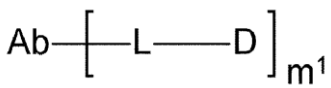
Claims

1. An antibody-drug conjugate represented by formula (II):



(II)

wherein

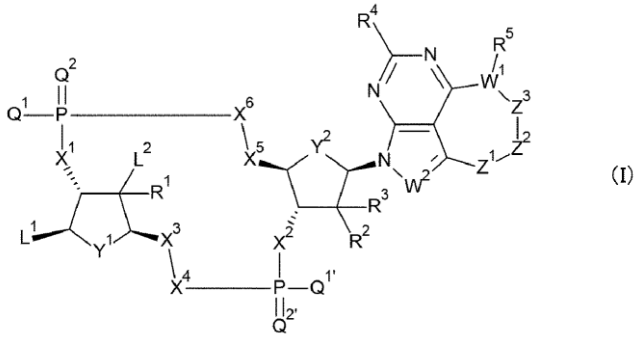
m^1 is in the range of 1 to 10;

Ab represents an antibody or a functional fragment of the antibody, where a glycan of the antibody is optionally remodeled;

L represents a linker linking Ab and D;

Ab bonds directly from an amino acid residue of Ab to L, or optionally bonds via a glycan or remodeled glycan of Ab to L; and

D represents a compound represented by formula (I):

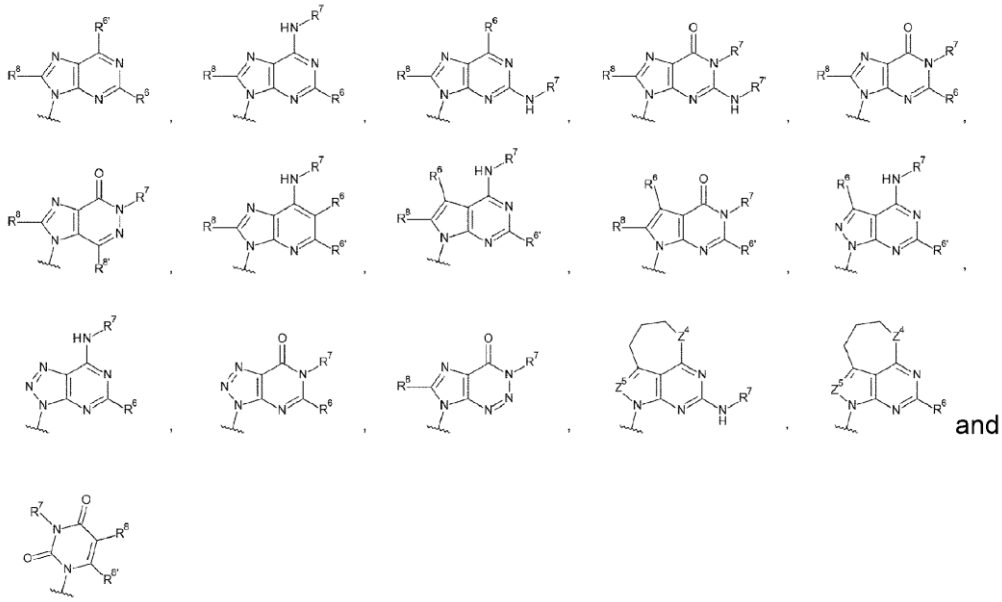


(I)

wherein

L bonds to any $-NH_2$ or hydroxy group included in L^1 or L^2;

L^1 represents a group selected from the group consisting of the following formulas:



and optionally substituted at any position with one to three groups selected from the group consisting of a hydroxy group, -NH_2, a 2-hydroxyacetylaminomethyl group, and a 2-[(2-hydroxyacetyl)amino]ethyl group,

wherein

R^6 and $R^{6'}$ each independently represent a hydrogen atom, a halogen atom, a hydroxy group, -NH_2, a C1-C6 alkyl group, a C2-C6 alkenyl group, or a C2-C6 alkynyl group;

R^7 and $R^{7'}$ each independently represent a hydrogen atom or a C1-C6 alkyl group, wherein the C1-C6 alkyl group is optionally substituted with one or two substituents selected from the group consisting of a halogen atom and an oxo group;

R^8 and $R^{8'}$ each independently represent a hydrogen atom or a halogen atom;

Z^4 represents -CH_2-, -NH-, or an oxygen atom; and

Z^5 represents a nitrogen atom or -CH=,

L^2 represents a group selected from (i) and (ii):

(i) when bonding to L, L^2 represents -NHR', a hydroxy C1-C6 alkyl group, or an amino C1-C6 alkyl group, wherein R' represents a hydrogen atom, a C1-C6 alkyl group, a C2-C6 alkenyl group, a C2-C6 alkynyl group, or a C3-C6 cycloalkyl

group, and the C1-C6 alkyl group, C2-C6 alkenyl group, or C2-C6 alkynyl group is optionally substituted with one to six halogen atoms; and

(ii) when not bonding to L, L^2 represents a hydrogen atom or a halogen atom;

Q^1 and $Q^{1'}$ each independently represent a hydroxy group, a thiol group, or a borano group (BH_3^-);

Q^2 and $Q^{2'}$ each independently represent an oxygen atom or a sulfur atom;

X^1 and X^2 each independently represent an oxygen atom, a sulfur atom, or -CH_2-;

Y^1 and Y^2 each represent an oxygen atom or -CH_2-;

X^3 and X^4 represent a group selected from (iii) and (iv):

(iii) when Y^1 is an oxygen atom, X^3-X^4 represents -CH_2-O-, -CH_2-S-, -CH_2-CH_2-, or -CH_2-CF_2-; and

(iv) when Y^1 is -CH_2-, X^3-X^4 represents -O-CH_2-;

X^5 and X^6 represent a group selected from (v) and (vi):

(v) when Y^2 is an oxygen atom, X^5-X^6 represents -CH_2-O-, -CH_2-S-, -CH_2-CH_2-, or -CH_2-CF_2-; and

(vi) when Y^2 is -CH_2-, X^5-X^6 represents -O-CH_2-;

R^1, R^2 and R^3 each independently represent a hydrogen atom, a halogen atom, -OR', -OC(=O)R', -N_3, -NHR', -NR'R", or -NHC(=O)R', wherein R' is as defined above, and R" represents a C1-C6 alkyl group, a C2-C6 alkenyl group, a C2-C6 alkynyl group, or a C3-C6 cycloalkyl group;

W^1 represents a nitrogen atom, an oxygen atom, a sulfur atom, or -CH-;

W^2 represents a nitrogen atom or -CH=;

R^4 represents a hydrogen atom, a halogen atom, or -NH_2;

R^5 represents a group selected from (vii) to (x):

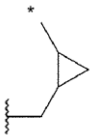
(vii) when W^1 is a nitrogen atom, R^5 represents a hydrogen atom, a C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, or an amino C1-C6 alkyl group;

(viii) when W^1 is an oxygen atom, R^5 is absent;

(ix) when W^1 is a sulfur atom, R^5 is absent; and

(x) when W^1 is -CH-, R^5 represents a hydrogen atom, a halogen atom, a hydroxy group, $-NH_2$, or a C1-C6 alkyl group;

Z^1-Z^2-Z^3 together represents $-CH_2-CH_2-CH_2-$, $-CH_2-CH_2-R'''-$, $-CH=CH-CH_2-$, $-CH=CX-CH_2-$, $-CX=CH-CH_2-$, $-CX=CX-CH_2-$, $-C(=O)-CH_2-CH_2-$, $-CH_2-CH_2-C(=O)-$, $-CH_2-CH(CH_3)-CH_2-$, or $-CH_2-CH_2-CH(CH_3)-$, wherein R''' represents -O- or $-CH_2-CH_2-$ and X represents a halogen atom, or a group represented by either one of the following formulas:


and


wherein

each asterisk indicates bonding to W^1, and each wavy line indicates bonding to the carbon atom of =C-.

2. The antibody-drug conjugate according to claim 1, wherein W^1 is a nitrogen atom.

3. The antibody-drug conjugate according to claim 2, wherein W^1 is a nitrogen atom, and R^5 is a hydrogen atom.

4. The antibody-drug conjugate according to claim 1, wherein W^1 is an oxygen atom.

5. The antibody-drug conjugate according to claim 1, wherein W^1 is a sulfur atom.

6. The antibody-drug conjugate according to claim 1, wherein W^1 is -CH-.

7. The antibody-drug conjugate according to claim 6, wherein W^1 is -CH-, and R^5 is a hydrogen atom.

8. The antibody-drug conjugate according to any one of claims 1 to 7, wherein Z^1, Z^2 and Z^3 together form $-CH_2-CH_2-CH_2-$ or $-CH=CH-CH_2-$.

9. The antibody-drug conjugate according to any one of claims 1 to 7, wherein Z^1, Z^2 and Z^3 together form $-CH_2-CH(CH_3)-CH_2-$ or $-CH_2-CH_2-CH(CH_3)-$.

10. The antibody-drug conjugate according to any one of claims 1 to 7, wherein Z^1, Z^2 and Z^3 together form $-CH_2-CH_2-R'''-$, wherein R''' represents -O- or $-CH_2-CH_2-$.

11. The antibody-drug conjugate according to any one of claims 1 to 10, wherein W^2 is -CH=.

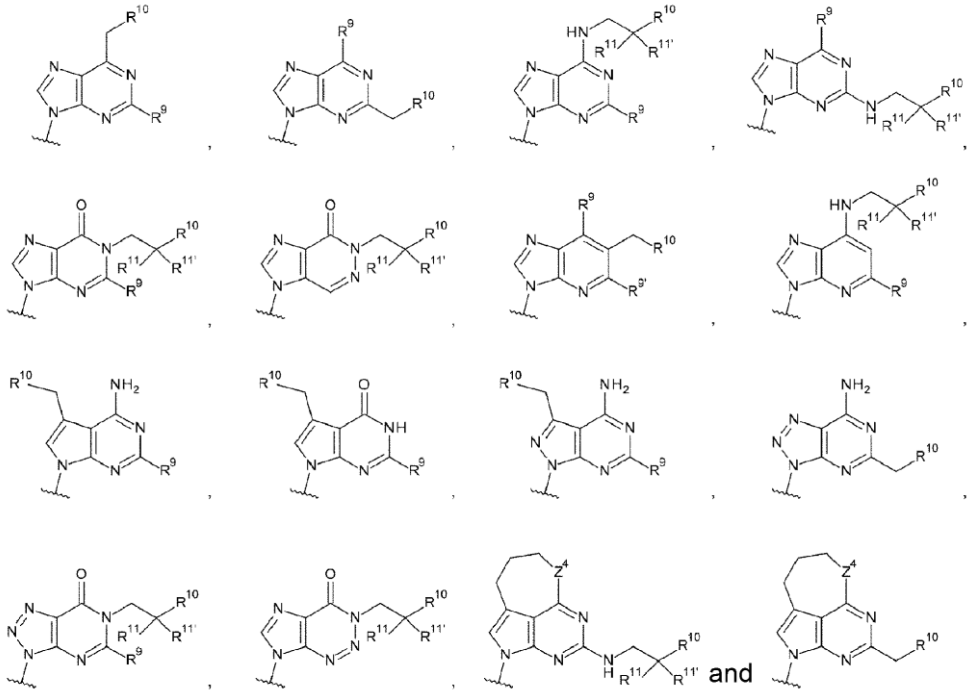
12. The antibody-drug conjugate according to any one of claims 1 to 10, wherein W^2 is a nitrogen atom.

13. The antibody-drug conjugate according to any one of claims 1 to 12, wherein R^4 represents a hydrogen atom.

14. The antibody-drug conjugate according to any one of claims 1 to 12, wherein R^4 represents a fluorine atom.

15. The antibody-drug conjugate according to any one of claims 1 to 14, wherein R^8 and $R^{8'}$ in L^1 are each independently a hydrogen atom.

16. The antibody-drug conjugate according to any one of claims 1 to 15, wherein L^1 is a group selected from the group consisting of the following formulas:



wherein

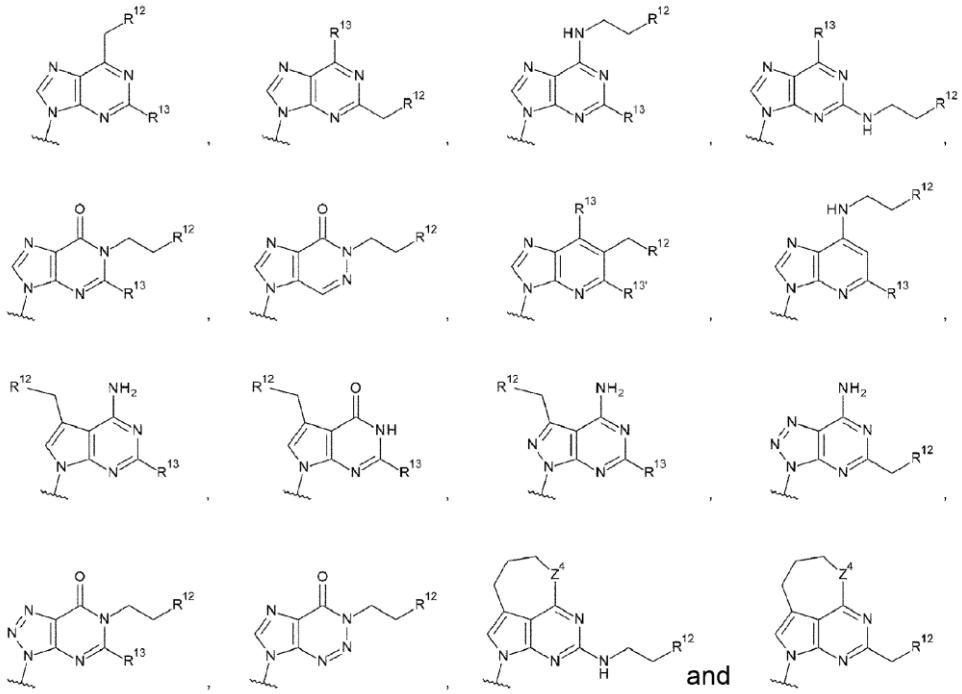
R^9 and $R^{9'}$ each represent a hydrogen atom, a halogen atom, a hydroxy group, or $-NH_2$;

R^{10} represents a hydroxy group, $-NH_2$, $-NHC(=O)CH_2OH$, $-CH_2NHC(=O)CH_2OH$, $-CH_2CH_2NHC(=O)CH_2OH$, a hydroxy C1-C3 alkyl group, or an amino C1-C3 alkyl group;

R^{11} and $R^{11'}$ each independently represent a hydrogen atom, a fluorine atom, or a methyl group, or R^{11} and $R^{11'}$ bond together to form cyclopropane; and

Z^4 represents $-CH_2-$, -NH-, or an oxygen atom.

17. The antibody-drug conjugate according to any one of claims 1 to 15, wherein L^1 is a group selected from the group consisting of the following formulas:


and

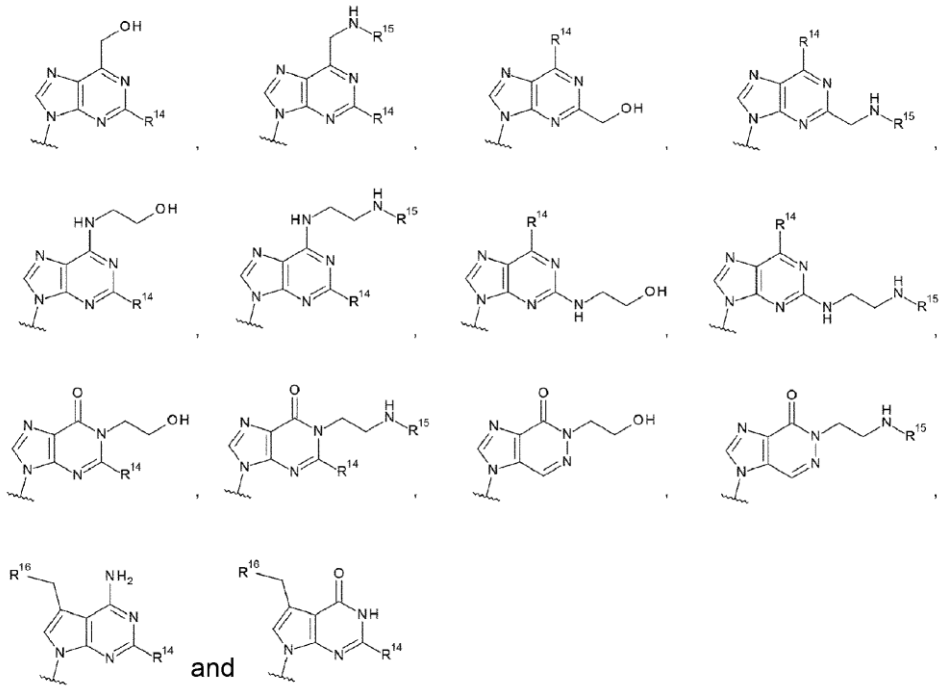
wherein

R^{13} and $R^{13'}$ each independently represent a hydrogen atom, a hydroxy group, or $-NH_2$;

R^{12} represents a hydroxy group, $-NH_2$, $-CH_2OH$, $-NHC(=O)CH_2OH$, $-CH_2NHC(=O)CH_2OH$, or $-CH_2CH_2NHC(=O)CH_2OH$; and

Z^4 is as defined above.

18. The antibody-drug conjugate according to any one of claims 1 to 15, wherein L^1 is a group selected from the group consisting of the following formulas:



wherein

R^{14} represents a hydrogen atom or $-NH_2$;

R^{15} represents a hydrogen atom or $-C(=O)CH_2OH$; and

R^{16} represents a hydroxy group, $-NH_2$, $-CH_2OH$, $-CH_2CH_2OH$, $-CH_2NH_2$, or $-CH_2CH_2NH_2$.

19. The antibody-drug conjugate according to any one of claims 1 to 18, wherein L^2 bonds to L and represents $-NH_2$, $-CH_2NH_2$, or $-CH_2OH$.

20. The antibody-drug conjugate according to any one of claims 1 to 18, wherein L^2 does not bond to L and represents a hydrogen atom or a fluorine atom.

21. The antibody-drug conjugate according to any one of claims 1 to 20, wherein Q^1 and $Q^{1'}$ each independently represent a hydroxy group or a thiol group.

22. The antibody-drug conjugate according to any one of claims 1 to 21, wherein X^1 and X^2 each represent an oxygen atom.

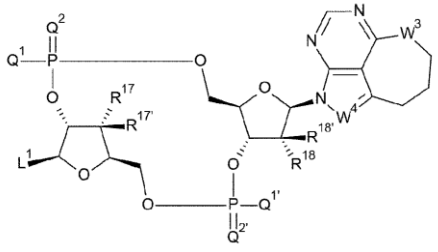
23. The antibody-drug conjugate according to any one of claims 1 to 22, wherein Y^1 and Y^2 each represent an oxygen atom.

24. The antibody-drug conjugate according to any one of claims 1 to 23, wherein X^3 and X^4 represent $-CH_2-O-$.

25. The antibody-drug conjugate according to any one of claims 1 to 24, wherein X^5 and X^6 represent $-CH_2-O-$.

26. The antibody-drug conjugate according to any one of claims 1 to 25, wherein R^1, R^2, and R^3 are each independently a hydrogen atom, a hydroxy group, or a fluorine atom.

27. The antibody-drug conjugate according to any one of claims 1 to 26, wherein D is represented by either one of the following two formulas: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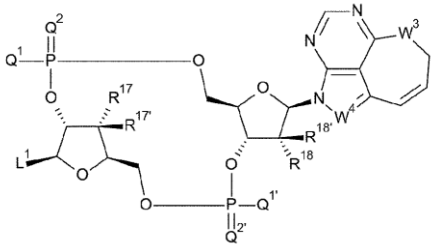


wherein

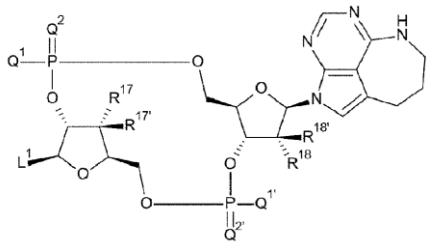
L^1, Q^1, $Q^{1'}$, Q^2, and $Q^{2'}$ are as defined above;

R^{17}, $R^{17'}$, R^{18}, and $R^{18'}$ each independently represent a hydrogen atom, a halogen atom, a hydroxy group, or $-NH_2$;

W^3 represents -NH-, an oxygen atom, a sulfur atom, or $-CH_2-$; and

W^4 represents -CH= or a nitrogen atom.

28. The antibody-drug conjugate according to claim 27, wherein D is represented by either one of the following two formulas: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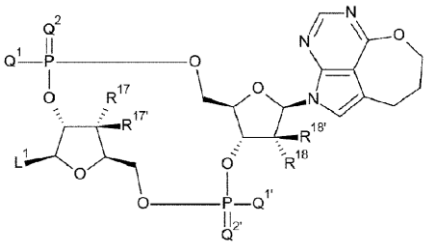
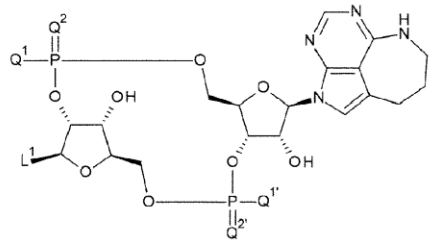


wherein

L^1, Q^1, $Q^{1'}$, Q^2, $Q^{2'}$, R^{17}, $R^{17'}$, R^{18}, and $R^{18'}$ are as defined above.

29. The antibody-drug conjugate according to claim 27 or 28, wherein D is represented by any one of the following eight formulas: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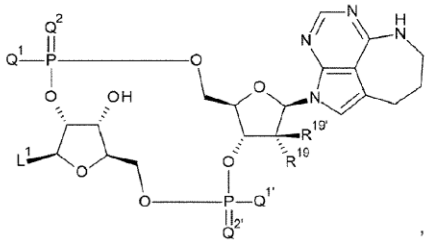
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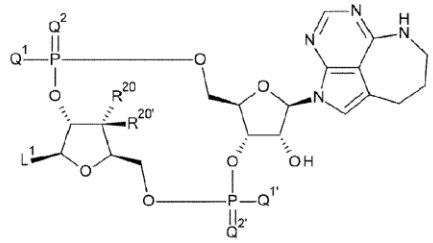
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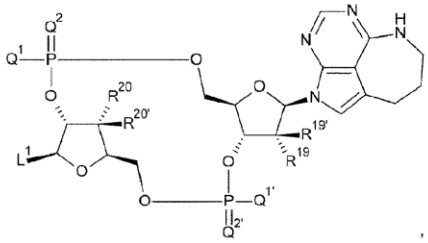
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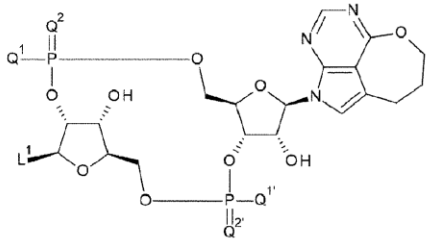
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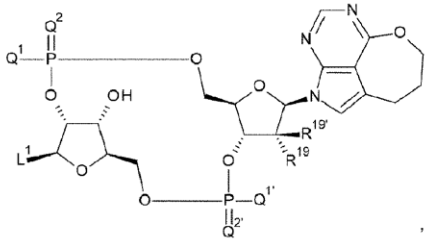
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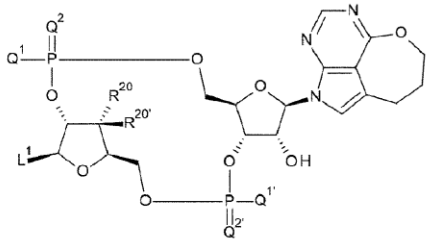
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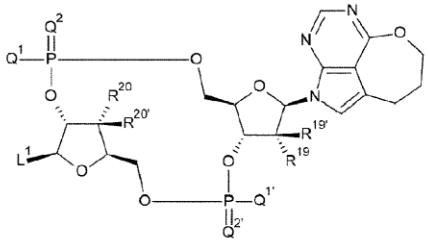
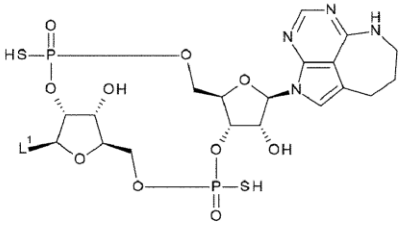


wherein

L^1, Q^1, $Q^{1'}$, Q^2, and $Q^{2'}$ are as defined above; and

R^{19}, $R^{19'}$, R^{20}, and $R^{20'}$ each independently represent a hydrogen atom or a fluorine atom.

30. The antibody-drug conjugate according to any one of claims 27 to 29, wherein D is represented by any one of the following four formulas: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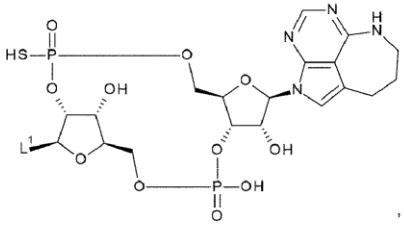
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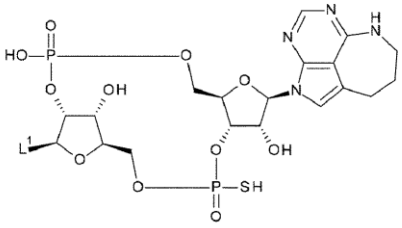
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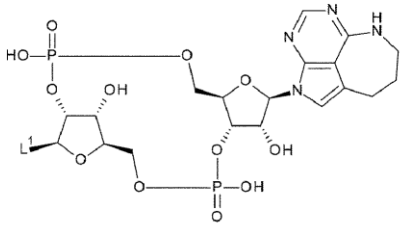
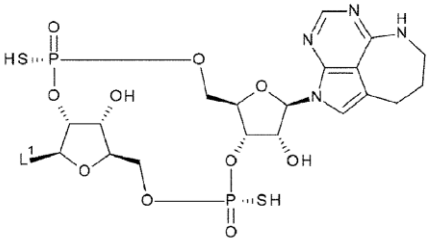


wherein

L^1 is as defined above.

31. The antibody-drug conjugate according to any one of claims 27 to 30, wherein D is represented by any one of the following four formulas: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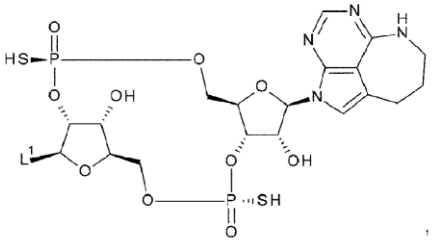
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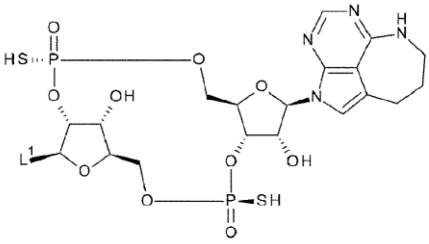
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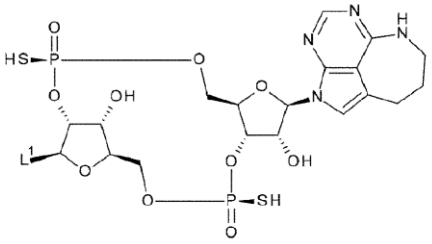
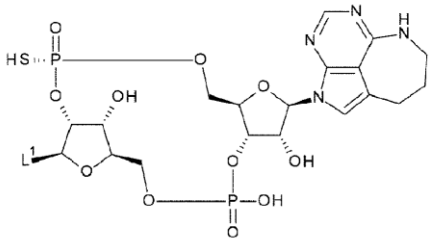


wherein

L^1 is as defined above.

32. The antibody-drug conjugate according to any one of claims 27 to 30, wherein D is represented by any one of the following four formulas: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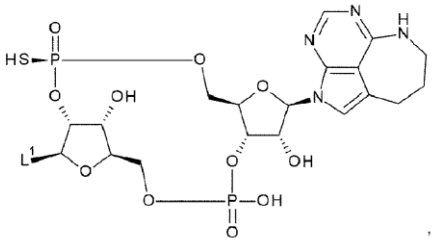
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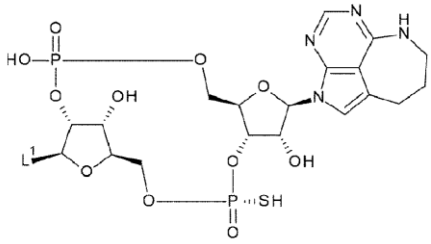
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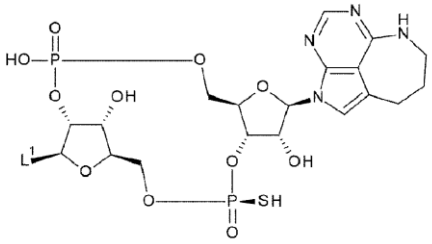
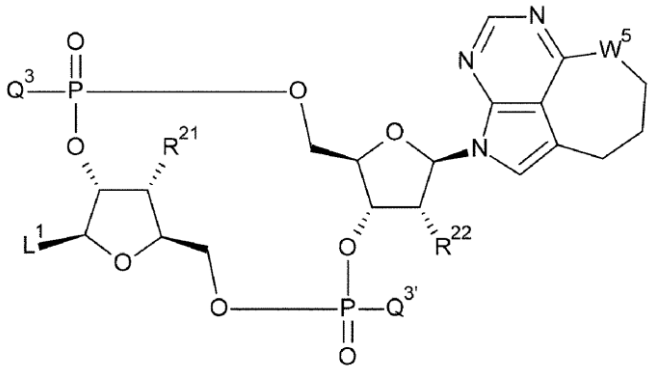


wherein

L^1 is as defined above.

33. The antibody-drug conjugate according to any one of claims 1 to 26, wherein D is represented by the following formula:



wherein

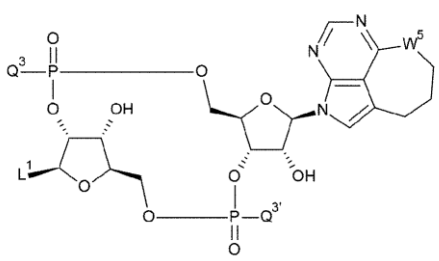
L^1 is as defined above;

Q^3 and $Q^{3'}$ each independently represent a hydroxy group or a thiol group;

R^{21} and R^{22} each independently represent a hydroxy group or a fluorine atom; and

W^5 represents -NH- or a sulfur atom.

34. The antibody-drug conjugate according to claim 33, wherein D is represented by either one of the following two formulas:



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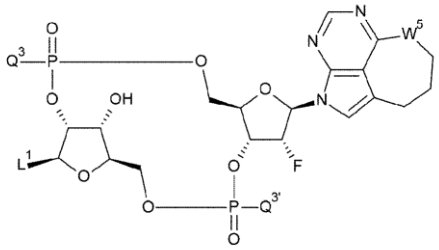
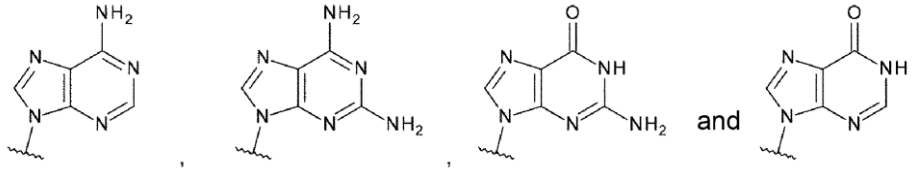


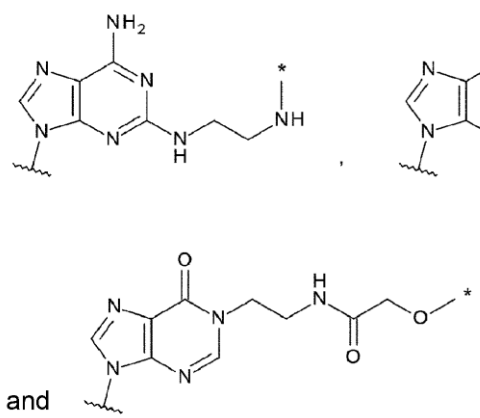
wherein

L^1, Q^3, $Q^{3'}$, and W^5 are as defined above.

35. The antibody-drug conjugate according to any one of claims 1 to 34, wherein L^1 is represented by any one of the following four formulas:



36. The antibody-drug conjugate according to any one of claims 1 to 34, wherein L^1 is represented by any one of the following four formulas:

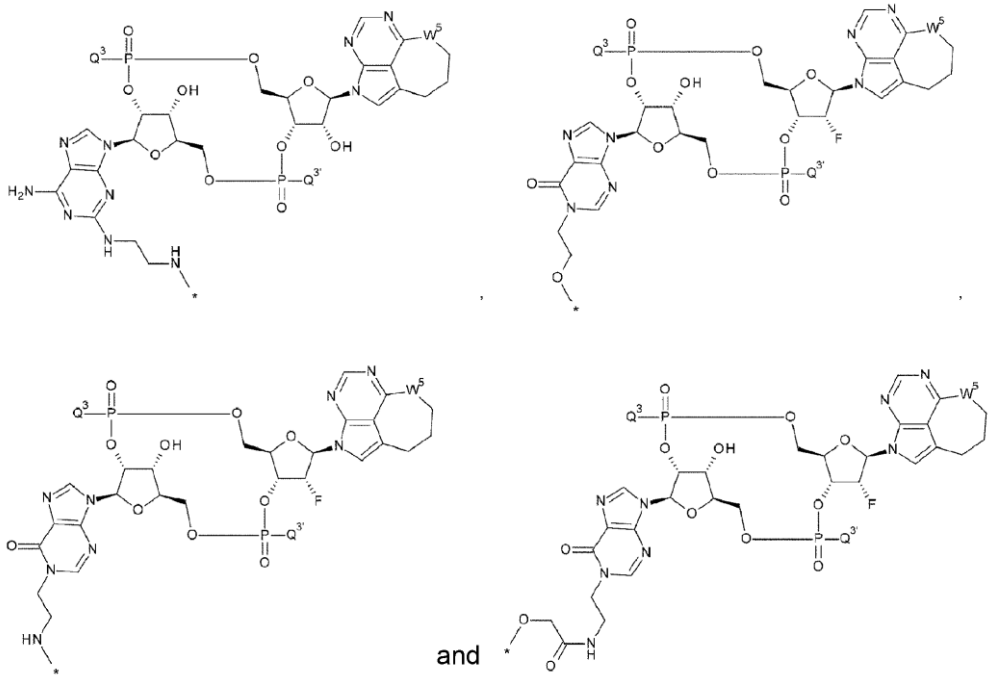


and

wherein

each asterisk indicates bonding to L.

37. The antibody-drug conjugate according to any one of claims 33, 34, and 36, wherein D is represented by any one of the following four formulas:



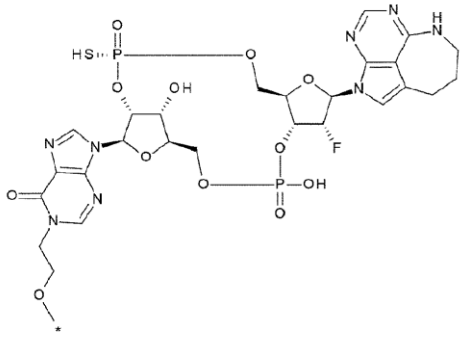
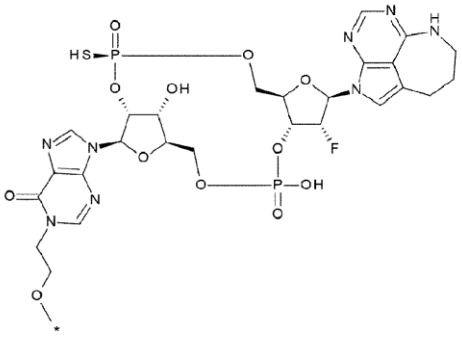
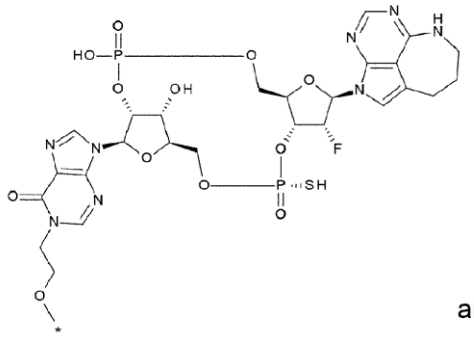
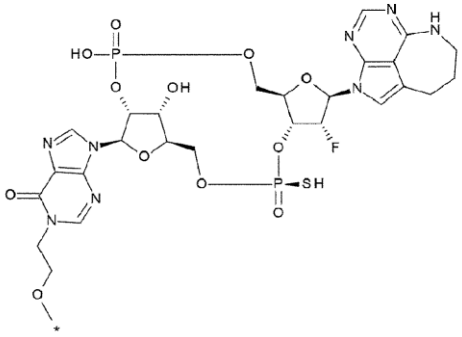
and

wherein

each asterisk indicates bonding to L; and

Q^3, $Q^{3'}$, and W^5 are as defined above.

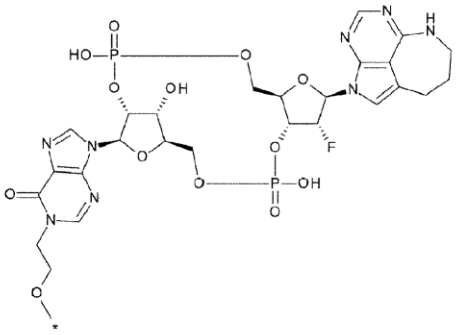
38. The antibody-drug conjugate according to any one of claims 33, 34, 36, and 37, wherein D is represented by any one of the following four formulas:


,


and


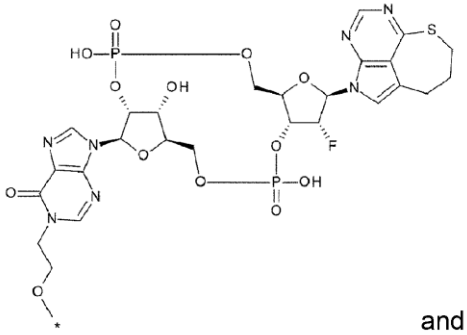
wherein

each asterisk indicates bonding to L.

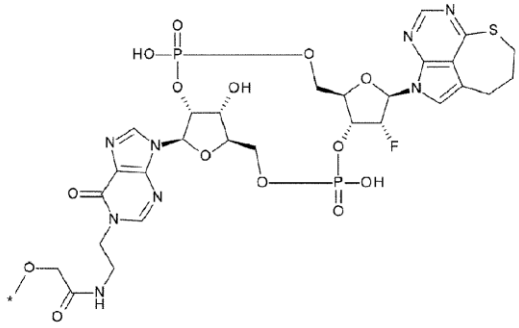
39. The antibody-drug conjugate according to any one of claims 33, 34, 36, and 37, wherein D is represented by any one of the following three formulas:



,



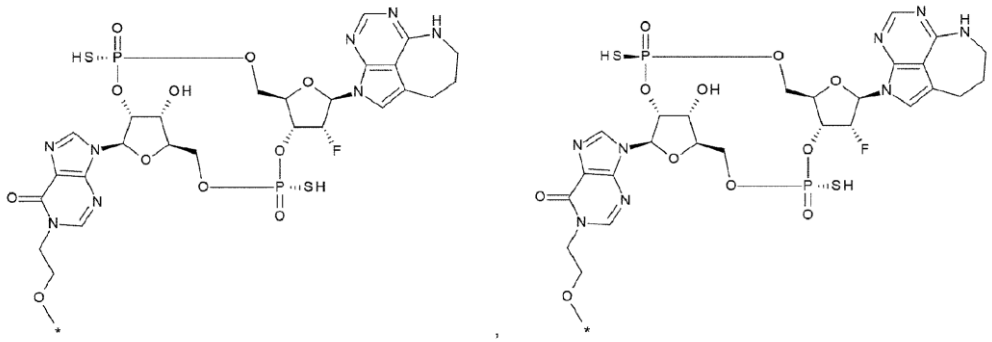
and

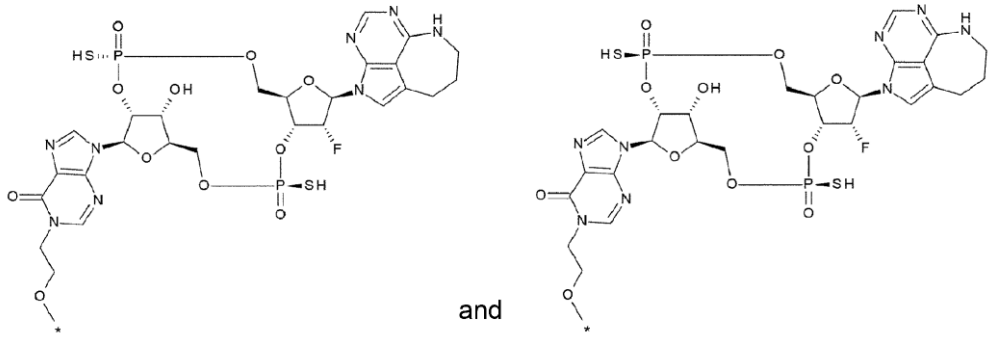


wherein

each asterisk indicates bonding to L.

40. The antibody-drug conjugate according to any one of claims 33, 34, 36, and 37, wherein D is represented by any one of the following four formulas:





and

wherein

each asterisk indicates bonding to L.

41. The antibody-drug conjugate according to any one of claims 1 to 40, wherein linker L is represented by -Lb-La-Lp-Lc-*, wherein

the asterisk indicates bonding to drug D;

Lp represents a linker consisting of an amino acid sequence cleavable in a target cell, or is absent;

La represents any one selected from the following group:

$-C(=O)-(CH_2CH_2)n^2-C(=O)-$,

$-C(=O)-(CH_2CH_2)n^2-CH_2-C(=O)-$,

$-C(=O)-(CH_2CH_2)n^2-C(=O)-NH-(CH_2CH_2)n^3-C(=O)-$,

$-C(=O)-(CH_2CH_2)n^2-C(=O)-NH-(CH_2CH_2)n^3-CH_2-C(=O)-$,

$-C(=O)-(CH_2CH_2)n^2-C(=O)-NH-(CH_2CH_2O)n^3-CH_2-C(=O)-$,

$-(CH_2)n^4-O-C(=O)-$, and

-$(CH_2)n^9$-C(=O)-, wherein

n^2 represents an integer of 1 to 3, n^3 represents an integer of 1 to 5, n^4 represents an integer of 0 to 2, and n^9 represents an integer of 2 to 7;

Lb represents a spacer bonding La and a glycan or remodeled glycan of Ab or a spacer bonding La and a cysteine residue of Ab; and

Lc represents -NH-CH_2-, -NH-phenyl group-CH_2-O(C=O)-, or -NH-heteroaryl group-CH_2-O(C=O)-, or is absent.

42. The antibody-drug conjugate according to claim 41, wherein Lc is absent.

43. The antibody-drug conjugate according to claim 41, wherein Lc is -NH-CH_2-.

44. The antibody-drug conjugate according to any one of claims 41 to 43, wherein Lp represents any one selected from the group consisting of:
-GGVA-, -VA-, -GGFG-, -FG-, -GGPI-, -PI-, -GGVCit-, -VCit-, -GGVK-, -VK-, -GGFCit-, -FCit-, -GGFM-, -FM-, -GGLM-, -LM-, -GGICit-, and -ICit-.

45. The antibody-drug conjugate according to claim 44, wherein Lp is any one of -GGVA-, -VA-, -GGFG-, -FG-, -GGVCit-, -VCit-, -GGFCit-, and -FCit-.

46. The antibody-drug conjugate according to any one of claims 41 to 43, wherein Lp is any one of -GGFG-, -GGPI-, -GGVA-, -GGFM-, -GGVCit-, -GGFCit-, -GGICit-, -GGPL-, -GGAQ-, and -GGPP-.

47. The antibody-drug conjugate according to claim 46, wherein Lp is -GGFG- or -GGPI-.

48. The antibody-drug conjugate according to any one of claims 41 to 47, wherein La represents any one selected from the group consisting of:

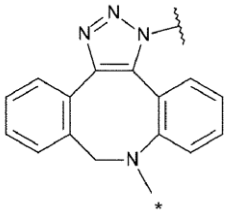
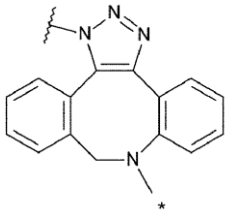
-C(=O)-CH_2CH_2-C(=O)-,

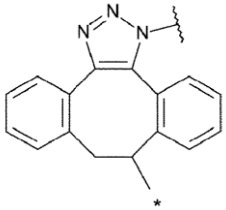
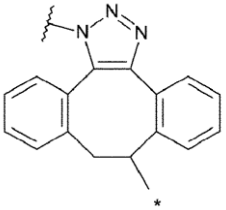
-C(=O)-CH_2CH_2-C(=O)-NH-$(CH_2CH_2O)_3$-CH_2-C(=O)-,

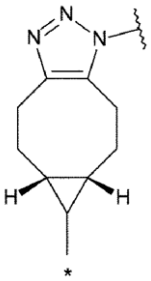
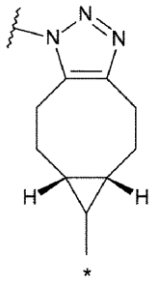
-C(=O)-CH_2CH_2-C(=O)-NH-$(CH_2CH_2O)_4$-CH_2-C(=O)-, and

-$(CH_2)_5$-C(=O)-.

49. The antibody-drug conjugate according to any one of claims 41 to 48, wherein Lb is represented by any one of the following formulas:


and


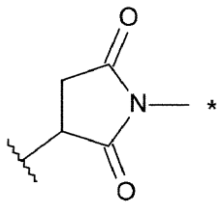

and

, and


and


wherein, in the structural formulas for Lb shown above,

each asterisk indicates bonding to La, and each wavy line indicates bonding to a glycan or remodeled glycan of Ab.

50. The antibody-drug conjugate according to any one of claims 41 to 48, wherein Lb is -(succinimid-3-yl-N)-, wherein -(succinimid-3-yl-N)- represents the following structural formula:



wherein the asterisk indicates bonding to La, and the wavy line indicates bonding to a side chain of a cysteine residue of the antibody through forming thioether.

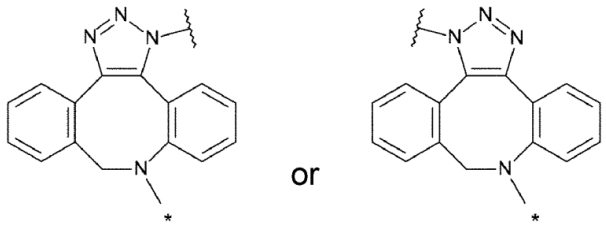
51. The antibody-drug conjugate according to any one of claims 41 and 46 to 49, wherein linker L is represented by -Lb-La-Lp-Lc-*, wherein

the asterisk indicates bonding to drug D;

Lp is -GGFG- or -GGPI-;

La represents -C(=O)-CH_2CH_2-C(=O)-;

Lb represents the following formula:



wherein, in the structural formulas for Lb shown above,

each asterisk indicates bonding to La, and each wavy line indicates bonding to a glycan or remodeled glycan of Ab; and

Lc represents -NH-CH_2-.

52. The antibody-drug conjugate according to any one of claims 1 to 51, wherein the average number of conjugated drug molecules per antibody molecule in the antibody-drug conjugate is in the range of 1 to 10.

53. The antibody-drug conjugate according to claim 52, wherein the average number of conjugated drug molecules per antibody molecule in the antibody-drug conjugate is in the range of 1 to 5.

54. The antibody-drug conjugate according to any one of claims 1 to 53, wherein the antibody bonds via a glycan bonding to Asn297 of the antibody (N297 glycan) to L.

55. The antibody-drug conjugate according to claim 54, wherein the N297 glycan is a remodeled glycan.

56. The antibody-drug conjugate according to claim 54 or 55, wherein the N297 glycan is N297-(Fuc)MSG1 or N297-(Fuc)SG.

57. The antibody-drug conjugate according to any one of claims 1 to 56, wherein the antibody or an antigen-binding fragment of the antibody is an anti-HER2 antibody, an anti-HER3 antibody, an anti-DLL3 antibody, an anti-FAP antibody, an anti-CDH11 antibody, an anti-CDH6 antibody, an anti-A33 antibody, an anti-CanAg antibody, an anti-CD19 antibody, an anti-CD20 antibody, an anti-CD22 antibody, an anti-CD30 antibody, an anti-CD33 antibody, an anti-CD56 antibody, an anti-CD70 antibody, an anti-CD98 antibody, an anti-TROP2 antibody, an anti-CEA antibody, an anti-Cripto antibody, an anti-EphA2 antibody, an anti-G250 antibody, an anti-MUC1 antibody, an anti-GPNMB antibody, an anti-Integrin antibody, an anti-PSMA

antibody, an anti-Tenascin-C antibody, an anti-SLC44A4 antibody, an anti-Mesothelin antibody, an anti-ENPP3 antibody, an anti-CD47 antibody, an anti-EGFR antibody, an anti-GPR20 antibody, or an anti-DR5 antibody or an antigen-binding fragment of the antibody.

58. The antibody-drug conjugate according to any one of claims 1 to 57, wherein the antibody or an antigen-binding fragment of the antibody is any one selected from the group consisting of IgG being IgG1, IgG2, IgG3, or IgG4, IgE, IgM, IgD, IgA being IgA1 or IgA2, and IgY.

59. The antibody-drug conjugate according to claim 58, wherein the antibody or an antigen-binding fragment of the antibody is IgG1.

60. The antibody-drug conjugate according to claim 59, wherein a part of the amino acid residues in the constant region is substituted.

61. The antibody-drug conjugate according to claim 60, wherein the substition comprises substitution of leucine with alanine at positions 234 and 235 specified by EU Index numbering.

62. The antibody-drug conjugate according to any one of claims 1 to 61, wherein the antibody or an antigen-binding fragment of the antibody is a protein produced in host cells by using a genetically engineered antibody gene.

63. The antibody-drug conjugate according to claim 57, wherein the antibody or an antigen-binding fragment of the antibody is an anti-HER2 antibody or an antigen-binding fragment of the antibody.

64. The antibody-drug conjugate according to claim 63, wherein the antibody or an antigen-binding fragment of the antibody is any one of the following (i) to (iii):

(i) an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 1 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 2 or an antigen-binding fragment of the antibody, or an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 1 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 3 or an antigen-binding fragment of the antibody;

(ii) the antibody or an antigen-binding fragment of the antibody as defined in (i) wherein a part of the amino acid residues in the constant region is substituted; and

(iii) a protein produced in host cells by using a gene (a) which is modified by genetical engineering from a gene (b) of the antibody or an antigen-binding fragment of the antibody as defined in (i).

65. The antibody-drug conjugate according to claim 63, wherein the antibody or an antigen-binding fragment of the antibody is any one of the following (i) to (iii):

(i) an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 29 or an antigen-binding fragment of the antibody, or an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 30 or an antigen-binding fragment of the antibody;

(ii) the antibody or an antigen-binding fragment of the antibody as defined in (i) wherein a part of the amino acid residues in the constant region is substituted; and

(iii) a protein produced in host cells by using a gene (a) which is modified by genetical engineering from a gene (b) of the antibody or an antigen-binding fragment of the antibody as defined in (i).

66. The antibody-drug conjugate according to claim 64 or 65, wherein the substition comprises substitution of leucine with alanine at positions 234 and 235 specified by EU Index numbering.

~~67. The antibody-drug conjugate according to claim 57, wherein the antibody or an antigen-binding fragment of the antibody is an anti-CD33 antibody, an anti-EphA2 antibody, or an anti-CDH6 antibody or an antigen-binding fragment of the antibody.~~

67. The antibody-drug conjugate according to any one of claims 63 to 66, wherein one or two amino acids are deleted at the carboxyl terminus of the heavy chain of the antibody or an antigen-binding fragment of the antibody.

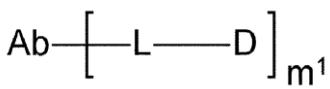
68. The antibody-drug conjugate according to claim 57, wherein the antibody or an antigen-binding fragment of the antibody is an anti-CD33 antibody, an anti-EphA2 antibody, or an anti-CDH6 antibody or an antigen-binding fragment of the antibody.

~~68~~69. The antibody-drug conjugate according to claim ~~57~~67~~68~~, wherein the antibody is an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 31 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 32, an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 33 and a heavy

chain consisting of an amino acid sequence represented by SEQ ID NO: 34, or an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 35 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 36.

~~69. The antibody-drug conjugate according to any one of claims 63 to 68, wherein one or two amino acids are deleted at the carboxyl terminus of the heavy chain of the antibody or an antigen-binding fragment of the antibody.~~

70. An antibody-drug conjugate represented by formula (II):



(II)

wherein

m^1 is in the range of 3 to 5;

Ab represents an anti-HER2 antibody, where a glycan of the antibody is remodeled;

L represents a linker linking Ab and D;

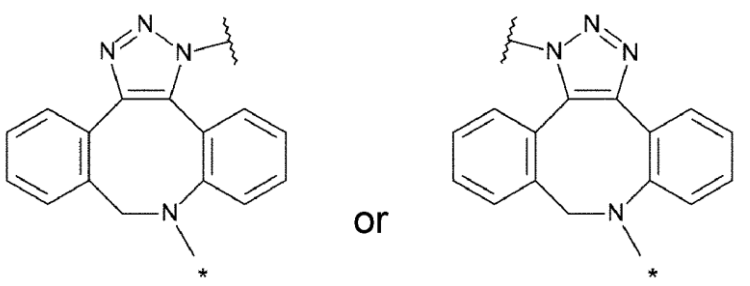
wherein linker L is represented by -Lb-La-Lp-Lc-*, wherein

the asterisk indicates bonding to drug D;

Lp is -GGFG-;

La represents -C(=O)-CH_2CH_2-C(=O)-;

Lb represents the following formula:



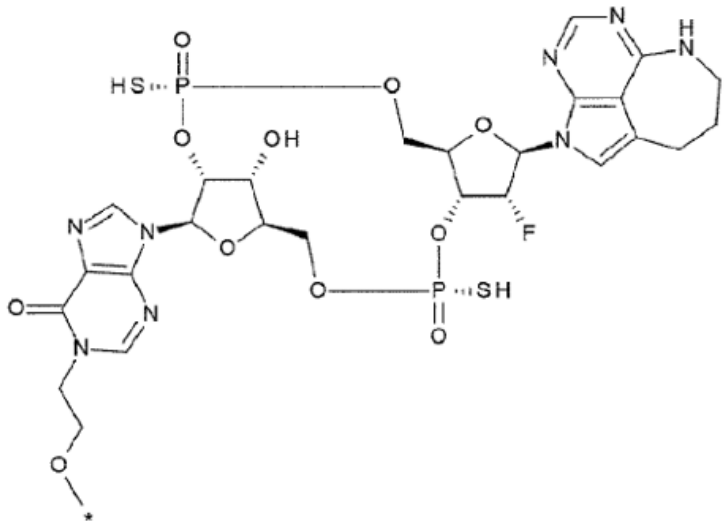
wherein, in the structural formulas for Lb shown above,

each asterisk indicates bonding to La, and each wavy line indicates bonding to a remodeled glycan of Ab; and

Lc represents -NH-CH_2-;

Ab bonds via a glycan bonding to Asn297 of the antibody (N297-(Fuc) SG) to L; and

D represents a compound represented by formula (I):



wherein

the asterisk indicates bonding to L.

71. The antibody-drug conjugate according to claim 70, wherein the antibody is any one of the following (i) to (iii):

(i) an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 29, or an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 30;

(ii) the antibody as defined in (i) wherein a part of the amino acid residues in the constant region is substituted; and

(iii) a protein produced in host cells by using a gene (a) which is modified by genetic engineering from a gene (b) of the antibody as defined in (i).

72. The antibody-drug conjugate according to claim 71, wherein the substition comprises substitution of leucine with alanine at positions 234 and 235 specified by EU Index numbering.

73. The antibody-drug conjugate according to claim 70 or 71,
wherein the antibody is an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 29,
wherein a part of the amino acid residues in the constant region of the antibody is substituted.

74. The antibody-drug conjugate according to claim 73, wherein the antibody or an antigen-binding fragment of the antibody is IgG1.

75. The antibody-drug conjugate according to claim 70 or 71,
wherein the antibody is an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 29,
wherein the constant region of the antibody comprises substitution of leucine with alanine at positions 234 and 235 specified by EU Index numbering.

76. The antibody-drug conjugate according to claim 70 or 71,

wherein the antibody is an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 30,
wherein a part of the amino acid residues in the constant region of the antibody is substituted.

77. The antibody-drug conjugate according to claim 76, wherein the antibody or an antigen-binding fragment of the antibody is IgG1.

78. The antibody-drug conjugate according to claim 70 or 71,
wherein the antibody is an antibody comprising a light chain consisting of an amino acid sequence represented by SEQ ID NO: 28 and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 30,
wherein the constant region of the antibody comprises substitution of leucine with alanine at positions 234 and 235 specified by EU Index numbering.

79. The antibody-drug conjugate according to any one of claims 70 to 78, wherein one or two amino acids are deleted at the carboxyl terminus of the heavy chain of the antibody.

~~69~~80. A STING agonist comprising any one selected from the group consisting of the antibody-drug conjugate according to any one of claims 1 to ~~68~~79.

~~70~~81. A pharmaceutical composition comprising any one selected from the group consisting of the antibody-drug conjugate according to any one of claims 1 to ~~68~~79.

~~71~~82. An anti-tumor agent comprising any one selected from the group consisting of the antibody-drug conjugate according to any one of claims 1 to ~~68~~79.

~~72. The anti-tumor agent according to claim 71, wherein the tumor is lung cancer, kidney cancer, urothelial cancer, colorectal cancer, prostate cancer, glioblastoma multiforme, ovarian cancer, pancreatic cancer, breast cancer, melanoma, liver cancer, bladder cancer, gastric cancer, esophageal cancer, endometrial cancer, testicular cancer, uterine cervix cancer, placental choriocarcinoma, glioblastoma multiforme, brain tumor, head-and-neck cancer, thyroid cancer, mesothelioma, gastrointestinal stromal tumor (GIST), gallbladder cancer, bile duct cancer, adrenal cancer, squamous cell carcinoma, leukemia, malignant lymphoma, plasmacytoma, myeloma, or sarcoma.~~

~~73~~83. The antibody-drug conjugate according to any one of claims 1 to ~~68~~79, the STING agonist according to claim ~~69~~80, the pharmaceutical composition according to claim ~~70~~81, or the anti-tumor agent according to claim ~~71 or 72~~82 for use in the treatment of cancer.

~~74~~84. The ~~antibody-drug conjugate, the STING agonist, the pharmaceutical composition, or the anti-tumor agent~~use according to claim ~~73~~83, wherein the cancer is lung cancer, kidney cancer, urothelial cancer, colorectal cancer, prostate cancer, glioblastoma multiforme, ovarian cancer, pancreatic cancer, breast cancer, melanoma, liver cancer, bladder cancer, gastric cancer, esophageal cancer, endometrial cancer, testicular cancer, uterine cervix cancer, placental choriocarcinoma, glioblastoma multiforme, brain tumor, head-and-neck cancer, thyroid cancer, mesothelioma, gastrointestinal stromal tumor (GIST), gallbladder cancer, bile duct cancer, adrenal cancer, squamous cell carcinoma, leukemia, malignant lymphoma, plasmacytoma, myeloma, or sarcoma.

85. Use of the antibody-drug conjugate according to any one of claims 1 to 79, the STING agonist according to claim 80, the pharmaceutical composition according to claim 81, or the anti-tumor agent according to claim 82 in the manufacture of a medicament for the treatment of cancer.

86. The use according to claim 85, wherein the cancer is lung cancer, kidney cancer, urothelial cancer, colorectal cancer, prostate cancer, glioblastoma multiforme, ovarian cancer, pancreatic cancer, breast cancer, melanoma, liver cancer, bladder cancer, gastric cancer, esophageal cancer, endometrial cancer, testicular cancer, uterine cervix cancer, placental choriocarcinoma, glioblastoma multiforme, brain tumor, head-and-neck cancer, thyroid cancer, mesothelioma, gastrointestinal stromal tumor (GIST), gallbladder cancer, bile duct cancer, adrenal cancer, squamous cell carcinoma, leukemia, malignant lymphoma, plasmacytoma, myeloma, or sarcoma.