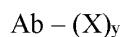


WHAT IS CLAIMED

1. An antibody conjugate of the General Formula I, or a pharmaceutically acceptable salt thereof:

[General Formula I]



wherein:

Ab is an antibody, or an antigen-binding fragment thereof specifically binding to the extracellular domain of ROR1, the antibody comprising a heavy chain variable region and a light chain variable region,

the antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region comprising a CDRH1 comprising the amino acid sequence of any one of SEQ ID NOs. 1-5; a CDRH2 comprising the amino acid sequence of any one of SEQ ID NOs. 6-13 and 96; and a CDRH3 comprising the amino acid sequence of any one of SEQ ID NOs. 14-21 and 97; and

a light chain variable region comprising a CDRL1 comprising the amino acid sequence of any one of SEQ ID NOs. 22-29; a CDRL2 comprising the amino acid sequence of any one of SEQ ID NOs. 30-37; and a CDRL3 comprising the amino acid sequence of any one of SEQ ID NOs. 38-42;

X is a chemical residue which independently includes at least one active agent and a linker; wherein the linker links Ab and the at least one active agent; and

y is an integer from 1 to 20.

2. The antibody conjugate of claim 1, wherein the antibody comprises a set of CDRs: CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, in which:

(a) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 1, 6 and 14, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 22, 30 and 38, respectively;

(b) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 2, 7 and 15, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 23, 31 and 39, respectively;

- (c) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 1, 8 and 16, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 24, 32 and 40, respectively;
- (d) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 3, 9 and 17, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 25, 33 and 41, respectively;
- (e) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 1, 10 and 18, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 26, 34 and 41, respectively;
- (f) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 4, 11 and 19, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 27, 35 and 42, respectively;
- (g) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs 5, 12 and 20, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs 28, 36 and 41, respectively;
- (h) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 3, 13 and 21, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 29, 37 and 41, respectively;
- (i) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 2, 96 and 15, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 23, 31 and 39, respectively; or
- (j) CDRH1, CDRH2 and CDRH3 comprise the amino acid sequence of SEQ ID NOs. 3, 9 and 97, respectively, and CDRL1, CDRL2 and CDRL3 comprise the amino acid sequence of SEQ ID NOs. 25, 33 and 41, respectively.

3. The antibody conjugate of claim 1 or 2, wherein the antibody comprises a heavy chain variable region comprising:

the amino acid sequence of any one of SEQ ID NOs. 43-50, 98 and 99;

at least 90% sequence identity to the amino acid sequence of any one of SEQ ID NOs 43-50, 98 and 99, or;

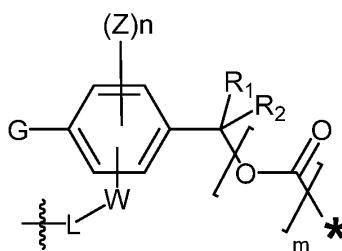
at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs 43-50, 98 and 99,

or a pharmaceutically acceptable salt or solvate thereof.

4. The antibody conjugate of any one of claims 1-3, wherein the antibody comprises a light chain variable region comprising:
the amino acid sequence of any one of SEQ ID NOs 51-58;
at least 90% sequence identity to the amino acid sequence of any one of SEQ ID NOs 51-58;
or
at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs 51-58,
or a pharmaceutically acceptable salt thereof.
5. The antibody conjugate of any one of claims 1-4, wherein the antibody comprises a combination of heavy chain and light chain variable regions comprising the amino acid sequence of: SEQ ID NOs. 43 and 51, respectively; SEQ ID NOs. 44 and 52, respectively; SEQ ID NOs. 45 and 53, respectively; SEQ ID NOs. 46 and 54, respectively; SEQ ID NOs. 47 and 55, respectively; SEQ ID NOs. 48 and 56, respectively; SEQ ID NOs. 49 and 57, respectively; SEQ ID NOs. 50 and 58, respectively; SEQ ID NOs. 98 and 52, respectively, or; SEQ ID NOs. 99 and 54, respectively.
6. The antibody conjugate of any one of claims 1-5, wherein the antibody comprises a combination of heavy chain and light chain variable regions comprising the amino acid sequence of: SEQ ID NOs. 59 and 67, respectively; SEQ ID NO 60 and 68, respectively; SEQ ID NO 61 and 69, respectively; SEQ ID NO 62 and 70, respectively; SEQ ID NO 63 and 71, respectively; SEQ ID NO 64 and 72, respectively; SEQ ID NO 65 and 73, respectively; or SEQ ID NO 66 and 74, respectively.
7. The antibody conjugate of claim 1 or 2, wherein the antibody 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 antibody conjugate of claim 1 or 2, wherein the antibody is a rabbit, mouse, chimeric, humanized, or fully human monoclonal antibody.

9. The antibody conjugate of any one of claims 1-8, wherein the antibody is of the IgG1, IgG2, IgG3 or IgG4 type.
10. The antibody conjugate of any one of claims 1-9, wherein the ROR1 is human ROR1 or mouse ROR1.
11. The antibody conjugate of any one of claims 1-10, wherein the linker between the antibody and the active agent comprises a cleavable bond (e.g., a bond cleavable by an enzyme).
12. The antibody conjugate of any one of claim 1-11, wherein the antibody drug conjugate has a structure represented by General Formula IIa:

[Chemical Formula (IIa)]



or a pharmaceutically acceptable salt thereof, wherein

G is a sugar, a sugar acid or a sugar derivative;

W is $-C(O)-$, $-C(O)NR'-$, $-C(O)O-$, $SO_2NR'-$, $-P(O)R''NR'-$, $-SONR'-$ or $-PO_2NR'-$; wherein the C , S or P is directly bound to the phenyl ring;

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

n is an integer from 0 to 3; and

m is 0 or 1;

L is absent, C_1 - C_{50} alkylene or 1-50 atom heteroalkylene, or L contains at least one branching unit (BR) and at least one connection unit;

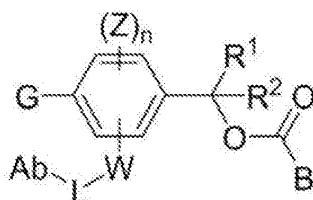
R^1 and R^2 are independently hydrogen, C_1 - C_8 alkyl or C_3 - C_8 cycloalkyl; or R_1 and R_2 , combine to complete a (C_3 - C_8) cycloalkyl ring;

$*$ represents a connection point to the active agent; and

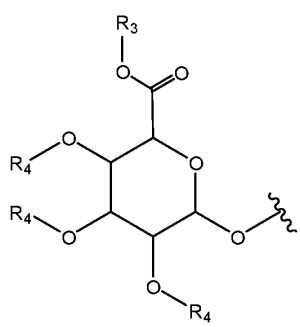
~~~~~ represents a connection point to the antibody.

13. The antibody conjugate of any one of claim 1-12, wherein the antibody drug conjugate has a structure represented by General Formula II:

[General Formula II]



or a pharmaceutically acceptable salt thereof, wherein



G is a glucuronic acid moiety or

R<sup>3</sup> is a hydrogen or carboxyl protecting group;

each of the R<sub>4</sub> are independently a hydrogen or hydroxyl protecting group;

B is an active agent;

R<sup>1</sup> and R<sup>2</sup> are respectively and independently hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

W is -C(O)-, -C(O)NR', -C(O)O-, SO<sub>2</sub>NR', -P(O)R''NR', -SONR' or -PO<sub>2</sub>NR'; wherein the C, S or P is directly bound to the phenyl ring;

R' and R'' are each independently are hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylthio, mono-or di- C<sub>1</sub>-C<sub>8</sub> alkylamino, C<sub>3</sub>-C<sub>20</sub> heteroaryl or C<sub>6</sub>-C<sub>20</sub> aryl;

each Z is independently C<sub>1</sub>-C<sub>8</sub> alkyl, halogen, cyano or nitro;

n is an integer of 0 to 3; and

L comprises:

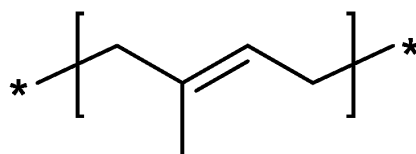
A) a C<sub>1</sub>-C<sub>50</sub> alkylene or 1-50 atom heteroalkylene satisfying at least one of the following:

- (i) L includes at least one unsaturated bond;
- (ii) L is substituted by a bivalent substituent where 2 atoms in L are the same as in a substituent, this completing a heteroarylene;

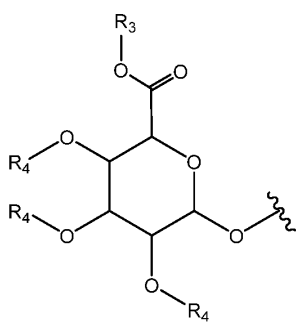
- (iii) L is a 1 to 50 atom heteroalkylene;
- (iv) L is substituted by at least one C<sub>1-20</sub> alkyl; or
- (v) L is interrupted by a heteroarylene; or

B) at least one isoprenyl derivative unit of General Formula III below which can be recognized by isoprenoid transferase :

[General Formula III]



14. The antibody conjugate of claim 12 or 13, wherein



G is

R<sup>3</sup> is a hydrogen or a carboxyl protecting group; and

each R<sup>4</sup> is, respectively and independently, a hydrogen or a hydroxyl protecting group.

15. The antibody conjugate of any one of claims 12-14, wherein R<sup>3</sup> is hydrogen, and each R<sup>4</sup> is hydrogen.

16. The antibody conjugate of any one of claims 12-15, wherein R<sup>1</sup> and R<sup>2</sup> are hydrogen.

17. The antibody conjugate of any one of claims 12-16, wherein Z is independently C<sub>1</sub>-C<sub>8</sub> alkyl, halogen, cyano or nitro.

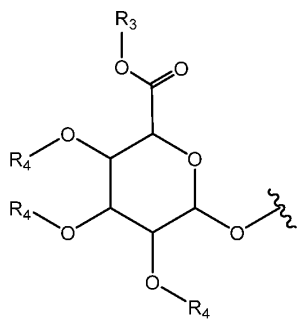
18. The antibody conjugate of any one of claims 12-17, wherein n is 0.

19. The antibody conjugate of any one of claims 12-18, wherein W is -C(O)-, -C(O)NR'-, -C(O)O-, SO<sub>2</sub>NR'-, -P(O)R''NR'-, -SONR'- or -PO<sub>2</sub>NR'-; the C, S or P is directly bound to the phenyl ring; the R' and R'' are respectively and independently compounds which are hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylthio, mono-or di- C<sub>1</sub>-C<sub>8</sub> alkylamino, C<sub>3</sub>-C<sub>20</sub> heteroaryl or C<sub>6</sub>-C<sub>20</sub> aryl.

20. The antibody conjugate of any one of claims 12-19, wherein W is -C(O)-, -C(O)NR'- or -C(O)O-.

21. The antibody conjugate of any one of claims 12-20, wherein W is -C(O)NR'-; and the C(O) binds to a phenyl ring, and NR' binds to L.

22. The antibody conjugate of any one of claims 12-21, wherein



G is ;

W is -C(O)NR'-, the C(O) is bound to the phenyl ring, NR' binds to L; and R<sub>3</sub> and R<sub>4</sub> are hydrogen.

23. The antibody conjugate of any one of claims 12-22, wherein L is C<sub>1</sub>-C<sub>50</sub> alkylene or a 1-50 atom heteroalkylene comprising at least one of:

- (i) L includes at least one unsaturated bond;
- (ii) L is substituted by a bivalent substituent where 2 atoms in L are the same as in a substituent, this completing a heteroarylene;
- (iii) L is a 1 to 50 atom heteroalkylene;
- (iv) L is substituted by at least one C<sub>1-20</sub> alkyl; or
- (v) L is interrupted by a heteroarylene.

24. The antibody conjugate of any one of claims 12-23, wherein L is C<sub>1</sub>-C<sub>50</sub> alkylene or a 1-50 atom heteroalkylene comprising at least one of:

- (i) an unsaturated bond;
- (ii) a heteroarylene;
- (iii) a 1 to 50 atom heteroalkylene; or
- (iv) at least one C<sub>1-20</sub> alkyl substituent.

25. The antibody conjugate of any one of claims 12-23, wherein L is a nitrogen-comprising 1-50 atom heteroalkylene, the linker includes at least 2 atoms of a hydrophilic amino acid; and the nitrogen forms a peptide bond with a carbonyl of a hydrophilic amino acid.

26. The antibody conjugate of any one of claims 12-25, wherein W is -C(O)NR', and the nitrogen of W is a nitrogen atom of a hydrophilic amino acid.

27. The antibody conjugate of claim 25 or 26, wherein the hydrophilic amino acid any one selected from a group comprising arginine, aspartate, asparagine, glutamate, glutamine, histidine, lysine, ornithine, proline, serine and threonine.

28. The antibody conjugate of any one of claims 25-27, wherein the amino acid covalently bonds an oxime of a linker to a polyethylene glycol unit of the linker.

29. The antibody conjugate of any one of claims 25-28, wherein the amino acid is selected from arginine, aspartate, asparagine, glutamate, glutamine, histidine, lysine, ornithine, proline, serine and threonine.

30. The antibody conjugate of any one of claims 25-29, wherein the hydrophilic amino acid comprises a side chain having a moiety which has electric charge in aqueous solution at a neutral pH.

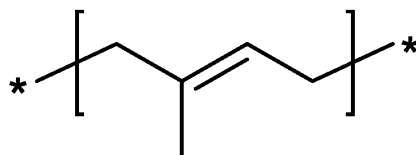
31. The antibody conjugate of any one of claims 25-30, wherein the hydrophilic amino acid is aspartate or glutamate.

32. The antibody conjugate of any one of claims 25-30, wherein the hydrophilic amino acid is ornithine or lysine.

33. The antibody conjugate of any one of claims 25-30, wherein the hydrophilic amino acid is arginine.
34. The antibody conjugate of any one of claims 25-33, wherein L further comprises a peptide, and the peptide comprises at least once hydrophilic amino acid and includes a side chain having a moiety which has electric charge in aqueous solution at a neutral pH.
35. The antibody conjugate of claim 34, wherein each amino acid of the peptide is independently selected from alanine, aspartate, asparagine, glutamate, glutamine, glycine, lysine, ornithine, proline, serine and threonine.
36. The antibody conjugate of claim 34 or 35, wherein the peptide comprises at least one aspartate or glutamate.
37. The antibody conjugate of any one of claims 12-36, wherein W is  $-C(O)NR'$ -, and in that the nitrogen of W is a nitrogen atom of an N-terminal amino acid of a peptide.
38. The antibody conjugate of claim 37, wherein the peptide covalently bonds an oxime of a linker to a polyethylene glycol unit of the linker.
39. The antibody conjugate of any one of claims 34-38, wherein the peptide comprises 2 to 20 amino acids.
40. The antibody conjugate of any one of claims 12-39, wherein L is covalently bonded to the antibody by a thioether bond, and the thioether bond includes a sulfur atom of the cysteine of the antibody.
41. The antibody conjugate of any one of claims 12-40, wherein the antibody comprises an amino acid motif which can be recognized by isoprenoid transferase at the C-terminal of the antibody, and the thioether bond includes a sulfur atom of the cysteine of the antibody.
42. The antibody conjugate of claim 41, wherein the amino acid motif is a CYYX sequence; C is cysteine; Y is an aliphatic amino acid; X is any one selected from glutamine, glutamate, serine, cysteine, methionine, alanine and leucine; and the thioether bond includes a sulfur atom of the cysteine of the antibody.

43. The antibody conjugate of claim 42 or 43, wherein the amino acid motif is a CYYX sequence; and Y is any one selected from alanine, isoleucine, leucine, methionine and valine.
44. The antibody conjugate of any one of claims 41-43, wherein the amino acid motif is a CVIM or CVLL sequence.
45. The antibody conjugate of any one of claims 41-44, wherein at least one of the 1 to 20 amino acids preceding the amino acid motif is glycine.
46. The antibody conjugate of any one of claims 41-45, wherein at least three of the 1 to 20 amino acids preceding the amino acid motif is glycine or proline.
47. The antibody conjugate of any one of claims 41-46, wherein at least one of the 1 to 20 amino acids preceding the amino acid motif is any one selected from glycine, aspartic acid, arginine and serine.
48. The antibody conjugate of any one of claims 41-47, wherein at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids preceding the amino acid motif is (are) respectively glycine.
49. The antibody conjugate of any one of claims 41-48, wherein L further comprises the amino acid sequence GGGGGGCVIM at the C-terminal.
50. The antibody conjugate of any one of claims 12-49, wherein L further comprises at least one isoprenyl derivative unit of General Formula III:

[General Formula III]

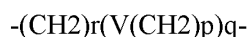


51. The antibody conjugate of any one of claims 12-50, wherein L is a 3 to 50 heteroalkylene comprising oxime and the oxygen atom of the oxime is on the side of L linked to W and the carbon atom of the oxime is on the side of L linked to Ab; or the carbon atom of the oxime is on the side of L linked to W and the oxygen atom of the oxime is on the side of L linked to Ab.

52. The antibody conjugate of any one of claims 12-51, wherein L further comprises an oxime and at least one isoprenyl unit covalently binds the oxime to Ab.

53. The antibody conjugate of any one of claims 12-52, wherein L further comprises a connecting units represented by General Formula VIII or General Formula IX:

[General Formula VIII]



[General Formula IX]



wherein

V is a single bond, -O-, -S-, -NR<sup>21</sup>-, -C(O)NR<sup>22</sup>-, NR<sup>23</sup>C(O)-, NR<sup>24</sup>SO<sub>2</sub>-, or -SO<sub>2</sub>NR<sup>25</sup>-;

X is -O-, C<sub>1</sub>-C<sub>8</sub> alkylene or -NR<sup>21</sup>-;

R<sup>21</sup> to R<sup>25</sup> are, independently and respectively hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkyl (C<sub>6</sub>-C<sub>20</sub>) aryl, or (C<sub>1</sub>-C<sub>6</sub>) alkyl (C<sub>3</sub>-C<sub>20</sub>) heteroaryl;

r is an integer of 0 to 10;

p is an integer of 0 to 10;

q is an integer of 1 to 20; and

w is an integer of 1 to 20.

54. The antibody conjugate of claim 53, wherein q is an integer of 4 to 20.

55. The antibody conjugate of claim 53 or 54, wherein q is an integer of 2 to 12.

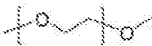
56. The antibody conjugate of claim 53 or 54, wherein q is an integer of 6 to 20.

57. The antibody conjugate of claim any one of claims 53-55, wherein q is an integer of 2, 5 or 11.

58. The antibody conjugate of any one of claims 53-57, wherein r is an integer of 2.

59. The antibody conjugate of any one of claims 53-58, wherein p is an integer of 2.

60. The antibody conjugate of any one of claims 53-59, wherein V is -O-.

61. The antibody conjugate of claim 53, wherein :  
r is an integer of 2;  
p is an integer of 2;  
q is an integer of 2, 5 or 11; and  
V is -O-.
62. The antibody conjugate of any one of claims 53-61, wherein X is -O-.
63. The antibody conjugate of any one of claims 63-62, wherein w is an integer of 6 to 20.
64. The antibody conjugate of any one of claims 53-63, wherein X is -O-, and w is an integer of 6 to 20.
65. The antibody conjugate of any one of claims 12-64, wherein L further comprises at least one polyethylene glycol unit represented by  or .
66. The antibody conjugate of any one of claims 12-65, wherein L further comprises 1 to 12 -OCH<sub>2</sub>CH<sub>2</sub>- units.
67. The antibody conjugate of any one of claims 12-66, wherein L further comprises 3 to 12 -OCH<sub>2</sub>CH<sub>2</sub>- units.
68. The antibody conjugate of any one of claims 12-67, wherein L comprises 5 to 12 -OCH<sub>2</sub>CH<sub>2</sub>- units.
69. The antibody conjugate of any one of claims 12-68, wherein L comprises 6 to 12 -OCH<sub>2</sub>CH<sub>2</sub>- units.
70. The antibody conjugate of any one of claims 12-67, wherein L further comprises 3 -OCH<sub>2</sub>CH<sub>2</sub>- units.

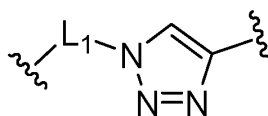
71. The antibody conjugate of any one of claims 12-68, wherein L further comprise an oxime and at least one polyethylene glycol unit covalently bonds the oxime to an active agent.

72. The antibody conjugate of any one of claims 12-71, wherein L further comprises a unit formed by 1,3-dipolar cycloaddition reactions, hetero-diels reactions, nucleophilic substitution reactions, nonaldol type carbonyl reactions, additions to carbon-carbon multiple bonds, oxidation reactions or click reactions.

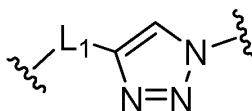
73. The antibody conjugate of claim 72, wherein the binding units are formed through reaction of acetylene and azide, or through reaction of an aldehyde or ketone group with hydrazine or hydroxylamine.

74. The antibody conjugate of any one of claims 12-73, wherein L further comprises a binding unit represented by General Formulae IV, V, VI or VII below:

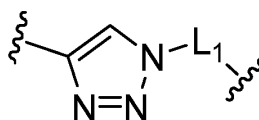
[General Formula IV]



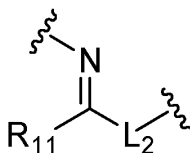
[General Formula V]



[General Formula VI]



[General Formula VII]



wherein

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

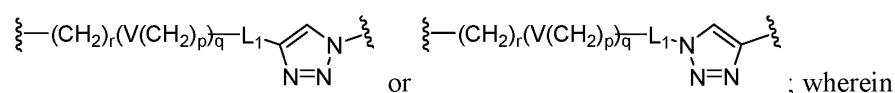
$R^{11}$  is a hydrogen or an alkyl of  $C_1$ - $C_{10}$ .

75. The antibody conjugate of claim 74, wherein  $L^1$  is a single bond.

76. The antibody conjugate of claim 74, wherein  $L^1$  is a  $C_{11}$ -alkylene.

77. The antibody conjugate of claim 74, wherein  $L^1$  is a  $C_{12}$ -alkylene.

78. The antibody conjugate of claim 74, wherein L further comprises



V is a single bond, -O-, -S-, -NR<sup>21</sup>-, -C(O)NR<sup>22</sup>-, NR<sup>23</sup>C(O)-, NR<sup>24</sup>SO<sub>2</sub>-, or -SO<sub>2</sub>NR<sup>25</sup>-;

R<sup>21</sup> to R<sup>25</sup> are, independently and respectively 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 an integer of 1 to 10;

p is an integer of 0 to 10;

q is an integer of 1 to 20; and

$L^1$  is a single bond.

79. The antibody conjugate of claim 78, wherein r is an integer of 2 or 3.

80. The antibody conjugate of claim 78 or 79, wherein p is an integer of 1 or 2.

81. The antibody conjugate of any one of claims 78-80, wherein q is an integer of 1 to 6.

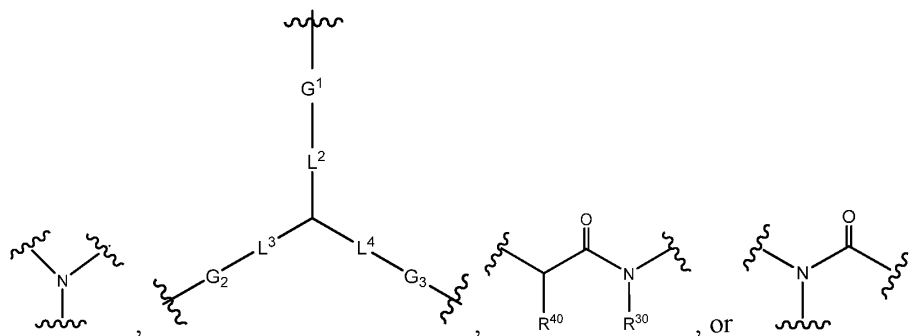
82. The antibody conjugate of claim 78, wherein r is an integer of 2 or 3; p is an integer of 1 or 2; and q is an integer of 1 to 6.

83. The antibody conjugate of any one of claims 12-83, wherein the isoprenoid transferase is a farnesyl protein transferase (FTase) or a geranylgeranyl transferase (GGTase).

84. The antibody conjugate of any one of claims 12-83, wherein L further comprises one or more branched linkers covalently coupled to Ab, wherein

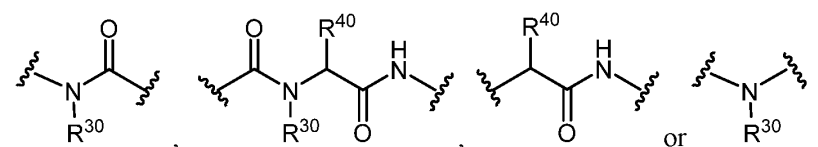
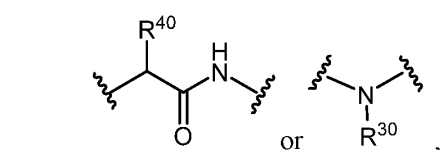
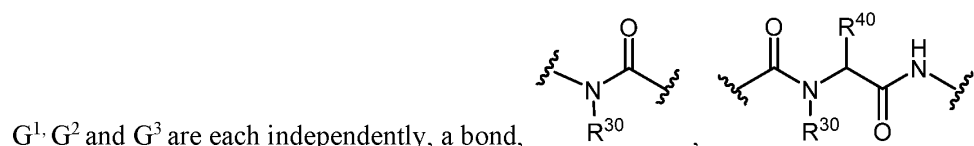
- i) each branched linker comprises a branching unit (BR) covalently coupled to Ab by a primary linker (PL);
  - ii) each branched linker comprises a first branch (B1), in which a first active agent is covalently coupled to the branching unit by a secondary linker (SL) and a cleavage group (CG); and
  - iii) each branched linker further comprises a second branch (B2), in which either a) a second active agent is covalently coupled to the branching unit by a secondary linker (SL) and a cleavage group (CG) or b) a polyethylene glycol moiety is covalently coupled to the branching unit,
- wherein each cleavage group can be hydrolyzed to release the active agent from the antibody-drug conjugate.

85. The antibody conjugate of claim 84, wherein the branching unit is represented by:



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

n is an integer of 1 to 30;



R<sup>30</sup> is hydrogen or C<sub>1-30</sub> alkyl;

L<sup>5</sup> is a direct bond or C<sub>1-10</sub> alkylene; and  
R<sup>50</sup> is hydrogen C<sub>1-30</sub> alkyl.

86. The antibody conjugate of claim 84 or 85, wherein the antibody conjugate comprises at least one branched linker covalently bonded to Ab; and at least two active agents covalently linked to the branched linker.

87. The antibody conjugate of any one of claims 84-86, wherein the antibody conjugate comprises at two or more branched linker covalently bonded to Ab; and the branched linkers bind to at least two active agents.

88. The antibody conjugate of claim 86 or 87, wherein the antibody conjugate comprises 3 branched linkers.

89. The antibody conjugate of claim 86 or 87, wherein the antibody conjugate comprises 4 branched linkers.

90. The antibody conjugate of claim 86 or 87, wherein the antibody conjugate comprises 1 branched linker.

91. The antibody conjugate of claim 86 or 87, wherein the respective branched linkers each bind to two active agents.

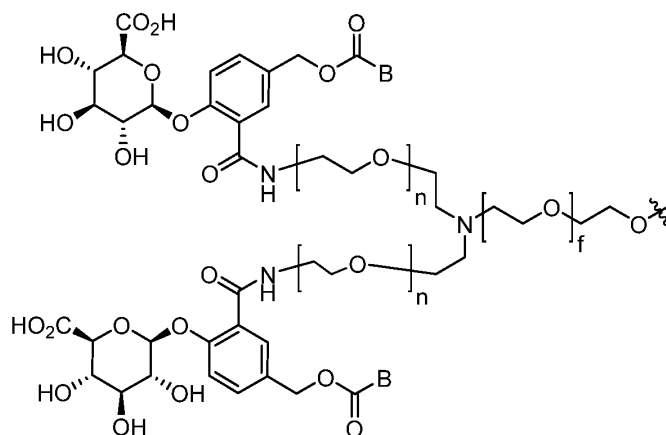
92. The antibody conjugate of claim 86 or 87, wherein the conjugate comprises at least two different active agents.

93. The antibody conjugate of any one of claims 86-92, wherein the branched linker is bonded to at least two active agents.

94. The antibody conjugate of any one of claims 84-93, wherein the active agents are bonded to a branched linker by a cleavable bond.

95. The antibody conjugate of claim 84 or 85, wherein the active agents bind to a branching unit through a second linker; and the branching units are bonded to an anti-ROR1 antibody by a first linker.

96. The antibody conjugate of any one of claims 84-95, wherein the branching unit is a nitrogen atom.
97. The antibody conjugate of any one of claims 84-96, wherein the branching unit is an amide, and the first linker comprises a carbonyl of the amide.
98. The antibody conjugate of any one of claims 84-96, wherein the branching unit is an amide, and the second linker comprises a carbonyl of the amide.
99. The antibody conjugate of any one of claims 84-98, wherein the branching unit is a lysine unit.
100. The antibody conjugate of claim 12-85, wherein the antibody conjugate comprises a structure represented by:



wherein

B active agents;

each n is independently an integer of 0 to 30; and

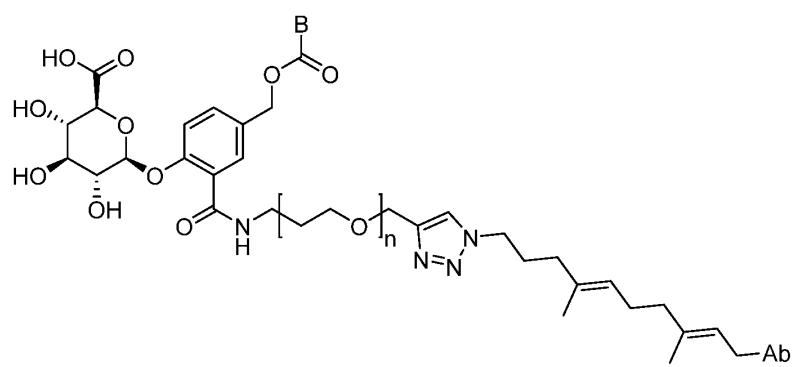
each n is independently an integer of 0 to 30.

101. The antibody conjugate of claim 100, wherein n is an integer of 1 to 10.
102. The antibody conjugate of claim 100, wherein n is an integer of 4 to 20.
103. The antibody conjugate of any one of claims 100-102, wherein L comprises oxime, and at least one polyethylene glycol unit covalently binds the oxime to an active agent.

104. The antibody conjugate according to any one of claims 11-103, wherein the cleavable bond is cleavable within a target cell.

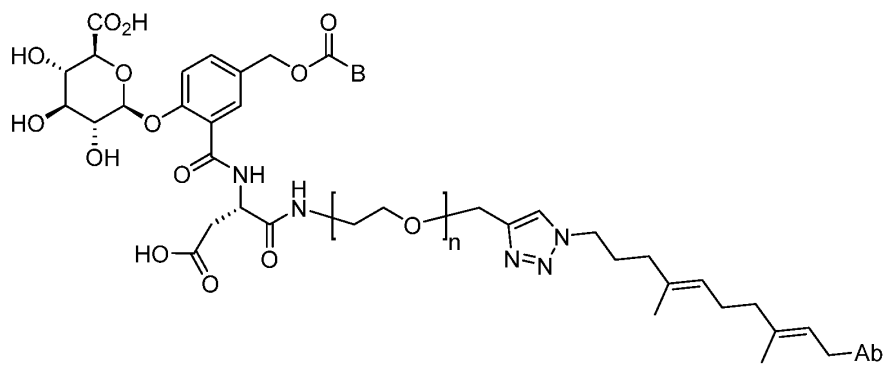
105. The antibody conjugate according to any one of claims 11-103, wherein the cleavable bond is cleavable by an activator (e.g., radiation, acid, base, or an enzyme).

106. The antibody conjugate of any one of claims 1-11, wherein the conjugate is represented by the following structure or a pharmaceutically acceptable salt thereof:



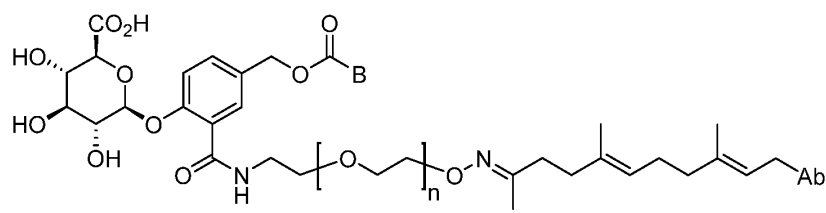
wherein Ab is an anti-ROR1 antibody; B is an active agent and; n is an integer of 1 to 20.

107. The antibody conjugate of any one of claims 1-11, wherein the conjugate is represented by the following structure or a pharmaceutically acceptable salt thereof:



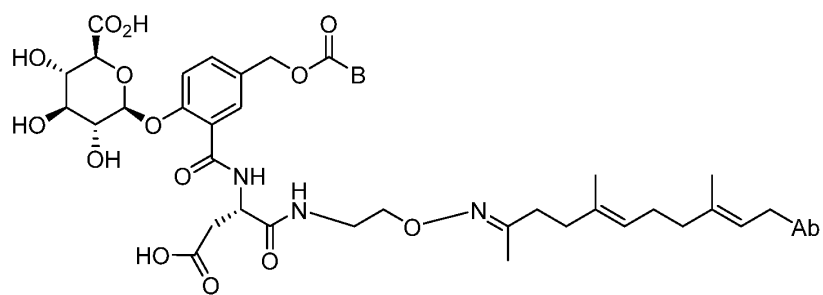
wherein Ab is an anti-ROR1 antibody; B is an active agent and; n is an integer of 1 to 20.

108. The antibody conjugate of any one of claims 1-11, wherein the conjugate is represented by the following structure or a pharmaceutically acceptable salt thereof:



wherein Ab is an anti-ROR1 antibody; B is an active agent and; n is an integer of 1 to 20.

109. The antibody conjugate of any one of claims 1-11, wherein the conjugate is represented by the following structure or a pharmaceutically acceptable salt thereof:



wherein Ab is an anti-ROR1 antibody; B is an active agent and; n is an integer of 1 to 20.

110. The antibody conjugate of any one of claims 1-109, wherein the active agent is a chemotherapeutic agent or a toxin.

111. The antibody conjugate of any one of claims 1-110, wherein the active agent is an immunoregulatory compound, anti-cancer agent, antiviral, antibacterial, antifungal, antiparasitic or a combination of these.

112. The antibody conjugate of any one of claims 1-111, 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, triethylenephosphoramidate, triethylenethiophosphoramidate, teimethylolomelamine, bullatacin, bullatacinone, camptothecin, topotecan, bryostatin, calyculin, 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, antrymycin, azaserine, bleomycins, catcinomycin, carabycin, carinomycin, carzinophilin, chromomycins, dactinomycin, daunorubicin, detorubicin, 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, tudecridin, ubenimex, zinostatin, zorubicin, 5-fluororacil, denopterin, methotrexate, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thiguanine, ancitabine, azacytidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, calusterone, dromostanolone, propionate, epitio stanol, mepitio stane, testolactone, aminoglutethimide, mitotane, trilostane, folinic acid, aceglatone, aldophosphamide glycoside, aminolevulinic acid, eniluracil, amsacrine, bestrabucil, bisantrene, edatrexate, defofamine, democolcine, 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, triaquizuone, 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 pharmaceutically acceptable salts, solvates or acids thereof;

- (b) monokine, lymphokine, traditional polypeptide hormone, parathyroid hormone, thyroxine, relaxin, prolaxin, 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- $\alpha$ , tumor necrosis factor- $\beta$ , Mullerian inhibiting substance, mouse gonadotropin associated peptide, inhibin, activin, vascular endothelial growth factor, thrombopoietin, erythropoietin, osteoinductive factor, interferon, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , colony stimulating factor (CSF), macrophage-CSF, granulocyte-macrophage-CSF, granulocyte-macrophage-CSF, granulocyte-CSF, interleukin (IL), IL-1, IL-1 $\beta$ , 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 mixtures thereof;
- (c) diphtheria toxin, botulinum toxin, tetanus toxin, dysentery toxin, cholera toxin, amanitin, -amanitin, 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, toxoid, or mixtures thereof;
- (d) affinity ligand, where the affinity ligand is a substrate, inhibitor, active agent, neurotransmitter, radioactive isotope, or mixtures thereof;
- (e) radioactive label,  $^{32}\text{P}$ ,  $^{35}\text{S}$ , fluorescent dye, electron dense reagent, enzyme, biotin, streptavidin, dioxigenin, hapten, immunogenic protein, nucleic acid molecule with a sequence complementary to a target, or mixtures thereof;
- (f) immunomodulatory compound, anti-cancer agent, anti-viral agent, anti-bacterial agent, anti-fungal agent, anti-parasitic agent, or mixtures 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) aromatase inhibitor;
- (k) protein kinase inhibitor;
- (l) lipid kinase inhibitor;

- (m) antisense oligonucleotide;
- (n) ribozyme;
- (o) vaccine; and
- (p) anti-angiogenic agent.

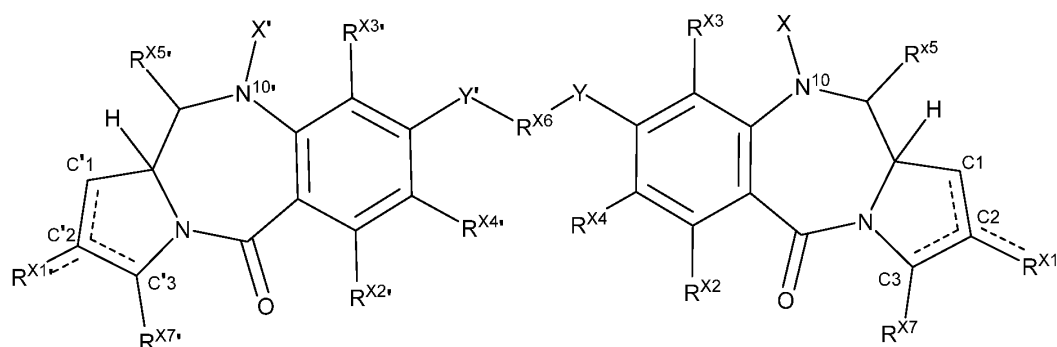
113. The antibody conjugate of any one of claims 1-110, wherein :  
 Ab is an anti-ROR1 antibody;  
 the active agent is a pyrrolobenzodiazepine dimer;  
 the linker links Ab to the N10 or N'10 position of the pyrrolobenzodiazepine dimer; and  
 y is an integer of 1 to 20.

114. The antibody conjugate of claim 113, wherein:  
 the active agent is a pyrrolobenzodiazepine dimer;  
 the pyrrolobenzodiazepine dimer is substituted by X at the N10 position or by X' at the N'10 position, where X or X' links the pyrrolobenzodiazepine dimer to the linker;  
 X and X' are, respectively and independently, -C(O)O\*, -S(O)O-\*, -C(O)-\*, -C(O)NR<sup>X</sup>-,  
 -S(O)<sub>2</sub>NR<sup>X</sup>-, -P(O)R'NR<sup>X</sup>-, -S(O)NR<sup>X</sup>-, or -PO<sub>2</sub>NR<sup>X</sup>-;  
 R<sup>X</sup> is C<sub>1-8</sub> alkyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-20</sub> heteroaryl or C<sub>5-20</sub> aryl;  
 R<sup>X'</sup> is OH, N<sub>3</sub>, CN, SH, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> cycloalkyl, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> alkylthio, C<sub>3-20</sub> heteroaryl, C<sub>5-20</sub> aryl or amino; and  
 \* is a binding site between the pyrrolobenzodiazepine dimer and the linker.

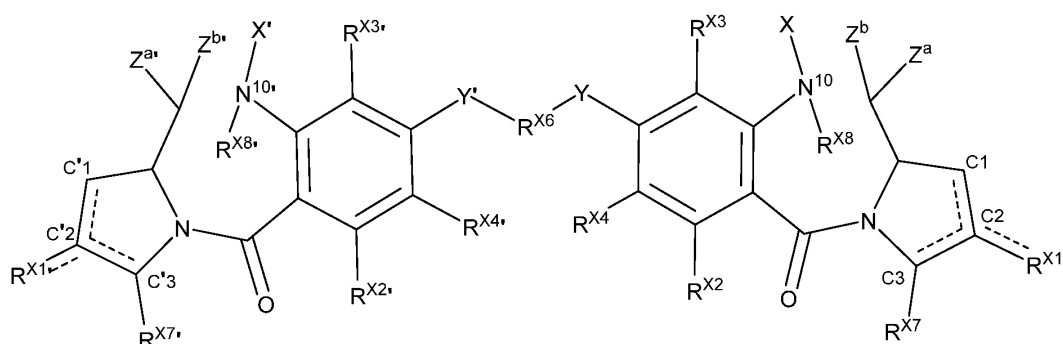
115. The antibody conjugate of claim 114, wherein X and X' are each independently -C(O)O\*, -C(O)-\* or -C(O)NR<sup>X</sup>-\*.

116. The antibody conjugate of claim 114 or 115, wherein the pyrrolobenzodiazepine dimer is represented by General Formula X or General Formula XI below :

[General Formula X]



[General Formula XI]



wherein:

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

$R^{X1}$  and  $R^{X1'}$  are independently selected from H, OH, =O, =CH<sub>2</sub> CN,  $R^m$ ,  $OR^m$ , =CH- $R^m$ , =C( $R^m$ )<sub>2</sub>,  $OSO_2-R^m$ ,  $CO_2R^m$ ,  $COR^m$ , 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 of C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>2-12</sub> alkynyl, C<sub>5-20</sub> aryl, C<sub>5-20</sub> heteroaryl, C<sub>3-6</sub> cycloalkyl, 3-7 membered heterocyclyl, 3-7 membered heterocycloalkyl and 5 to 7 heteroaryl; or  $R^m$  is X or X' ;

$R^{X2}$ ,  $R^{X2'}$ ,  $R^{X3}$ ,  $R^{X3'}$ ,  $R^{X5}$  and  $R^{X5'}$  are independently selected from H,  $R^m$ , OH,  $OR^m$ , SH,  $SR^m$ , NH<sub>2</sub>,  $NHR^m$ ,  $NR^m$ , NO<sub>2</sub>, Me<sub>3</sub>Sn and halo;

$R^{X4}$  and  $R^{X4'}$  are independently selected from H,  $R^m$ , OH,  $OR^m$ , SH,  $SR^m$ , NH<sub>2</sub>,  $NHR^m$ ,  $NR^m$ , NO<sub>2</sub>, Me<sub>3</sub>Sn, halo, C<sub>1-6</sub> alkyl C<sub>1-6</sub> alkoxy, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, 3-7 membered heterocycloalkyl, C<sub>5-12</sub> aryl, 5 to 7 heteroaryl, -CN, -NCO, -OR<sup>n</sup>, -OC(O) $R^n$ , -OC(O) $NR^nR^m$ , -OS(O) $R^n$ , -OS(O)<sub>2</sub> $R^n$ , -SR<sup>n</sup>, -S(O) $R^n$ , -S(O)<sub>2</sub> $R^n$ , -S(O) $NR^nR^m$ , -S(O)<sub>2</sub> $NR^nR^m$ , -OS(O) $NR^nR^m$ , -OS(O)<sub>2</sub> $NR^nR^m$ , -NR<sup>n</sup> $R^m$ , -NR<sup>n</sup>C(O) $R^o$ , -

$\text{NR}^n\text{C}(\text{O})\text{OR}^o$ ,  $-\text{NR}^n\text{C}(\text{O})\text{NR}^o\text{R}^{o'}$ ,  $-\text{NR}^n\text{S}(\text{O})\text{R}^o$ ,  $-\text{NR}^n\text{S}(\text{O})_2\text{R}^o$ ,  $-\text{NR}^n\text{S}(\text{O})\text{NR}^o\text{R}^{o'}$ ,  $-\text{NR}^n\text{S}(\text{O})_2\text{NR}^o\text{R}^{o'}$ ,  $-\text{C}(\text{O})\text{R}^n$ ,  $-\text{C}(\text{O})\text{OR}^n$  and  $-\text{C}(\text{O})\text{NR}^n\text{R}^{n'}$ ;

$\text{R}^X$  and  $\text{R}^{X'}$  are each independently selected from H, OH,  $\text{N}_3$ , CN,  $\text{NO}_2$ , SH,  $\text{NH}_2$ ,  $\text{ONH}_2$ ,  $\text{NHNH}_2$ , halo,  $\text{C}_{1-8}$  alkyl,  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{1-8}$  alkoxy,  $\text{C}_{1-8}$  alkylthio,  $\text{C}_{3-20}$  heteroaryl,  $\text{C}_{5-20}$  aryl or mono- or di- $\text{C}_{1-8}$  alkylamino;

Y and  $\text{Y}'$  are each independently selected from O, S and N(H);

each  $\text{R}^{X6}$  is independently selected from  $\text{C}_{3-12}$  alkylene,  $\text{C}_{3-12}$  alkenylene, or  $\text{C}_{3-12}$  heteroalkylene;

$\text{R}^{X7}$  and  $\text{R}^{X7'}$  are independently selected from H,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $\text{C}_{6-10}$  aryl, 5 to 7 heteroaryl,  $-\text{OR}^f$ ,  $-\text{OC}(\text{O})\text{R}^f$ ,  $-\text{OC}(\text{O})\text{NR}^f\text{R}^n$ ,  $-\text{OS}(\text{O})\text{R}^f$ ,  $-\text{OS}(\text{O})_2\text{R}^f$ ,  $-\text{SR}^f$ ,  $-\text{S}(\text{O})\text{R}^f$ ,  $-\text{S}(\text{O})_2\text{R}^f$ ,  $-\text{S}(\text{O})\text{NR}^f\text{R}^n$ ,  $-\text{S}(\text{O})_2\text{NR}^f\text{R}^n$ ,  $-\text{OS}(\text{O})\text{NR}^f\text{R}^n$ ,  $-\text{OS}(\text{O})_2\text{NR}^f\text{R}^n$ ,  $-\text{NR}^f\text{R}^n$ ,  $-\text{NR}^f\text{C}(\text{O})\text{R}^s$ ,  $-\text{NR}^f\text{C}(\text{O})\text{OR}^s$ ,  $-\text{NR}^f\text{C}(\text{O})\text{NR}^s\text{R}^{s'}$ ,  $-\text{NR}^f\text{S}(\text{O})\text{R}^s$ ,  $-\text{NR}^f\text{S}(\text{O})_2\text{R}^s$ ,  $-\text{NR}^f\text{S}(\text{O})\text{NR}^s\text{R}^{s'}$ ,  $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^s\text{R}^{s'}$ ,  $-\text{C}(\text{O})\text{R}^f$ ,  $-\text{C}(\text{O})\text{OR}^s$  or  $-\text{C}(\text{O})\text{NR}^f\text{R}^n$ ;

Each  $\text{R}^f$ ,  $\text{R}^f$ ,  $\text{R}^s$  and  $\text{R}^{s'}$  is independently selected from H,  $\text{C}_{1-7}$  alkyl,  $\text{C}_{2-7}$  alkenyl,  $\text{C}_{2-7}$  alkynyl,  $\text{C}_{3-13}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $\text{C}_{5-10}$  aryl and 5 to 7 heteroaryl;

each  $\text{R}^{X8}$  and  $\text{R}^{X8'}$  is independently selected from H,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{3-6}$  heteroalkyl, 3-7 membered heterocycloalkyl,  $\text{C}_{5-10}$  aryl, 5 to 7 heteroaryl,  $-\text{S}(\text{O})\text{R}^m$ ,  $-\text{S}(\text{O})_2\text{R}^m$ ,  $-\text{S}(\text{O})\text{NR}^m\text{R}^{m'}$ ,  $-\text{S}(\text{O})_2\text{NR}^m\text{R}^{m'}$ ,  $-\text{NR}^m\text{R}^{m'}$ ,  $-\text{NR}^m\text{C}(\text{O})\text{R}^n$ ,  $\text{NR}^m\text{C}(\text{O})\text{OR}^n$ ,  $-\text{NR}^m\text{C}(\text{O})\text{NR}^n\text{R}^{n'}$ ,  $-\text{NR}^m\text{S}(\text{O})\text{R}^n$ ,  $-\text{NR}^m\text{S}(\text{O})_2\text{R}^n$ ,  $-\text{NR}^m\text{S}(\text{O})\text{NR}^n\text{R}^{n'}$ ,  $-\text{NR}^m\text{S}(\text{O})_2\text{NR}^n\text{R}^{n'}$ ,  $-\text{C}(\text{O})\text{R}^m$ ,  $-\text{C}(\text{O})\text{OR}^m$  and  $-\text{C}(\text{O})\text{NR}^m\text{R}^{m'}$ ;

$\text{Z}^a$  is selected from  $\text{OR}^{X12a}$ ,  $\text{NR}^{X12a}\text{R}^{X12a}$ , or  $\text{SR}^{X12a}$ ;

$\text{Z}^b$  is selected from  $\text{OR}^{X13a}$ ,  $\text{NR}^{X13a}\text{R}^{X13a}$ , or  $\text{SR}^{X13a}$ ;

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

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

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

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

each  $\text{R}^{X13a}$  and  $\text{R}^{X14a}$  is independently H or alkyl; or  $\text{R}^{X13a}$  and  $\text{R}^{X14a}$ , together with the atom to which it is connected, form 3-7 membered heterocycloalkyl, form 3-7 membered

heterocycloalkyl, or form 3-7 membered heteroaryl, and the  $R^{X13a'}$  and  $R^{X14a'}$  arbitrarily bind to the atoms to which they are attached to form 3-7 membered heterocyclyl, 3-7 membered heterocycloalkyl, or 3-7 membered heteroaryl; and each of  $R^n$ ,  $R^{n'}$ ,  $R^o$ ,  $R^{o'}$ ,  $R^p$  and  $R^{p'}$  is independently selected from H,  $C_{1-7}$  alkyl,  $C_{2-7}$  alkenyl,  $C_{2-7}$  alkynyl,  $C_{3-13}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{5-10}$  aryl, and 5 to 7 heteroaryl.

117. The antibody conjugate of claim 116, wherein:

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

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

118. The antibody conjugate of claim 116 or 117, wherein:

$R^{X4}$  and  $R^{X4'}$  are independently selected from H,  $R^m$ , OH,  $OR^m$ , SH,  $SR^m$ ,  $NH_2$ ,  $NHR^m$ ,  $NR^mR^m$ ,  $NO_2$ ,  $Me_3SN$ , halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{5-12}$  5 to 7 heteroaryl, -CN, -NCO, - $OR^n$ , - $OC(O)R^n$ , - $OC(O)NR^nR^m$ , - $OS(O)R^n$ , - $OS(O)_2R^n$ , - $SR^n$ , - $S(O)R^n$ , - $S(O)_2R^n$ , - $S(O)NR^nR^m$ , - $S(O)_2NR^nR^m$ , - $OS(O)NR^nR^m$ , - $OS(O)_2NR^nR^m$ , - $NR^nR^m$ , - $NR^nC(O)R^o$ , - $NR^nC(O)OR^o$ , - $NR^nC(O)NR^oR^{o'}$ , - $NR^nS(O)R^o$ , - $NR^nS(O)_2R^o$ , - $NR^nS(O)NR^oR^{o'}$ , - $NR^nS(O)_2NR^oR^{o'}$ , - $C(O)R^n$ , - $C(O)OR^n$  and - $C(O)NR^nR^m$ ; and

$R^{X4}$  or  $R^{X4'}$  is  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{5-12}$  aryl or 5 to 7 heteroaryl, and additionally is 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, 3-7 membered heterocycloalkyl,  $C_{5-10}$  aryl, 5 to 7 heteroaryl, - $OR^p$ , - $OC(O)R^p$ , - $C(O)NR^pR^p$ , - $OS(O)R^p$ , - $OS(O)_2R^p$ , - $SR^p$ , - $S(O)R^p$ , - $S(O)_2R^p$ , - $S(O)NR^pR^p$ , - $S(O)_2NR^pR^p$ , - $OS(O)NR^pR^p$ , - $OS(O)_2NR^pR^p$ , - $NR^pR^p$ , - $NR^pC(O)R^q$ , - $NR^pC(O)OR^q$ , - $NR^pC(O)NR^qR^q$ , - $NR^pS(O)R^q$ , - $NR^pS(O)_2R^q$ , - $NR^pS(O)NR^qR^q$ , - $NR^pS(O)_2NR^qR^q$ , - $C(O)R^p$ , - $C(O)OR^p$  or - $C(O)NR^pR^p$ .

119. The antibody conjugate of any one of claims 116-118, wherein:

$R^{X7}$  and  $R^{X7'}$  are independently selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{6-10}$  aryl, 5 to 7 heteroaryl,  $-OR^f$ ,  $-OC(O)R^f$ ,  $-OC(O)NR^fR^n$ ,  $-OS(O)R^f$ ,  $-OS(O)_2R^f$ ,  $-SR^f$ ,  $-S(O)R^f$ ,  $-S(O)_2R^f$ ,  $-S(O)NR^fR^n$ ,  $-S(O)_2NR^fR^n$ ,  $-OS(O)NR^fR^n$ ,  $-OS(O)_2NR^fR^n$ ,  $-NR^fR^n$ ,  $-NR^fC(O)R^s$ ,  $-NR^fC(O)OR^s$ ,  $-NR^fC(O)NR^sR^s$ ,  $-NR^fS(O)R^s$ ,  $-NR^fS(O)_2R^s$ ,  $-NR^fS(O)NR^sR^s$ ,  $-NR^fS(O)_2NR^sR^s$ ,  $-C(O)R^f$ ,  $-C(O)OR^s$  or  $-C(O)NR^fR^n$ ;

$R^{X7}$  and  $R^{X7'}$  are  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{6-10}$  aryl, or 5 to 7 heteroaryl, and additionally  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{6-10}$  aryl, or 5 to 7 heteroaryl,  $-OR^t$ ,  $-OC(O)R^t$ ,  $-OC(O)NR^tR^u$ ,  $-OS(O)R^t$ ,  $-OS(O)_2R^t$ ,  $-SR^t$ ,  $-S(O)R^t$ ,  $-S(O)_2R^t$ ,  $-S(O)NR^tR^u$ ,  $-S(O)_2NR^tR^u$ ,  $-OS(O)NR^tR^u$ ,  $-OS(O)_2NR^tR^u$ ,  $-NR^tR^u$ ,  $-NR^tC(O)R^u$ ,  $-NR^tC(O)OR^u$ ,  $-NR^tC(O)NR^uR^w$ ,  $-NR^tS(O)R^u$ ,  $-NR^tS(O)_2R^u$ ,  $-NR^tS(O)NR^uR^w$ ,  $-NR^tS(O)_2NR^uR^w$ ,  $-C(O)R^t$ ,  $-C(O)OR^t$  or  $-C(O)NR^tR^u$ ; and

$R^f$ ,  $R^t$ ,  $R^s$ ,  $R^s$ ,  $R^t$ ,  $R^t$ ,  $R^u$  and  $R^u$  are each independently selected from H,  $C_{1-7}$  alkyl,  $C_{2-7}$  alkenyl,  $C_{2-7}$  alkynyl,  $C_{3-13}$  cycloalkyl, 3-7 membered heterocycloalkyl,  $C_{5-10}$  aryl, and 5 to 7 heteroaryl.

120. The antibody conjugate of any one of claims 116-119, wherein  $R^{X1}$  and  $R^{X1'}$  are both  $R^m$ ; and  $R^m$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{5-7}$  aryl, or  $C_{3-6}$  heteroaryl.

121. The antibody conjugate of any one of claims 116-120, wherein each of  $R^{X2}$ ,  $R^{X2'}$ ,  $R^{X3}$ ,  $R^{X3'}$ ,  $R^{X5}$  and  $R^{X5'}$  are independently selected from H or OH.

122. The antibody conjugate of any one of claims 116-121, wherein  $R^{X4}$  and  $R^{X4'}$  are both  $R^m$ ; and  $R^m$  is  $C_{1-6}$  alkoxy.

123. The antibody conjugate of any one of claims 116-122, wherein  $R^{X4}$  and  $R^{X4'}$  are each independently selected from methoxy, ethoxy and butoxy.

124. The antibody conjugate of any one of claims 116-123, wherein Y and Y' are O.

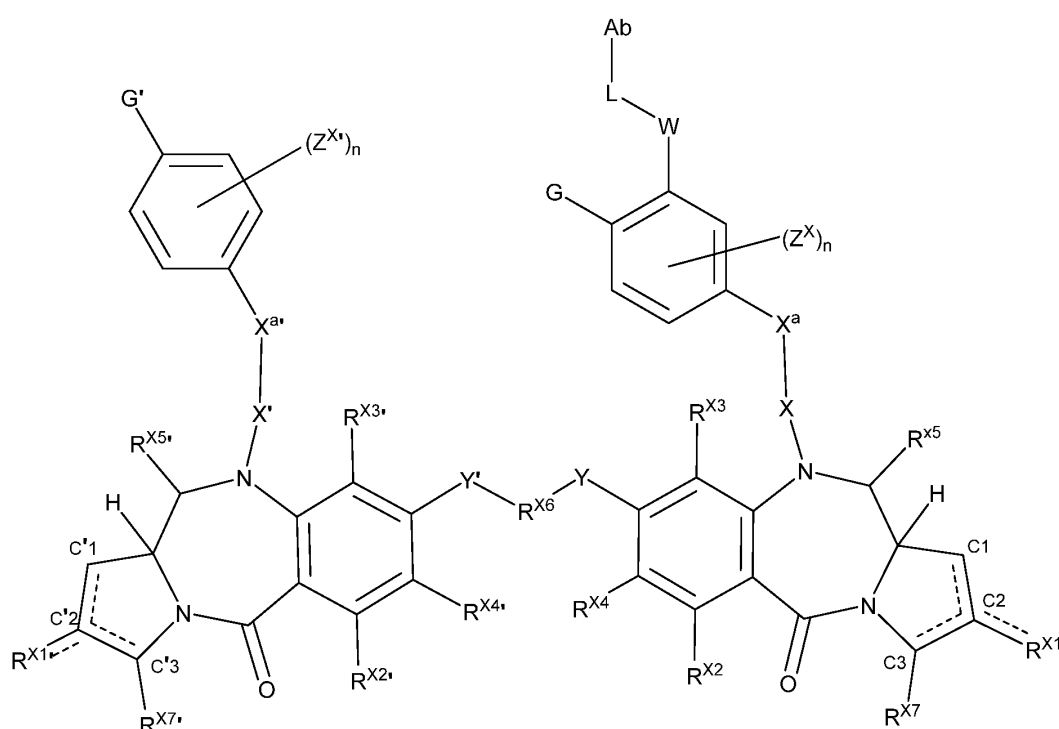
125. The antibody conjugate of any one of claims 116-124, wherein:

$R^{X6}$  is  $C_{3-12}$  alkylene,  $C_{3-12}$  alkenylene or  $C_{3-12}$  heteroalkylene, where  $R^{X6}$  is substituted with  $-NH_2$ ,  $-NHR^m$ ,  $-NHC(O)R^m$ ,  $-NHC(O)R^m$ ,  $-NHC(O)CH_2-[OCH_2CH_2]_n-R^{XX}$ , or  $-[CH_2CH_2O]_n-R^{XX}$ ;

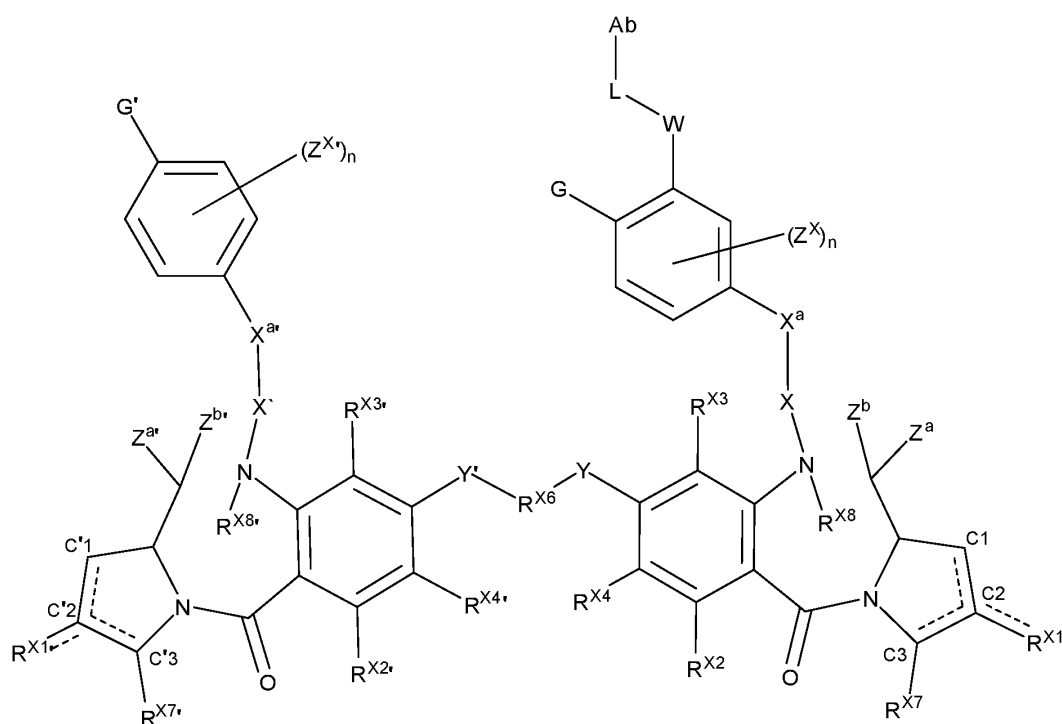
$R^{XX}$  is H, OH,  $N_3$ , CN,  $NO_2$ , SH,  $NH_2$ ,  $ONH_2$ ,  $NHNH_2$ , halo,  $C_{1-8}$  alkyl,  $C_{3-8}$  cycloalkyl,  $C_{1-8}$  alkoxy,  $C_{1-8}$  alkylthio,  $C_{3-20}$  heteroaryl,  $C_{5-20}$  aryl or mono- or di- $C_{1-8}$  alkyl amino; and n is an integer of 1 through 6.

126. The antibody conjugate of any one of claims 1-125, wherein the active agent has a structure represented by General Formula XII or General Formula XIII;

[General Formula XII]



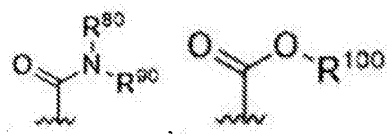
[General Formula XIII]



wherein

$X^a$  and  $X^b$  are each independently a bond or  $C_{1-6}$  alkylene;

$Z^X$  and  $Z^{X'}$  are each independently selected from hydrogen,  $C_{1-8}$  alkyl, halogen, cyano, nitro,

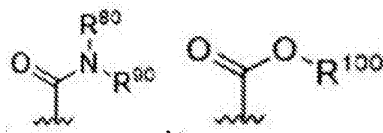


and  $-(CH_2)_m-OCH_3$ ;

each  $R^{80}$ ,  $R^{90}$  and  $R^{100}$  is independently selected from hydrogen,  $C_{1-8}$  alkyl,  $C_{2-6}$  alkenyl and  $C_{1-6}$  alkoxy; and

$m$  is an integer of 0 to 12.

127. The antibody conjugate of any one of claims 116-126, wherein the  $Z^{X'}$  and  $Z^X$  are

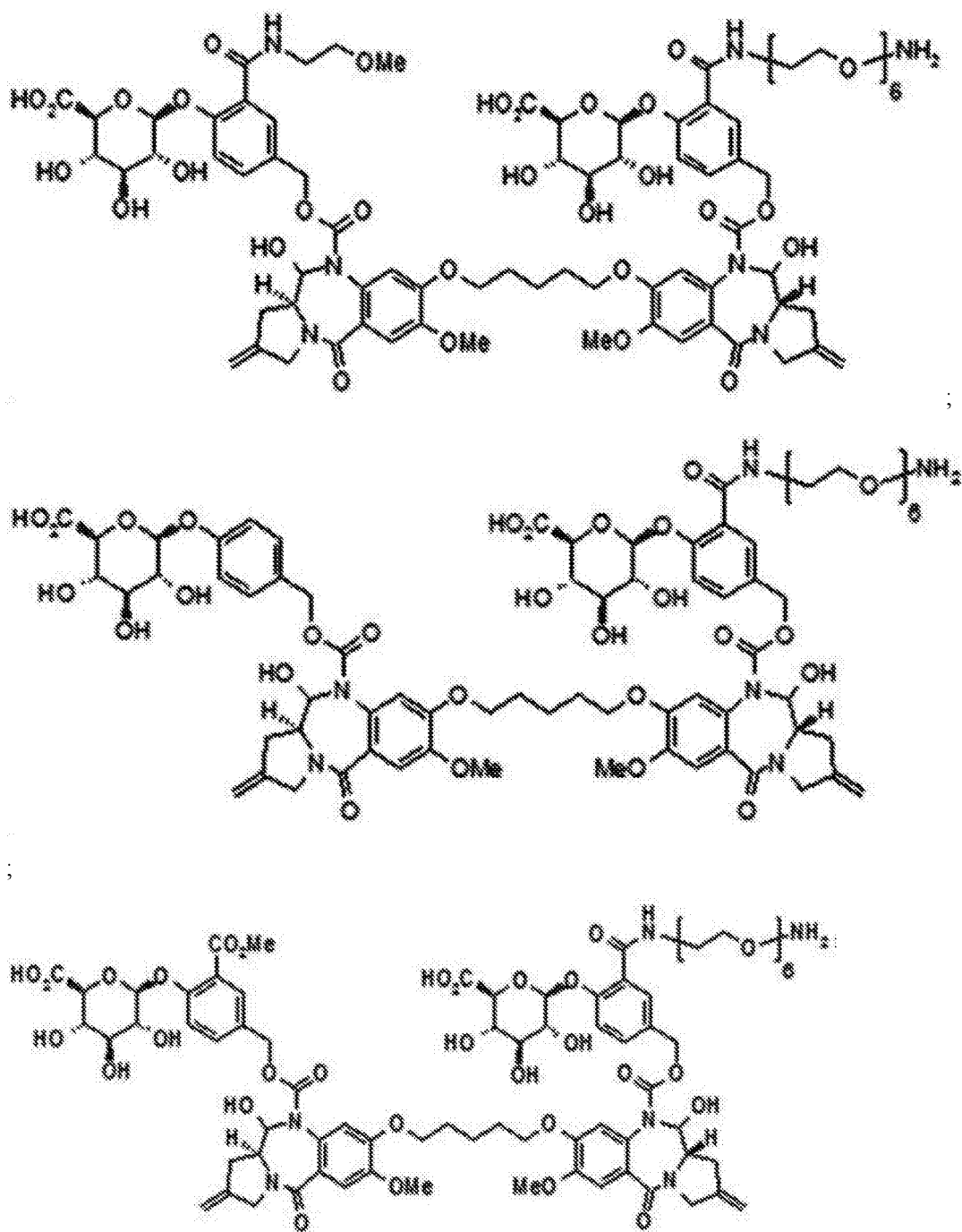


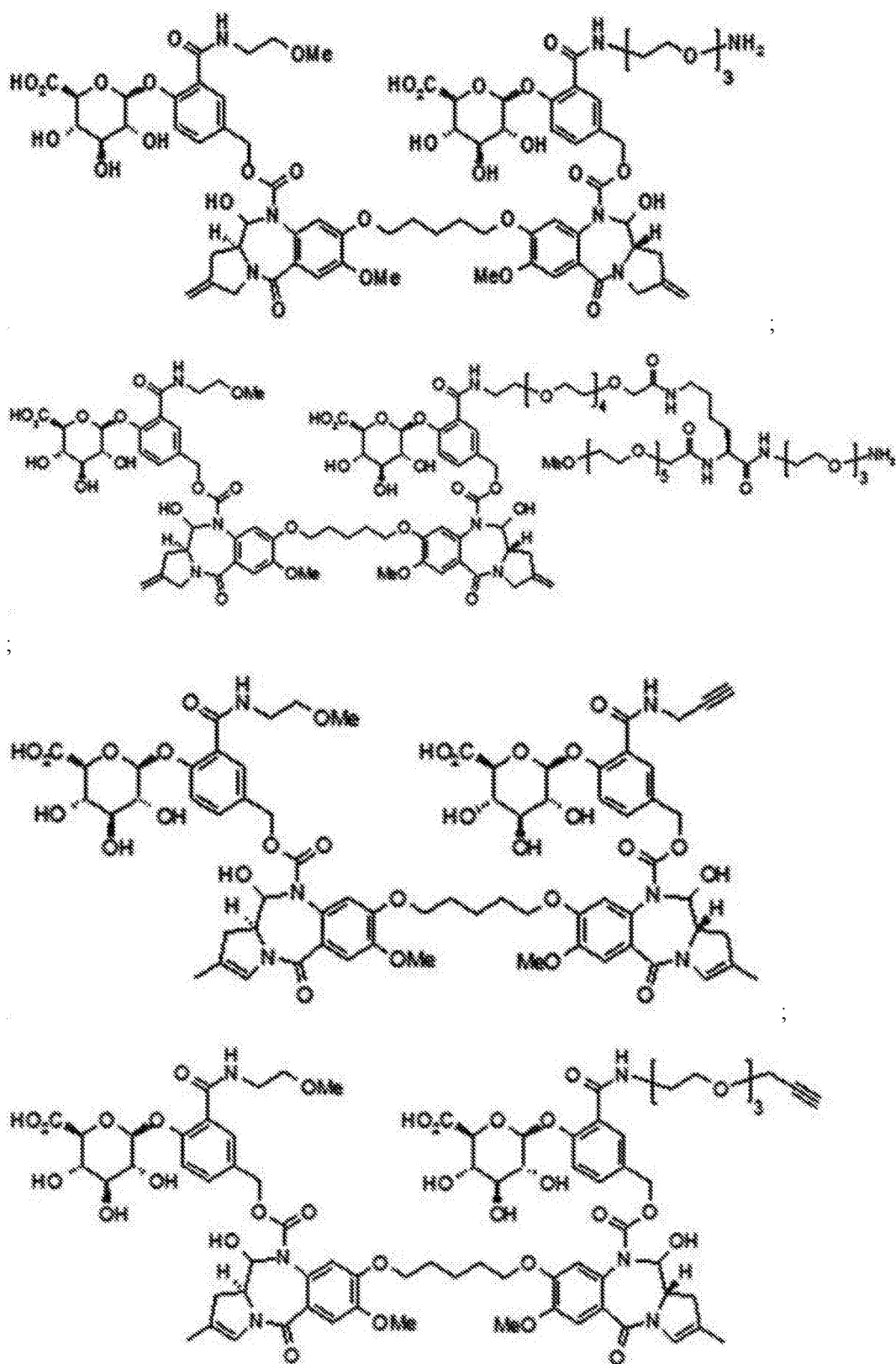
each independently selected from hydrogen,  $-(CH_2)_m-OCH_3$ ;

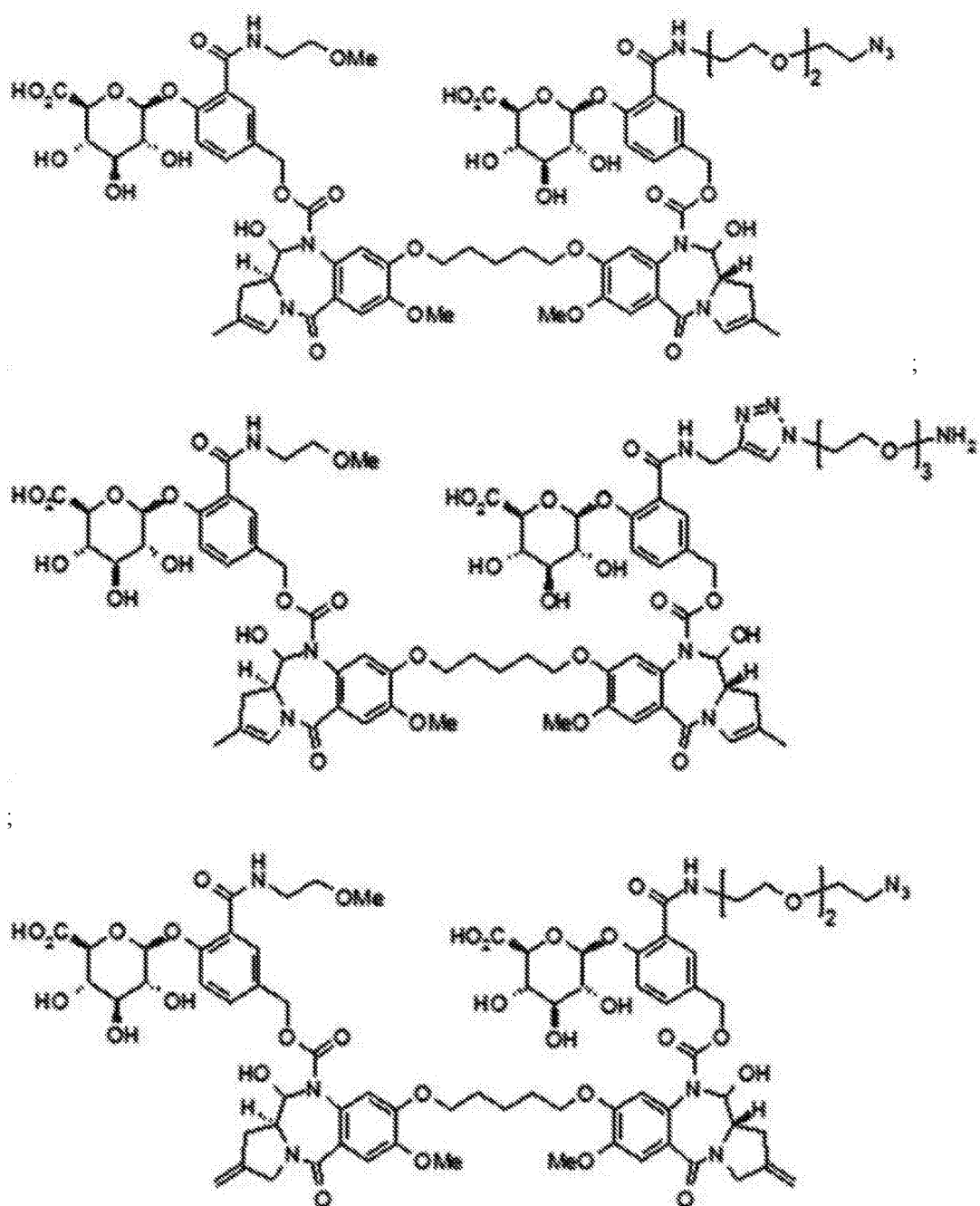
$R^{80}$ ,  $R^{90}$  and  $R^{100}$  are each independently selected from hydrogen,  $C_{1-3}$  alkyl and  $C_{1-3}$  alkoxy; and

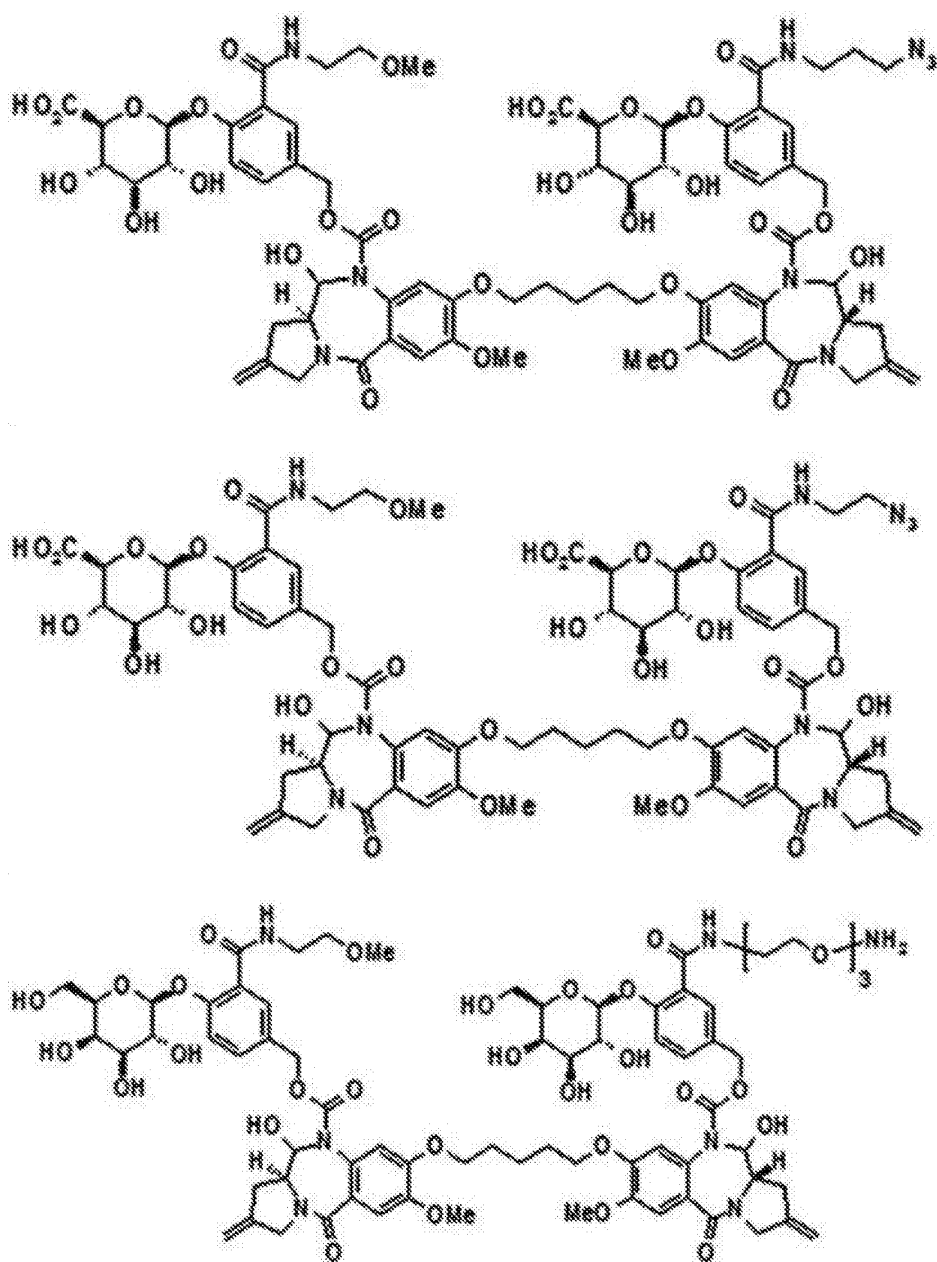
$m$  is an integer of 1 to 6.

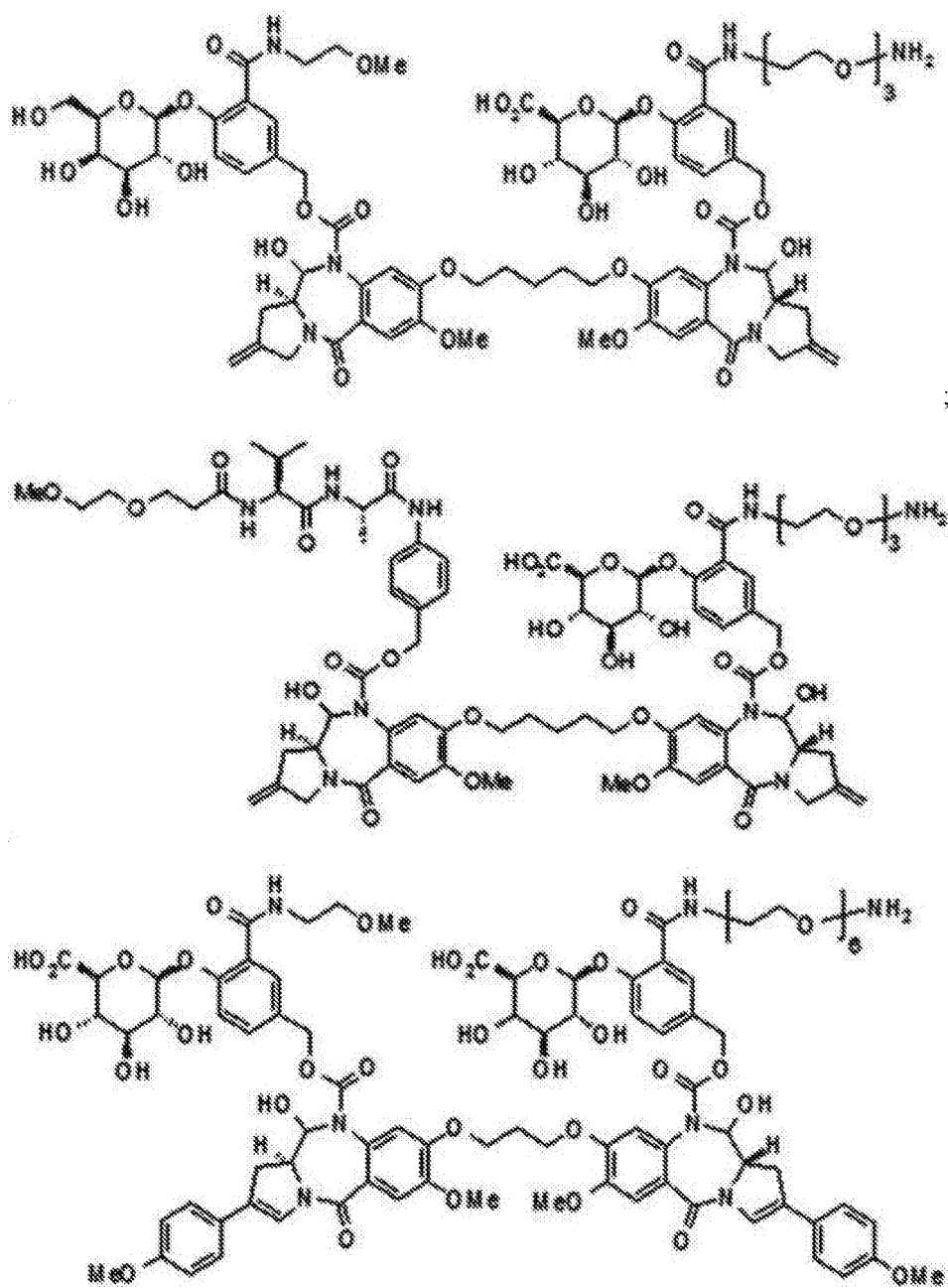
128. The antibody conjugate of any one of claims 1-127, wherein the active agent is selected from

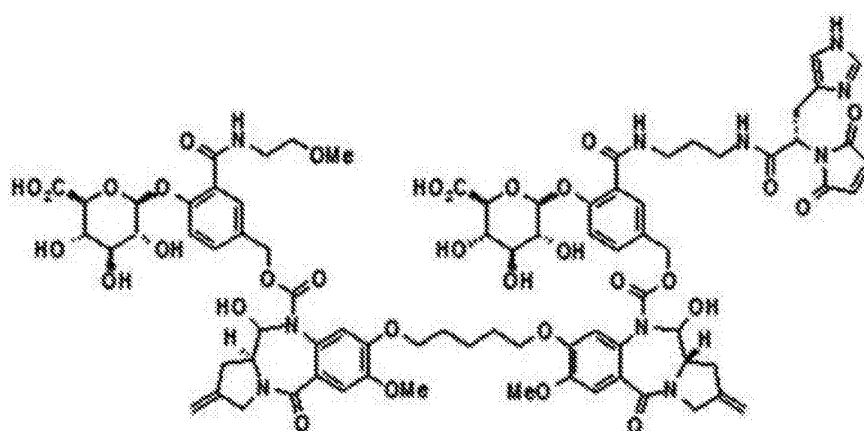
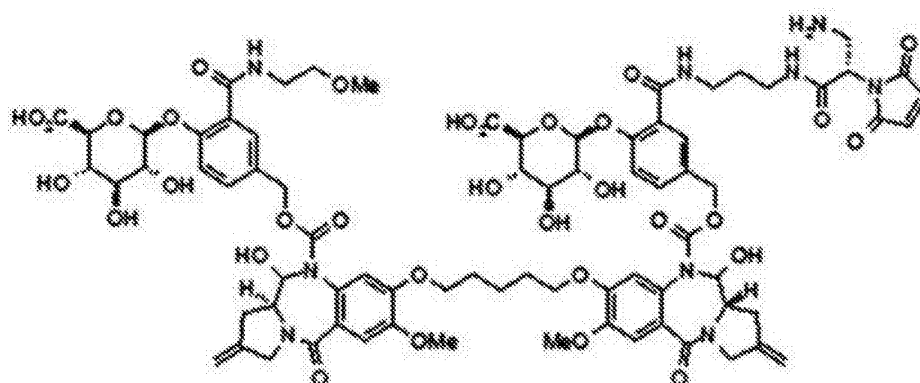
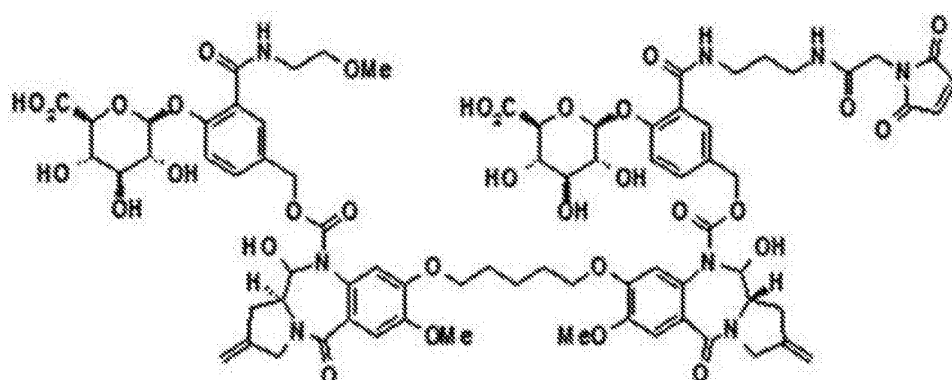


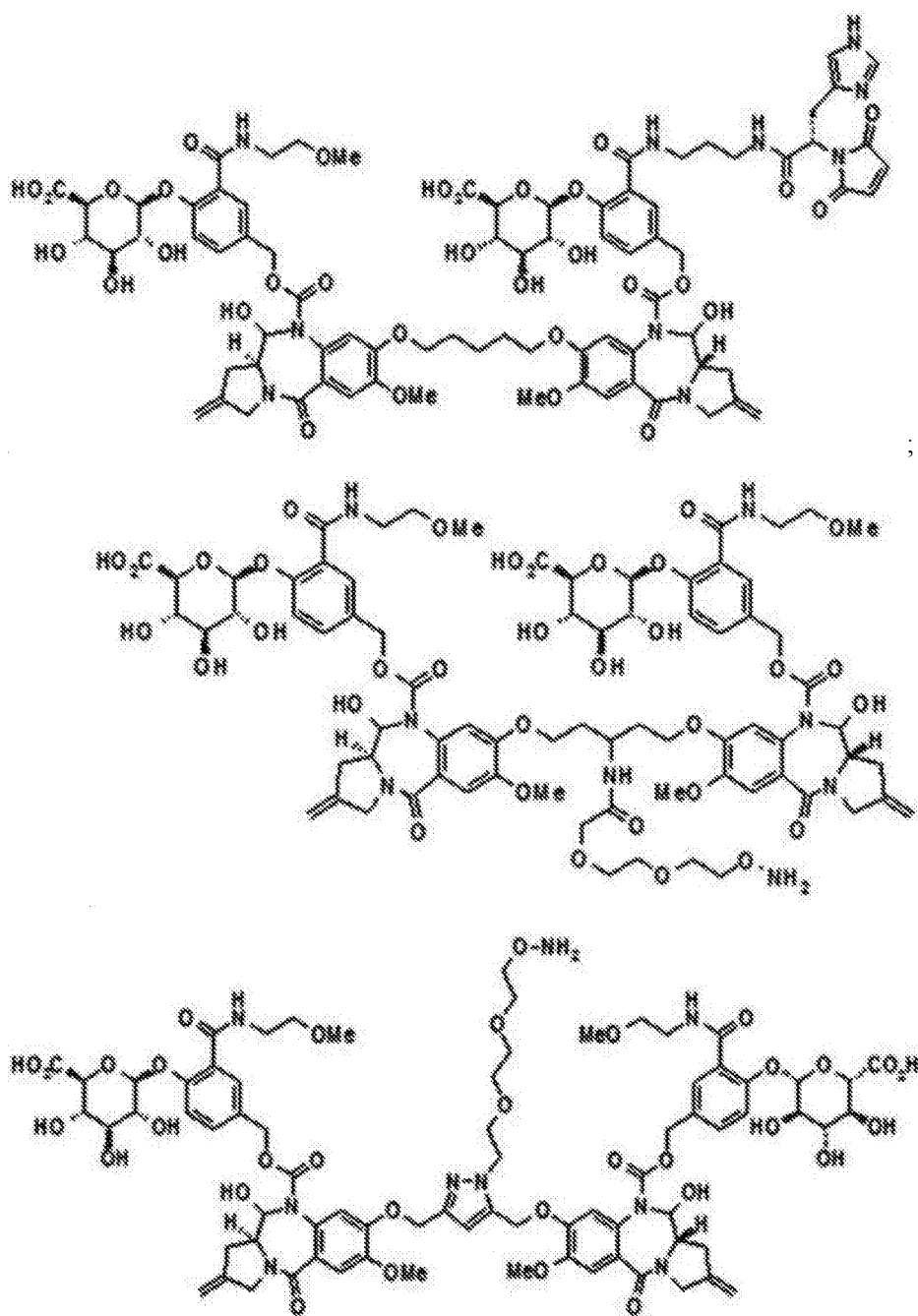


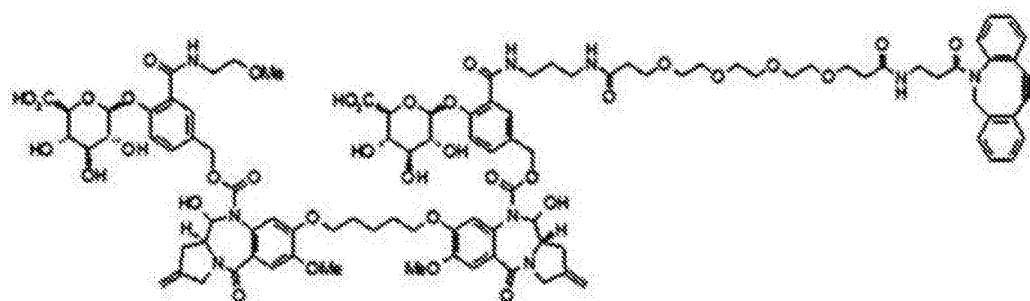
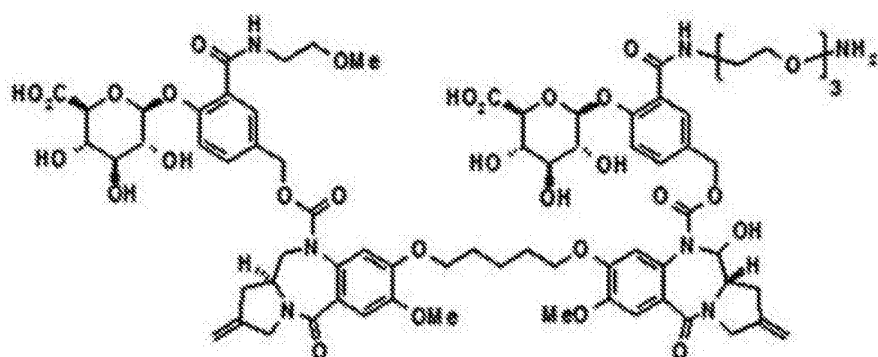
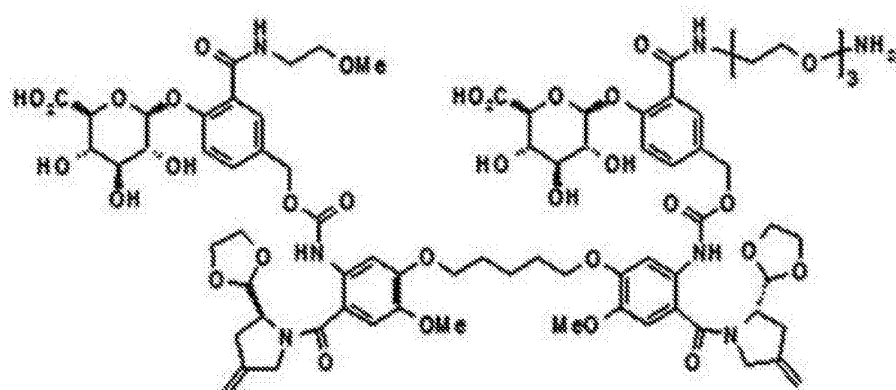
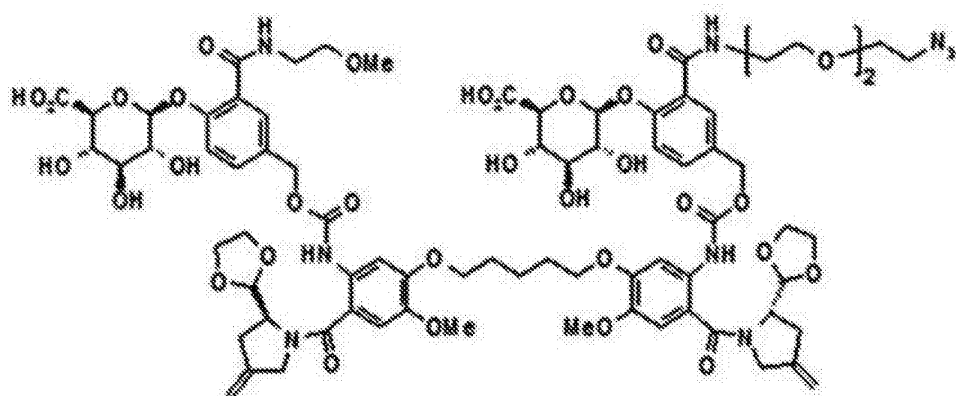






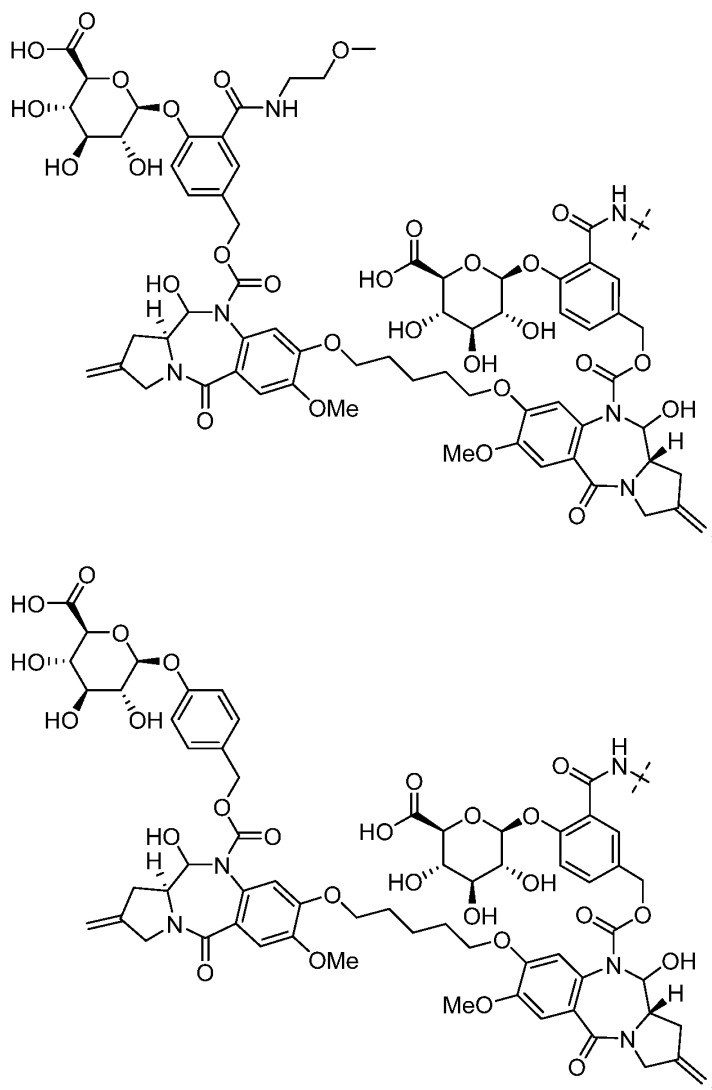


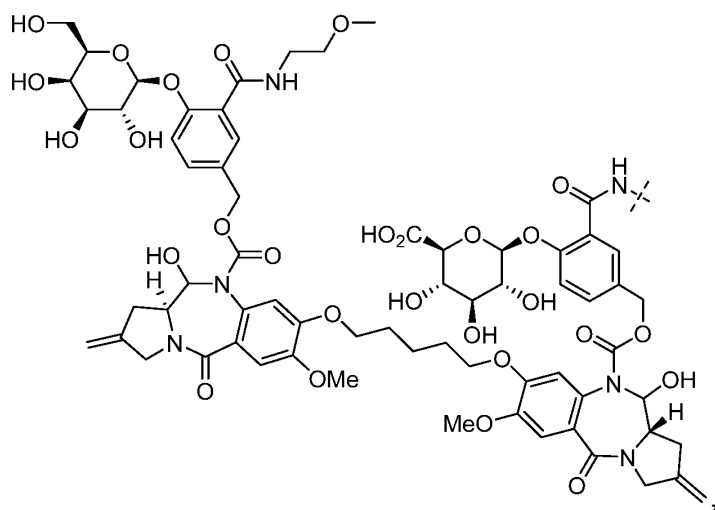
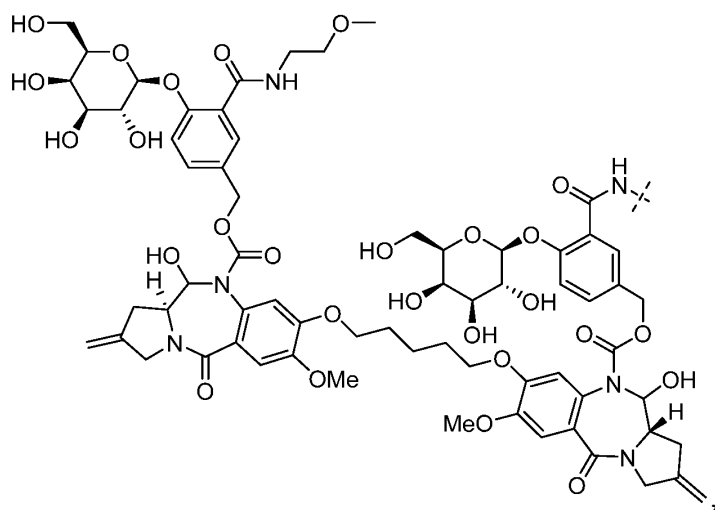
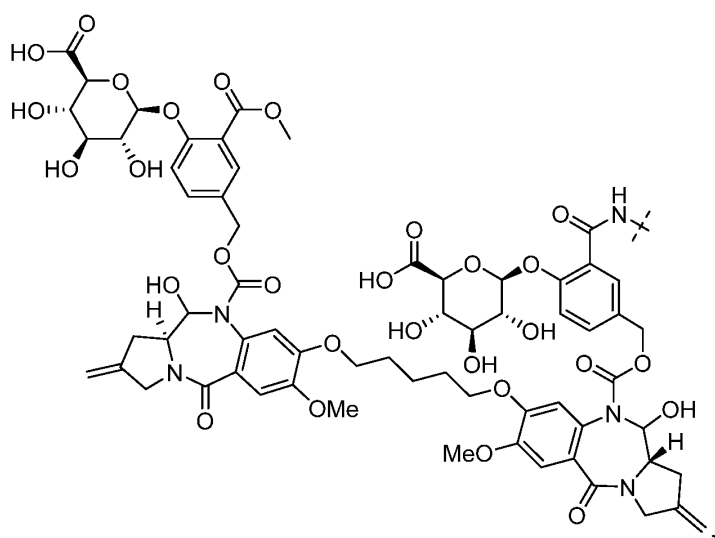


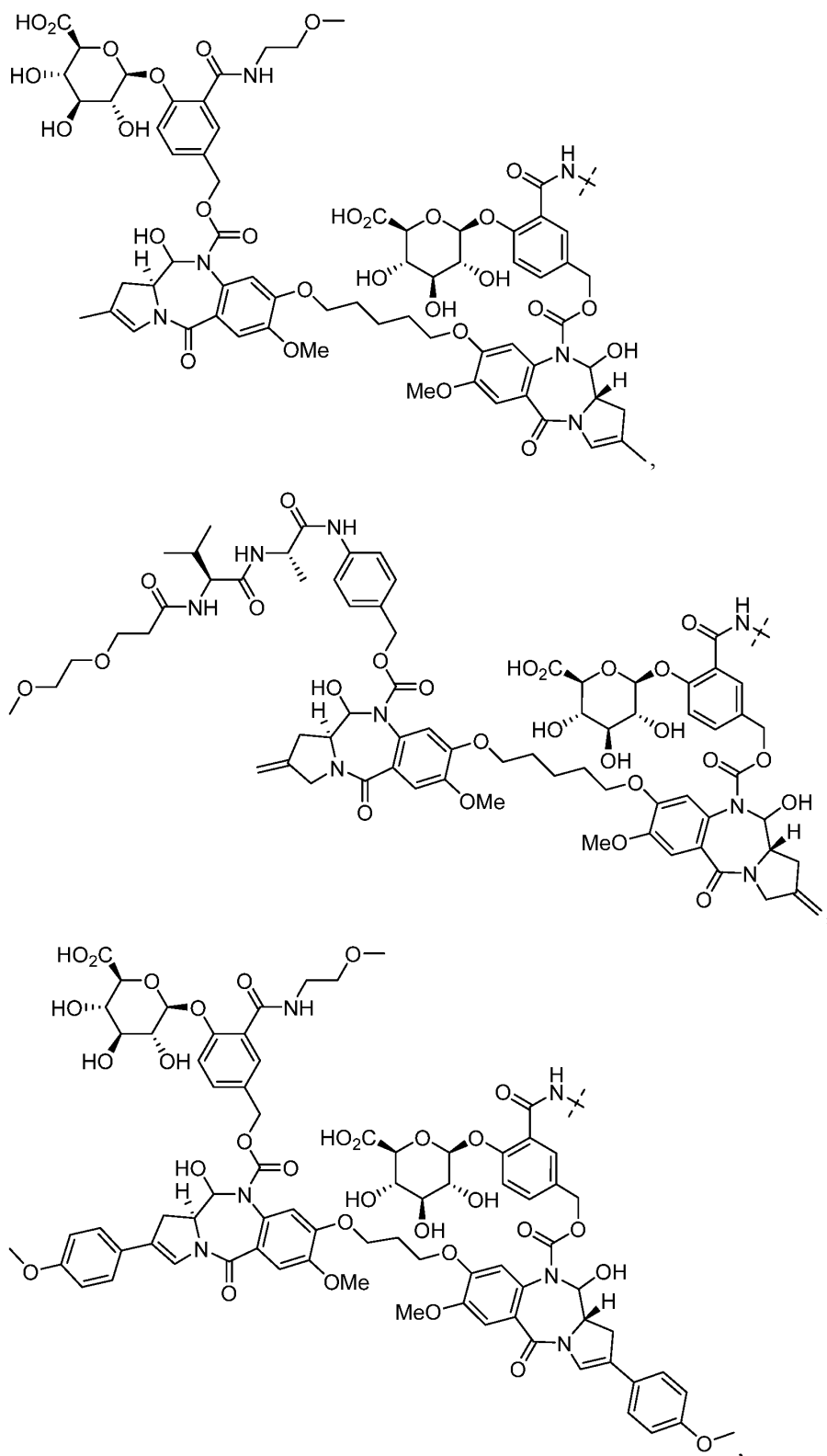


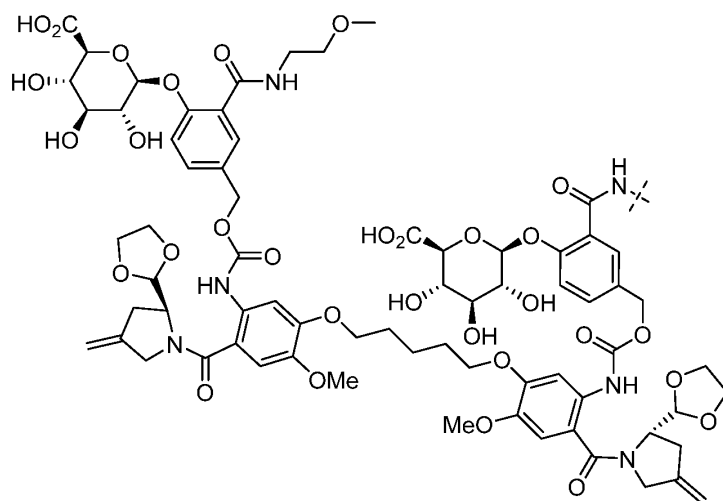
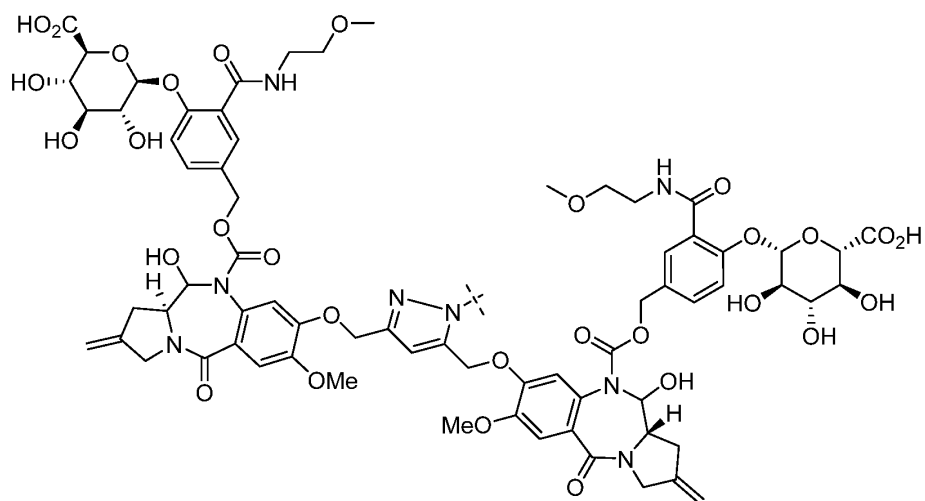
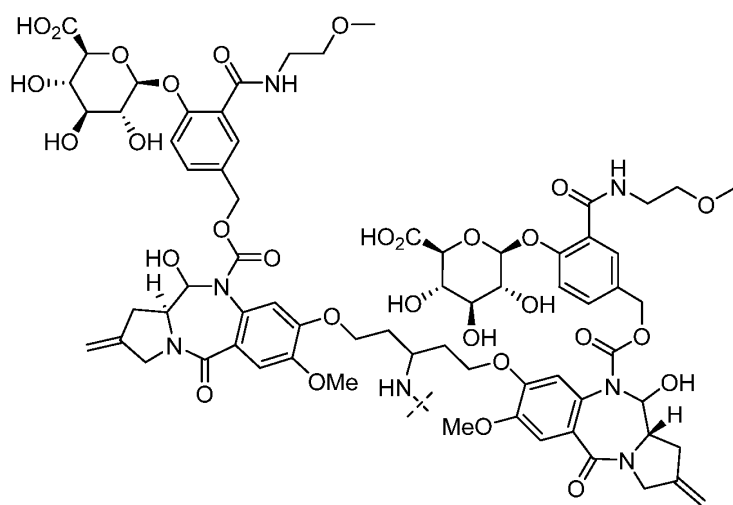
or a pharmaceutically acceptable salt thereof.

129. The antibody conjugate of any one of claims 1-127, wherein the active agent is selected from:









acceptable salt thereof; and

; or a pharmaceutically

the bond overlaid with a dashed line represents a connection point to L.

130. A pharmaceutical composition comprising an antibody drug conjugate of any one of claims 1-129 and a pharmaceutically acceptable excipient.

131. A pharmaceutical composition for prevention, amelioration or treatment of illness associated with over-expression of ROR1, the composition comprising the antibody conjugate of any one of claims 1-129 or a pharmaceutically acceptable salt or solvate thereof.

132. The pharmaceutical composition according to claim 131, wherein the pharmaceutical composition further comprises a pharmaceutically efficacious amount of a chemotherapeutic agent.

133. The pharmaceutical composition according to claim 131 or 132, wherein the illness associated with over-expression of ROR1 is cancer.

134. The pharmaceutical composition of any one of claims 131-133, wherein the cancer is selected from chronic lymphocytic leukemia (CLL), B-cell leukemia, lymphoma, acute myeloid leukemia (AML), Burkitt lymphoma, mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), Diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and marginal zone lymphoma (MZL), breast cancer, renal cancer, ovarian cancer, gastric cancer, liver cancer, lung cancer, colorectal cancer, pancreatic cancer, skin cancer, bladder cancer, testicular cancer, uterine cancer, prostate cancer, non-small cell lung cancer (NSCLC), neuroblastoma, brain cancer, colon cancer, squamous cell carcinoma, melanoma, myeloma, cervical cancer, thyroid cancer, head and neck cancer and adrenal cancer.

135. A method of treating a disease or disorder associated with the over-expression of ROR1 in a subject, comprising administering an antibody drug conjugate of any one of claims 1-129 or a pharmaceutically acceptable salt thereof to the subject.

136. The method of claim 135, wherein the disease or disorder associated with the over-expression of ROR1 is cancer.

137. The method of claim 136, wherein the cancer is selected from chronic lymphocytic leukemia (CLL), B-cell leukemia, lymphoma, acute myeloid leukemia (AML), Burkitt lymphoma, mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), Diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and marginal zone lymphoma (MZL), breast cancer, renal cancer, ovarian cancer, gastric cancer, liver cancer, lung cancer, colorectal cancer, pancreatic cancer, skin cancer, bladder cancer, testicular cancer, uterine cancer, prostate cancer, non-small cell lung cancer (NSCLC), neuroblastoma, brain cancer, colon cancer, squamous cell carcinoma, melanoma, myeloma, cervical cancer, thyroid cancer, head and neck cancer and adrenal cancer.

138. A method of treating cancer in a subject, comprising administering an antibody drug conjugate of any one of claims 1-129 or a pharmaceutically acceptable salt thereof to the subject.

139. The method of claim 138, wherein the cancer is selected from chronic lymphocytic leukemia (CLL), B-cell leukemia, lymphoma, acute myeloid leukemia (AML), Burkitt lymphoma, mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), Diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and marginal zone lymphoma (MZL), breast cancer, renal cancer, ovarian cancer, gastric cancer, liver cancer, lung cancer, colorectal cancer, pancreatic cancer, skin cancer, bladder cancer, testicular cancer, uterine cancer, prostate cancer, non-small cell lung cancer (NSCLC), neuroblastoma, brain cancer, colon cancer, squamous cell carcinoma, melanoma, myeloma, cervical cancer, thyroid cancer, head and neck cancer and adrenal cancer.