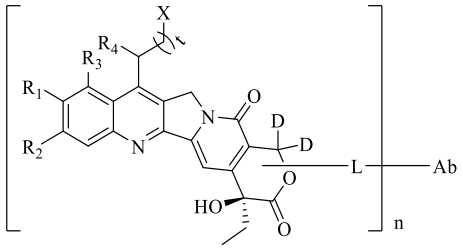
CLAIMS

1. A compound of Formula I, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof:



Formula I

wherein Ab represents an antibody or an antigen-binding fragment; L represents a linker connecting Ab and a payload drug molecule; n is selected from the group consisting of 1-12;

R_1 is H, halogen, OH, SH, NH_2, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy;

R_2 is H, halogen, C_{1-4} alkyl, or C_{1-4} alkoxy;

or R_1 and R_2 are cyclized to form -O-$(CH_2)_m$-O-, wherein m is 1, 2, or 3;

R_3 and R_4 are each independently H, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, or C_{1-4} haloalkoxy;

or R_3 and R_4 are cyclized to form -$(CH_2)_k$-, wherein k is 1, 2, 3, or 4;

X is H, OH, HO-CH(R_5)-$(CH_2)_p$-CO-NH-, or -N(R_6)(R_7), wherein p is 0, 1, or 2;

R_5 is H, C_{1-4} alkyl, C_{1-4} haloalkyl, 3- to 6-membered cycloalkyl, or 3- to 6-membered heterocycloalkyl;

R_6 is H, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_7 is H or R_8-S(O)$_2$-;

R_8 is C_{1-4} alkyl; and

t is 0, 1, 2, 3, 4, or 5.

2. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 1, wherein the compound meets one or more of the following conditions:

(1) R_1 is C_{1-4} alkyl, and R_2 is halogen; or R_1 is methyl, and R_2 is F; or R_1 is H, and R_2 is H; or R_1 and R_2 are cyclized to form -O-CH_2-O-; or R_1 is NH_2, and R_2 is H or halogen; or R_1 is NH_2, and R_2 is H or F;

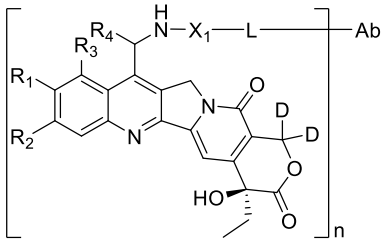
(2) R_3 is H, and R_4 is H; or R_3 is H, and R_4 is C_{1-4} alkyl; or R_3 is H, and R_4 is methyl; or R_3 and R_4 are cyclized to form -CH_2-CH_2-;

(3) X is HO-CH(R_5)-(CH_2)$_p$-CO-NH-, wherein p is 0, 1, or 2; or X is OH or NH_2; or X is H, and t is 0; or X is -N(R_6)(R_7);

(4) n is 4-9; or n is 6-8, 7-8, 7.4-8.0, or 7.5-8.5; or n is 6, 7, or 8; or n is 7-8, 7.3-7.9, 7.4-7.8, 7.5-7.7, 7.5-7.6, 7.5-7.8, or 7.4-7.7; and

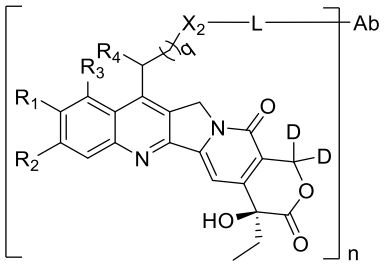
(5) the Ab is an anti-Her2 antibody, an anti-Trop2 antibody, or an anti-Claudin18.2 antibody.

3. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 1 or 2, wherein the compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof is a compound of Formula Ia, Formula Ib, Formula Ic or Formula Id, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof:



Formula Ia

wherein in the compound of Formula Ia, R_1, R_2, R_3, and R_4 are as defined in claim 1 or 2; X_1 is a chemical bond or -O-CH(R_5)-(CH_2)$_p$-CO-, wherein the -CO- end is connected to -NH-; p is 0, 1, or 2; R_5 is H, C_{1-4} alkyl, 3- to 6-membered cycloalkyl, or 3- to 6-membered heterocycloalkyl;



Formula Ib

wherein in the compound of Formula Ib, Ab, L, and n are as defined in claim 1;

R_1 is H, OH, halogen, NH_2, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy;

R_2 is H, halogen, C_{1-4} alkyl, or C_{1-4} alkoxy;

or R_1 and R_2 are cyclized to form -O-(CH_2)$_m$-O-, wherein m is 1, 2, or 3;

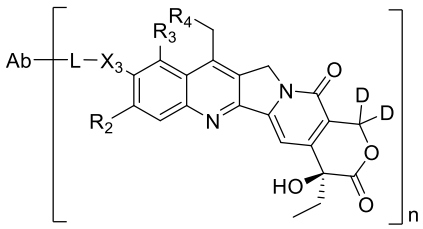
R_3 and R_4 are each independently H, C_{1-4} alkyl, or C_{1-4} alkoxy;

or R_3 and R_4 are cyclized to form -(CH_2)$_k$-, wherein k is 1, 2, or 3;

X_2 is O or -N(R_6)-;

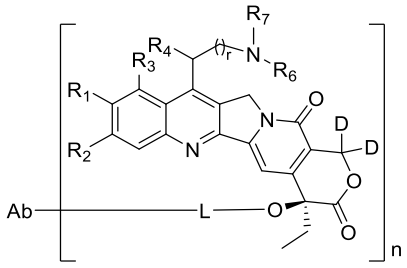
R_6 is H or C_{1-4} alkyl;

q is 0, 1, 2, 3, or 4;



Formula Ic

wherein in the compound of Formula Ic, X_3 is NH, O, or S, or X_3 is NH or O; R_2, R_3, and R_4 are as defined in claim 1 or 2; and Ab, L, and n are as defined in claim 1;

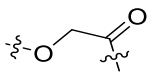
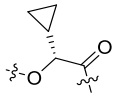
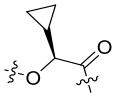
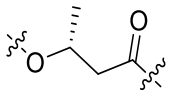
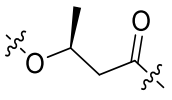


Formula Id

wherein in the compound of Formula Id, L, n, R_6, and R_7 are as defined in claim 1; R_1, R_2, R_3, and R_4 are as defined in claim 1 or 2, and r is 0, 1, 2, or 3.

4. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 3, wherein the compound of Formula Ia meets one or more of the following conditions:

(1) R_1 is methyl or methoxy; or R_2 is F or Cl; or R_1 is methyl, and R_2 is F; or R_3 and R_4 are cyclized to form -$(CH_2)_k$-, wherein k is 2; or R_3 is H; and R_4 is H; and

(2) X_1 is -O-CH(R_5)-$(CH_2)_p$-CO-, p is 0 or 1, R_5 is H, C_{1-4} alkyl, or 3- to 6-membered cycloalkyl; or X_1 is -O-CH(R_5)-CO-, R_5 is H or 3- to 6-membered cycloalkyl; or X_1 is -O-CH(R_5)-CO-, and R_5 is H or cyclopropyl; or X_1 is -O-CH(R_5)-CH_2-CO-; R_5 is C_{1-4} alkyl; or X_1 is -O-CH(R_5)-CH_2-CO-, R_5 is methyl; or X_1 is the following group: , , , , or ; wherein the -CO- end of X_1 is connected to NH;

the compound of Formula Ib meets one or more of the following conditions:

(1) R_1 is methyl, and R_2 is H, Cl, or F; or R_1 and R_2 are cyclized to form -O-$(CH_2)_m$-O-, wherein m is 1 or 2;

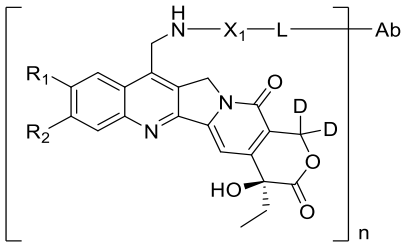
(2) R_3 and R_4 are both H; or R_3 is H, and R_4 is methyl; and

(3) X_2 is -O- or -NH-; or X_2 is -O- or -NH-, and q is 0, 1, 2, 3, or 4; or X_2 is -O- or -NH-, and q is 1, 2, 3, or 4;

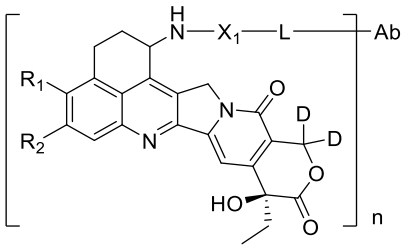
in the compound of Formula Ic, R_2 is H or F; or R_3 is H, and R_4 is methyl; or R_3 and R_4 are cyclized to form -$(CH_2)_k$-, wherein k is 1, 2, or 3; or R_3 and R_4 are cyclized to form -$(CH_2)_2$-; or X_3 is NH; or X_3 is O;

in the compound of Formula Id, R_1 and R_2 are both H; or R_3 and R_4 are both H; or r is 1; or R_6 is methyl, ethyl, or isopropyl; or R_6 is isopropyl; or R_7 is H; or R_7 is R_8-$S(O)_2$-, R_8 is methyl or ethyl, or R_8 is methyl.

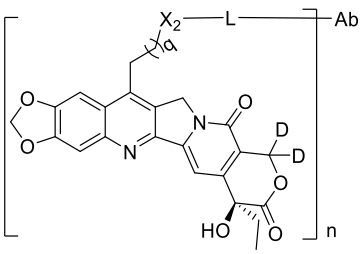
5. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 3 or 4, wherein the compound of Formula Ia is a compound of Formula Ia-1 or Formula Ia-2, or the compound of Formula Ib is a compound of Formula Ib-1;



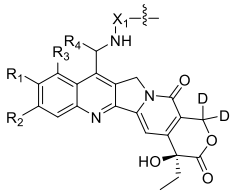
Formula Ia-1

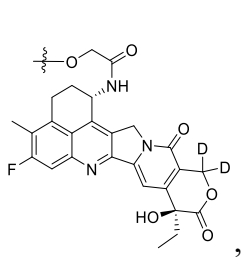
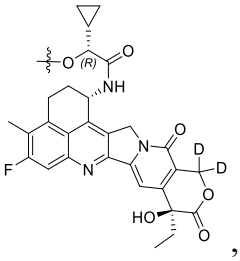
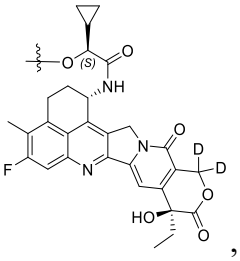
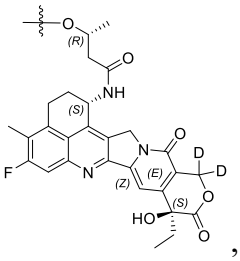


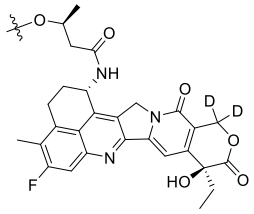
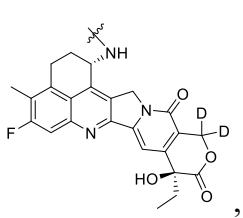
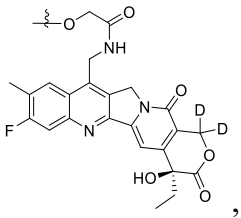
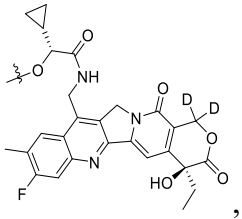
Formula Ia-2

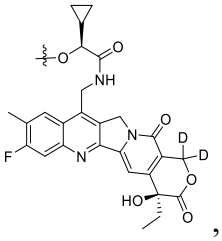
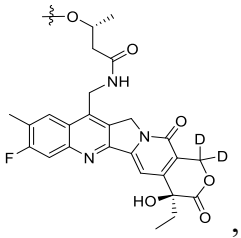
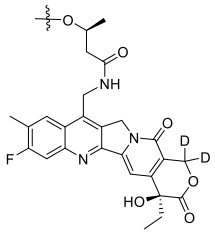


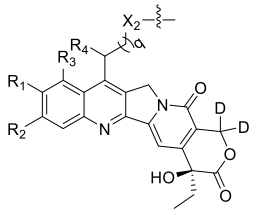
Formula Ib-1wherein Ab, L, R_1, R_2, X_1, X_2, q and n are as defined in claim 3 or 4.

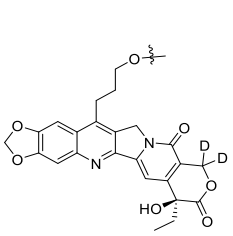
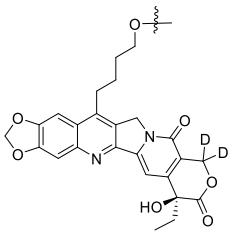
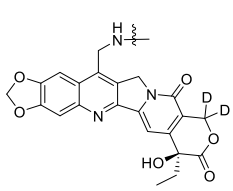
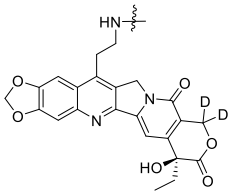
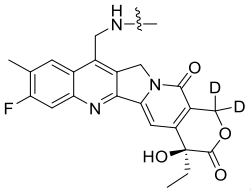
6. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 3 or 4, wherein in the compound of Formula Ia,  is the following compound moiety:

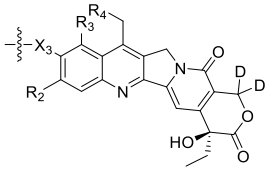
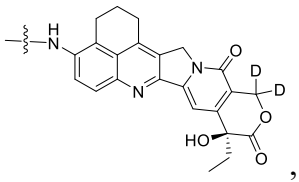
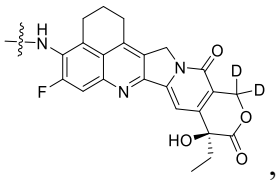
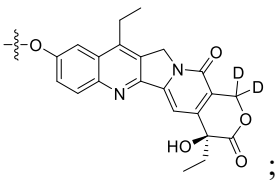
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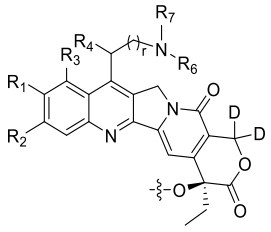
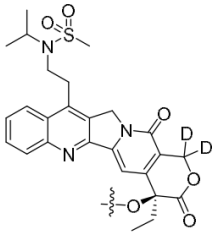
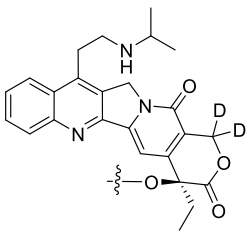
5 , , , ,

, , or , wherein " ∿∿ " indicates that this position is connected to the linker L via a chemical bond;

in the compound of Formula Ib,  is the following compound moiety:

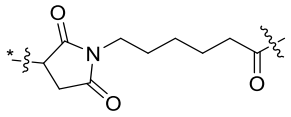
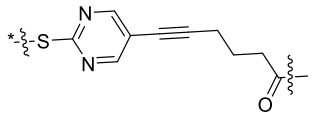
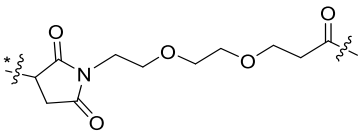
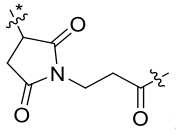
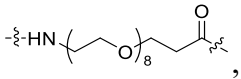
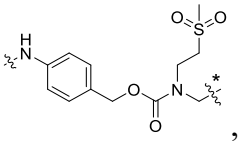
, , , , or , wherein " ∿∿ " indicates that this position is connected to the linker L via a chemical bond;

in the compound of Formula Ic,  is the following compound moiety: , , or ;

in the compound of Formula Id,  is the following compound moiety:  or .

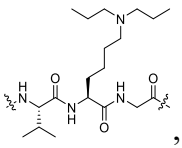
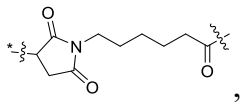
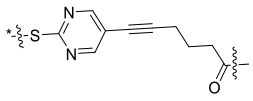
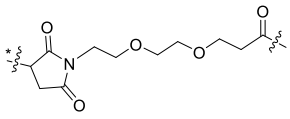
7. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to any one of claims 1-6, wherein the compound meets one or more of the following conditions:

(1) the Ab is an anti-Her2 antibody, having HCDR1, HCDR2, and HCDR3 as set forth in SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, respectively, and LCDR1, LCDR2, and LCDR3 as set forth in SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, respectively; and

(2) the L is -L_1-L_2-L_3-L_4-, wherein L_1 is connected to the Ab at one end, and L_4 is connected to the payload drug molecule at the other end; L_1 is the following group, and the end of L_1 marked with an asterisk * is connected to the Ab: , , , or ; L_2 is a chemical bond, -N(R_{10})-CH_2-CO-, or , and the CO end of L_2 is connected to L_3, while the other end is connected to L_1; R_{10} is C_{1-4} alkyl or C_{1-4} haloalkyl; L_3 is a polypeptide residue composed of 2-6 amino acids, and the C-terminus of the polypeptide residue is connected to L_4; and L_4 is a chemical bond, -NH-CH-, or , wherein the CH end is connected to the payload drug molecule, and the -NH- end is connected to L_3.

8. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to any one of claims 1-7, wherein the compound meets one or more of the following conditions:

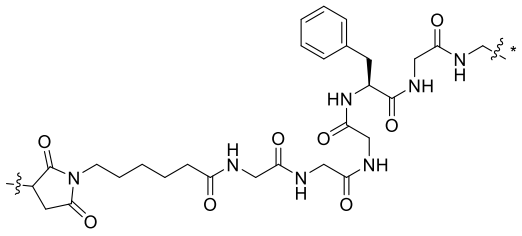
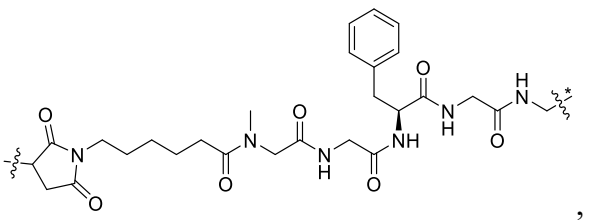
(1) the Ab is an anti-Her2 antibody, having a heavy chain variable region as set forth in SEQ ID NO: 4 and a light chain variable region as set forth in SEQ ID NO: 9; and

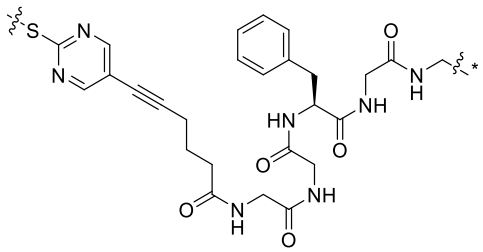
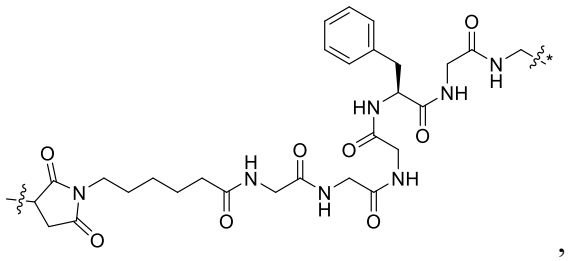
(2) L_2 is a chemical bond; or L_2 is -N(CH_3)-CH_2-CO-; or/and L_3 is the following polypeptide residue: GFG, GGFG, GGGFG, GGVA, V-Cit, , or VA; or L_1 is , , or , L_2 is a chemical bond or -N(CH_3)-CH_2-CO-, L_3 is GFG, GGFG, or GGGFG, and L_4 is -NH-CH-.

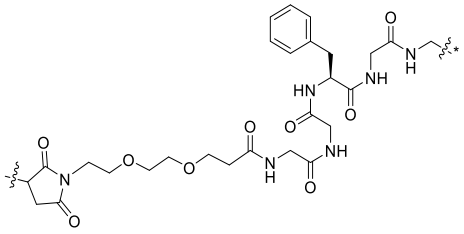
9. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to any one of claims 1-8, wherein the compound meets one or more of the following conditions:

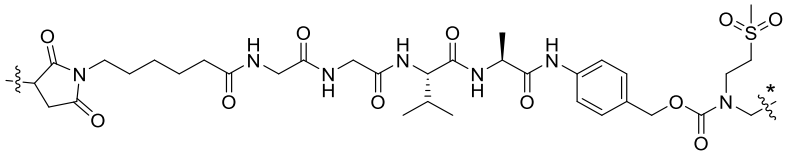
(1) the Ab is an anti-Her2 antibody, having a heavy chain as set forth in SEQ ID NO: 5 and a light chain as set forth in SEQ ID NO: 10; and

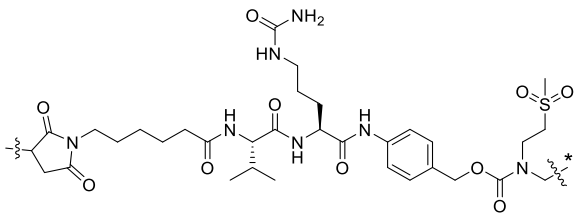
(2) wherein L is the following moiety:

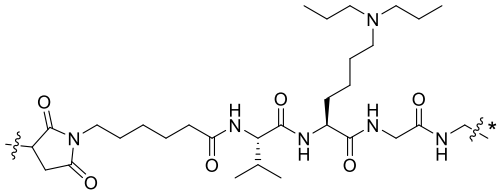
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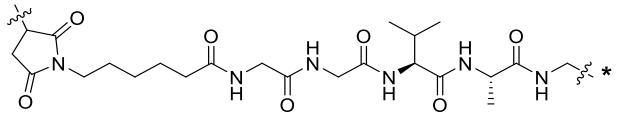
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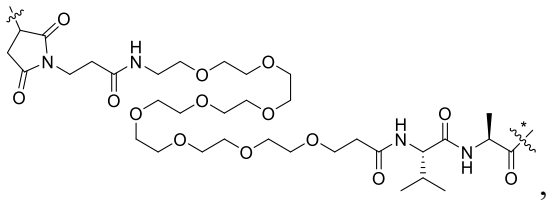

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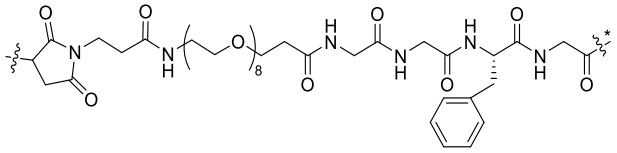

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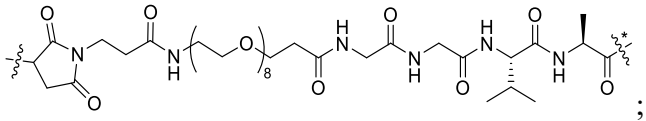

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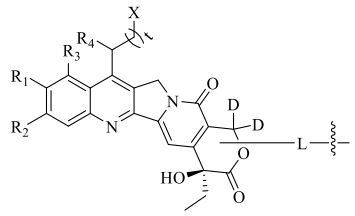

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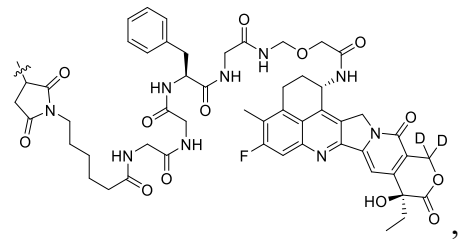

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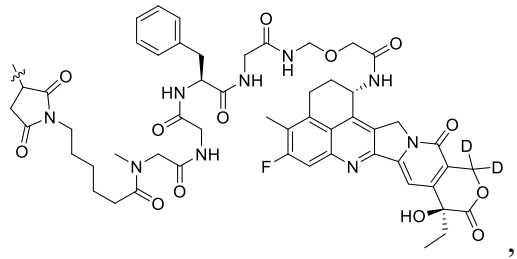
wherein "*" indicates the position where the linker connects to the payload drug molecule, and the other end indicates the position where the linker connects to the Ab.

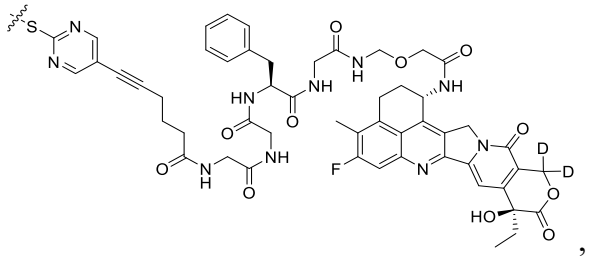
10. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to claim 1 or 2, wherein the compound meets one or more of the following conditions:

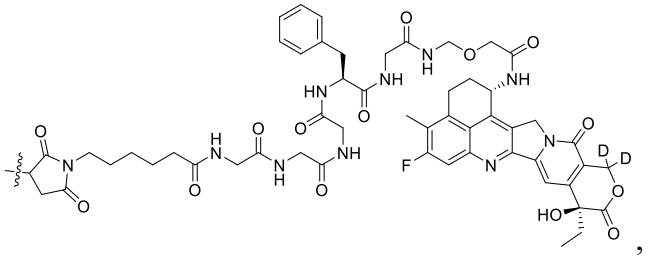
(1) the Ab is Trastuzumab, Pertuzumab, Sacituzumab, or zolbetuximab; and

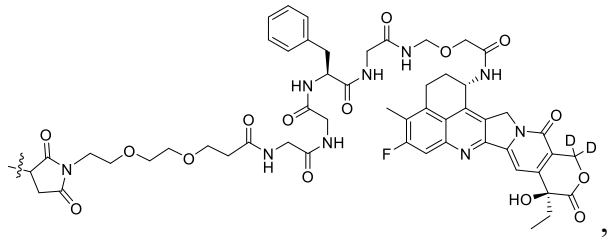
(2)  is the following structural moiety:

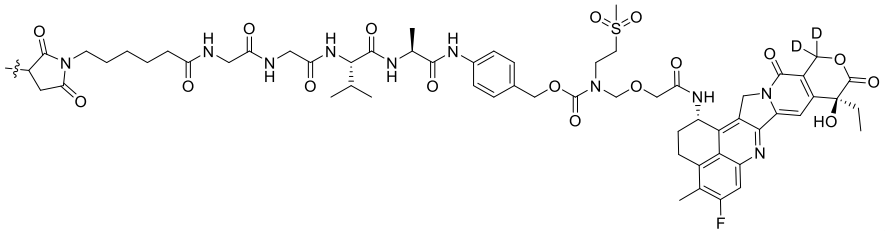
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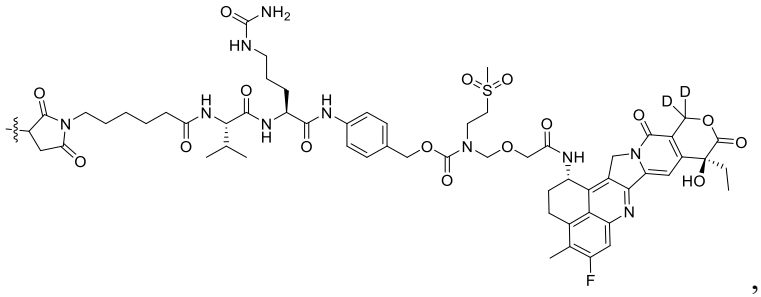
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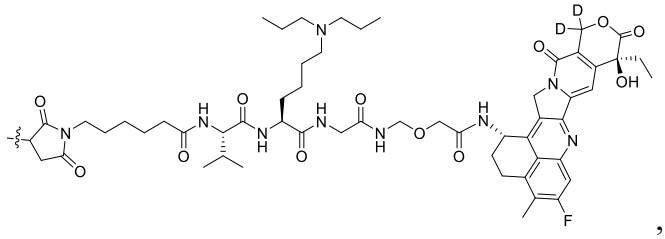
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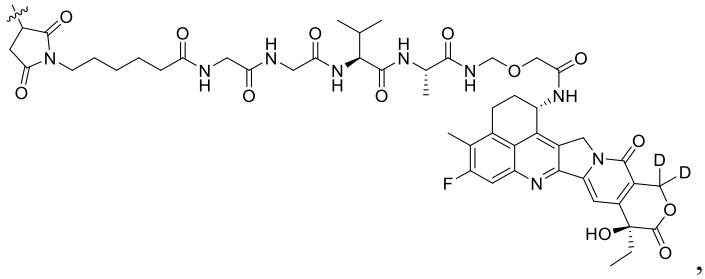
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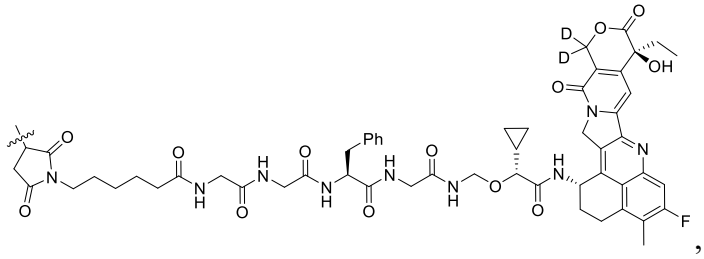
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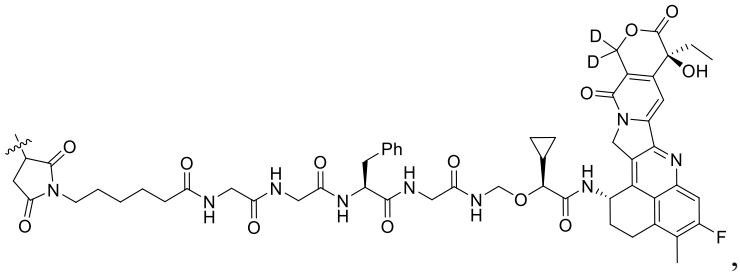

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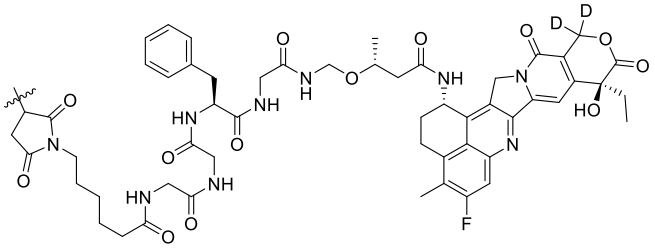

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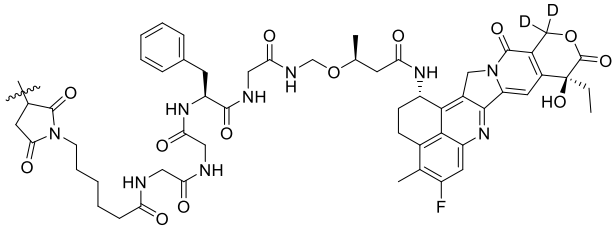

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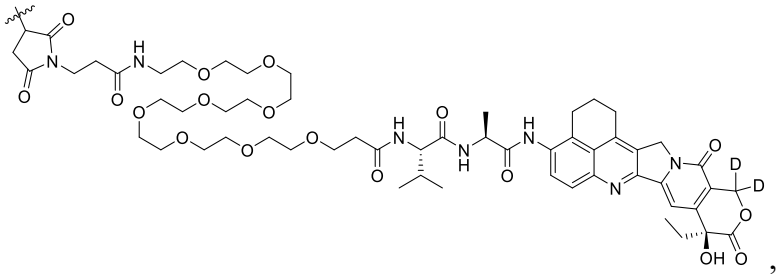

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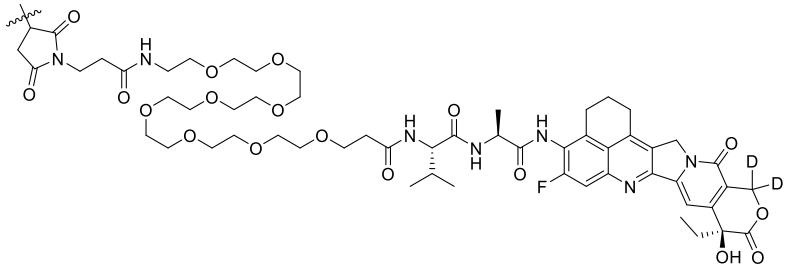

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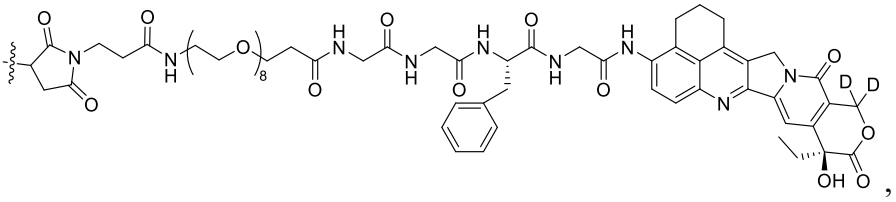

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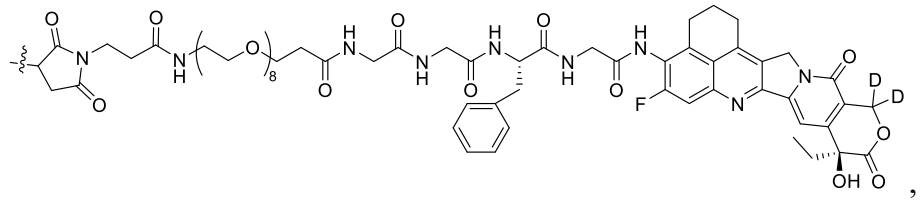

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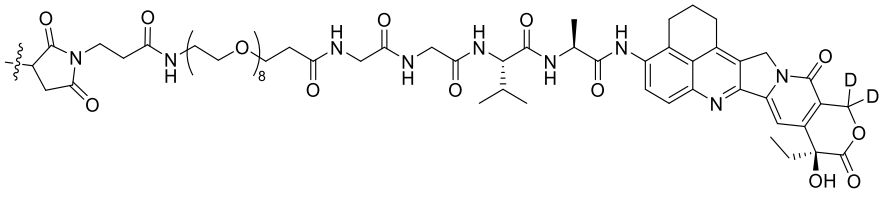

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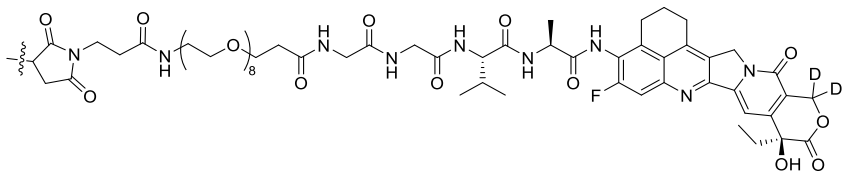

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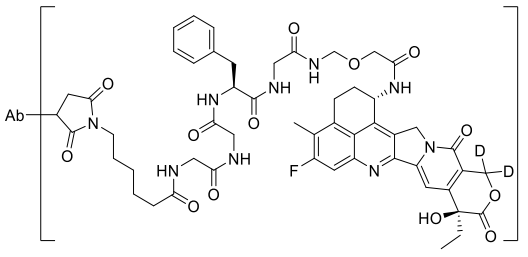

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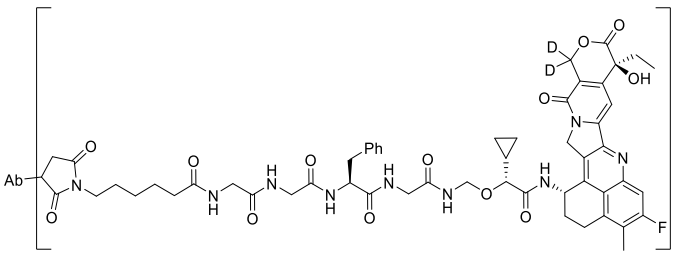

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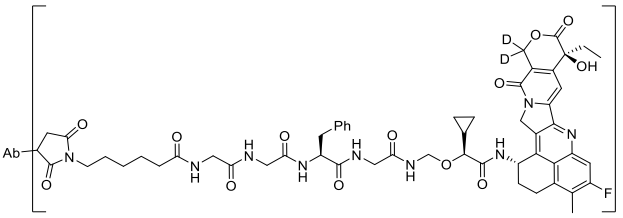

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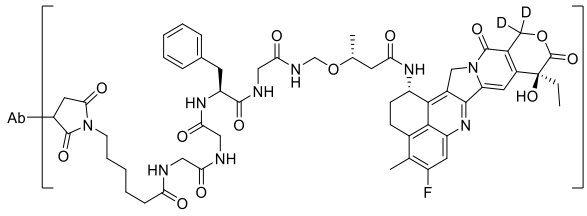
11. The compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof according to any one of claims 1, 2 and 7-10, wherein the compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof is the following compound, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof:


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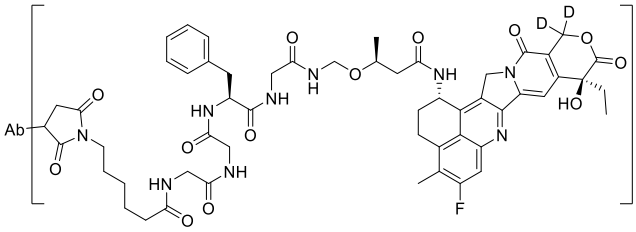

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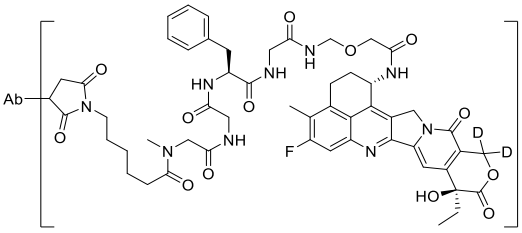
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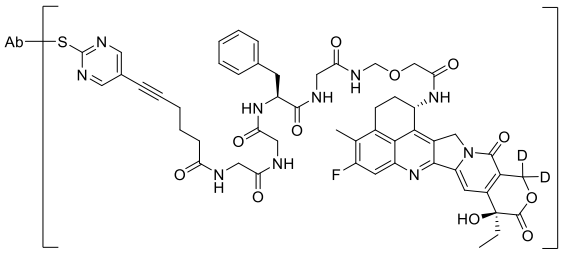
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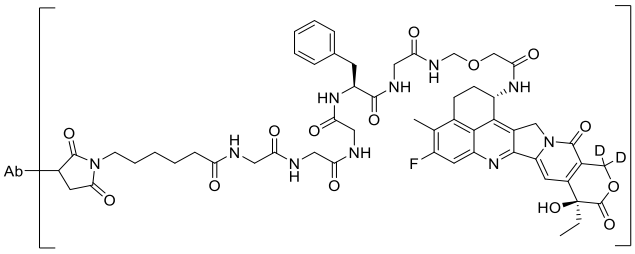
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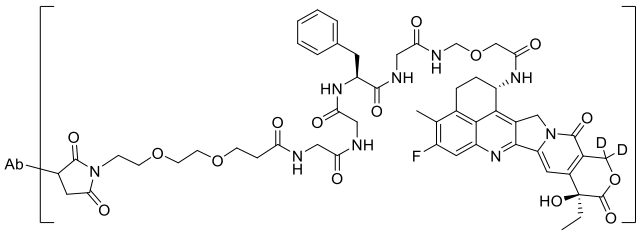
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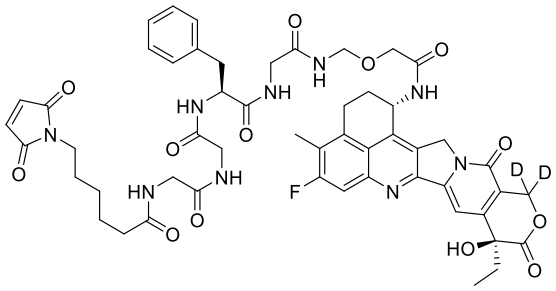
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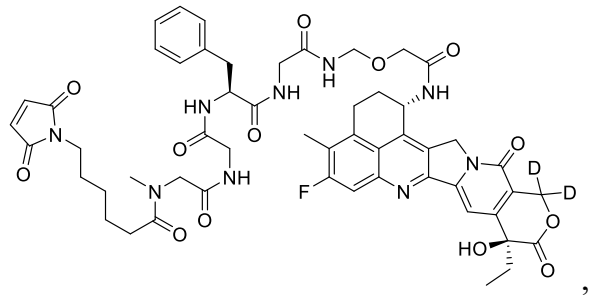


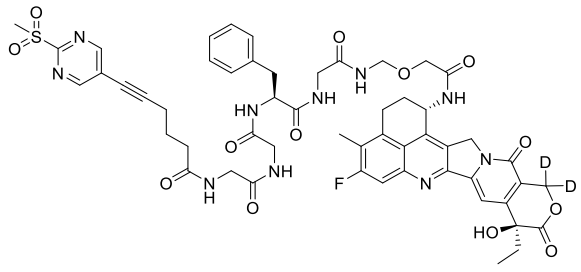
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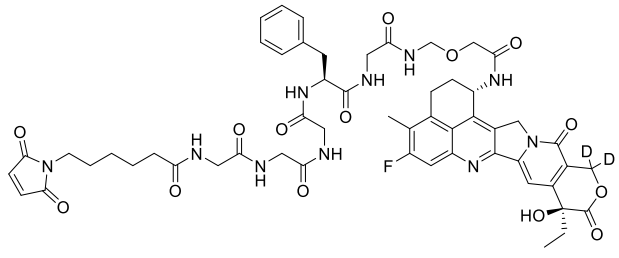

, wherein n is 7.0-8.0, or n is 7.4-7.8, or n is 7.4-8.0, or n is 7.5-8.5.

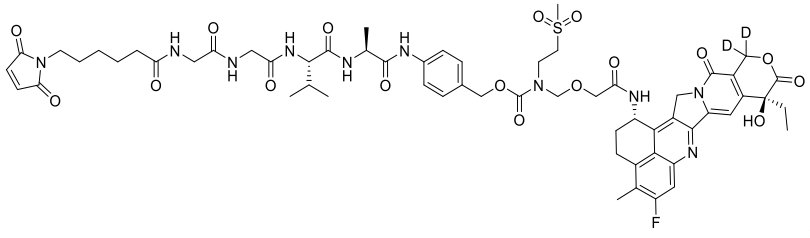
12. A compound, wherein the compound is one of the following compounds, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof:

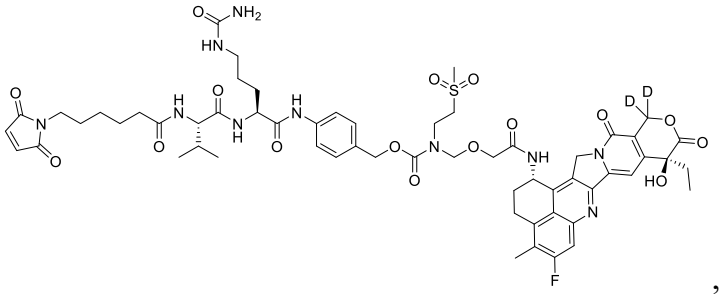

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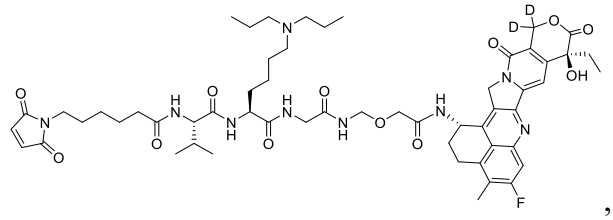

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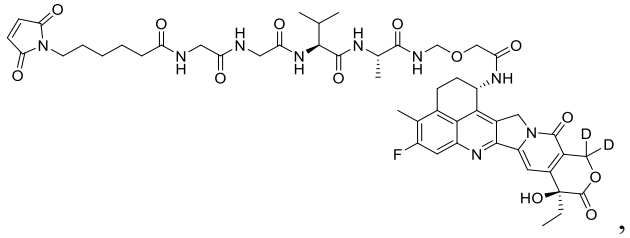

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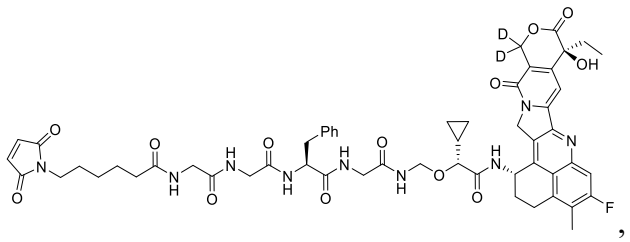

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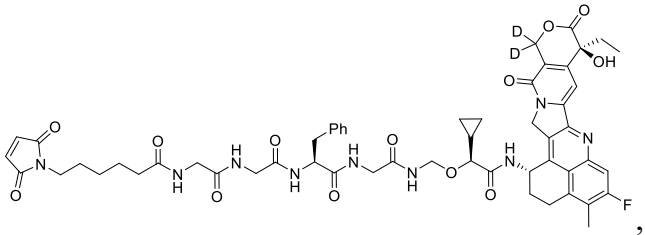

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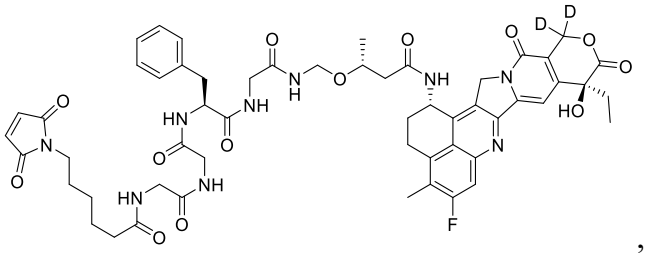

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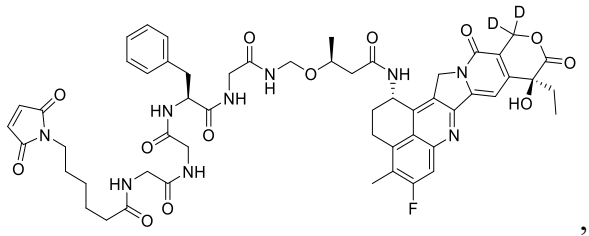

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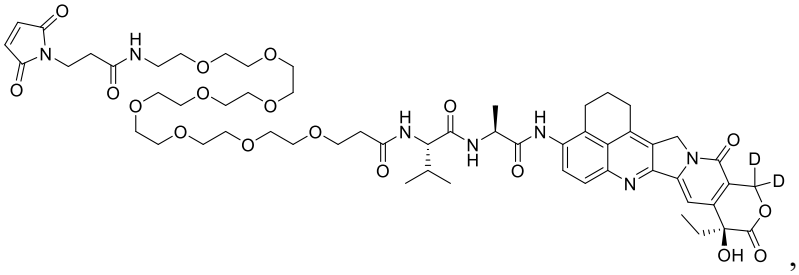

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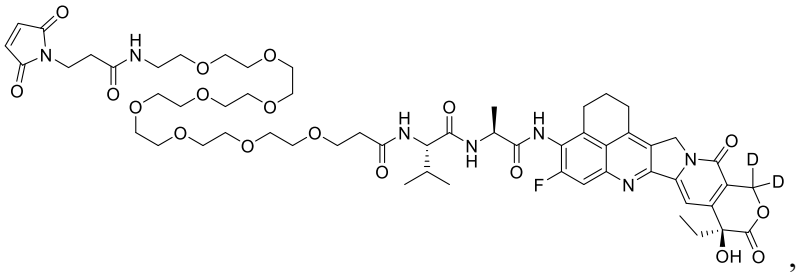

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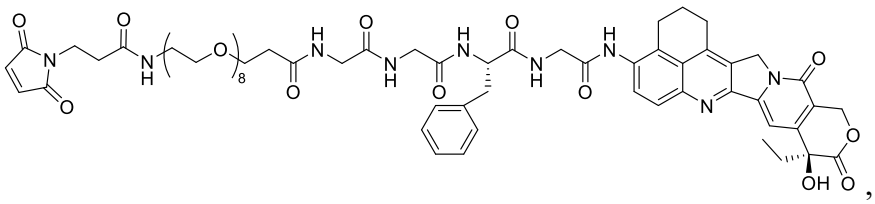

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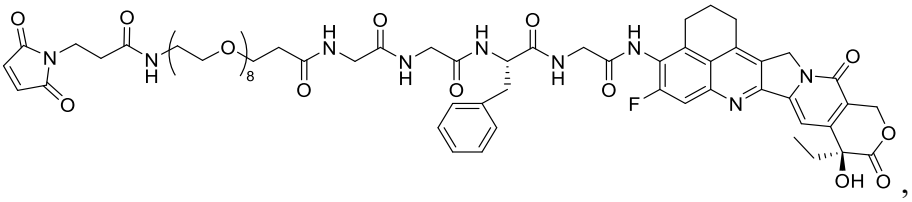

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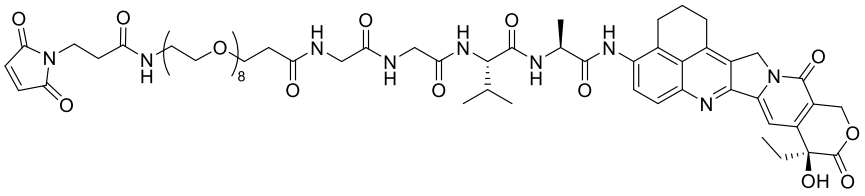

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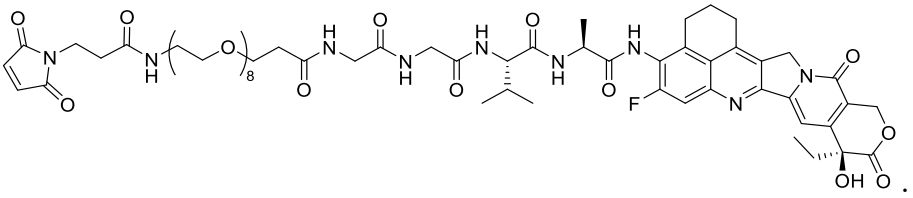

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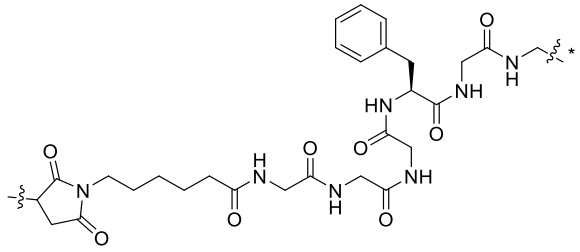

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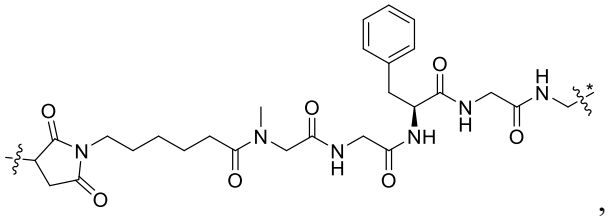

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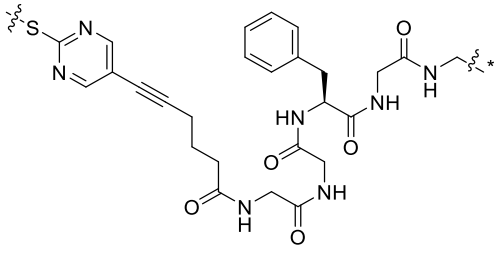

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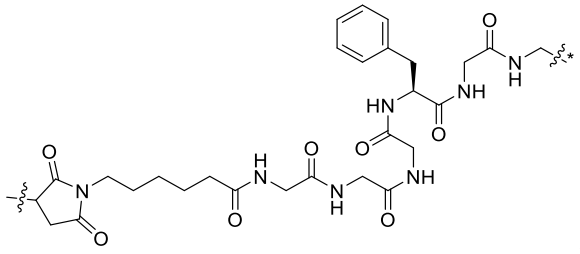
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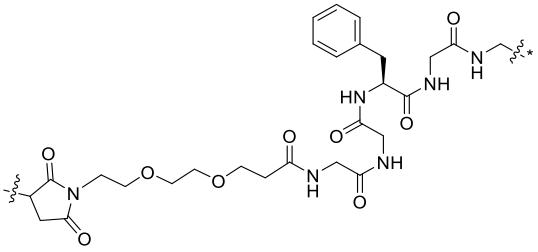

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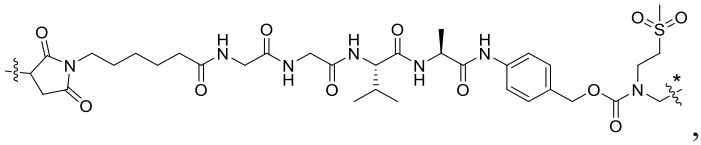

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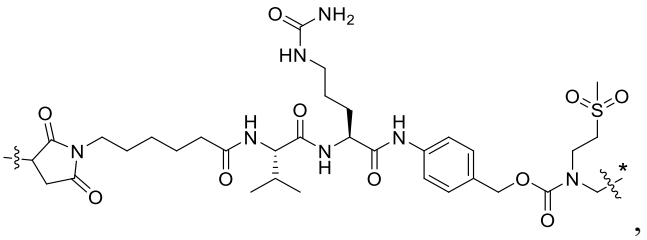
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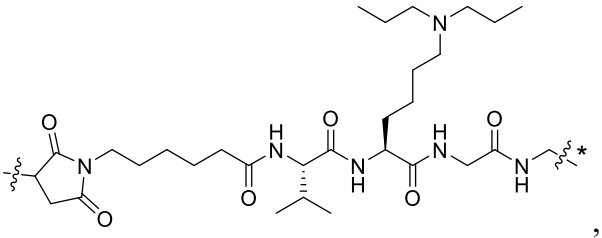

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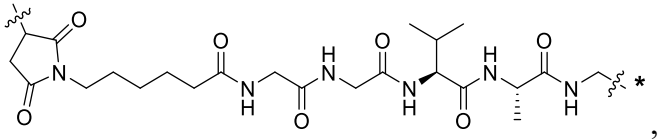

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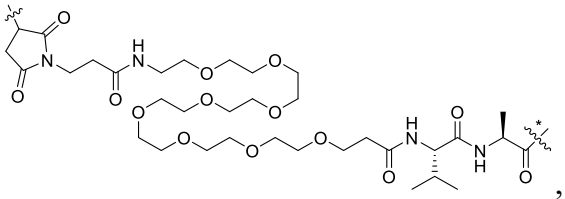
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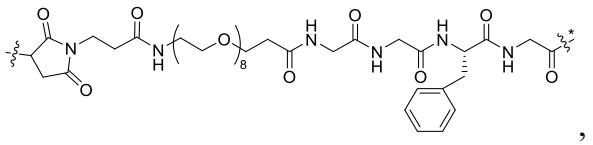
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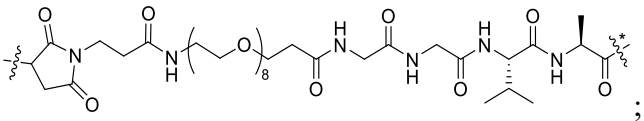


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or



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wherein the asterisk * end is connected to the payload drug molecule.

14. A pharmaceutical composition comprising the compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof as defined in any one of claims 1-11, and a pharmaceutically acceptable excipient.

15. Use of the compound, the pharmaceutically acceptable salt thereof, or the stereoisomer thereof as defined in any one of claims 1-11, or the pharmaceutical composition as defined in claim 14, in the manufacture of a medicament for treating tumors.