CLAIMS

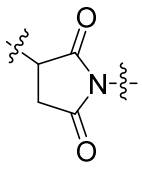
1. An immunoconjugate having Formula (I),

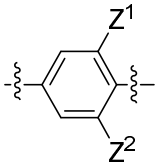
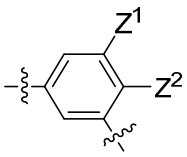
$$Ab\text{-}[S\text{-}L^1\text{-}\ L^2\text{-}\ L^3\text{-}\ L^4\text{-}\ L^5\text{-}\ L^6\text{-}\ L^7\text{-}D]_n$$

(I)

wherein:

Ab is an antibody or an antigen-binding fragment;

L^1 is ;

L^2 is absent, , or ;

Z^1 and Z^2 are each individually hydrogen, halogen, NO_2, –O–(C_1-C_6 alkyl), or C_1-C_6 alkyl;

L^3 is $–(CH_2)n^1\text{-}C(=O)–$ or $–(CH_2CH_2O)n^1\text{-}(CH_2)n^1C(=O)–$;

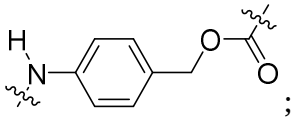
each n^1 is independently integer of 0 to 12;

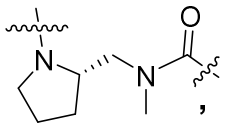
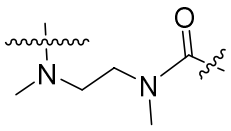
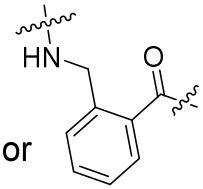
L^4 is a tetrapeptide residue;

L^5 is absent or $–[NH(CH_2)n^2]n^3–$;

n^2 is an integer of 0 to 6;

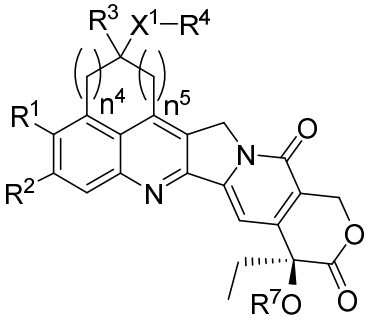
n^3 is an integer of 0 to 2;

L^6 is absent or ;

L^7 is absent, , , or ;

D is a drug moiety; and

n is an integer from 1 to 10, wherein D is a drug moiety of Formula (II) having the structure:



(II)

wherein:

R^1 and R^2 are each individually selected from the group consisting of hydrogen, halogen, –CN, –OR^5, –NR^5R^6, a substituted or an unsubstituted C_1-C_6 alkyl, a substituted or an unsubstituted C_1-C_6 haloalkyl, a substituted or an unsubstituted –O–(C_1-C_6 alkyl), a substituted or an unsubstituted –O–(C_1-C_6 haloalkyl), –$[(CY_2)_pO(CY_2)_q]_tCY_3$, or a substituted or an unsubstituted –O-$(CR^5R^6)_m$–O– such that R^1 and R^2 taken together form a ring;

R^3 is hydrogen or a substituted or an unsubstituted C_1-C_6 alkyl, a substituted or an unsubstituted C_1-C_6 haloalkyl, or –$[(CY_2)_pO(CY_2)_q]_tCY_3$;

R^4 is hydrogen, a substituted or an unsubstituted –(C_1-C_6 alkyl)-X^2, a substituted or an unsubstituted –(C_1-C_6 haloalkyl)-X^2, a substituted or an unsubstituted –(C_1-C_6 alkenyl)-X^2, a substituted or an unsubstituted –(C_1-C_6 haloalkenyl)-X^2, a substituted or an unsubstituted –(C_1-C_6 alkynyl)-X^2, or a substituted or an unsubstituted –(C_1-C_6 haloalkynyl)-X^2;

X^1 is –O–;

X^2 is –OR^9, -SR^9, or -NHR^9;

R^5 and R^6 are each individually hydrogen, halogen, a substituted or an unsubstituted C_1-C_6 alkyl, a substituted or an unsubstituted C_1-C_6 haloalkyl, or –$[(CY_2)_pO(CY_2)_q]_tCY_3$;

m is 1 or 2;

n^4 and n^5 are each individually 0, 1 or 2, with the proviso that n^4 and n^5 are not both 0;

each Y is individually H or halogen;

each p is individually 1, 2, 3, 4, 5, or 6;

each q is individually 0, 1, 2, 3, 4, 5, or 6;

each t is individually 1, 2, 3, 4, 5, or 6;

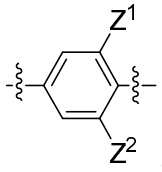
R^7 is H, $–COR^8$, $–CO_2R^8$, $–(CO)-NHR^8$, L^4, L^5, L^6, or L^7;

R^8 is a substituted or an unsubstituted C_1-C_6 alkyl-X^3, a substituted or an unsubstituted C_1-C_6 haloalkyl-X^3, or $–[(CY_2)_pO(CY_2)_q]_tCY_2$-$X^3$;

R^9 is H, $–COR^8$, $–CO_2R^8$, $–(CO)-NHR^8$, L^4, L^5, L^6, or L^7, with the proviso that exactly one of R^7 and R^9 is L^4, L^5, L^6, or L^7; and

each X^3 is individually –H, –OH, –SH, or $–NH_2$.

2. The immunoconjugate of claim 1, wherein L^2 is absent.

3. The immunoconjugate of claim 1, wherein L^2 is 

.

4. The immunoconjugate of any one of claims 1 to 3, wherein at least one of Z^1 and Z^2 is hydrogen.

5. The immunoconjugate of any one of claims 1 to 4, wherein L^3 is $–(CH_2)n^1$-C(=O)–.

6. The immunoconjugate of any one of claims 1 to 5, wherein L^4 is gly-gly-phe-gly (GGFG).

7. The immunoconjugate of any one of claims 1 to 5, wherein L^5 is $–[NH(CH_2)n^2]n^3$–.

8. The immunoconjugate of any one of claims 1 to 7, wherein L^6 is absent.

9. The immunoconjugate of any one of claims 1 to 8, wherein L^7 is absent.

10. The immunoconjugate of any one of claims 1 to 9, wherein:

a) R^1 and R^2 are each individually selected from the group consisting of hydrogen, fluoro, methoxy, methyl, difluoromethyl, and -O-(CH_2)-O- such that R^1 and R^2 taken together form a ring;

b) R^3 is hydrogen;

c) R^4 is a substituted or unsubstituted $–(C_1$-C_6 alkyl)-X^2;

d) X^2 is $–OR^9$;

e) n^4 is 2 and n^5 is 0;

f) R^7 is H; and/or

g) R^9 is L^4, L^5, L^6, or L^7.

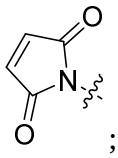
11. The immunoconjugate of any one of claims 1-10, wherein Ab specifically binds to human receptor tyrosine kinase like orphan receptor 1 (ROR1).

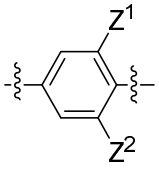
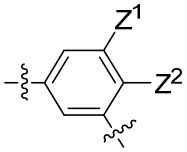
12. A process of producing an immunoconjugate of claim 1, comprising: reacting an effective amount of a thiol-functionalized antibody or antigen-binding fragment with a conjugate of Formula (III) under reaction conditions effective to form the immunoconjugate, wherein the conjugate of Formula (III) is:

$$Mi\text{-}\ L^2\text{-}\ L^3\text{-}\ L^4\text{-}\ L^5\text{-}\ L^6\text{-}\ L^7\text{-}D$$

(III)

wherein:

Mi is ;

L^2 is absent, , or ;

Z^1 and Z^2 are each individually hydrogen, halogen, NO_2, –O–(C_1-C_6 alkyl), or C_1-C_6 alkyl;

L^3 is $–(CH_2)n^1\text{-}C(=O)–$ or $–(CH_2CH_2O)n^1\text{-}(CH_2)n^1C(=O)–$;

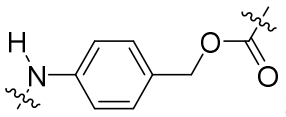
each n^1 is independently integer of 0 to 12;

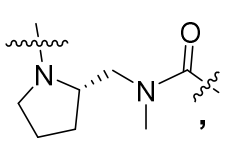
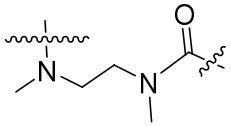
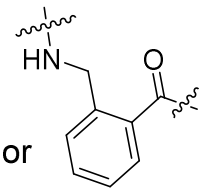
L^4 is a tetrapeptide residue;

L^5 is absent or $–[NH(CH_2)n^2]n^3–$;

n^2 is an integer of 0 to 6;

n^3 is an integer of 0 to 2;

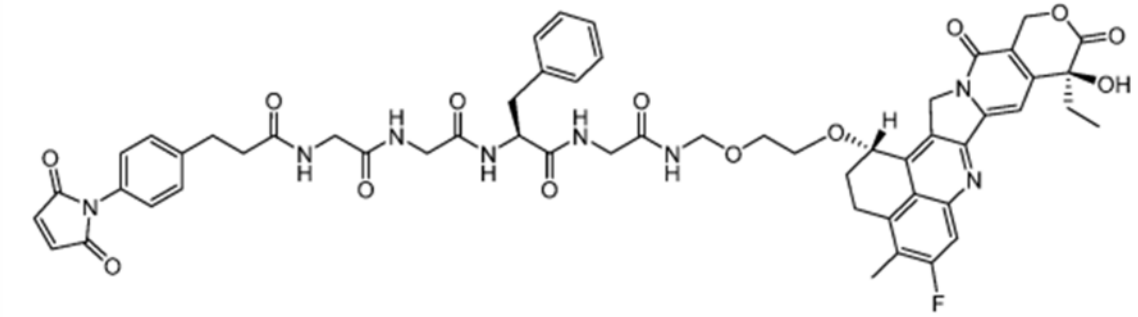
L^6 is absent or ;

L^7 is absent, , , or ; and

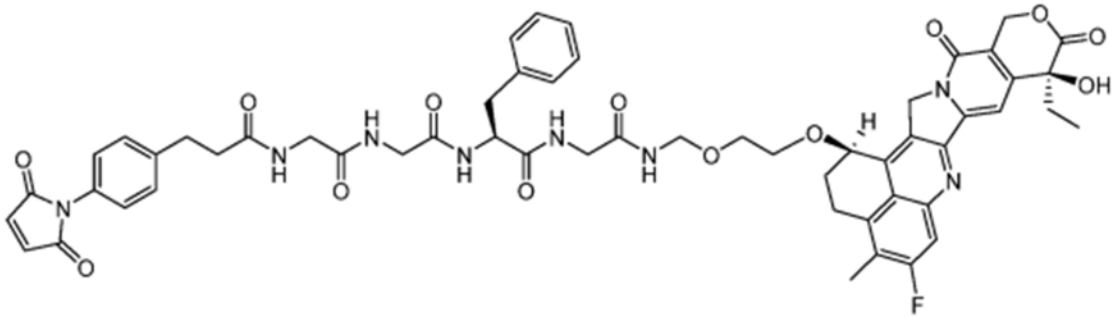
D is a drug moiety of Formula (II) as defined in claim 1.

13. The process of claim 12, further comprising reducing an antibody or antigen-binding fragment under reducing conditions effective to form the thiol-functionalized antibody or antigen-binding fragment.

14. The process of claim 12 or 13, wherein the conjugate is selected from:



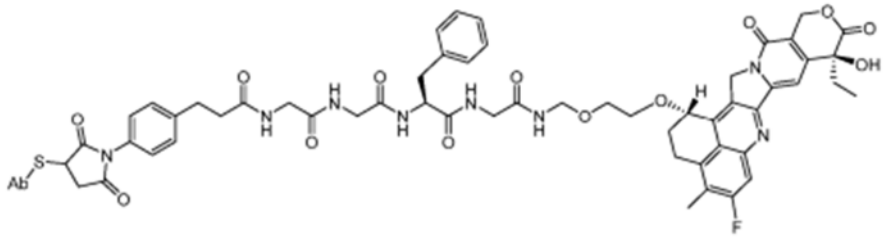
and



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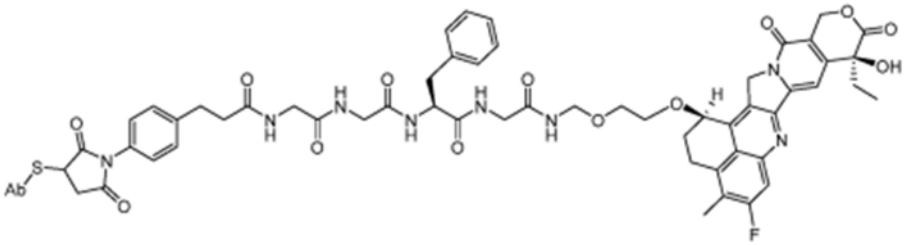
15. An immunoconjugate produced by the process of any one of claims 12-14.

16. An immunoconjugate of claim 1, selected from:



,

and



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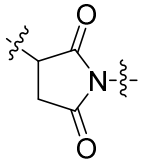
17. An immunoconjugate having Formula (I),

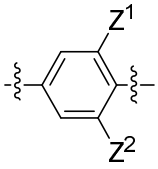
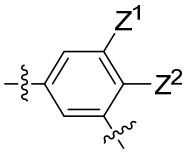
$$Ab\text{-}[S\text{-}L^1\text{-}\ L^2\text{-}\ L^3\text{-}\ L^4\text{-}\ L^5\text{-}\ L^6\text{-}\ L^7\text{-}D]_n$$

(I)

wherein:

Ab is an antibody or an antigen-binding fragment;

L^1 is ;

L^2 is absent, , or ;

Z^1 and Z^2 are each individually hydrogen, halogen, NO_2, –O–(C_1-C_6 alkyl), or C_1-C_6 alkyl;

L^3 is $–(CH_2)n^1$-C(=O)– or $–(CH_2CH_2O)n^1$-$(CH_2)n^1$C(=O)–;

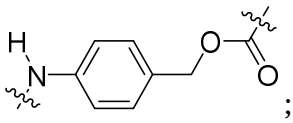
each n^1 is independently integer of 0 to 12;

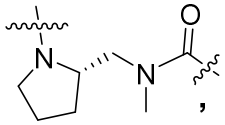
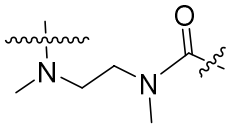
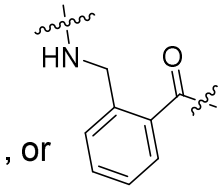
L^4 is a tetrapeptide residue;

L^5 is absent or $–[NH(CH_2)n^2]n^3$–;

n^2 is an integer of 0 to 6;

n^3 is an integer of 0 to 2;

L^6 is absent or ;

L^7 is absent, , , or ;

D is a drug moiety; and

n is an integer from 1 to 10, wherein said antibody or antigen-binding fragment thereof comprises:

a) a heavy chain comprising:

VHCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1;

VHCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2; and

VHCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:3; and

b) a light chain comprising:

VLCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8;

VLCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of AAS; and

VLCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 10;

wherein the antibody or antigen-binding fragment thereof specifically binds to the extracellular domain of human receptor tyrosine kinase like orphan receptor 1 (ROR1).

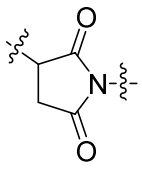
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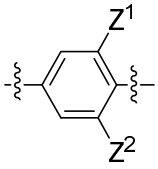
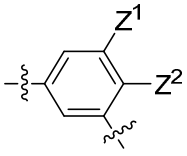
$$Ab\text{-}[S\text{-}L^1\text{-}\ L^2\text{-}\ L^3\text{-}\ L^4\text{-}\ L^5\text{-}\ L^6\text{-}\ L^7\text{-}D]_n$$

(I)

wherein:

Ab is an antibody or an antigen-binding fragment;

L^1 is ;

L^2 is absent,  , or ;

Z^1 and Z^2 are each individually hydrogen, halogen, NO_2, –O–(C_1-C_6 alkyl), or C_1-C_6 alkyl;

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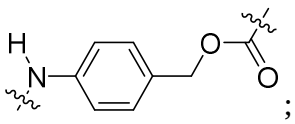
each n^1 is independently integer of 0 to 12;

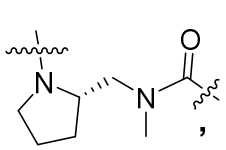
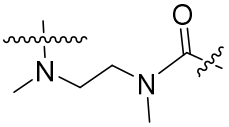
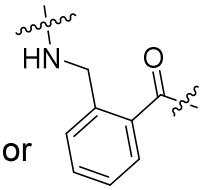
L^4 is a tetrapeptide residue;

L^5 is absent or $–[NH(CH_2)n^2]n^3–$;

n^2 is an integer of 0 to 6;

n^3 is an integer of 0 to 2;

L^6 is absent or ;

L^7 is absent, , , or ;

D is a drug moiety; and

n is an integer from 1 to 10, wherein said antibody or antigen-binding fragment thereof comprises:

a) a heavy chain comprising:

VHCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 15;

VHCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 16; and

VHCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17; and b) a light chain comprising:

VLCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:22;

VLCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of DAY; and

VLCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:24;

wherein the antibody or antigen-binding fragment thereof specifically binds to the extracellular domain of human receptor tyrosine kinase like orphan receptor 1

(ROR1).

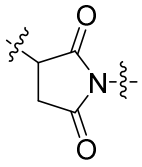
19. An immunoconjugate having Formula (I),

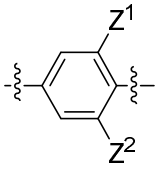
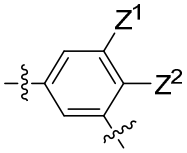
$$Ab\text{-}[S\text{-}L^1\text{-}L^2\text{-}L^3\text{-}L^4\text{-}L^5\text{-}L^6\text{-}L^7\text{-}D]_n$$

(I)

wherein:

Ab is an antibody or an antigen-binding fragment;

L^1 is ;

L^2 is absent, , or ;

Z^1 and Z^2 are each individually hydrogen, halogen, NO_2, –O–(C_1-C_6 alkyl), or C_1-C_6 alkyl;

L^3 is $–(CH_2)n^1$-C(=O)– or $–(CH_2CH_2O)n^1$-$(CH_2)n^1$C(=O)–;

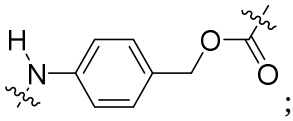
each n^1 is independently integer of 0 to 12;

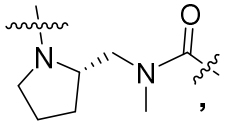
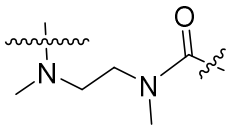
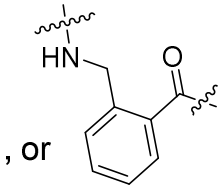
L^4 is a tetrapeptide residue;

L^5 is absent or $–[NH(CH_2)n^2]n^3$–;

n^2 is an integer of 0 to 6;

n^3 is an integer of 0 to 2;

L^6 is absent or ;

L^7 is absent, , , or ;

D is a drug moiety; and

n is an integer from 1 to 10, wherein said antibody or antigen-binding fragment thereof comprises:

a) a heavy chain comprising:

VHCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:29;

VHCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:30; and

VHCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:31; and

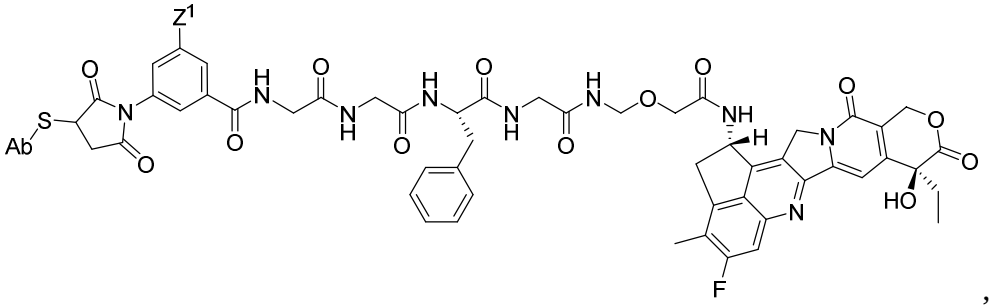
b) a light chain comprising:

VLCDR 1 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:36;

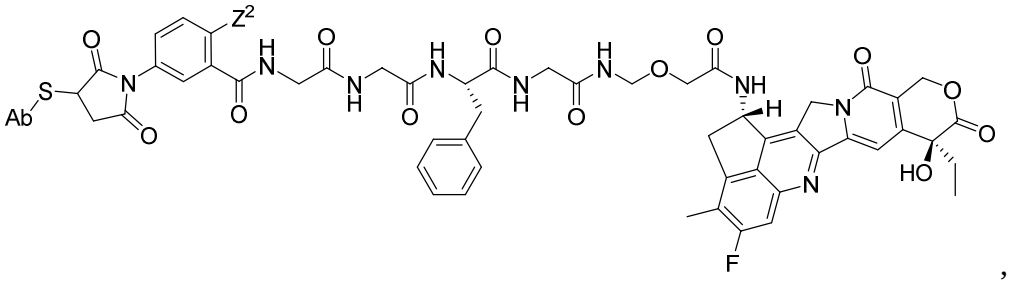
VLCDR 2 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of DAS; and

VLCDR 3 comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:38; wherein the antibody or antigen-binding fragment specifically binds to the extracellular domain of human receptor tyrosine kinase like orphan receptor 1 (ROR1).

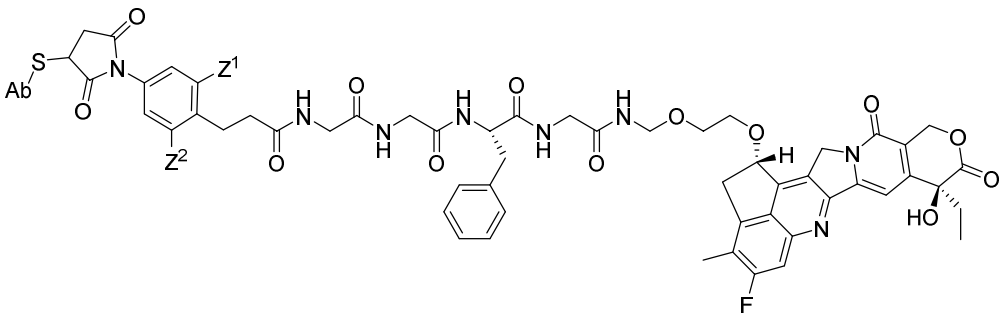
20. The immunoconjugate of any one of claims 17-19, wherein Formula (I) is selected from:



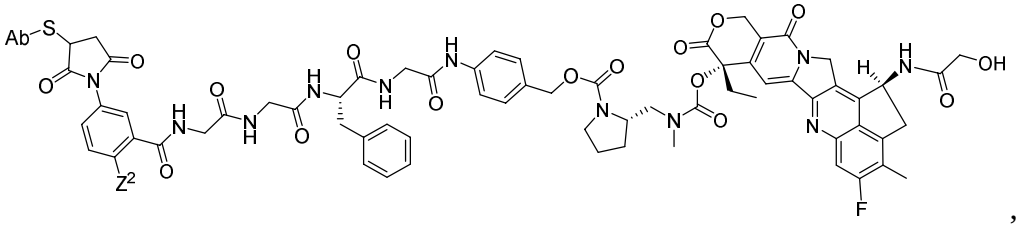
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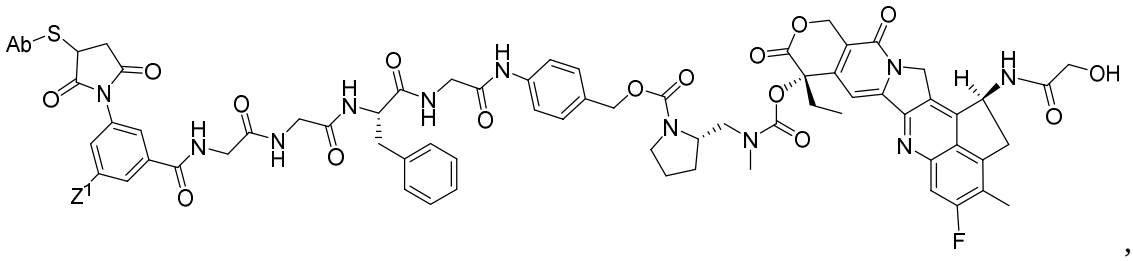


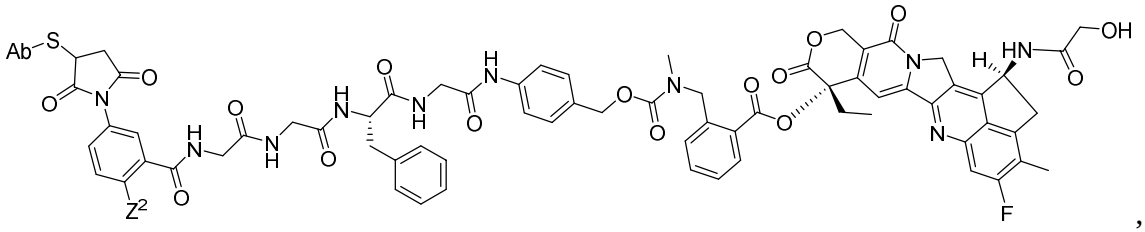
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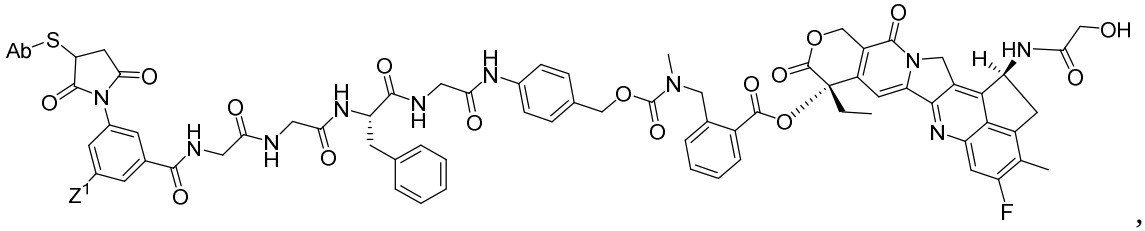


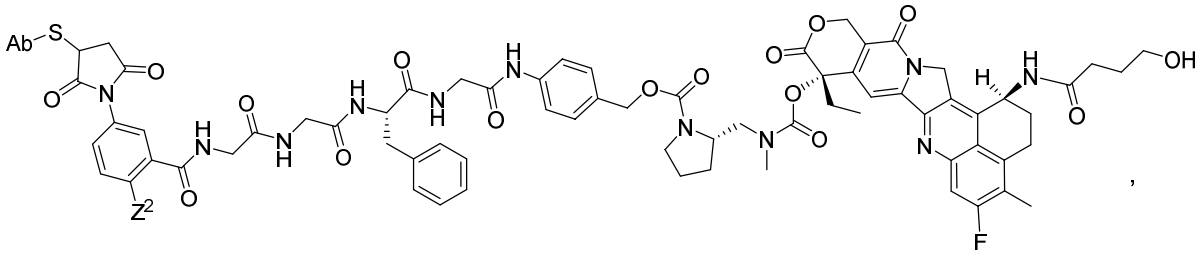
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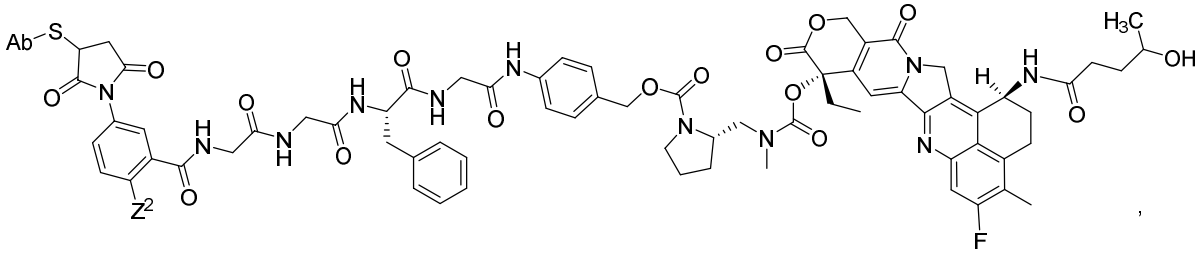

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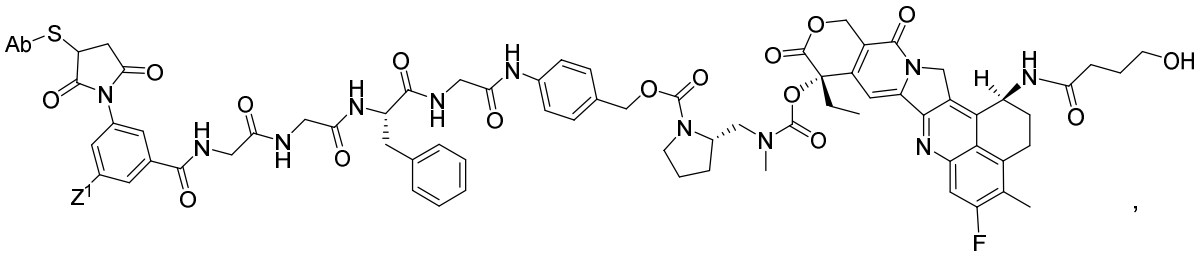

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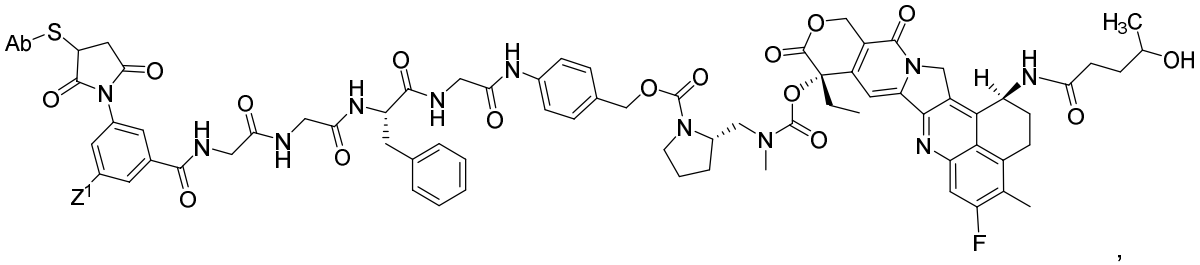

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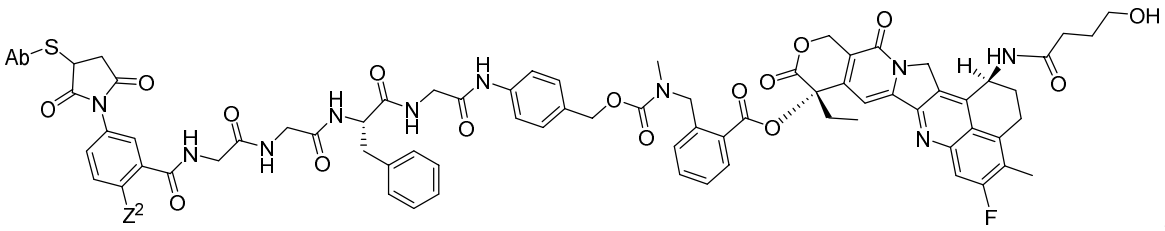

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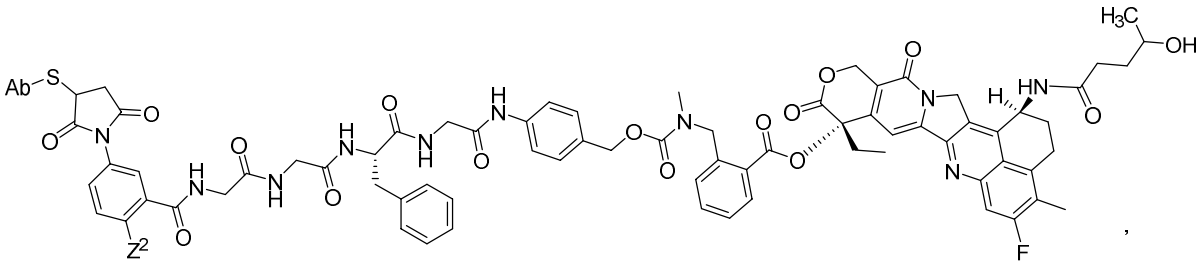

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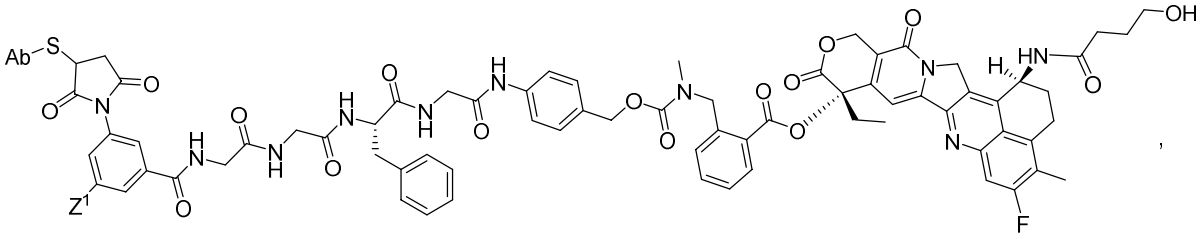

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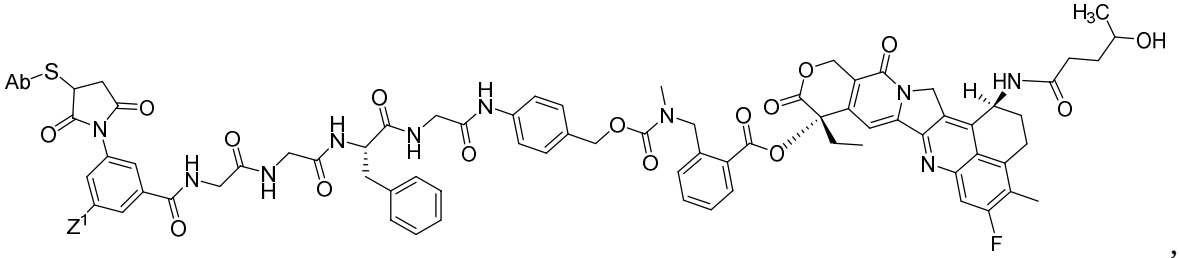

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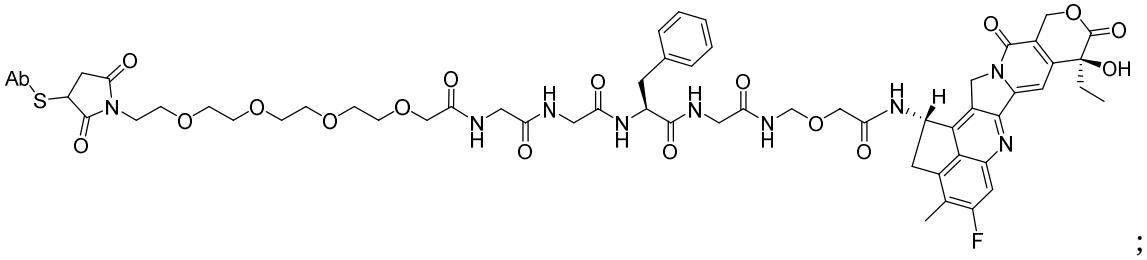

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, and



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wherein Z^1 and Z^2 are each individually selected from hydrogen, fluoro, chloro, $–NO_2$, and $–OCH_3$.

21. A pharmaceutical composition comprising an immunoconjugate of any one of claims 1 to 20, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

22. Use of an immunoconjugate of any one of claims 1 to 20, or a pharmaceutical composition of claim 21, in the manufacture of a medicament for treating a cancer or a tumor in a subject having the cancer or the tumor.

23. The use of claim 22, wherein the cancer or the tumor is selected from lung cancer, urothelial cancer, colorectal cancer, prostate cancer, ovarian cancer, pancreatic cancer, breast cancer, bladder cancer, gastric cancer, gastrointestinal stromal tumor, uterine cervix cancer, esophageal cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, colon cancer, rectal cancer, colorectal cancer, endometrial cancer, uterine cancer, salivary gland cancer, kidney cancer, vulval cancer, thyroid cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, or sarcoma.

24. Use of an immunoconjugate of any one of claims 1 to 20, or a pharmaceutical composition of claim 21, in the manufacturing of a medicament for use in therapy.