CLAIMS

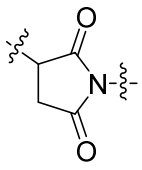
1. An immunoconjugate having Formula (I),

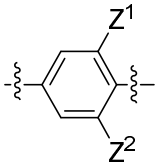
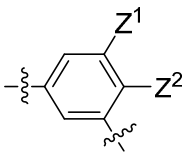
$$Ab\text{-}[S\text{-}L^1\text{-}\ L^2\text{-}\ L^3\text{-}\ L^4\text{-}\ L^5\text{-}\ L^6\text{-}\ L^7\text{-}D]_n$$

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

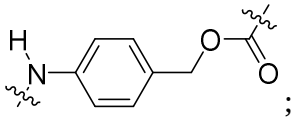
n^1 are independently integers of 0 to 12;

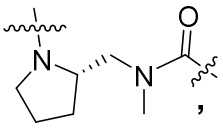
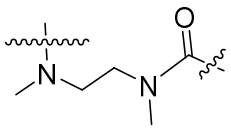
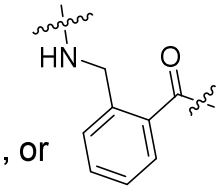
L^4 is a tetrapeptide residue;

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;

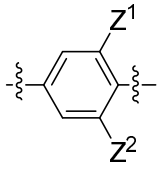
L^6 is absent or ;

L^7 is absent, , , or ;

D is a drug moiety; and

n is an integer from 1 to 10.

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 $–(CH_2)n^1\text{-}C(=O)$.

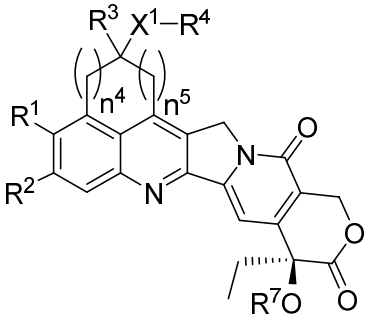
6. The immunoconjugate of any one of claims 1 to 5, wherein L^4 is gly-gly-phe-gly (GGFG).

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 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 $–O–(C_1\text{-}C_6$ alkyl), a substituted or an unsubstituted $–O–(C_1\text{-}C_6$ haloalkyl), $–[(CY_2)_pO(CY_2)_q]_tCY_3$, or a substituted or an unsubstituted $–O\text{-}(CR^5R^6)_m–O–$ 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–, –S(O_{n6})–, –NH–, –O-(C=O)–, –NH-(C=O)–, –NH-(C=O)-O–, –NH-(C=O)-NH–, or –NH-S(O_{n6})–;

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;

n^6 is 0, 1 or 2;

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;

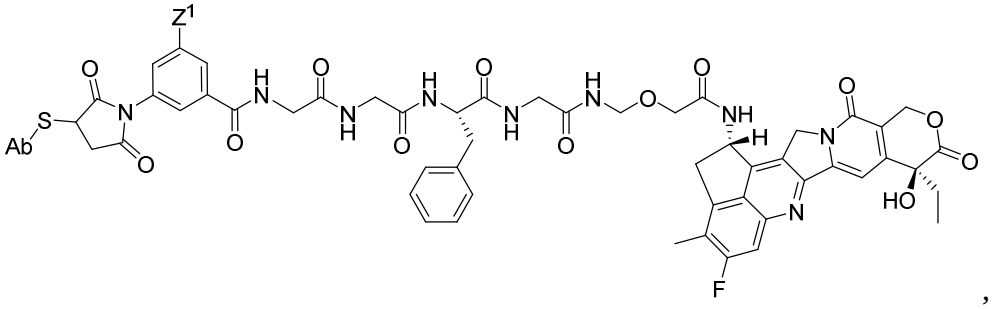
R^8 is a substituted or an unsubstituted C_1-C_6 alkyl-X^3, a substituted or an unsubstituted C_1-C_6 haloalkyl-X^3, or –$[(CY_2)_pO(CY_2)_q]_tCY_2$-$X^3$;

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.

11. The immunoconjugate of claim 10, wherein the drug moiety is exatecan.

12. The immunoconjugate of claim 1, wherein Formula (I) is selected from



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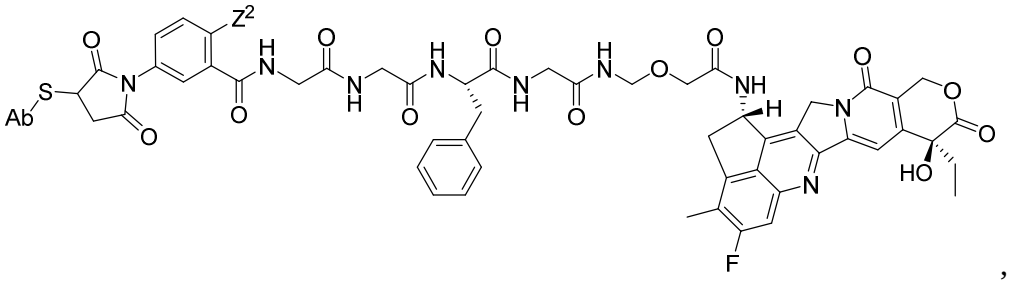

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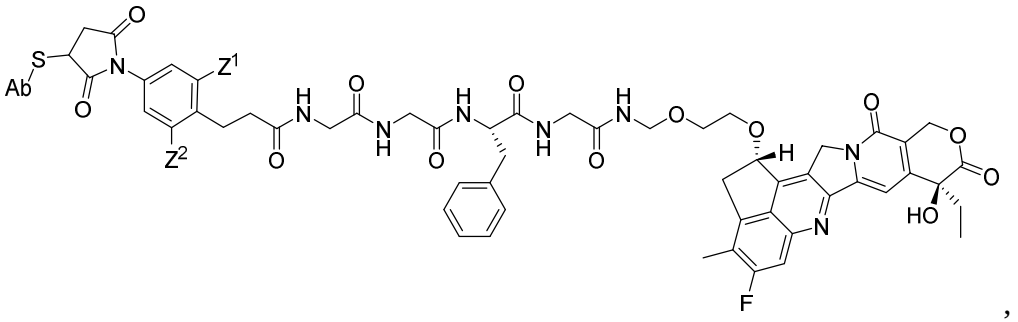

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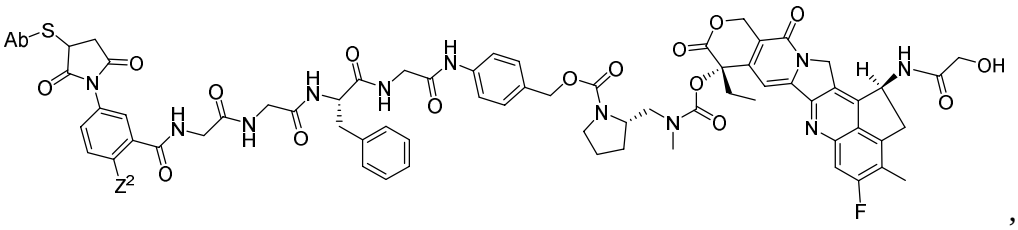

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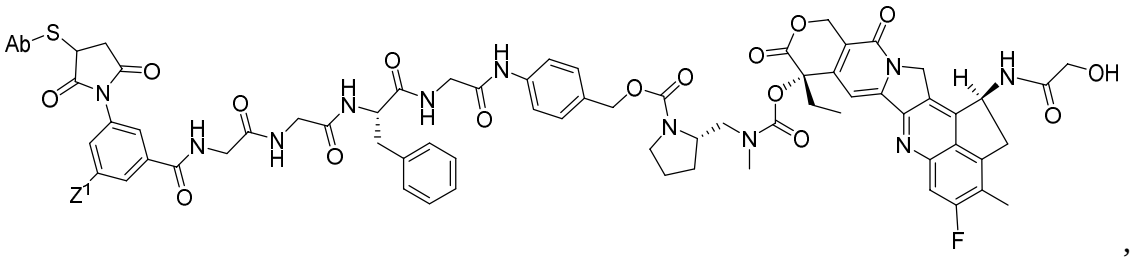

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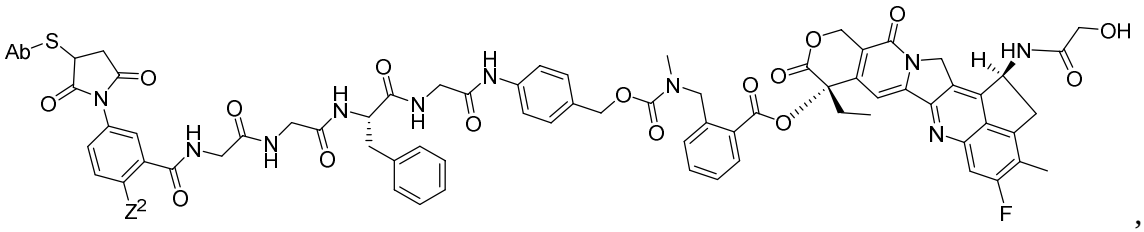
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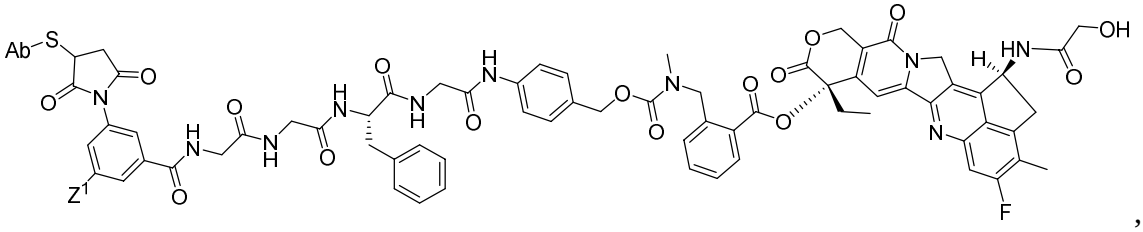
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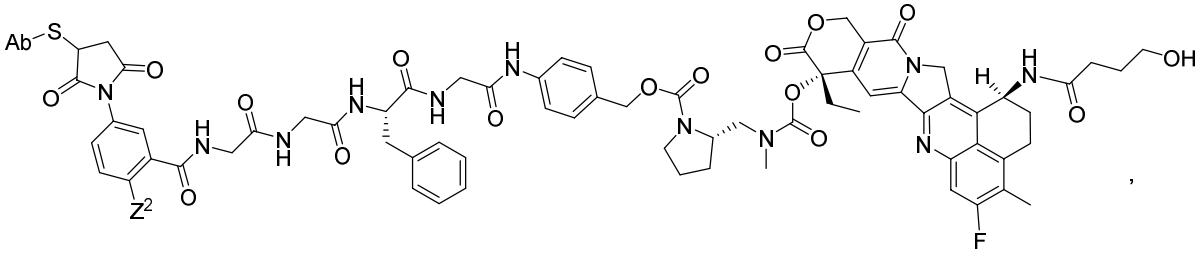
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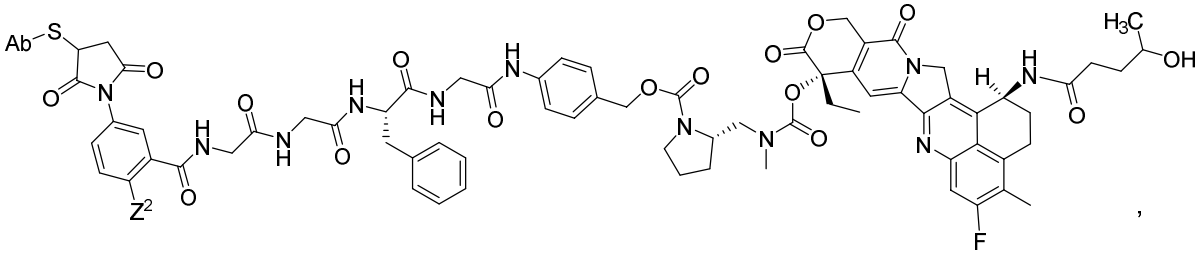
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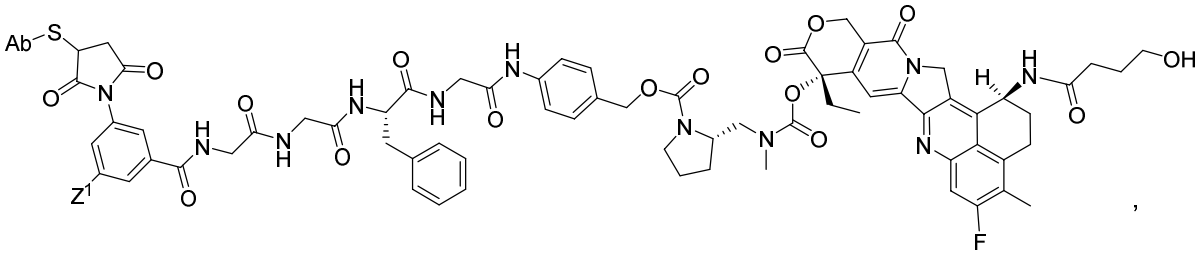
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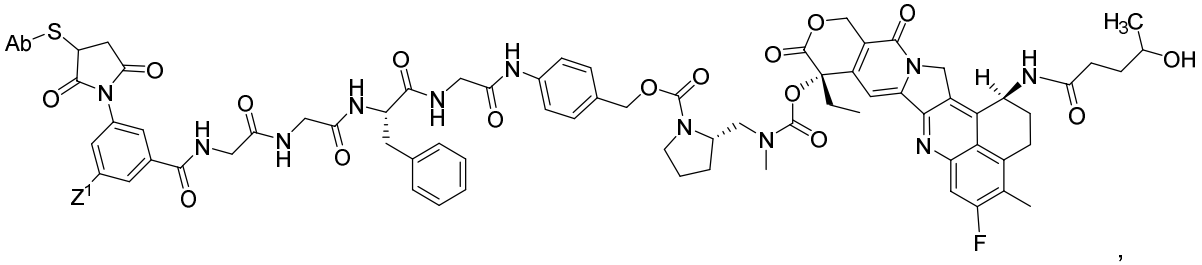
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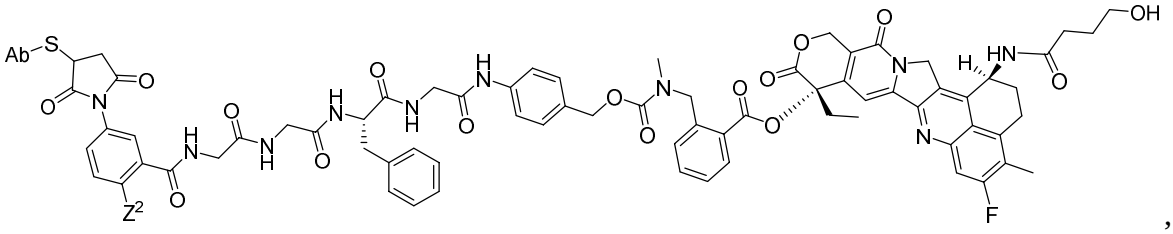
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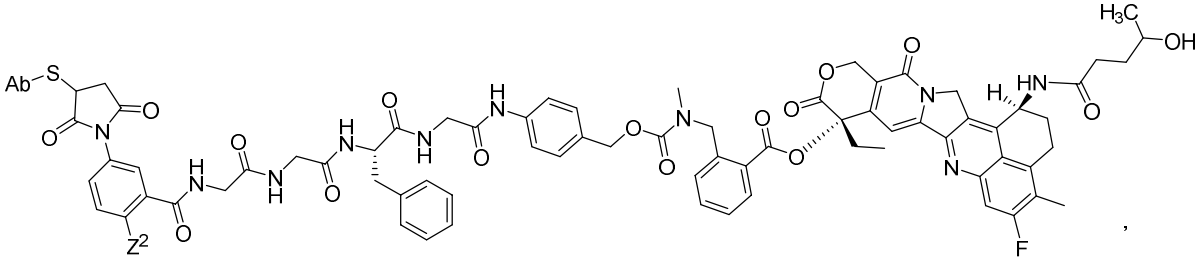
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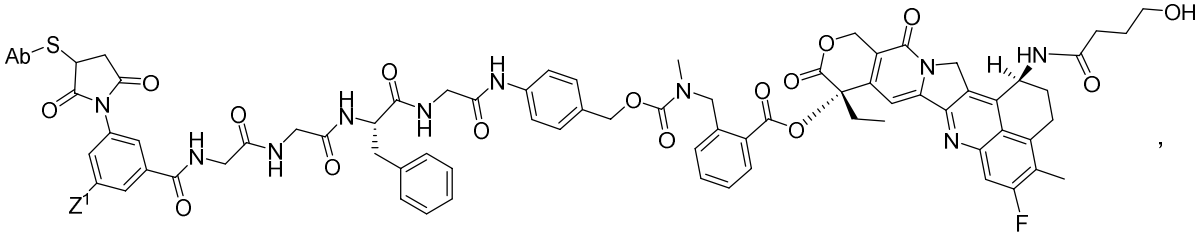
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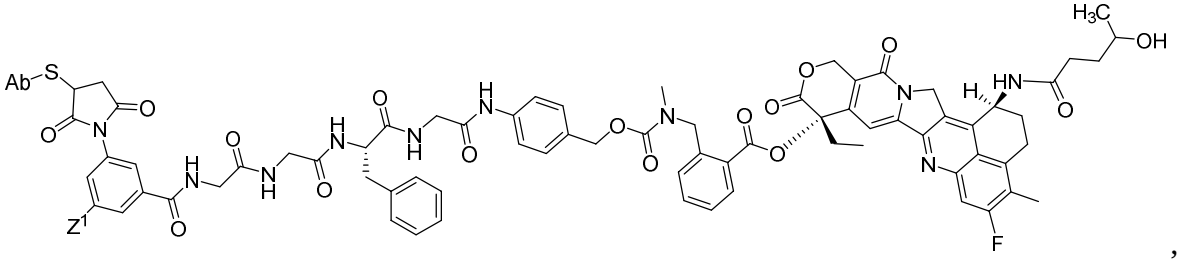
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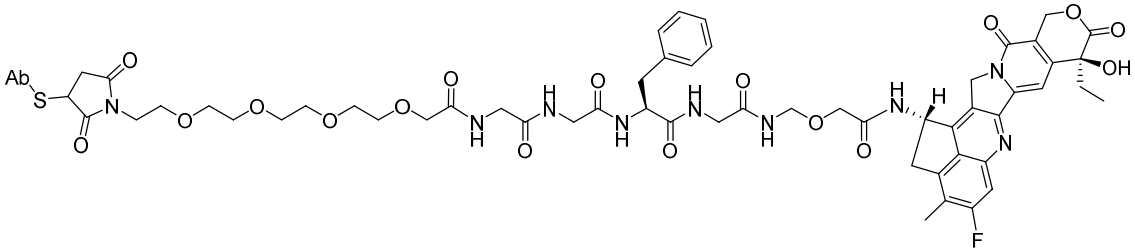
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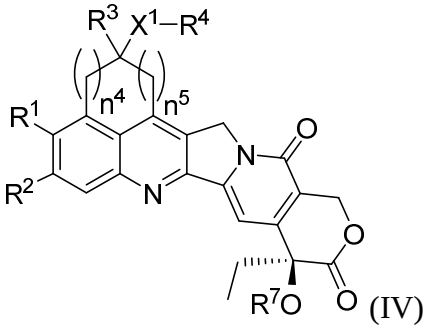
wherein Z^1 and Z^2 are each individually selected from hydrogen, fluoro, chloro, $–NO_2$, and $–OCH_3$.

13. A compound of Formula (IV), or a pharmaceutically acceptable salt thereof, having the structure:



(IV)

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–, $–S(O_{n6})–$, –NH–, –O-(C=O)–, –NH-(C=O)–, –NH-(C=O)-O–, –NH-(C=O)-NH–, or $–NH-S(O_{n6})–$;

X^2 is –OH, –SH, or $–NR^5R^6$;

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 $–[(CY_2)_pO(CY_2)_q]_tCY_3$;

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

R^8 is 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;

n^6 is 0, 1 or 2; and

each Y is individually H or halogen;

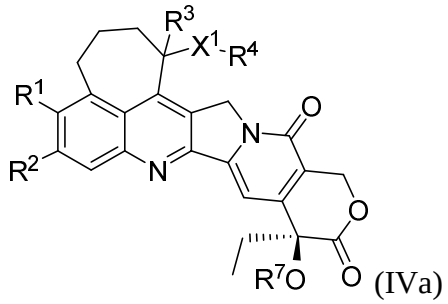
each p is individually 1, 2, 3, 4, 5, or 6;

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

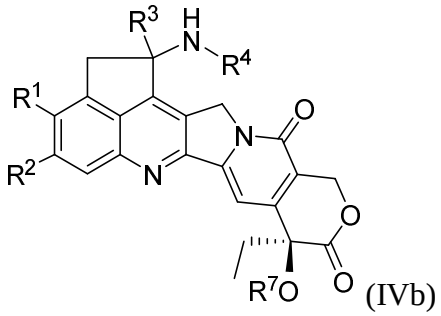
each t is individually 1, 2, 3, 4, 5, or 6;

with the proviso that Formula (IV) does not represent deruxtecan or exatecan.

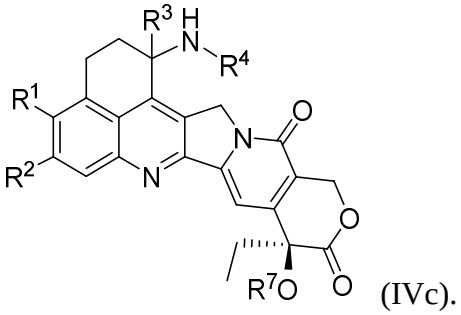
14. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (IV) is represented by Formula (IVa), Formula (IVb), or Formula (VIc):



(IVa)

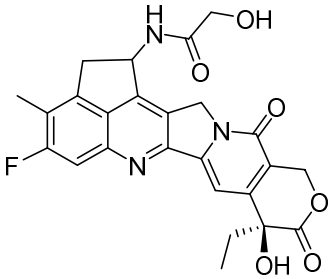


(IVb)



(IVc).

15. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (IV) is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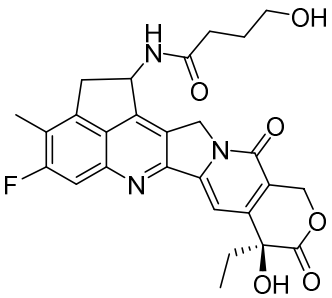
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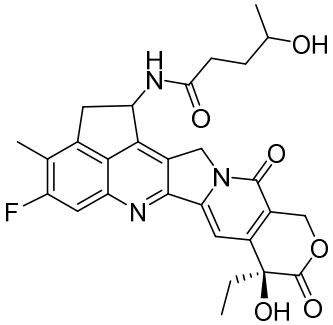
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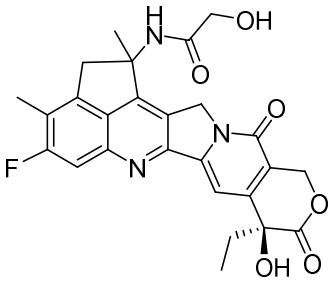
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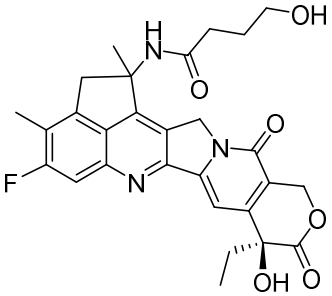
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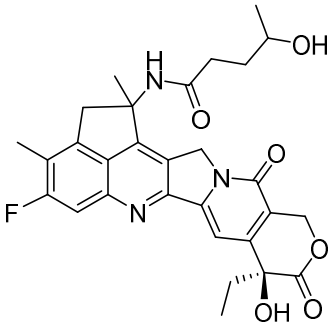
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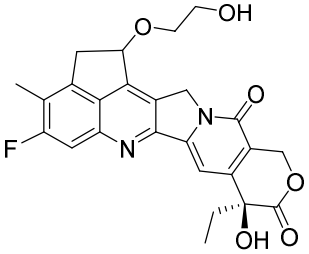
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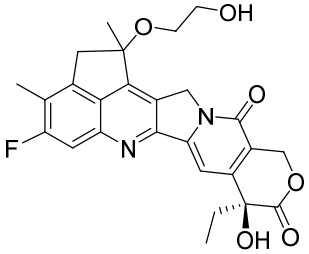
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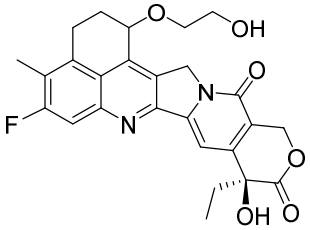
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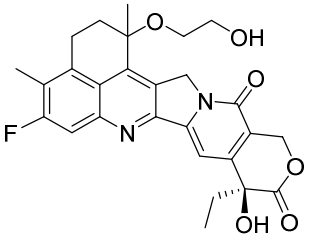
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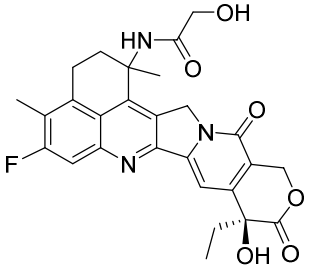
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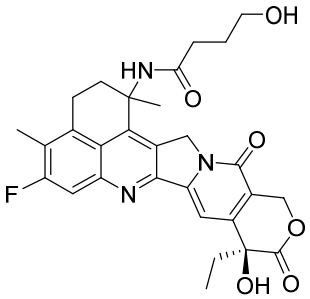
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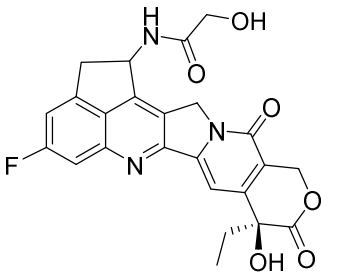
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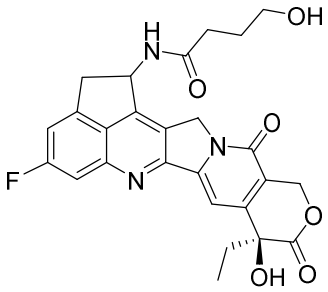
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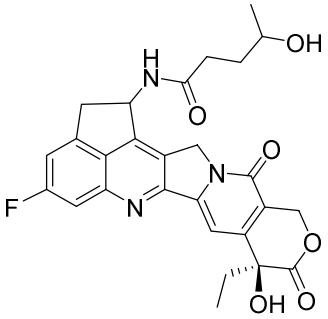
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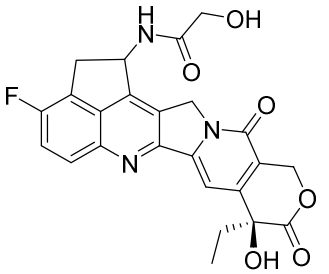
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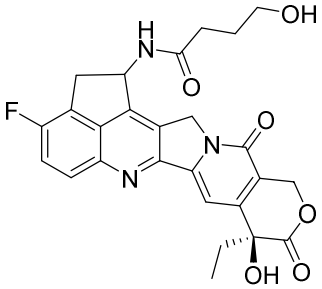
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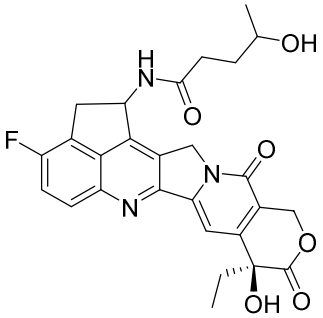
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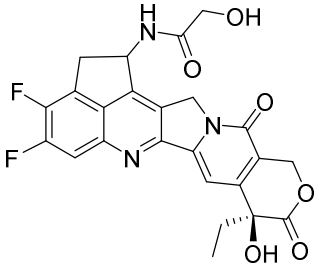
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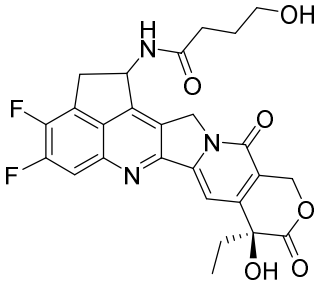
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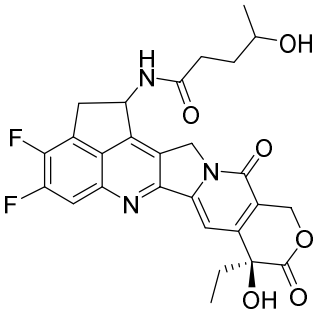
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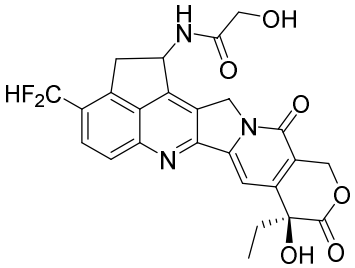
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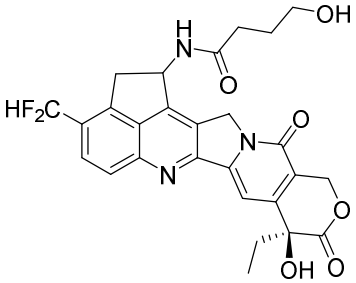
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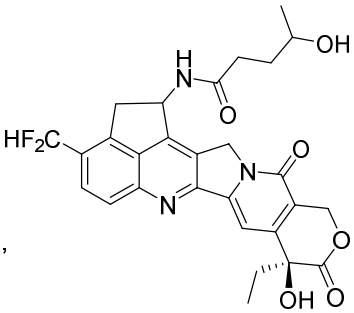
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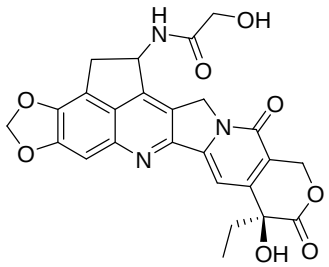
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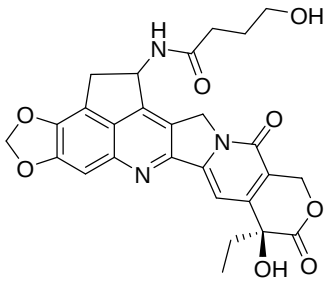
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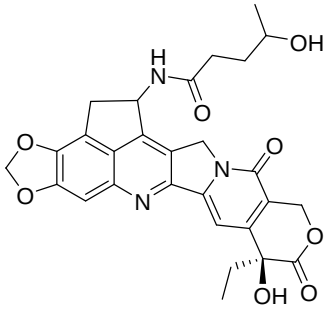
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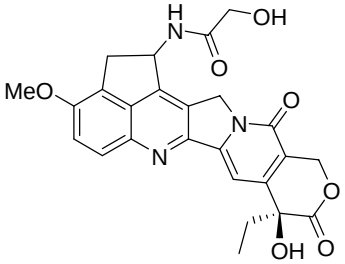
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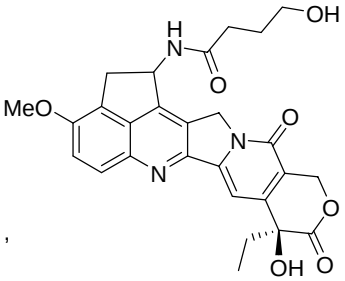
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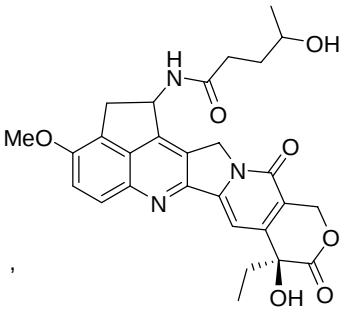
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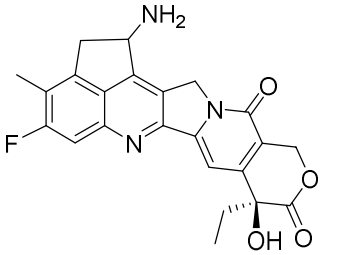
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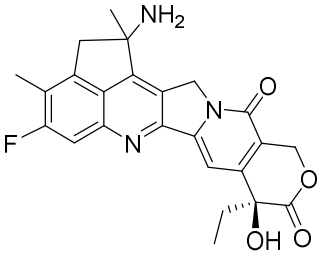
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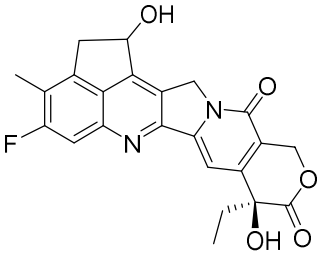
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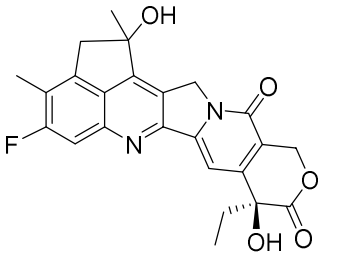
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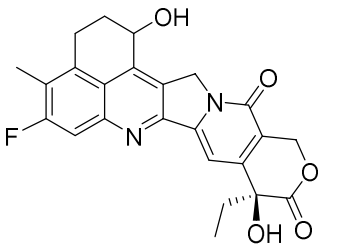
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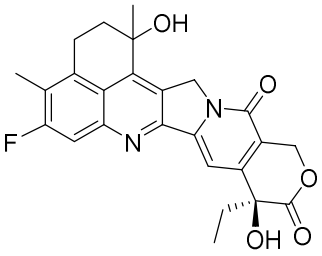
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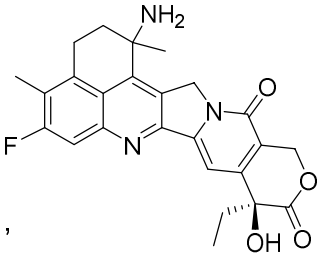
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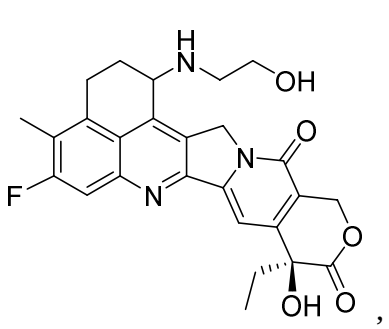
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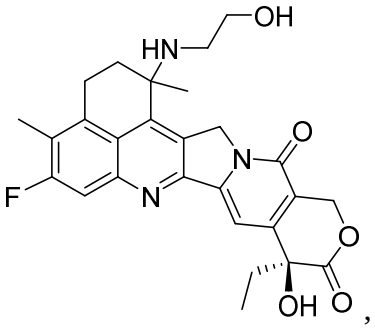
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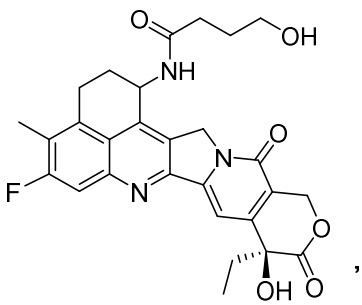
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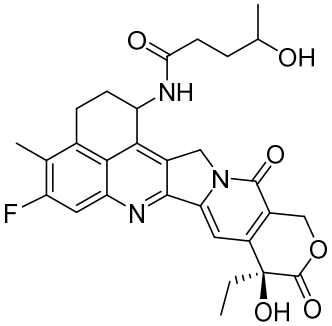
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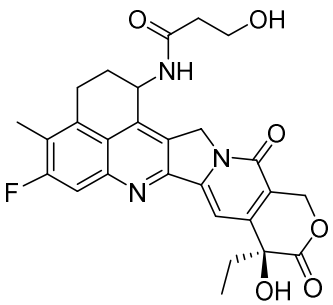
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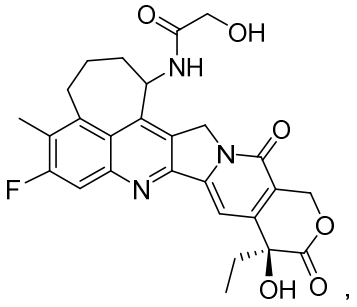
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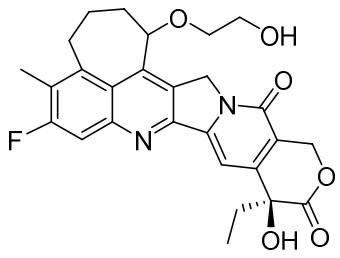
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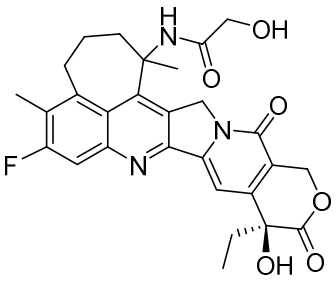
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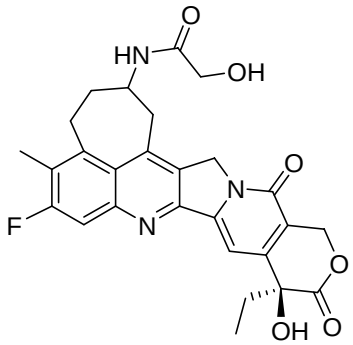
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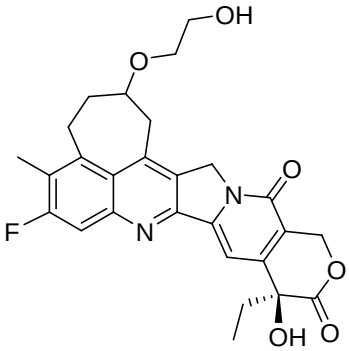
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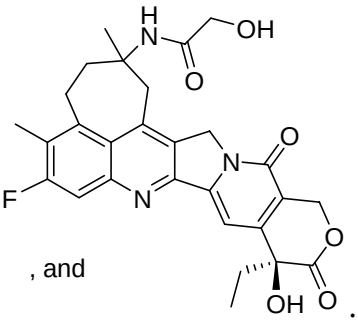
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16. A pharmaceutical composition comprising an immunoconjugate of any one of claims 1 to 12, a compound of any one of claims 13 to 15, or a pharmaceutically active salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

17. Use of an immunoconjugate of any one of claims 1 to 12, a compound of any one of claims 13 to 15, or a pharmaceutically active salt thereof, or a pharmaceutical composition of

claim 16, in the manufacture of a medicament for treating a cancer or a tumor in a subject having the cancer or the tumor.

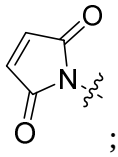
18. The use of claim 17, wherein the cancer or the tumor is selected from lung cancer, urothelial cancer, colorectal cancer, prostate cancer, ovarian cancer, pancreatic cancer, breast cancer, bladder cancer, gastric cancer, gastrointestinal stromal tumor, uterine cervix cancer, esophageal cancer, squamous 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.

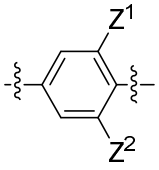
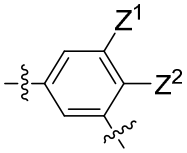
19. A conjugate having Formula (III),

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

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

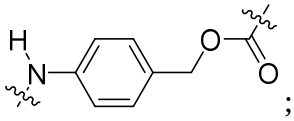
n^1 are independently integers of 0 to 12;

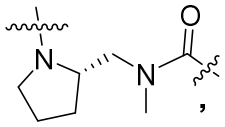
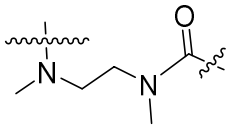
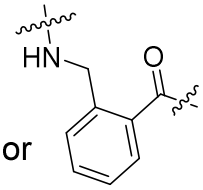
L^4 is a tetrapeptide residue;

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

n^2 is an integer of 0 to 6;

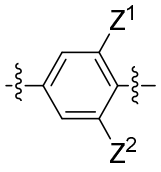
n^3 is an integer of 0 to 2;

L^6 is absent or ;

L^7 is absent,  ,  , or  ; and

D is a drug moiety.

20. The conjugate of claim 19, wherein L^2 is absent.

21. The conjugate of claim 19, wherein L^2 is  .

22. The conjugate of any one of claims 19 to 20, wherein at least one of Z^1 and Z^2 is hydrogen.

23. The conjugate of any one of claims 19 to 22, wherein L^3 is $–(CH_2)n^1\text{-}C(=O)–$.

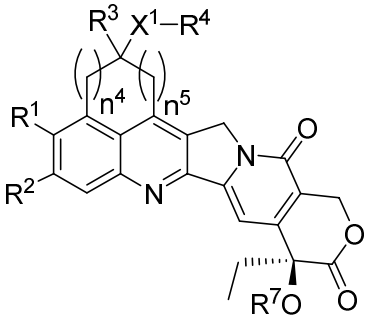
24. The conjugate of any one of claims 19 to 23, wherein L^4 is gly-gly-phe-gly (GGFG).

25. The conjugate of any one of claims 19 to 24, wherein L^5 is $–[NH(CH_2)n^2]n^3–$.

26. The conjugate of any one of claims 19 to 25, wherein L^6 is absent.

27. The conjugate of any one of claims 19 to 26, wherein L^7 is absent.

28. The conjugate of any one of claims 19 to 27, wherein D is a compound 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 $–O–(C_1\text{-}C_6$ 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–, –$S(O_{n6})$–, –NH–, –O-(C=O)–, –NH-(C=O)–, –NH-(C=O)-O–, –NH-(C=O)-NH–, or –NH-$S(O_{n6})$–;

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;

n^6 is 0, 1 or 2

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;

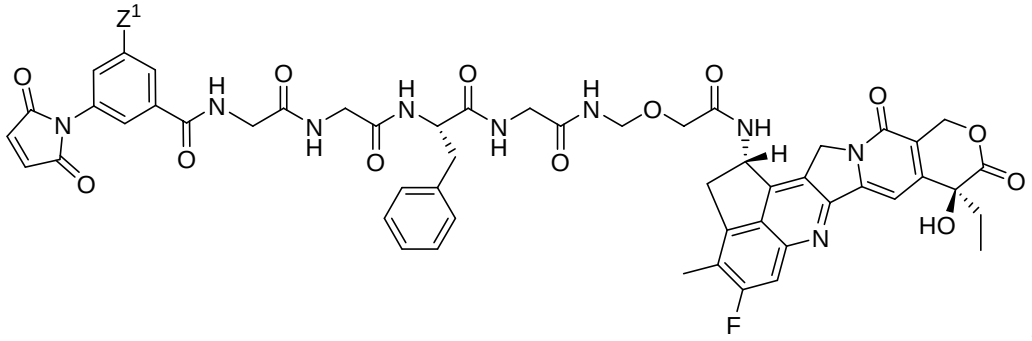
R^7 is H, -COR^8, -CO_2R^8, -(CO)-NHR^8, L^4, L^5, L^6, or L^7;

each R^8 is individually 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.

29. The conjugate of any one of claims 19 to 28, wherein Formula (III) is selected from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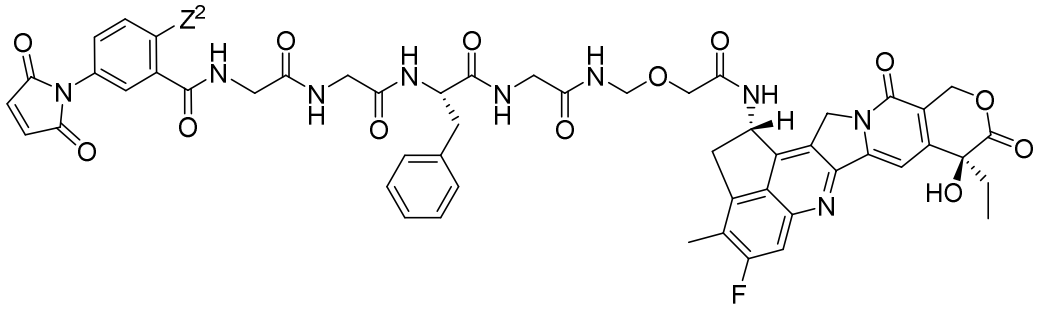
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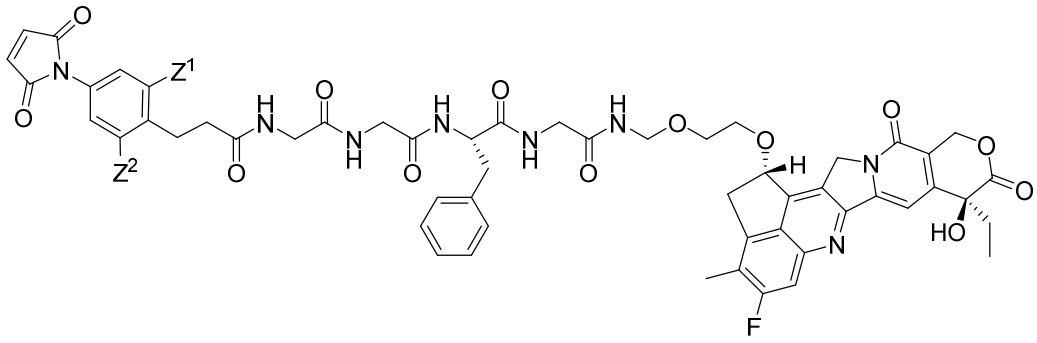
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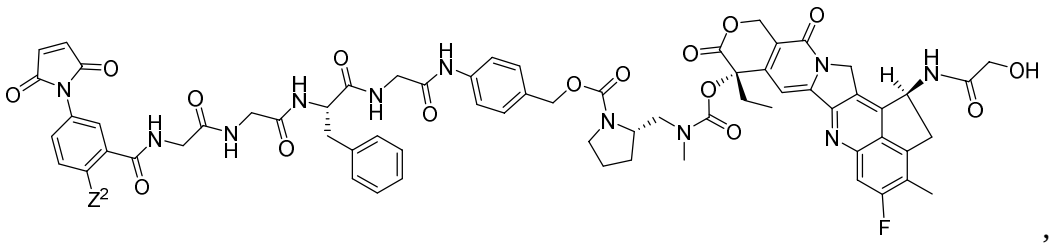
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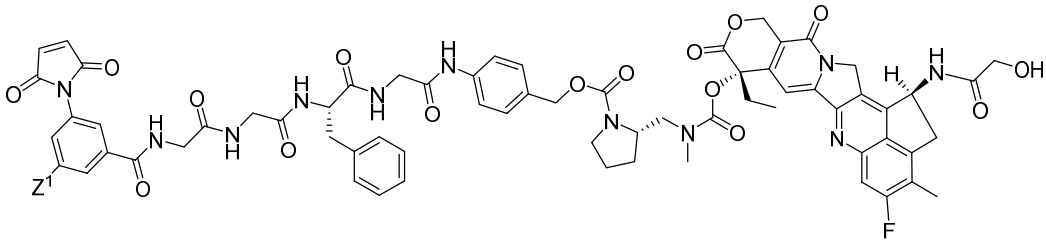
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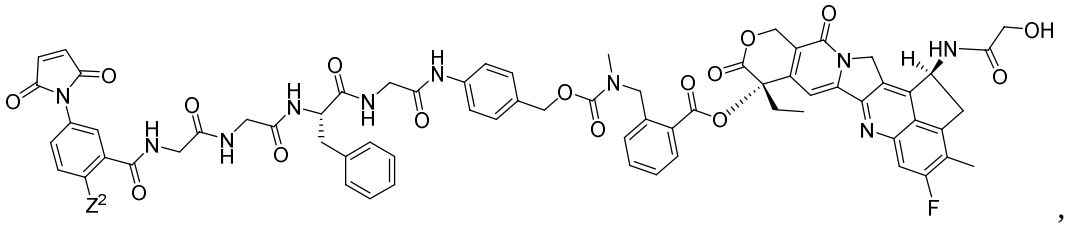
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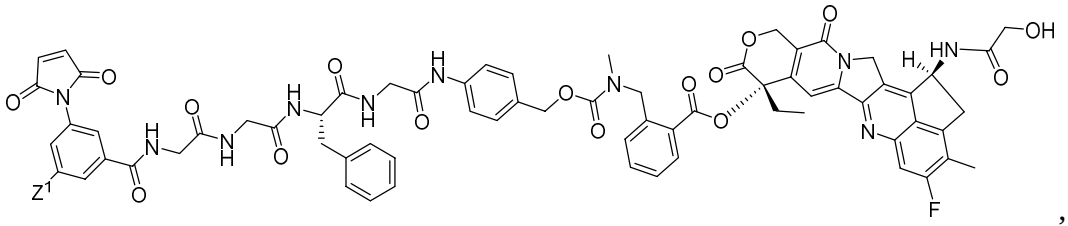
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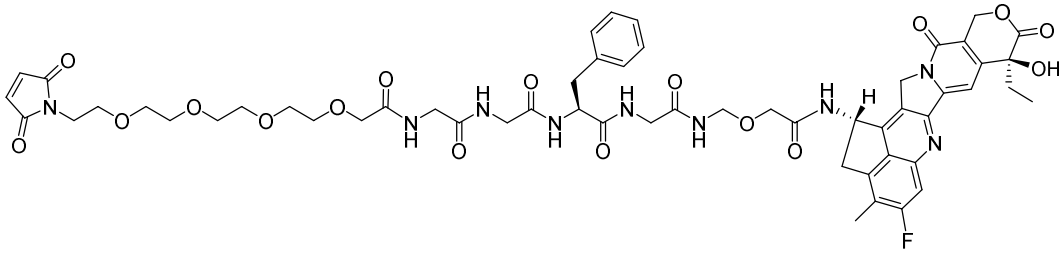
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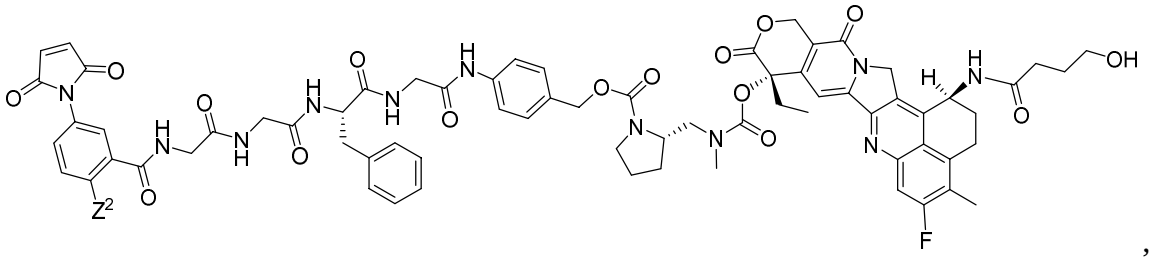
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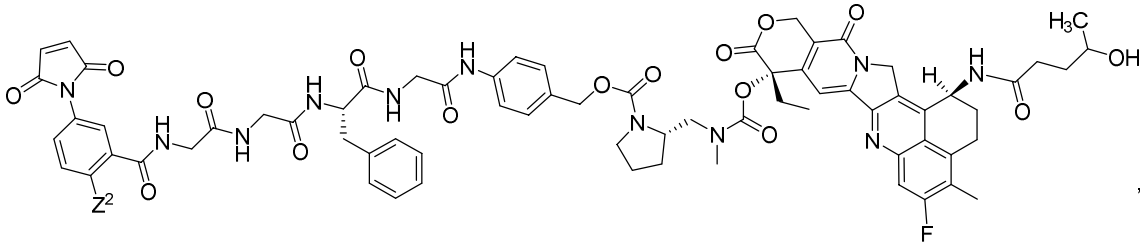
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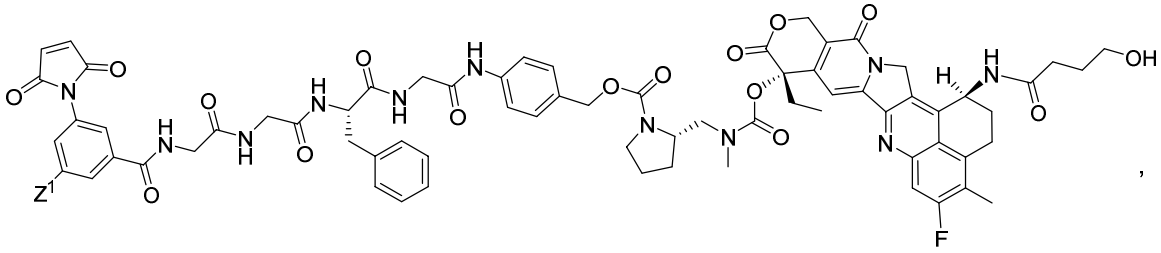
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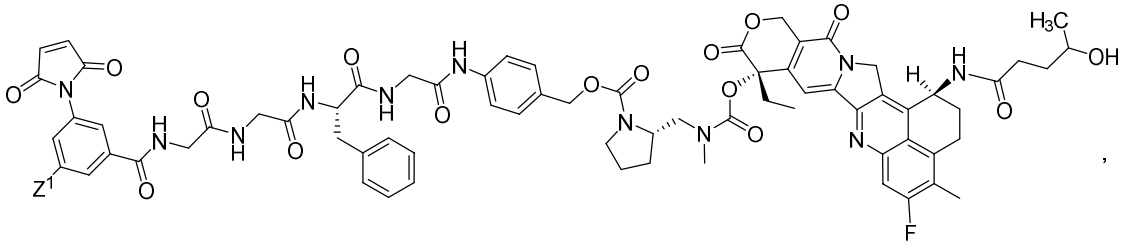

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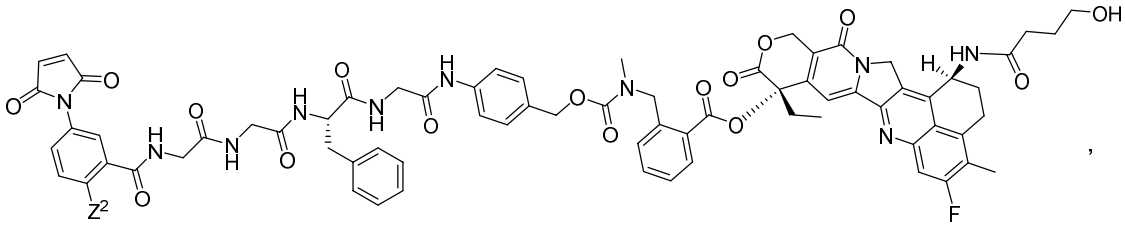

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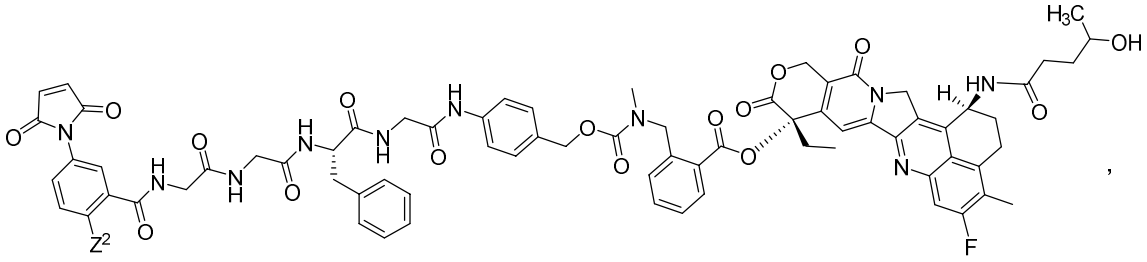

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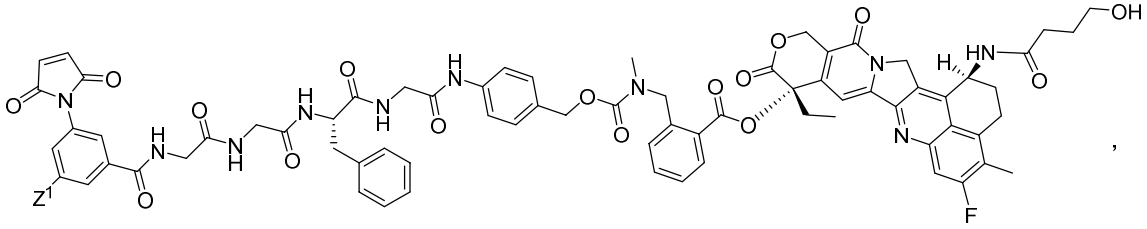

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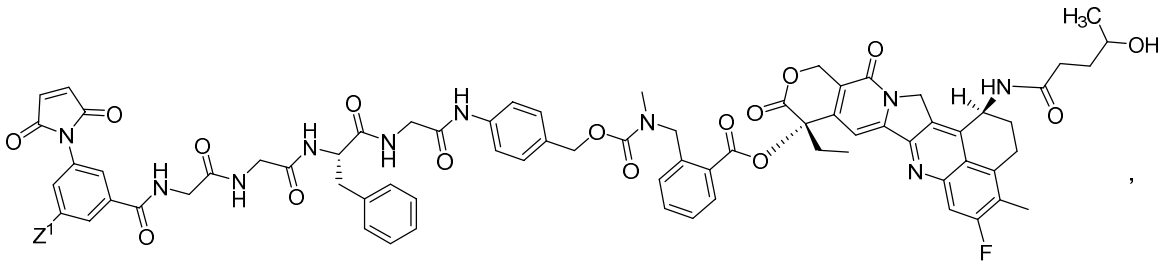

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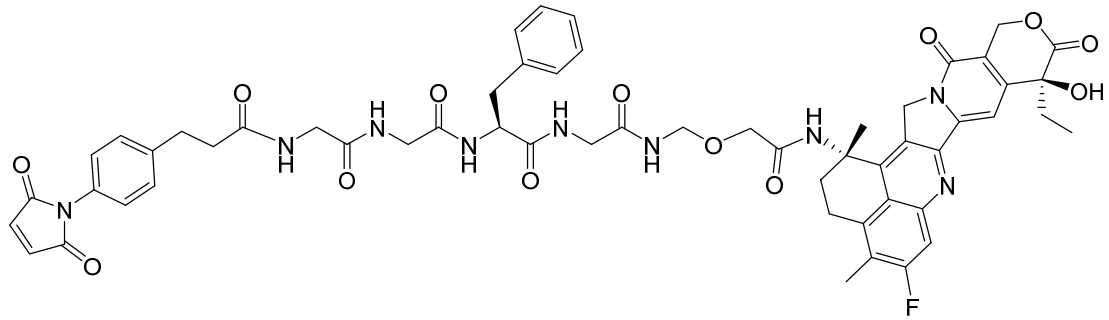

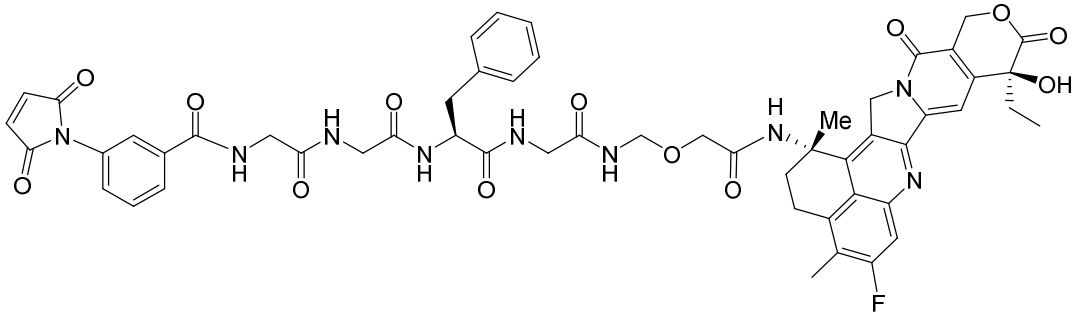

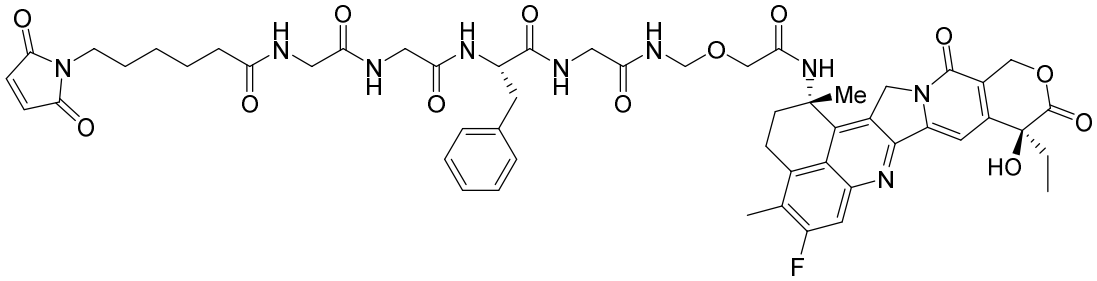

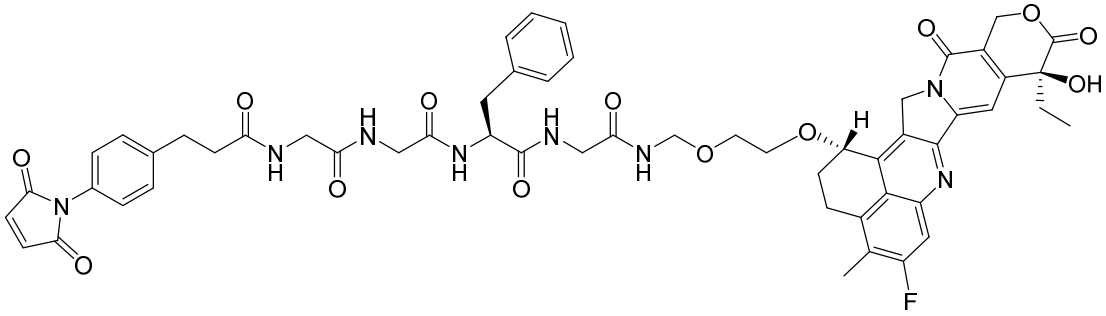

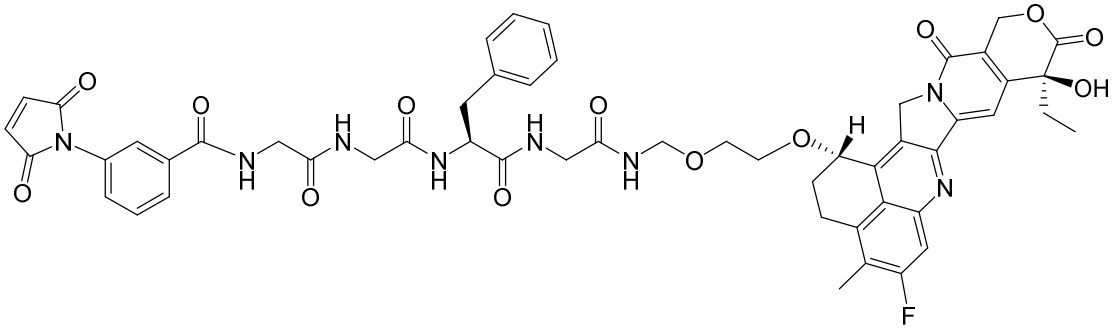
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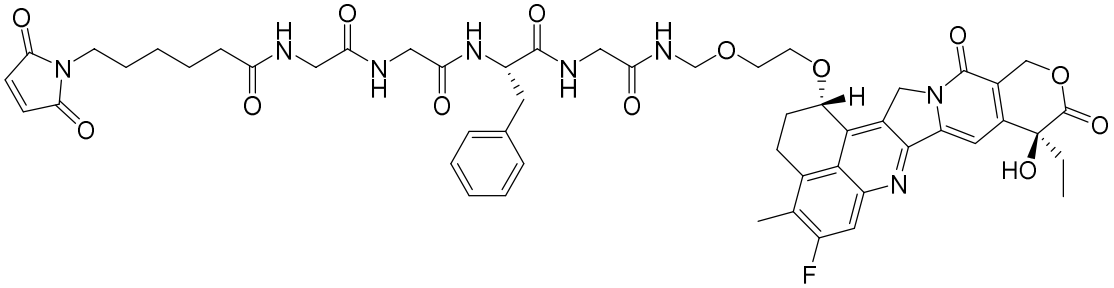
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30. Use of an immunoconjugate of any one of claims 1 to 12, a compound of any one of claims 13 to 15, or a pharmaceutically active salt thereof, or a pharmaceutical composition of claim 16, for use as a medicament.