We claim:

1. An antibody conjugate represented by General Formula I or a pharmaceutically acceptable salt thereof:

[General Formula I] Ab – (X)y

wherein:

Ab is an antibody or antigen-binding fragment thereof that specifically binds to DLK1, wherein Ab comprises a variable heavy chain complementarity determining region 1 (CDRH1), a variable heavy chain complementarity determining region 2 (CDRH2), a variable heavy chain complementarity determining region 3 (CDRH3), a variable light chain complementarity determining region 1 (CDRL1), a variable light chain complementarity determining region 2 (CDRL2), and a variable light chain complementarity determining region 3 (CDRL3); wherein:

(a) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 16;
(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 18;
(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 20;
(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 23;
(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 25; and
(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 27;

(b) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 58;
(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 60;
(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 62;
(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 65;
(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 67; and
(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 69;

(c) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 72;
(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 74;
(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 76;
(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 79;
(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 81; and

(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 83;

(d) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 86;

(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 88;

(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 90;

(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 93;

(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 95; and

(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 97;

(e) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 16;

(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 18;

(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 20;

(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 115;

(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 95; and

(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 116; or

(f) (i) CDRH1 comprises the amino acid sequence of SEQ ID NO: 16;

(ii) CDRH2 comprises the amino acid sequence of SEQ ID NO: 18;

(iii) CDRH3 comprises the amino acid sequence of SEQ ID NO: 20;

(iv) CDRL1 comprises the amino acid sequence of SEQ ID NO: 121;

(v) CDRL2 comprises the amino acid sequence of SEQ ID NO: 39; and

(vi) CDRL3 comprises the amino acid sequence of SEQ ID NO: 124;

each X is independently a chemical moiety comprising at least one active agent and a linker, wherein the linker links the antibody to the at least one active agent, and

y is 1 to 20.

2. The antibody conjugate of claim 1, wherein the antibody or the antigen-binding fragment thereof comprises:

at least one heavy chain framework region (FR) 1 comprising a sequence selected from: 15, 57, 71, 85 and 119;

at least one heavy chain FR2 comprising a sequence selected from: SEQ ID NO: 17, 59, 73 and 87;

at least one heavy chain FR3 comprising a sequence selected from: SEQ ID NO: 19, 61, 75 and 89;

at least one heavy chain FR4 comprising a sequence selected from: SEQ ID NO: 21, 63, 77 and 91;

at least one light chain FR1 comprising a sequence selected from: SEQ ID NO: 22, 64, 78, 92, 117 and 120;

at least one light chain FR2 comprising a sequence selected from: SEQ ID NO: 24, 66, 80, 94 and 122;

at least one light chain FR3 comprising a sequence selected from: SEQ ID NO: 26, 68, 82, 96, 118 and 123; and

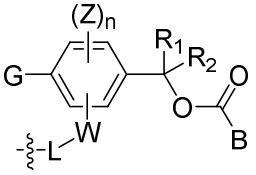
at least one light chain FR4 comprising a sequence selected from: SEQ ID NO: 28, 70, 84, 98 and 125.

3. The antibody conjugate of claim 1, wherein the antibody or an antigen-binding fragment thereof comprises a sequence comprising at least 90% sequence identity to a sequence selected from: SEQ ID NO: 101, 107, 109, 111 and 127.

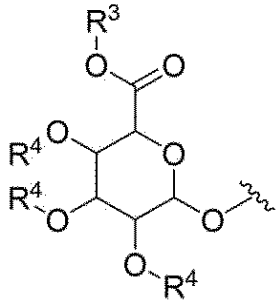
4. The antibody conjugate of claim 1, wherein the antibody or an antigen-binding fragment thereof comprises a light chain variable region comprising a sequence comprising at least 90% sequence identity to a sequence selected from SEQ ID No. 102, 108, 110, 112, 126 and 128.

5. The antibody conjugate of claim 1, wherein at least one X has a structure represented by General Formula II or a pharmaceutically acceptable salt thereof:

[General Formula II]




wherein:

G is a glucuronic acid moiety or  ;

$R^3$ is hydrogen or a carboxyl protecting group;

each $R^4$ is independently hydrogen or a hydroxyl protecting group;

B is the active agent;

$R_1$ and $R_2$ are each independently hydrogen, ($C_1$-$C_8$) alkyl or ($C_3$-$C_8$) cycloalkyl;

W is -C(O)-, -C(O)NR'-, -C(O)O-, -$SO_2$NR'-, -P(O)R"NR'-, -SONR'- or -$PO_2$NR'-,wherein the C, S or P is directly bound to the phenyl ring;

R' and R'' are each independently, hydrogen, ($C_1$-$C_8$) alkyl, ($C_3$-$C_8$) cycloalkyl, ($C_1$-$C_8$) alkoxy, ($C_1$-$C_8$) alkylthio, mono- or di-($C_1$-$C_8$) alkylamino, (C3-$C_{20}$) heteroaryl, or ($C_6$-$C_{20}$) aryl;

each Z is independently ($C_1$-$C_8$) alkyl, halogen, cyano or nitro;

n is 0 to 3;

L comprises:

A) a $C_1$-$C_{50}$ alkylene or a 1 to 50 atom heteroalkylene and:

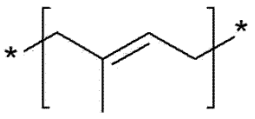
(i) comprises at least one unsaturated bond;

(ii) a heteroarylene; or

(iii) an alkylene substituted with one or more $C_{1-20}$ alkyl; or

B) at least one isoprenyl group of General Formula III, which can be recognized by isoprenoid transferase:

[General Formula III]

 ; and

the bond overlaid with the wavy line represents a connection to Ab.

6. The antibody conjugate of claim 5, wherein L is a nitrogen-containing 1 to 50 atom heteroalkylene and further comprises at least 2 atoms of a hydrophilic amino acid; and the

nitrogen forms a peptide bond with a carbonyl of a hydrophilic amino acid selected from arginine, aspartate, asparagine, glutamate, glutamine, histidine, lysine, ornithine, proline, serine and threonine.

7. The antibody conjugate of claim 6, wherein W is -C(O)NR'-, and the nitrogen of W is a nitrogen atom of the hydrophilic amino acid.

8. The antibody conjugate of claim 6 or 7, wherein L further comprises an oxime and the hydrophilic amino acid bonds the oxime to a polyethylene glycol unit of L.

9. The antibody conjugate of claim 6 or 7, wherein the hydrophilic amino acid is an amino acid selected from aspartate, glutamate, ornithine, lysine, and arginine.

10. The antibody conjugate of claim 5, wherein L comprises 2 to 20 amino acids selected from alanine, aspartate, asparagine, glutamate, glutamine, glycine, lysine, ornithine, proline, serine and threonine, and comprising at least one hydrophilic amino acid selected from aspartate, glutamate, ornithine, lysine and arginine comprising a side chain having a moiety that exhibits charge at neutral pH in an aqueous solution.

11. The antibody conjugate of claim 10, wherein W is -C(O)NR'- and the nitrogen of W is the nitrogen atom of the hydrophilic amino acid.

12. The antibody conjugate of claim 10, wherein L comprises an oxime and the hydrophilic amino acid bonds the oxime to a polyethylene glycol unit of L.

13. The antibody conjugate of claim 5, wherein the L is covalently bonded to Ab by a thioether bond, and the thioether bond comprises a sulfur atom of the cysteine of Ab.

14. The antibody conjugate of claim 13, wherein Ab comprises an amino acid motif which can be recognized by isoprenoid transferase at the C-terminal of Ab, and the thioether bond comprises a sulfur atom of the cysteine of Ab.

15. The antibody conjugate of claim 14, wherein the amino acid motif is a CYYX sequence; wherein

C is cysteine;

Y is an aliphatic amino acid selected from: alanine, isoleucine, leucine, methionine and valine;

X is any one selected from: glutamine, glutamate, serine, cysteine, methionine, alanine and leucine; and

the thioether bond comprises a sulfur atom of cysteine of the amino acid sequence.

16. The antibody conjugate of claim 15, wherein the amino acid motif is a CVIM or CVLL sequence.

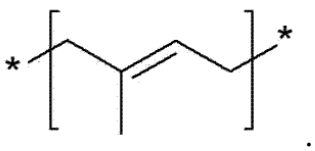
17. The antibody conjugate of any one of claims 14-16, wherein at least one of the 1 to 10 amino acids preceding the amino acid motif is selected from: glycine, proline, aspartic acid, arginine and serine.

18. The antibody conjugate of claim 17, wherein the 1 to 10 amino acids preceding the amino acid motif are each glycine.

19. The antibody conjugate of claim 5, wherein Ab comprises the amino sequence GGGGGGGCVIM at the C-terminus.

20. The antibody conjugate of claim 5, wherein L comprises at least one isoprenyl derivative unit of General Formula III, which can be recognized by isoprenoid transferase:

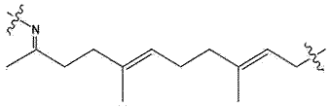
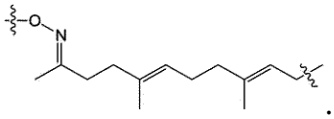
[General Formula III]



21. The antibody conjugate of claim 5, wherein L is a 3 to 50 heteroalkylene comprising an oxime, the oxygen atom of the oxime is on the side of L linked to W and the carbon atom of the

oxime is on the side of L linked to Ab, or the carbon atom of the oxime is on the side of L linked to W and the oxygen atom of the oxime is on the side of L linked to Ab.

22. The antibody conjugate of claim 21, wherein at least one isoprenyl unit covalently links the oxime to Ab.

23. The antibody conjugate of claim 5, wherein L comprises  or .

24. The antibody conjugate of claim 5, wherein L further comprises a connecting unit represented by General Formula VIII or General Formula IX:

[General Formula VIII]

$-(CH_2)_r(V(CH_2)_p)_q-$

[General Formula IX]

$-(CH_2CH_2X)_w-$

wherein: V is a single bond, -O-, -S-, $-NR^{21}-$, $-C(O)NR^{22}-$, $NR^{23}C(O)-$, $NR^{24}SO_2-$, or $-SO_2NR^{25}-$;

X is -O-, $C_1$-$C_8$ alkylene or $-NR^{21}-$;

$R^{21}$ to $R^{25}$ are each independently hydrogen, ($C_1$-$C_6$) alkyl, ($C_1$-$C_6$) alkyl ($C_6$-$C_{20}$) aryl, or ($C_1$-$C_6$) alkyl ($C_3$-$C_{20}$) heteroaryl;

r is 0 to 10;

p is 0 to 10;

q is 1 to 20; and

w is 1 to 20.

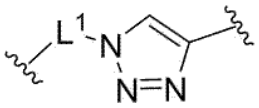
25. The antibody conjugate of claim 5, wherein L comprises 1 to 20 polyethylene glycol units.

26. The antibody conjugate of claim 25, wherein L comprises 1 to 12 $-OCH_2CH_2-$ units.

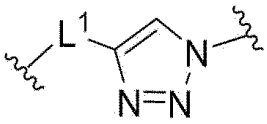
27. The antibody conjugate of claim 25, wherein L comprises an oxime and 1 to 20 polyethylene glycol units.

28. The antibody conjugate of claim 5, wherein L further comprises binding units represented by General Formulae IV, V, VI or VII:

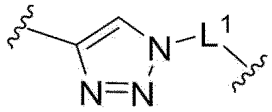
[General Formula IV]



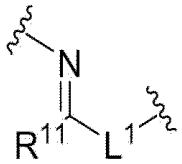
[General Formula V]



[General Formula VI]



[General Formula VII]



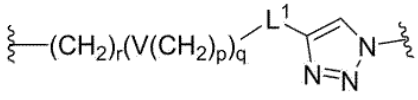
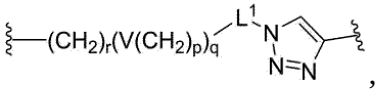
wherein:

$L^1$ is a single bond or a $C_1$-$C_{30}$ alkylene; and

$R^{11}$ is hydrogen or a $C_1$-$C_{10}$ alkyl.

29. The antibody conjugate of claim 28, wherein $L^1$ is a single bond or a $C_{11}$ or $C_{12}$ alkylene.

30. The antibody conjugate of claim 5, wherein L further comprises

 or , wherein

V is a single bond, -O-, -S-, -$NR^{21}$-, -C(O)$NR^{22}$-, $NR^{23}$C(O)-, $NR^{24}SO_2$-, or -$SO_2NR^{25}$-;

$R^{21}$ to $R^{25}$ are each independently, hydrogen, ($C_{1-6}$) alkyl, ($C_{1-6}$) alkyl ($C_{6-20}$) aryl, or ($C_{1-6}$) alkyl ($C_{3-20}$) heteroaryl;

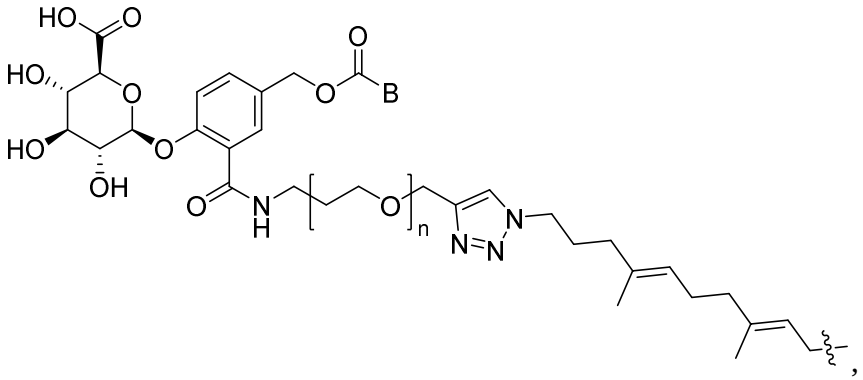
r is 0 to 10;

p is 0 to 10;

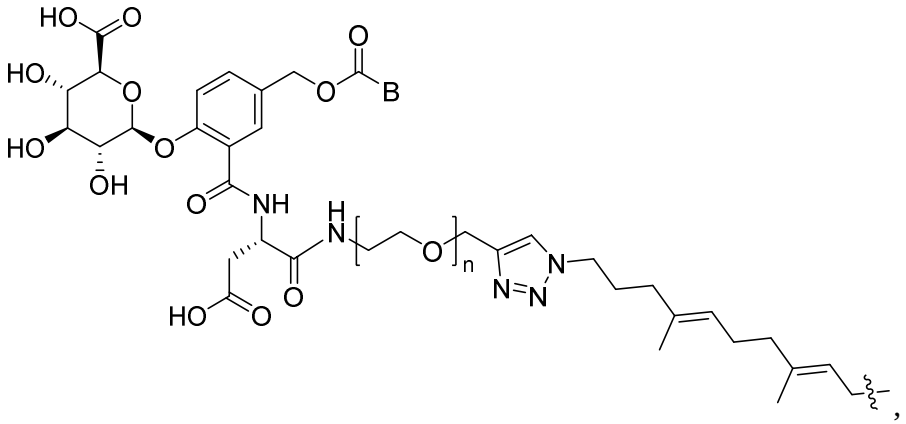
q is 1 to 20; and

$L^1$ is a single bond.

31. The antibody conjugate of claim 1, wherein at least one X has a structure represented by:



,



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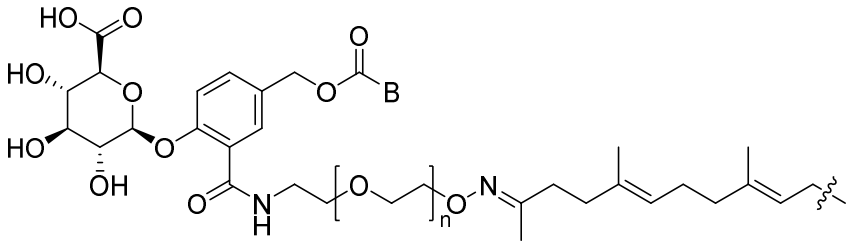
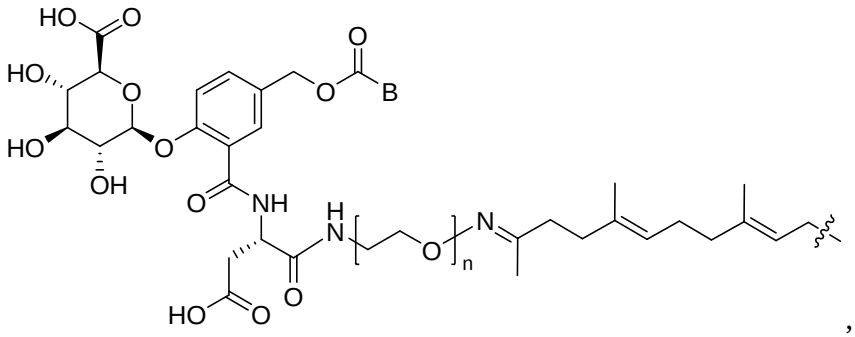


and;



,

B is the active agent;

n is 0 to 20; and

the bond overlaid with the wavy line represents a connection to Ab.

32. The antibody conjugate of claim 5, wherein the isoprenoid transferase is a farnesyl protein transferase (FTase) or a geranylgeranyl transferase (GGTase).

33. The antibody conjugate of claim 5, wherein L is branched and comprises:

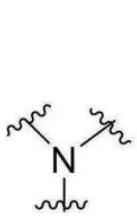
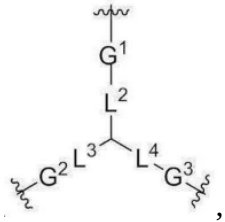
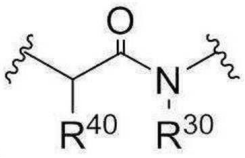
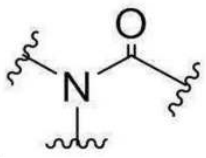
i) a branching unit covalently coupled to the antibody by a primary linker;

ii) a first branch, in which a first active agent is covalently coupled to the branching unit by a secondary linker and a cleavage group; and

iii) a second branch, in which:

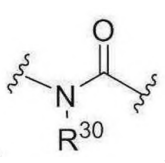
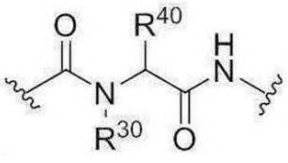
a) a second active agent is covalently coupled to the branching unit by a secondary linker and a cleavage group; or

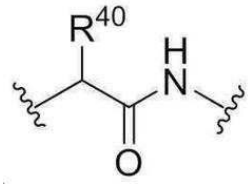
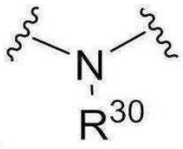
b) a polyethylene glycol moiety is covalently coupled to the branching unit.

34. The antibody conjugate of claim 33, wherein the branching unit has a structure represented by , ,  or ;


$L^2$, $L^3$ and $L^4$ are each independently a bond or $-C_nH_{2n}-$;

n is 1 to 30;

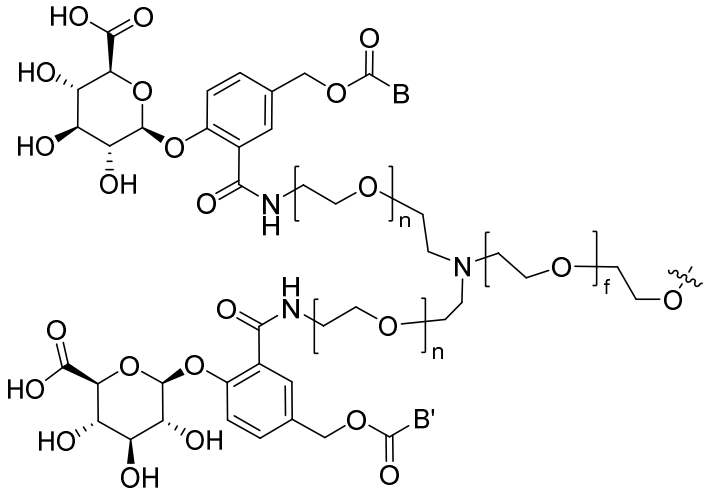
$G^{1,}$ $G^2$ and $G^3$ are each independently a bond , ,

 or ;

$R^{30}$ is hydrogen or $C_{1-30}$ alkyl; and

$R^{40}$ is $L^5$-$COOR^{50}$, wherein $L^5$ is a direct bond or $C_{1-10}$ alkylene, and $R^{50}$ is hydrogen or $C_{1-30}$ alkyl.

35. The antibody conjugate of claim 1, wherein at least one X is represented by:



B and B' are each active agents;

each n is independently 0 to 30;

f is 0 to 30; and

the bond overlaid with the wavy line represents a connection to Ab.

36. The antibody conjugate of claim 5, wherein the active agent is a chemotherapeutic agent or a toxin.

37. The antibody conjugate of claim 5, wherein the active agent is an immunoregulatory compound, anti-cancer agent, antiviral agent, antibacterial agent, antifungal agent, or antiparasitic agent.

38. The antibody conjugate of claim 5, wherein the active agent is selected from:

(a) erlotinib, bortezomib, fulvestrant, sunitinib, letrozole, imatinib mesylate, PTK787/ZK 222584, oxaliplatin, 5-fluorouracil, leucovorin, rapamycin, lapatinib, lonafarnib, sorafenib, gefitinib, AG1478, AG1571, thiotepa, cyclophosphamide, busulfan, improsulfan, piposulfan, benzodopa, carboquone, meturedopa, uredopa, ethylenimine, altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide, trimethylolmelamine, bullatacin, bullatacinone, camptothecin, topotecan, bryostatin, callystatin, CC-1065, adozelesin, carzelesin, bizelesin, cryptophycin 1, cryptophycin 8, dolastatin, duocarmycin, KW-2189, CB1-TM1, eleutherobin, pancratistatin, sarcodictyin, spongistatin, chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard, carmustine, chlorozotoxin, fotemustine, lomustine, nimustine, ranimustine, calicheamicin, calicheamicin gamma 1, calicheamicin omega 1, dynemicin, dynemicin A, clodronate, esperamicin, neocarzinostatin chromophore, aclacinomysins, actinomycin, antimycin, azaserine, bleomycins, catcinomycin, carabicin, carninomycin, carzinophilin, chromomycins, dactinomycin, daunorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubucin, liposomal doxorubicin, deoxydoxorubicin, epirubicin, esorubicin, marcellomycin, mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptomigrin, streptozocin, tudercidin, ubenimex, zinostatin, zorubicin, denopterin, methotrexate, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thioguanine, ancitabine, azacytidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, calusterone, dromostanolone, propionate, epitiostanol, mepitiostane, testolactone, aminoglutethimide,mitotane, trilostane, folinic acid, aceglatone, aldophosphamide glycoside, aminolevulinic acid, eniluracil, amsacrine, bestrabucil, bisantrene, edatrexate,

demecolcine, diaziquone, elfornithine, elliptinium acetate, etoglucid, gallium nitrate, hydroxyurea, lentinan, lonidainine, maytansine, ansamitocins, mitoguazone, mitoxantrone, mopidanmol, pentostatin, phenamet, pirarubicin, losoxantrone, 2-ethylhydrazide, procarbazine, polysaccharide-k, razoxane, rhizoxin, sizofiran, spirogermanium, tenuazonic acid, 2,2', 2''-trichlorotriethylamine, T-2 toxin, verracurin A, roridin A, anguidine, urethane, vindesine, dacarbazine, mannomustine, mitobronitol, mitolactol, pipobroman, gacytosine, arabinoside, cyclophosphamide, paclitaxel, albumin-engineered nanoparticle formulation of paclitaxel, docetaxel, chlorambucil, gemcitabine, 6-thioguanine, mercaptopurine, cisplatin, carboplatin, vinblastine, platinum, etoposide, vincristine, vinorelbine, novantrone, teniposide, edatrexate, daunomycin, aminopterin, ibandronate, CPT-11, topoisomerase inhibitor RFS 2000, difluoromethylornithine, retinoic acid, capecitabine, or pharmaceutically acceptable salts, solvates or acids thereof;

(b) monokine, lympokine, traditional polypeptide hormone, parathyroid hormone, thyroxine, relaxin, prorelaxin, glycoprotein hormone, follicle stimulating hormone, thyroid stimulating hormone, luteinizing hormone, hepatic growth factor, fibroblast growth factor, prolactin, placental lactogen, tumor necrosis factor, tumor necrosis factor-α, tumor necrosis factor-β, Mullerian inhibiting substance, mouse gonadotropin associated peptide, inhibin, activin, vascular endothelial growth factor, thrombopoietin, erythropoietin, osteoinductive factor, interferon, interferon-α, interferon-β, interferon-γ, colony stimulating factor (CSF), macrophage-CSF, granulocyte-macrophage-CSF), granulocyte-macrophage-CSF, granulocyte-CSF, interleukin (IL), IL-1, IL-1α, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, I L-12, TNF-α, TNF-β, polypeptide factor, LIF, kit, or ligand;

(c) diphtheria toxin, botulinum toxin, tetanus toxin, dysentery toxin, cholera toxin, amanitin, α-amatinin, pyrrolobenzodiazepine, pyrrolobenzodiazepine derivative, indolinobenzodiazepine, pyridobenzodiazepine, tetrodotoxin, brevetoxin, ciguatoxin, ricin, AM toxin, auristatin, tubulysin, geldanamycin, maytansinoid, calicheamicin, daunomycin, doxorubicin, methotrexate, vindesine, SG2285, dolastatin, dolastatin analog, auristatin, cryptophycin, camptothecin, rhizoxin, rhizoxin derivatives, CC-1065, CC-1065 analogs or derivatives, duocarmycin, enediyne antibiotic, esperamicin, epothilone, or toxoid;

(d) affinity ligand, where the affinity ligand is a substrate, inhibitor, active agent, neurotransmitter, or radioactive isotope;

(e) radioactive label, 32P, 35S, fluorescent dye, electron dense reagent, enzyme, biotin, streptavidin, digoxigenin, hapten, immunogenic protein, or nucleic acid molecule with a sequence complementary to a target;

(f) tamoxifen, raloxifene, droloxifene, 4-hydroxytamoxifen, trioxifene, LY117018, onapristone or toremifene;

(g) 4(5)-imidazole, aminoglutethimide, megestrol acetate, exemestane, letrozole or anastrozole

(h) flutamide, nilutamide, bicalutamide, leuprolide, goserelin, or troxacitabine;

(i) aromatase inhibitor;

(j) protein kinase inhibitor;

(k) lipid kinase inhibitor;

(l) antisense oligonucleotide;

(m) ribozyme;

(n) vaccine; and

(o) anti-angiogenic agent.

39. The antibody conjugate of claim 1, wherein the active agent is a pyrrolobenzodiazepine dimer, wherein the linker links Ab to the N10 or N'10 position of the pyrrolobenzodiazepine dimer.

40. The antibody conjugate of claim 39, wherein

the pyrrolobenzodiazepine dimer is substituted by X at the N10 position or by X' at the N'10 position, where X or X' binds the pyrrolobenzodiazepine dimer to the linker;

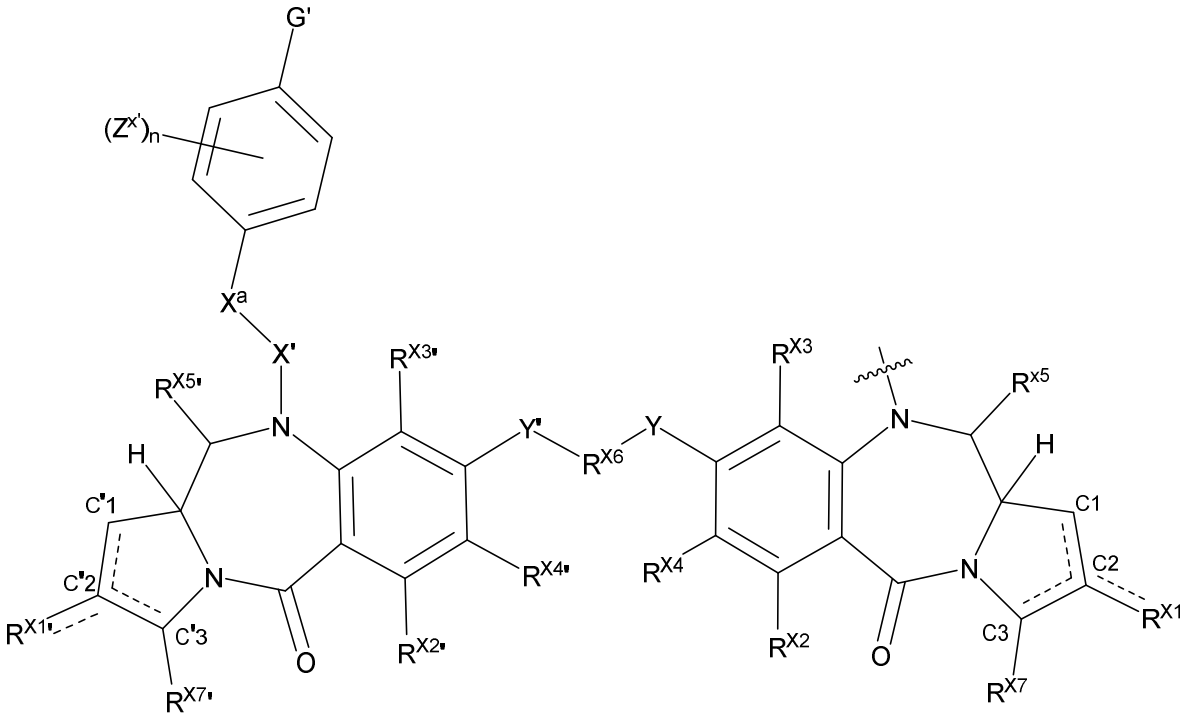
X and X' are, respectively and independently, -C(O)O*, -S(O)O-*, -C(O)-*, -C(O)$NR^X$-*, -$S(O)_2NR^X$-*, -P(O)$R^x$'$NR^X$-*, -S(O)$NR^X$-*, or -$PO_2NR^X$-*;

$R^X$ is $C_{1-8}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-20}$ heteroaryl or $C_{5-20}$ aryl;

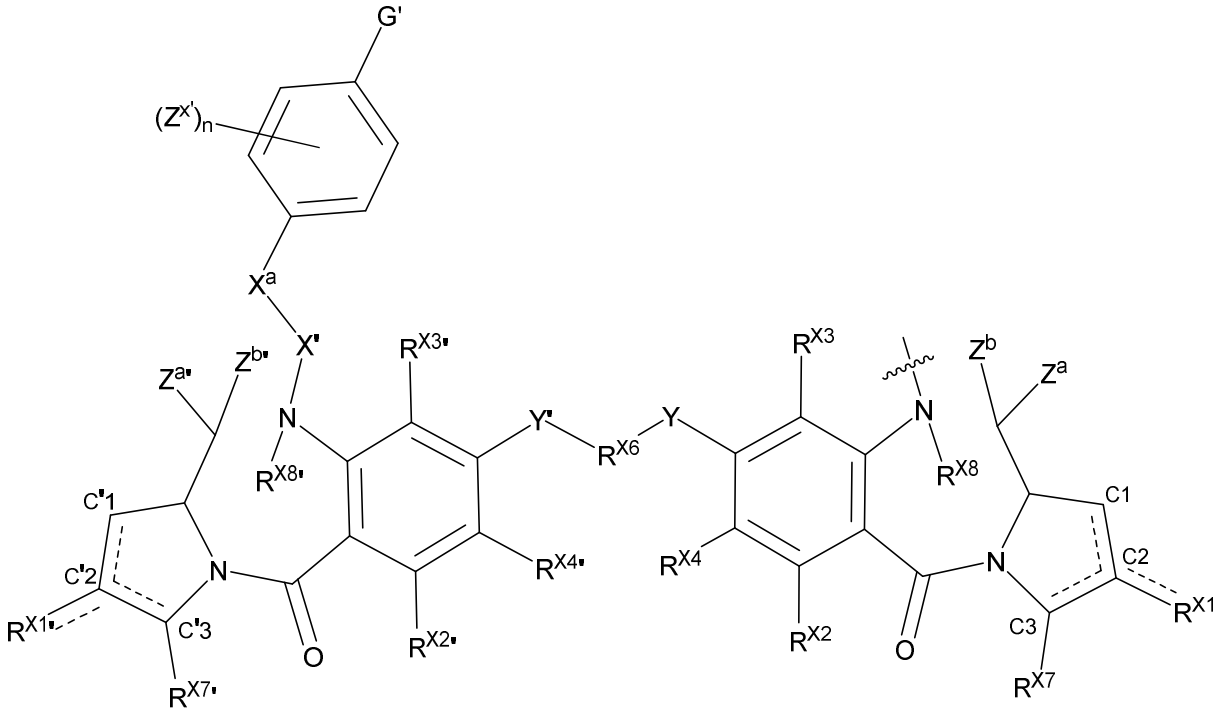
$R^X$' is OH, $N_3$, CN, SH, $C_{1-8}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{1-8}$ alkoxy, $C_{1-8}$ alkylthio, $C_{3-20}$ heteroaryl, $C_{5-20}$ aryl or amino; and

* is a binding site between the pyrrolobenzodiazepine dimer and the linker.

41. The antibody conjugate of claim 5, wherein B has a structure represented by

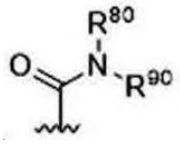


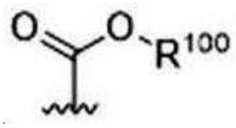
[General Formula X]



[General Formula XI]

$X^a$ is independently selected from a bond or $C_{1-6}$ alkylene;

$Z^{X'}$ is independently selected from $C_{1-8}$ alkyl, halogen, cyano, nitro, ,

, and–$(CH_2)_m$-$OCH_3$;

n is an integer of 1 to 3;

$R^{80}$ and $R^{90}$ are each independently selected from hydrogen, $C_{1-8}$ alkyl, $C_{2-6}$ alkenyl, $C_{1-6}$ alkoxy, and methoxyethyl;

$R^{100}$ is selected from H, $C_{1-8}$ alkyl, $C_{2-6}$ alkenyl, and $C_{1-6}$ alkoxy; and

m is an integer of 1 to 12;

the dotted line represents an optional double bond, as permitted by valency;

X' is independently selected from -C(O)O-, -S(O)O-, -C(O)-, -C(O)NR-, -$S(O)_2$NR-, -P(O)R'NR-, -S(O)NR-, and -$PO_2$NR-;

$R^{X1}$ and $R^{X1'}$ are independently selected from H, OH, =O, $=CH_2$, CN, $R^m$, $OR^m$, $=CH\text{-}R^{m'}$, $=C(R^{m'})_2$, O-$SO_2$-$R^m$, $CO_2R^m$, $COR^m$, halo and dihalo;

$R^{m'}$ is selected from $R^m$, $CO_2R^m$, $COR^m$, CHO, $CO_2H$ and halo;

each $R^m$ is independently selected from $C_{1-12}$ alkyl, $C_{2-12}$ alkenyl, $C_{2-12}$ alkynyl, $C_{5-20}$ aryl, $C_{5-20}$ heteroaryl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl and 5- to 7-membered heteroaryl;

$R^{X2}$, $R^{X2'}$, $R^{X3}$, $R^{X3'}$, $R^{X5}$ and $R^{X5'}$ are each independently selected from H, $R^m$, OH, $OR^m$, SH, $SR^m$, $NH_2$, $NHR^m$, $NR^m{}_2$, $NO_2$, $Me_3Sn$ and halo;

$R^{X4}$ and $R^{X4'}$ are each independently selected from H, $R^m$, OH, $OR^m$, SH, $SR^m$, $NH_2$, $NHR^m$, $NR^m{}_2$, $NO_2$, $Me_3Sn$, halo, $C_{1-6}$ alkyl, $C_{1-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{2-6}$ aryl, $C_{3-6}$ heteroaryl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-12}$ aryl, 5- to 7-membered heteroaryl, -CN, -NCO, -$OR^n$, -OC(O)$R^n$, -OC(O)$NR^nR^{n'}$, -OS(O)$R^n$, -$OS(O)_2R^n$, -$SR^n$, -S(O)$R^n$, -$S(O)_2R^n$, -S(O)$NR^nR^{n'}$, -$S(O)_2NR^nR^{n'}$, -OS(Or)$NR^nR^{n'}$, -$OS(O)_2NR^nR^{n'}$, -

$NR^nR^{n'}$, $-NR^nC(O)R^o$, $-NR^nC(O)OR^o$, $-NR^nC(O)NR^oR^{o'}$, $-NR^nS(O)R^o$, $-NR^nS(O)_2R^o$, $-NR^nS(O)NR^oR^{o''}$, $-NR^nS(O)_2NR^oR^{o''}$, $-C(O)R^n$, $-C(O)OR^n$ and $-C(O)NR^nR^{n''}$;

$R^X$ and $R^{X'}$ are each independently selected from H, OH, and $C_{1-8}$ alkyl;

Y and Y' are each independently selected from O, S and N(H);

$R^{x6}$ is $C_{3-12}$ alkylene, $C_{3-12}$ alkenylene, or $C_{3-12}$ heteroalkylene;

$R^{X7}$ and $R^{X7'}$ are each independently selected from H, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{6-10}$ aryl, 5- to 7-membered heteroaryl, $-OR^r$, $-OC(O)R^r$, $-OC(O)NR^rR^{r'}$, $-OS(O)R^r$, $-OS(O)_2R^r$, $-SR^r$, $-S(O)R^r$, $-S(O)_2R^r$, $-S(O)NR^rR^{r'}$, $-S(O)_2NR^rR^{r''}$, $-OS(O)NR^rR^{r''}$, $-OS(O)_2NR^rR^{r''}$, $-NR^rR^{r''}$, $-NR^rC(O)R^s$, $-NR^rC(O)OR^s$, $-NR^rC(O)NR^sR^{s'}$, $-NR^rS(O)R^s$, $-NR^rS(O)_2R^s$, $-NR^rS(O)NR^sR^{s'}$, $-NRr^S(O)_2NR^sR^s$, $-C(O)R^r$, $-C(O)OR^s$ and $-C(O)NR^rR^{r''}$;

each $R^r$, $R^{r'}$, $R^s$ and $R^{s'}$ is independently selected from H, $C_{1-7}$ alkyl, $C_{2-7}$ alkenyl, $C_{2-7}$ alkynyl, $C_{3-13}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl and 5- to 7-membered heteroaryl;

each $R^{X8}$ and $R^{X8'}$ is independently selected from H, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ heteroalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, 5- to 7-membered heteroaryl, $-S(O)R^m$, $-S(O)_2R^m$, $-S(O)NR^mR^{m'}$, $-S(O)_2NR^mR^{m'}$, $-NR^mR^{m'}$, $-NR^mC(O)R^m$, $-NR^mC(O)OR^n$, $-NR^mC(O)NR^nR^{n'}$, $-NR^mS(O)R^n$, $-NR^mS(O)_2R^n$, $-NR^mS(O)NR^nR^{n'}$, $-NR^mS(O)_2NR^nR^{n'}$, $-C(O)R^m$, $-C(O)OR^m$ and $-C(O)NR^mR^{m'}$;

$Z^a$ is $OR^{X12a}$, $NR^{X12a}R^{X12a}$, or $SR^{X12a}$;

$Z^b$ is $OR^{X13a}$, $NR^{X13a}R^{X13a}$, or $SR^{X13a}$;

$Z^{a'}$ is $OR^{X12a'}$, $NR^{X12a'}R^{X12a'}$, or $SR^{X12a'}$;

$Z^{b'}$ is $OR^{X13a'}$, $NR^{X13a'}R^{X13a'}$, or $SR^{X13a'}$;

each $R^{X12a}$, $R^{X12a'}$, $R^{X13a}$ and $R^{x13a'}$ is independently selected from H, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, 5- to 7-membered heteroaryl, $-C(O)R^{X15a}$, $-C(O)OR^{X15a}$ and $-C(O)NR^{X15a}R^{X15a'}$;

each $R^{X15a}$ and $R^{x15a'}$ is independently selected from $C_{1-12}$ alkyl, $C_{2-12}$ alkenyl, $C_{2-12}$ alkynyl, $C_{5-20}$ aryl, $C_{5-20}$ heteroaryl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl, and 5- to 7-membered heteroaryl;

$R^{X12a}$ and $R^{X13a}$ optionally join the atoms to which they are attached to form a 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl, or 3- to 7-membered heteroaryl, and

$R^{X12a'}$ and $R^{X13a'}$ optionally join the atoms to which they are attached to form a 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl, or 3- to 7-membered heteroaryl; and

each of the $R^{n}$, $R^{n'}$, $R^{o}$, $R^{o'}$, $R^{p}$ and $R^{p'}$ is independently selected from H, $C_{1-7}$ alkyl, $C_{2-7}$ alkenyl, $C_{2-7}$ alkynyl, $C_{3-13}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, and 5- to 7-membered heteroaryl.

42. The antibody conjugate of claim 41, wherein the $R^{m}$ is $C_{1-12}$ alkyl, $C_{2-12}$ alkenyl, $C_{2-12}$ alkynyl, $C_{5-20}$ aryl, $C_{5-20}$ heteroaryl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl, or 5- to 7-membered heteroaryl;

and the $R^{m}$ is additionally substituted with $C_{1-12}$ alkyl, $C_{2-12}$ alkenyl, $C_{2-12}$ alkynyl, $C_{5-20}$ aryl, $C_{5-20}$ heteroaryl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocyclyl, 3- to 7-membered heterocycloalkyl or 5- to 7-membered heteroaryl.

43. The antibody conjugate of claim 41, wherein each $R^{X4}$ or $R^{X4'}$ is $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-12}$ aryl, or 5- to 7-membered heteroaryl; the $R^{X4}$ or $R^{X4'}$ is additionally substituted with at least one $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, 5- to 7-membered heteroaryl, $-OR^{p}$, $-OC(O)R^{p}$, $-C(O)NR^{p}R^{p'}$, $-OS(O)R^{p}$, $-OS(O)_2R^{p}$, $-SR^{p}$, $-S(O)R^{p}$, $-S(O)_2R^{p}$, $-S(O)NR^{p}R^{p'}$, $-S(O)_2NR^{p}R^{p'}$, $-OS(O)NR^{p}R^{p'}$, $-OS(O)_2NR^{p}R^{p'}$, $-NR^{p}R^{p'}$, $-NR^{p}C(O)R^{q}$, $-NR^{p}C(O)OR^{q}$, $-NR^{p}C(O)NR^{q}R^{q'}$, $-NR^{p}S(O)R^{q}$, $-NR^{p}S(O)_2R^{q}$, $-NR^{p}S(O)NR^{q}R^{q'}$, $-NR^{p}S(O)_2NR^{q}R^{q'}$, $-C(O)R^{p}$, $-C(O)OR^{p}$ or $-C(O)NR^{p}R^{p}$; and

the $R^{p}$, $R^{p'}$, $R^{q}$, and $R^{q'}$ are each H, $C_{1-7}$ alkyl, $C_{2-7}$ alkenyl, $C_{2-7}$ alkynyl, $C_{3-13}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, or 5- to 7-membered heteroaryl.

44. The antibody conjugate of claim 41, wherein each $R^{X7}$ or $R^{X7'}$ is H, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{6-10}$ aryl, or 5- to 7-membered heteroaryl; the $R^{X7}$ or $R^{X7'}$ is additionally substituted with $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{6-10}$ aryl, 5- to 7-membered heteroaryl, $-OR^{t}$, $-OC(O)R^{t}$, $-OC(O)NR^{t}R^{t'}$, $-OS(O)R^{t}$, $-OS(O)_2R^{t}$, $-SR^{t}$, $-S(O)R^{t}$, $-S(O)_2R^{t}$, $-S(O)NR^{t}R^{t'}$, $-S(O)_2NR^{t}R^{t'}$, $-OS(O)NR^{t}R^{t'}$, $-OS(O)_2NR^{t}R^{t'}$, $-NR^{t}R^{t'}$, $-NR^{t}C(O)R^{u}$, $-NR^{t}C(O)OR^{u}$, -

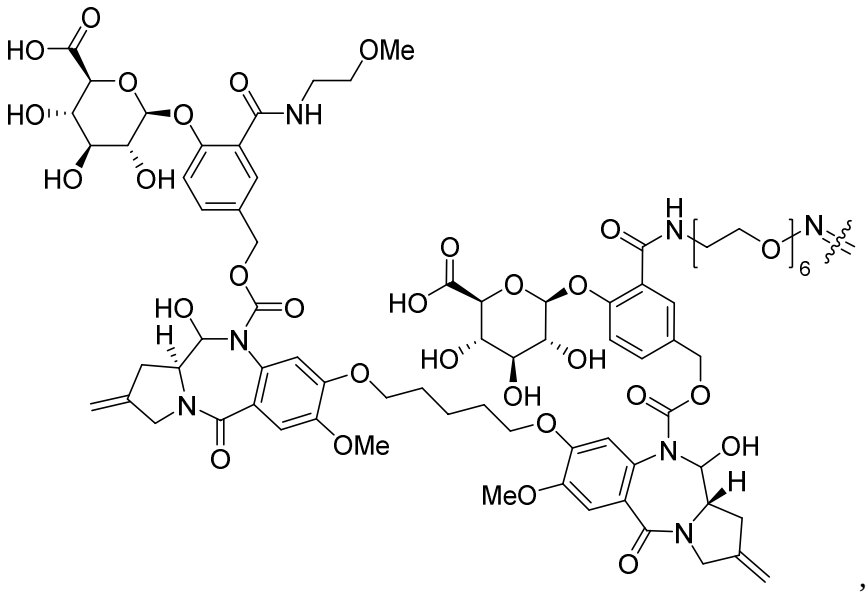
$NR^tC(O)NR^uR^{u'}$, $-NR^tS(O)R^u$, $-NR^tS(O)_2R^u$, $-NR^tS(O)NR^uR^{u'}$, $-NR^tS(O)_2NR^uR^{u'}$, $-C(O)R^t$, $-C(O)OR^t$ or $-C(O)NR^tR^{t'}$; and

the $R^t$, $R^{t'}$, $R^u$ and $R^{u'}$ are each H, $C_{1-7}$ alkyl, $C_{2-7}$ alkenyl, $C_{2-7}$ alkynyl, $C_{3-13}$ cycloalkyl, 3- to 7-membered heterocycloalkyl, $C_{5-10}$ aryl, or 5- to 7-membered heteroaryl.

45. The antibody conjugate of claim 41, wherein $R^{x6}$ is $C_{3-12}$ alkylene, $C_{3-12}$ alkenylene or $C_{3-12}$ heteroalkylene; $R^{x6}$ is additionally substituted with $-NH_2$, $-NHR^m$, $-NHC(O)R^m$, $-NHC(O)CH_2$, $[OCH_2CH_2]_n$-$R^{XX}$, or $-[CH_2CH_2O]_n$-$R^{XX}$; the $R^{XX}$ is H, OH, $N_3$, CN, $NO_2$, SH, $NH_2$, $ONH_2$, $NHNH_2$, halo, $C_{1-8}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{1-8}$ alkoxy, $C_{1-8}$ alkylthio, $C_{3-20}$ heteroaryl, $C_{5-20}$ aryl or mono- or di-$C_{1-8}$ alkyl amino; n is 1 to 6; and

each $R^m$ is independently substituted or unsubstituted $C_{1-12}$ alkyl, substituted or unsubstituted $C_{2-12}$ alkenyl, substituted or unsubstituted $C_{2-12}$ alkynyl, substituted or unsubstituted $C_{5-20}$ aryl, substituted or unsubstituted $C_{5-20}$ heteroaryl, substituted or unsubstituted $C_{3-6}$ cycloalkyl, substituted or unsubstituted 3- to 7-membered heterocyclyl, substituted or unsubstituted 3- to 7-membered heterocycloalkyl, or substituted or unsubstituted 5- to 7-membered heteroaryl.

46. The antibody conjugate of claim 28, wherein X comprises:



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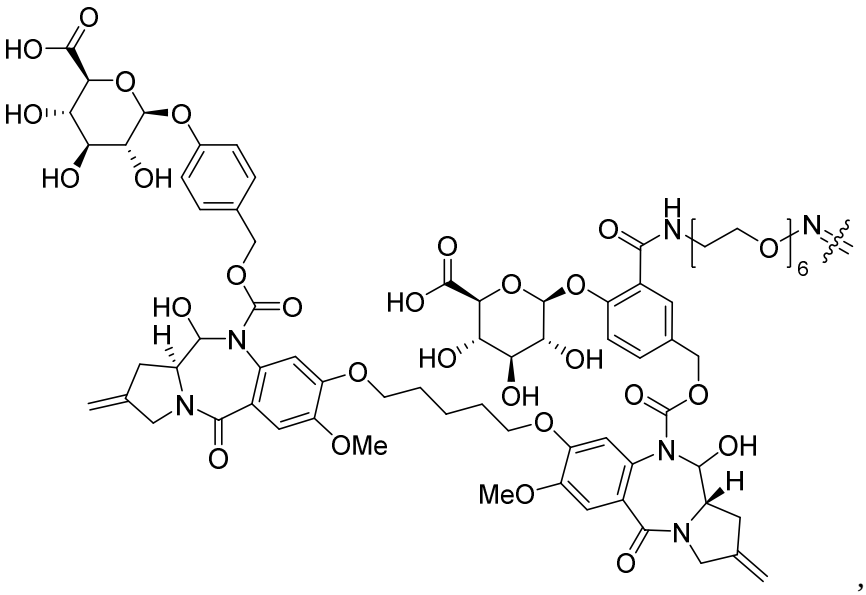

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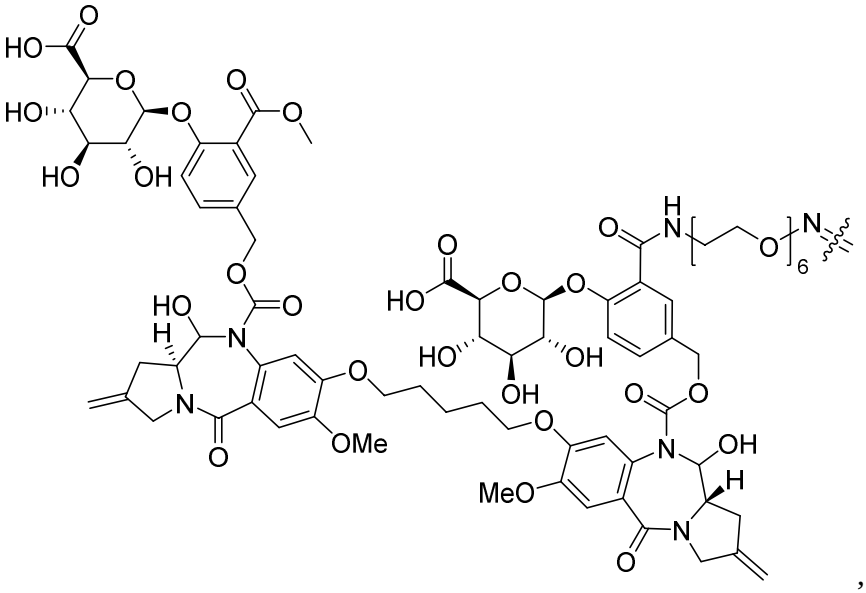

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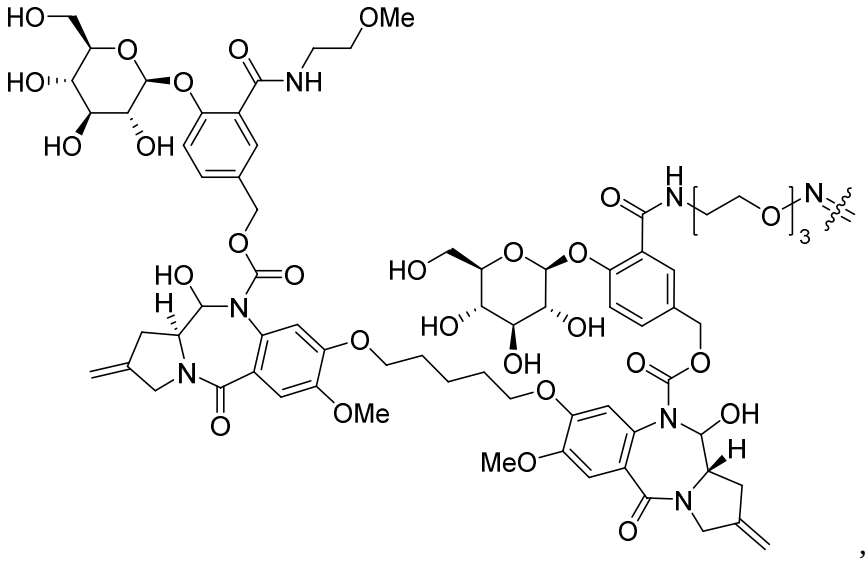

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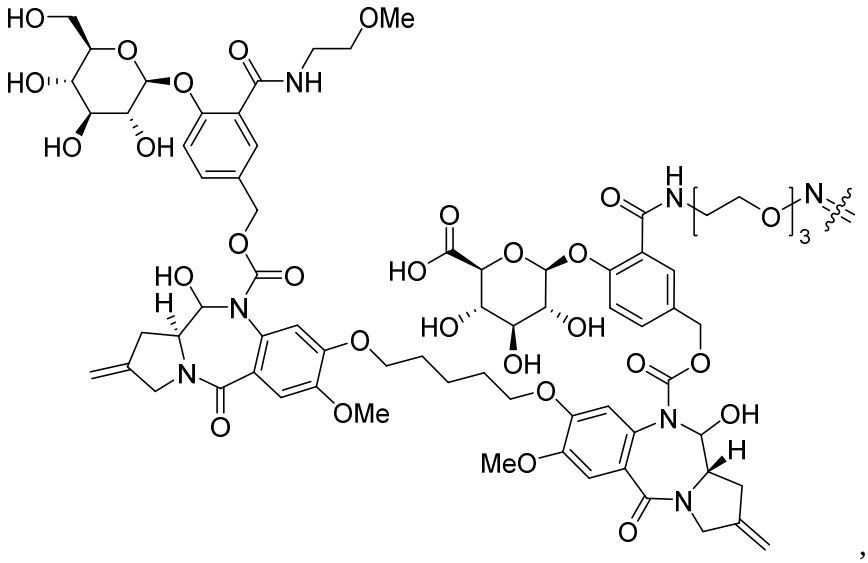

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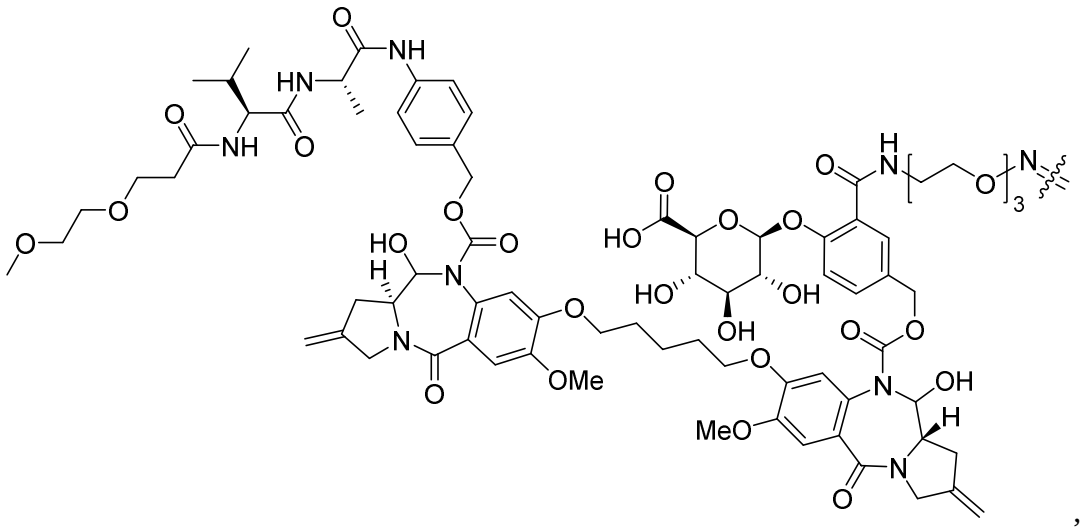
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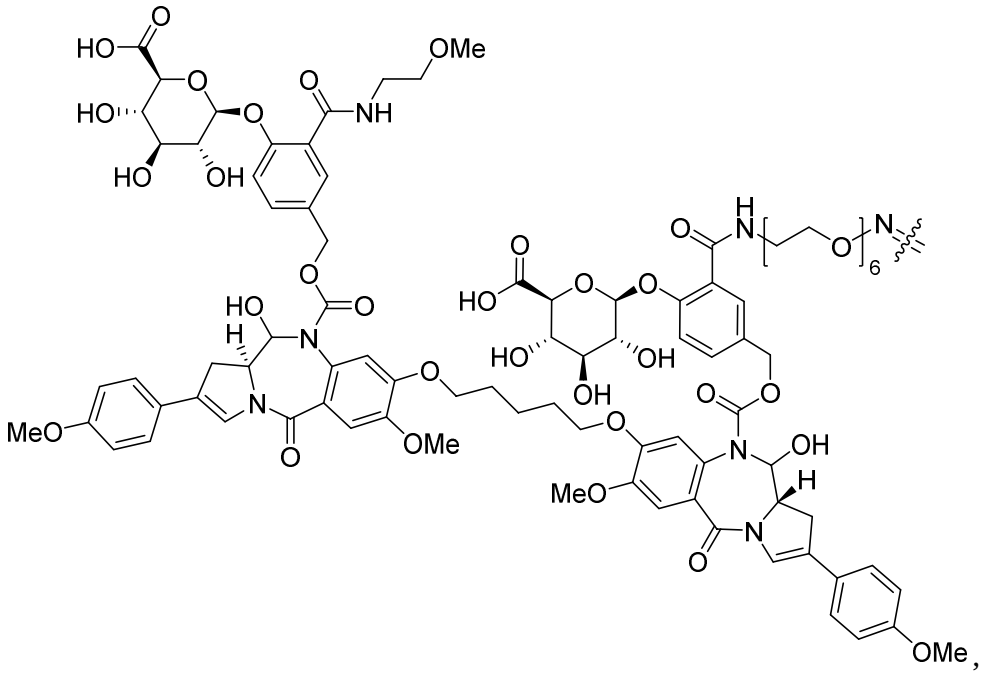
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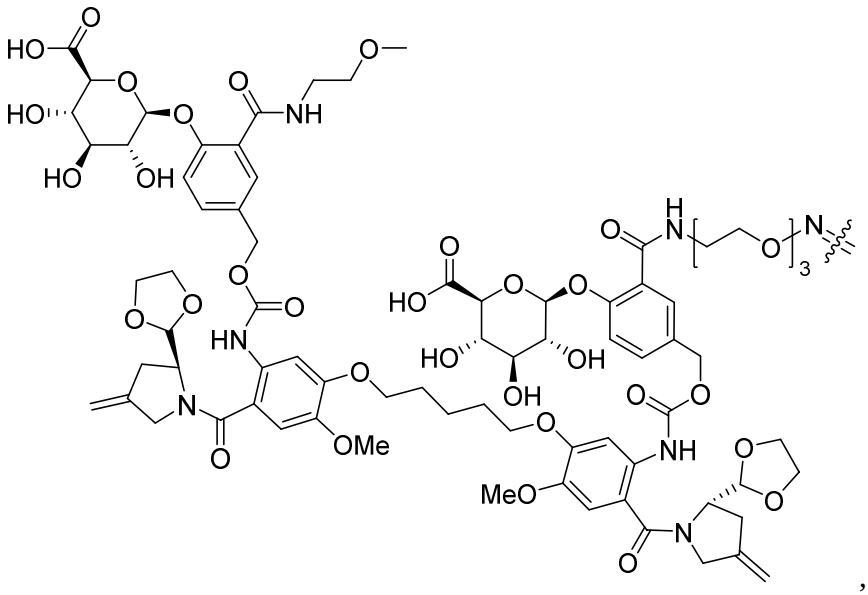
or



wherein the bond overlaid with the wavy line represents a connection to the carbon atom adjacent to $R^{11}/L^1$.

47. A pharmaceutical composition comprising the antibody conjugate of any one of claims 1-46 and a pharmaceutically acceptable carrier or diluent.

48. A pharmaceutical composition for use in prevention or treatment of cancer or an angiogenetic disease, the composition comprising the antibody conjugate of any one of claims 1-46.

49. The pharmaceutical composition for use according to claim 48, wherein the cancer is characterized by DLK1 expression.

50. The pharmaceutical composition for use according to claim 48 or 49, wherein the cancer is lung cancer, gastrointestinal cancer, colon cancer, intestinal cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, liver cancer, kidney cancer, bladder cancer, pancreatic cancer, brain cancer, sarcoma, or melanoma.

51. The pharmaceutical composition for use according to claim 50, wherein the lung cancer is small cell lung carcinoma.

52. The pharmaceutical composition for use according to claim 50, wherein the sarcoma is osteosarcoma or Kaposi’s sarcoma.

53. A use of the antibody conjugate of any one of claims 1-46 in the manufacture of a medicament for prevention or treatment of cancer or an angiogenetic disease.

54. The use of claim 53, wherein the medicament further comprises a pharmaceutically efficacious amount of a chemotherapeutic agent.

55. The use of claim 53 or 54, wherein the cancer is lung cancer, gastrointestinal cancer, colon cancer, intestinal cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, liver cancer, kidney cancer, bladder cancer, pancreatic cancer, brain cancer, sarcoma, or melanoma.

56. The use of claim 55, wherein the lung cancer is small cell lung carcinoma.

57. The use of claim 55, wherein the sarcoma is osteosarcoma or Kaposi’s sarcoma.