[CLAIMS]

1. A conjugate comprising a structure represented by General Formula I, or a pharmaceutically acceptable salt thereof:

[General Formula I]

$Ab-[LINKER-(B)_l]_m$

wherein

Ab is an anti-Claudin 18 isoform 2 (CLDN18.2) antibody or antigen-binding fragment thereof, comprising a heavy chain CDR1 consisting of the amino acid sequence represented by SEQ ID NO: 2, a heavy chain CDR2 consisting of the amino acid sequence represented by SEQ ID NO: 4, and a heavy chain CDR3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and

a light chain CDR1 consisting of the amino acid sequence represented by SEQ ID NO: 9, a light chain CDR2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and a light chain CDR3 consisting of the amino acid sequence represented by SEQ ID NO: 13;

B is an active agent;

LINKER is a covalent linker linking Ab to the active agent(s); and

l and m are each independently an integer selected from 1 to 20.

2. The conjugate of claim 1, wherein Ab comprises a variable heavy chain FR of a human antibody encoded by a gene derived from germline V gene IGHV3-23.

3. The conjugate of claim 2, wherein the variable heavy chain FR comprises:
a heavy chain FR1 consisting of the amino acid sequence represented by SEQ ID NO: 1;
a heavy chain FR2 consisting of the amino acid sequence represented by SEQ ID NO: 3;
a heavy chain FR3 consisting of the amino acid sequence represented by SEQ ID NO: 5; and
a heavy chain FR4 consisting of the amino acid sequence represented by SEQ ID NO: 7.

4. The conjugate of any one of claims 1-3, wherein Ab comprises a variable light chain FR of a human encoded by a gene derived from germline V gene IGKV3-11 or IGKV3-15.

5. The conjugate of claim 4, wherein the variable light chain FR comprises:

a light chain FR1 consisting of the amino acid sequence represented by SEQ ID NO: 8;

a light chain FR2 consisting of the amino acid sequence represented by SEQ ID NO: 10;

a light chain FR3 consisting of the amino acid sequence represented by SEQ ID NO: 12; and

a light chain FR4 consisting of the amino acid sequence represented by SEQ ID NO: 14 or 20.

6. The conjugate of any one of claims 1-5, wherein Ab comprises:

a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 15 or an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 15; and

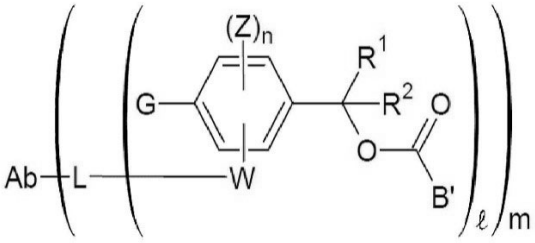
a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 16 or an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 16.

7. The conjugate of any one of claims 1-6, wherein Ab is a monoclonal antibody, a domain antibody (dAb), a single chain antibody (scAb), a Fab fragment, a Fab' fragment, a F(ab')2 fragment, an scFab fragment, an Fv fragment, a dsFv fragment, a single chain variable fragment (scFv), an scFv-Fc fragment, a single domain heavy chain antibody, a single domain light chain antibody, a variant antibody, a multimeric antibody, a minibody, a diabody, a bispecific antibody, or a multispecific antibody.

8. The conjugate of any one of claims 1-7, wherein the linker is cleavable.

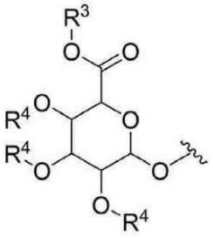
9. The conjugate of any one of claims 1-8, wherein the conjugate comprises a structure represented by General Formula IIa:

[General Formula IIa]



wherein

each B' is independently an active agent;

each G is independently a glucuronic acid moiety or  ;

R^3 is hydrogen or a carboxyl-protecting group, and each R^4 is independently hydrogen or a hydroxyl-protecting group;

R^1 and R^2 are each independently hydrogen, C_{1-8} alkyl, or C_{3-8} cycloalkyl;

each W is independently -C(O)-, -C(O)NR'-, -C(O)O-, -SO_2NR'-, -P(O)R"NR', -SONR'-, or -PO_2NR'-, wherein C, S, or P is directly bonded to the phenyl ring and NR' is bonded to L; R' and R" are each independently hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, mono- or di-C_{1-8} alkylamino, C_{3-20} heteroaryl, or C_{6-20} aryl;

each Z is independently hydrogen, C_{1-8} alkyl, halogen, cyano, or nitro;

n is an integer from 0 to 3;

each L is independently:

A) a C_{1-50} alkylene or 1-50 atom heteroalkylene comprising:

(i) one or more unsaturated bonds;

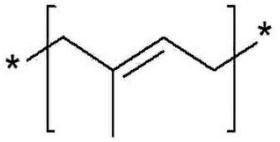
(ii) a heteroarylene;

or

(iii) a C_{1-20} alkyl substituent on the C_{1-50} alkylene; and/or

B) at least one isoprenyl unit having a structure represented by General Formula III which is recognizable by an isoprenoid transferase:

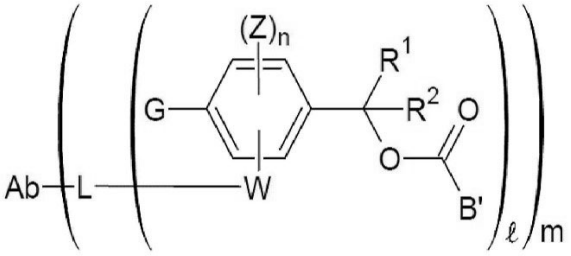
[General Formula III]


; and

l and m are each independently an integer selected from 1 to 20.

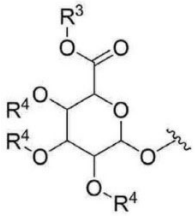
10. A conjugate comprising a structure represented by General Formula IIa, or a pharmaceutically acceptable salt thereof:

[General Formula IIa]



wherein

Ab is an anti-Claudin 18 isoform 2 (CLDN18.2) antibody or antigen-binding fragment thereof;

each G is independently a glucuronic acid moiety or ;

R^3 is hydrogen or a carboxyl-protecting group, and each R^4 is independently hydrogen or a hydroxyl-protecting group;

R^1 and R^2 are each independently hydrogen, C_{1-8} alkyl, or C_{3-8} cycloalkyl;

each W is independently -C(O)-, -C(O)NR'-, -C(O)O-, -SO_2NR'-, -P(O)R"NR', -SONR'-, or -PO_2NR'-, wherein C, S, or P is directly bonded to the phenyl ring and NR' is bonded to L; R' and R" are each independently hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, mono- or di-C_{1-8} alkylamino, C_{3-20} heteroaryl, or C_{6-20} aryl;

each Z is independently hydrogen, C_{1-8} alkyl, halogen, cyano, or nitro;

n is an integer from 0 to 3; and

each L is independently:

A) a C_{1-50} alkylene or 1-50 atom heteroalkylene comprising:

(i) one or more unsaturated bonds;

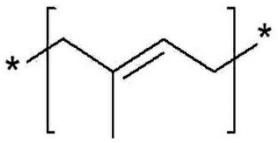
(ii) a heteroarylene;

or

(iii) a C_{1-20} alkyl substituent on the C_{1-50} alkylene; and/or

B) at least one isoprenyl unit having a structure represented by General Formula III which is recognizable by an isoprenoid transferase:

[General Formula III]

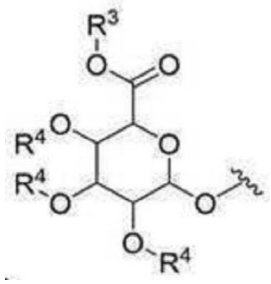


;

each B' is independently an active agent; and

l and m are each independently an integer selected from 1 to 20.

11. The conjugate of claim 9 or 10, wherein

each G is 

; and

each R^3 and R^4 are hydrogen.

12. The conjugate of any one of claims 9-11, wherein:

R^1 and R^2 are each hydrogen;

n is 0; and

each W is independently -C(O)NR'-, C is directly bonded to the phenyl ring; R' is hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, mono- or di-C_{1-8} alkylamino, C_{3-20} heteroaryl, or C_{6-20} aryl; and NR' is bonded to L.

13. The conjugate of any one of claims 9-12, wherein

L is a 1-50 atom heteroalkylene comprising nitrogen,

L comprises two or more atoms of a hydrophilic amino acid, and

the nitrogen forms a peptide bond with a carbonyl of the hydrophilic amino acid.

14. The conjugate of any one of claims 9-13, wherein

L is covalently bonded to the antibody by a thioether bond,

wherein the thioether bond comprises a sulfur atom of a cysteine of the antibody.

15. The conjugate of claim 14, wherein

a C-terminus of the antibody comprises an amino acid motif that is recognized by an isoprenoid transferase, and

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

16. The conjugate of claim 15, wherein:

the amino acid motif has a CYYX sequence, wherein C is cysteine, Y is an aliphatic amino acid, and X is selected from glutamine, glutamate, serine, cysteine, methionine, alanine, and leucine.

17. The conjugate of claim 16, wherein

the amino acid motif has a CYYX sequence, wherein Y is selected from alanine, isoleucine, leucine, methionine, and valine; or

the amino acid motif has a CVIM or CVLL sequence.

18. The conjugate of any one of claims 15-17, wherein at least one of 1 to 20 amino acids preceding the amino acid motif is glycine.

19. The conjugate of claim 9 or 10, wherein the antibody comprises the amino acid sequence of GGGGGGGCVIM at the C-terminus.

20. The conjugate of any one of claims 9-19, wherein

L is 3 to 50 heteroalkylene containing an oxime, and

(1) 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

(2) 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.

21. The conjugate of any one of claims 9-20, wherein L comprises an oxime, and at least one isoprenyl unit that covalently binds the oxime to Ab.

22. The conjugate of any one of claims 9-21, wherein L further comprises a second unit represented by General Formula VIII or General Formula IX:

[General Formula VIII]

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

[General Formula IX]

$-(CH_2CH_2X)_w-$

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_{1-8} alkylene, or $-NR^{21}-$;

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 an integer from 0 to 10;

p is an integer from 0 to 10;

q is an integer from 1 to 20; and

w is an integer from 1 to 20.

23. The conjugate of claim 22, wherein:

q is an integer from 1 to 10;

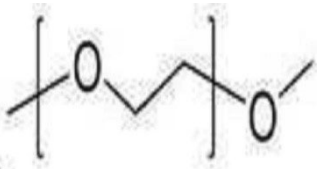
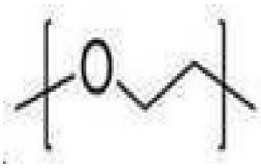
r and p are each 1 or 2; and

V is -O-.

24. The conjugate of claim 22 or 23, wherein:

X is -O-; and

w is an integer from 1 to 10.

25. The conjugate of claim 22, wherein L comprises at least one polyethylene glycol unit represented by  or .

26. The conjugate of any one of claims 9-25, wherein

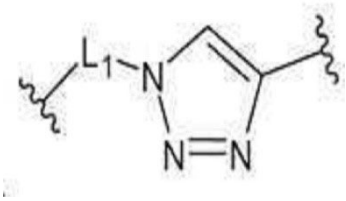
L comprises an oxime, and

at least one polyethylene glycol unit covalently bonds the oxime to an active agent.

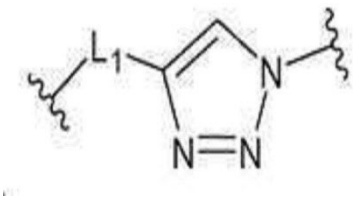
27. The conjugate of any one of claims 9-26, wherein L further comprises a third unit formed by 1,3-dipolar cycloaddition reactions, hetero-Diels-Alder reactions, nucleophilic substitution reactions, non-aldol type carbonyl reactions, addition to a carbon-carbon multiple bond, oxidation reactions, or click reactions or a third unit formed by a reaction between an alkyne and an azide or between an aldehyde or ketone group and hydrazine or hydroxylamine.

28. The conjugate of any one of claims 9-27, wherein L further comprises a third unit represented by General Formula IVa, IVb, IVc, IVd or IVe:

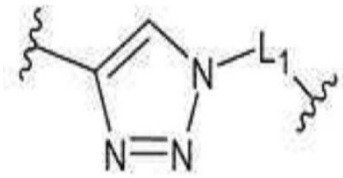
[General Formula IVa]



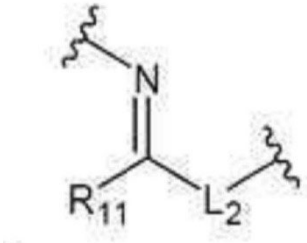
[General Formula IVb]



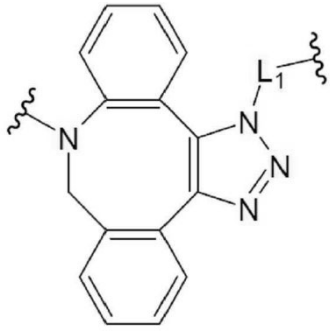
[General Formula IVc]



[General Formula IVd]



[General Formula IVe]



wherein

L_1 and L_2 are each independently a single bond or C_{1-30} alkylene; and

R_{11} is hydrogen or C_{1-10} alkyl.

29. The conjugate of claim 28, wherein L_1 and L_2 are each independently a single bond, C_{11} alkylene, or C_{12} alkylene.

30. The conjugate of any one of claims 9-29, wherein the isoprenoid transferase is farnesyl protein transferase (FTase) or geranylgeranyl transferase (GGTase).

31. The conjugate of any one of claims 9-30, wherein

L comprises one or more branched linkers covalently bonded to Ab, wherein each branched linker comprises:

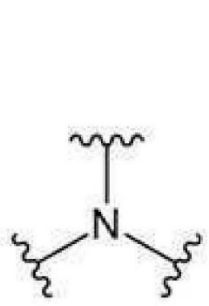
i) a fifth unit covalently bonded to Ab by a primary linker (PL);

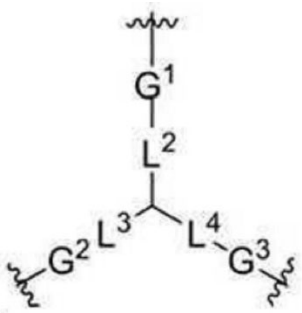
ii) a first branch (B1) in which a first active agent is covalently bonded to the fifth unit by a secondary linker (SL) and a cleavage group (CG); and

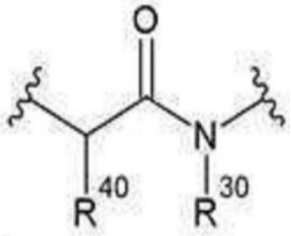
iii) a second branch (B2) in which a) a second active agent is covalently bonded to the fifth unit by a secondary linker (SL) and the cleavage group (CG); or b) a polyethylene glycol moiety is covalently bonded to the fifth unit; and

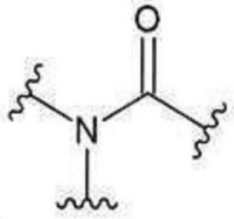
each cleavage group is hydrolyzed to release the active agent from the conjugate.

32. The conjugate of claim 31, wherein

the fifth unit is 

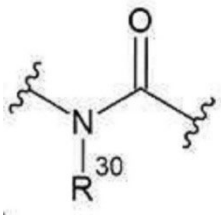
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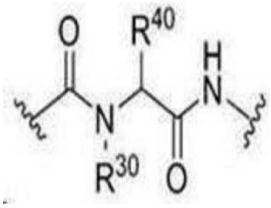
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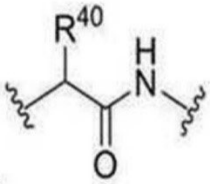
, or 

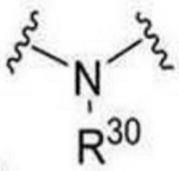
;

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

R^{40} is hydrogen or L^5-$COOR_6$; and

L^5 is a bond or $-C_{n'}H_{2n'}-$, wherein n' is an integer from 1 to 10; and

R_6 is hydrogen or C_{1-30} alkyl.

33. The conjugate of claim 31 or 32, wherein the cleavage group is cleavable in a target cell, or is capable of releasing one or more active agents.

34. The conjugate of any one of claims 31-33, wherein

the conjugate comprises

1, 2, 3, 4 or more branched linkers; and

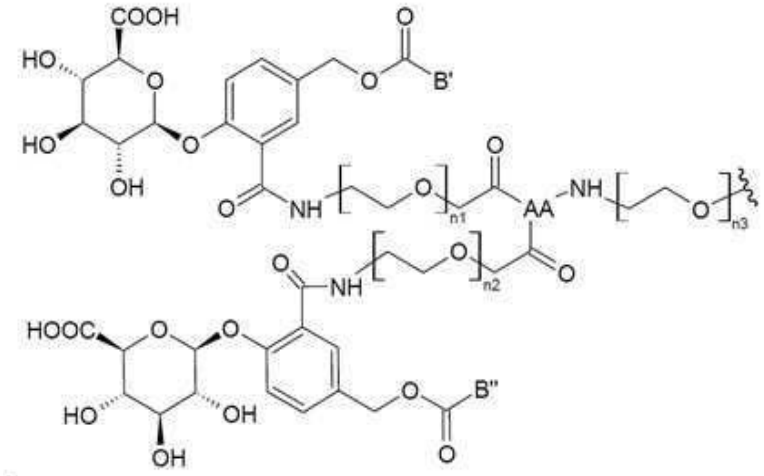
each branched linker is bonded to one or more active agents.

35. The conjugate of any one of claims 31-34, wherein

the fifth unit is

a lysine, and the primary linker is bound to the C-terminus of the lysine.

36. The conjugate of claim 31, wherein the conjugate comprises a structure represented by:



wherein B' and B" are each active agents which are identical to or different from each other;

n1 to n3 each independently are an integer from 0 to 30; and

AA is an amino acid group.

37. The conjugate of any one of claims 1-36, wherein the active agent is a chemotherapeutic agent or a toxin.

38. The conjugate any one of claims 1-37, wherein the active agent is an immunomodulatory compound, an anticancer agent, an anti-viral agent, an anti-bacterial agent, an anti-fungal agent, an anti-parasitic agent, or a combination thereof.

39. The conjugate of any one of claims 1-38, wherein the active agent is:

(a) erlotinib, bortezomib, fulvestrant, sutent, 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, triethiylenethiophosphoramide, trimethylolomelamine, 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, chlorozotocin, fotemustine, lomustine, nimustine, ranimnustine, calicheamicin, calicheamicin gamma 1, calicheamicin omega 1, dynemicin, dynemicin A, clodronate, esperamicin, neocarzinostatin chromophore, aclacinomysins, actinomycin, antrmycin, azaserine, bleomycins, cactinomycin, carabicin, carninomycin, carzinophilin, chromomycins, dactinomycin, daunorubicin, detorubucin, 6-diazo-5-oxo-L-norleucine, doxorubicin, morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin, liposomal doxorubicin, deoxydoxorubicin, epirubicin, esorubicin, marcellomycin, mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptomigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, 5-fluorouracil, denopterin, methotrexate, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thiguanine, ancitabine, azacitidine, 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, edatraxate, defofamine, demecolcine, diaziquone, elfornithine, elliptinium acetate, etoglucid, gallium nitrate, hydroxyurea, lentinan, lonidainine, maytansine, ansamitocins, mitoguazone, mitoxantrone, mopidanmol, nitraerine, pentostatin, phenamet, pirarubicin, losoxantrone, 2-ethylhydrazide, procarbazine, polysaccharide-k, razoxane, rhizoxin, sizofiran, spirogermanium, tenuazonic acid, triaziquone, 2,2',2"-trichlorotriethylamine, T-2 toxin, verracurin A, roridin A, anguidine, urethane, vindesine, dacarbazine, mannomustine, mitobronitol, mitolactol, pipobroman, gacytosine, arabinoside, cyclophosphamide, thiotepa, paclitaxel, albumin-engineered nanoparticle formulation of paclitaxel, docetaxel, chlorambucil, gemcitabine, 6-thioguanine, mercaptopurine, cisplatin, carboplatin, vinblastine, platinum, etoposide, ifosfamide, mitoxantrone, vincristine, vinorelbine, novantrone, teniposide, edatrexate, daunomycin, aminopterin, xeloda, ibandronate, CPT-11, topoisomerase inhibitor RFS 2000, difluoromethylornithine, retinoic acid, capecitabine, or a pharmaceutically acceptable salt, solvate or acid thereof;

(b) monokines, lymphokines, traditional polypeptide hormones, parathyroid hormones, 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-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, IL-12, tumor necrosis factor, polypeptide factor, LIF, kit ligand, or a combination thereof;

(c) diphtheria toxin, botulinum toxin, tetanus toxin, decentretoxin, cholera toxin, amanitin, α-amanitin, pyrrolobenzodiazepines, pyrrolobenzodiazepine derivatives, indolinobenzodiazepines, pyridinobenzodiazepines, tetrodotoxin, brevetoxin, ciguatoxin, ricin, AM toxin, auristatin, tubulysin, geldanamycin, maytansinoid, calicheamycin, daunomycin, doxorubicin, methotrexate, vindesine, SG2285, dolastatin, dolastatin analog, cryptophycin, camptothecin, rhizoxin, rhizoxin derivatives, CC-1065, CC-1065, analogs or derivatives, duocarmycin, enediyne antibiotics, esperamicin, epothilone, toxoid, or a combination thereof;

(d) an affinity ligand, wherein the affinity ligand is a substrate, an inhibitor, an active

agent, a neurotransmitter, a radioisotope, or a combination thereof;

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

(f) an immunomodulatory compound, an anticancer agent, an anti-viral agent, an anti-bacterial agent, an anti-fungal agent, an anti-parasitic agent, or a combination thereof;

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

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

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

(j) an aromatase inhibitor;

(k) a protein kinase inhibitor;

(l) a lipid kinase inhibitor;

(m) an antisense oligonucleotide;

(n) a ribozyme;

(o) a vaccine; or

(p) an anti-angiogenic agent.

40. The conjugate of claims 1-39, wherein:

the active agent is a pyrrolobenzodiazepine dimer;

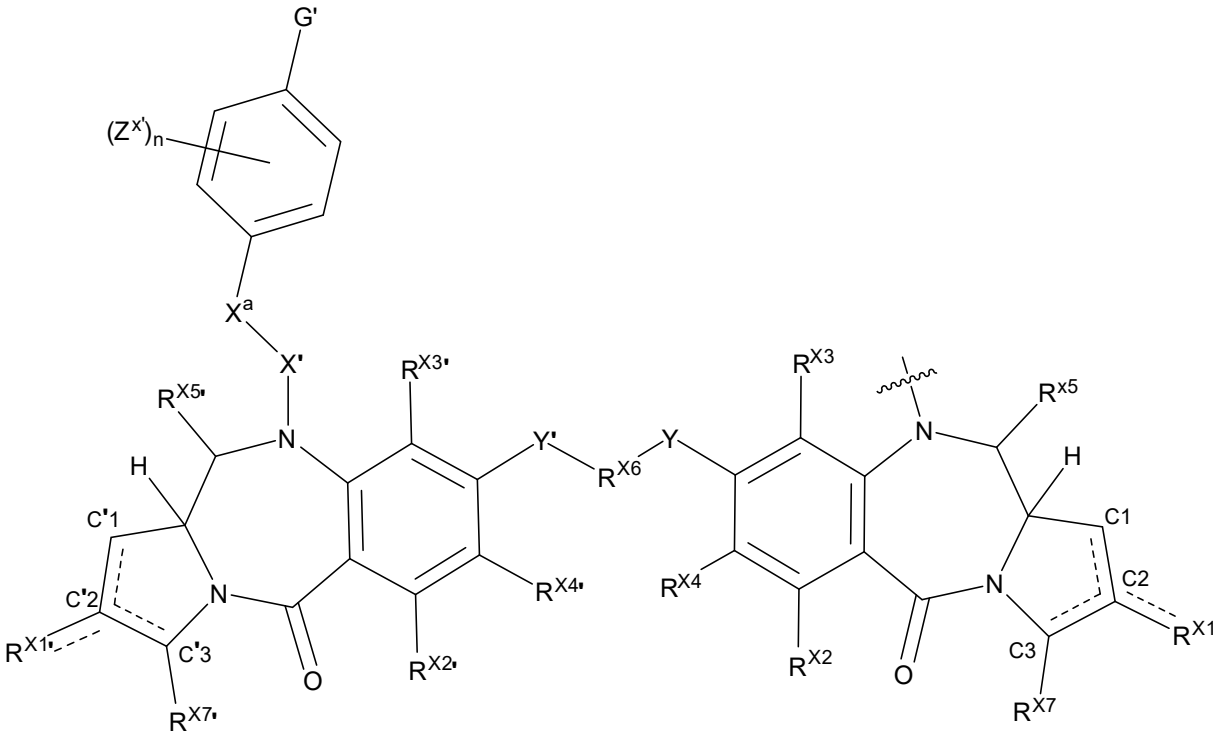
position N10 of the pyrrolobenzodiazepine dimer is substituted with X or position N'10 is substituted with X' wherein X or X' links the pyrrolobenzodiazepine dimer to the conjugate;

X and X' are each independently -C(O)O-* or -C(O)-*; and

* refers to a binding site between the pyrrolobenzodiazepine dimer and the linker.

41. The conjugate of claim 40, wherein the active agent comprises a structure represented by General Formula XII:

[General Formula XII]

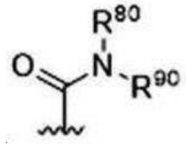
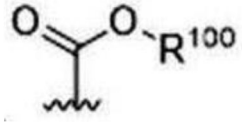


wherein

each dotted line represents an optional double bond;

G' is a glucuronide group or a galactoside group;

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 $–(CH_2)_m\text{-}OCH_3$;

n is an integer of 1 to 3;

R^{80} and R^{90} are each independently selected from H, 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;

m is an integer of 1 to 12;

X' is independently selected from -C(O)O-, -S(O)O-, -C(O)-, $-C(O)NR^X$-, $-S(O)_2NR^X$-, $-P(O)R^{X'}NR^X$-, $-S(O)NR^X$-, and $-PO_2NR^X$-;

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

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

R^{X2}, $R^{X2'}$, R^{X3}, and $R^{X3'}$ are each independently selected from H, R^m, OH, OR^m, NR^m_2, NO_2, 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, halo, and C_{1-6} alkyl;

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, $-NR^mR^{m'}$, NO_2, $-NR^mC(O)R^{m'}$, $-NR^mC(O)OR^{m'}$, $-NR^mC(O)NR^mR^{m'}$, $-S(O)R^m$, $-S(O)_2R^m$, $-S(O)NR^mR^{m'}$, $-S(O)_2NR^mR^{m'}$, $-NR^mS(O)R^{m'}$, $-NR^mS(O)_2R^{m'}$, $-P(O)R^m$, $-P(O)_2R^m$, $-P(O)NR^mR^{m'}$, $-P(O)_2NR^mR^{m'}$, $-NR^mP(O)R^{m'}$, $-NR^mP(O)_2R^{m'}$, and halo;

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

R^{X6} is independently C_{3-12} alkylene, C_{3-12} alkenylene, or C_{3-12} heteroalkylene;

R^{X6} is unsubstituted or substituted with $-NH_2$, $-NHR^m$, $-NHC(O)R^m$, $-NHC(O)CH_2-[OCH_2CH_2]_n-R^{XX}$, or $-[CH_2CH_2O]_n-R^{XX}$;

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} alkylamino, wherein n is an integer from 1 to 6;

R^{X7} and $R^{X7'}$ are each independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $-C(O)R^r$, $-C(O)OR^s$, or $-C(O)NR^rR^{r'}$;

R^r, $R^{r'}$, and R^s are each independently 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;

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

each R^m is independently selected from H, OH, C_{1-12} alkyl, C_{1-12} alkoxy, 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, wherein at least one hydrogen atom of 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 is substituted with OH, =O, C_{1-12} alkyl, or C_{1-12} alkoxy.

42. The conjugate of claim 41, wherein R^{X1} and $R^{X1'}$ are each independently $=CH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{5-7} aryl, C_{3-6} heteroaryl, or C_{5-7} aryl substituted with C_{1-6} alkyl or C_{1-6}

alkoxy.

43. The conjugate of claim 41 or 42, wherein R^{X2}, $R^{X2'}$, R^{X3}, and $R^{X3'}$ are each independently H or OH.

44. The conjugate of any one of claims 41-43, wherein R^{X5} and $R^{X5'}$ are each independently selected from H, OH, -S(O)R^m, S(O)$_2R^m$, -P(O)R^m, and -P(O)$_2R^m$, wherein R^m is H, OH, C_{1-12} alkyl, C_{1-12} alkoxy, C_{2-12} alkenyl, or C_{2-12} alkynyl.

45. The conjugate of any one of claims 41-44, wherein R^{X4} and $R^{X4'}$ are each independently C_{1-6} alkoxy.

46. The conjugate of any one of claims 41-45, wherein Y and Y' are each independently O.

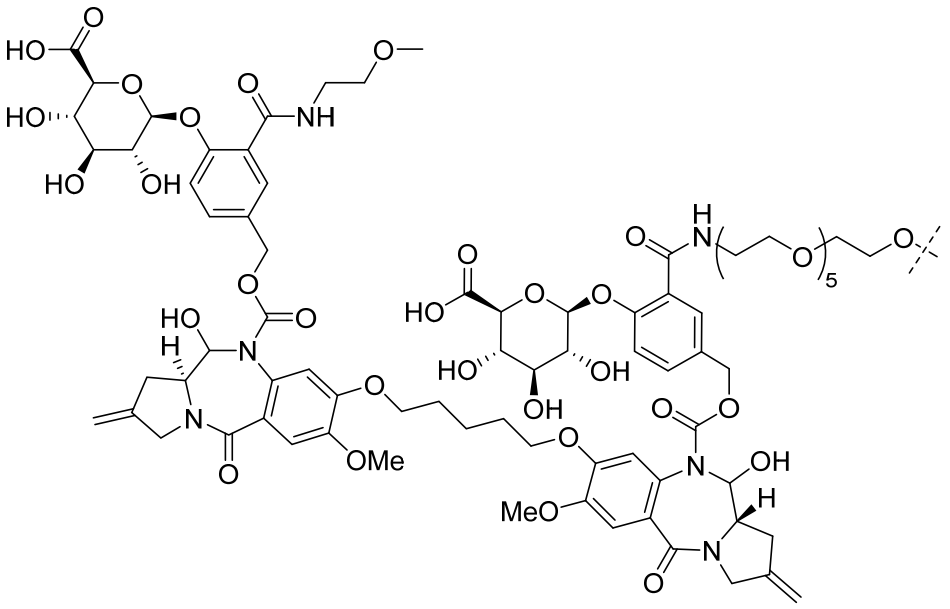
47. The conjugate of any one of claims 41-46, wherein:

R^{X6} is C_{3-12} alkylene, C_{3-12} alkenylene, or C_{3-12} heteroalkylene, and R^{X6} is 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};

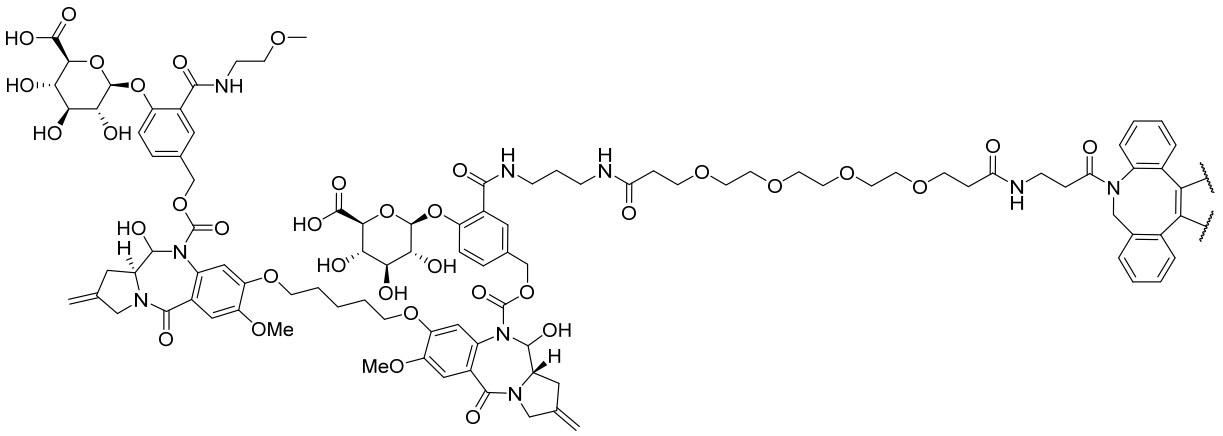
R^{XX} is H, OH, N_3, CN, NO_2, SH, NH_2, ONH_2, $NHNH_2$, halo, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, C_{3-20} heteroaryl, C_{5-20} aryl, or mono- or di-C_{1-8} alkylamino; and

n is an integer from 1 to 6.

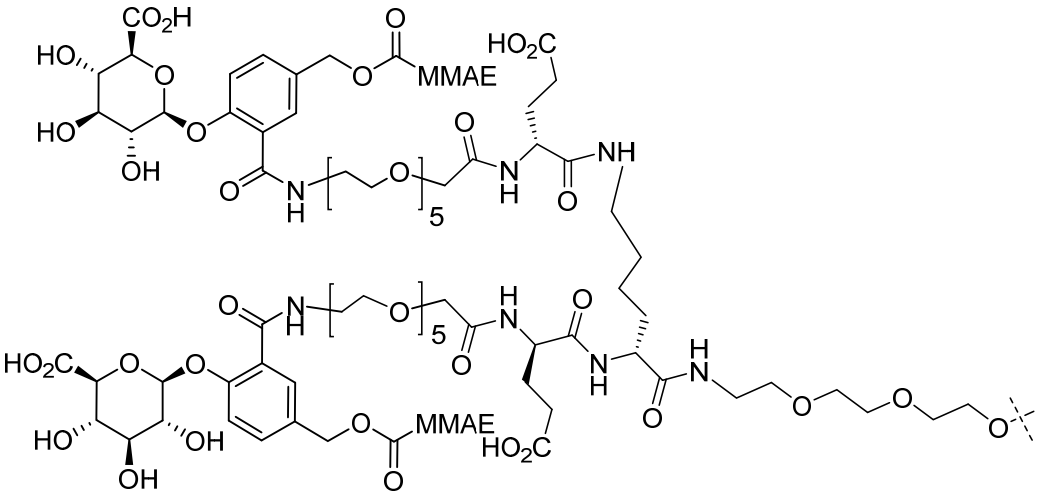
48. The conjugate of any one of claims 1-47, comprising:



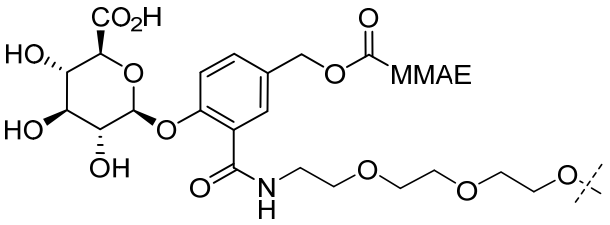
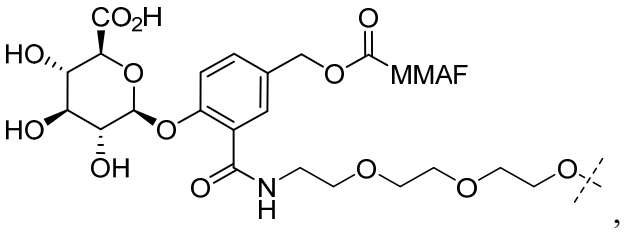
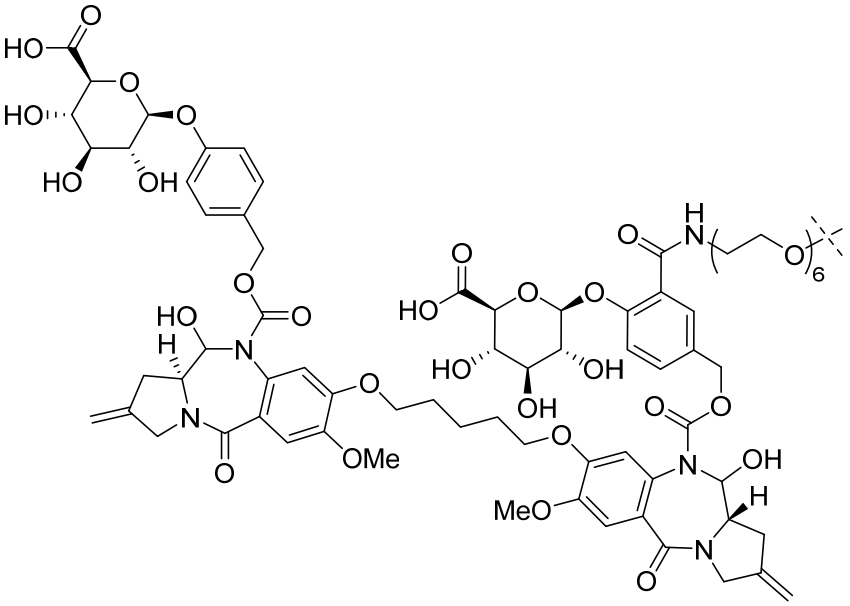
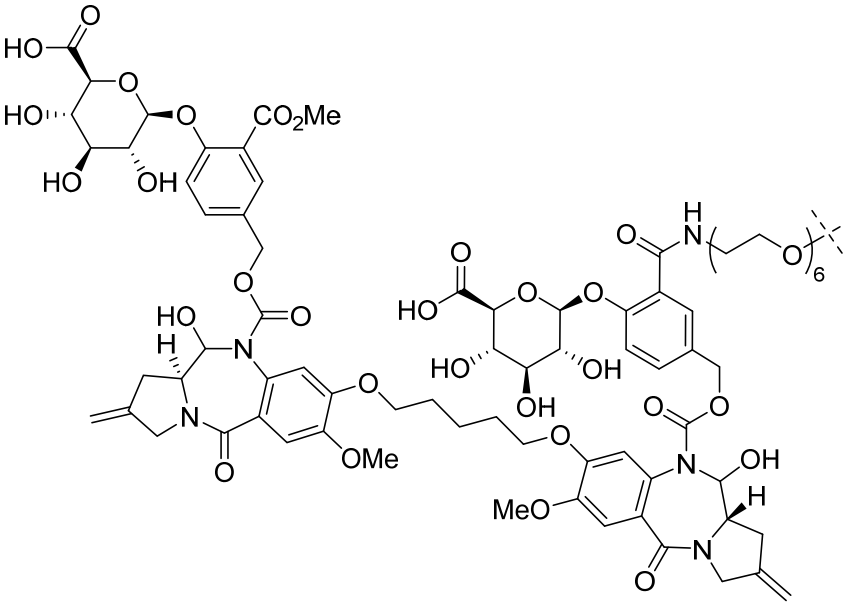
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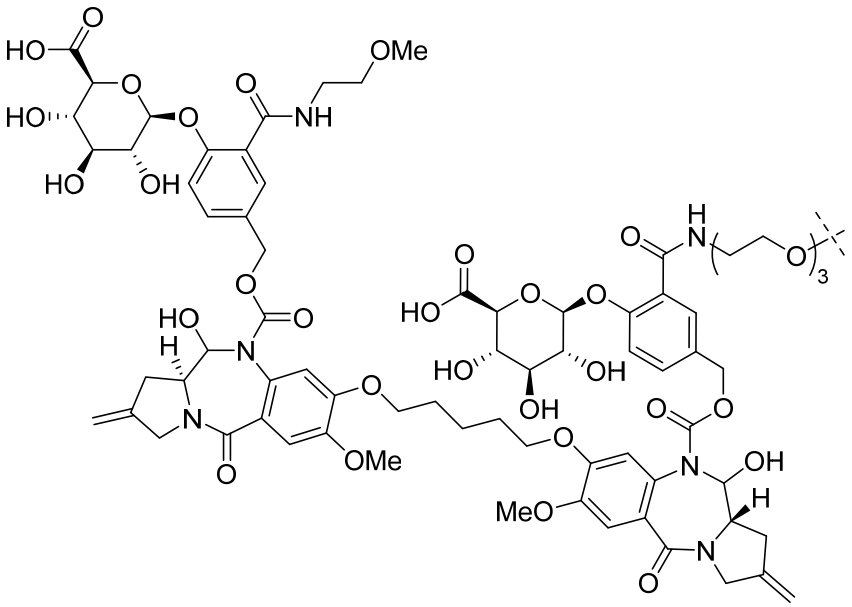


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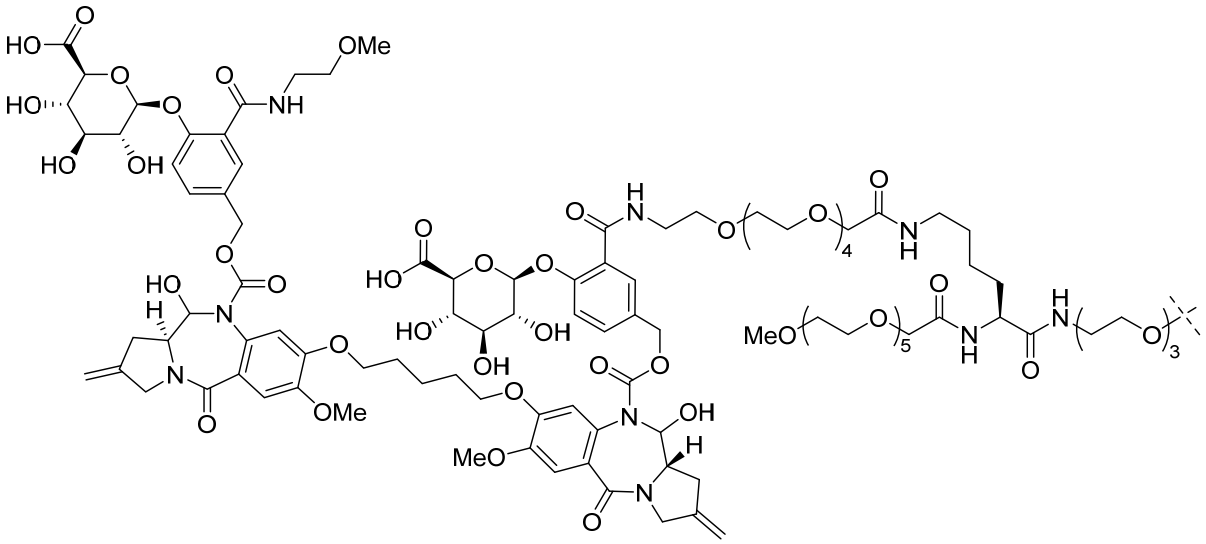


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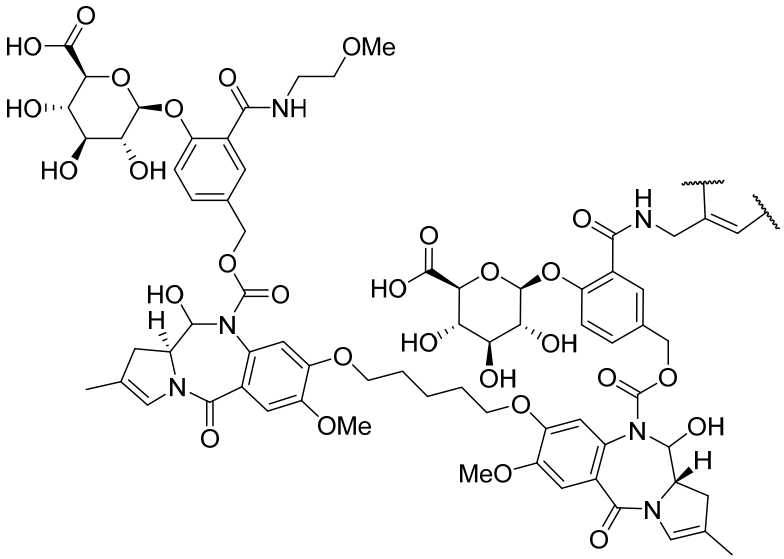

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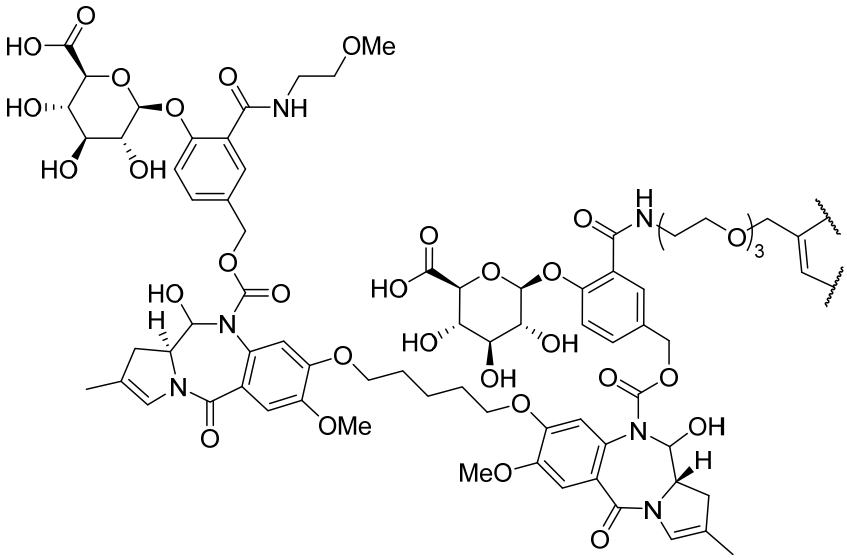
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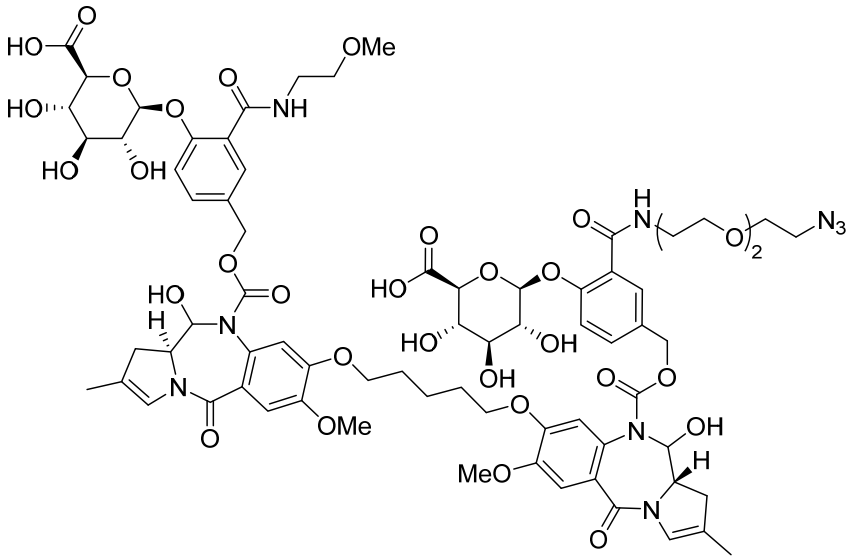
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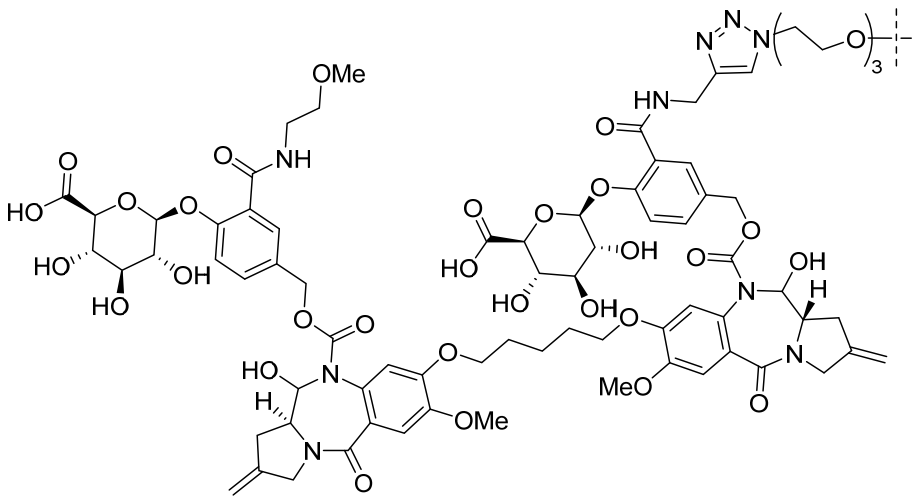
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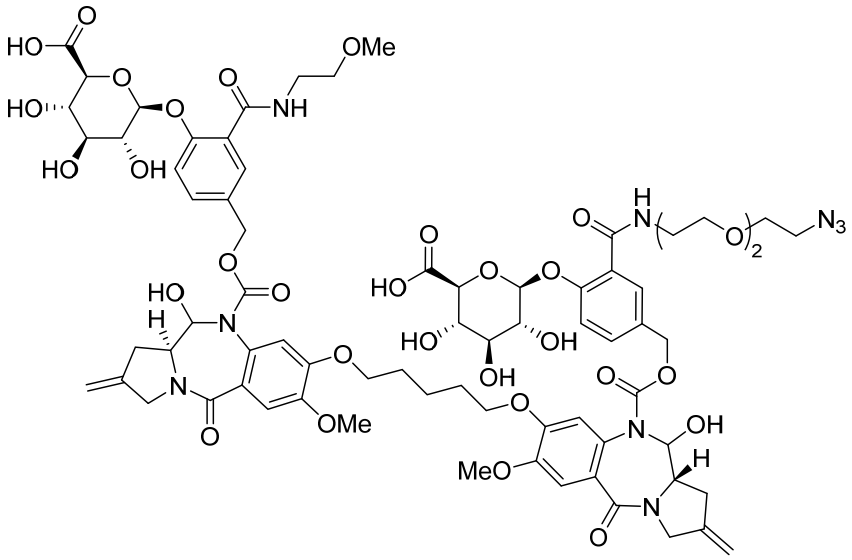
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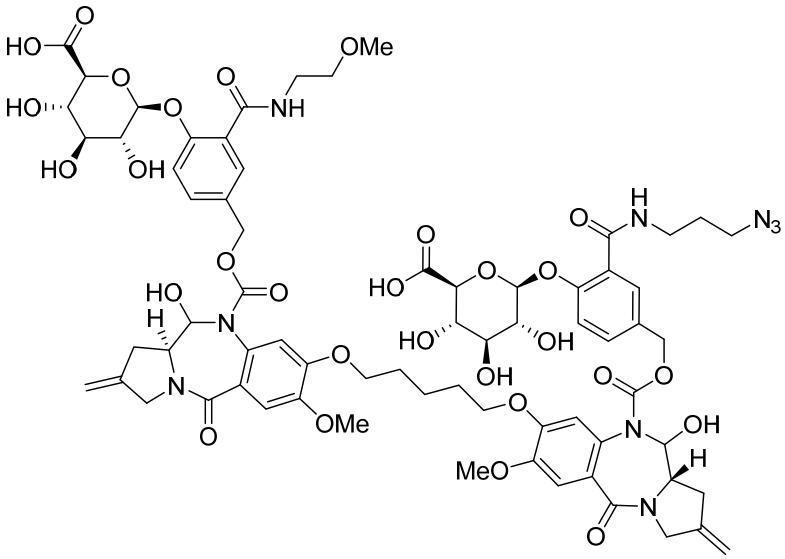
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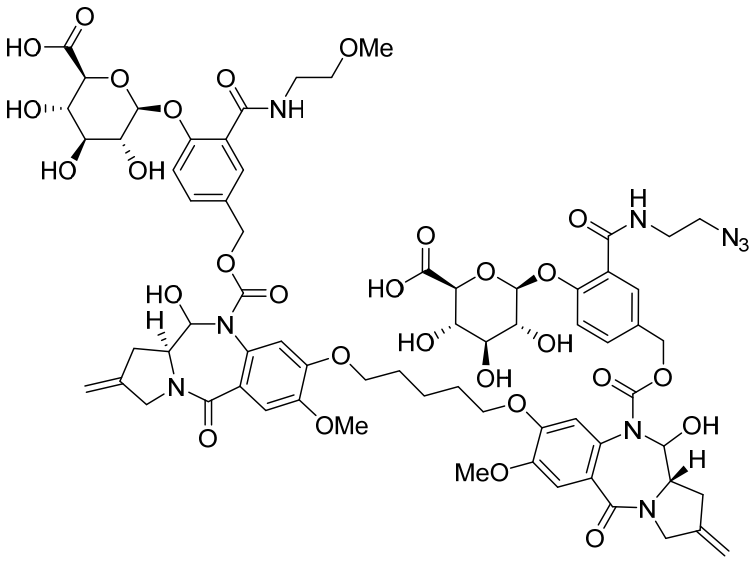
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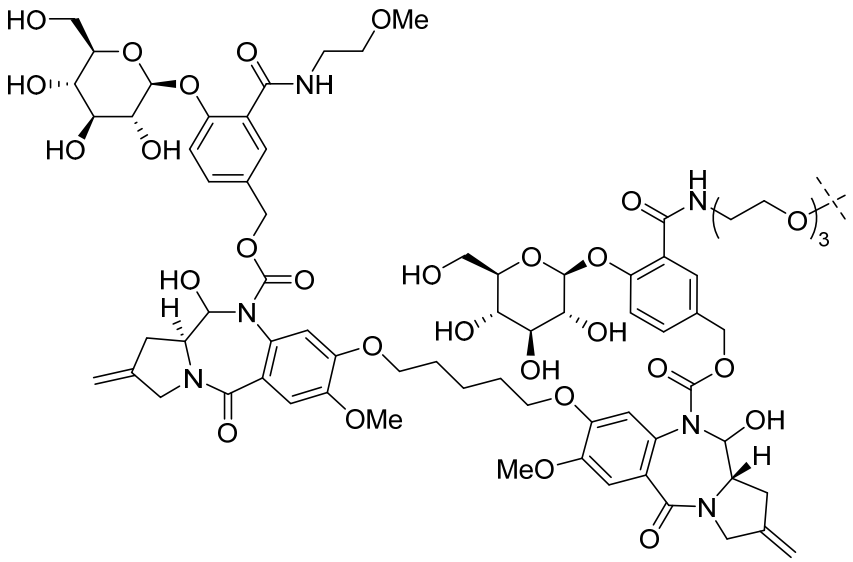
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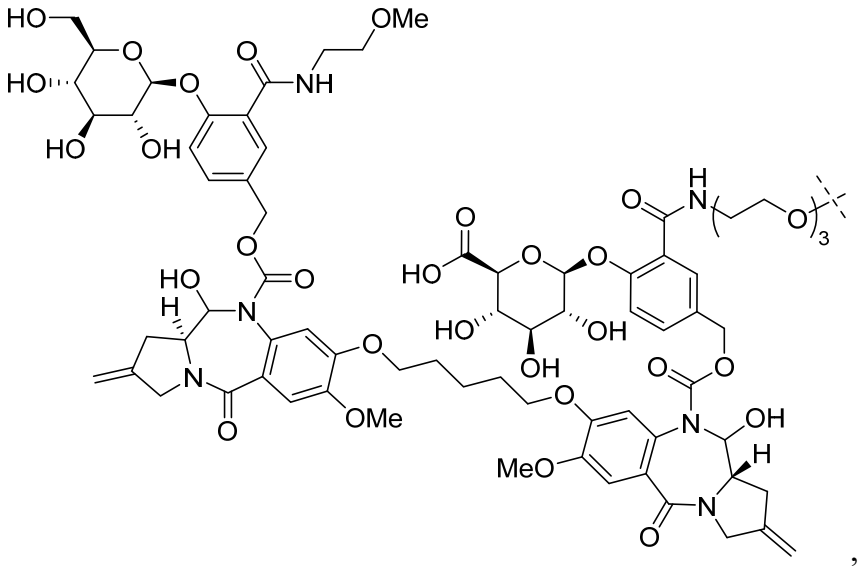
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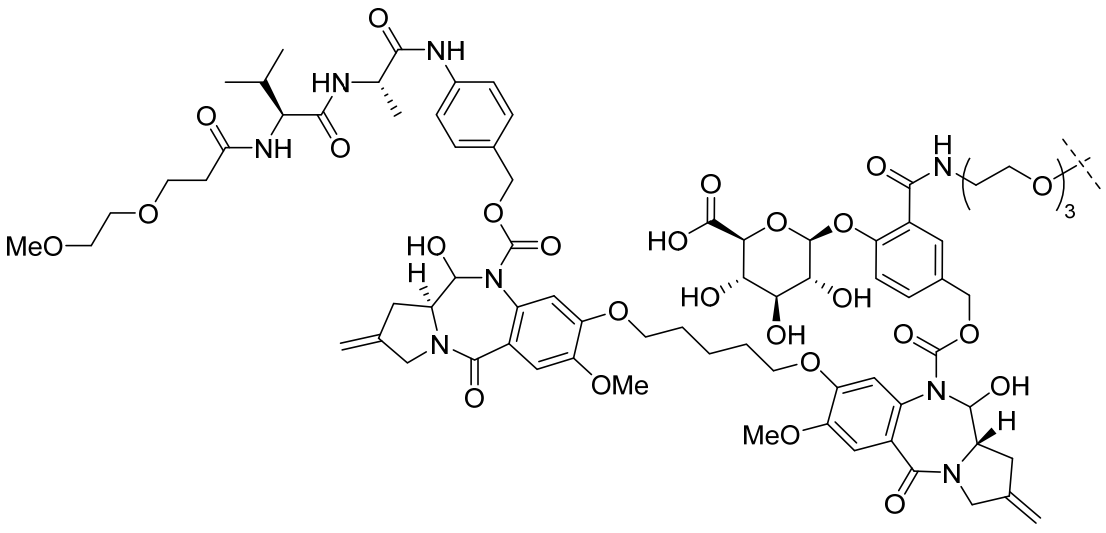
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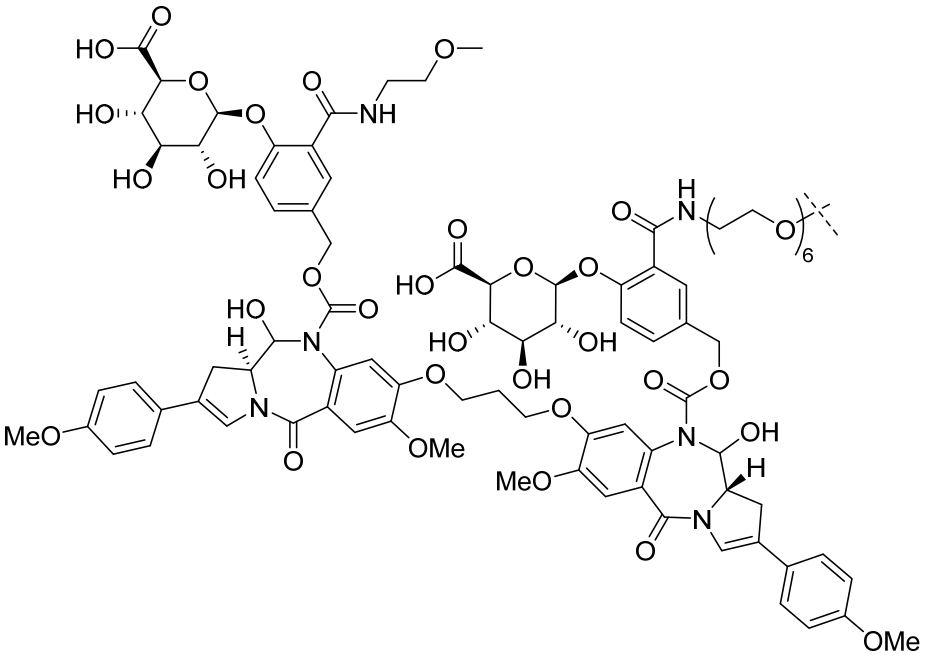
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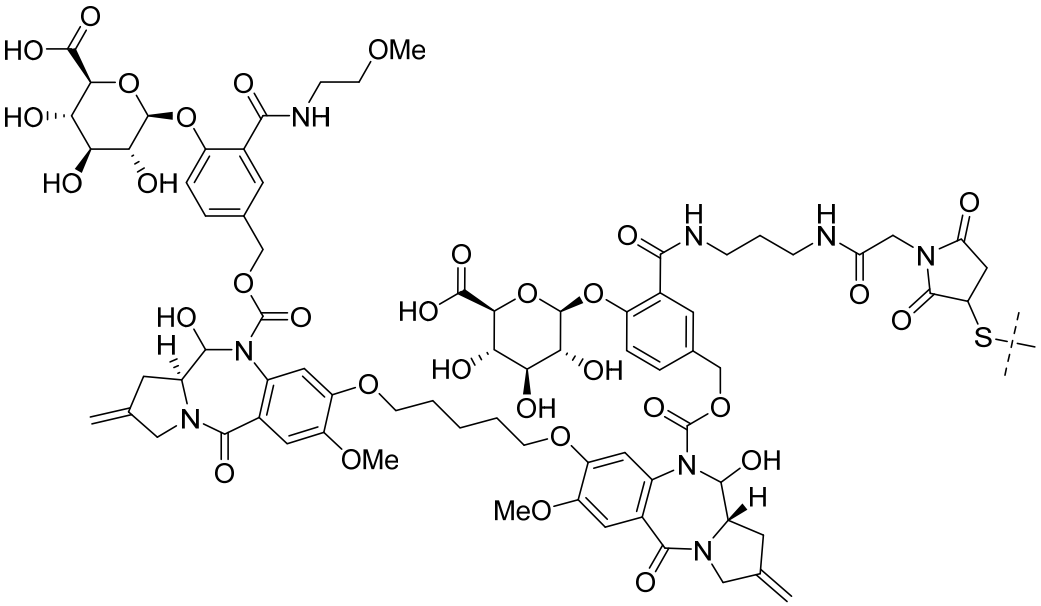
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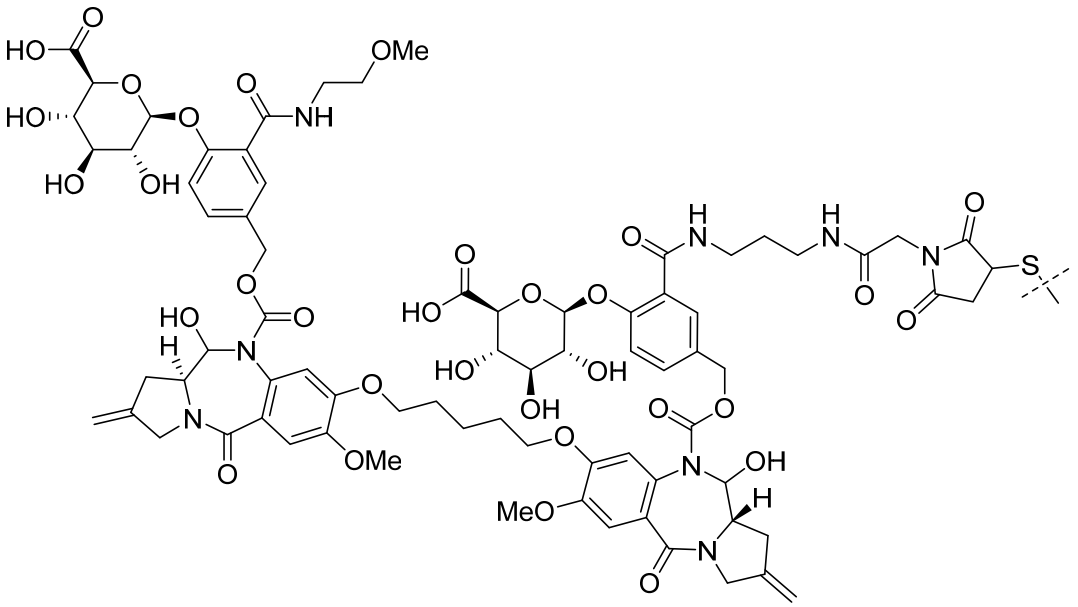
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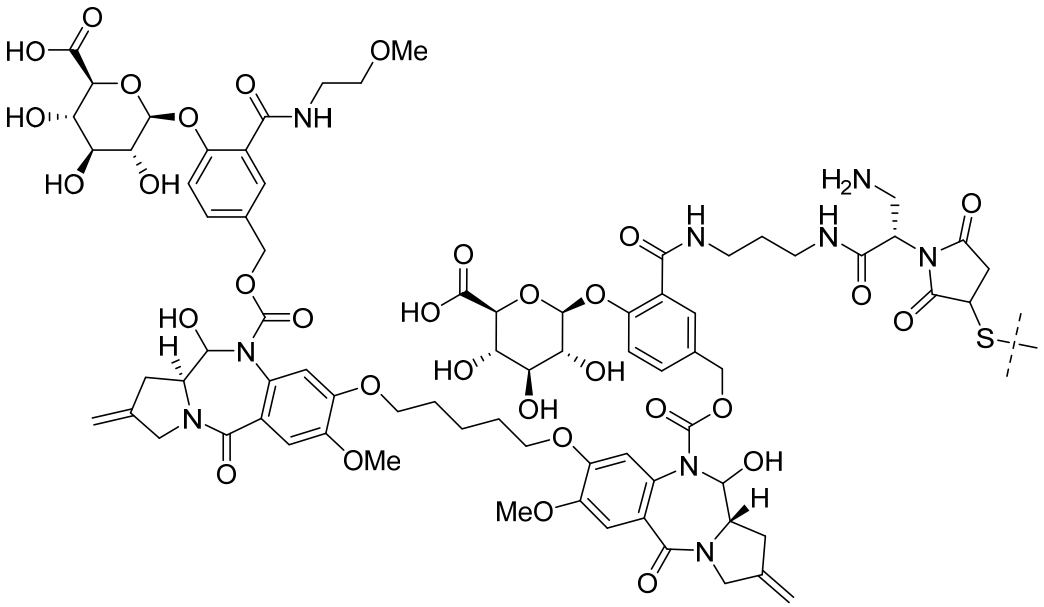
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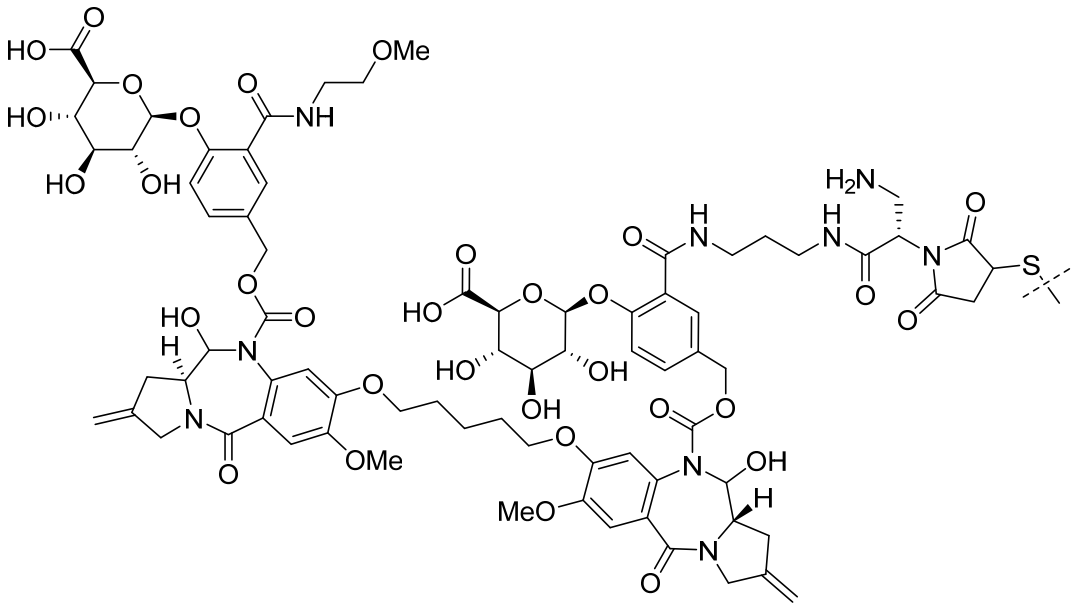
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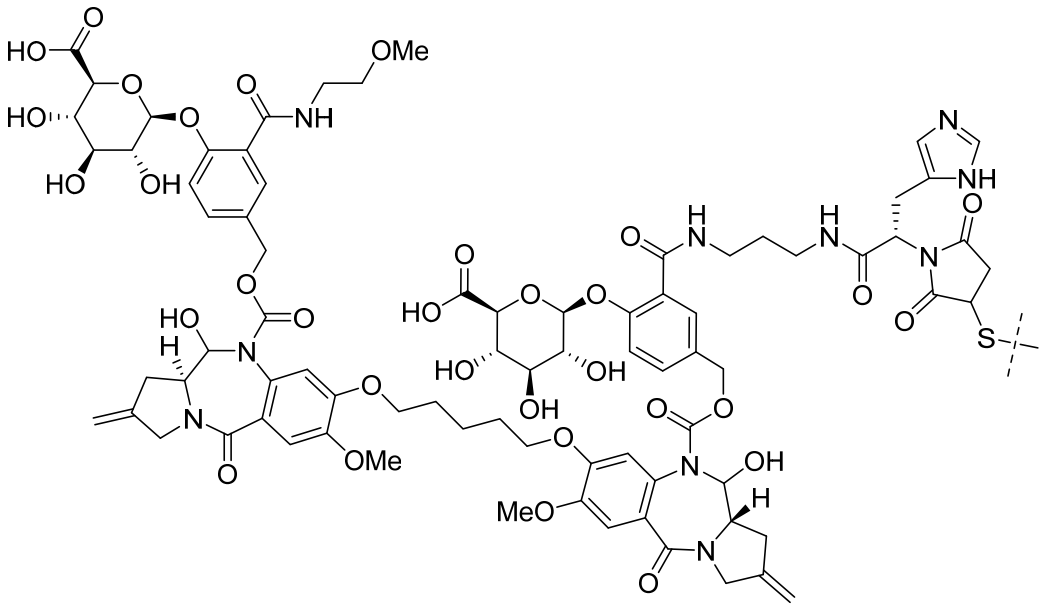
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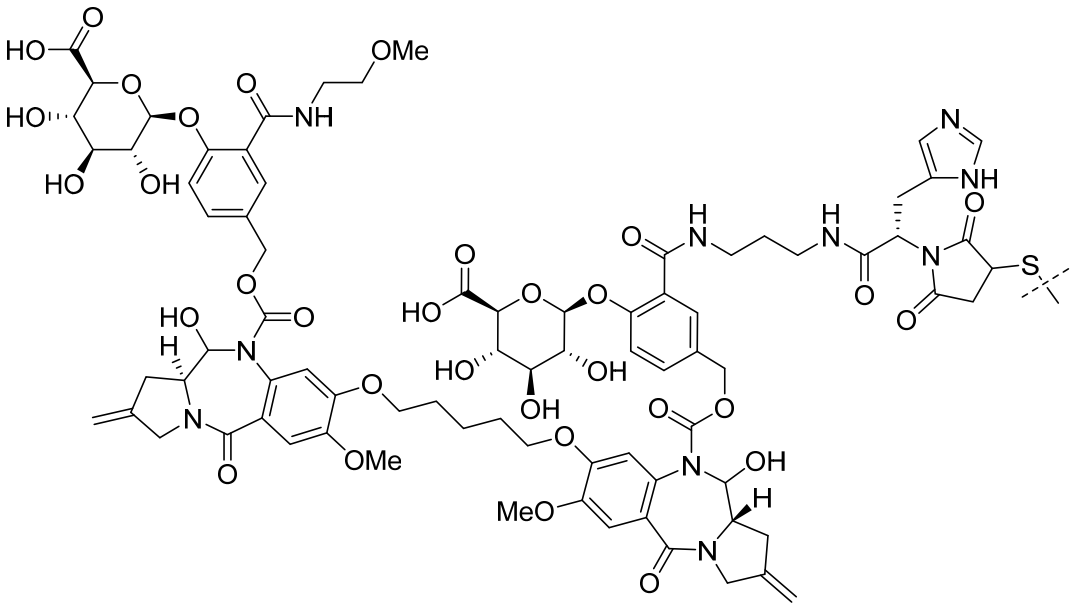
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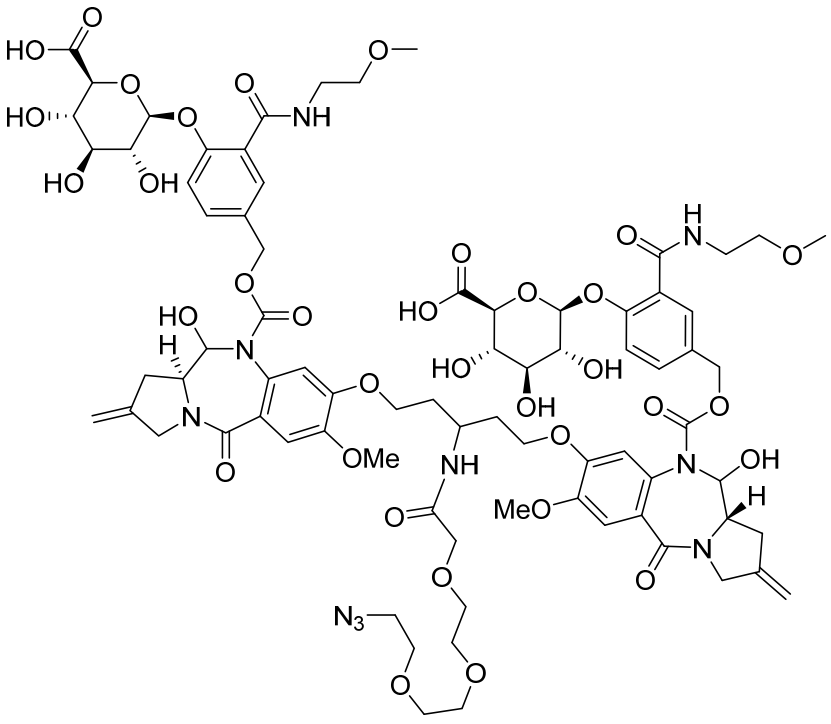
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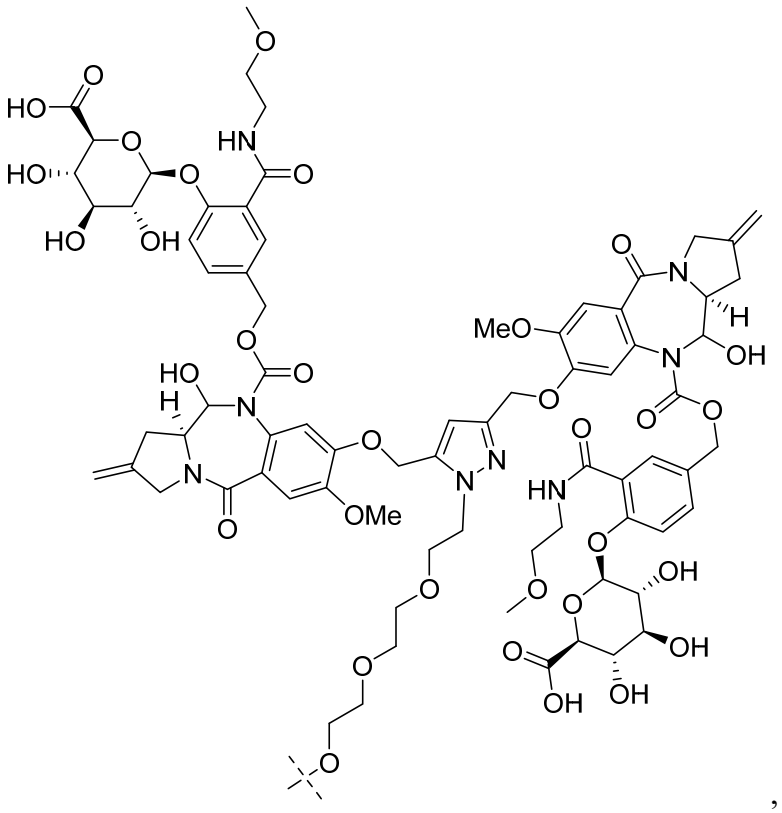
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wherein MMAE is monomethyl auristatin E, and

MMAF is monomethyl auristatin F.

49. A pharmaceutical composition comprising the conjugate of any one of claims 1-48 and a pharmaceutically acceptable excipient.

50. The pharmaceutical composition of claim 49, further comprising a chemotherapeutic agent.

51. Use of the conjugate of any one of claims 1-48 for the manufacture of a medicament for the prevention or treatment of hyperproliferation, cancer, or an angiogenic disease.

52. The use of claim 51, wherein the cancer is selected from lung cancer, gastrointestinal cancer, colon cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, liver cancer, kidney cancer, bladder cancer, pancreatic cancer, brain cancer, sarcoma, osteosarcoma, Kaposi's sarcoma, and melanoma.

53. The use of claim 52, wherein the lung cancer is small cell lung cancer.

54. A pharmaceutical preparation comprising the conjugate of any one of claims 1-48, and a pharmaceutically acceptable carrier, the pharmaceutical preparation being selected from injections, tablets, pills, powders, granules, capsules, troches, suspending agents, liquids for internal use, emulsions, syrups, freeze-dried preparations, and suppositories.