CLAIMS

1. A conjugate compound or a pharmaceutically acceptable salt thereof, comprising: a targeted molecule comprising at least two ligands specifically binding to a cell surface protein and a payload linked to the targeted molecule, wherein the payload is a proteolysis targeting chimera.

2. The conjugate compound or the pharmaceutically acceptable salt thereof according to claim 1, wherein the conjugate compound has one or more of the following definitions:

i) wherein the targeted molecule binds to the following cell surface proteins: FOLR1, TRPV6, PSMA, LHRH, EGFR, Her2, Trop2, Her3, Claudin18.2, c-Met, or any combination thereof;

ii) wherein the targeted molecule binds to the following cell surface proteins: FOLR1, TRPV6, PSMA, c-Met, or any combination thereof;

iii) wherein the targeted molecule binds to the following cell surface protein combinations: FOLR1 and TRPV6; FOLR1 and PSMA; TRPV6 and PSMA; TRPV6 and c-Met; FOLR1 and c-Met; PSMA and c-Met; FOLR1, TRPV6, and PSMA; FOLR1, TRPV6, and c-Met; FOLR1, PSMA, and c-Met; TRPV6, PSMA, and c-Met; or FOLR1, PSMA, TRPV6, and c-Met; and

iv) wherein the targeted molecule comprises two ligands respectively binding to FOLR1 and TRPV6, FOLR1 and PSMA, TRPV6 and PSMA, FOLR1 and c-Met, PSMA and c-Met, or TRPV6 and c-Met.

3. The conjugate compound or the pharmaceutically acceptable salt thereof according to claim 2, wherein the conjugate compound has one or more of the following definitions:

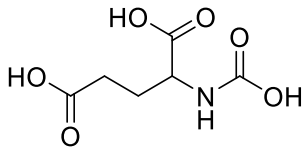
i) wherein the ligand binding to FOLR1 comprises folic acid or an analog thereof and pteroic acid; preferably the folic acid analog is selected from: 5-methyltetrahydrofolic acid, 5-formyltetrahydrofolic acid, 10-formyltetrahydrofolic acid, methotrexate, 5,10-

formyltetrahydrofolic acid, 5,10-methenyltetrahydrofolic acid, aminopterin, and raltitrexed;

ii) wherein the ligand binding to TRPV6 comprises the amino acid sequence set forth in SEQ ID NO: 1, the amino acid sequence set forth in SEQ ID NO: 2, or an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2;

iii) wherein the ligand binding to PSMA comprises a peptide, an antibody, or a small molecule;

iv) wherein the ligand binding to PSMA is selected from the following structures: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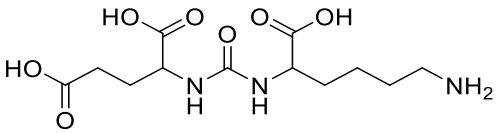
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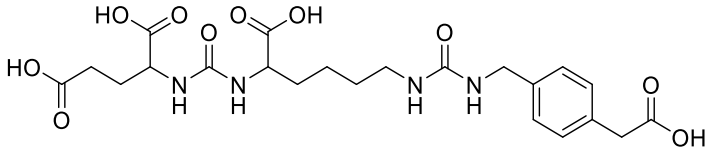
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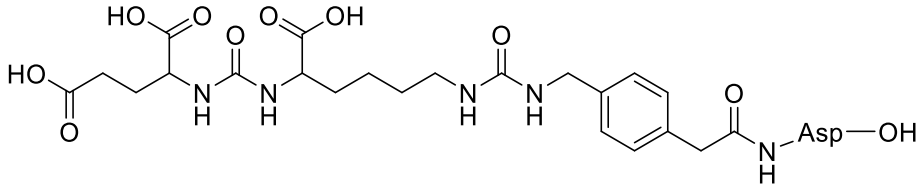
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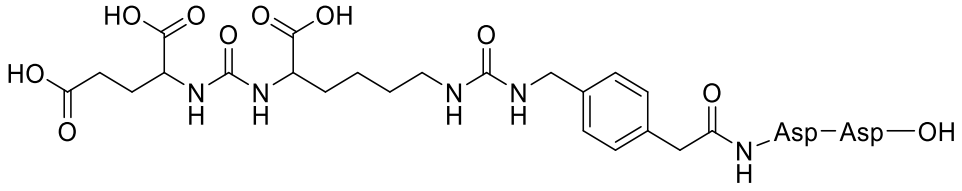
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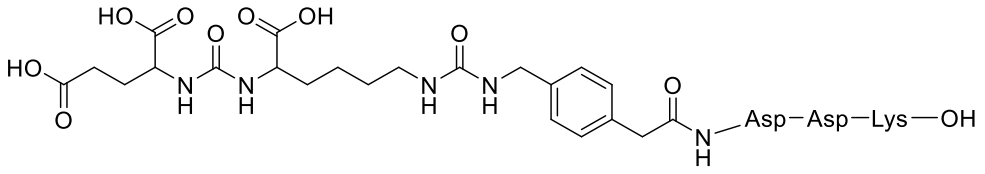
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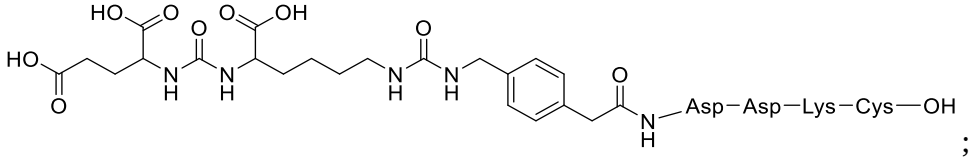
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v) wherein the ligand binding to c-MET comprises the amino acid sequence set forth in

SEQ ID NO: 3: Cys^a-X1-Cys^c-X2-Gly-Pro-Pro-X3-Phe-Glu-Cys^d-Trp-Cys^b-Tyr-X4-X5-X6; X1 is Asn, His, or Tyr; X2 is Gly, Ser, Thr, or Asn; X3 is Thr or Arg; X4 is Ala, Asp, Glu, Gly, or Ser; X5 is Ser or Thr; X6 is Asp or Glu; Cys^{a-d} are cysteine residues; preferably, residues Cys^a and Cys^b, as well as residues Cys^c and Cys^d, are separately cyclized to form two independent disulfide bonds;

vi) wherein the ligand binding to c-MET comprises the amino acid sequence set forth in SEQ ID NO: 4: Ala-Gly-Ser-Cys^a-Tyr-Cys^c-Ser-Gly-Pro-Pro-Arg-Phe-Glu-Cys^d-Trp-Cys^b-Tyr-Glu-Thr-Glu-Gly-Thr-Gly-Gly-Gly-Lys; Cys^{a-d} are cysteine residues; preferably, residues Cys^a and Cys^b, as well as residues Cys^c and Cys^d, are separately cyclized to form two independent disulfide bonds; optionally, the carboxyl of the terminal lysine may be amidated; optionally, the alanine at the N-terminus may be acetylated; and

vii) wherein the ligand binding to c-MET comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 4; Cys^{a-d} are cysteine residues; preferably, residues Cys^a and Cys^b and residues Cys^c and Cys^d are separately cyclized to form two independent disulfide bonds.

4. The conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-3, wherein the ligands are linked to each other directly or via a spacer region; preferably the linkage is by means of a dehydration reaction;

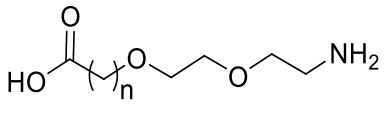
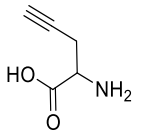
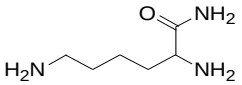
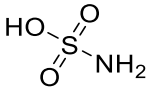
optionally, wherein the conjugate compound further has any one of the following definitions:

i) wherein the spacer region comprises an amino acid or an amino acid combination selected from the following group: Lys, Cys, Lys-Cys, Cys-Cys, Lys-Cys-Lys, Arg-Arg, Ala-Ser-Asn, Ala-Ala-Ala, Ser-Ser-Arg, Pro-Arg, Asp-Asp-Lys-Cys, and Pro-Leu-Gly; optionally, the amino acid may be amidated;

ii) wherein the spacer region comprises an amino acid or an amino acid combination selected from the following group: Lys, Cys, Lys-Cys, Cys-Cys, Lys-Cys-Lys, Arg-Arg, Ala-Ser-Asn, Ala-Ala-Ala, Ser-Ser-Arg, Pro-Arg, Asp-Asp-Lys-Cys, and Pro-Leu-Gly; optionally, the amino acid may be amidated;

wherein Lys is amidated, e.g., to 2,6-diaminohexanamide; and

iii) wherein the spacer region is formed by one or more identical or different compounds selected from the following group by means of a dehydration reaction:


, 
, 
, and 
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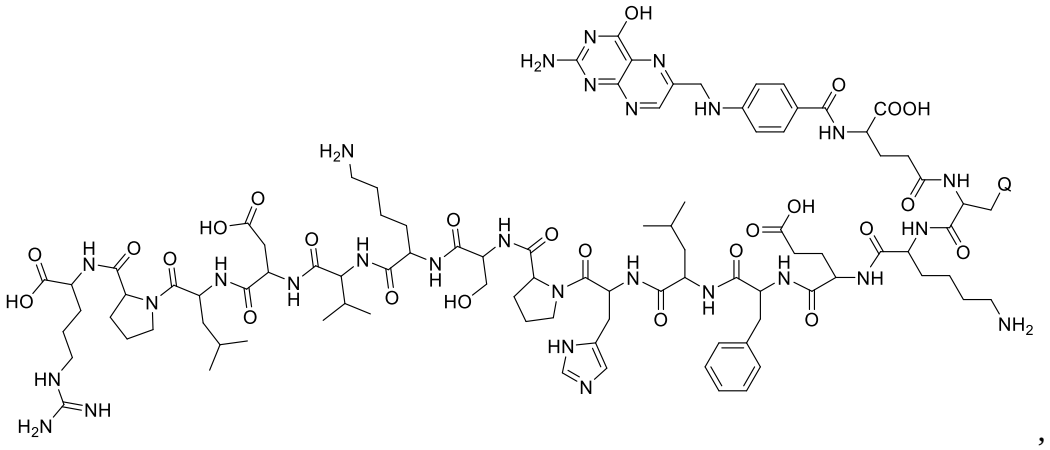
wherein n is 0 or 1.

5. The conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-4, wherein the targeted molecule having the following structures is linked to the payload to form the conjugate compound: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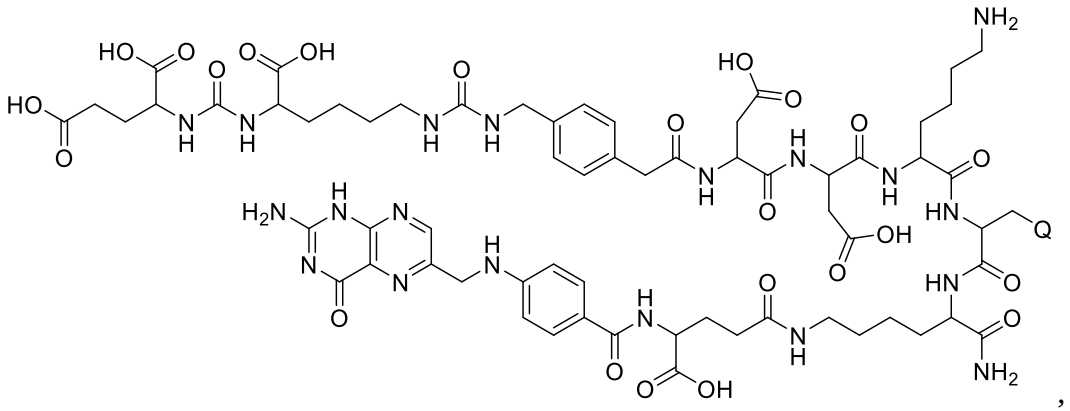
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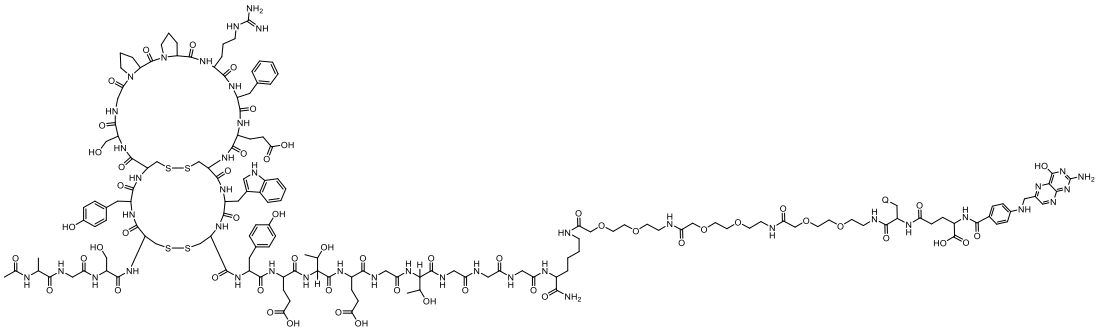

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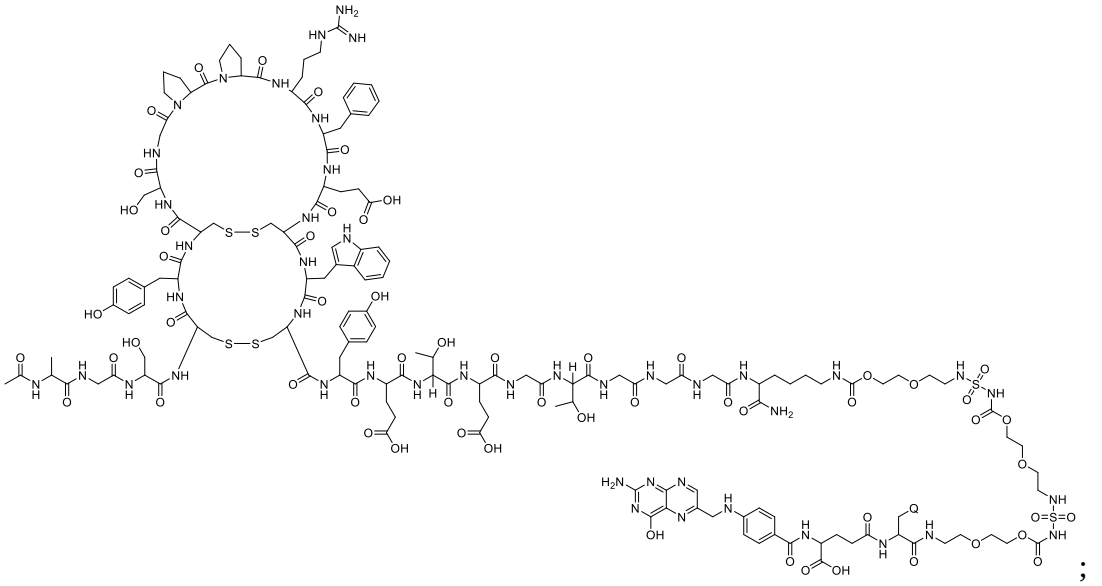

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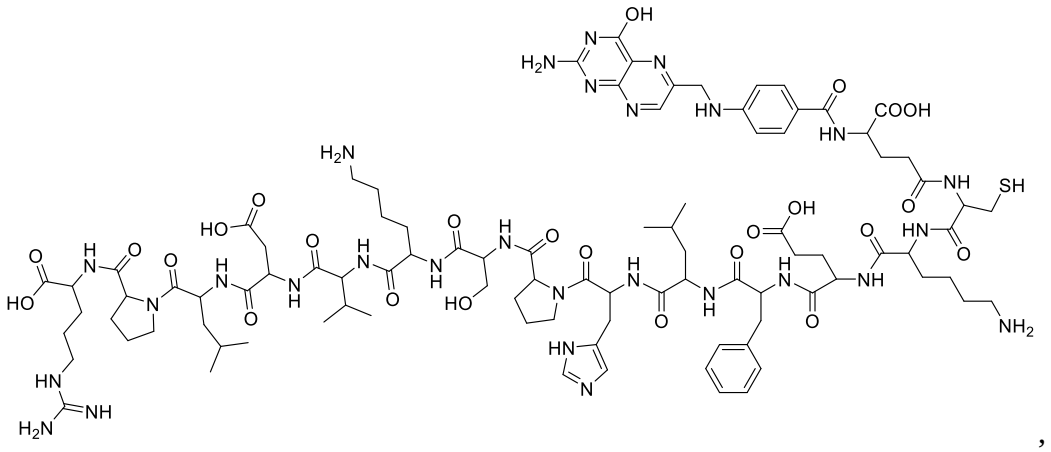
wherein Q is an active group, and the targeted molecule is linked to the payload through the active group Q; preferably, the active group Q is alkynyl or sulfhydryl; preferably, the targeted molecule has the following structures:



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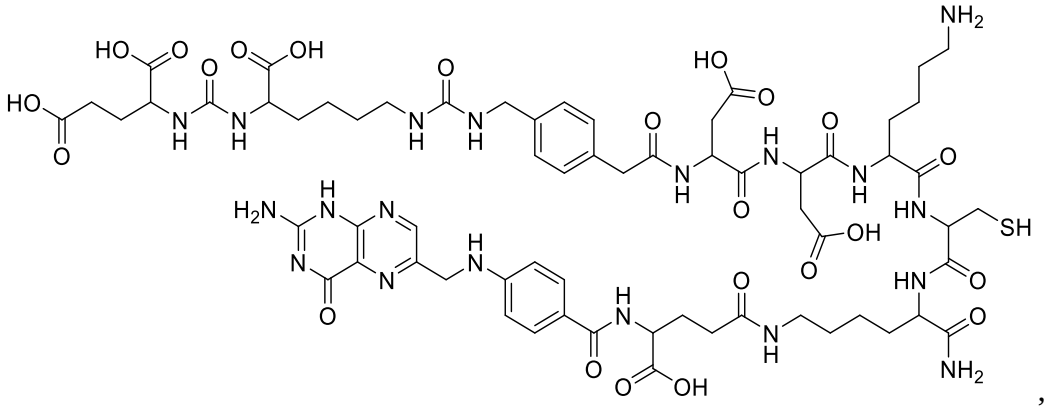

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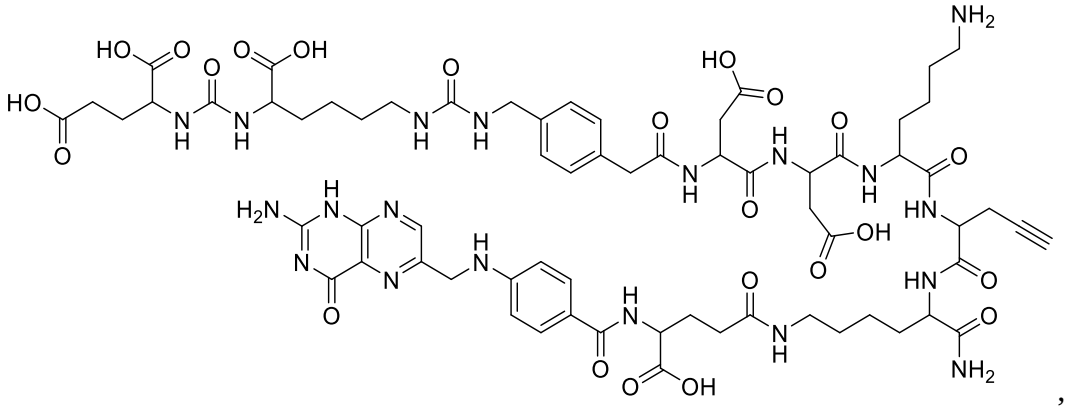

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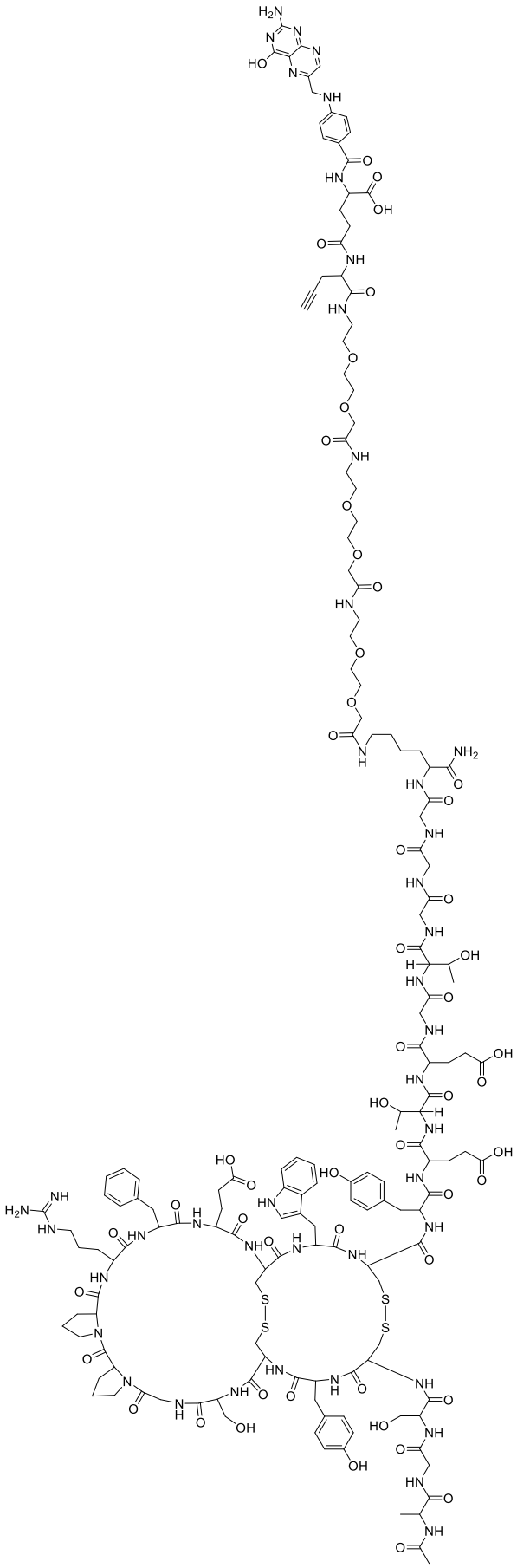

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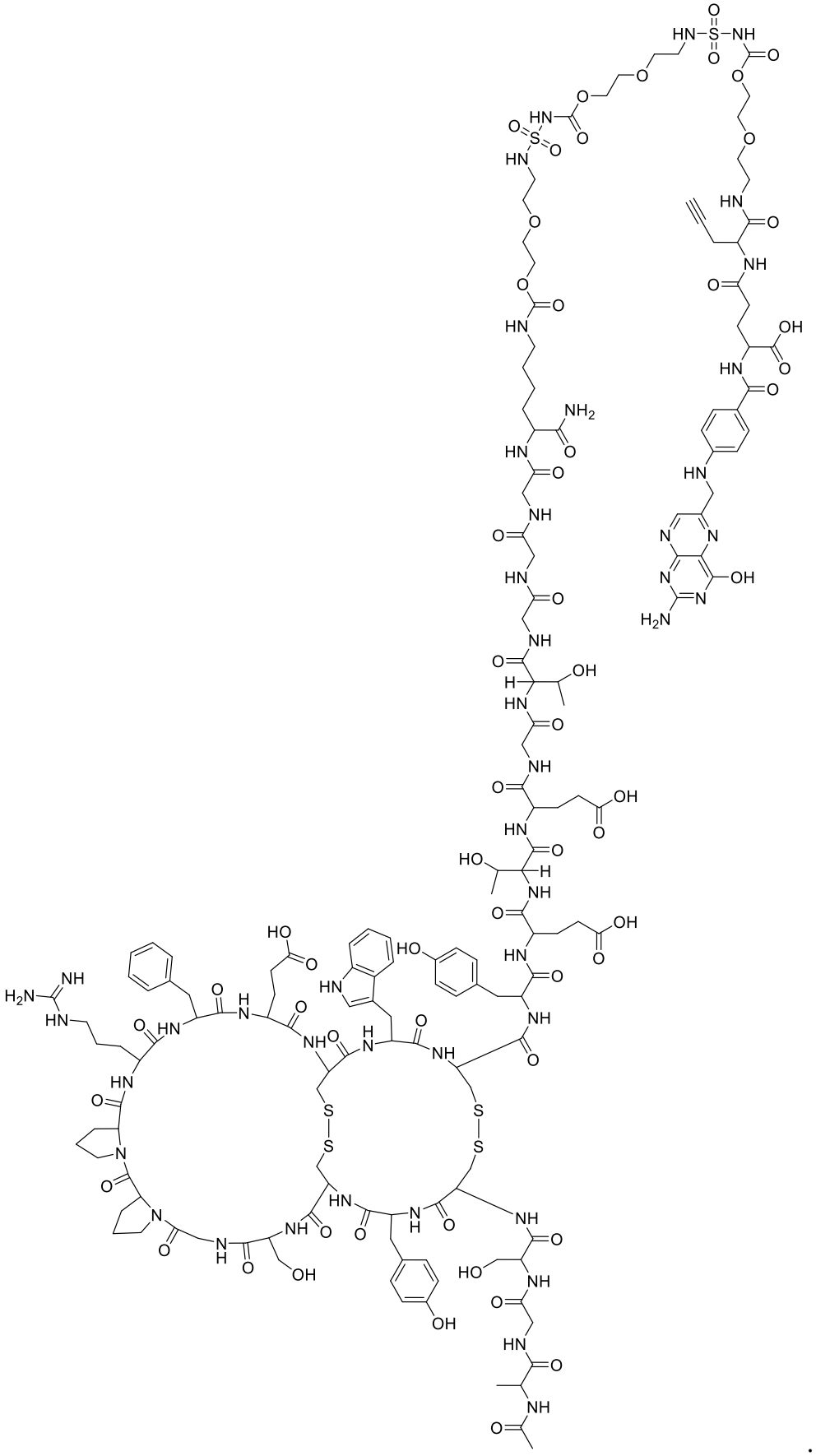


6. The conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-5, wherein the proteolysis targeting chimera having the structure represented by formula (I) is linked to the targeted molecule to form the conjugate compound:

$$(T_P)_n\text{-}L\text{-}T_{E3} \quad (I),$$

wherein,

T_P is a target protein ligand moiety for binding to a target protein, wherein n is 1, 2, or 3;

L is a linking moiety for linking T_P to T_{E3};

T_{E3} is an E3 ligase ligand moiety for binding to E3 ligase;

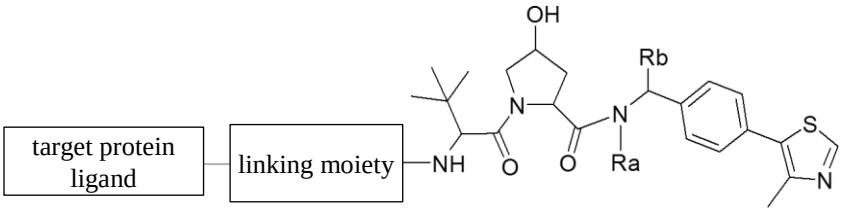
optionally, wherein the conjugate compound further has one or more of the following definitions:

i) wherein the E3 ligase ligand binds to VHL (Von Hippel-Lindau) protein, CRBN (cereblon) protein, MDM2 protein, or XIAP protein; preferably, the E3 ligase ligand is a VHL ligand or a CRBN ligand;

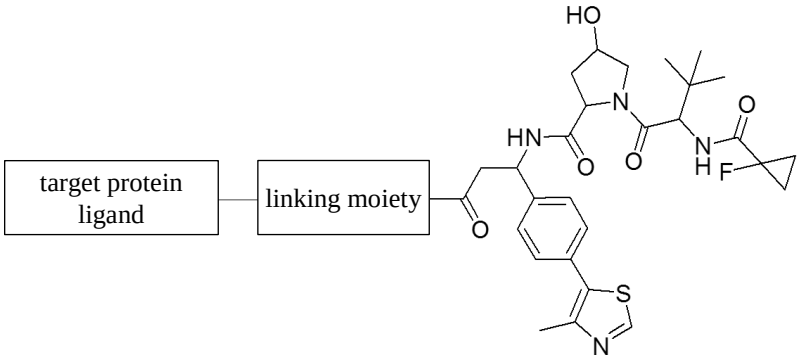
ii) wherein the E3 ligase ligand binds to VHL (Von Hippel-Lindau) protein, CRBN (cereblon) protein, MDM2 protein, or XIAP protein; preferably, the E3 ligase ligand is a VHL ligand or a CRBN ligand;

wherein the VHL ligand is VHL-L or an analog thereof, and the CRBN ligand is lenalidomide, pomalidomide, thalidomide, or an analog thereof;

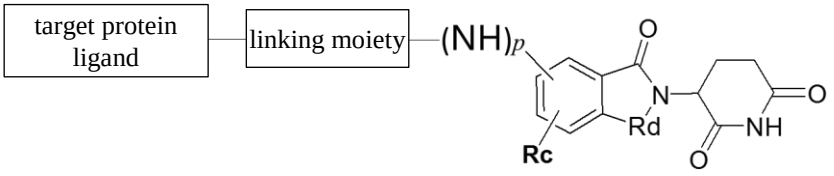
iii) wherein the proteolysis targeting chimera has a structure selected from the following group:



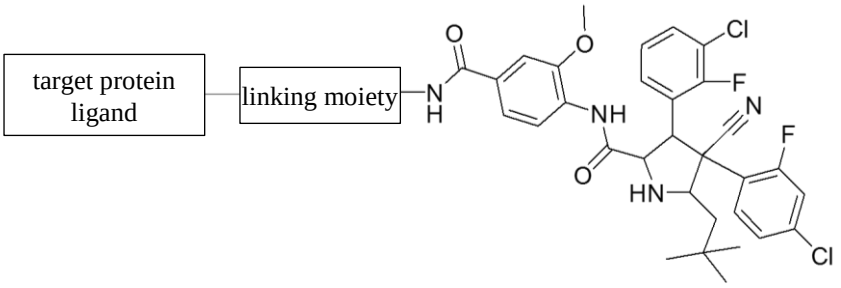
(II),



(III),



(IV), or



(V),

wherein,

Ra, Rb and Rc are each independently hydrogen, alkyl, NH_2, OH, or halogen; preferably the alkyl is methyl, and the halogen is fluorine;

Rd is CH_2, C=O, or C=S;

p is 0 or 1;

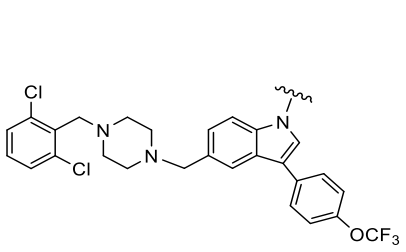
the target protein ligand can bind to a specific target protein;

the target protein ligand is linked to the E3 ligase group through the linking moiety;

iv) wherein the target protein is a nuclear receptor (e.g., AR and ER), a kinase-like protein (e.g., RIPK2, BCR-ABL, EGFR, HER2, c-Met, TBK1, CDK2/4/6/9, ALK, Akt, CK2, ERK1/2, FLT3, PI3K, BTK, and FAK), AKT, PAN-BET protein, BET protein (e.g., BRD2, BRD3, BRD4, and BRD6), BLK, BRAF1, BCL-xl, ERRα, FKBP12, FRS2α, JAK1, JAK3, IKZF1, IRAK4, MDM2, MetAP2, PLK1, PSK-J3, RAS, TACC3, Tau, TrkB, MDM2, or any combination thereof;

v) wherein the target protein is AR protein, ER protein, RAS protein, BRD4 protein, PLK1 protein, FAK protein, MDM2 protein, or any combination thereof;

vi) wherein the target protein ligand moiety has a structure selected from: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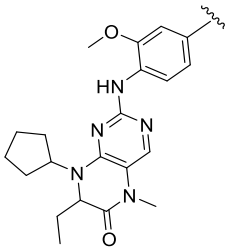
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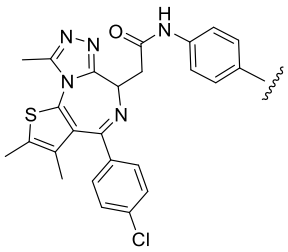
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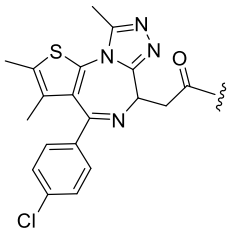
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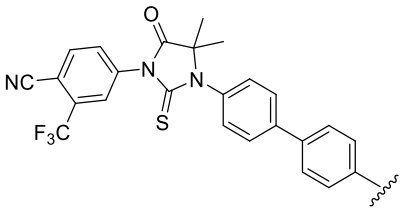
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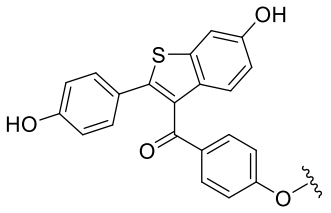
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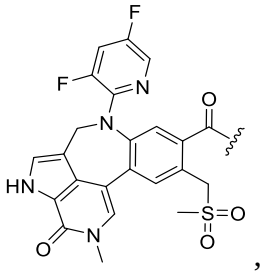
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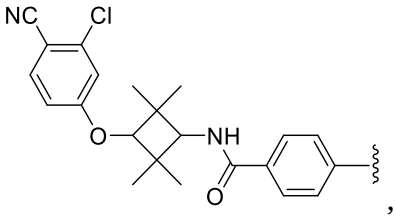
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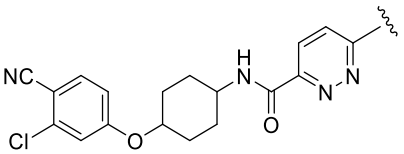
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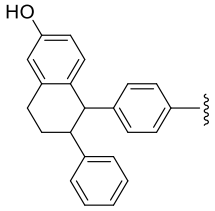
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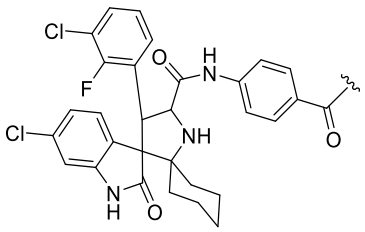
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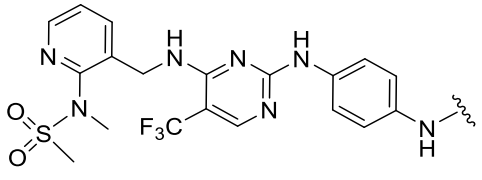
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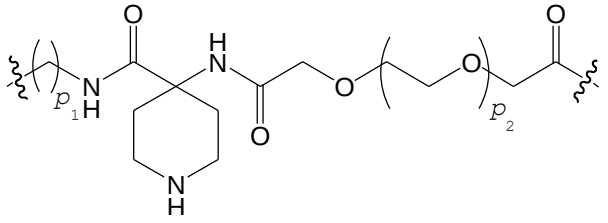
vii) wherein the linking moiety has a structure selected from the following group: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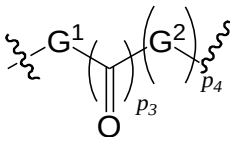
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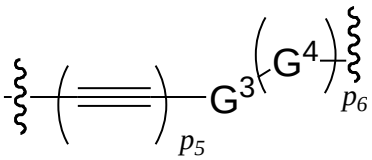

(L3)

wherein,

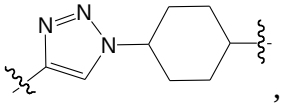
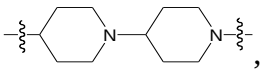
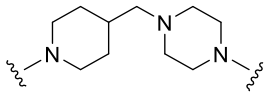
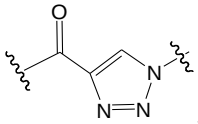
p_1 is an integer of 0-4;

p_2 is an integer of 0-6;

p_3, p_4, p_5, and p_6 are each independently 0 or 1;

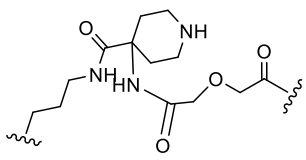
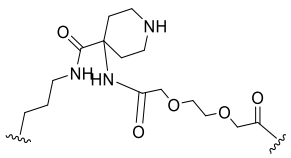
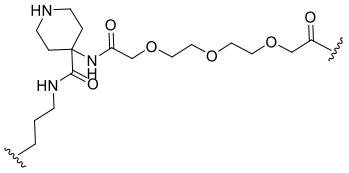
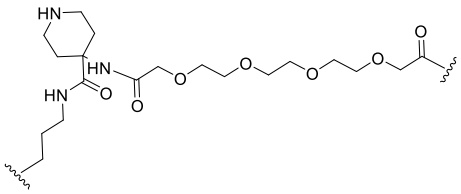
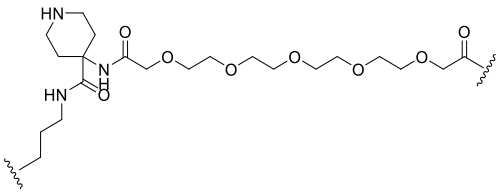
G^1 is a 4-14 membered linear alkylene, optionally 2-5 carbon atoms of the 4-14 membered linear alkylene may be substituted by -O-, -NH-, -N(C_{1-6} alkyl)-, or -C≡C-;

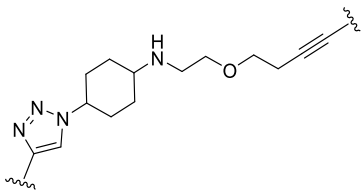
G^2 is an amino acid residue, wherein preferably G^2 is a Lys residue;

G^3 is selected from the following group: , , , and ;

G^4 is a 5-9 membered linear alkylene, optionally 2-4 carbon atoms of the 5-9 membered linear alkylene may be substituted by -O-, -NH-, -N(C_{1-6} alkyl)-, or -C≡C-;

viii) wherein the linking moiety has a structure selected from the following group:

, , , , ,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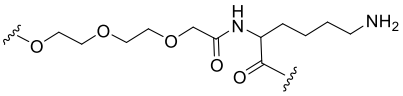
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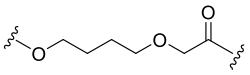
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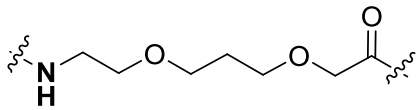
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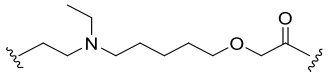
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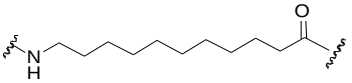
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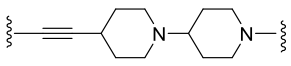
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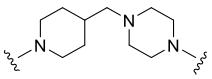
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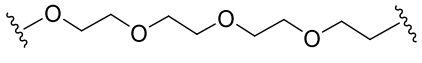
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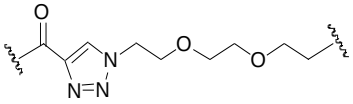
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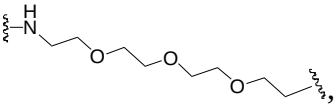
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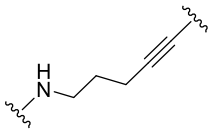
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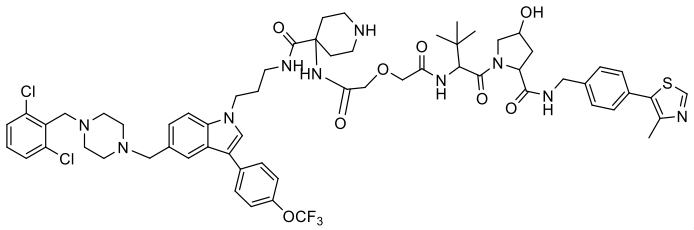
ix) wherein the proteolysis targeting chimera has the structures shown below:

CR202CC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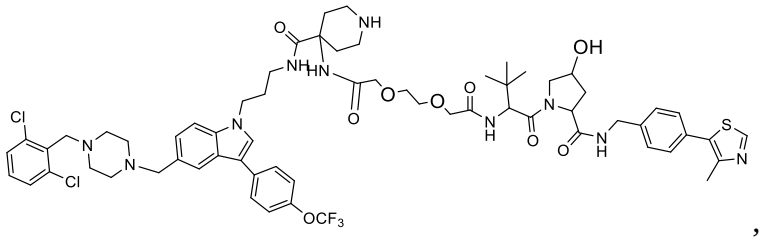
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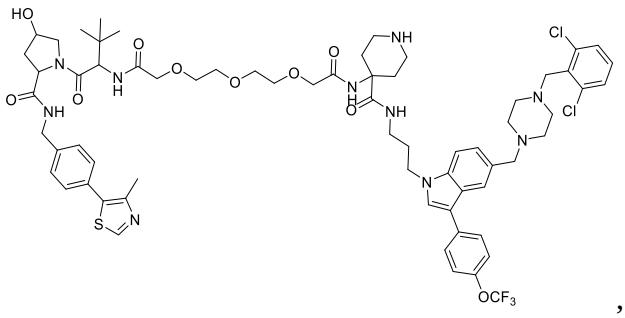
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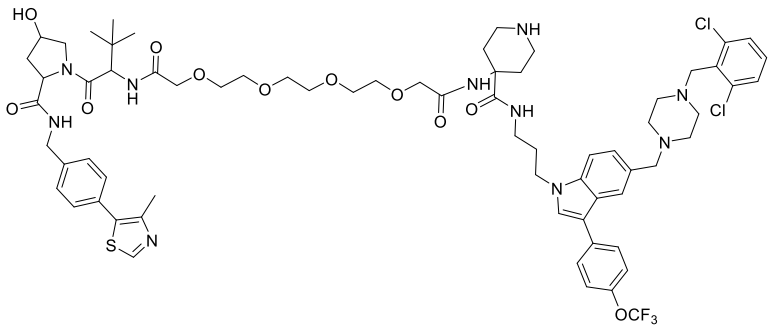
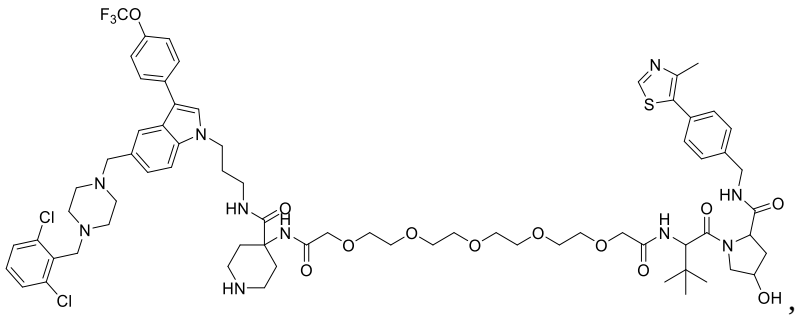
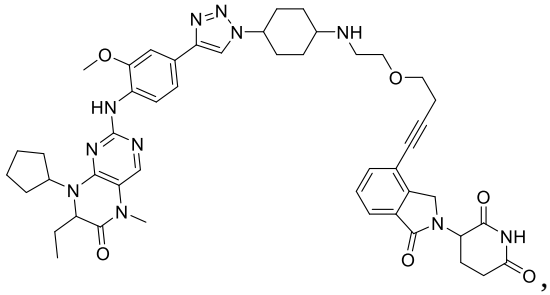
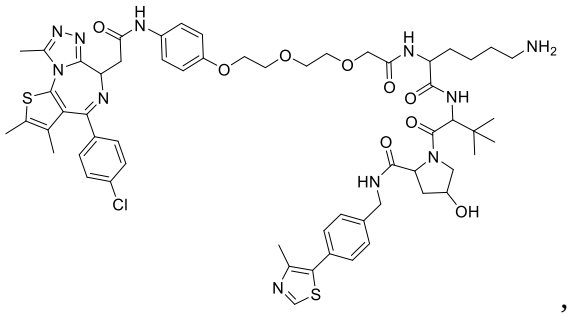
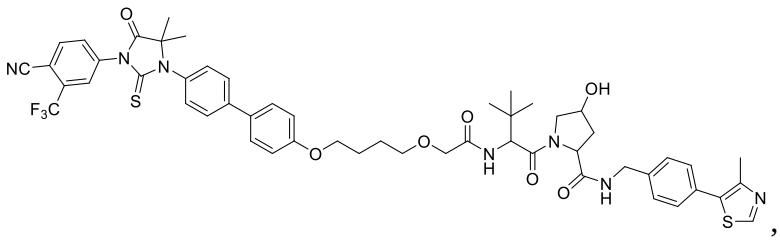
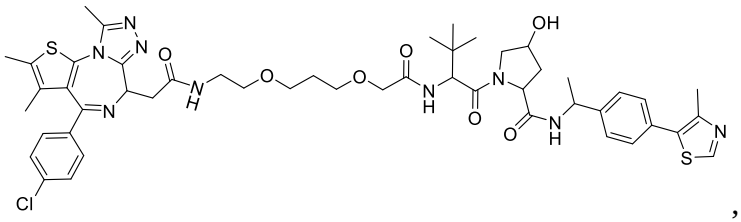
CR202CL ,

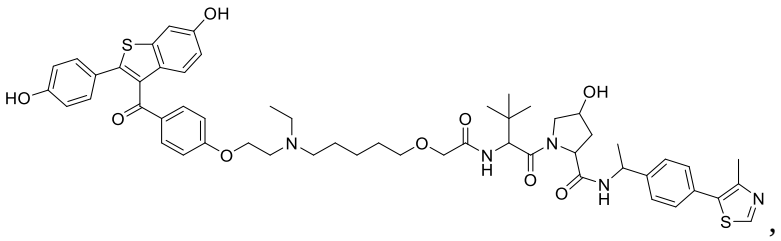
CR202CP ,

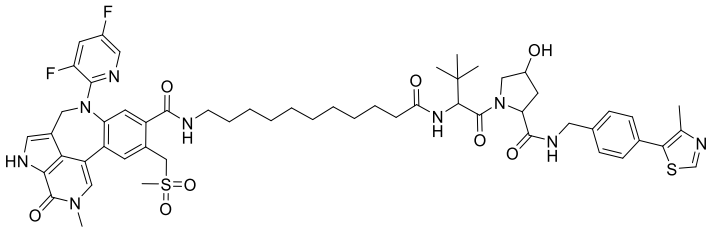
CR20274 ,

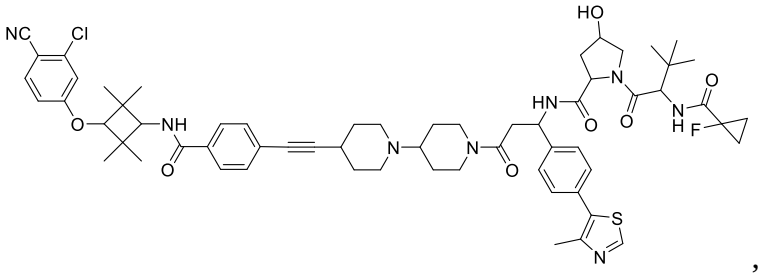
CR202EE ,

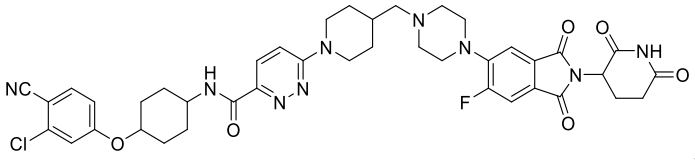
CR202Z5 ,

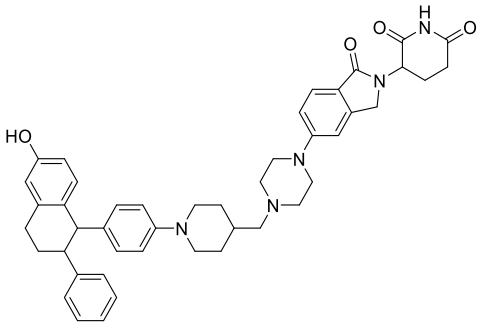
CR202ES ,

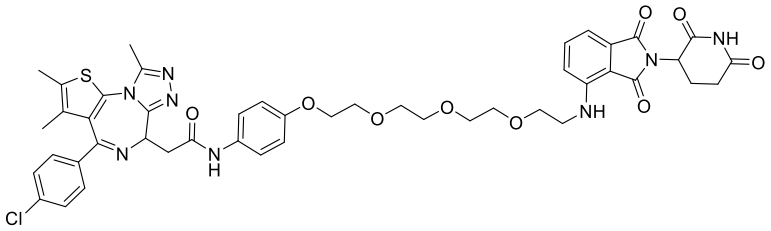
CR202Z7 ,

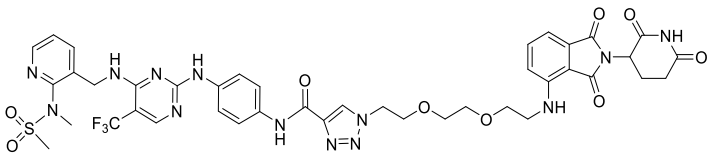
CR202Z8 ,

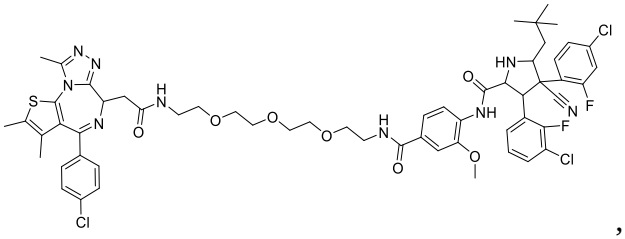
CR202Z9 ,

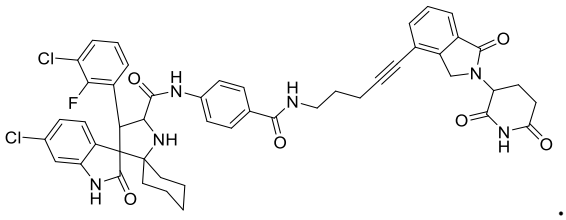
CR202Z1 ,

CR202Z2 ,

CR202Z3 ,

CR202Z4 ,

CR202Y2 , or

CR202Y4 .

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

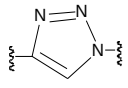
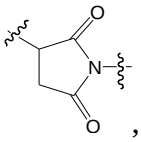
i) wherein the payload is linked to the targeted molecule directly, or the payload is linked to the targeted molecule via a linker;

ii) wherein the linkage between the payload and the targeted molecule, the payload and the linker, or the linker and the targeted molecule is accomplished by a chemical reaction; preferably, the linkage between the targeted molecule and the linker is accomplished by a click reaction;

iii) wherein the conjugate compound has the following structure

$$W^1\text{-}L^1\text{-}(EG)n^1\text{-}(D)n^5\text{-}(CH_2)n^2\text{-}(B)n^6\text{-}(AA)n^3\text{-}(CH_2CH_2\text{-}Q)n^4\text{-}L^2\text{-}W^2,$$

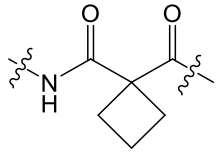
wherein,

L^1 is  or , -S-S-, or a bond;

EG is $-CH_2CH_2O-$ or $-OCH_2CH_2-$; n^1 is an integer of 0-6;

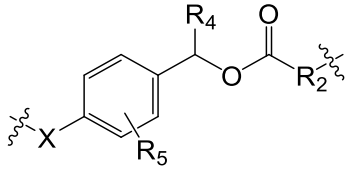
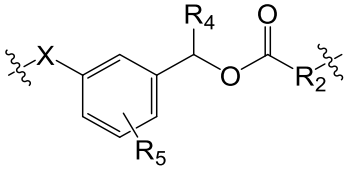
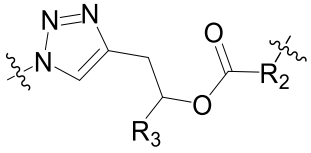
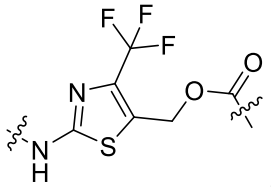
n^2 is an integer of 0-8;

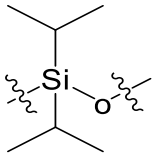
D is $-C(=O)-NH-S(=O)_2-NH-$; n^5 is 0 or 1;

B is each independently -C(=O)-, , -NH-CH_2CH_2-C(=O)-, -C(=O)-NH-, -CH(CH_3)-CH_2-O-, -CH_2CH_2O-, -NH-C(=O)-, or -NH-; n^6 is an integer of 0-3;

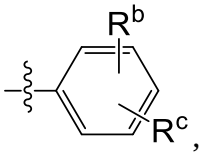
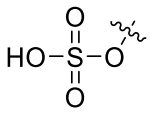
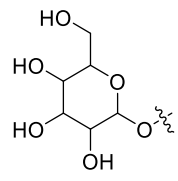
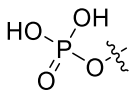
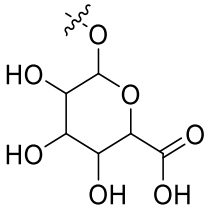
AA is each independently an amino acid residue; n^3 is an integer of 0-5;

Q is each independently -C(=O)-, -O-, or a bond; n^4 is an integer of 0-3;

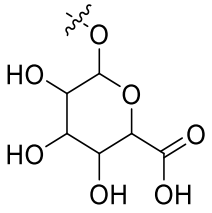
L^2 is , , , , -NH-CH_2-O-, or a bond;

wherein X is a bond, -NH-, -C(=O)-, oxygen, or ;

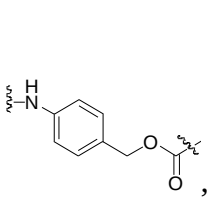
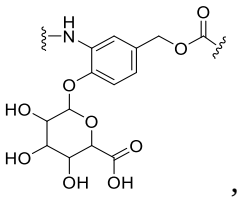
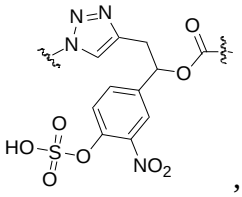
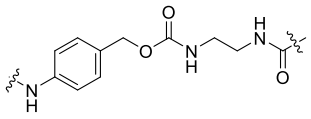
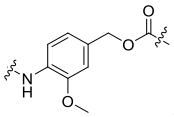
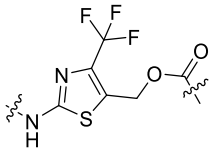
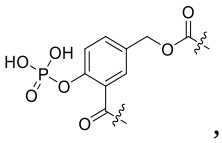
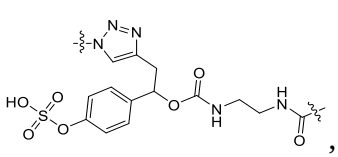
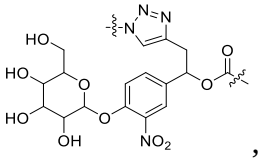
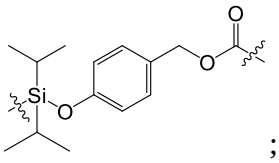
R_2 is a bond, -O-CH_2-, or -NH-CH_2CH_2-NH-C(=O)-;

R_3 is hydrogen or , wherein R^b and R^c are each independently hydrogen, nitro, , , , or ;

R_4 is hydrogen or C_{1-8} alkyl;

R_5 is hydrogen, amino, nitro, phosphate group, -OR^a, or  ; wherein R^a is methyl, ethyl, propyl, or isopropyl;

W^1 is the targeted molecule capable of binding to the cell surface protein, and W^2 is the payload;

preferably, L^2 is a bond,  ,  ,  , -NH-CH_2-O-,  ,  ,  ,  ,  ,  , or  ;

preferably, EG is -CH_2CH_2O-;

preferably, n^1 is 2 or 0;

preferably, n^2 is 1, 4, or 5;

preferably, n^5 is 0;

preferably, n^6 is 1 or 3;

preferably, n^1 is 2, n^2 is 1, n^3 and n^4 are 0, and L^2 is a bond;

preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu, Leu, Lys, Ala, Gly, Phe, Gln, Pro, or Asn;

preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, -Phe-Cit-, -Val-Ala-, -Gly-Gly-Phe-Gly-, -Cit-, -Val-Leu-Lys-, Val-Cit-Pro-Gly-, -Gly-Asn-Asn-, and Ala-Ala-Asn-;

preferably, when n^4 is 1, Q is -C(=O)-;

preferably, when n^4 is 2, Q are -O- and -C(=O)-, respectively;

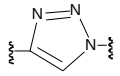
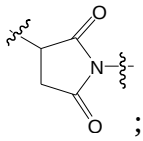
preferably, when n^4 is 3, Q are -O-, -O-, and a bond, respectively; or

preferably, n^4 is 0;

iv) wherein the conjugate compound has the following structure

$$W^1\text{-}L^1\text{-}(EG)n^1\text{-}(D)n^5\text{-}(CH_2)n^2\text{-}(B)n^6\text{-}(AA)n^3\text{-}(CH_2CH_2\text{-}Q)n^4\text{-}L^2\text{-}W^2$$

wherein,

L^1 is  or ;

EG is $-CH_2CH_2O-$; n^1 is an integer of 0-4;

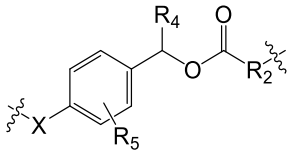
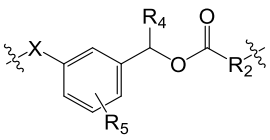
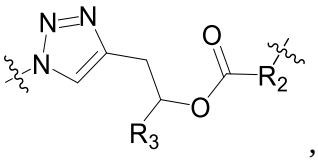
D is $-C(=O)-NH-S(=O)_2-NH-$; n^5 is 0 or 1;

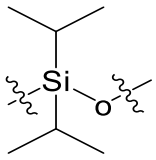
n^2 is an integer of 0-5;

B is $-C(=O)-$, $-C(=O)-NH-$, $-CH_2CH_2O-$, $-NH-CH_2CH_2-C(=O)-$, or $-NH-$; n^6 is an integer of 0-3;

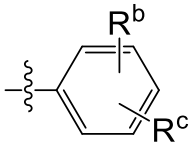
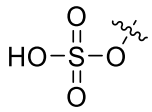
AA is each independently an amino acid residue; n^3 is an integer of 0-3;

Q is each independently $-C(=O)-$, $-O-$, or a bond; n^4 is an integer of 0-3;

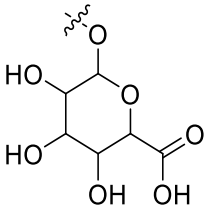
L^2 is , , or ,

wherein X is a bond, $-NH-$, $-C(=O)-$, or ;

R_2 is a bond;

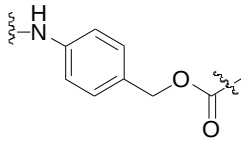
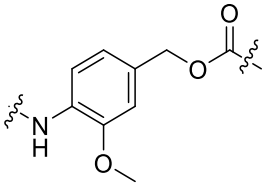
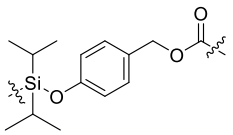
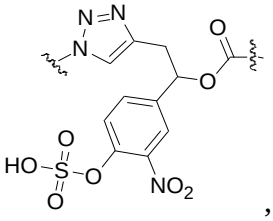
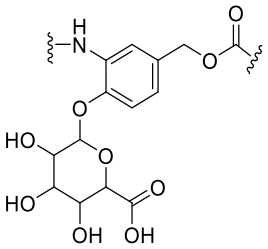
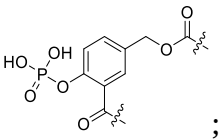
R_3 is , wherein R^b and R^c are each independently hydrogen, nitro, or ;

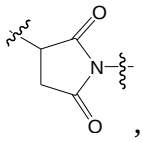
R_4 is hydrogen;

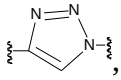
R_5 is hydrogen, $-OCH_3$, or ;

W^1 is the targeted molecule capable of binding to the cell surface protein, and W^2 is the

payload;

preferably, L^2 is , , , , , or ;

preferably, L^1 is , and n^1, n^5, and n^4 are all 0;

preferably, L^1 is , and n^2 is 1 or 2;

preferably, when n^5 is 1, n^2 and n^4 are both 0;

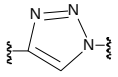
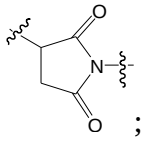
preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu, or Ala; or

preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, and -Val-Ala-; and

v) wherein the conjugate compound has the following structure

$$W^1\text{-}L^1\text{-}(EG)n^1\text{-}(CH_2)n^2\text{-}(C{=}O)\text{-}(AA)n^3\text{-}L^2\text{-}W^2$$

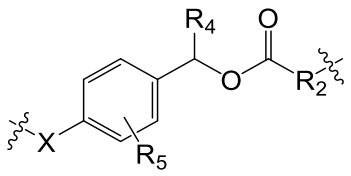
wherein,

L^1 is  or ;

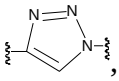
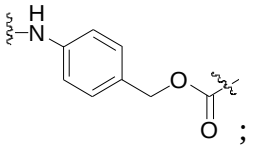
EG is $-CH_2CH_2O-$; n^1 is an integer of 0-4;

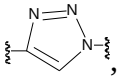
n^2 is an integer of 0-5;

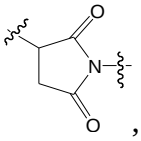
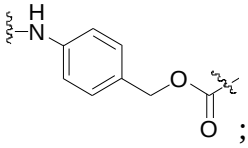
AA is each independently an amino acid residue; n^3 is an integer of 1-4;

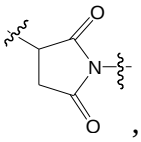
L^2 is  or a bond,

wherein X is -NH-; R_2 is a bond; R_4 is hydrogen; R_5 is hydrogen or $-OCH_3$;
W^1 is the targeted molecule capable of binding to the cell surface protein, and W^2 is the payload;

preferably, L^1 is , n^1 is 2, n^2 is 1, and L^2 is ;

preferably, L^1 is , n^1 is 2, n^2 is 1, and L^2 is a bond;

preferably, L^1 is , n^1 is 0, n^2 is 5, and L^2 is ;

preferably, L^1 is , n^1 is 0, n^2 is 5, and L^2 is a bond;

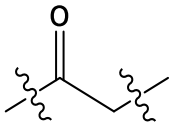
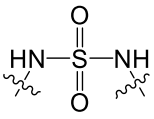
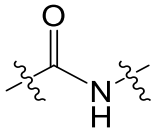
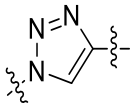
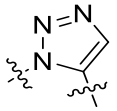
preferably, AA is each independently Val, Cit, Glu, or Ala amino acid residue; or

preferably, $-(AA)n^3-$ is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, -Phe-Cit-, -Val-Ala-, -Gly-Gly-Phe-Gly-, -Val-Leu-Lys-, and -Gly-Asn-Asn-.

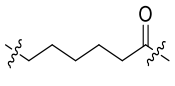
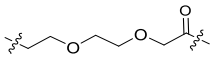
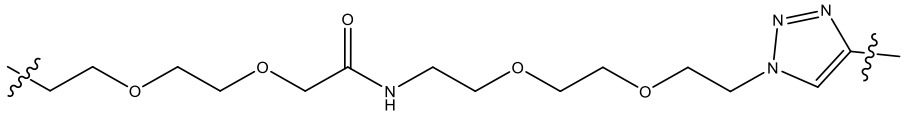
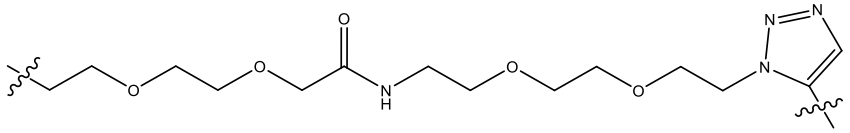
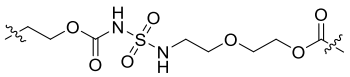
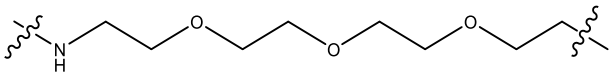
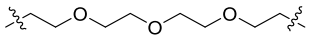
8. The conjugate compound or the pharmaceutically acceptable salt thereof according to claim 7, wherein the conjugate compound has any one of the following definitions:

i) wherein the linker comprises a linking module 1 and a linking module 2; optionally the linking module 1 is linked to the linking module 2 via a bond; optionally, the linking module 1 is linked to the linking module 2 via a chemical group;

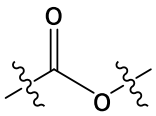
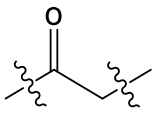
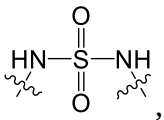
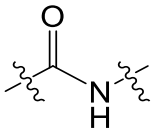
optionally, wherein the conjugate compound further has the following definition:

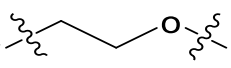
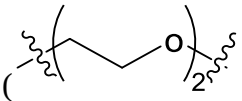
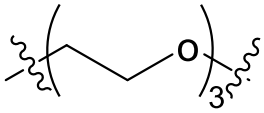
wherein the chemical group is a PEG chain, , , , C_1-C_8 alkyl chain, -NH-, -O-, -C(O)-, , , or any combination thereof;

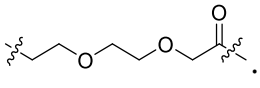
preferably, the PEG chain is PEG1, PEG2, or PEG3;

preferably, the chemical group is , , , , , , or ;

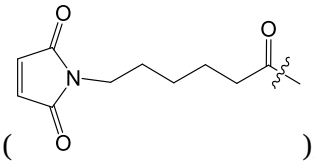
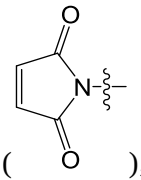
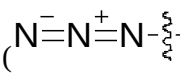
ii) wherein the linker comprises a linking module 2; preferably, the linking module 2 may be enzymatically cleavable or acid-labile; and

iii) wherein the linker comprises a linking module 1 and a group binding to the linking module 1; optionally, the group binding to the linking module 1 is a PEG chain, , , , , C_1-C_8 alkyl chain, -NH-, -O-, -C(O)-, or any combination thereof;

preferably, the PEG chain is PEG1 (), PEG2 (), or PEG3 ();

optionally, the group binding to the linking module 1 is .

9. The conjugate compound or the pharmaceutically acceptable salt thereof according to claim 8, wherein the conjugate compound has one or more of the following definitions:

i) wherein the linking module 1 is maleimidocaproyl (), maleimido (), or azido (); and

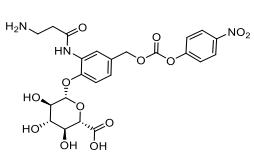
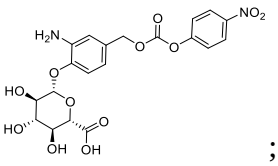
ii) wherein

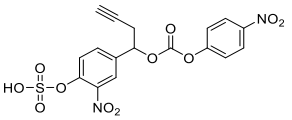
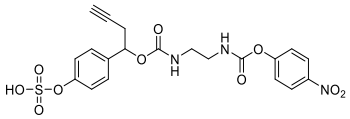
- the linking module 2, before linked to the targeted molecule, the linking module 1, the chemical group, or the payload, has a structure comprising the following groups: a CB enzyme-cleavable group, a plasmin-cleavable group, a legumain-cleavable group, a β-glucuronidase-cleavable group, a sulfatase-cleavable group, a phosphatase-cleavable group, a β-galactosidase-cleavable group, a glutathione enzyme-cleavable group, or an acid-labile group
- optionally, wherein:

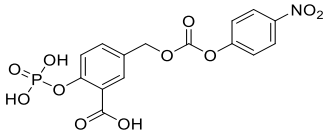
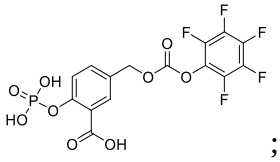
the CB enzyme-cleavable group comprises an amino acid or a combination of an amino acid and a self-decomposing fragment, and the amino acid is Val-Cit, Gly-Gly-Phe-Gly, CycloBut-Cit, Phe-Cit, Val-Ala, Glu-Val-Cit, Ala-Cit, Val-Cit-Pro, or Val-Cit-Pro-Gly;

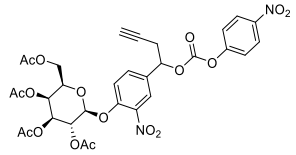
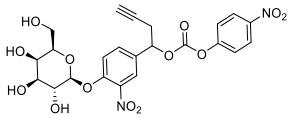
the plasmin-cleavable group comprises an amino acid or a combination of an amino acid and a self-decomposing fragment, and the amino acid is Val-Leu-Lys;

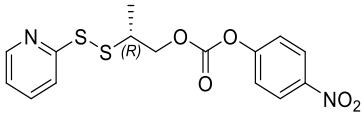
the legumain-cleavable group comprises an amino acid or a combination of an amino acid and a self-decomposing fragment, and the amino acid is selected from Gly-Asn-Asn or Ala-Ala-Asn;

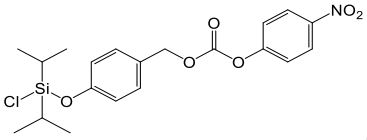
the β-glucuronidase-cleavable group is  or  ;

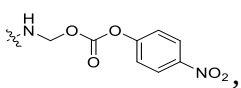
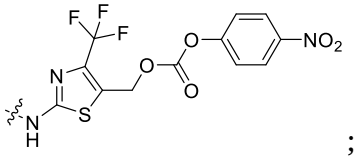
the sulfatase-cleavable group is  or ;

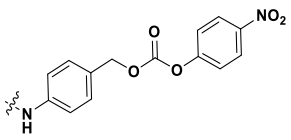
the phosphatase-cleavable group is  or ;

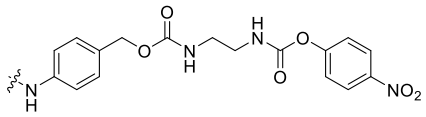
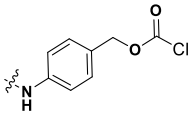
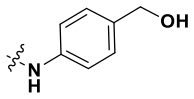
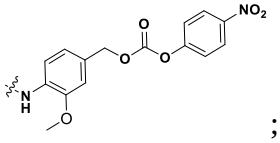
the β-galactosidase-cleavable group is  or ;

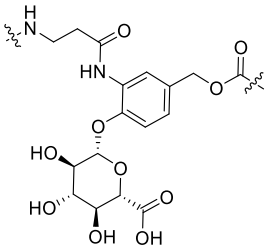
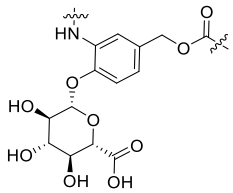
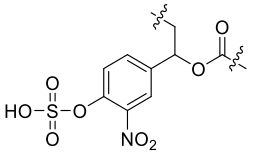
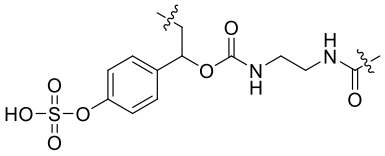
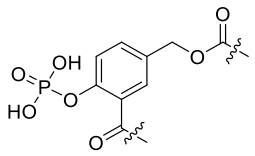
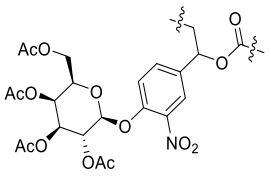
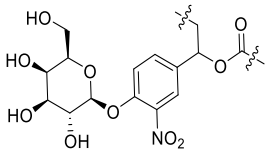
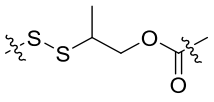
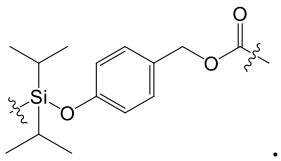
the glutathione enzyme-cleavable group is ;

the acid-labile group is ;

optionally, the self-decomposing fragment is PAB and a derivative thereof, , or ;

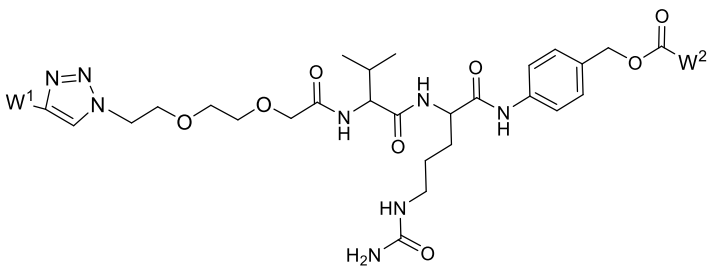
preferably, the PAB is ;

preferably, the PAB derivative is , , , or ; and

- optionally, wherein the linking module 2, upon operative linkage to the linking module 1, the chemical group, the targeted molecule, or the payload, has the following structures: , , , , , , , , or .

10. The conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-9, wherein the conjugate compound has any one of the following definitions:

i) wherein the conjugate compound has the following structures:



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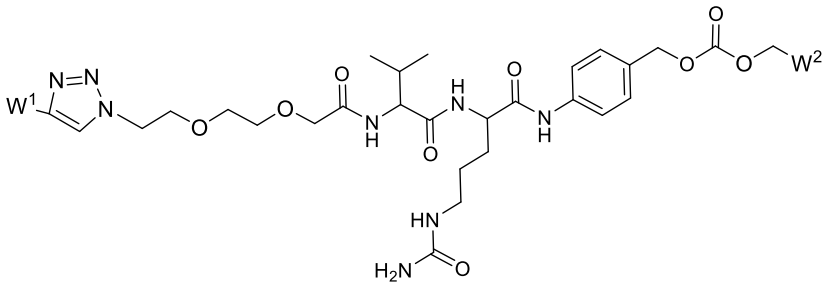

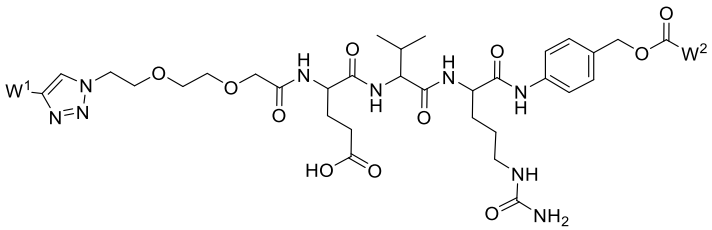

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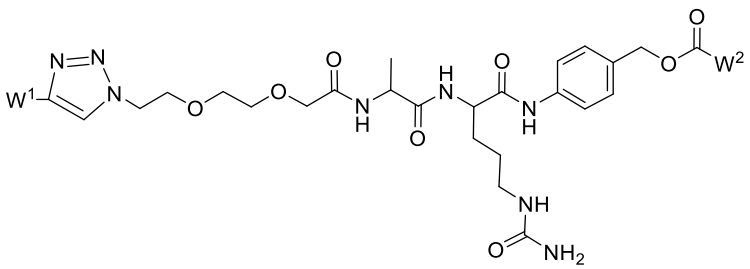

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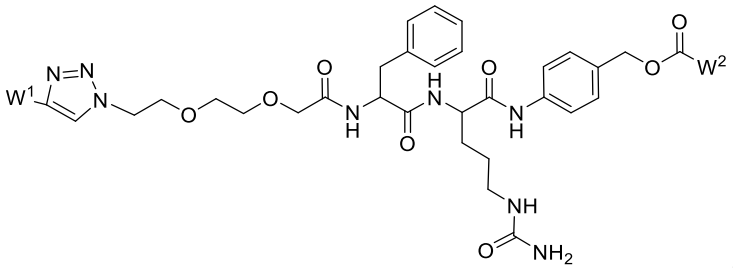

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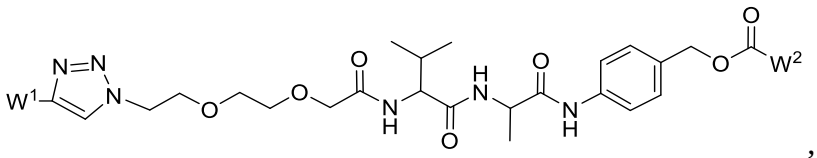

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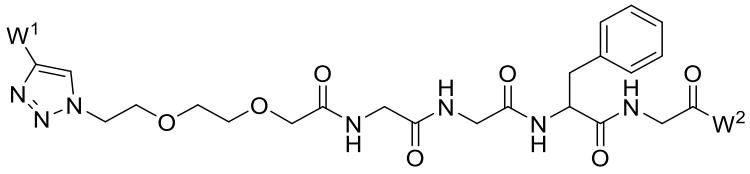

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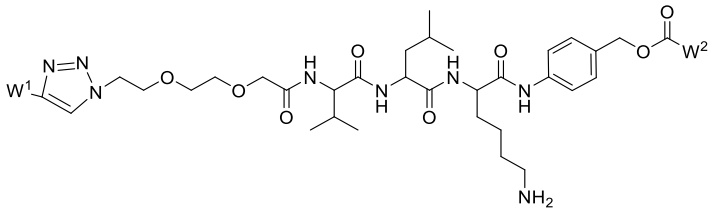

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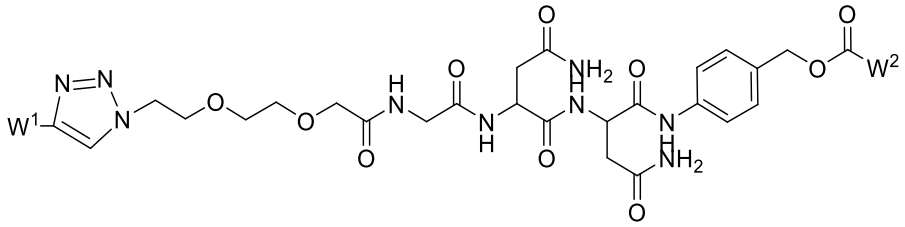

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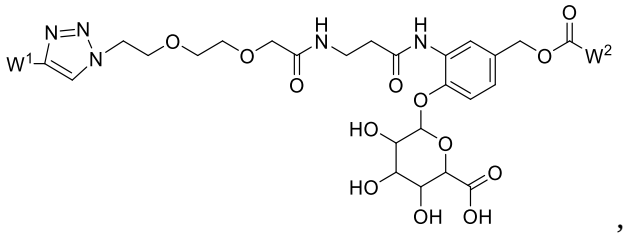

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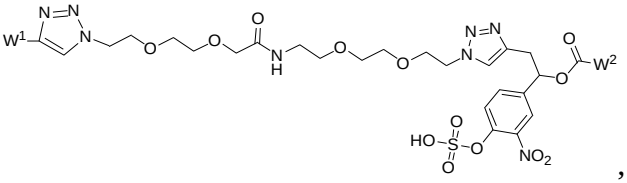

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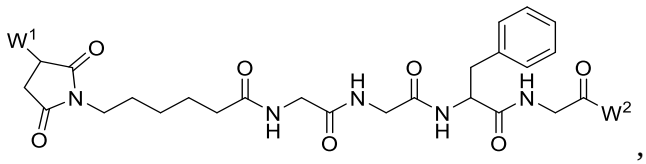

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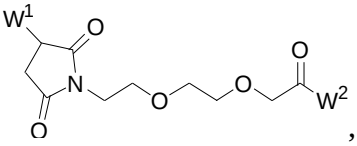

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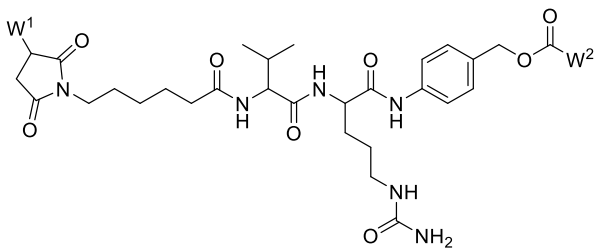

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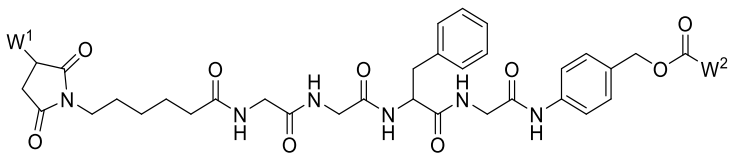

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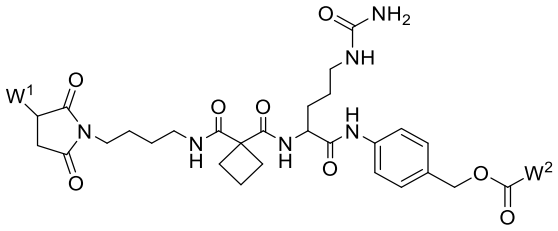

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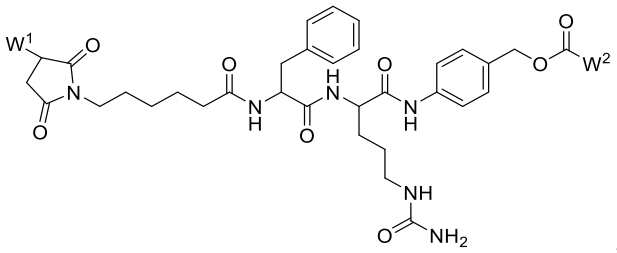

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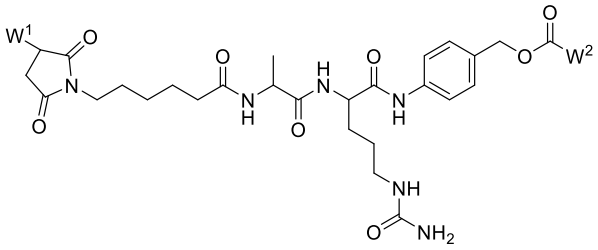

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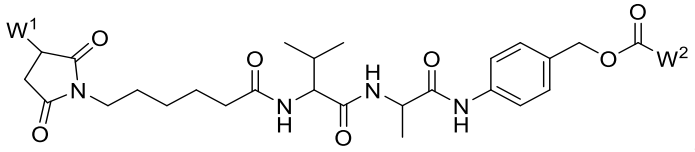

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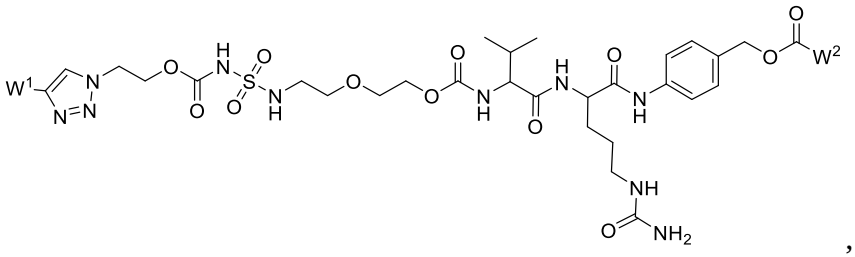

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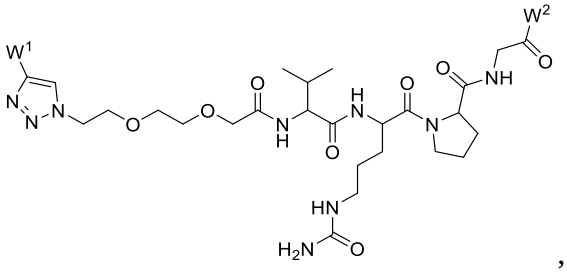

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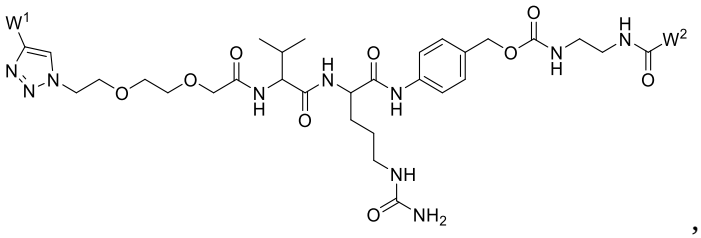

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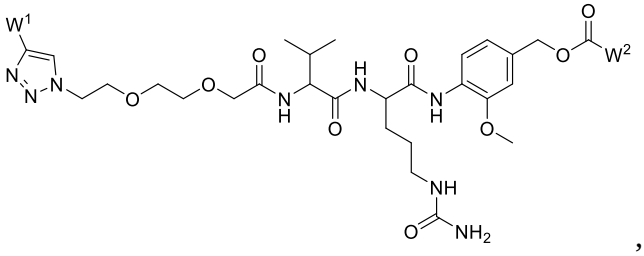

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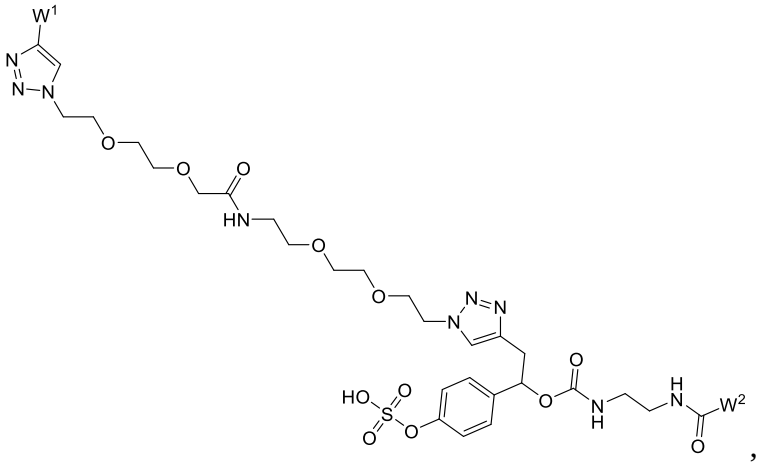

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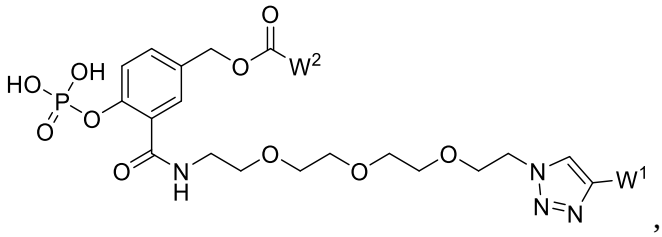

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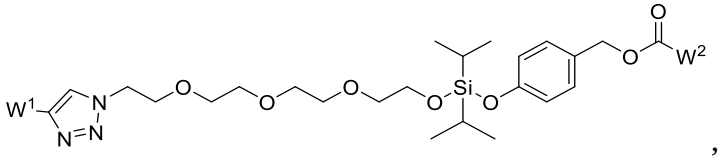

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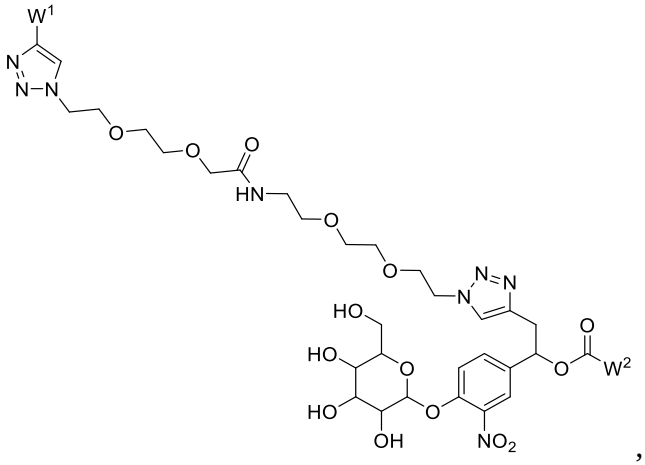

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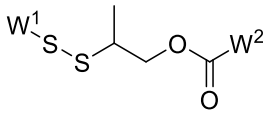

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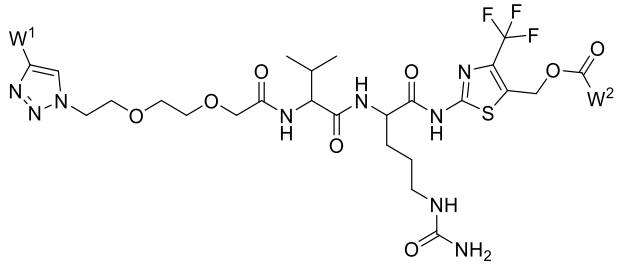

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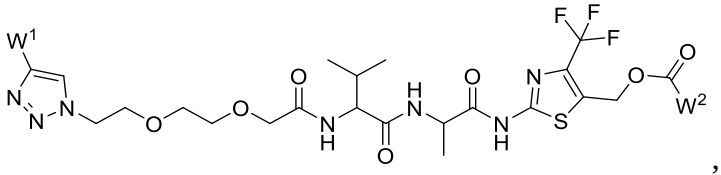

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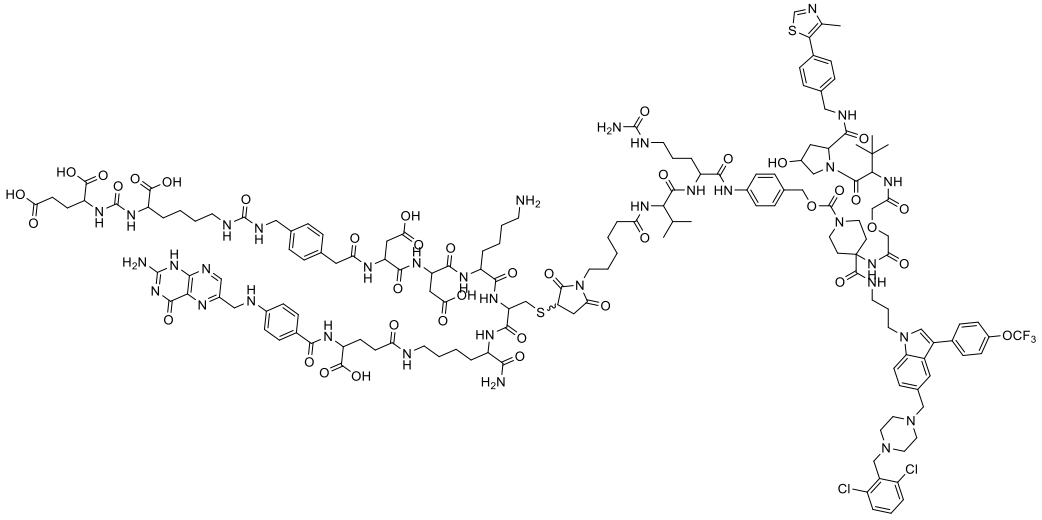
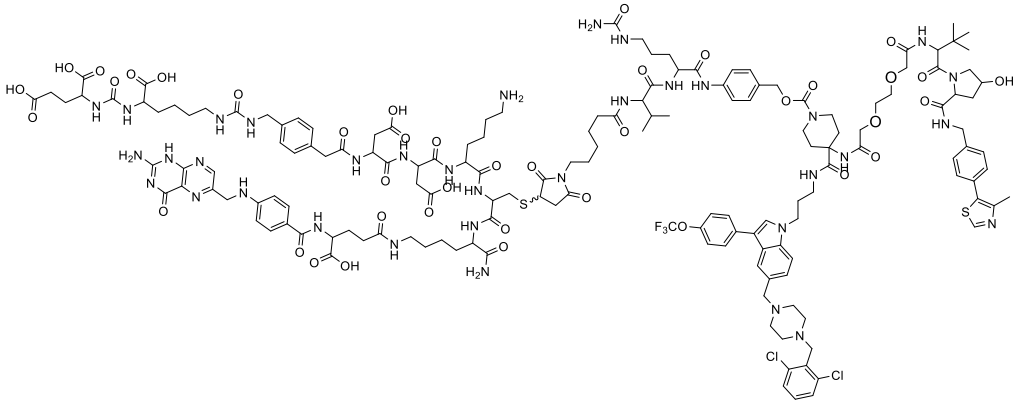
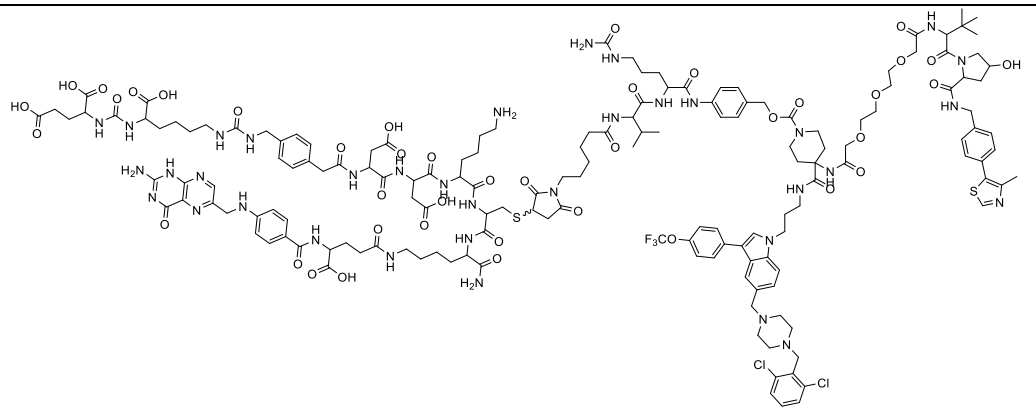
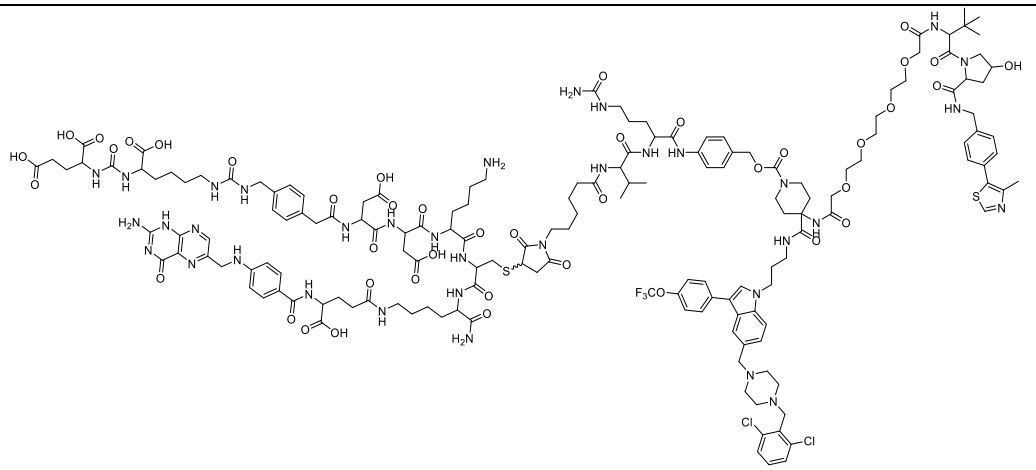
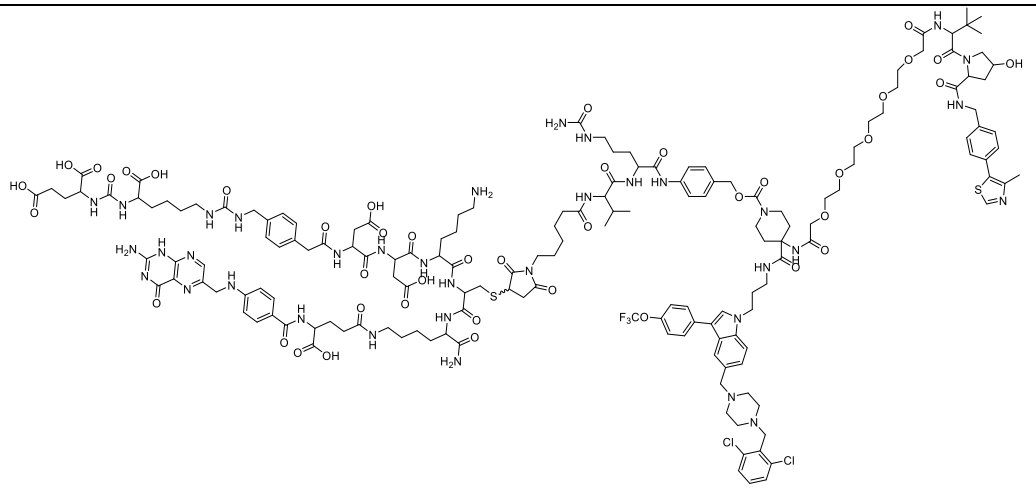
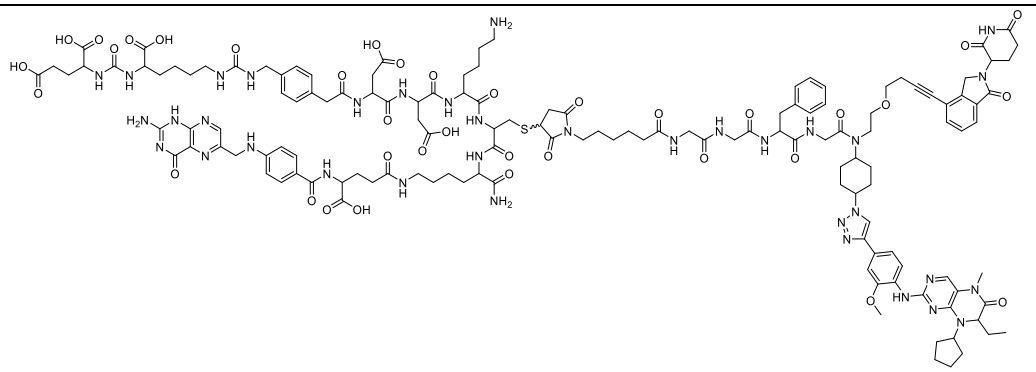
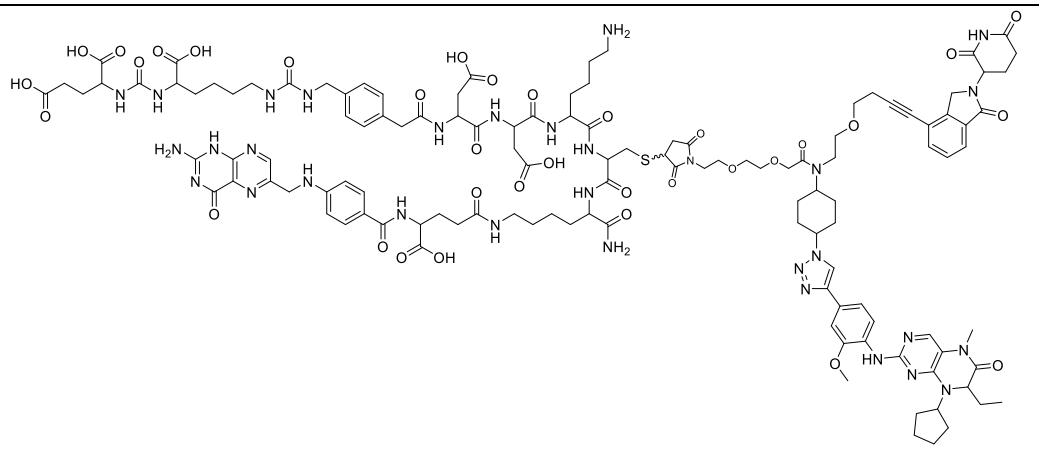
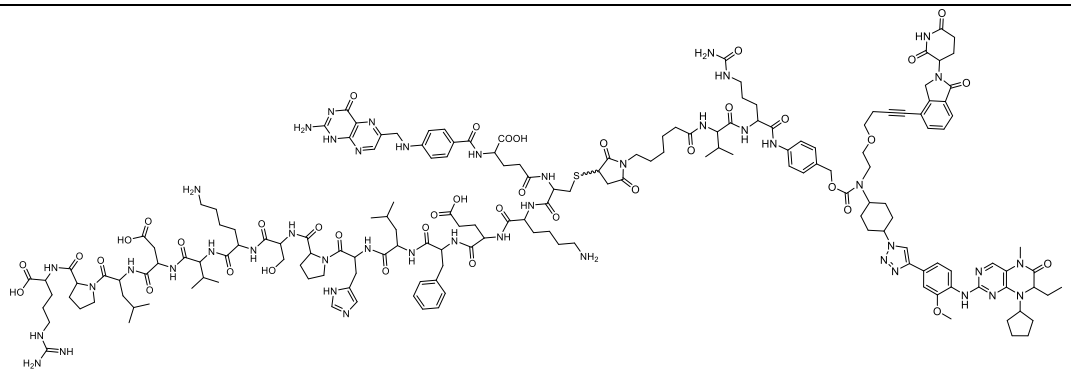
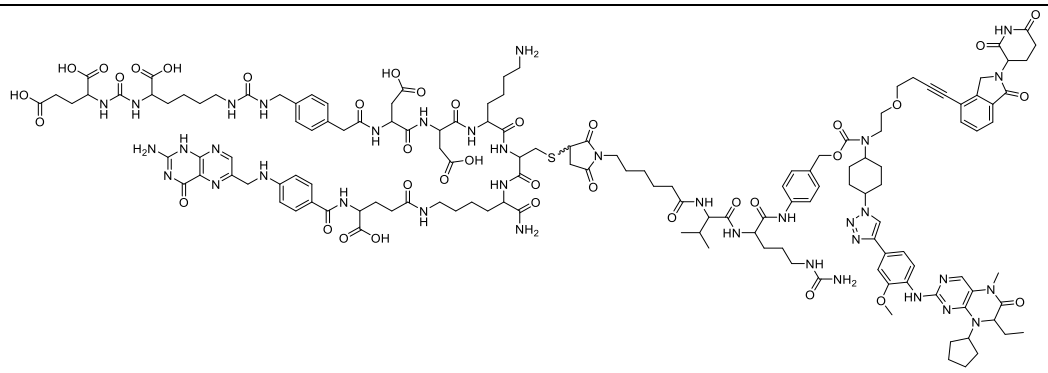
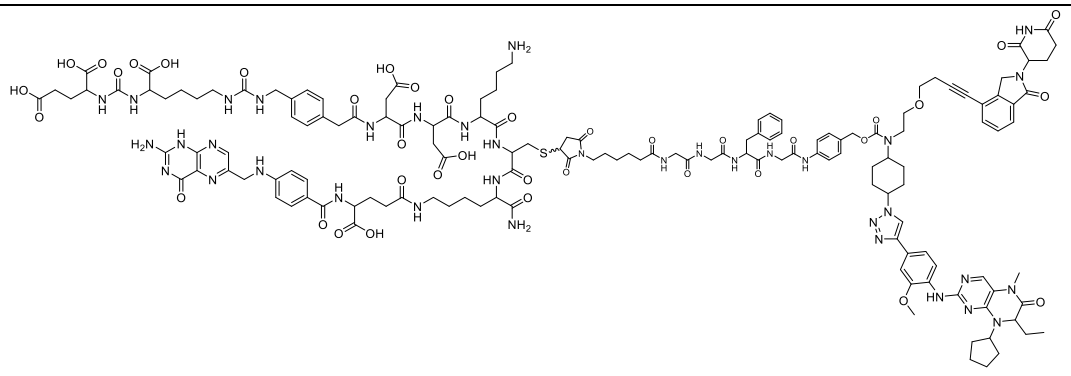
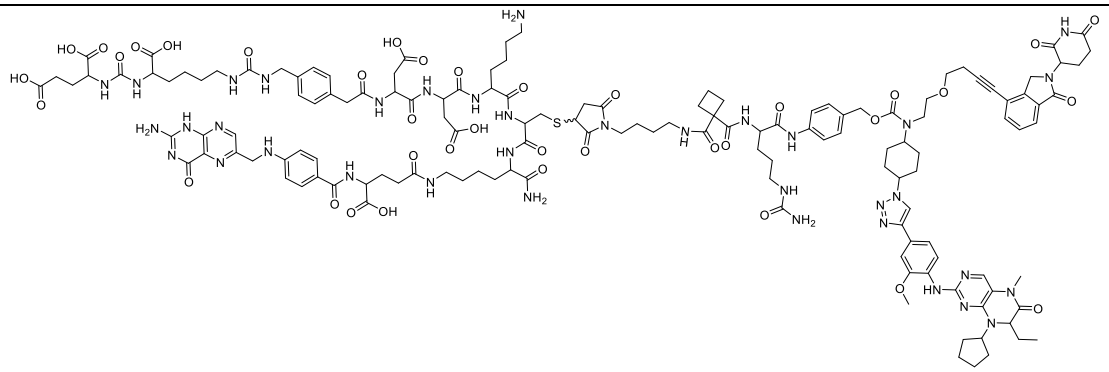
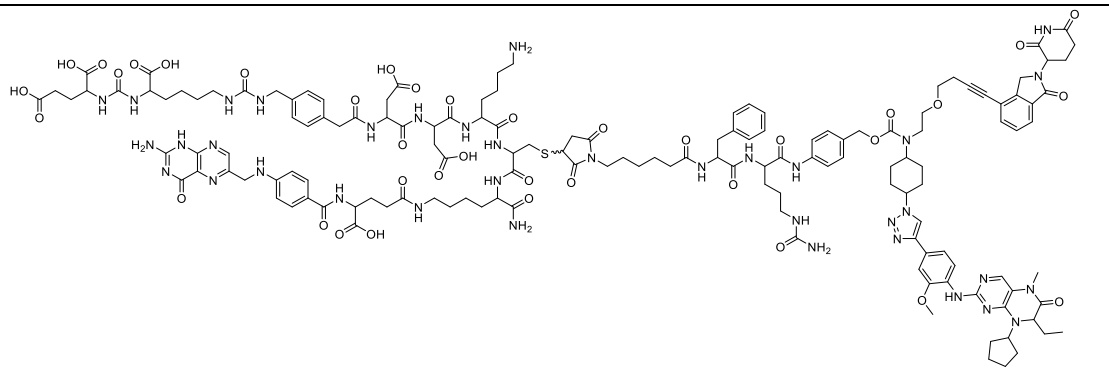
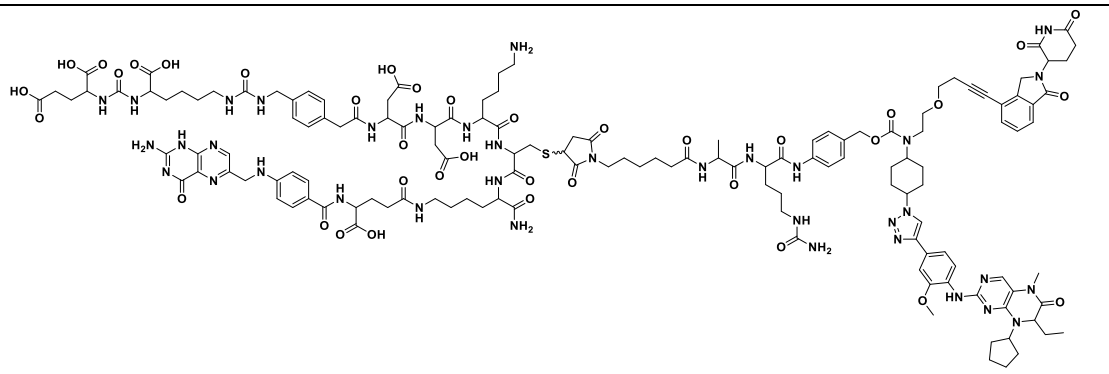
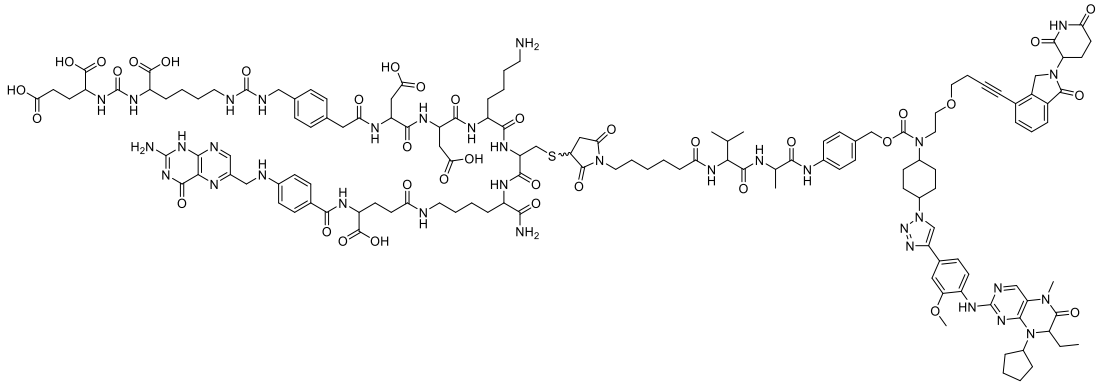
wherein W^1 is the targeted molecule capable of binding to the cell surface protein, and W^2 is the payload; and

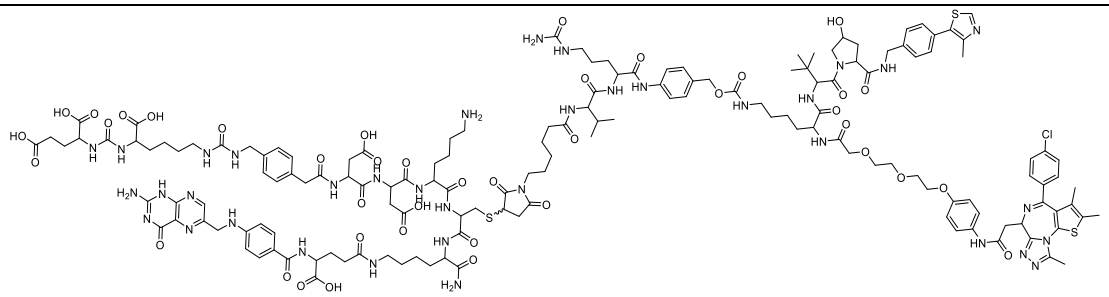
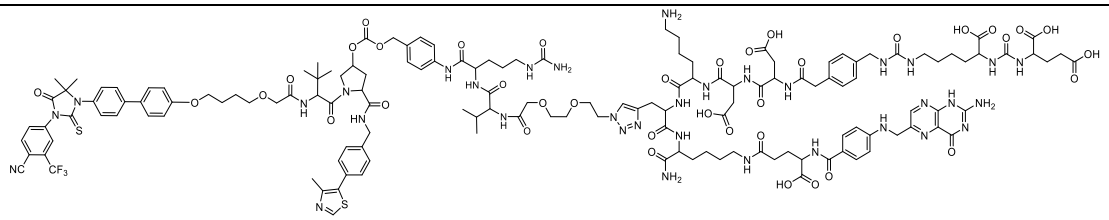
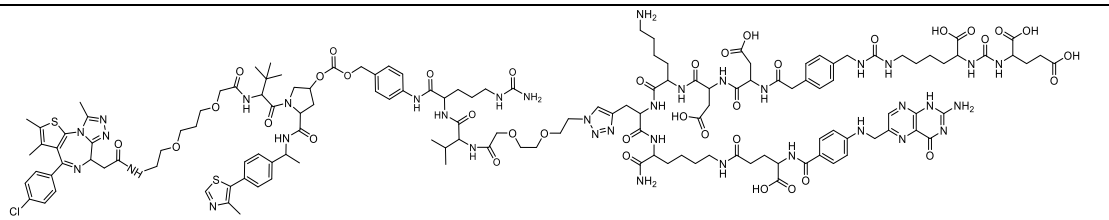
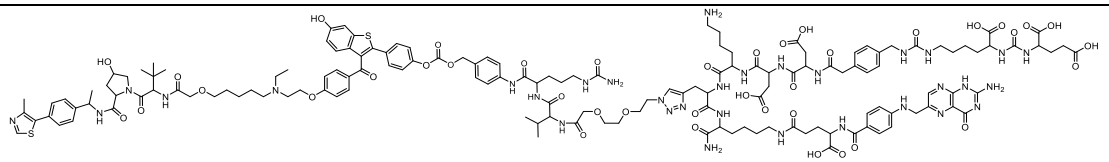
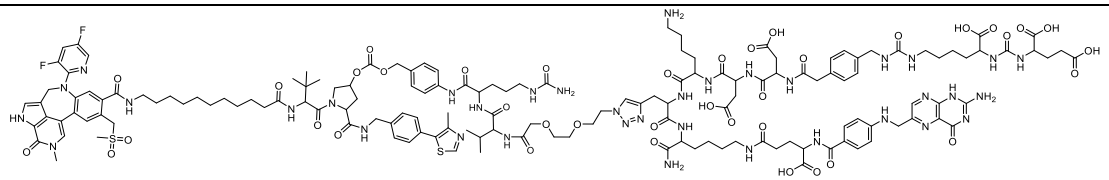
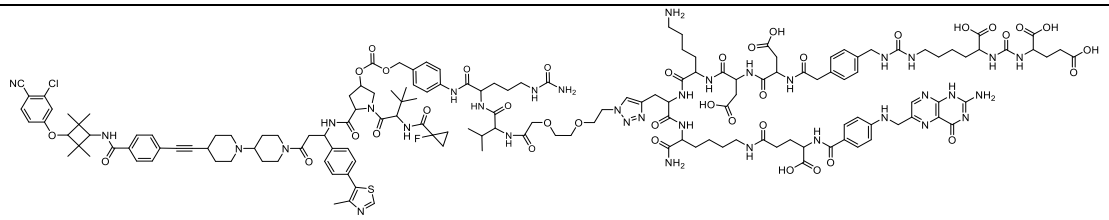
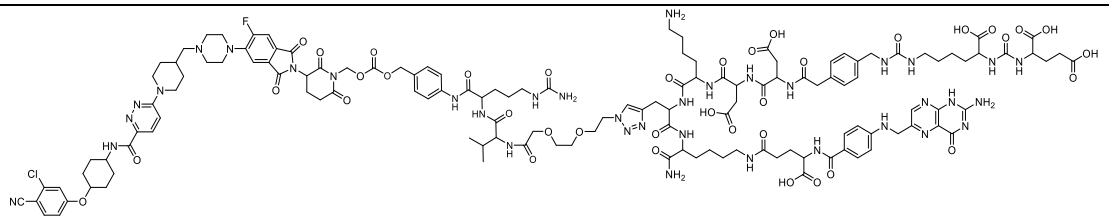
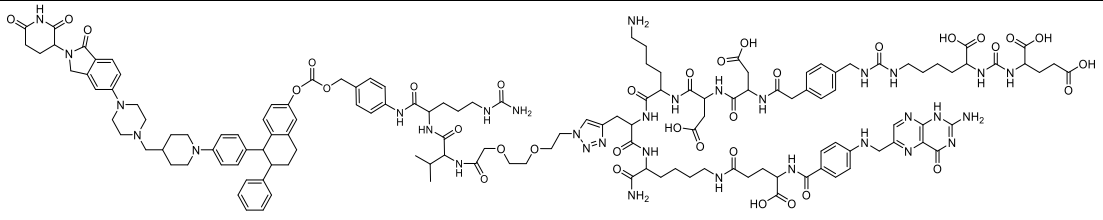
ii) wherein the conjugate compound has the following structures:

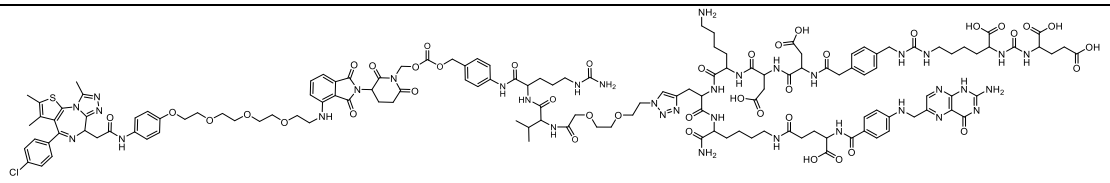
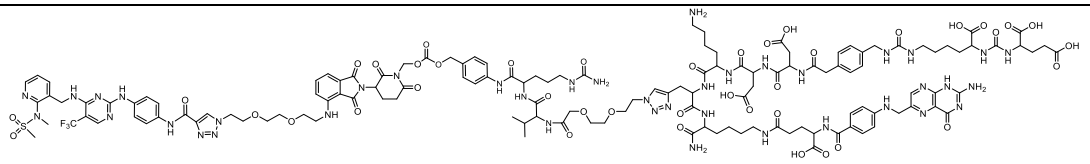
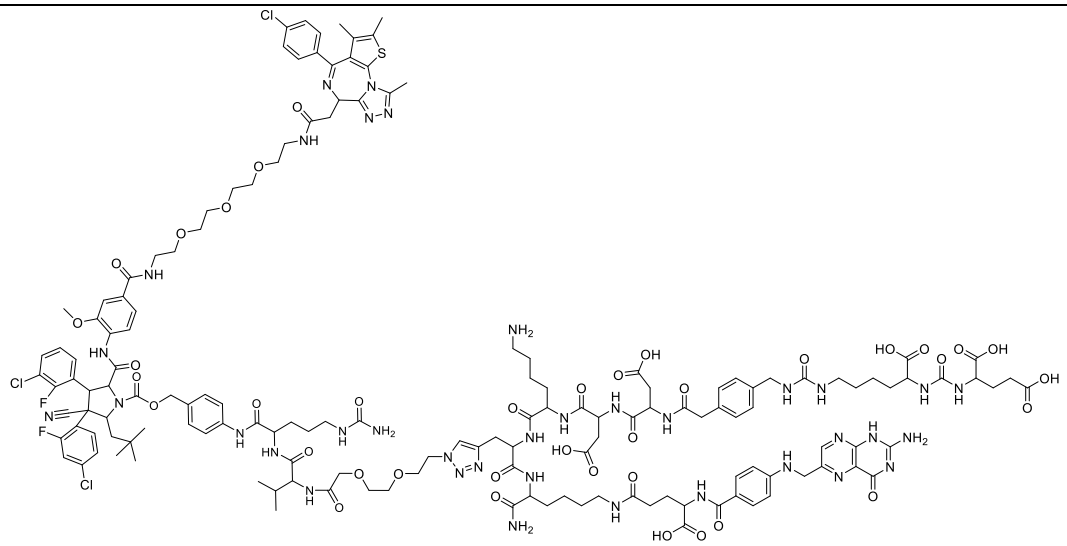
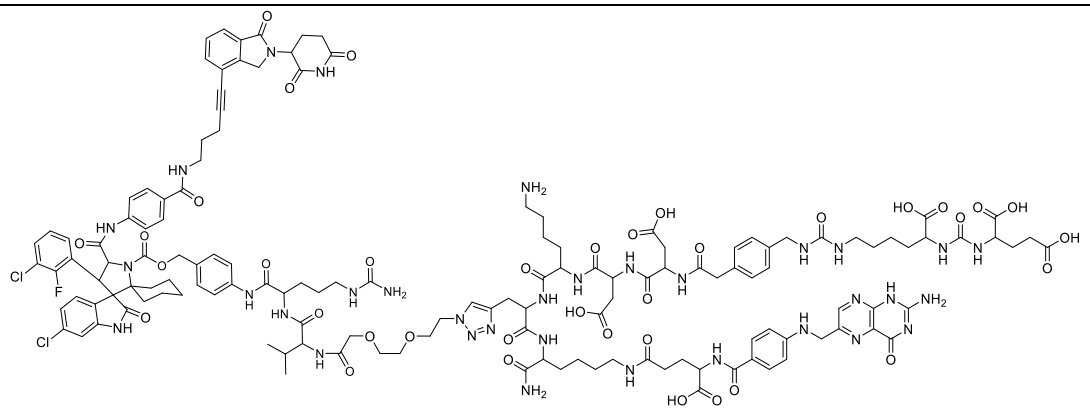
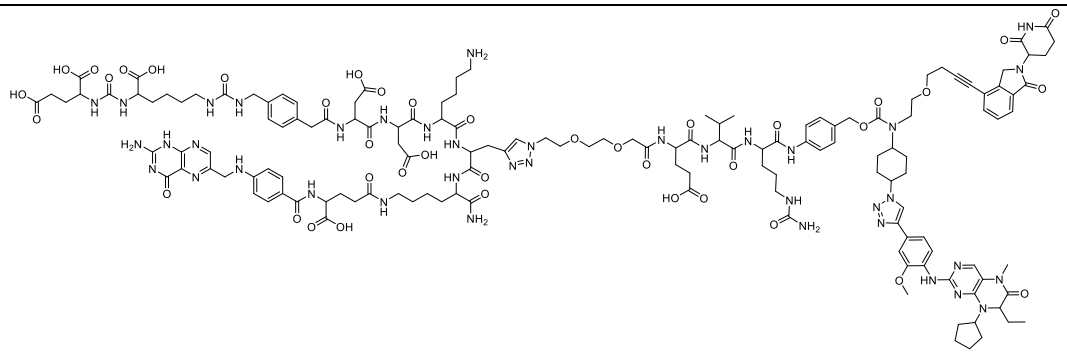
CR202CE	
CR202CH	

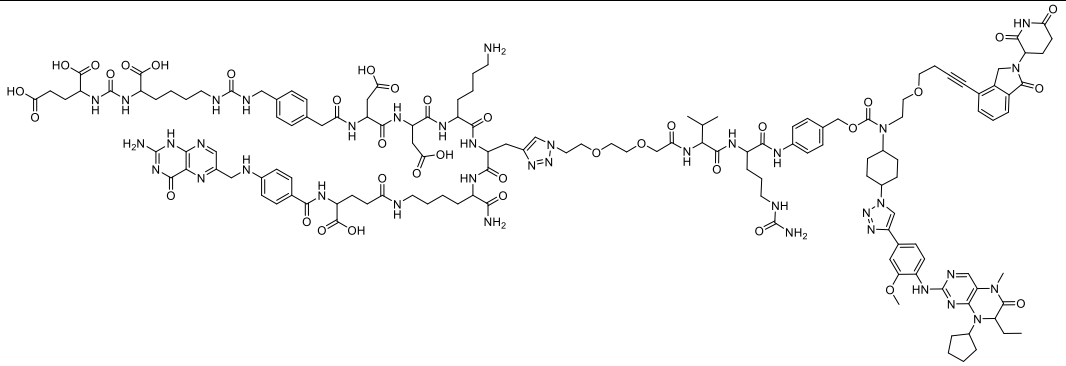
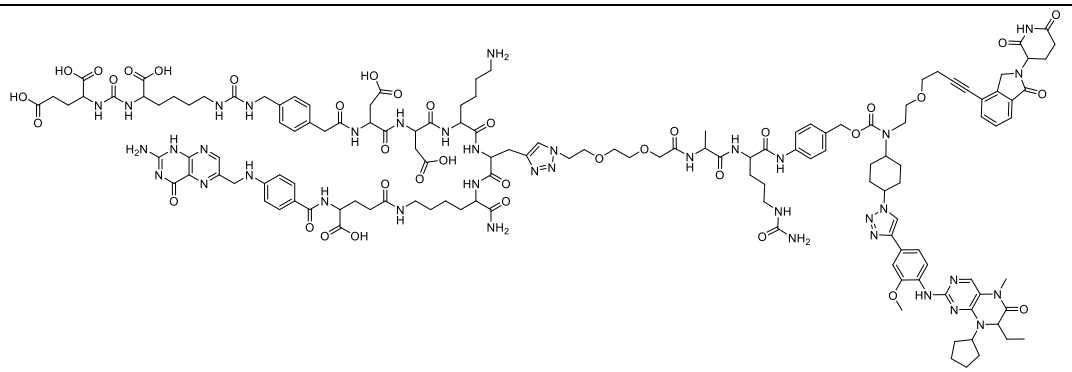
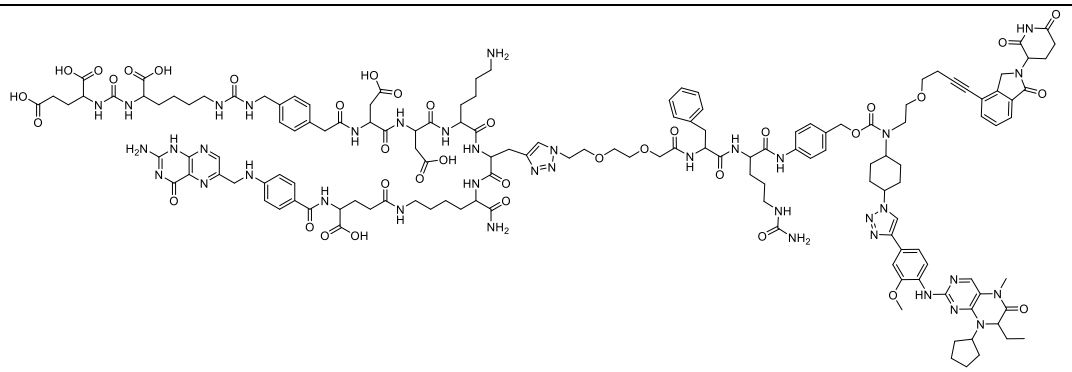
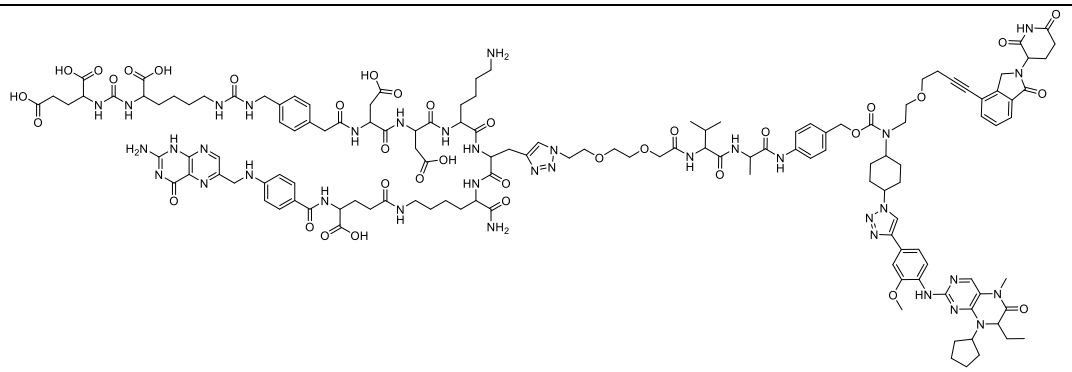
CR202CK	
CR202CN	
CR202CR	
CR202F0	

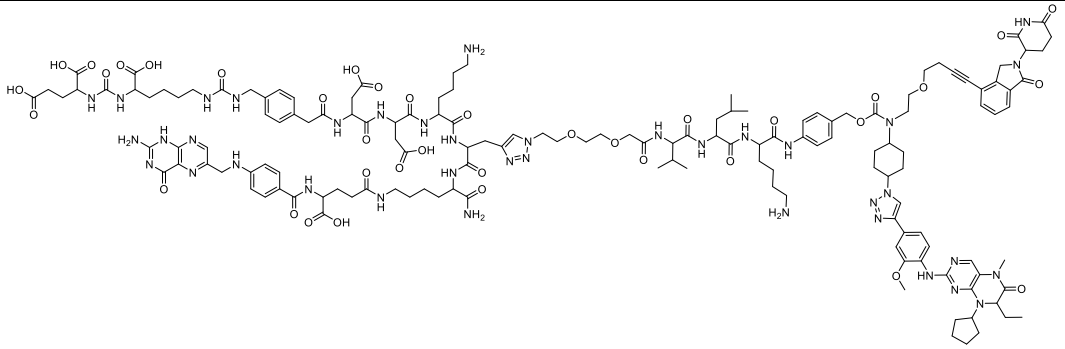
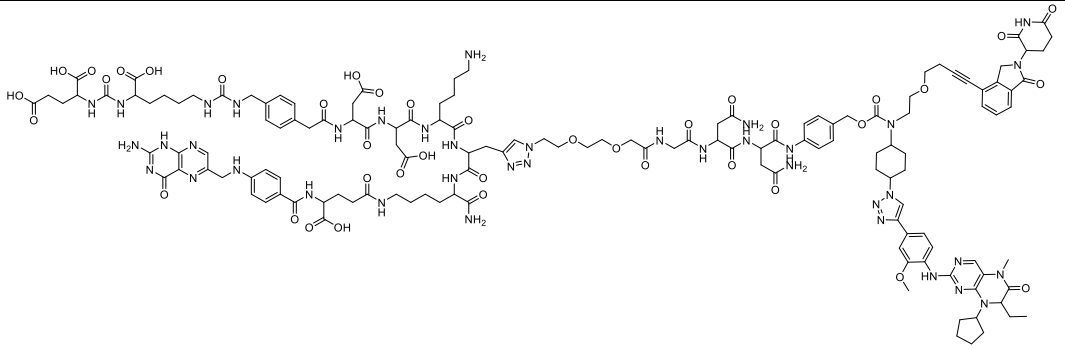
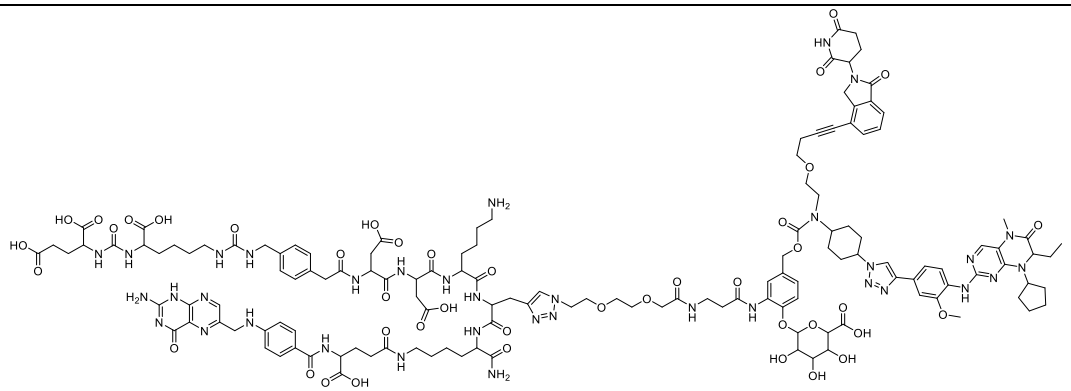
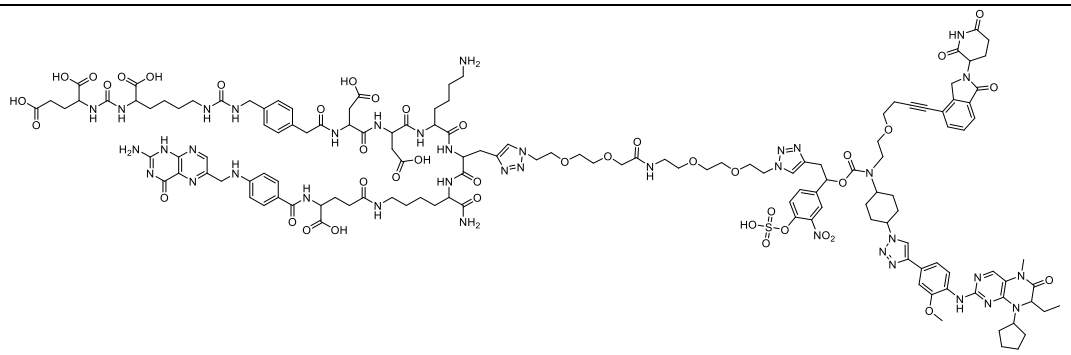
CR202F2	
CR20214	
CR20282	
CR20285	

CR20287	
CR20293	
CR20295	
CR20297	

CR202EF	
CR202W5	
CR202W6	
CR202W7	
CR202W8	
CR202W9	
CR202X0	
CR202X1	

CR202X2	
CR202X3	
CR202Y3	
CR202Y5	
CR202V4	

CR202V5	
CR202V6	
CR202V7	
CR202Z6	

CR202V8	
CR202V9	
CR202AL	
CR202W1	
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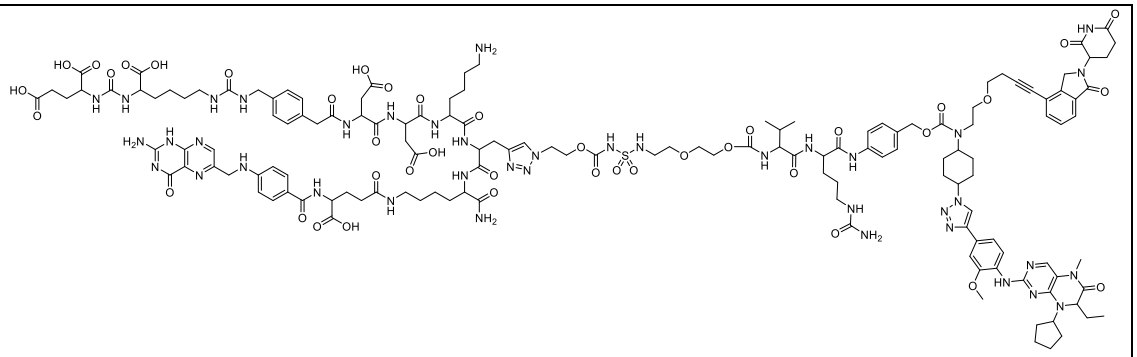
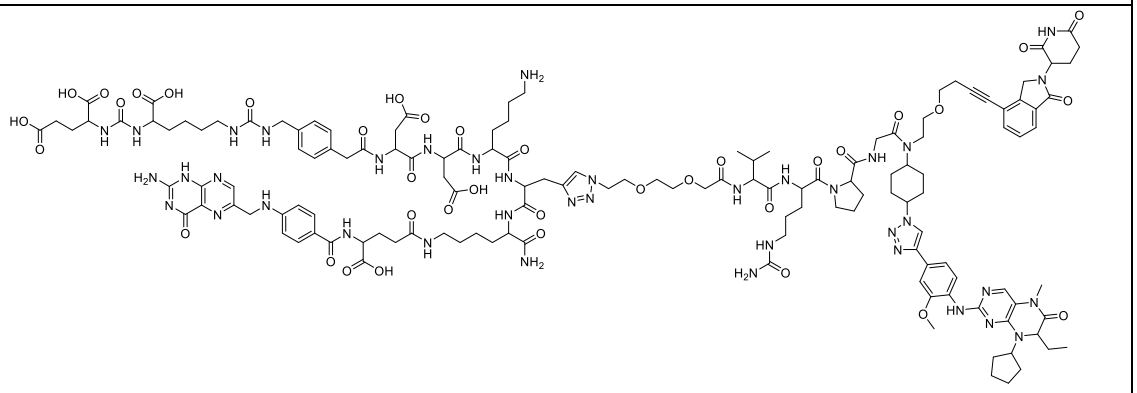
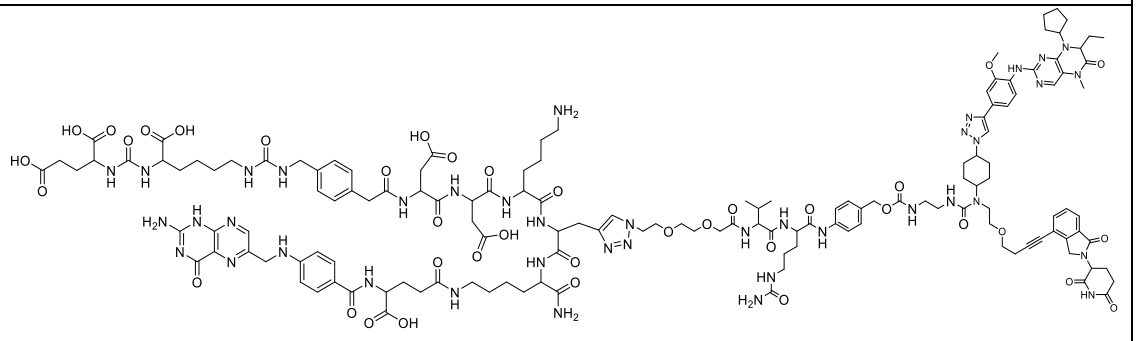
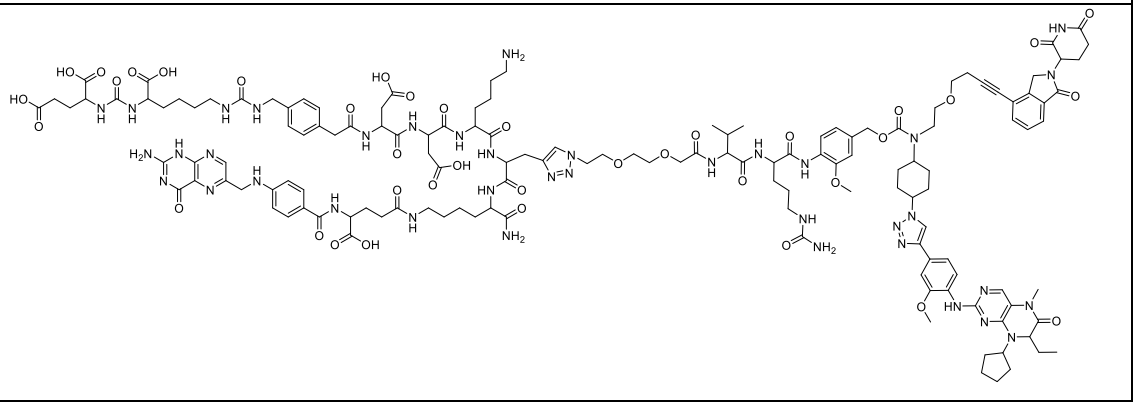
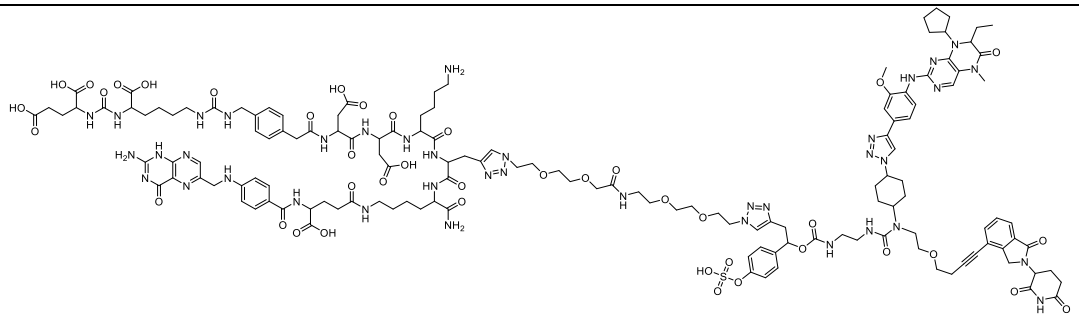
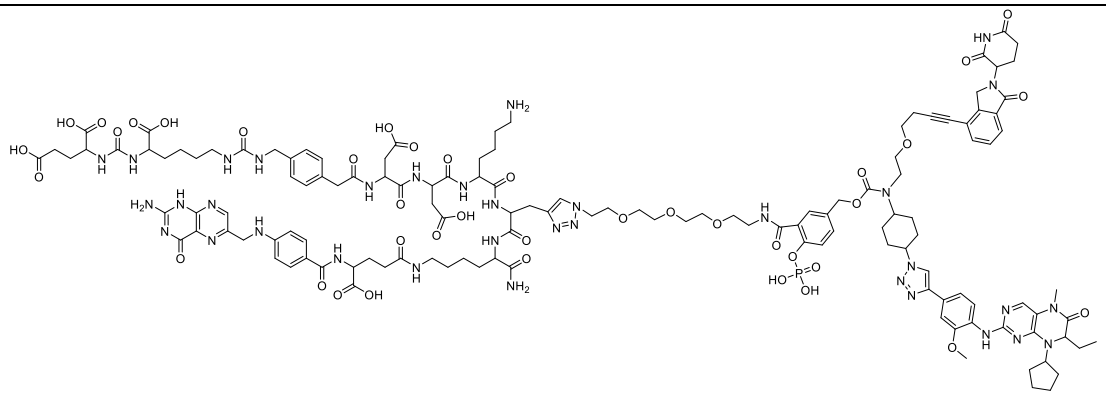
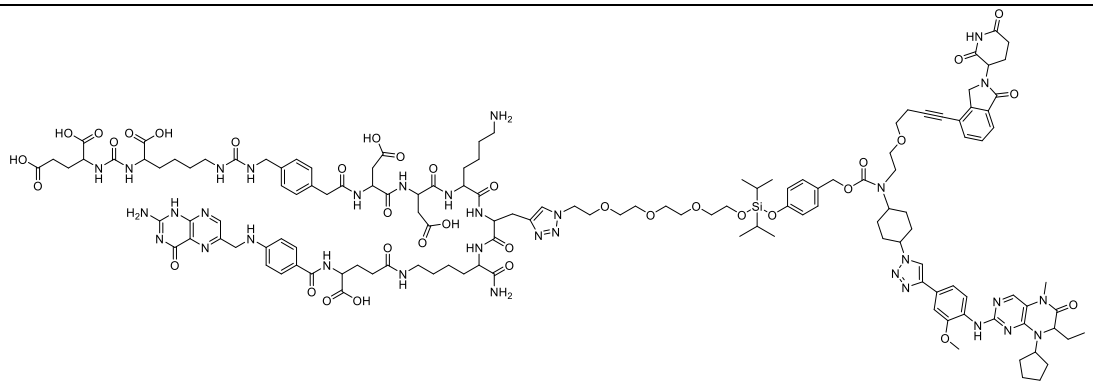
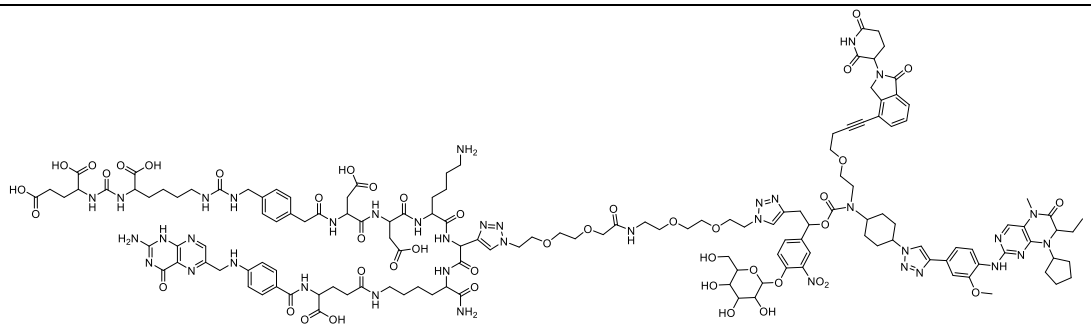
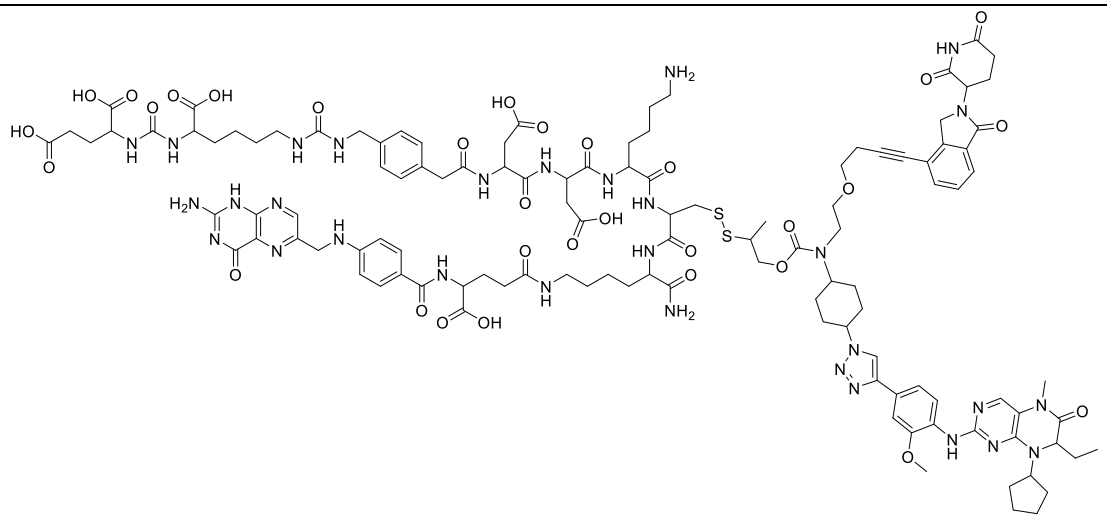
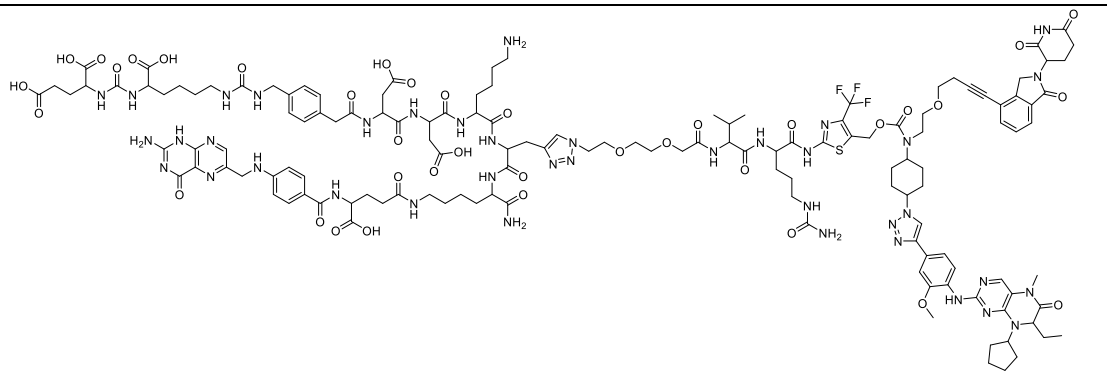
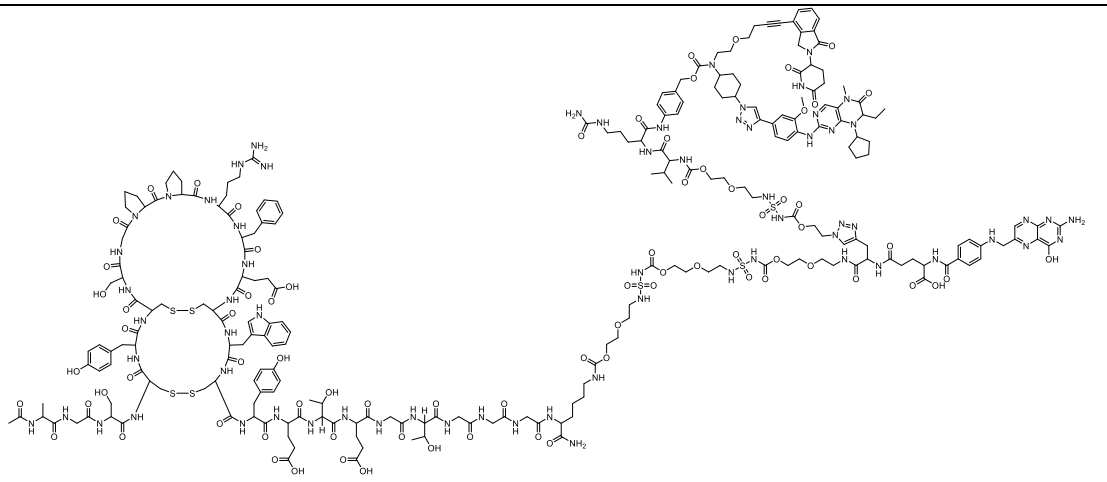
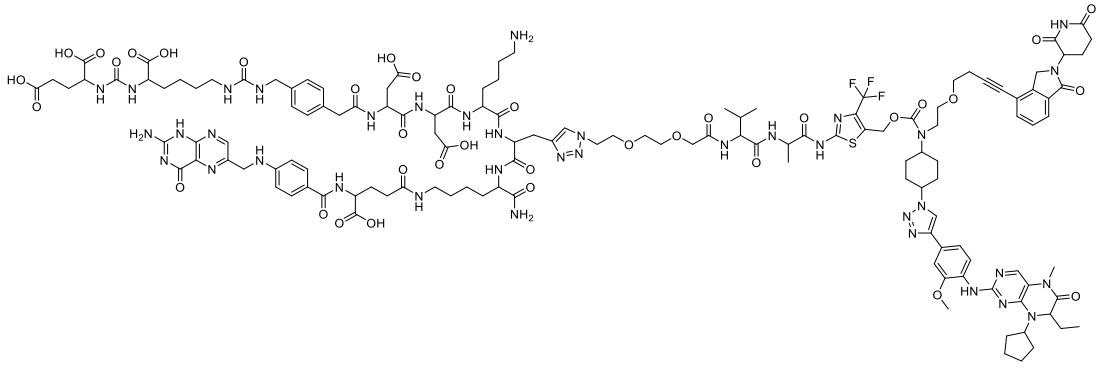
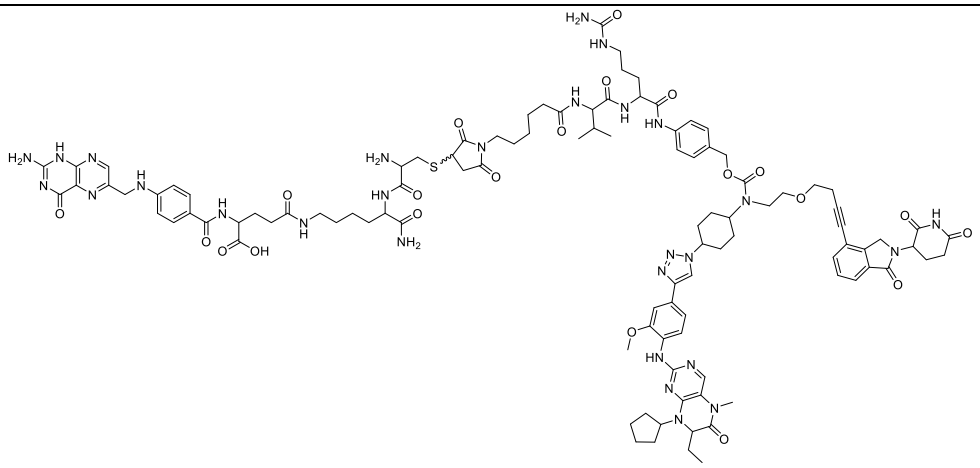
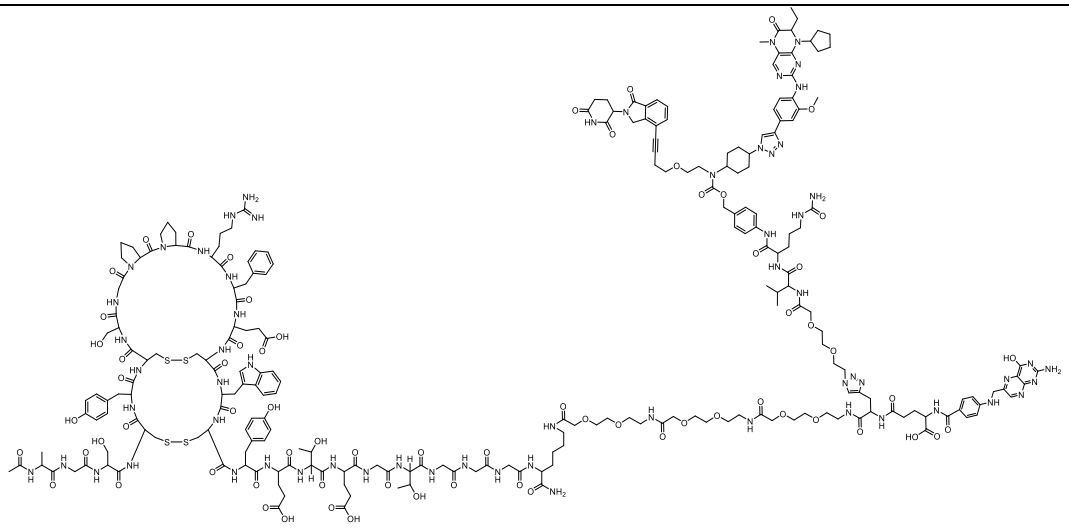
	
CR202GQ	
CR202HJ	
CR202FU	

CR202JG	
CR202LB	
CR202HT	
CR202HU	

CR202HV	
CR202FX	
CR202HR	
CR202GC	

CR202MT	
CR202EZ	

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11. A pharmaceutical composition, wherein the pharmaceutical composition has any one of the following definitions:

i) comprising the conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-10, and a pharmaceutically acceptable carrier; and

ii) comprising the conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-10, and a pharmaceutically acceptable carrier;

wherein the composition is for intravenous, subcutaneous, oral, intramuscular, or intraventricular administration.

12. A conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-10 or the pharmaceutical composition according to claim 11 for use in treating a disease, optionally, wherein the disease is: a cancer, an immune disease, a cardiovascular disease, a metabolic disease, or a neurological disease.

13. Use of the conjugate compound or the pharmaceutically acceptable salt thereof according to any one of claims 1-10 or the pharmaceutical composition according to claim 11 in the manufacture of a medicament for treating a disease, optionally, wherein the disease is selected from the following group: a cancer, an immune disease, a cardiovascular disease, a metabolic disease, and a neurological disease.

14. The conjugate compound or the pharmaceutically acceptable salt thereof or the pharmaceutical composition for use according to claim 12, or the use according to claim 13, wherein any one of the following definitions is met:

i) wherein the cancer is characterized by cancer cells overexpressing FOLR1, TRPV6, PSMA, or c-MET;

ii) wherein the cancer is characterized by cancer cells overexpressing FOLR1, TRPV6, PSMA, or c-MET;

wherein the cancer is characterized by cancer cells overexpressing FOLR1 and TRPV6, FOLR1 and c-MET, c-MET and TRPV6, c-MET and PSMA, PSMA and TRPV6, or FOLR1 and PSMA;

iii) wherein the disease is characterized by expression of the target protein or abnormal expression of the target protein in the subject;

iv) wherein the cancer is selected from the following group: human breast ductal carcinoma, human brain astroblastoma, transitional cell papilloma of the bladder, prostate cancer, breast cancer, lung cancer, kidney cancer, leukemia, ovarian cancer, gastric cancer, cervical cancer, uterine cancer, endometrial cancer, liver cancer, colon cancer, thyroid cancer, pancreatic cancer, colorectal cancer, esophageal cancer, testicular cancer, skin cancer, lymphoma, and multiple myeloma;

v) wherein the immune disease is an autoimmune disease; optionally, the autoimmune disease is selected from the following group: connective tissue disorder, systemic sclerosis, rheumatoid arthritis, and systemic lupus erythematosus;

vi) wherein the cardiovascular disease is selected from the following group: angina pectoris, myocardial infarction, stroke, heart attack, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, cardiac arrhythmia, and congenital heart disease;

vii) wherein the metabolic disease is selected from the following group: diabetes, gout, obesity, hypoglycemia, hyperglycemia, and dyslipidemia; and

viii) wherein the neurological disease is selected from the following group: Alzheimer's disease, Parkinson's disease, Huntington's disease, head injury, multiple sclerosis, vertigo, coma, and epilepsy.

15. The conjugate compound or the pharmaceutically acceptable salt thereof or the pharmaceutical composition for use according to claim 12, wherein the conjugate compound or the pharmaceutically acceptable salt thereof or the pharmaceutical composition is used in combination with one or more therapeutic agents.

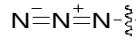
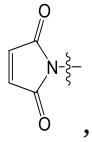
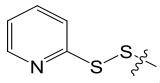
16. The use according to claim 13, wherein the medicament comprises one or more therapeutic agents in combination with the conjugate compound or the pharmaceutically acceptable salt thereof or the pharmaceutical composition.

17. A compound or a salt thereof, wherein the compound has any one of the following definitions:

i) wherein the compound has the following structure:

$$L^{a}\text{-}(EG)n^{1}\text{-}(D)n^{5}\text{-}(CH_2)n^{2}\text{-}(B)n^{6}\text{-}(AA)n^{3}\text{-}(CH_2CH_2\text{-}Q)n^{4}\text{-}L^{b},$$

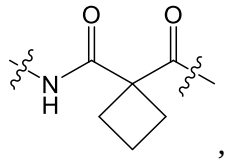
wherein,

L^a is , , or ;

EG is $-CH_2CH_2O-$ or $-OCH_2CH_2-$; n^1 is an integer of 0-6;

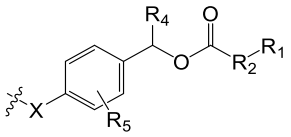
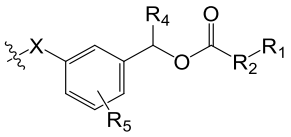
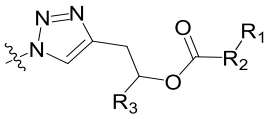
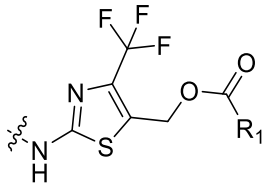
n^2 is an integer of 0-8;

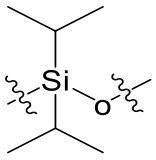
D is $-C(=O)-NH-S(=O)_2-NH-$; n^5 is 0 or 1;

B is $-C(=O)-$, , $-NH-CH_2CH_2-C(=O)-$, $-C(=O)-NH-$, $-CH(CH_3)-CH_2-O-$, $-CH_2CH_2O-$, $-NH-C(=O)-$, or $-NH-$; n^6 is an integer of 0-3;

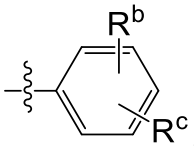
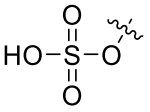
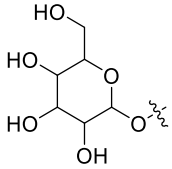
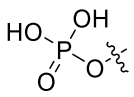
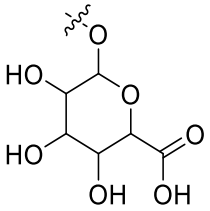
AA is each independently an amino acid residue; n^3 is an integer of 0-5;

Q is each independently $-C(=O)-$, $-O-$, or a bond; n^4 is an integer of 0-3;

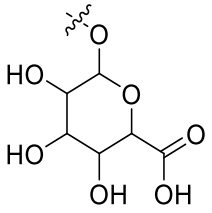
L^b is , , , , $-OH$, or $-NH-CH_2-OH$;

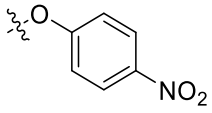
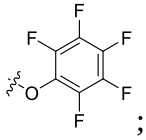
wherein X is a bond, $-NH-$, $-C(=O)-$, oxygen, or ;

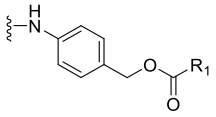
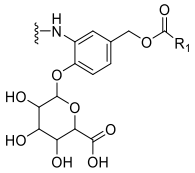
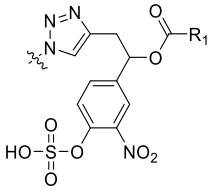
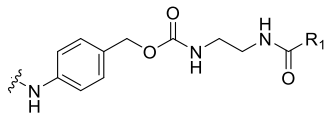
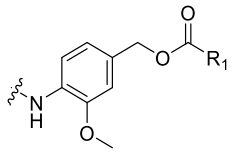
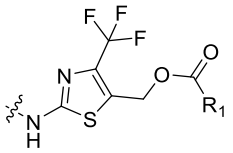
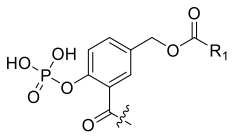
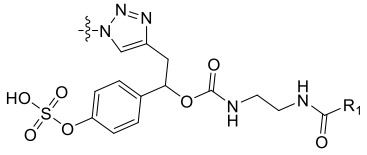
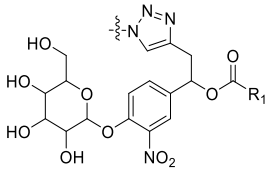
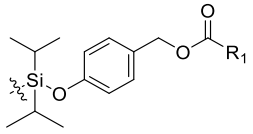
R_2 is a bond, $-O-CH_2-$, or $-NH-CH_2CH_2-NH-C(=O)-$;

R_3 is hydrogen or , wherein R^b and R^c are each independently hydrogen, nitro, , , , or ;

R_4 is hydrogen or C_{1-8} alkyl;

R_5 is hydrogen, amino, nitro, phosphate group, -OR[a], or  ; wherein R[a] is methyl, ethyl, propyl, or isopropyl;

R_1 is a leaving group, preferably R_1 is halogen (e.g., chlorine), , or ;

preferably, L^b is , , , -OH, -NH-CH_2-OH, , , , , , , or ;

preferably, EG is -CH_2CH_2O-;

preferably, n^1 is 0 or 2;

preferably, n^2 is 1, 4, or 5;

preferably, n^5 is 0;

preferably, n^6 is 1 or 3;

preferably, n^1 is 2, n^2 is 1, n^3 and n^4 are 0, and L^b is -OH;

preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu,

Leu, Lys, Ala, Gly, Phe, Gln, Pro, or Asn;

preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, -Phe-Cit-, -Val-Ala-, -Gly-Gly-Phe-Gly-, -Cit-, -Val-Leu-Lys-, -Val-Cit-Pro-Gly-, -Gly-Asn-Asn-, and -Ala-Ala-Asn-;

preferably, when n^4 is 1, Q is -C(=O)-;

preferably, when n^4 is 2, Q are -O- and -C(=O)-, respectively;

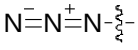
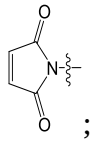
preferably, when n^4 is 3, Q are -O-, -O-, and a bond, respectively; or

preferably, n^4 is 0;

ii) wherein the compound has the following structure:

$$L^a\text{-}(EG)n^1\text{-}(D)n^5\text{-}(CH_2)n^2\text{-}(B)n^6\text{-}(AA)n^3\text{-}(CH_2CH_2\text{-}Q)n^4\text{-}L^b$$

wherein,

L^a is  or ;

EG is -CH_2CH_2O-; n^1 is an integer of 2-4;

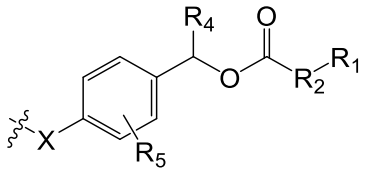
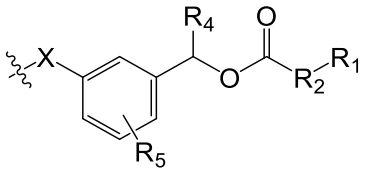
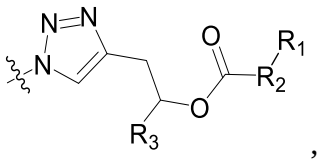
D is -C(=O)-NH-$S(=O)_2$-NH-; n^5 is 0 or 1;

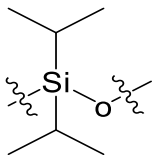
n^2 is an integer of 0-5;

B is -C(=O)-, -C(=O)-NH-, -CH_2CH_2O-, -NH-CH_2CH_2-C(=O)-, or -NH-; n^6 is an integer of 0-3;

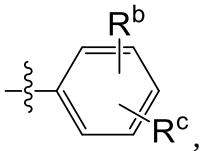
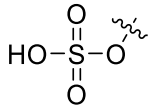
AA is each independently an amino acid residue; n^3 is an integer of 0-3;

Q is each independently -C(=O)-, -O-, or a bond; n^4 is an integer of 0-3;

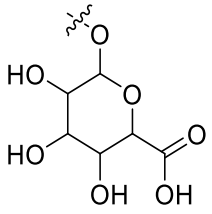
L^b is -OH, , , or ,

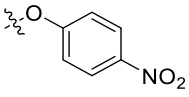
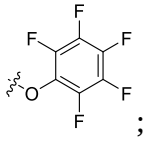
wherein X is a bond, -NH-, -C(=O)-, or ;

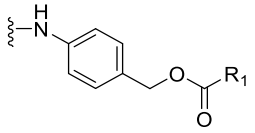
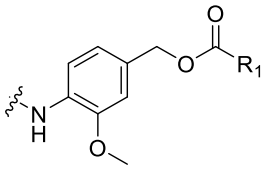
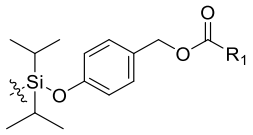
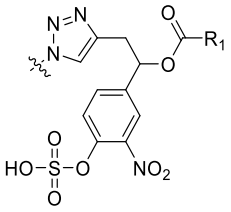
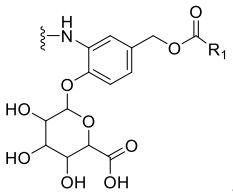
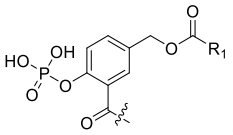
R_2 is a bond;

R_3 is , wherein R^b and R^c are each independently hydrogen, nitro, or ;

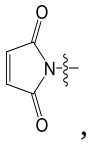
R_4 is hydrogen;

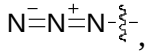
R_5 is hydrogen, -OCH_3, or ;

R_1 is a leaving group, preferably R_1 is halogen (e.g., chlorine), , or ;

preferably, L^b is -OH, , , , , , or ;

preferably, when n^5 is 1, n^2 and n^4 are both 0;

preferably, L^a is , and n^1, n^5, and n^4 are all 0;

preferably, L^a is , and n^2 is 1 or 2;

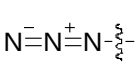
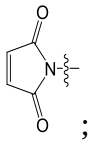
preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu, or Ala; or

preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, and -Val-Ala-;

iii) wherein the compound has the following structure:

$$L^a\text{-}(EG)n^1\text{-}(CH_2)n^2\text{-}(C{=}O)\text{-}(AA)n^3\text{-}L^b$$

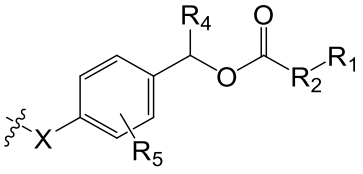
wherein,

L^a is  or ;

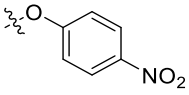
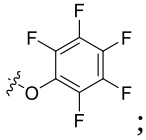
EG is $-CH_2CH_2O-$; n^1 is an integer of 0-4;

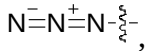
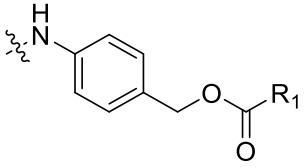
n^2 is an integer of 0-5;

AA is each independently an amino acid residue; n^3 is an integer of 0-3;

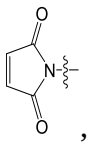
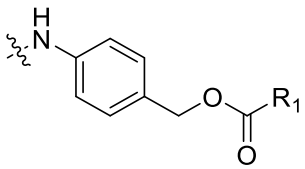
L^b is  or -OH,

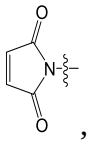
wherein X is -NH-; R_2 is a bond; R_4 is hydrogen; R_5 is hydrogen or $-OCH_3$;

R_1 is a leaving group, preferably R_1 is halogen (e.g., chlorine), , or ;

preferably, L^a is , n^1 is 2, n^2 is 1, and L^b is ;

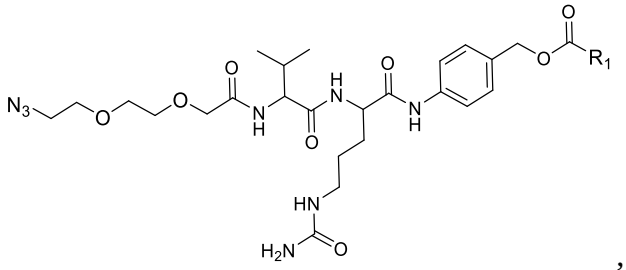
preferably, L^a is , n^1 is 2, n^2 is 1, and L^b is -OH;

preferably, L^a is , n^1 is 0, n^2 is 5, and L^b is ;

preferably, L^a is , n^1 is 0, n^2 is 5, and L^b is -OH;

preferably, AA is each independently Val, Cit, Glu, or Ala amino acid residue; or preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, -Phe-Cit-, -Val-Ala-, -Gly-Gly-Phe-Gly-, -Val-Leu-Lys-, and -Gly-Asn-Asn-;

iv) wherein the compound has a structure selected from the following group: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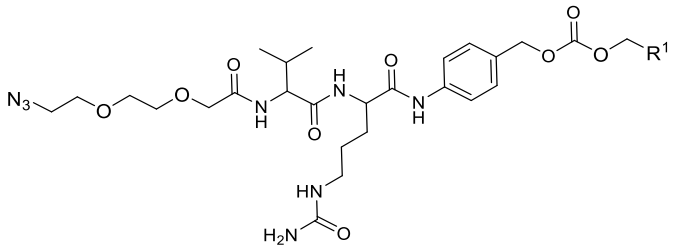
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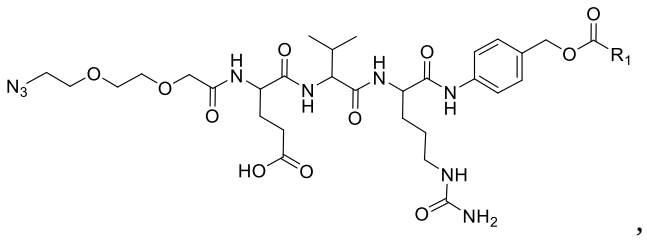
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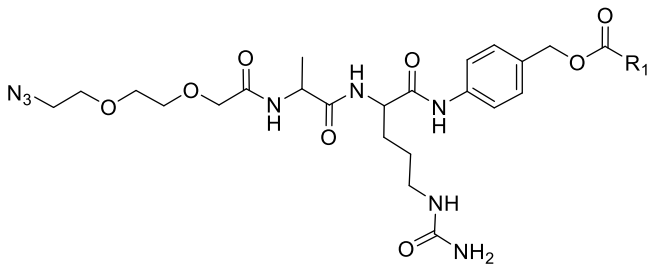
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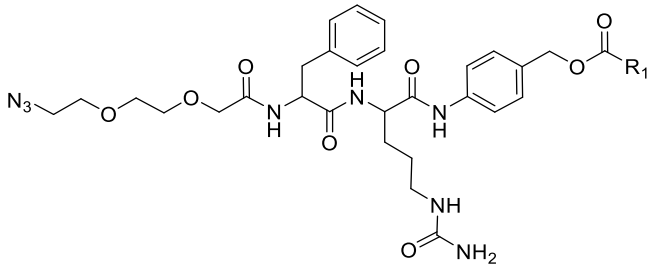
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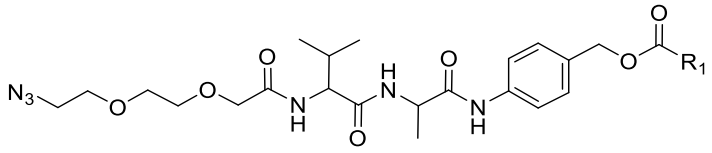

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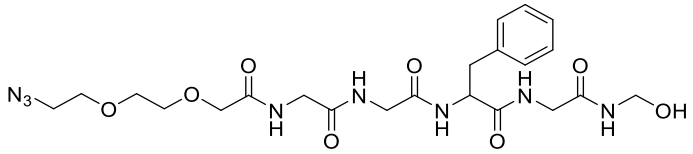

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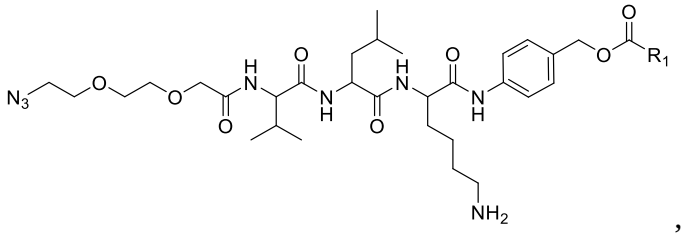

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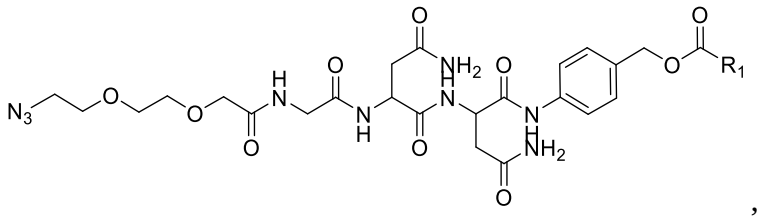

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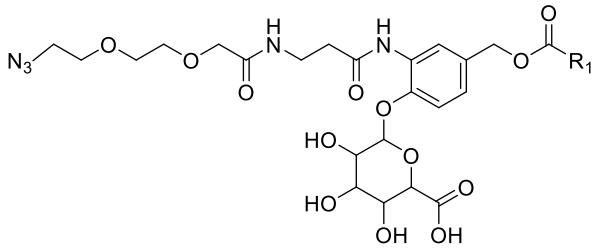

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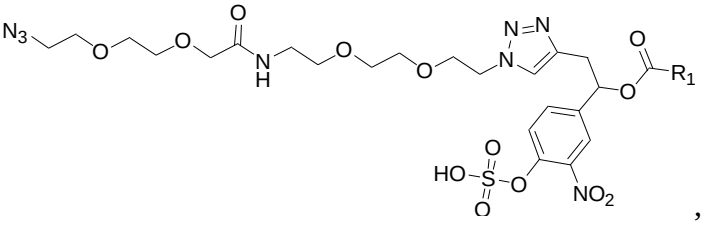

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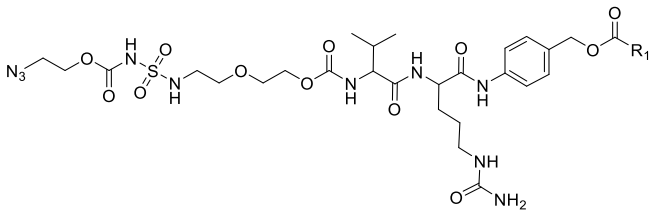

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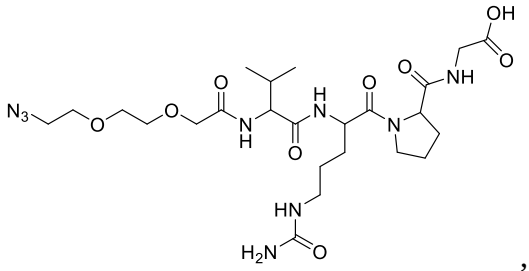
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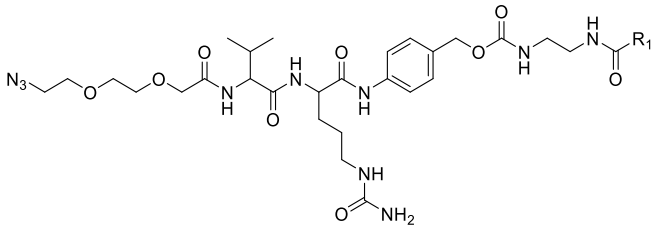
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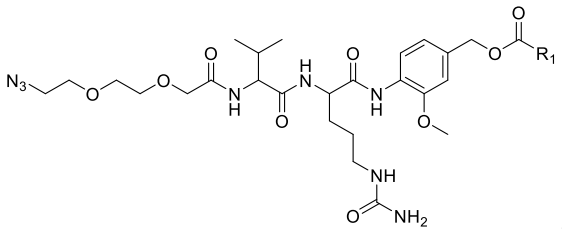
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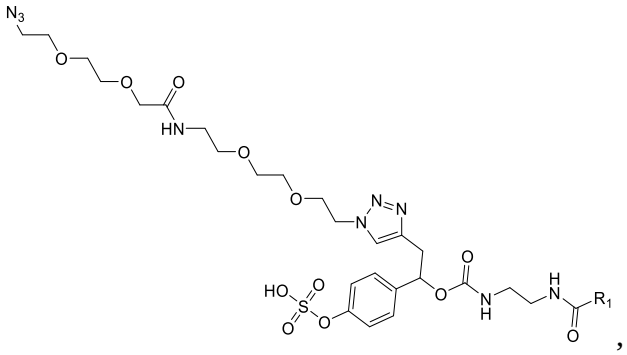
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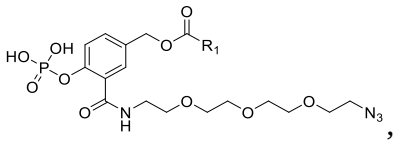
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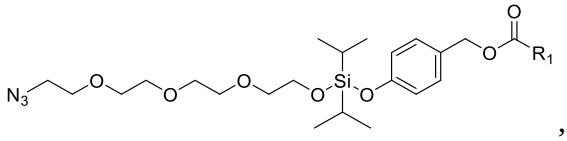
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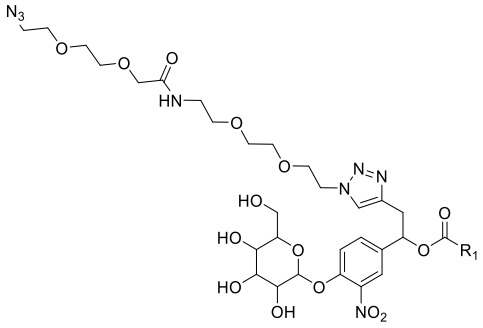
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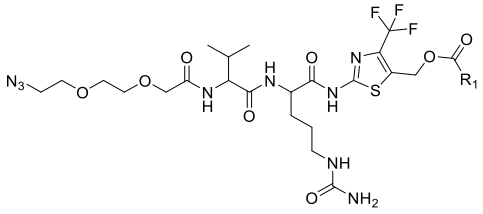
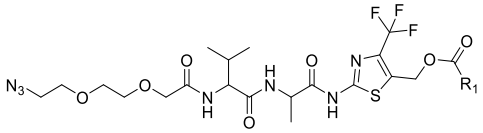
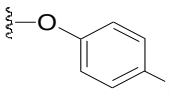
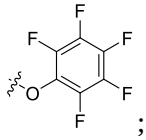
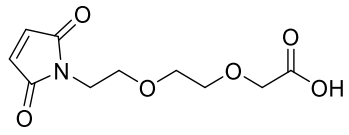

, and


, wherein R_1 is a leaving group, preferably R_1 is halogen (e.g., chlorine), , or ; and

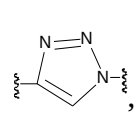
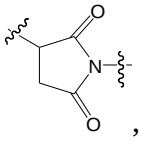
v) wherein the compound is .

18. A conjugate compound or a pharmaceutically acceptable salt thereof, wherein the conjugate compound has any one of the following definitions:

i) wherein the conjugate compound has the following structure:

$$W^a\text{-}L^1\text{-}(EG)n^1\text{-}(D)n^5\text{-}(CH_2)n^2\text{-}(B)n^6\text{-}(AA)n^3\text{-}(CH_2CH_2\text{-}Q)n^4\text{-}L^2\text{-}W^b,$$

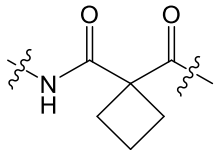
wherein,

L^1 is , , -S-S-, or a bond;

EG is $-CH_2CH_2O-$ or $-OCH_2CH_2-$; n^1 is an integer of 0-6;

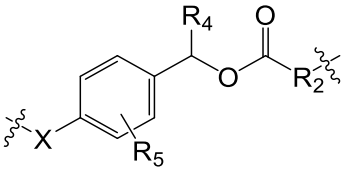
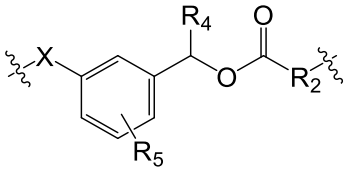
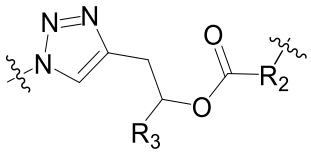
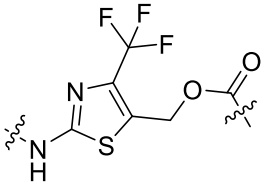
n^2 is an integer of 0-8;

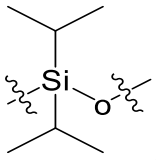
D is $-C(=O)-NH-S(=O)_2-NH-$; n^5 is 0 or 1;

B is each independently -C(=O)-, , -NH-CH_2CH_2-C(=O)-, -C(=O)-NH-, -$CH(CH_3)$-CH_2-O-, -CH_2CH_2O-, -NH-C(=O)-, or -NH-; n^6 is an integer of 0-3;

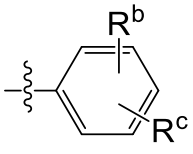
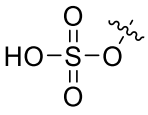
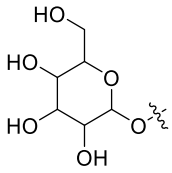
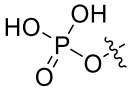
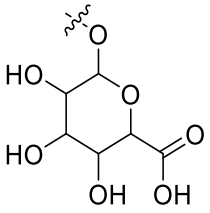
AA is each independently an amino acid residue; n^3 is an integer of 0-5;

Q is each independently -C(=O)-, -O-, or a bond; n^4 is an integer of 0-3;

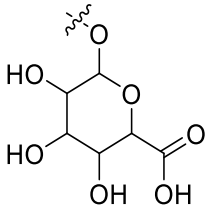
L^2 is , , , , -NH-CH_2-OH, or a bond;

wherein X is a bond, -NH-, -C(=O)-, oxygen, or ;

R_2 is a bond, -O-CH_2-, or -NH-CH_2CH_2-NH-C(=O)-;

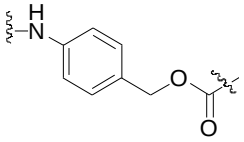
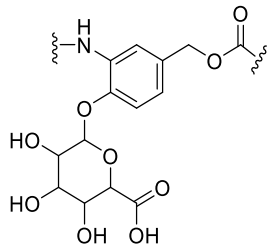
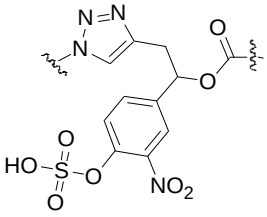
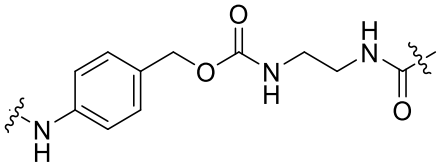
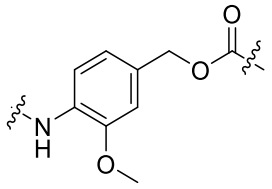
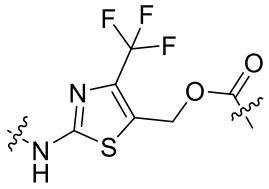
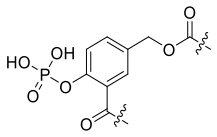
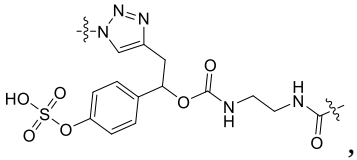
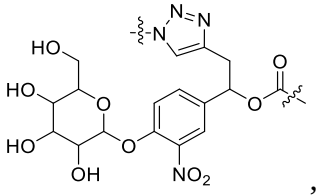
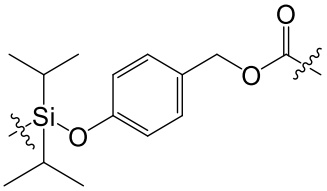
R_3 is hydrogen or , wherein R^b and R^c are each independently hydrogen, nitro, , , , or ;

R_4 is hydrogen or C_{1-8} alkyl;

R_5 is hydrogen, amino, nitro, phosphate group, -OR^a, or ; wherein R^a is methyl, ethyl, propyl, or isopropyl;

W^a and W^b are each independently a payload or a targeted molecule capable of binding

to a cell surface protein;

preferably, L^2 is a bond, , , , -NH-CH_2-O-, , , , , , , or ,

preferably, EG is -CH_2CH_2O-;

preferably, n^1 is 0 or 2;

preferably, n^2 is 1, 4, or 5;

preferably, n^5 is 0;

preferably, n^6 is 1 or 3;

preferably, n^1 is 2, n^2 is 1, n^3 and n^4 are 0, and L^2 is a bond;

preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu, Leu, Lys, Ala, Gly, Phe, Gln, Pro, or Asn;

preferably, -(AA)n^3- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, -Phe-Cit-, -Val-Ala-, -Gly-Gly-Phe-Gly-, -Cit-, -Val-Leu-Lys-, -Val-Cit-Pro-Gly-, -Gly-Asn-Asn-, and -Ala-Ala-Asn-;

preferably, when n^4 is 1, Q is -C(=O)-;

preferably, when n^4 is 2, Q are -O- and -C(=O)-, respectively;

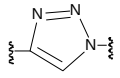
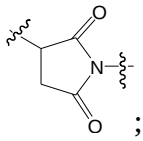
preferably, when n^4 is 3, Q are -O-, -O-, and a bond, respectively; or

preferably, n^4 is 0;

ii) wherein the conjugate compound has the following structure:

$$W^a\text{-}L^1\text{-}(EG)n^1\text{-}(D)n^5\text{-}(CH_2)n^2\text{-}(B)n^6\text{-}(AA)n^3\text{-}(CH_2CH_2\text{-}Q)n^4\text{-}L^2\text{-}W^b$$

wherein,

L^1 is  or ;

EG is $-CH_2CH_2O-$; n^1 is an integer of 2-4;

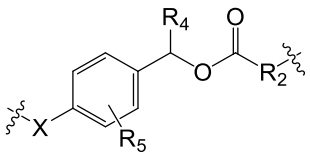
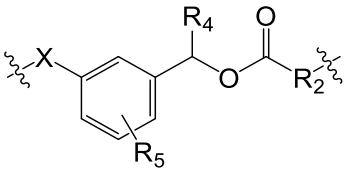
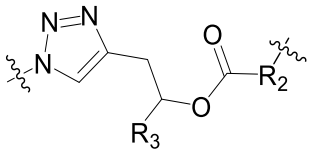
D is $-C(=O)-NH-S(=O)_2-NH-$; n^5 is 0 or 1;

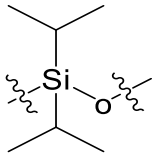
n^2 is an integer of 0-5;

B is $-C(=O)-$, $-C(=O)-NH-$, $-CH_2CH_2O-$, $-NH-CH_2CH_2-C(=O)-$, or $-NH-$; n^6 is an integer of 0-3;

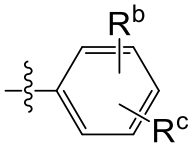
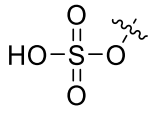
AA is each independently an amino acid residue; n^3 is an integer of 0-3;

Q is each independently $-C(=O)-$, $-O-$, or a bond; n^4 is an integer of 0-3;

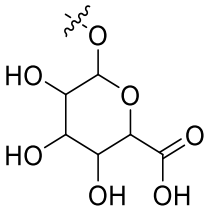
L^2 is , , or ,

wherein X is a bond, -NH-, -C(=O)-, or ;

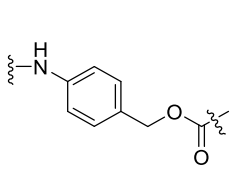
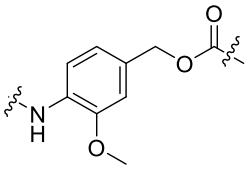
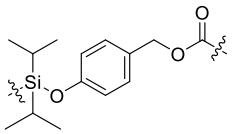
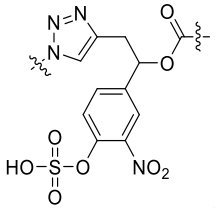
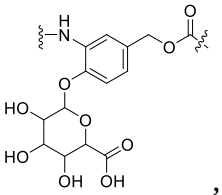
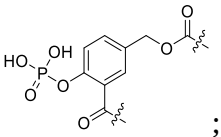
R_2 is a bond;

R_3 is , wherein R^b and R^c are each independently hydrogen, nitro, or ;

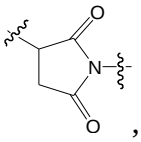
R_4 is hydrogen;

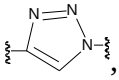
R_5 is hydrogen, -OCH_3, or  ;

W^a and W^b are each independently a payload or a targeted molecule capable of binding to a cell surface protein;

preferably, L^2 is  ,  ,  ,  ,  , or  ;

preferably, when n^5 is 1, n^2 and n^4 are both 0;

preferably, L^1 is  , and n^1, n^5, and n^4 are all 0;

preferably, L^1 is , and n^2 is 1 or 2;

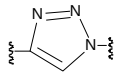
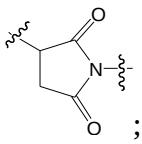
preferably, AA is each independently an amino acid residue formed by Val, Cit, Glu, or Ala; or

preferably, -$(AA)n^3$- is a peptide residue selected from the following group: -Val-Cit-, -Glu-Val-Cit-, -Ala-Cit-, and -Val-Ala-;

iii) wherein the conjugate compound has the following structure:

$$W^a\text{-}L^1\text{-}(EG)n^1\text{-}(CH_2)n^2\text{-}(C{=}O)\text{-}(AA)n^3\text{-}L^2\text{-}W^b$$

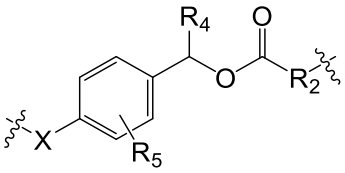
wherein,

L^1 is  or  ;

EG is -CH_2CH_2O-; n^1 is an integer of 0-4; preferably

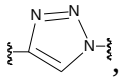
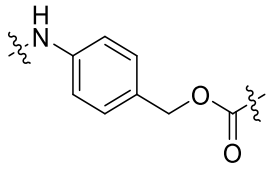
n^2 is an integer of 1-5;

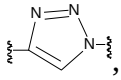
AA is each independently an amino acid residue; n^3 is an integer of 1-4;

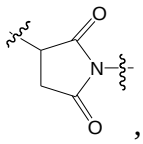
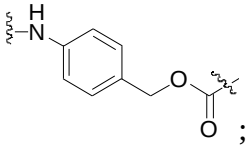
L^2 is  or a bond,

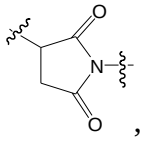
wherein X is -NH-; R_2 is a bond; R_4 is hydrogen; R_5 is hydrogen or $-OCH_3$;

W^a and W^b are each independently a payload or a targeted molecule capable of binding to a cell surface protein;

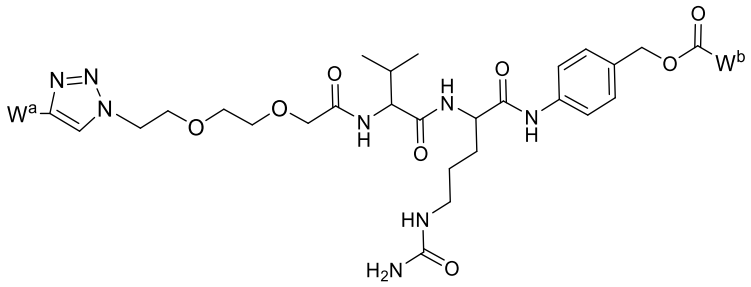
preferably, L^1 is , n^1 is 2, n^2 is 1, and L^2 is ;

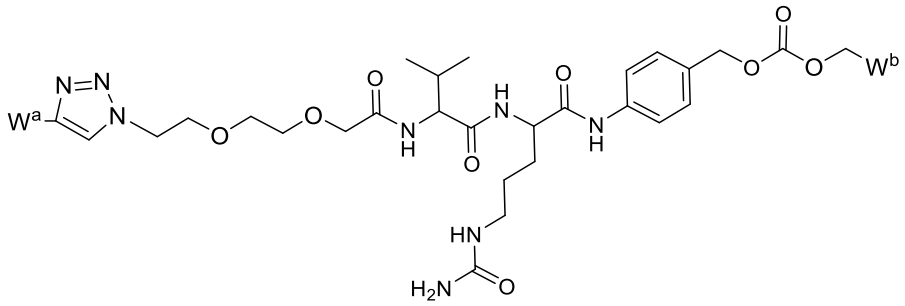
preferably, L^1 is , n^1 is 2, n^2 is 1, and L^2 is a bond;

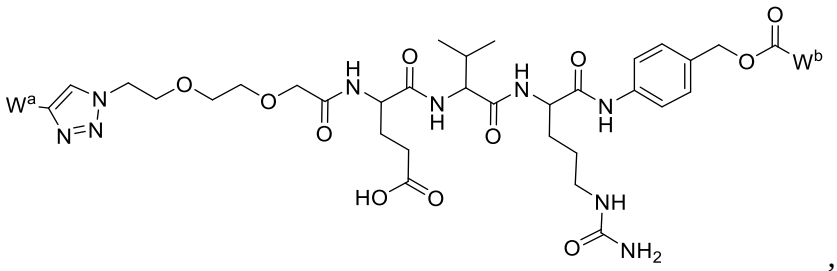
preferably, L^1 is , n^1 is 0, n^2 is 5, and L^2 is ;

preferably, L^1 is , n^1 is 0, n^2 is 5, and L^2 is a bond;

iv) wherein the compound has a structure selected from the following group:

,





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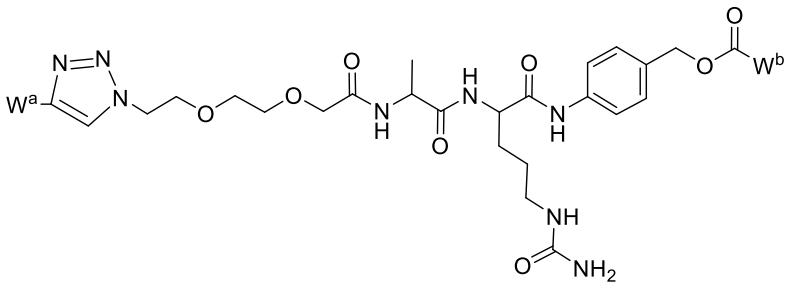

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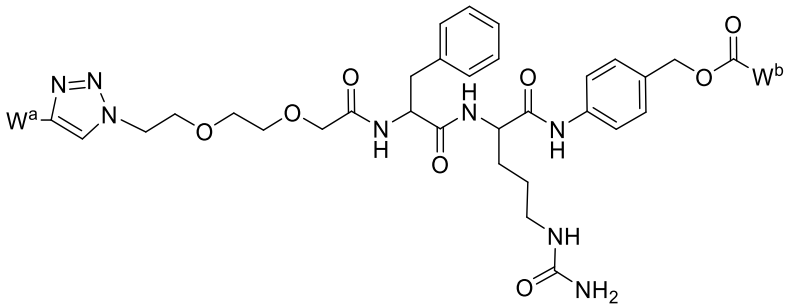

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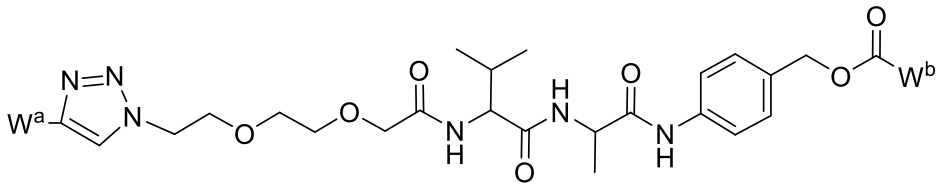

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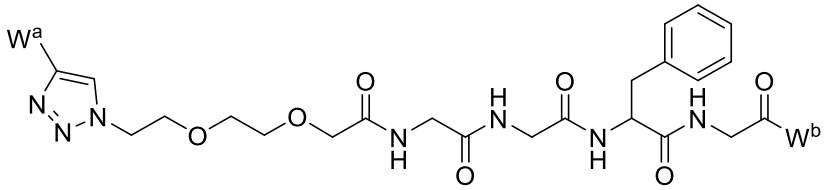

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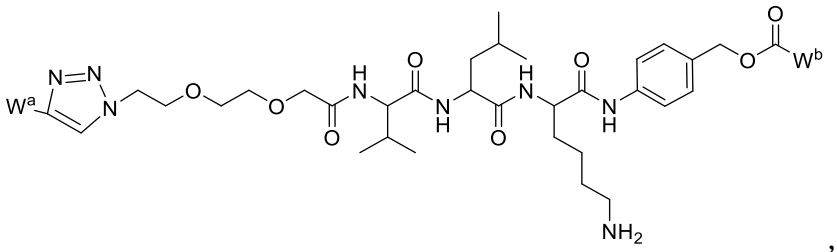

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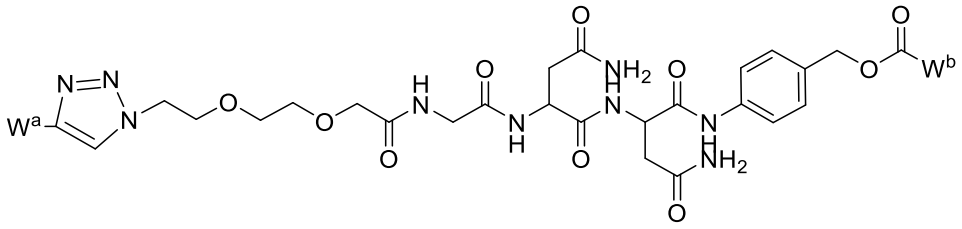

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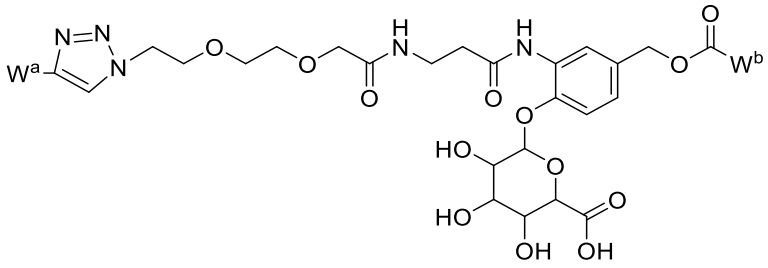

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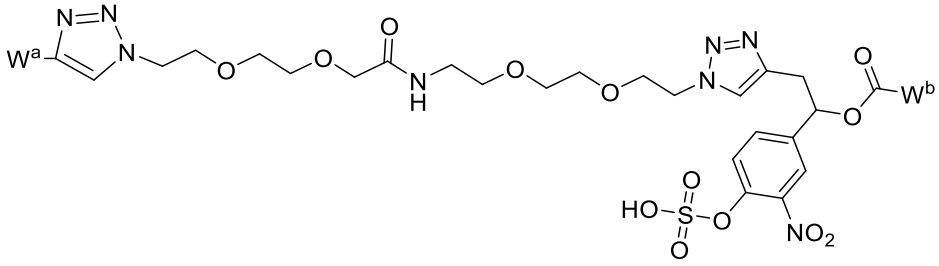

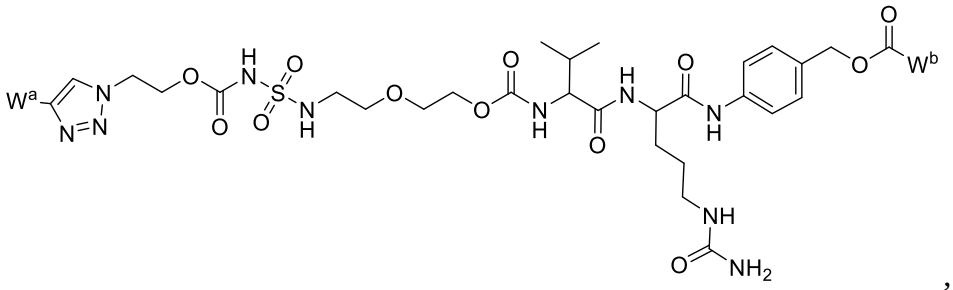

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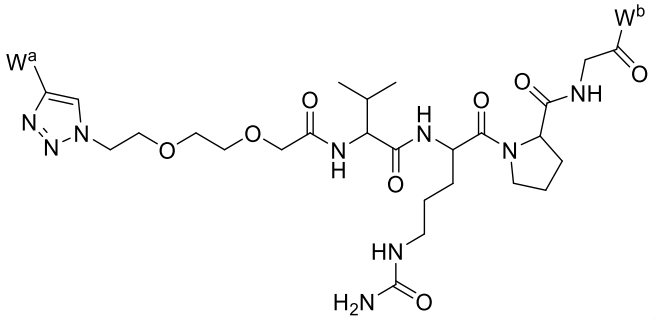

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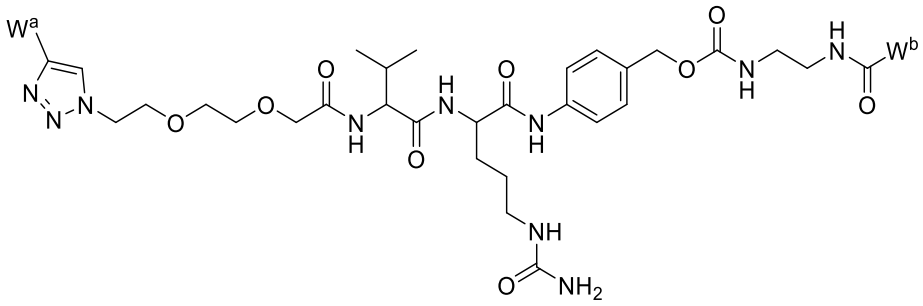

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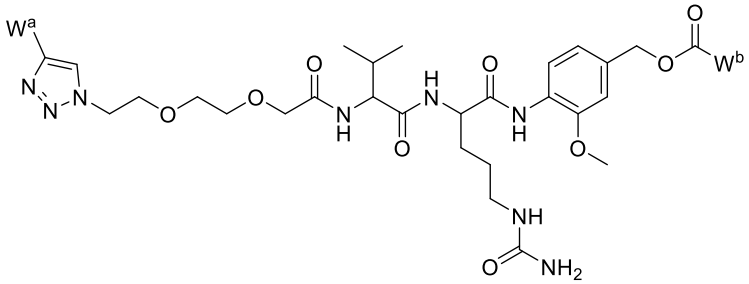

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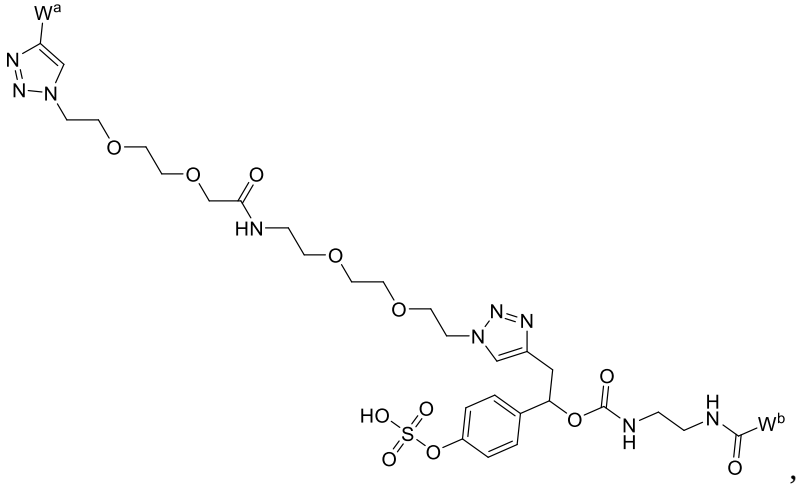

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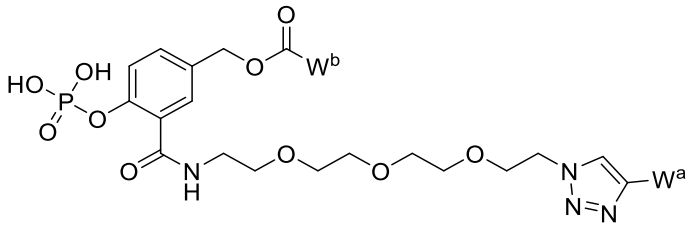

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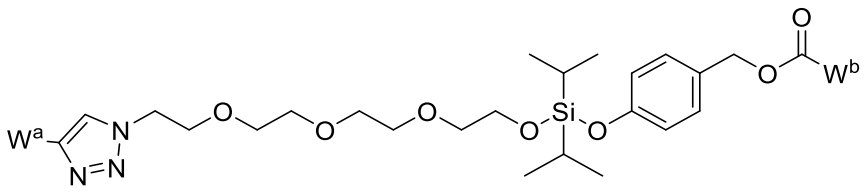

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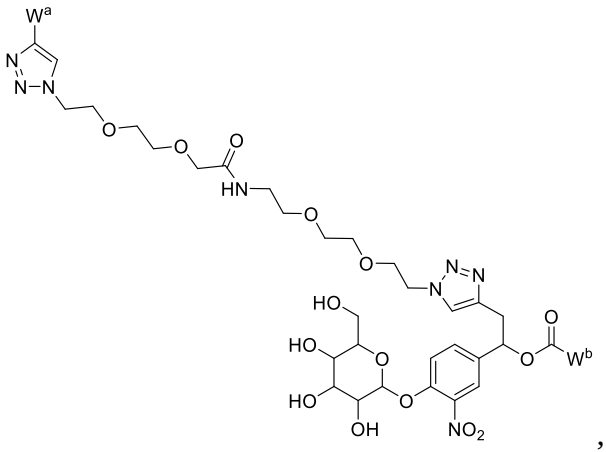
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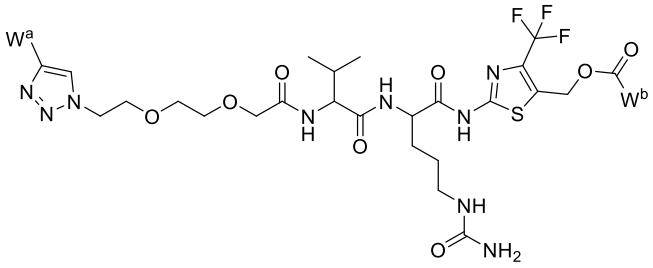
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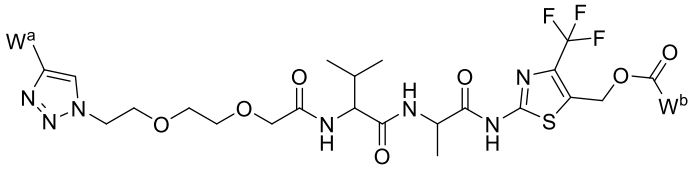
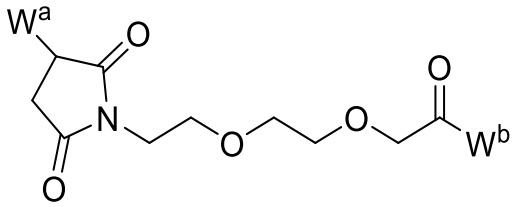
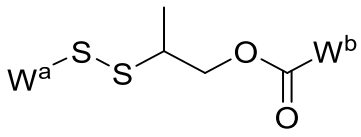
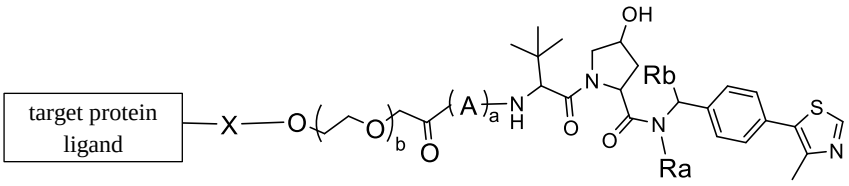

, wherein W^a and W^b are each independently a payload or a targeted molecule capable of binding to a cell surface protein;

v) wherein the conjugate compound is 
, wherein W^a and W^b are each independently a payload or a targeted molecule capable of binding to a cell surface protein; and

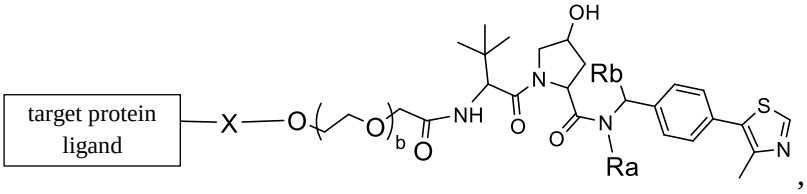
vi) wherein the conjugate compound is 
, wherein W^a and W^b are each independently a payload or a targeted molecule capable of binding to a cell surface protein.

19. A proteolysis targeting chimera or a pharmaceutically acceptable salt thereof,

wherein the proteolysis targeting chimera compound has the following structures:



or



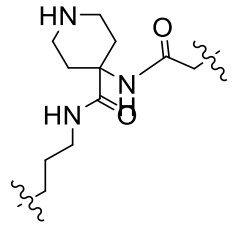
,

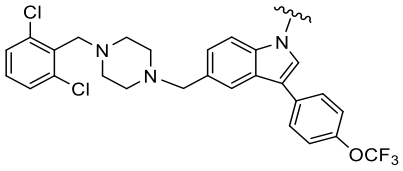
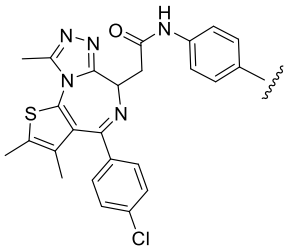
wherein,

Ra and Rb are each independently hydrogen, C_{1-4} alkyl, NH_2, OH, or halogen;

A is an amino acid residue; a is 0 or 1;

b is an integer of 0-5;

X is  or a bond;

the target protein ligand is  or .

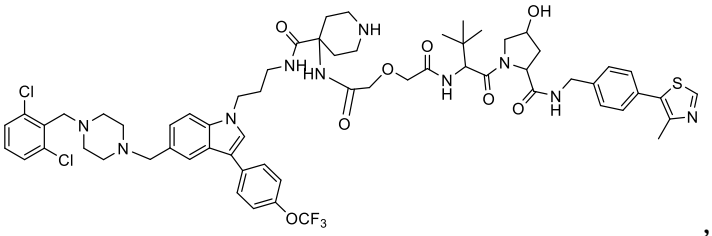
20. The proteolysis targeting chimera or the pharmaceutically acceptable salt thereof according to claim 19, wherein the proteolysis targeting chimera has any one of the following definitions:

i) wherein Ra is hydrogen;

ii) wherein Rb is hydrogen;

iii) wherein A is a Lys-formed amino acid residue; and

iv) wherein the proteolysis targeting chimera compound has a structure selected from the following group: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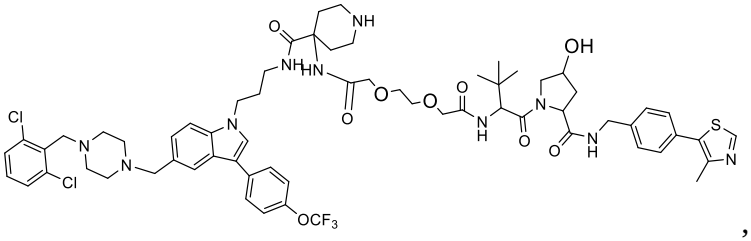
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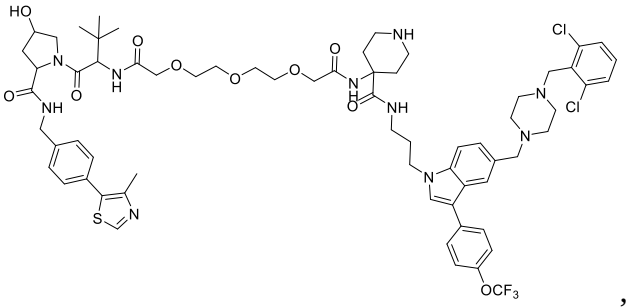
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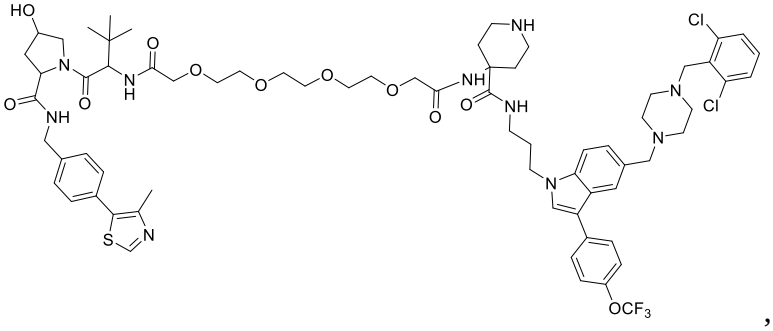
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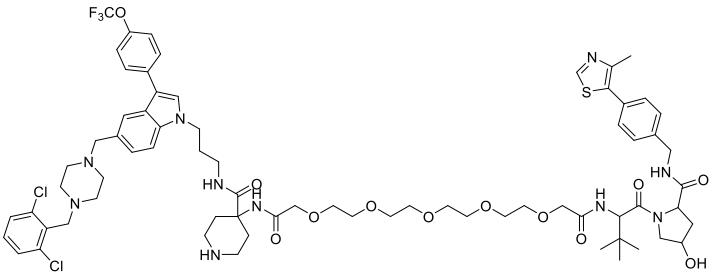
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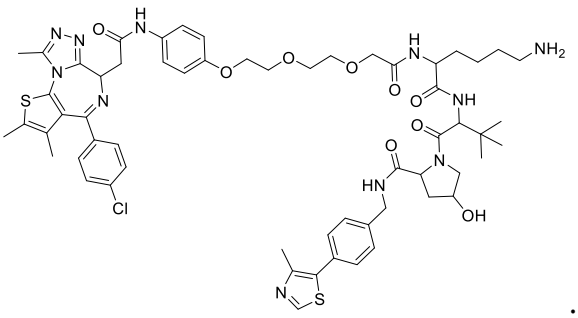

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