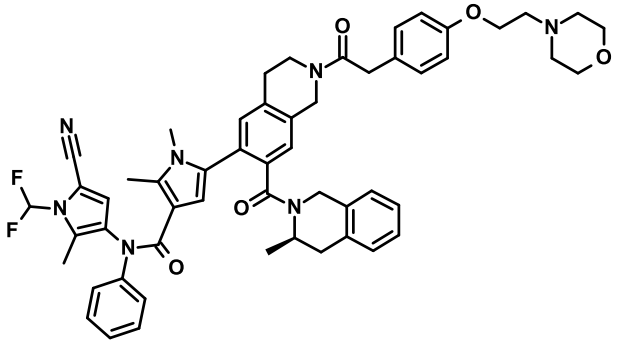
D3-10



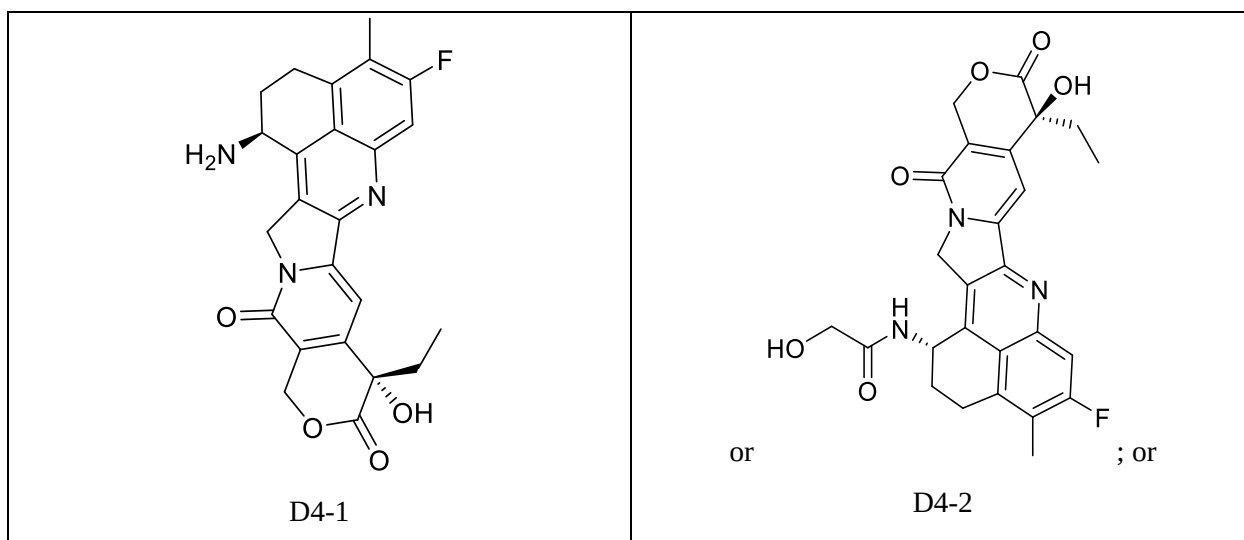
D3-11



D3-12

 <p>D3-13</p>	 <p>D3-14</p>
 <p>D3-15</p>	 <p>D3-16</p>
 <p>D3-17</p>	

34. The antibody-drug conjugate of claim 20, wherein:
 (i) the topoisomerase 1 inhibitor is:



(ii) the anti-mitotic drug is monomethyl auristatin E (MMAE) or a taxane; preferably wherein the taxane is selected from docetaxel, paclitaxel, or cabazitaxel

35. The antibody-drug conjugate of any one of claims 1 to 34, wherein:

(i) the antibody or antigen-binding fragment thereof binds to a target antigen on a cancer cell; optionally wherein:

(a) the target antigen is selected from BCMA, CD33, HER2, CD38, CD48, CD79b, PCAD, CD74, CD138, SLAMF7, CD123, CLL1, FLT3, CD7, CKIT, CD56, SEZ6, DLL3, DLK1, B7-H3, EGFR, CD71, EphA2, EPCAM, FOLR1, ENPP3, MET, AXL, SLC34A2, Nectin4, TROP2, LIV1, CD46, MSLN, F3, MUC16, SLC39A6, TFRC, TACSTD2, and GPNMB;

(b) the target antigen is selected from EGFR, CD7, HER2, EPCAM, FOLR1, ENPP3, MET, AXL, SLC34A2, Nectin4, MSLN, F3, MUC16, SLC39A6, TFRC, TACSTD2, and GPNMB; or

(c) the target antigen is selected from CD48, CD74, EphA2, PCAD, TROP2, B7-H3, or 5T4 or HER2; or

(ii) the antibody or antigen-binding fragment thereof is selected from Table D1.

36. The antibody-drug conjugate of claim 35, wherein the antibody or antigen-binding fragment thereof comprises i) three heavy chain CDR sequences and three light chain CDR sequences selected from an antibody in Tables D3 and D8, ii) a heavy chain variable region sequence and a light chain

variable region sequence selected from an antibody in Tables D2 and D8, or iii) a heavy chain sequence and light chain sequence selected from an antibody in Tables D4, D5, and D7.

37. The antibody-drug conjugate of claim 35, wherein:

(i) the antibody or antigen-binding fragment thereof is

(A) an anti-CD74 antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:256, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:257, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171; light chain CDR1 (LCDR1) consisting of SEQ ID NO:268, light chain CDR2 (LCDR2) consisting of SEQ ID NO:264, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:265;
- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:258, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:170, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171; light chain CDR1 (LCDR1) consisting of SEQ ID NO:172, light chain CDR2 (LCDR2) consisting of SEQ ID NO:173, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174;
- 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:259, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:260, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:261; light chain CDR1 (LCDR1) consisting of SEQ ID NO:269, light chain CDR2 (LCDR2) consisting of SEQ ID NO:264, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174;
- 4) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:169, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:170, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171; light chain CDR1 (LCDR1) consisting of SEQ ID NO:172, light chain CDR2 (LCDR2) consisting of SEQ ID NO:173, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174;
- 5) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:256, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:257, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171; light chain CDR1 (LCDR1) consisting of SEQ ID NO:263, light chain CDR2 (LCDR2) consisting of SEQ ID NO:264, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:265;
- 6) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:258, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:170, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171;

light chain CDR1 (LCDR1) consisting of SEQ ID NO:266, light chain CDR2 (LCDR2) consisting of SEQ ID NO:173, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174;

- 7) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:259, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:260, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:261; light chain CDR1 (LCDR1) consisting of SEQ ID NO:215, light chain CDR2 (LCDR2) consisting of SEQ ID NO:264, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174; and
- 8) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:169, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:170, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:171; light chain CDR1 (LCDR1) consisting of SEQ ID NO:266, light chain CDR2 (LCDR2) consisting of SEQ ID NO:173, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:174;

(B) an anti-CD74 antibody comprising (1) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:153, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:262, or (2) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:153, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:267; or

(C) an anti-CD74 antibody comprising:

(1) the heavy chain amino acid sequence of SEQ ID NO:118 or a sequence that is at least 95% identical to SEQ ID NO:118, and the light chain amino acid sequence of SEQ ID NO:237 or a sequence that is at least 95% identical to SEQ ID NO:237;

(2) the heavy chain amino acid sequence of SEQ ID NO:236 or a sequence that is at least 95% identical to SEQ ID NO:236, and the light chain amino acid sequence of SEQ ID NO:237 or a sequence that is at least 95% identical to SEQ ID NO:237; or

(3) the heavy chain amino acid sequence of SEQ ID NO:118 or a sequence that is at least 95% identical to SEQ ID NO:118, and the light chain amino acid sequence of SEQ ID NO:239 or a sequence that is at least 95% identical to SEQ ID NO:239;

(ii) the antibody or antigen-binding fragment thereof is:

(A) an anti-CD48 antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:271, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:272, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:273; light chain CDR1 (LCDR1) consisting of SEQ ID NO:281, light chain CDR2 (LCDR2)

- consisting of SEQ ID NO:282, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:283;
- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:274, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:275, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:273; light chain CDR1 (LCDR1) consisting of SEQ ID NO:284, light chain CDR2 (LCDR2) consisting of SEQ ID NO:285, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:286;
 - 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:276, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:277, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:278; light chain CDR1 (LCDR1) consisting of SEQ ID NO:287, light chain CDR2 (LCDR2) consisting of SEQ ID NO:282, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:286;
 - 4) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:279, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:275, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:273; light chain CDR1 (LCDR1) consisting of SEQ ID NO:284, light chain CDR2 (LCDR2) consisting of SEQ ID NO:288, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:286; and
 - 5) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:51, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:52, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:53; light chain CDR1 (LCDR1) consisting of SEQ ID NO:54, light chain CDR2 (LCDR2) consisting of SEQ ID NO:55, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:56;

(B) an anti-CD48 antibody comprising (1) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:270, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:280; or (2) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:13, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:14; or

(C) an anti-CD48 antibody comprising (1) the heavy chain amino acid sequence of SEQ ID NO:240 or a sequence that is at least 95% identical to SEQ ID NO:240, and the light chain amino acid sequence of SEQ ID NO:243 or a sequence that is at least 95% identical to SEQ ID NO:243; (2) the heavy chain amino acid sequence of SEQ ID NO:242 or a sequence that is at least 95% identical to SEQ ID NO:242, and the light chain amino acid sequence of SEQ ID NO:243 or a sequence that is at least 95% identical to SEQ ID NO:243; or (3) the heavy chain amino acid sequence of SEQ ID NO:240 or a sequence that is at least 95% identical to SEQ ID NO:240, and the light chain amino acid sequence of SEQ ID NO:69 or a sequence that is at least 95% identical to SEQ ID NO:70;

(iii) the antibody or antigen-binding fragment thereof is:

(A) an anti-Her2 antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:289, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:290, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:291; light chain CDR1 (LCDR1) consisting of SEQ ID NO:297, light chain CDR2 (LCDR2) consisting of SEQ ID NO:298, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:299;
- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:292, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:40, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:291; light chain CDR1 (LCDR1) consisting of SEQ ID NO:300, light chain CDR2 (LCDR2) consisting of SEQ ID NO:301, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:44;
- 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:293, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:294, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:295; light chain CDR1 (LCDR1) consisting of SEQ ID NO:302, light chain CDR2 (LCDR2) consisting of SEQ ID NO:298, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:44; and
- 4) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:39, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:40, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:291; light chain CDR1 (LCDR1) consisting of SEQ ID NO:300, light chain CDR2 (LCDR2) consisting of SEQ ID NO:301, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:44;

(B) an anti-Her2 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:9, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:296; or

(C) an anti-Her2 antibody comprising the heavy chain amino acid sequence of SEQ ID NO:245 or a sequence that is at least 95% identical to SEQ ID NO:245, and the light chain amino acid sequence of SEQ ID NO:66 or a sequence that is at least 95% identical to SEQ ID NO:66;

(iv) the antibody or antigen-binding fragment thereof is:

(A) an anti-PCAD antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:304, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:305, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:306; light chain CDR1 (LCDR1) consisting of SEQ ID NO:312, light chain CDR2 (LCDR2)

consisting of SEQ ID NO:313, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:314;

- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:307, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:308, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:306; light chain CDR1 (LCDR1) consisting of SEQ ID NO:315, light chain CDR2 (LCDR2) consisting of SEQ ID NO:25, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:316;
- 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:309, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:277, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:278; light chain CDR1 (LCDR1) consisting of SEQ ID NO:317, light chain CDR2 (LCDR2) consisting of SEQ ID NO:313, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:316; and
- 4) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:310, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:308, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:306; light chain CDR1 (LCDR1) consisting of SEQ ID NO:315, light chain CDR2 (LCDR2) consisting of SEQ ID NO:25, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:316;

(B) an anti-PCAD antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:303, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:311; or

(C) an anti-PCAD antibody comprising the heavy chain amino acid sequence of SEQ ID NO:248 or a sequence that is at least 95% identical to SEQ ID NO:248, and the light chain amino acid sequence of SEQ ID NO:250 or a sequence that is at least 95% identical to SEQ ID NO:250;

(v) the antibody or antigen-binding fragment thereof is

(A) an anti-EphA2 antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:319, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:320, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:321; light chain CDR1 (LCDR1) consisting of SEQ ID NO:330, light chain CDR2 (LCDR2) consisting of SEQ ID NO:331, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:332;
- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:322, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:323, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:324; light chain CDR1 (LCDR1) consisting of SEQ ID NO:333, light chain CDR2 (LCDR2) consisting of SEQ ID NO:334, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:335;

- 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:325, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:326, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:327; light chain CDR1 (LCDR1) consisting of SEQ ID NO:336, light chain CDR2 (LCDR2) consisting of SEQ ID NO:331, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:335; and
- 4) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:328, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:323, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:321; light chain CDR1 (LCDR1) consisting of SEQ ID NO:333, light chain CDR2 (LCDR2) consisting of SEQ ID NO:334, and light chain CDR3 (LCDR3) consisting of SEQ ID NO:335;

(B) an anti-EphA2 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:318, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:329; or

(C) an anti-EphA2 antibody comprising the heavy chain amino acid sequence of SEQ ID NO:252 or a sequence that is at least 95% identical to SEQ ID NO:252, and the light chain amino acid sequence of SEQ ID NO:254 or a sequence that is at least 95% identical to SEQ ID NO:254; or

(vi) the antibody or antigen-binding fragment thereof is

(A) an anti-MET antibody comprising three heavy chain CDRs and three light chain CDRs selected from the group consisting of:

- 1) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:349, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:350, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:351; light chain CDR1 (LCDR1) consisting of SEQ ID NO:352, light chain CDR2 (LCDR2) consisting of SEQ ID NO:353, and light chain CDR3 (LCDR3) consisting of SEQ ID NO: 354;
- 2) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:355, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:356, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:357; light chain CDR1 (LCDR1) consisting of SEQ ID NO:358, light chain CDR2 (LCDR2) consisting of SEQ ID NO:359, and light chain CDR3 (LCDR3) consisting of SEQ ID NO: 360; and
- 3) heavy chain CDR1 (HCDR1) consisting of SEQ ID NO:361, heavy chain CDR2 (HCDR2) consisting of SEQ ID NO:362, heavy chain CDR3 (HCDR3) consisting of SEQ ID NO:363; light chain CDR1 (LCDR1) consisting of SEQ ID NO:364, light chain CDR2 (LCDR2) consisting of SEQ ID NO:365, and light chain CDR3 (LCDR3) consisting of SEQ ID NO: 366;

(B) an anti- MET antibody comprising a heavy chain variable region and a light chain variable region selected from the group consisting of:

- 1) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:339, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:340;
- 2) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:341, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:342; and
- 3) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:343, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:344; or

(C) an anti-MET antibody comprising a heavy chain and a light chain selected from the group consisting of:

- 1) the heavy chain amino acid sequence of SEQ ID NO:367 or a sequence that is at least 95% identical to SEQ ID NO:367, and the light chain amino acid sequence of SEQ ID NO:368 or a sequence that is at least 95% identical to SEQ ID NO:368;
- 2) the heavy chain amino acid sequence of SEQ ID NO:369 or a sequence that is at least 95% identical to SEQ ID NO:369, and the light chain amino acid sequence of SEQ ID NO:370 or a sequence that is at least 95% identical to SEQ ID NO:370;
- 3) the heavy chain amino acid sequence of SEQ ID NO:371 or a sequence that is at least 95% identical to SEQ ID NO:371, and the light chain amino acid sequence of SEQ ID NO:372 or a sequence that is at least 95% identical to SEQ ID NO:372;
- 4) the heavy chain amino acid sequence of SEQ ID NO:373 or a sequence that is at least 95% identical to SEQ ID NO:373, and the light chain amino acid sequence of SEQ ID NO:374 or a sequence that is at least 95% identical to SEQ ID NO:374;
- 5) the heavy chain amino acid sequence of SEQ ID NO:375 or a sequence that is at least 95% identical to SEQ ID NO:375, and the light chain amino acid sequence of SEQ ID NO:370 or a sequence that is at least 95% identical to SEQ ID NO:370; and
- 6) the heavy chain amino acid sequence of SEQ ID NO:376 or a sequence that is at least 95% identical to SEQ ID NO:376, and the light chain amino acid sequence of SEQ ID NO:372 or a sequence that is at least 95% identical to SEQ ID NO:372.

38. The antibody-drug conjugate of claim 37 wherein the two antineoplastic payloads are Bcl-xL inhibitors.

39. The antibody-drug conjugate of claim 37, wherein:

(i) the antibody or antigen binding fragment thereof comprises one or more cysteine substitutions selected from E152C, S375C, or both E152C and S375C of the heavy chain of the antibody or antigen binding fragment thereof, wherein the position is numbered according to the EU system; or

(ii) the antibody or antigen binding fragment thereof comprises one or more Fc silencing mutations.

40. A composition comprising multiple copies of the antibody-drug conjugate of any one of claims 1 to 39, wherein the average *a* of the antibody-drug conjugates in the composition is from about 1 to about 8, *e.g.*, about 1 to about 6, about 1 to about 4, or about 1 to about 2.

41. A pharmaceutical composition comprising the antibody-drug conjugate of any one of claims 1 to 39 or the composition of claim 40, and a pharmaceutically acceptable carrier.

42. The antibody-drug conjugate of any one of claims 1 to 39, the composition of claim 40, or the pharmaceutical composition of claim 41, for use in:

(i) treating a subject having or suspected of having a cancer,

(ii) reducing or inhibiting the growth of a tumor in a subject;

(iii) reducing or inhibiting a hematological cancer in a subject; or

(iv) reducing or slowing the expansion of a cancer cell population in a subject,
optionally wherein

(a) the cancer is a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(b) the tumor is a breast cancer, gastric cancer, bladder cancer, brain cancer, cervical cancer, colorectal cancer, esophageal cancer, hepatocellular cancer, melanoma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(c) the hematological cancer is chronic lymphocytic leukemia (CLL), follicular lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML),

chronic myelomonocytic leukemia (CMML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphoma or myelodysplasia syndrome (MDS); or

(d) the cancer cell population is from a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer.

43. Use of the antibody-drug conjugate of any one of claims 1 to 39, the composition of claim 40, or the pharmaceutical composition of claim 41, in the manufacture of a medicament for:

- (i) treating a subject having or suspected of having a cancer,
 - (ii) reducing or inhibiting the growth of a tumor in a subject;
 - (iii) reducing or inhibiting a hematological cancer in a subject; or
 - (iv) reducing or slowing the expansion of a cancer cell population in a subject,
- optionally wherein

(a) the cancer is a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(b) the tumor is a breast cancer, gastric cancer, bladder cancer, brain cancer, cervical cancer, colorectal cancer, esophageal cancer, hepatocellular cancer, melanoma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer;

(c) the hematological cancer is chronic lymphocytic leukemia (CLL), follicular lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphoma or myelodysplasia syndrome (MDS); or

(d) the cancer cell population is from a breast cancer, multiple myeloma, plasma cell myeloma, leukemia, lymphoma, sarcoma, gastric cancer, acute myeloid leukemia, bladder cancer, brain cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia including acute lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer, spleen cancer, pancreatic cancer, stomach cancer, colon cancer, or head and neck cancer.