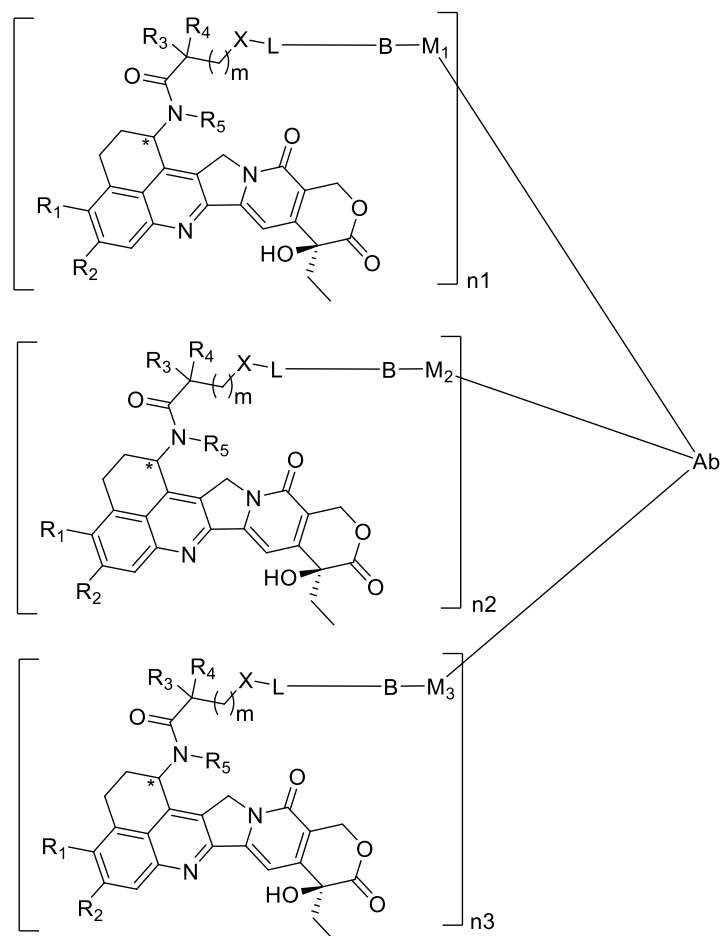


CLAIMS

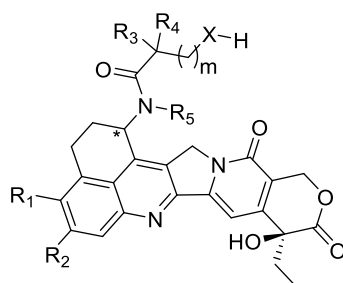
1. An antibody-drug conjugate of general formula **I** or its stereoisomer, pharmaceutically acceptable salt or solvate thereof,



I

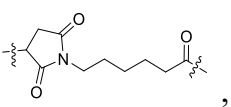
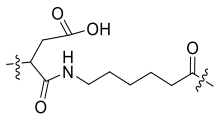
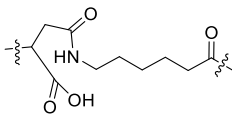
wherein:

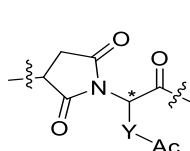
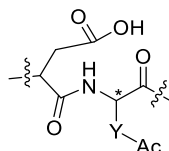
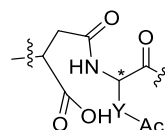
the drug in the antibody-drug conjugate is a camptothecin antitumor drug or a stereoisomer thereof, as shown in formula **II** below



II

Ab comprises an anti-CD33 antibody or an antigen-binding fragment thereof;

M₁, M₂, and M₃ are each independently selected from , , and , and M₁, M₂, and M₃ are not identical to each other; or M₁, M₂, and M₃ are each independently selected from the structure represented by formula A₁, formula A₂, and formula A₃, and M₁, M₂, and M₃ are different from each other;

A₁A₂A₃

wherein Y is a scaffold selected from C1-C6 alkyl, substituted C1-C6 alkyl, or C3-C8 cycloalkyl; preferably Y is C1-C6 alkyl; Ac is a hydrophilic structural unit; and the position indicated by the wavy line on the left is connected to Ab, and the position indicated by the wavy line on the right is connected to B or L;

B is present or absent, and, when present, B is a modifier unit;

L is a linker unit, preferably a peptide-containing linker unit;

X is selected from -NH-, -O- and -S-, preferably -O-;

R₁ and R₂ are the same or different and are each independently selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7-membered heterocyclyl, substituted 3-7-membered heterocyclyl, C6-C10 aryl, substituted C6-C10 aryl, 5-10-membered heteroaryl, and substituted 5-10-membered heteroaryl;

R₃ and R₄ are the same or different, each independently selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7-membered heterocyclyl, substituted 3-7-membered heterocyclyl, C6-C10 aryl, substituted C6-C10 aryl, C6-C10 aryl C1-C6 alkyl, 5-10-membered heteroaryl, and substituted 5-10-membered heteroaryl; preferably R₃, R₄ are each independently selected from hydrogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, and C6-C10 aryl C1-C6 alkyl;

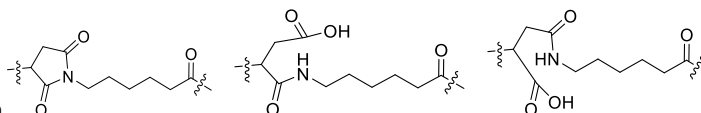
alternatively, R₃, R₄ and the carbon atoms to which they are attached constitute a C3-C8 cycloalkyl group, a 3-7-membered heterocyclic group, a substituted 3-7-membered heterocyclic group; preferably R₃, R₄ and the carbon atoms to which they are attached constitute a C3-C8 cycloalkyl group;

R₅ is selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, and C1-C6 alkoxy C1-C6 alkyl; preferably, R₅ is selected from hydrogen, and C1-C6 alkyl;

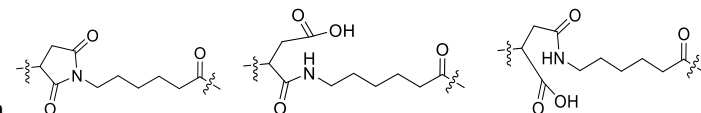
m is an integer from 0-5;

n₁, n₂, and n₃ are each independently an integer or a decimal from 0 to 10, n₁, n₂, and n₃ are not simultaneously 0, and $1 \leq n_1 + n_2 + n_3 \leq 10$;

the chiral carbon atom indicated at position * has an R or S absolute configuration; and the following conditions are met, when M₁, M₂, and M₃ are each independently

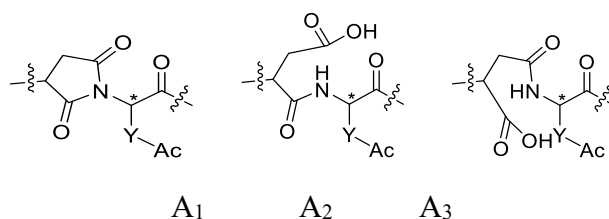
selected from , M₁, M₂, and M₃ are not identical to each other; B is present and is a modifier unit.

2. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein M₁, M₂, M₃ are each independently

selected from , and M₁, M₂, M₃ are not identical to each other;

alternatively, M₁, M₂, M₃ are each independently selected from the structure represented by formula A₁, formula A₂, formula A₃, and M₁, M₂, and M₃ are not identical to each other;

preferably, M₁, M₂, M₃ are each independently selected from the structures shown in formula A₁, formula A₂, formula A₃, and M₁, M₂, M₃ are not identical to each other;



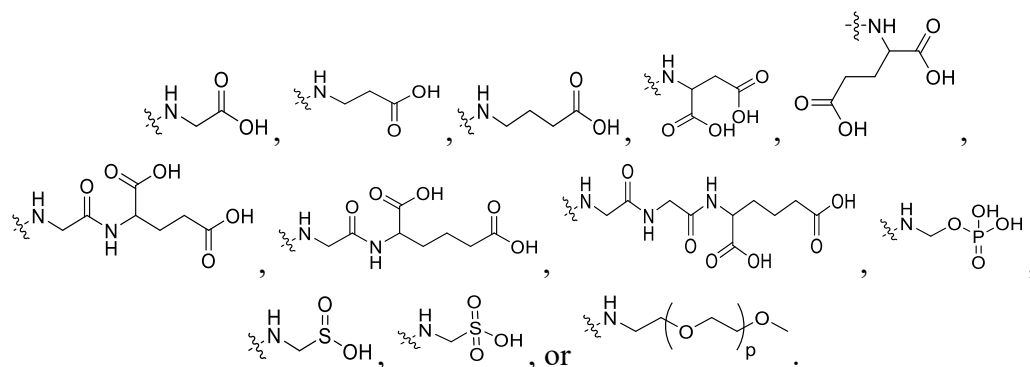
wherein Y is a scaffold selected from C1-C6 alkyl, substituted C1-C6 alkyl, and C3-C8 cycloalkyl; preferably Y is C1-C6 alkyl, more preferably C1-C3 alkyl, and most preferably methylene;

the chiral carbon atom indicated at position * has an R or S absolute configuration;

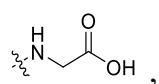
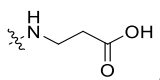
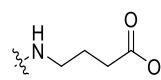
the position indicated by the left wavy line is connected to Ab, and the position shown by the right wavy line is connected to B or L;

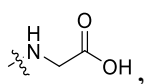
the hydrophilic structural unit Ac comprises a natural or non-natural amino acid,

1-20 polyethylene glycol, phosphate group, carboxylic acid group, sulfonic acid group, sulfinic acid group, or the following structures:

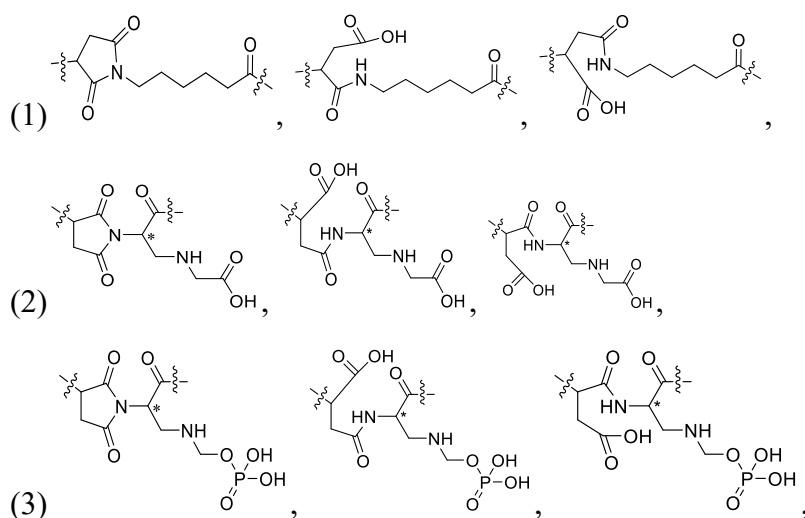


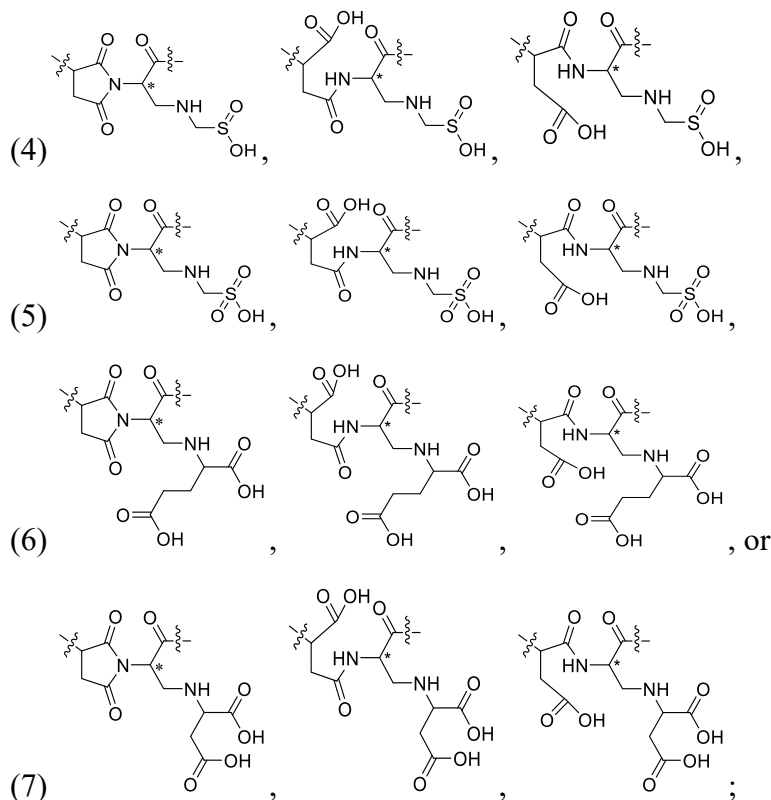
wherein p is an integer from 0 to 10; the position indicated by the wavy line is connected to the bracket Y;

preferably, the hydrophilic structural unit Ac is selected from , , , and is connected to the bracket Y at the position indicated by the wavy line;

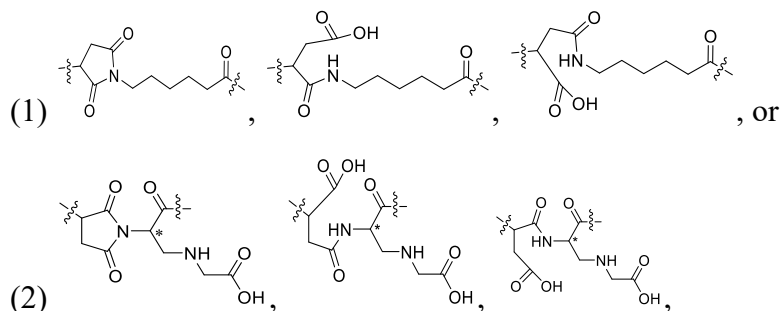
more preferably, the hydrophilic structural unit Ac is , connected to the bracket Y at the position indicated by the wavy line.

3. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to Claim 1 or 2, wherein M₁, M₂, M₃ are selected from any one of the following combinations (1)-(7), and M₁, M₂, M₃ are not identical to each other:

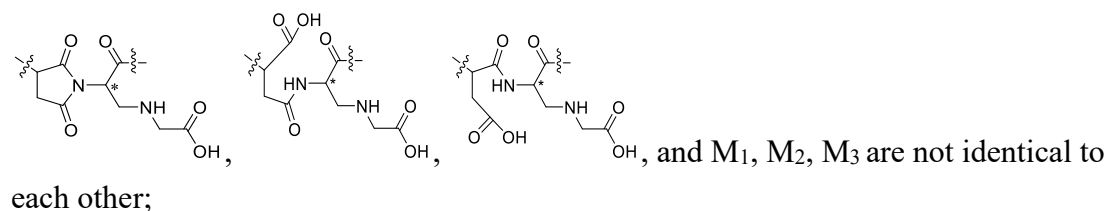




preferably, M_1 , M_2 , M_3 are selected from any one of the following combinations (1)-(2), and M_1 , M_2 , M_3 are not identical to each other,



more preferably, M_1 , M_2 , M_3 are each independently selected from



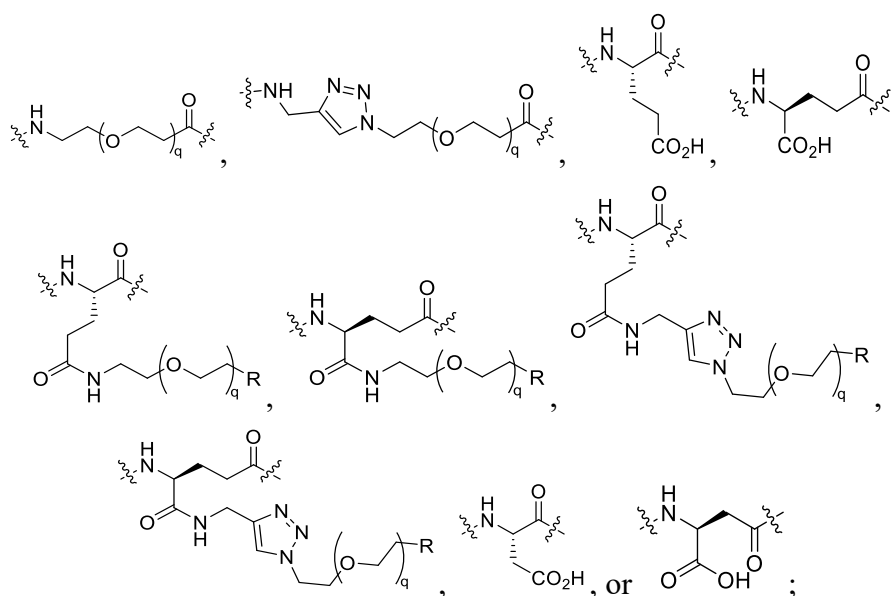
wherein:

the chiral carbon atom indicated at position * has an R or S absolute configuration;

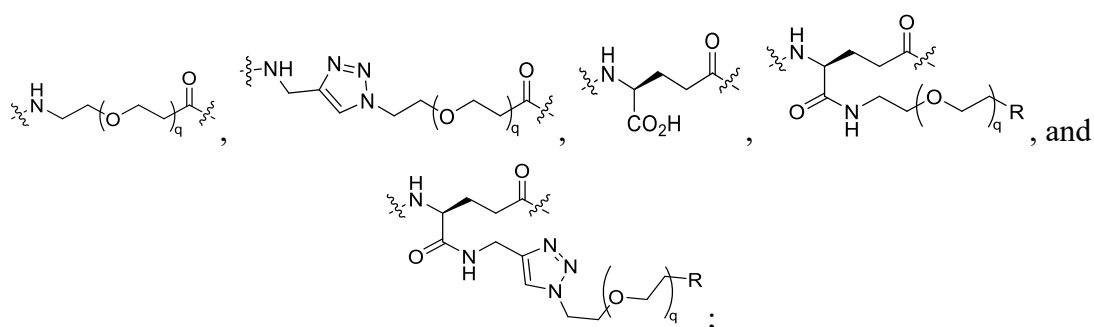
the position indicated by the left wavy line is connected to Ab; the position indicated by the right wavy line is connected to the modifier unit B or the linker unit L.

4. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 3, wherein the modifier unit B is present or absent, and when present, B comprises a hydrophilicity-enhancing structure or a stereoisomer thereof.

5. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 4, wherein the modifier unit B is present or absent, and when present, B comprises a hydrophilicity-enhancing structure or a stereoisomer thereof as shown in the following formula:



preferably, the modifier unit B is present or absent, and when present, the modifier unit B comprises a hydrophilicity-enhancing structure or a stereoisomer thereof as shown in the following formula .



wherein:

R comprises hydroxyl, amino, polyethylene glycol, carboxylic acid group, sulfonic acid group, sulfinic acid group, phosphoric acid group, C1-C6 alkyl, C1-C6 alkoxy, natural or non-natural amino acid residue, sugar or a derivative thereof, or a combination thereof;

preferably, R is selected from C1-C6 alkoxy, carboxylic acid group, and amino group;

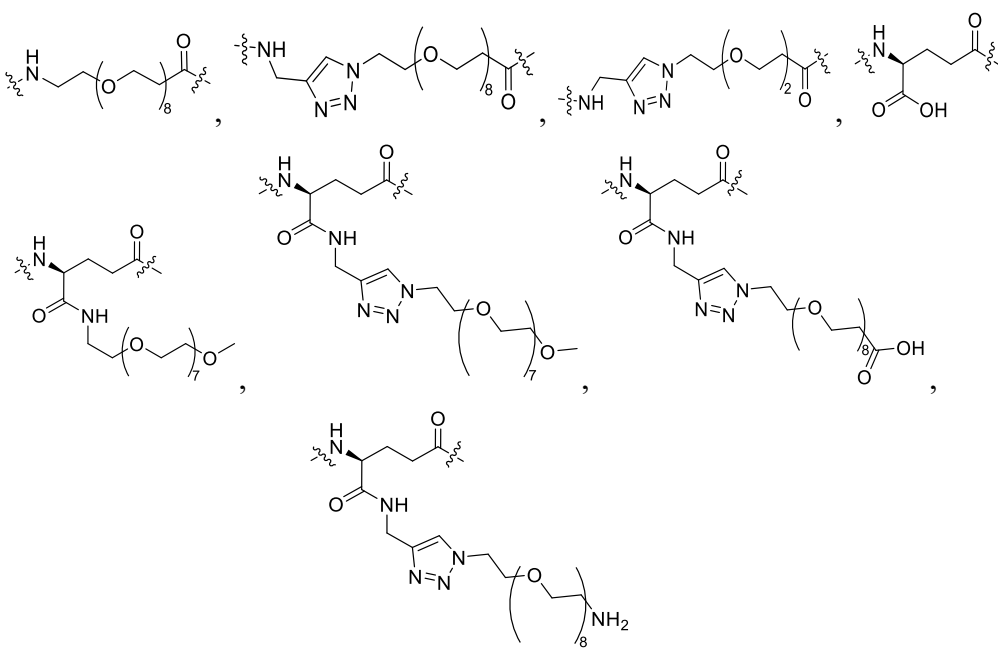
more preferably, R is selected from methoxy, carboxylic acid group, and amino group;

the position indicated by the wavy line on the left is connected to M₁, M₂, or M₃;

the position indicated by the wavy line on the right is connected to L;

q is an integer from 1-10, preferably 2, 7, or 8;

most preferably, the modifier unit B is selected from a hydrophilicity-enhancing structure or a stereoisomer thereof as shown in the following formula:



the position indicated by the left wavy line is connected to M₁, M₂, or M₃, and the position indicated by the right wavy line is connected to the linker unit L.

6. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 5, wherein the linker unit L is L₁-L₂,

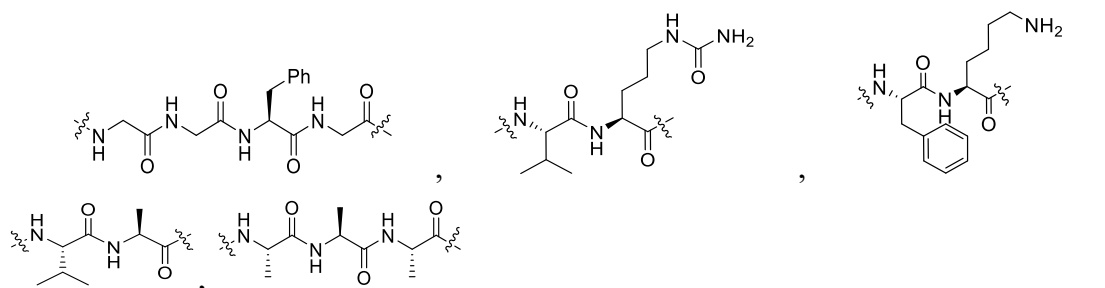
L₁ is a peptide residue comprising 2-10 amino acid residues, the peptide residue having an amino terminus connected to the modifier unit B or to M₁, M₂, M₃ and a carbonyl terminus connected to L₂;

preferably, L₁ is a peptide residue comprising 2-4 amino acid residues, the peptide residue having the amino terminus connected to B or to M₁, M₂, M₃, and the carbonyl terminus connected to L₂; preferably, the amino acid is selected from valine, alanine, phenylalanine, glycine, lysine, citrulline, serine, glutamic acid, and aspartic acid; more

preferably, the amino acid is selected from valine, alanine, phenylalanine, glycine, lysine, and citrulline; most preferably, the amino acid is selected from valine, phenylalanine, glycine, lysine, and citrulline;

more preferably, L_1 is selected from the following peptide residues: glycine-glycine-phenylalanine-glycine, valine-citrulline, phenylalanine-lysine, valine-alanine, and alanine-alanine-alanine (preferably selected from glycine-glycine-phenylalanine-glycine, valine-citrulline, and phenylalanine-lysine), the amino terminus of the peptide residues is connected to B or to M_1 , M_2 , M_3 , and the carbonyl terminus is connected to L_2 ;

most preferably, L_1 is selected from the following peptide residues:



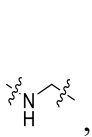
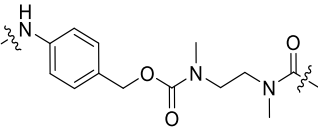
(preferably selected from

), the peptide residues having an amino terminus connected to B or to M_1 , M_2 , M_3 and a carbonyl terminus to L_2 ;

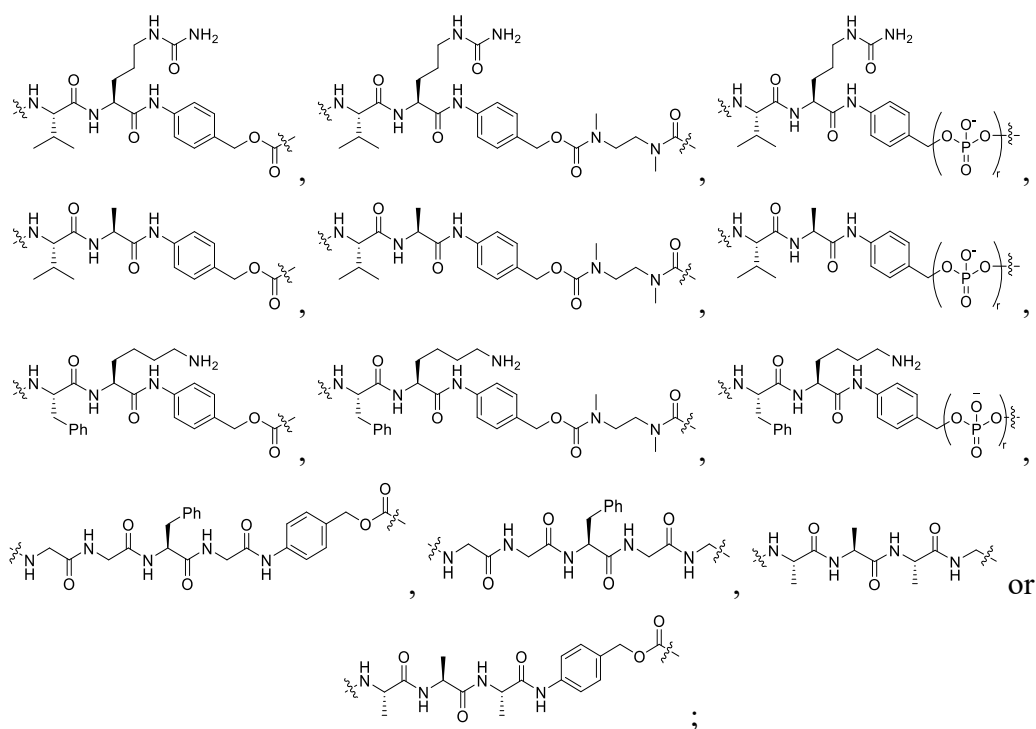
L_2 is selected from , and is connected to L_1 at the position indicated by the left wavy line, and to X at the position indicated by the right wavy line;

preferably, L_2 is selected from , and is connected to L_1 at the position indicated by the left

wavy line, and to X at the position indicated by the right wavy line;

more preferably, L₂ is selected from , , and is connected to L₁ at the position indicated by the left wavy line, and to X at the position indicated by the right wavy line;

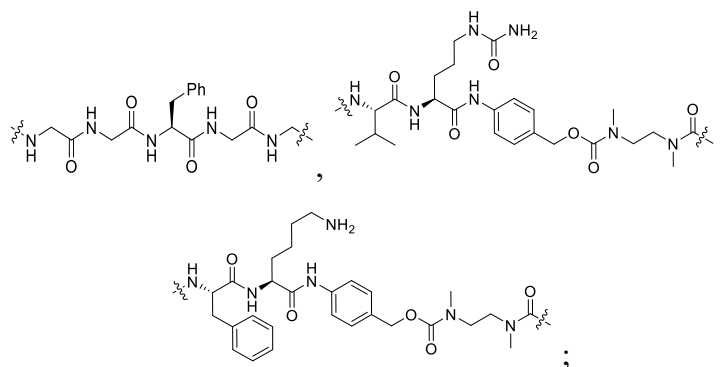
preferably, the linker unit L comprises the following structures or stereoisomers thereof.



wherein:

r is an integer from 1-10;

more preferably, the linker unit L is selected from the following structures or stereoisomers thereof:



the linker unit L is connected to the modifier unit B or to M₁, M₂, M₃ at the position

indicated by the wavy line on the left side;

the linker unit L is connected to X at the position indicated by the wavy line on the right side.

7. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 6, wherein R_1 and R_2 are the same or different and are each independently selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7-membered heterocyclyl, substituted 3-7-membered heterocyclyl, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, and substituted 5-10-membered heteroaryl;

preferably, R_1 and R_2 are the same or different and are each independently selected from halogen, and C1-C6 alkyl;

more preferably, R_1 is selected from C1-C6 alkyl and R_2 is selected from halogen;

most preferably, R_1 is methyl and R_2 is fluoride;

R_3 and R_4 are the same or different, each independently selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7-membered heterocyclic, substituted 3-7-membered heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, C6-C10 aryl C1-C6 alkyl, 5-10-membered heteroaryl, and substituted 5-10-membered heteroaryl;

preferably, R_3 , R_4 are the same or different, each independently selected from hydrogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl and C6-C10 aryl C1-C6 alkyl;

further preferably, R_3 , R_4 are the same or different, each independently selected from hydrogen, C1-C6 alkyl, halo-C1-C6 alkyl, C3-C6 cycloalkyl, C3-C6 cycloalkyl C1-C6 alkyl, and phenyl C1-C6 alkyl;

more preferably, R_3 , R_4 are the same or different, each independently selected from hydrogen, methyl, ethyl, trifluoromethyl, cyclopropyl, cyclopropylmethyl, and benzyl;

most preferably, of R_3 , R_4 , any one is selected from hydrogen, methyl, and the other is selected from hydrogen, methyl, ethyl, trifluoromethyl, cyclopropyl, cyclopropylmethyl, benzyl;

alternatively, R_3 , R_4 and the carbon atoms to which they are attached constitute a C3-C8 cycloalkyl group, a 3-7-membered heterocyclic group, a substituted 3-7-membered heterocyclic group;

preferably, R_3 , R_4 and the carbon atoms to which they are attached constitute a C3-

C8 cycloalkyl group;

more preferably, R₃, R₄ and the carbon atoms to which they are attached constitute a C3-C6 cycloalkyl group;

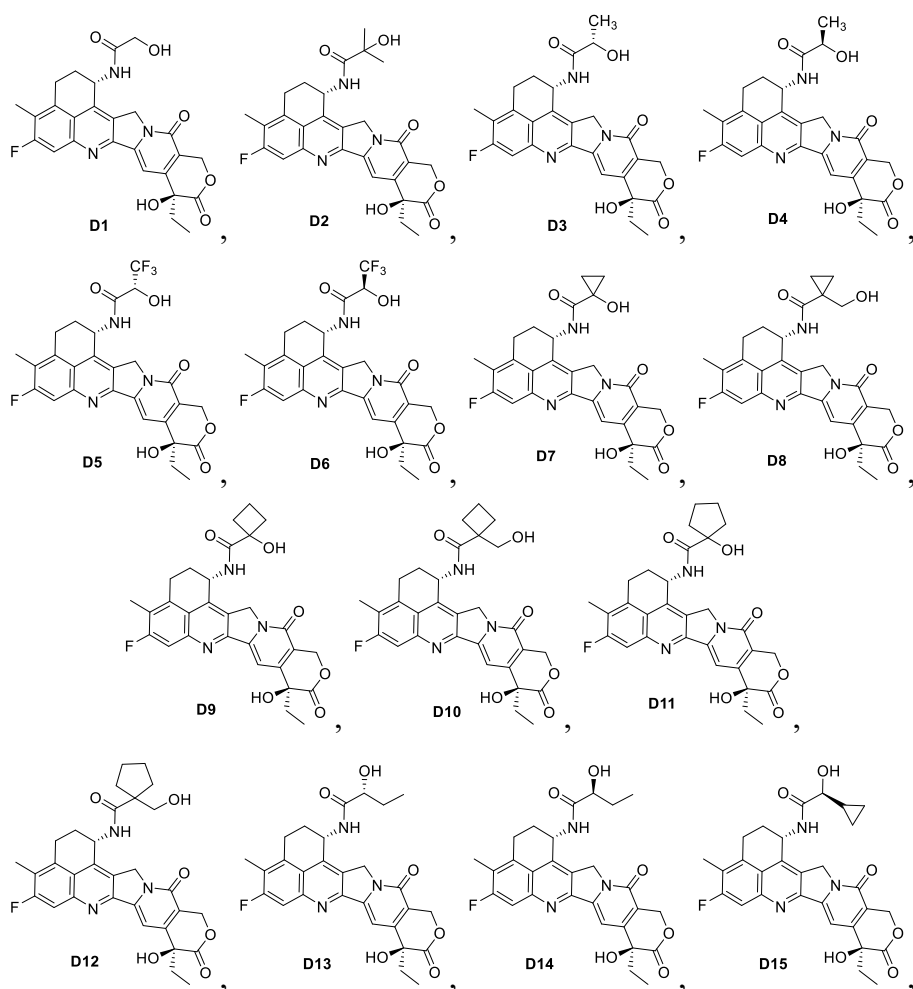
most preferably, R₃, R₄ and the carbon atom to which it is attached constitute a cyclopropyl, cyclobutyl or cyclopentyl group;

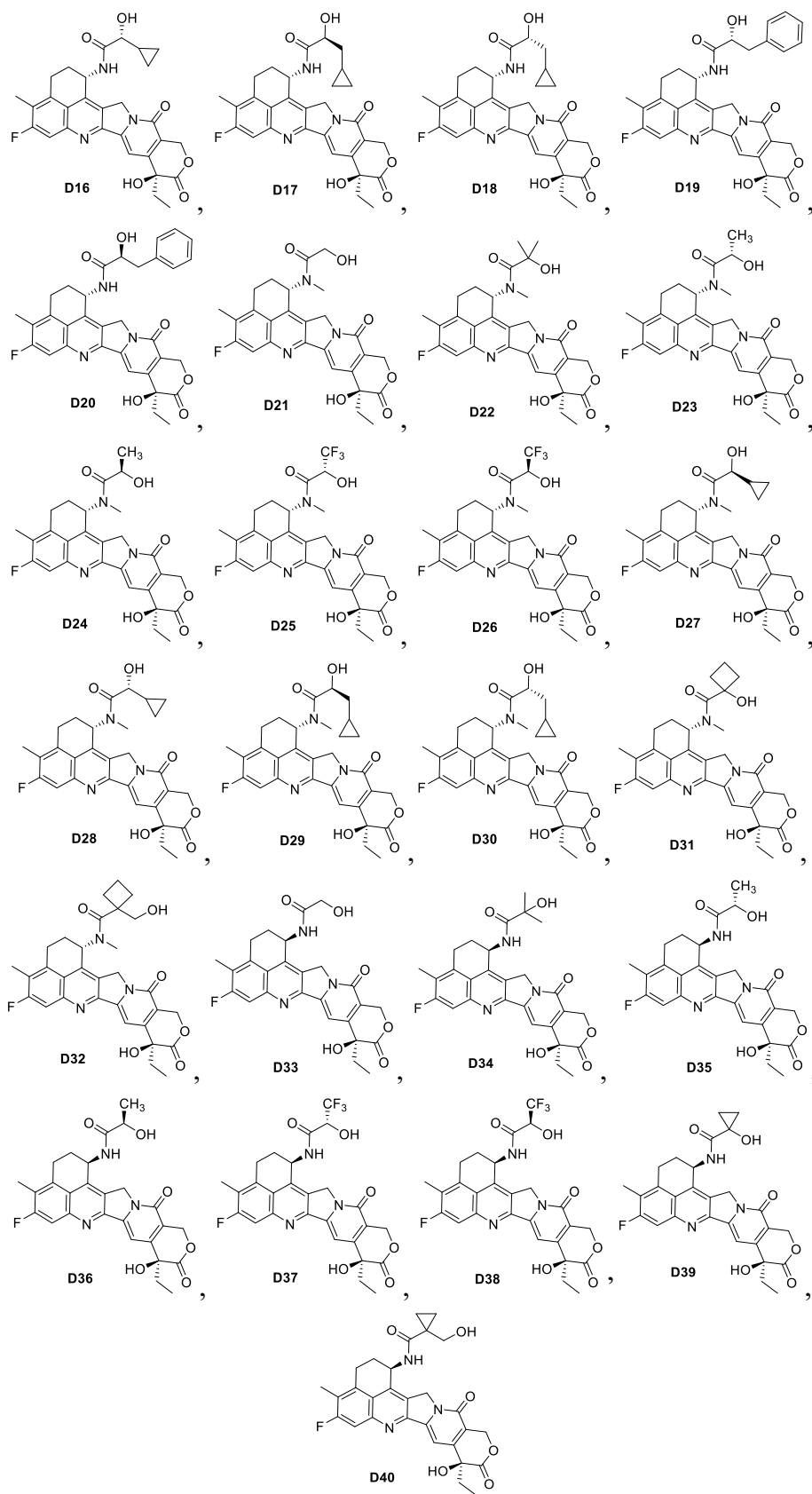
R₅ is selected from hydrogen, deuterium, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, and C1-C6 alkoxy C1-C6 alkyl, R₅ is preferably selected from hydrogen, and C1-C6 alkyl, R₅ is more preferably selected from hydrogen, and methyl;

X is selected from -NH-, -O- and -S-, preferably -O-;

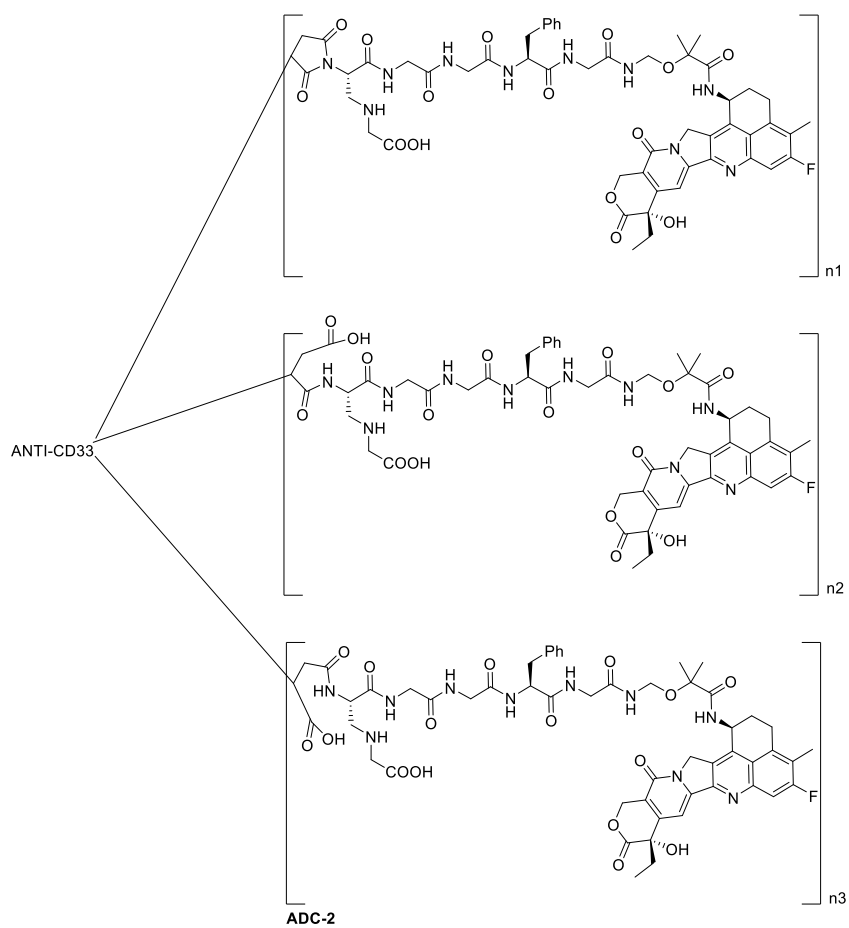
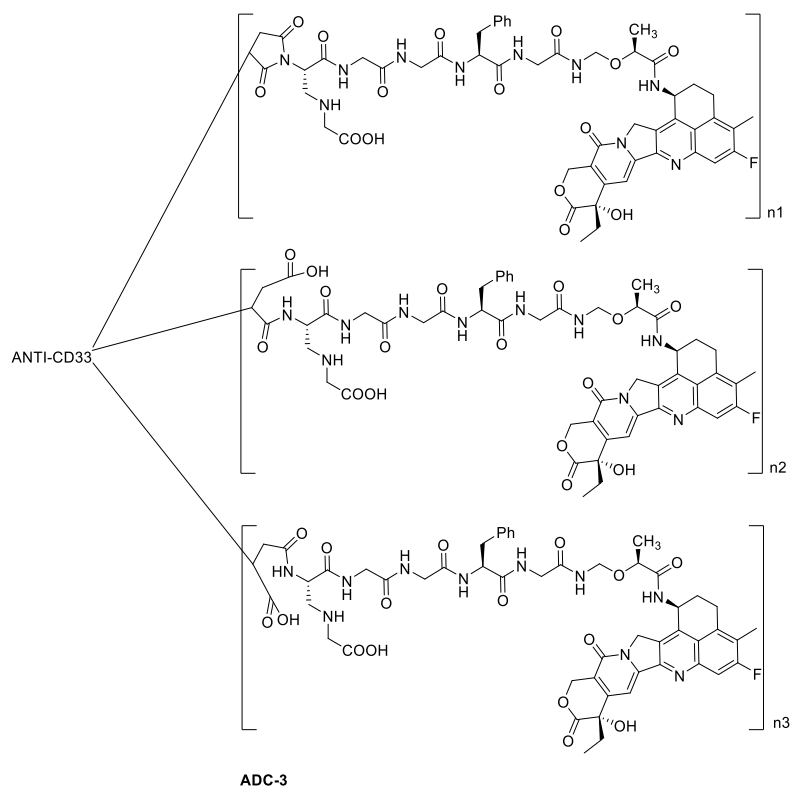
m is an integer from 0 to 5, preferably 0, or 1.

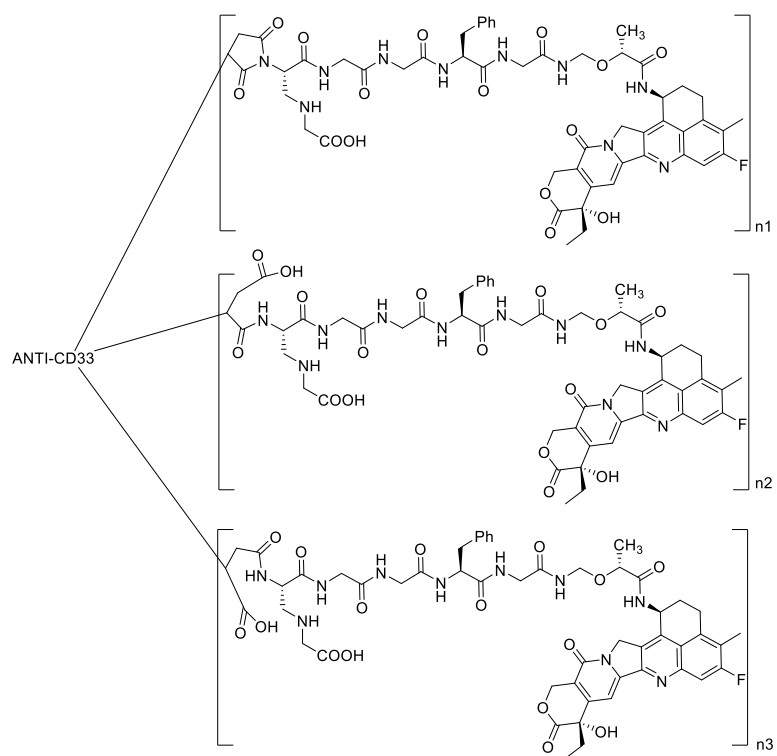
8. The antibody-drug conjugate or the stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 7, wherein the camptothecin antitumor drug comprises the following compounds or their stereoisomers :



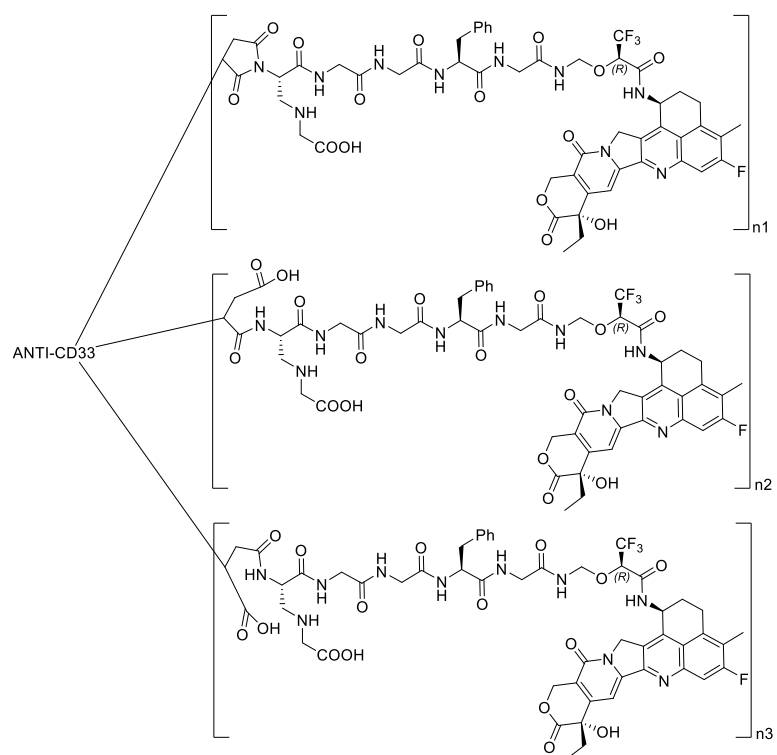


9. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 8, wherein the antibody-drug

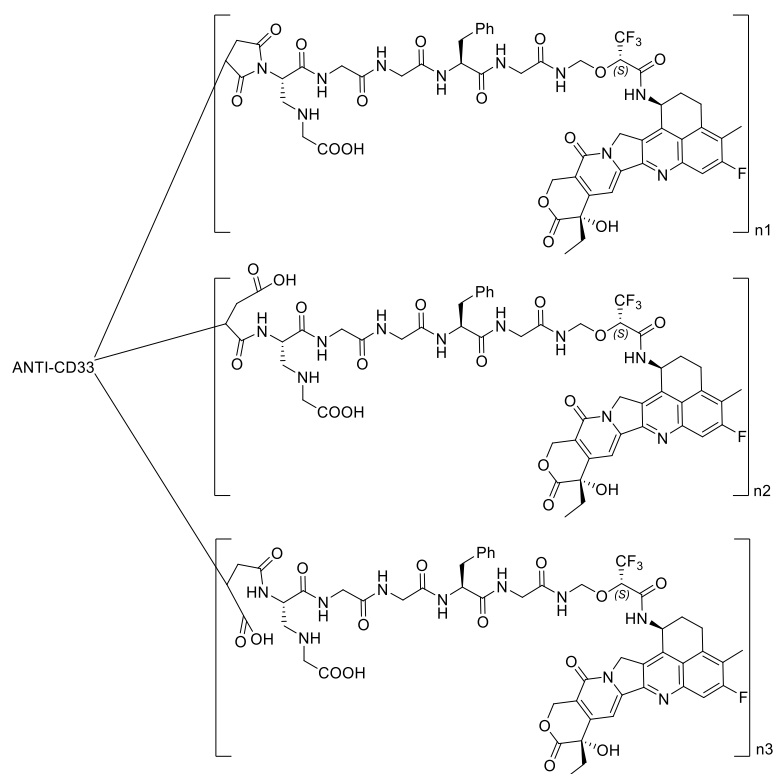




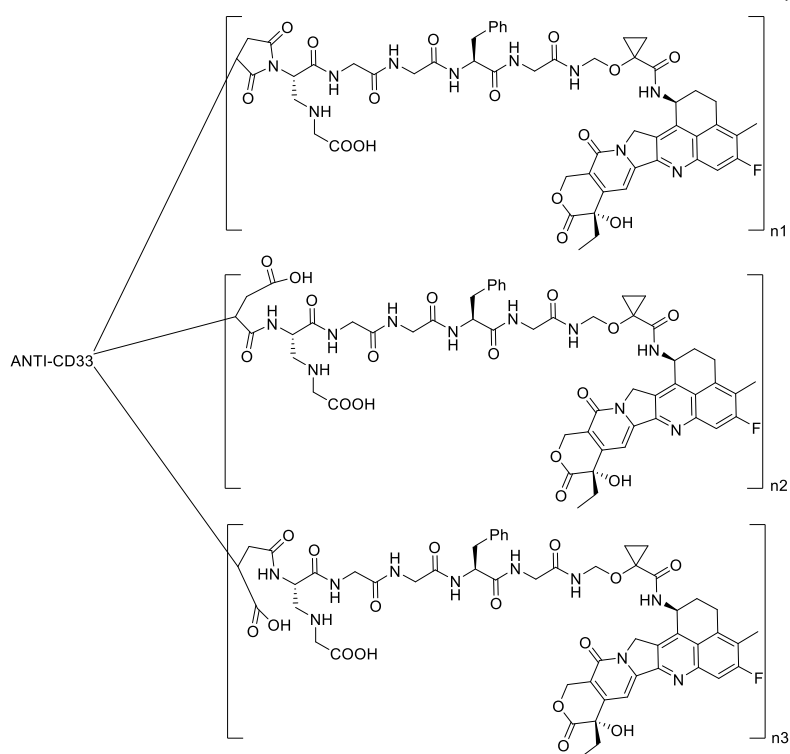
ADC-4



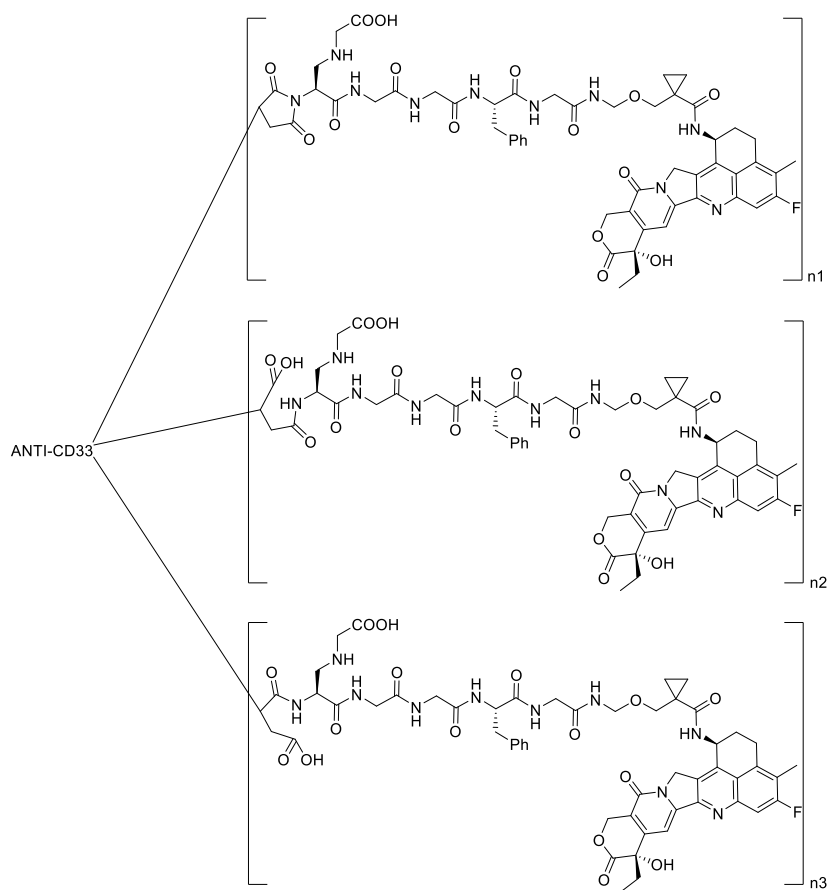
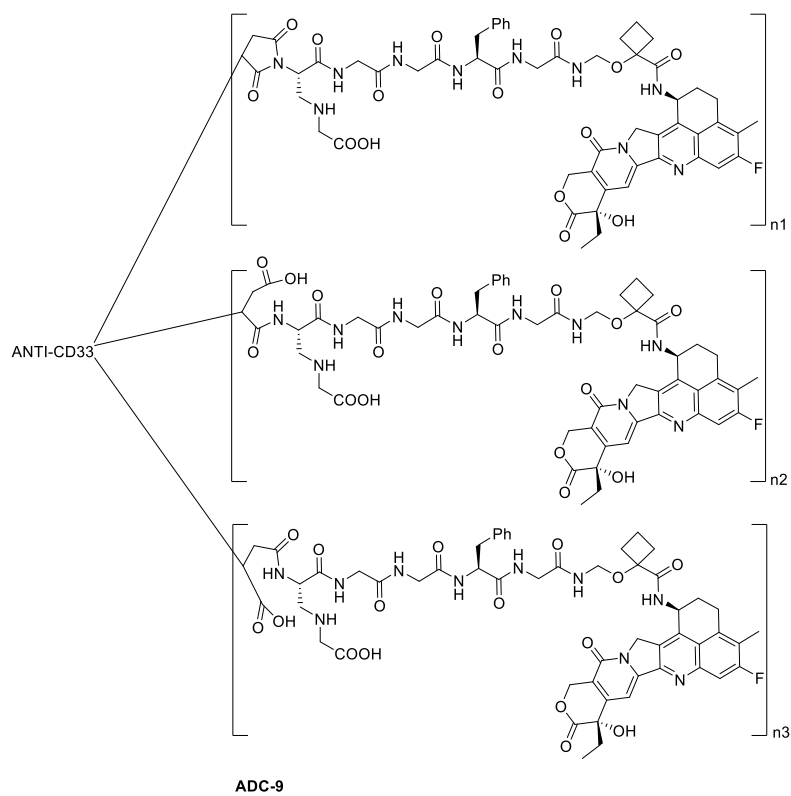
ADC-5

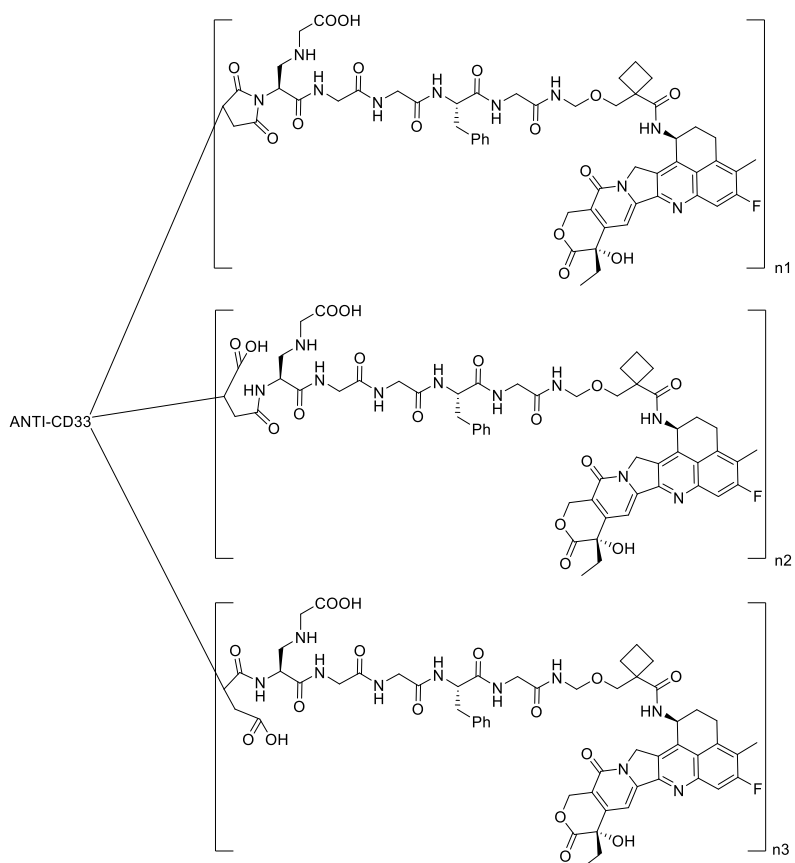
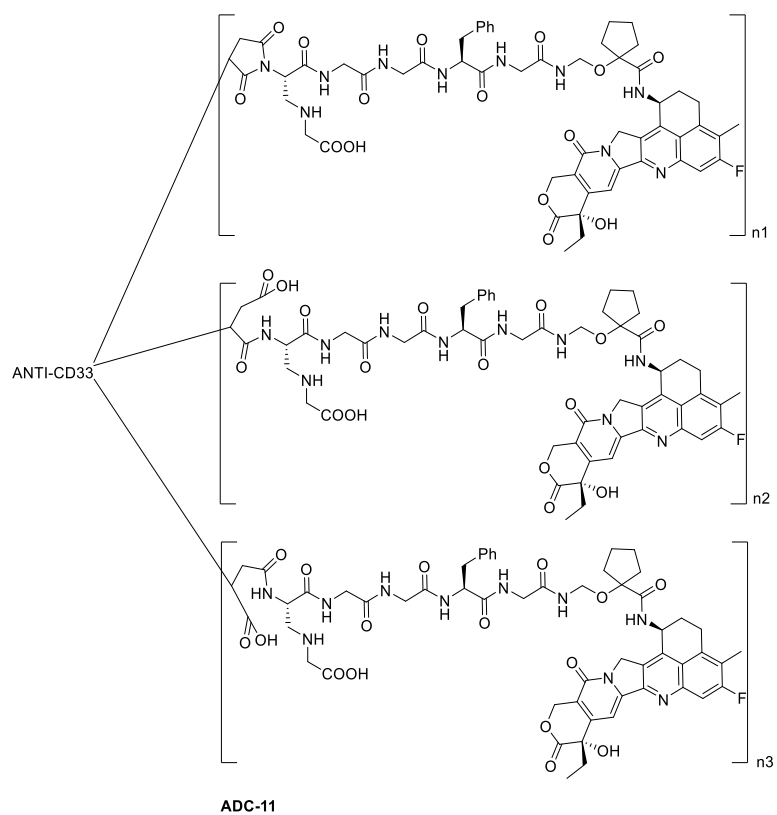


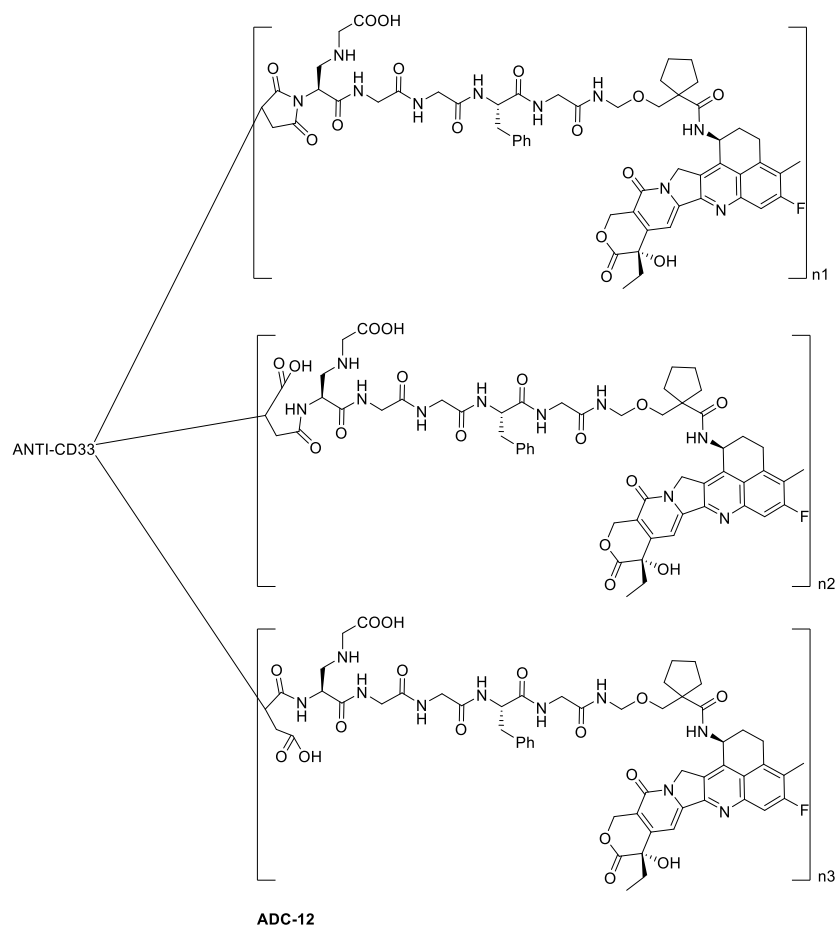
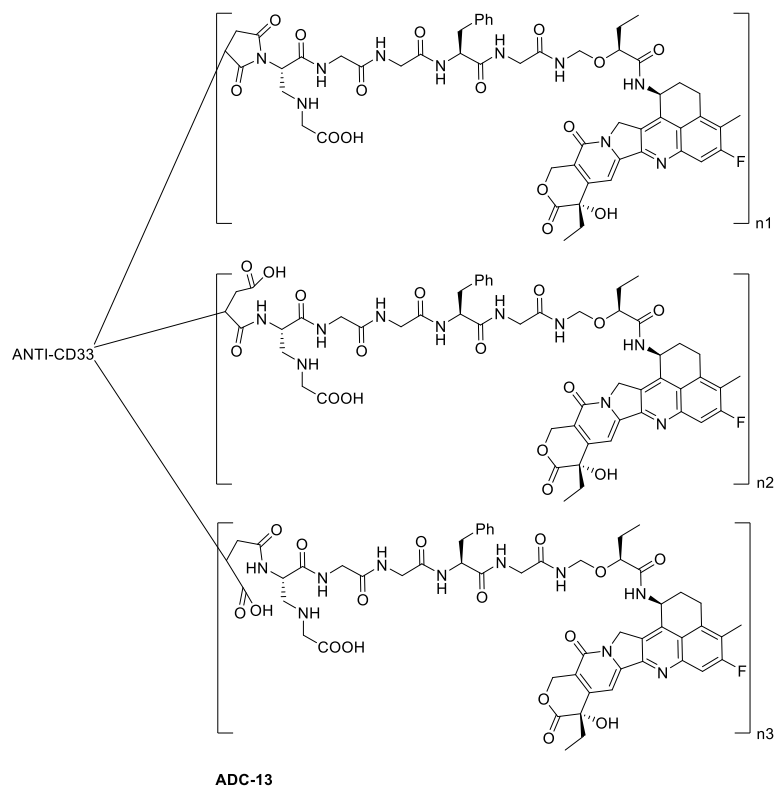
ADC-6

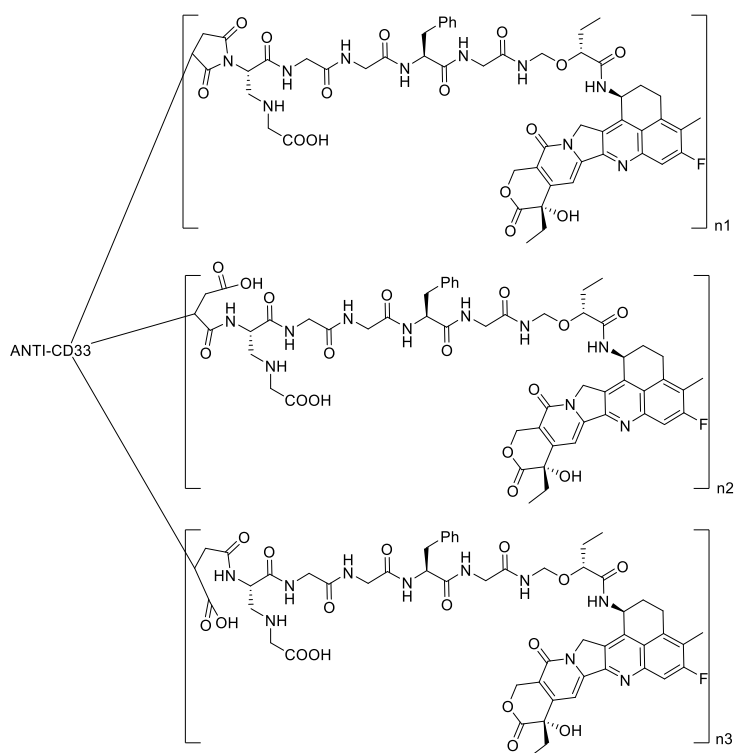
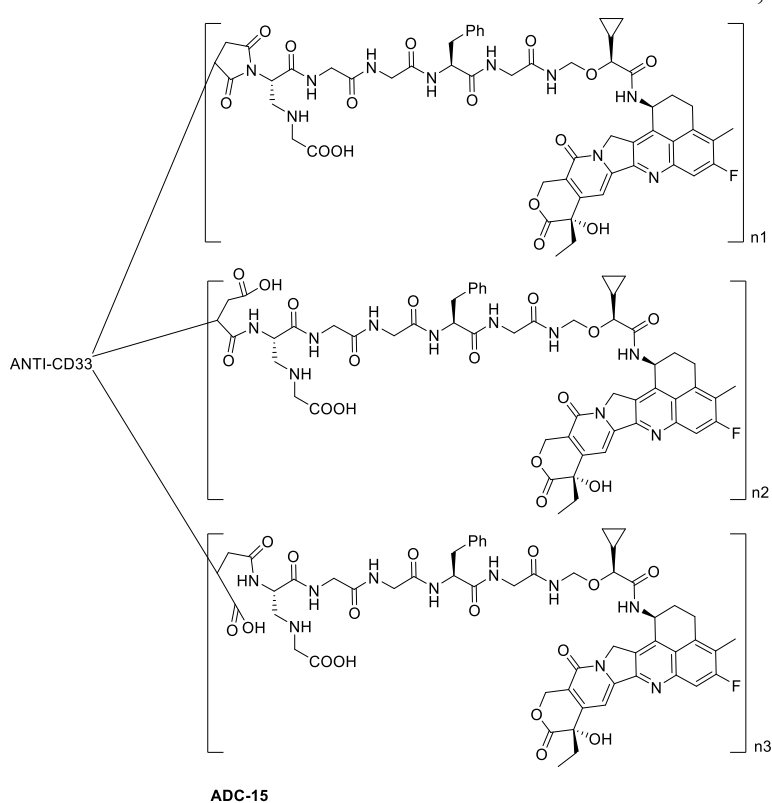


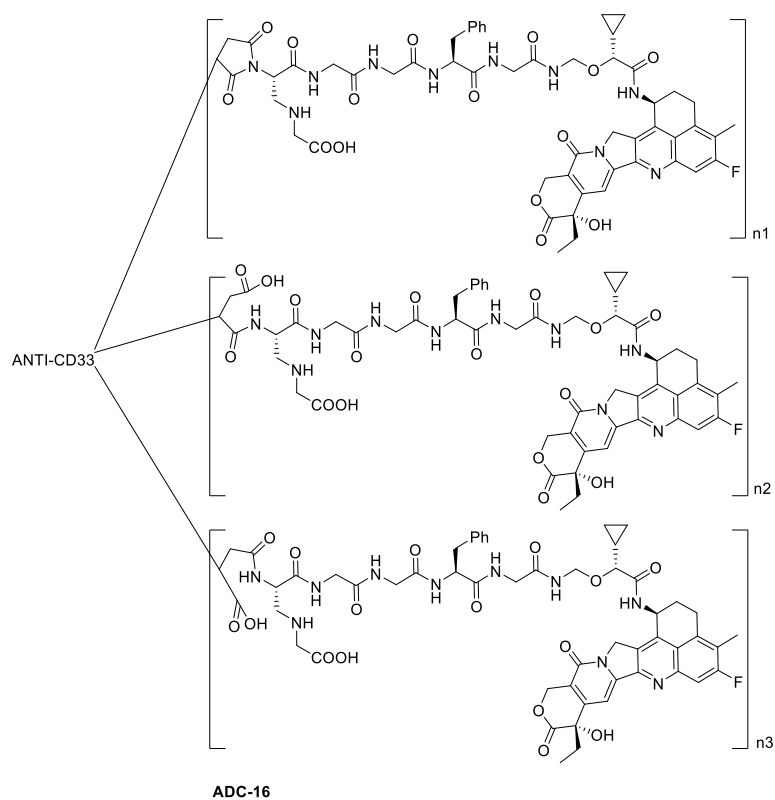
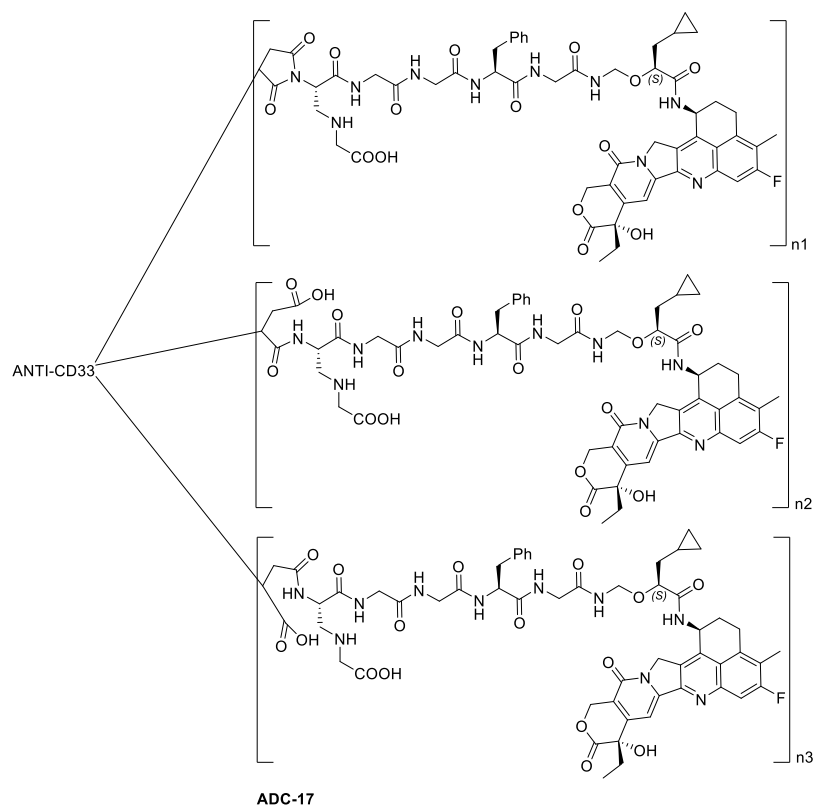
ADC-7

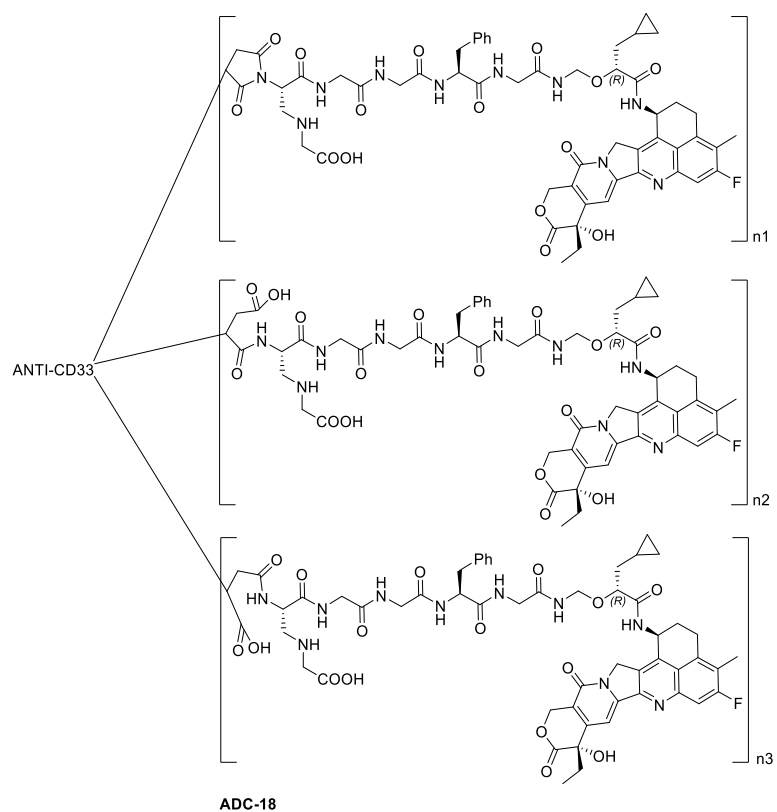
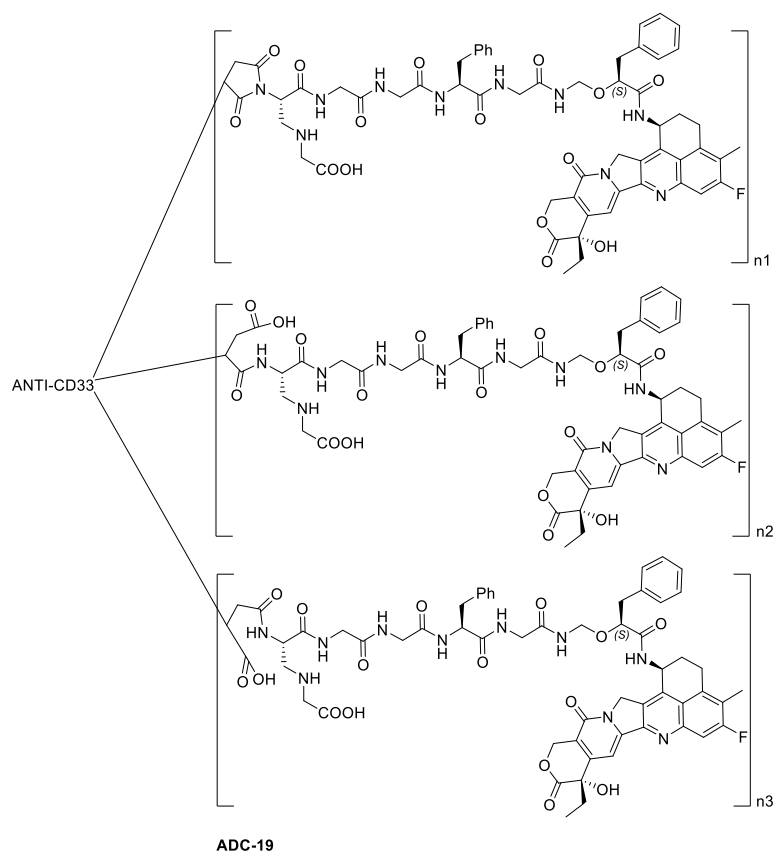


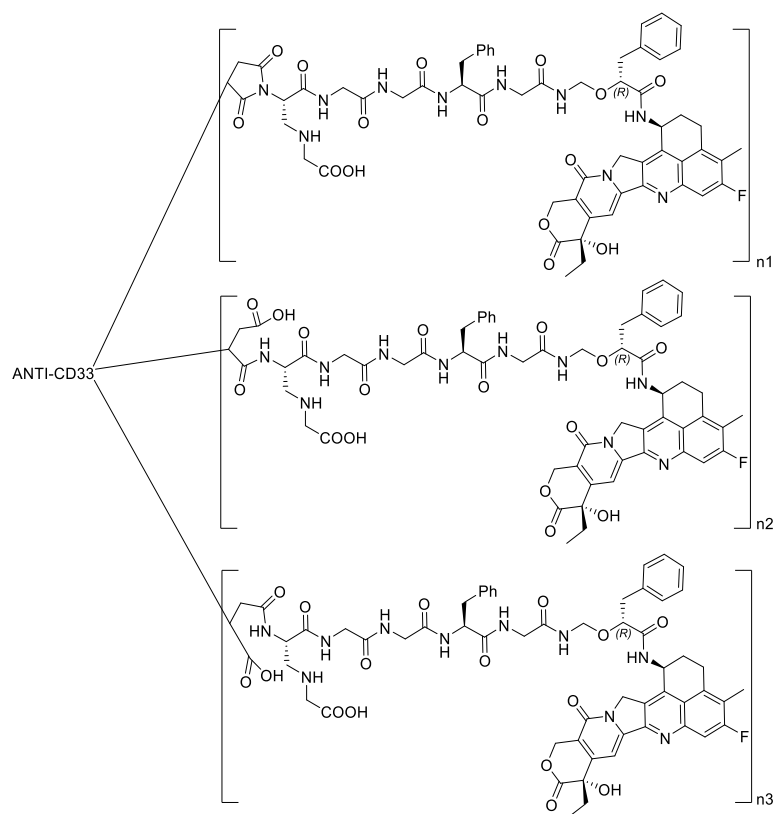




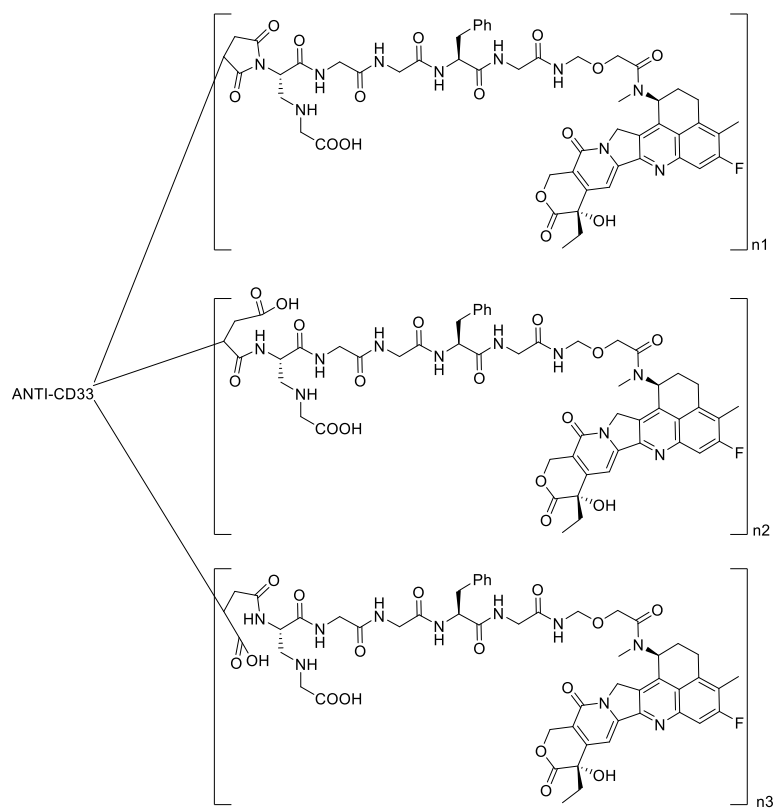




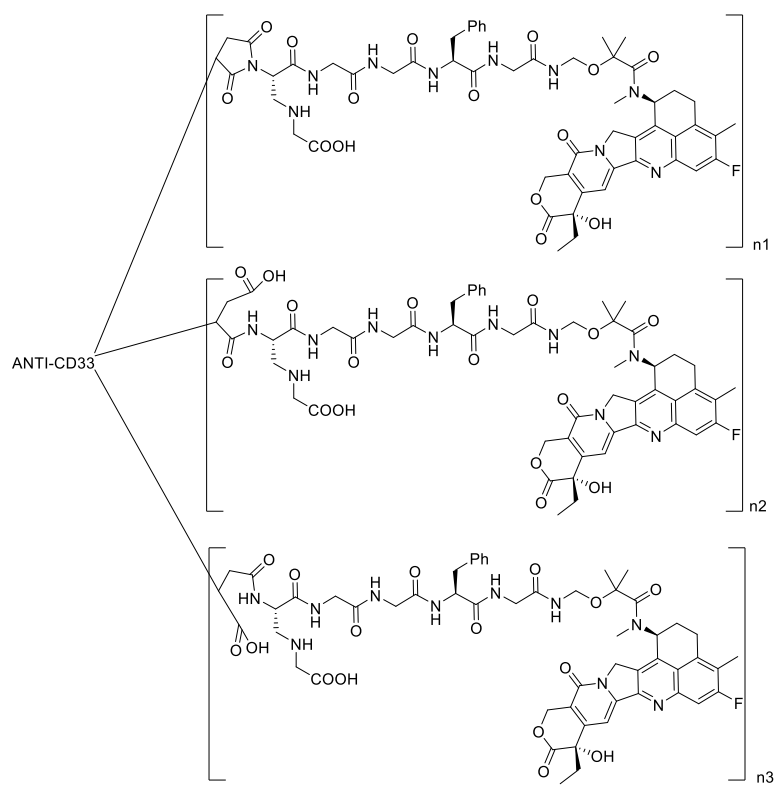




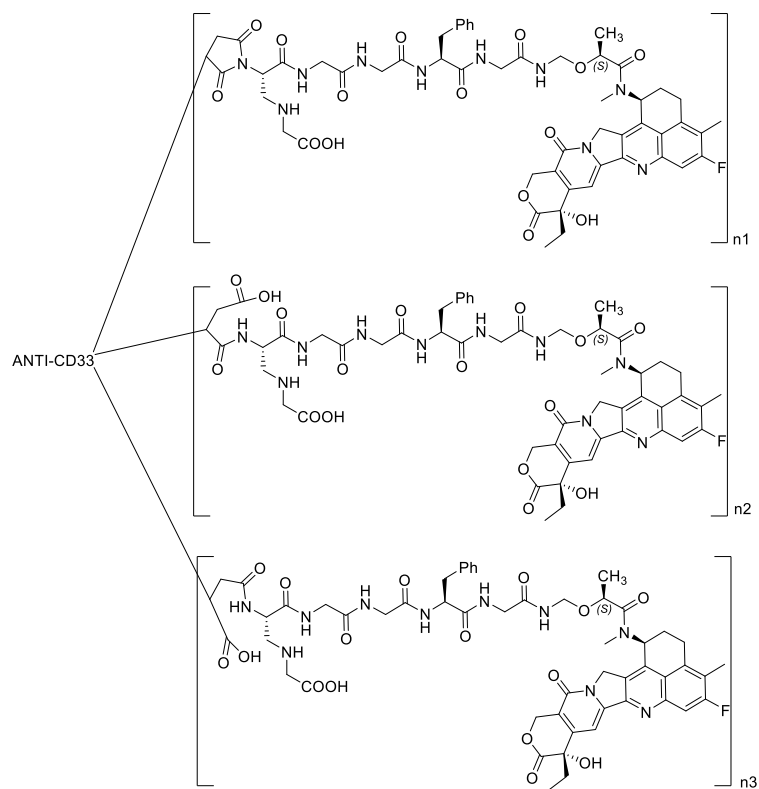
ADC-20



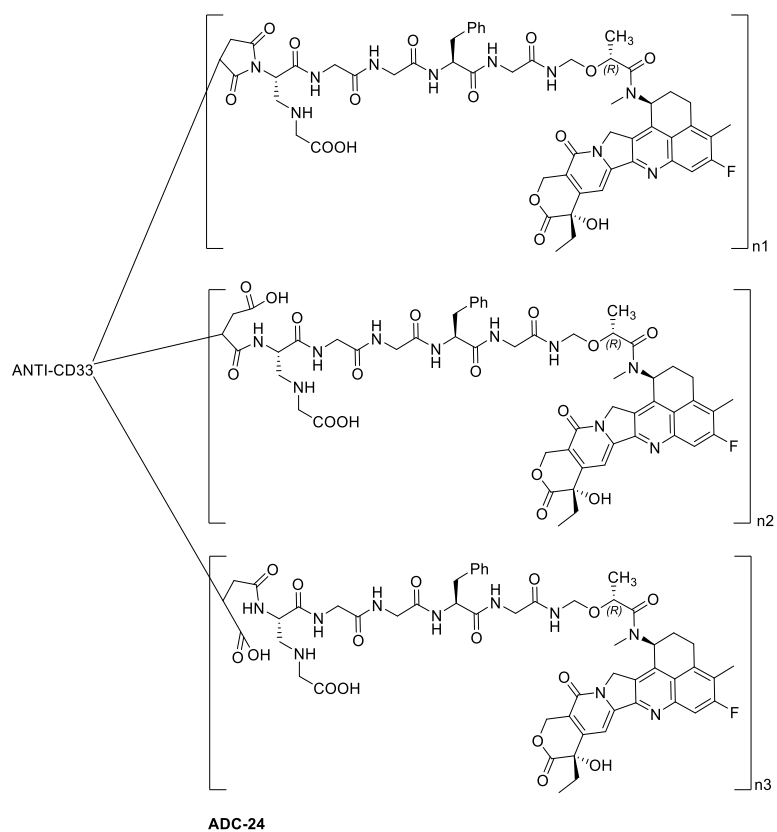
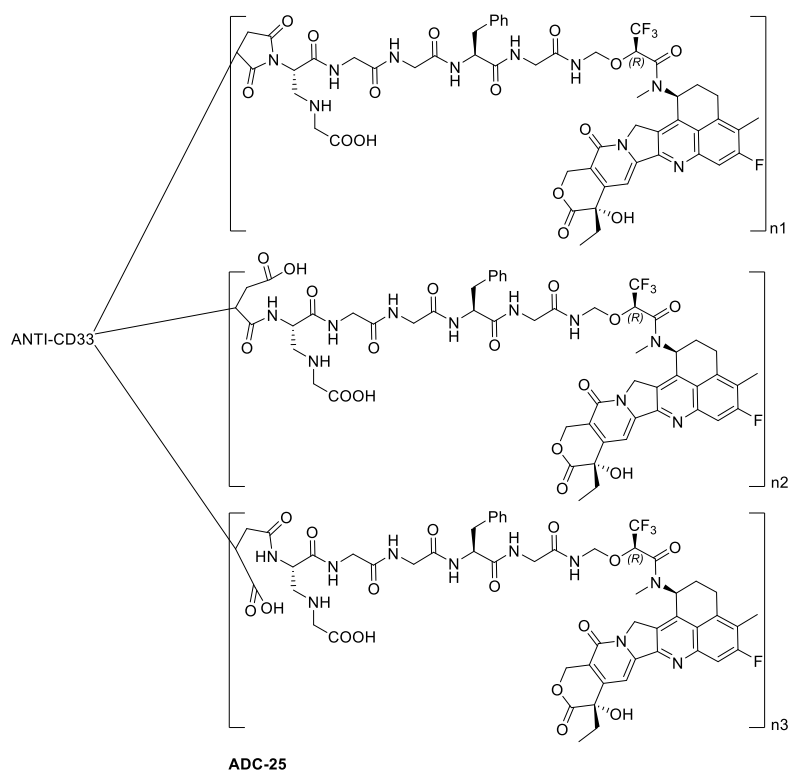
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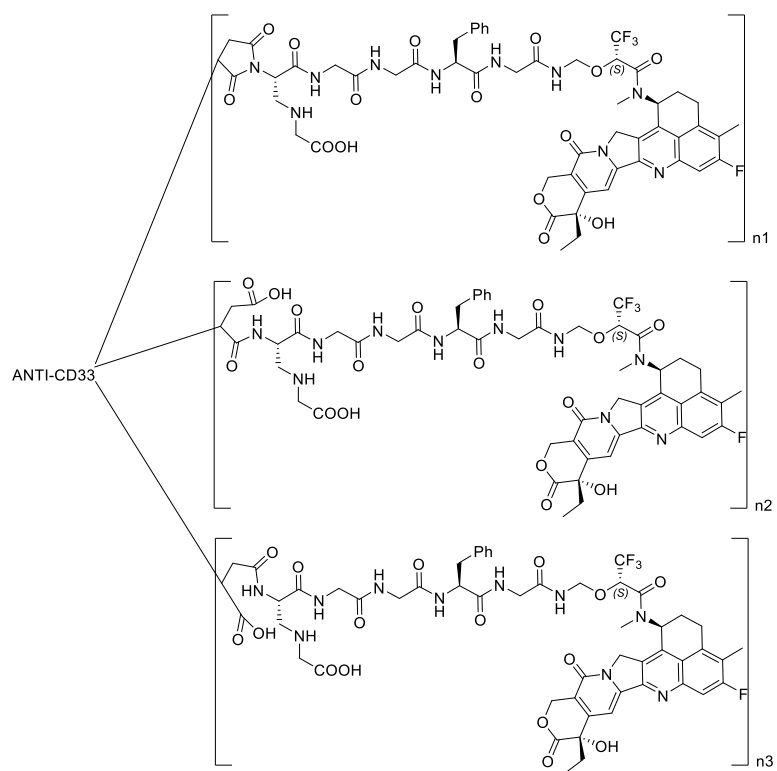
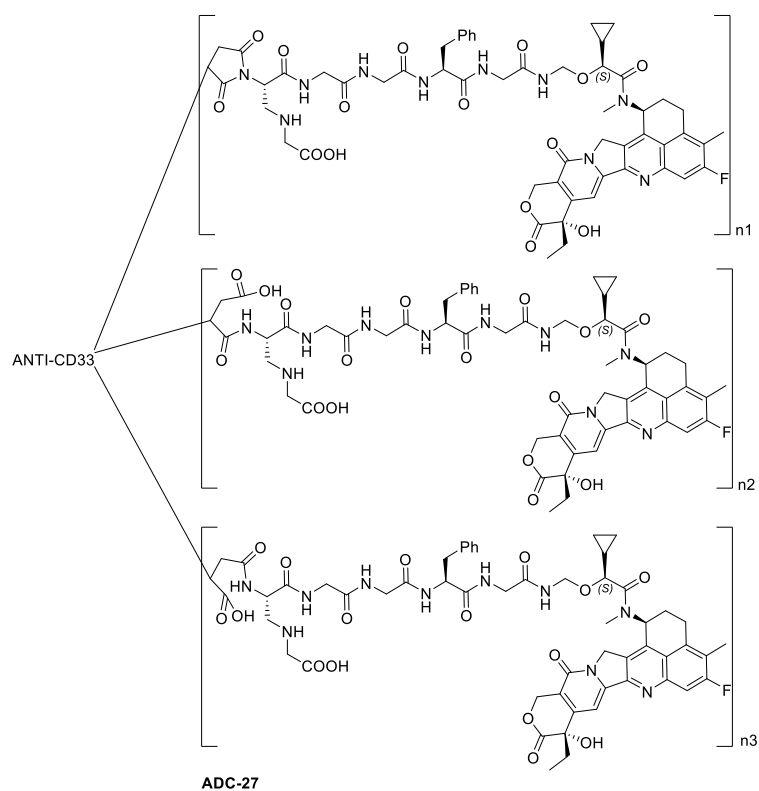


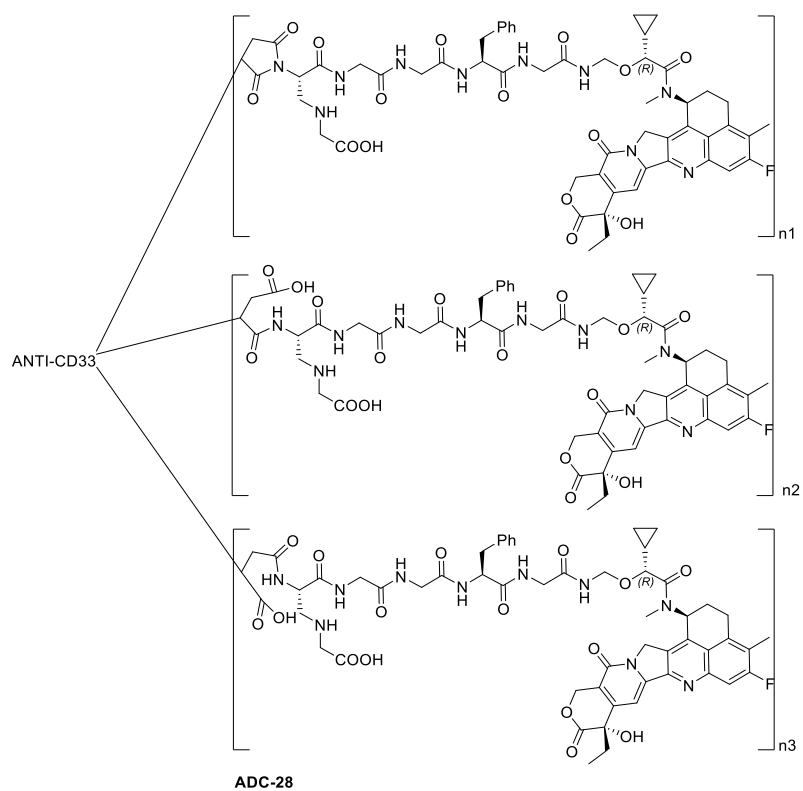
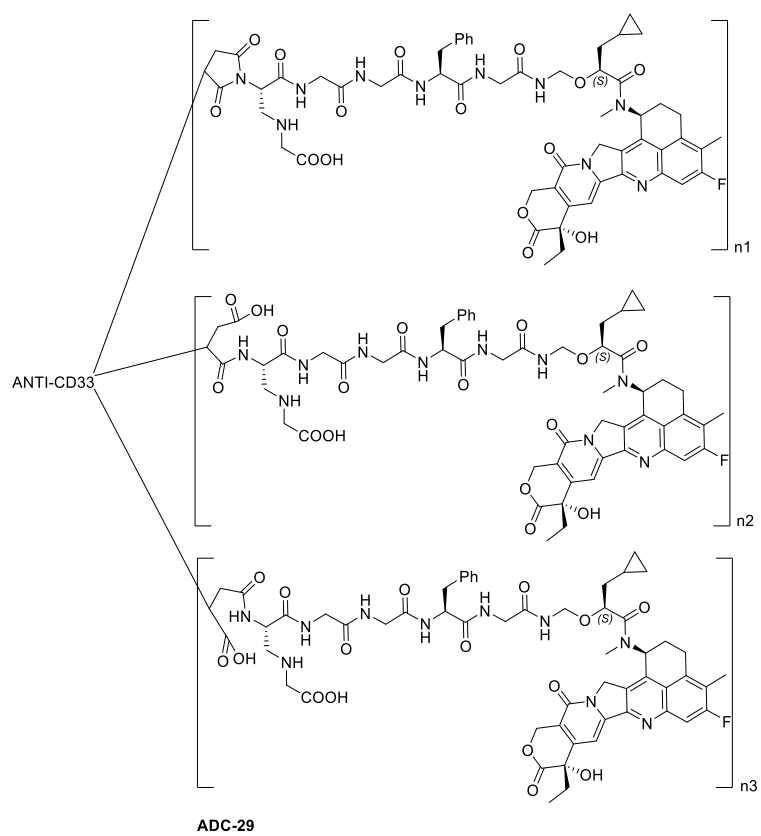
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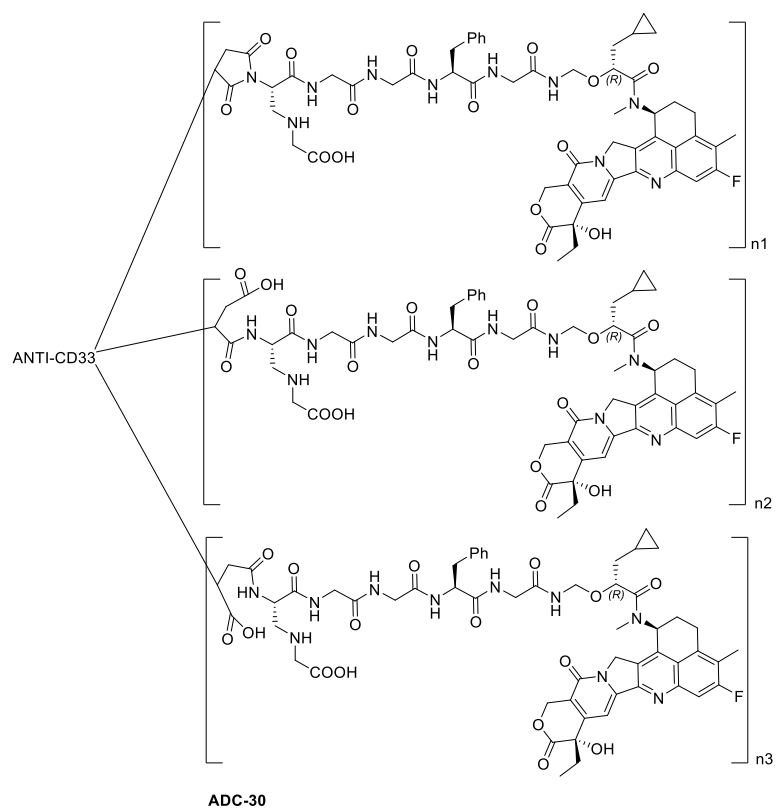
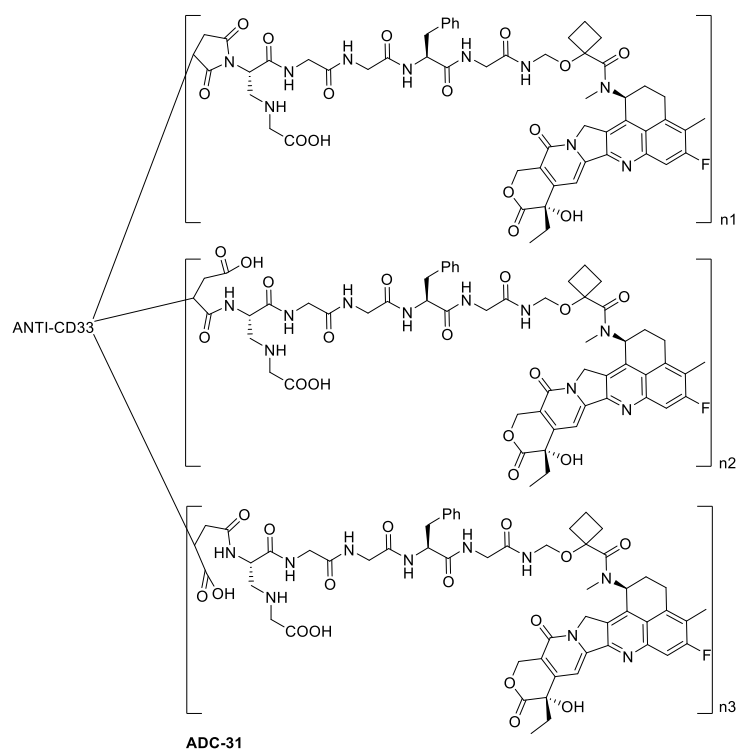


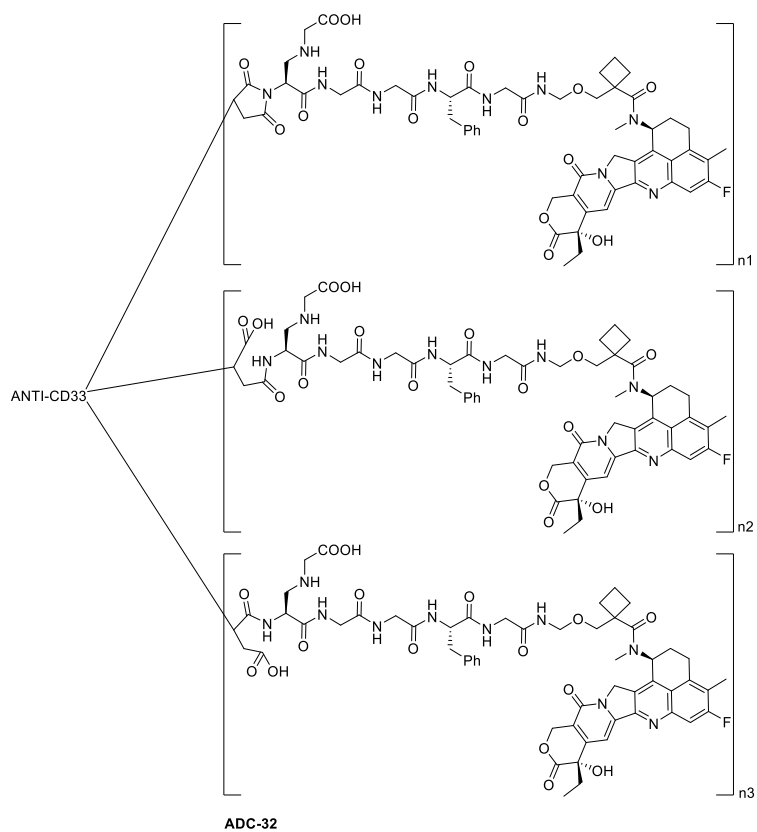
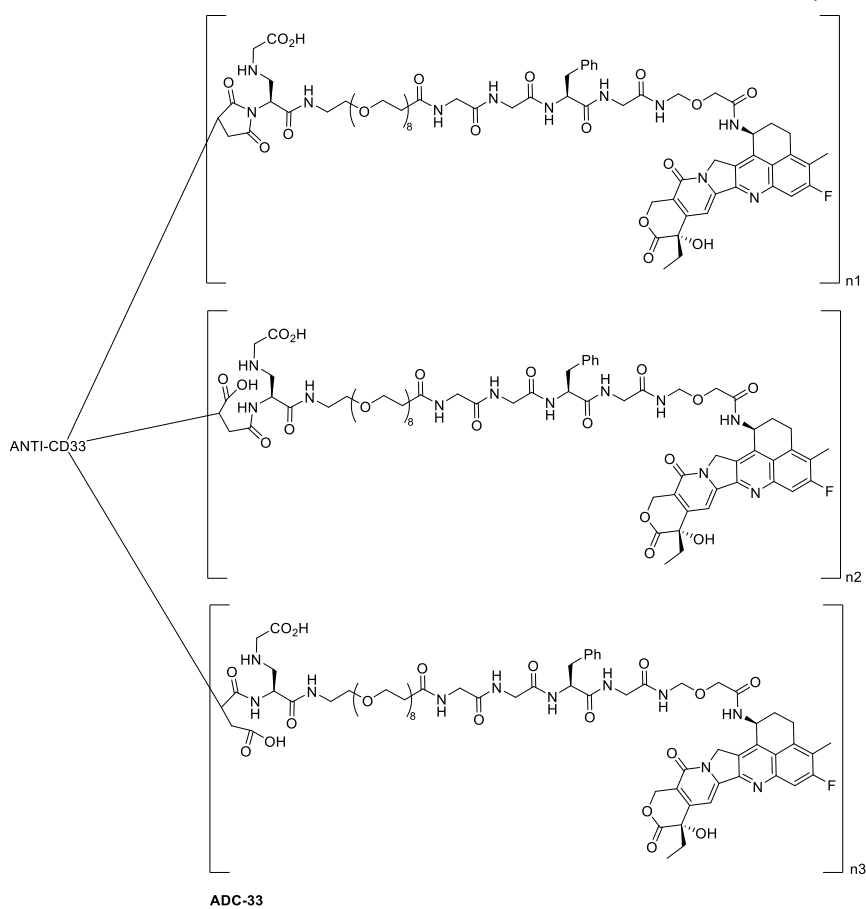
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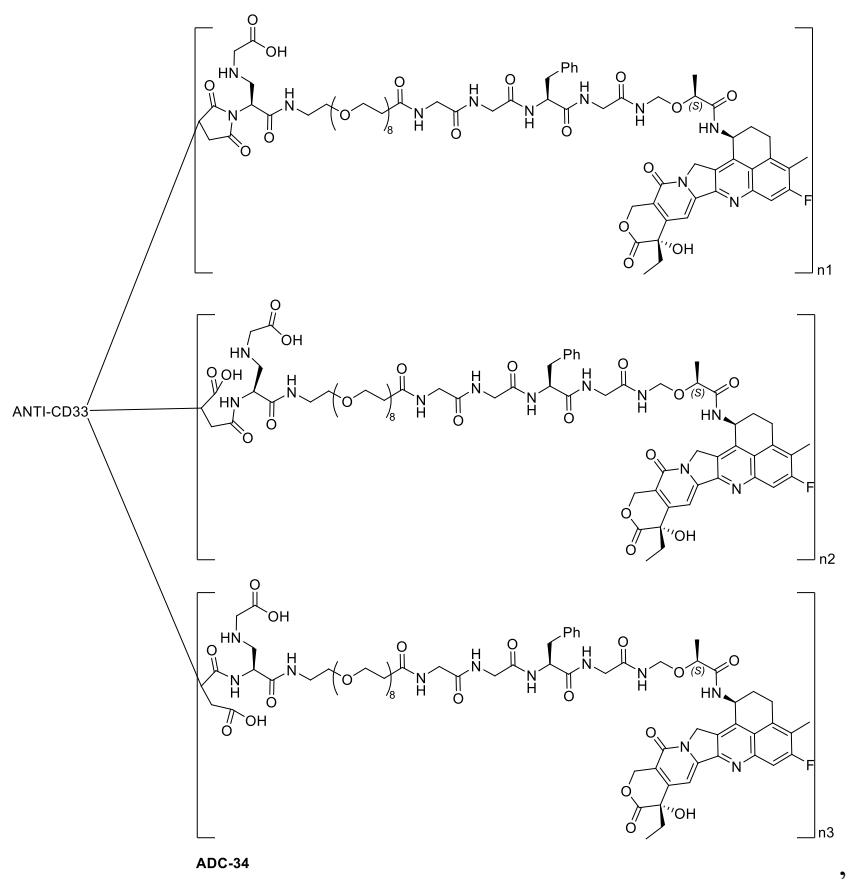
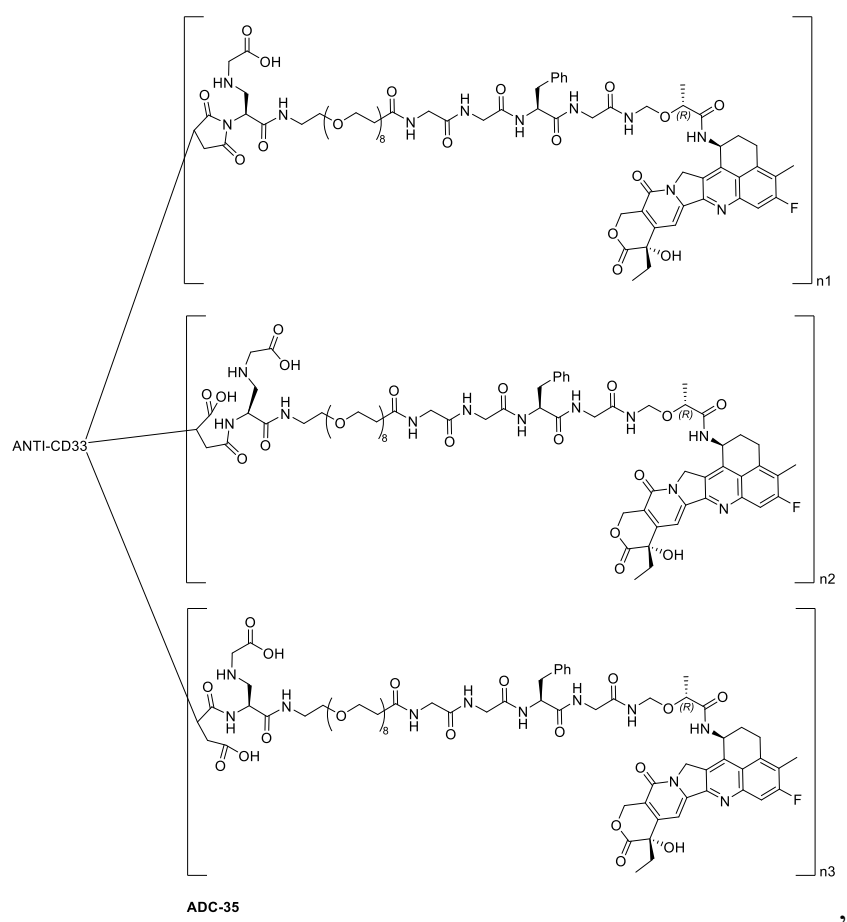


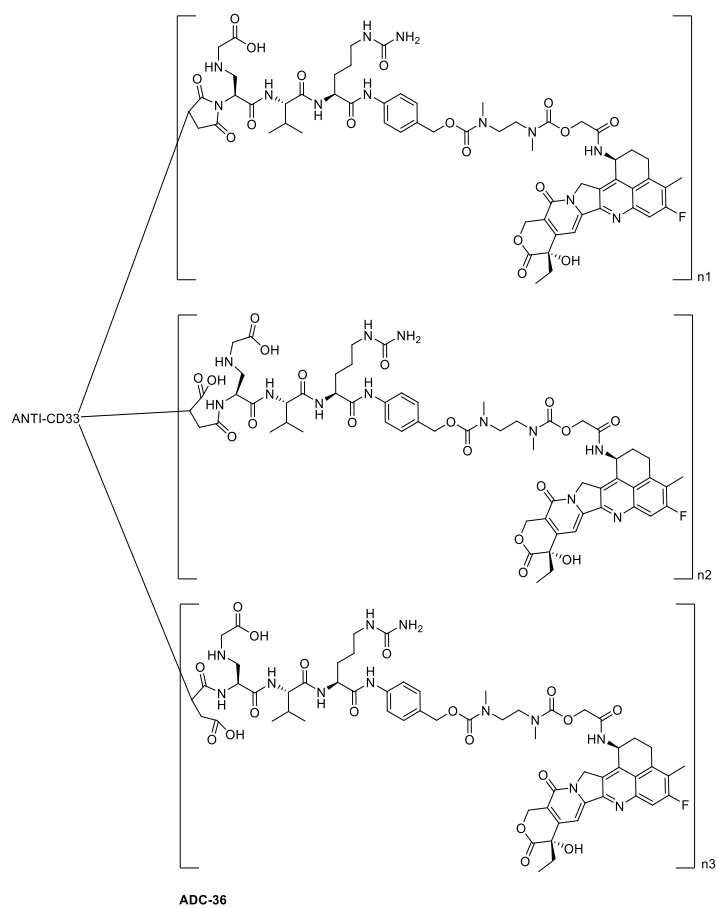
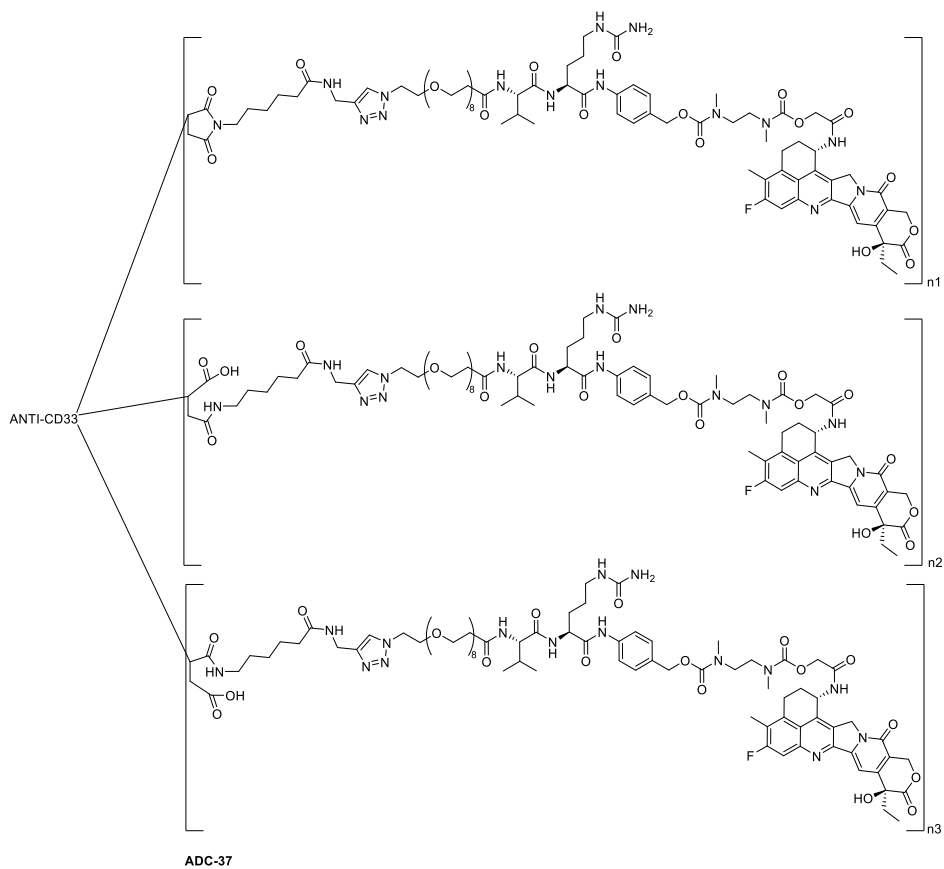


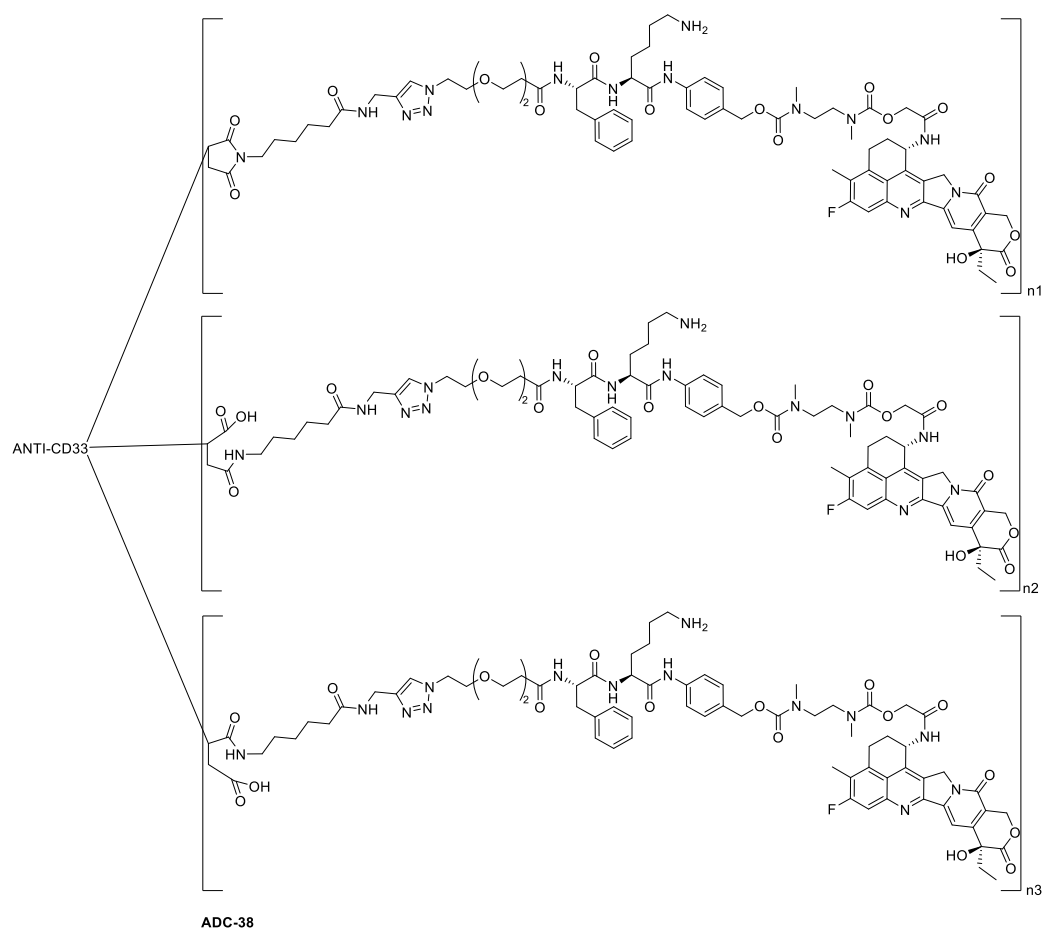
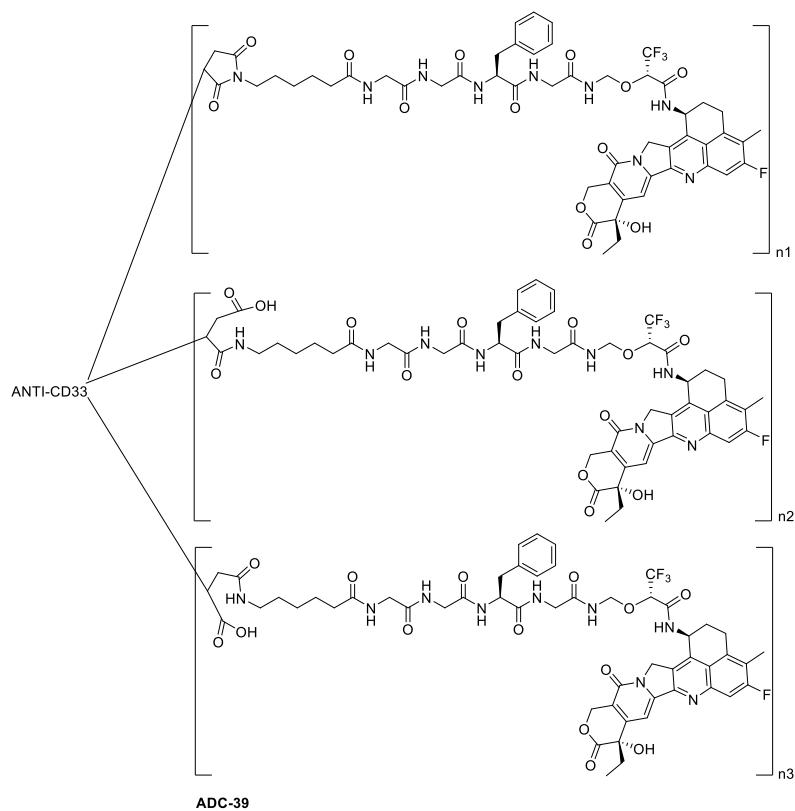


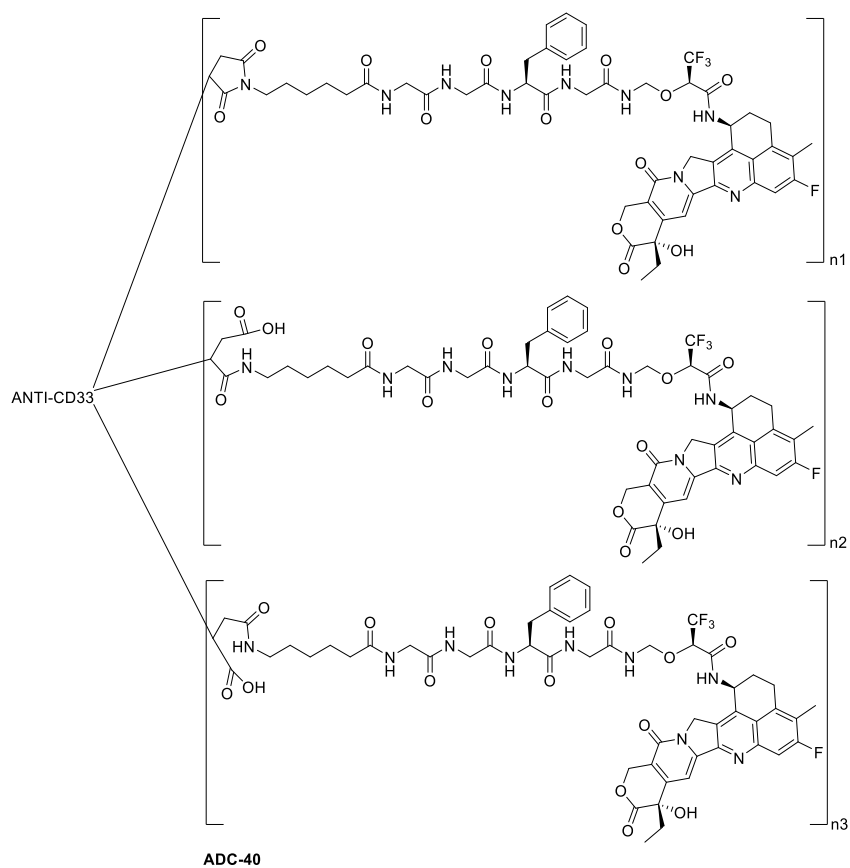
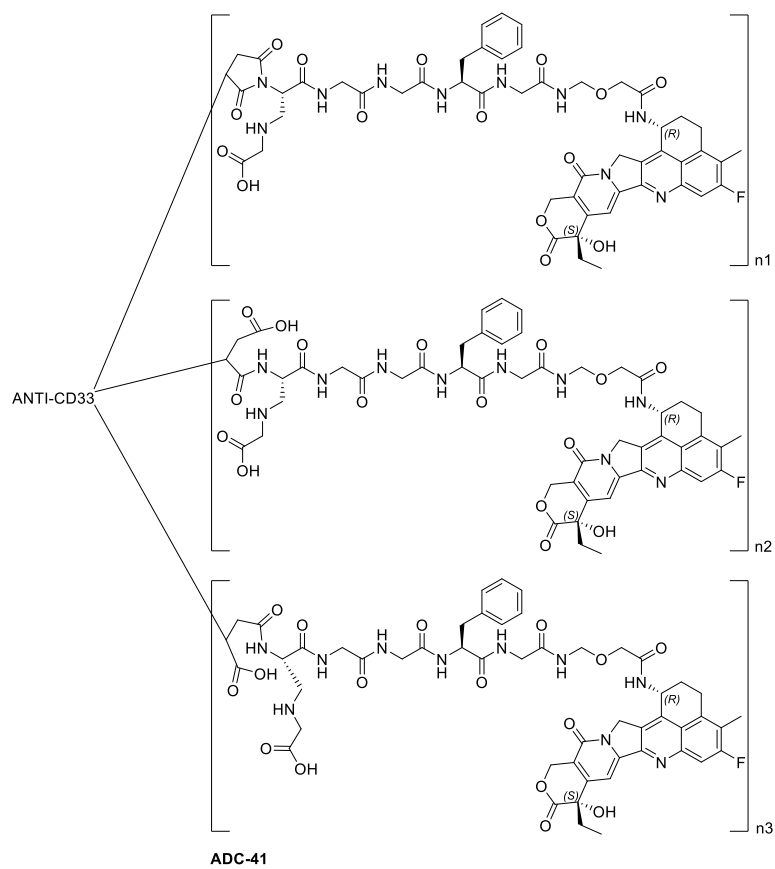


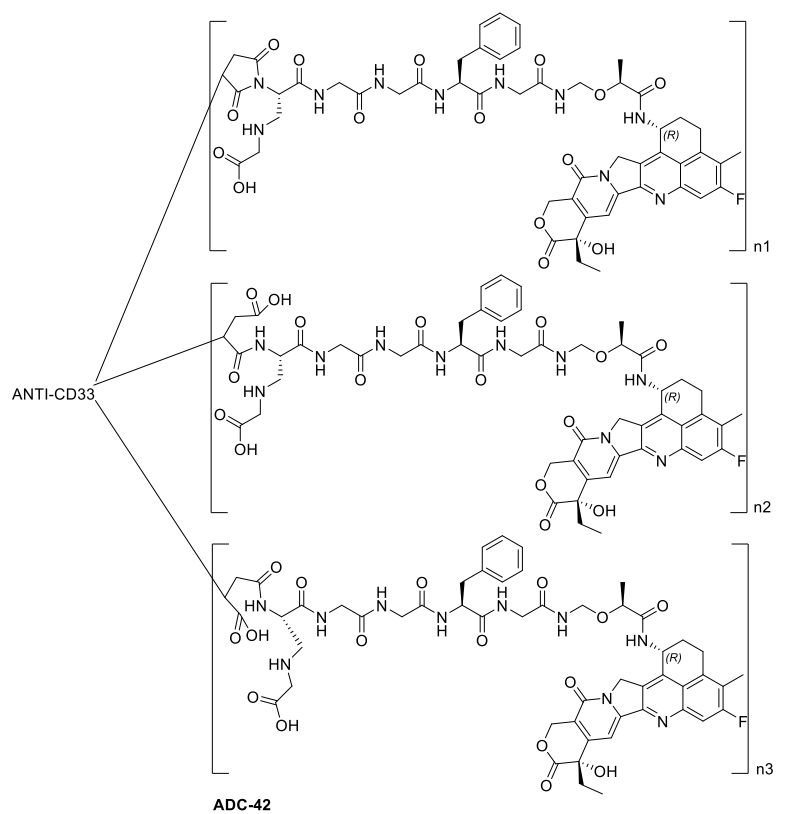
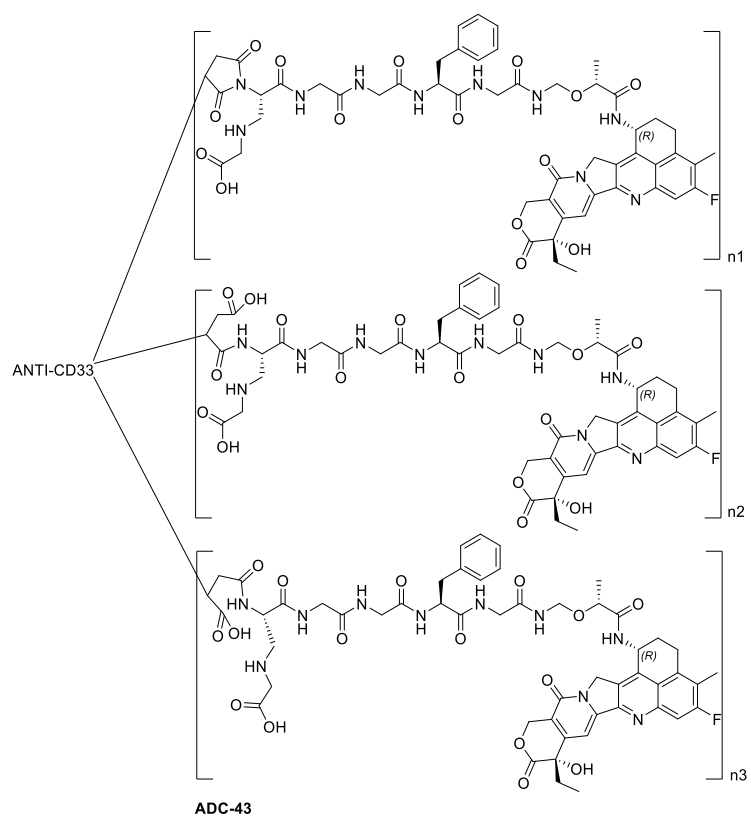


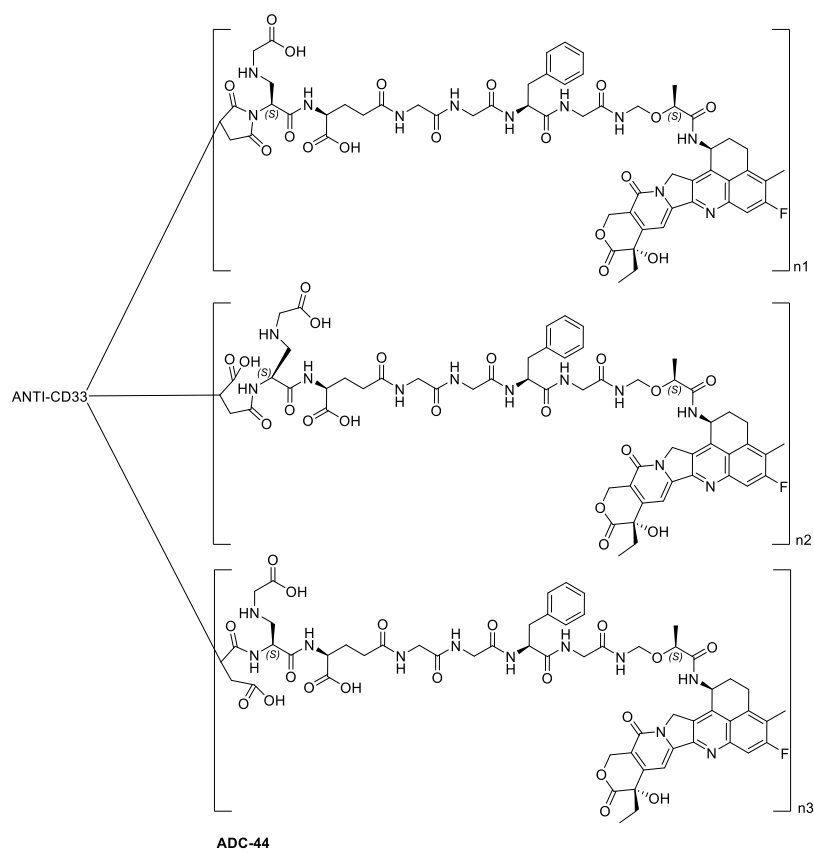
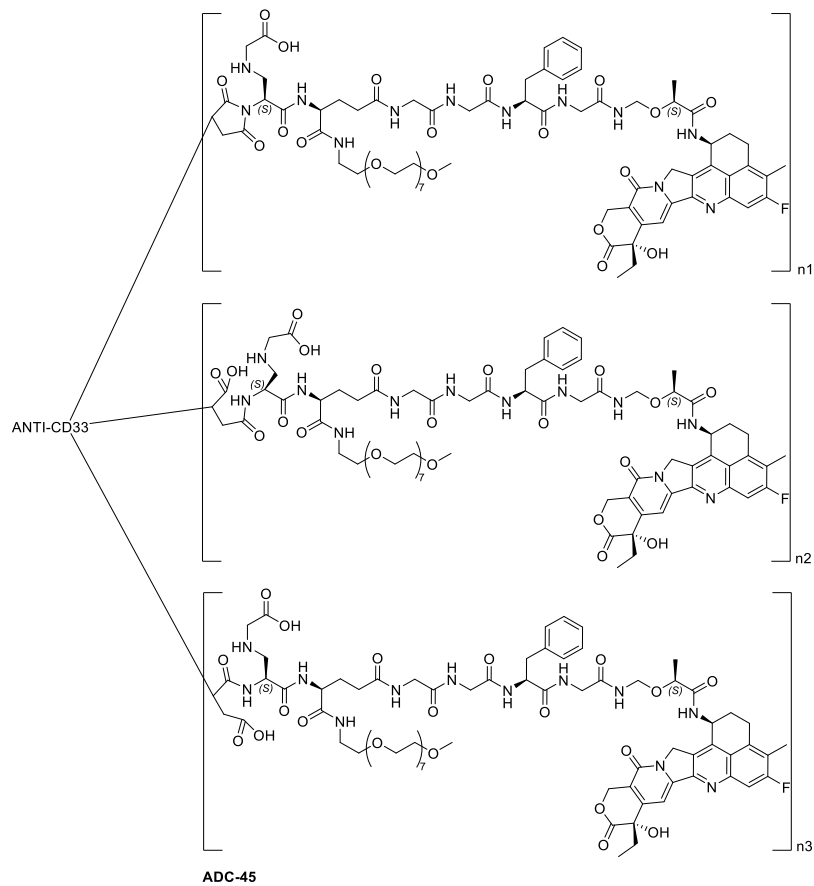


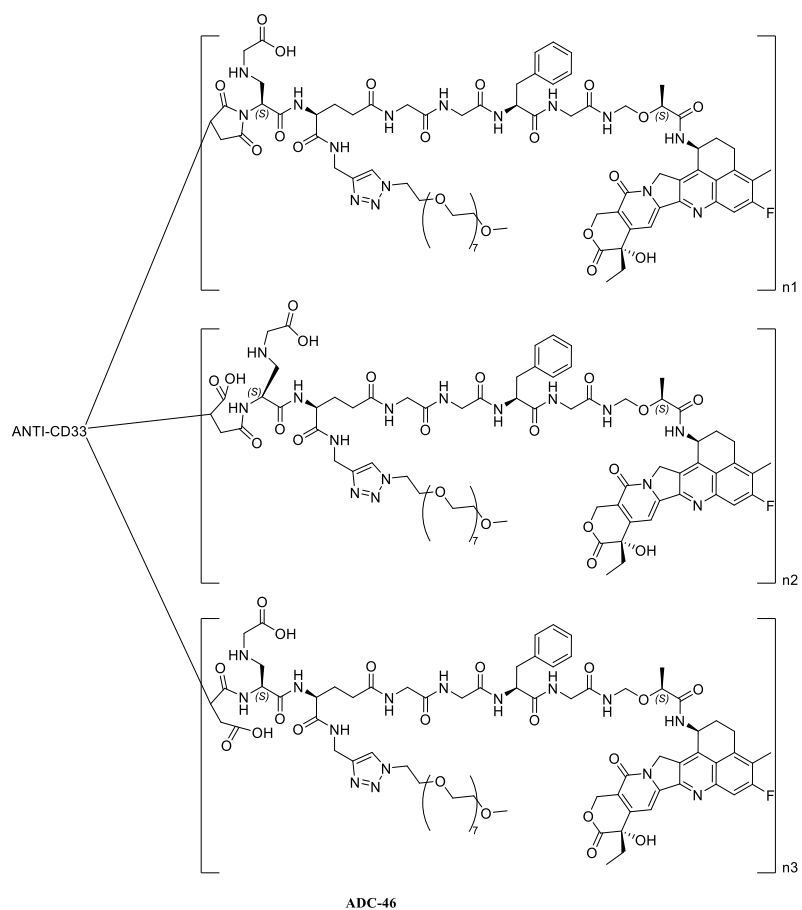
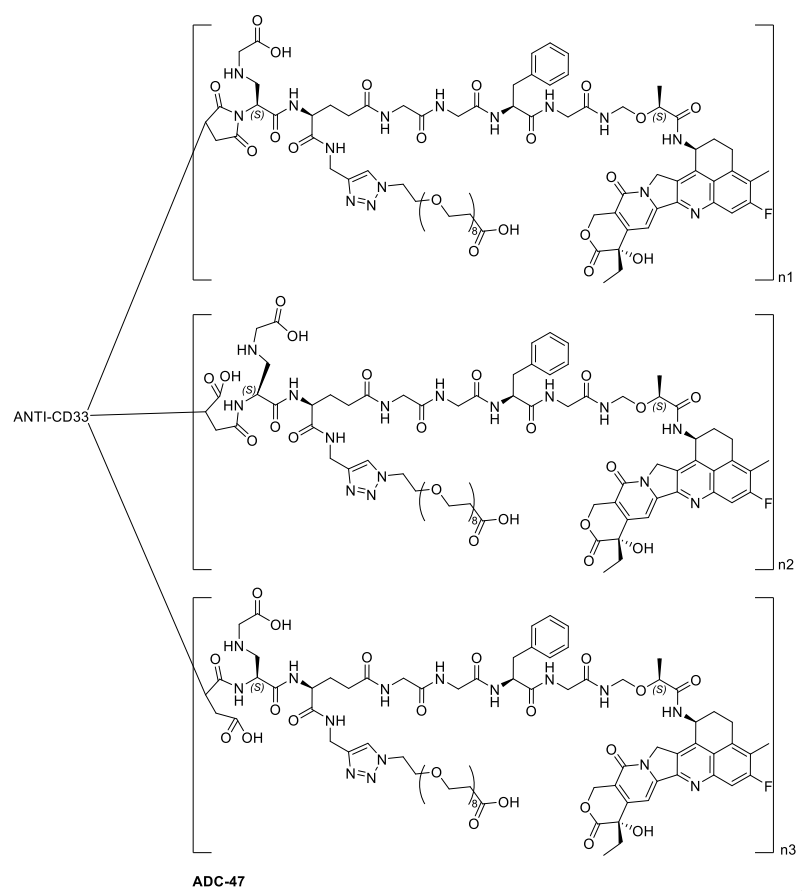


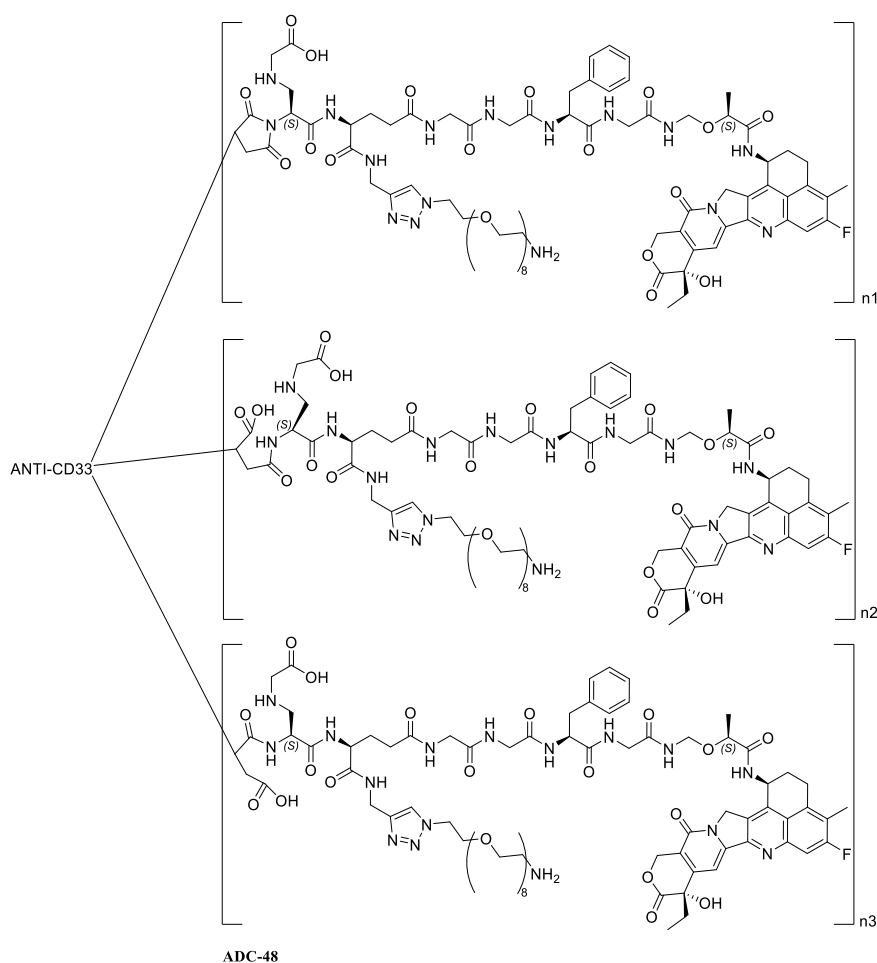












wherein:

ANTI-CD33 is an anti CD33 antibody or an antigen-binding fragment thereof;

n_1 , n_2 , and n_3 are each independently any integer or any decimal from 0 to 10, n_1 , n_2 , and n_3 are not simultaneously 0, and $1 \leq n_1 + n_2 + n_3 \leq 10$;

preferably, n_1 , n_2 , and n_3 each is independently an integer or a decimal number from 0 to 10, n_1 , n_2 , and n_3 are not simultaneously 0, and $8 \leq n_1 + n_2 + n_3 \leq 10$.

10. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any of Claims 1 to 9, wherein the light chain variable region of the anti-CD33 antibody or antigen-binding fragment thereof comprises CDR1, CDR2, CDR3 as shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, respectively, and the heavy chain variable region comprises CDR1, CDR2, CDR3 as shown in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, respectively.

11. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 10, wherein the anti-CD33

antibody or antigen-binding fragment thereof has a light-chain variable region as shown in SEQ ID NO: 7 and a heavy-chain variable region as shown in SEQ ID NO: 1.

12. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 11, wherein the anti-CD33 antibody comprises a constant region derived from human immunoglobulin;

preferably, the light chain of the anti-CD33 antibody comprises a light chain constant region derived from a human immunoglobulin (e.g., kappa or lambda); and the heavy chain of the antibody comprises a heavy chain constant region derived from a human immunoglobulin (e.g., IgG1, IgG2, IgG3, or IgG4),

preferably, the amino acid sequence of the light chain of the anti-CD33 antibody is SEQ ID NO: 11 and the amino acid sequence of the heavy chain is SEQ ID NO: 5;

preferably, the nucleic acid coding sequence for the light chain of the anti-CD33 antibody is SEQ ID NO: 23 and the nucleic acid coding sequence for the heavy chain is SEQ ID NO: 17.

13. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of claims 10 to 12, wherein the anti-CD33 antibody further comprises a site-specific cysteine insertion site;

preferably, the cysteine insertion site is in the light chain constant region;

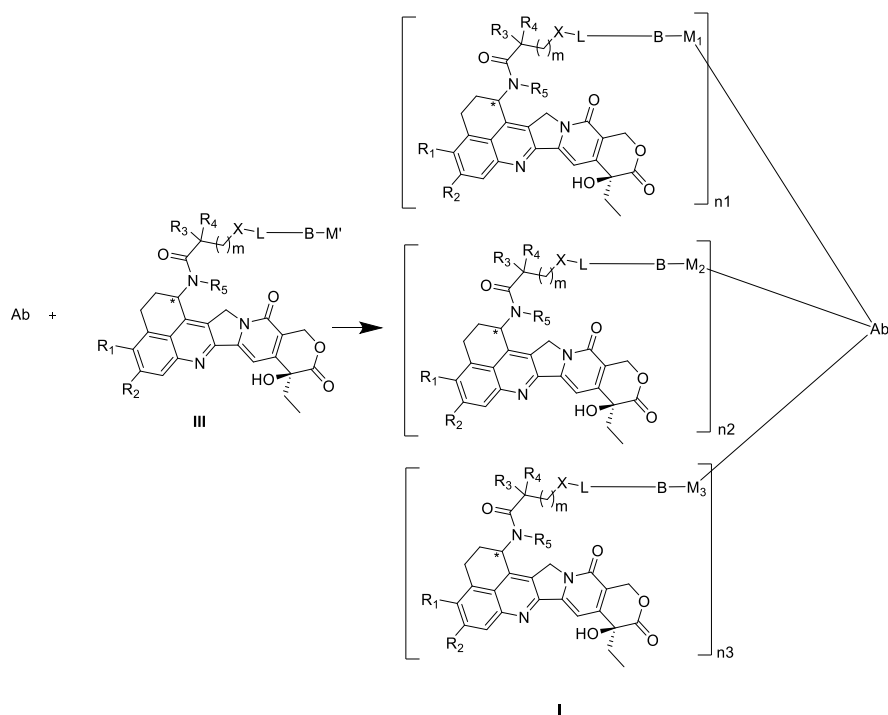
preferably, the cysteine insertion site is position 206 (Kabat numbering) of the kappa light chain constant region;

preferably, the anti-CD33 antibody has a light chain amino acid sequence of SEQ ID NO: 25 and a heavy chain amino acid sequence of SEQ ID NO: 5;

preferably, the nucleic acid coding sequence for the light chain of the anti-CD33 antibody is SEQ ID NO: 27 and the nucleic acid coding sequence for the heavy chain is SEQ ID NO: 17.

14. The antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 13, wherein the pharmaceutically acceptable salt comprises sodium, potassium, calcium or magnesium salts formed with acidic functional groups in the structural formula, and acetate, trifluoroacetate, citrate, oxalate, tartrate, malate, nitrate, chloride, bromide, iodide, sulfate, bisulfate, phosphate, lactate, oleate, ascorbate, salicylate, formate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, or p-toluenesulfonate formed with basic functional groups in the structure.

15. A method of preparing the antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claims 1 to 14, comprising:

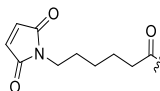


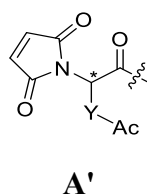
conjugating Ab with a linker-payload shown in general formula **III** to obtain the antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof shown in general formula **I** of any one of Claims 1 to 14,

wherein:

Ab is selected from anti-CD33 antibodies and antigen-binding fragments thereof; preferably, the anti-CD33 antibody is as defined in any one of claims 10 to 13;

M₁, M₂, M₃, B, L, X, R₁, R₂, R₃, R₄, R₅, m, n₁, n₂, n₃ are as defined in any one of Claims 1 to 8;

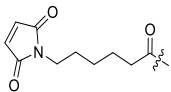
M' is selected from  or a connector unit shown in formula **A'** below



wherein Y is a scaffold selected from C1-C6 alkyl, substituted C1-C6 alkyl and C3-C8 cycloalkyl; preferably Y is C1-C6 alkyl; Ac is a hydrophilic structural unit; and

the position indicated by the wavy line on the right side is connected to B or L;

the chiral carbon atoms indicated at position * independently have an R or S absolute configuration; and

wherein when M' is , B is present and is a modifier unit.

16. A pharmaceutical composition comprising the antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claim 1 to 14, and optionally a pharmaceutically acceptable carrier.

17. A pharmaceutical formulation comprising the antibody-drug conjugate or its stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claim 1 to 14.

18. Use of the antibody-drug conjugate or the stereoisomer, pharmaceutically acceptable salt or solvate thereof according to any one of Claim 1 to 14, the pharmaceutical composition of Claim 16, or the pharmaceutical formulation of Claim 17, in the preparation of a drug for treating or prevention of cancer or tumors;

preferably, the cancer or tumor expresses CD33;

more preferably, the cancer or tumor is selected from solid tumors or hematologic tumors such as adenocarcinoma, ovarian cancer, cervical cancer, uterine cancer, prostate cancer, renal cancer, urethral cancer, bladder cancer, liver cancer, gastric cancer, endometrial cancer, salivary gland cancer, esophageal cancer, lung cancer (e.g., non-small cell lung cancer), colon cancer, breast cancer (e.g., triple-negative breast cancer), rectal cancer, colorectal cancer, bone cancer, skin cancer (e.g., epidermal cancer), thyroid cancer, pancreatic cancer, melanoma, glioma, neuroblastoma, glioblastoma multiforme, sarcoma, lymphoma, myeloma, and leukemia.