

ANTIBODY-DRUG CONJUGATE

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority to the prior application with the patent application No. 2023104680075 filed with China National Intellectual Property Administration on Apr. 27, 2023 and the prior application with the patent application No. 2024101290645 filed with China National Intellectual Property Administration on Jan. 30, 2024, both of which are entitled “ANTIBODY-DRUG CONJUGATE” and are incorporated herein by reference in their entirety.

TECHNICAL FIELD

The present disclosure relates to the field of biotechnology and pharmaceuticals, and particularly to an antibody-drug conjugate, a preparation method therefor, and use thereof.

BACKGROUND

Antibody-drug conjugates (ADCs) are currently one of the hottest spots in the research and development of anti-tumor drugs. To date, there are 14 types of antibody-drug conjugates on the market. They are: Mylotarg approved in 2000 for the treatment of CD33-positive acute myeloid leukemia (AML); Adcetris approved in 2011 for Hodgkin lymphoma; Kadcyla approved in 2013 for HER2-positive breast cancer; Besponsa approved in 2017 for B-cell lymphocytic leukemia; Lumoxiti approved in 2018 for recurrent or refractory hairy cell leukemia; Polivy approved in 2019 for recurrent or refractory diffuse large B-cell lymphoma; Padcev approved in 2019 for urothelial carcinoma; Enhertu approved in 2019 for HER2-positive breast cancer; Trodelvy approved in 2020 for triple negative breast cancer; Akalux approved in 2020 as a photoimmunotherapy drug for head and neck cancer; Zynlonta approved in 2021 for large B-cell lymphoma; Disitamab Vedotin approved in 2021 for HER2-positive gastric cancer; Tivdak approved in 2022 for cervical cancer; and Elahere approved in 2022 for ovarian cancer. It is worth mentioning that Mylotarg was withdrawn from the market in 2010 due to its excessive toxicity, and then re-launched in 2017 after adjusting the clinical dosage. Additionally, Blenrep was granted accelerated approval in 2020 for multiple myeloma, but was later withdrawn from the market due to its unsatisfactory subsequent clinical results.

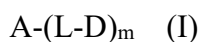
An antibody-drug conjugate comprises three parts: an antibody, a linker, and a bioactive molecule (drug), wherein the antibody is closely related to a disease target, while the linker and the drug determine the efficacy and safety of the ADC, thus being the most critical parts.

Among the marketed ADC drugs, the majority employ the technology developed several decades ago by Seattle Genetics, in which a microtubule inhibitor is used as an active molecule, combined with a cathepsin-cleavable linker, and then conjugated to antibody cysteine via maleimide. ADCs obtained using this technology often exhibit relatively high toxicity, strong hydrophobicity, and poor pharmacokinetic properties. The ADCs obtained by Daiichi Sankyo using a hydrophilic tetrapeptide linker have achieved great improvements, but still show considerable differences in properties compared to naked antibodies. Trodelvy adopts a linker containing polyethylene glycol and salt-forming lysine; although the resulting ADC has relatively good hydrophilicity, it has relatively poor stability. It has been reported in the literature that a linker containing polysarcosine can greatly improve the hydrophilicity of an ADC, but the linker is only suitable for an active molecule containing a secondary amine structure, such as MMAE. For an active molecule with a primary amine structure like exatecan, the carbonamide bond formed by linking the linker has relatively poor stability.

The object of the present disclosure is to solve the above problems by providing a hydrophilic linker that can meet the linkage requirements of most active molecules. Moreover, the resulting ADCs exhibit relatively good stability and hydrophilicity as well as excellent pharmacokinetic properties.

SUMMARY

The present disclosure provides an antibody-drug conjugate having a structure of formula (I), a tautomer, a mesomer, a racemate, an enantiomer, a diastereoisomer, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:



wherein A is a targeting ligand selected from an antibody (e.g., a monoclonal antibody) or an antigen-binding fragment, a small-molecule ligand, and a polypeptide;

L is a linker moiety, with one end linked to the ligand A and the other end linked to a bioactive molecule D;

D is an amino-containing bioactive molecule or a tautomer, a mesomer, a racemate, an enantiomer, a diastereoisomer or an isotopically labeled compound thereof, covalently linked to the linker moiety L via the amino group in its molecular structure;

m represents the molar ratio of the cytotoxic drug molecule to the antibody A (also called DAR, i.e., drug-to-antibody ratio).

m is an integer or a decimal from 1 to 12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

When m is a decimal, it refers to the average number of linker-drug molecules (L-D) conjugated

per antibody unit (A).

In some embodiments, A is selected from an antibody or an antigen-binding fragment thereof targeting HER2 (ErbB2), HER3 (ErbB3), HER4 (ErbB4), EGFR, DLL3, TROP2, B7H3, c-Met, CD20, CD22, CD30, CD33, CD44, CD47, CD56, CD70, CD73, CD79b, CD105, CEA, A33, Cripto, EphA2, G250, MUC1, Lewis Y, VEGFR, VEGF, PD-1, PD-L1, MET, RET, GPNMB, Integrin, PSMA, Tenascin-C, SLC44A4, FR α , or Mesothelin.

In some embodiments, A can be modified, for example by alteration, addition, or deletion of one or more amino acids.

In some embodiments, A is selected from an antibody or an antigen-binding fragment thereof targeting HER2, DLL3, B7H3, or FR α .

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 1, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 2, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 3; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 4, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 5, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 6, wherein the CDRs are determined according to the Kabat numbering scheme.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the anti-B7H3 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 7, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 8.

In some embodiments, A is an antibody targeting B7H3, wherein the anti-B7H3 antibody further comprises a heavy chain constant region sequence or a variant thereof, and/or a light chain constant region sequence or a variant thereof.

In some embodiments, A is an antigen-binding fragment targeting B7H3, wherein the antigen-binding fragment is selected from a Fab, a Fab', a Fab'-SH, an Fv, an scFv, and a F(ab')₂.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting B7H3,

wherein the anti-B7H3 antibody or the antigen-binding fragment thereof is a humanized or fully human antibody or an antigen-binding fragment thereof.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the anti-B7H3 antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 9 or SEQ ID NO: 10, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 11.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 12, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 13, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 14; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 15, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 16, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 17, wherein the CDRs are determined according to the Kabat numbering scheme.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the anti-DLL3 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 18, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 19.

In some embodiments, A is an antibody targeting DLL3, wherein the anti-DLL3 antibody further comprises a heavy chain constant region sequence or a variant thereof, and/or a light chain constant region sequence or a variant thereof.

In some embodiments, A is an antigen-binding fragment targeting DLL3, wherein the antigen-binding fragment is selected from a Fab, a Fab', a Fab'-SH, an Fv, an scFv, and a F(ab')₂.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the anti-DLL3 antibody or the antigen-binding fragment thereof is a humanized or fully human antibody or an antigen-binding fragment thereof.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the anti-DLL3 antibody comprises a heavy chain and/or a light chain, wherein

the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 20, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 21.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 22, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 23, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 24; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 25, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 26, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 27, wherein the CDRs are determined according to the Kabat numbering scheme.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the anti-FR α antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 28, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 29.

In some embodiments, A is an antibody targeting FR α , wherein the anti-FR α antibody further comprises a heavy chain constant region sequence or a variant thereof, and/or a light chain constant region sequence or a variant thereof.

In some embodiments, A is an antigen-binding fragment targeting FR α , wherein the antigen-binding fragment is selected from a Fab, a Fab', a Fab'-SH, an Fv, an scFv, and a F(ab')₂.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the anti-FR α antibody or the antigen-binding fragment thereof is a humanized or fully human antibody or an antigen-binding fragment thereof.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the anti-FR α antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 30 or SEQ ID NO: 32, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 31.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain

and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 37, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 38, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 39; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 40, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 41, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 42, wherein the CDRs are determined according to the Kabat numbering scheme. In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the anti-HER2 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 35, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 36.

In some embodiments, A is an antibody targeting HER2, wherein the anti-HER2 antibody further comprises a heavy chain constant region sequence or a variant thereof, and/or a light chain constant region sequence or a variant thereof.

In some embodiments, A is an antigen-binding fragment targeting HER2, wherein the antigen-binding fragment is selected from a Fab, a Fab', a Fab'-SH, an Fv, an scFv, and a F(ab')₂.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the anti-HER2 antibody or the antigen-binding fragment thereof is a humanized or fully human antibody or an antigen-binding fragment thereof.

In some embodiments, A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the anti-HER2 antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 33, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 34.

In some embodiments, A is selected from 43A or 43B targeting B7H3, 33B targeting DLL3, farletuzumab or farletuzumab-FcS targeting FR α , trastuzumab targeting HER2, or a biosimilar thereof.

43A comprises 2 identical heavy chains and 2 identical light chains, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 9, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 11.

> 43A heavy chain sequence (SEQ ID NO: 9)

QVQLVQSGAEVKKPGASVKVSCKASGYTFT**DYFMN**WVRQAPGQGLEWMGDVNP
KTGSPSYNQKFKGRVTMTRDTSTSTVYMELSSLRSEDTAVYYC**CARRYGFLYSMD**
YWQGQTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
 5 ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKS
 CDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
 WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA
 SIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
 NNYKTTTPVLDSDGSFFLYSKLTVDKSR
 10 WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

> 43A light chain sequence (SEQ ID NO: 11)

DIQMTQSPSSLSASVGDRVTITC**RASQDISNYLN**WYQQKPGKAVKVLIIYTSRLHSG
VPSRFSGSGSGTDFTFTISSLQPEDATYYC**QQGNTHPFT**FGGGTKVEIKRTVAAPSV
 FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
 15 YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

The amino acid sequences marked in bold are the heavy chain/light chain CDR sequences, and the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively:

HCDR1: DYFMN	SEQ ID NO:1
HCDR2: DVNPKTGSPSYNQKFKG	SEQ ID NO:2
HCDR3: RYGFLYSMDY	SEQ ID NO:3
LCDR1: RASQDISNYLN	SEQ ID NO:4
LCDR2: YTSRLHS	SEQ ID NO:5
LCDR3: QQGNTHPFT	SEQ ID NO:6

20 The amino acid sequences marked with underlines are the heavy chain/light chain variable region sequences, and the HV and LV are designated as SEQ ID NO: 7 and SEQ ID NO: 8, respectively.

43A heavy chain variable region (HV) sequence (SEQ ID NO: 7):

QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYFMNWVRQAPGQGLEWMGDVNP
 25 KTGSPSYNQKFKGRVTMTRDTSTSTVYMELSSLRSEDTAVYYC**CARRYGFLYSMDY**

WGQGTSVTVSS

43A light chain variable region (LV) sequence (SEQ ID NO: 8):

DIQMTQSPSSLSASVGDRVTITCRASQDISNYLNWYQQKPGKAVKVLIIYTSRLHSG
VPSRFSGSGSGTDFTFTISSLQPEDATYYCQQGNTHPFTFGGGTKVEIK

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43B comprises 2 identical heavy chains and 2 identical light chains, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 10, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 11.

> 43B heavy chain sequence (SEQ ID NO: 10)

10 QVQLVQSGAEVKKPGASVKVSCKASGYTFTD**YFMNWVRQAPGQGLEWMGDVNP**
KTGSPSYNQKFKGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARRYGFLYSMD
YWGQGTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKS
CDKTHSTPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
15 WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA
SIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTTPVLDSGDSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

> 43B light chain sequence (SEQ ID NO: 11)

20 DIQMTQSPSSLSASVGDRVTITCRASQDISNYLNWYQQKPGKAVKVLIIYTSRLHSG
VPSRFSGSGSGTDFTFTISSLQPEDATYYC**QQGNTHPFT**FGGGTKVEIKRRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

25 The amino acid sequences marked in bold are the heavy chain/light chain CDR sequences, and the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively:

HCDR1: DYFMN	SEQ ID NO:1
HCDR2: DVNPKTGSPSYNQKFKG	SEQ ID NO:2
HCDR3: RYGFLYSMDY	SEQ ID NO:3
LCDR1: RASQDISNYLN	SEQ ID NO:4

LCDR2: YTSRLHS

SEQ ID NO:5

LCDR3: QQGNTHPFT

SEQ ID NO:6

The amino acid sequences marked with underlines are the heavy chain/light chain variable region sequences, and the HV and LV are designated as SEQ ID NO: 7 and SEQ ID NO: 8, respectively.

43B heavy chain variable region (HV) sequence (SEQ ID NO: 7):

5 QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYFMNWVRQAPGQGLEWMGDVNP
KTGSPSYNQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARRYGFLYSMDY
WGQGTSVTVSS

43B light chain variable region (LV) sequence (SEQ ID NO:8):

DIQMTQSPSSLSASVGDRVTITCRASQDISNYLNWYQQKPGKAVKVLIIYTSRLHSG
10 VPSRFSGSGSGTDFTFTISSLQPEDATYYCQQGNTHPFTFGGGTKVEIK

33B comprises 2 identical heavy chains and 2 identical light chains, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 20, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 21.

15 > 33B heavy chain sequence (SEQ ID NO: 20)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYMKWVRQAPGQRLEWMGAFNL
NNGDTFYNQKFKGRVTITRDTASTAYMELSSLRSEDVAVYYCARDVYGYGDYW
GQGTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS
GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK
20 THTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAASIEK
TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

> 33B light chain sequence (SEQ ID NO: 21)

25 DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSYMHWYQQKPGQPPKLLIYLAS
NLDSGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSRELPTYFGGGTKLEIKRT
VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

30 The sequence of the heavy chain variable region is set forth in SEQ ID NO: 18, and the
sequence of the light chain variable region is set forth in SEQ ID NO: 19.

> 33B heavy chain variable region (HV) sequence (SEQ ID NO: 18)

QVQLVQSGAEVKKPGASVKVSCKASGYTFT**DYYMK**WVRQAPGQRLEWMGA**FN**L
NNGDTFYNQKFKGRVTITRDTASTAYMELSSLRSEDTAVYYCARD**VYGYGDY**W
 GQGTSVTVSS

5 > 33B light chain variable region (LV) sequence (SEQ ID NO: 19)

DIVMTQSPDSLAVSLGERATINC**RASKSVSTSGYSYMH**WYQQKPGQPPKLLIYLAS
NLDSGVDPDRFSGSGSGTDFTLTISLQAEDVAVYYC**QHSREL**PYTFGGG**TKLEIK**

The heavy chain CDR sequences HCDR1, HCDR2, and HCDR3 are designated as SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14, respectively, and the light chain CDR sequences

10 LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO: 15, SEQ ID NO: 16, and SEQ ID NO: 17, respectively.

HCDR1: DYYMK SEQ ID NO:12

HCDR2: AFNLNNGDTFYNQKFKG SEQ ID NO:13

HCDR3: DVYGYGDY SEQ ID NO:14

LCDR1: RASKSVSTSGYSYMH SEQ ID NO:15

LCDR2: LASNLDS SEQ ID NO:16

LCDR3: QHSRELPLYT SEQ ID NO:17

Farletuzumab comprises 2 identical heavy chains and 2 identical light chains (WO 2023/170247 A1), wherein the amino acid sequence of the heavy chain is set forth in SEQ ID

15 NO: 30, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 31.

> Farletuzumab heavy chain sequence (SEQ ID NO: 30):

EVQLVESGGGVVQPGRSLRLSCSASGFTFSGYGLSWVRQAPGKGLEWVAMISSGGS
YTTYADSVKGRFAISRDNAKNTLFLQMDSLRPEDTGVYFCARHGDDPAWFAYWG
QGTPVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
 20 **VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT**
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

> Farletuzumab light chain sequence (SEQ ID NO: 31):

DIQLTQSPSSLSASVGDRVTITCSVSSSISSNNLHWYQQKPGKAPKPWIYGTSNLAG
VPSRFSGSGSGTDYTFTISLQPEDATYYCQQWSSYPYMYTFGQGTKVEIKRTVAA
 PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK
 5 DSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

The amino acid sequences marked in bold are the heavy chain/light chain CDR sequences, and the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27, respectively:

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HCDR1: GYGLS	SEQ ID NO:22
HCDR2: MISSGGSYTTYADSVKG	SEQ ID NO:23
HCDR3: HGDDPAWFAY	SEQ ID NO:24
LCDR1: SVSSSISSNNLH	SEQ ID NO:25
LCDR2: GTSNLAG	SEQ ID NO:26
LCDR3: QQWSSYPYMYT	SEQ ID NO:27

The heavy chain/light chain variable region sequences HV and LV are designated as SEQ ID NO: 28 and SEQ ID NO: 29, respectively.

Farletuzumab heavy chain variable region (HV) sequence (SEQ ID NO: 28):

15 EVQLVESGGGVVQPGRSLRLSCSASGFTFS**GYGLSWVRQAPGKGLEWVAMISSGGS**
YTTYADSVKGRFAISRDNAKNTLFLQMDSLRPEDTGVYFCAR**HGDDPAWFAYWG**
 QGTPVTVSS

Farletuzumab light chain variable region (LV) sequence (SEQ ID NO: 29):

20 DIQLTQSPSSLSASVGDRVTITCSVSSSISSNNLHWYQQKPGKAPKPWIYGTSNLAG
 VPSRFSGSGSGTDYTFTISLQPEDATYYC**QQWSSYPYMYTFGQGTKVEIK**

Farletuzumab-FcS comprises 2 identical heavy chains and 2 identical light chains, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 32, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 31.

> Farletuzumab-FcS heavy chain sequence (SEQ ID NO: 32):

25 EVQLVESGGGVVQPGRSLRLSCSASGFTFS**GYGLSWVRQAPGKGLEWVAMISSGGS**

YTTYADSVKGRFAISRDNAKNTLFLQMDSLRLPEDTGVYFCARHGDDPAWFAYWG
QGTPVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
5 GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAASIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

> Farletuzumab-FcS light chain sequence (SEQ ID NO: 31):

DIQLTQSPSSLSASVGDRVTITCSVSSSISSNNLHWYQQKPGKAPKRWIYGTSNLSAG
10 **VPSRFSGSGSGTDYFTFSSISLQPEDIAITYYCQOWSSYPYMYTFGGQGTKVEIKRTVAA**
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK
DSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

The amino acid sequences marked in bold are the heavy chain/light chain CDR sequences, and
the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO:
15 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27,
respectively:

HCDR1: GYGLS	SEQ ID NO:22
HCDR2: MISSGGSYTTYADSVKG	SEQ ID NO:23
HCDR3: HGDDPAWFAY	SEQ ID NO:24
LCDR1: SVSSSISSNNLH	SEQ ID NO:25
LCDR2: GTSNLS	SEQ ID NO:26
LCDR3: QOWSSYPYMYT	SEQ ID NO:27

The heavy chain/light chain variable region sequences HV and LV are designated as SEQ ID
NO: 28 and SEQ ID NO: 29, respectively.

20 Farletuzumab-FcS heavy chain variable region (HV) sequence (SEQ ID NO: 28):
EVQLVESGGGVVQPGRSLRLSCSASGFTFS**GYGLSWVRQAPGKGLEWVAMISSGGS**
YTTYADSVKGRFAISRDNAKNTLFLQMDSLRLPEDTGVYFCARHGDDPAWFAYWG
QGTPVTVSS

Farletuzumab-FcS light chain variable region (LV) sequence (SEQ ID NO: 29):

25 **DIQLTQSPSSLSASVGDRVTITCSVSSSISSNNLHWYQQKPGKAPKRWIYGTSNLSAG**

VPSRFSGSGSGTDYFTFISLQPEDATYYC**QQWSSYPYMYTFGQGTKVEIK**

Trastuzumab comprises 2 identical heavy chains and 2 identical light chains, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 33, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 34.

5 > Trastuzumab heavy chain (SEQ ID NO: 33)

EVQLVESGGGLVQPGGSLRLSCAASGFMNIKDTYIHWRQAPGKGLEWVARIYPTNG
YTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY
WGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

> Trastuzumab light chain (SEQ ID NO: 34)

15 **DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSG**
VPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

The sequence of the heavy chain variable region is set forth in SEQ ID NO: 35, and the sequence of the light chain variable region is set forth in SEQ ID NO: 36.

> Trastuzumab heavy chain variable region (HV) sequence (SEQ ID NO: 35)

EVQLVESGGGLVQPGGSLRLSCAASGFMNIKDTYIHWRQAPGKGLEWVARIYPTNG
YTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY
WGQGTLLTVSS

25 > Trastuzumab light chain variable region (LV) sequence (SEQ ID NO: 36)

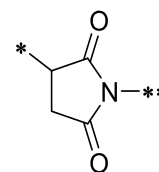
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSG
VPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK

The heavy chain CDR sequences HCDR1, HCDR2, and HCDR3 are designated as SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39, respectively, and the light chain CDR sequences LCDR1, LCDR2, and LCDR3 are designated as SEQ ID NO: 40, SEQ ID NO: 41, and SEQ ID NO: 42, respectively.

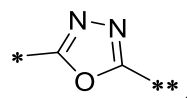
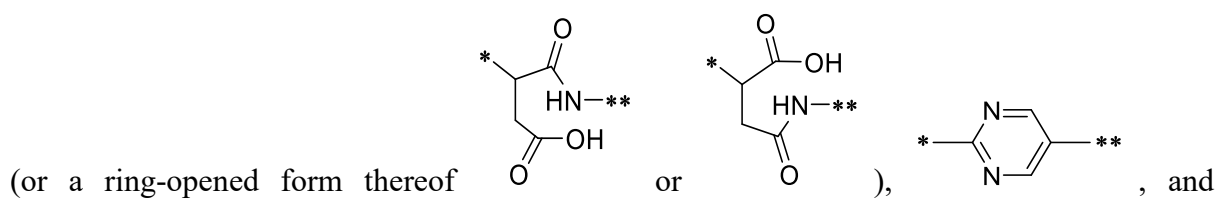
HCDR1: DTYIH	SEQ ID NO:37
HCDR2: RIYPTNGYTRYADSVKG	SEQ ID NO:38
HCDR3: WGGDGFYAMDY	SEQ ID NO:39
LCDR1: RASQDVNTAVA	SEQ ID NO:40
LCDR2: SASFLYS	SEQ ID NO:41
LCDR3: QQHYTTPPT	SEQ ID NO:42

In some embodiments, the linker moiety -L- is represented by the following formula:

-L₁-L₂-L₃-L₄-,



wherein L₁ is a moiety of L linked to the ligand A; preferably, L₁ is selected from



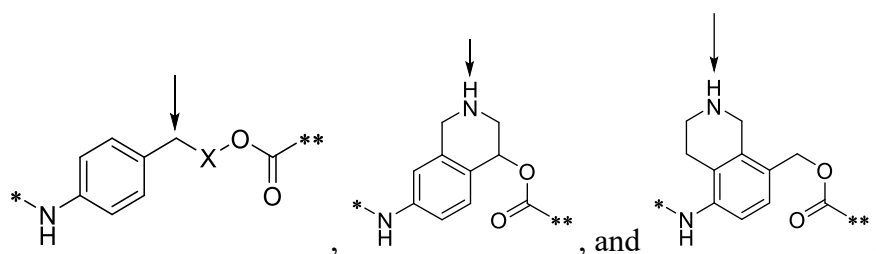
5 *, wherein * represents linkage to a sulfhydryl group of A (e.g., a monoclonal antibody), and ** represents linkage to L₂;

L₂ is a spacer, preferably selected from -L_{2a}-C(O)-, -L_{2a}-L_{2b}-C(O)-, -L_{2a}-NH-C(O)-, -L_{2a}-C(O)-NH-, -L_{2a}-L_{2b}-NH-C(O)-, -L_{2a}-L_{2b}-C(O)-NH-, -L_{2a}-C(O)-NH-L_{2b}-C(O)-, -L_{2a}-NH-C(O)-L_{2b}-C(O)-, -L_{2a}-C(O)-NH-L_{2b}-C(O)-NH-, -L_{2a}-NH-C(O)-L_{2b}-NH-C(O)-, -L_{2a}-NR¹-SO₂-NH-C(O)-O-L_{2b}-C(O)-, and -L_{2a}-NR¹-SO₂-NH-C(O)-O-L_{2b}-NH-C(O)-, wherein L_{2a} is selected from -C₁-C₈ alkylene-, -C₁-C₈ alkylene-C₃-C₈ cycloalkylene-, -C₆-C₁₄ arylene-, -C₆-C₁₄ arylene-C₁-C₈ alkylene-, -(5- to 6-membered heteroarylene)-, -(5- to 6-membered heteroarylene)-C₁-C₈ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 8-membered heterocyclylene),

wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, C₁-C₆ heteroalkyl, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more (e.g., two or three) of N, O, and S; L_{2b} is selected from -C₁-C₈ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R¹ is selected from hydrogen, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, 3- to 8-membered heterocyclyl, C₁-C₆ haloalkyl, heteroalkyl having 2-8 atoms, C₆-C₁₄ aryl, and 5- to 6-membered heteroaryl, wherein the alkyl, heterocyclyl, heteroalkyl, aryl, and heteroaryl are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, heteroalkylene, or heteroarylene is selected from one or more (e.g., two or three) of N, O, and S;

L₃ is a polypeptide sequence, preferably selected from a peptide residue consisting of 2-8 (e.g., 2, 3, 4, 5, 6, 7, or 8) natural or unnatural amino acids, wherein the amino acid is optionally further substituted with one or more substituents selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl;

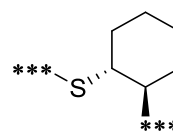
L₄ is a hydrophilic group-modified self-immolative fragment, and the self-immolative fragment is selected from:



wherein * represents linkage to a carboxyl group of L₃ via an amide bond, ** represents linkage

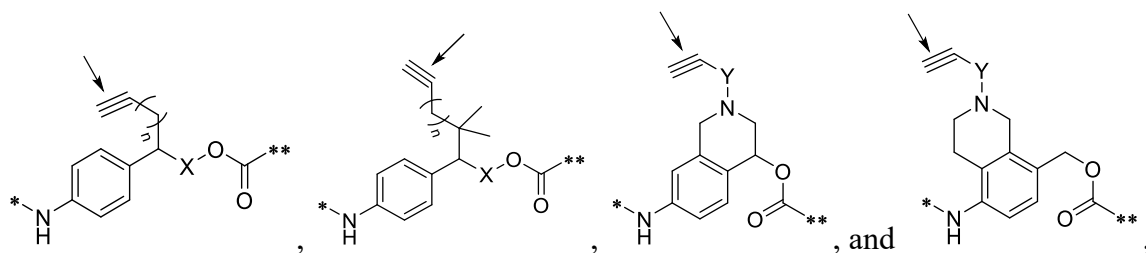
to the amino group of the bioactive molecule D, X is absent or

linkage to a carbon atom, **** represents linkage to an oxygen atom, and the arrow indicates



a modification site of the hydrophilic group;

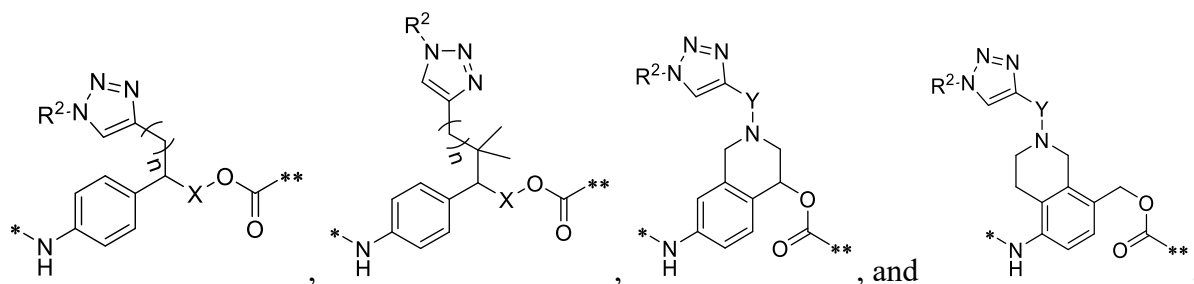
further preferably, the self-immolative fragment, prior to modification by the hydrophilic group, is selected from the following structures:



- 5 wherein Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6;

the hydrophilic group has at least one azido group and comprises a polyethylene glycol group, a poly-natural or unnatural amino acid group, a monosaccharide, an oligosaccharide, or a polysaccharide, or a combination thereof;

- 10 preferably, L₄ is selected from:



wherein * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule D;

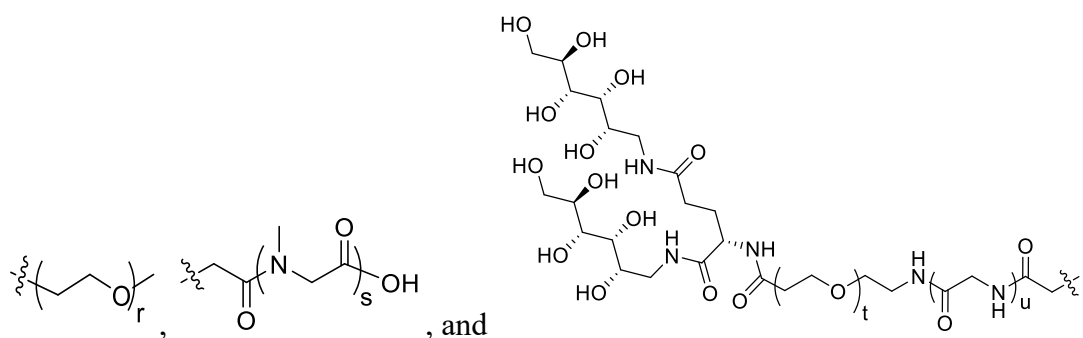
- 15 R² is a hydrophilic fragment, preferably selected from linear or branched heteroalkyl containing 4-50 (preferably 4-24, more preferably 6-24, and most preferably 8-24, e.g., 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) -OCH₂CH₂- structural units, a peptide chain containing 4-50 (preferably 4-24, more preferably 8-24, and most preferably 10-24, e.g., 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) proteinogenic amino acids (e.g., glycines) or non-proteinogenic amino acids (e.g., sarcosines), and linear or branched heteroalkyl containing a monosaccharide, an oligosaccharide, or a

polysaccharide; X is absent or , *** represents linkage to a carbon atom, and

$$\begin{array}{c} \text{---} \text{Ra} (\text{---} \text{CH}_2 \text{CH}_2 \text{O})_r \text{---} \text{Rb} \\ \text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{N} (\text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{OH})_s \text{---} \end{array}$$
,
$$\text{HOCH}_2 \text{CH}(\text{OH}) \text{CH}(\text{OH}) \text{CH}_2 \text{NH} \text{C}(=\text{O}) (\text{---} \text{CH}_2 \text{CH}_2 \text{O})_t \text{CH}_2 \text{NH} \text{C}(=\text{O}) \text{CH}_2 \text{NH} (\text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{OH})_u \text{---}$$
,
$$\text{HOCH}_2 \text{CH}(\text{OH}) \text{CH}(\text{OH}) \text{CH}_2 \text{NH} \text{C}(=\text{O}) (\text{---} \text{CH}_2 \text{CH}_2 \text{O})_t \text{CH}_2 \text{N} (\text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{OH})_u \text{---}$$
,
$$\text{HOCH}_2 \text{CH}(\text{OH}) \text{CH}(\text{OH}) \text{CH}_2 \text{NH} \text{C}(=\text{O}) (\text{---} \text{CH}_2 \text{CH}_2 \text{O})_t \text{CH}_2 \text{N} (\text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{OH})_u \text{---}$$
, and
$$\text{HOCH}_2 \text{CH}(\text{OH}) \text{CH}(\text{OH}) \text{CH}_2 \text{NH} \text{C}(=\text{O}) (\text{---} \text{CH}_2 \text{CH}_2 \text{O})_t \text{CH}_2 \text{N} (\text{---} \text{CH}_2 \text{CH}_2 \text{C}(=\text{O}) \text{OH})_u \text{---}$$

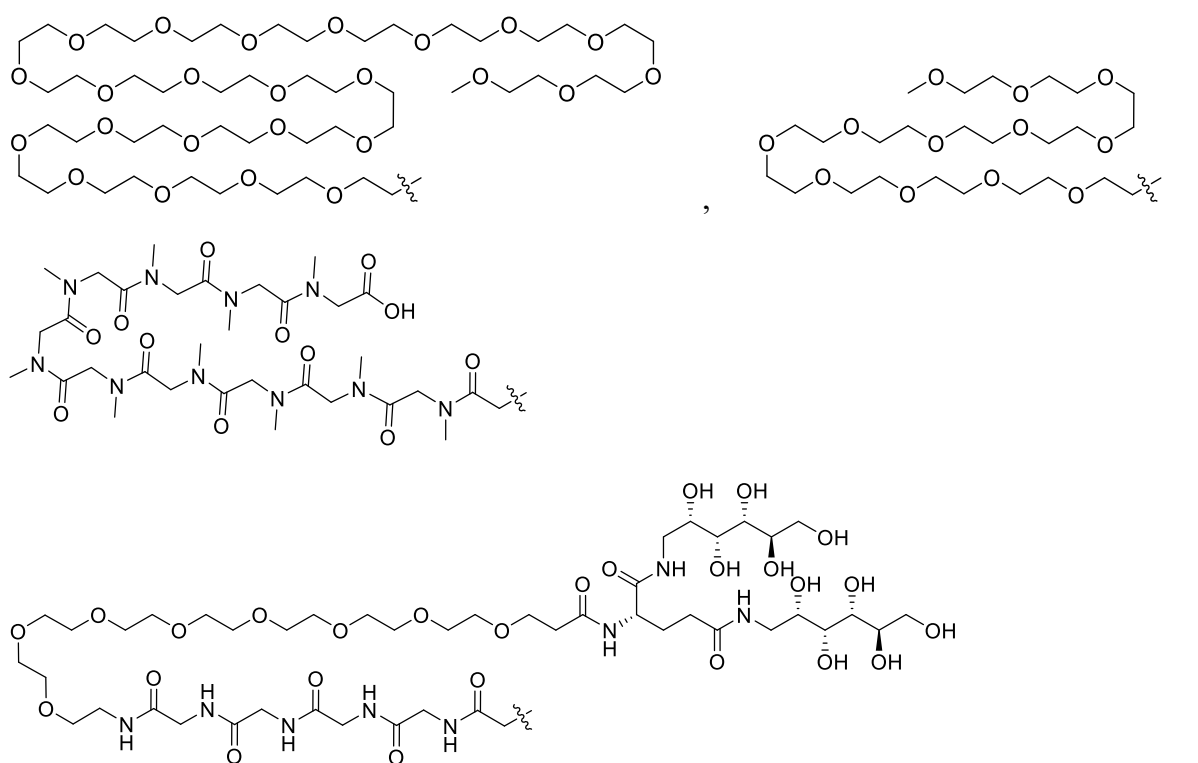
wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50); R_a is selected from a bond and C₁-C₃ alkylene, such as methylene, ethylidene, *n*-propylidene, or isopropylidene; R_b is selected from C₁-C₃ alkyl, such as methyl, ethyl, *n*-propyl, or isopropyl.

In some embodiments, R^2 is selected from the following structures:



wherein r , s , t , and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50).

5 In some embodiments, R^2 is selected from the following structures:



10 In some embodiments, Y is C_1 - C_6 alkylene or $-R^3-C(O)-$, wherein R^3 is C_1 - C_6 alkylene or $-C_1$ - C_6 alkylene- $(OCH_2CH_2)_v-$, wherein v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, Y is C_1 - C_3 alkylene or $-R^3-C(O)-$, wherein R^3 is C_1 - C_3 alkylene or $-C_1$ - C_3 alkylene- $(OCH_2CH_2)_v-$, wherein v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

15 In some embodiments, Y is methylene, ethylidene, n -propylidene, isopropylidene, or $-R^3-C(O)-$, wherein R^3 is methylene- $(OCH_2CH_2)_v-$, ethylidene- $(OCH_2CH_2)_v-$, n -propylidene- $(OCH_2CH_2)_v-$, or isopropylidene- $(OCH_2CH_2)_v-$, wherein v is an integer selected from 1-12

(e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, Y is selected from $-\text{CH}_2-(\text{OCH}_2\text{CH}_2)_4\text{C}(\text{O})-$.

In some embodiments, L_2 is selected from $-\text{L}_{2a}-\text{C}(\text{O})-$, $-\text{L}_{2a}-\text{NH}-\text{C}(\text{O})-\text{L}_{2b}-\text{C}(\text{O})-$, and $-\text{L}_{2a}-\text{NR}^1-\text{SO}_2-\text{NH}-\text{C}(\text{O})-\text{O}-\text{L}_{2b}-\text{C}(\text{O})-$, wherein L_{2a} is selected from $-\text{C}_1-\text{C}_6$ alkylene-, $-\text{C}_1-\text{C}_6$ alkylene-

5 C_3-C_6 cycloalkylene-, $-\text{C}_6-\text{C}_{10}$ arylene-, $-\text{C}_6-\text{C}_{10}$ arylene- C_1-C_6 alkylene-, $-(5\text{- to } 6\text{-membered heteroarylene})-$, $-(5\text{- to } 6\text{-membered heteroarylene})-\text{C}_1-\text{C}_6$ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 6-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from halogen, C_1-C_3 alkyl, heteroalkyl having 1-3 atoms, C_1-C_3 alkoxy, hydroxyl, amino, carboxyl, and C_3-C_6 cycloalkyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more of N, O, and S; L_{2b} is selected from $-\text{C}_1-\text{C}_6$ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R^1 is selected from hydrogen, C_1-C_3 alkyl, C_3-C_6 cycloalkyl, 3- to 6-membered heterocyclyl, C_1-C_3 haloalkyl, heteroalkyl having 2-6 atoms, C_6-C_{10} aryl, and 5- to 6-membered heteroaryl, wherein the alkyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents independently selected from C_1-C_3 alkyl, heteroalkyl having 2-3 atoms, C_1-C_3 alkoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, or heteroalkylene is selected from one or more of N, O, and S.

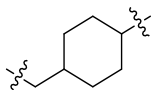
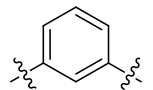
In some embodiments, L_2 is selected from $-\text{L}_{2a}-\text{C}(\text{O})-$, $-\text{L}_{2a}-\text{NH}-\text{C}(\text{O})-\text{L}_{2b}-\text{C}(\text{O})-$, and $-\text{L}_{2a}-\text{NR}^1-\text{SO}_2-\text{NH}-\text{C}(\text{O})-\text{O}-\text{L}_{2b}-\text{C}(\text{O})-$, wherein L_{2a} is selected from methylene, ethylidene, *n*-propylidene, *n*-butylidene, *n*-pentylidene, *n*-hexylidene, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{C}_1-\text{C}_3$ alkylene-cyclohexylidene-, $-\text{phenylene}-$, $-\text{phenylene}-\text{C}_1-\text{C}_3$ alkylene-, $-(5\text{- to } 6\text{-membered$

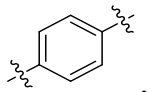
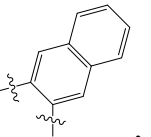
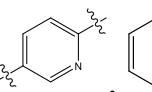
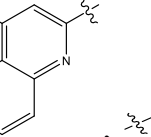
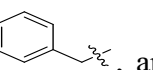
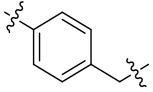
heteroarylene)-C₁-C₃ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 6-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from halogen, methyl, ethyl, *n*-propyl, isopropyl, heteroalkyl having 1-3 atoms, methoxy, ethoxy, *n*-propoxy, isopropoxy, hydroxyl, amino, carboxyl or cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more of N, O, and S; L_{2b} is selected from methylene, ethylidene, *n*-propylidene, *n*-butylidene, *n*-pentylidene, *n*-hexylidene, -CH(CH₃)CH₂CH₂CH₂CH₂-, and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R¹ is selected from hydrogen, methyl, ethyl, *n*-propyl, isopropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 3- to 6-membered heterocyclyl, -CF₃, -CF₂CF₃, heteroalkyl having 2-3 atoms, phenyl, and 5- to 6-membered heteroaryl, wherein the alkyl, heteroalkyl, phenyl, heteroaryl, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents independently selected from methyl, ethyl, *n*-propyl, isopropyl, heteroalkyl having 2-3 atoms, methoxy, ethoxy, *n*-propoxy, isopropoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, or heteroalkylene is selected from one or more of N, O, and S.

In some embodiments, L_{2a} is selected from -C₁-C₈ alkylene-, -C₁-C₈ alkylene-C₃-C₈ cycloalkylene, C₆-C₁₄ arylene-C₁-C₈ alkylene, and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8) atoms, wherein the alkylene, cycloalkylene, arylene, and heteroalkylene are each optionally substituted with one or more substituents independently selected from halogen, C₁-C₆ alkyl, heteroalkyl having 2-6

atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl, the heteroalkylene or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene or heteroalkyl is selected from one or more of N, O, and S; L_{2b} is selected from -C₁-C₈ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8) atoms, and R¹ is selected from hydrogen, C₁-C₆ alkyl, heteroalkyl having 2-8 atoms, and C₆-C₁₄ aryl, wherein the alkyl, heteroalkyl, and aryl are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, amino, and carboxyl, the heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl or heteroalkylene is selected from one or more of N, O, and S.

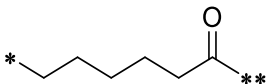
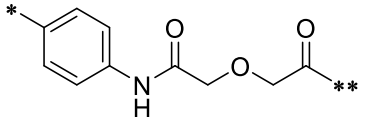
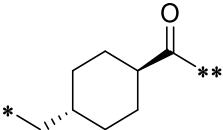
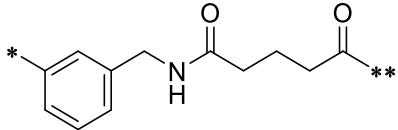
In some embodiments, L_{2a} is selected from -CH₂CH₂CH₂CH₂CH₂-, -CH₂CH₂(OCH₂CH₂)_p-, - (OCH₂CH₂)_p-, -CH₂(OCH₂CH₂)_p-, -CH₂CH₂(OCH₂CH₂)_pCH₂-, -

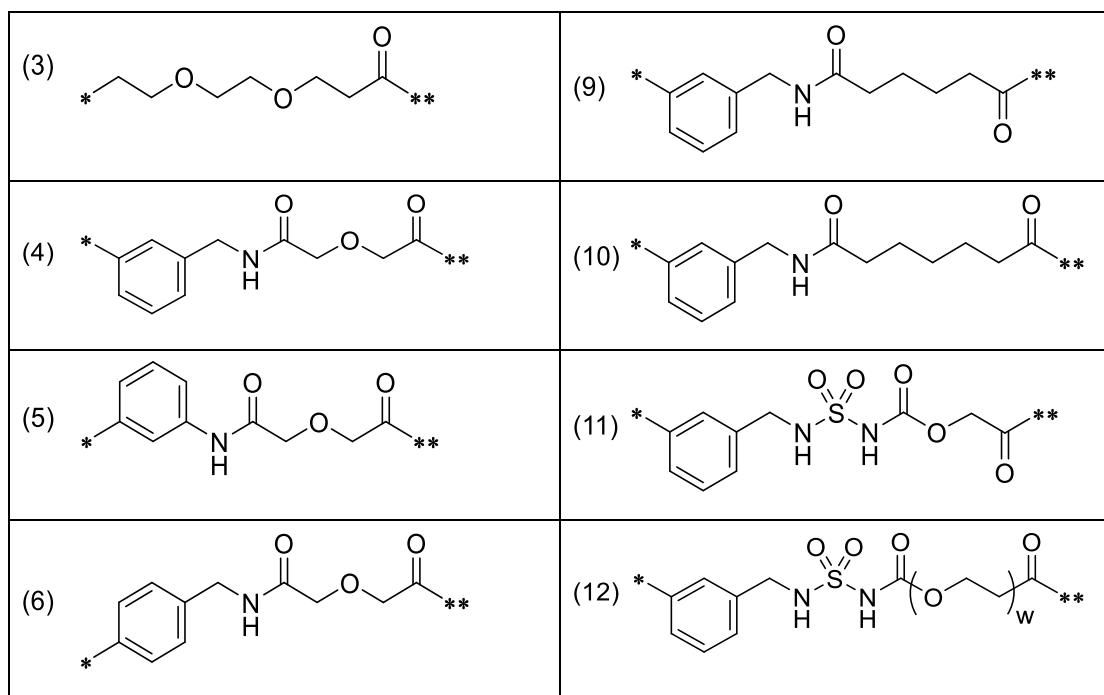
CH₂CH₂(OCH₂CH₂)_pCH₂CH₂-, -CH₂(OCH₂CH₂)_pCH₂CH₂-, , ,

, , , , , and , wherein p is an

integer from 1 to 12 (preferably 2-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12); L_{2b} is selected from -CH₂OCH₂-, -CH₂CH₂OCH₂-, -CH₂CH₂OCH₂CH₂-, -CH₂O-, -CH₂CH₂O-, -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -(OCH₂CH₂)_q-, -CH₂CH₂(OCH₂CH₂)_q-, -CH₂(OCH₂CH₂)_q-, -CH₂CH₂(OCH₂CH₂)_qCH₂-, -CH₂CH₂(OCH₂CH₂)_qCH₂CH₂-, and -CH₂(OCH₂CH₂)_qCH₂CH₂-, and R¹ is selected from hydrogen, methyl, ethyl, *n*-propyl, isopropyl, and cyclopropyl, wherein q is an integer from 1 to 12 (preferably 2-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, L₂ is selected from the following structures:

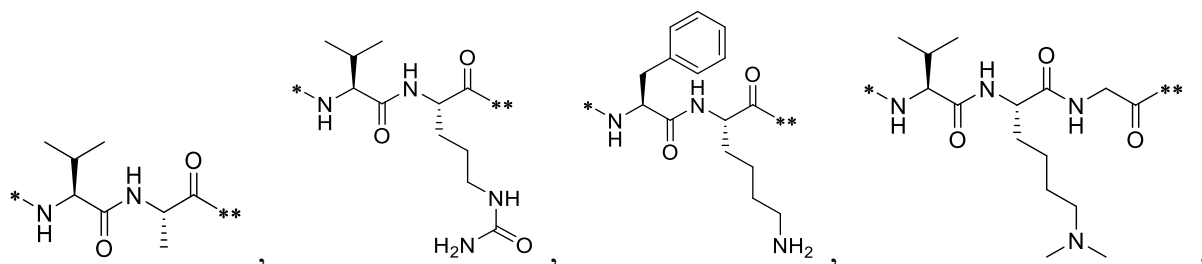
(1) 	(7) 
(2) 	(8) 

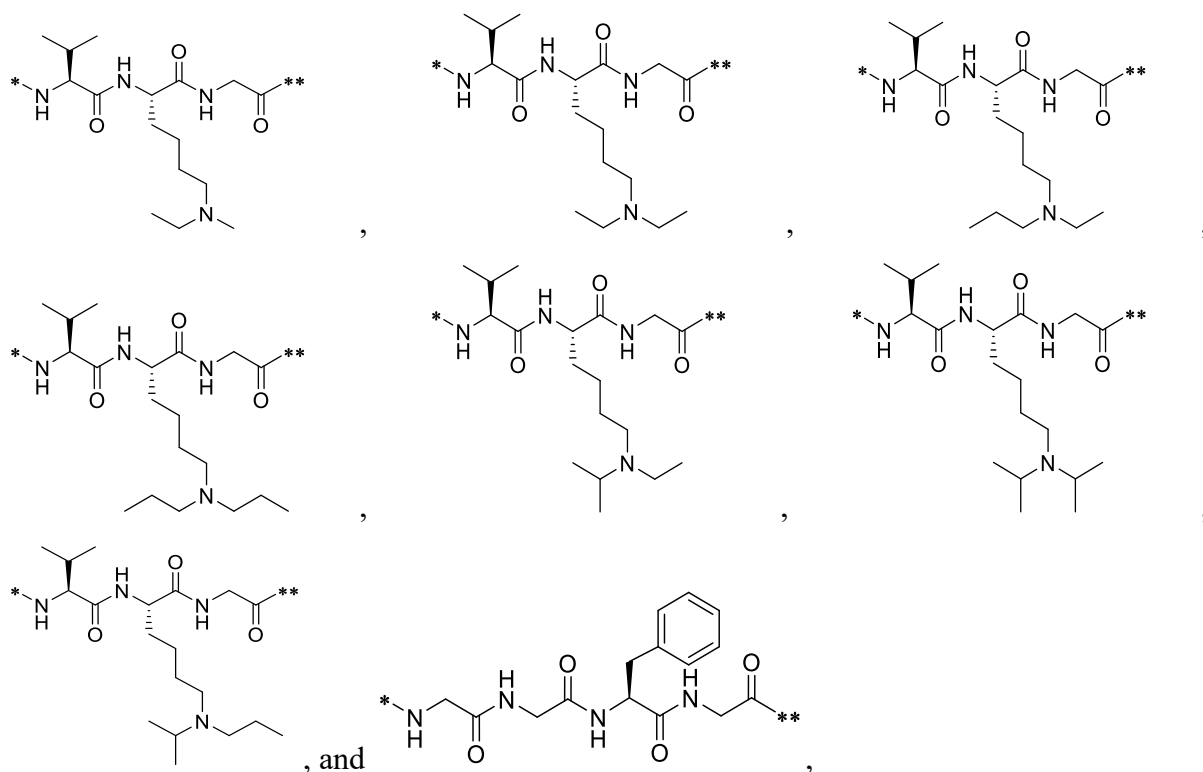


wherein w is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to L₁, and ** represents linkage to L₃.

In some embodiments, L₃ is selected from a peptide residue formed from 2-8 amino acids selected from phenylalanine (F), glycine (G), valine (V), citrulline (C), glutamic acid (E), alanine (A), lysine (K), C₁-C₆ alkyl-substituted lysine (e.g., C₁-C₃ alkyl-substituted lysine, such as methyl-substituted lysine, ethyl-substituted lysine, *n*-propyl-substituted lysine, or isopropyl-substituted lysine), etc. For example, L₃ is: -ValCit-; -CitVal-; -AlaAla-; -AlaCit-; -CitAla-; -AsnCit-; -CitAsn-; -CitCit-; -ValGlu-; -GluVal-; -SerCit-; -CitSer-; -LysCit-; -CitLys-; -AspCit-; -CitAsp-; -AlaVal-; -ValAla-; -PheAla-; -AlaPhe-; -PheLys-; -LysPhe-; -ValLys-; -LysVal-; -AlaLys-; -LysAla-; -PheCit-; -CitPhe-; -LeuCit-; -CitLeu-; -IleCit-; -CitIle-; -PheArg-; -ArgPhe-; -CitTrp-; -TrpCit-; -AlaAlaAla-; -PhePheLys-; -LysPhePhe-; -DPhePheLys-; -DLysPhePhe-; -GlyPheLys-; -LysPheGly-; -GlyPheLeuGly-; -GlyLeuPheGly-; -GluValCit-; -AlaLeuAlaLeu-; -GlyGlyGly-; -GlyGlyGlyGly-; -GlyPheValGly-; -GlyValPheGly-; -GlyGlyPheGly-; or -GlyGlyValGly-.

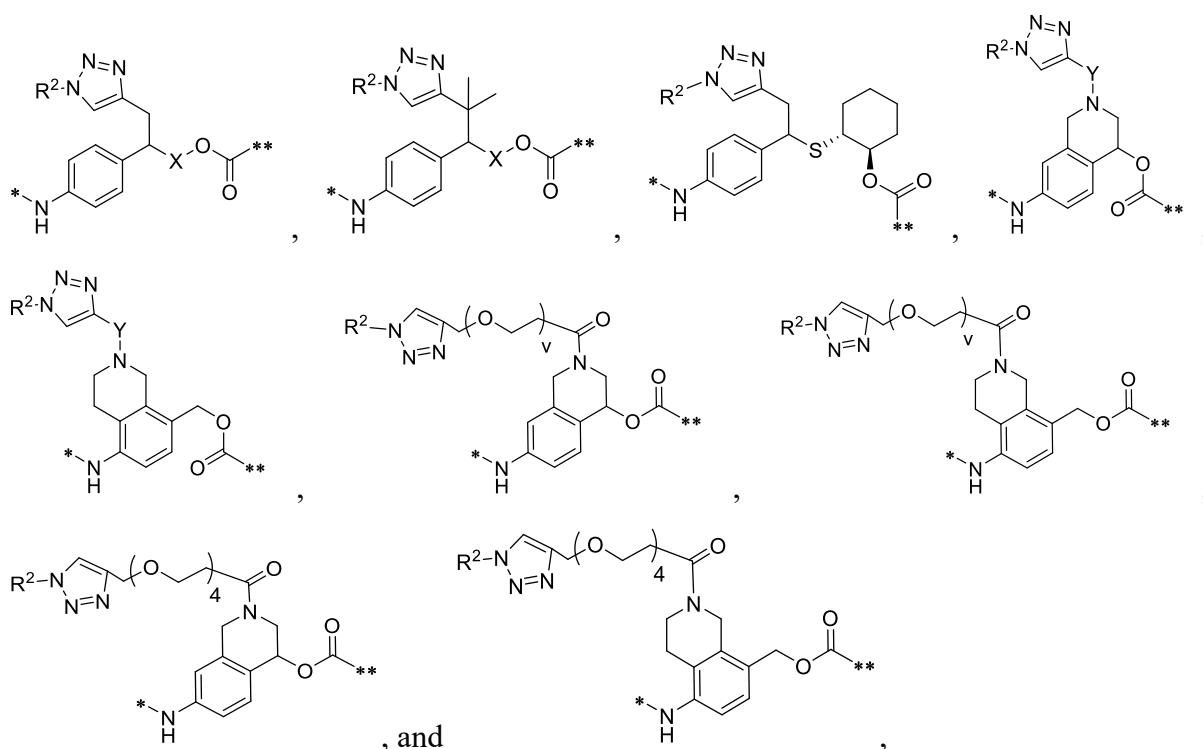
In some embodiments, L₃ is selected from the following structures:





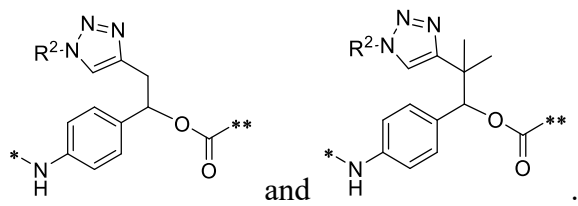
wherein * represents linkage to L₂, and ** represents linkage to L₄.

5 In some embodiments, L₄ is selected from:

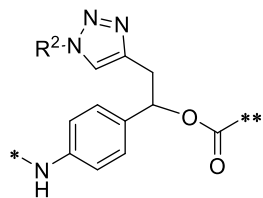


wherein v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule D.

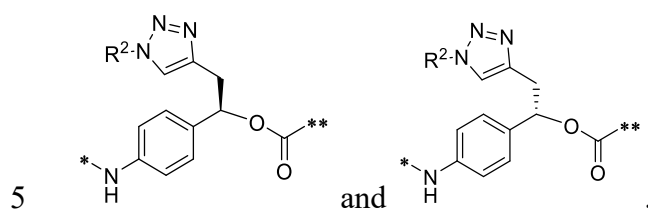
In some embodiments, L₄ is selected from:



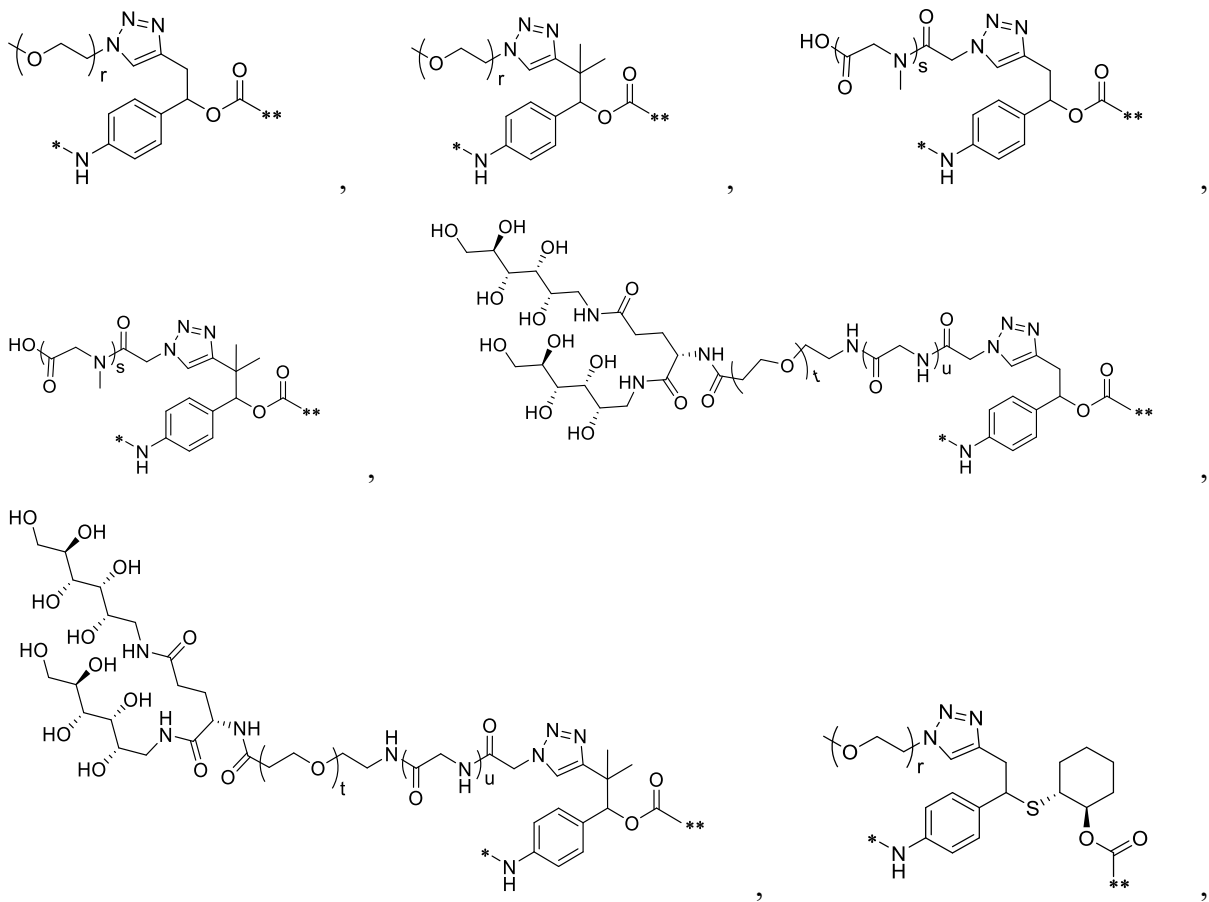
In some embodiments, L_4 is selected from:

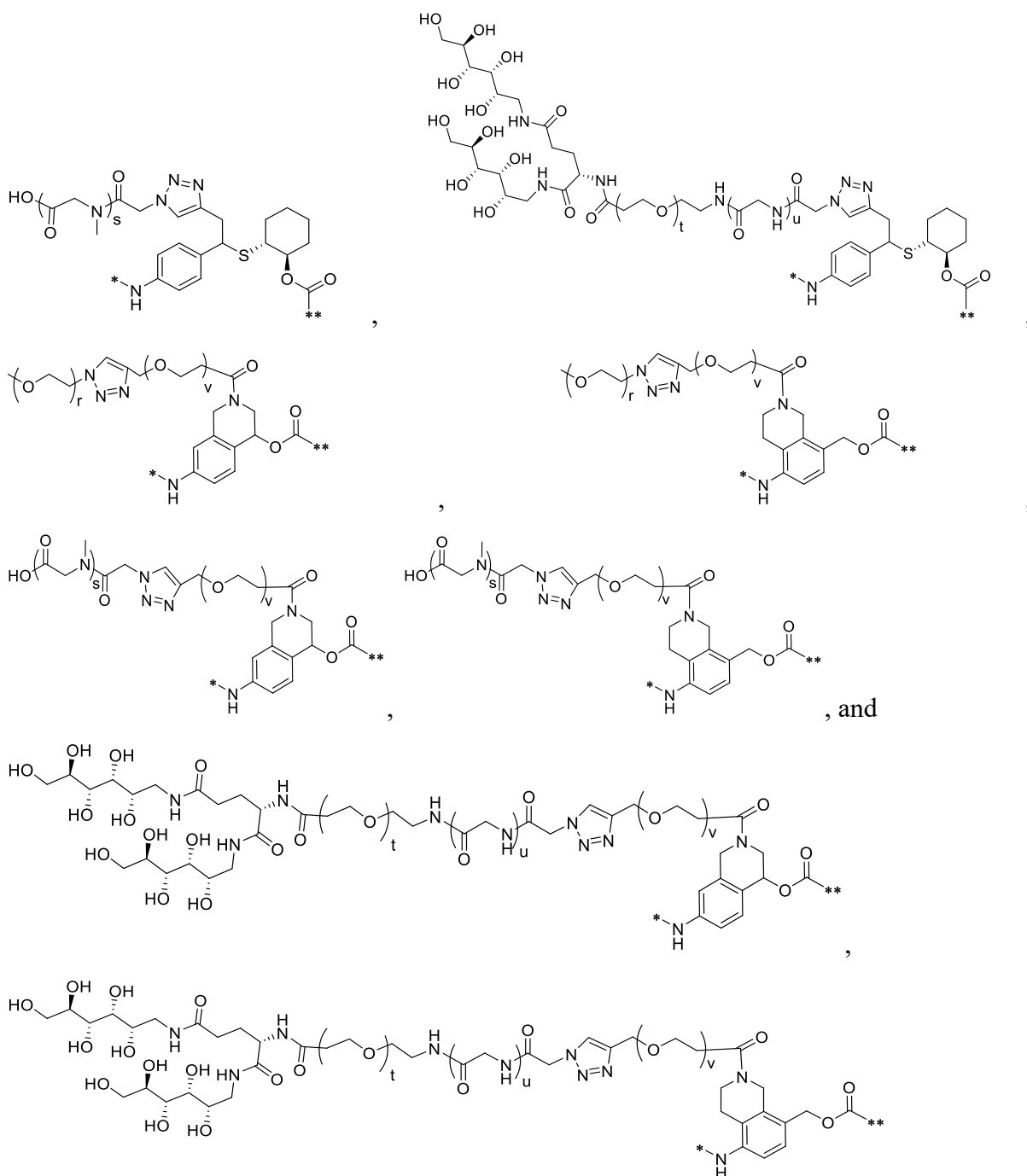


In some embodiments, L_4 is selected from:



In some embodiments, L₄ is selected from:



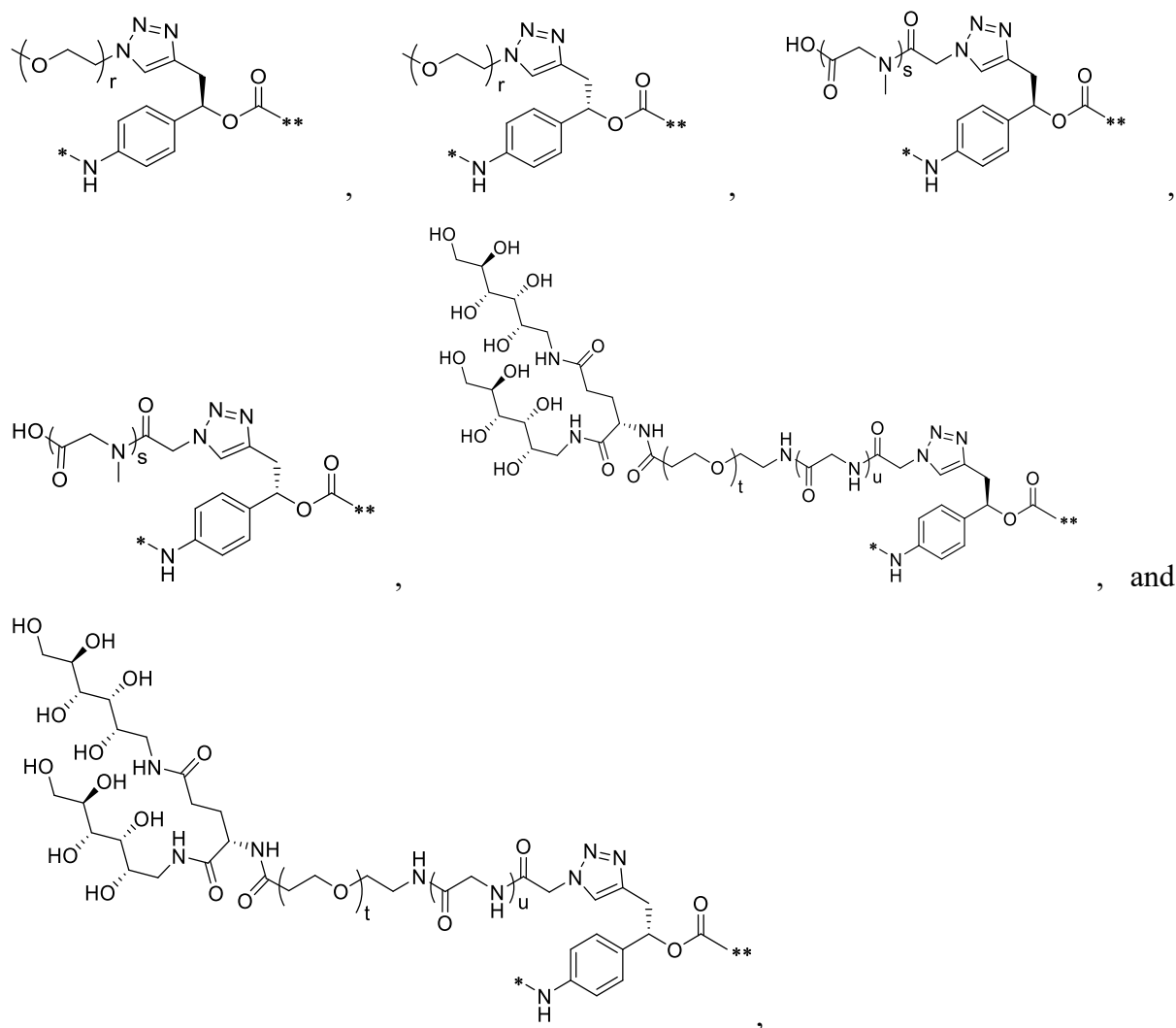


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wherein r , s , t , and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), $*$ represents linkage to a carboxyl group of L_3 via an amide bond, and $**$ represents linkage to the amino group of the bioactive molecule D.

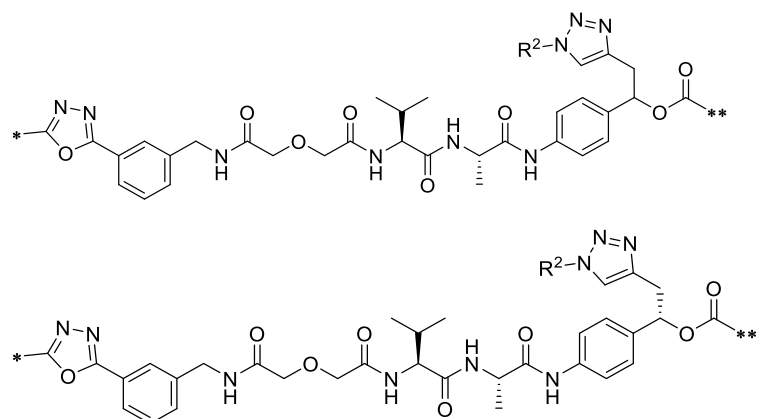
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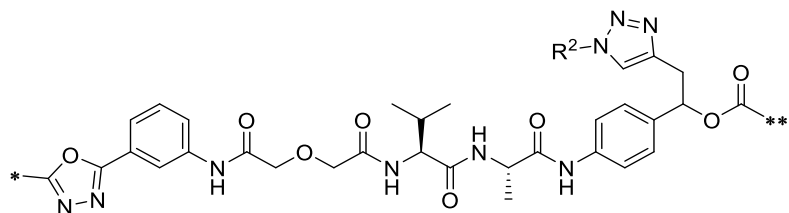
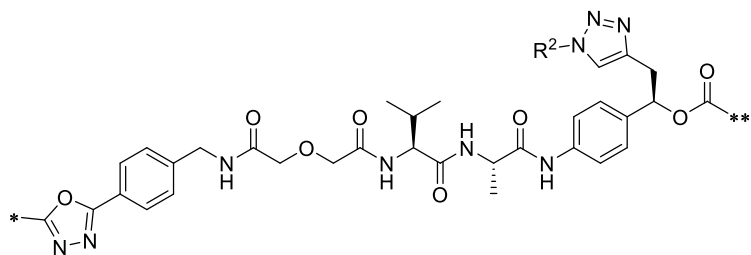
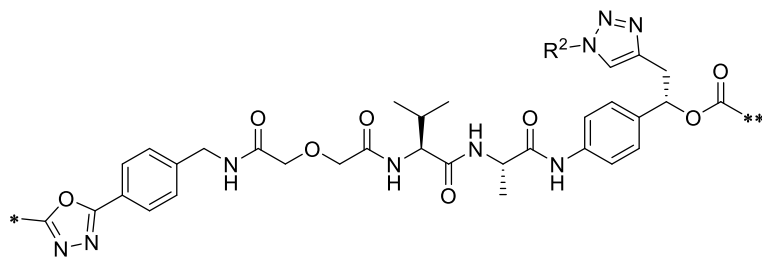
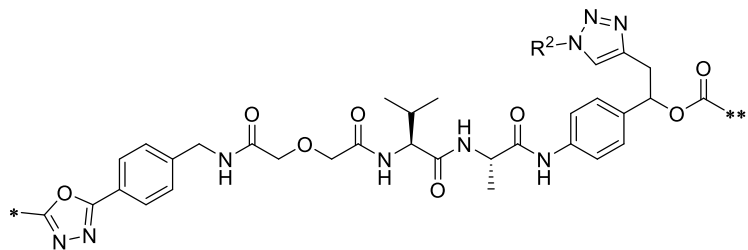
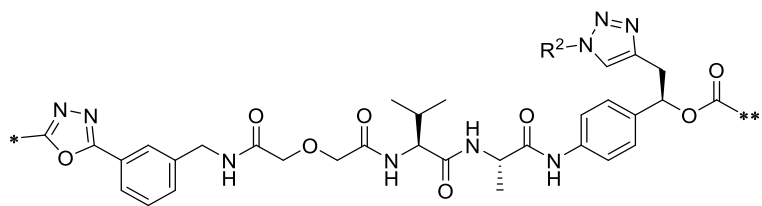
In some embodiments, L_4 is selected from:



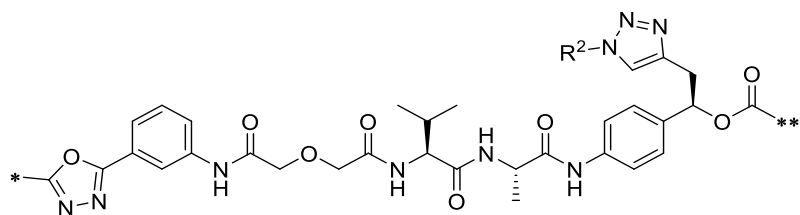
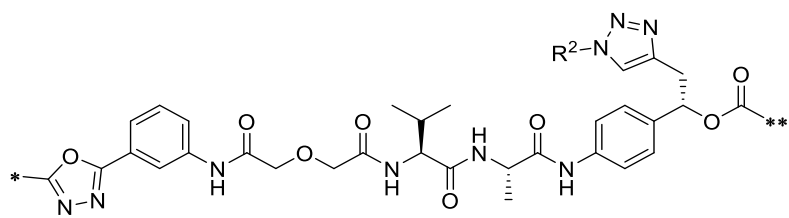
wherein r , s , t , and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), $*$ represents linkage to a carboxyl group of L_3 via an amide bond, and $**$ represents linkage to the amino group of the bioactive molecule D .

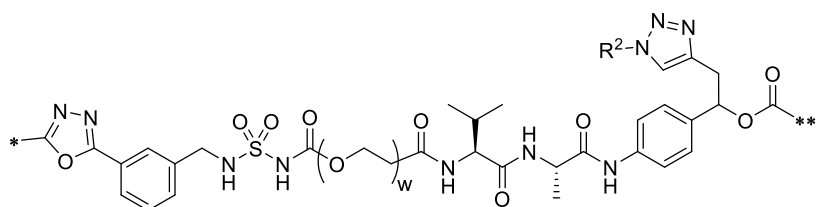
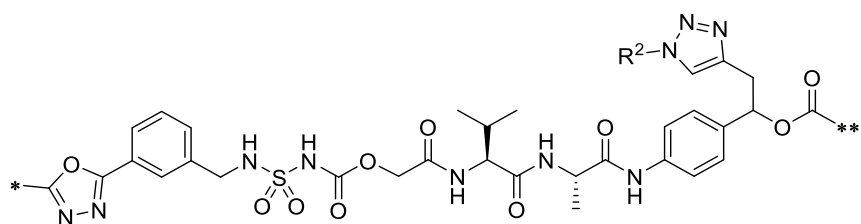
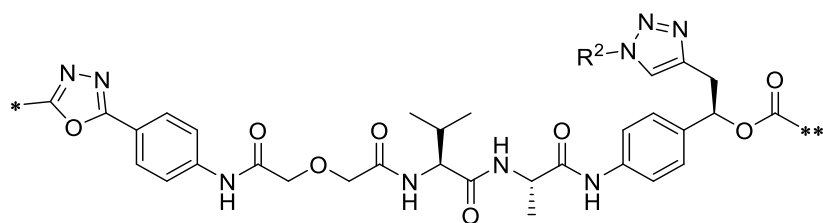
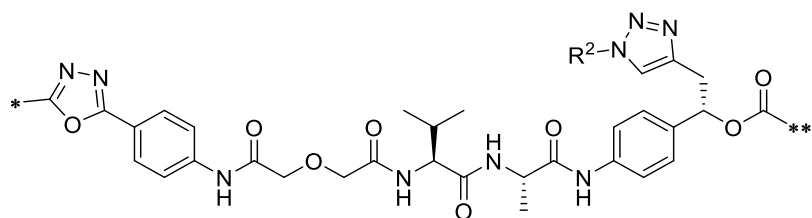
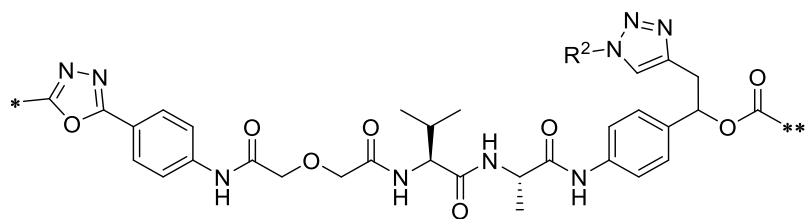
In some embodiments, L is selected from the following structures:



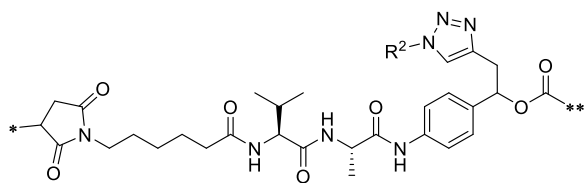
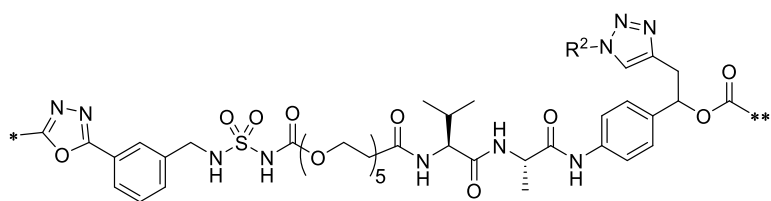


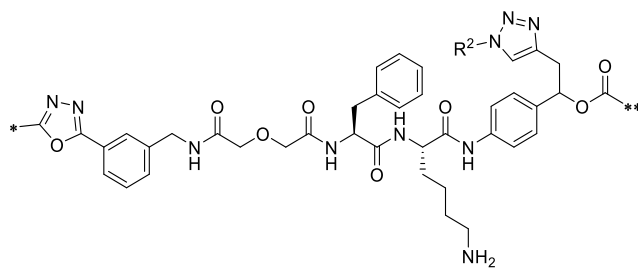
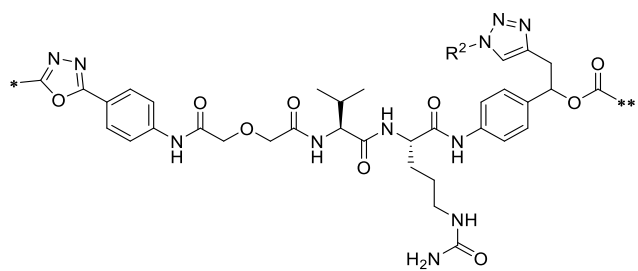
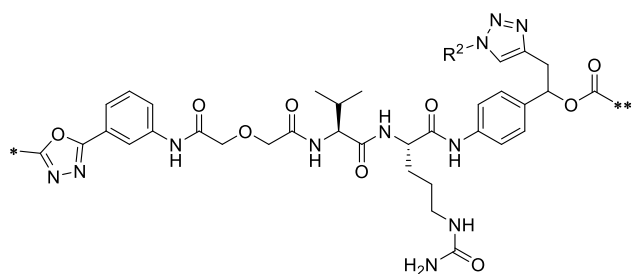
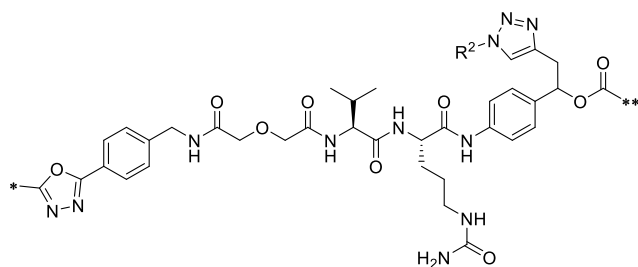
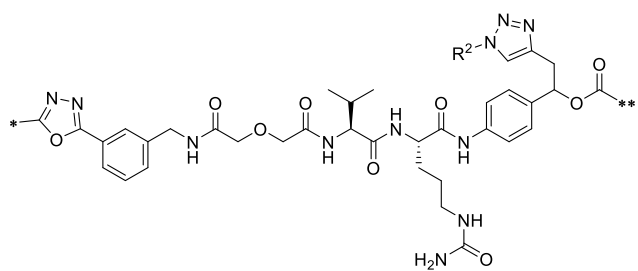
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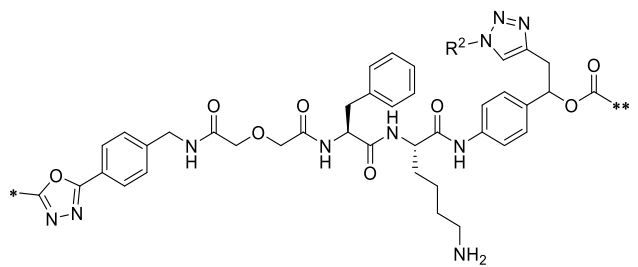


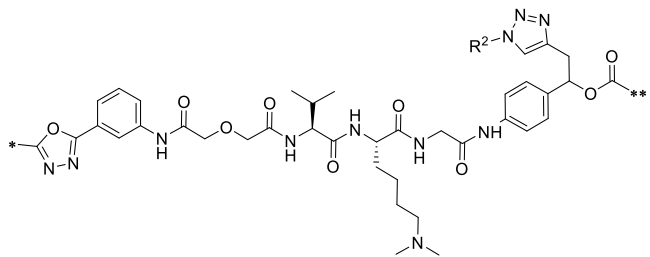
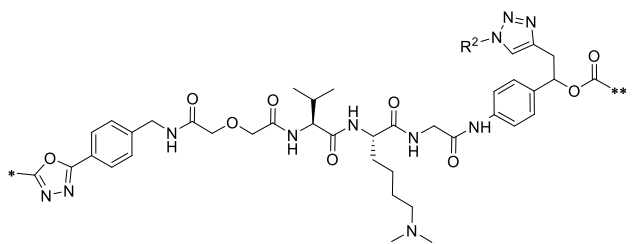
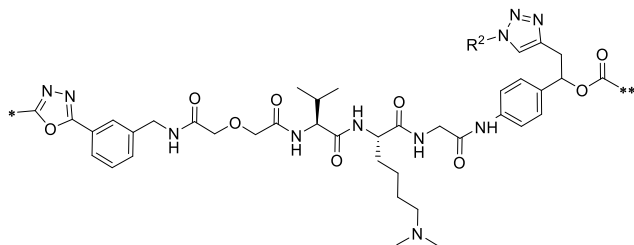
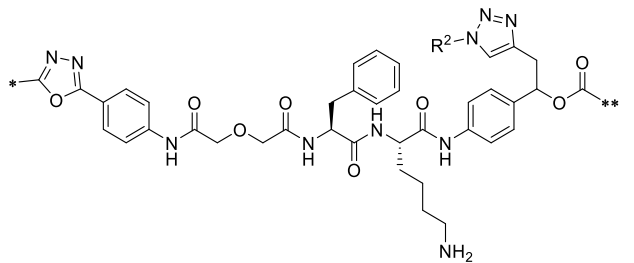
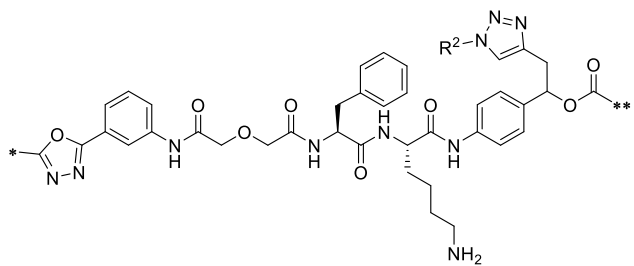
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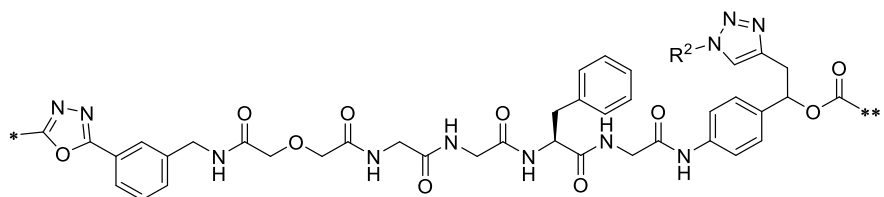
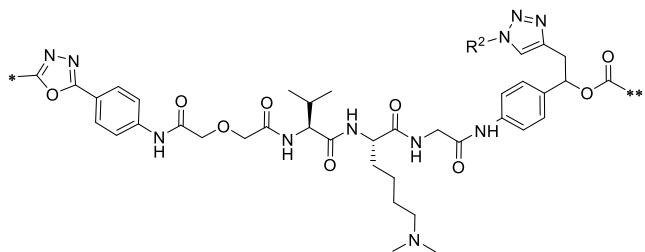


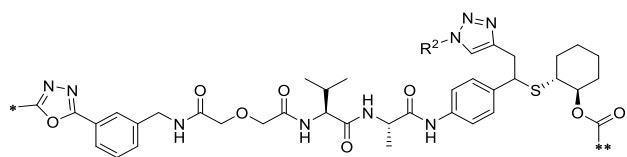
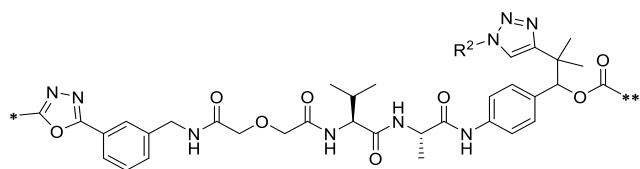
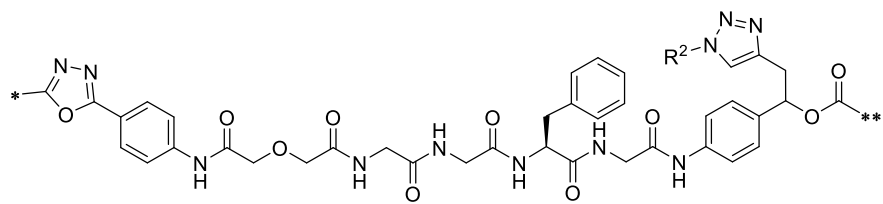
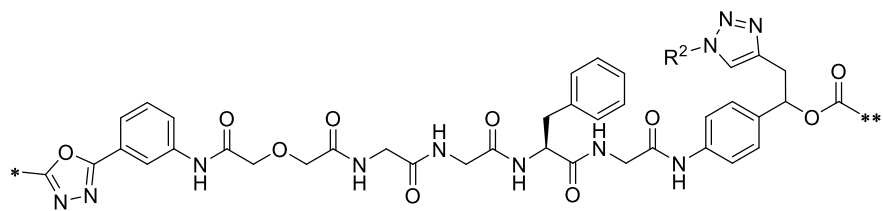
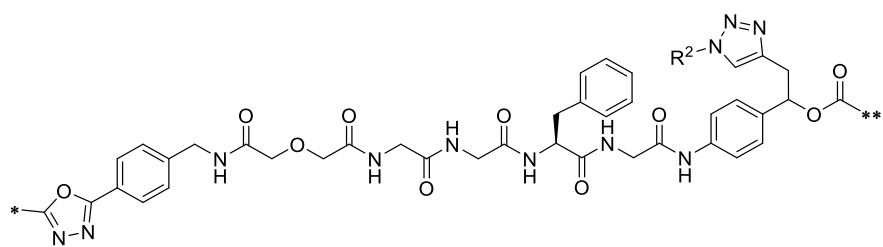
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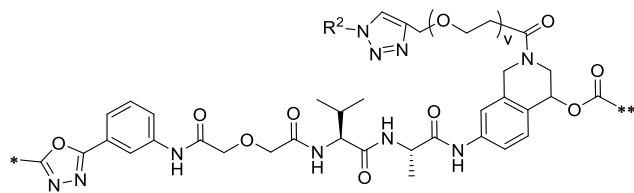
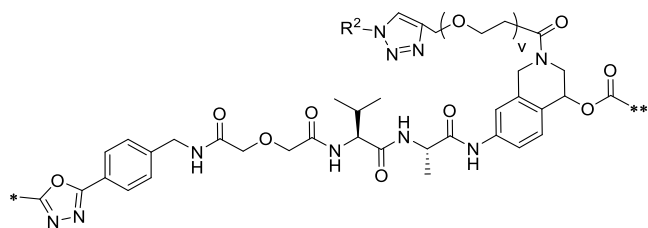
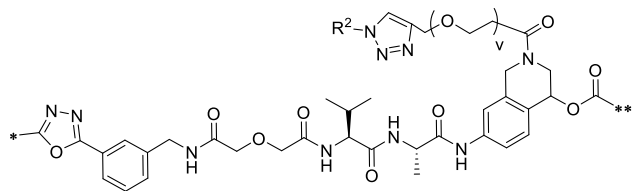


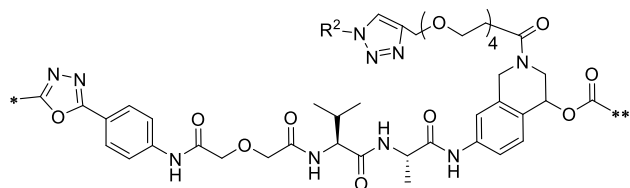
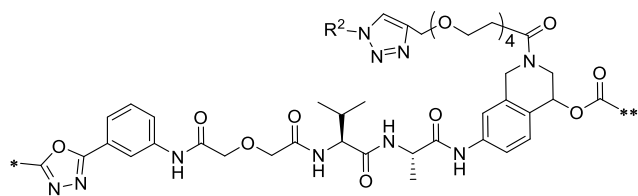
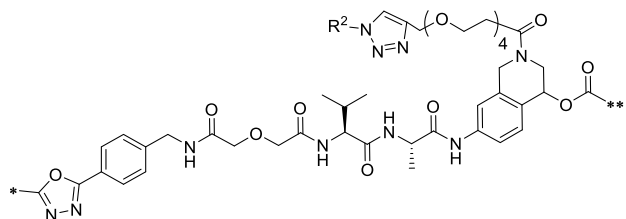
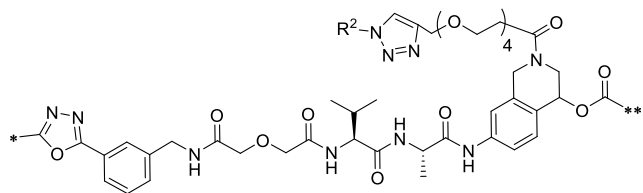
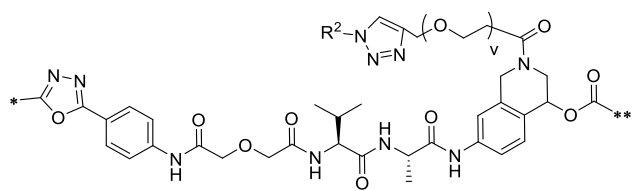
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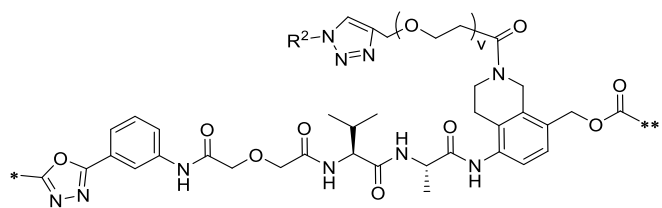
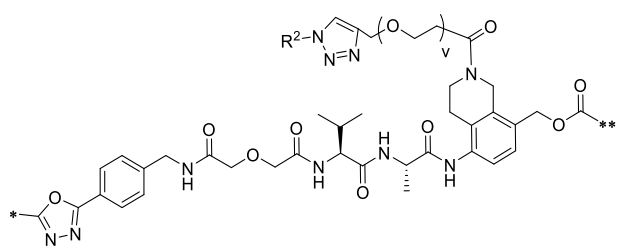
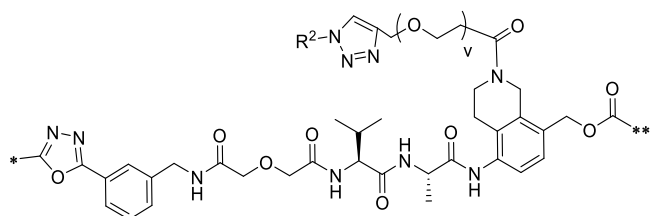


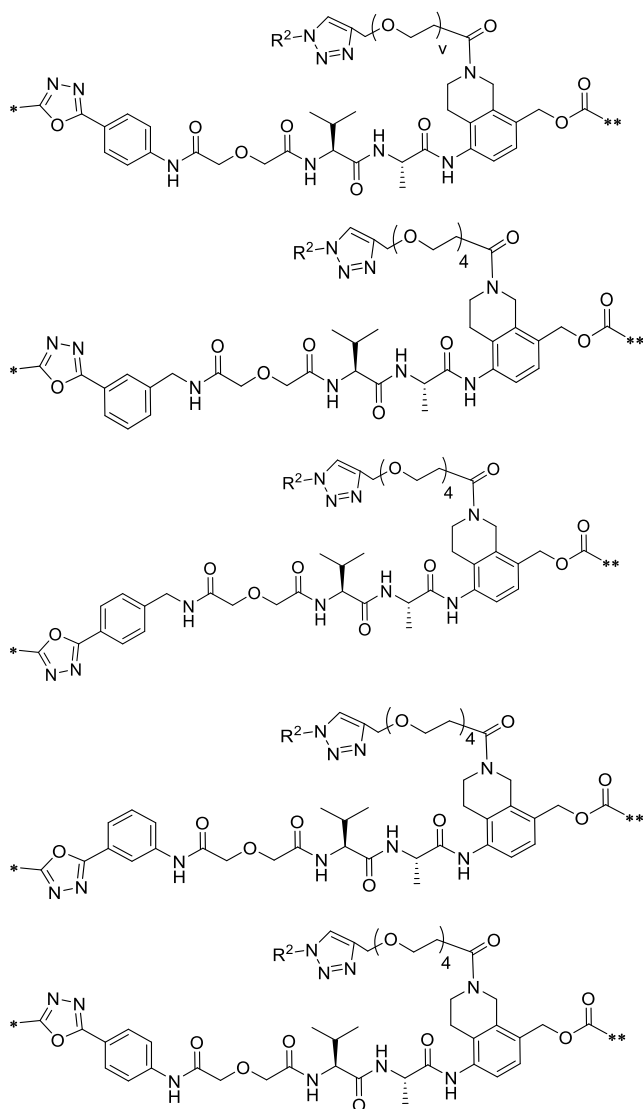
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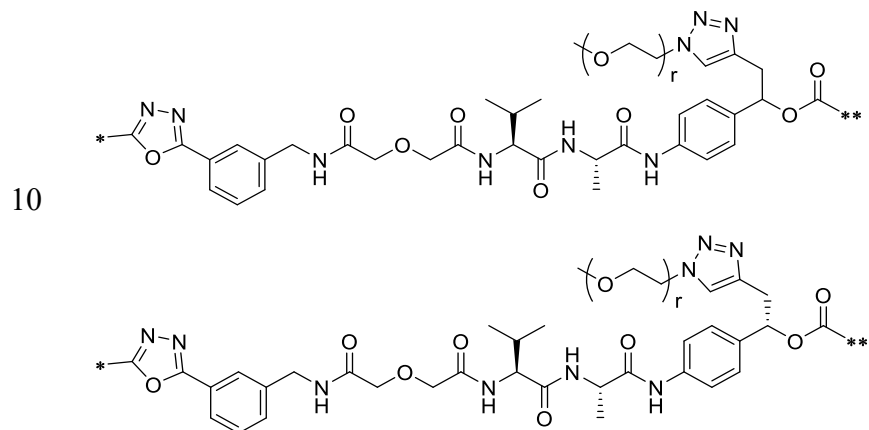
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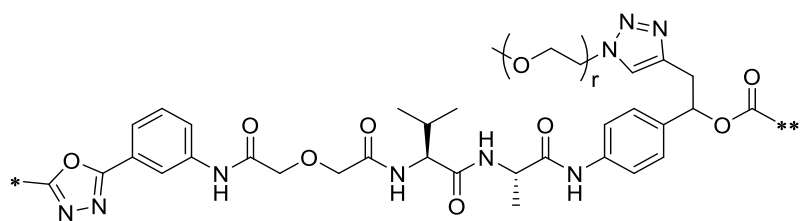
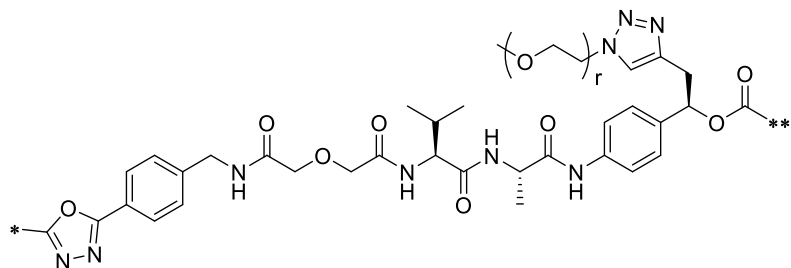
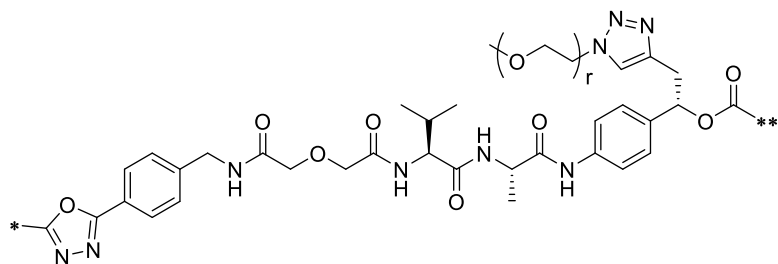
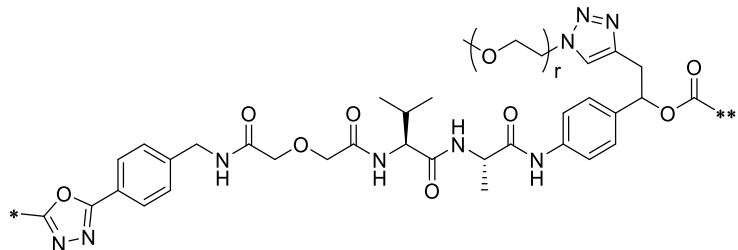
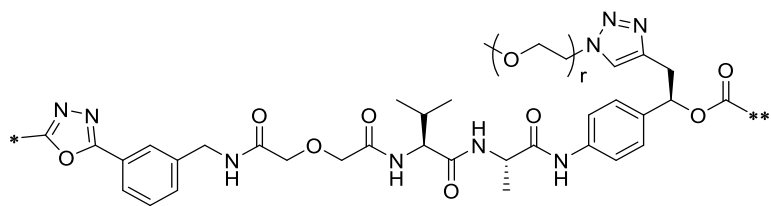




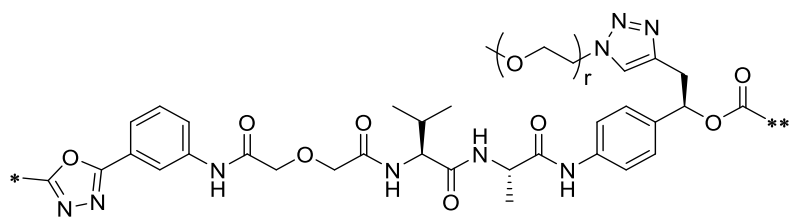
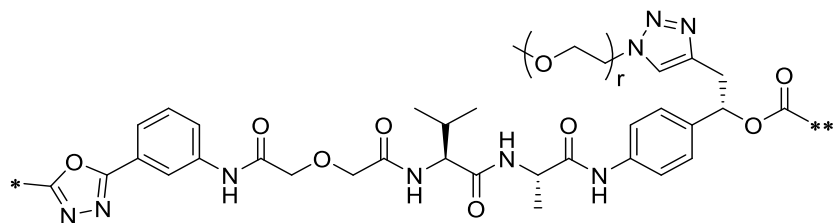
wherein v and w are each independently an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), $*$ represents linkage to a sulfhydryl group of the antibody A, and $**$ represents linkage to the amino group of the bioactive molecule D.

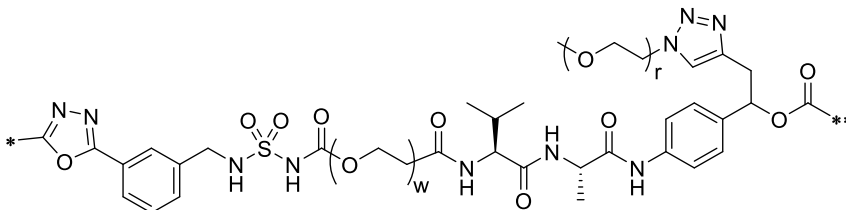
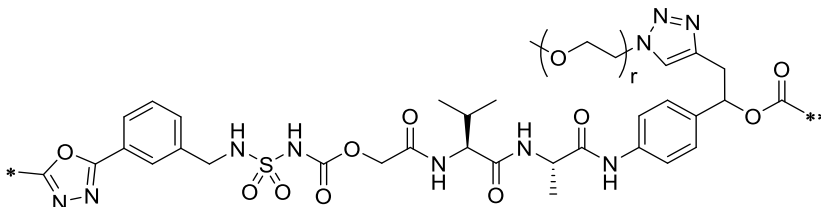
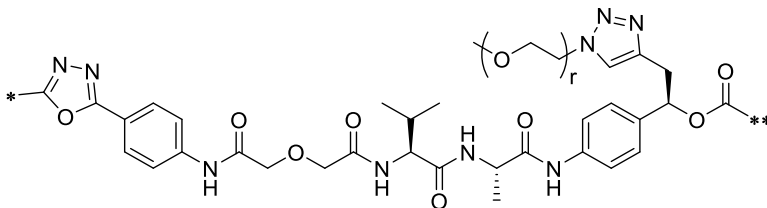
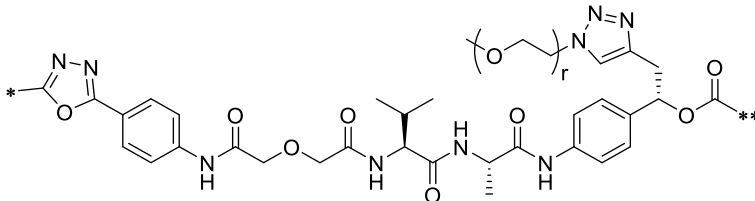
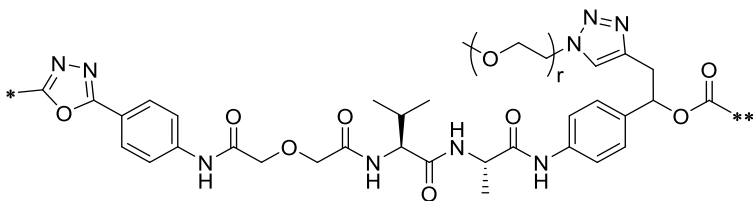
In some embodiments, L is selected from the following structures:



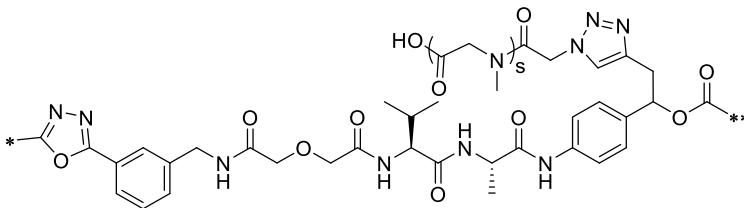
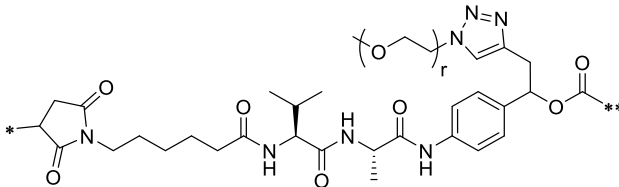
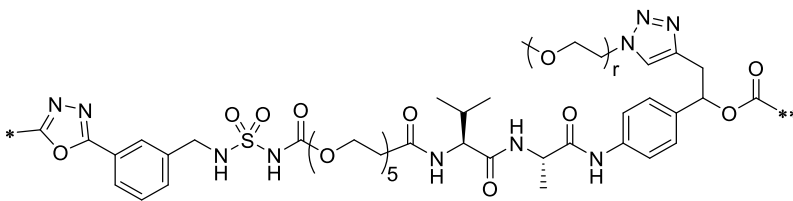


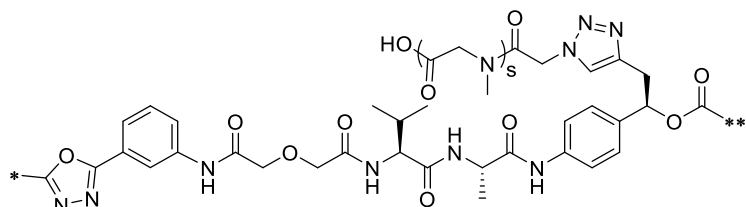
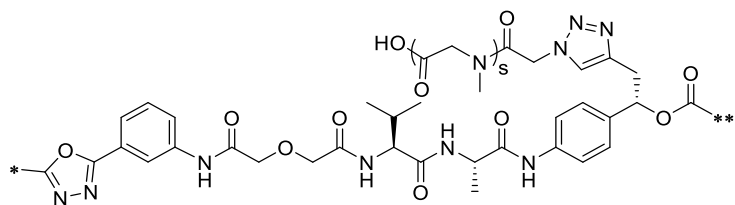
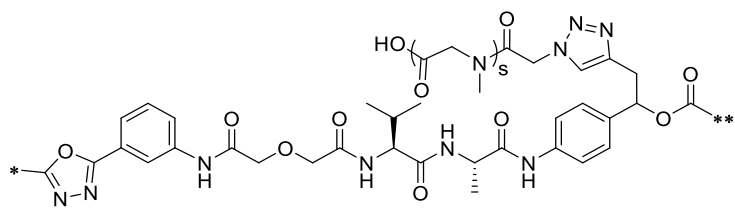
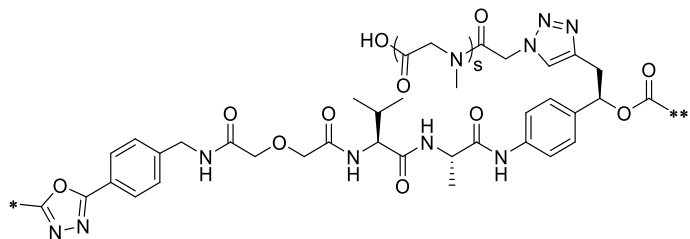
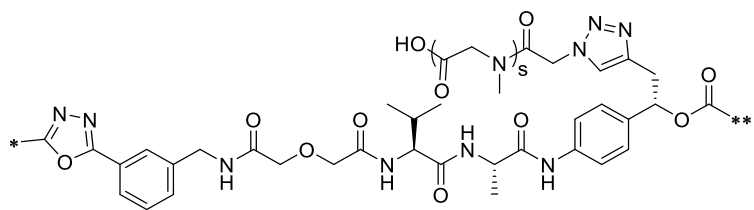
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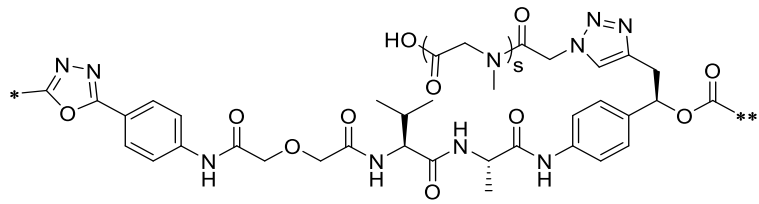
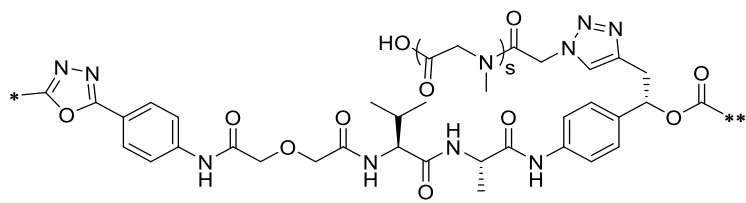
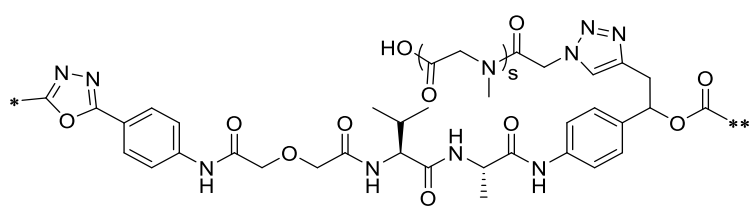


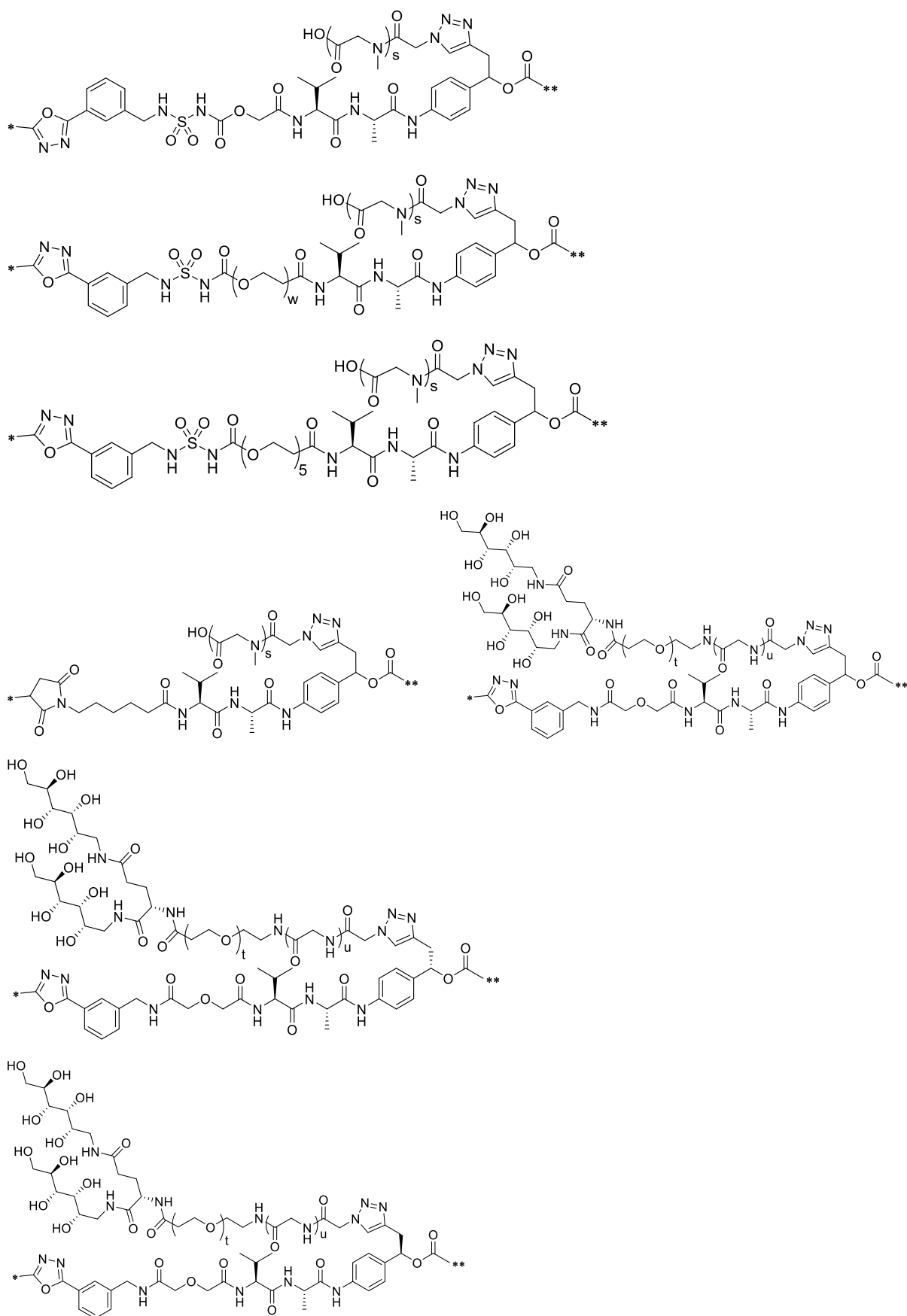
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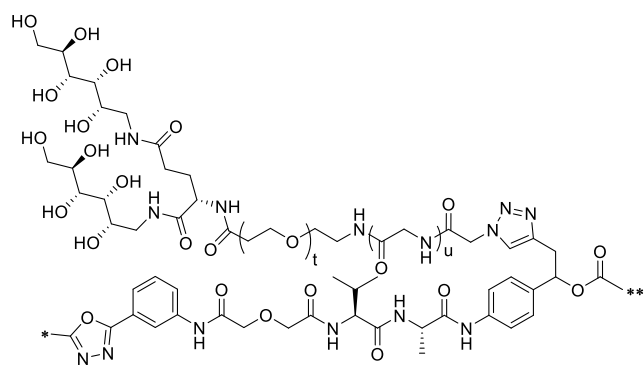
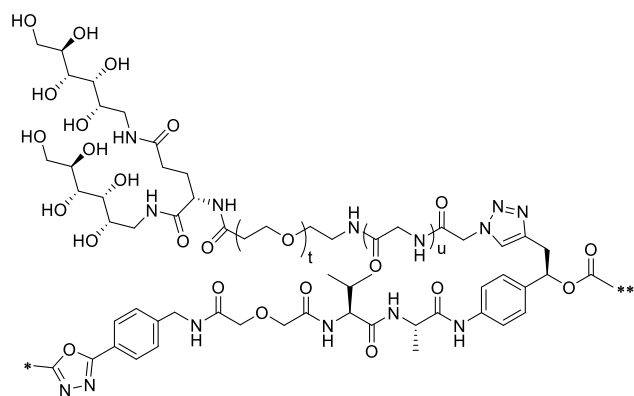
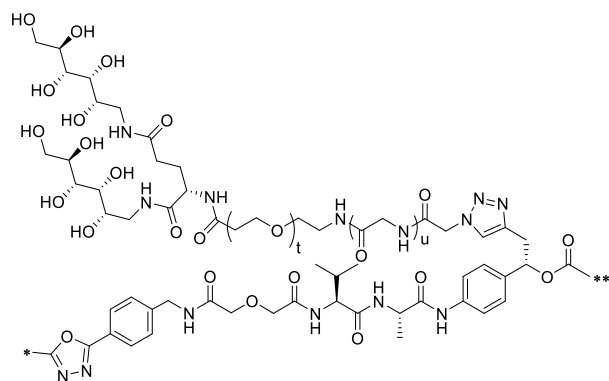
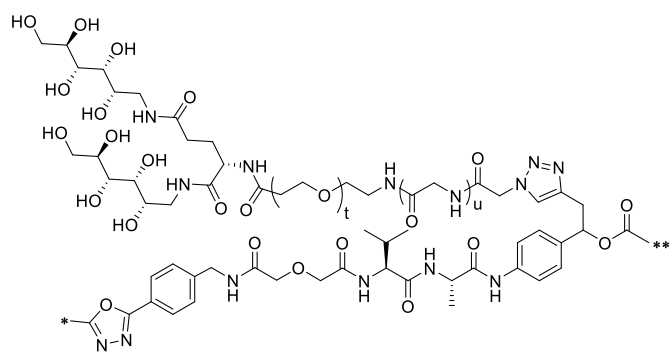


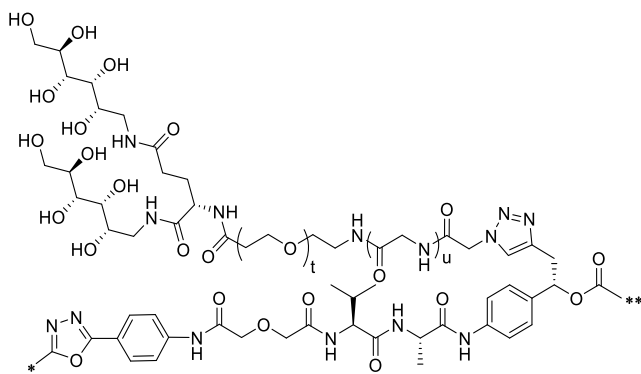
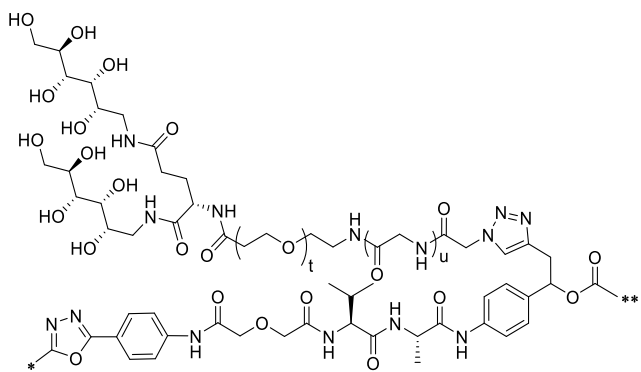
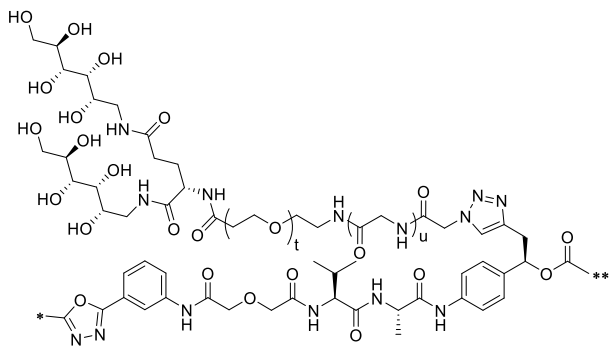
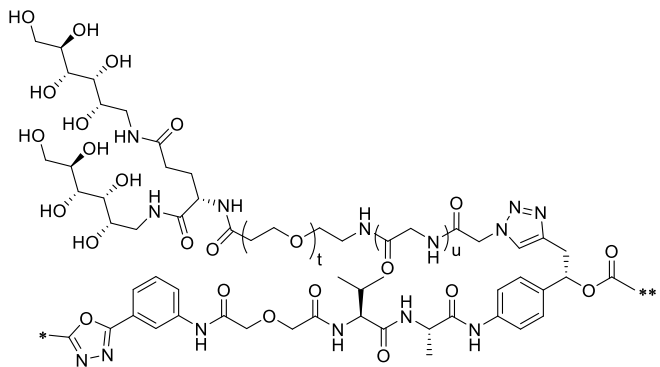


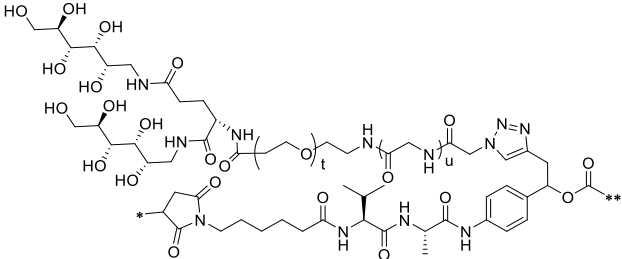
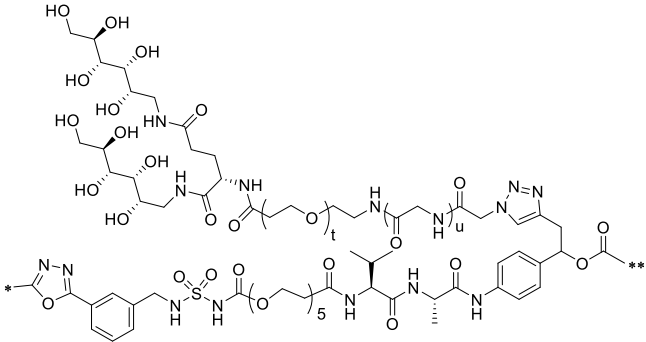
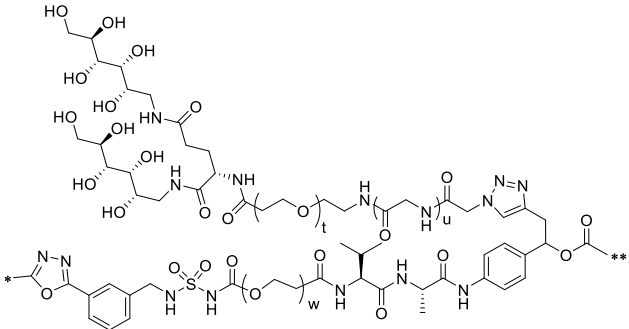
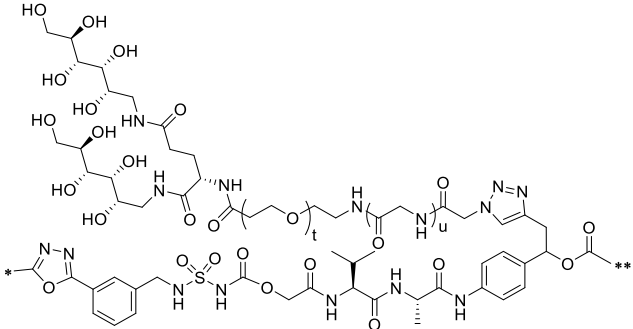
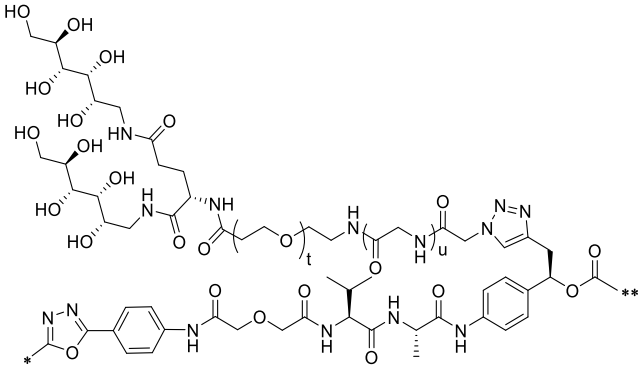
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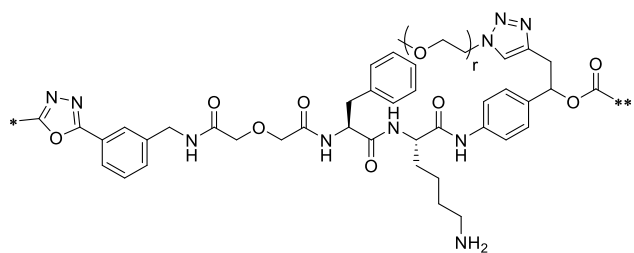
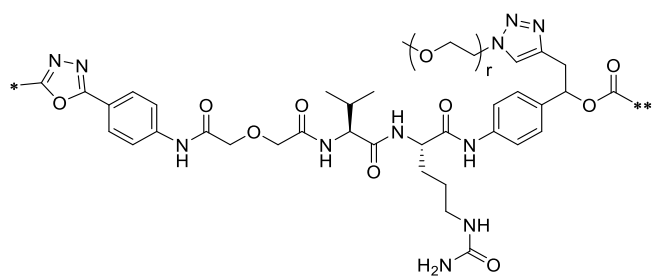
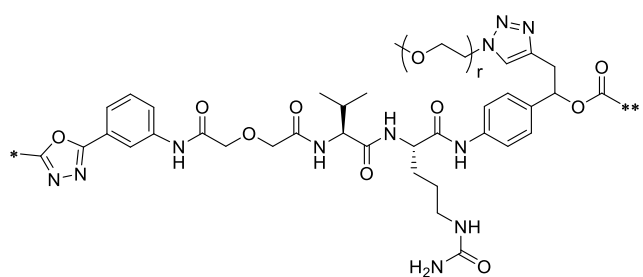
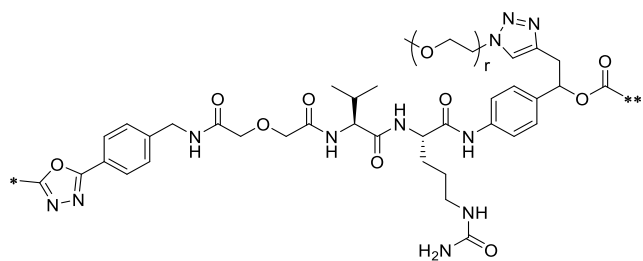
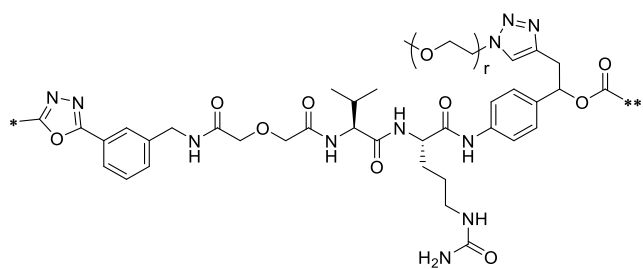




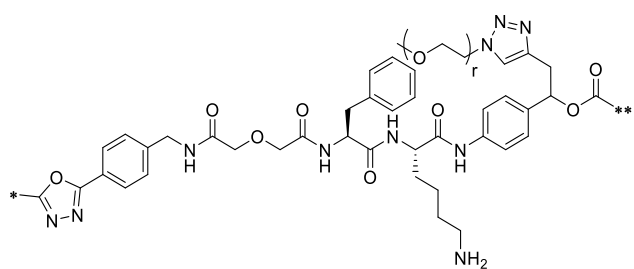


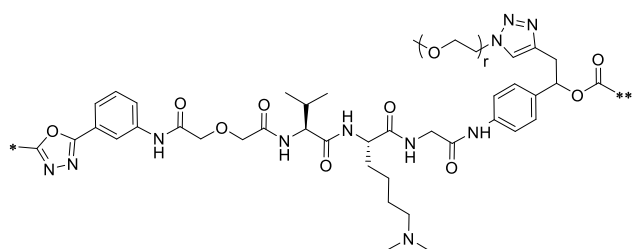
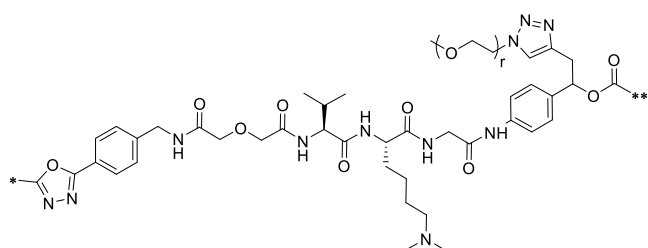
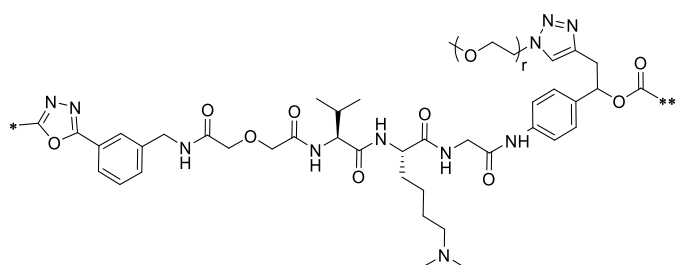
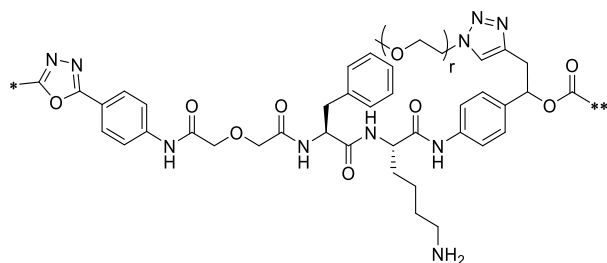
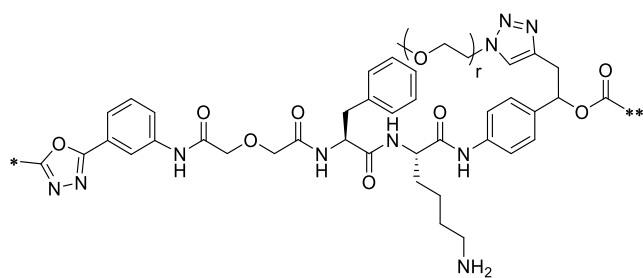




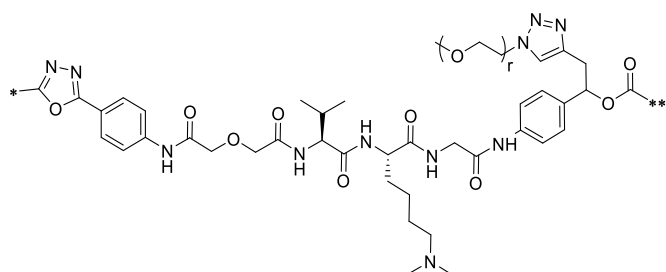


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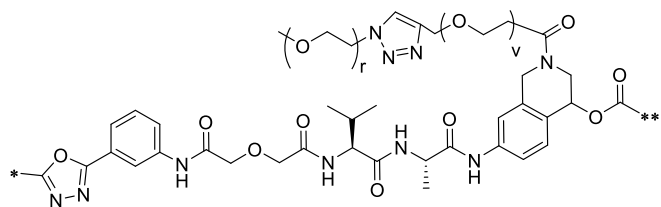
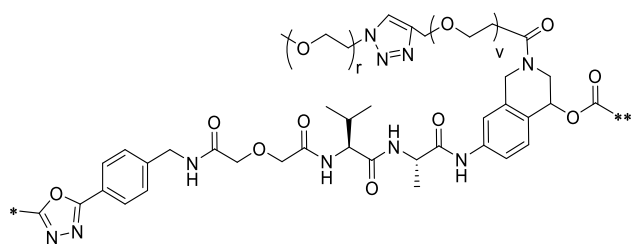
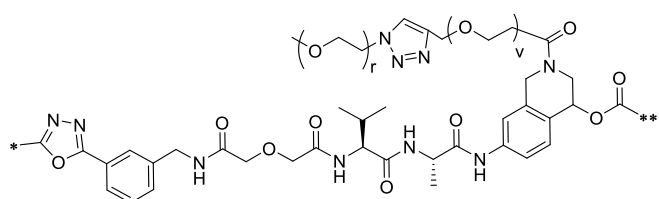
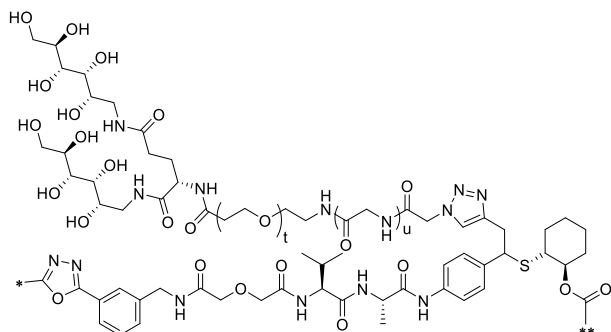
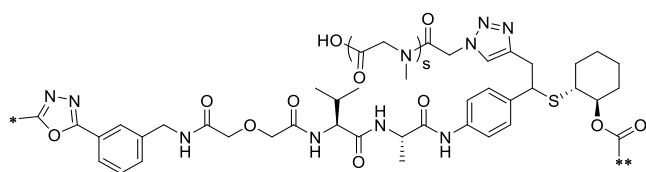




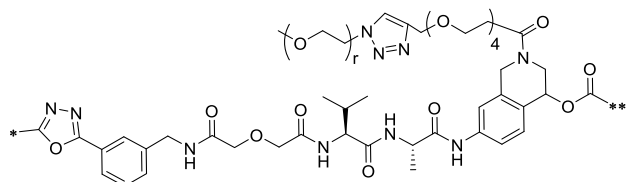
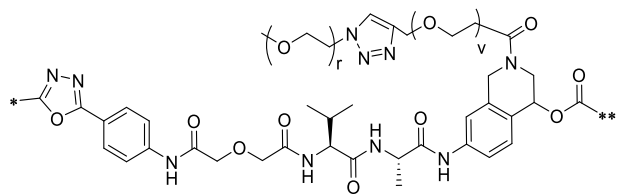
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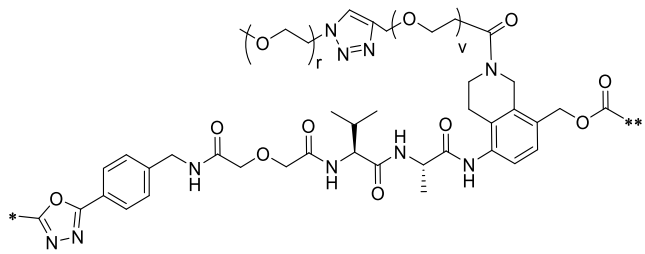
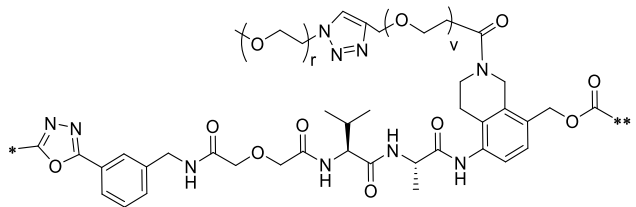
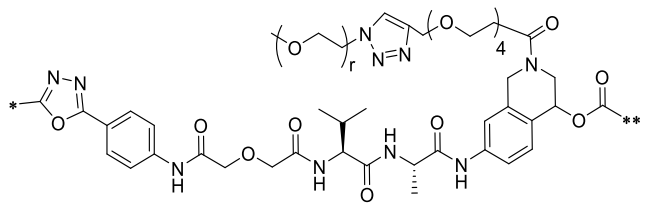
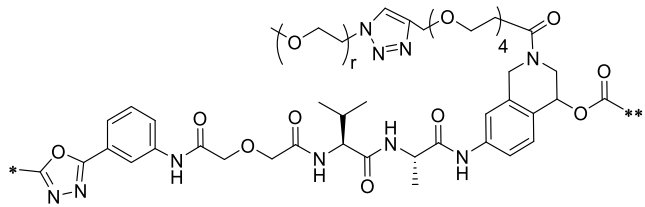
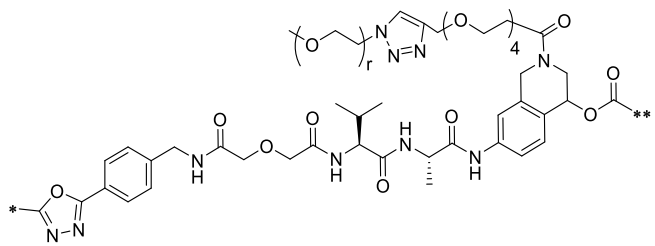




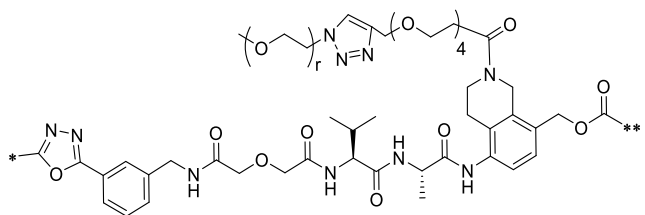
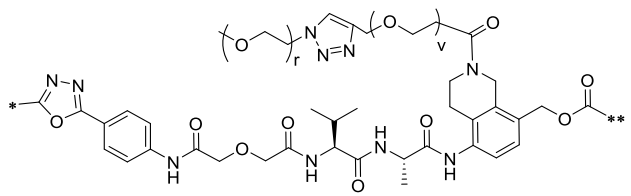
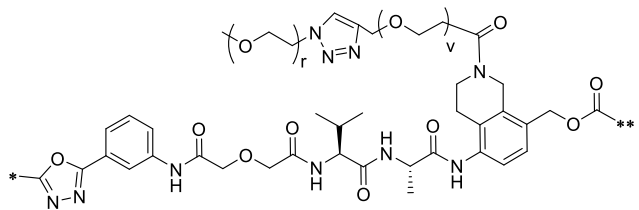


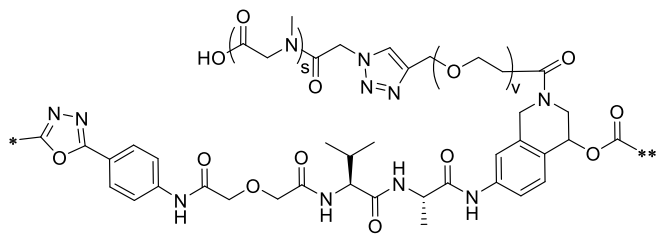
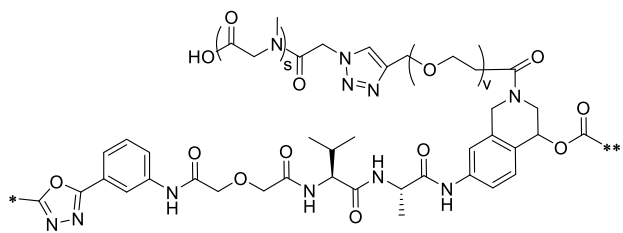
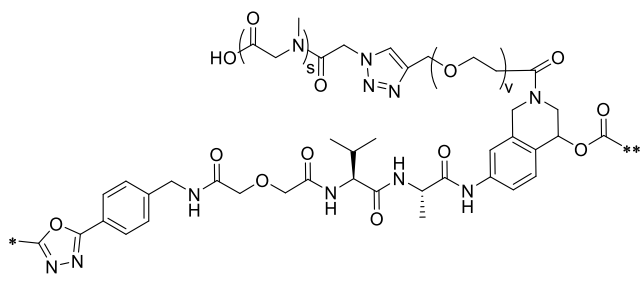
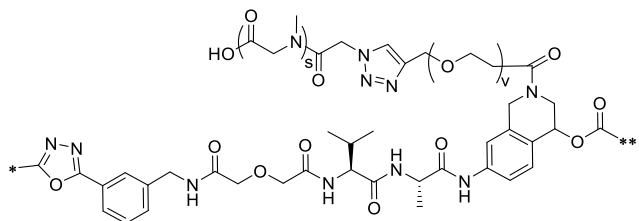
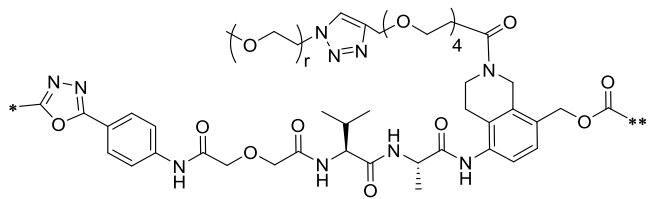
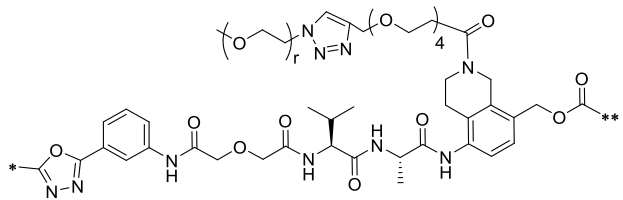
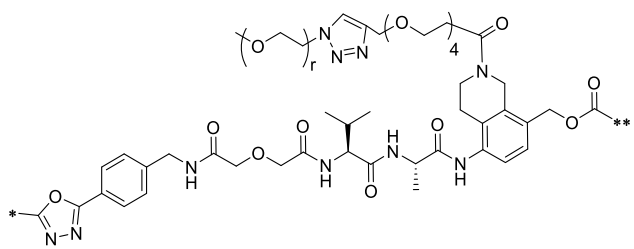
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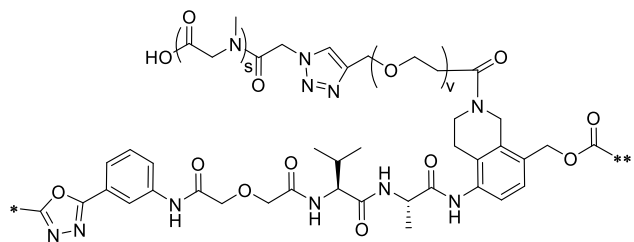


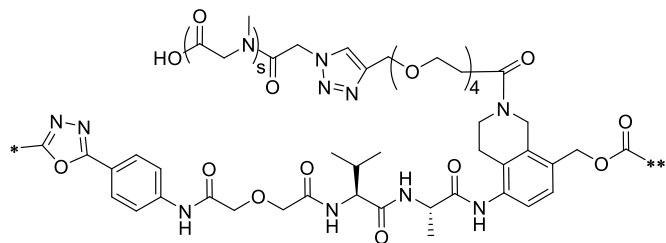
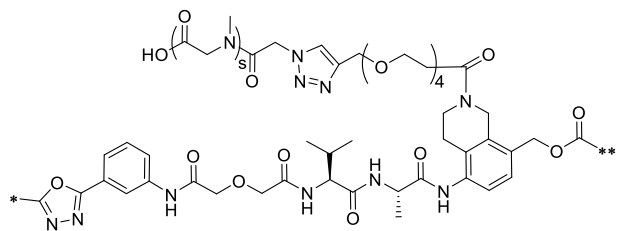
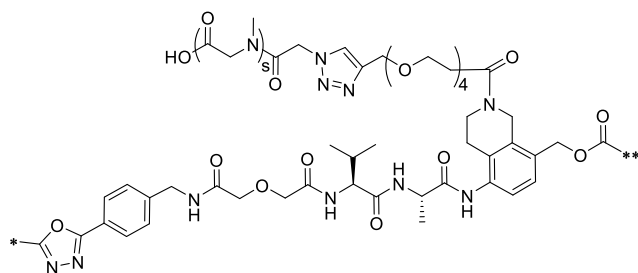
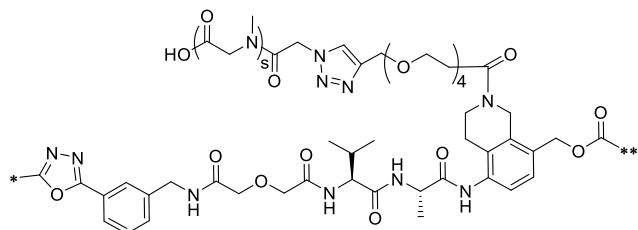
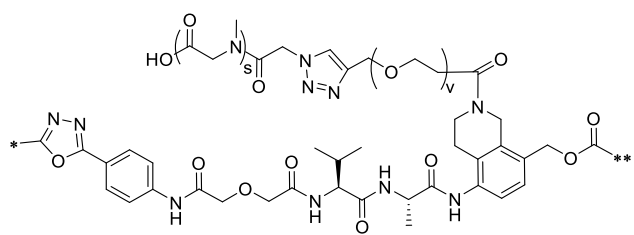


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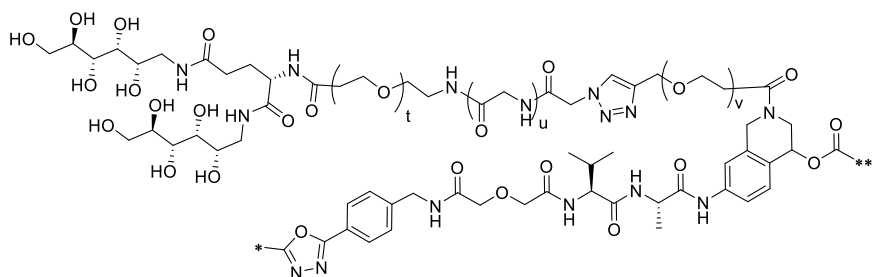
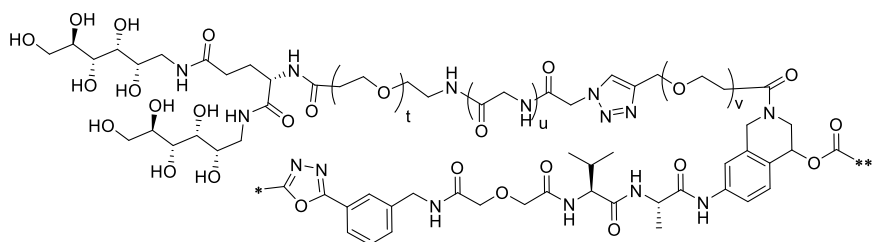


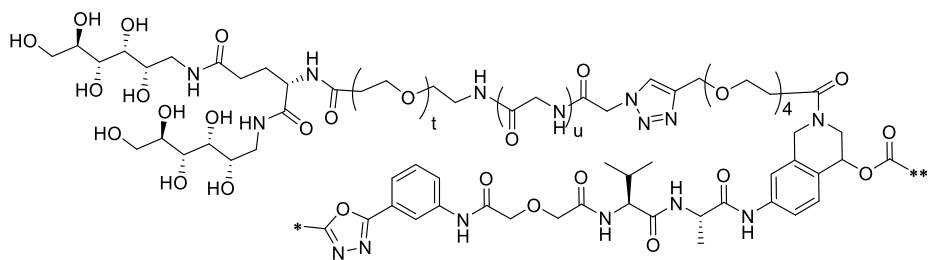
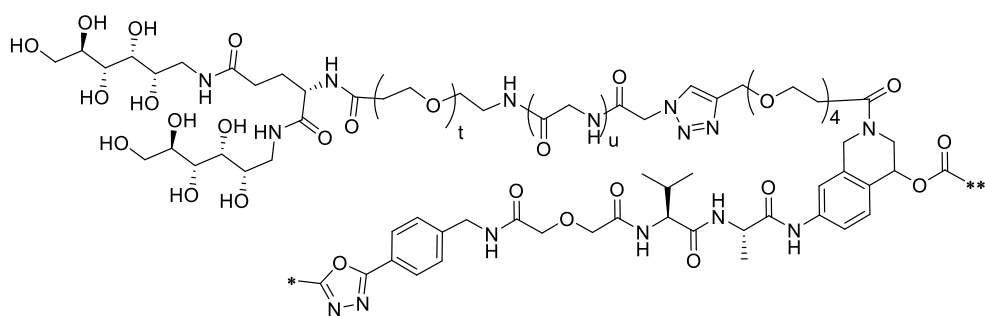
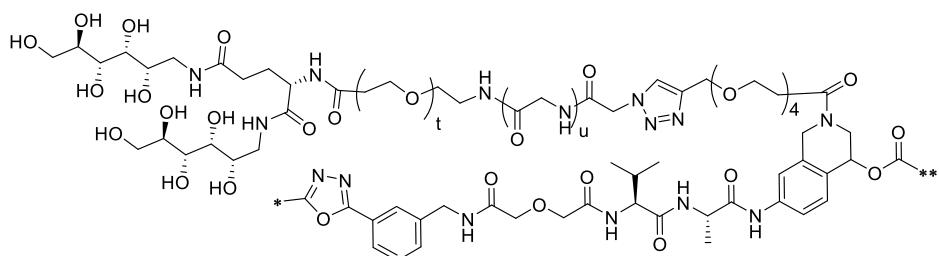
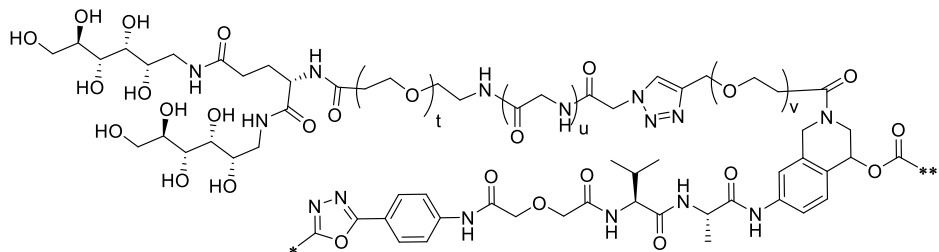
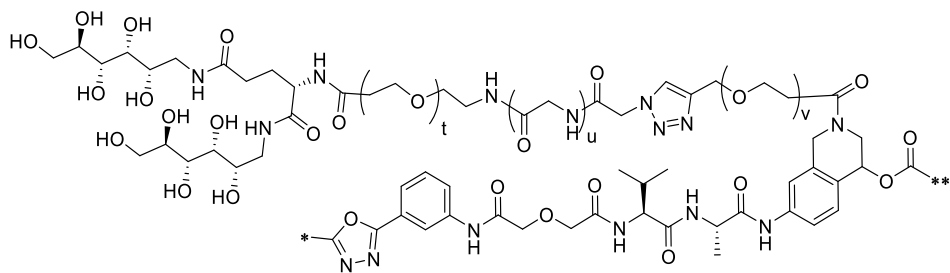




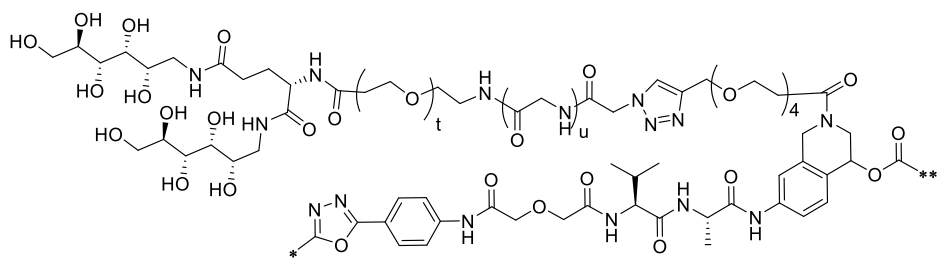


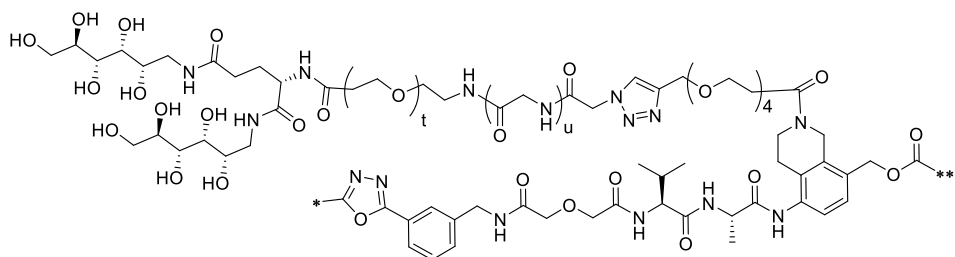
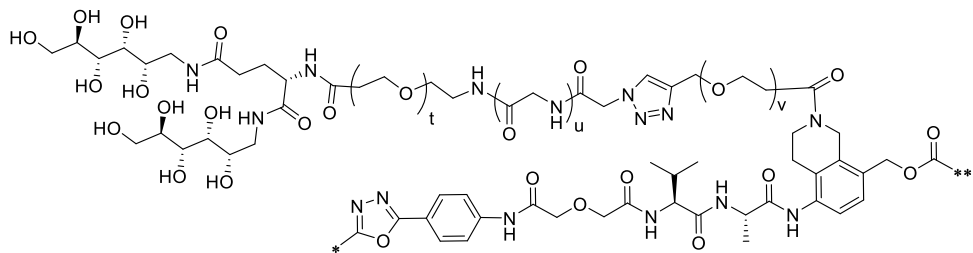
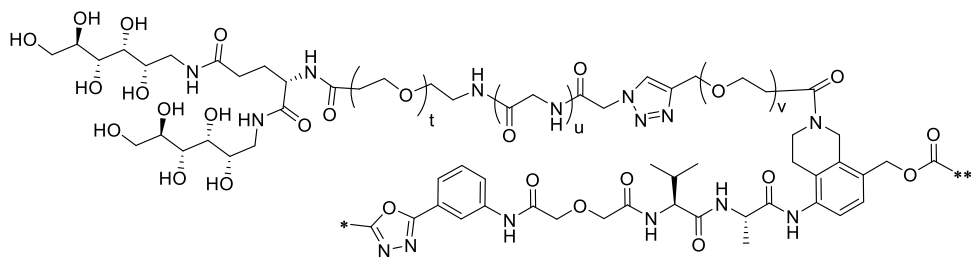
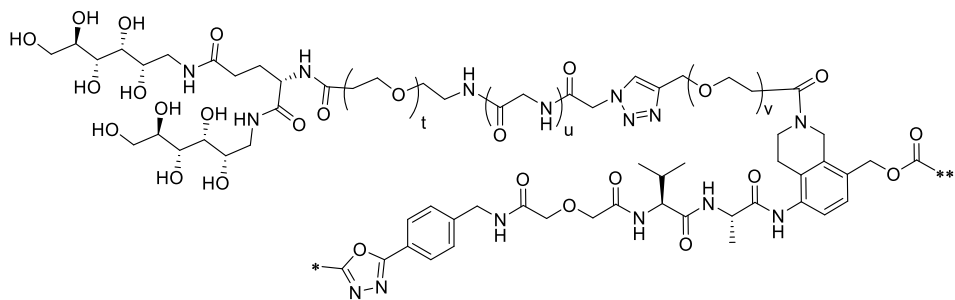
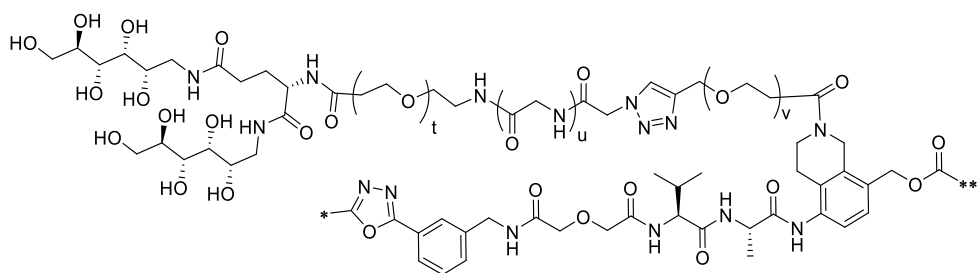
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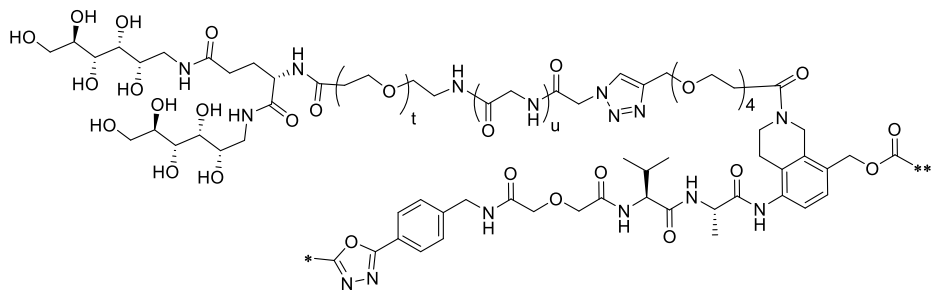


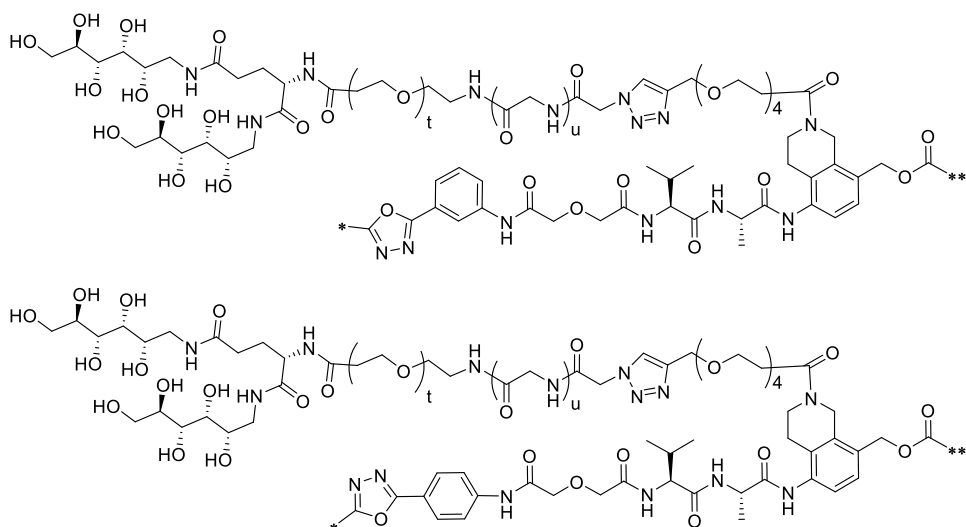
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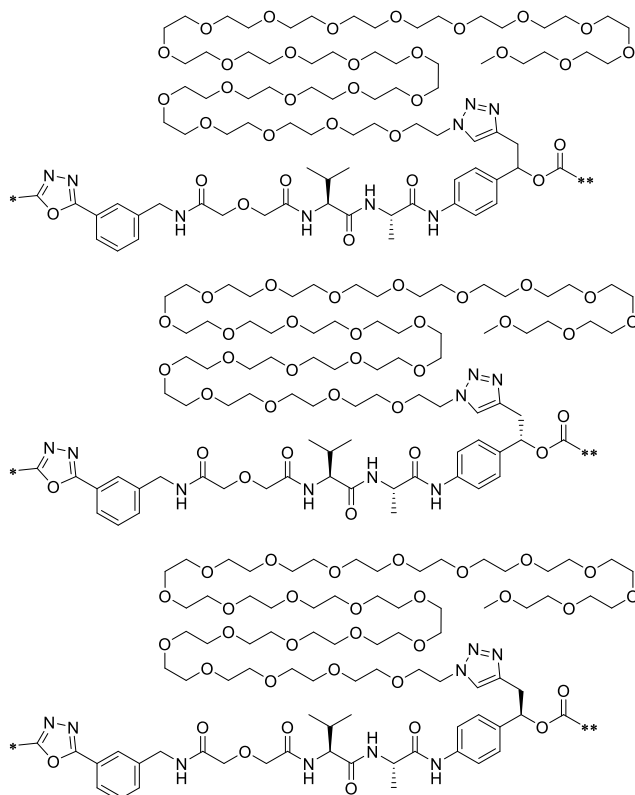
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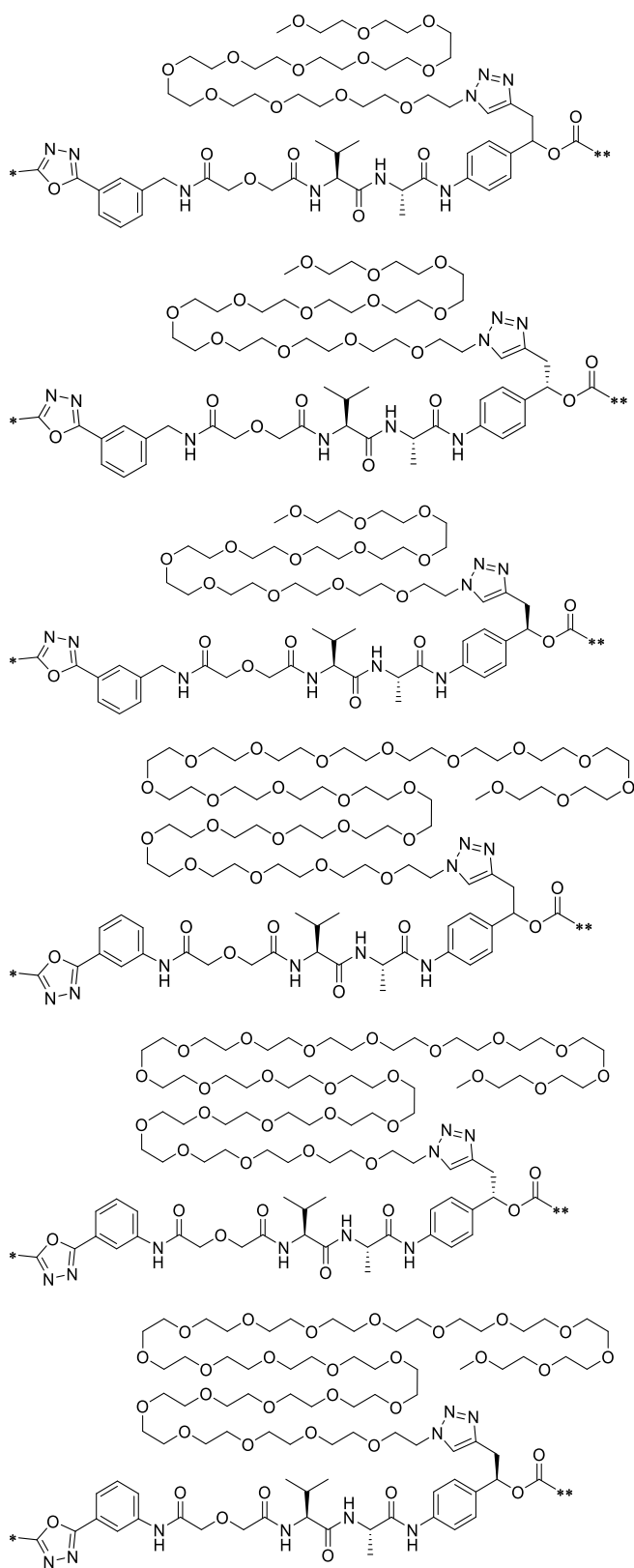


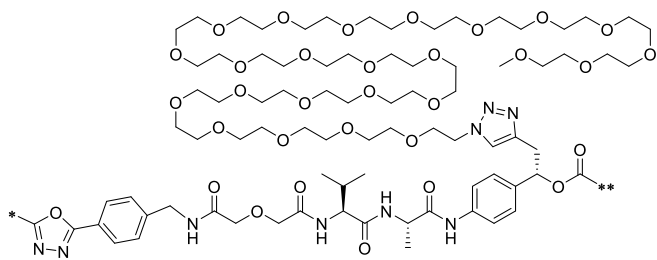
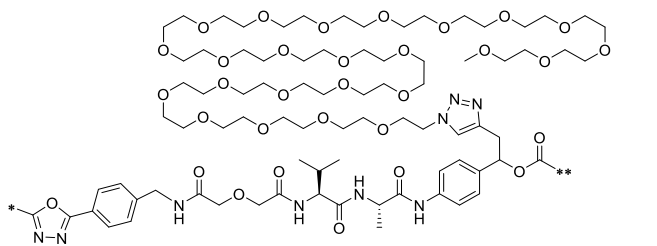
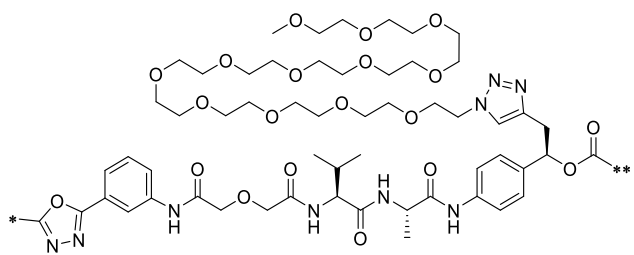
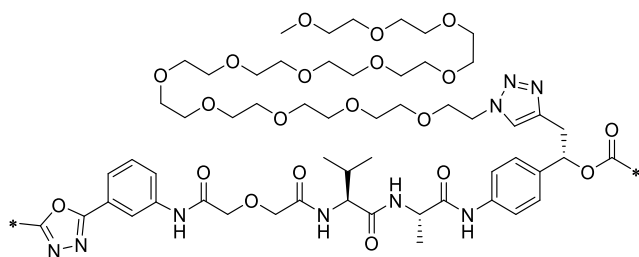
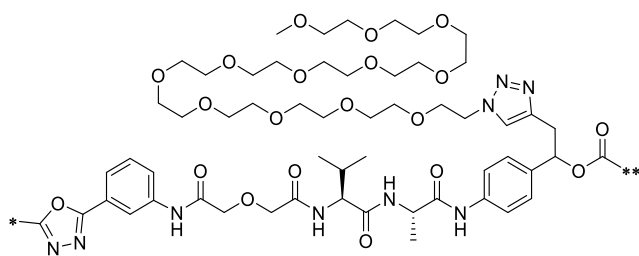


wherein v and w are each independently an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to a sulfhydryl group of the antibody A, and ** represents linkage to the amino group of the bioactive molecule D; r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50).

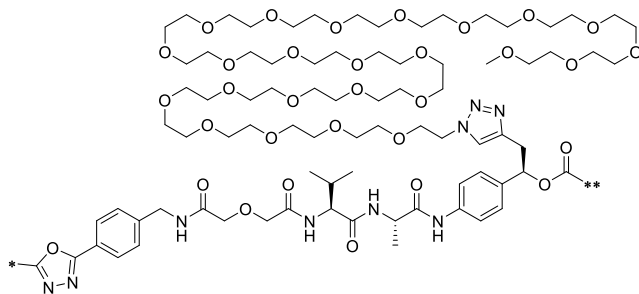
In some embodiments, L is selected from the following structures:

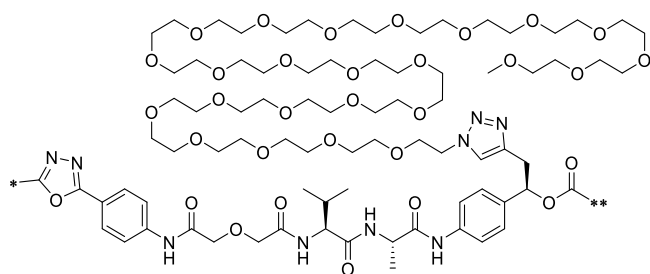
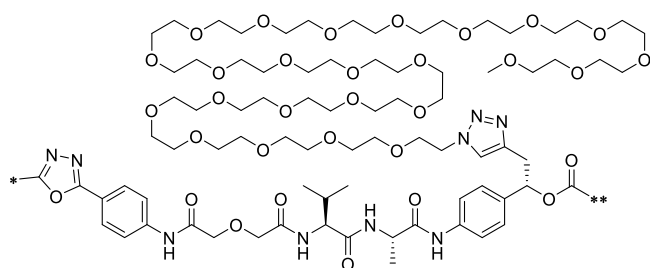
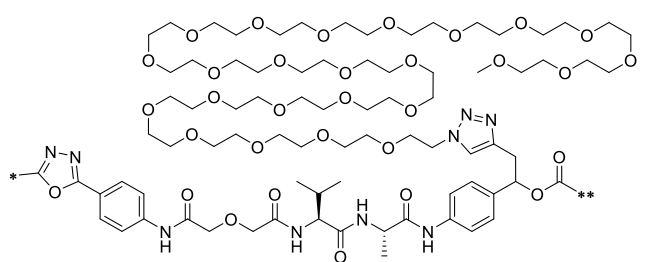
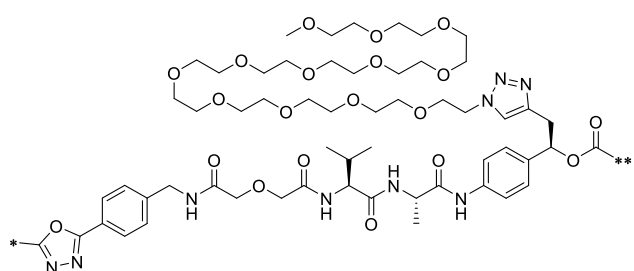
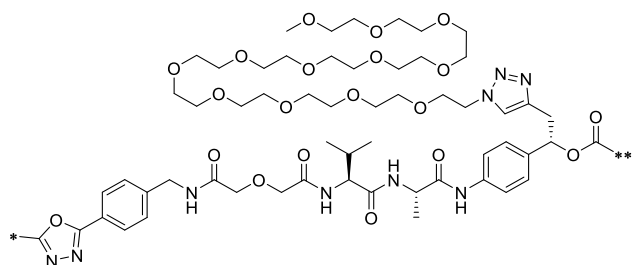
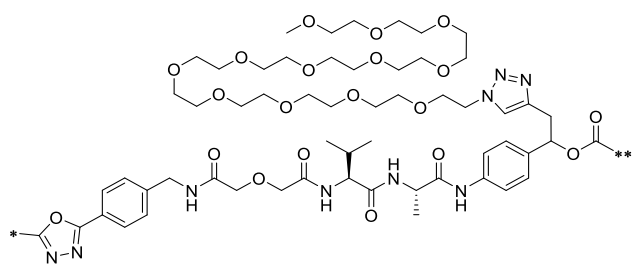


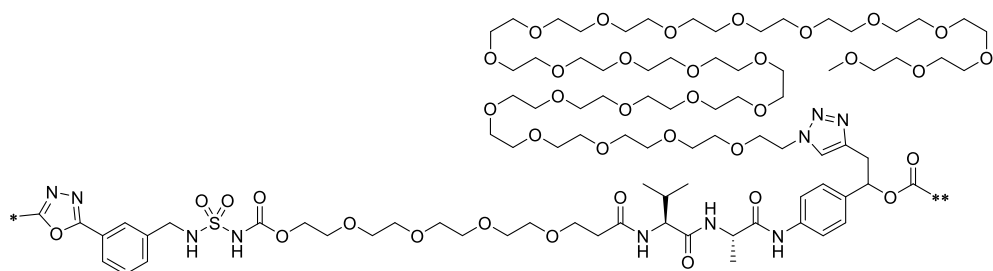
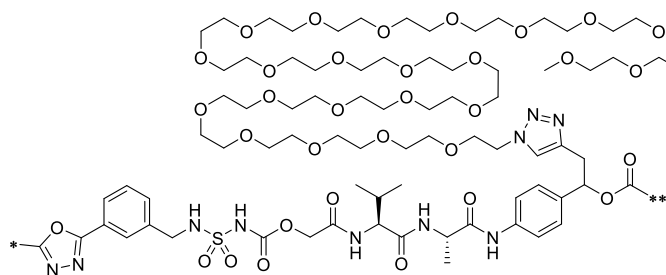
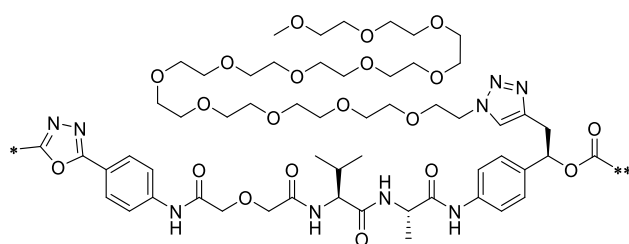
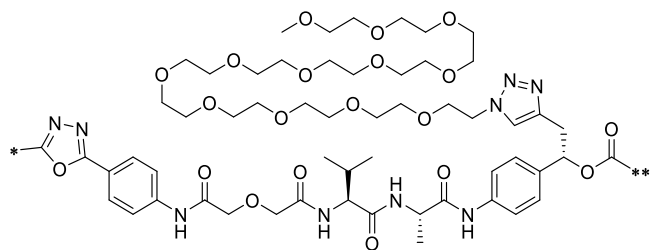
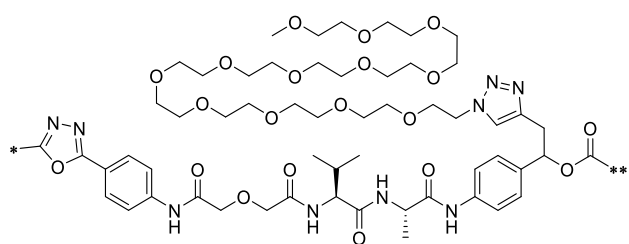




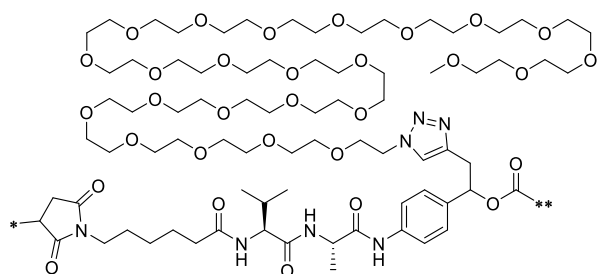
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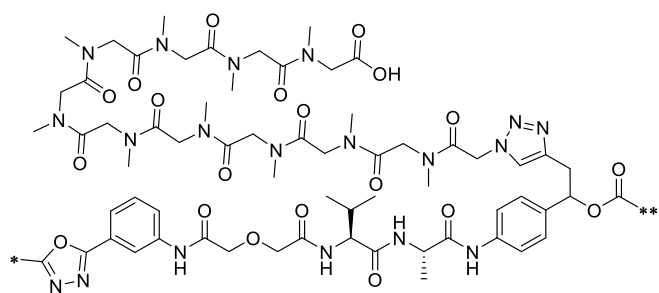
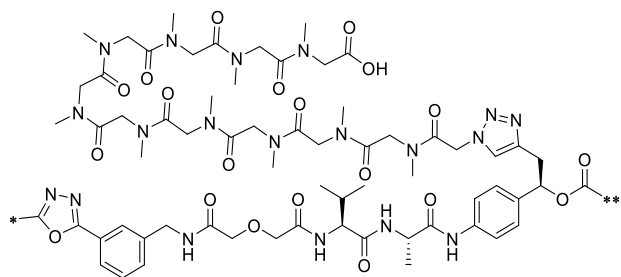
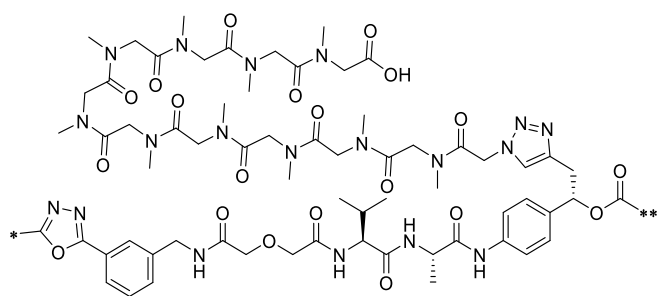
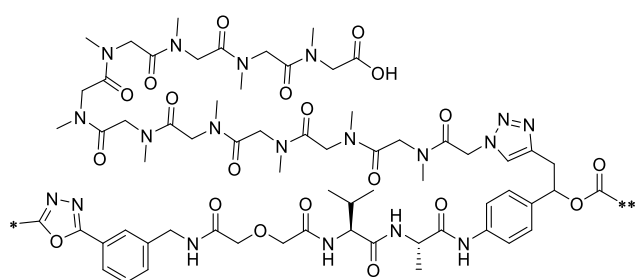
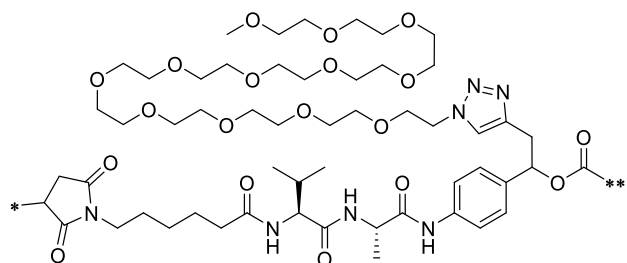
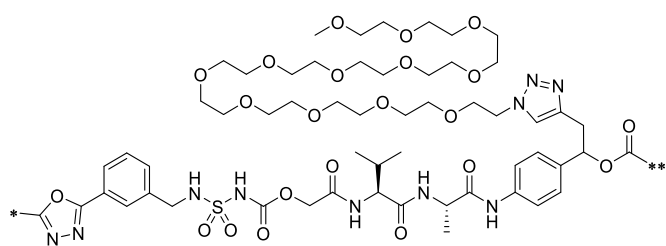


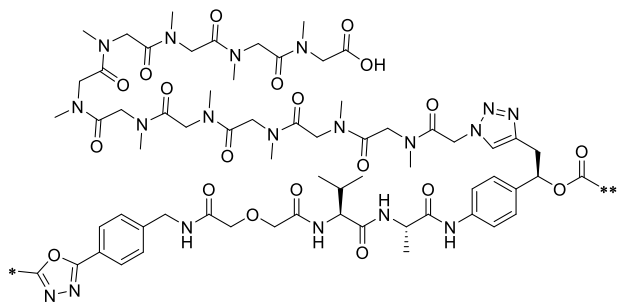
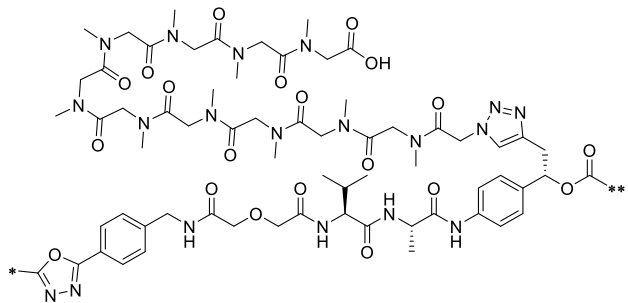
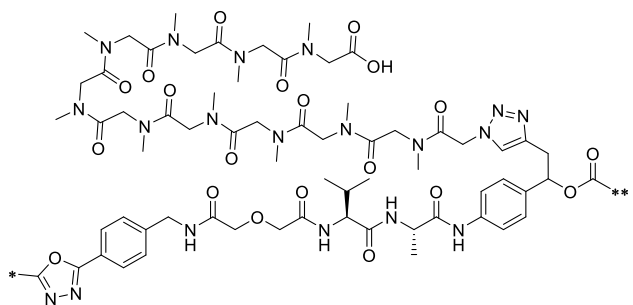
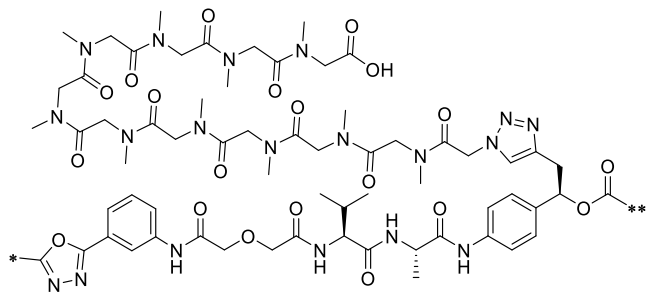
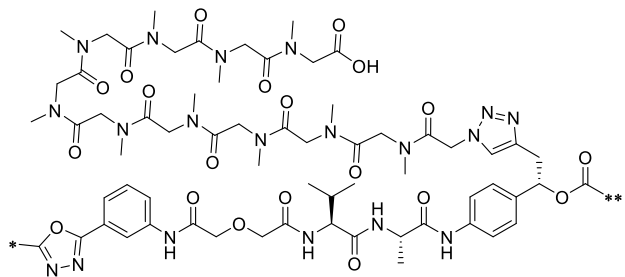




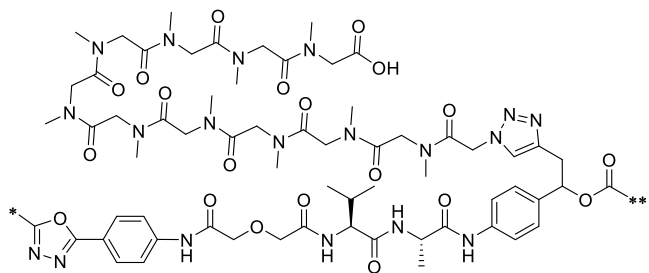
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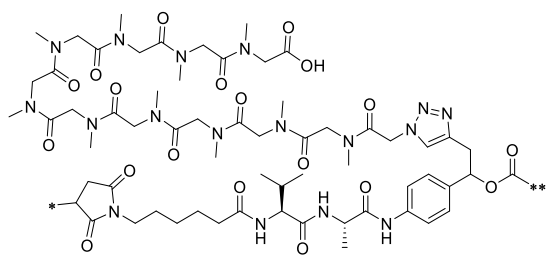
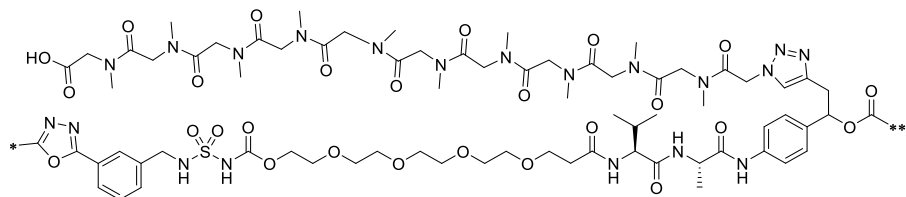
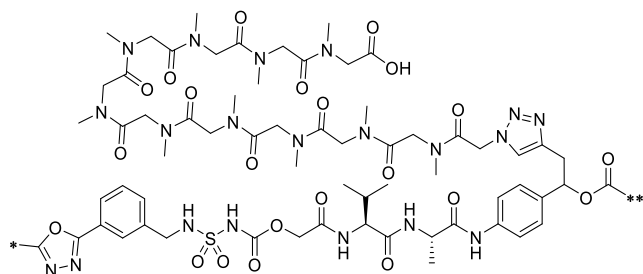
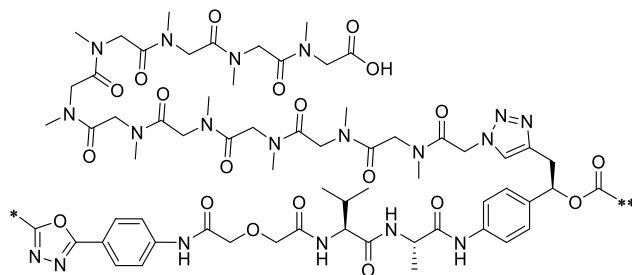
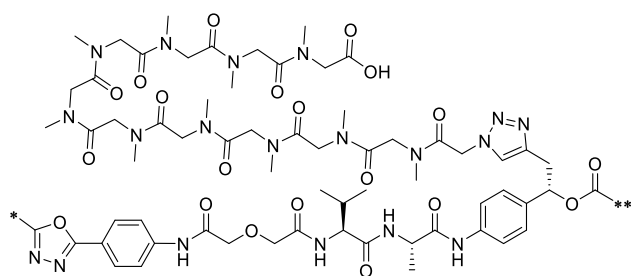




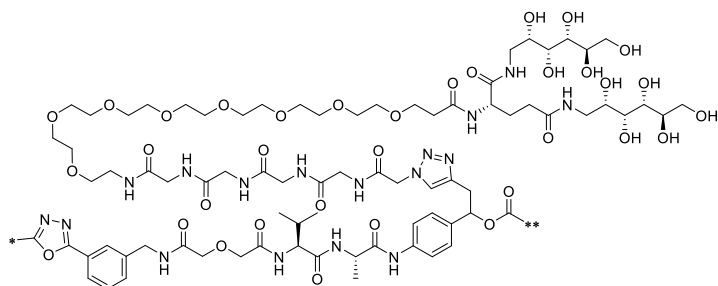


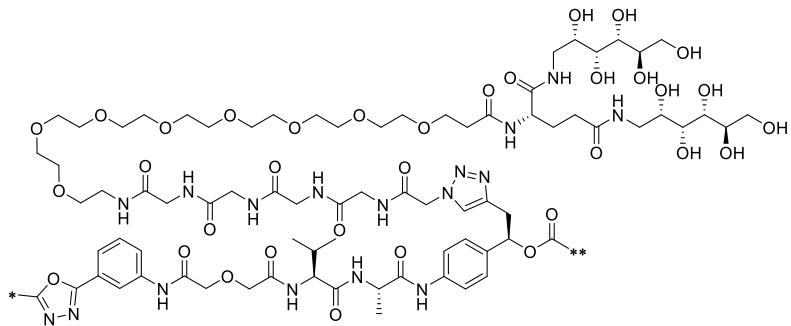
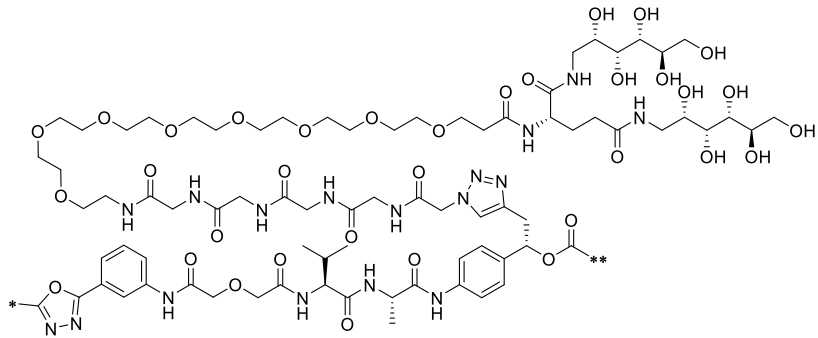
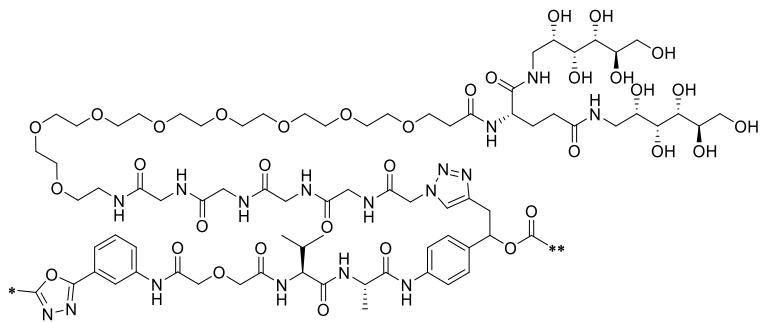
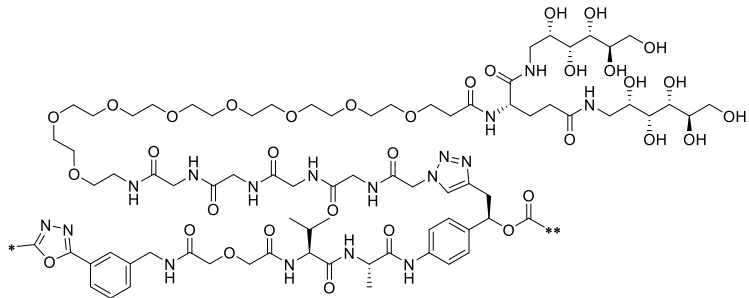
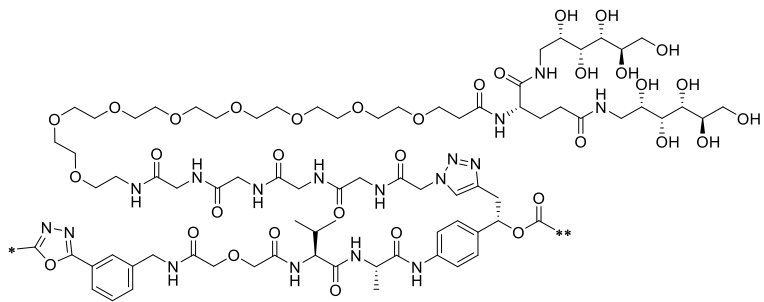
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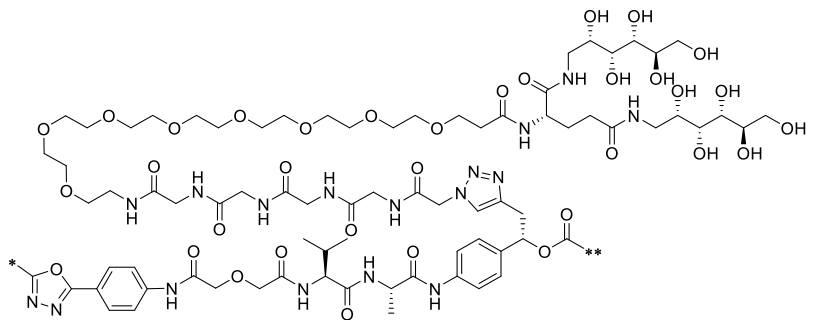
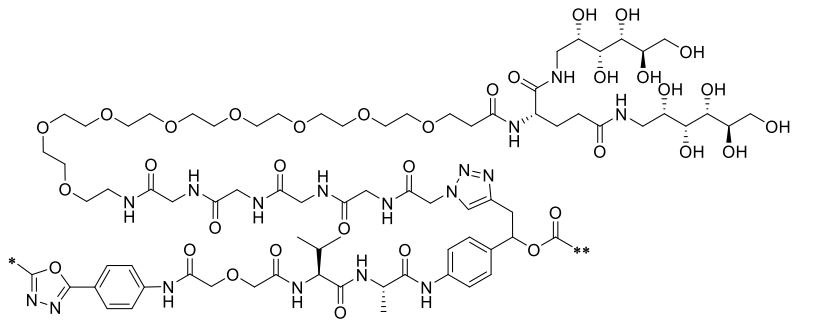
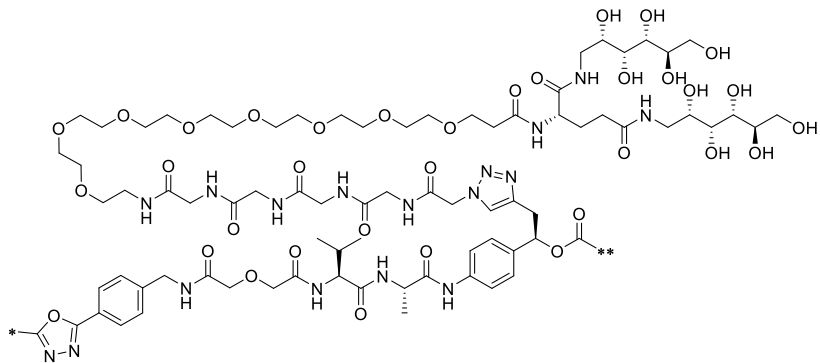
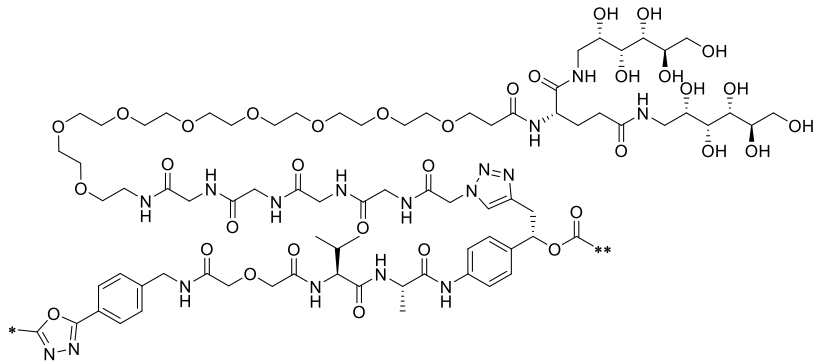
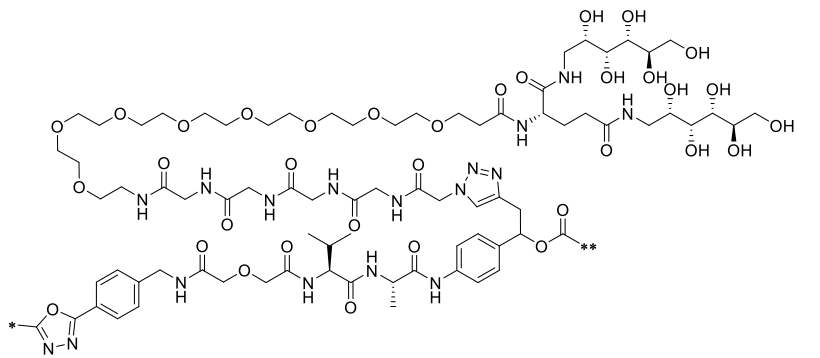


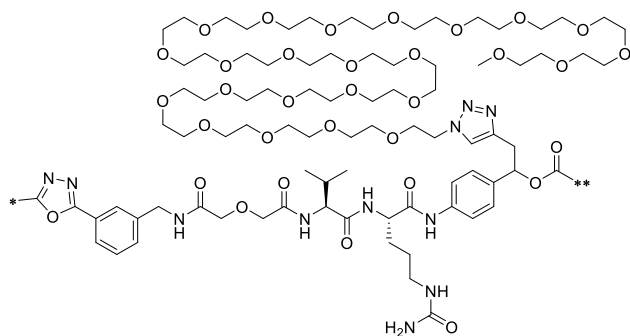
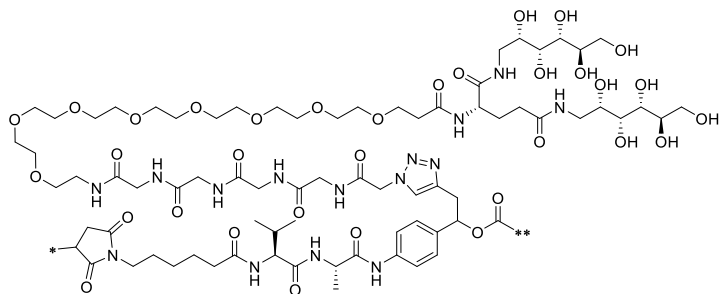
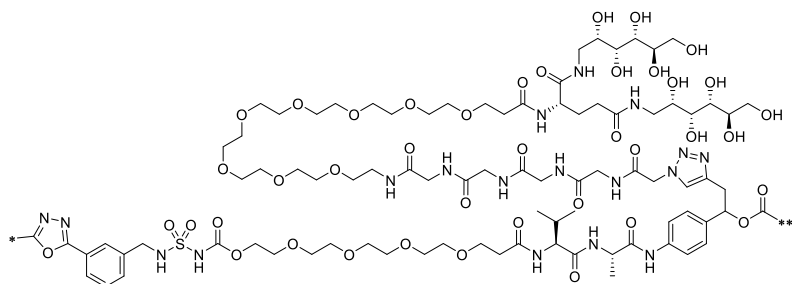
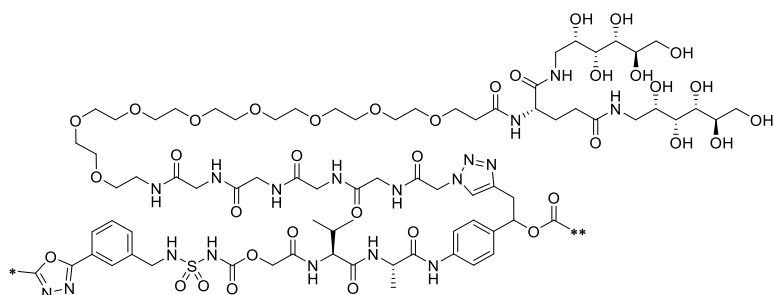
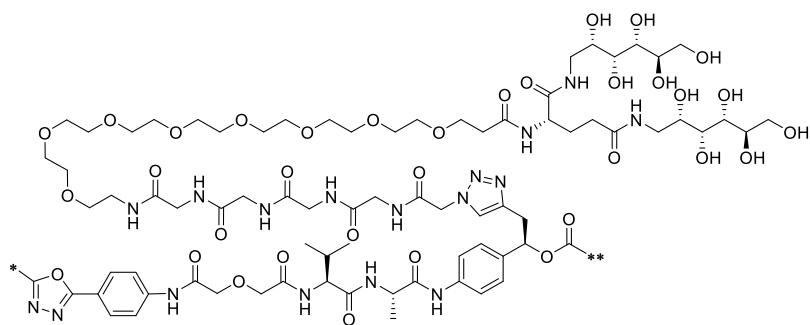


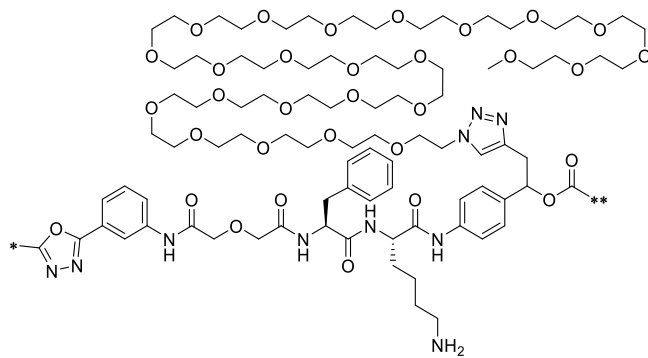
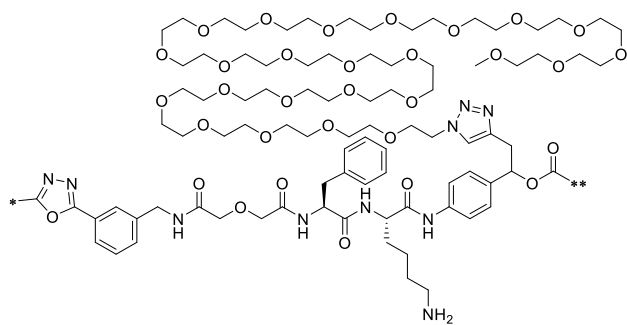
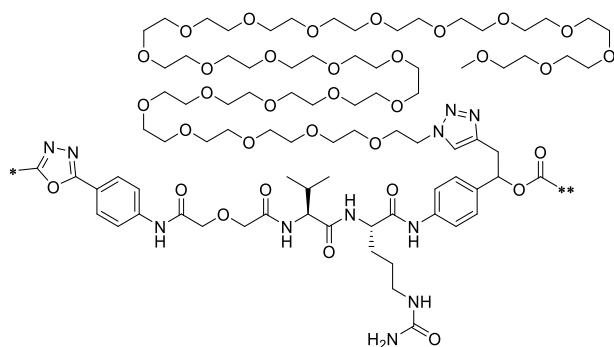
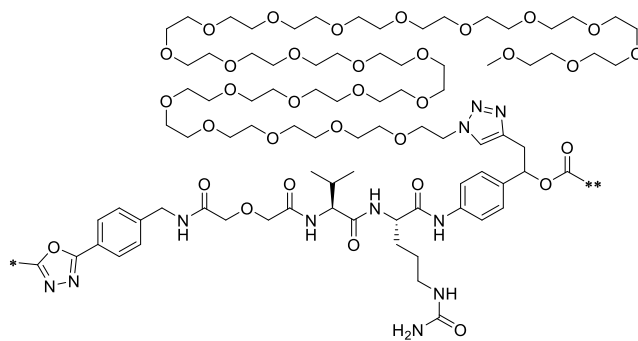
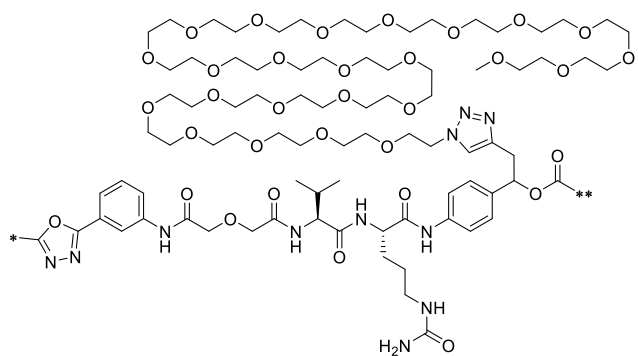
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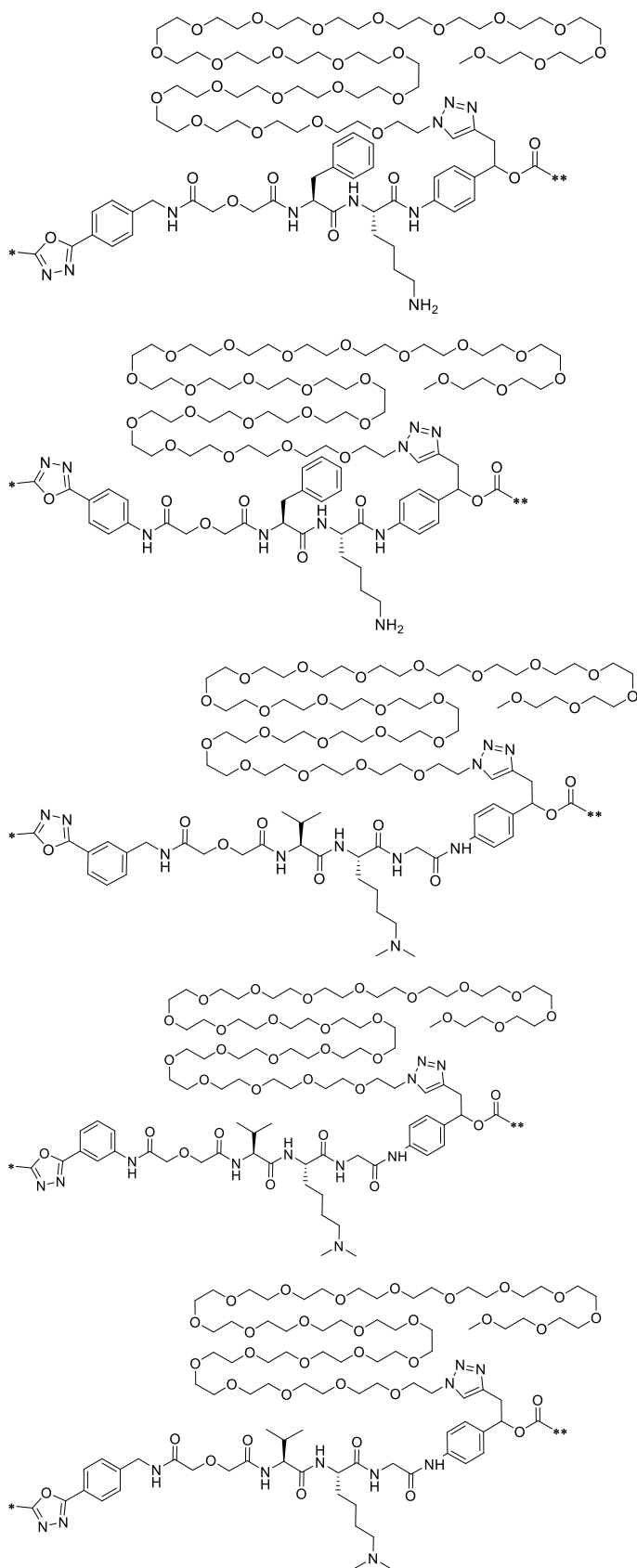


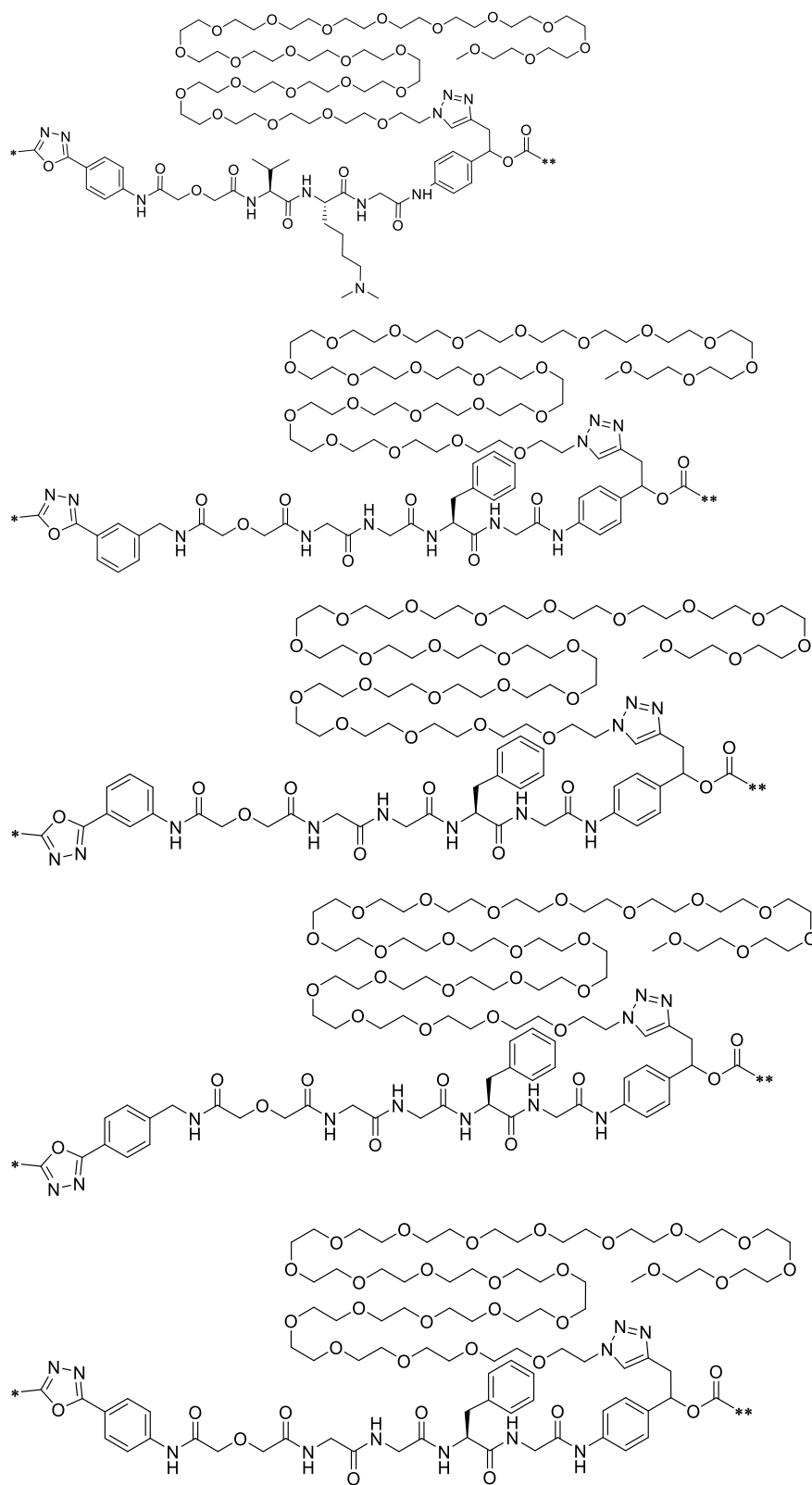


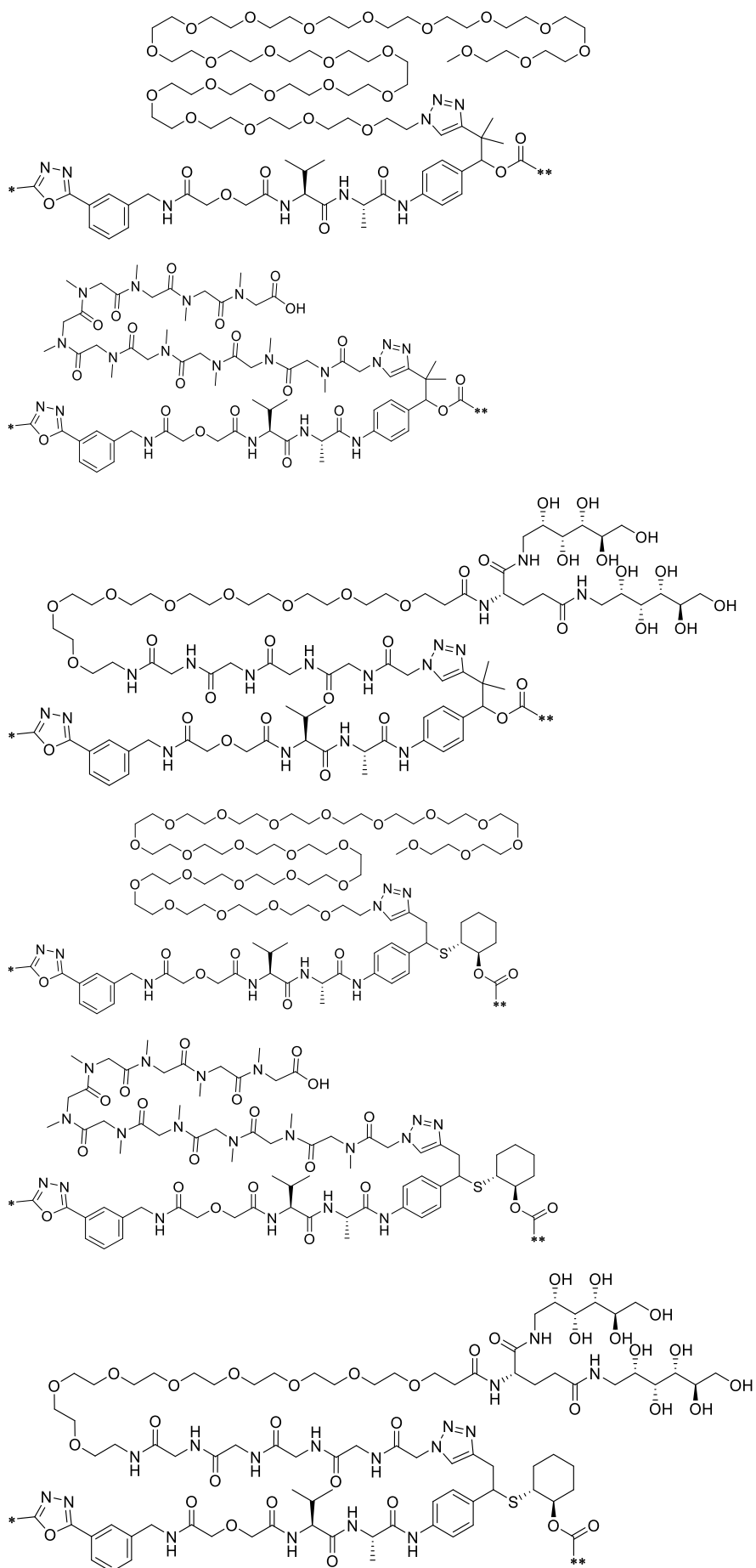


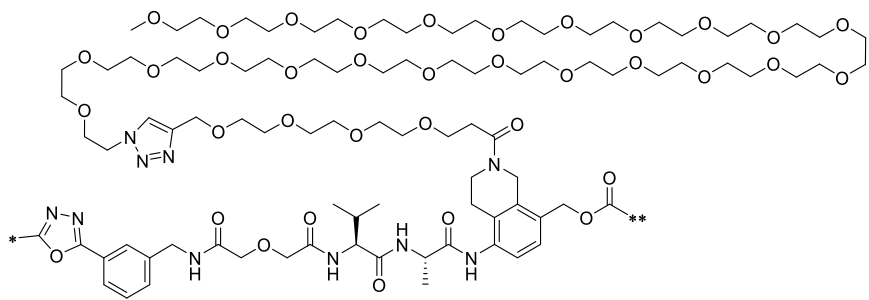
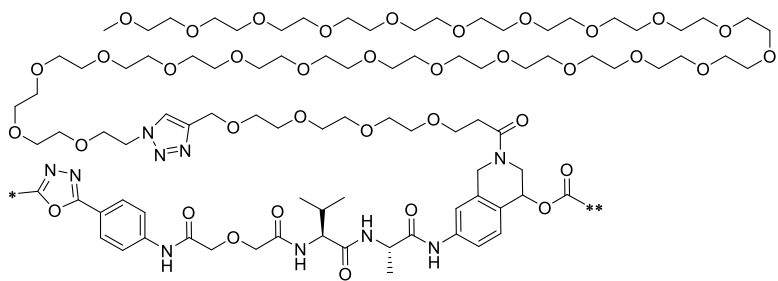
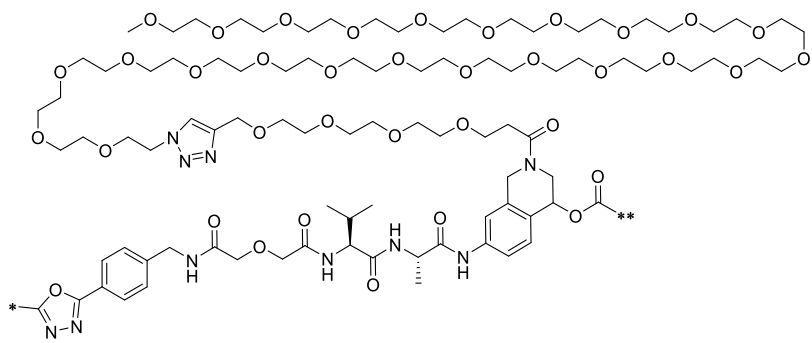
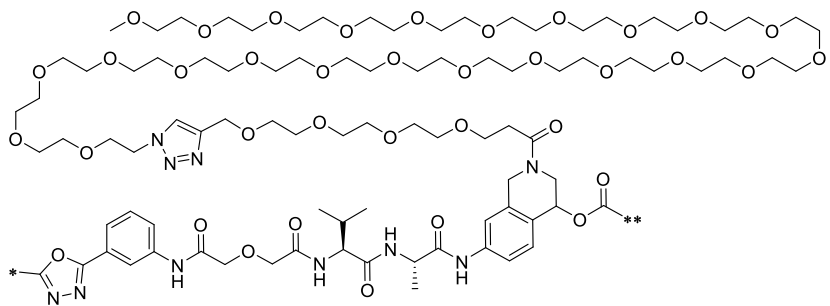
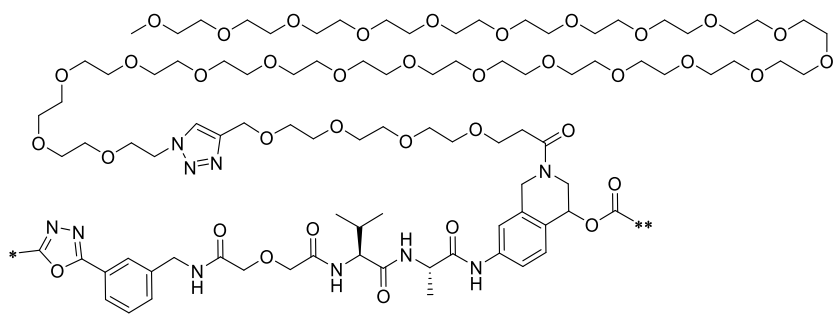


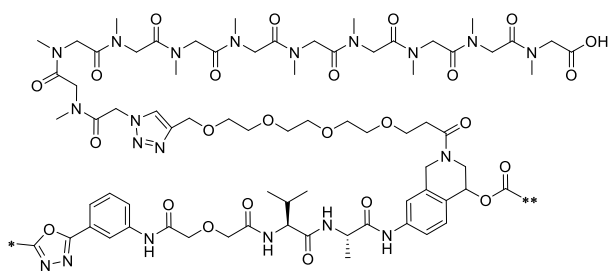
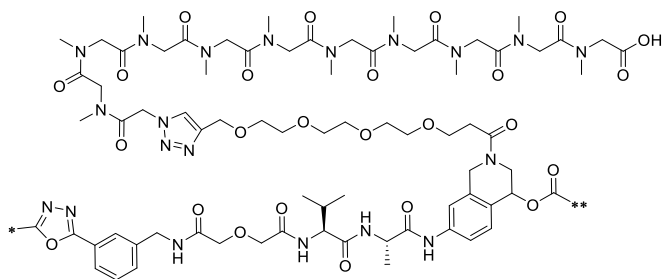
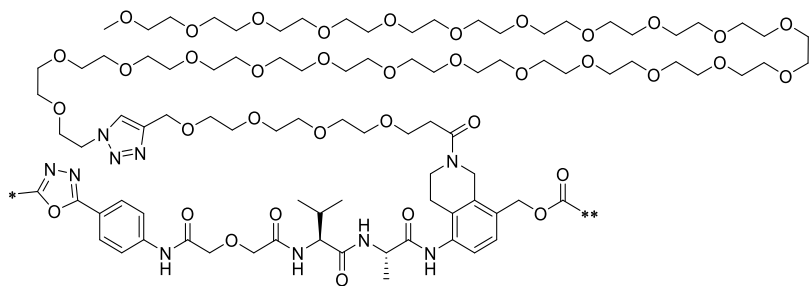
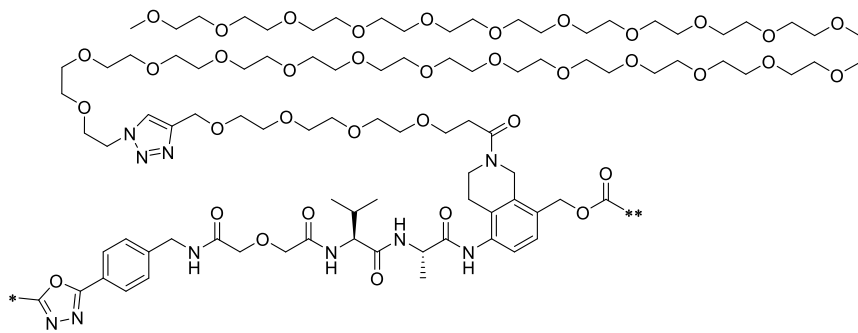
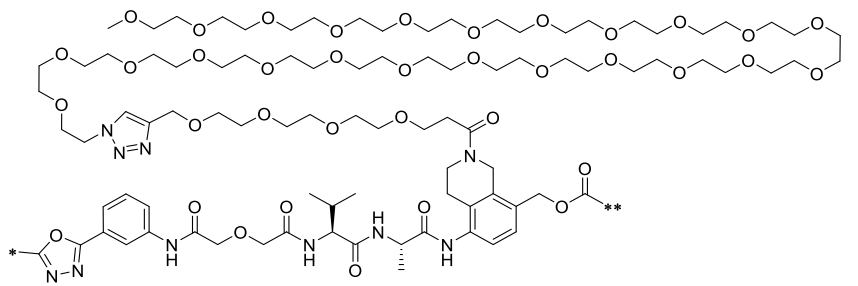




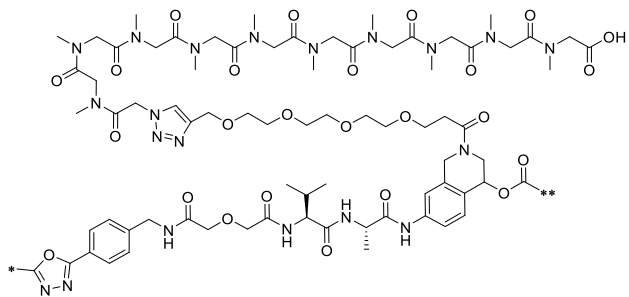


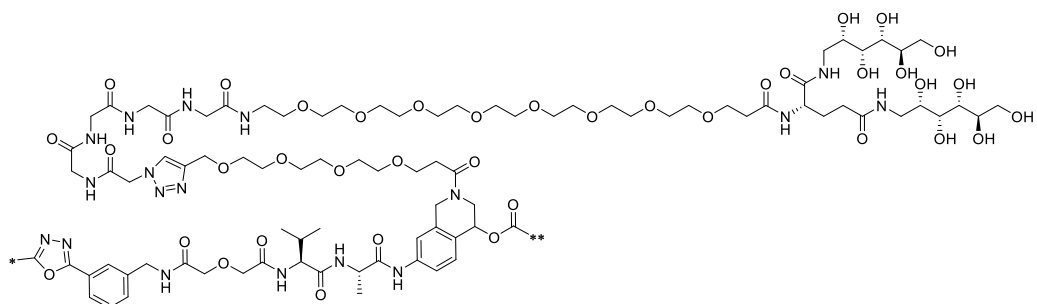


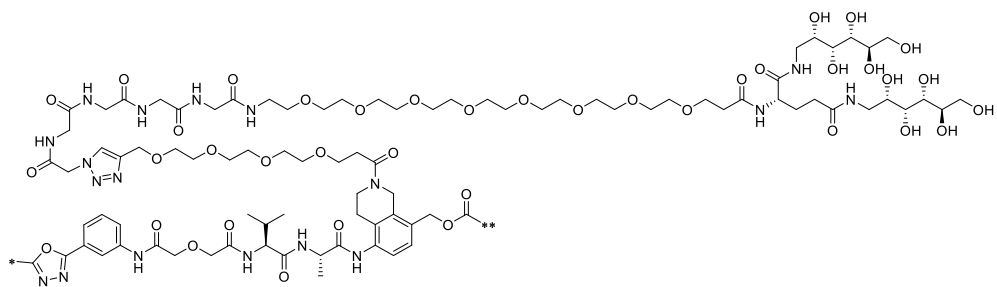
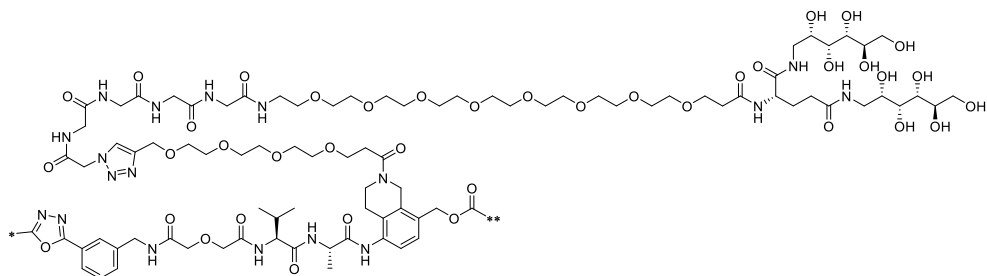
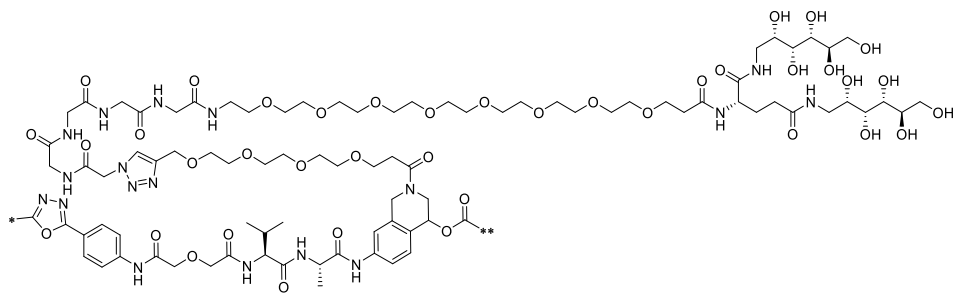
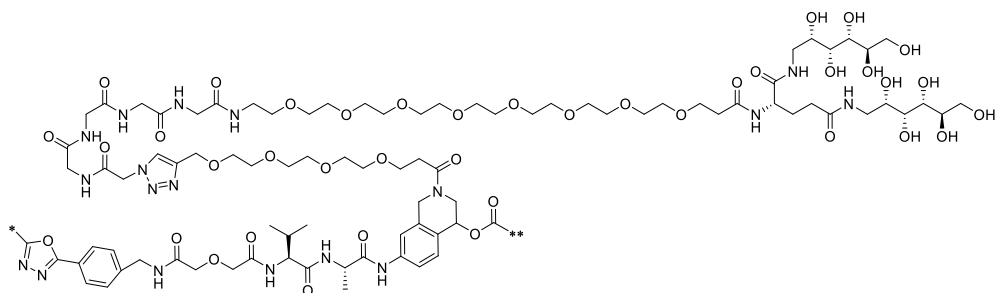
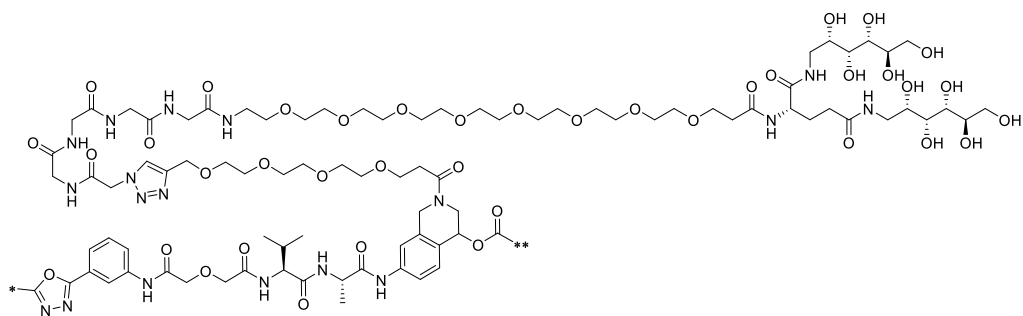


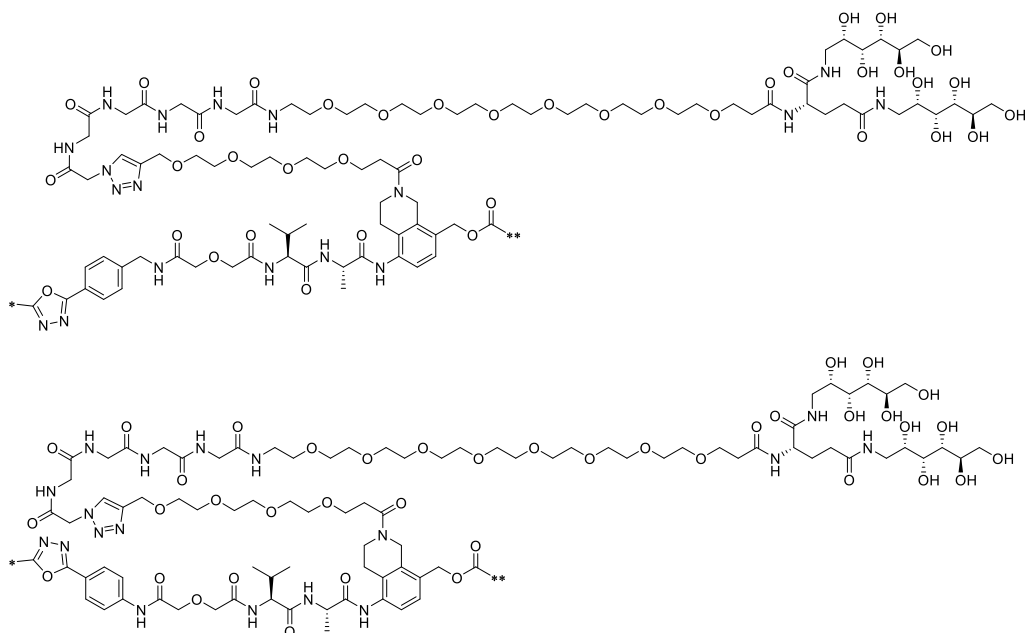


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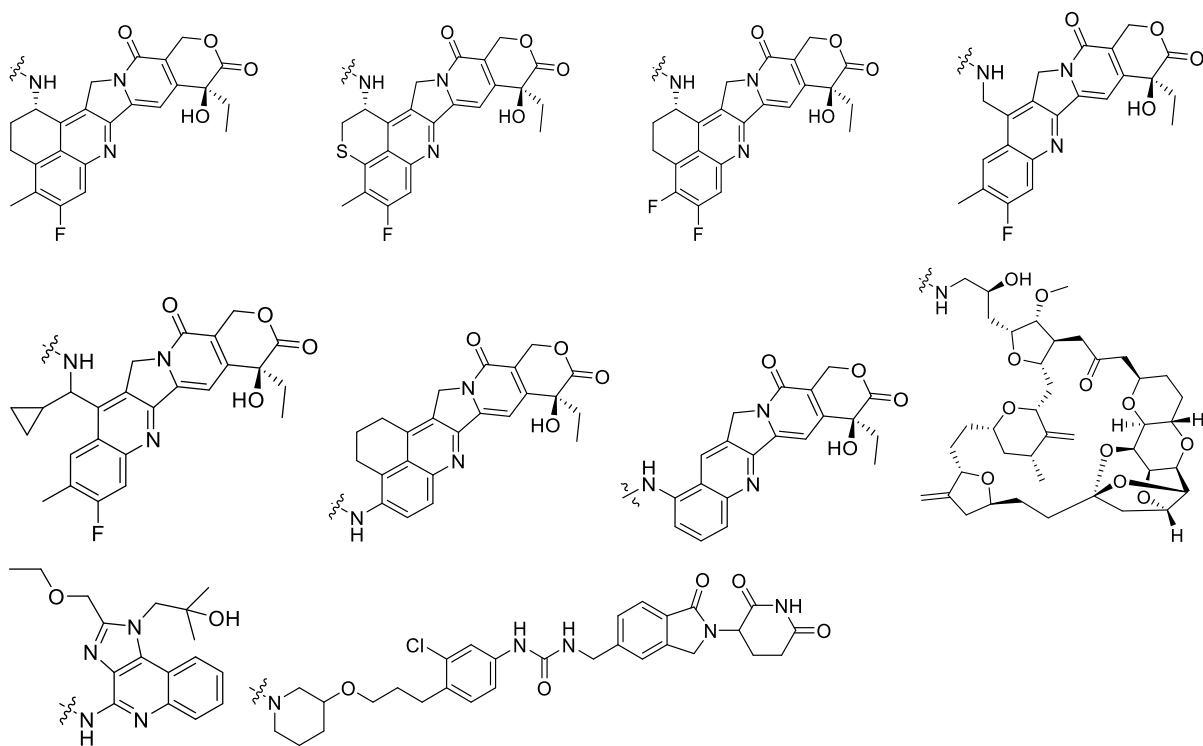


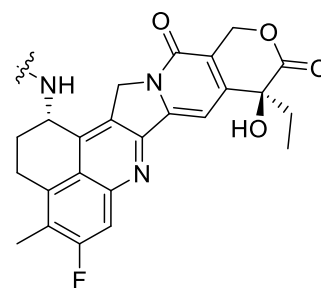
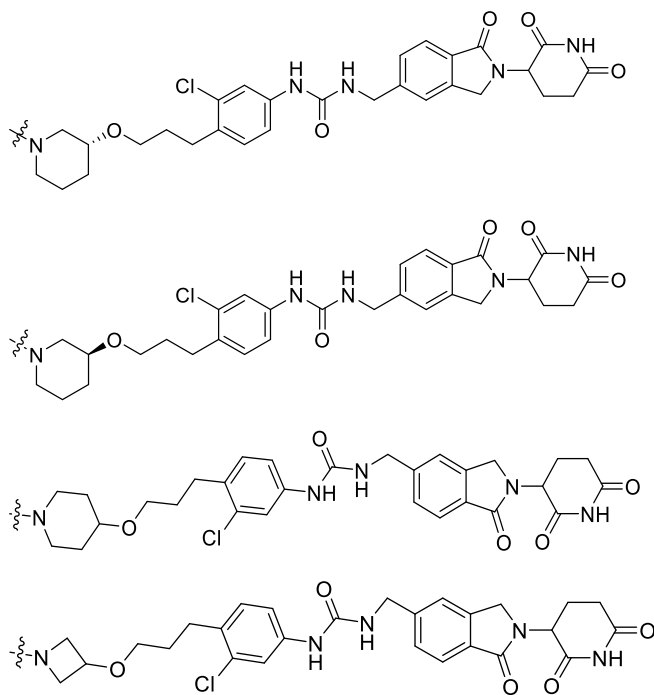


wherein * represents linkage to a sulfhydryl group of the antibody A, and ** represents linkage to the amino group of the bioactive molecule D.

- 5 In some embodiments, the bioactive molecule D is selected from a camptothecin derivative, eribulin, and a molecular glue.

In some embodiments, the bioactive molecule D is selected from compounds of the following formulas:

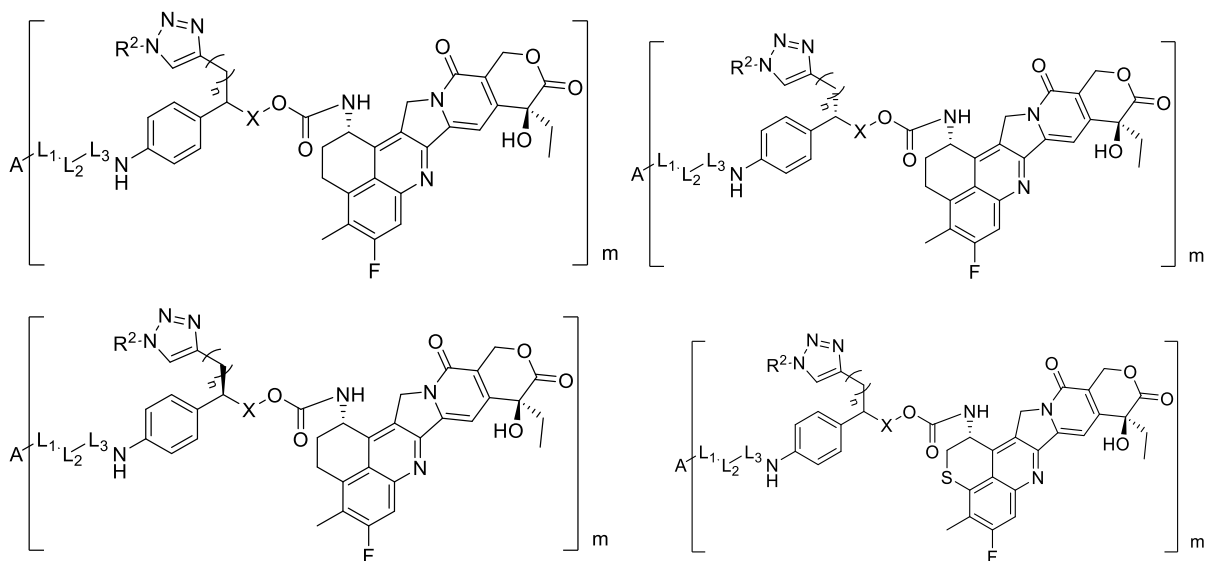


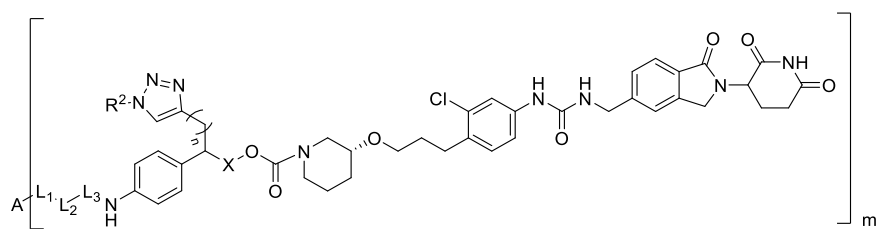
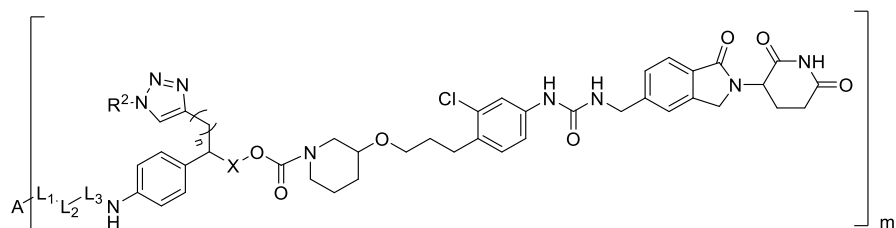
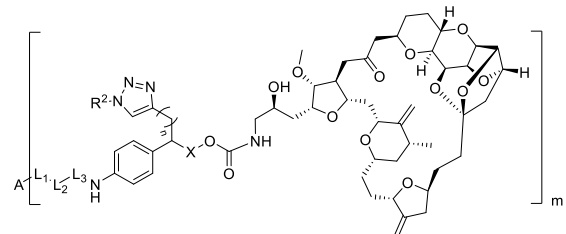
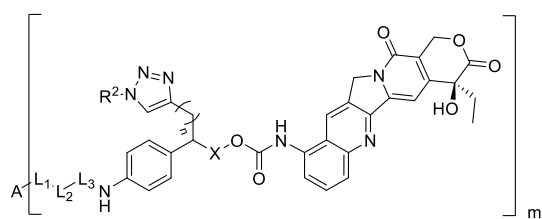
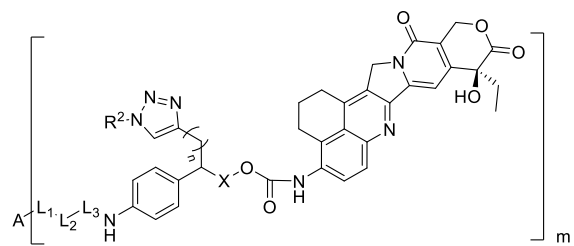
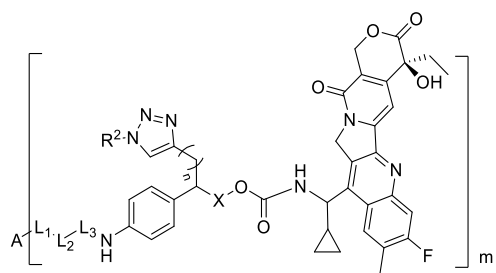
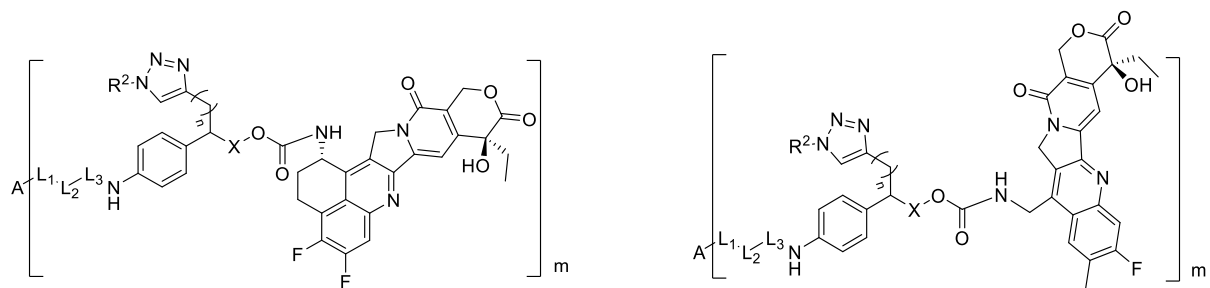


5 In some embodiments, the bioactive molecule D is selected from:

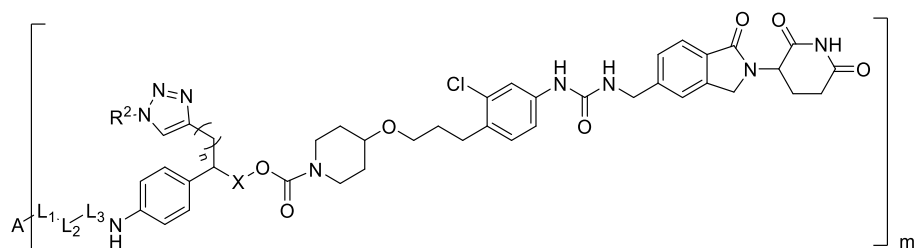
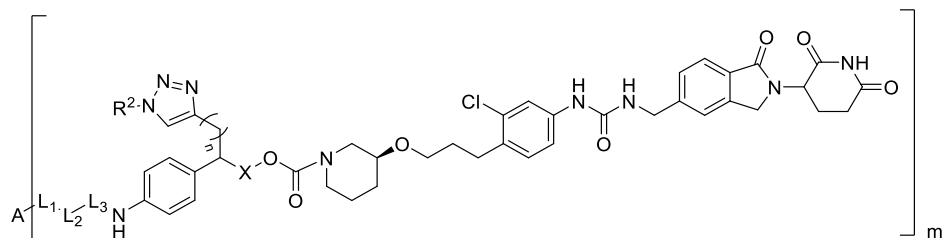
In some embodiments, the antibody-drug conjugate represented by formula I, the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

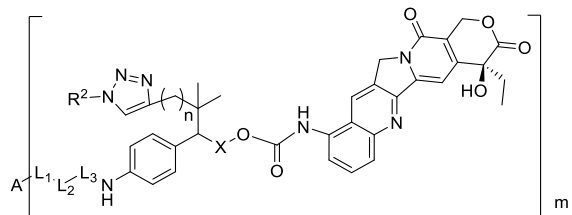
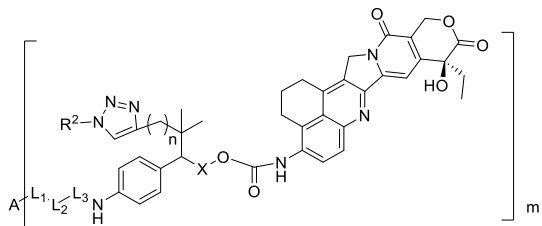
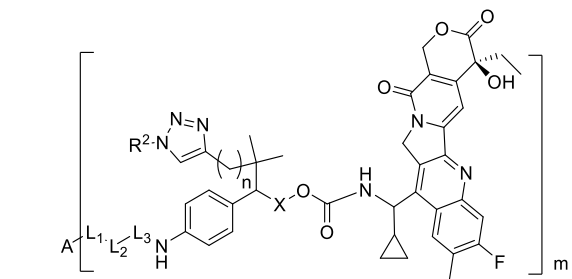
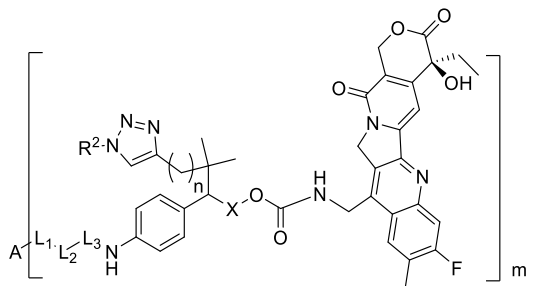
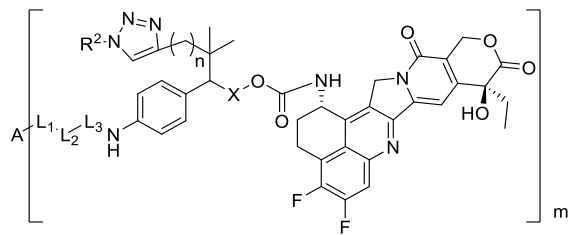
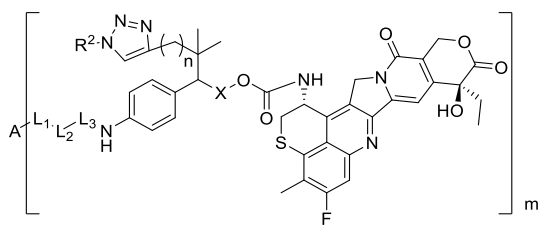
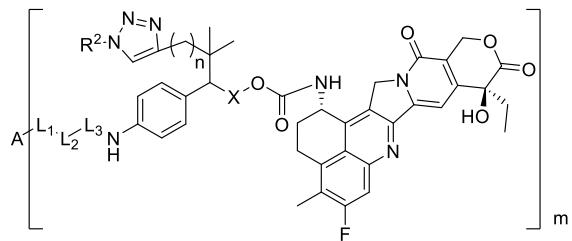
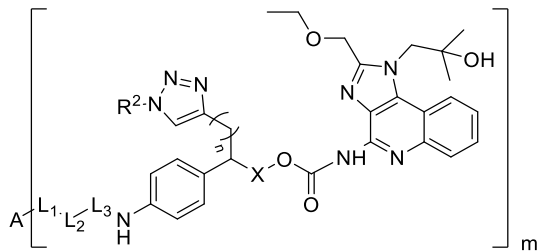
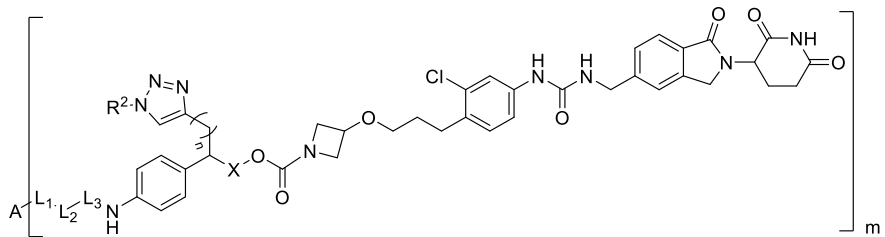
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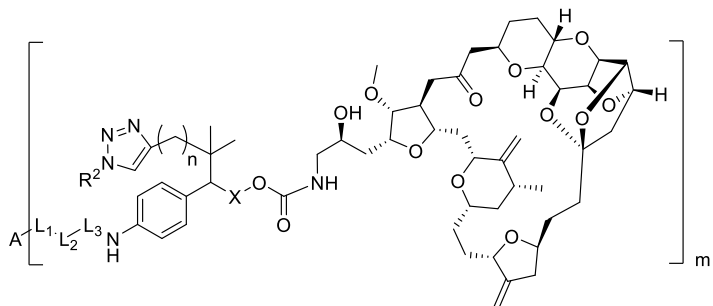


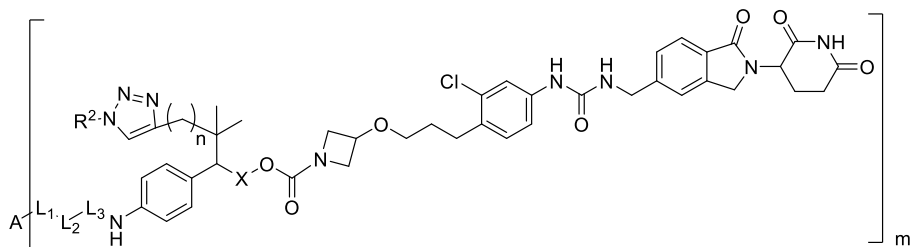
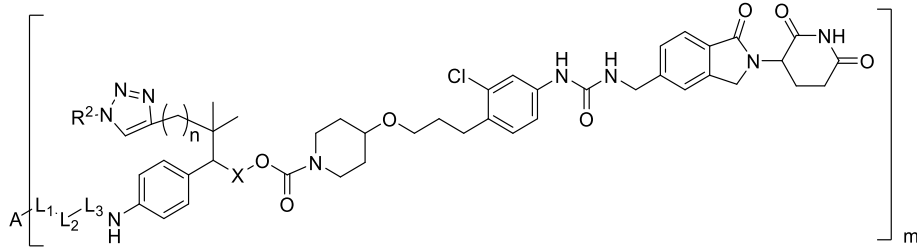
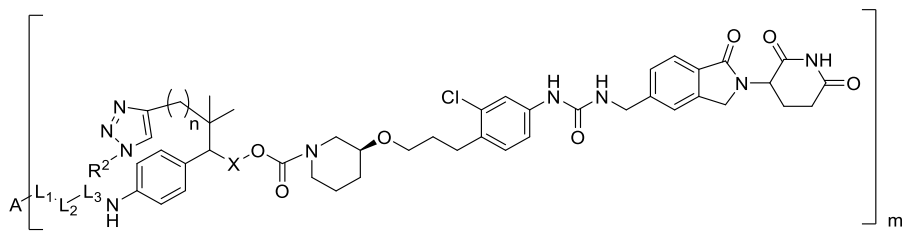
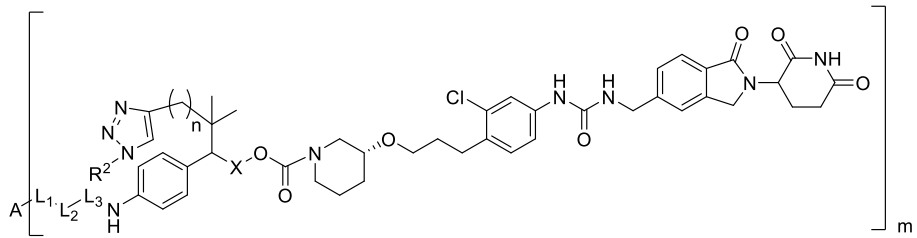
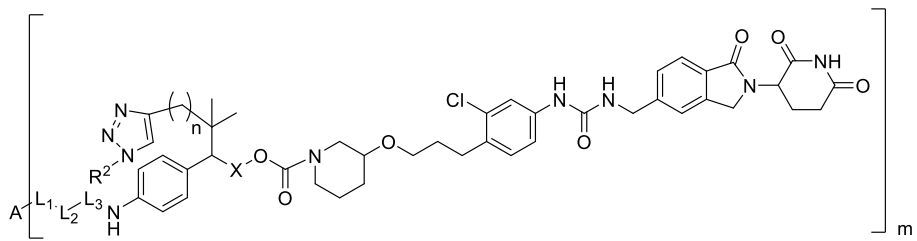
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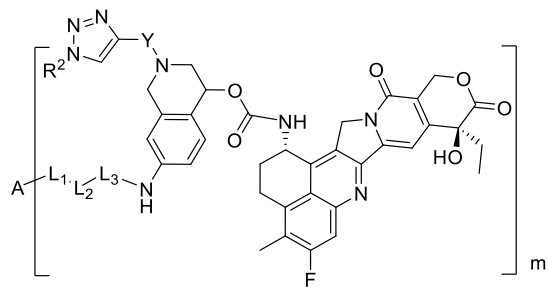
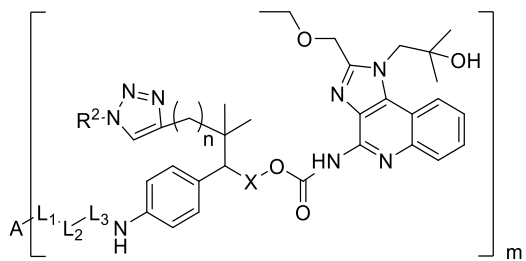


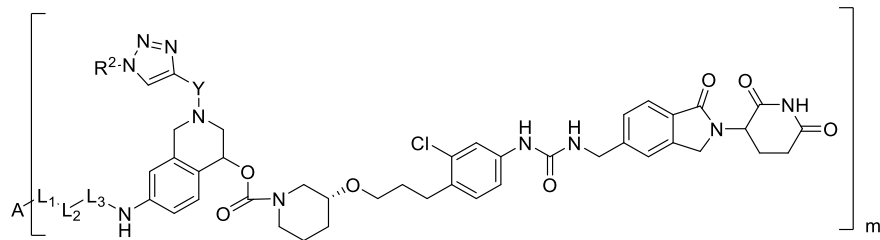
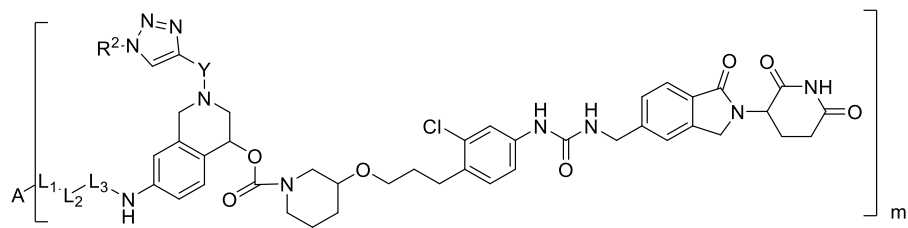
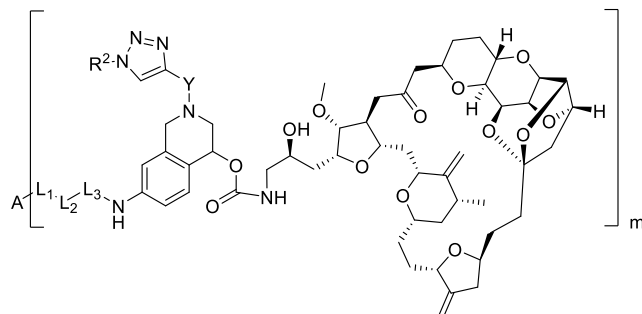
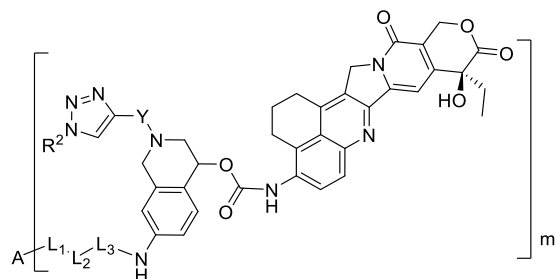
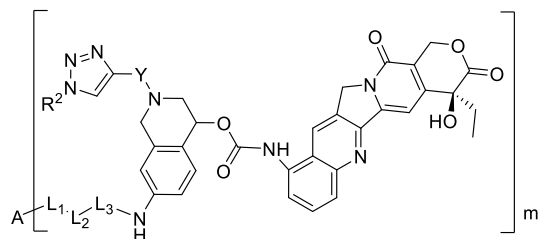
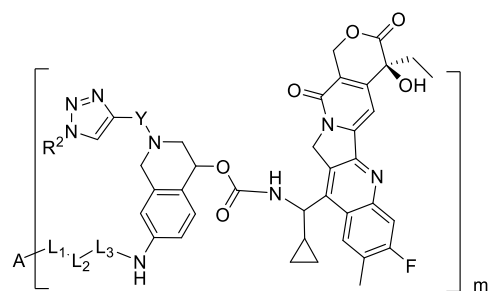
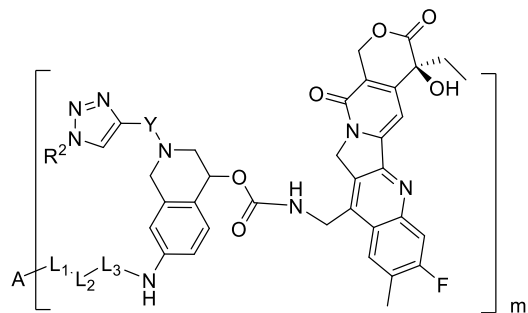
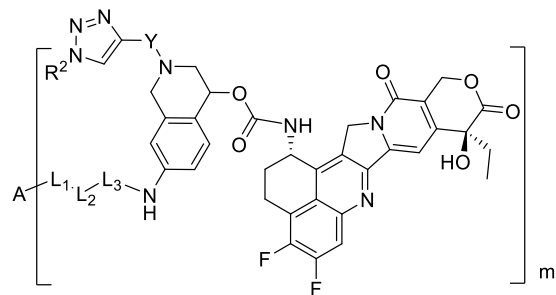
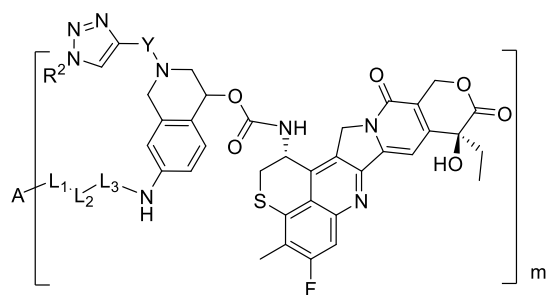
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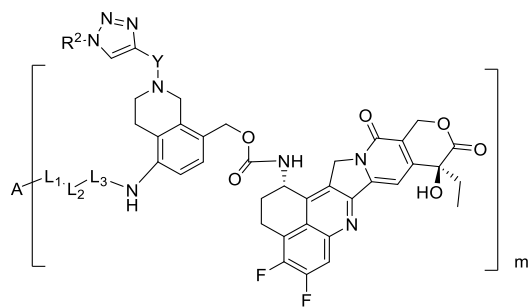
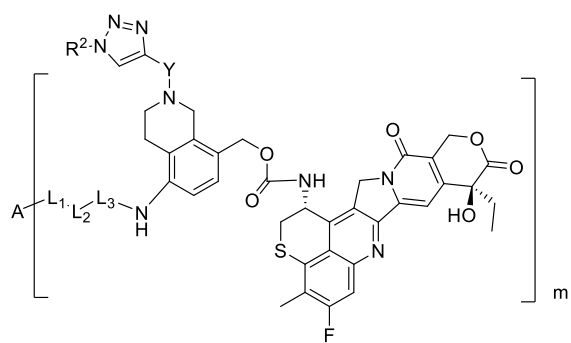
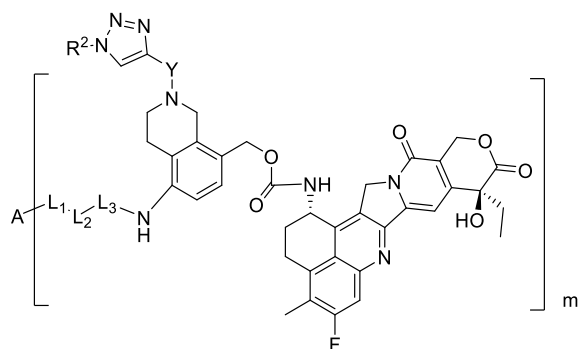
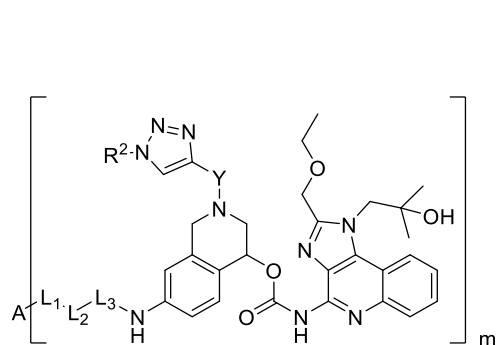
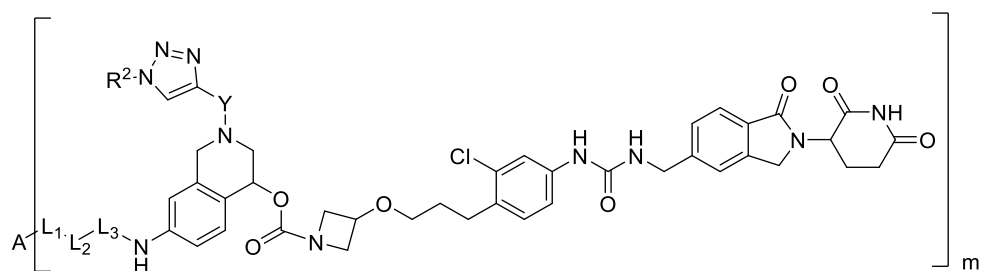
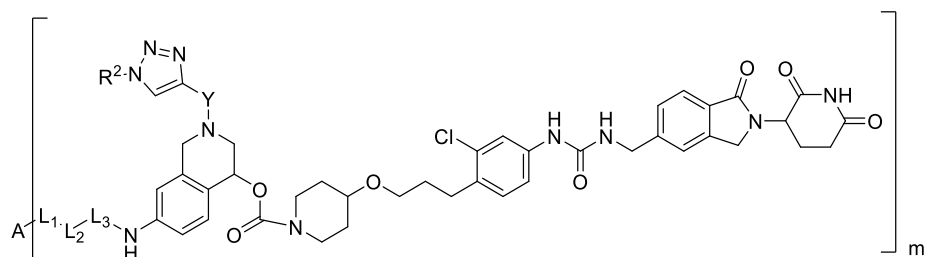
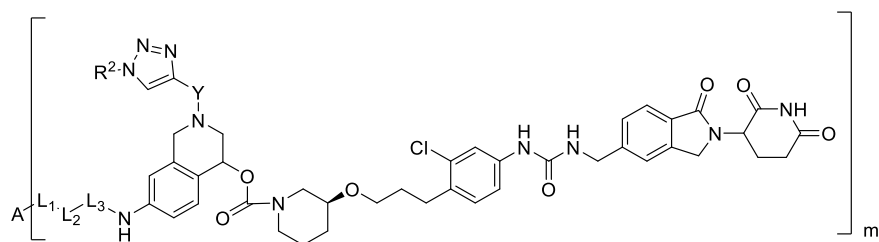


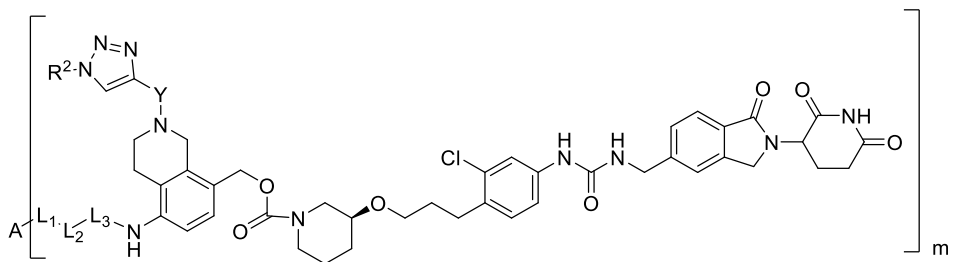
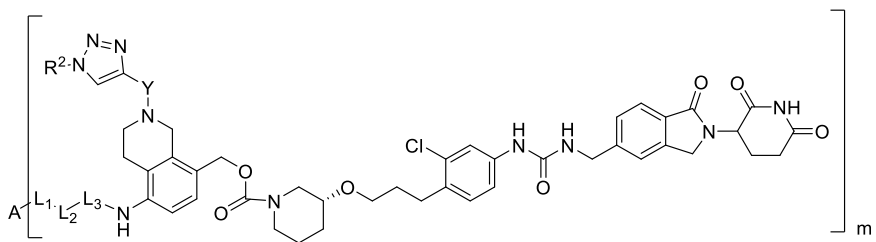
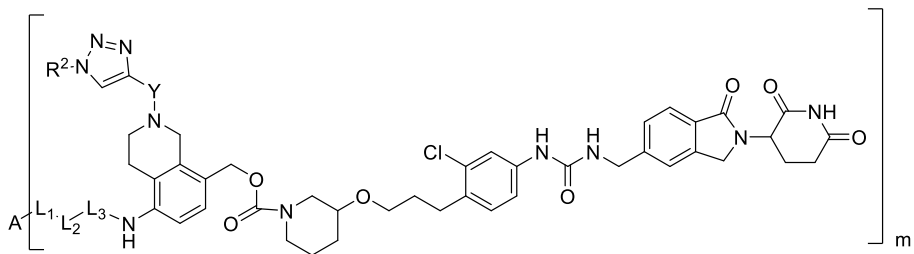
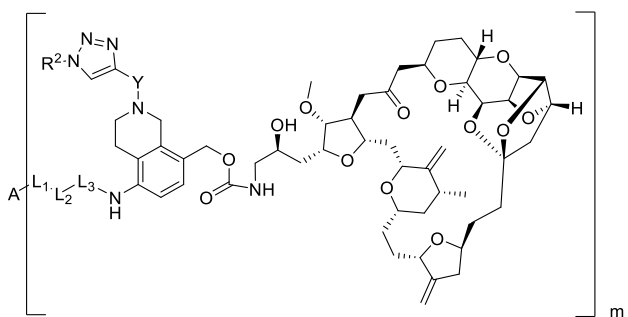
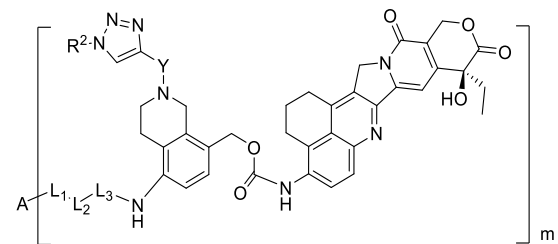
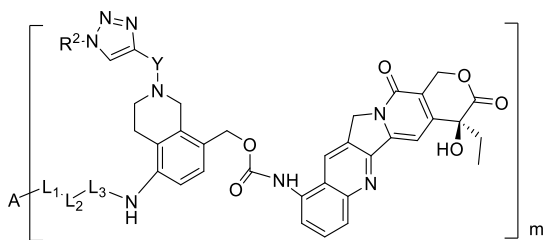
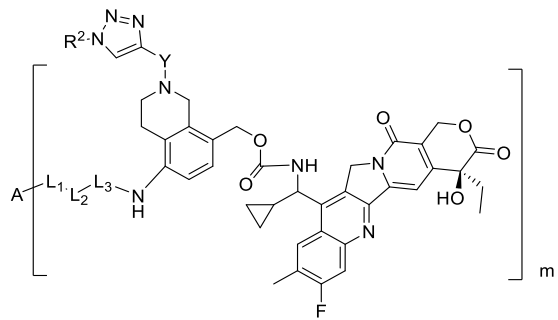
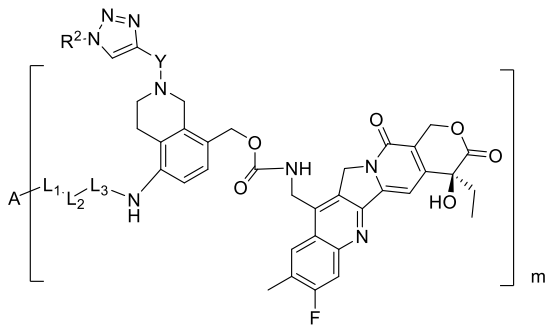


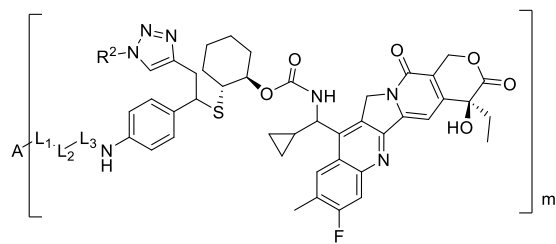
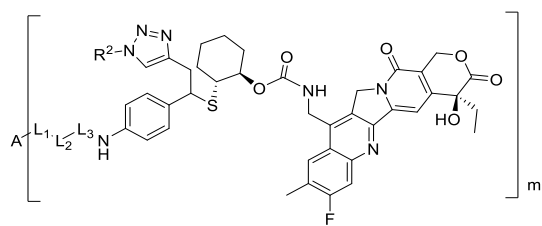
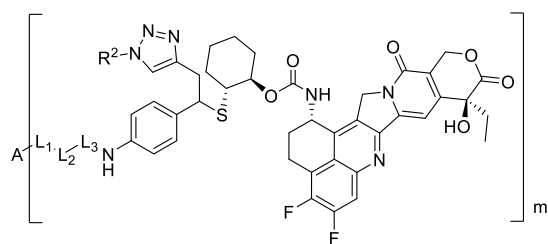
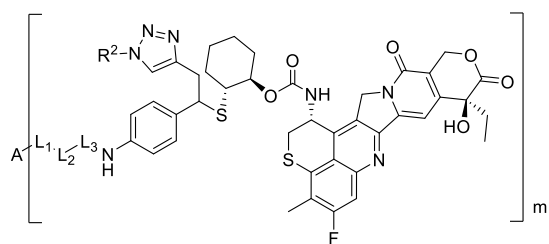
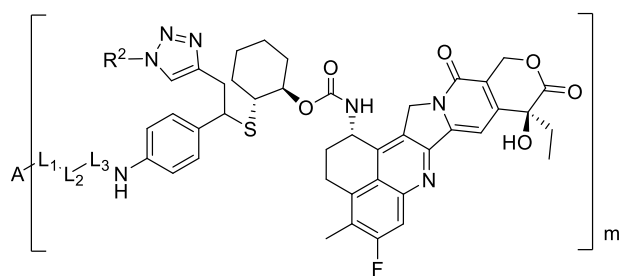
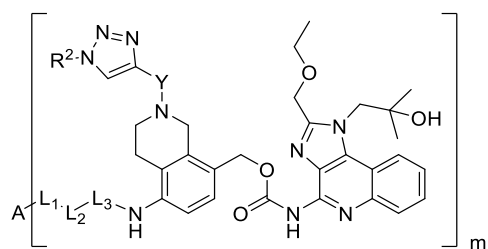
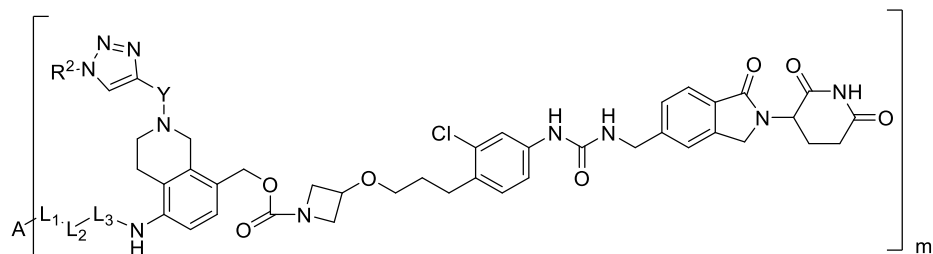
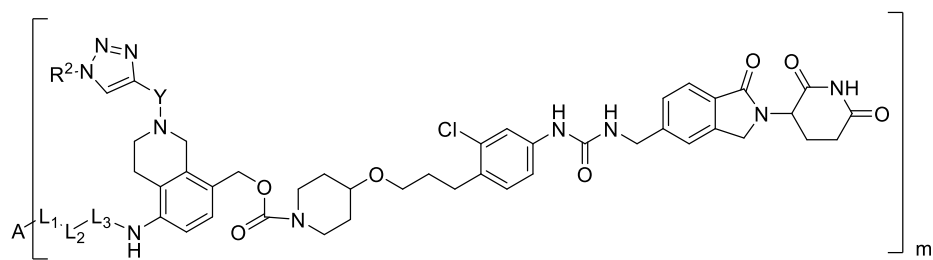
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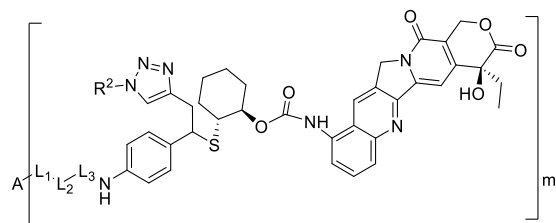
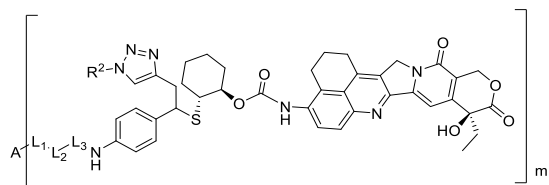


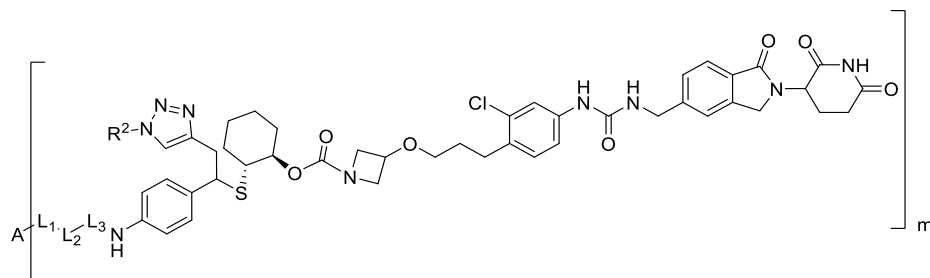
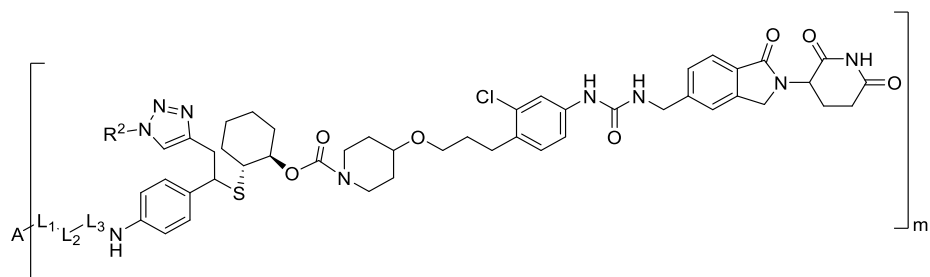
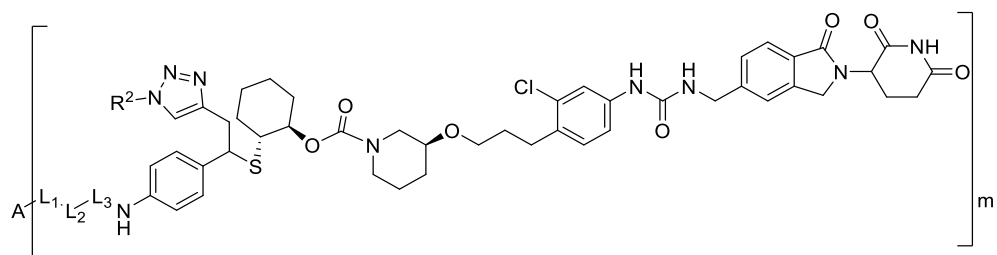
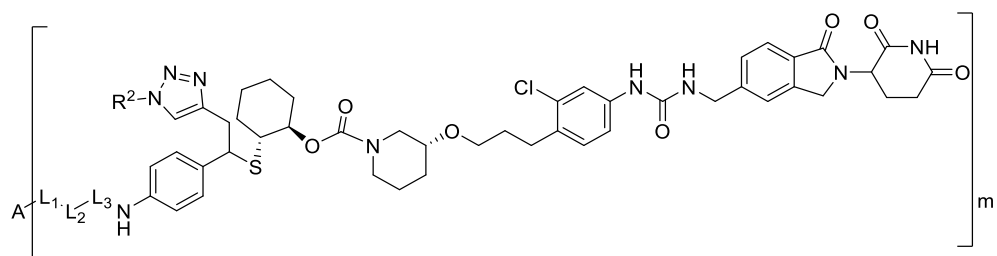
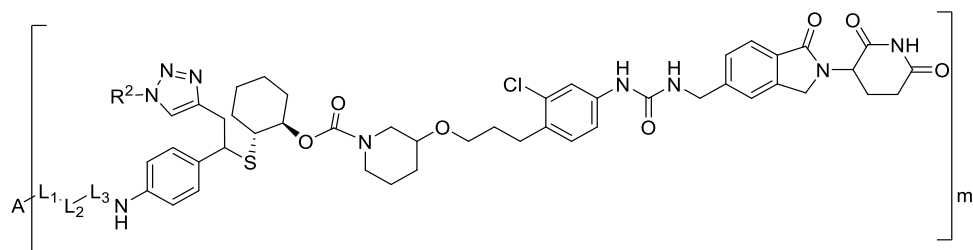
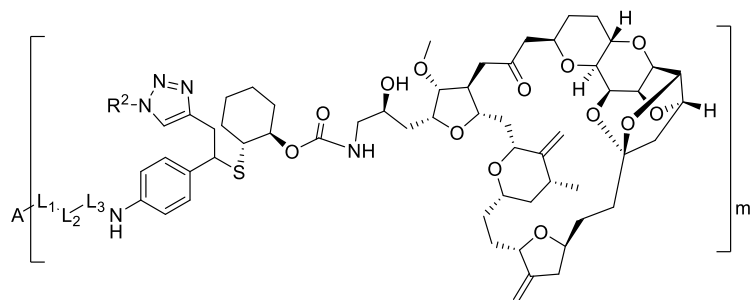


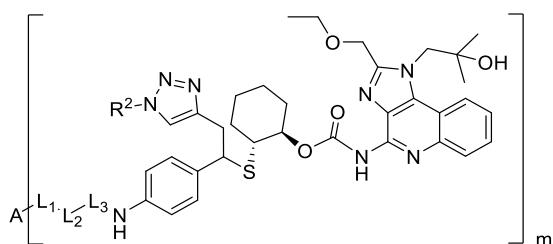




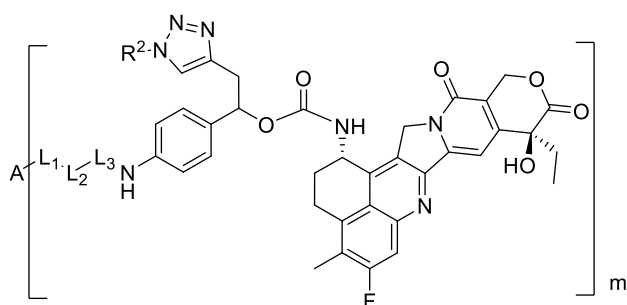
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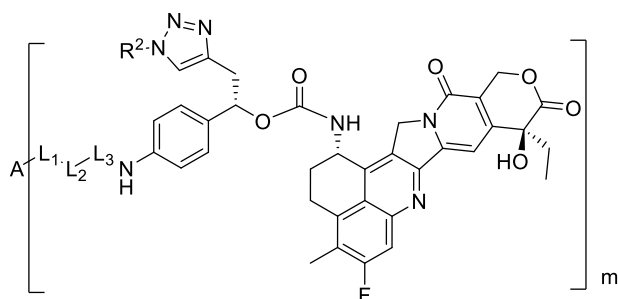
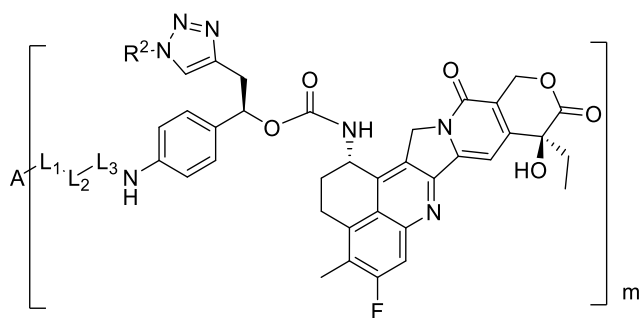




In some embodiments, the antibody-drug conjugate represented by formula I, the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

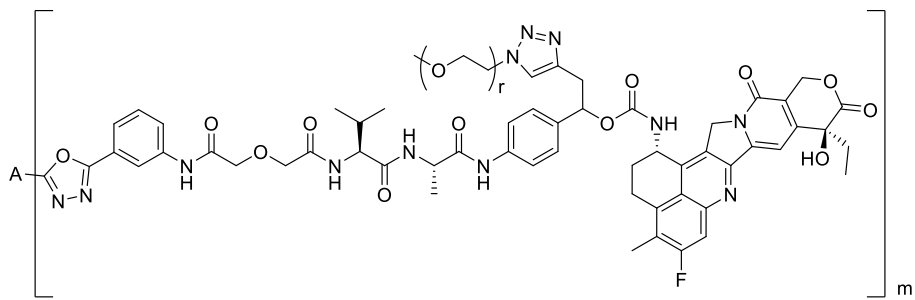
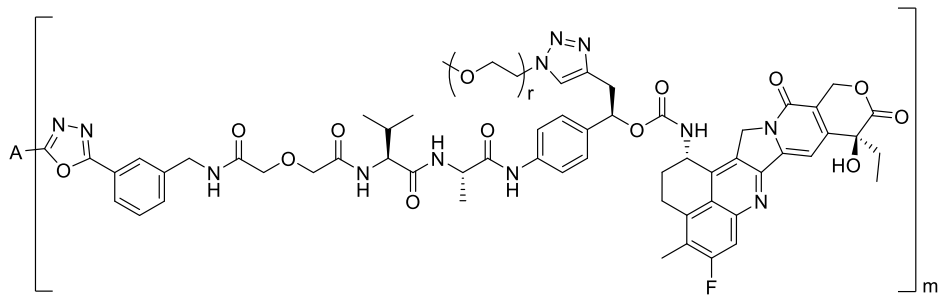
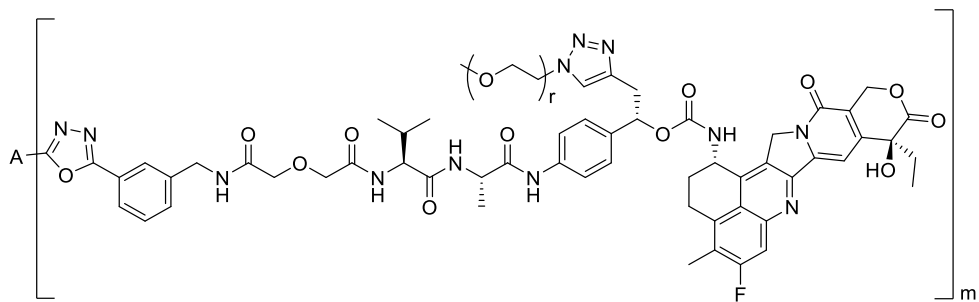
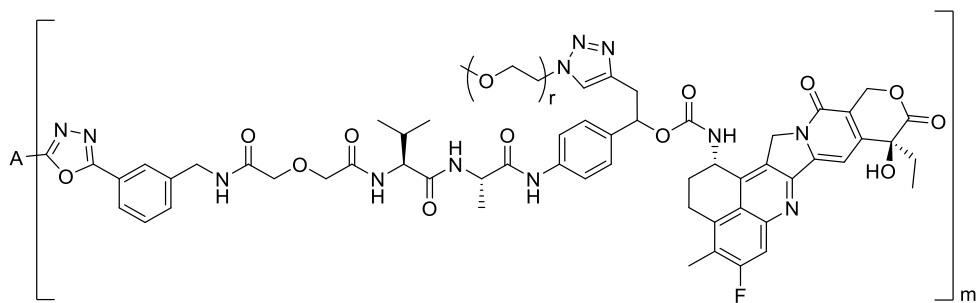


In some embodiments, the antibody-drug conjugate represented by formula I, and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

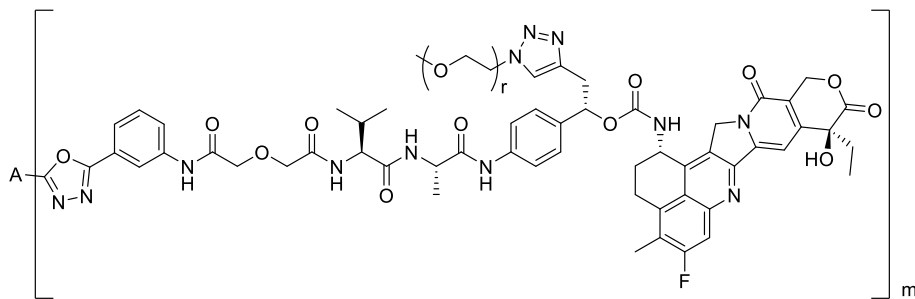


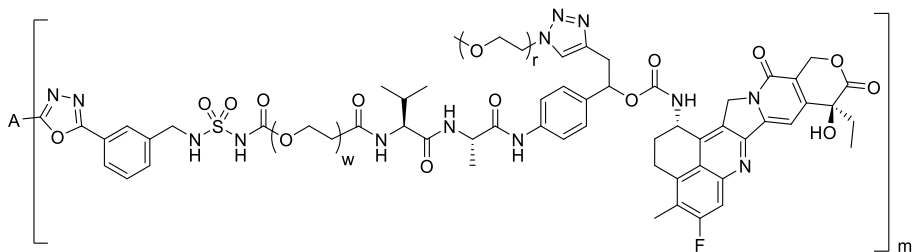
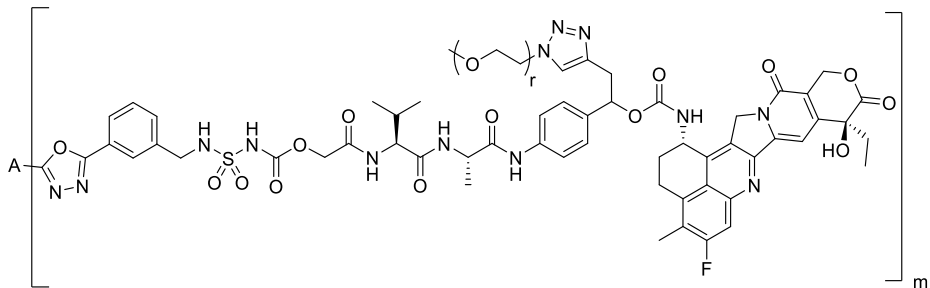
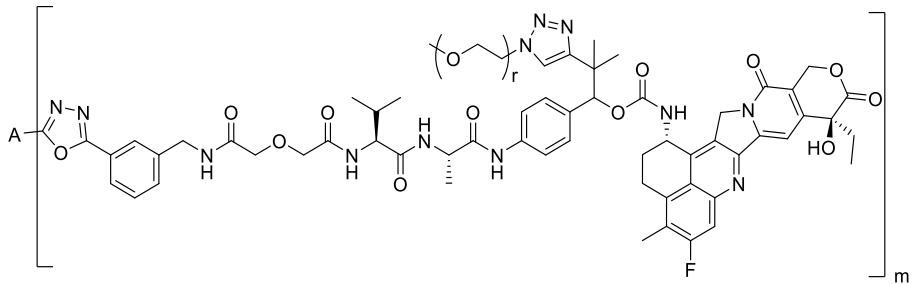
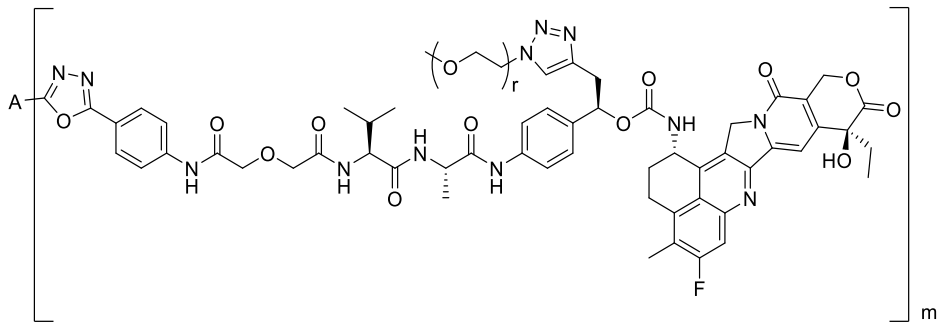
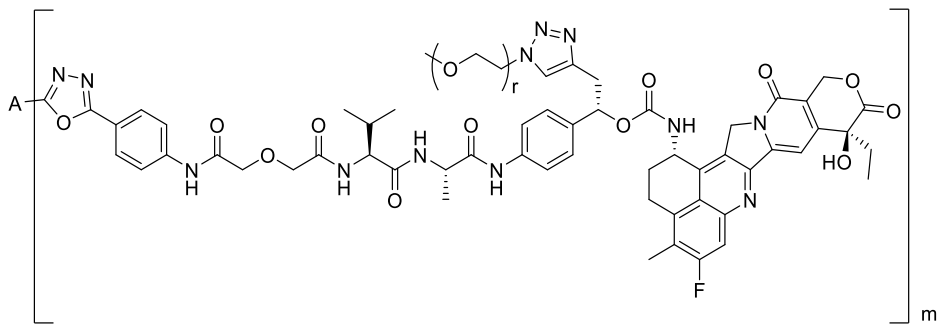
In some embodiments, the antibody-drug conjugate represented by formula I, the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the

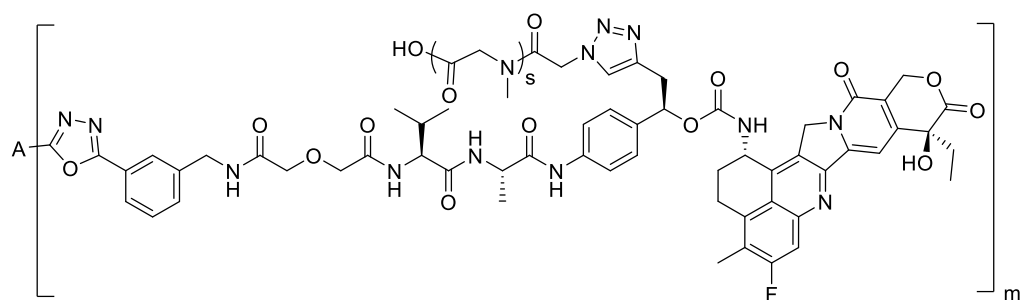
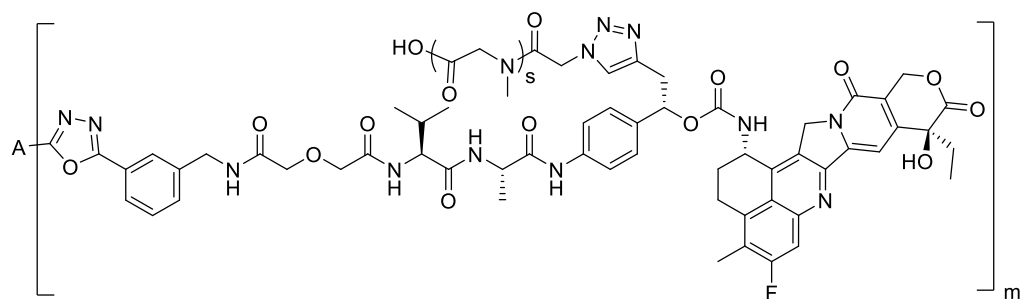
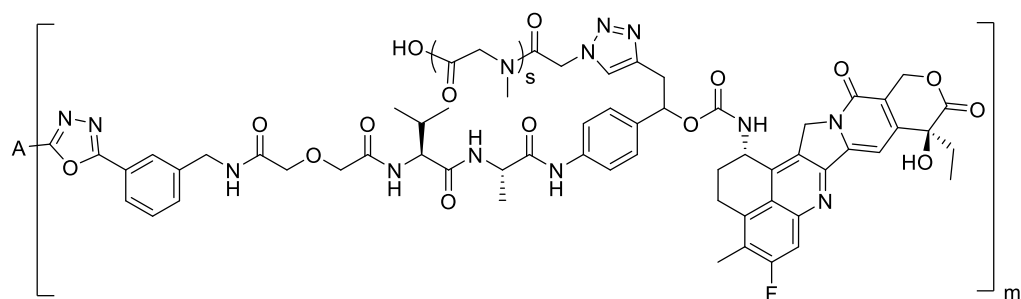
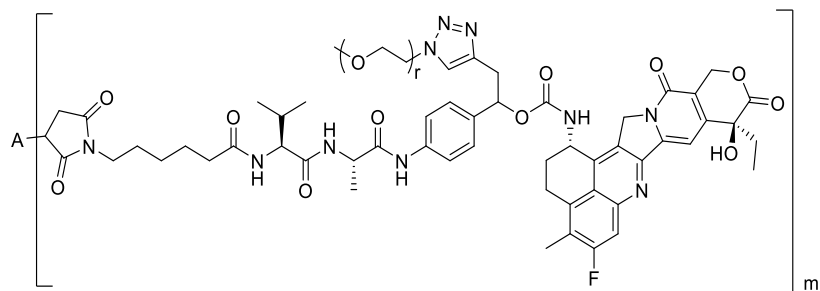
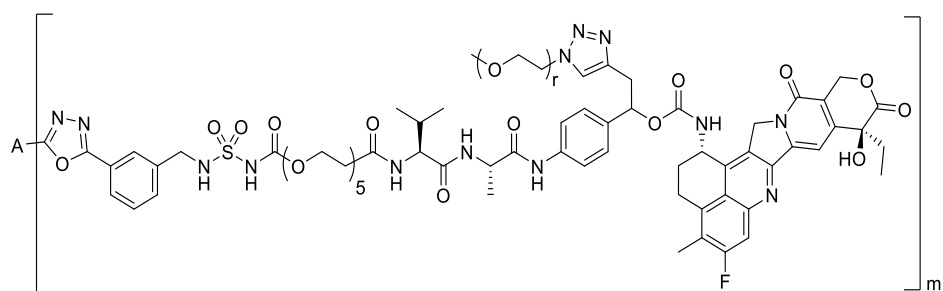
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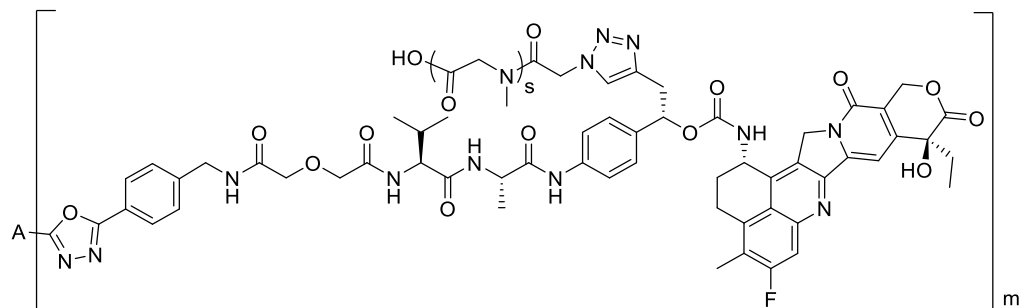
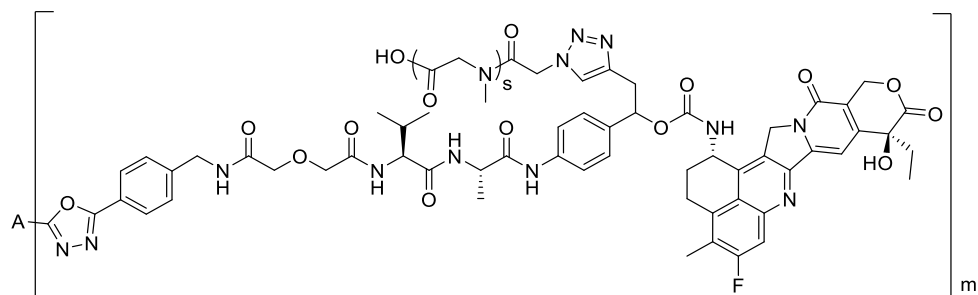
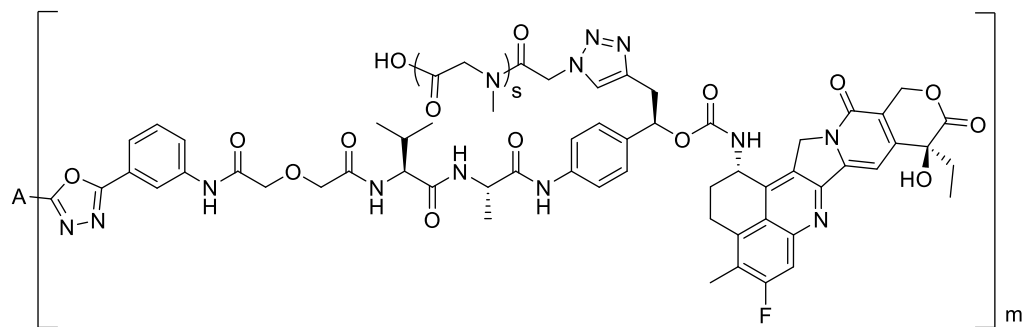
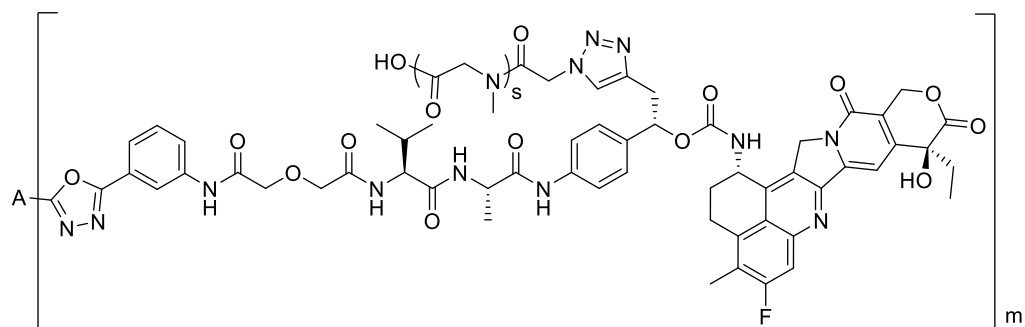
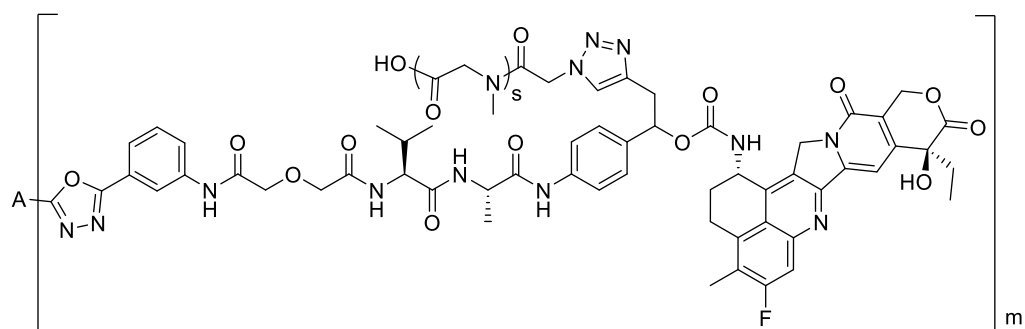


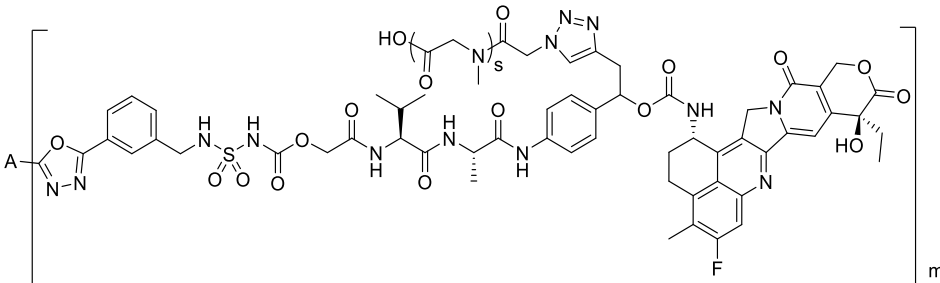
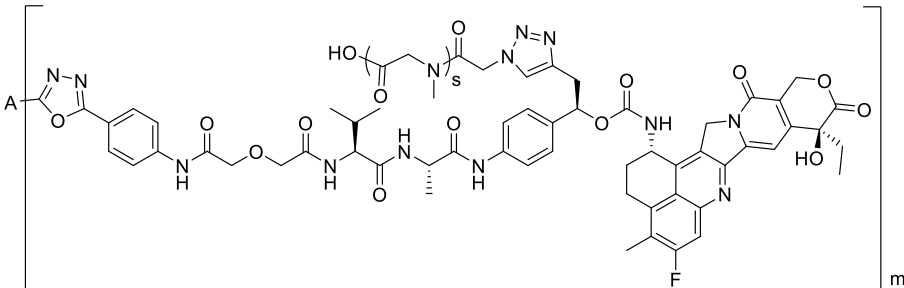
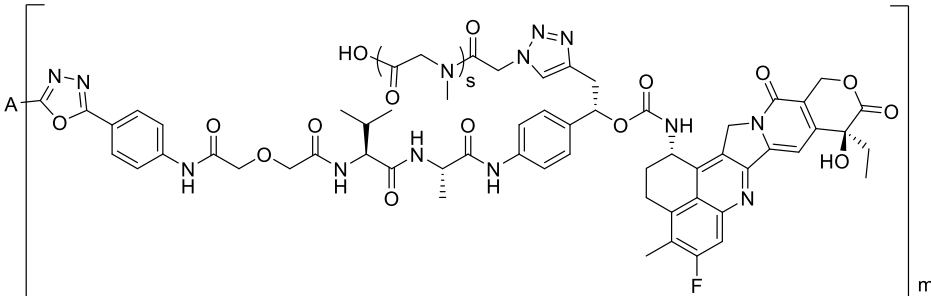
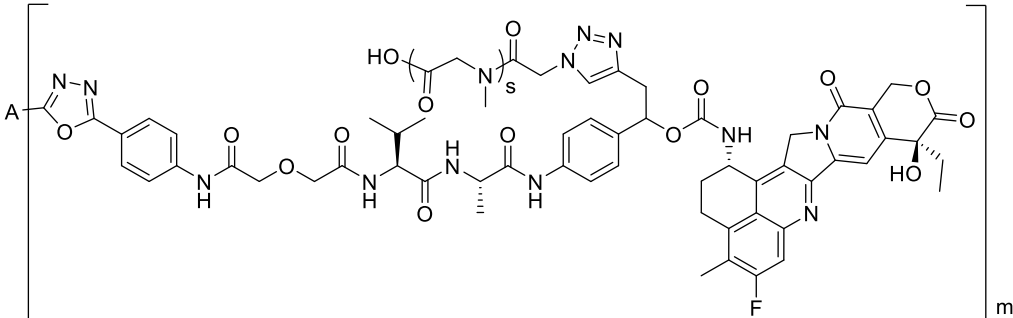
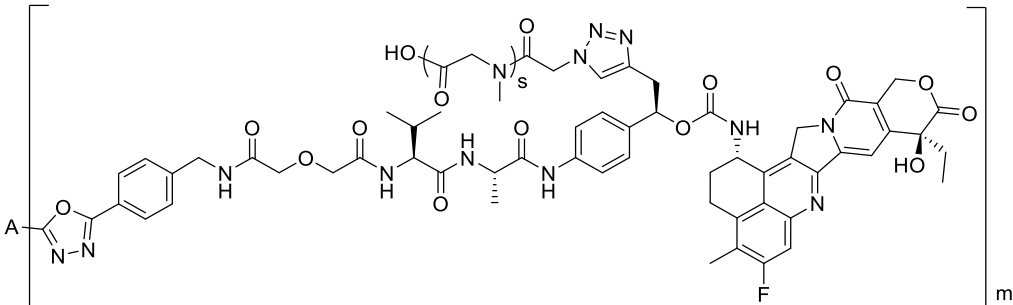
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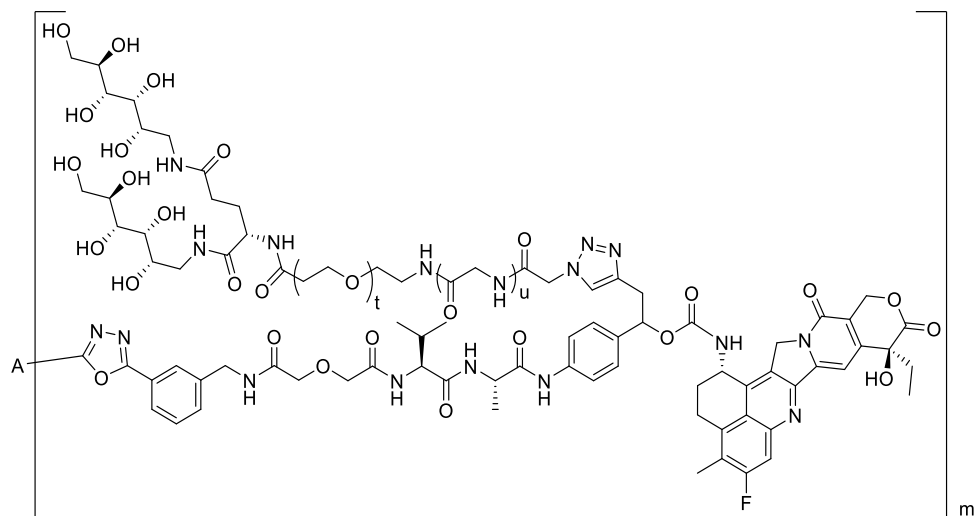
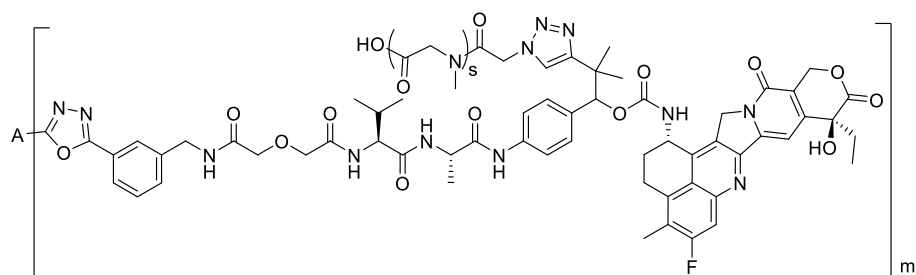
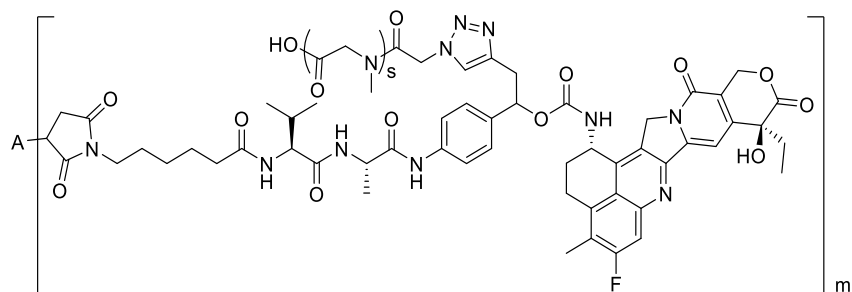
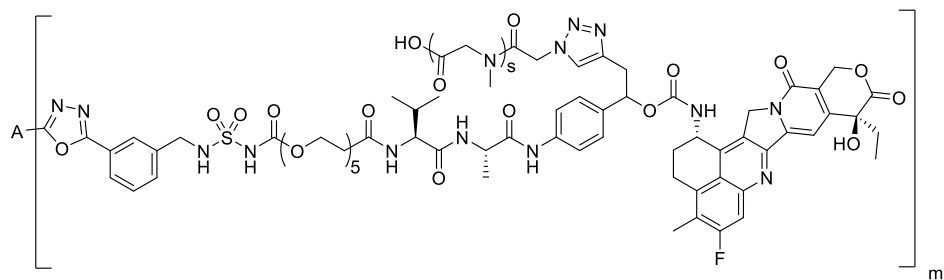
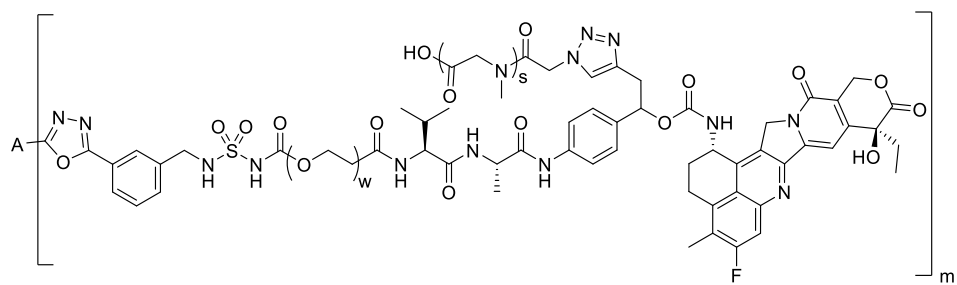


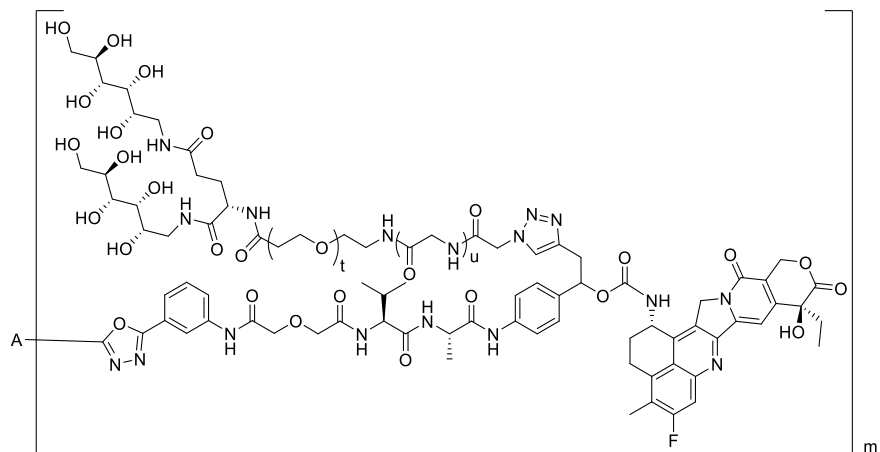
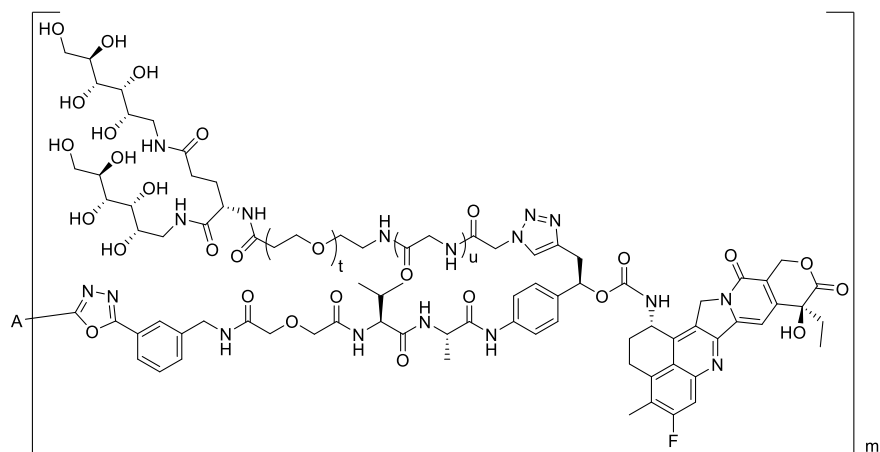
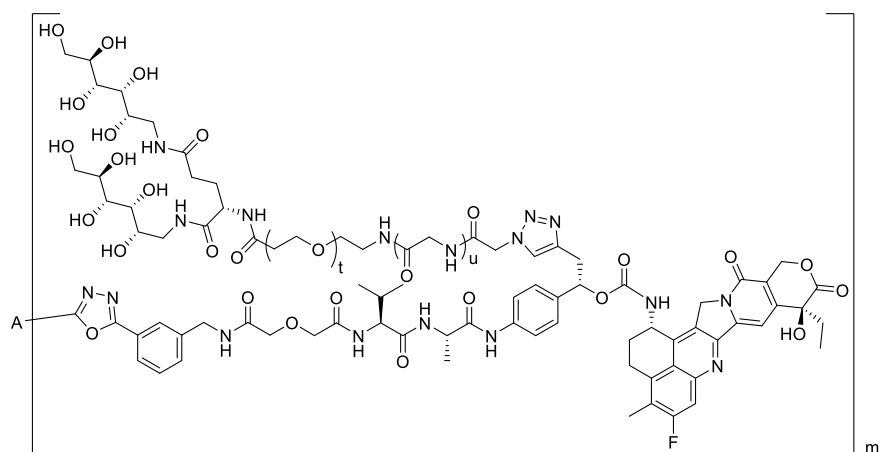


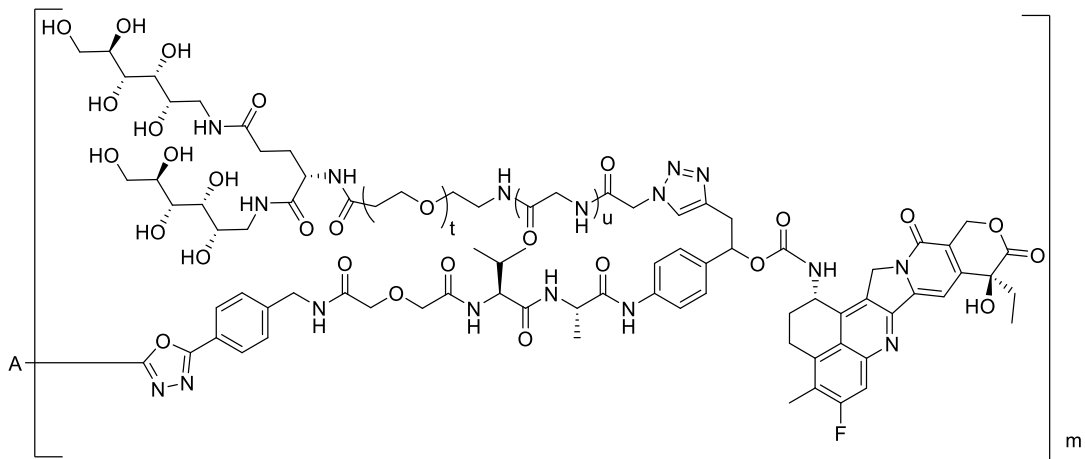
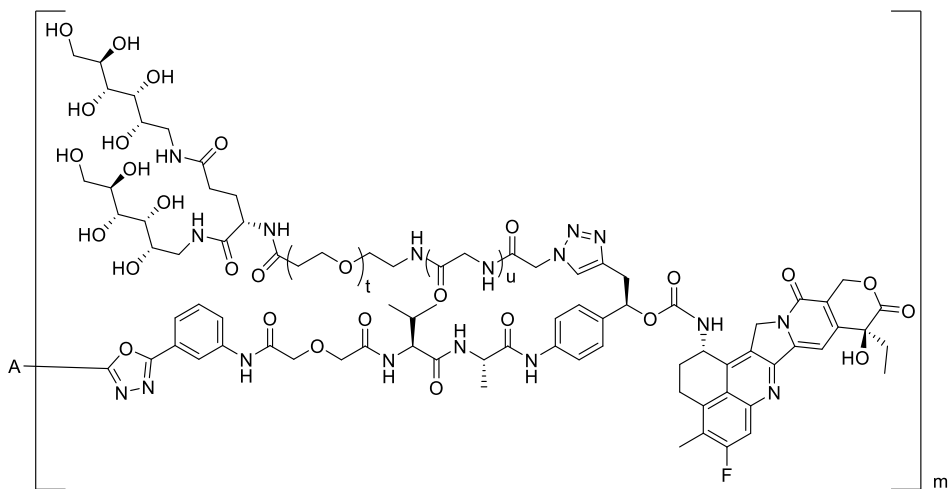
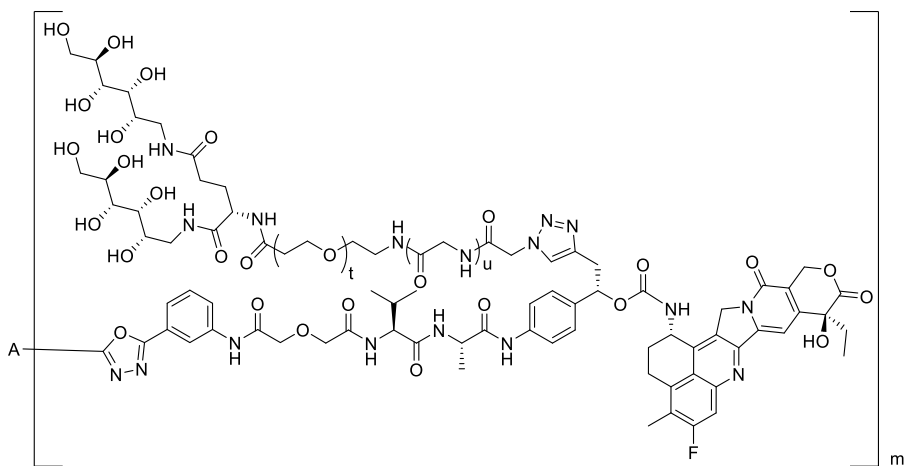


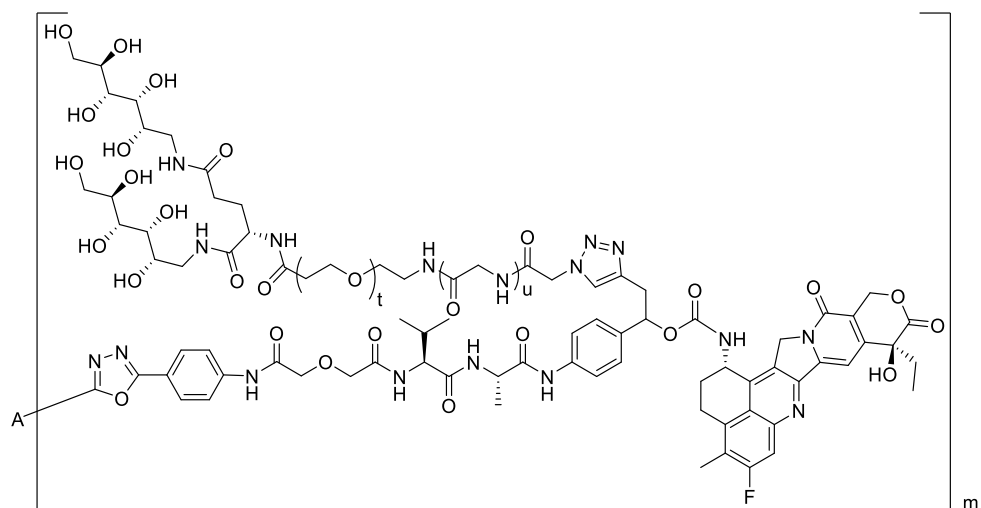
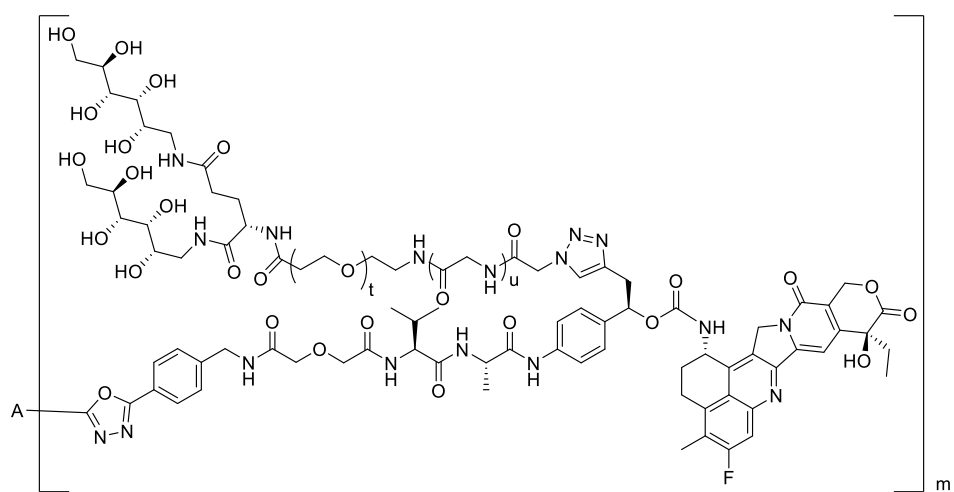
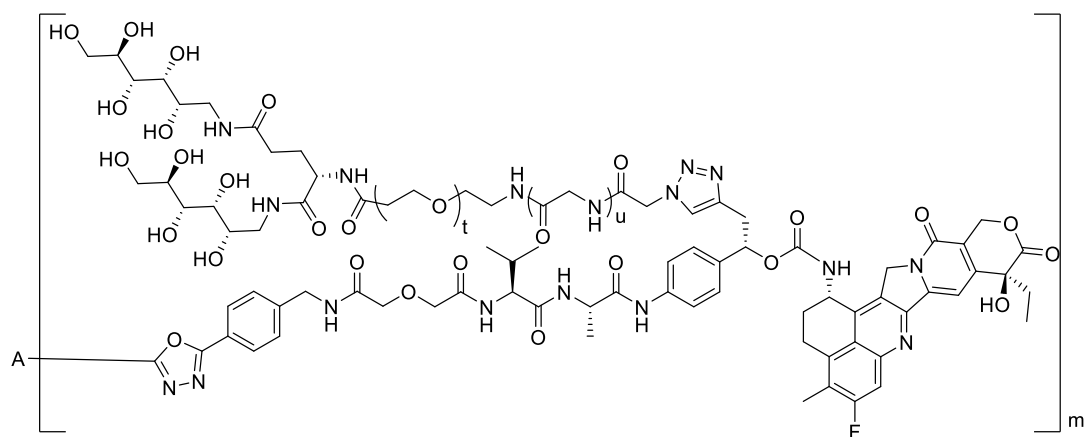


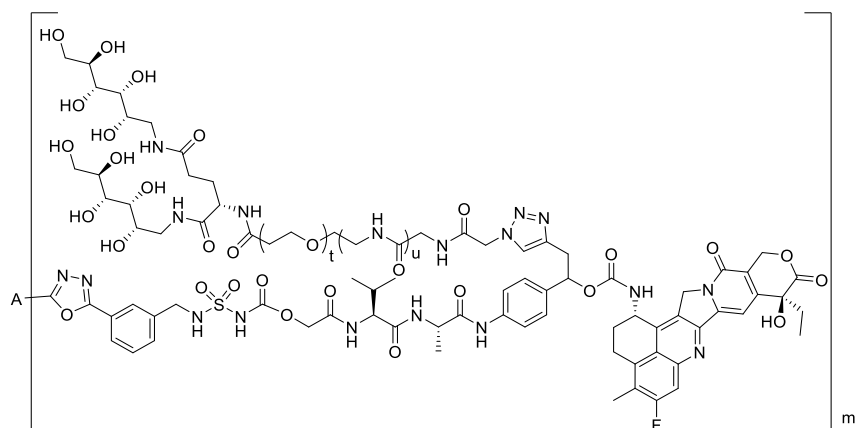
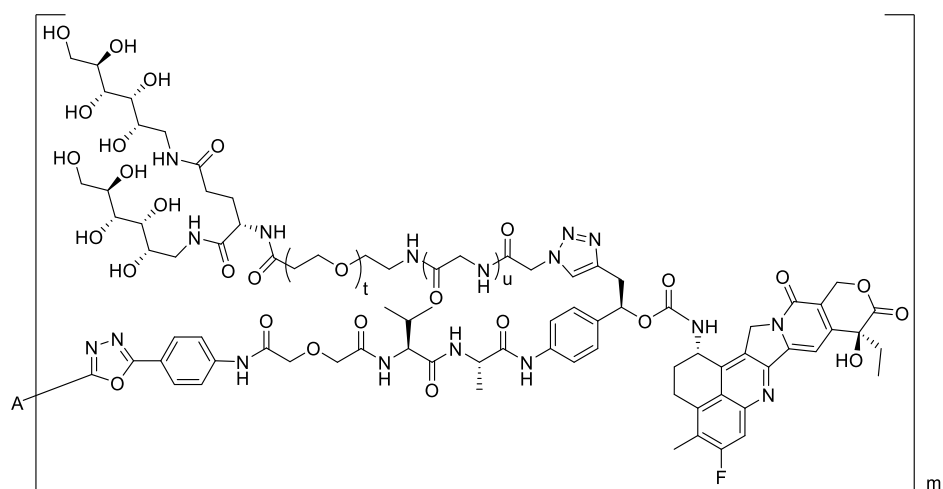
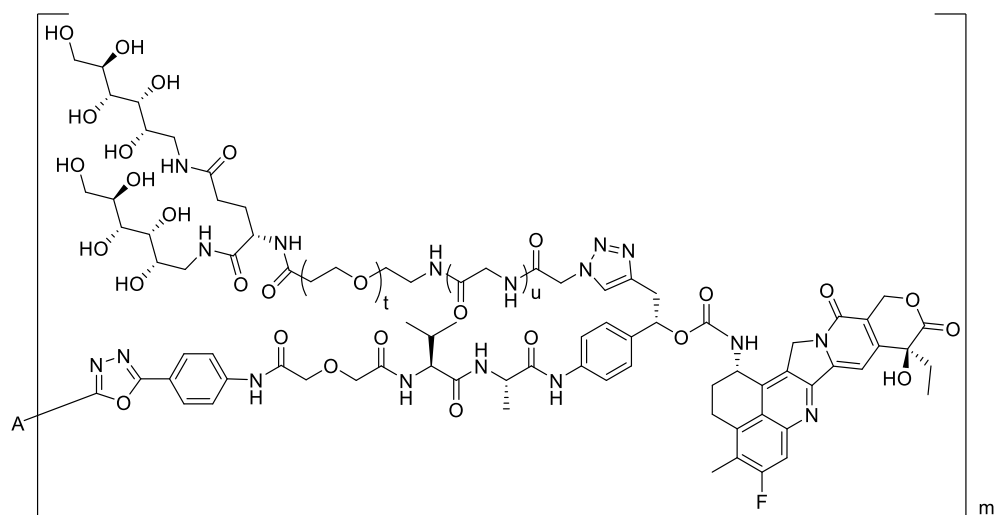


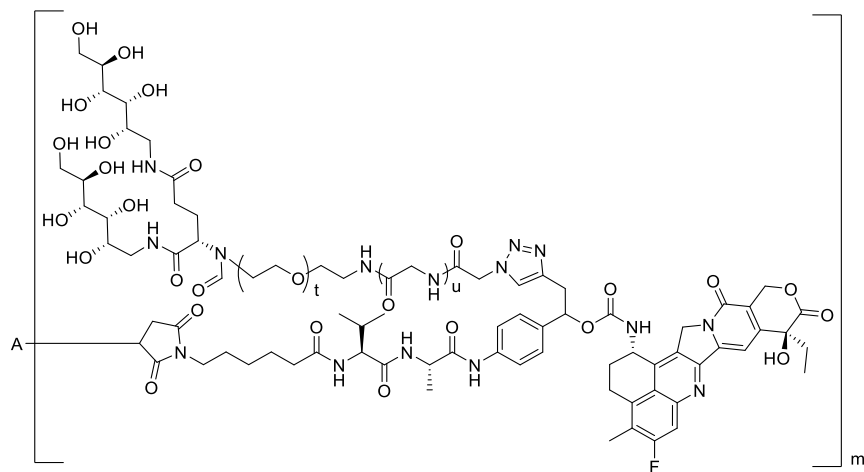
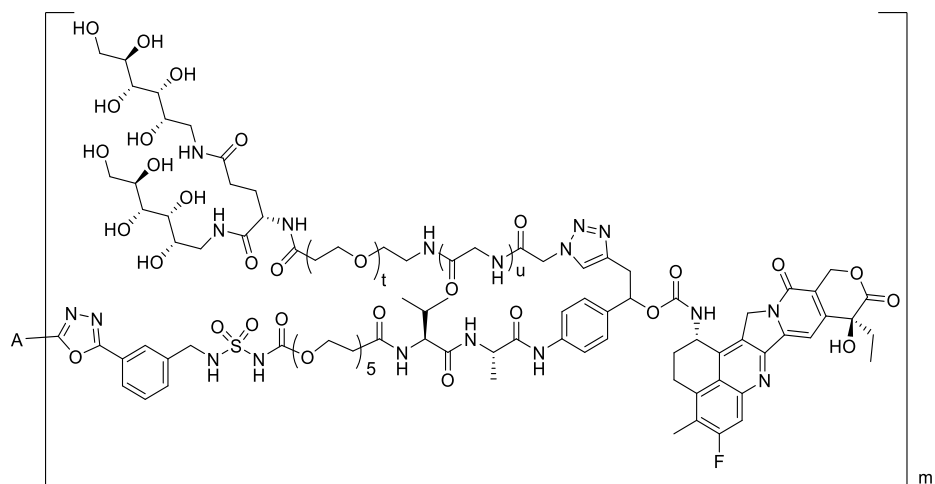
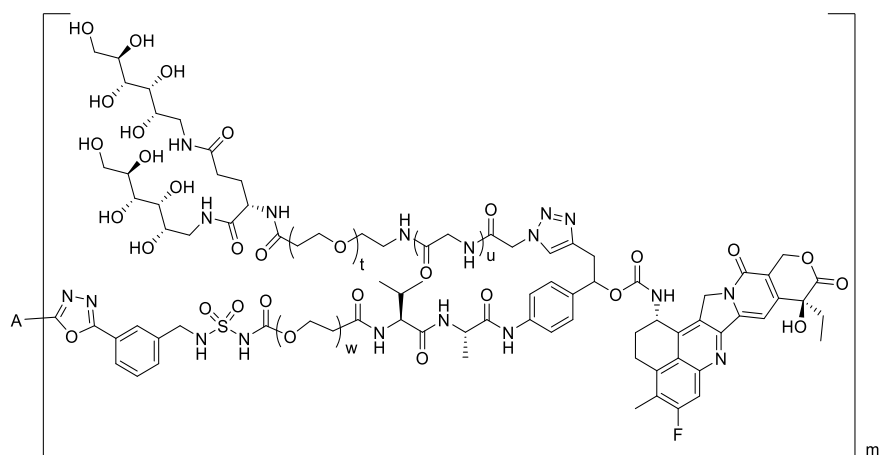


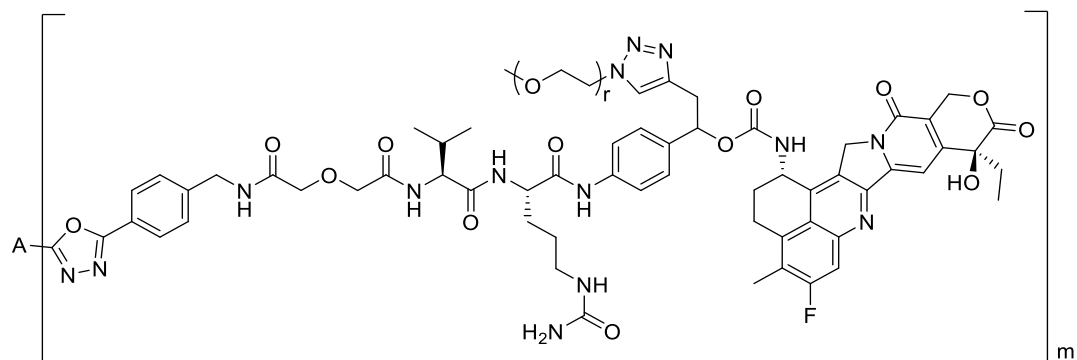
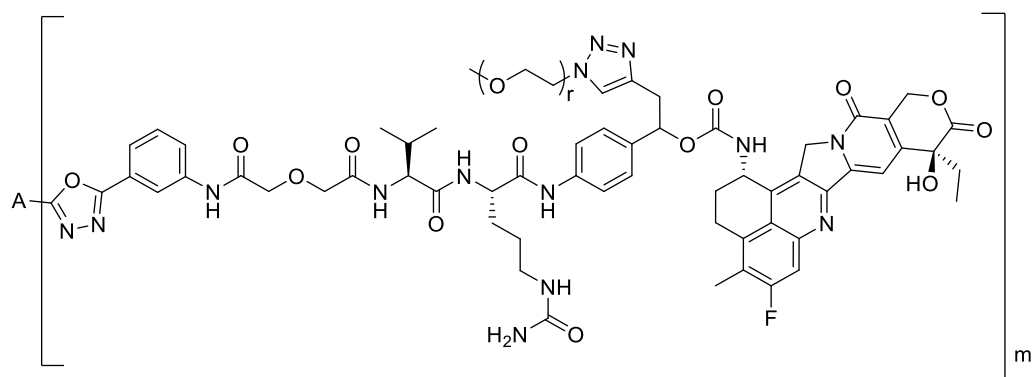
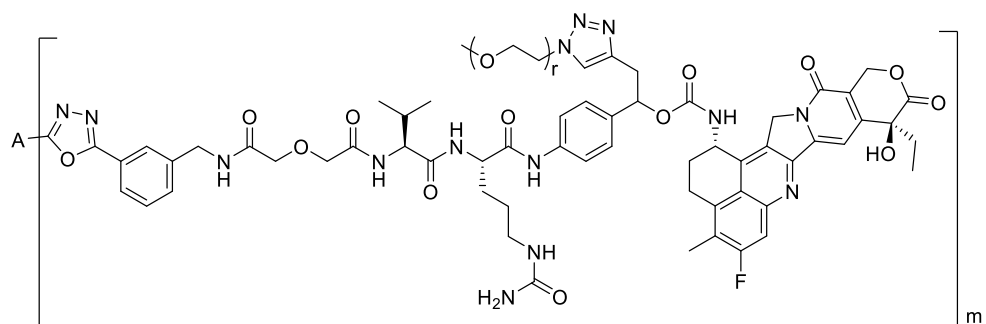
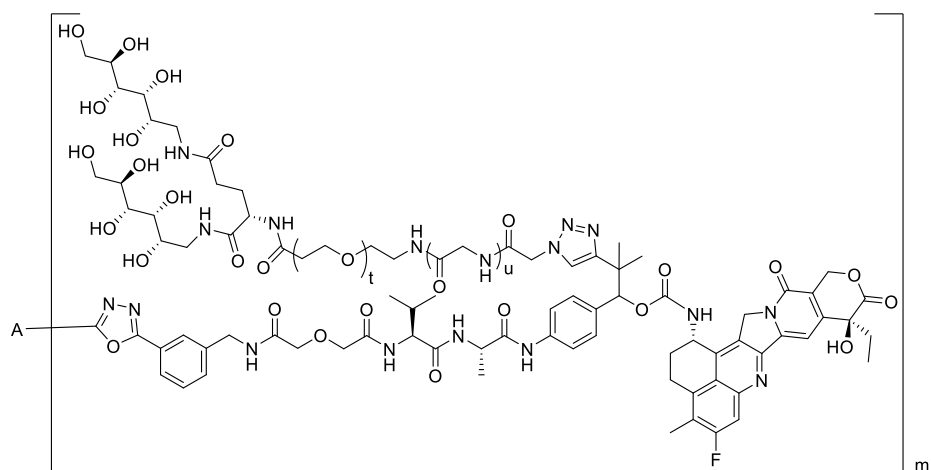


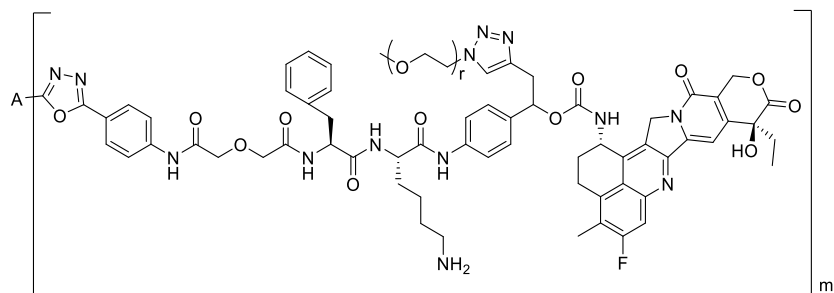
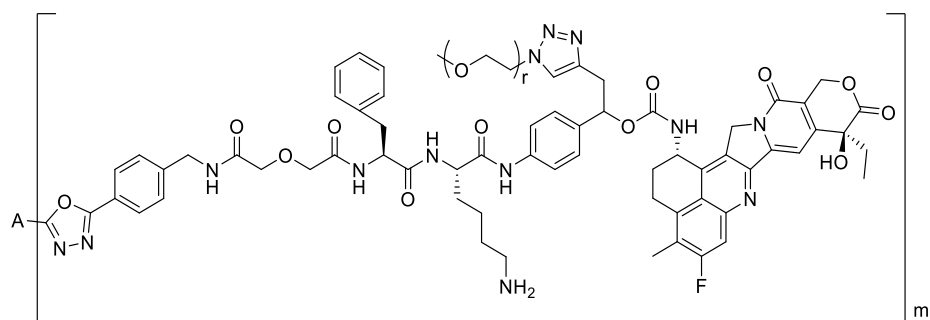
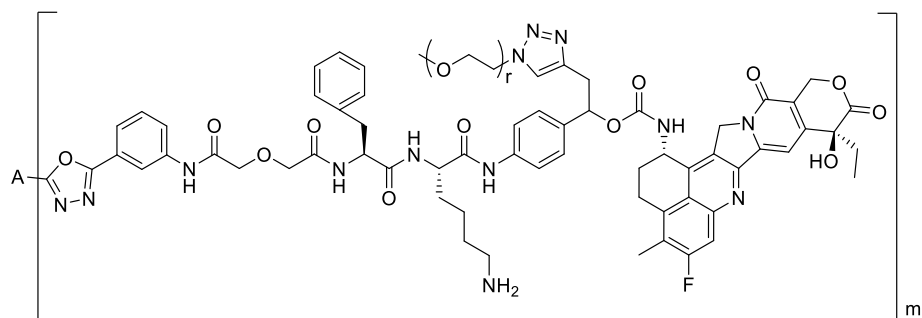
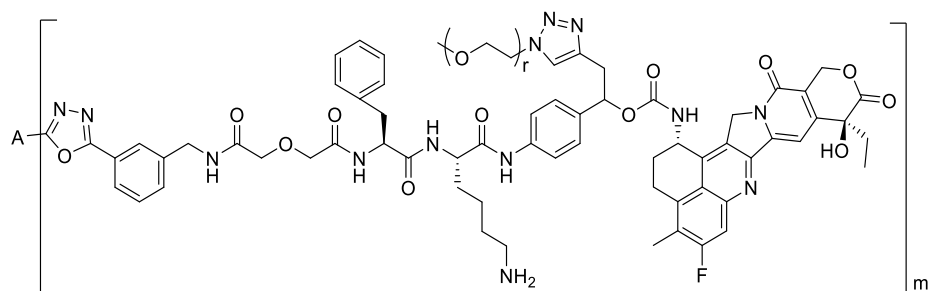
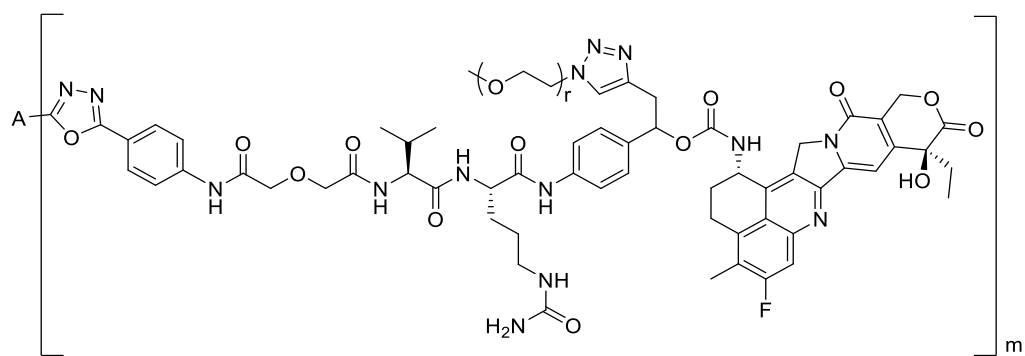


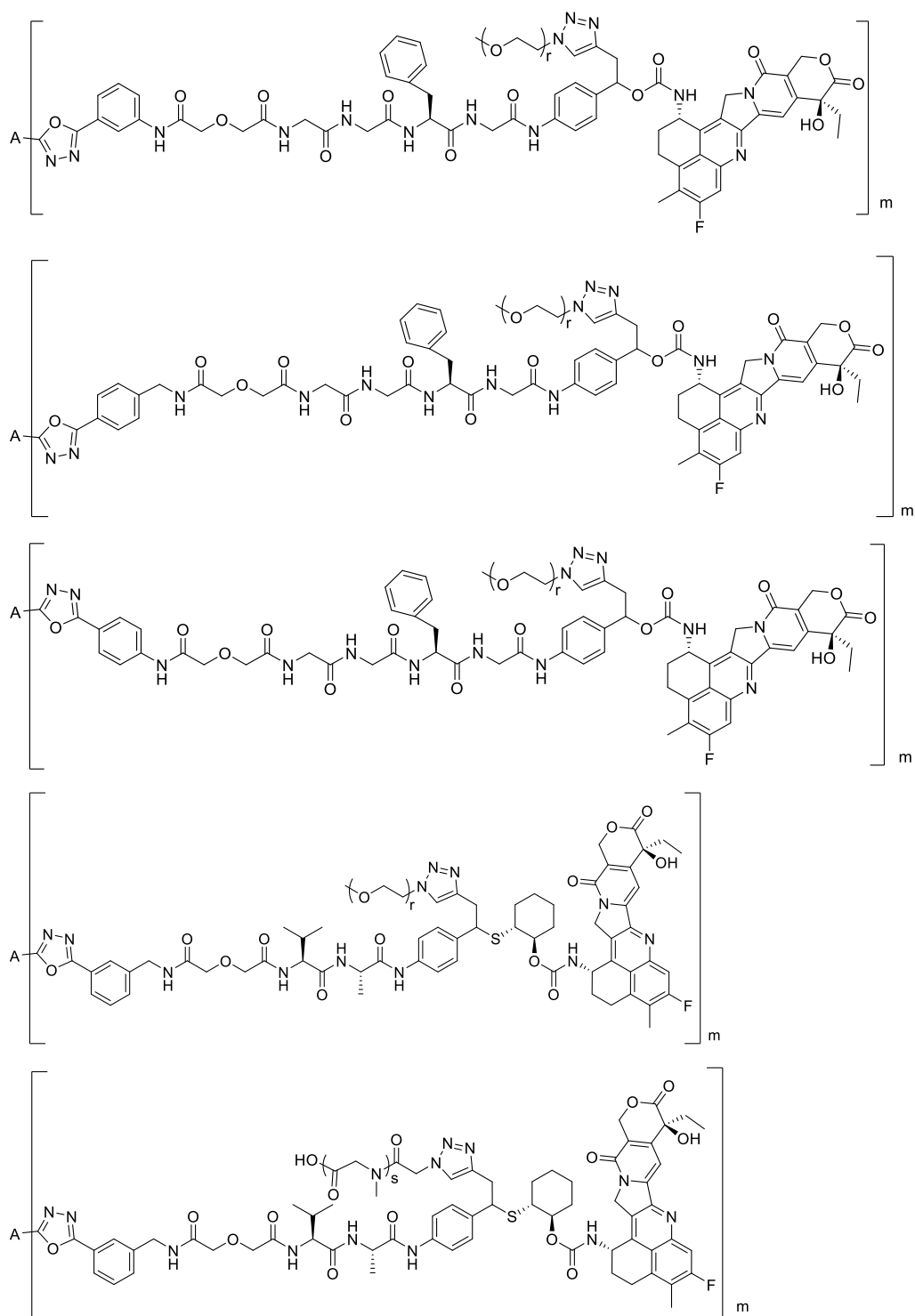


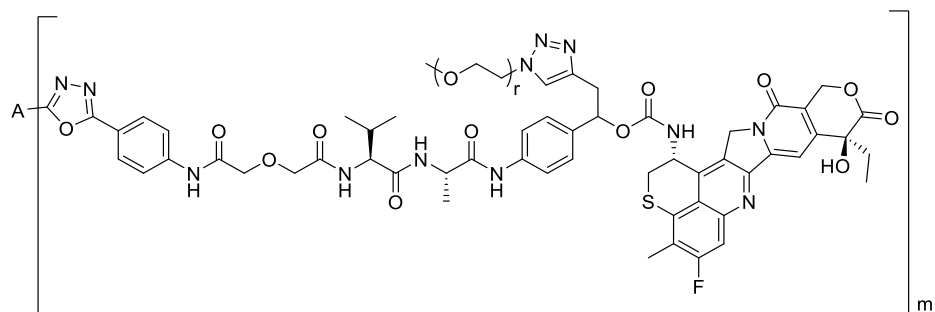
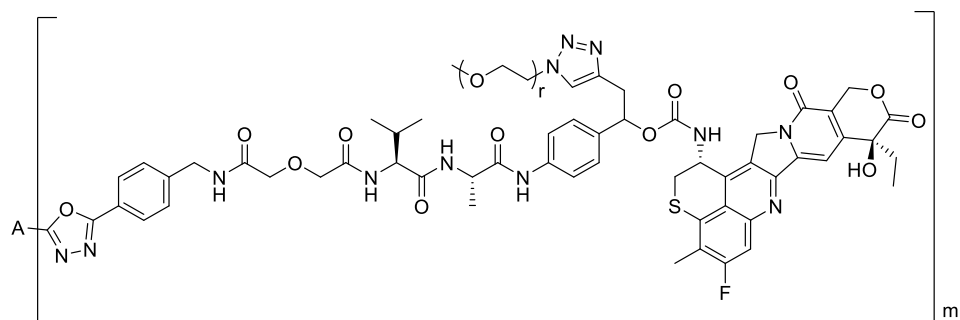
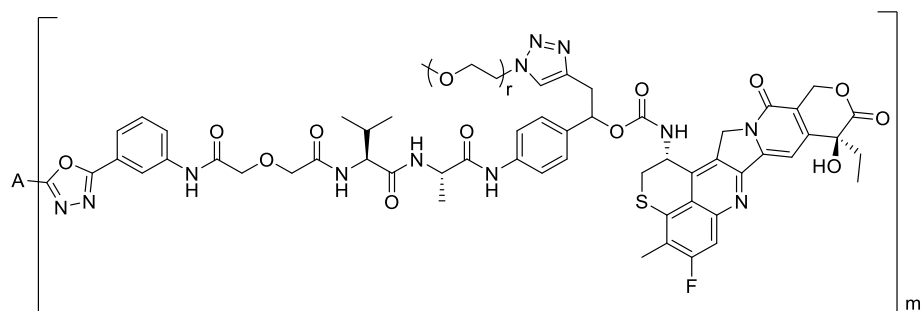
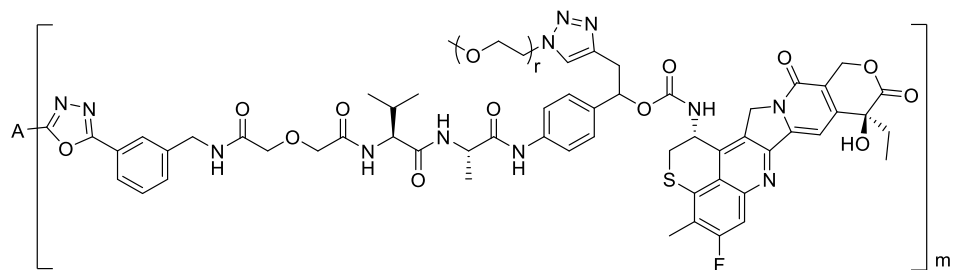
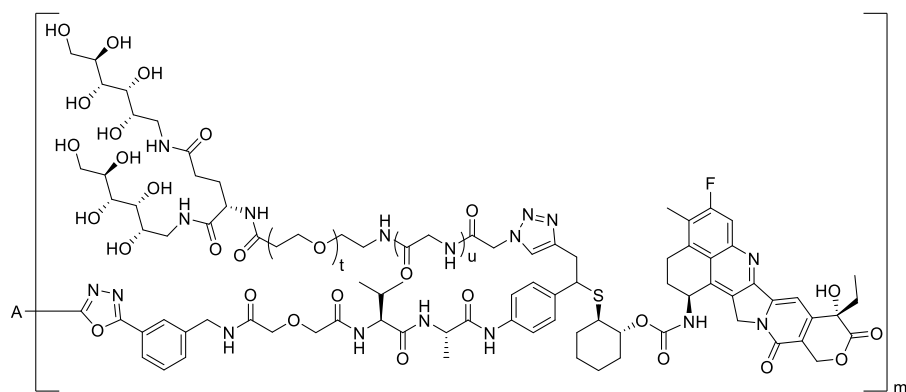


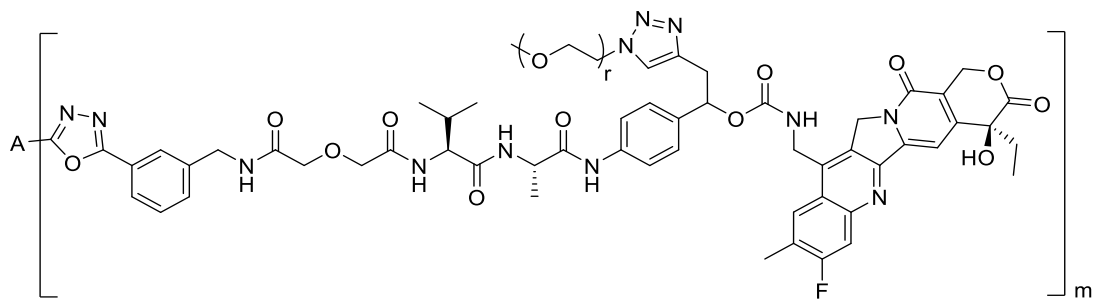
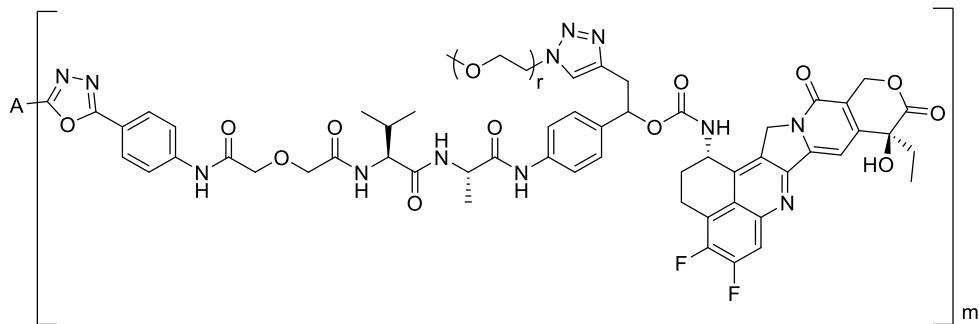
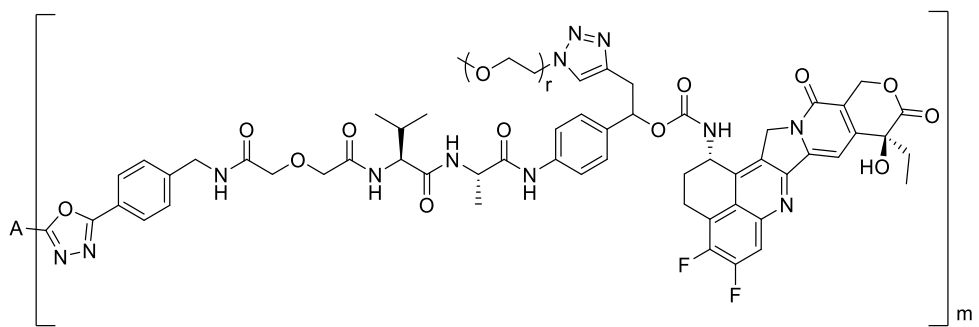
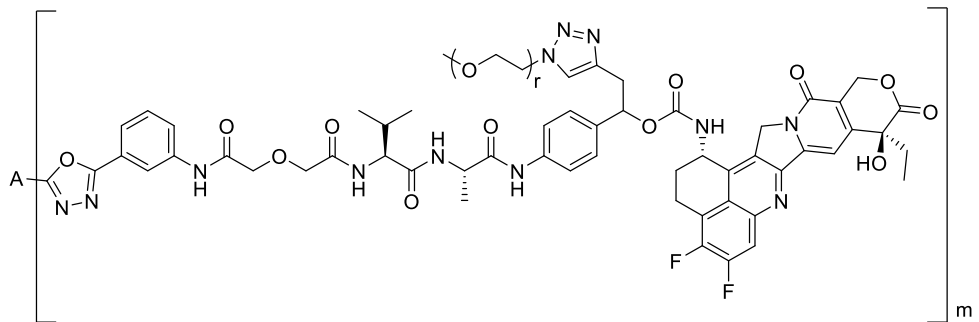
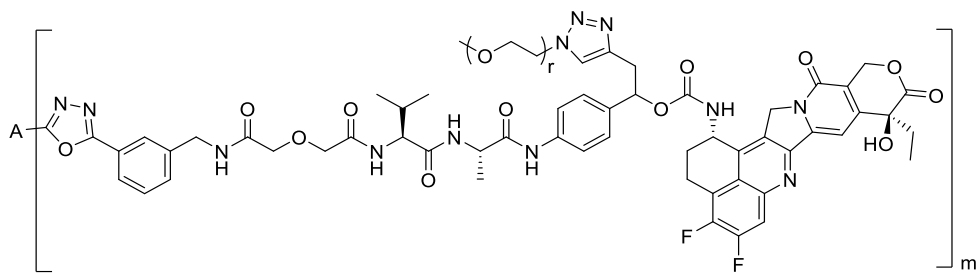


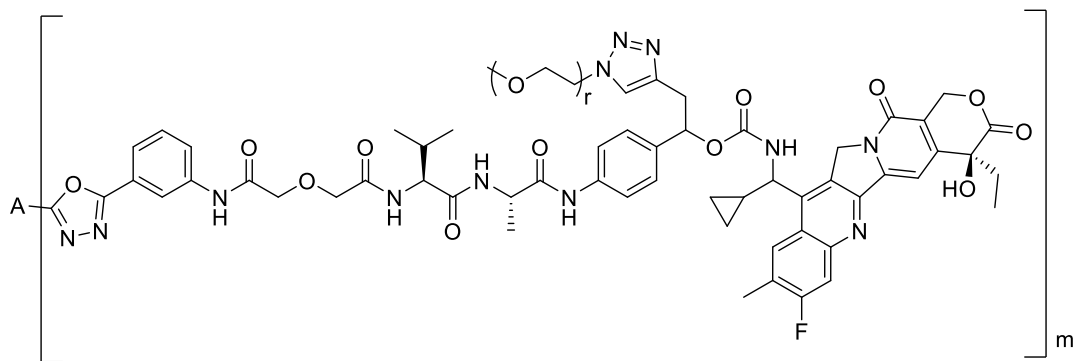
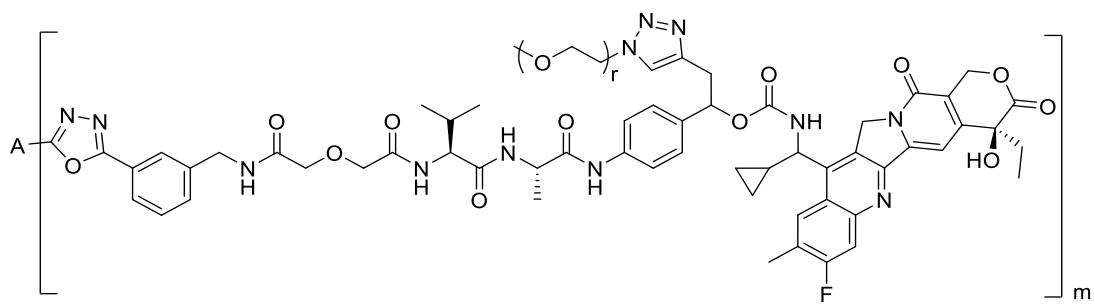
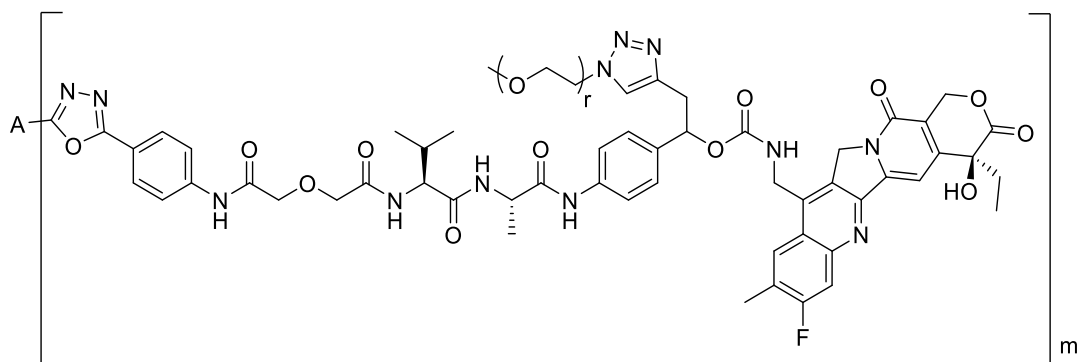
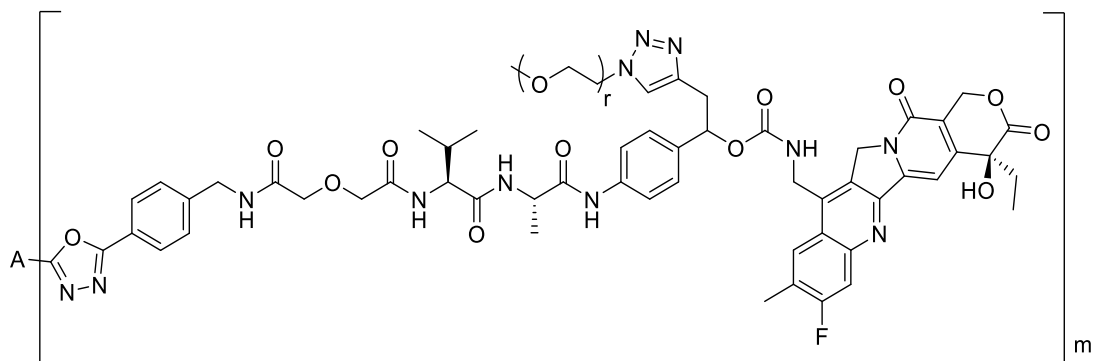
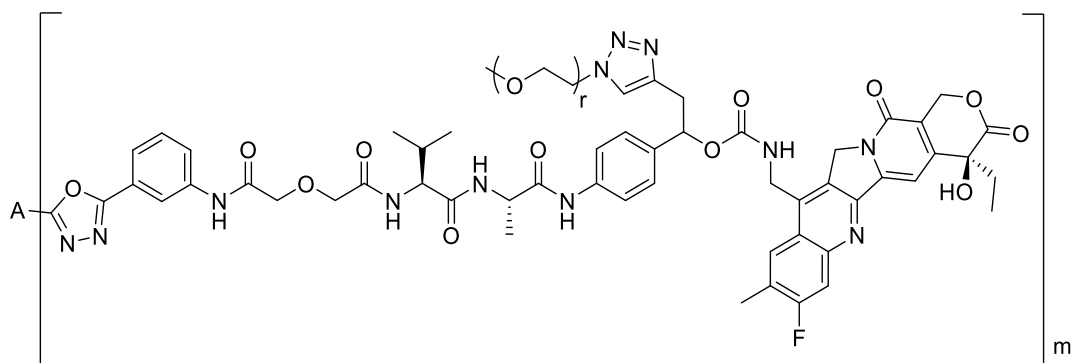


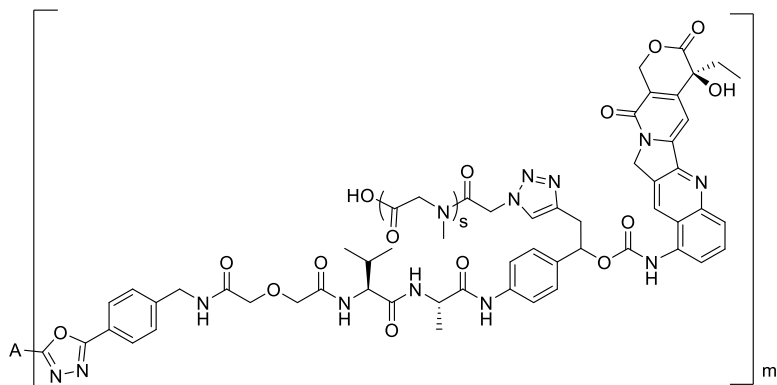
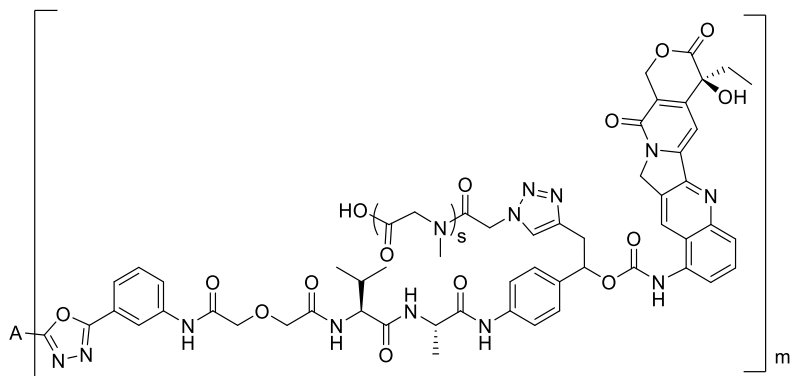
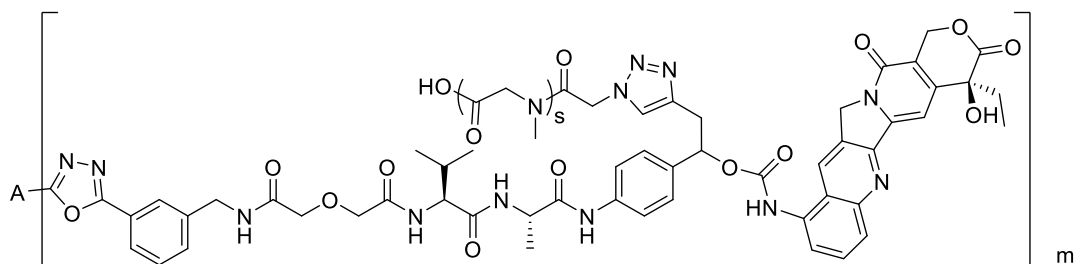
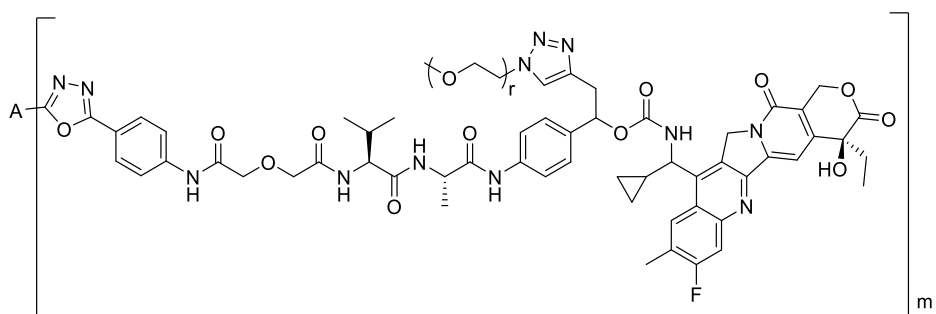
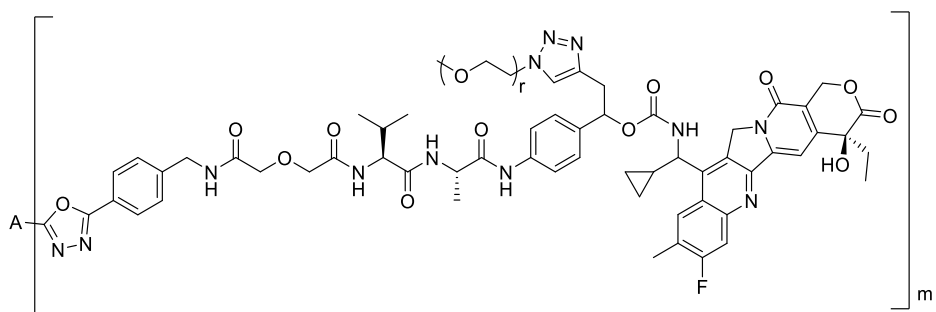


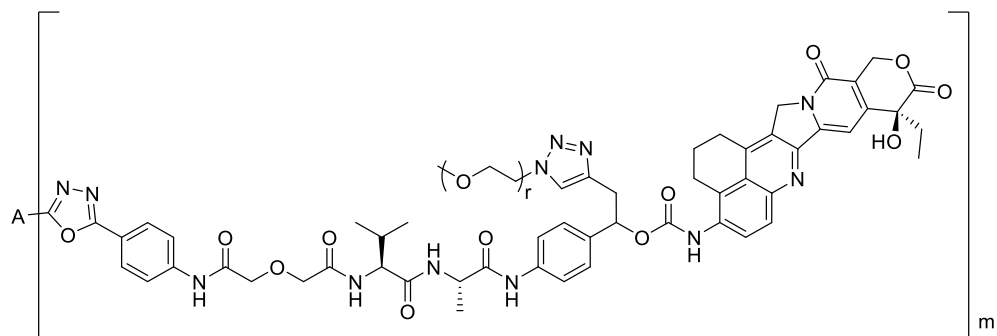
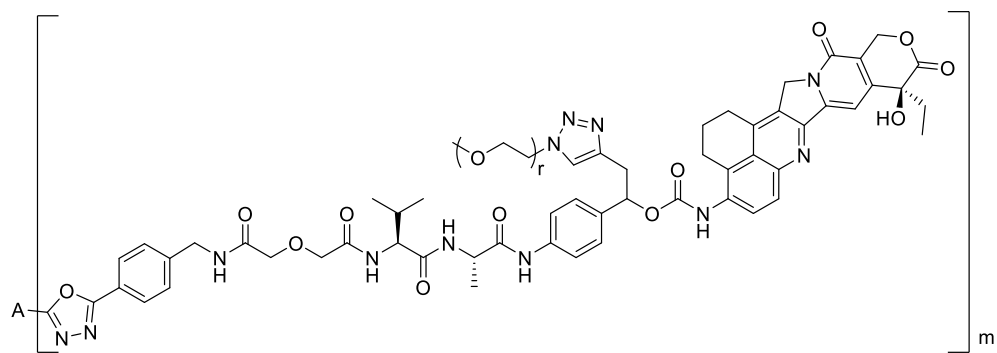
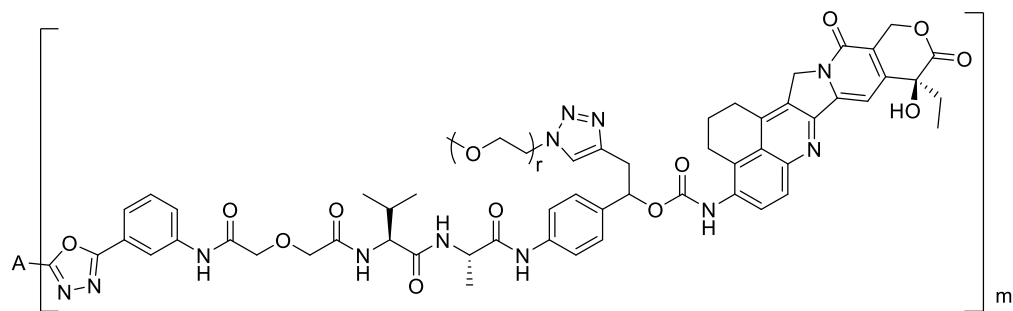
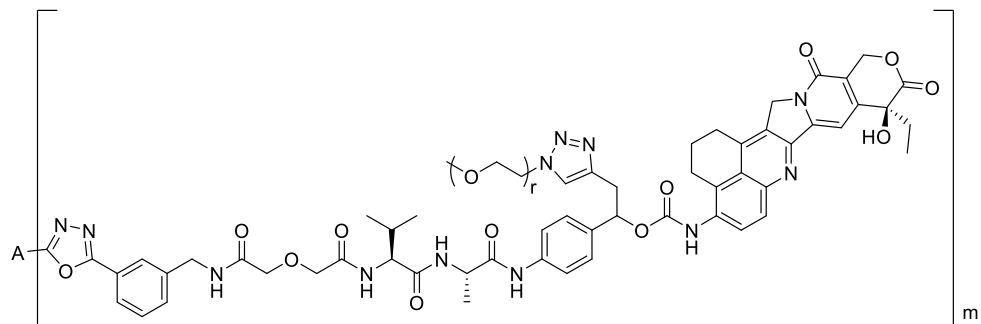
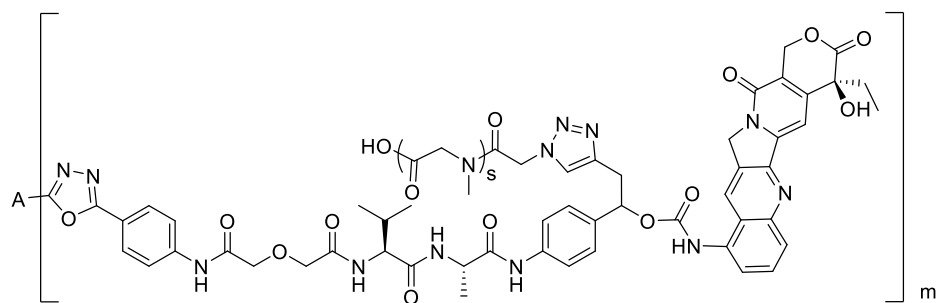


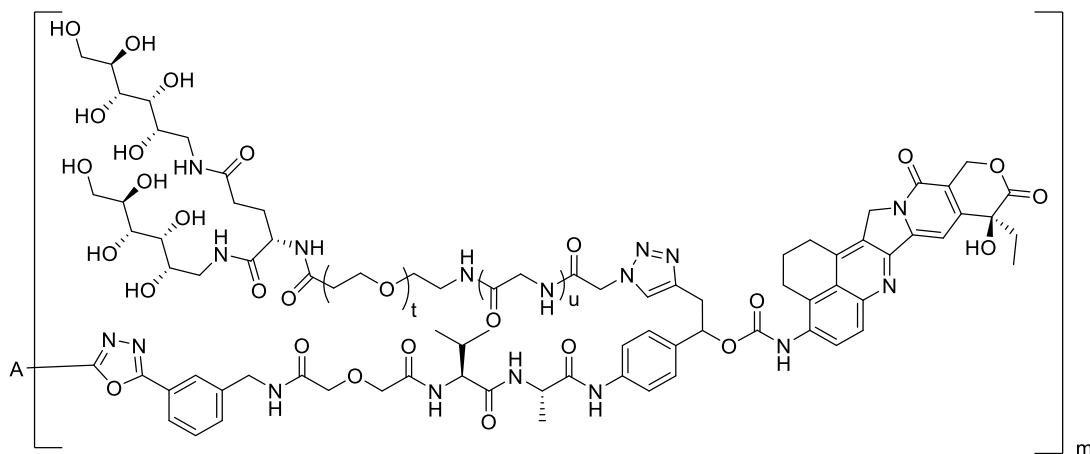
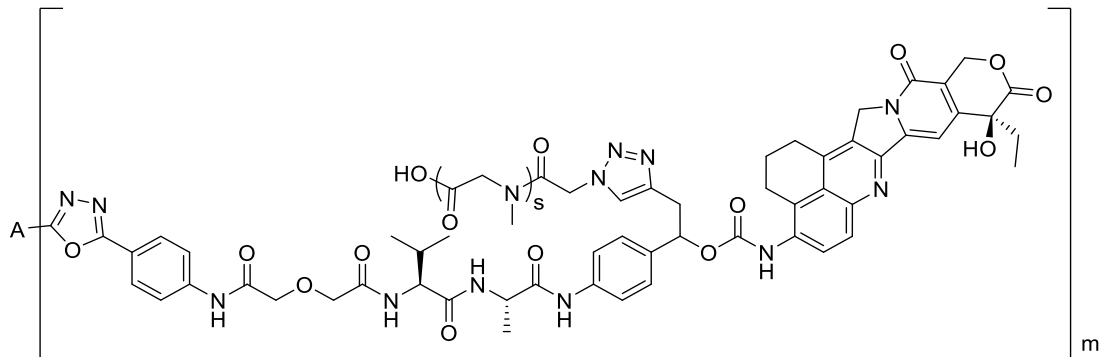
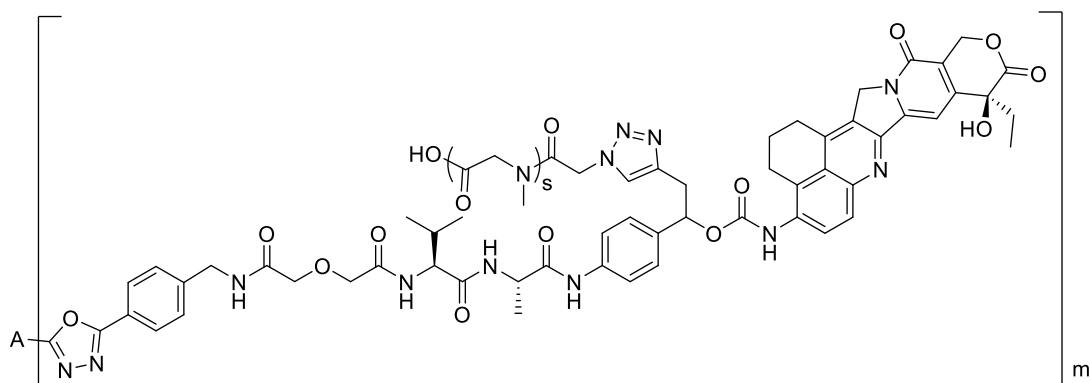
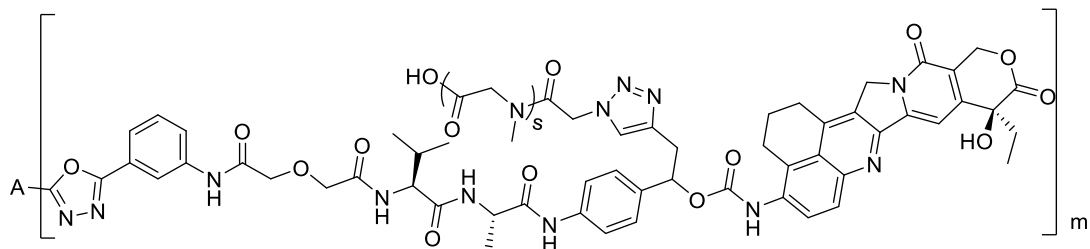
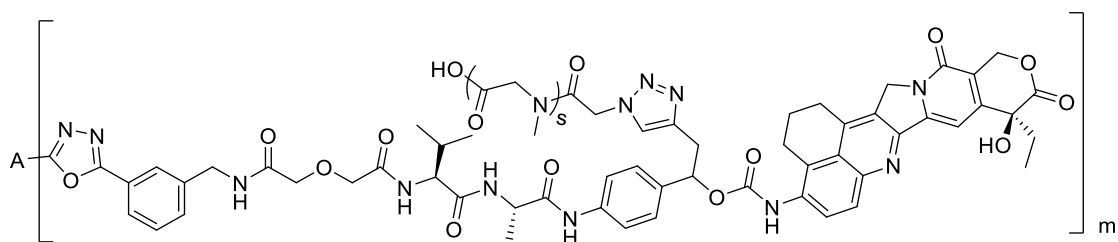


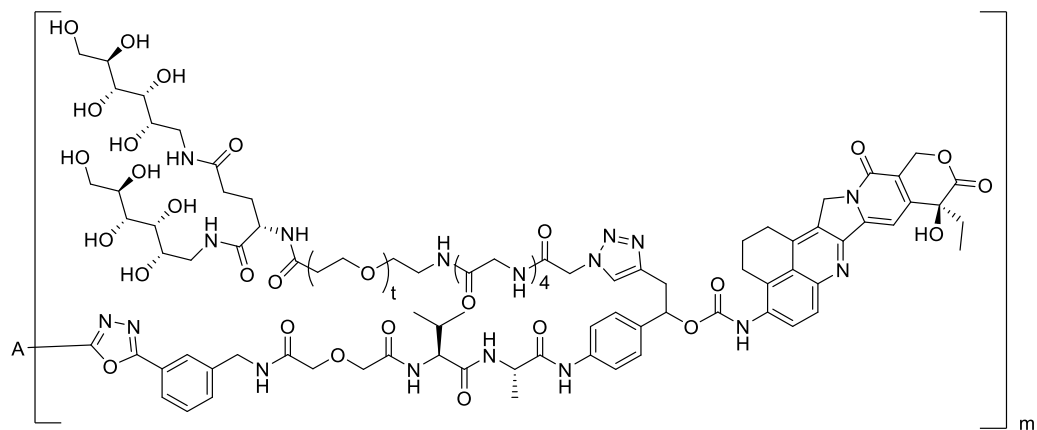
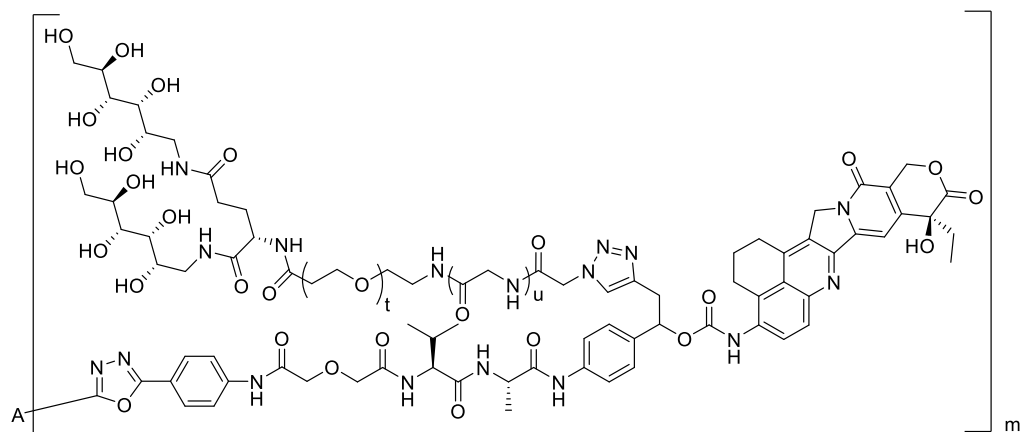
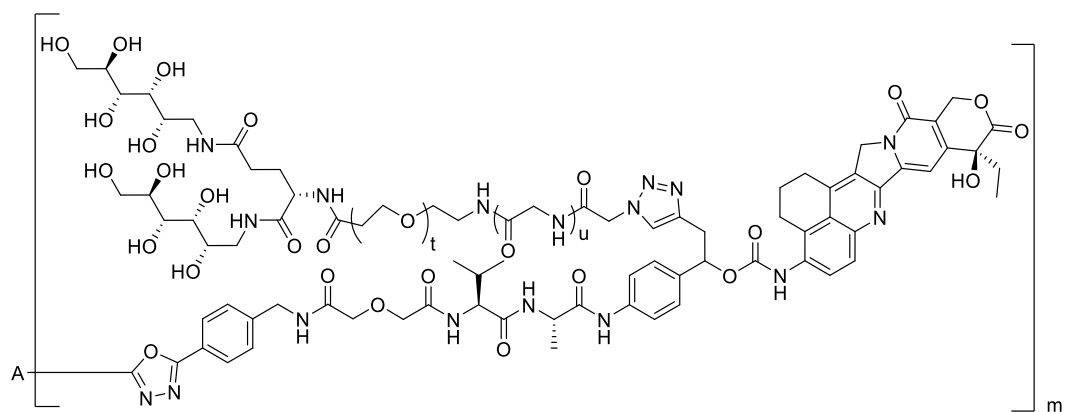
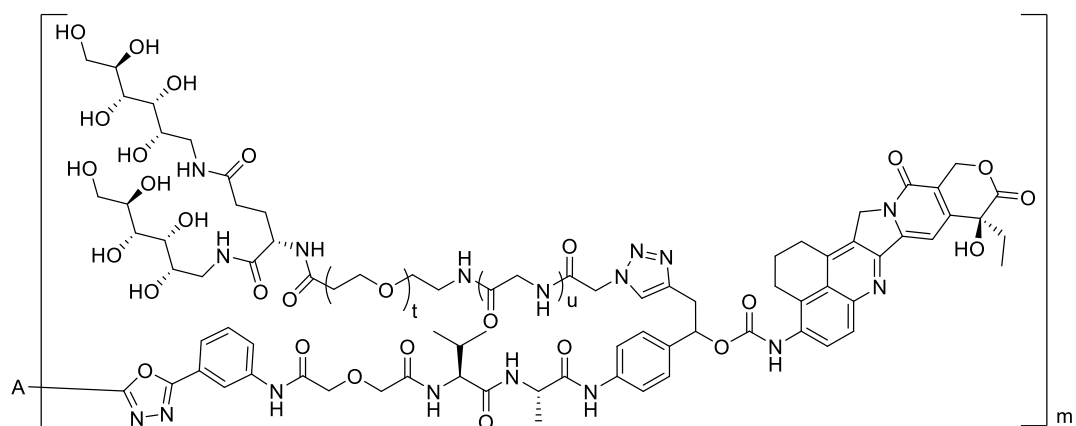


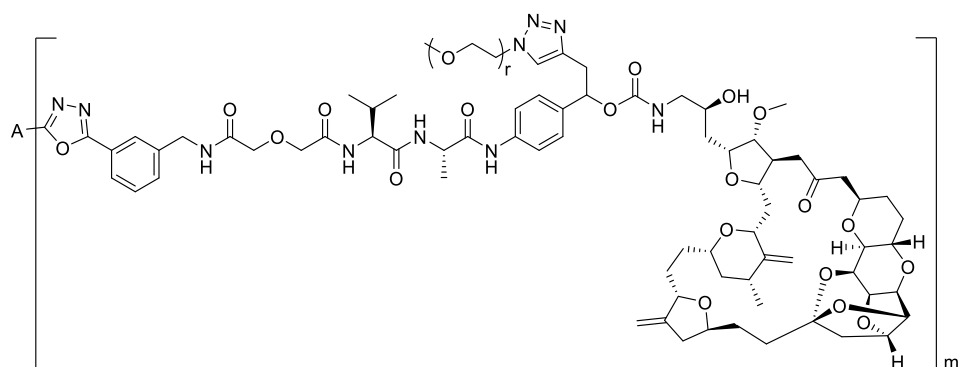
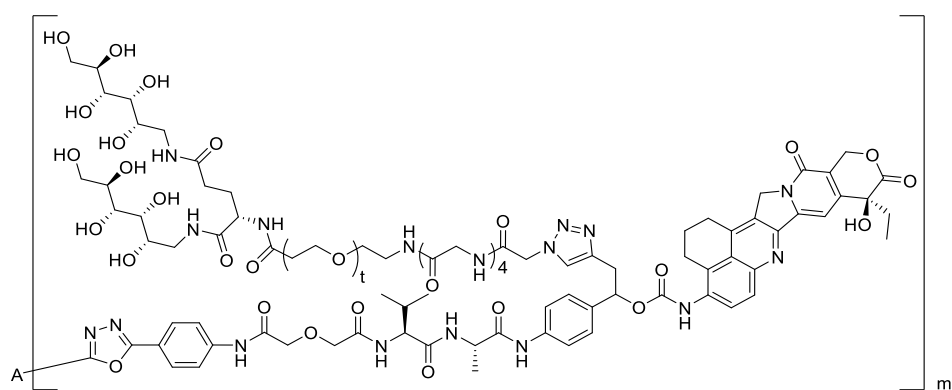
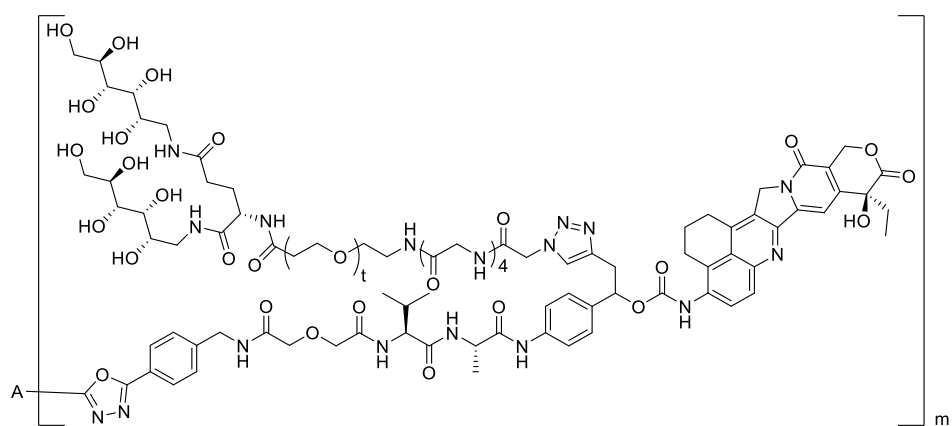
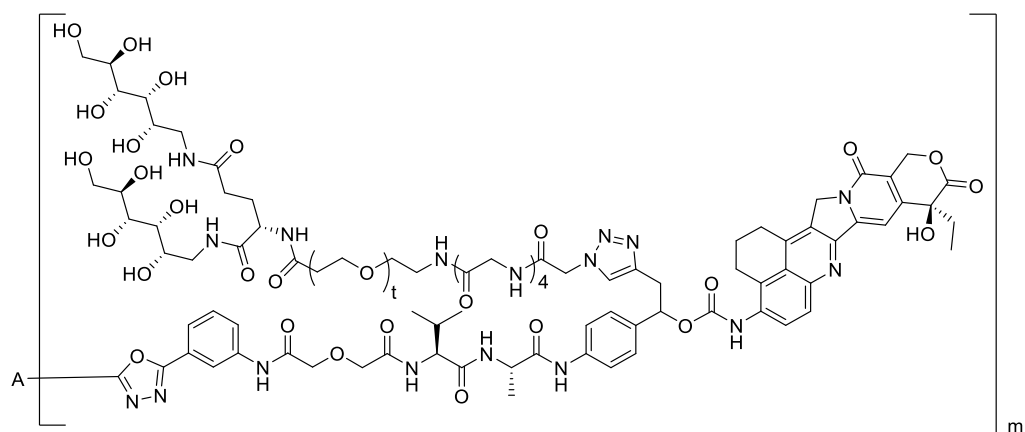


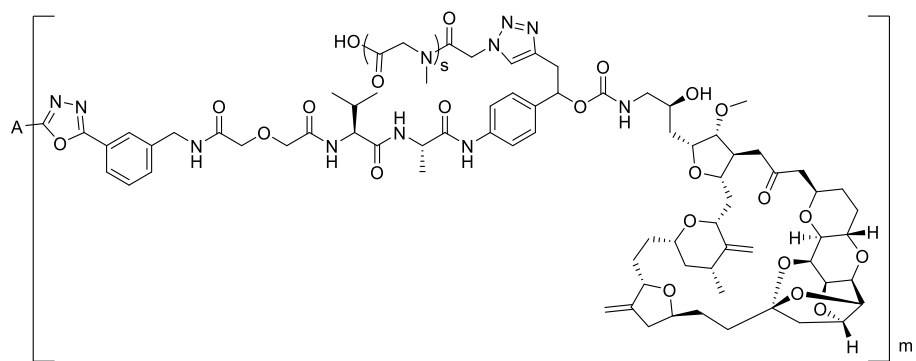
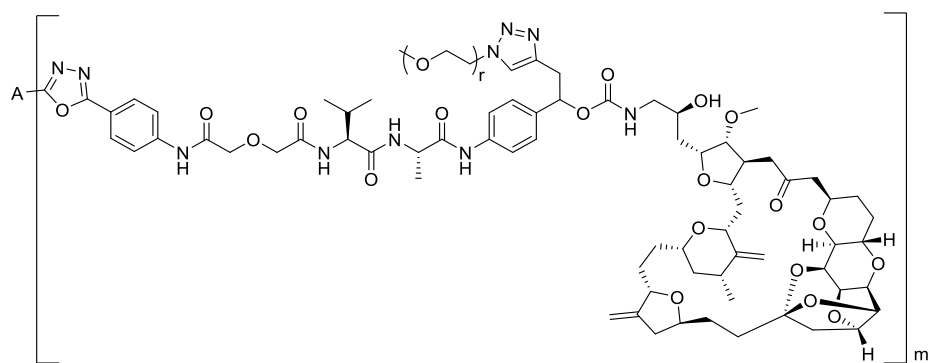
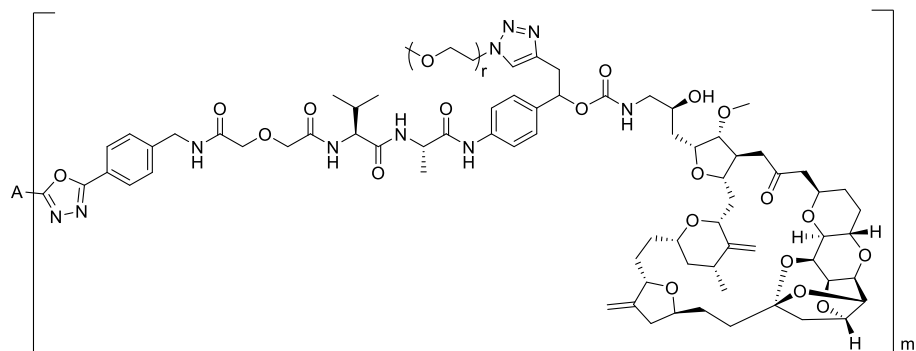
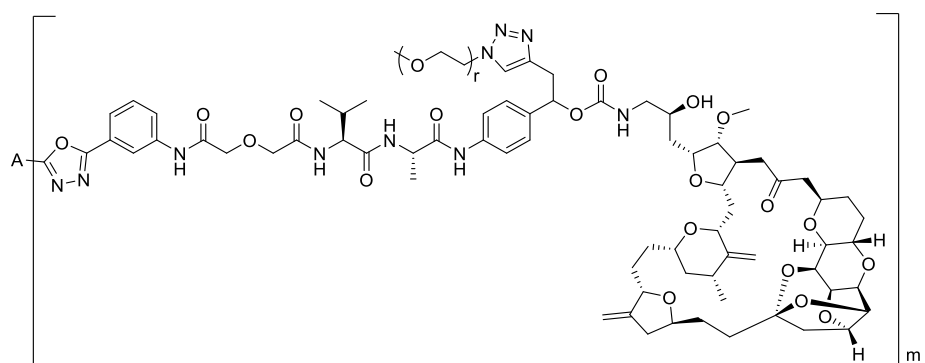


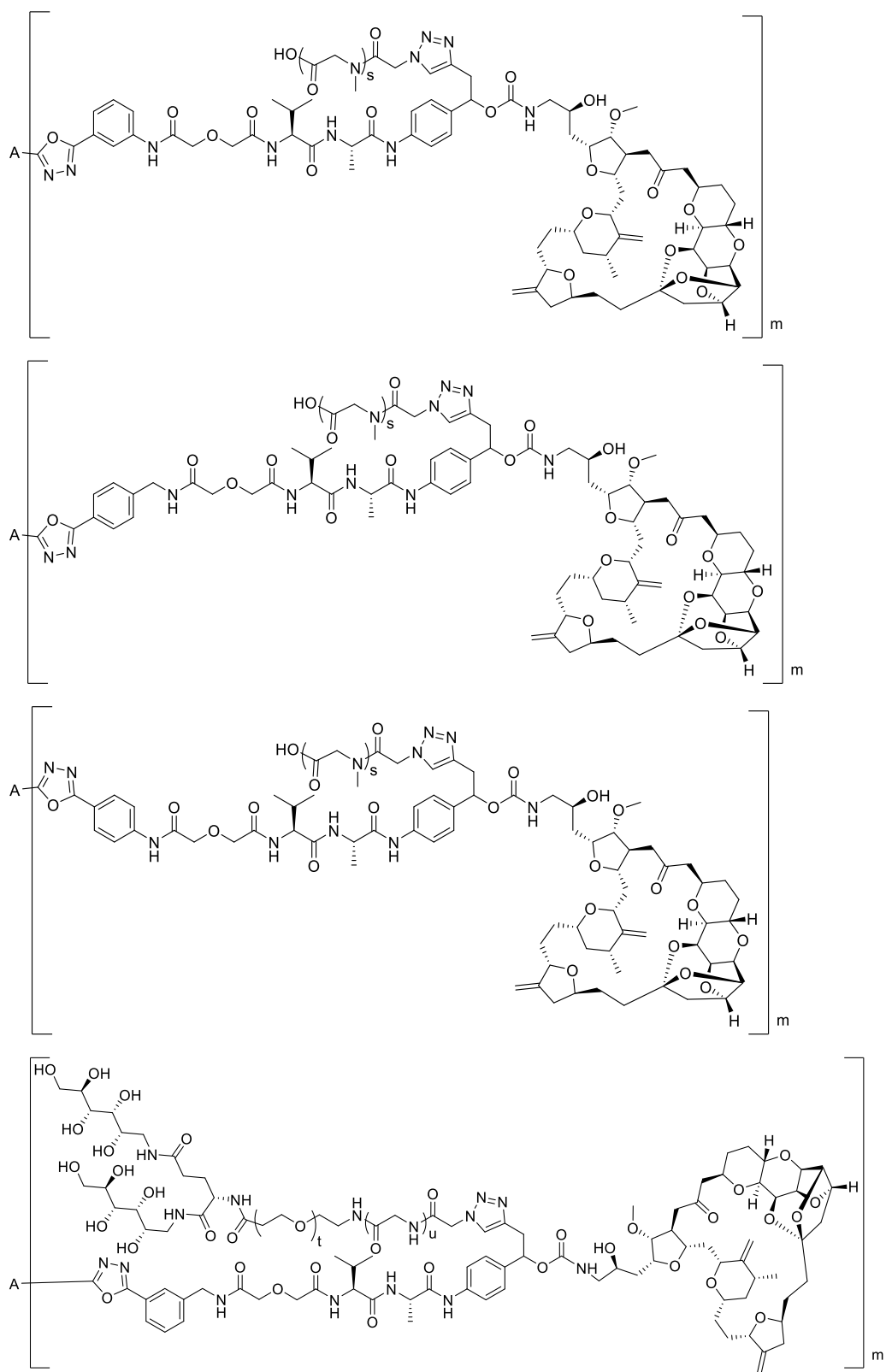


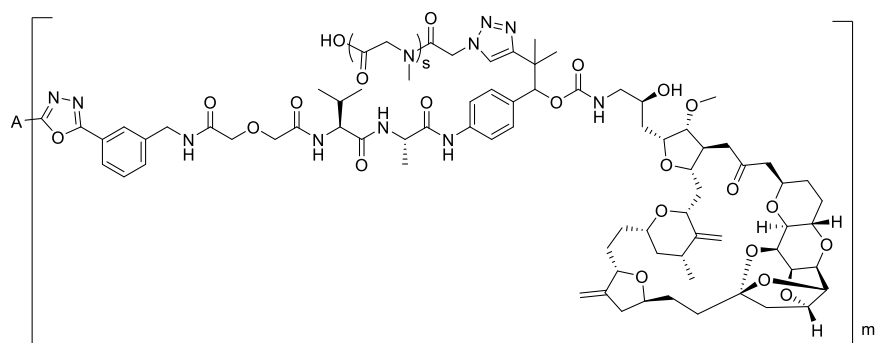
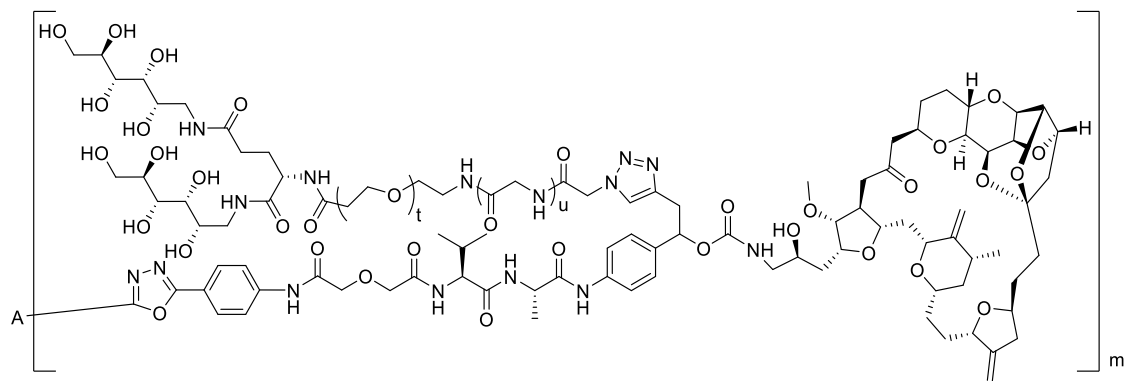
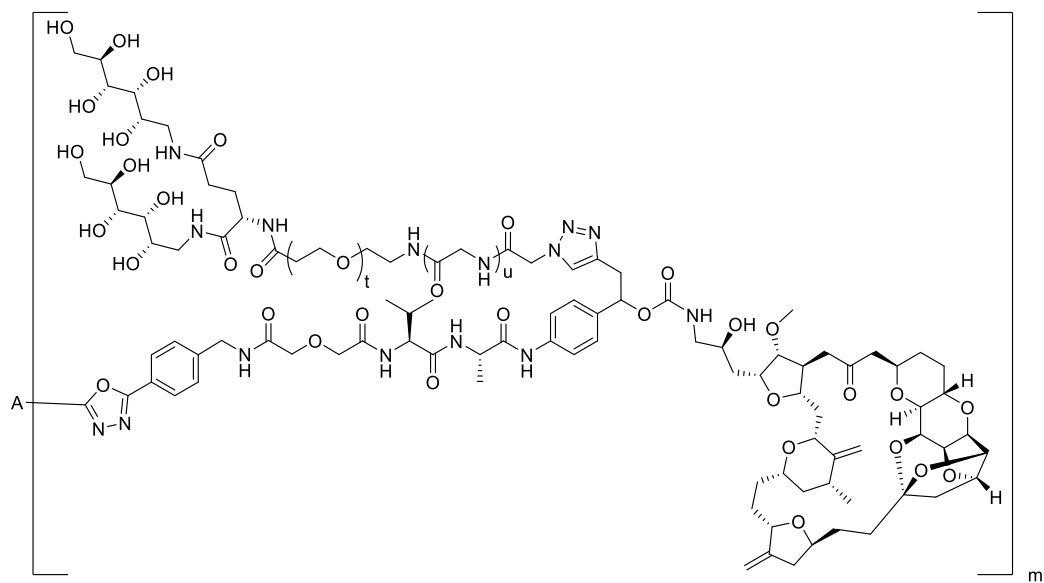
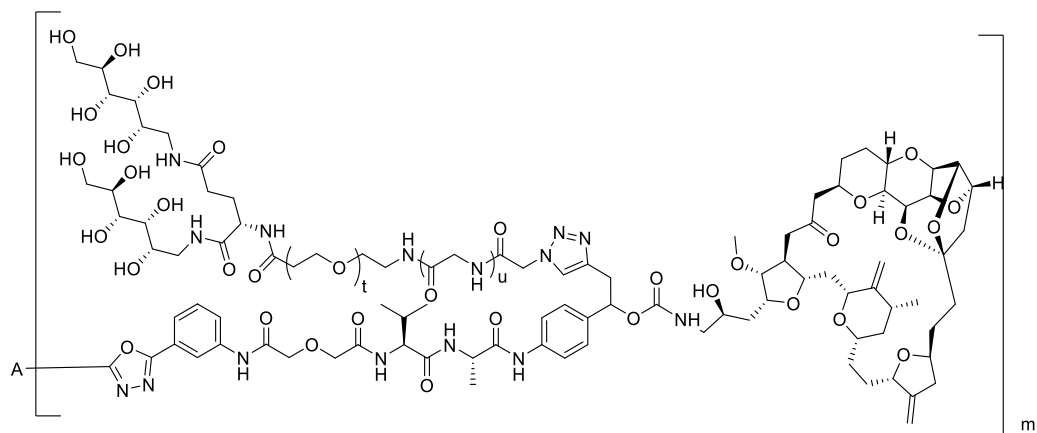


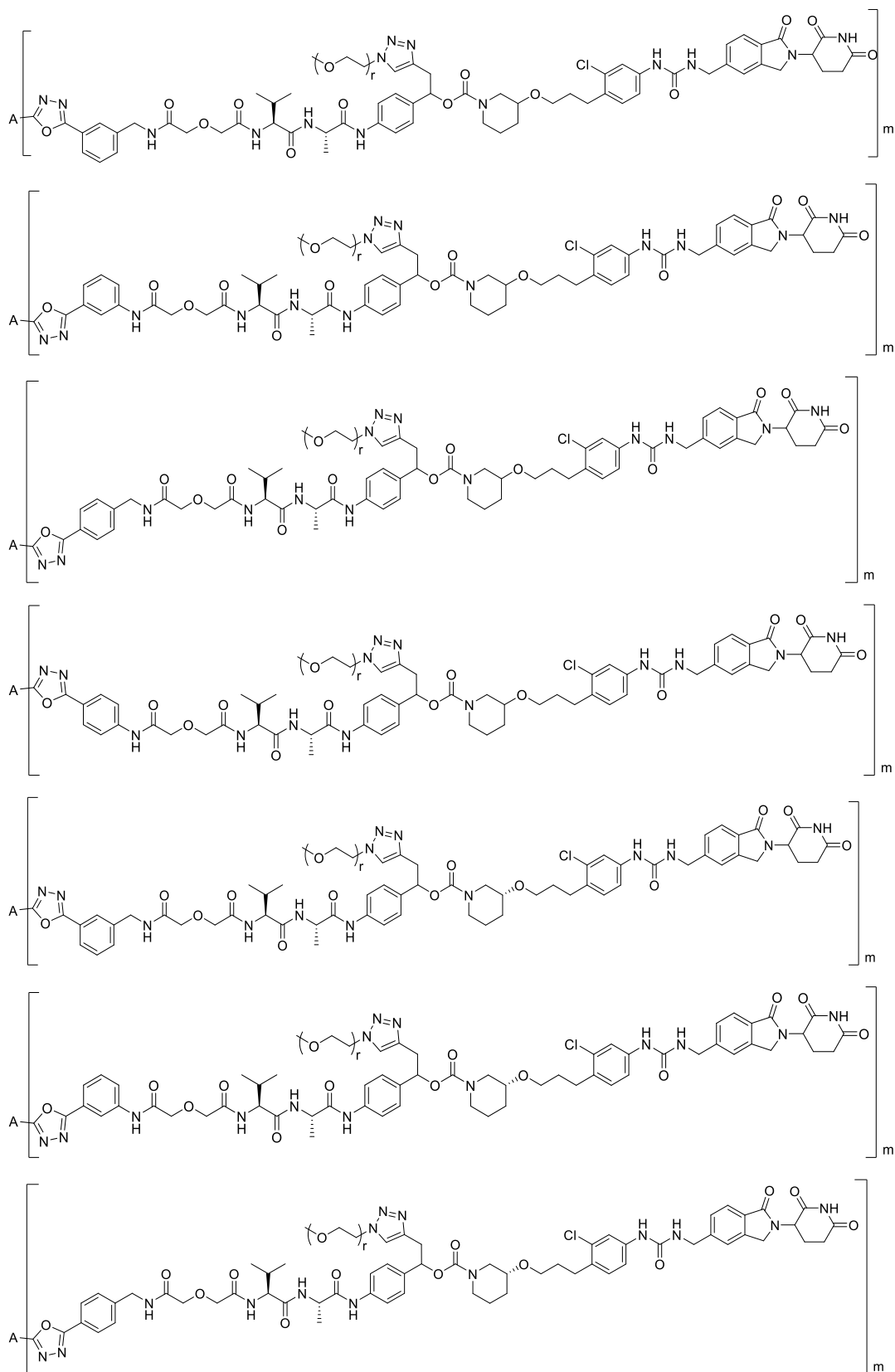




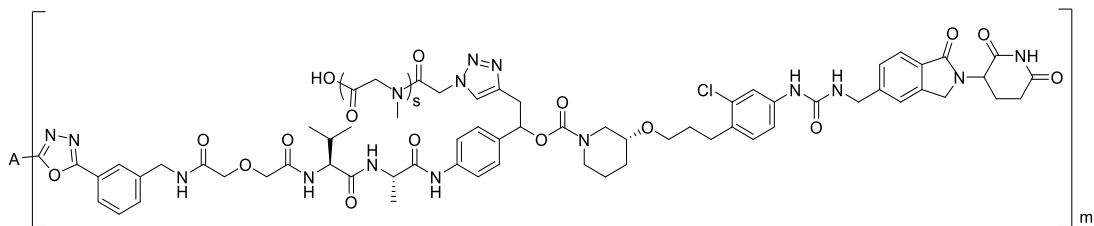
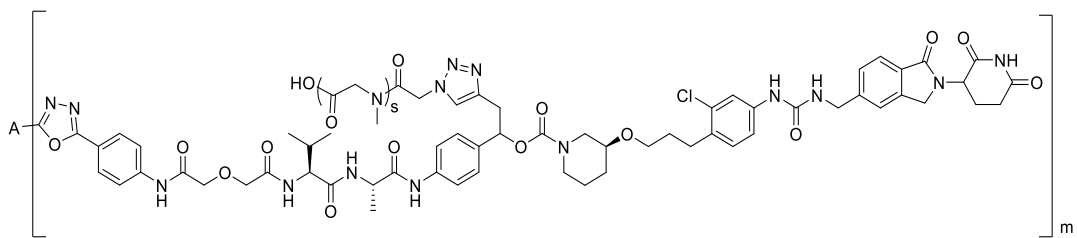
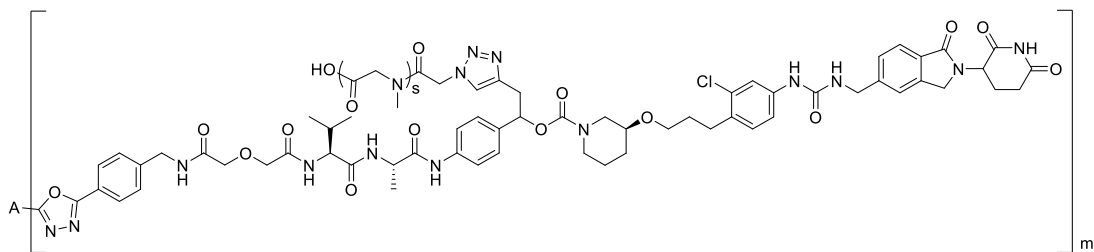
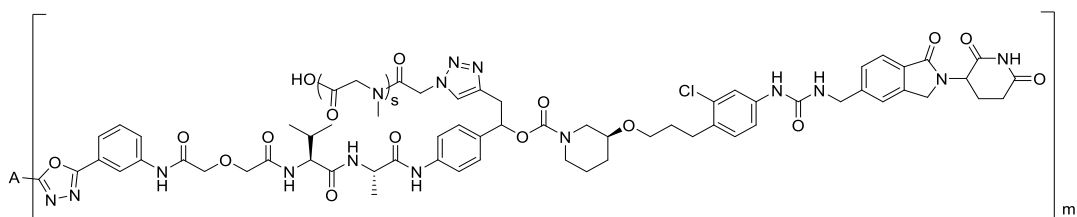
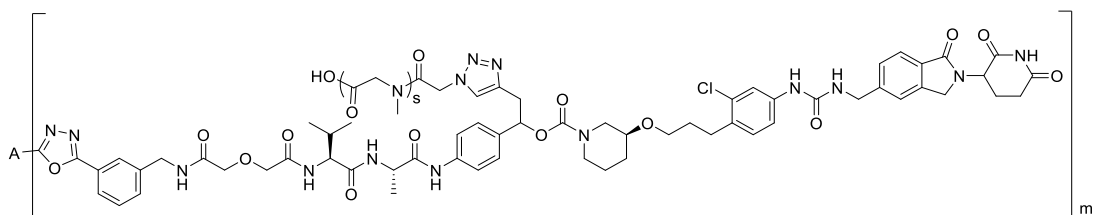
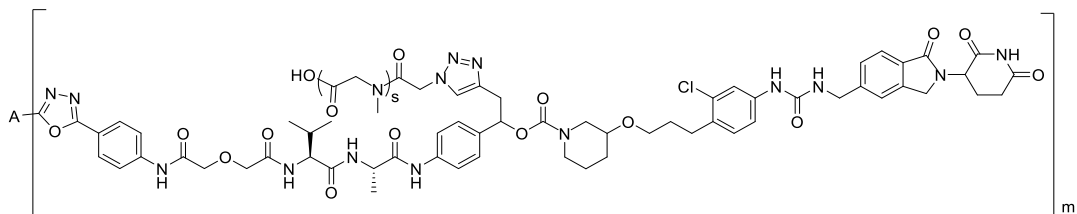
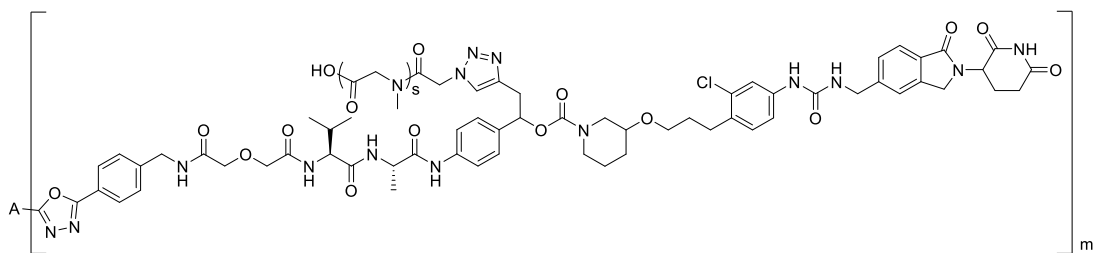


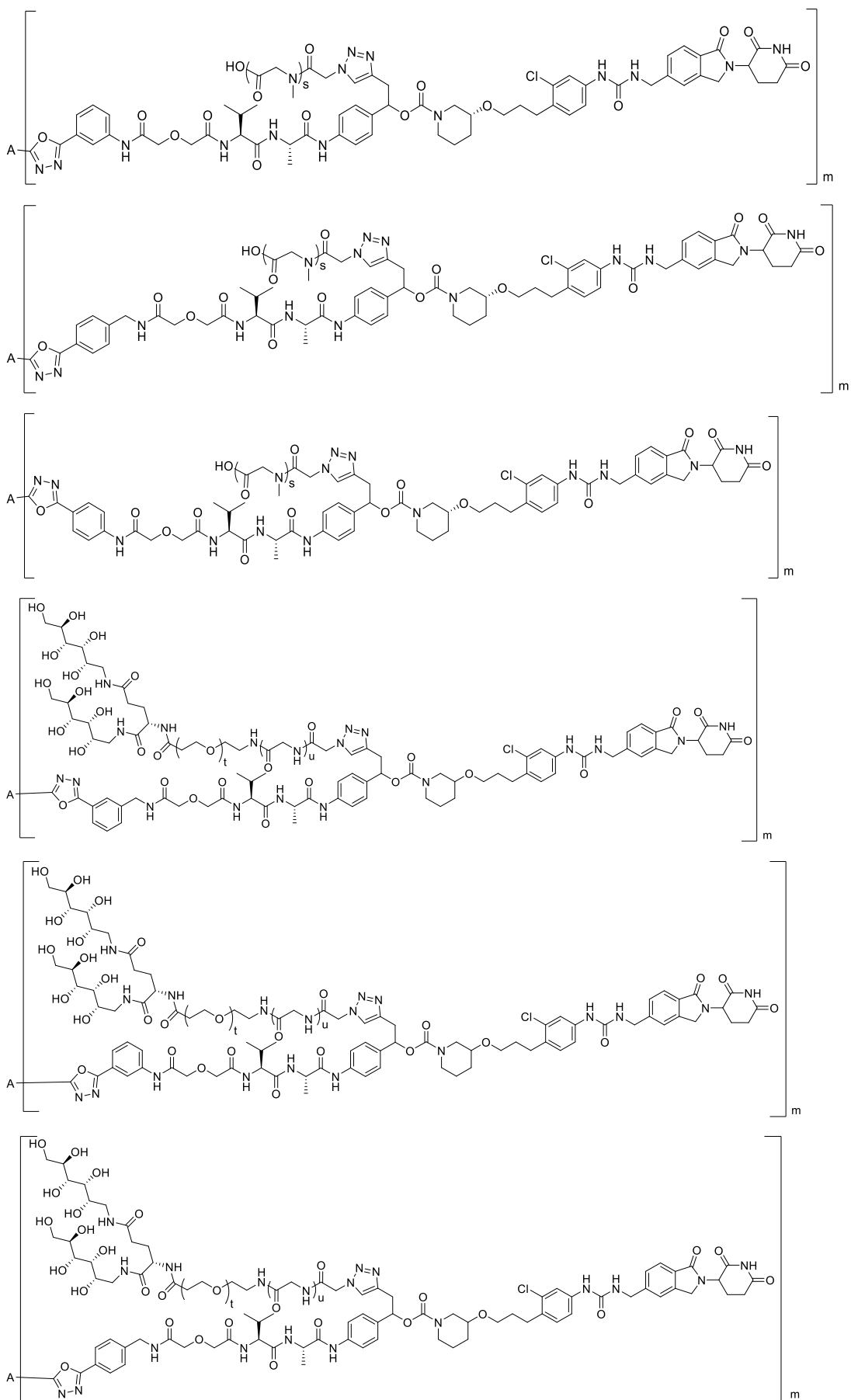


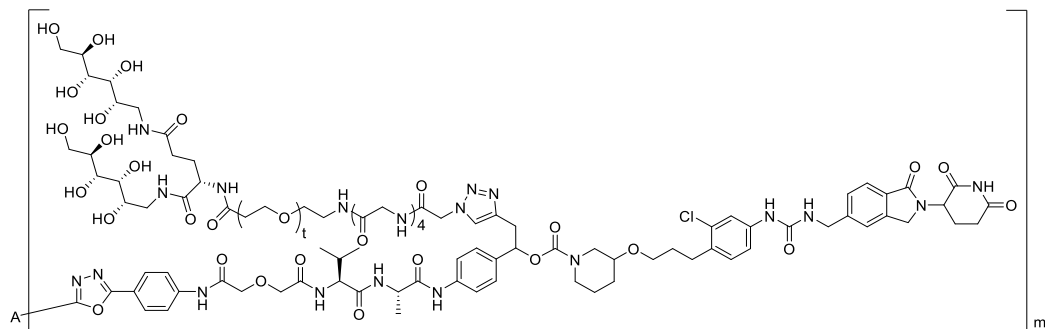
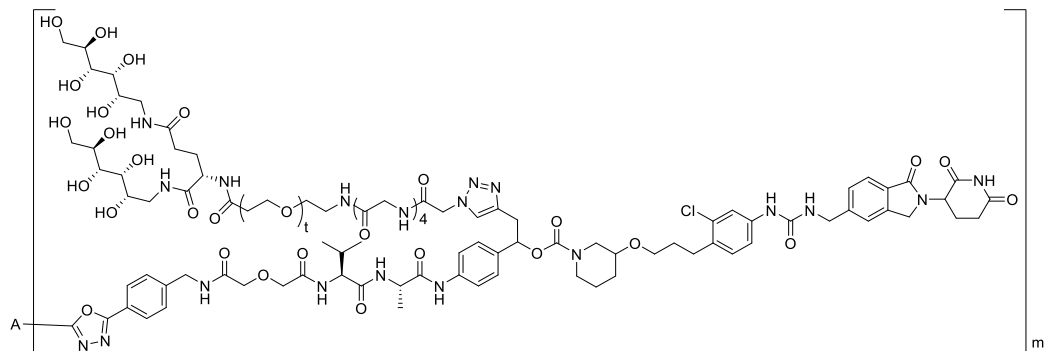
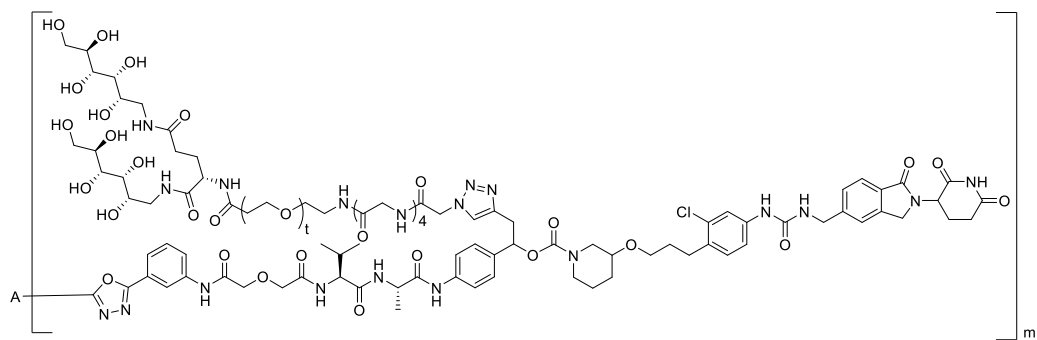
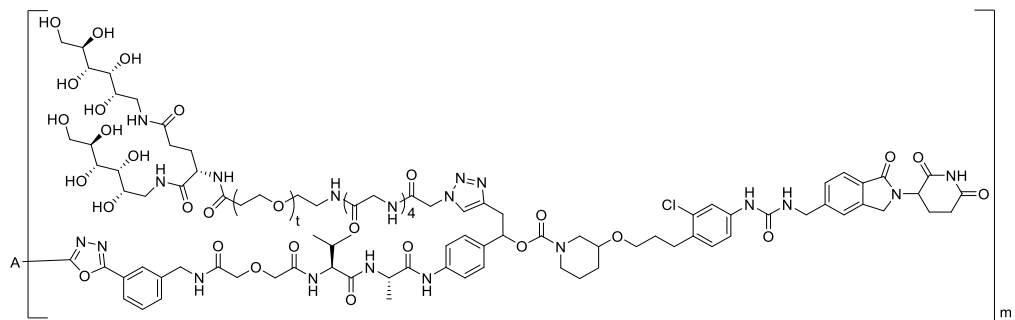
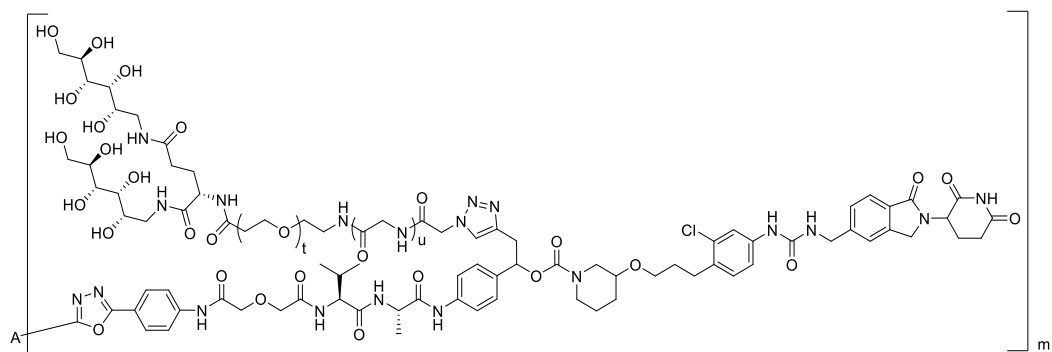


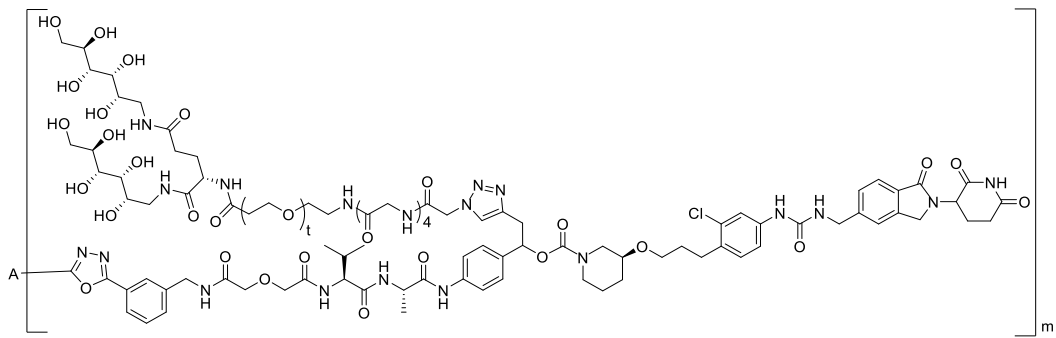
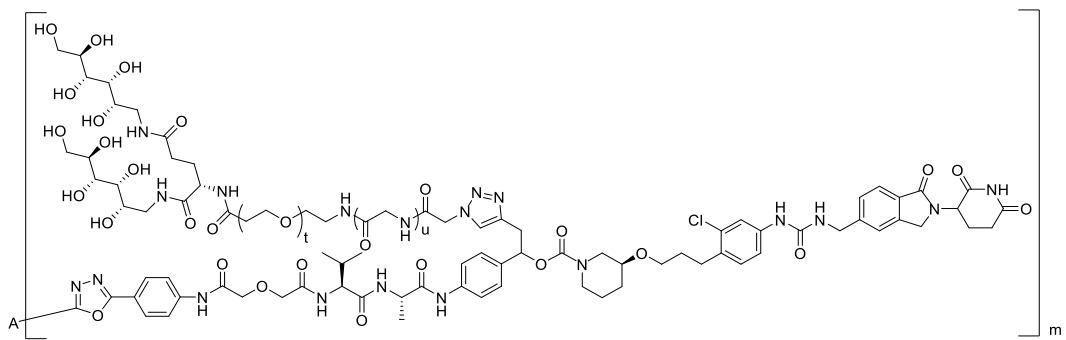
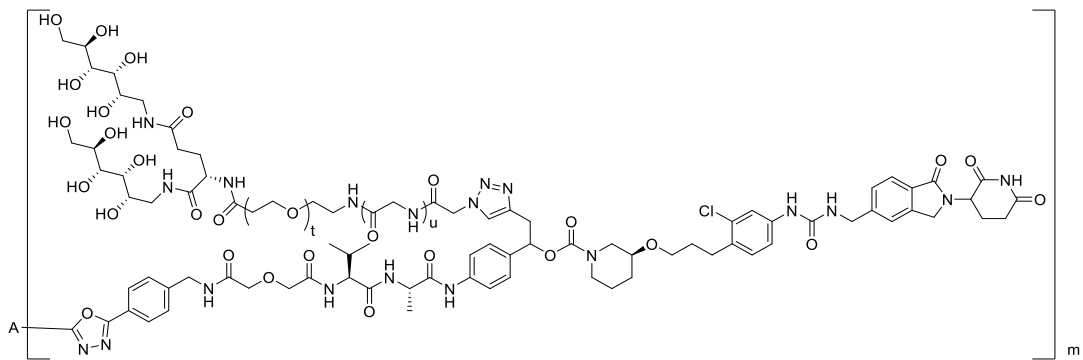
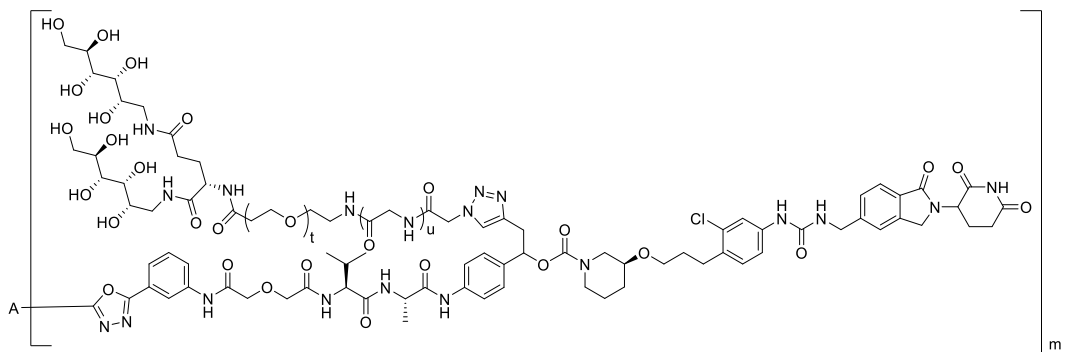
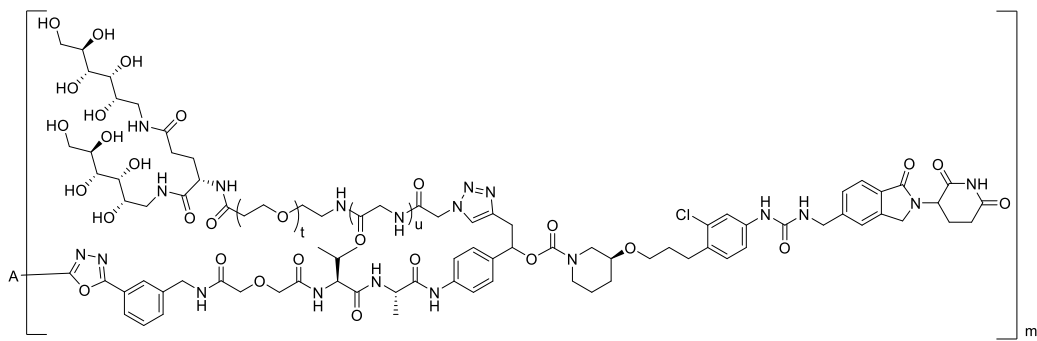


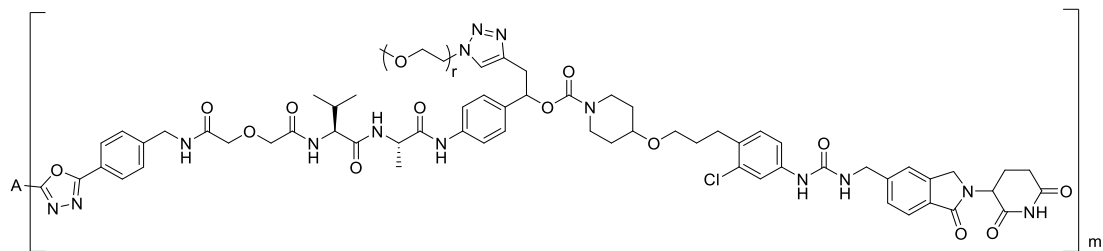
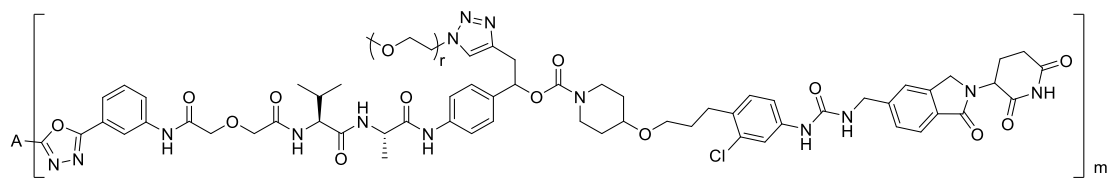
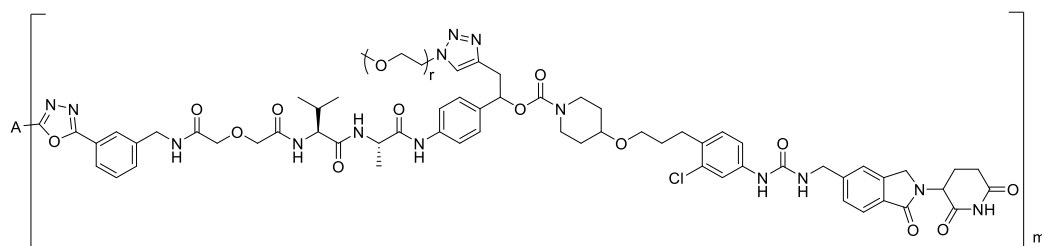
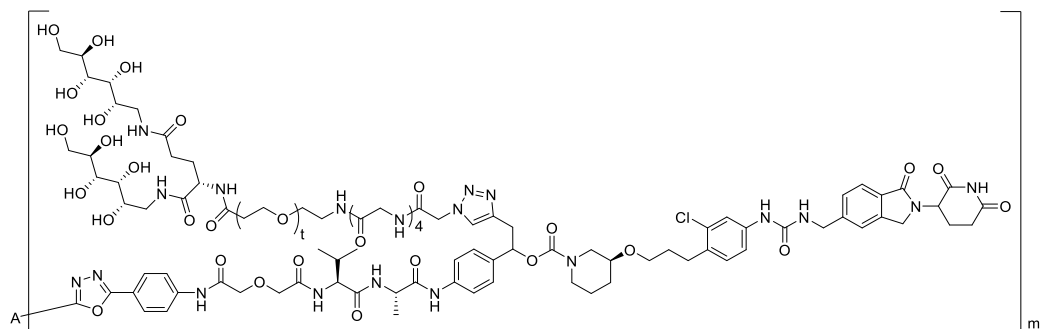
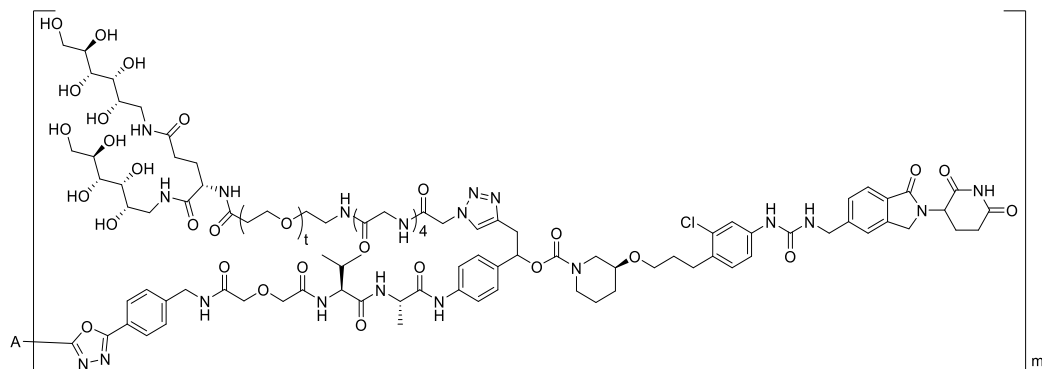
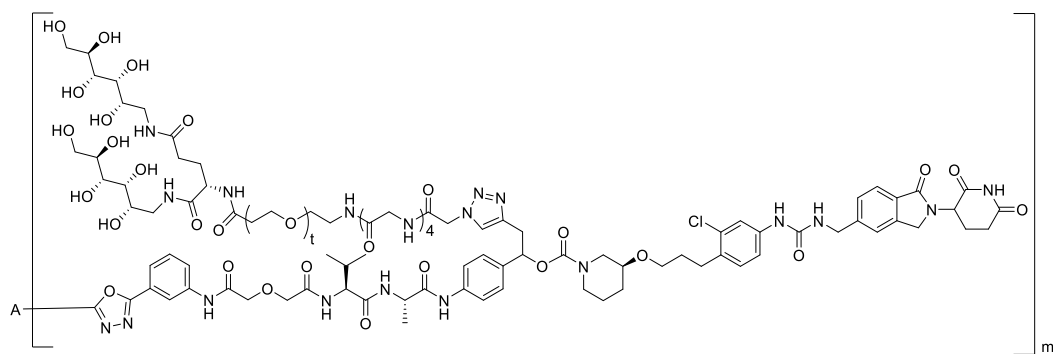


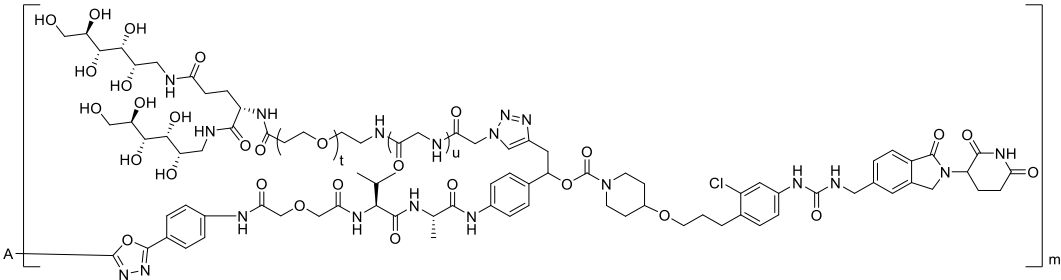
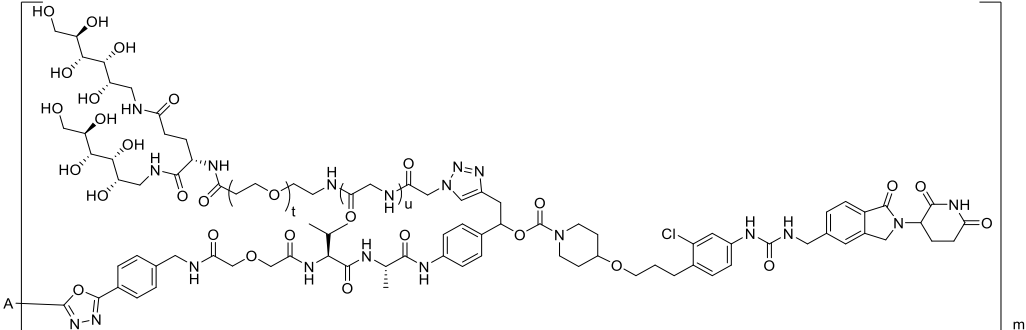
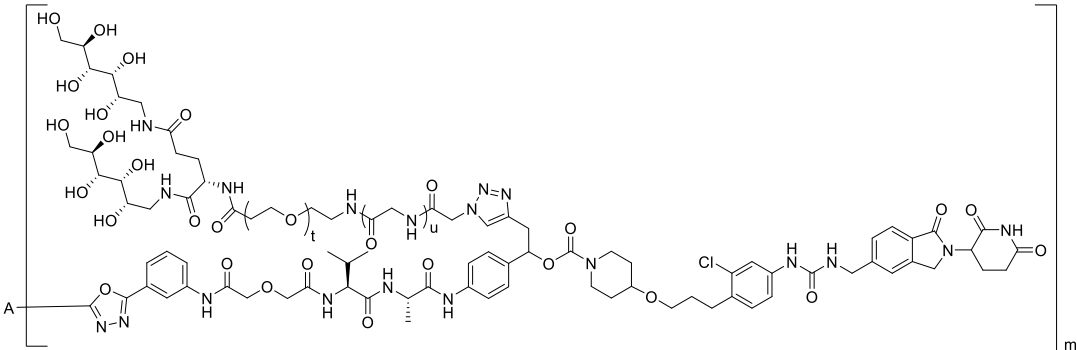
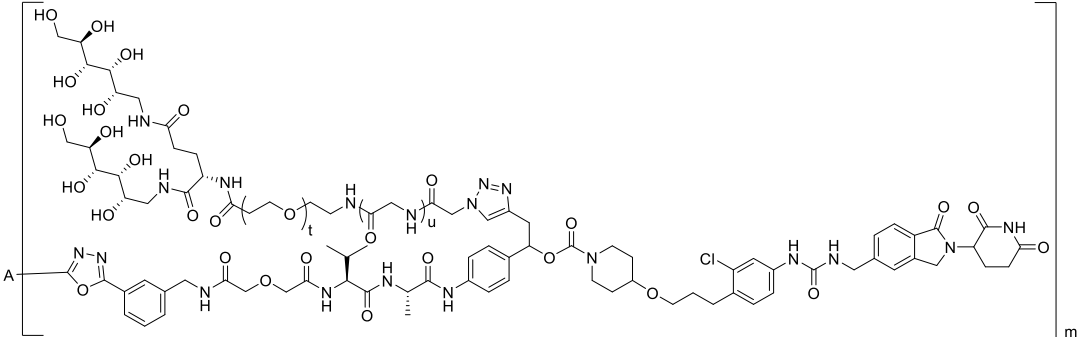
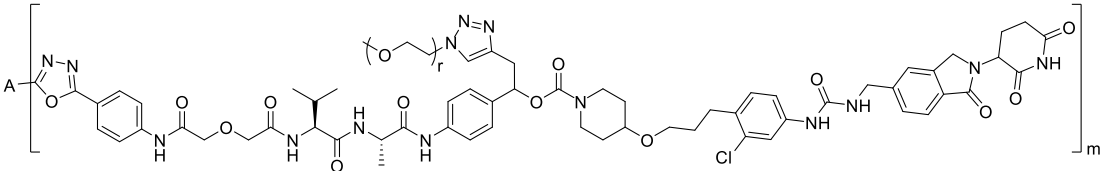


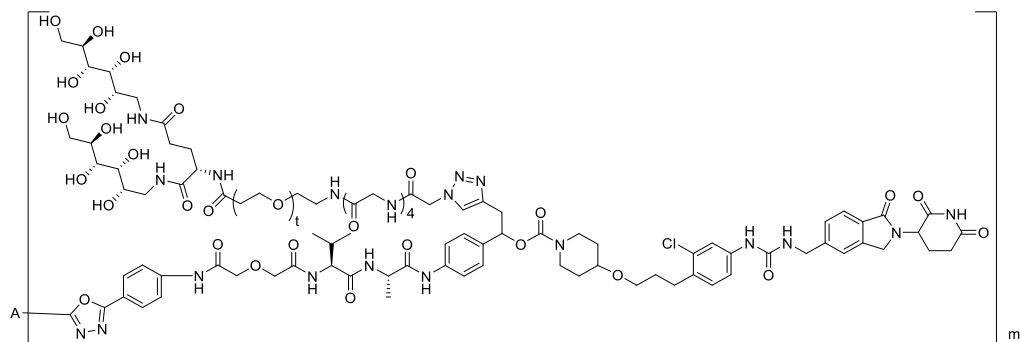
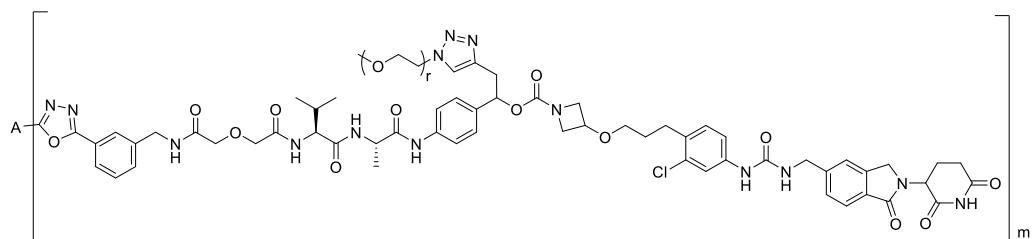
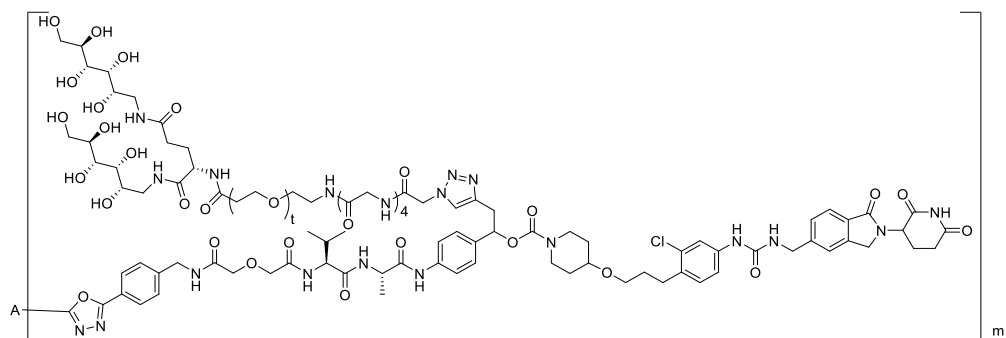
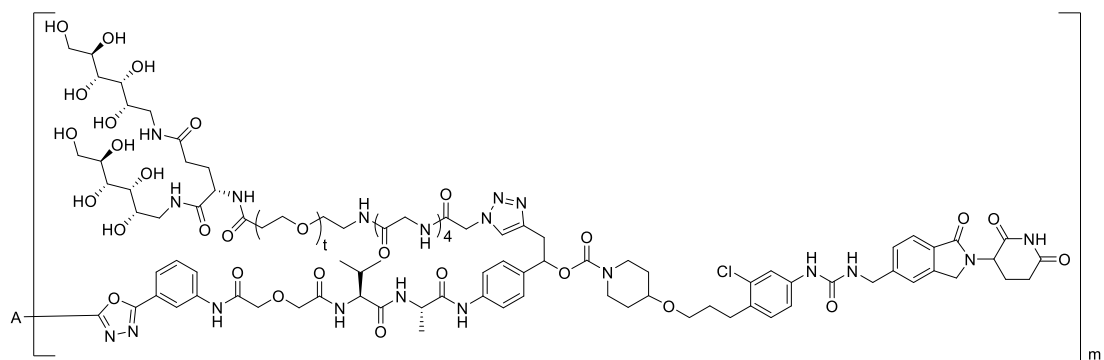
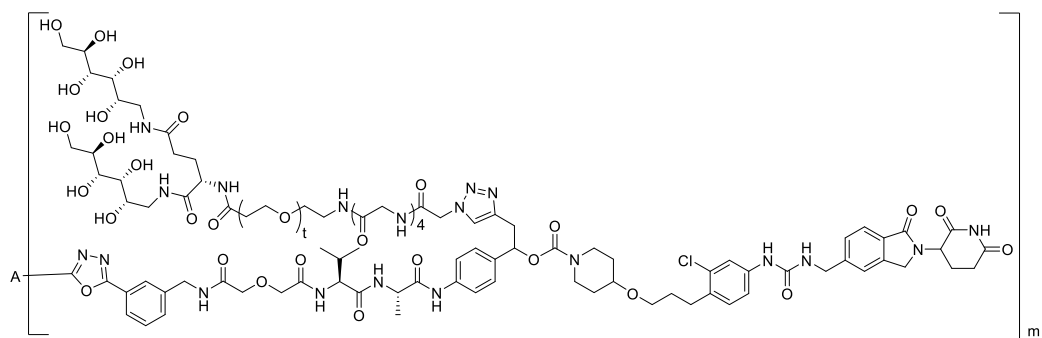


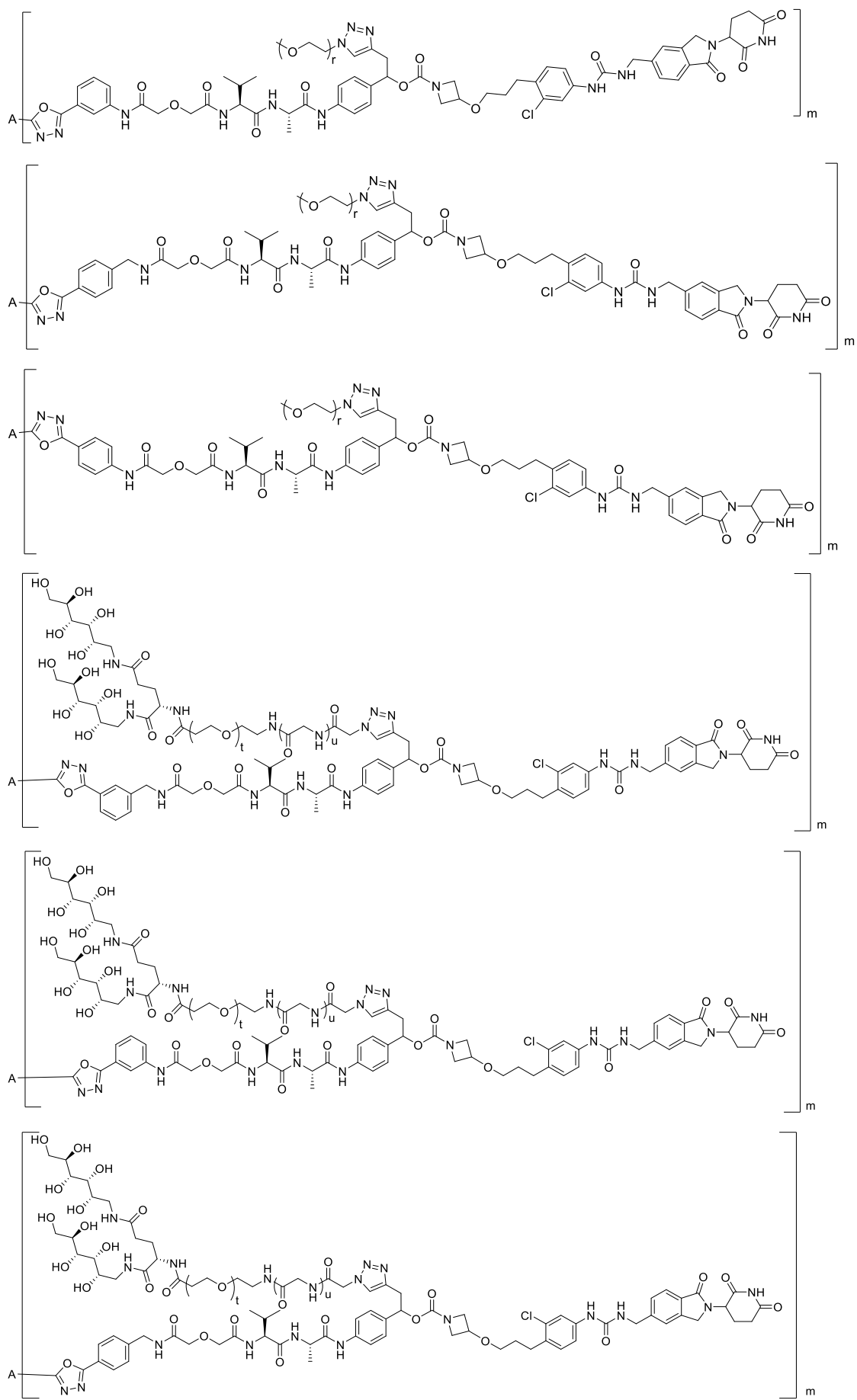


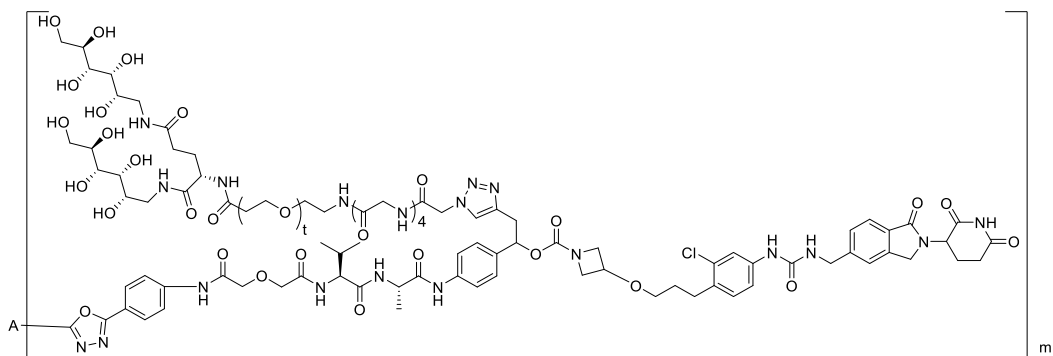
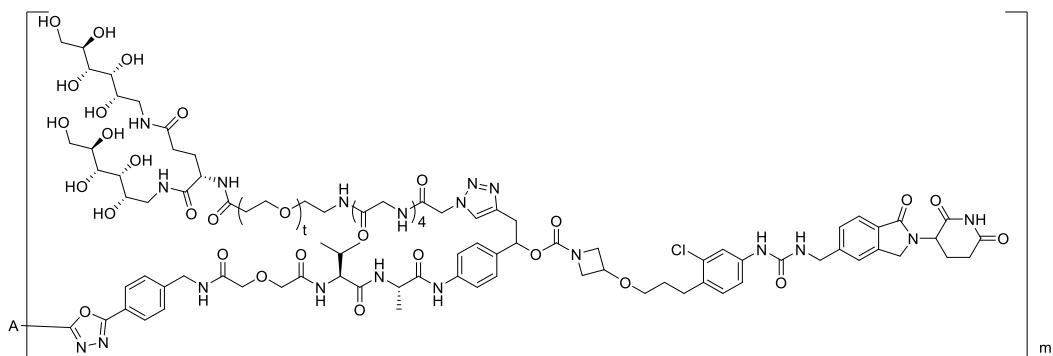
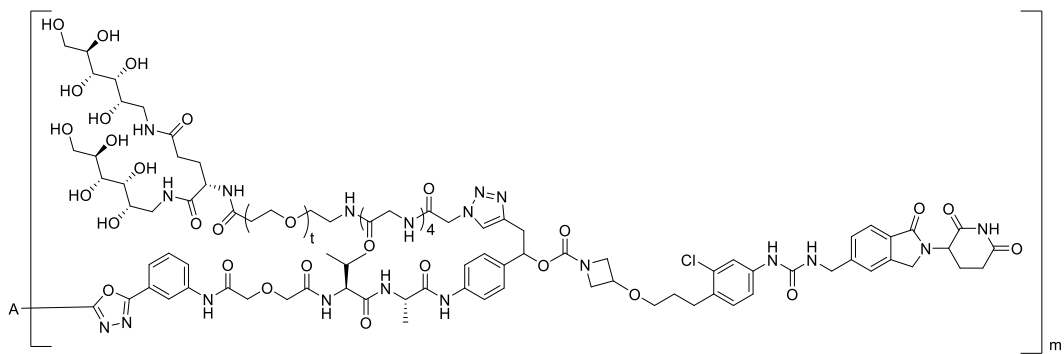
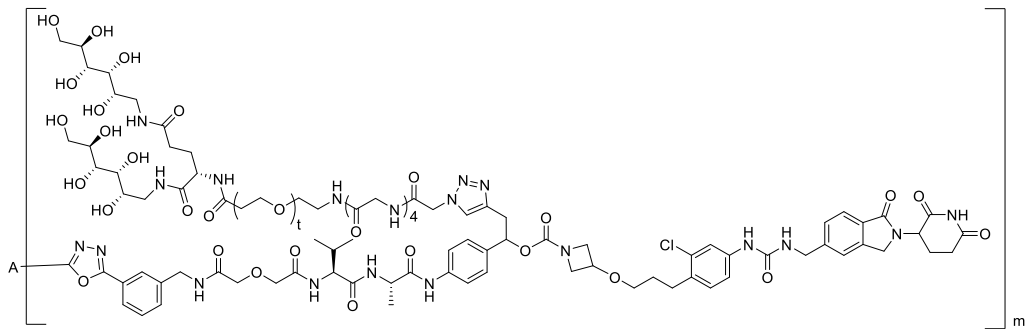
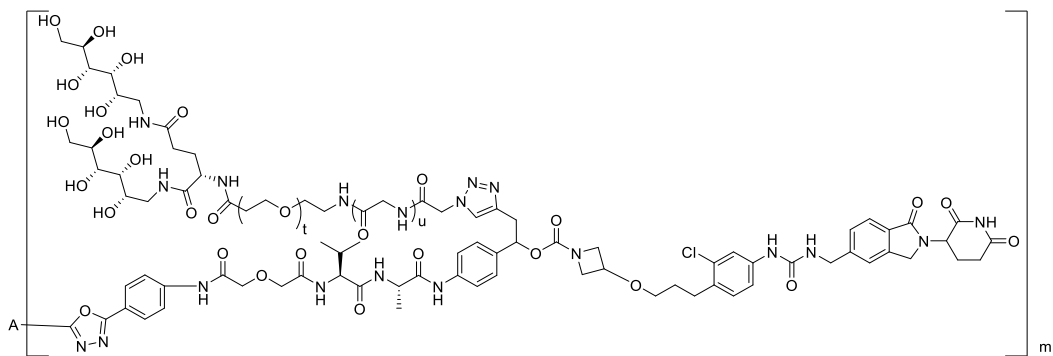


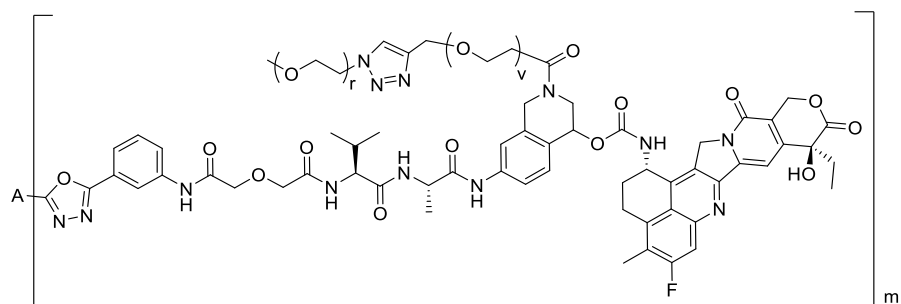
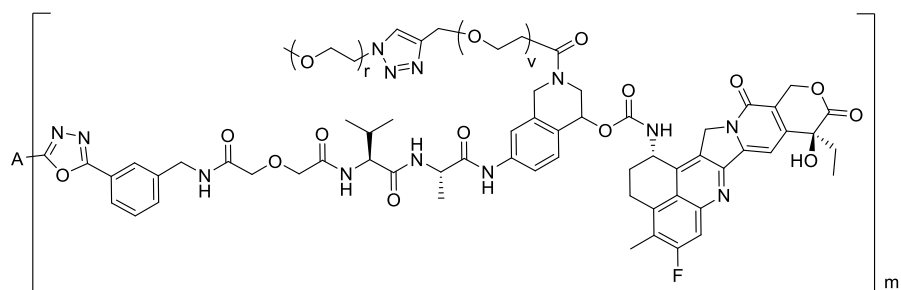
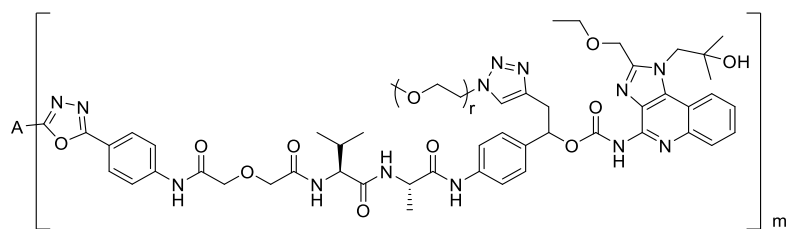
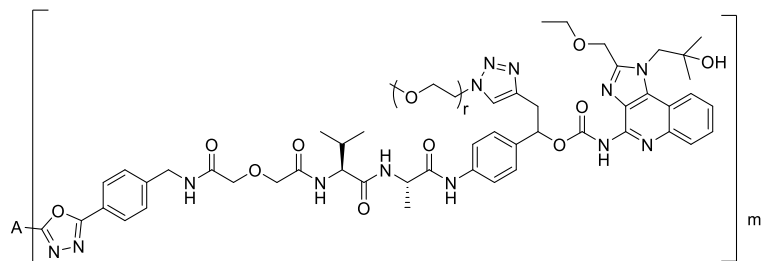
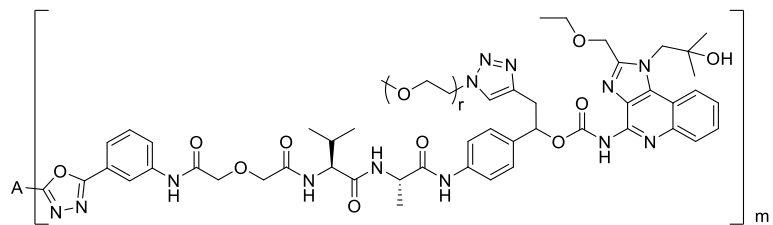
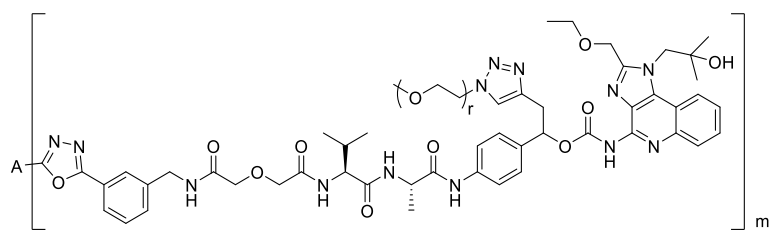


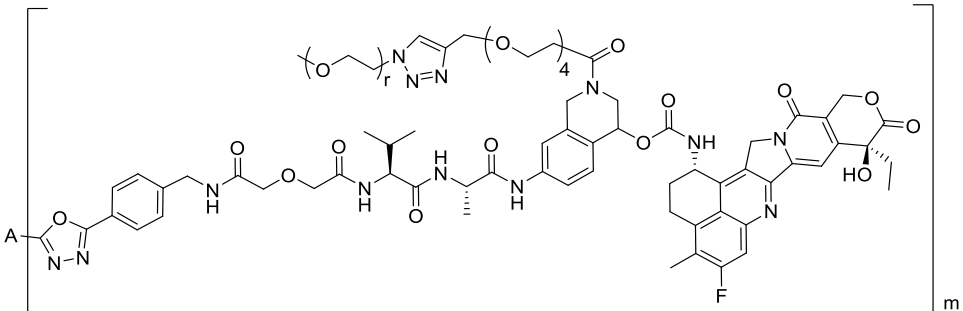
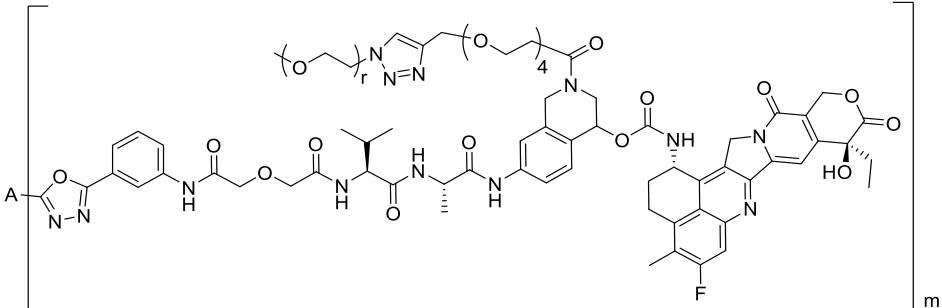
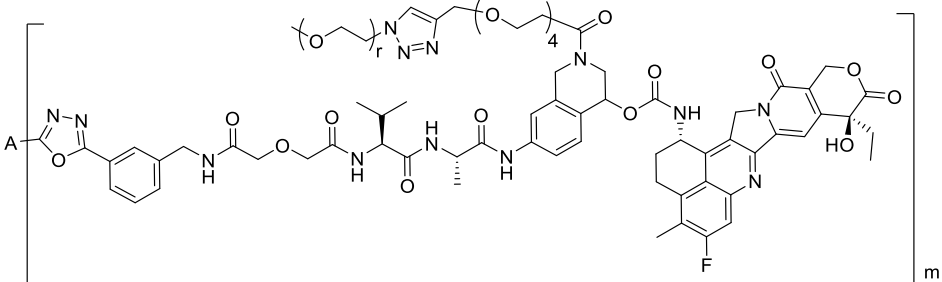
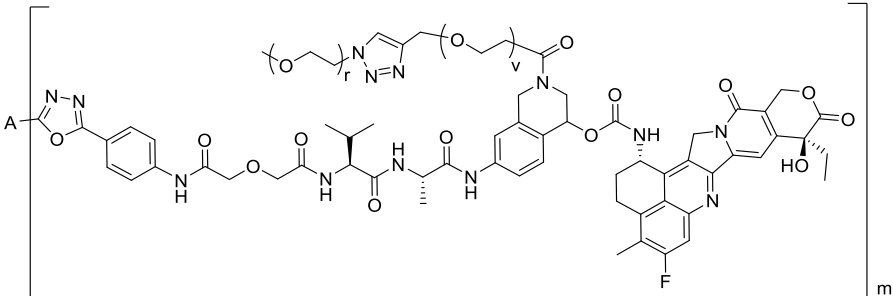
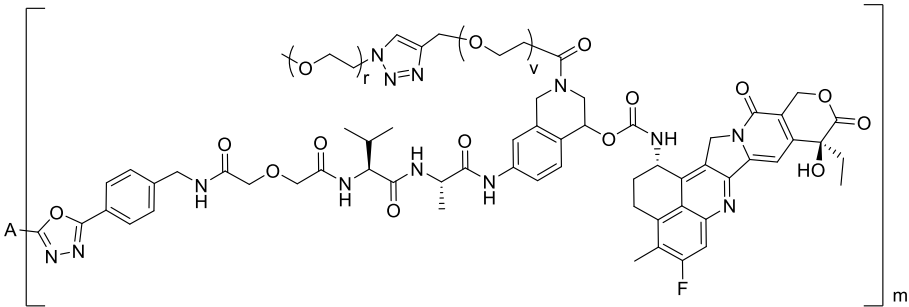


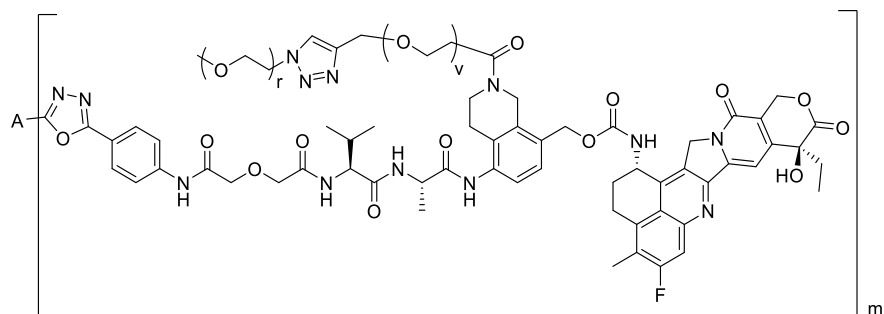
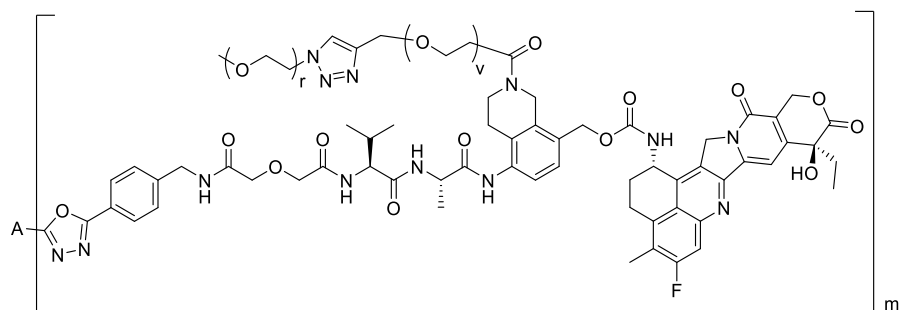
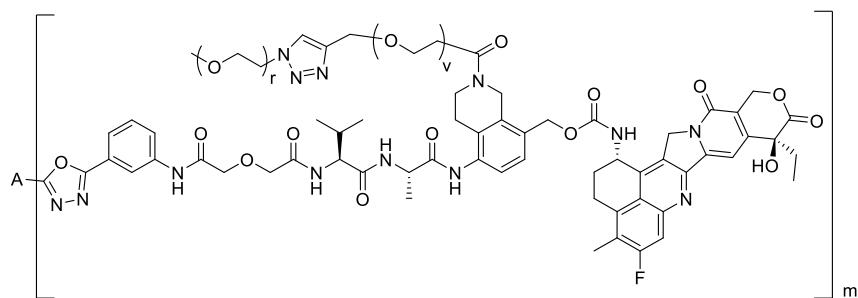
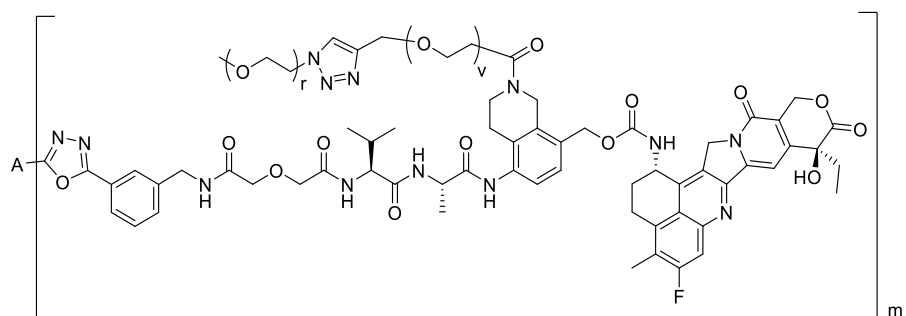
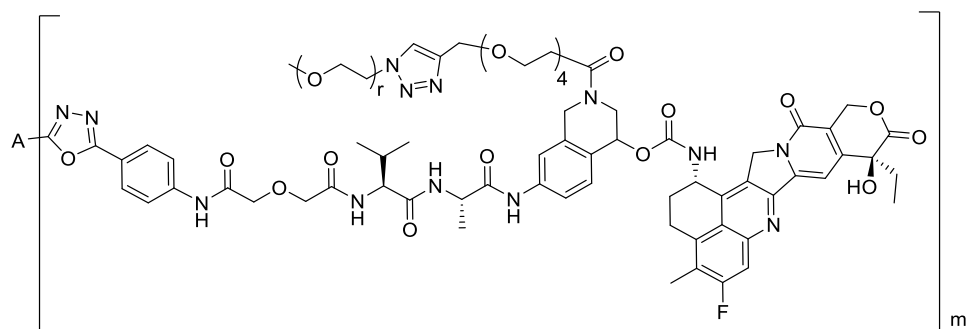


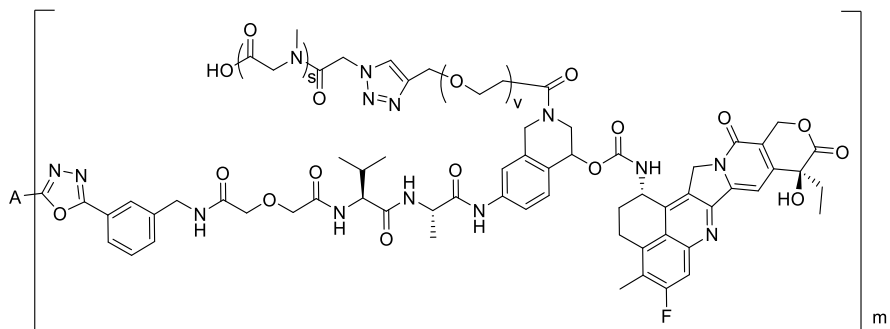
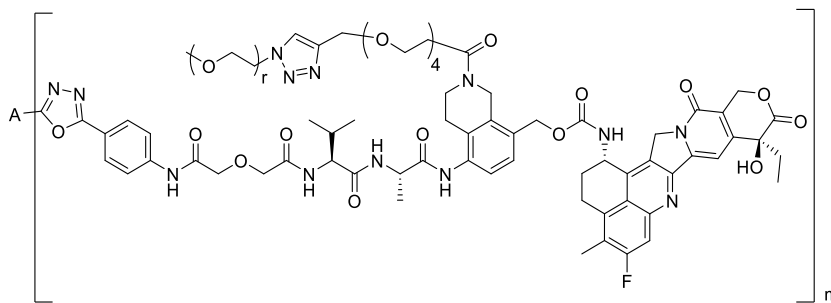
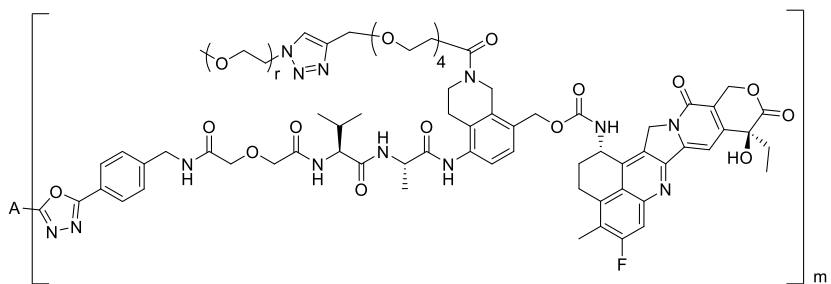
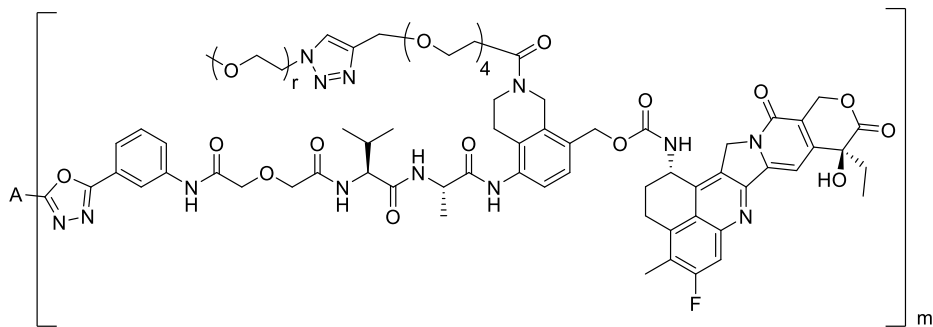
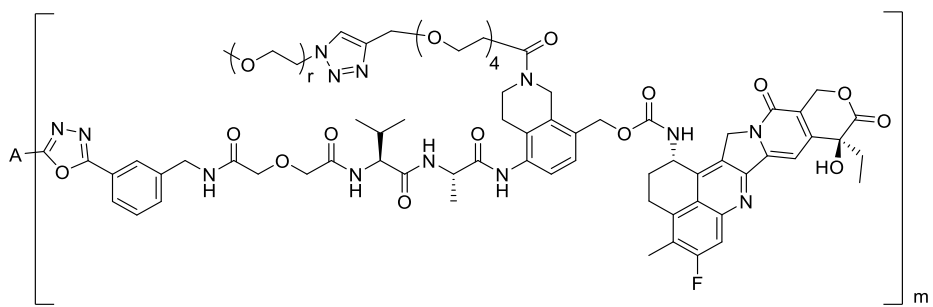


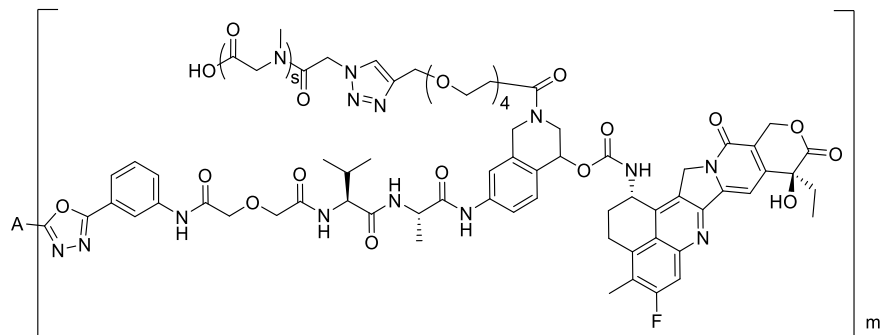
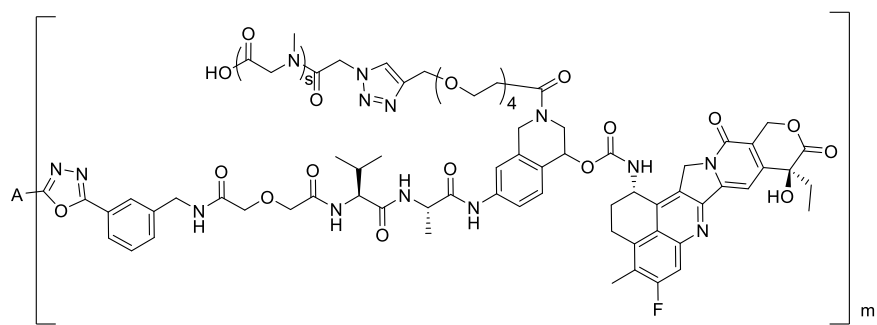
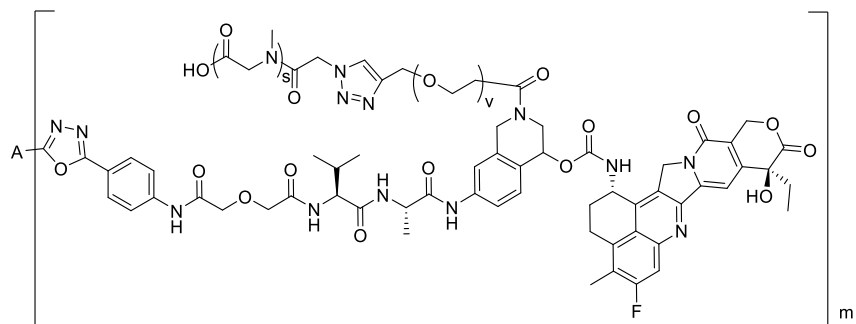
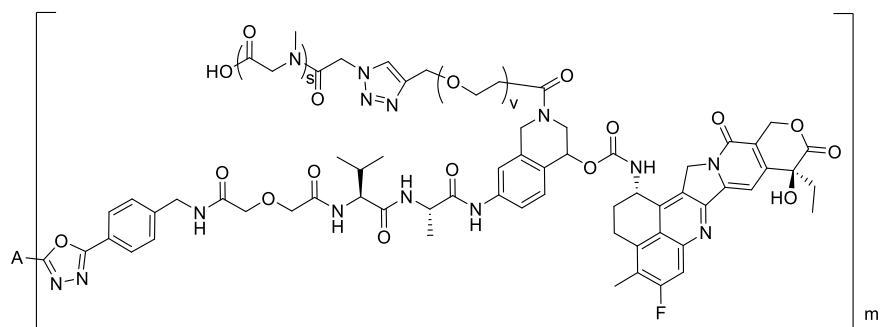
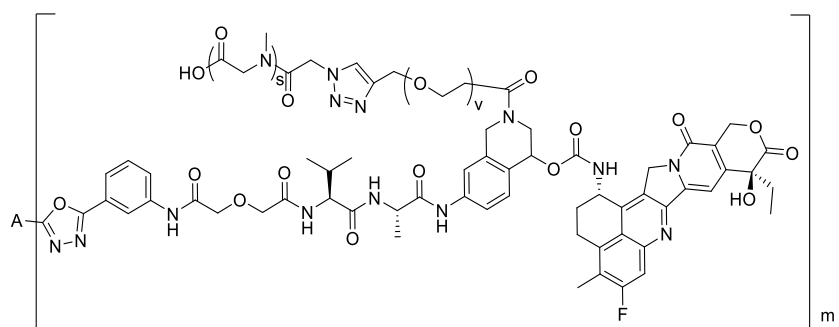


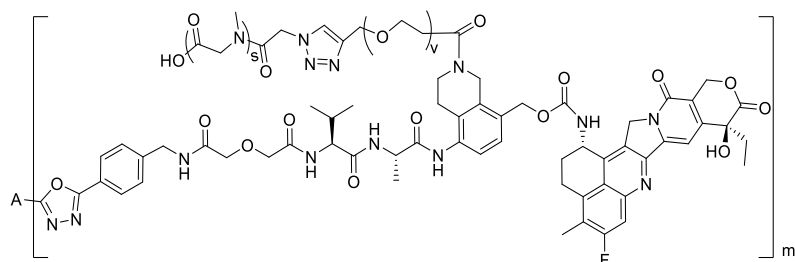
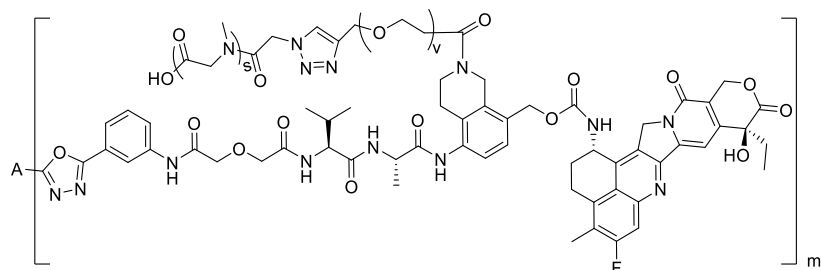
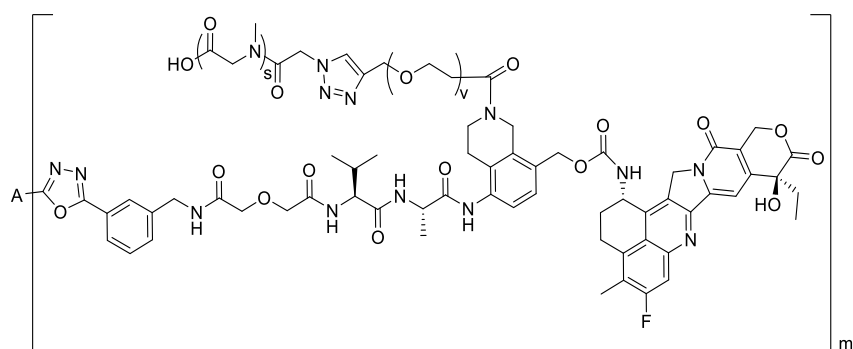
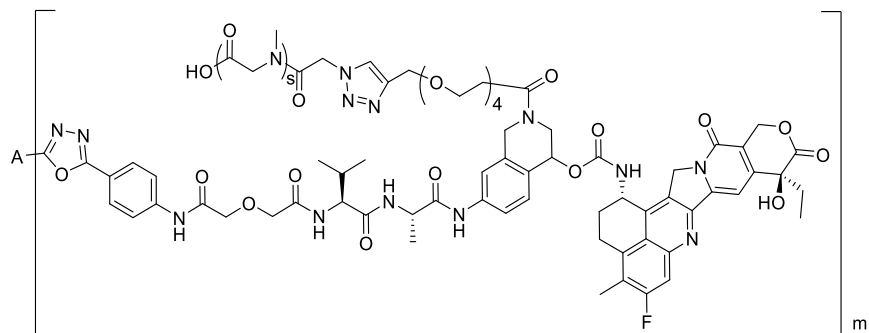
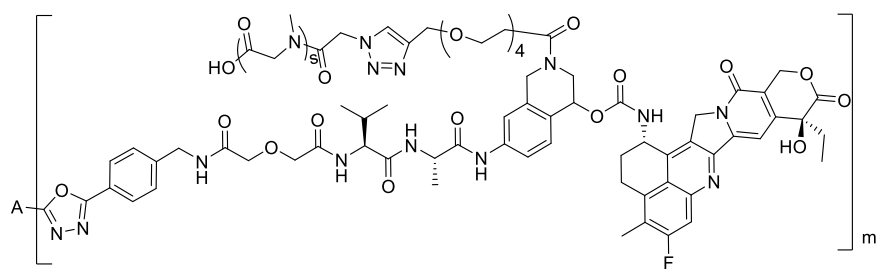


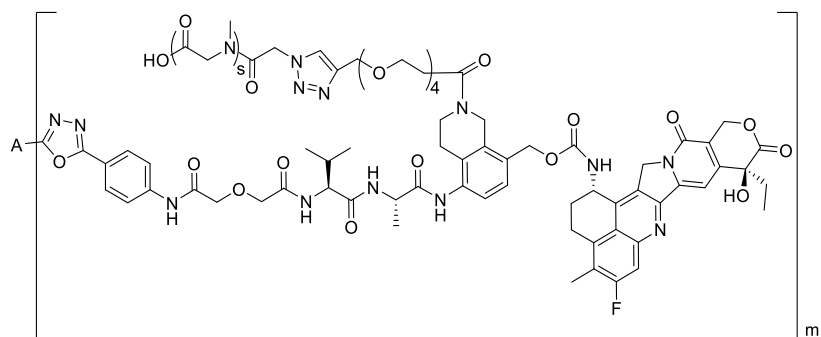
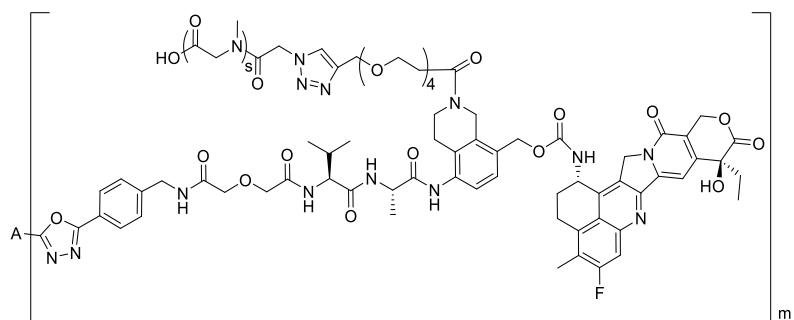
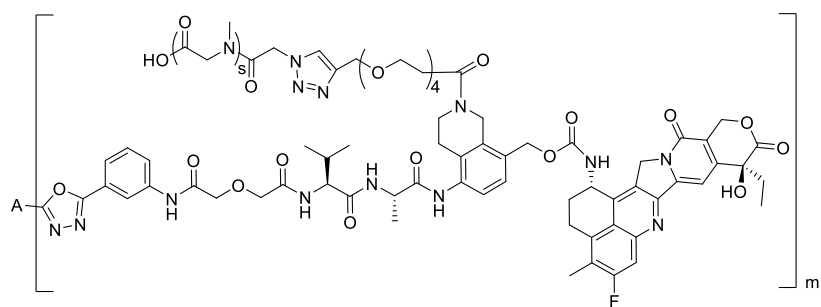
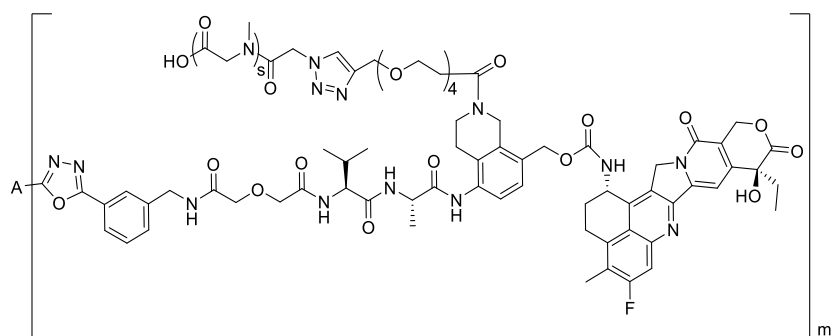
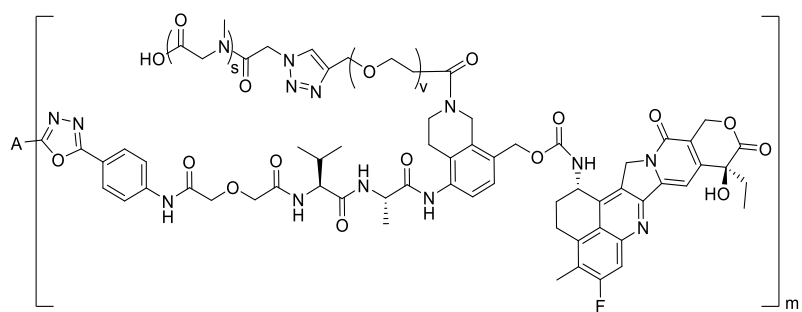


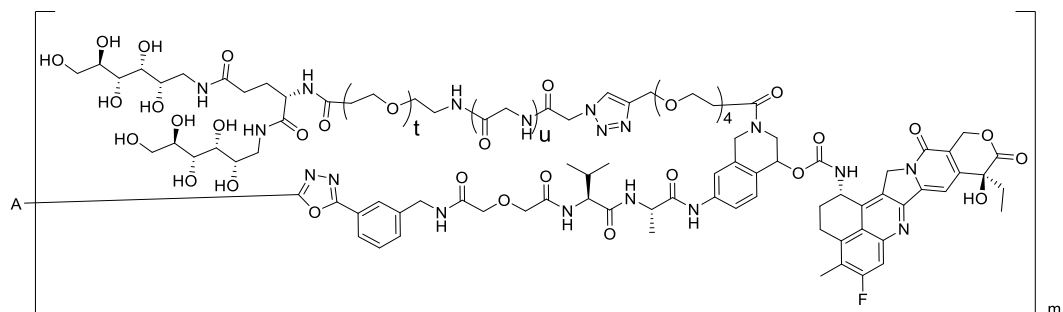
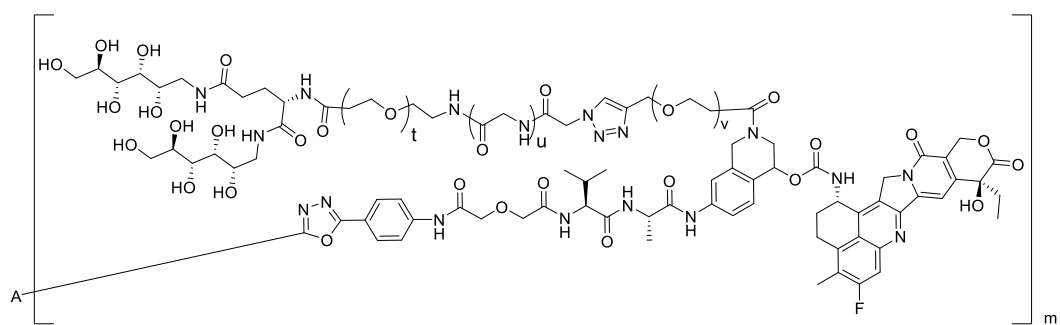
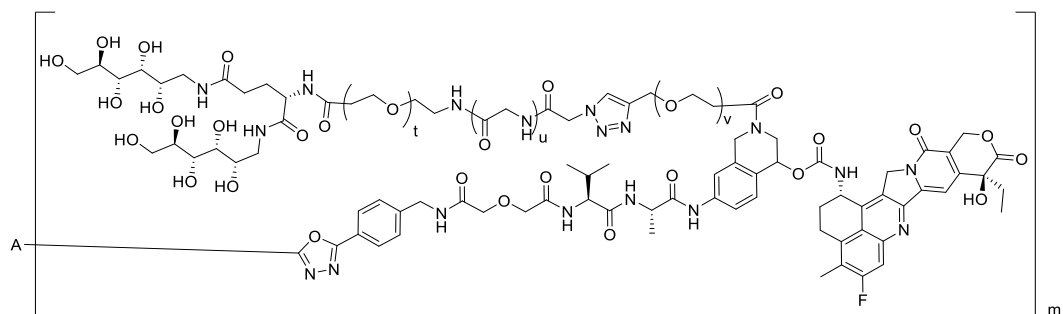
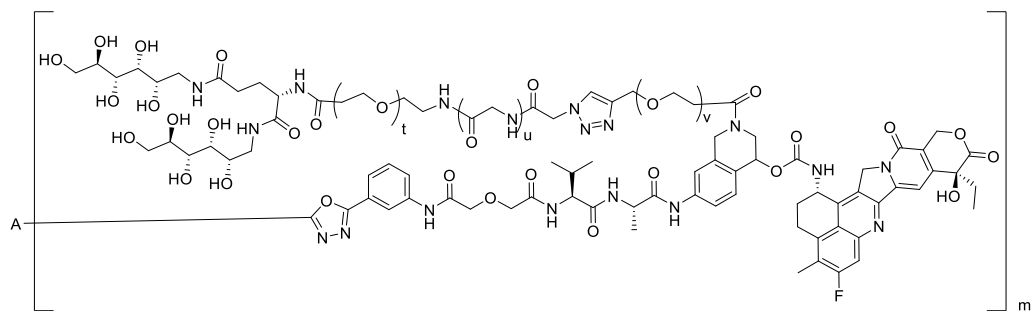
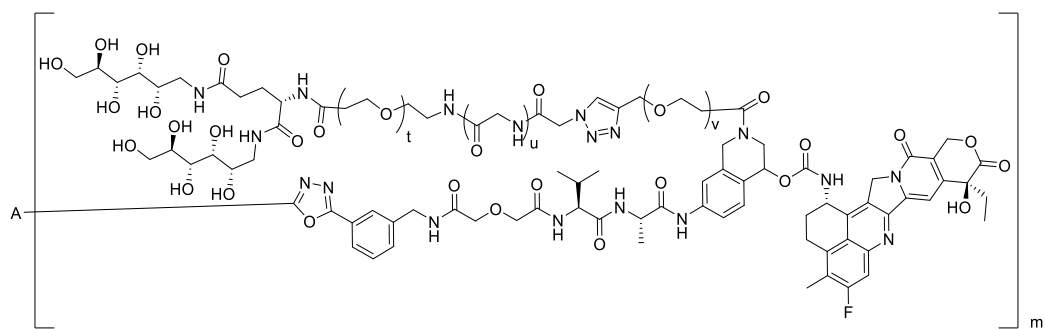


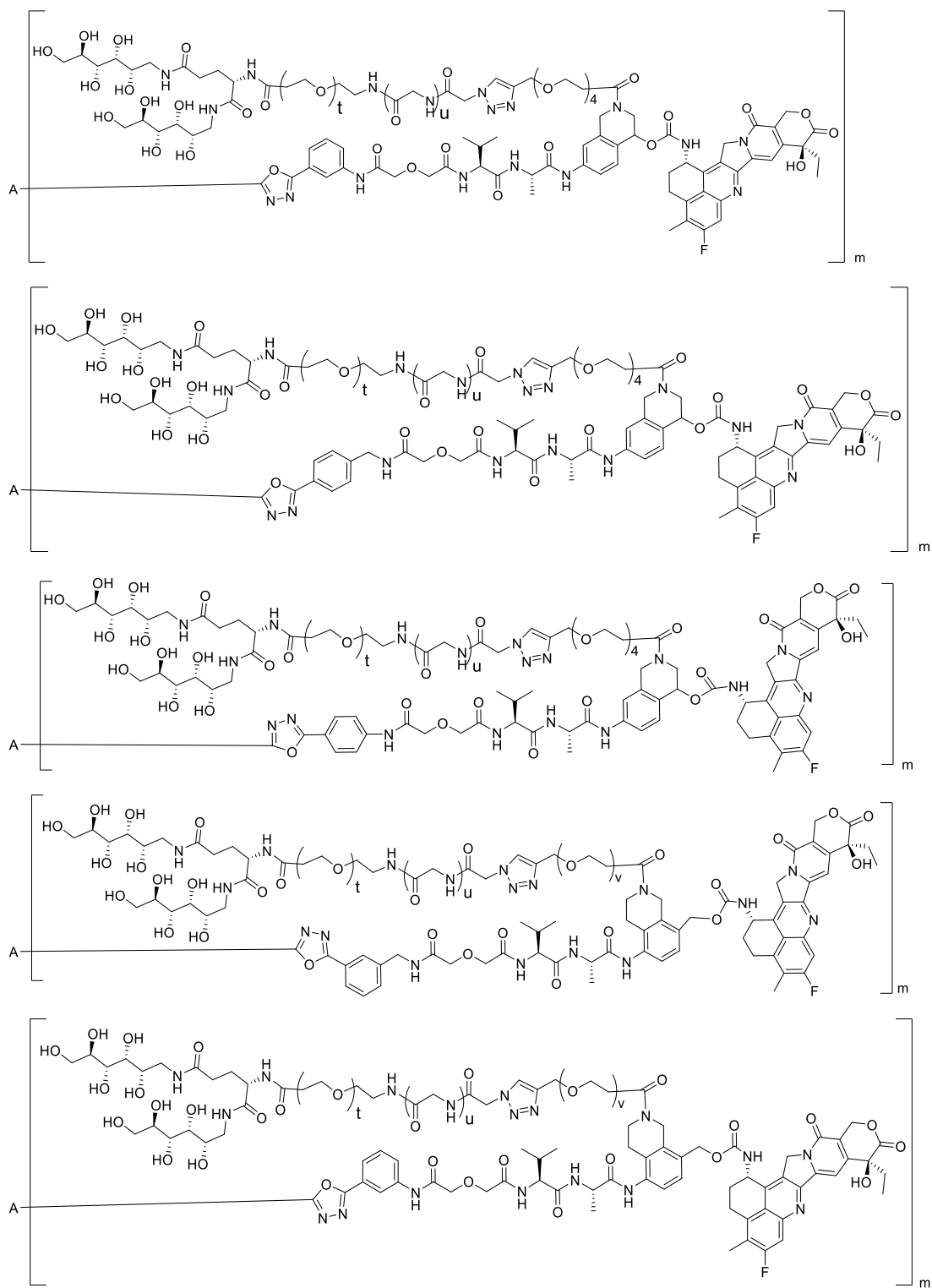


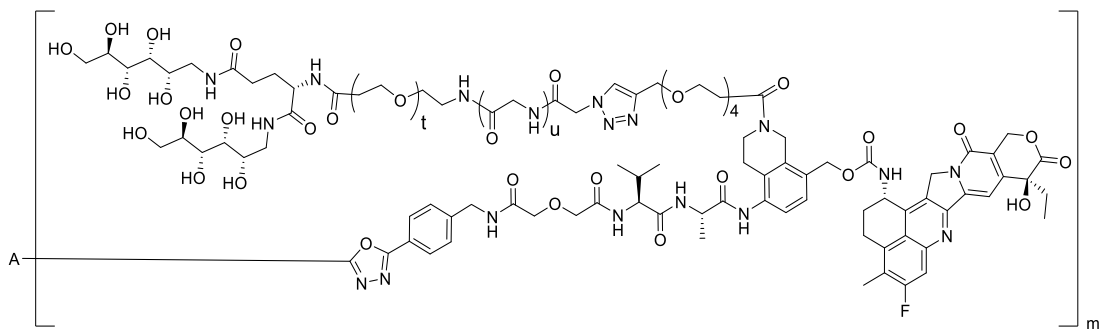
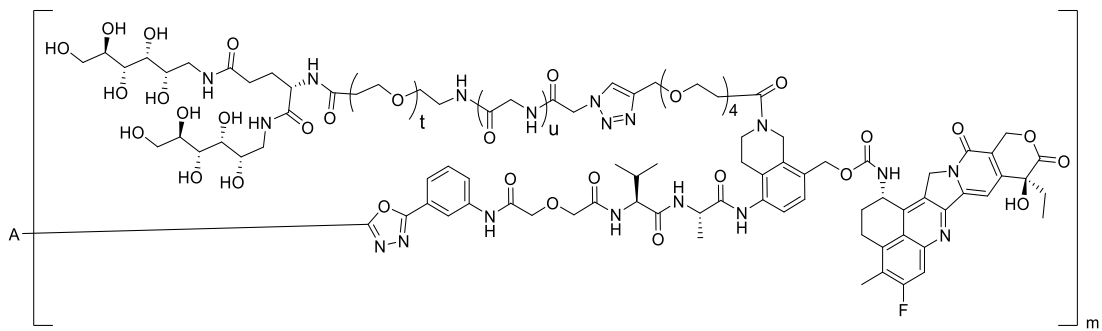
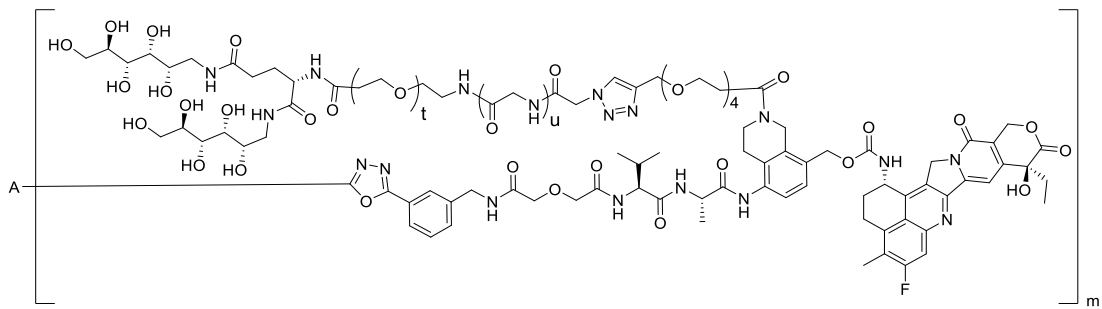
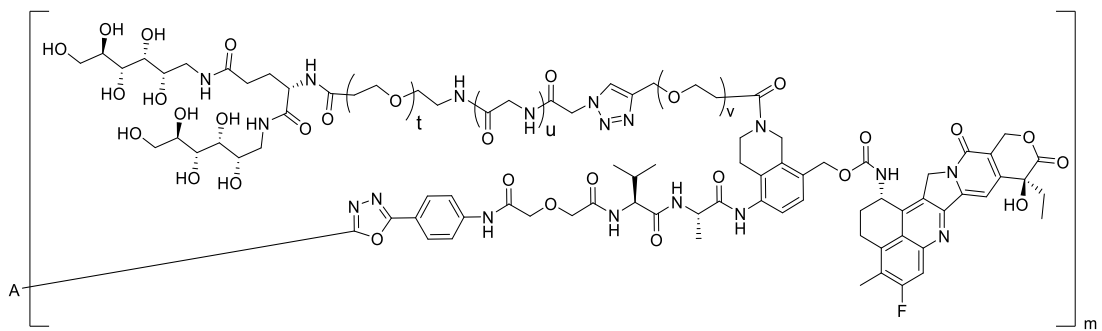
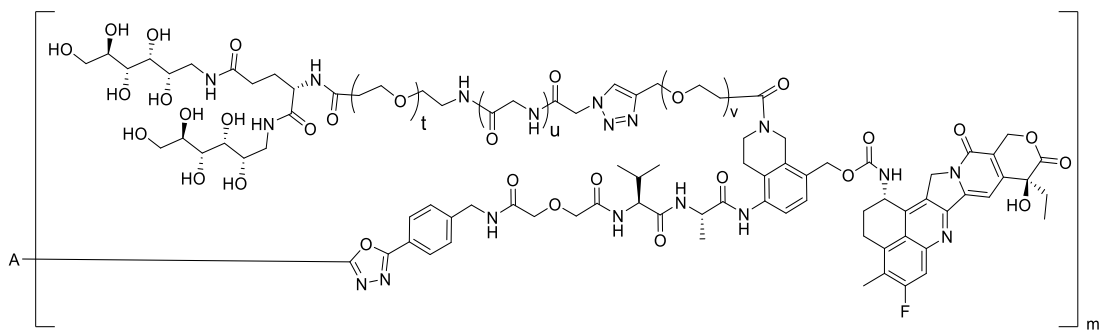


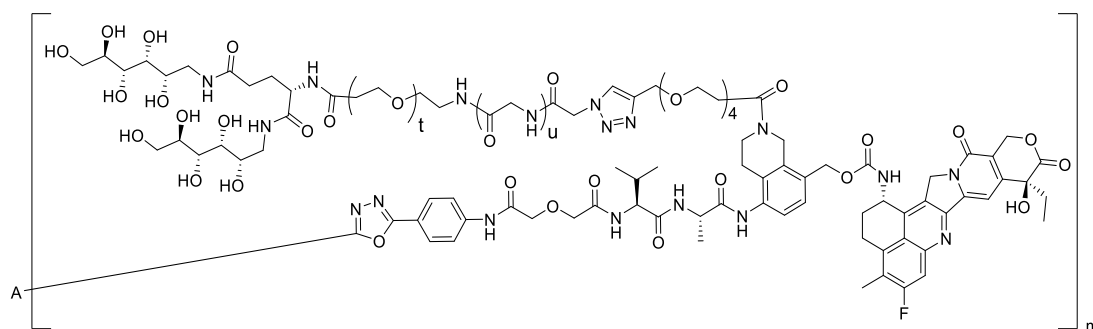








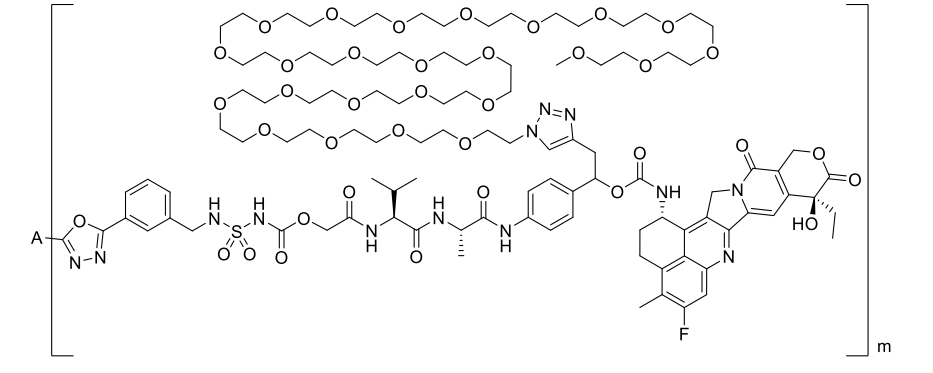
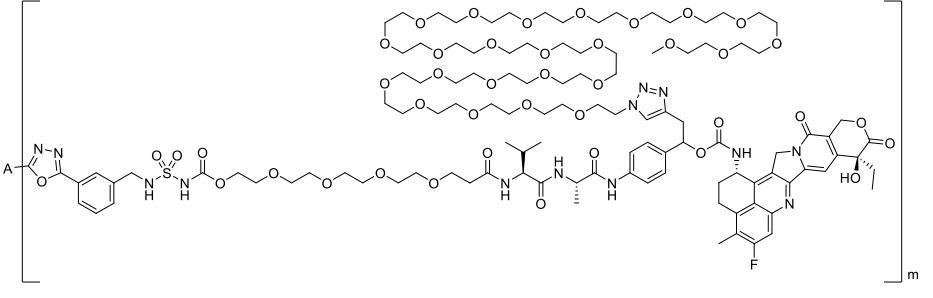
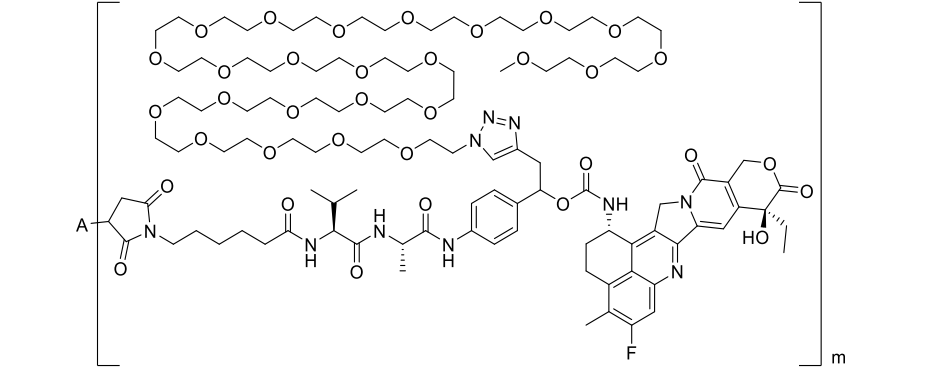
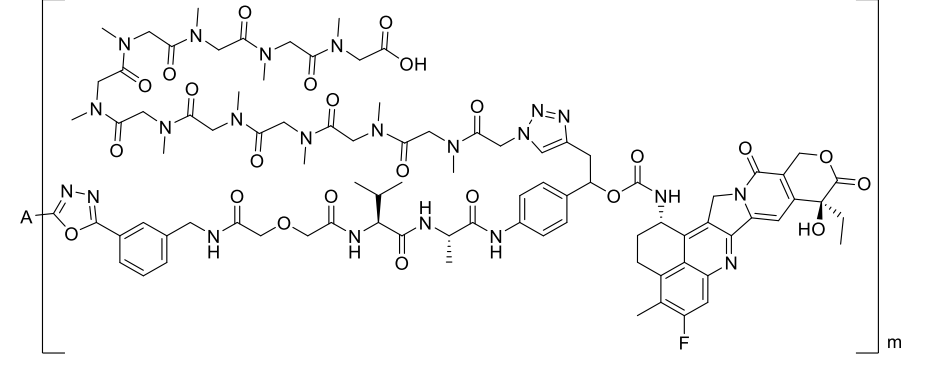




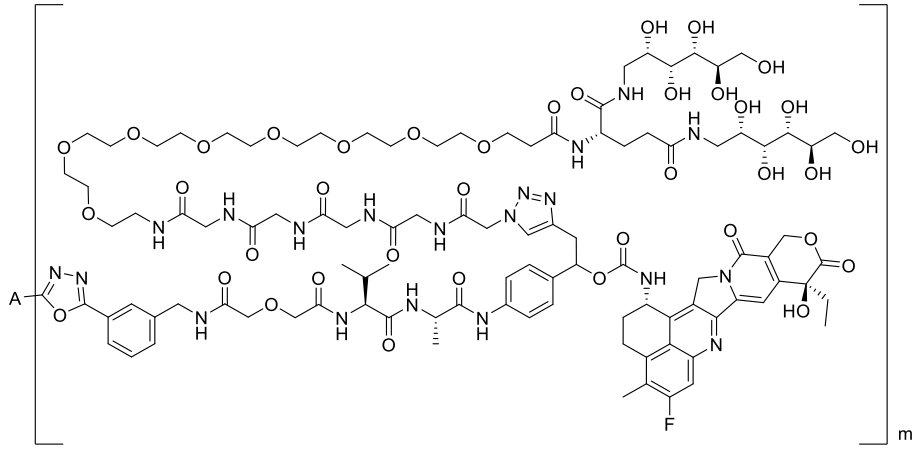
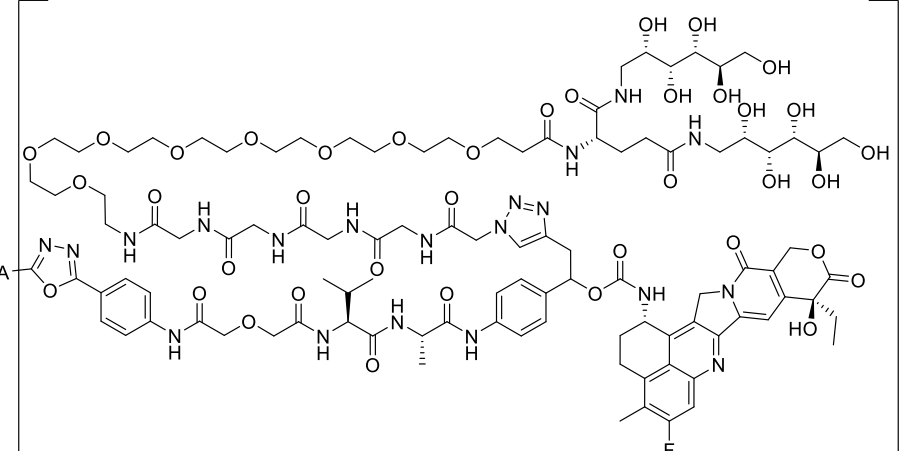
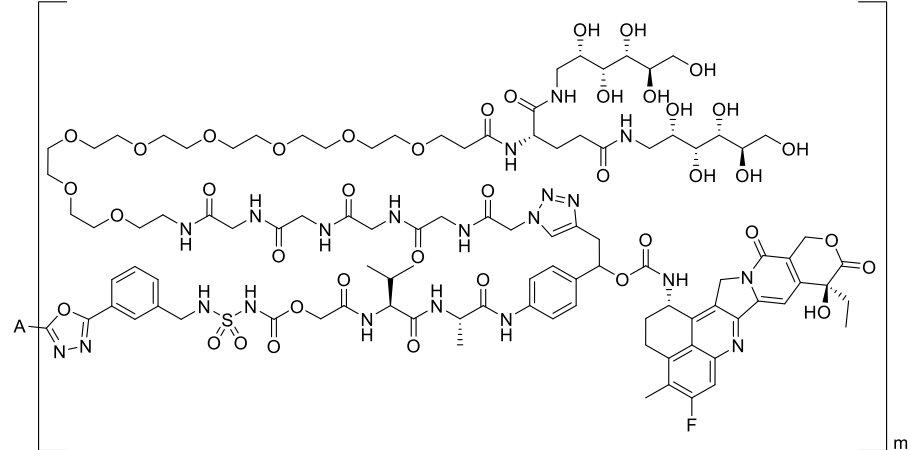
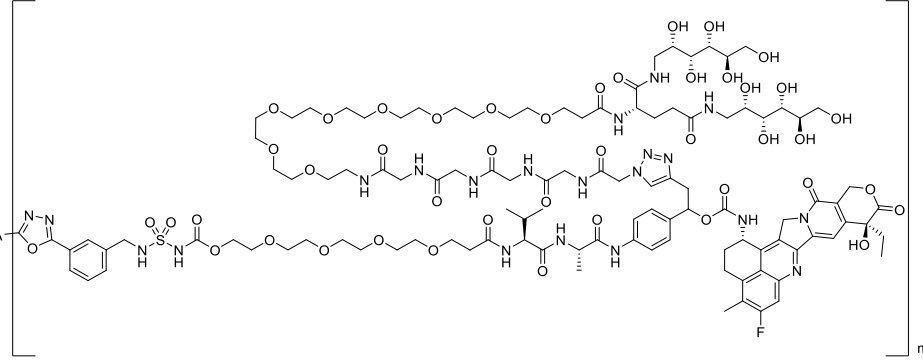
wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), and v and w are each independently an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

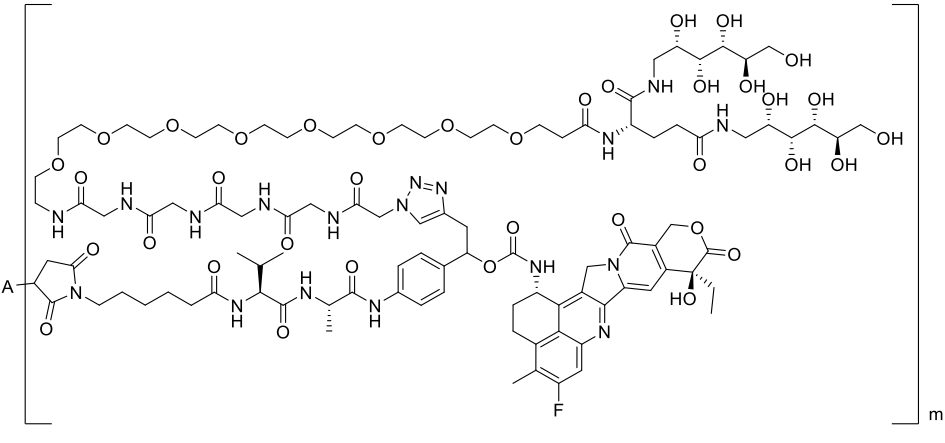
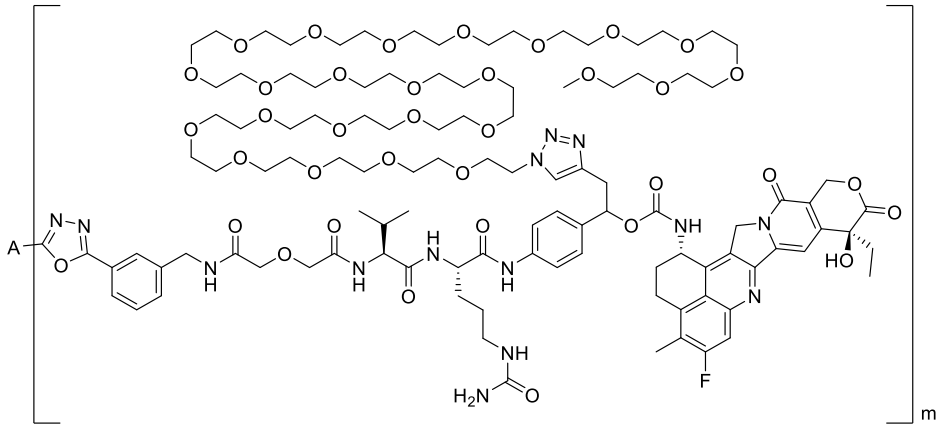
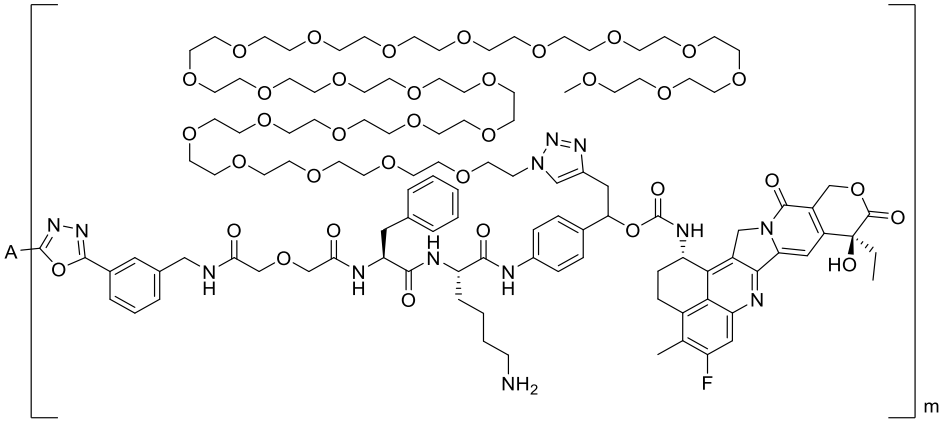
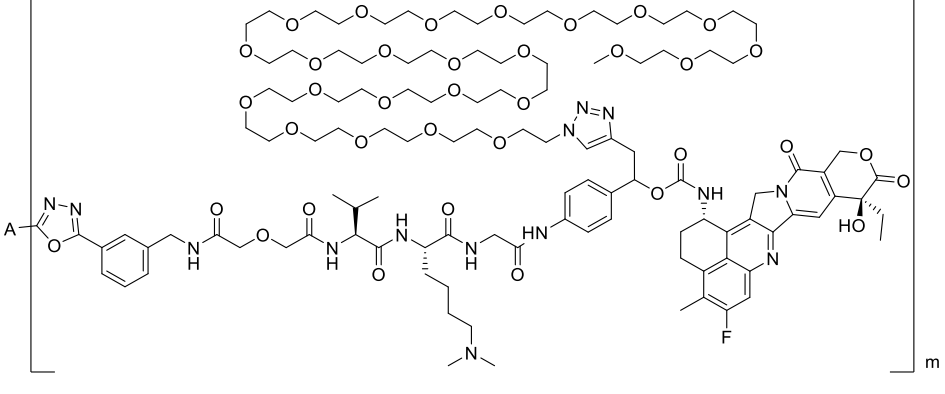
In some embodiments, the antibody-drug conjugate represented by formula I, the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

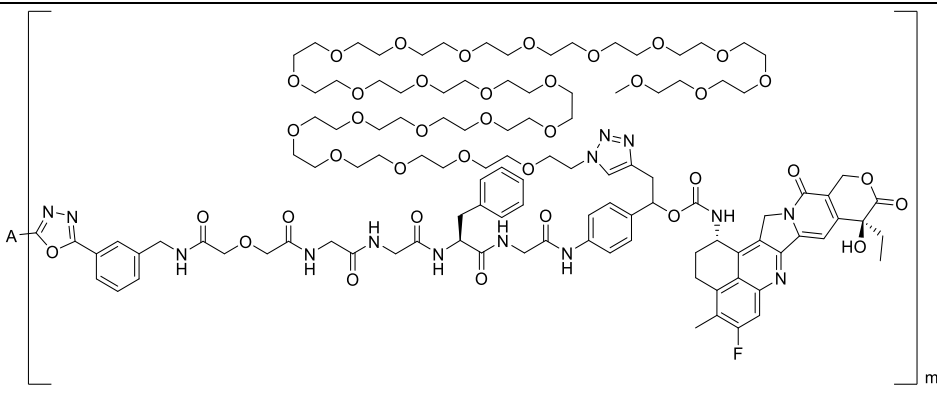
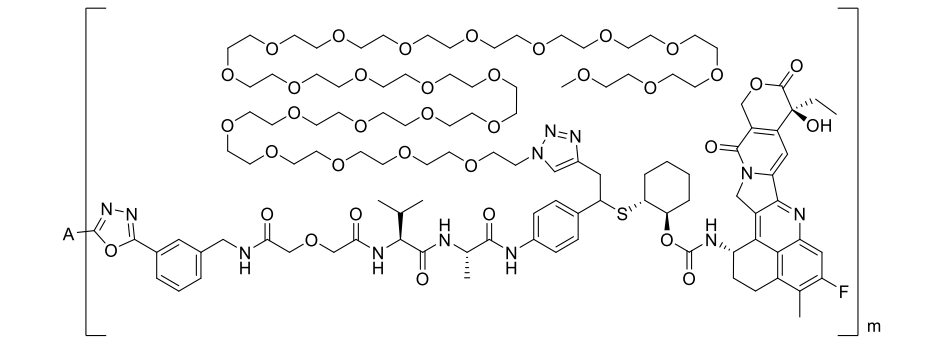
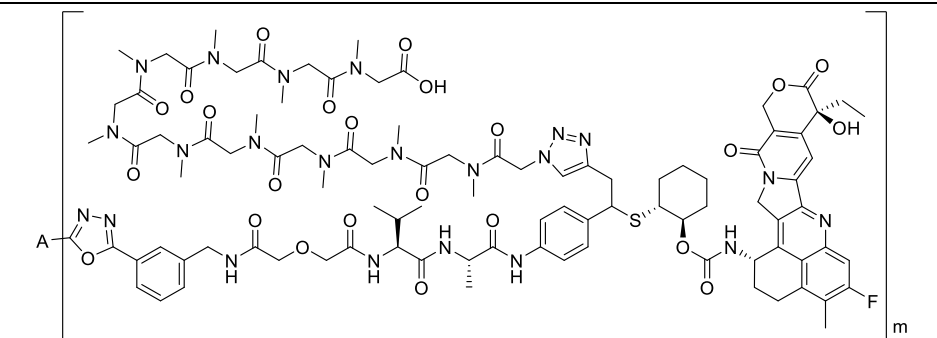
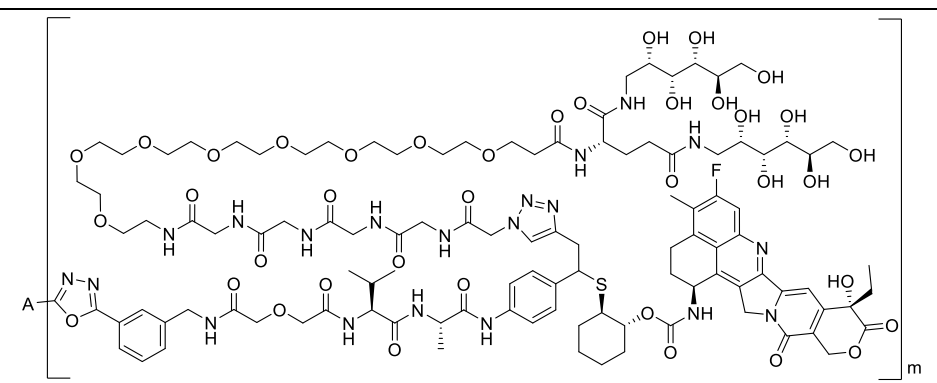
No.	Structure
ADC1	
ADC2	

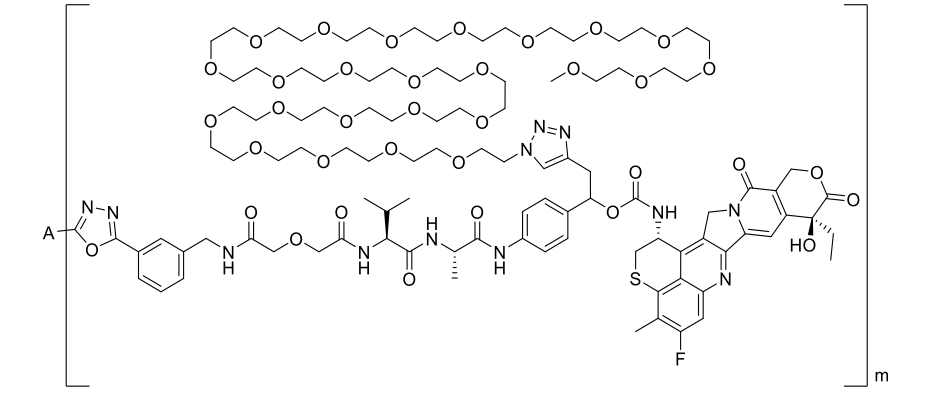
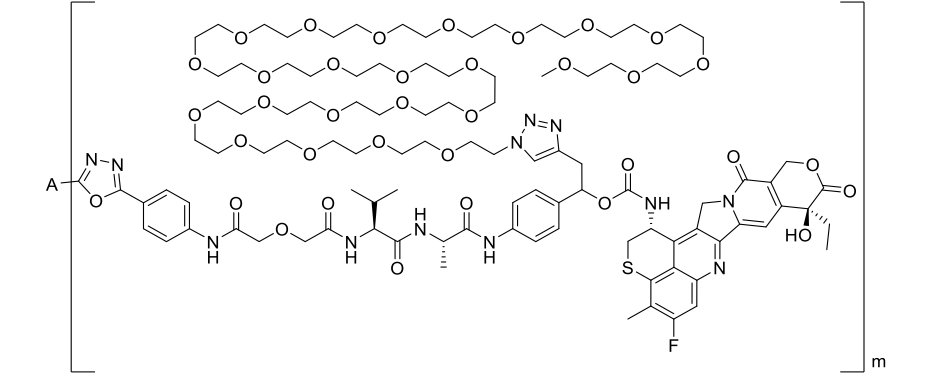
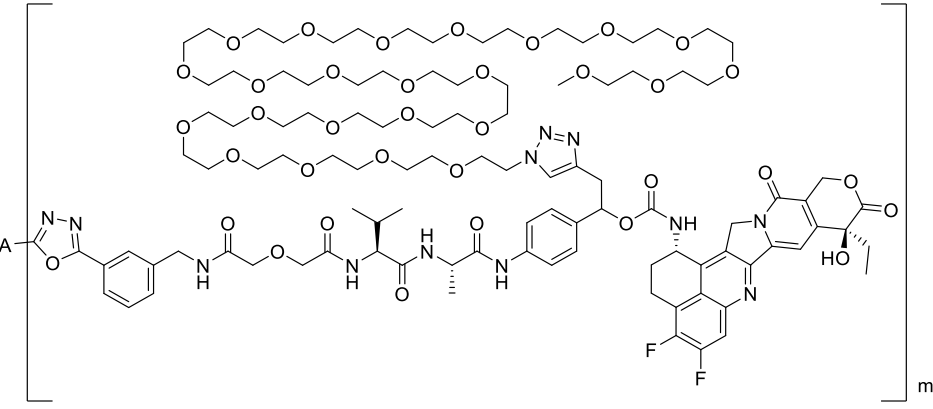
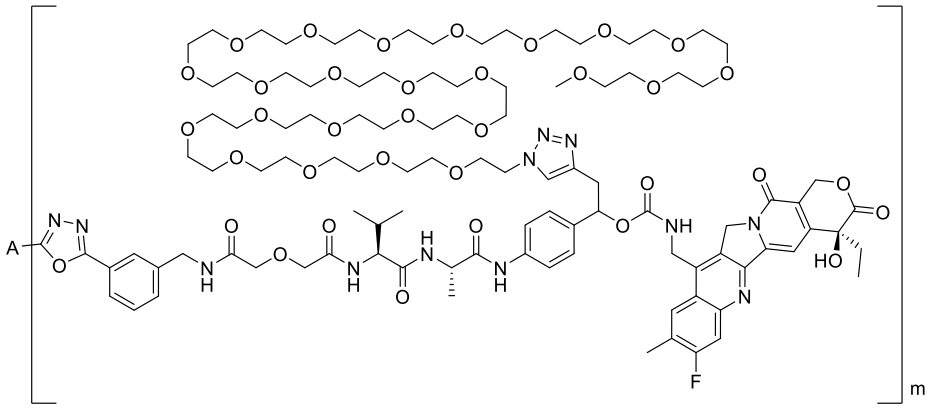
ADC3	 Chemical structure of ADC3, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl group, which is further linked to a sulfonamide group. This is followed by a chain of amide bonds, including a chiral center with a methyl group. The linker terminates in a triazole ring connected to a phenyl group, which is linked to a carbonyl group. The carbonyl group is connected to a complex polycyclic system, including a quinoline ring and a fused ring system with a fluorine atom and a hydroxyl group.
ADC4	 Chemical structure of ADC4, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl group, which is further linked to a sulfonamide group. This is followed by a chain of amide bonds, including a chiral center with a methyl group. The linker terminates in a triazole ring connected to a phenyl group, which is linked to a carbonyl group. The carbonyl group is connected to a complex polycyclic system, including a quinoline ring and a fused ring system with a fluorine atom and a hydroxyl group.
ADC5	 Chemical structure of ADC5, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl group, which is further linked to a sulfonamide group. This is followed by a chain of amide bonds, including a chiral center with a methyl group. The linker terminates in a triazole ring connected to a phenyl group, which is linked to a carbonyl group. The carbonyl group is connected to a complex polycyclic system, including a quinoline ring and a fused ring system with a fluorine atom and a hydroxyl group.
ADC6	 Chemical structure of ADC6, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl group, which is further linked to a sulfonamide group. This is followed by a chain of amide bonds, including a chiral center with a methyl group. The linker terminates in a triazole ring connected to a phenyl group, which is linked to a carbonyl group. The carbonyl group is connected to a complex polycyclic system, including a quinoline ring and a fused ring system with a fluorine atom and a hydroxyl group.

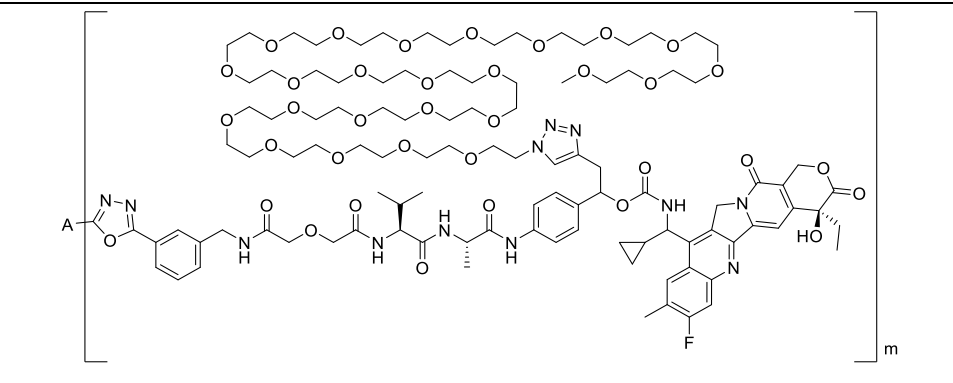
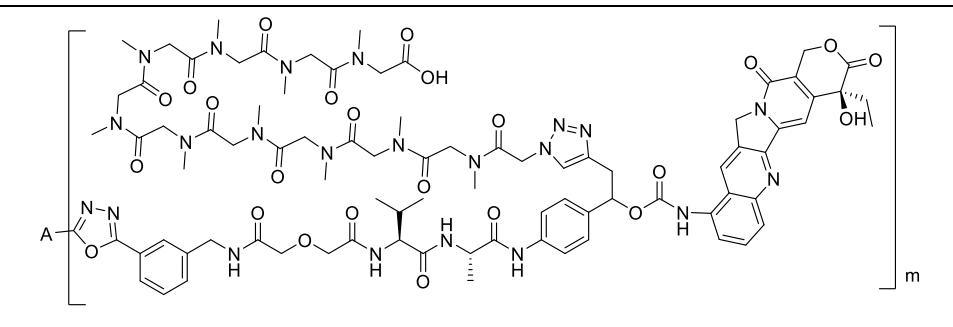
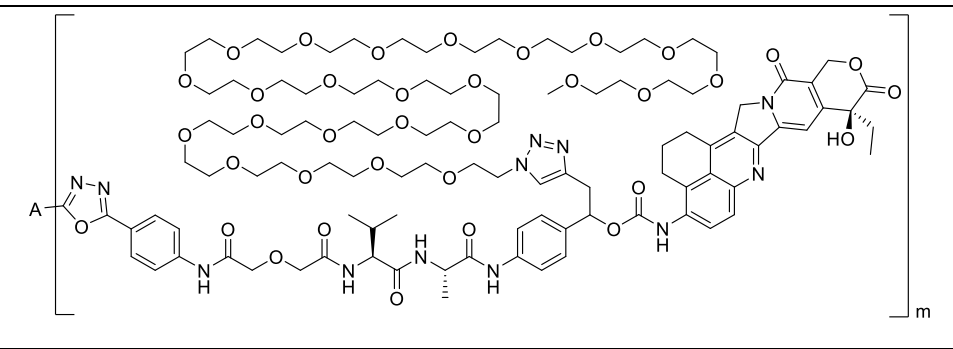
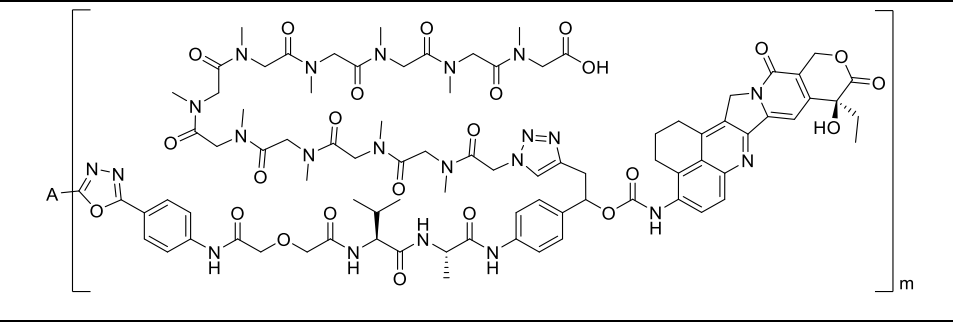
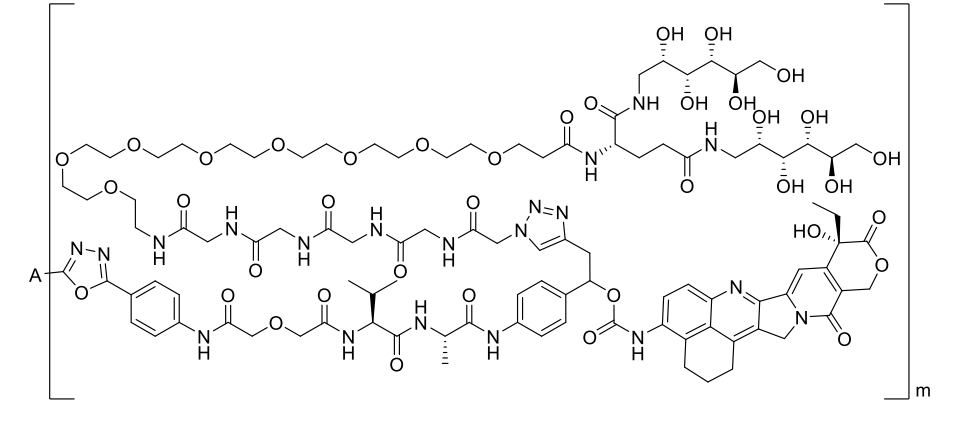
ADC7	
ADC8	
ADC9	
ADC10	

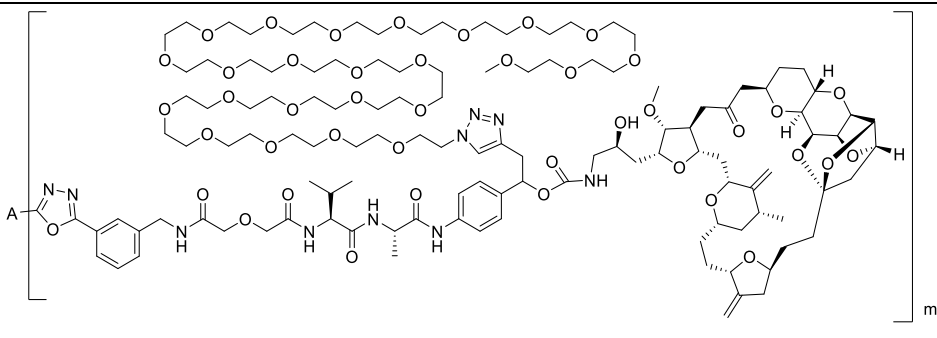
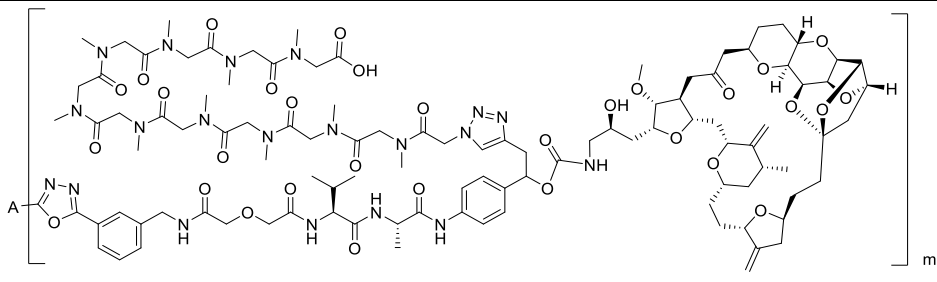
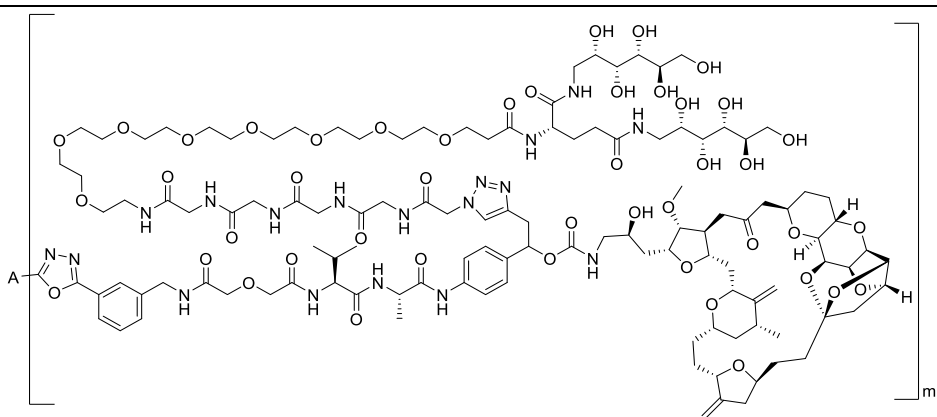
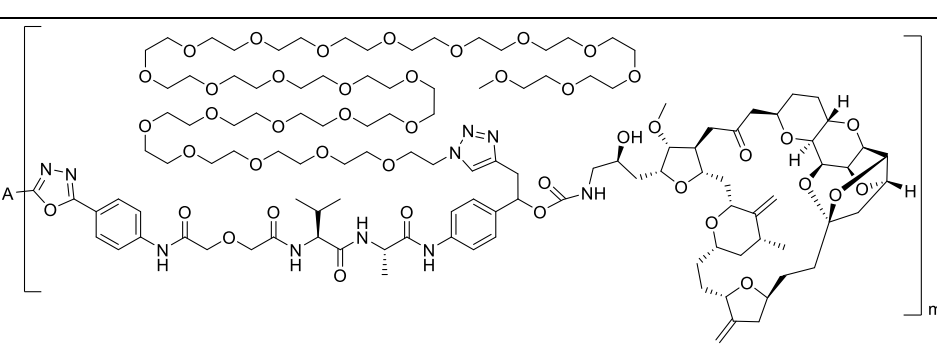
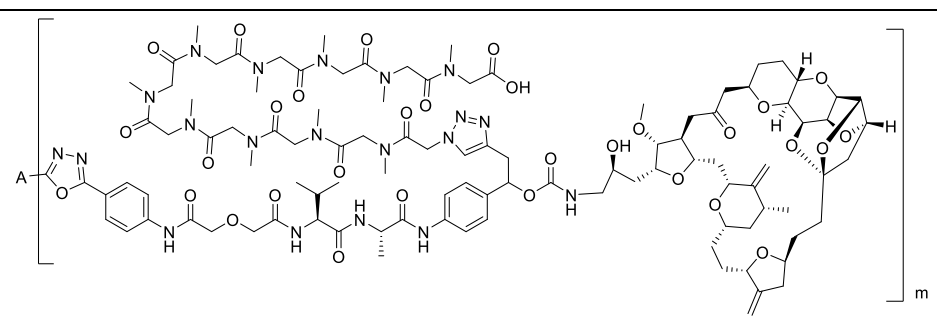
ADC11	 Chemical structure of ADC11, a conjugate consisting of a fluorinated nucleoside derivative linked via a linker to a poly(ethylene glycol) (PEG) chain, which is further linked to a fluorinated nucleoside derivative. The structure is shown within brackets with a subscript 'm'.
ADC12	 Chemical structure of ADC12, a conjugate consisting of a fluorinated nucleoside derivative linked via a linker to a poly(ethylene glycol) (PEG) chain, which is further linked to a fluorinated nucleoside derivative. The structure is shown within brackets with a subscript 'm'.
ADC13	 Chemical structure of ADC13, a conjugate consisting of a fluorinated nucleoside derivative linked via a linker to a poly(ethylene glycol) (PEG) chain, which is further linked to a fluorinated nucleoside derivative. The structure is shown within brackets with a subscript 'm'.
ADC14	 Chemical structure of ADC14, a conjugate consisting of a fluorinated nucleoside derivative linked via a linker to a poly(ethylene glycol) (PEG) chain, which is further linked to a fluorinated nucleoside derivative. The structure is shown within brackets with a subscript 'm'.

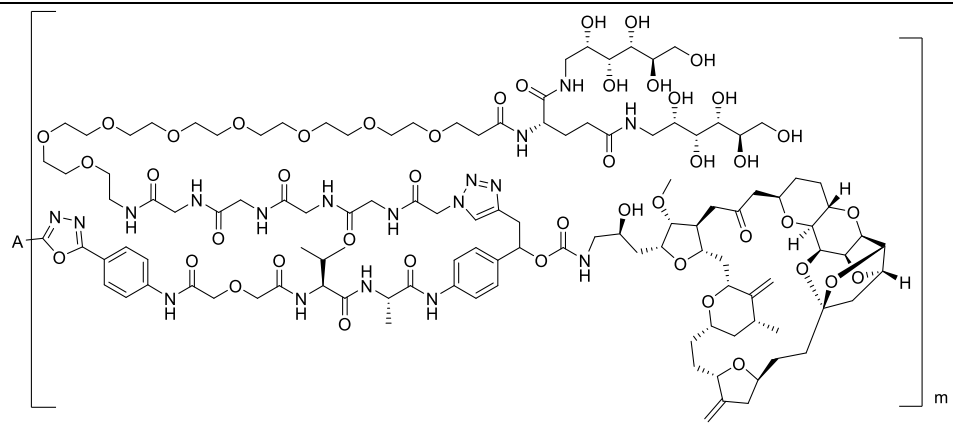
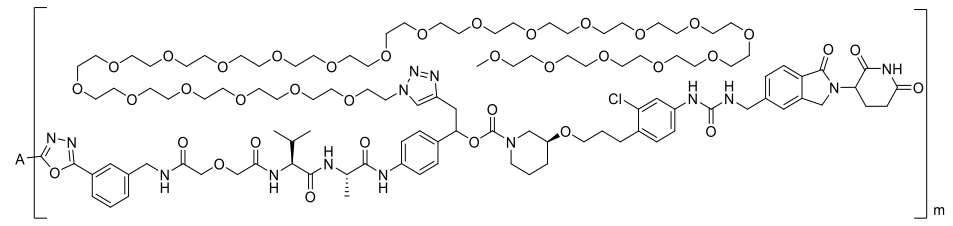
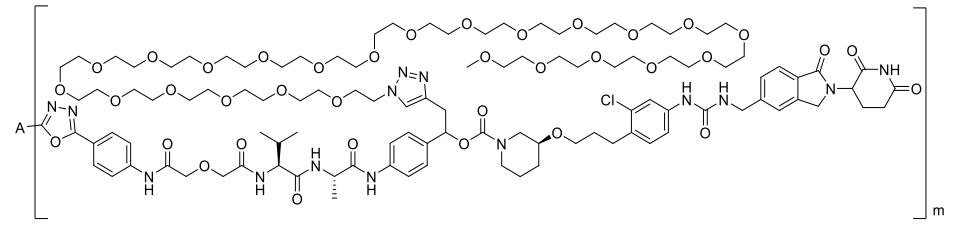
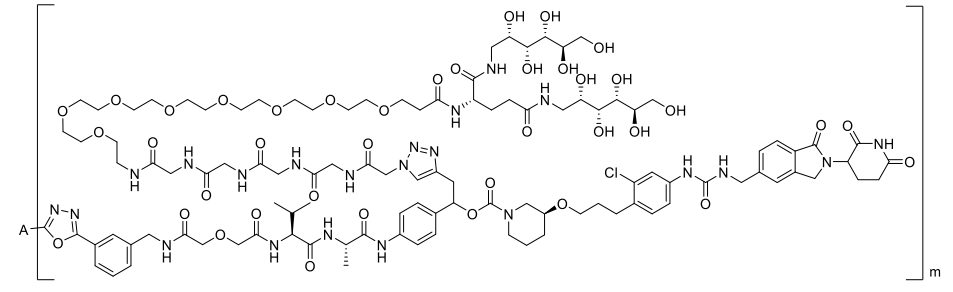
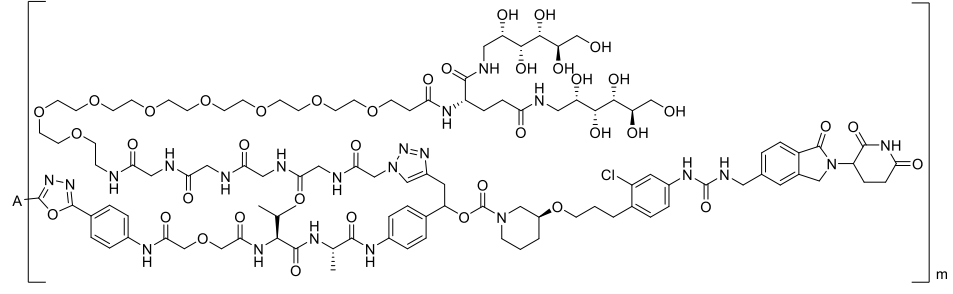
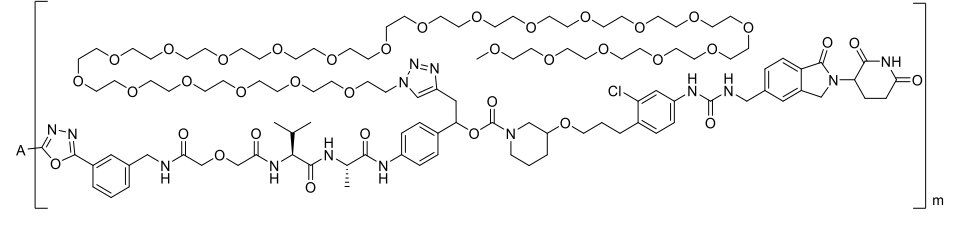
ADC15	 Chemical structure of ADC15, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The linker also contains a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The structure is enclosed in brackets with a subscript 'm'.
ADC16	 Chemical structure of ADC16, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The linker also contains a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The structure is enclosed in brackets with a subscript 'm'.
ADC17	 Chemical structure of ADC17, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The linker also contains a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The structure is enclosed in brackets with a subscript 'm'.
ADC18	 Chemical structure of ADC18, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The linker also contains a fluorinated nucleoside derivative (5'-F) and a complex sugar moiety (2',3'-O-isopropylidene-β-D-ribofuranose). The structure is enclosed in brackets with a subscript 'm'.

ADC19	 Chemical structure of ADC19, a conjugate consisting of a fluorinated quinoline core linked via a sulfonamide group to a triazole-containing linker. The linker is further connected to a poly(ethylene glycol) (PEG) chain, which is terminated by a triazole group. The structure is shown within brackets with a subscript 'm'.
ADC20	 Chemical structure of ADC20, a conjugate consisting of a fluorinated quinoline core linked via a sulfonamide group to a triazole-containing linker. The linker is further connected to a PEG chain, which is terminated by a triazole group. The structure is shown within brackets with a subscript 'm'.
ADC21	 Chemical structure of ADC21, a conjugate consisting of a fluorinated quinoline core linked via a sulfonamide group to a triazole-containing linker. The linker is further connected to a PEG chain, which is terminated by a triazole group. The structure is shown within brackets with a subscript 'm'.
ADC22	 Chemical structure of ADC22, a conjugate consisting of a fluorinated quinoline core linked via a sulfonamide group to a triazole-containing linker. The linker is further connected to a PEG chain, which is terminated by a triazole group. The structure is shown within brackets with a subscript 'm'.

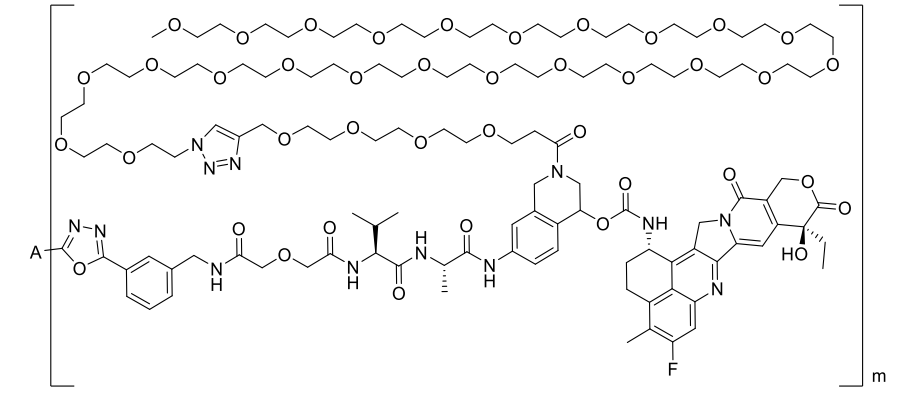
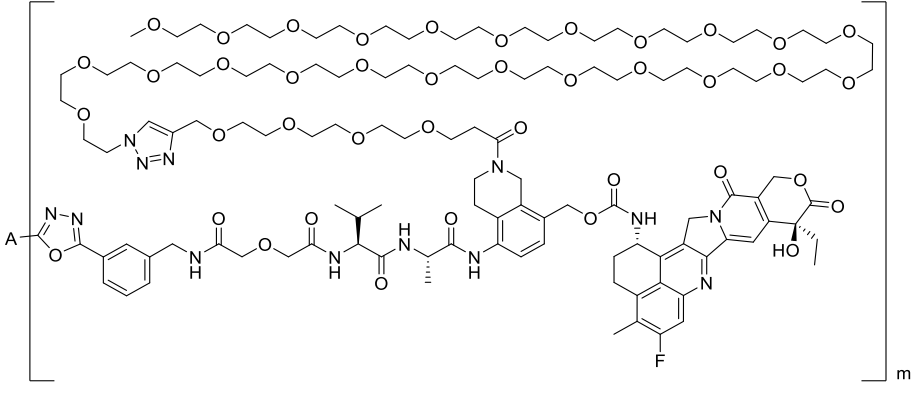
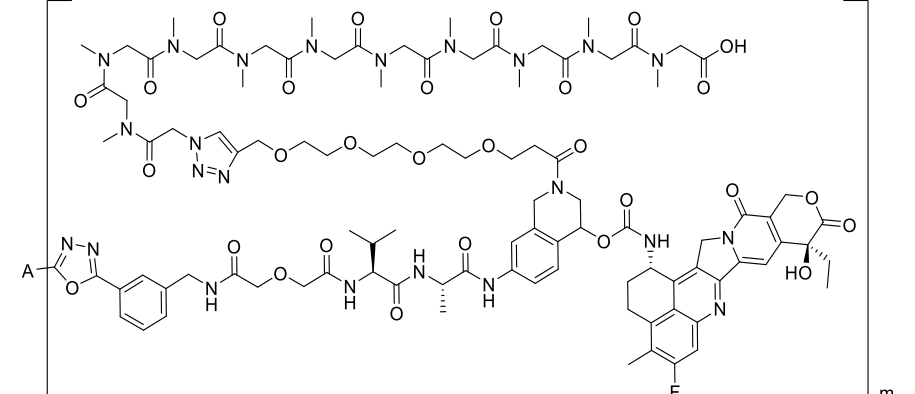
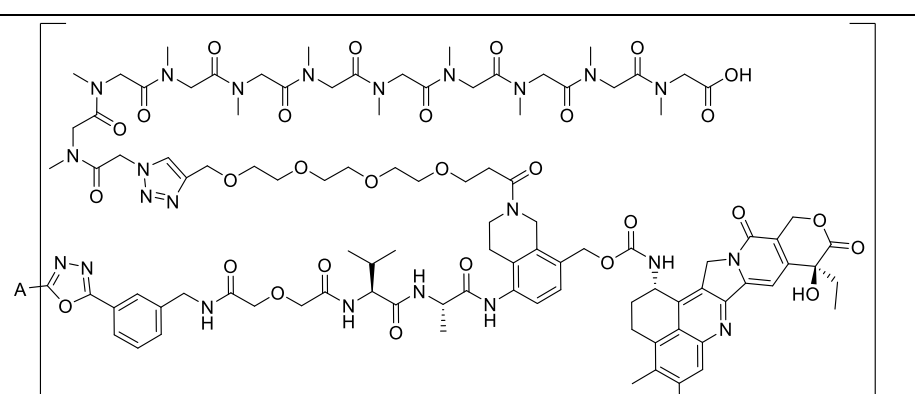
ADC23	 Chemical structure of ADC23, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain consists of several amino acid residues, including a chiral center with a methyl group. The peptide chain is terminated by a fluorinated heterocyclic moiety, which is a benzothiazine derivative with a fluorine atom and a hydroxyl group.
ADC24	 Chemical structure of ADC24, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain consists of several amino acid residues, including a chiral center with a methyl group. The peptide chain is terminated by a fluorinated heterocyclic moiety, which is a benzothiazine derivative with a fluorine atom and a hydroxyl group.
ADC25	 Chemical structure of ADC25, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain consists of several amino acid residues, including a chiral center with a methyl group. The peptide chain is terminated by a fluorinated heterocyclic moiety, which is a benzothiazine derivative with two fluorine atoms and a hydroxyl group.
ADC26	 Chemical structure of ADC26, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain consists of several amino acid residues, including a chiral center with a methyl group. The peptide chain is terminated by a fluorinated heterocyclic moiety, which is a benzothiazine derivative with a fluorine atom and a hydroxyl group.

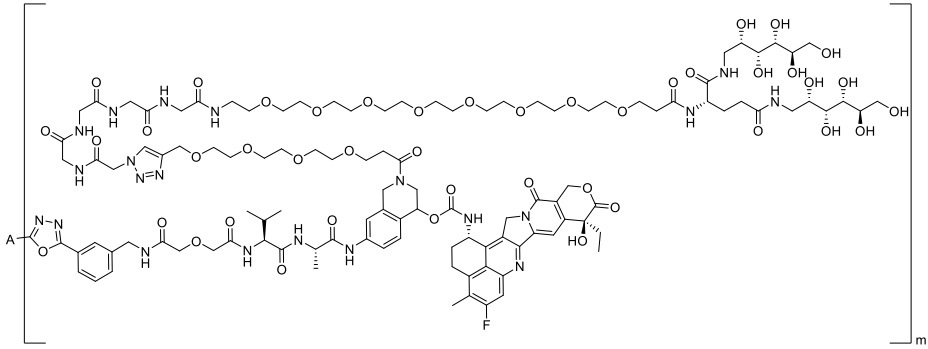
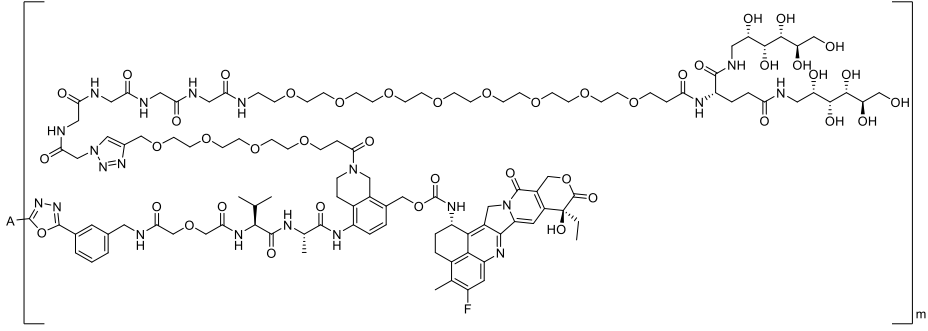
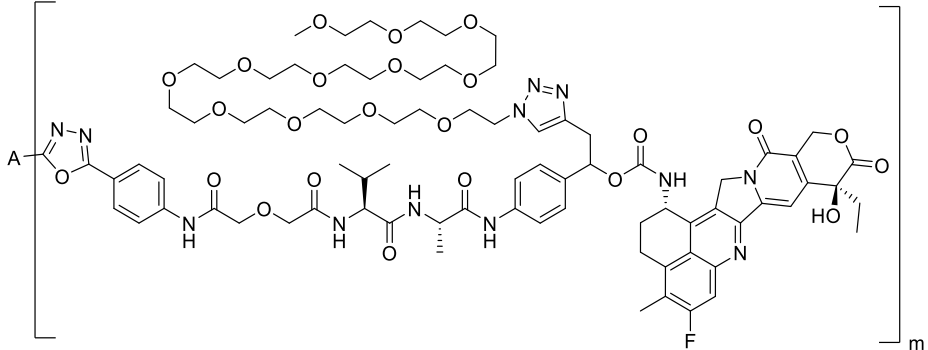
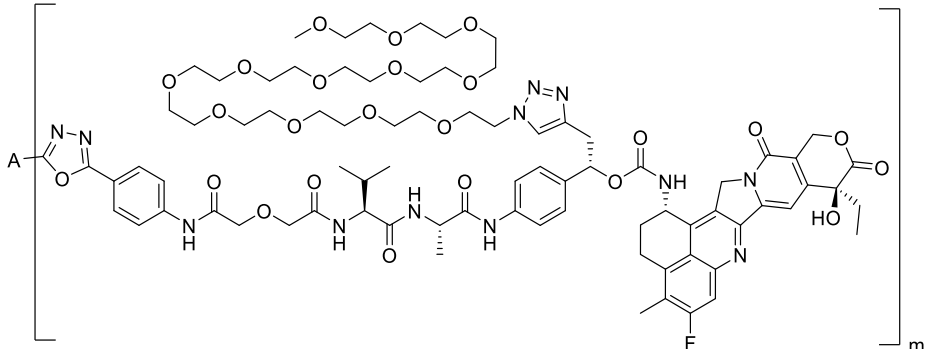
ADC27	 Chemical structure of ADC27, a conjugate consisting of a linker (A) connected to a fluorinated benzimidazole derivative via a triazole ring. The linker contains a long poly(ethylene glycol) (PEG) chain and a hydrophobic moiety. The fluorinated benzimidazole derivative is attached to the linker via an amide bond.
ADC28	 Chemical structure of ADC28, a conjugate consisting of a linker (A) connected to a fluorinated benzimidazole derivative via a triazole ring. The linker contains a long poly(ethylene glycol) (PEG) chain and a hydrophobic moiety. The fluorinated benzimidazole derivative is attached to the linker via an amide bond.
ADC29	 Chemical structure of ADC29, a conjugate consisting of a linker (A) connected to a fluorinated benzimidazole derivative via a triazole ring. The linker contains a long poly(ethylene glycol) (PEG) chain and a hydrophobic moiety. The fluorinated benzimidazole derivative is attached to the linker via an amide bond.
ADC30	 Chemical structure of ADC30, a conjugate consisting of a linker (A) connected to a fluorinated benzimidazole derivative via a triazole ring. The linker contains a long poly(ethylene glycol) (PEG) chain and a hydrophobic moiety. The fluorinated benzimidazole derivative is attached to the linker via an amide bond.
ADC31	 Chemical structure of ADC31, a conjugate consisting of a linker (A) connected to a fluorinated benzimidazole derivative via a triazole ring. The linker contains a long poly(ethylene glycol) (PEG) chain and a hydrophobic moiety. The fluorinated benzimidazole derivative is attached to the linker via an amide bond.

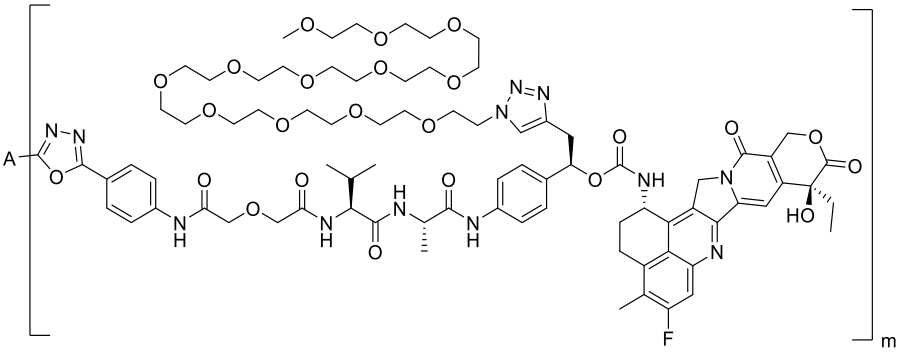
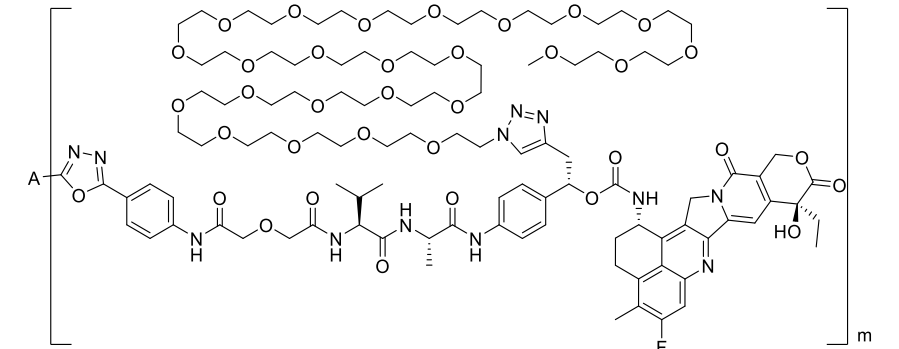
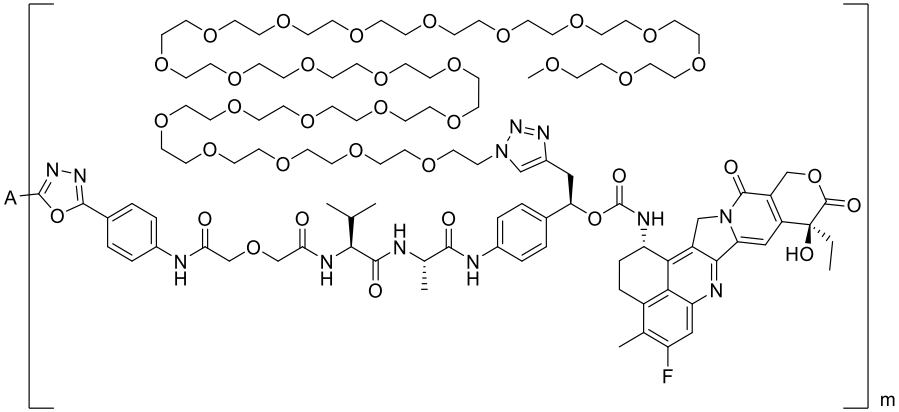
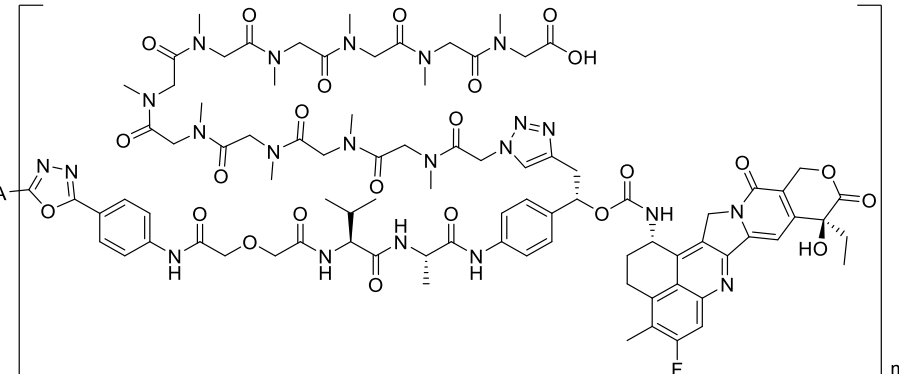
ADC32	 Chemical structure of ADC32, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a complex molecule containing a triazole ring, a sugar moiety, and a complex polycyclic structure. The structure is enclosed in brackets with a subscript 'm'.
ADC33	 Chemical structure of ADC33, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a complex molecule containing a triazole ring, a sugar moiety, and a complex polycyclic structure. The structure is enclosed in brackets with a subscript 'm'.
ADC34	 Chemical structure of ADC34, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a complex molecule containing a triazole ring, a sugar moiety, and a complex polycyclic structure. The structure is enclosed in brackets with a subscript 'm'.
ADC35	 Chemical structure of ADC35, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a complex molecule containing a triazole ring, a sugar moiety, and a complex polycyclic structure. The structure is enclosed in brackets with a subscript 'm'.
ADC36	 Chemical structure of ADC36, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a complex molecule containing a triazole ring, a sugar moiety, and a complex polycyclic structure. The structure is enclosed in brackets with a subscript 'm'.

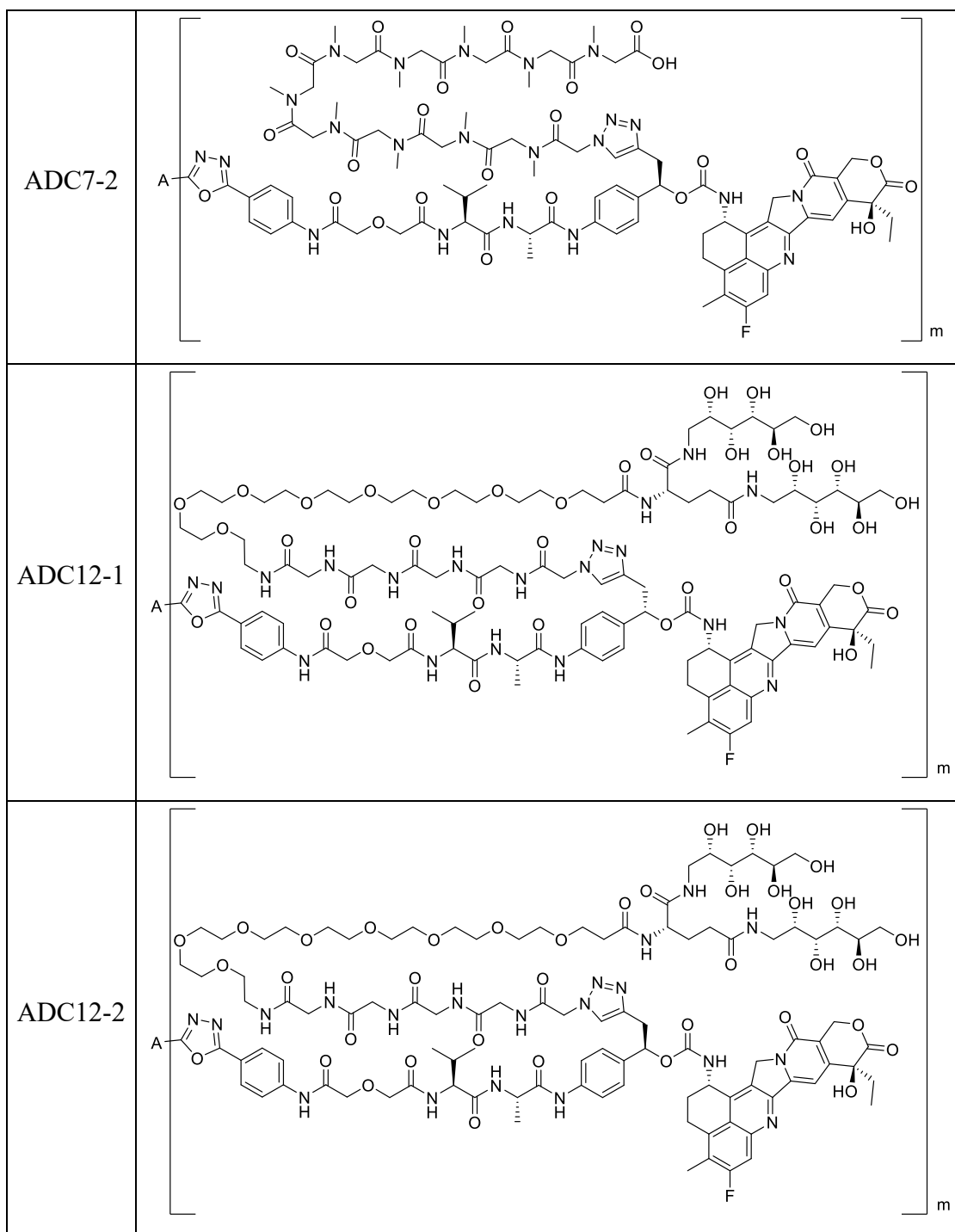
ADC37	
ADC38	
ADC39	
ADC40	
ADC41	
ADC42	

ADC43	The structure shows a repeating unit enclosed in large square brackets with a subscript 'm'. It features a long poly(ethylene glycol) chain at the top, connected via ether linkages to two triazole rings. The left triazole ring is attached to a benzyl group which is part of a peptide backbone containing several amide bonds and chiral centers (including a methyl group). The right triazole ring is attached to another benzyl group, which is also part of a peptide backbone. This second peptide backbone terminates in a chlorophenyl group linked to a pyrazole-containing moiety.
ADC44	This structure is similar to ADC43, showing a repeating unit with a subscript 'm'. It contains a long PEG chain, two triazole rings, and peptide backbones. However, the terminal moiety on the right is different, featuring a pyrazole ring system instead of the one seen in ADC43.
ADC45	The structure of ADC45 repeating unit, indicated by a subscript 'm', is very similar to ADC44. It includes a long PEG chain, two triazole rings, and peptide backbones, with a distinct terminal functional group on the right side.
ADC46	ADC46's repeating unit, shown with a subscript 'm', differs significantly from the previous three. It lacks the long PEG chains. Instead, it features multiple ether-linked segments and two triazole rings. The rightmost part of the molecule contains a complex polycyclic aromatic system with a quaternary carbon bearing two hydroxyl groups.
ADC47	The structure of ADC47 repeating unit, with a subscript 'm', shows a more complex architecture. It includes a long PEG chain, two triazole rings, and a dense network of amide bonds forming a cyclic or branched peptide-like structure. The right end features a polycyclic aromatic system with a quaternary carbon and hydroxyl groups.
ADC48	ADC48's repeating unit, indicated by a subscript 'm', is highly complex. It features a long PEG chain, two triazole rings, and a very intricate peptide backbone with numerous amide bonds and chiral centers. The right side of the molecule terminates in a polycyclic aromatic system with a quaternary carbon and hydroxyl groups.

ADC49	 Chemical structure of ADC49, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a piperidine ring. The piperidine ring is connected to a linker containing a triazole ring, which is further linked to a phenyl ring. The phenyl ring is substituted with a triazole ring. The entire structure is enclosed in brackets with a subscript 'm'.
ADC50	 Chemical structure of ADC50, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a piperidine ring. The piperidine ring is connected to a linker containing a triazole ring, which is further linked to a phenyl ring. The phenyl ring is substituted with a triazole ring. The entire structure is enclosed in brackets with a subscript 'm'.
ADC51	 Chemical structure of ADC51, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a piperidine ring. The piperidine ring is connected to a linker containing a triazole ring, which is further linked to a phenyl ring. The phenyl ring is substituted with a triazole ring. The entire structure is enclosed in brackets with a subscript 'm'.
ADC52	 Chemical structure of ADC52, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a piperidine ring. The piperidine ring is connected to a linker containing a triazole ring, which is further linked to a phenyl ring. The phenyl ring is substituted with a triazole ring. The entire structure is enclosed in brackets with a subscript 'm'.

ADC53	 Chemical structure of ADC53, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated aromatic system on the left and a complex polycyclic system on the right, which includes a fluorinated benzene ring and a complex polycyclic system with a fluorine atom and a hydroxyl group. The structure is enclosed in brackets with a subscript 'm'.
ADC54	 Chemical structure of ADC54, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated aromatic system on the left and a complex polycyclic system on the right, which includes a fluorinated benzene ring and a complex polycyclic system with a fluorine atom and a hydroxyl group. The structure is enclosed in brackets with a subscript 'm'.
ADC55	 Chemical structure of ADC55, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated aromatic system on the left and a complex polycyclic system on the right, which includes a fluorinated benzene ring and a complex polycyclic system with a fluorine atom and a hydroxyl group. The structure is enclosed in brackets with a subscript 'm'.
ADC55-1	 Chemical structure of ADC55-1, a complex molecule featuring a long poly(ethylene glycol) (PEG) linker. The linker is connected to a fluorinated aromatic system on the left and a complex polycyclic system on the right, which includes a fluorinated benzene ring and a complex polycyclic system with a fluorine atom and a hydroxyl group. The structure is enclosed in brackets with a subscript 'm'.

ADC55-2	 Chemical structure of ADC55-2, a conjugate consisting of a fluorinated indole derivative linked via an amide bond to a triazole-containing linker, which is further connected to a poly(ether amide) chain. The structure is shown within brackets with a subscript 'm'.
ADC2-1	 Chemical structure of ADC2-1, a conjugate consisting of a fluorinated indole derivative linked via an amide bond to a triazole-containing linker, which is further connected to a poly(ether amide) chain. The structure is shown within brackets with a subscript 'm'.
ADC2-2	 Chemical structure of ADC2-2, a conjugate consisting of a fluorinated indole derivative linked via an amide bond to a triazole-containing linker, which is further connected to a poly(ether amide) chain. The structure is shown within brackets with a subscript 'm'.
ADC7-1	 Chemical structure of ADC7-1, a conjugate consisting of a fluorinated indole derivative linked via an amide bond to a triazole-containing linker, which is further connected to a poly(ether amide) chain. The structure is shown within brackets with a subscript 'm'.



In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from trastuzumab.

In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from farletuzumab.

5 In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from farletuzumab FcS.

In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from 33B.

In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from 43A.

In some embodiments, the antibodies of ADC1 to ADC55, and ADC2-1, ADC2-2, ADC7-1, ADC7-2, ADC12-1, ADC12-2, ADC55-1, and ADC55-2 are selected from 43B.

- 5 In some embodiments, the antibody-drug conjugate represented by formula I, the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

10

No. Structure Antibody	Trastuzuma b	Farletuzum ab	Farletuzumab- FcS	33B	43B
ADC1	T-ADC1	F-ADC1	FS-ADC1	D-ADC1	B-ADC1
ADC2	T-ADC2	F-ADC2	FS-ADC2	D-ADC2	B-ADC2
ADC2-1	T-ADC2-1	F-ADC2-1	FS-ADC2-1	D-ADC2-1	B-ADC2-1
ADC2-2	T-ADC2-2	F-ADC2-2	FS-ADC2-2	D-ADC2-2	B-ADC2-2
ADC3	T-ADC3	F-ADC3	FS-ADC3	D-ADC3	B-ADC3
ADC4	T-ADC4	F-ADC4	FS-ADC4	D-ADC4	B-ADC4
ADC5	T-ADC5	F-ADC5	FS-ADC5	D-ADC5	B-ADC5
ADC6	T-ADC6	F-ADC6	FS-ADC6	D-ADC6	B-ADC6
ADC7	T-ADC7	F-ADC7	FS-ADC7	D-ADC7	B-ADC7
ADC7-1	T-ADC7-1	F-ADC7-1	FS-ADC7-1	D-ADC7-1	B-ADC7-1
ADC7-2	T-ADC7-2	F-ADC7-2	FS-ADC7-2	D-ADC7-2	B-ADC7-2
ADC8	T-ADC8	F-ADC8	FS-ADC8	D-ADC8	B-ADC8
ADC9	T-ADC9	F-ADC9	FS-ADC9	D-ADC9	B-ADC9

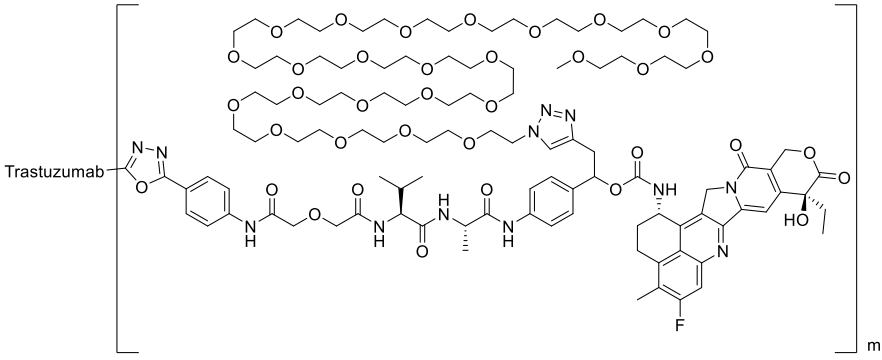
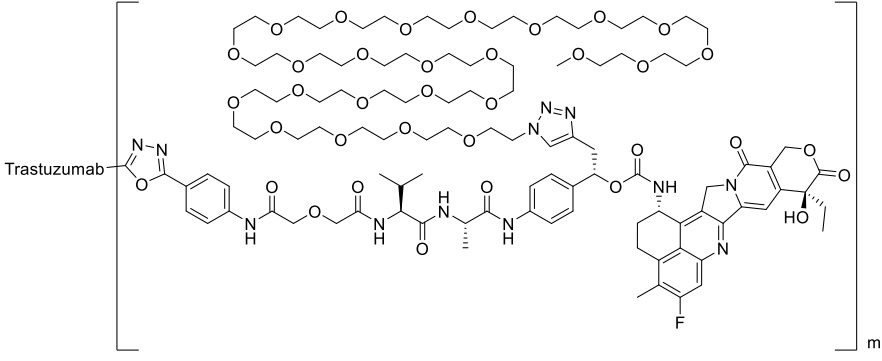
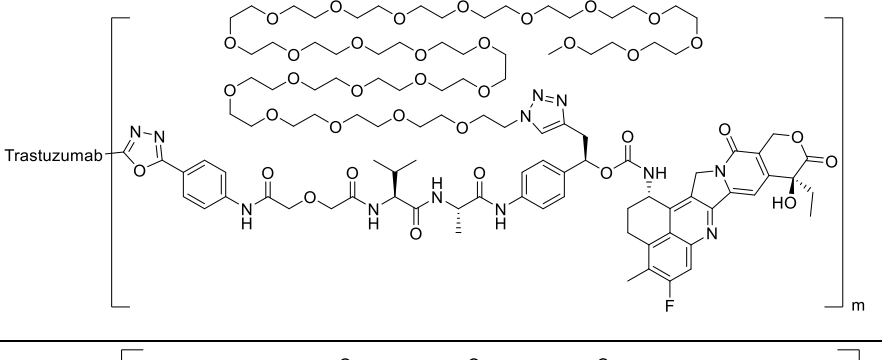
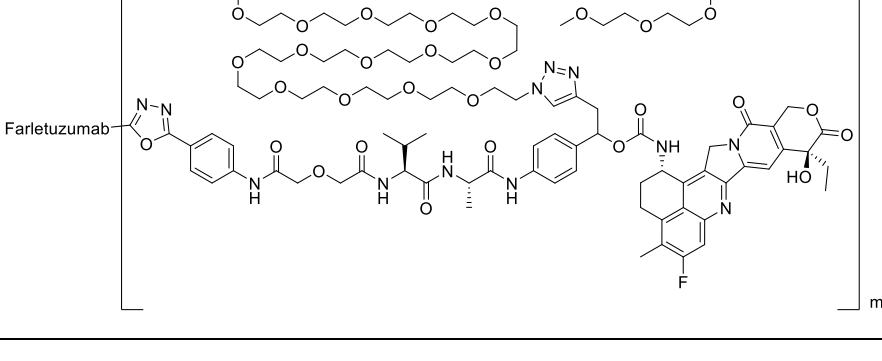
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ADC13	T-ADC13	F-ADC13	FS-ADC13	D-ADC13	B-ADC13
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ADC16	T-ADC16	F-ADC16	FS-ADC16	D-ADC16	B-ADC16
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ADC19	T-ADC19	F-ADC19	FS-ADC19	D-ADC19	B-ADC19
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ADC22	T-ADC22	F-ADC22	FS-ADC22	D-ADC22	B-ADC22
ADC23	T-ADC23	F-ADC23	FS-ADC23	D-ADC23	B-ADC23
ADC24	T-ADC24	F-ADC24	FS-ADC24	D-ADC24	B-ADC24
ADC25	T-ADC25	F-ADC25	FS-ADC25	D-ADC25	B-ADC25
ADC26	T-ADC26	F-ADC26	FS-ADC26	D-ADC26	B-ADC26
ADC27	T-ADC27	F-ADC27	FS-ADC27	D-ADC27	B-ADC27
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ADC37	T-ADC37	F-ADC37	FS-ADC37	D-ADC37	B-ADC37

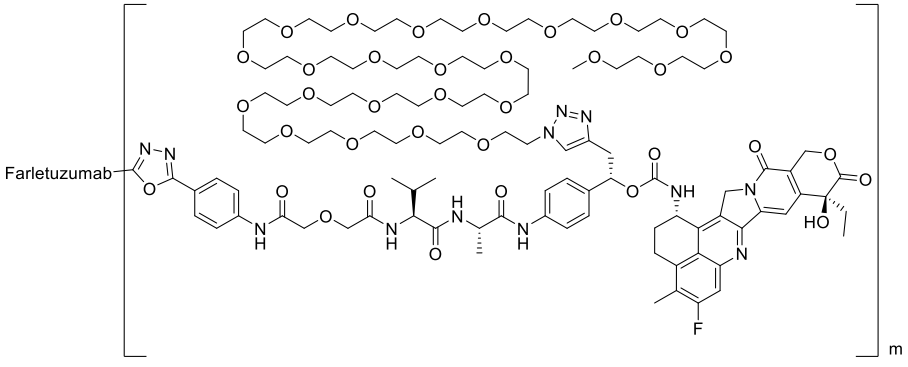
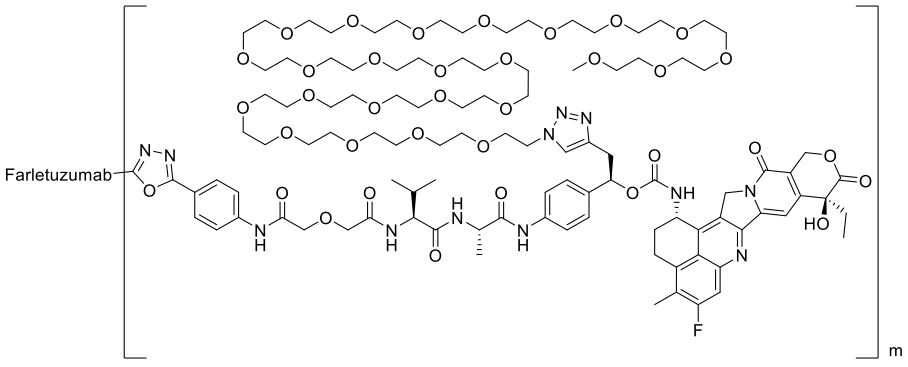
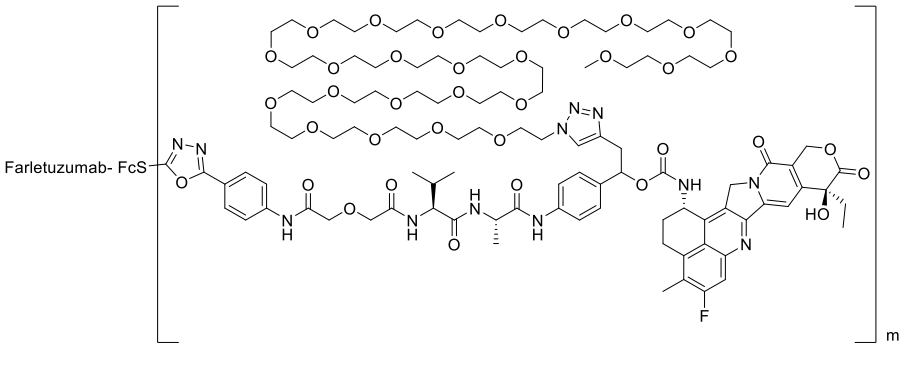
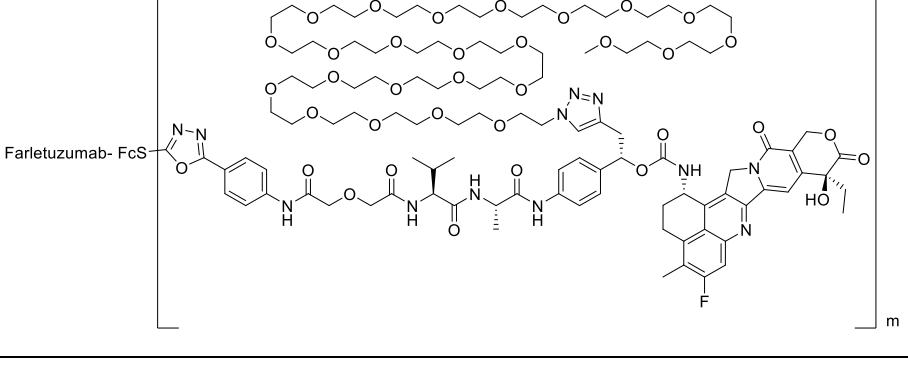
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ADC41	T-ADC41	F-ADC41	FS-ADC41	D-ADC41	B-ADC41
ADC42	T-ADC42	F-ADC42	FS-ADC42	D-ADC42	B-ADC42
ADC43	T-ADC43	F-ADC43	FS-ADC43	D-ADC43	B-ADC43
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ADC45	T-ADC45	F-ADC45	FS-ADC45	D-ADC45	B-ADC45
ADC46	T-ADC46	F-ADC46	FS-ADC46	D-ADC46	B-ADC46
ADC47	T-ADC47	F-ADC47	FS-ADC47	D-ADC47	B-ADC47
ADC48	T-ADC48	F-ADC48	FS-ADC48	D-ADC48	B-ADC48
ADC49	T-ADC49	F-ADC49	FS-ADC49	D-ADC49	B-ADC49
ADC50	T-ADC50	F-ADC50	FS-ADC50	D-ADC50	B-ADC50
ADC51	T-ADC51	F-ADC51	FS-ADC51	D-ADC51	B-ADC51
ADC52	T-ADC52	F-ADC52	FS-ADC52	D-ADC52	B-ADC52
ADC53	T-ADC53	F-ADC53	FS-ADC53	D-ADC53	B-ADC53
ADC54	T-ADC54	F-ADC54	FS-ADC54	D-ADC54	B-ADC54
ADC55	T-ADC55	F-ADC55	FS-ADC55	D-ADC55	B-ADC55
ADC55-1	T-ADC55-1	F-ADC55-1	FS-ADC55-1	D-ADC55-1	B-ADC55-1
ADC55-2	T-ADC55-2	F-ADC55-2	FS-ADC55-2	D-ADC55-2	B-ADC55-2

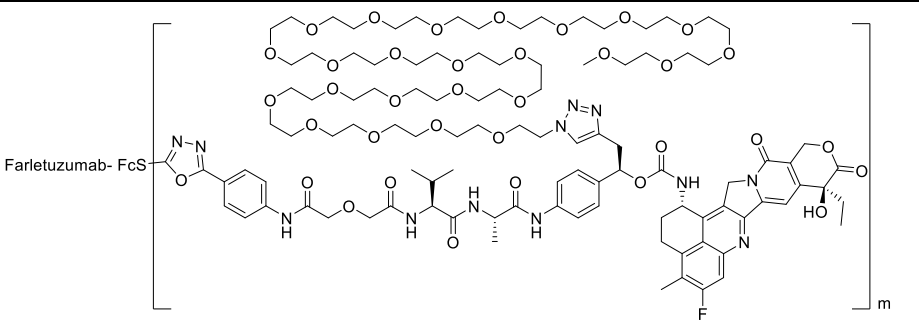
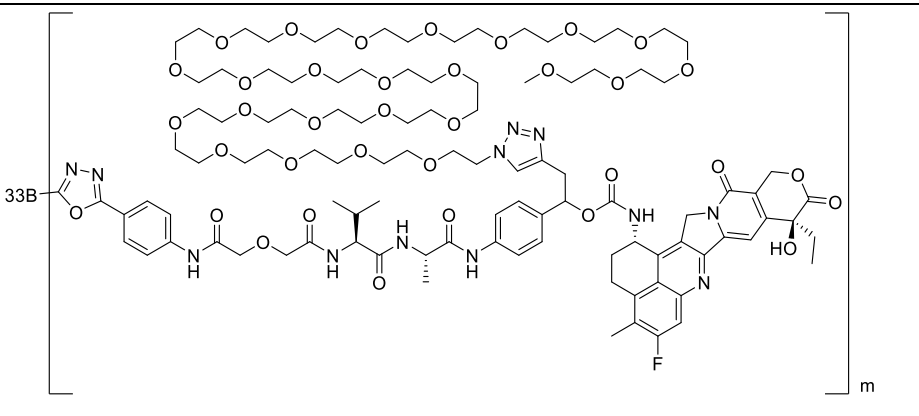
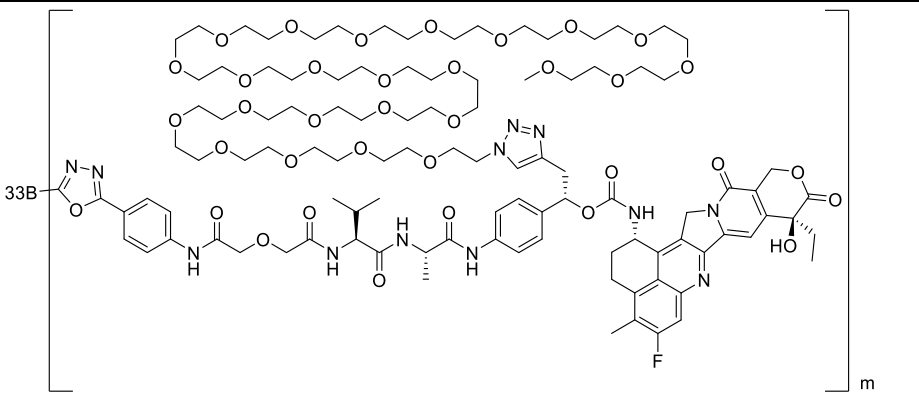
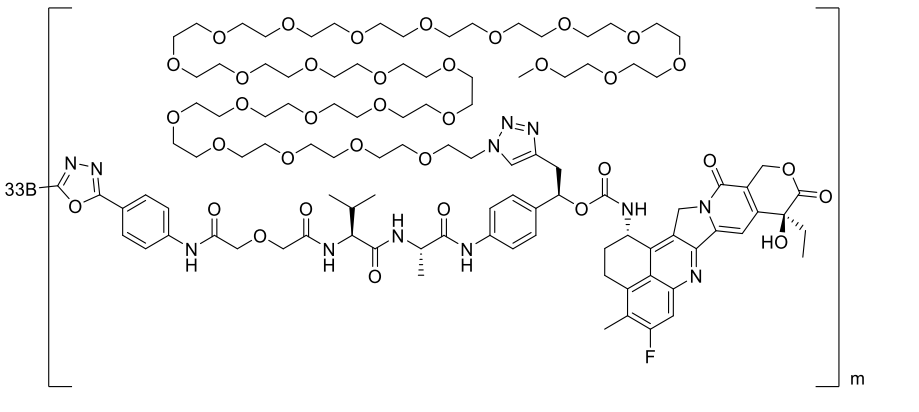
Note: In the table, T-ADC1 refers to the ADC in ADC1 where antibody A is trastuzumab, and the same naming convention applies to other ADCs.

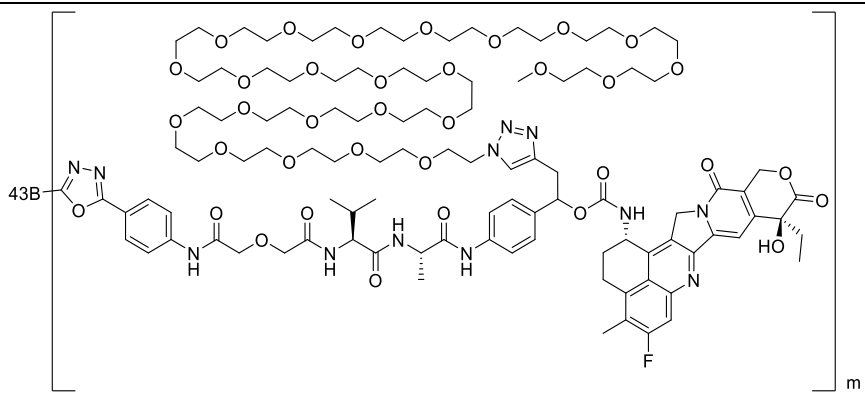
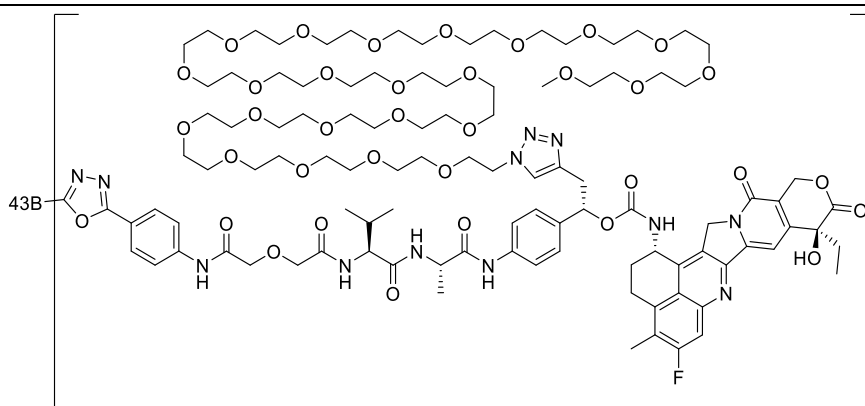
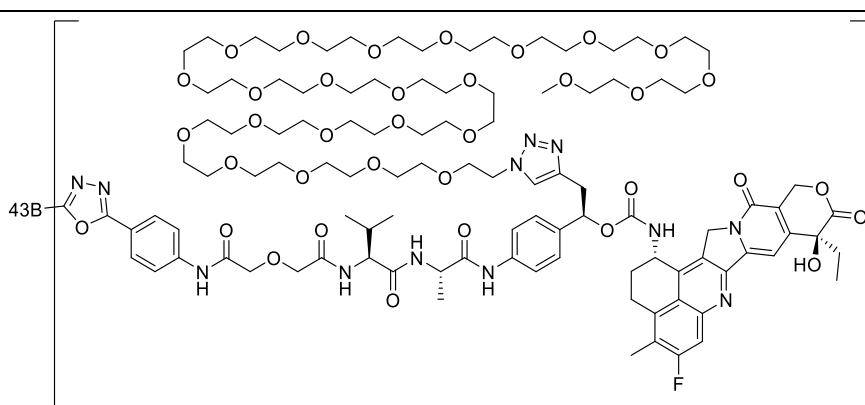
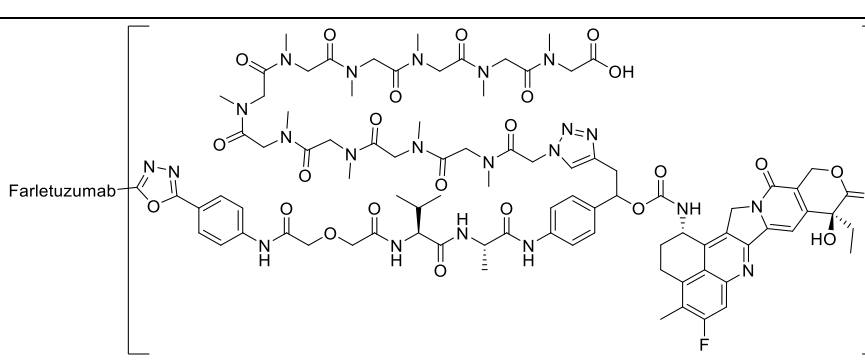
In some embodiments, the antibody-drug conjugate represented by formula I, and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof are selected from the following structures:

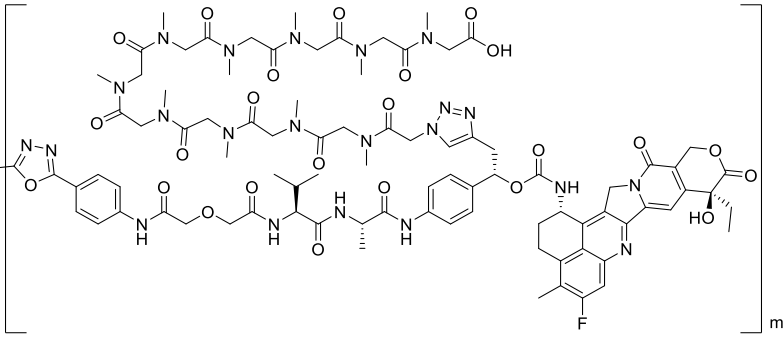
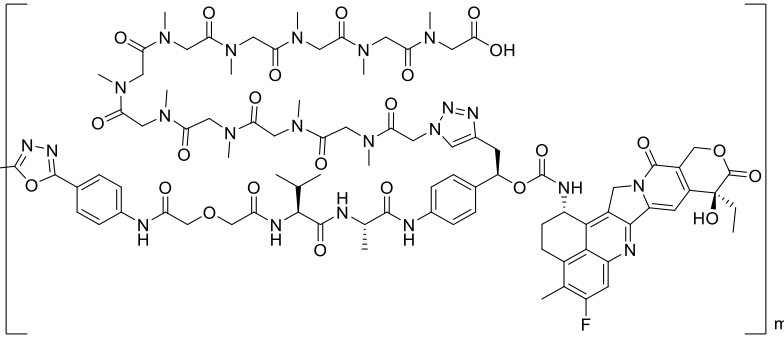
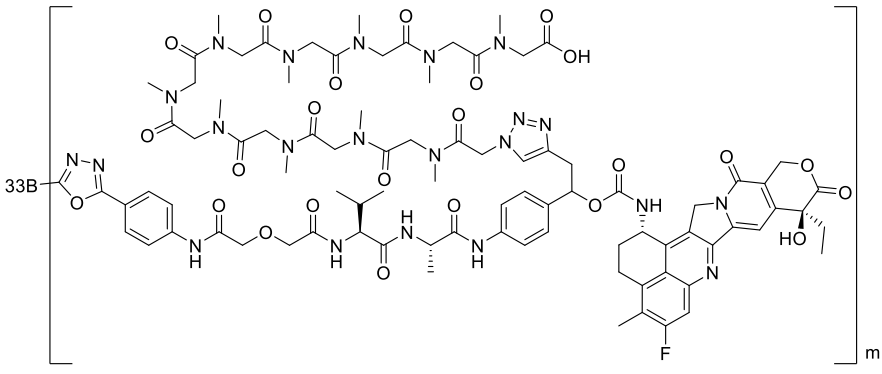
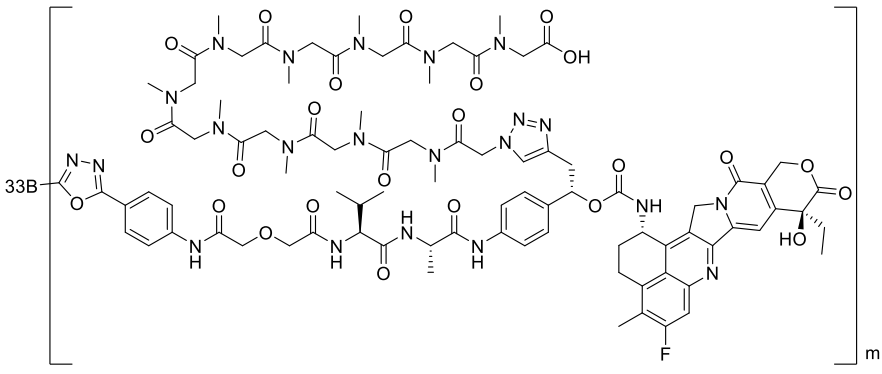
No.	Structure
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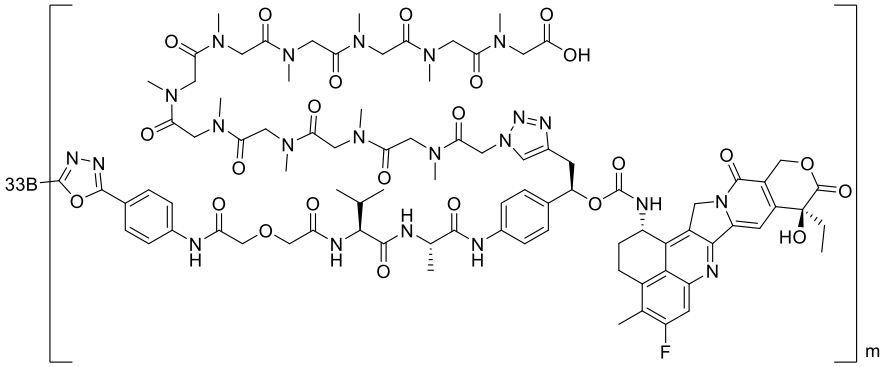
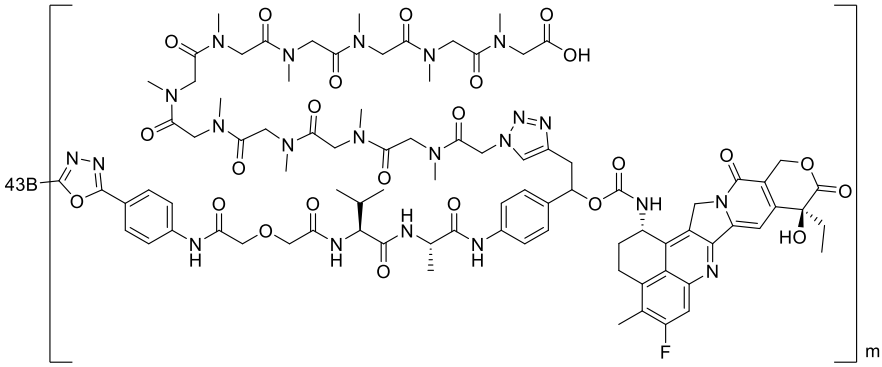
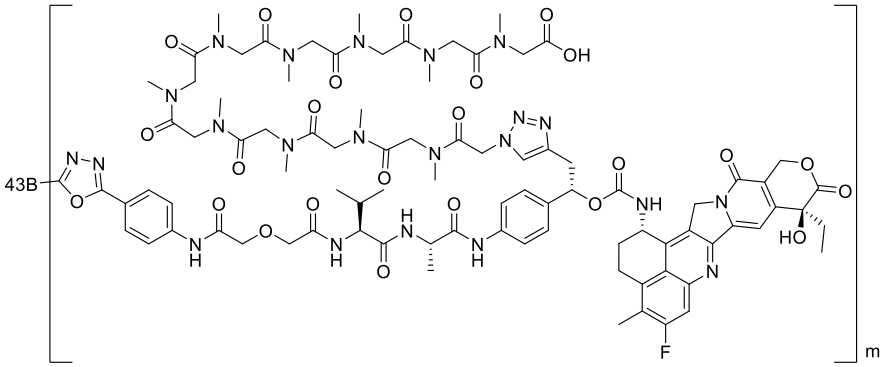
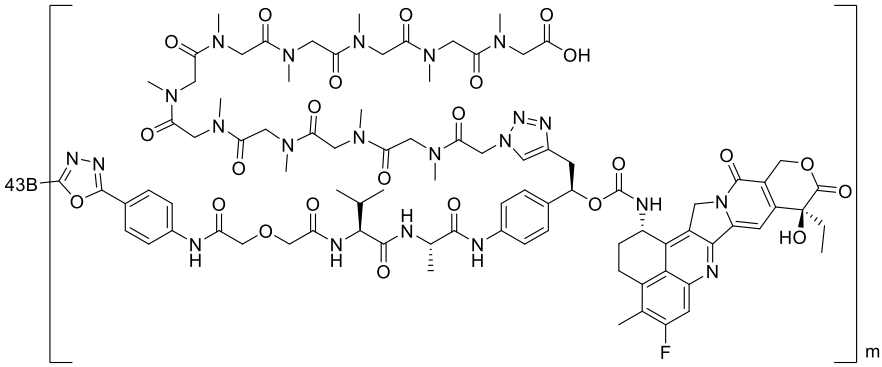
T-ADC2	 Chemical structure of T-ADC2 conjugate. The structure shows a Trastuzumab antibody (labeled "Trastuzumab") linked via a linker to a fluorinated pyridine derivative. The linker consists of a phenyl ring connected to a carbonyl group, which is further connected to a chain of amide and ether linkages. The fluorinated pyridine derivative is a 6-fluoro-2-methyl-4-(hydroxymethyl)pyridine-3-carboxamide derivative. The entire conjugate is enclosed in brackets with a subscript "m".
T-ADC2-1	 Chemical structure of T-ADC2-1 conjugate. The structure is identical to T-ADC2, showing a Trastuzumab antibody (labeled "Trastuzumab") linked via a linker to a fluorinated pyridine derivative. The linker consists of a phenyl ring connected to a carbonyl group, which is further connected to a chain of amide and ether linkages. The fluorinated pyridine derivative is a 6-fluoro-2-methyl-4-(hydroxymethyl)pyridine-3-carboxamide derivative. The entire conjugate is enclosed in brackets with a subscript "m".
T-ADC2-2	 Chemical structure of T-ADC2-2 conjugate. The structure is identical to T-ADC2, showing a Trastuzumab antibody (labeled "Trastuzumab") linked via a linker to a fluorinated pyridine derivative. The linker consists of a phenyl ring connected to a carbonyl group, which is further connected to a chain of amide and ether linkages. The fluorinated pyridine derivative is a 6-fluoro-2-methyl-4-(hydroxymethyl)pyridine-3-carboxamide derivative. The entire conjugate is enclosed in brackets with a subscript "m".
F-ADC2	 Chemical structure of F-ADC2 conjugate. The structure shows a Farletuzumab antibody (labeled "Farletuzumab") linked via a linker to a fluorinated pyridine derivative. The linker consists of a phenyl ring connected to a carbonyl group, which is further connected to a chain of amide and ether linkages. The fluorinated pyridine derivative is a 6-fluoro-2-methyl-4-(hydroxymethyl)pyridine-3-carboxamide derivative. The entire conjugate is enclosed in brackets with a subscript "m".

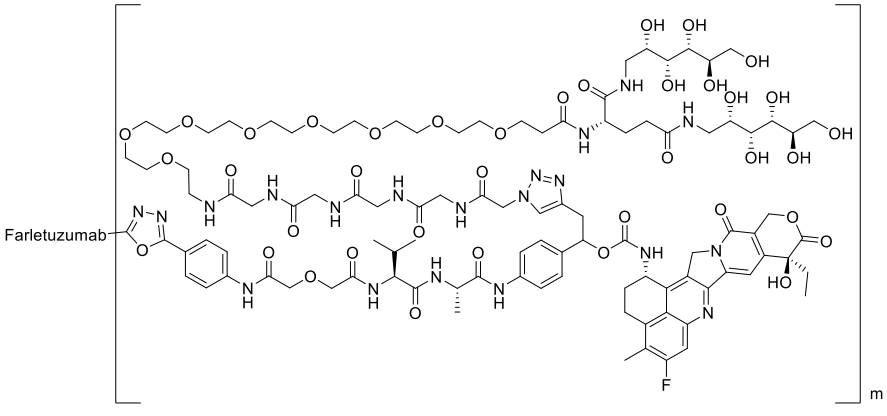
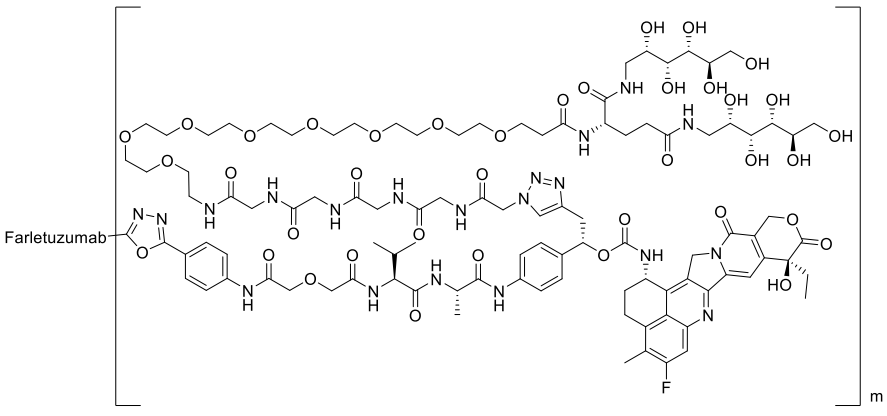
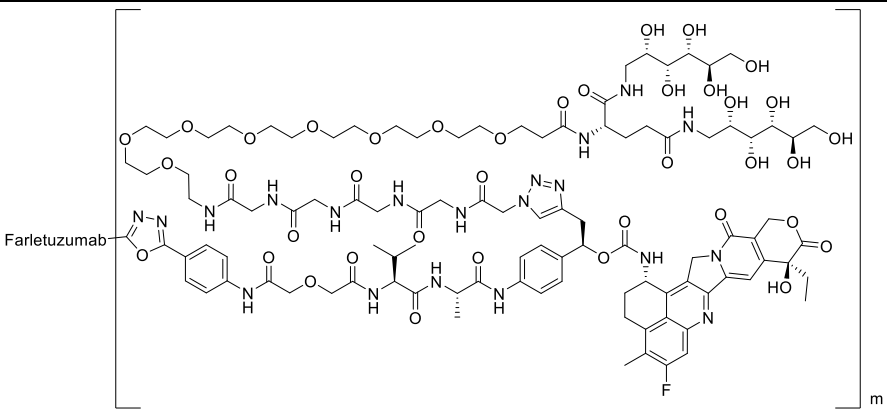
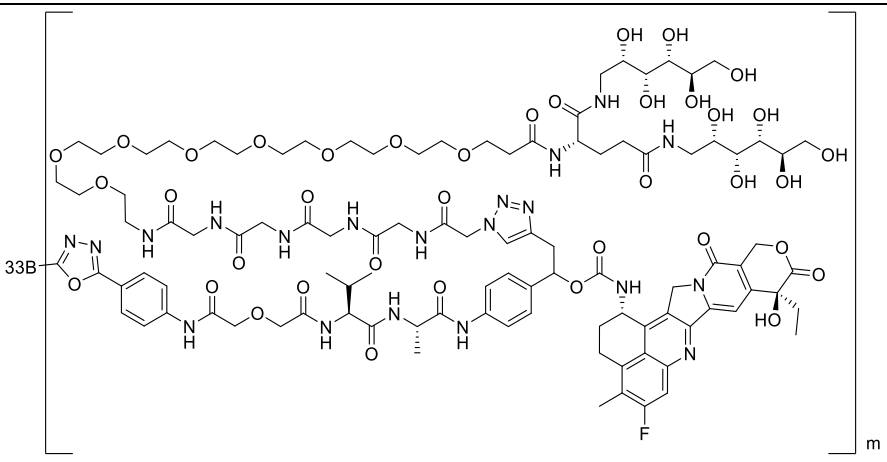
F-ADC2-1	 Chemical structure of F-ADC2-1, showing a Farletuzumab antibody linked via a triazole bridge to a long PEG chain, which is further linked to a fluorinated quinoline derivative. The structure is enclosed in brackets with a subscript 'm'.
F-ADC2-2	 Chemical structure of F-ADC2-2, showing a Farletuzumab antibody linked via a triazole bridge to a long PEG chain, which is further linked to a fluorinated quinoline derivative. The structure is enclosed in brackets with a subscript 'm'.
FS-ADC2	 Chemical structure of FS-ADC2, showing a Farletuzumab-FcS antibody linked via a triazole bridge to a long PEG chain, which is further linked to a fluorinated quinoline derivative. The structure is enclosed in brackets with a subscript 'm'.
FS-ADC2-1	 Chemical structure of FS-ADC2-1, showing a Farletuzumab-FcS antibody linked via a triazole bridge to a long PEG chain, which is further linked to a fluorinated quinoline derivative. The structure is enclosed in brackets with a subscript 'm'.

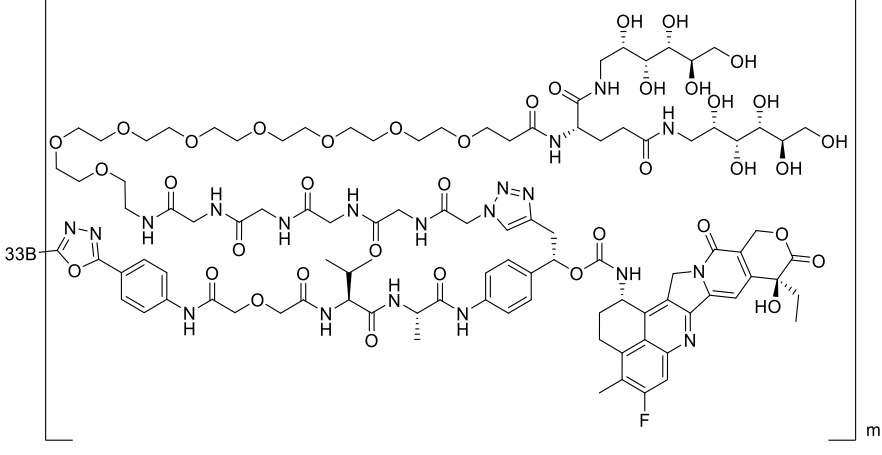
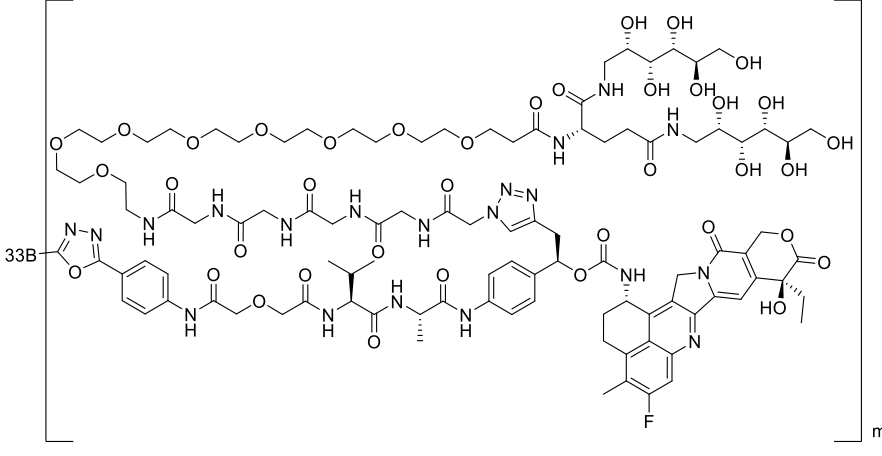
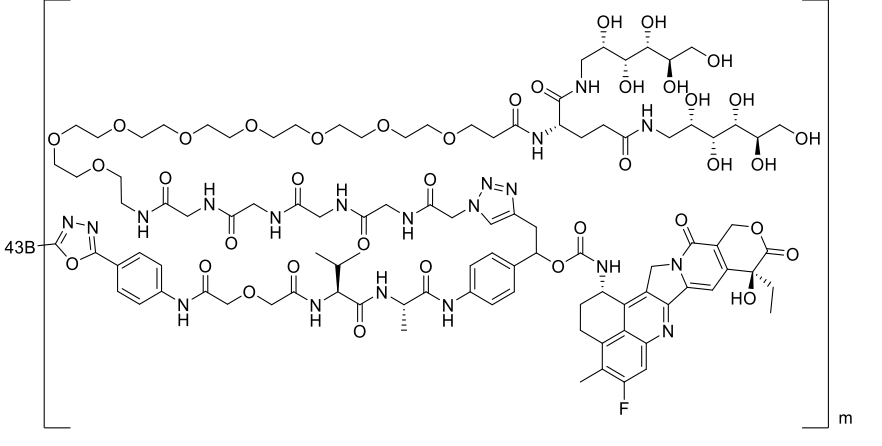
FS-ADC2-2	 Chemical structure of FS-ADC2-2, showing a Farletuzumab- FcS conjugate linked to a fluorinated nucleoside derivative via a triazole bridge. The structure is enclosed in brackets with a subscript 'm'.
D-ADC2	 Chemical structure of D-ADC2, showing a 33B conjugate linked to a fluorinated nucleoside derivative via a triazole bridge. The structure is enclosed in brackets with a subscript 'm'.
D-ADC2-1	 Chemical structure of D-ADC2-1, showing a 33B conjugate linked to a fluorinated nucleoside derivative via a triazole bridge. The structure is enclosed in brackets with a subscript 'm'.
D-ADC2-2	 Chemical structure of D-ADC2-2, showing a 33B conjugate linked to a fluorinated nucleoside derivative via a triazole bridge. The structure is enclosed in brackets with a subscript 'm'.

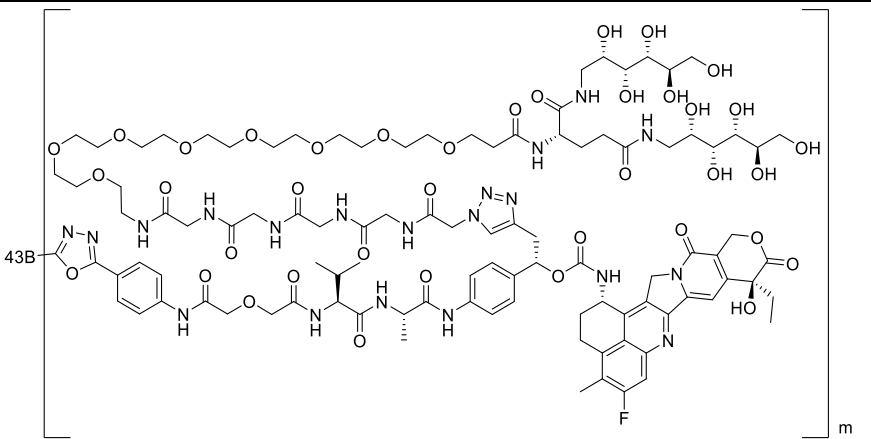
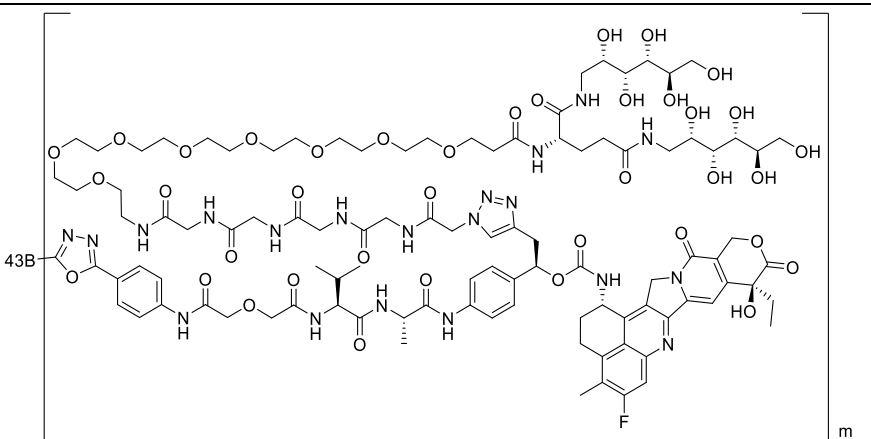
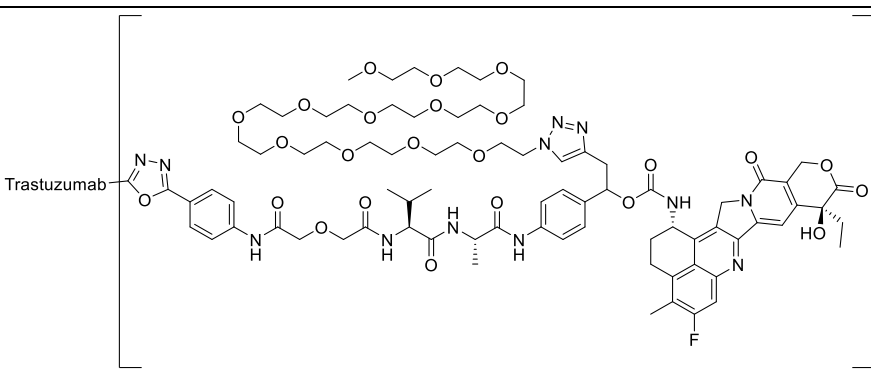
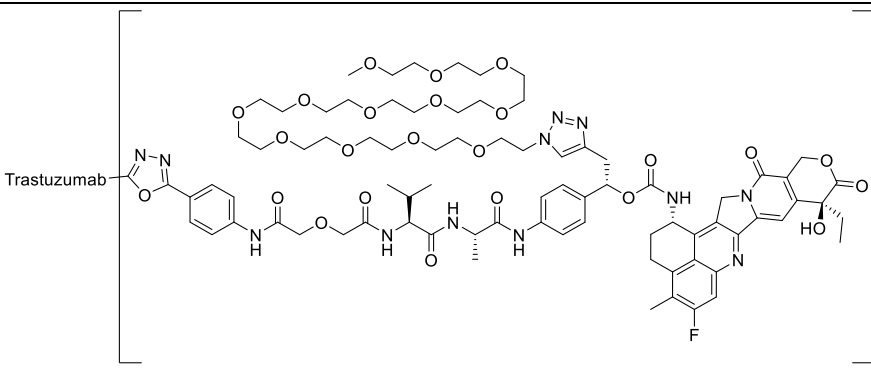
B-ADC2	
B-ADC2-1	
B-ADC2-2	
F-ADC7	

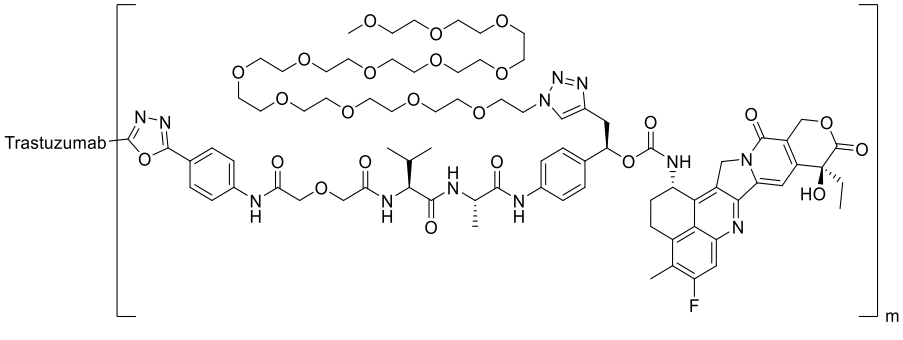
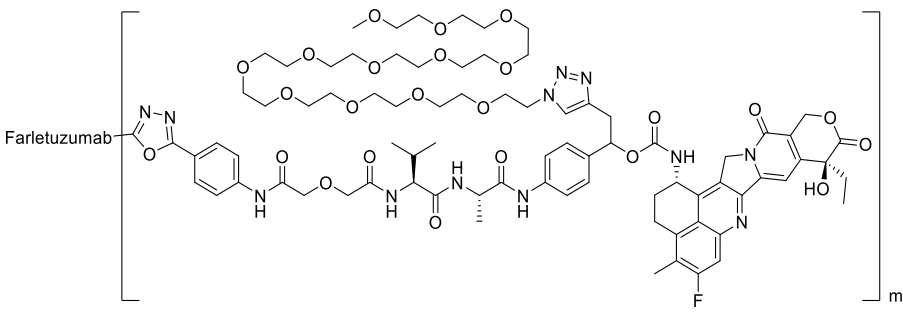
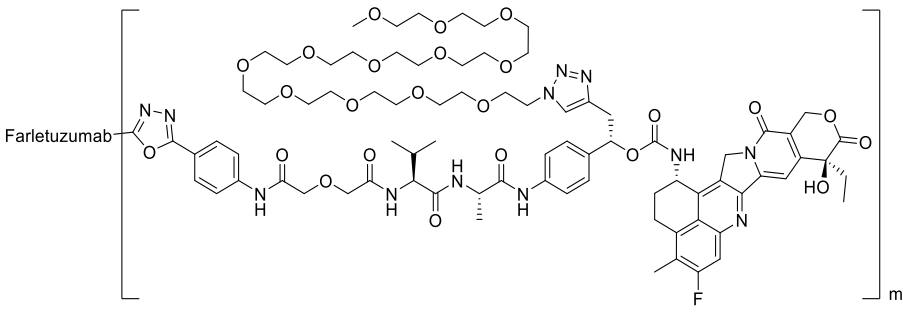
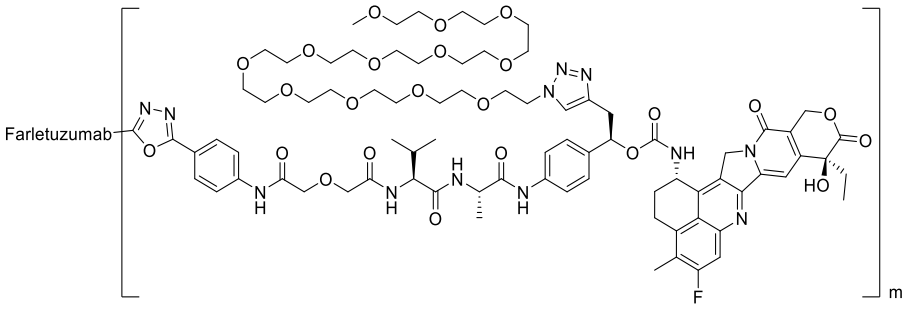
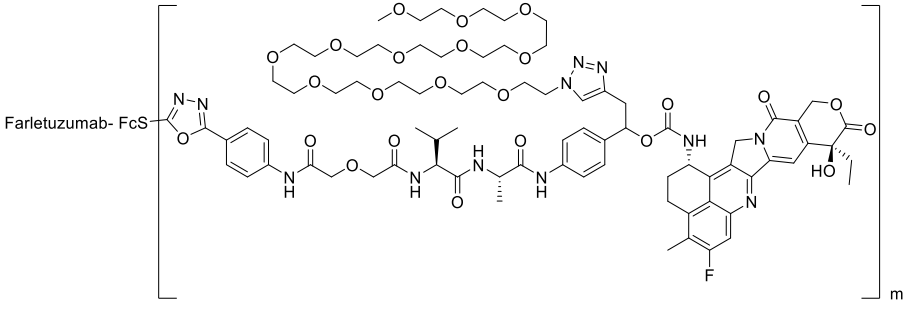
F-ADC7-1	Farletuzumab 
F-ADC7-2	Farletuzumab 
D-ADC7	33B 
D-ADC7-1	33B 

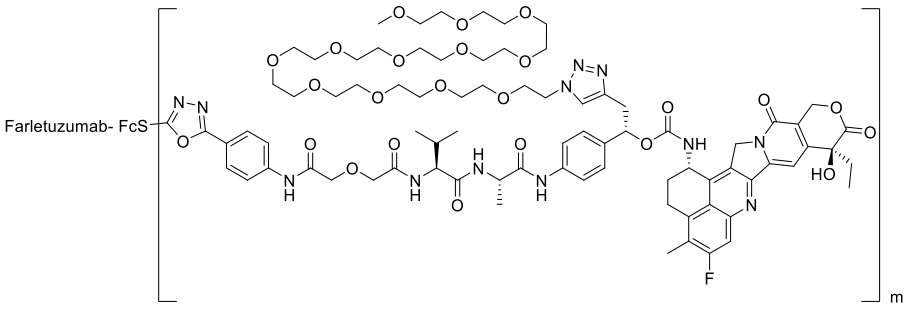
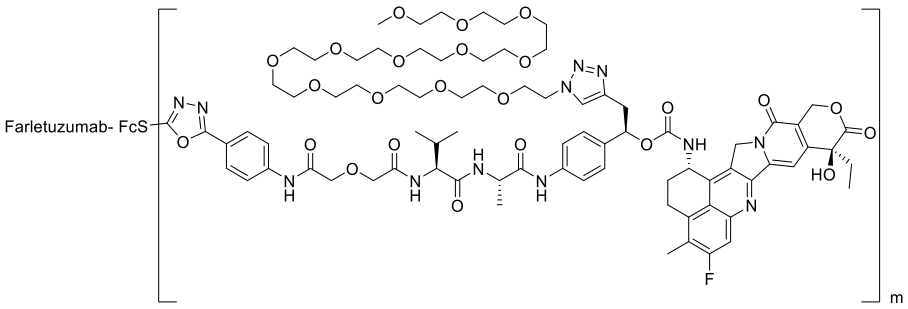
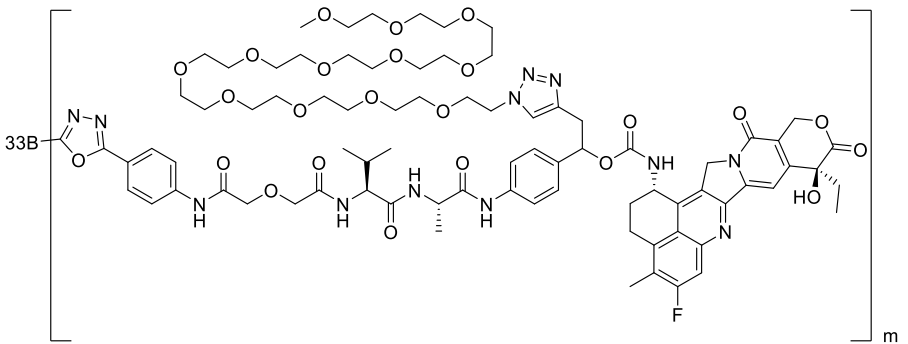
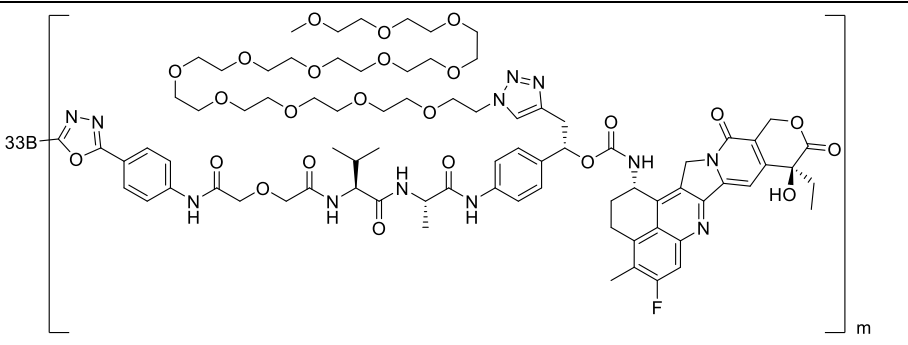
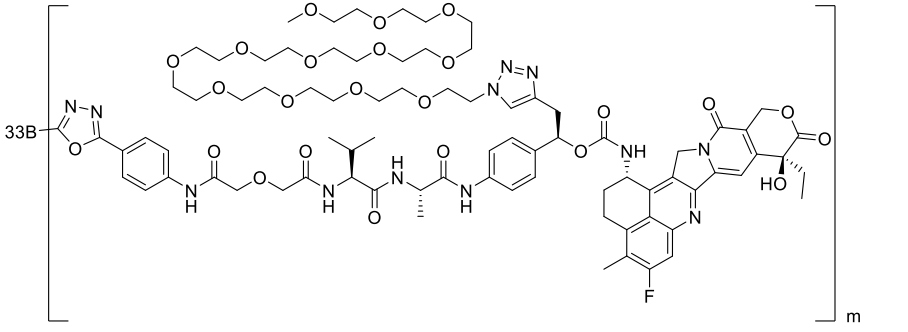
D-ADC7-2	
B-ADC7	
B-ADC7-1	
B-ADC7-2	

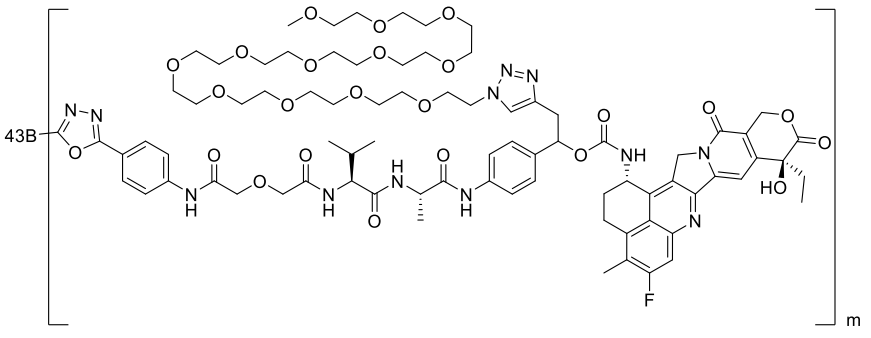
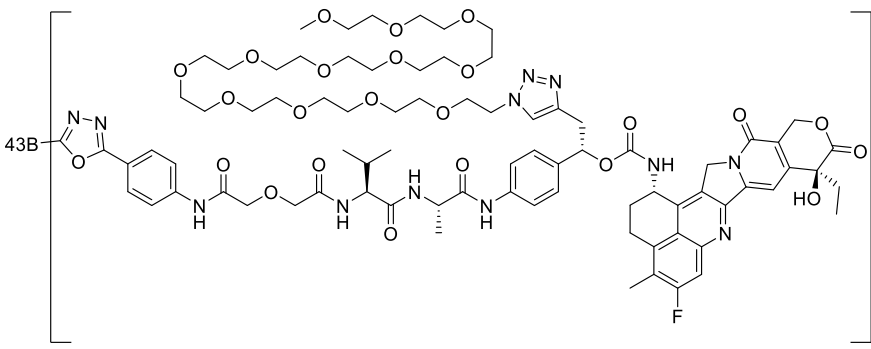
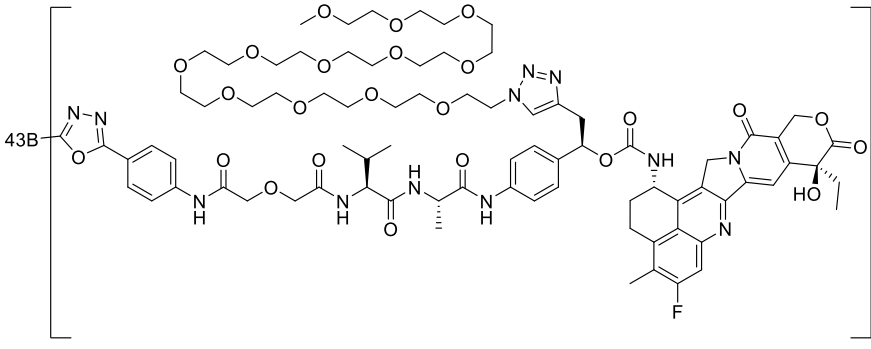
F-ADC12	 Chemical structure of F-ADC12, showing a Farletuzumab antibody (labeled "Farletuzumab") linked via a linker to a fluorinated quinoline derivative. The linker consists of a long poly(ethylene glycol) (PEG) chain connected to a series of amide bonds. The quinoline moiety is substituted with a fluorine atom (F) and a hydroxyl group (OH). The structure is enclosed in brackets with a subscript "m".
F-ADC12-1	 Chemical structure of F-ADC12-1, showing a Farletuzumab antibody (labeled "Farletuzumab") linked via a linker to a fluorinated quinoline derivative. The linker consists of a long poly(ethylene glycol) (PEG) chain connected to a series of amide bonds. The quinoline moiety is substituted with a fluorine atom (F) and a hydroxyl group (OH). The structure is enclosed in brackets with a subscript "m".
F-ADC12-2	 Chemical structure of F-ADC12-2, showing a Farletuzumab antibody (labeled "Farletuzumab") linked via a linker to a fluorinated quinoline derivative. The linker consists of a long poly(ethylene glycol) (PEG) chain connected to a series of amide bonds. The quinoline moiety is substituted with a fluorine atom (F) and a hydroxyl group (OH). The structure is enclosed in brackets with a subscript "m".
D-ADC12	 Chemical structure of D-ADC12, showing a Farletuzumab antibody (labeled "33B") linked via a linker to a fluorinated quinoline derivative. The linker consists of a long poly(ethylene glycol) (PEG) chain connected to a series of amide bonds. The quinoline moiety is substituted with a fluorine atom (F) and a hydroxyl group (OH). The structure is enclosed in brackets with a subscript "m".

D-ADC12- 1	
D-ADC12- 2	
B-ADC12	

B-ADC12-1	 Chemical structure of B-ADC12-1, a conjugate consisting of a long poly(ethylene glycol) (PEG) linker chain. The linker is terminated at one end by a 43B group (a 1,2,4-triazole ring) and at the other end by a fluorinated benzimidazole moiety. The structure is shown within brackets with a subscript 'm'.
B-ADC12-2	 Chemical structure of B-ADC12-2, a conjugate consisting of a long poly(ethylene glycol) (PEG) linker chain. The linker is terminated at one end by a 43B group (a 1,2,4-triazole ring) and at the other end by a fluorinated benzimidazole moiety. The structure is shown within brackets with a subscript 'm'.
T-ADC55	 Chemical structure of T-ADC55, a conjugate consisting of a long poly(ethylene glycol) (PEG) linker chain. The linker is terminated at one end by a Trastuzumab antibody (labeled 43B) and at the other end by a fluorinated benzimidazole moiety. The structure is shown within brackets with a subscript 'm'.
T-ADC55-1	 Chemical structure of T-ADC55-1, a conjugate consisting of a long poly(ethylene glycol) (PEG) linker chain. The linker is terminated at one end by a Trastuzumab antibody (labeled 43B) and at the other end by a fluorinated benzimidazole moiety. The structure is shown within brackets with a subscript 'm'.

T-ADC55- 2	
F-ADC55	
F-ADC55- 1	
F-ADC55- 2	
FS-ADC55	

FS- ADC55-1	 Chemical structure of FS-ADC55-1, a Farletuzumab-FCs conjugate. The structure shows a Farletuzumab antibody (FcS) linked via a triazole ring to a linker containing a poly(ethylene glycol) (PEG) chain and a fluorinated pyridine moiety. The linker is connected to a fluorinated pyridine moiety, which is further linked to a fluorinated pyridine moiety. The structure is enclosed in brackets with a subscript 'm'.
FS- ADC55-2	 Chemical structure of FS-ADC55-2, a Farletuzumab-FCs conjugate. The structure shows a Farletuzumab antibody (FcS) linked via a triazole ring to a linker containing a poly(ethylene glycol) (PEG) chain and a fluorinated pyridine moiety. The linker is connected to a fluorinated pyridine moiety, which is further linked to a fluorinated pyridine moiety. The structure is enclosed in brackets with a subscript 'm'.
D-ADC55	 Chemical structure of D-ADC55, a Farletuzumab-FCs conjugate. The structure shows a Farletuzumab antibody (FcS) linked via a triazole ring to a linker containing a poly(ethylene glycol) (PEG) chain and a fluorinated pyridine moiety. The linker is connected to a fluorinated pyridine moiety, which is further linked to a fluorinated pyridine moiety. The structure is enclosed in brackets with a subscript 'm'.
D-ADC55- 1	 Chemical structure of D-ADC55-1, a Farletuzumab-FCs conjugate. The structure shows a Farletuzumab antibody (FcS) linked via a triazole ring to a linker containing a poly(ethylene glycol) (PEG) chain and a fluorinated pyridine moiety. The linker is connected to a fluorinated pyridine moiety, which is further linked to a fluorinated pyridine moiety. The structure is enclosed in brackets with a subscript 'm'.
D-ADC55- 2	 Chemical structure of D-ADC55-2, a Farletuzumab-FCs conjugate. The structure shows a Farletuzumab antibody (FcS) linked via a triazole ring to a linker containing a poly(ethylene glycol) (PEG) chain and a fluorinated pyridine moiety. The linker is connected to a fluorinated pyridine moiety, which is further linked to a fluorinated pyridine moiety. The structure is enclosed in brackets with a subscript 'm'.

B-ADC55	
B-ADC55-1	
B-ADC55-2	

wherein m is selected from 2, 4, 6, and 8.

In some embodiments, the present disclosure provides use of the antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof for the manufacturing of a medicament for the treatment of a cancer. The cancer includes liver cancer, kidney cancer, lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), gastric cancer, esophageal cancer, oral cancer, urethral cancer, bladder cancer, colon cancer, rectal cancer, prostate cancer, breast cancer, ovarian cancer, pancreatic cancer, melanoma, hematological tumors or glioblastoma multiforme, lymphoma (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or recurrent anaplastic large cell lymphoma), cervical cancer, uterine cancer, endometrial cancer, salivary gland cancer, glioma, neuroblastoma, sarcoma, colorectal cancer, leukemia (e.g., acute lymphoblastic leukemia, acute myeloid leukemia, acute promyelocytic leukemia, chronic

myeloid leukemia, or chronic lymphocytic leukemia), bone cancer, skin cancer, thyroid cancer, etc.

In some embodiments, the present disclosure provides use of the antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof for the treatment of a cancer. The cancer includes liver cancer, kidney cancer, lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), gastric cancer, esophageal cancer, oral cancer, urethral cancer, bladder cancer, colon cancer, rectal cancer, prostate cancer, breast cancer, ovarian cancer, pancreatic cancer, melanoma, hematological tumors or glioblastoma multiforme, lymphoma (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or recurrent anaplastic large cell lymphoma), cervical cancer, uterine cancer, endometrial cancer, salivary gland cancer, glioma, neuroblastoma, sarcoma, colorectal cancer, leukemia (e.g., acute lymphoblastic leukemia, acute myeloid leukemia, acute promyelocytic leukemia, chronic myeloid leukemia, or chronic lymphocytic leukemia), bone cancer, skin cancer, thyroid cancer, etc.

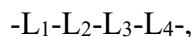
In some embodiments, the cancer is a tumor expressing HER2 (HER2+), DLL3 (DLL3+), FR α (FR α +), or B7H3 (B7H3+) on the surface of tumor cells.

In some embodiments, the present disclosure provides use of the antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof for the treatment of a cancer. The cancer is preferably a cancer associated with abnormal expression of FR α , DLL3, B7H3, or HER2. The cancer associated with abnormal expression of FR α includes lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), breast cancer, ovarian cancer, cervical cancer, uterine cancer, endometrial cancer, etc. The cancer associated with abnormal expression of DLL3 includes lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), etc. The cancer associated with abnormal expression of B7H3 includes lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), colon cancer, rectal cancer, prostate cancer, pancreatic cancer, breast cancer, ovarian cancer, etc. The cancer associated with abnormal expression of HER2 includes lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), breast cancer, ovarian cancer, endometrial cancer, gastric cancer, prostate cancer, etc.

In some embodiments, the present disclosure provides a pharmaceutical composition, which comprises the antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically

acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof, and one or more pharmaceutically acceptable auxiliary materials.

In some embodiments, the present disclosure provides a linker represented by the following formula for use in obtaining an antibody-drug conjugate formed by linking a drug to an antibody via the linker:



wherein the left terminus is a linkage site to the antibody, the right terminus is a linkage site to the anti-tumor compound, and L_1 , L_2 , L_3 , and L_4 are as defined in formula (I).

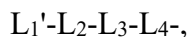
In another aspect of the present disclosure, provided is a linker-drug compound represented by formula (II), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:

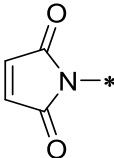
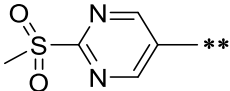
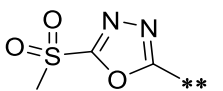


wherein L' is a linker moiety;

D is an amino-containing bioactive molecule or a pharmaceutically acceptable salt thereof, covalently linked to the linker moiety L' via an amine group in its molecular structure;

In some embodiments, the linker moiety L' is represented by the following formula:



wherein L_1' is selected from , , and , wherein $**$

represents linkage to L_2 ;

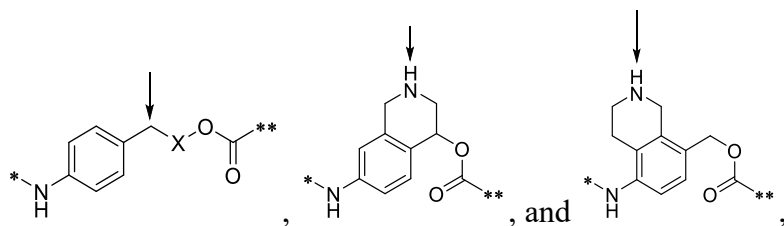
L_2 , L_3 , L_4 , and D are as defined in formula (I).

L_2 is a spacer, preferably selected from $-L_{2a}-C(O)-$, $-L_{2a}-L_{2b}-C(O)-$, $-L_{2a}-NH-C(O)-$, $-L_{2a}-C(O)-NH-$, $-L_{2a}-L_{2b}-NH-C(O)-$, $-L_{2a}-L_{2b}-C(O)-NH-$, $-L_{2a}-C(O)-NH-L_{2b}-C(O)-$, $-L_{2a}-NH-C(O)-L_{2b}-C(O)-$, $-L_{2a}-C(O)-NH-L_{2b}-C(O)-NH-$, $-L_{2a}-NH-C(O)-L_{2b}-NH-C(O)-$, $-L_{2a}-NR^1-SO_2-NH-C(O)-O-L_{2b}-C(O)-$, and $-L_{2a}-NR^1-SO_2-NH-C(O)-O-L_{2b}-NH-C(O)-$, wherein L_{2a} is selected from $-C_1-C_8$ alkylene-, $-C_1-C_8$ alkylene- C_3-C_8 cycloalkylene-, $-C_6-C_{14}$ arylene-, $-C_6-C_{14}$ arylene- C_1-C_8 alkylene-, $-(5- \text{ to } 6\text{-membered heteroarylene})-$, $-(5- \text{ to } 6\text{-membered heteroarylene})-C_1-C_8$ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably

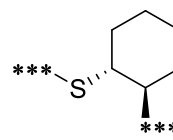
1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 8-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from halogen, C₁-C₆ alkyl, heteroalkyl having 1-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more (e.g., two or three) of N, O, and S; L_{2b} is selected from -C₁-C₈ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R¹ is selected from hydrogen, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, 3- to 8-membered heterocyclyl, C₁-C₆ haloalkyl, heteroalkyl having 2-8 atoms, C₆-C₁₄ aryl, and 5- to 6-membered heteroaryl, wherein the alkyl, heterocyclyl, heteroalkyl, aryl, and heteroaryl are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, heteroalkylene, or heteroarylene is selected from one or more of N, O, and S;

L₃ is a polypeptide sequence, preferably selected from a peptide residue consisting of 2-8 (e.g., 2, 3, 4, 5, 6, 7, or 8) natural or unnatural amino acids, wherein the amino acid is optionally further substituted with one or more substituents selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl;

L₄ is a hydrophilic group-modified self-immolative fragment, and the self-immolative fragment is selected from:

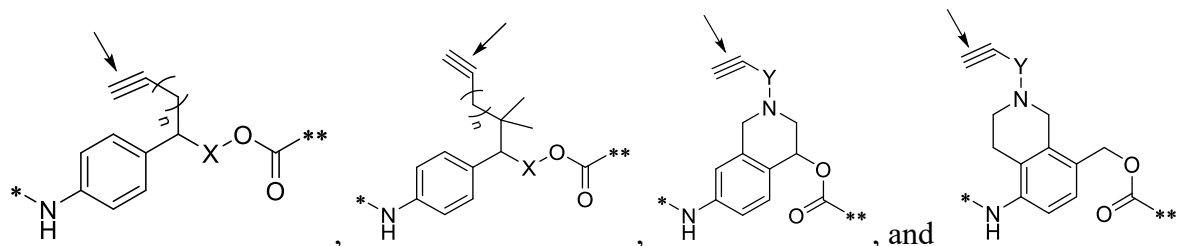


wherein * represents linkage to a carboxyl group of L₃ via an amide bond, ** represents linkage



to the amino group of the bioactive molecule D, X is absent or linkage to a carbon atom, **** represents linkage to an oxygen atom, and the arrow indicates a modification site of the hydrophilic group;

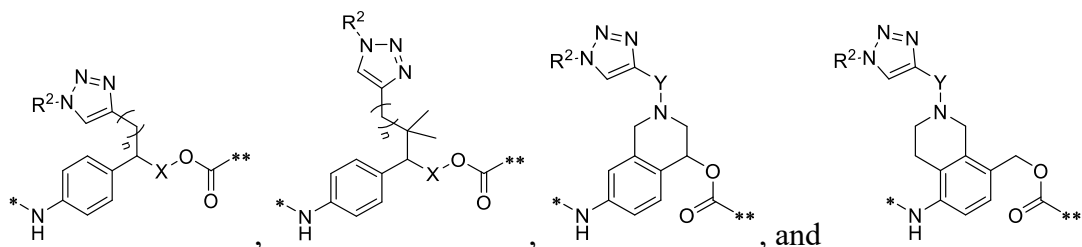
further preferably, the self-immolative fragment, prior to modification by the hydrophilic group, is selected from the following structures:



wherein Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6;

the hydrophilic group has at least one azido group and comprises a polyethylene glycol group, a poly-natural or unnatural amino acid group, a monosaccharide, an oligosaccharide, or a polysaccharide, or a combination thereof;

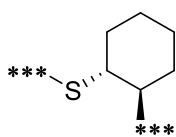
preferably, L₄ is selected from:



wherein * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule D;

R² is a hydrophilic fragment, preferably selected from linear or branched heteroalkyl containing 4-50 (preferably 4-24, more preferably 6-24, and most preferably 8-24, e.g., 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) (OCH₂CH₂) structural units, a peptide chain containing 4-50 (preferably 4-24, more preferably 8-24, and most preferably 10-24, e.g., 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) proteinogenic amino acids (e.g., glycines) or non-proteinogenic amino acids (e.g., sarcosines),

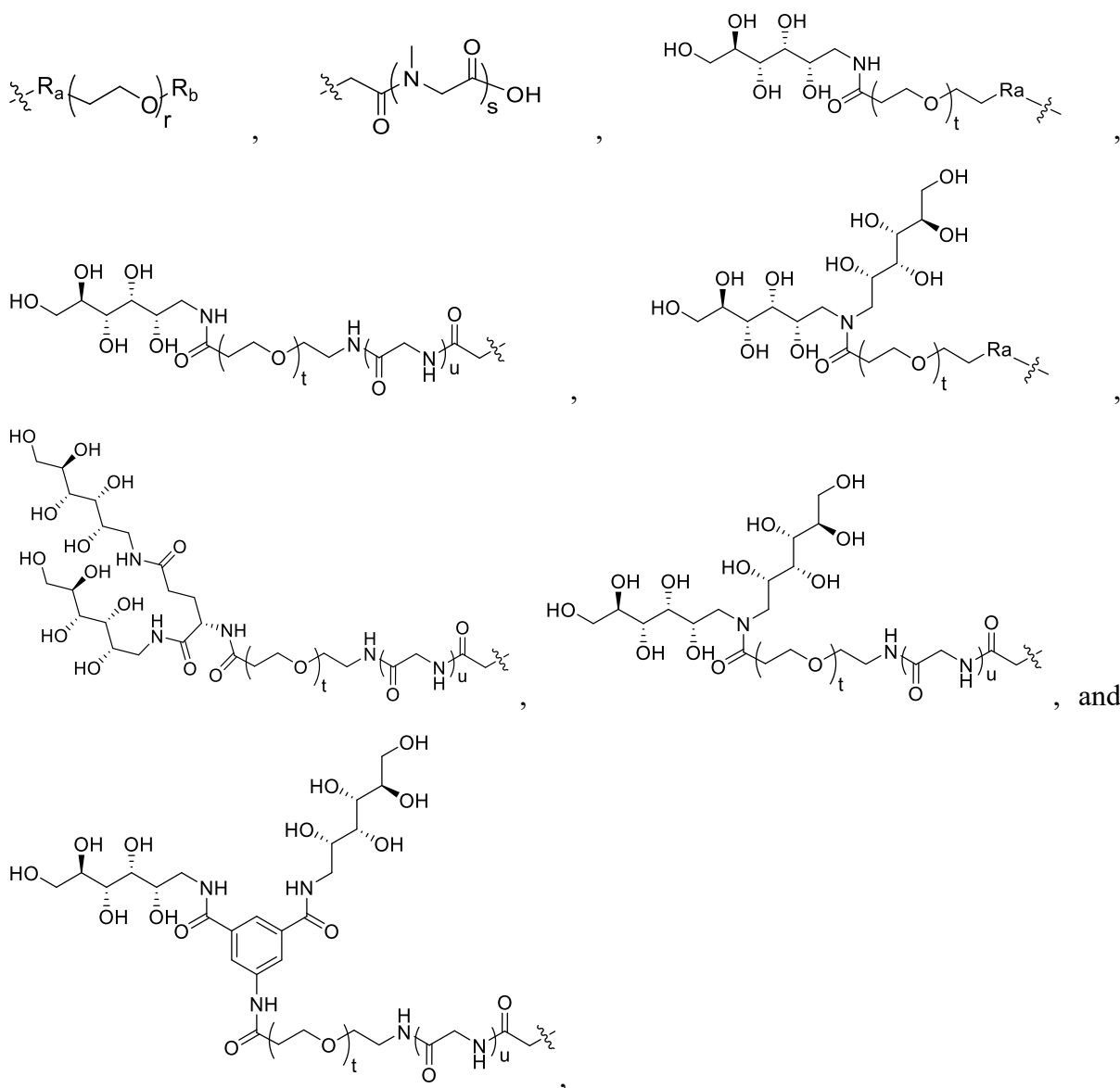
and linear or branched heteroalkyl containing a monosaccharide, an oligosaccharide, or a



polysaccharide; X is absent or

polysaccharide; X is absent or ********, ******* represents linkage to a carbon atom, and ******** represents linkage to an oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-24 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) -OCH₂CH₂- structural units; n is an integer from 0 to 6 (e.g., 0, 1, 2, 3, 4, 5, or 6).

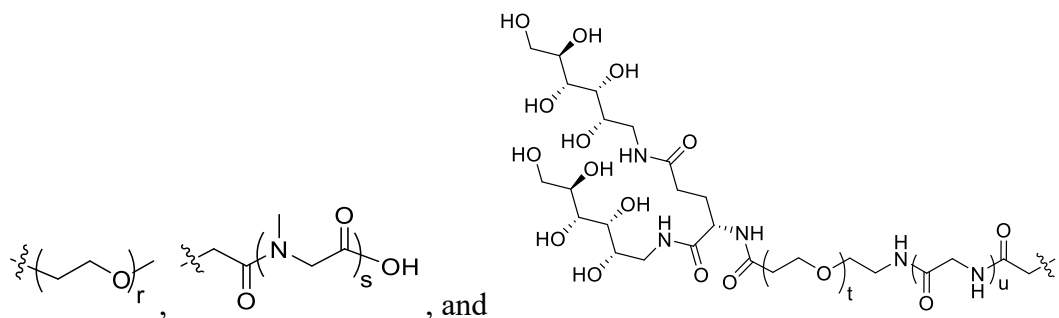
In some embodiments, R^2 is selected from the following structures:



wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50); R_a is selected from a

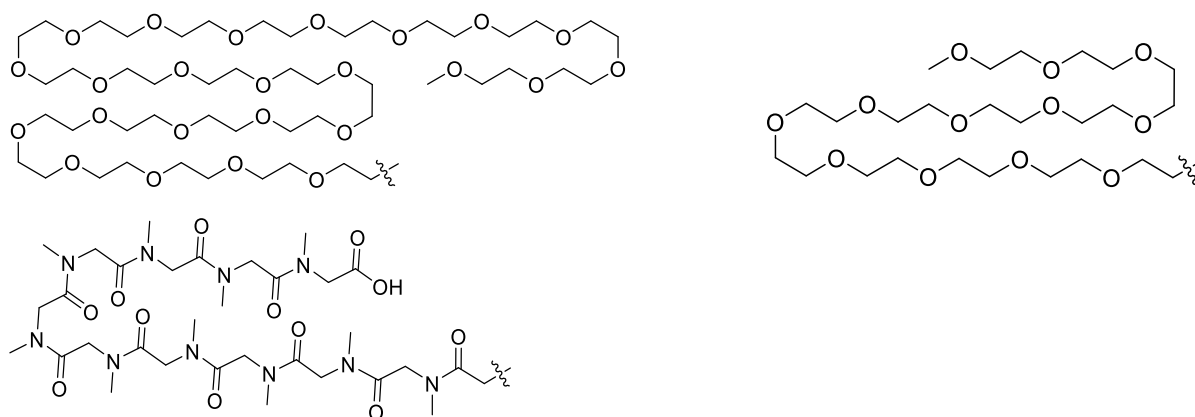
bond and C₁-C₃ alkylene, such as methylene, ethylidene, *n*-propylidene, or isopropylidene; R_b is selected from C₁-C₃ alkyl, such as methyl, ethyl, *n*-propyl, or isopropyl.

In some embodiments, R² is selected from the following structures:

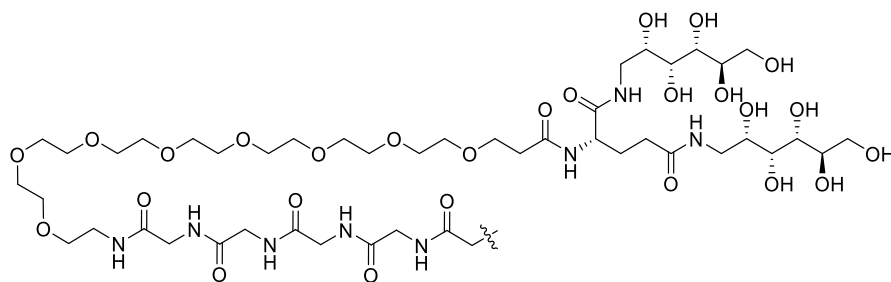


- 5 wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50).

In some embodiments, R² is selected from the following structures:



10



In some embodiments, Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or -C₁-C₆ alkylene-(OCH₂CH₂)_v-, wherein v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

- 15 In some embodiments, Y is C₁-C₃ alkylene or -R³-C(O)-, wherein R³ is C₁-C₃ alkylene or -C₁-C₃ alkylene-(OCH₂CH₂)_v-, wherein v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, Y is methylene, ethylidene, *n*-propylidene, isopropylidene, or -R³-

C(O)-, wherein R^3 is methylene-(OCH₂CH₂)_v-, ethylidene-(OCH₂CH₂)_v-, *n*-propylidene-(OCH₂CH₂)_v-, or isopropylidene-(OCH₂CH₂)_v-, wherein *v* is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, Y is selected from -CH₂-(OCH₂CH₂)₄C(O)-.

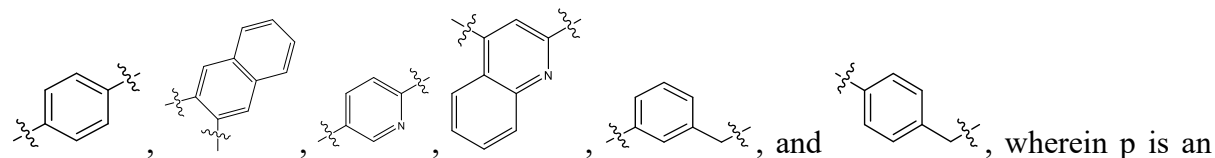
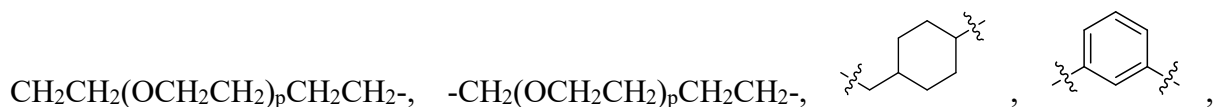
- 5 In some embodiments, L₂ is selected from -L_{2a}-C(O)-, -L_{2a}-NH-C(O)-L_{2b}-C(O)-, and -L_{2a}-NR¹-SO₂-NH-C(O)-O-L_{2b}-C(O)-, wherein L_{2a} is selected from -C₁-C₆ alkylene-, -C₁-C₆ alkylene-C₃-C₆ cycloalkylene-, -C₆-C₁₀ arylene-, -C₆-C₁₀ arylene-C₁-C₆ alkylene-, -(5- to 6-membered heteroarylene)-, -(5- to 6-membered heteroarylene)-C₁-C₆ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 6-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from halogen, C₁-C₃ alkyl, heteroalkyl having 1-3 atoms, C₁-C₃ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₆ cycloalkyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more (e.g., two or three) of N, O, and S; L_{2b} is selected from -C₁-C₆ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R¹ is selected from hydrogen, C₁-C₃ alkyl, C₃-C₆ cycloalkyl, 3- to 6-membered heterocyclyl, C₁-C₃ haloalkyl, heteroalkyl having 2-6 atoms, C₆-C₁₀ aryl, and 5- to 6-membered heteroaryl, wherein the alkyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents independently selected from C₁-C₃ alkyl, heteroalkyl having 2-3 atoms, C₁-C₃ alkoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, or heteroalkylene is selected from one or more (e.g., two or three) of N, O, and S.

In some embodiments, L₂ is selected from -L_{2a}-C(O)-, -L_{2a}-NH-C(O)-L_{2b}-C(O)-, and -L_{2a}-NR¹-

$\text{SO}_2\text{-NH-C(O)-O-L}_{2b}\text{-C(O)-}$, wherein L_{2a} is selected from methylene, ethylidene, *n*-propylidene, *n*-butylidene, *n*-pentylidene, *n*-hexylidene, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{C}_1\text{-C}_3$ alkylene-cyclohexylidene-, -phenylene-, -phenylene- $\text{C}_1\text{-C}_3$ alkylene-, -(5- to 6-membered heteroarylene)- $\text{C}_1\text{-C}_3$ alkylene-, linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and (linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms)-(3- to 6-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from halogen, methyl, ethyl, *n*-propyl, isopropyl, heteroalkyl having 1-3 atoms, methoxy, ethoxy, *n*-propoxy, isopropoxy, hydroxyl, amino, carboxyl or cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more (e.g., two or three) of N, O, and S; L_{2b} is selected from methylene, ethylidene, *n*-propylidene, *n*-butylidene, *n*-pentylidene, *n*-hexylidene, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50) atoms, and R^1 is selected from hydrogen, methyl, ethyl, *n*-propyl, isopropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 3- to 6-membered heterocyclyl, $-\text{CF}_3$, $-\text{CF}_2\text{CF}_3$, heteroalkyl having 2-3 atoms, phenyl, and 5- to 6-membered heteroaryl, wherein the alkyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl are each optionally substituted with one or more substituents independently selected from methyl, ethyl, *n*-propyl, isopropyl, heteroalkyl having 2-3 atoms, methoxy, ethoxy, *n*-propoxy, isopropoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, or heteroalkylene is selected from one or more (e.g., two or three) of N, O, and S.

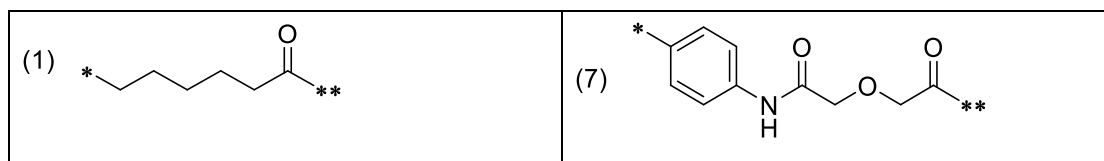
In some embodiments, L_{2a} is selected from $-\text{C}_1\text{-C}_8$ alkylene-, $-\text{C}_1\text{-C}_8$ alkylene- $\text{C}_3\text{-C}_8$ cycloalkylene, $\text{C}_6\text{-C}_{14}$ arylene- $\text{C}_1\text{-C}_8$ alkylene, and linear or branched heteroalkylene having 1-

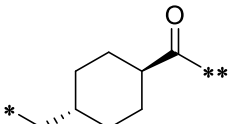
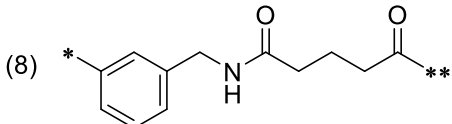
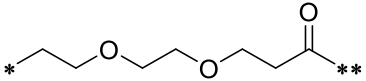
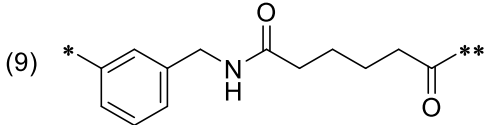
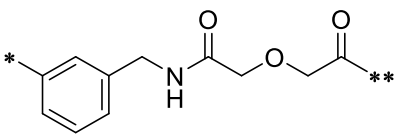
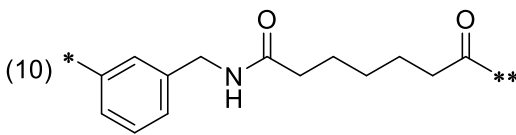
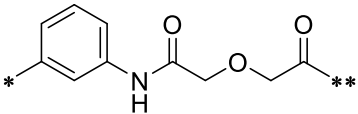
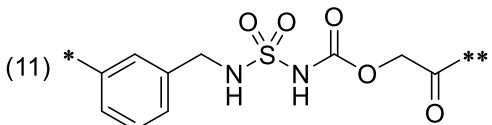
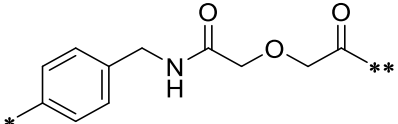
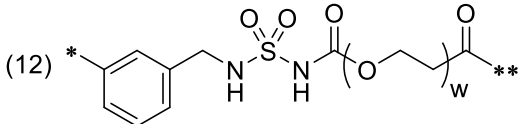
- 50 (preferably 1-20, more preferably 1-12, and most preferably 1-8) atoms, wherein the alkylene, cycloalkylene, arylene, and heteroalkylene are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl, the heteroalkylene or heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkylene or heteroalkyl is selected from one or more (e.g., two or three) of N, O, and S; L_{2b} is selected from -C₁-C₈ alkylene- and linear or branched heteroalkylene having 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8) atoms, and R¹ is selected from hydrogen, C₁-C₆ alkyl, heteroalkyl having 2-8 atoms, and C₆-C₁₄ aryl, wherein the alkyl, heteroalkyl, and aryl are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, amino, and carboxyl, the heteroalkyl contains 1-12 (preferably 1-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms, and the heteroatom in the heteroalkyl or heteroalkylene is selected from one or more (e.g., two or three) of N, O, and S.
- 15 In some embodiments, L_{2a} is selected from -CH₂CH₂CH₂CH₂CH₂-, -CH₂CH₂(OCH₂CH₂)_p-, -(OCH₂CH₂)_p-, -CH₂(OCH₂CH₂)_p-, -CH₂CH₂(OCH₂CH₂)_pCH₂-, -



- integer from 1 to 12 (preferably 2-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12); L_{2b} is selected from -CH₂OCH₂-, -CH₂CH₂OCH₂-, -CH₂CH₂OCH₂CH₂-, -CH₂O-, -CH₂CH₂O-, -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -(OCH₂CH₂)_q-, -CH₂CH₂(OCH₂CH₂)_q-, -CH₂(OCH₂CH₂)_q-, -CH₂CH₂(OCH₂CH₂)_qCH₂-, -CH₂CH₂(OCH₂CH₂)_qCH₂CH₂-, and -CH₂(OCH₂CH₂)_qCH₂CH₂-, and R¹ is selected from hydrogen, methyl, ethyl, *n*-propyl, isopropyl, and cyclopropyl, wherein q is an integer from 1 to 12 (preferably 2-8, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

In some embodiments, L₂ is selected from the following structures:

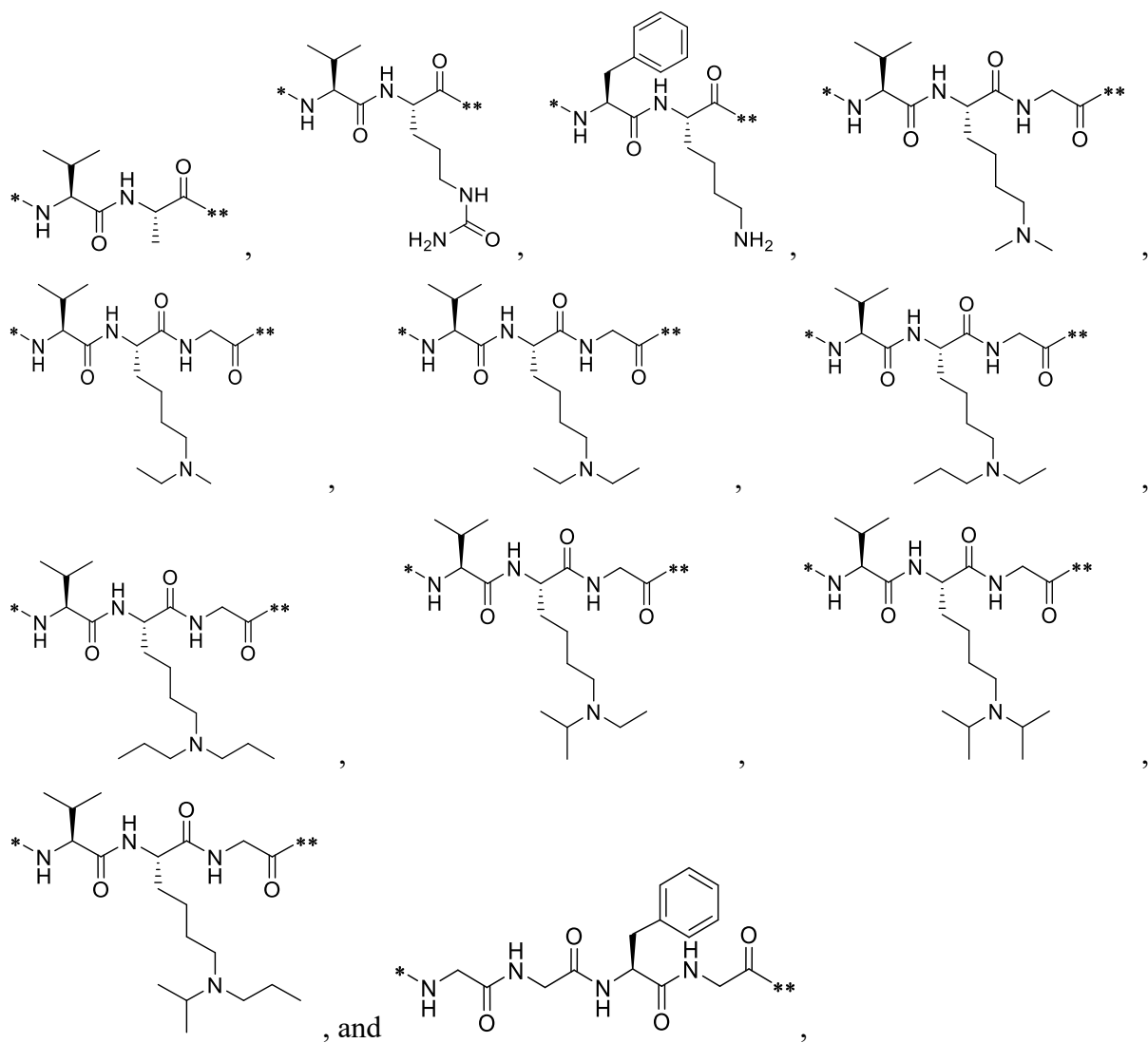


(2) 	(8) 
(3) 	(9) 
(4) 	(10) 
(5) 	(11) 
(6) 	(12) 

wherein w is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to L₁, and ** represents linkage to L₃.

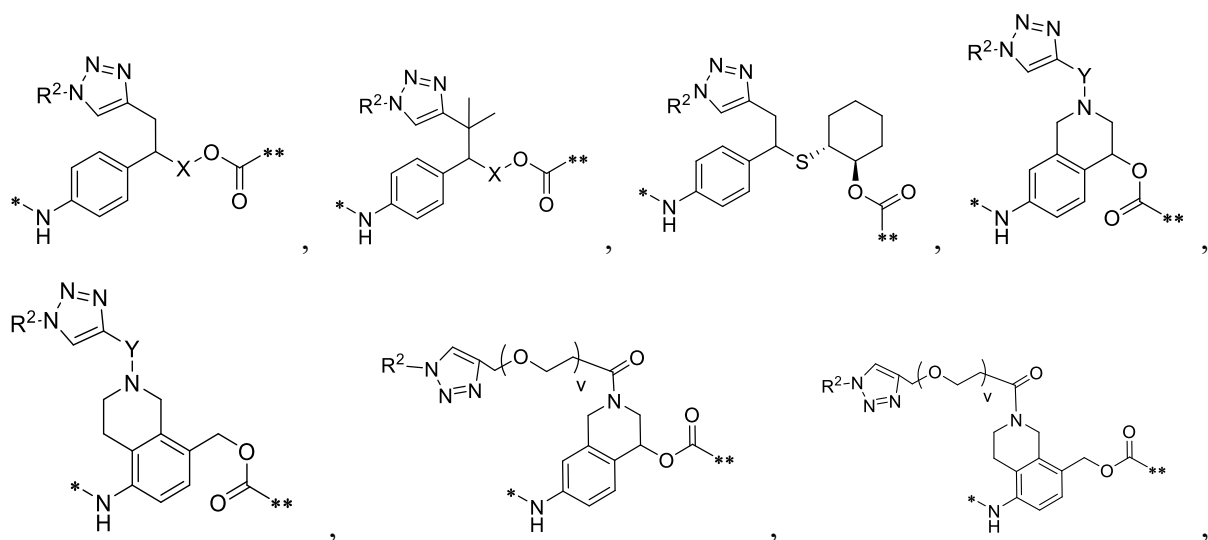
In some embodiments, L₃ is selected from a peptide residue formed from 2-8 amino acids selected from phenylalanine (F), glycine (G), valine (V), citrulline (Cit), glutamic acid (E), alanine (A), lysine (K), C₁-C₆ alkyl-substituted lysine (e.g., C₁-C₃ alkyl-substituted lysine, such as methyl-substituted lysine, ethyl-substituted lysine, *n*-propyl-substituted lysine, or isopropyl-substituted lysine), etc. For example, L₃ is: -ValCit-; -CitVal-; -AlaAla-; -AlaCit-; -CitAla-; -AsnCit-; -CitAsn-; -CitCit-; -ValGlu-; -GluVal-; -SerCit-; -CitSer-; -LysCit-; -CitLys-; -AspCit-; -CitAsp-; -AlaVal-; -ValAla-; -PheAla-; -AlaPhe-; -PheLys-; -LysPhe-; -ValLys-; -LysVal-; -AlaLys-; -LysAla-; -PheCit-; -CitPhe-; -LeuCit-; -CitLeu-; -IleCit-; -CitIle-; -PheArg-; -ArgPhe-; -CitTrp-; -TrpCit-; -AlaAlaAla-; -PhePheLys-; -LysPhePhe-; -DPhePheLys-; -DLysPhePhe-; -GlyPheLys-; -LysPheGly-; -GlyPheLeuGly-; -GlyLeuPheGly-; -GluValCit-; -AlaLeuAlaLeu-; -GlyGlyGly-; -GlyGlyGlyGly-; -GlyPheValGly-; -GlyValPheGly-; -GlyGlyPheGly-; or -GlyGlyValGly-.

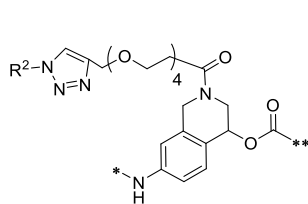
In some embodiments, L₃ is selected from the following structures:



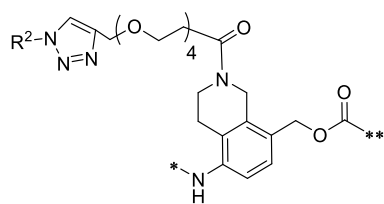
5 wherein * represents linkage to L₂, and ** represents linkage to L₄.

In some embodiments, L₄ is selected from:





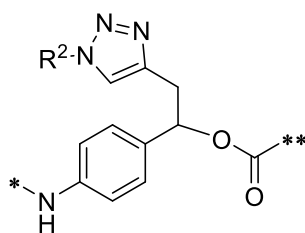
, and



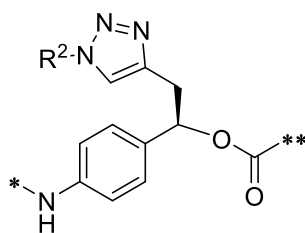
, wherein v is an integer selected

from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule D.

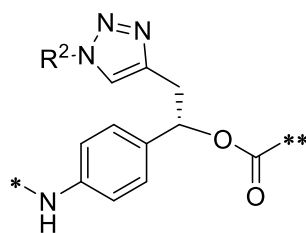
5 In some embodiments, L₄ is selected from:



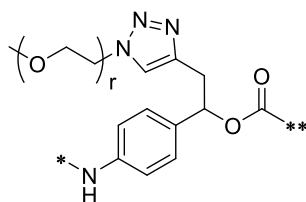
In some embodiments, L₄ is selected from:



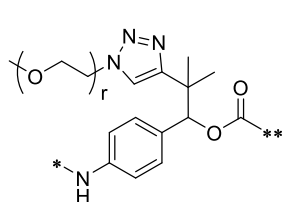
and



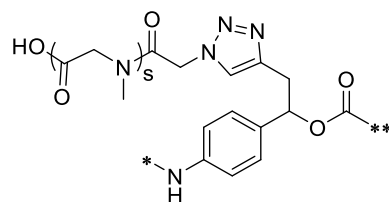
In some embodiments, L₄ is selected from:



,

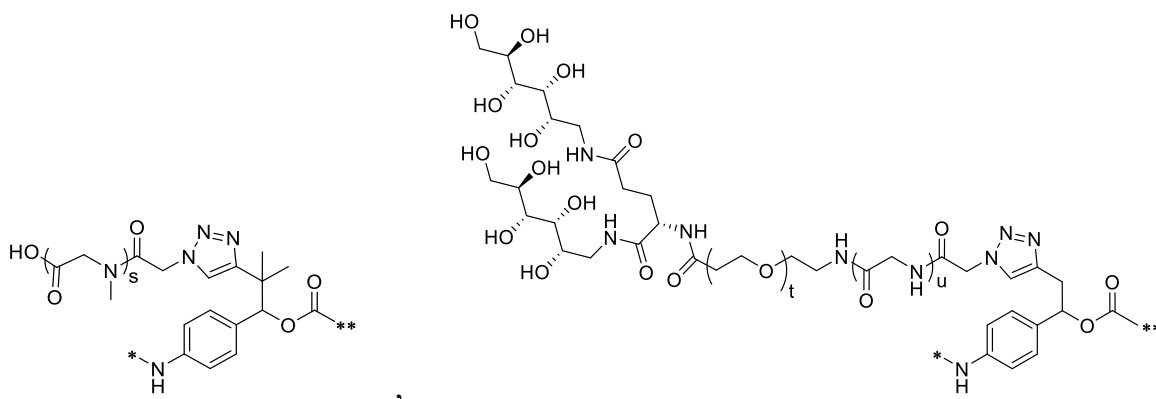


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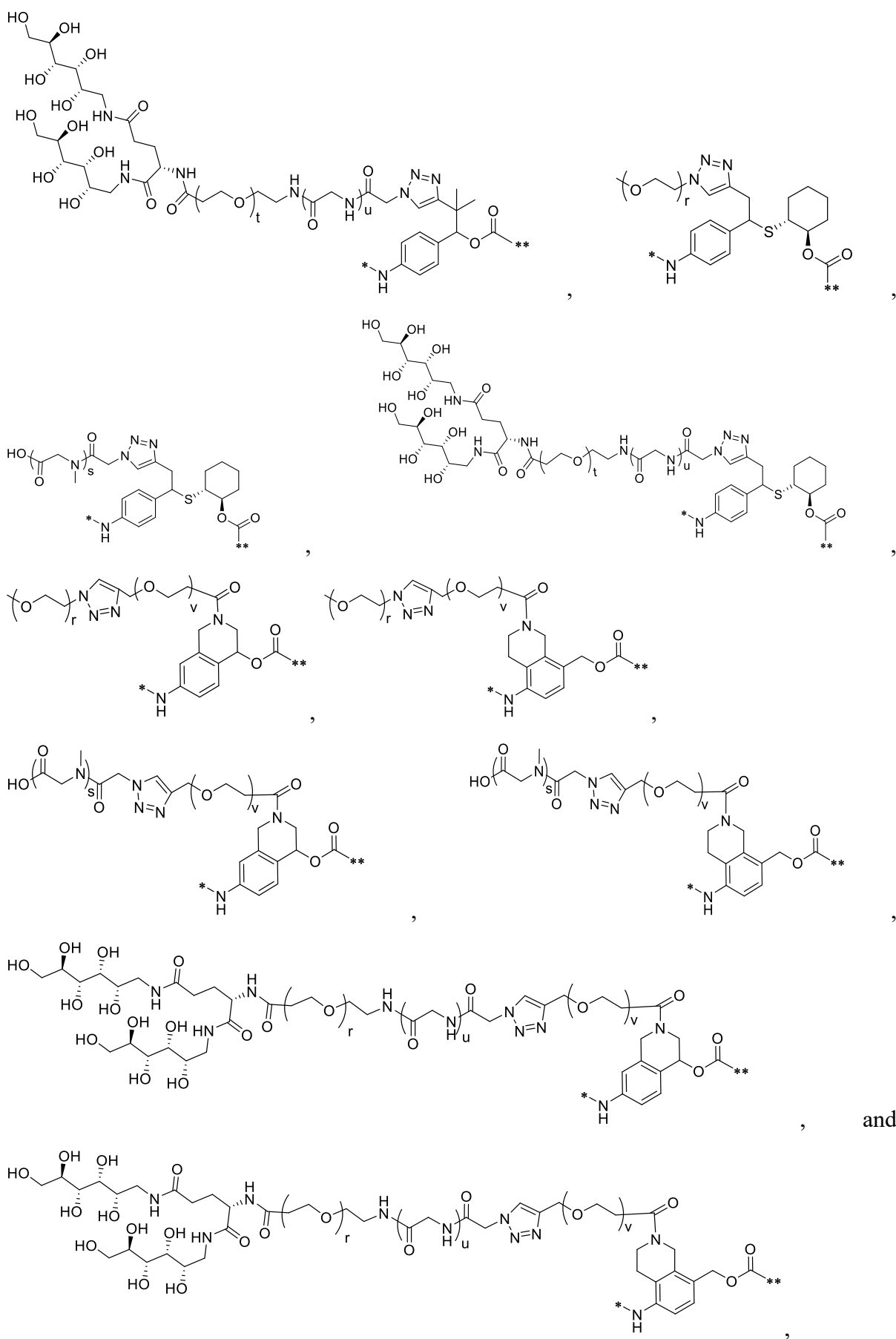
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10



,

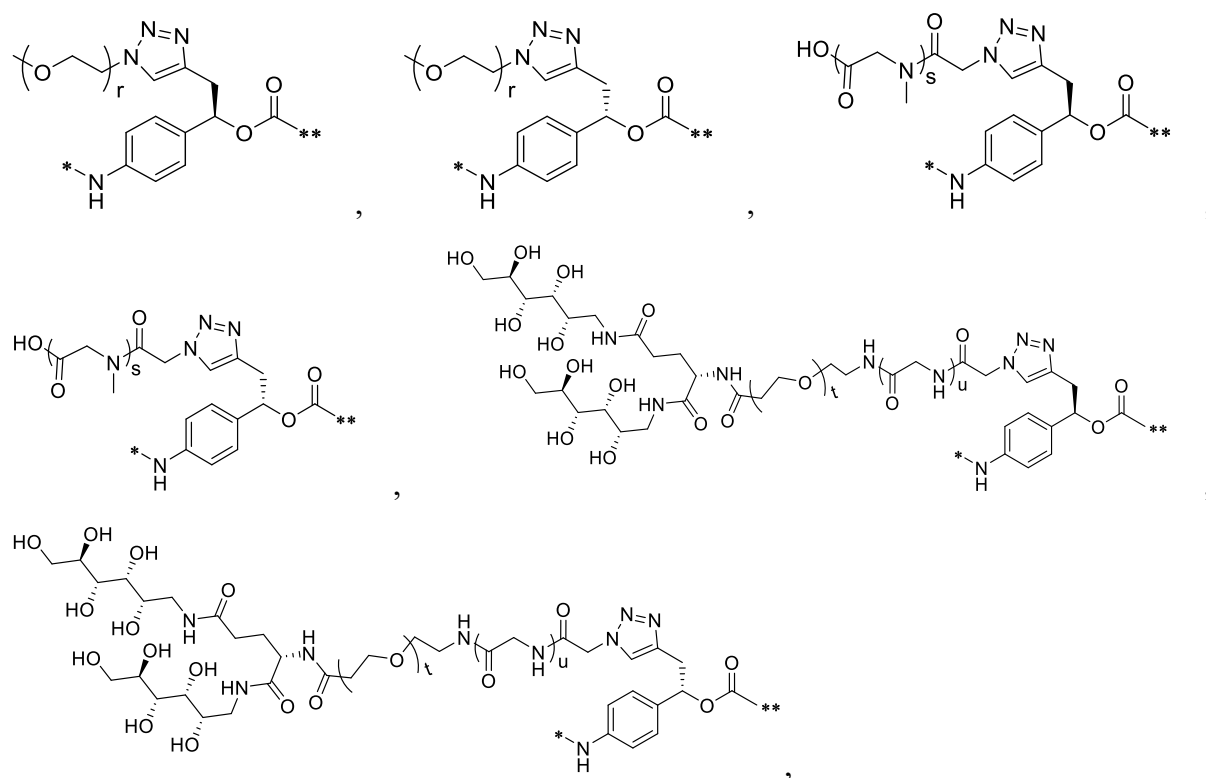
,



7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule

5 D.

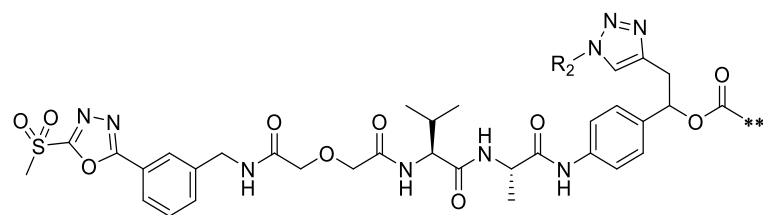
In some embodiments, L₄ is selected from:

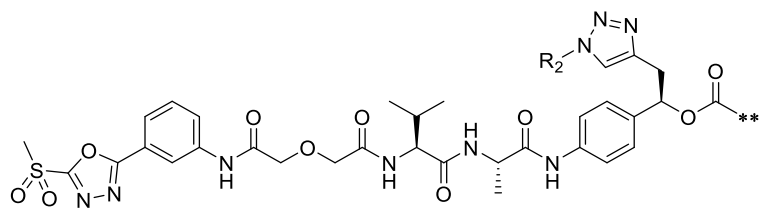
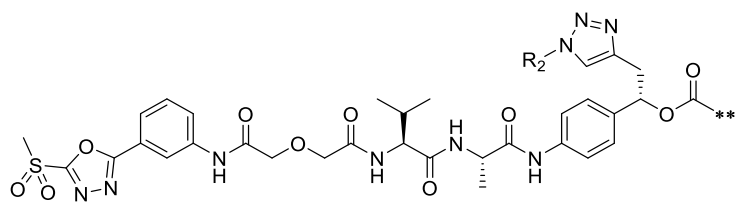
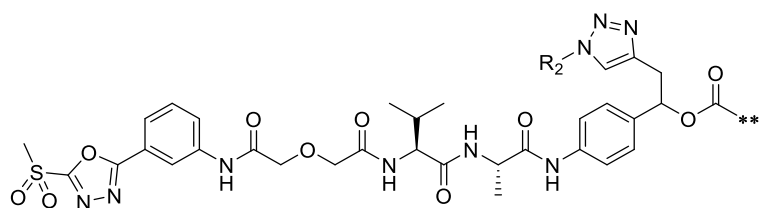
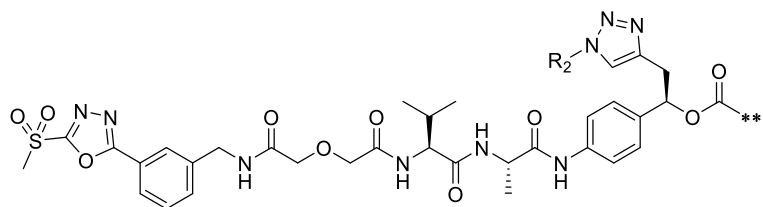
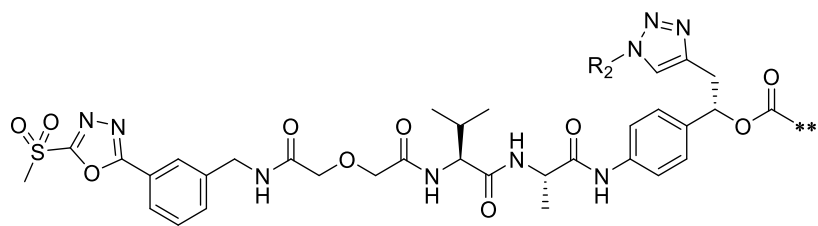


10 wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), v is an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule

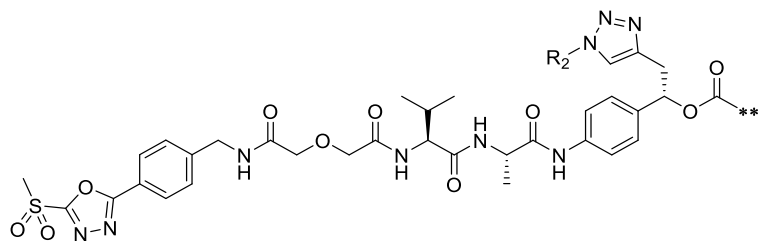
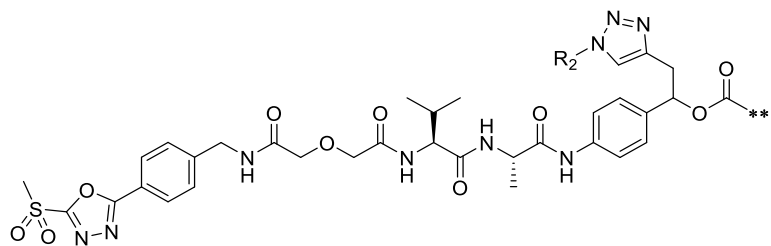
15 D.

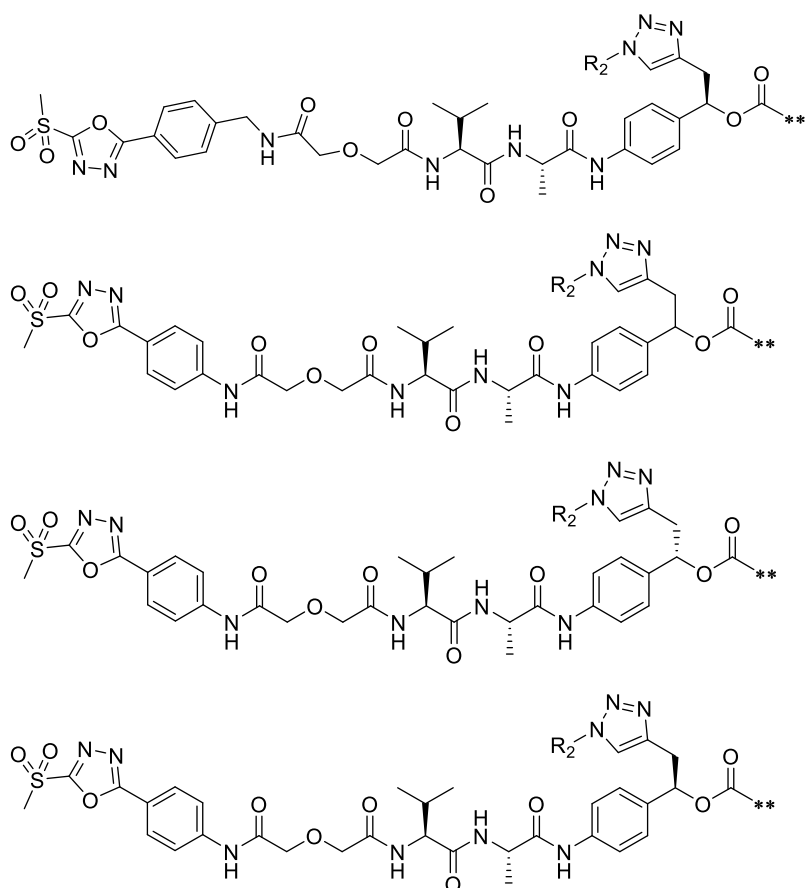
In some embodiments, L' is selected from the following structures:



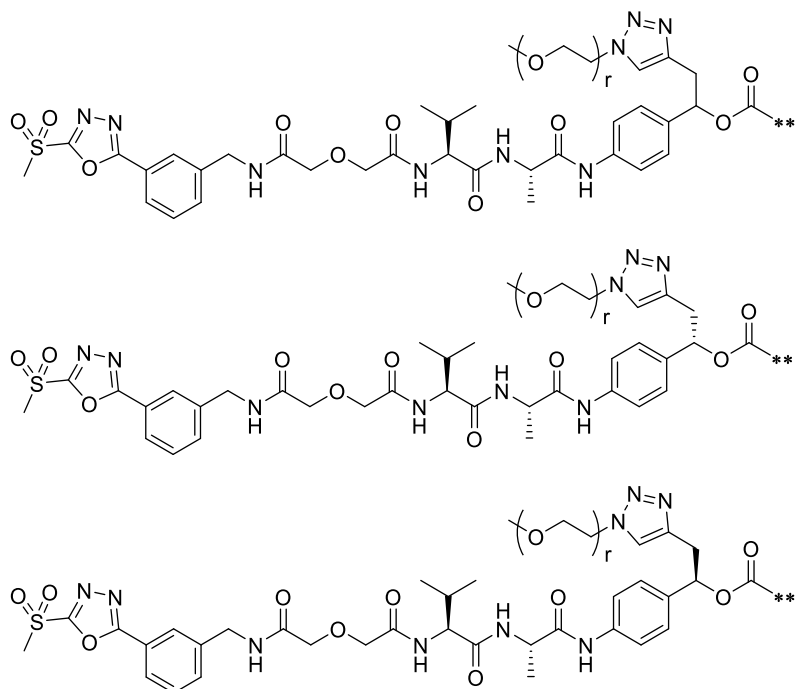


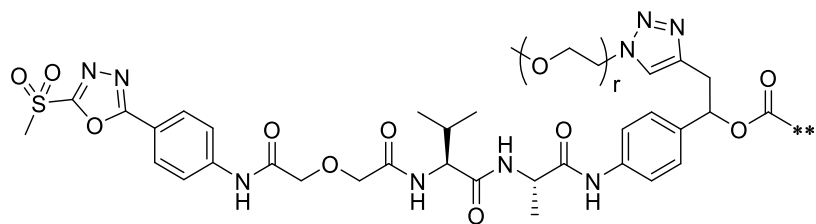
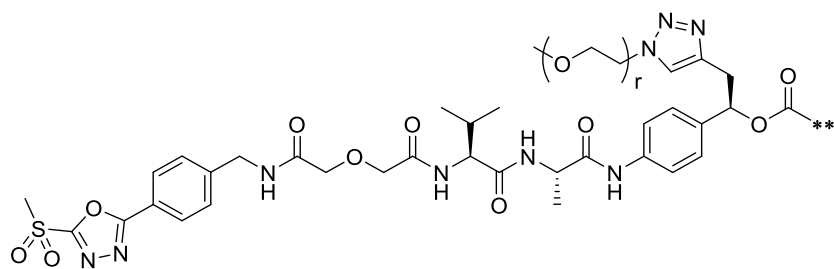
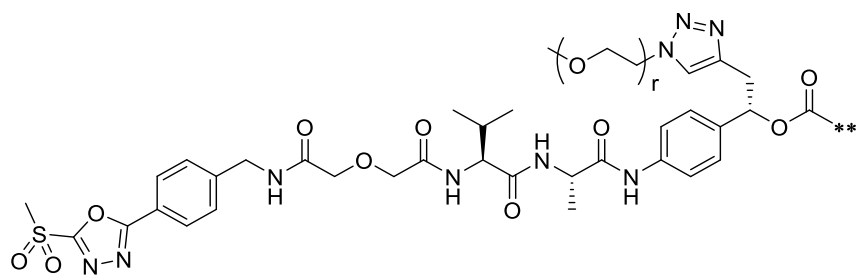
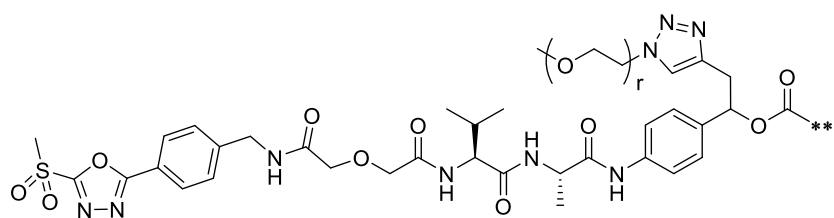
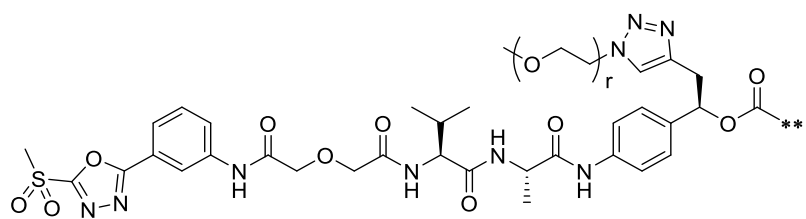
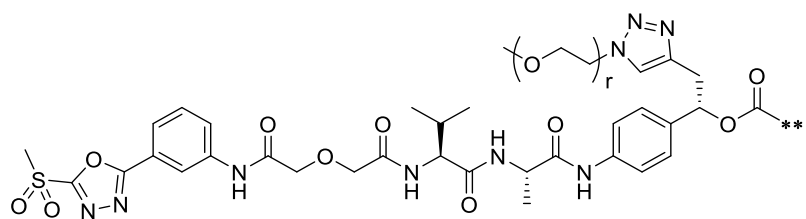
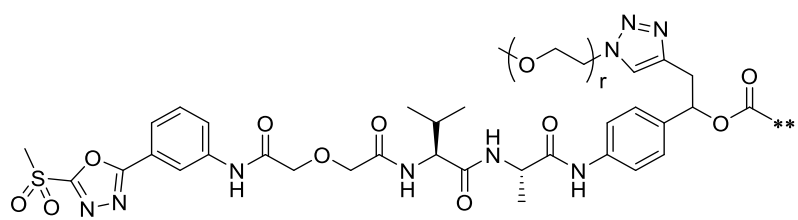
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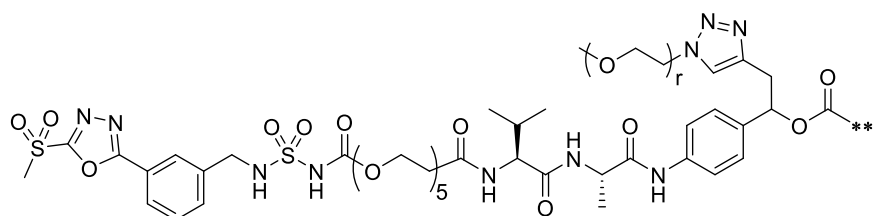
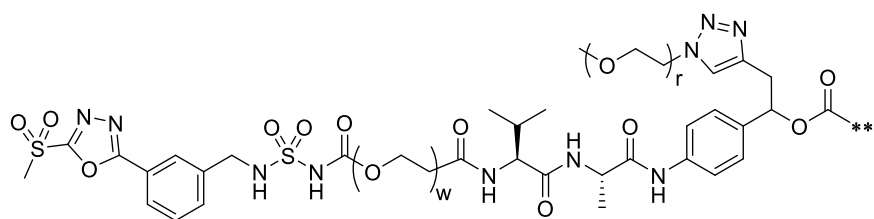
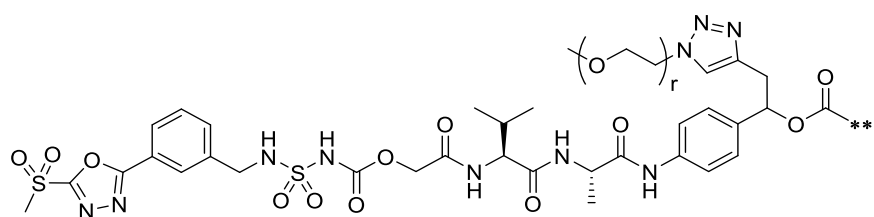
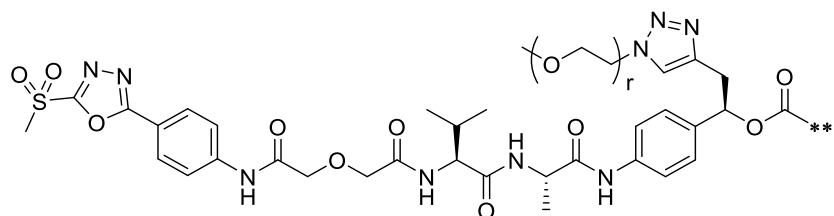
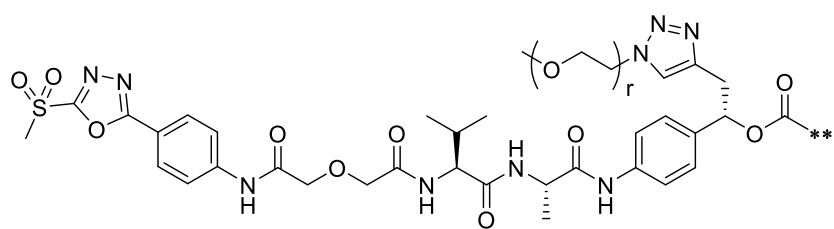




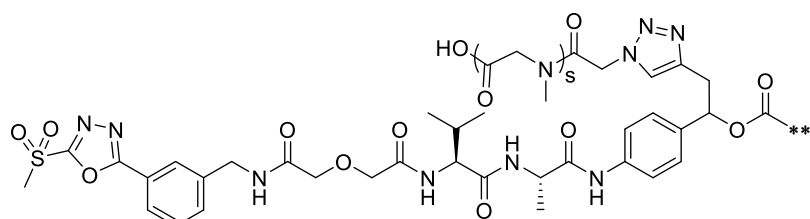
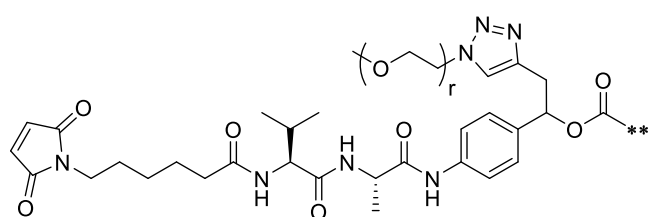
5 In some embodiments, L' is selected from the following structures:

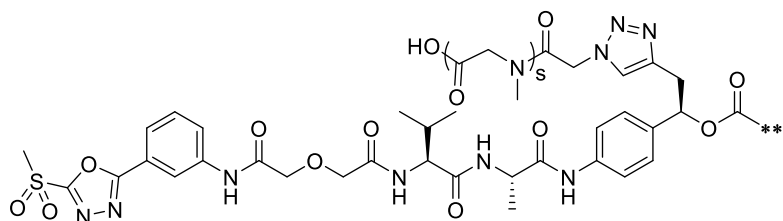
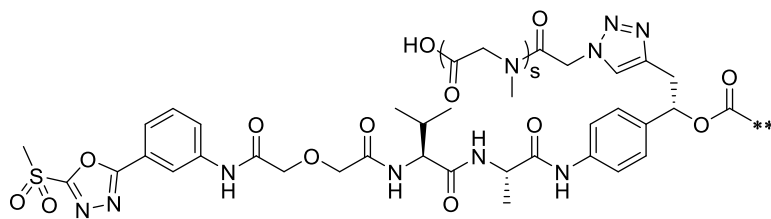
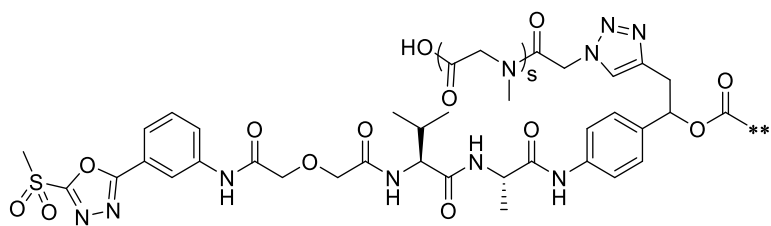
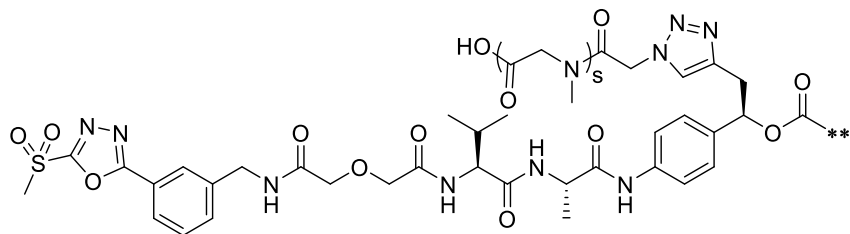
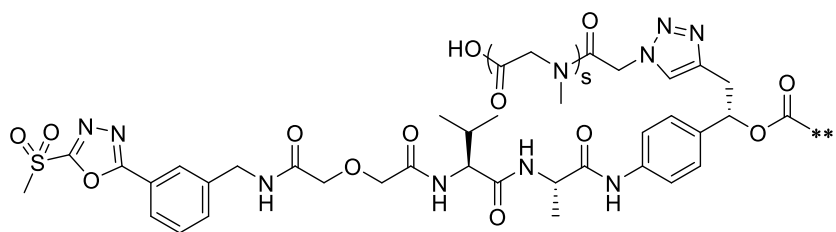




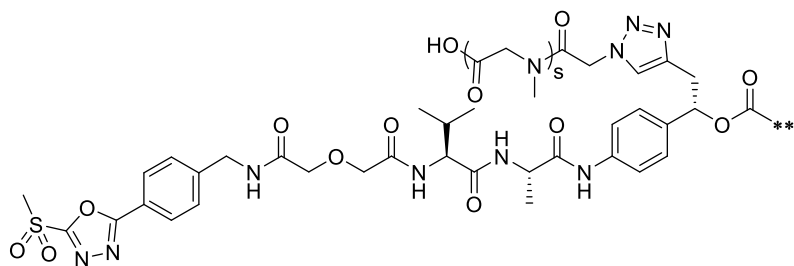
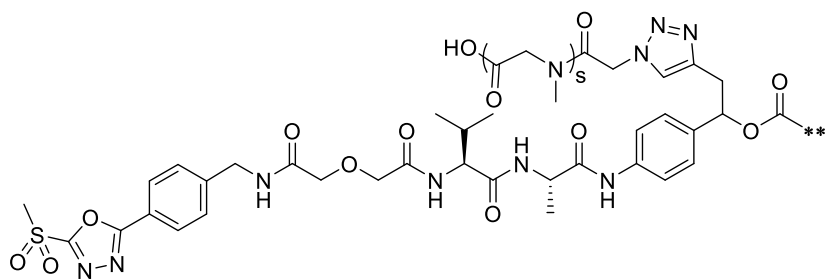


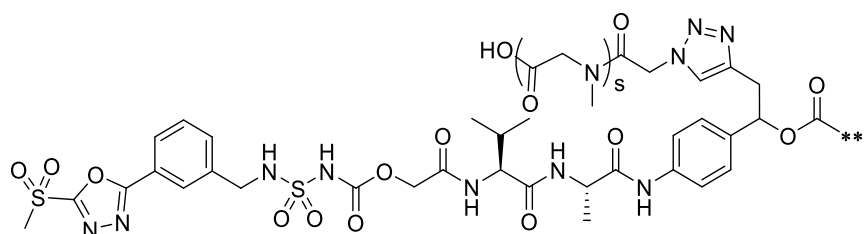
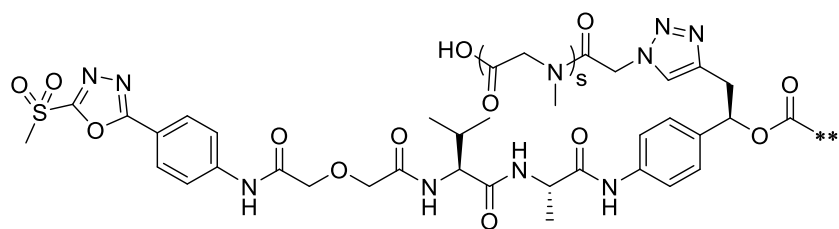
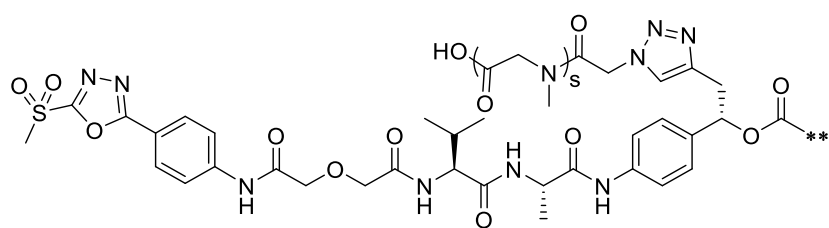
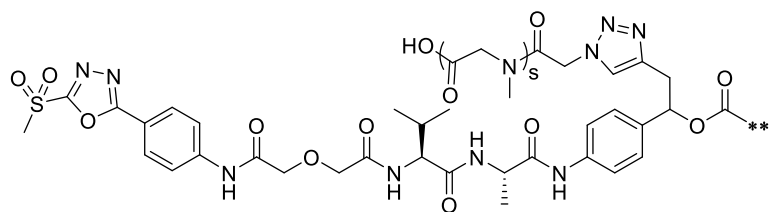
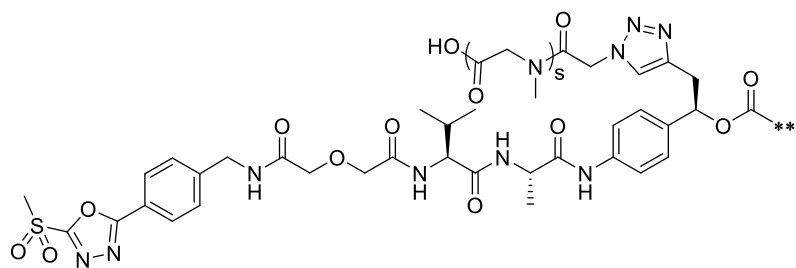
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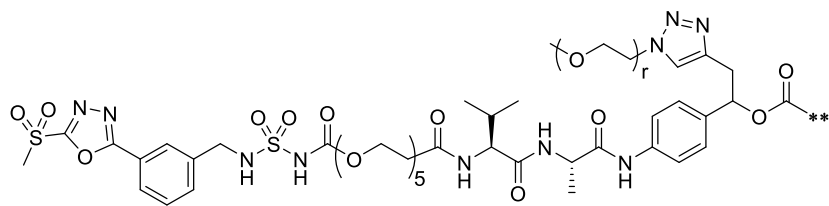
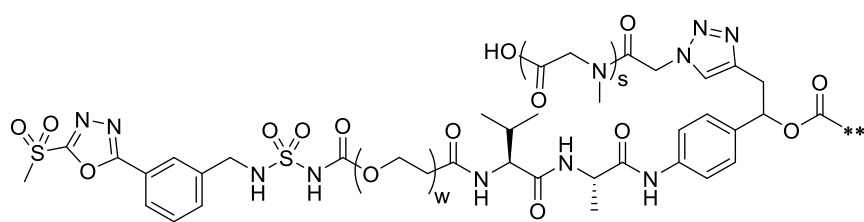


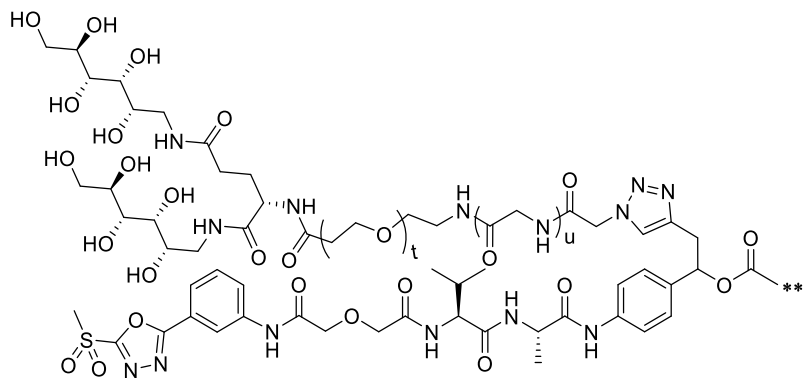
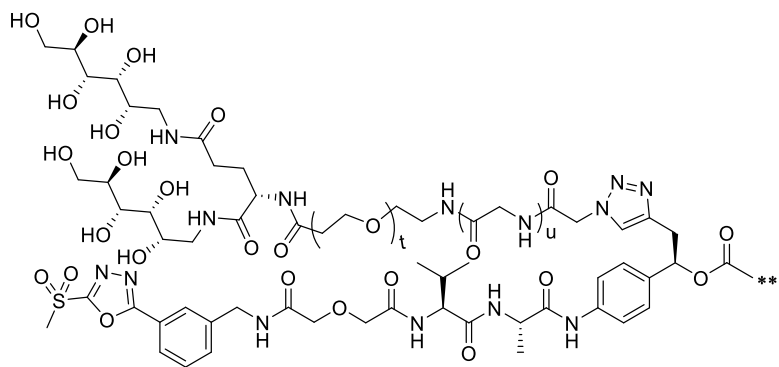
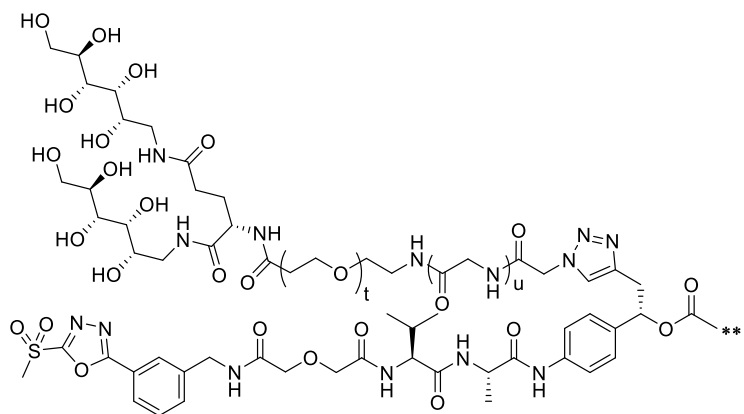
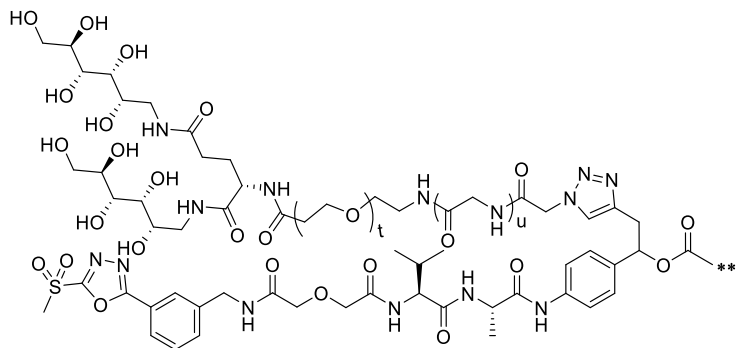
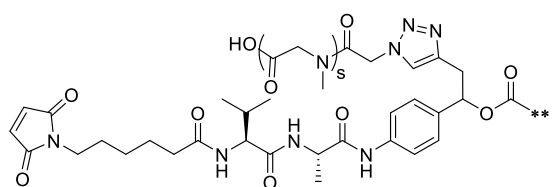
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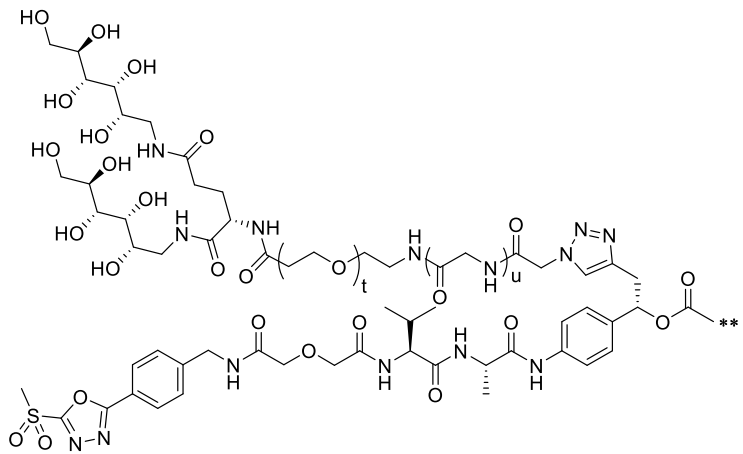
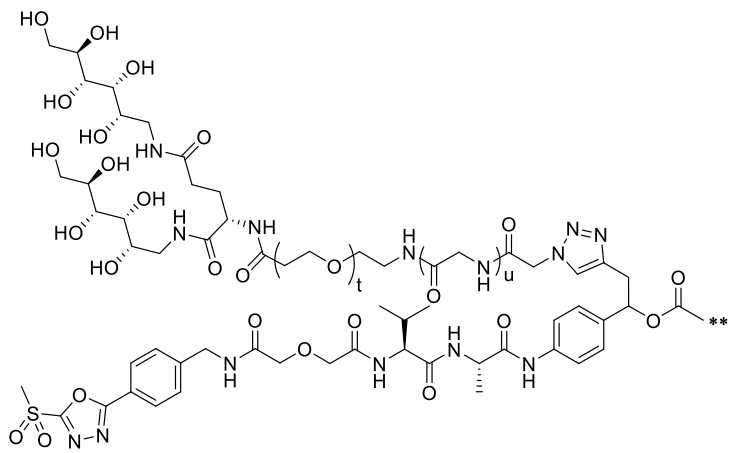
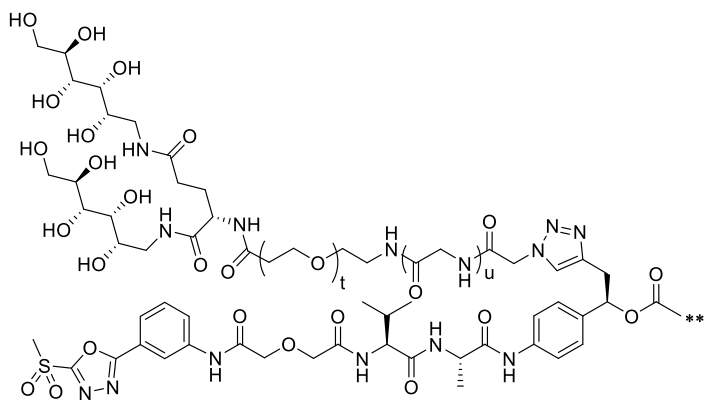
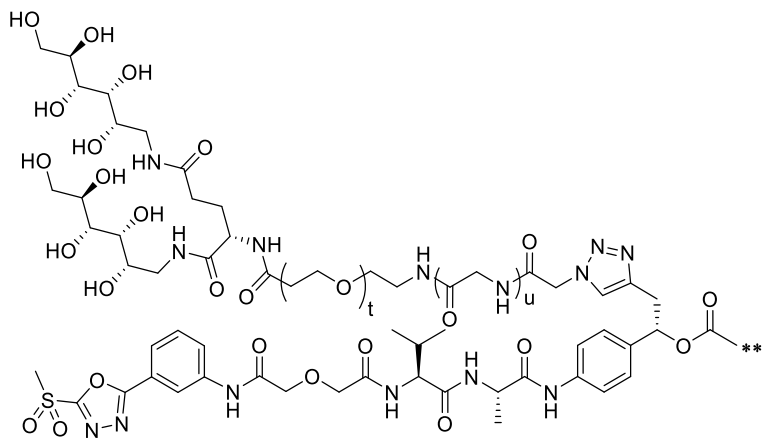


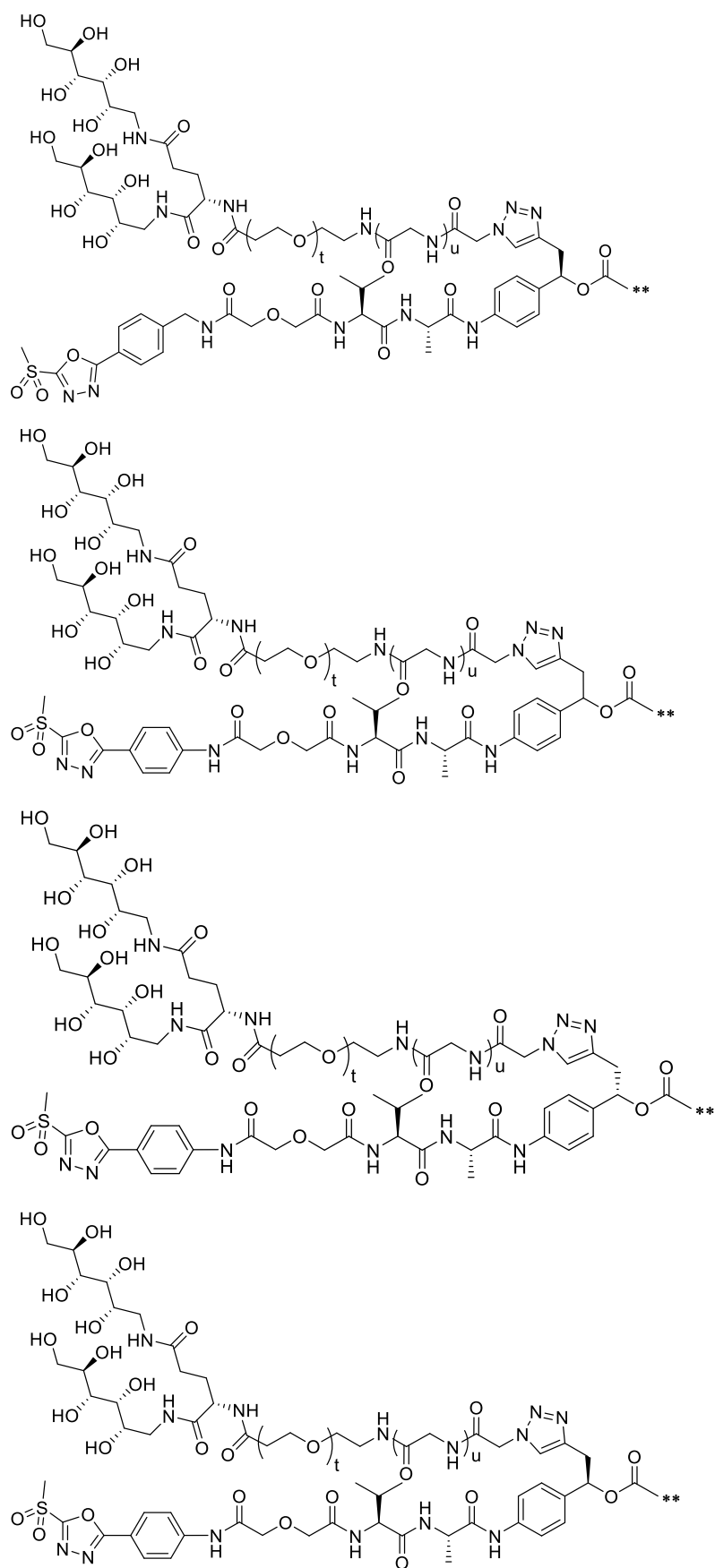


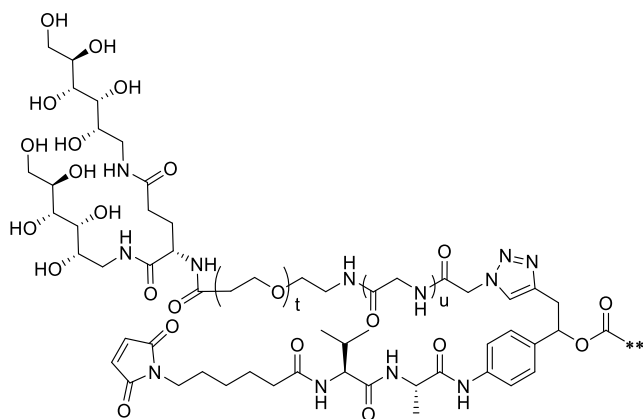
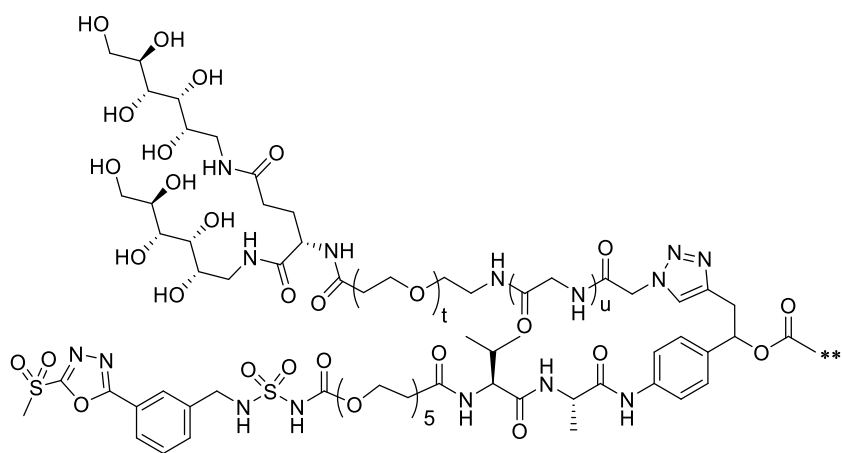
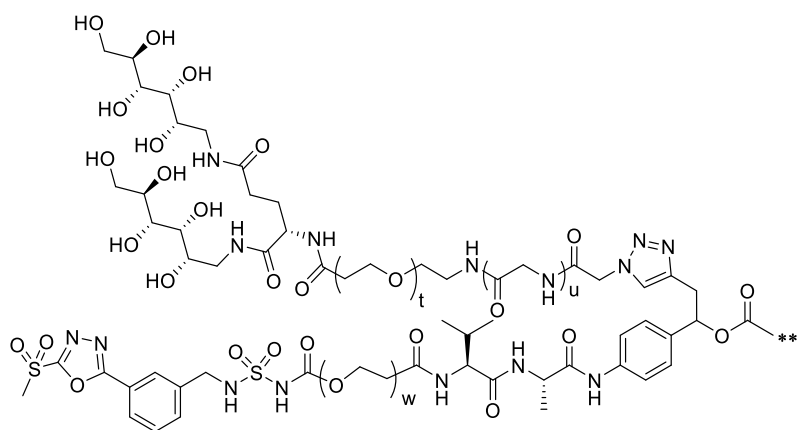
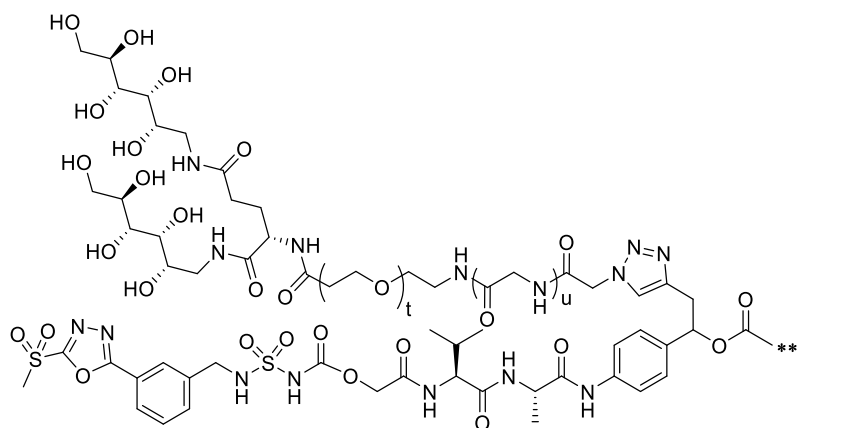
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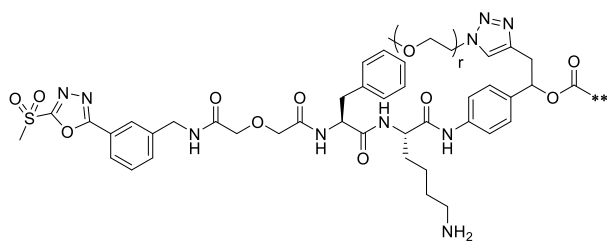
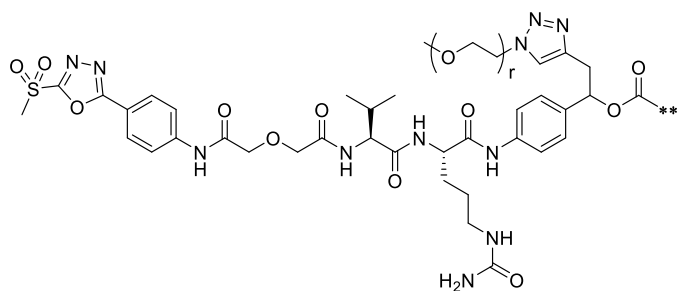
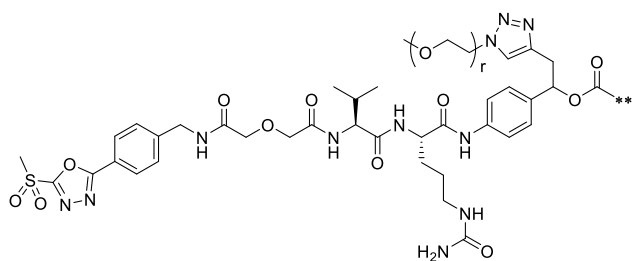
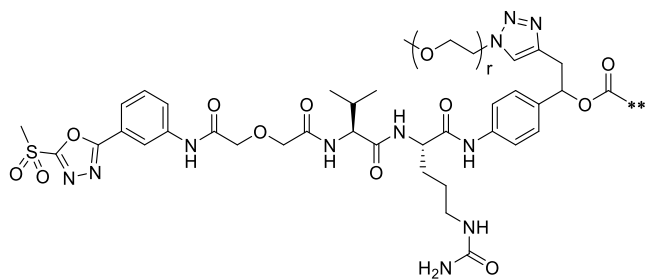
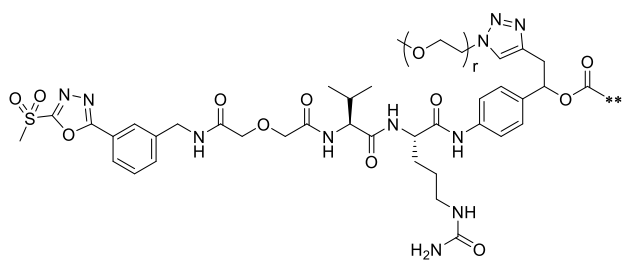




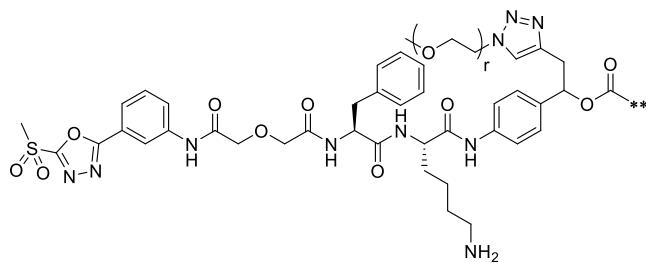


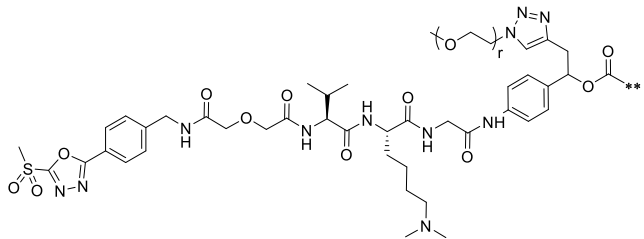
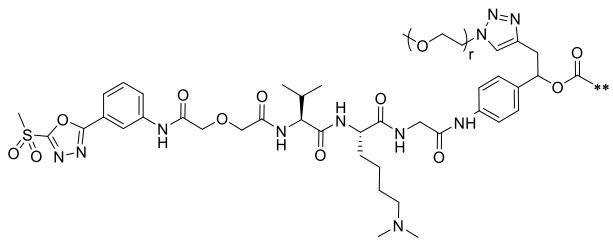
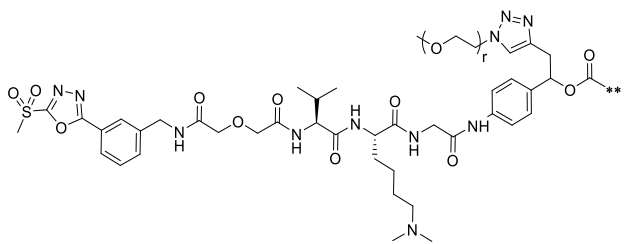
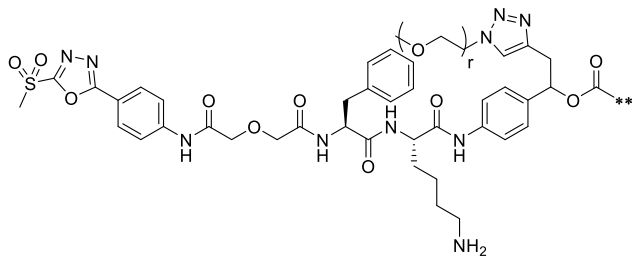
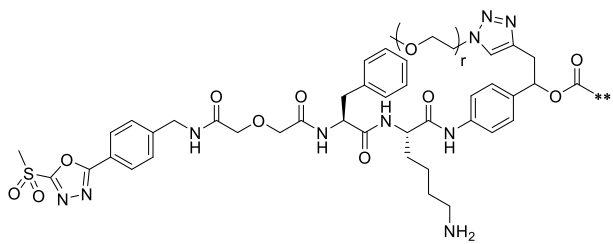




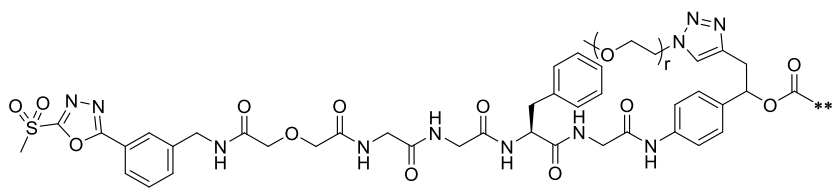
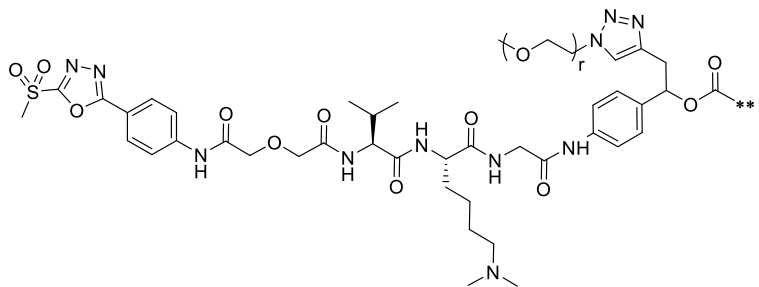


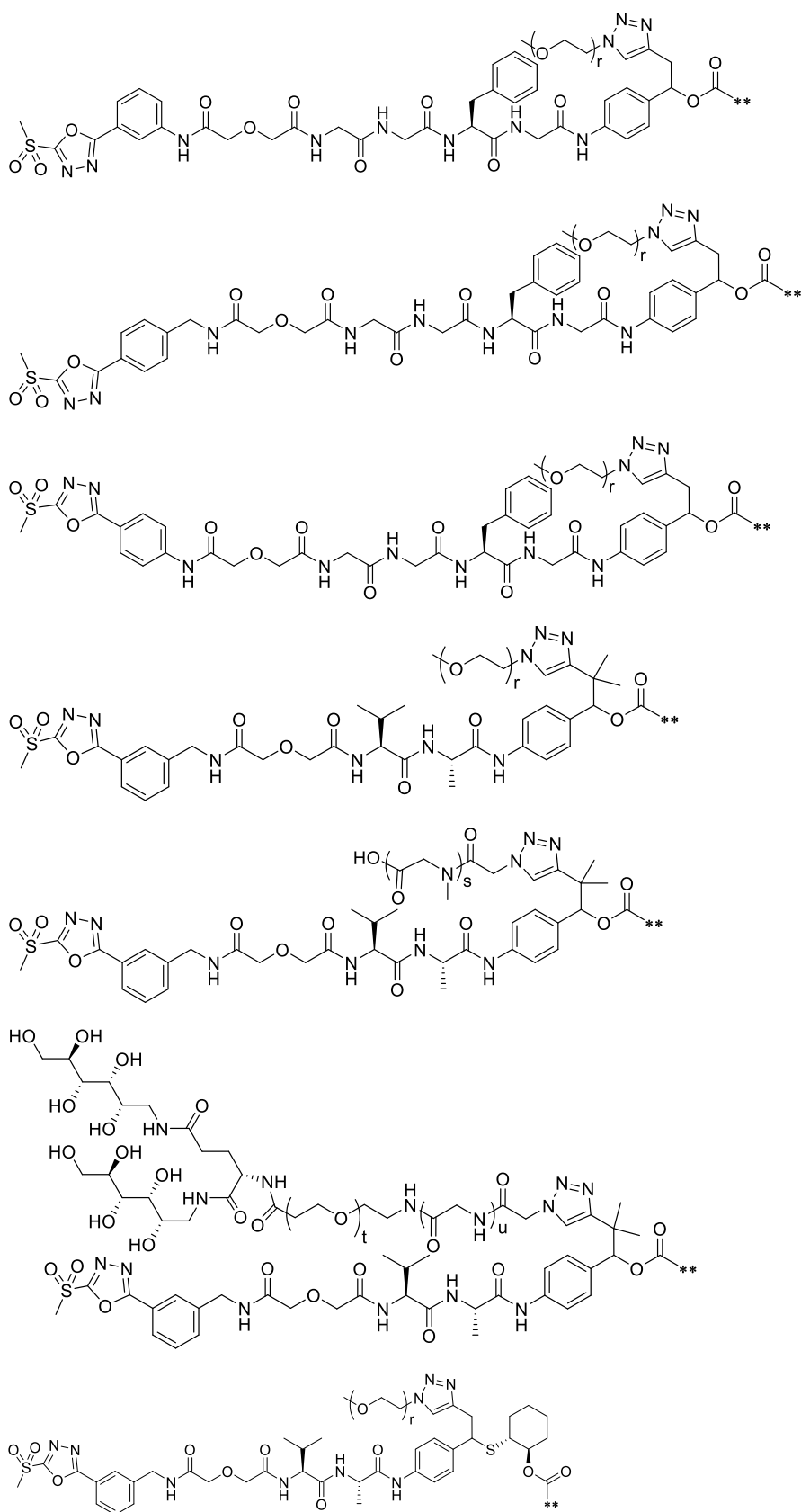
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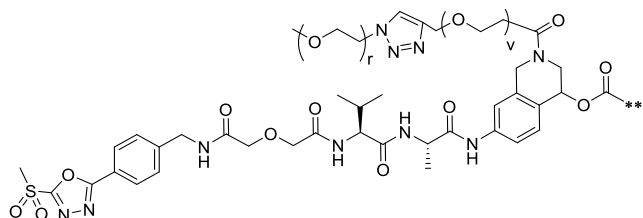
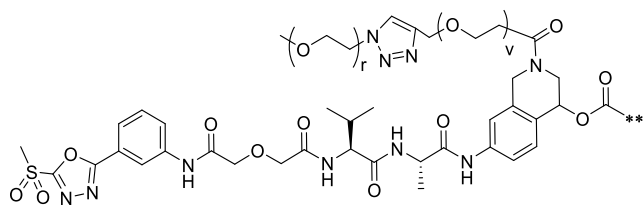
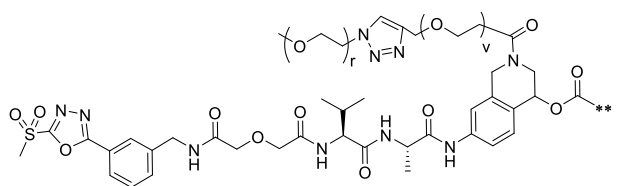
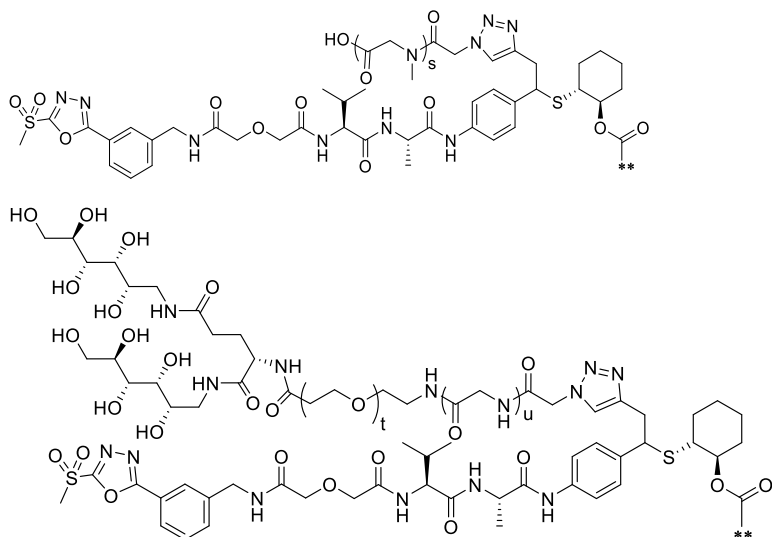




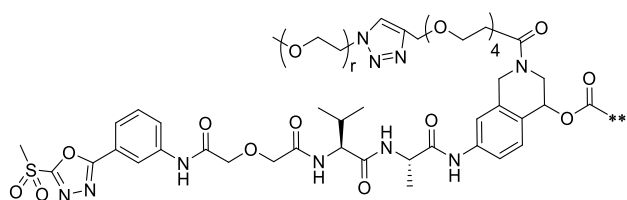
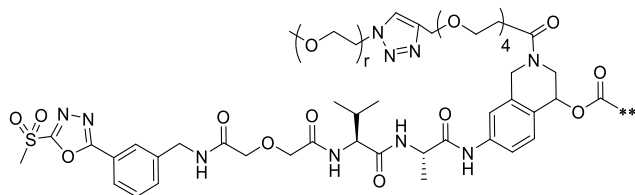
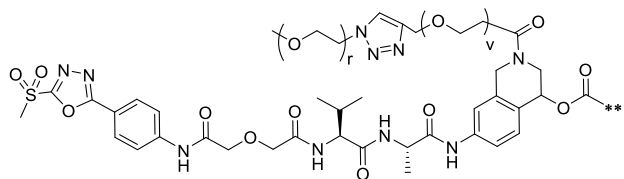
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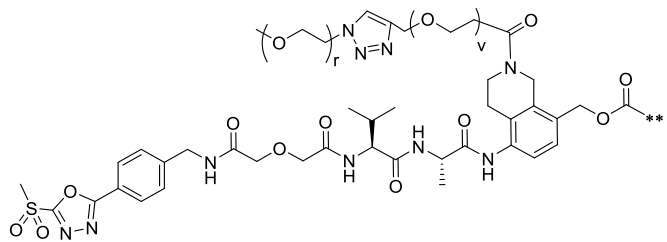
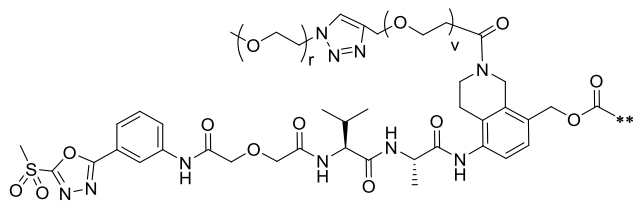
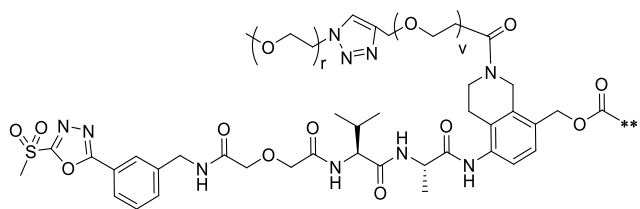
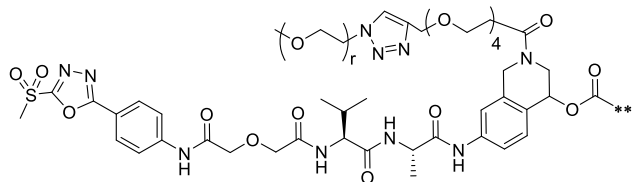
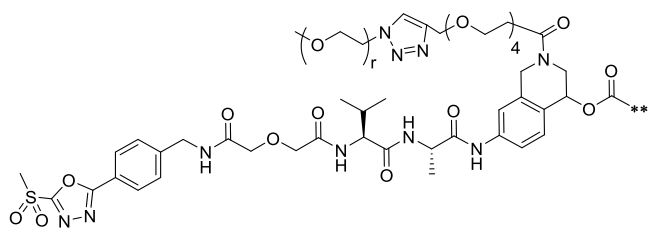




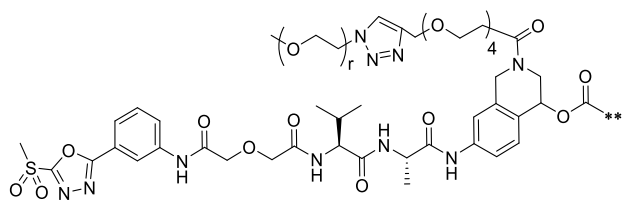
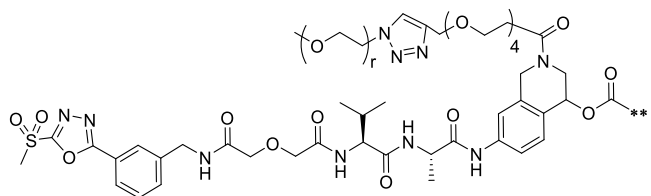
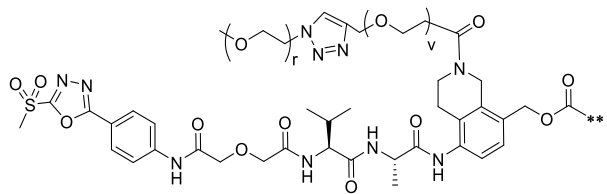


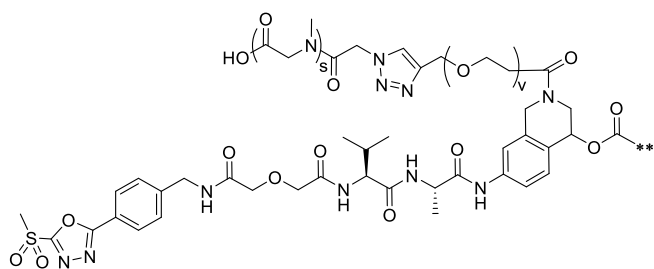
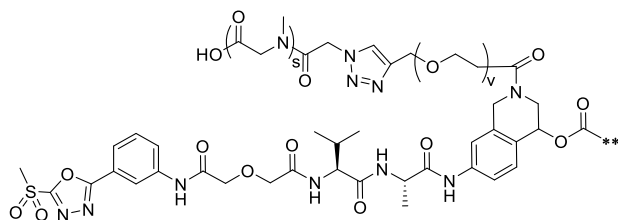
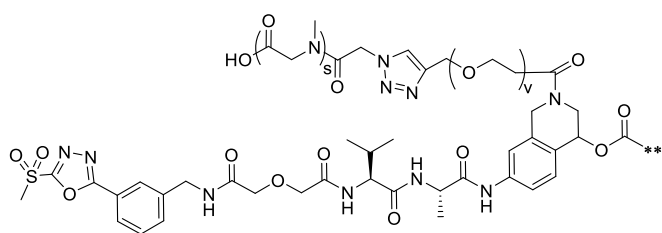
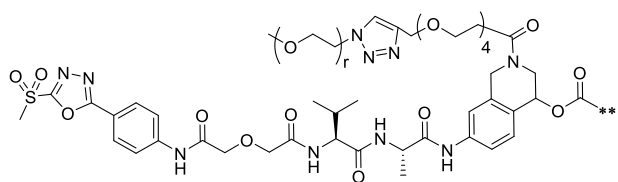
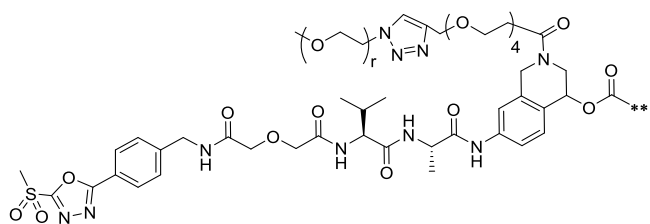
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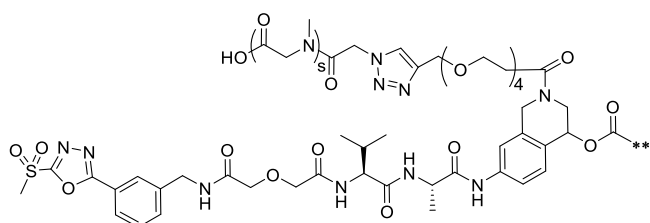
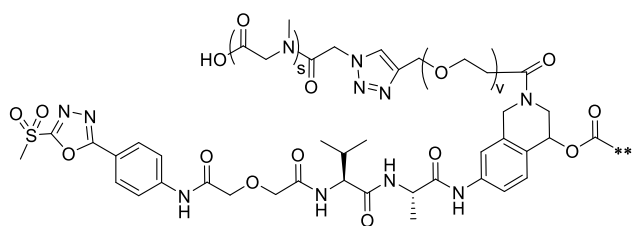


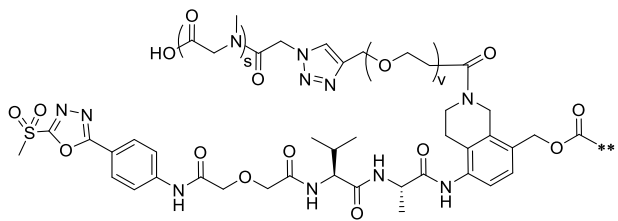
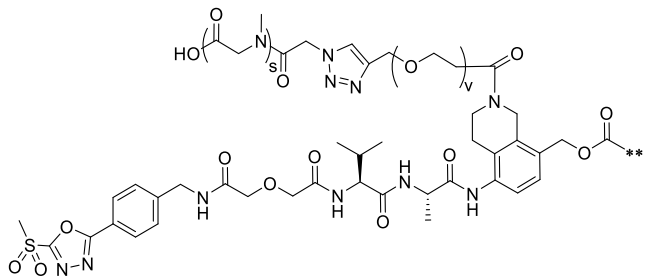
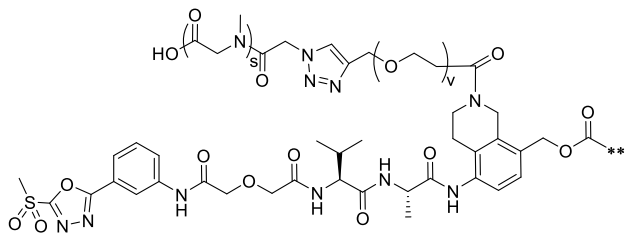
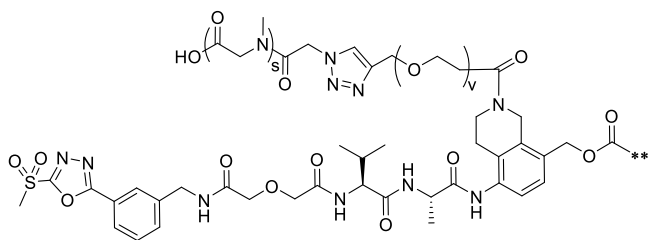
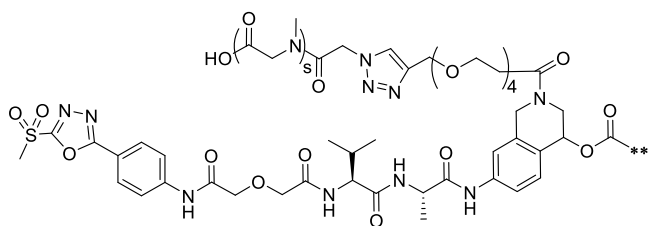
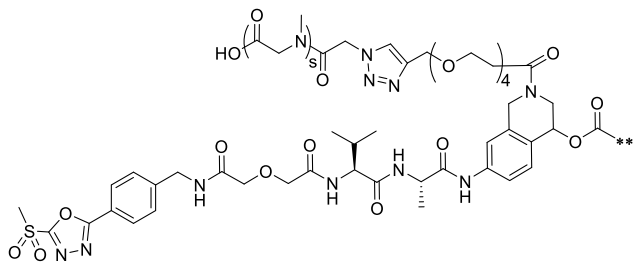
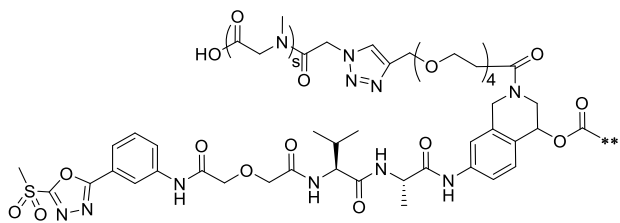
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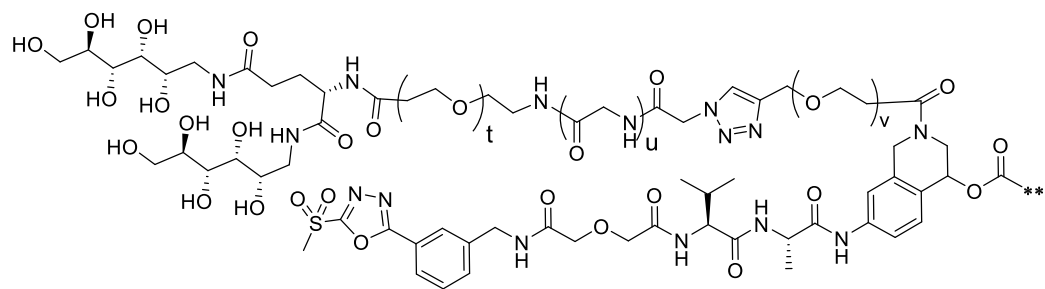
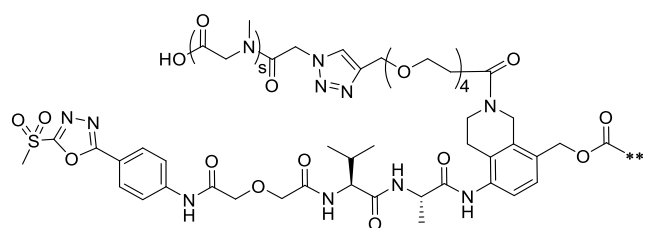
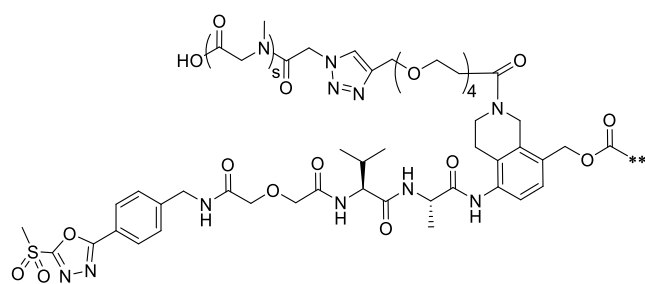
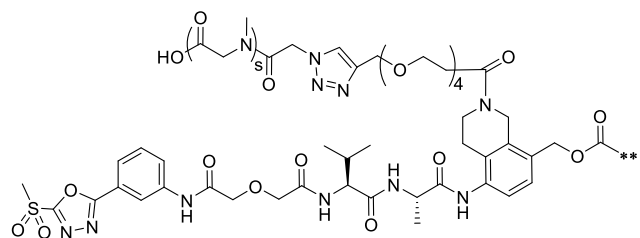
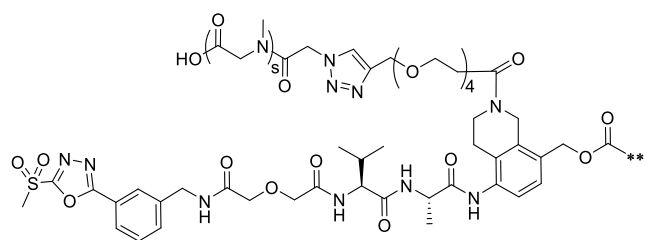


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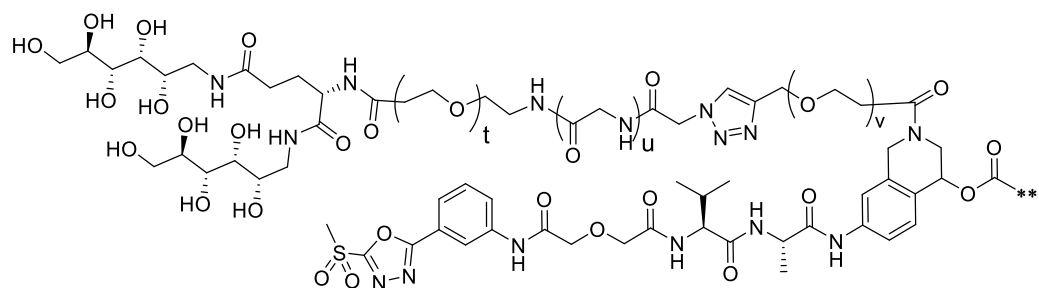


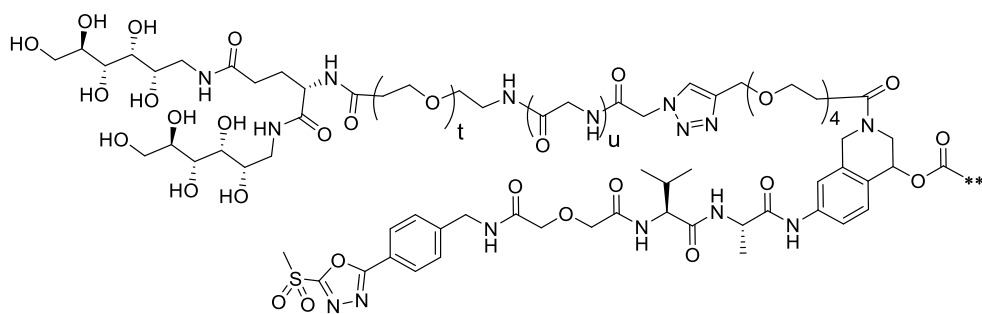
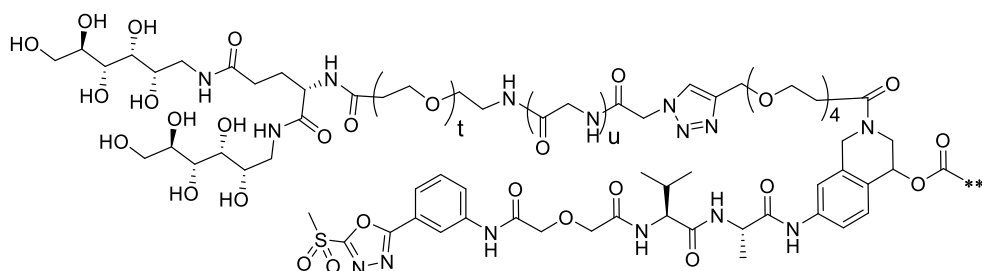
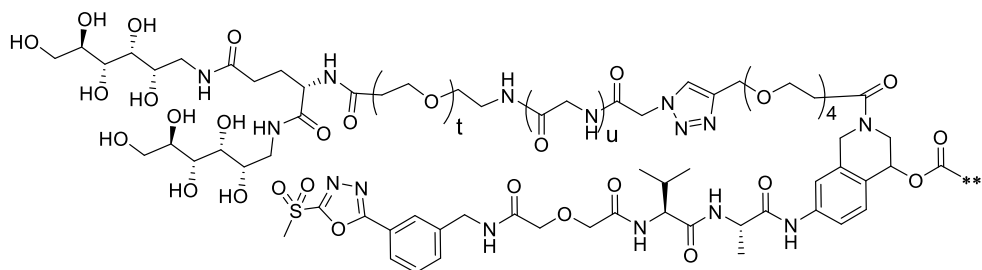
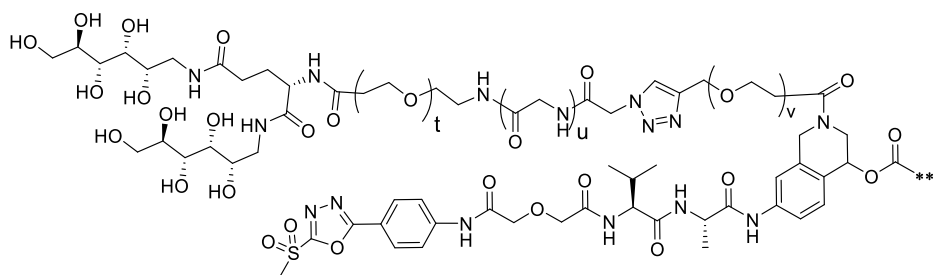
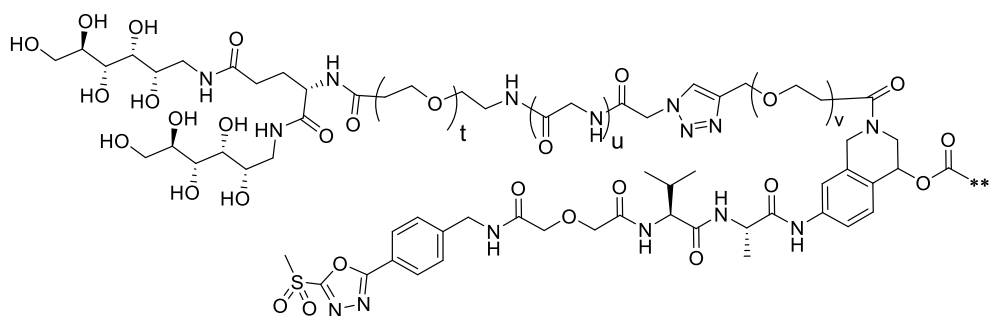


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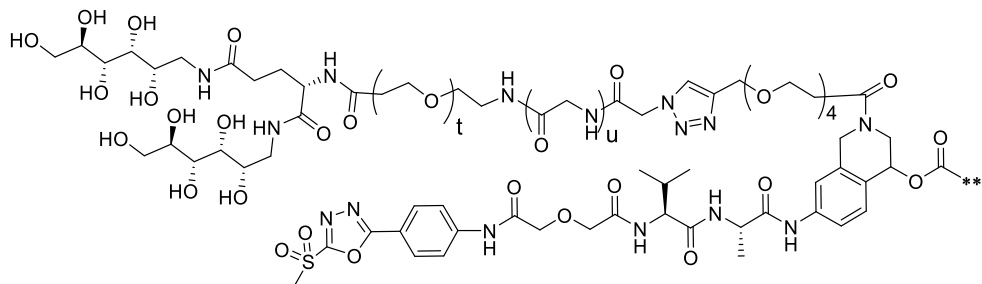


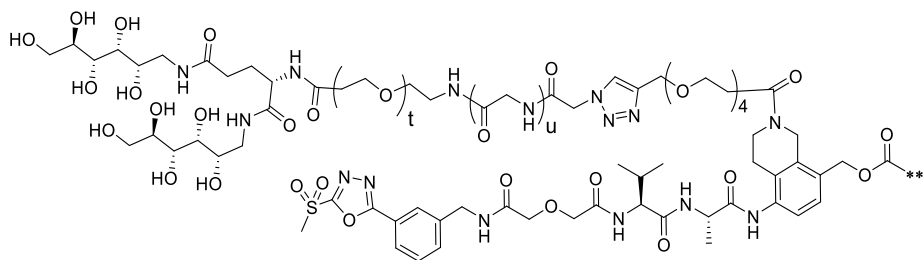
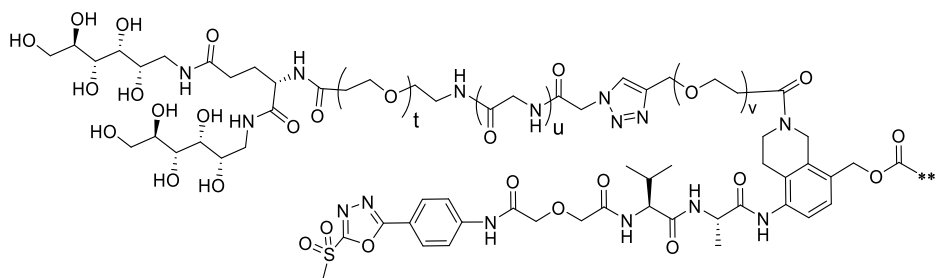
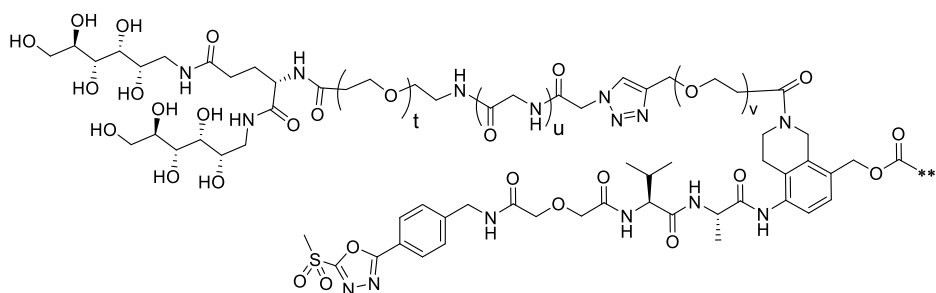
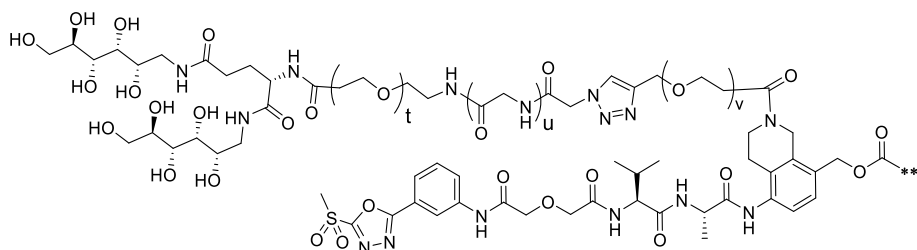
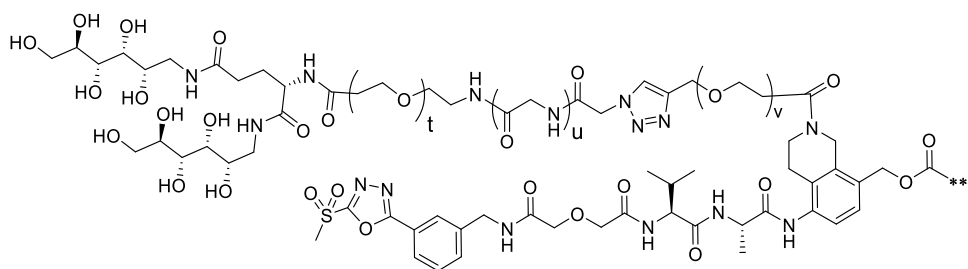
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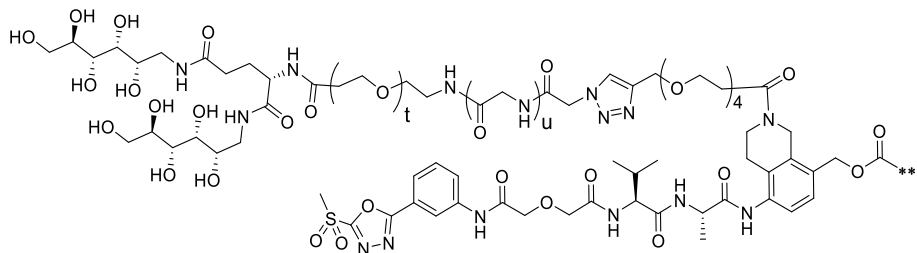


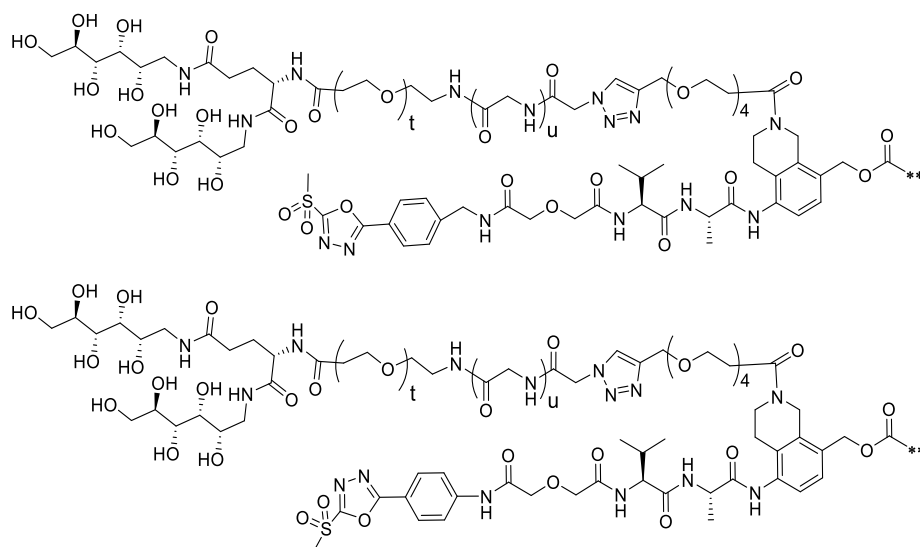
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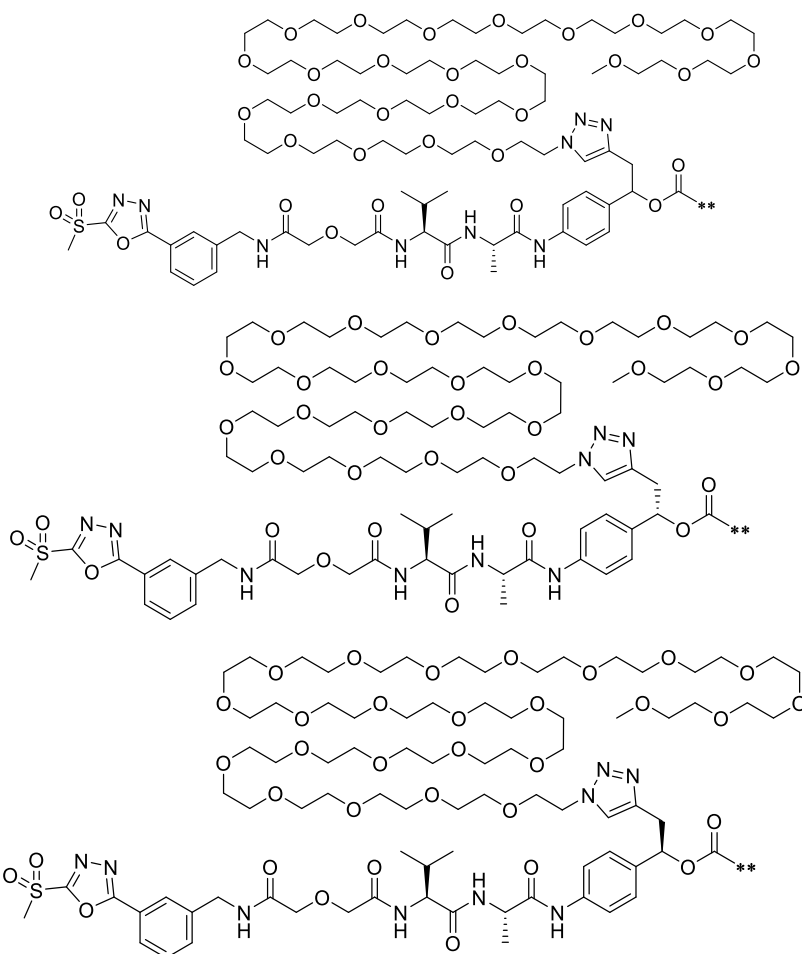


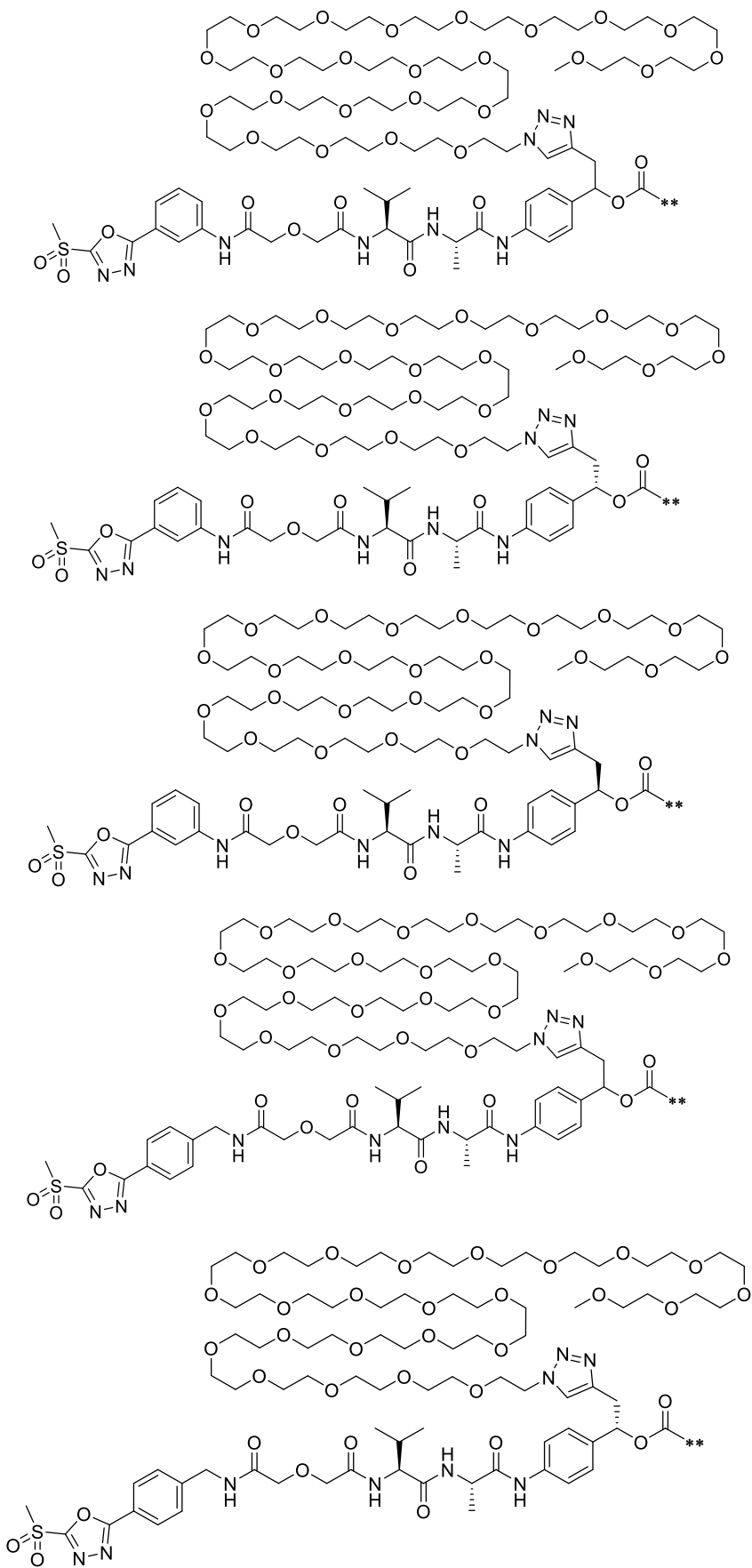


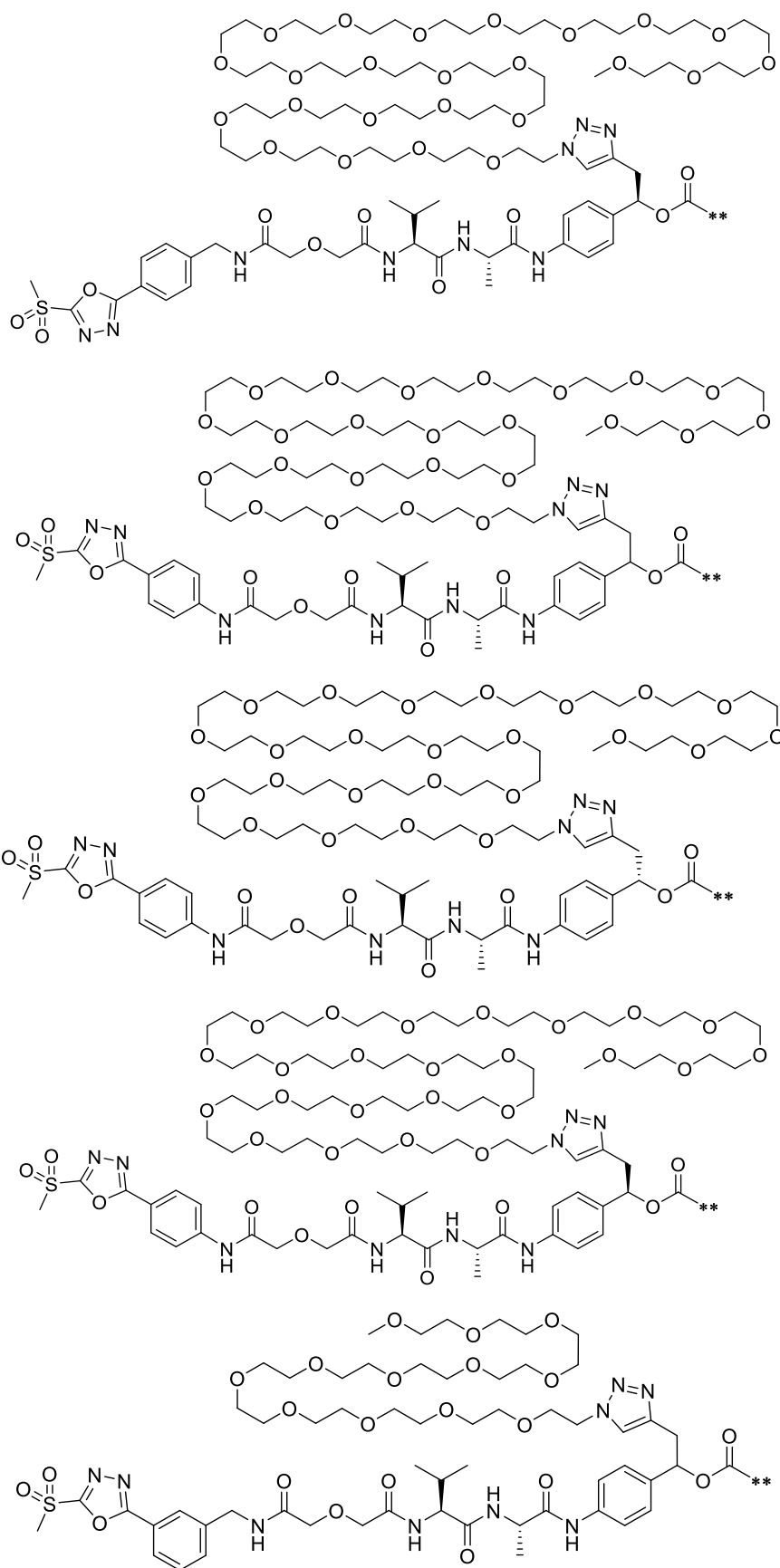
wherein v and w are each independently an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12), and ** represents linkage to the amino group of the bioactive molecule D;

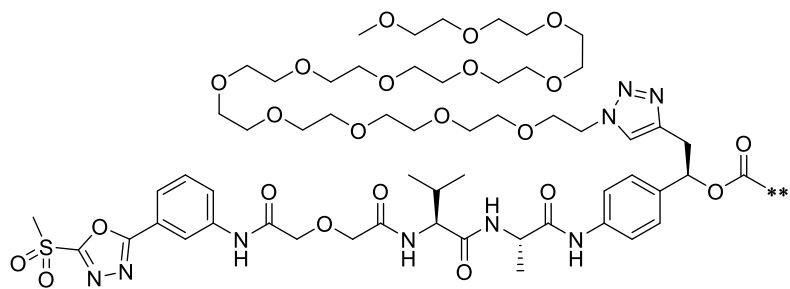
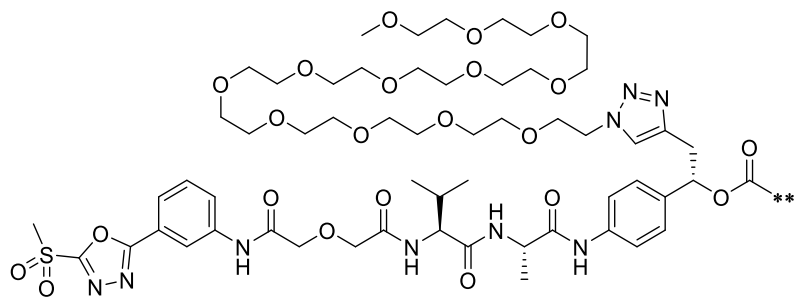
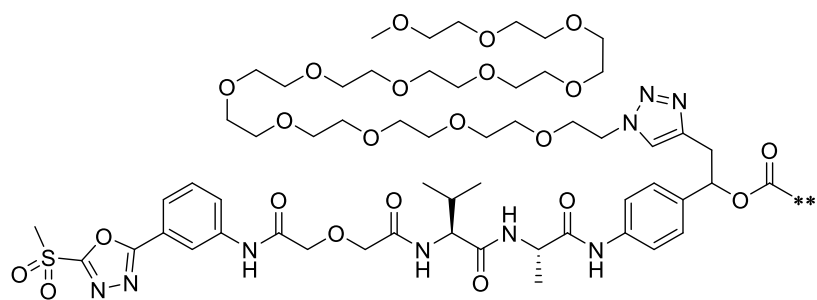
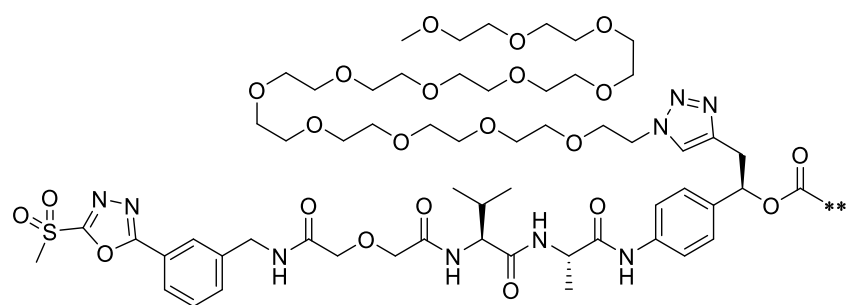
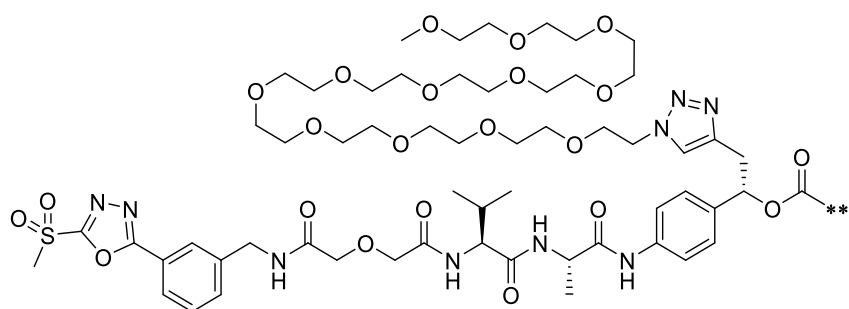
5 r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9,
10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34,
35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50).

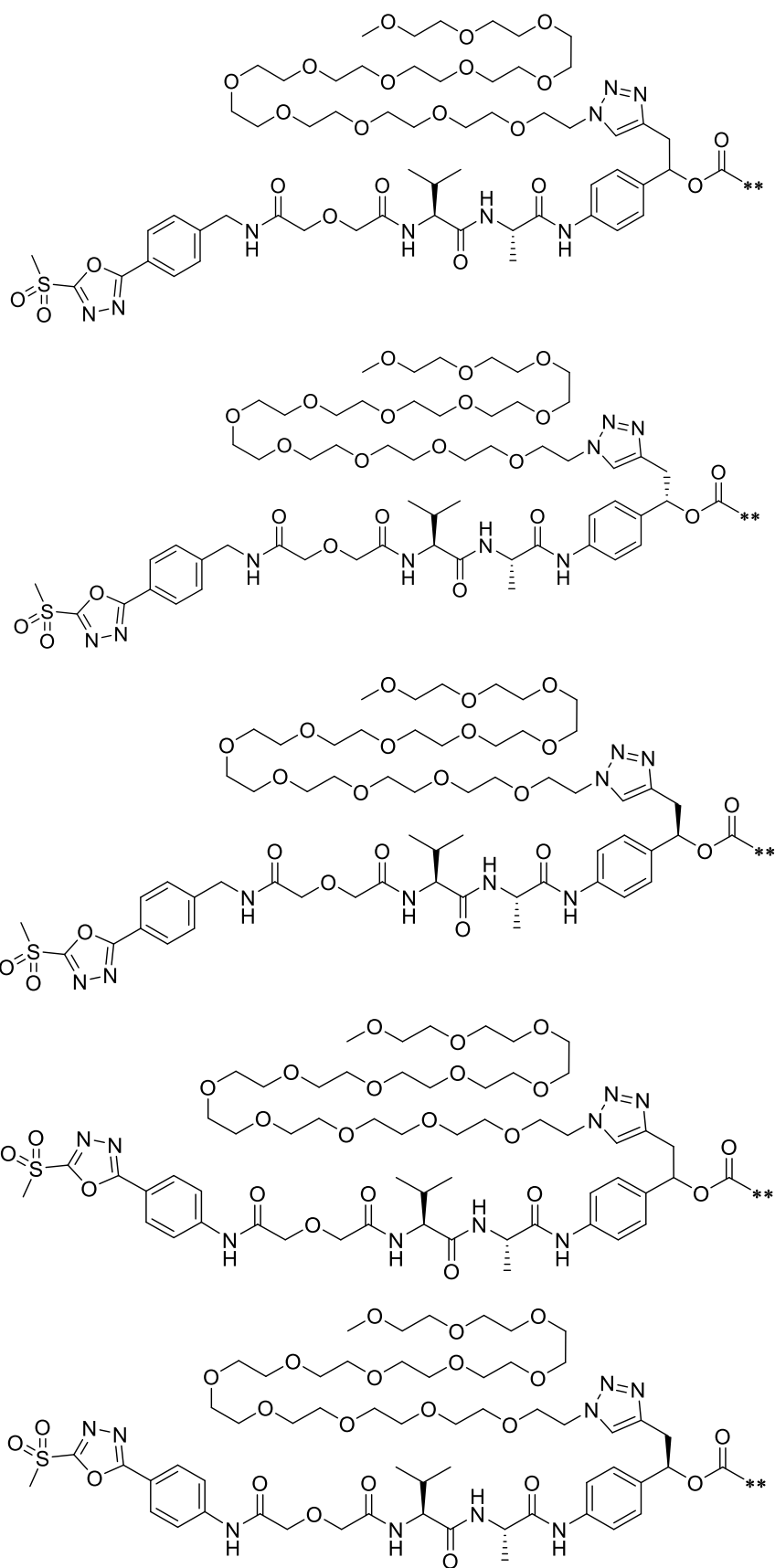
In some embodiments, L' is selected from the following structures:

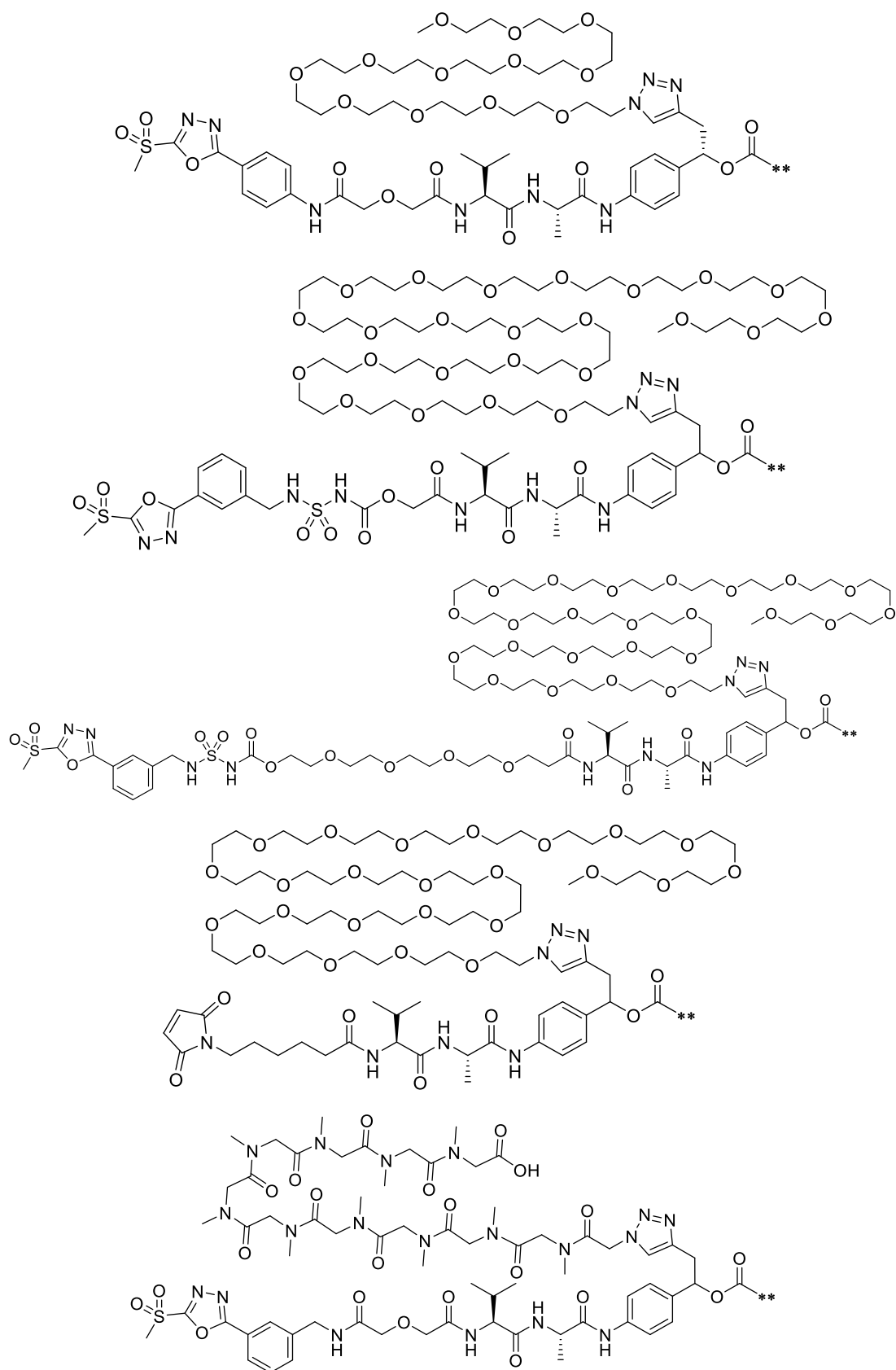


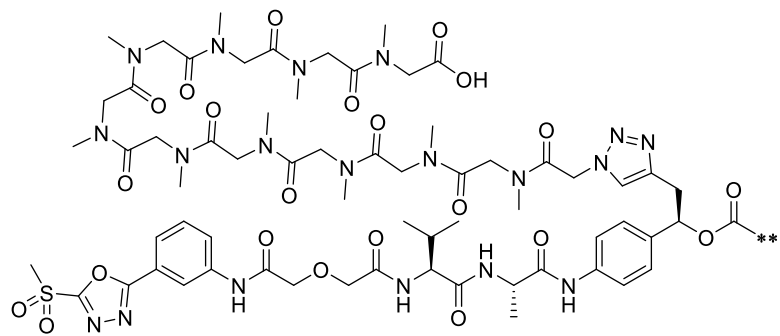
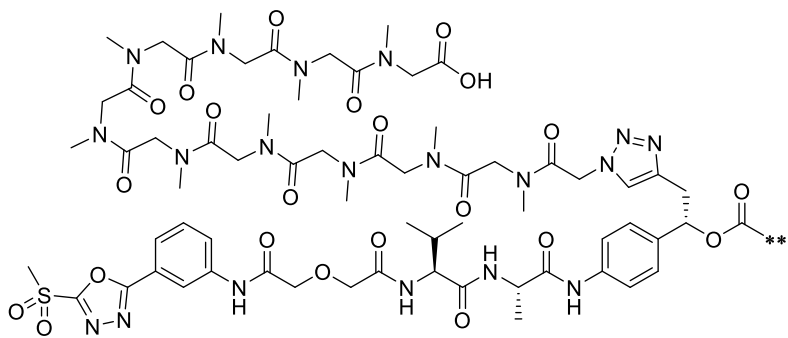
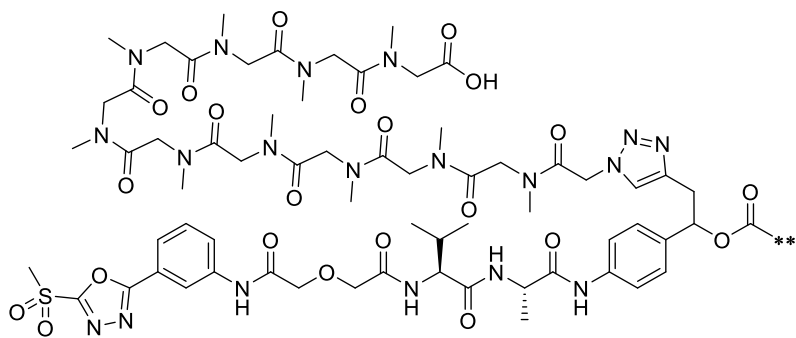
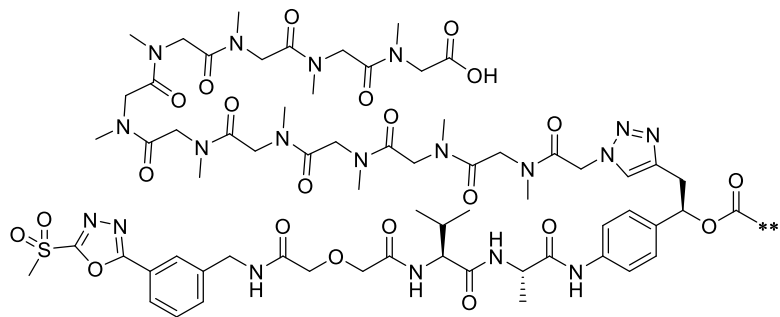
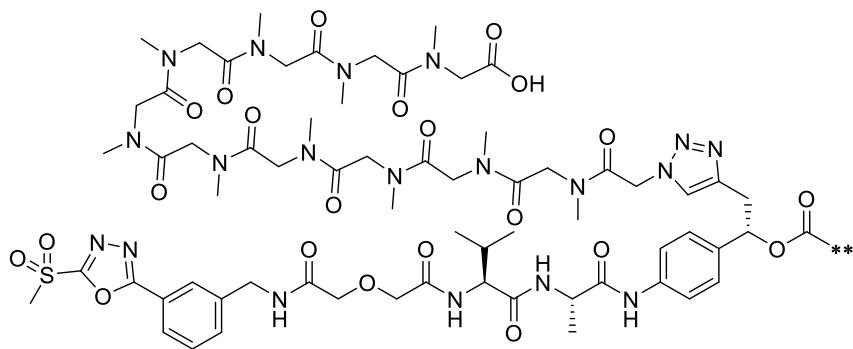


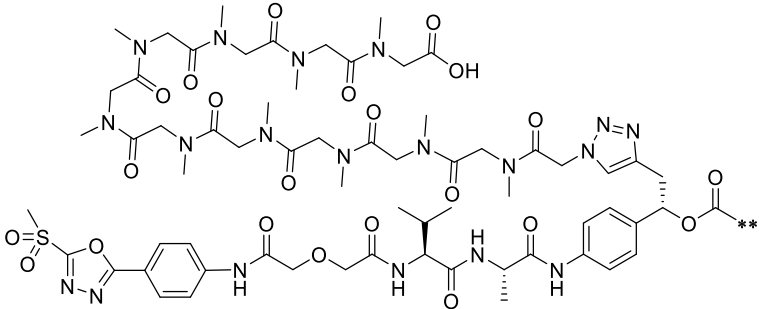
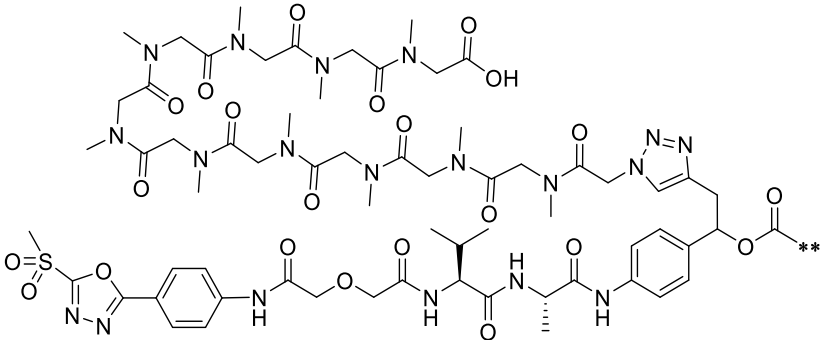
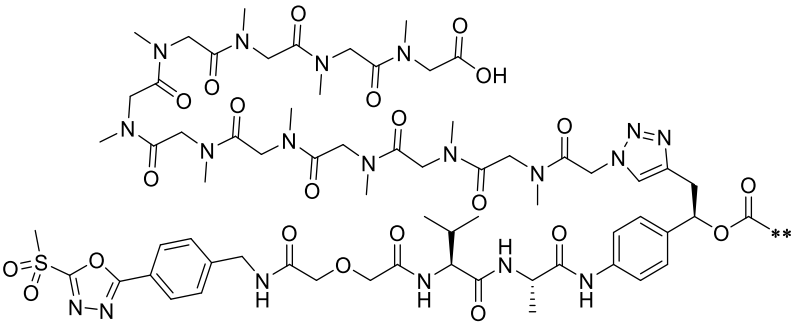
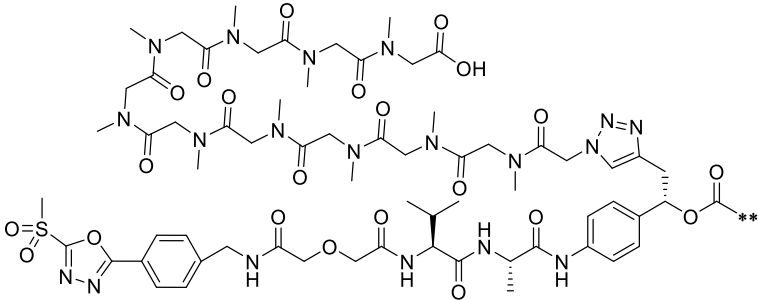
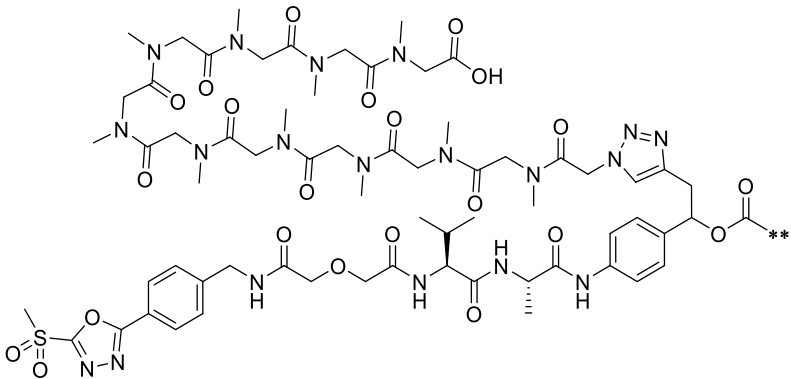


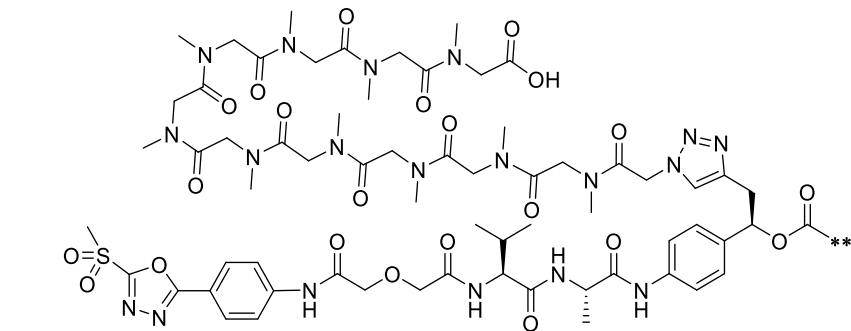


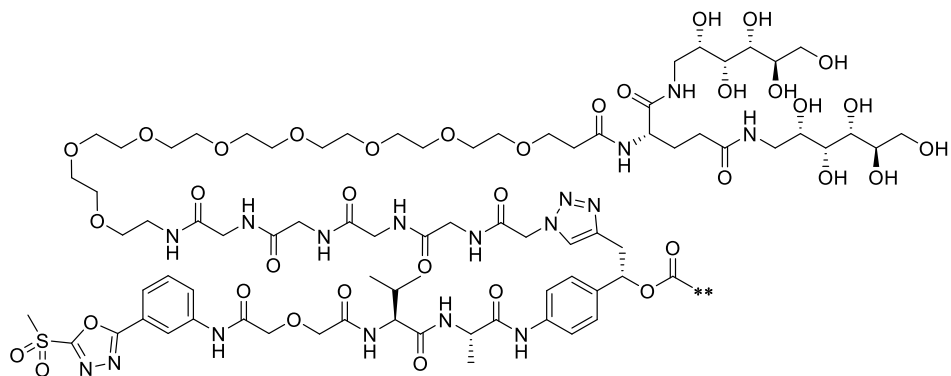
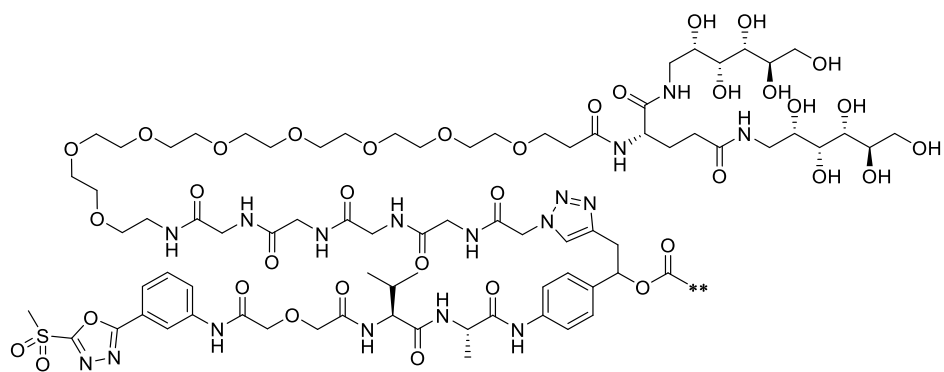
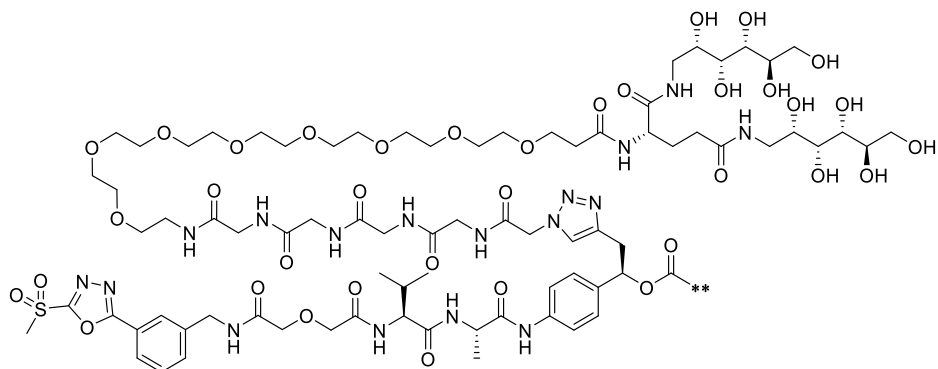
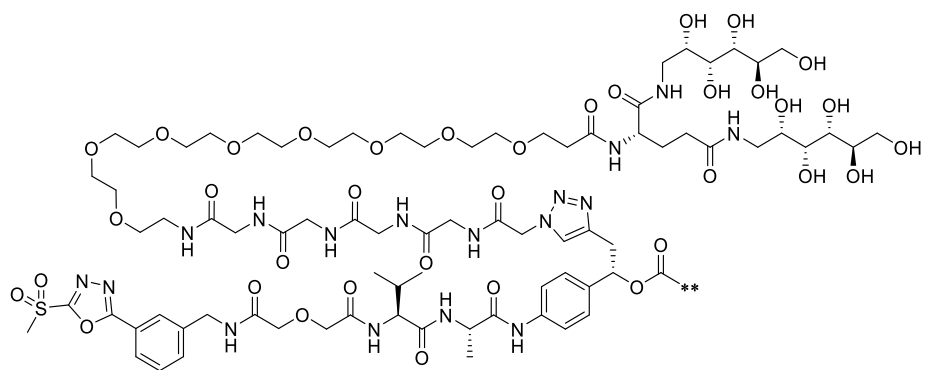


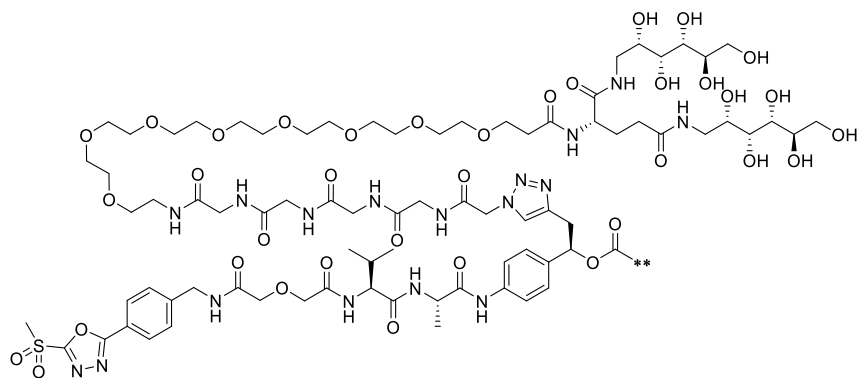
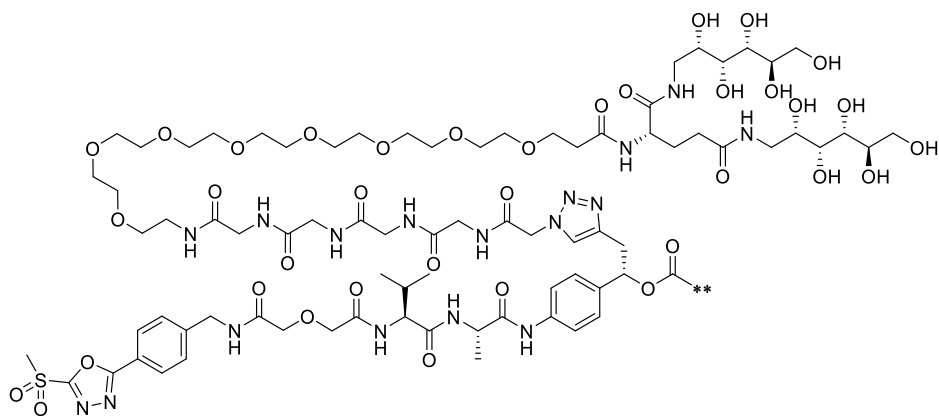
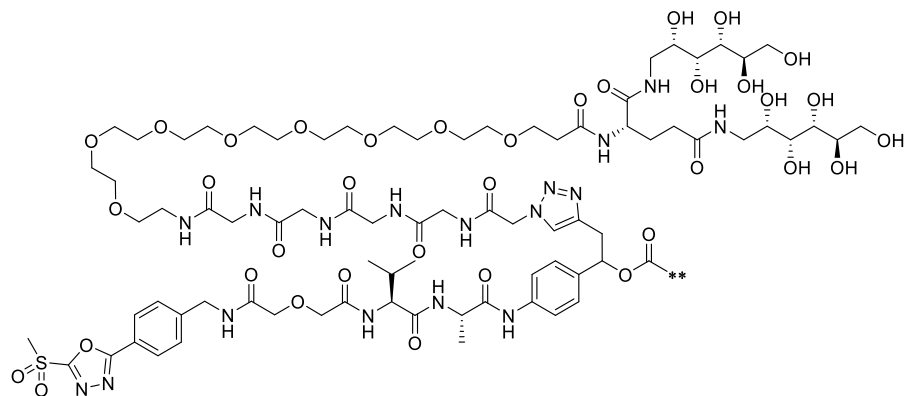
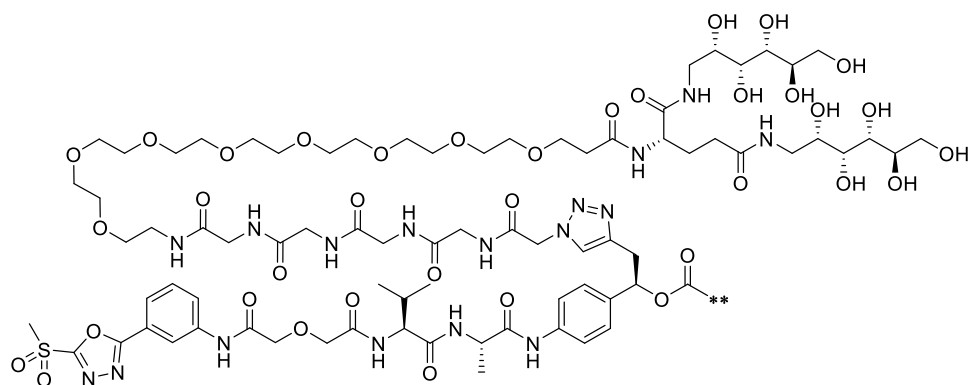


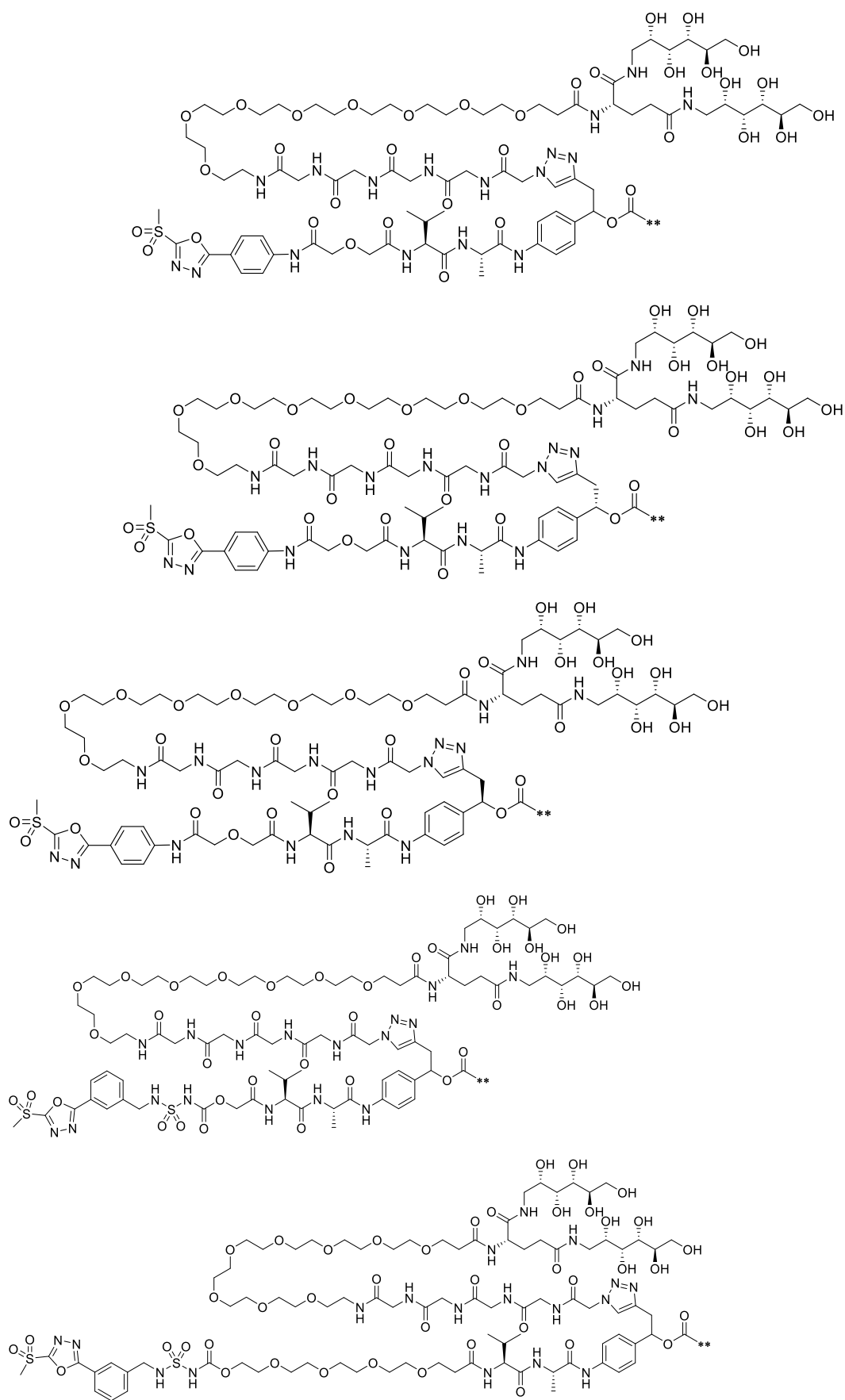


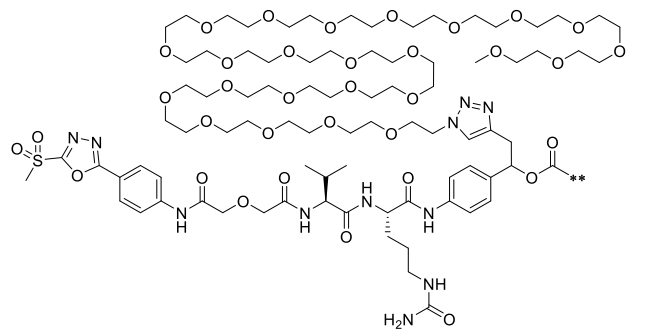
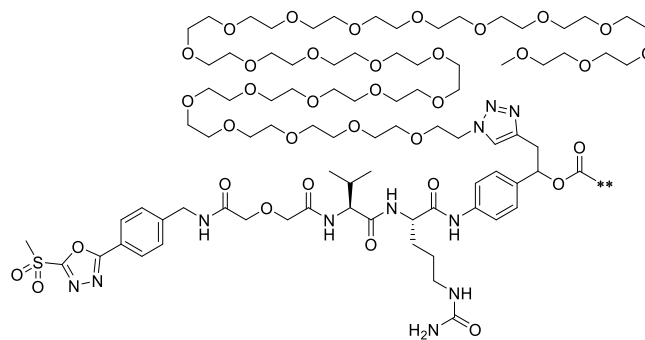
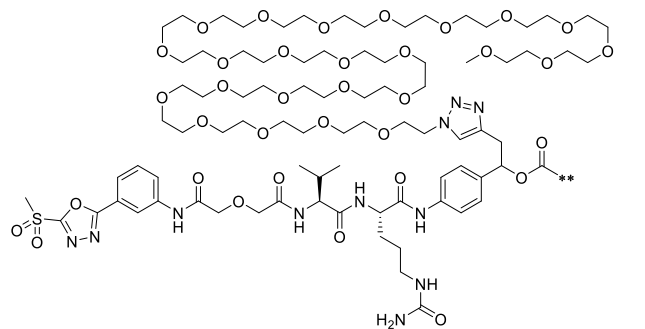
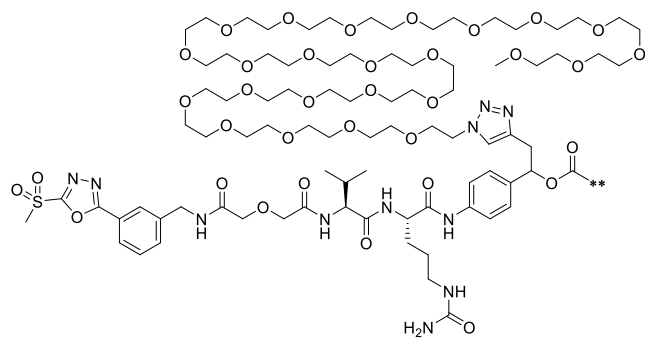
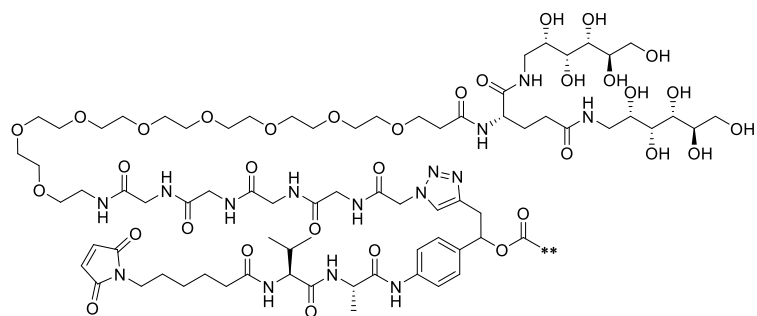


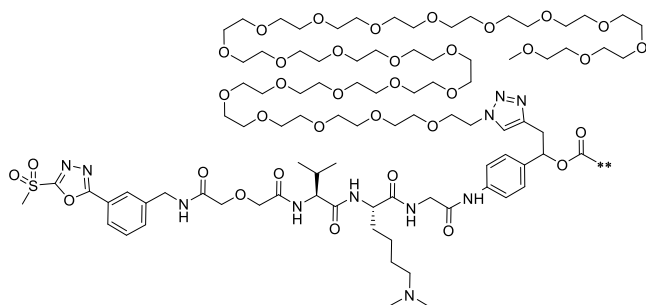
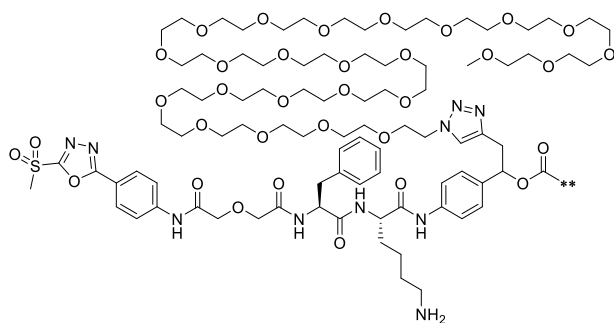
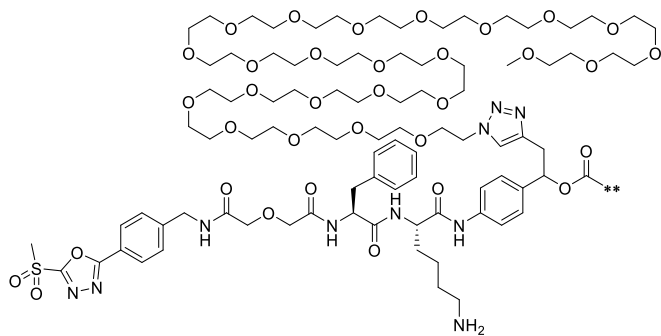
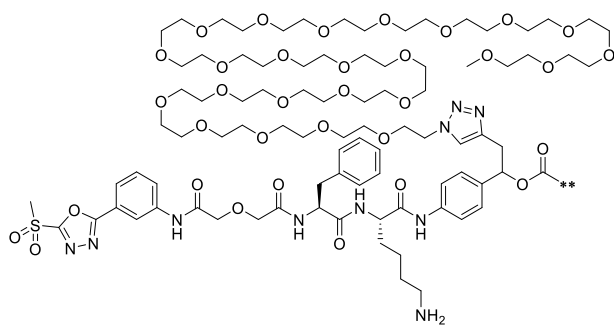
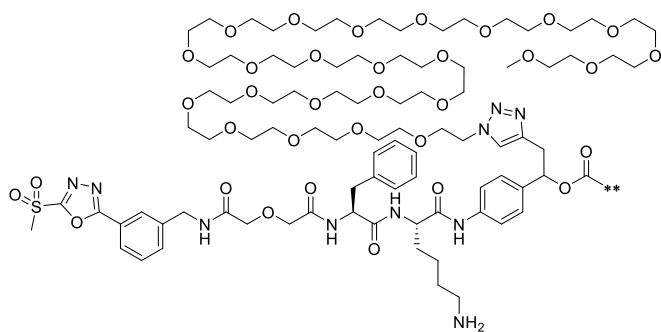
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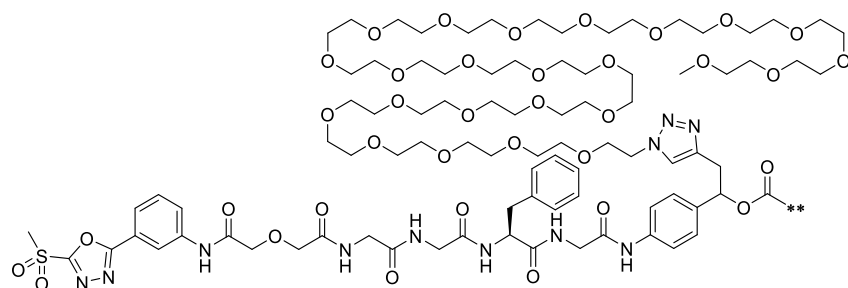
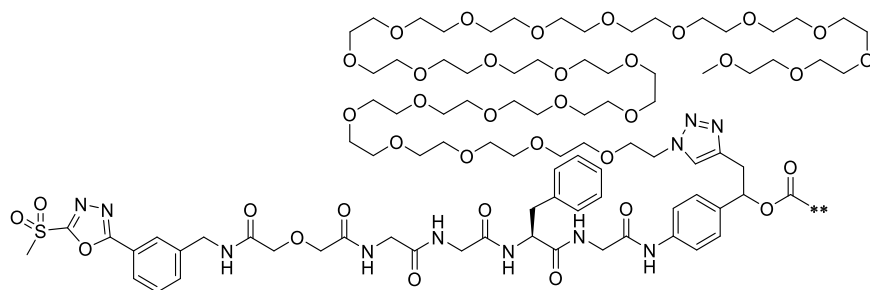
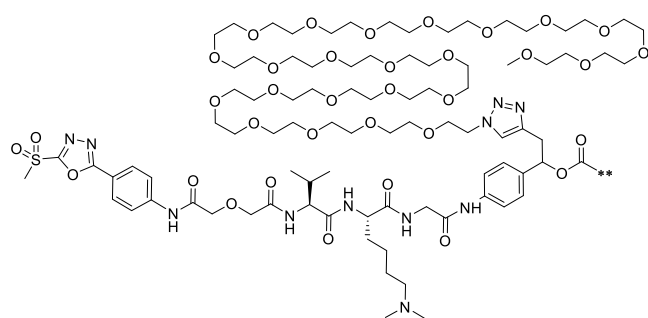
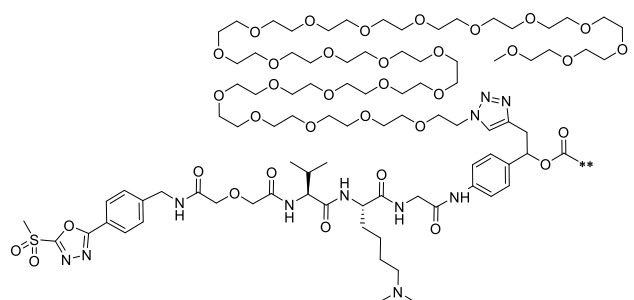
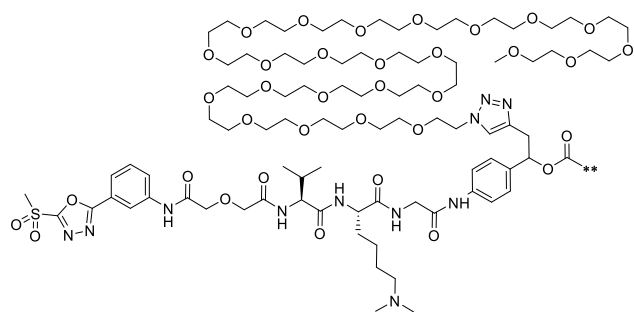


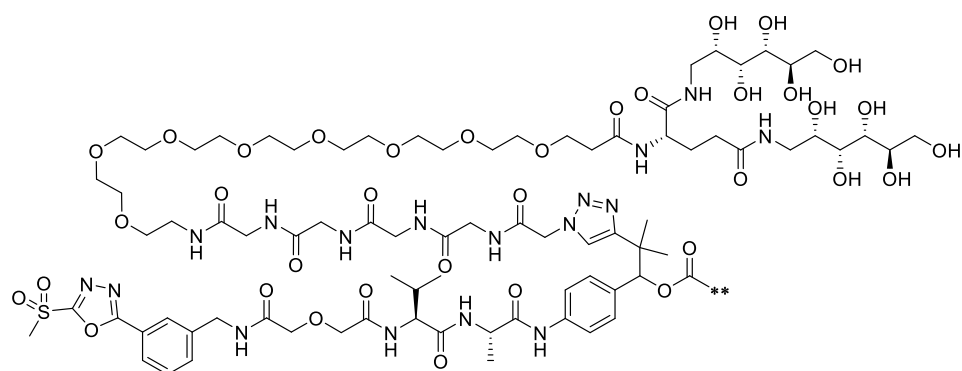
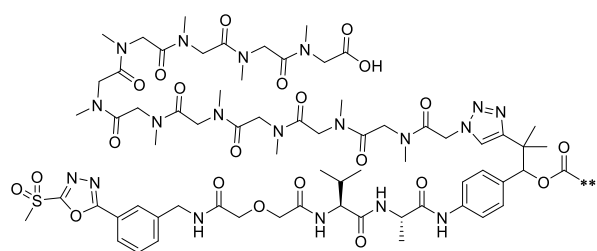
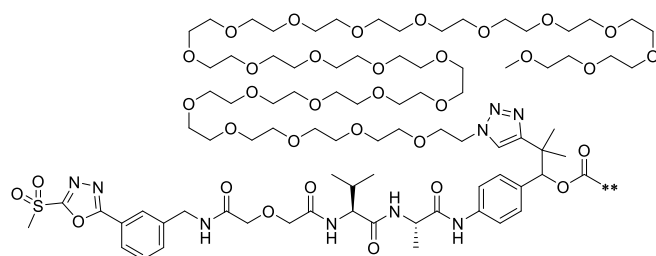
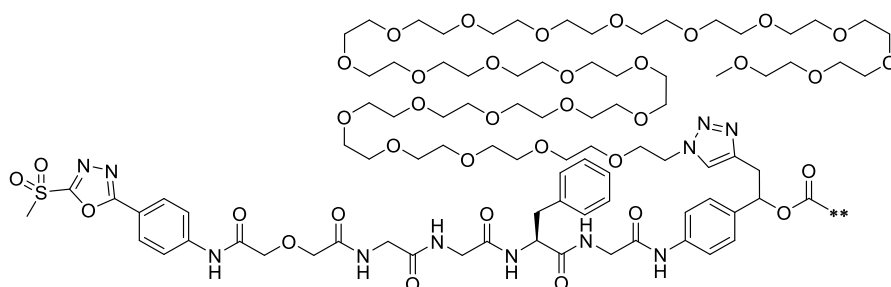
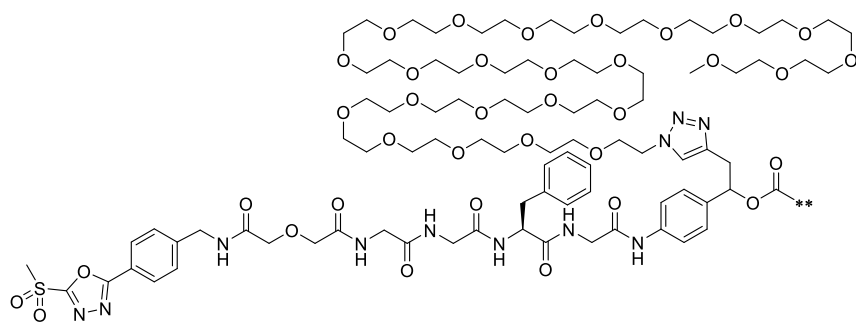




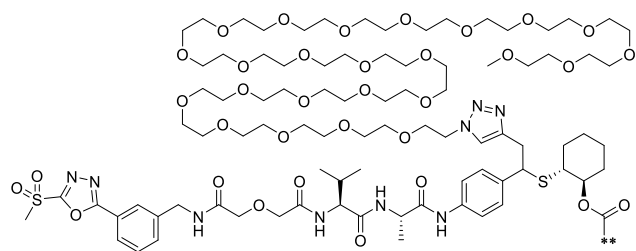


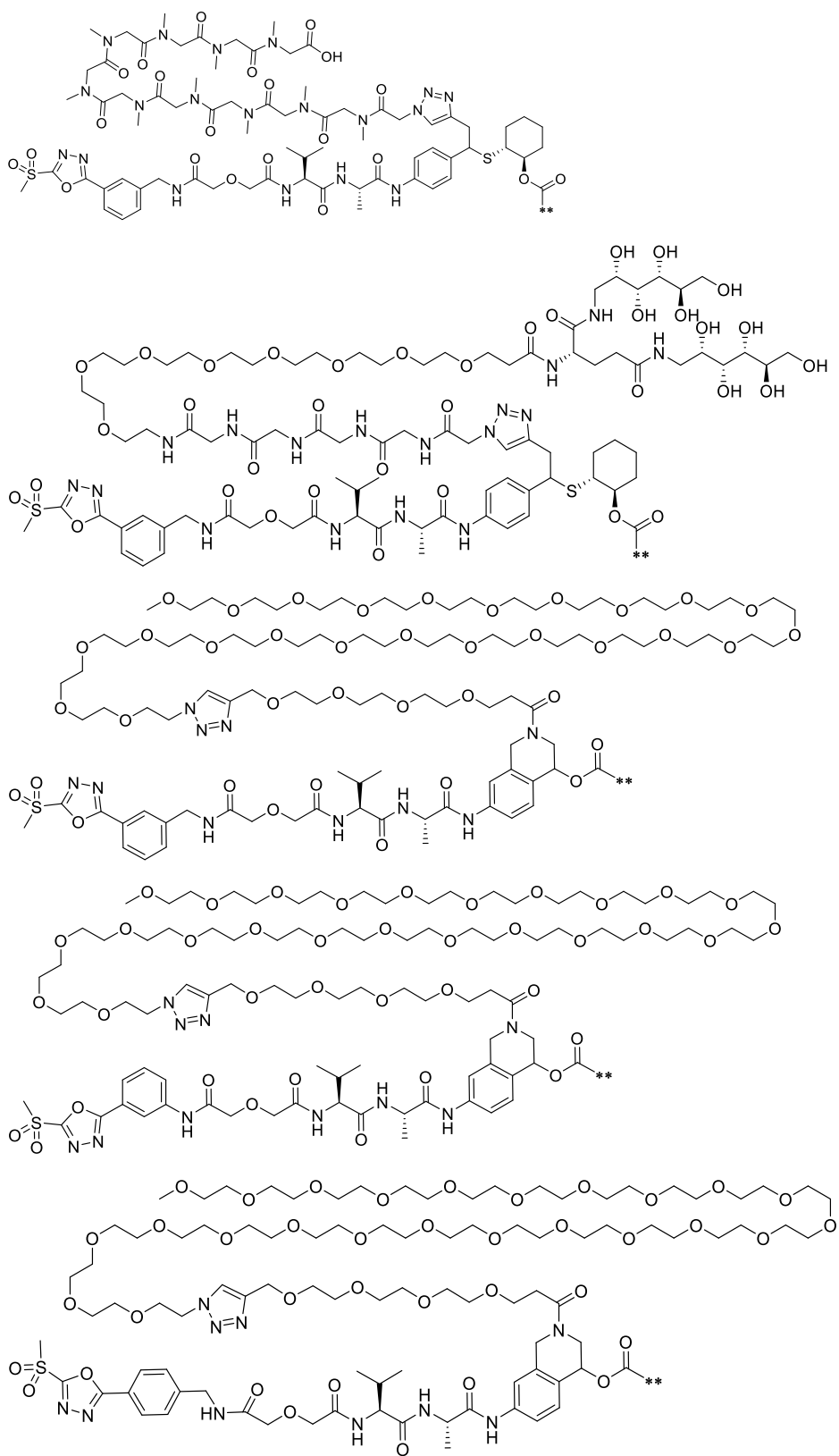


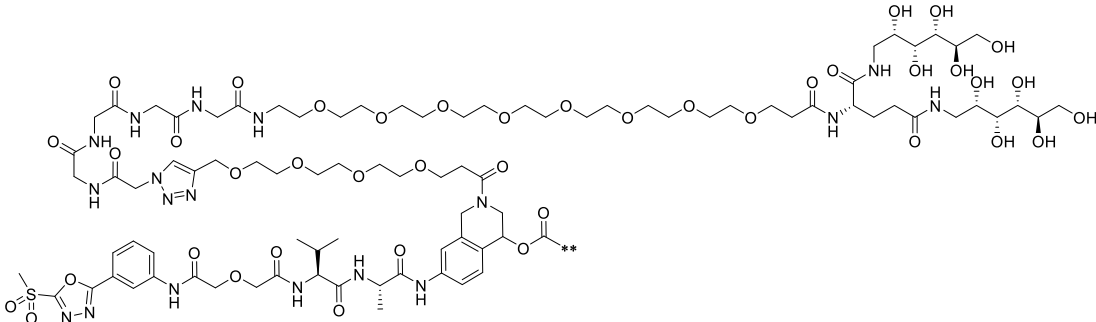
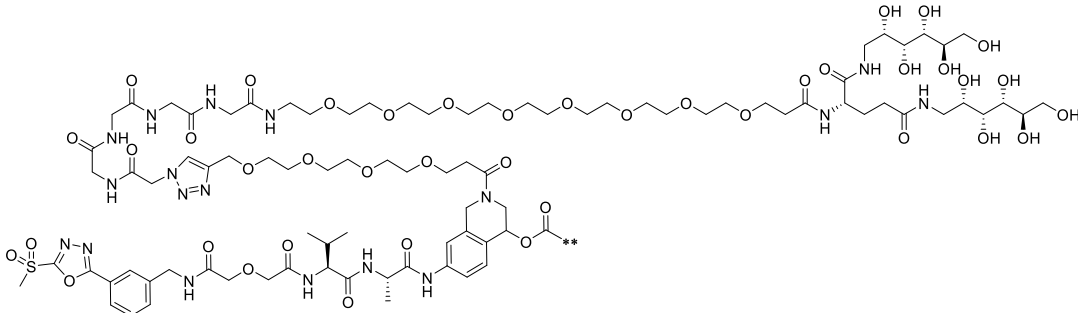
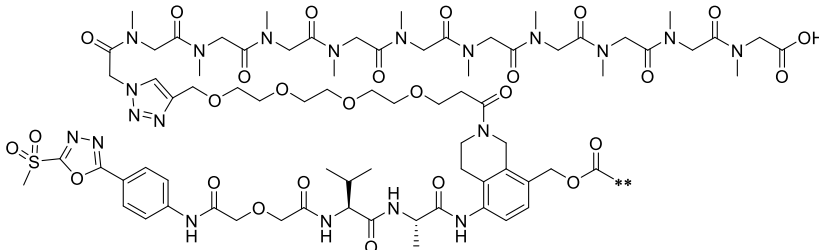
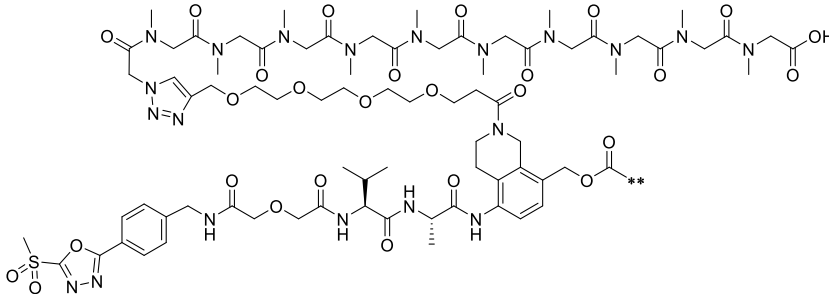
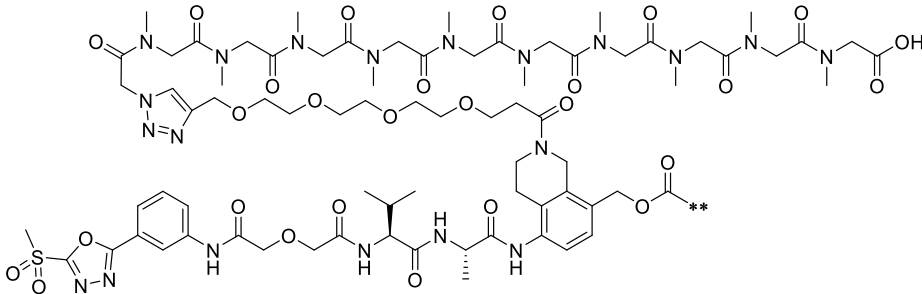


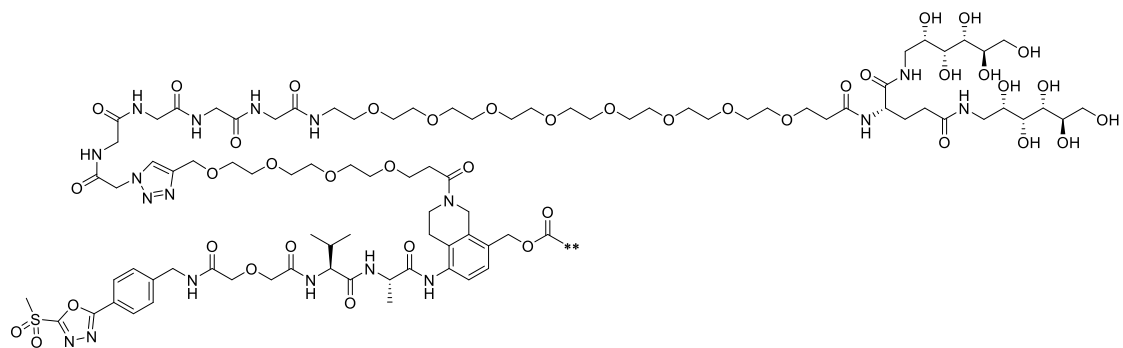
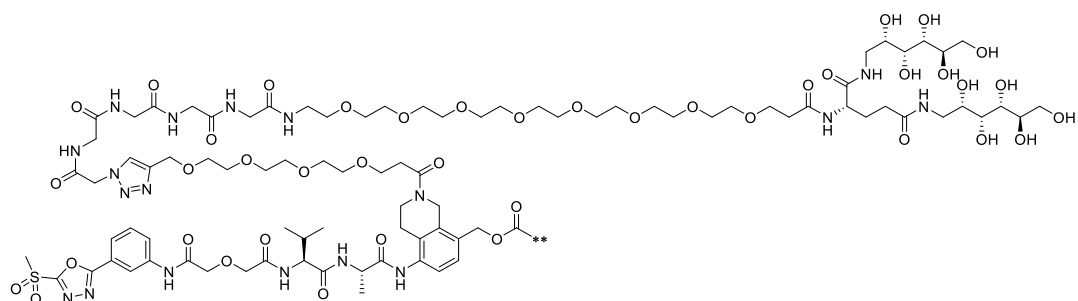
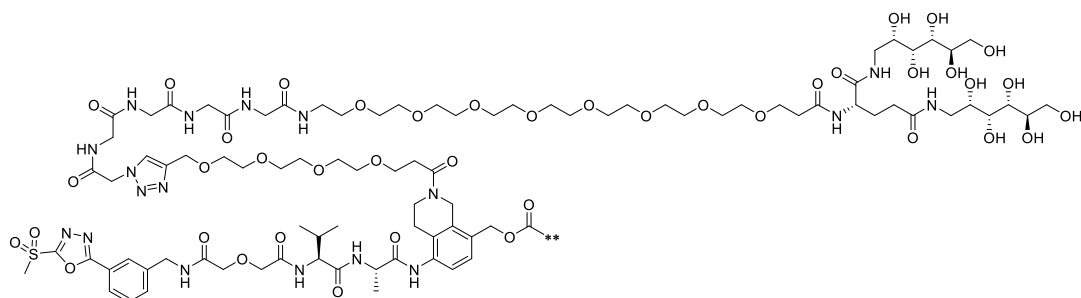
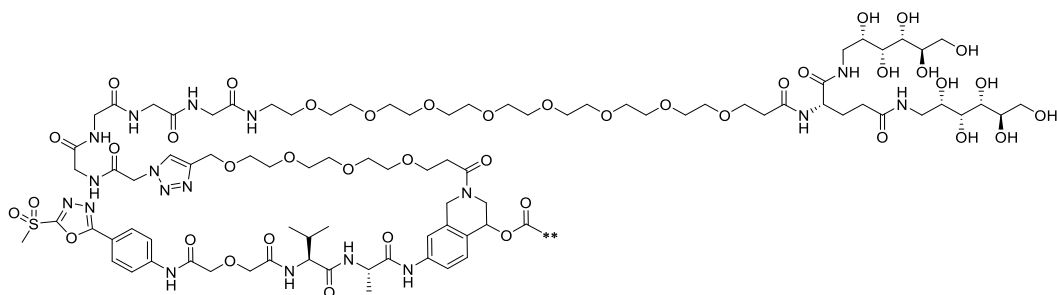
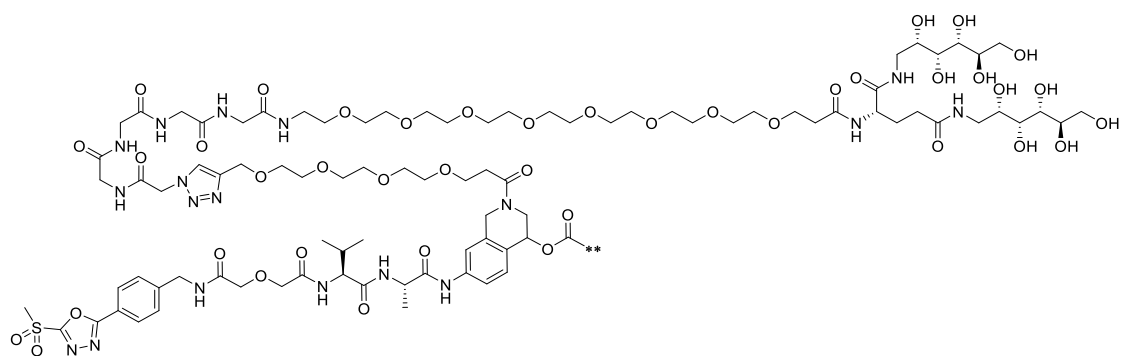


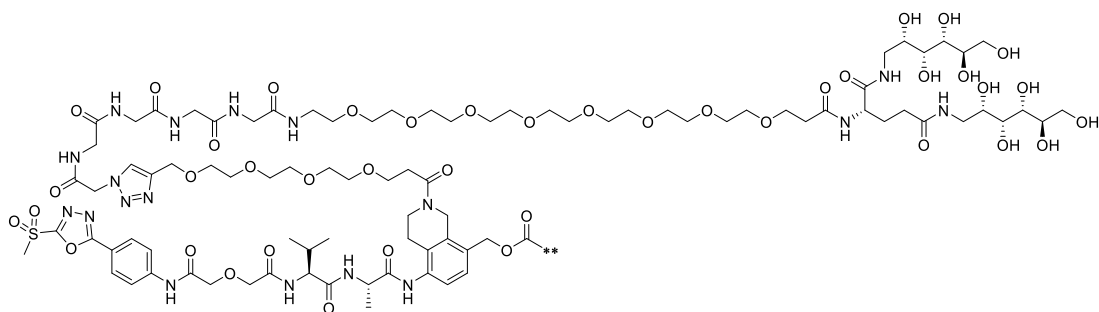
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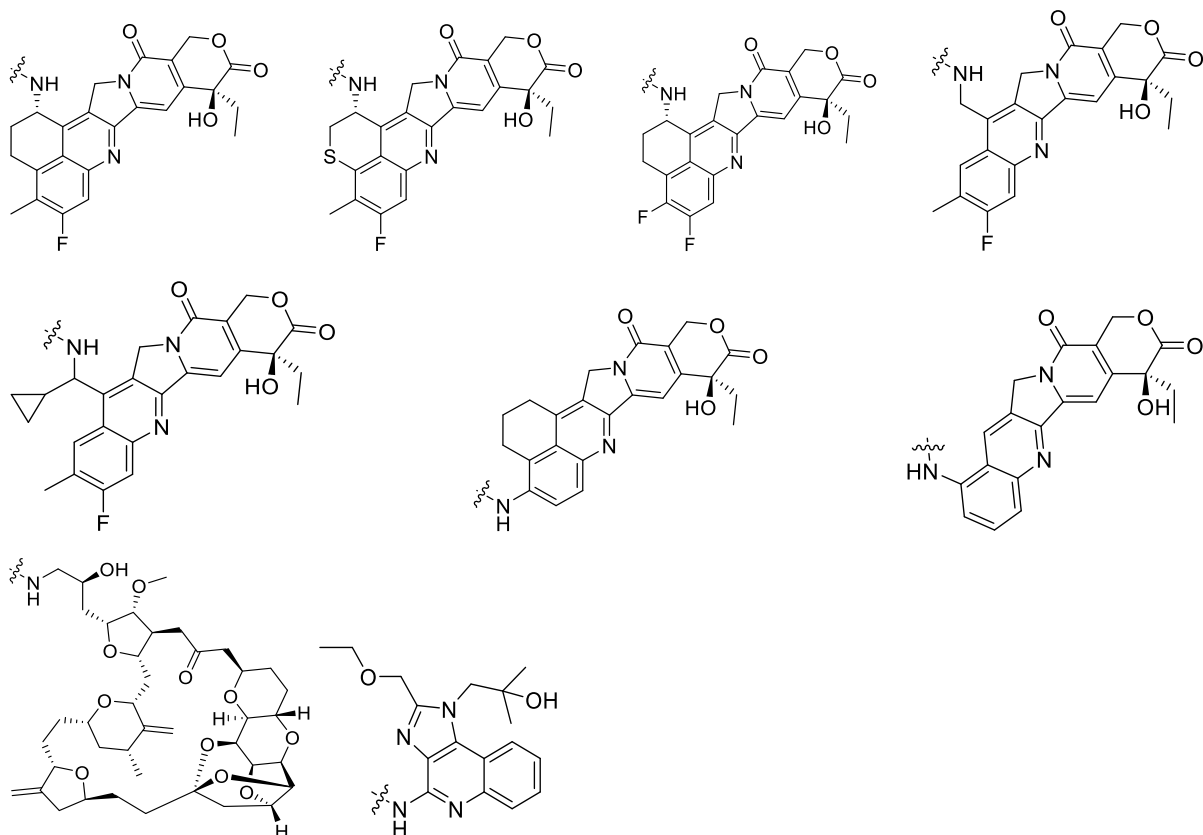


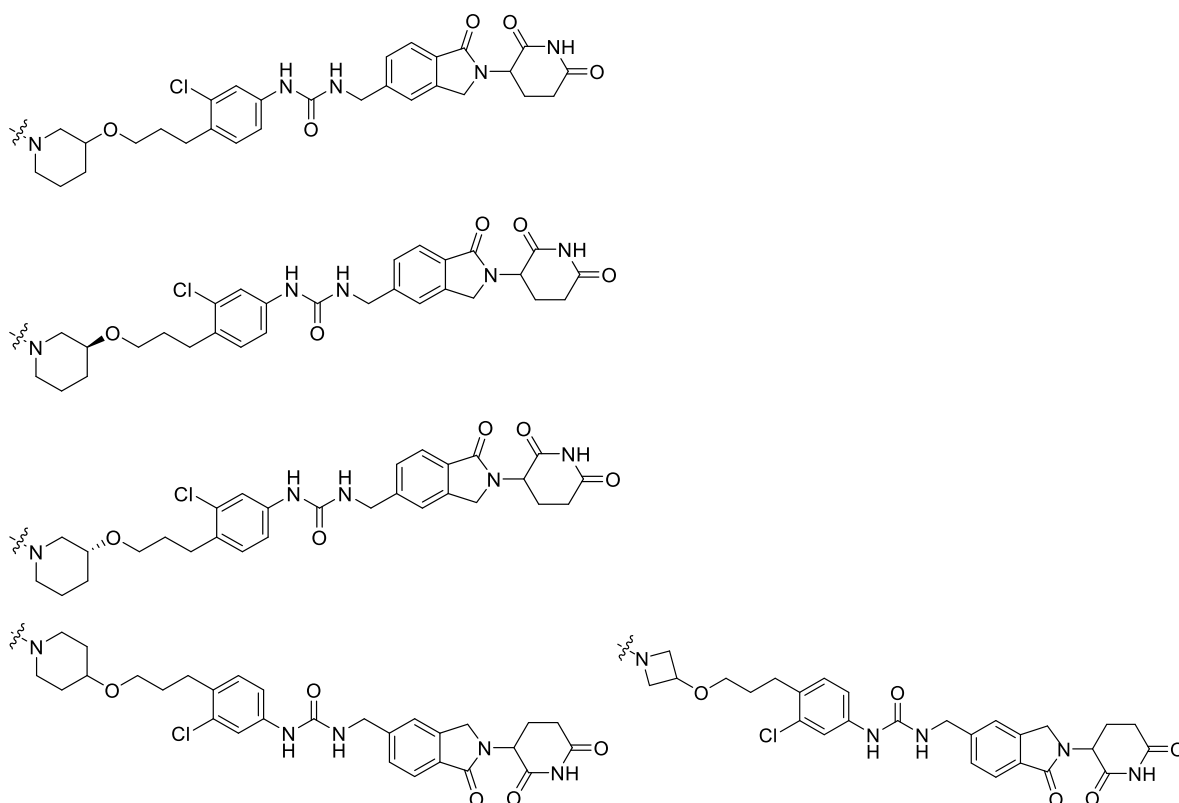


wherein ** represents linkage to the amino group of the bioactive molecule D.

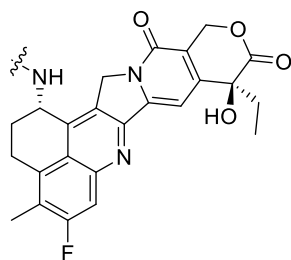
In some embodiments, in the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof, the bioactive molecule D is selected from a camptothecin derivative, eribulin, and a molecular glue.

In some embodiments, in the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof, the bioactive molecule D is selected from compounds of the following formulas:

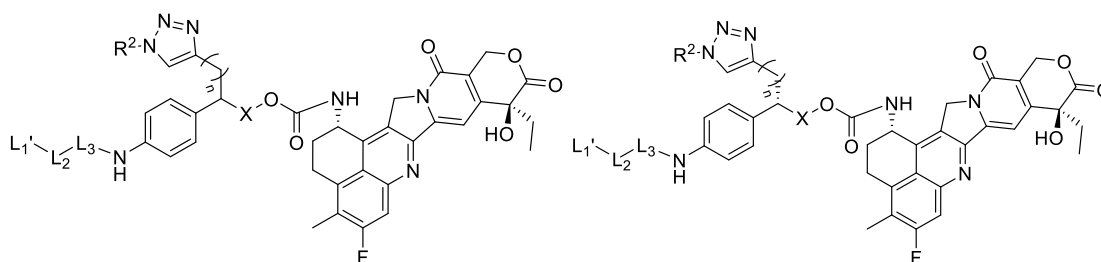


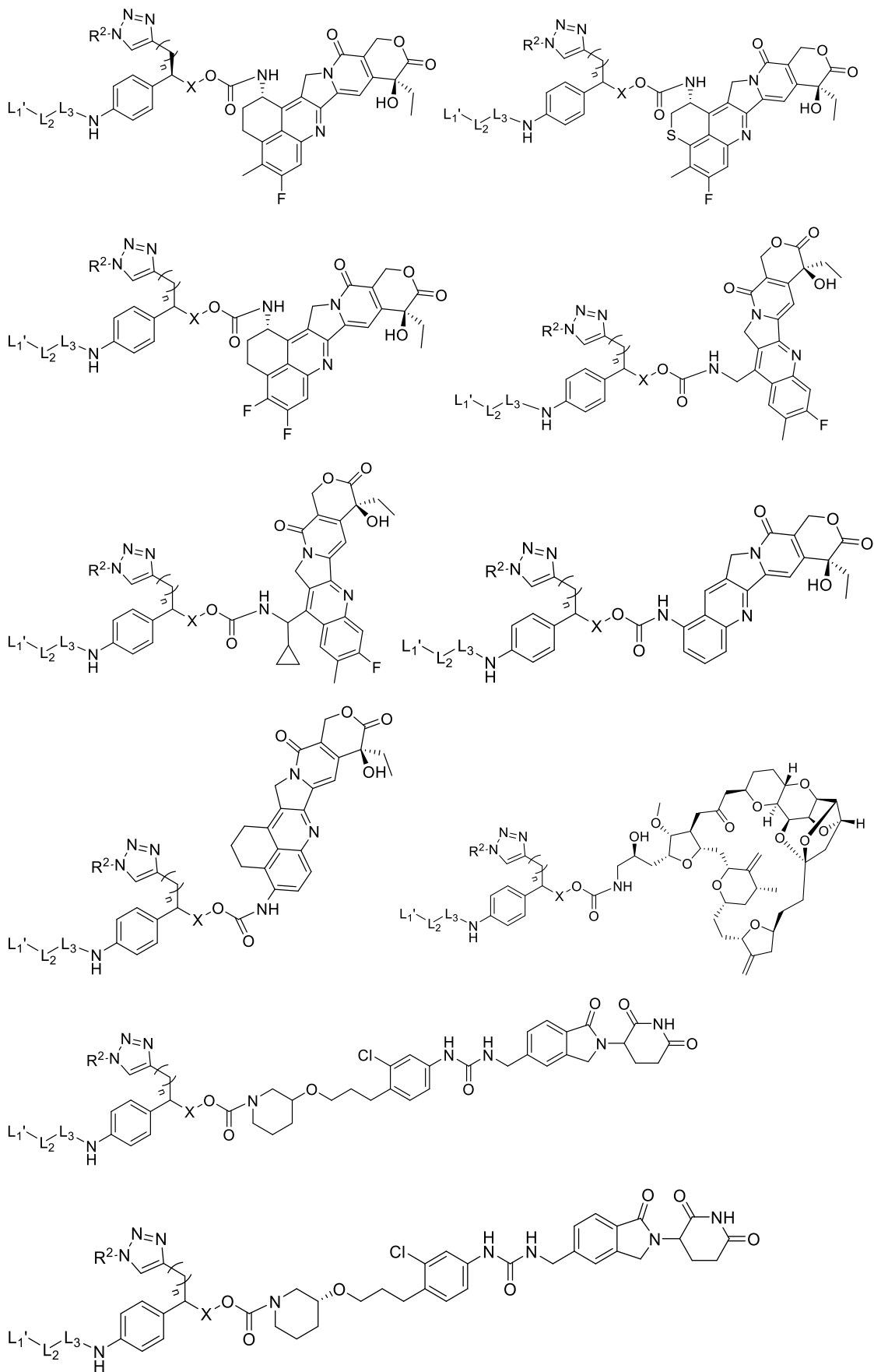


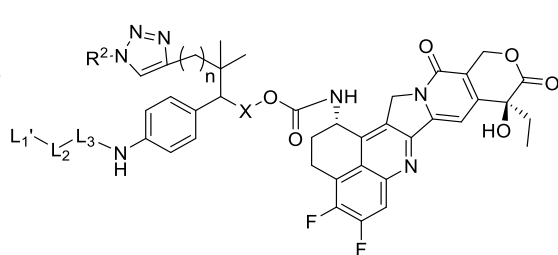
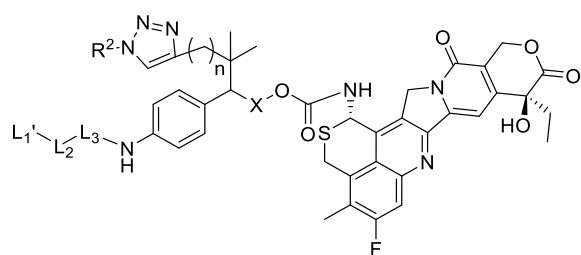
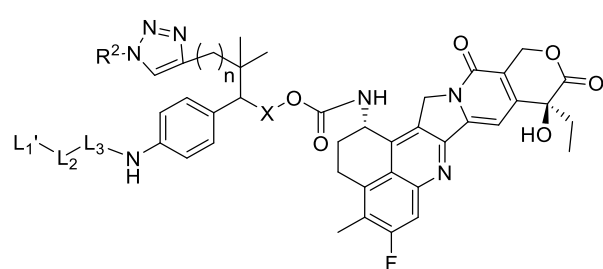
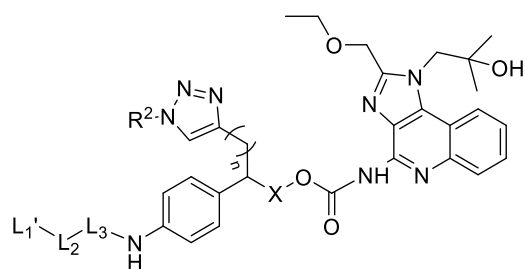
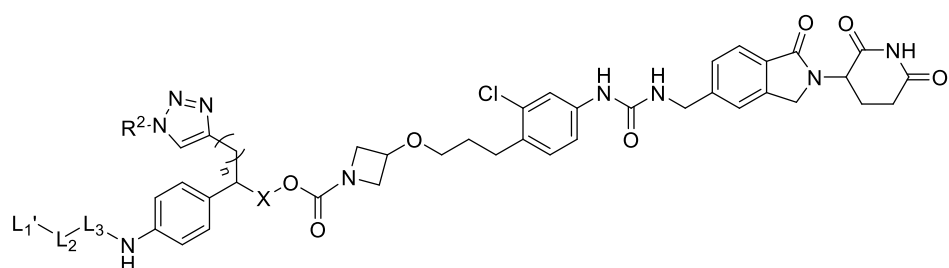
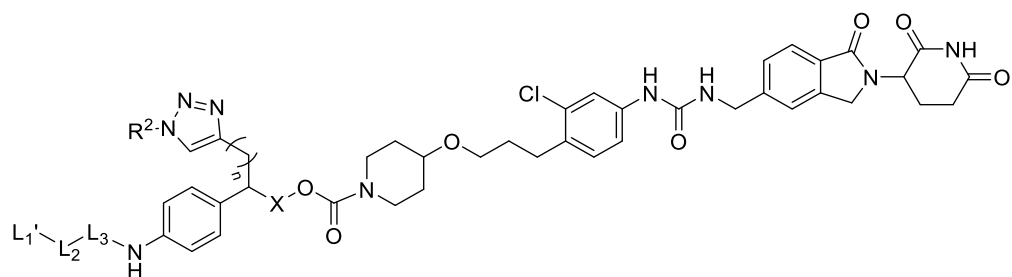
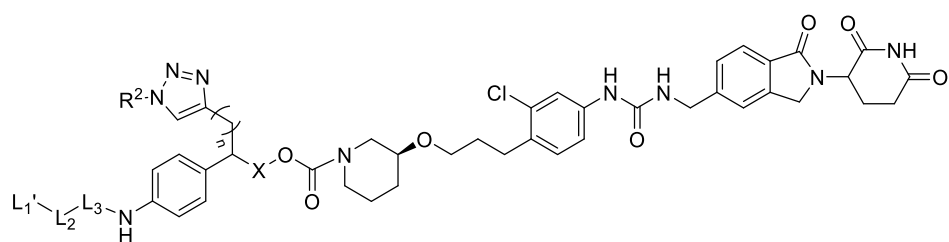
- 5 In some embodiments, in the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof, the bioactive molecule D is selected from:



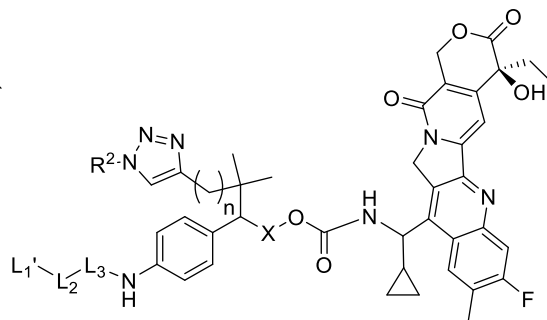
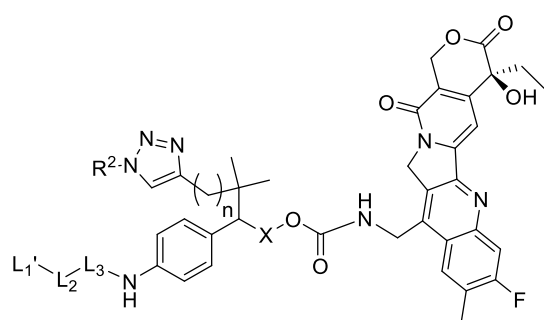
- 10 In some embodiments, the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof have a structure shown as follows:

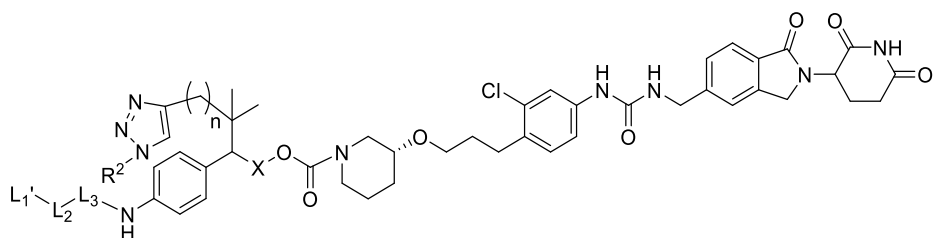
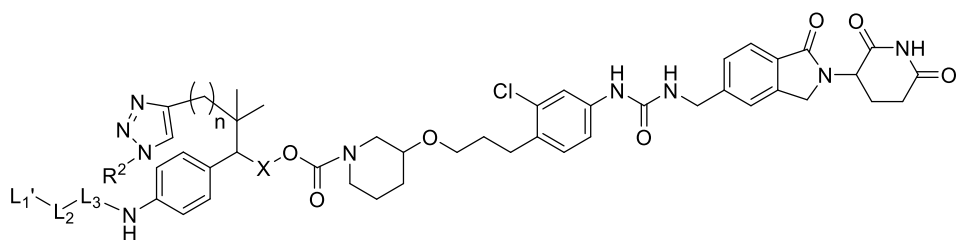
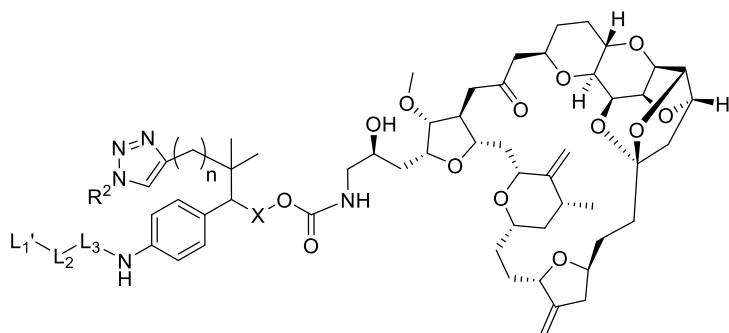
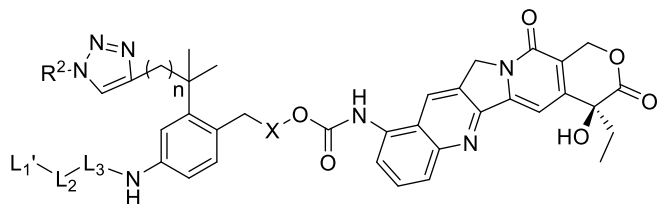
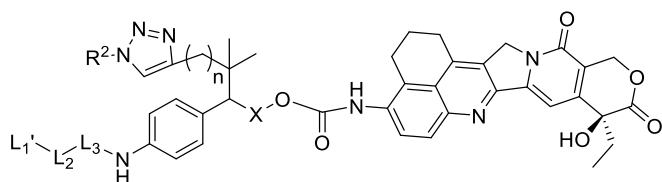




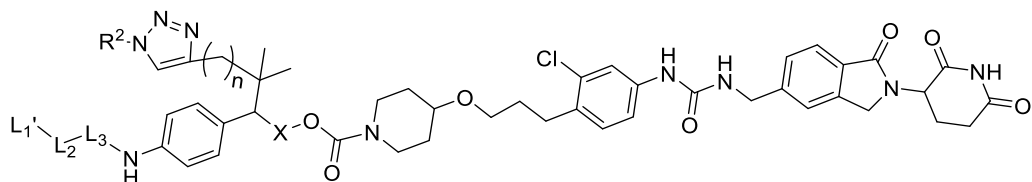
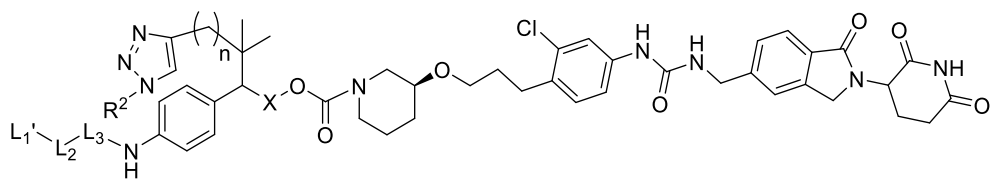


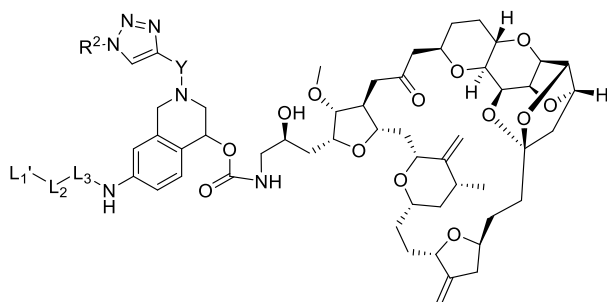
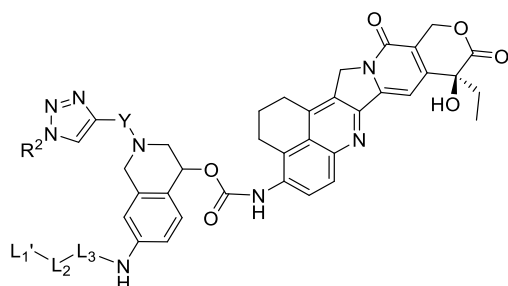
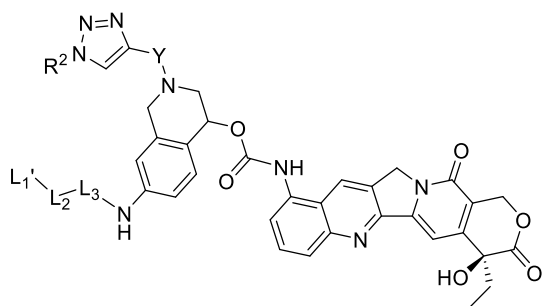
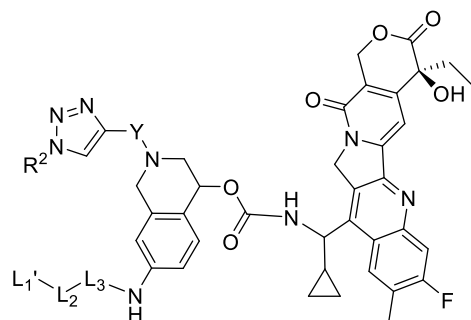
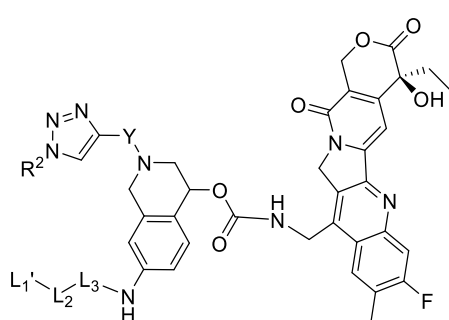
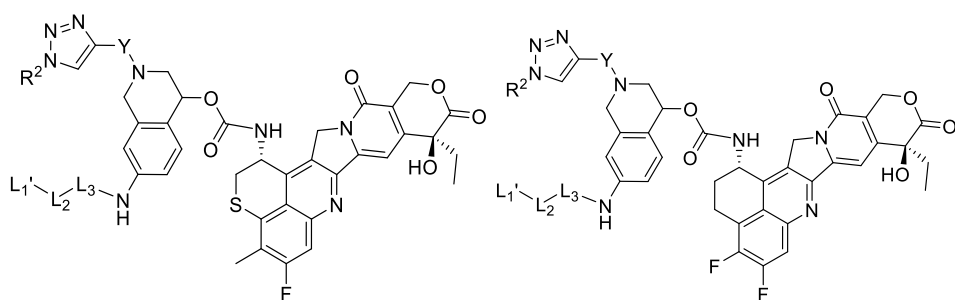
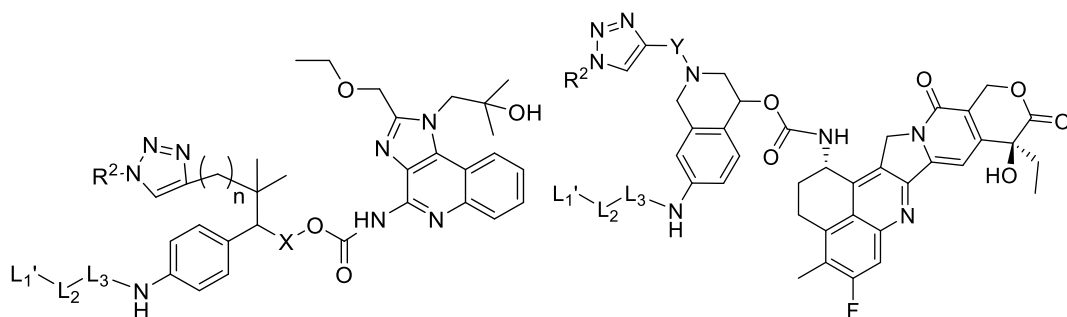
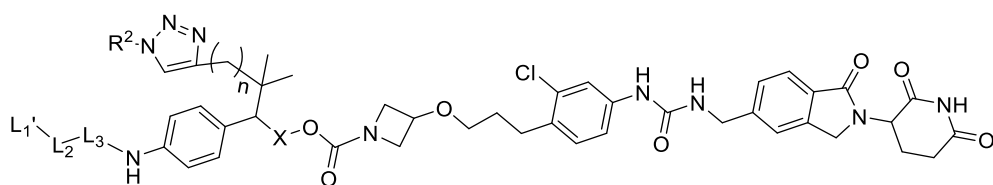
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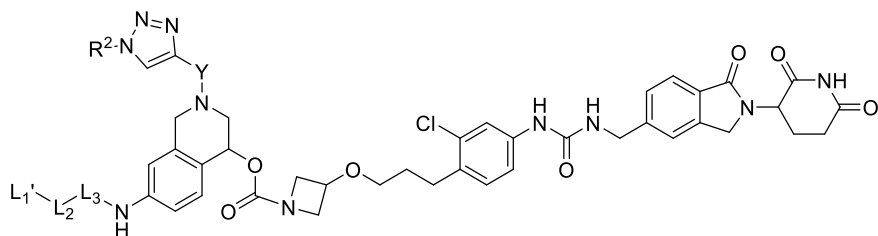
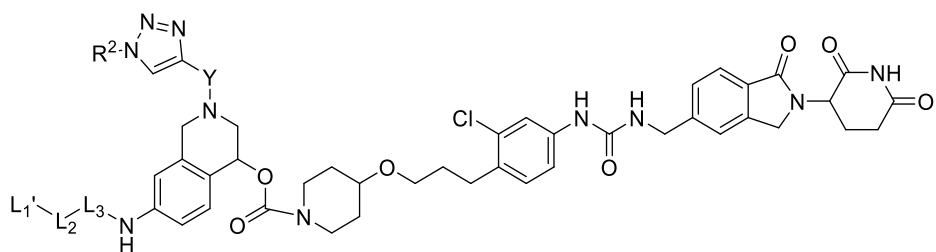
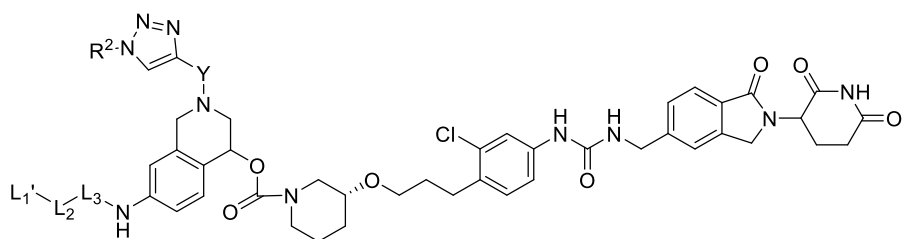
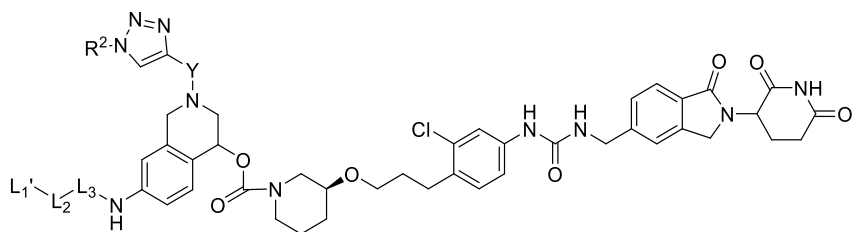
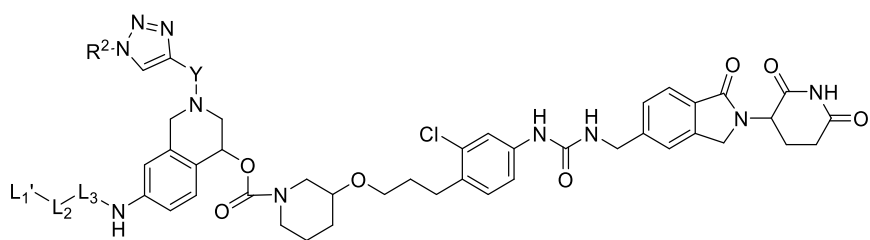




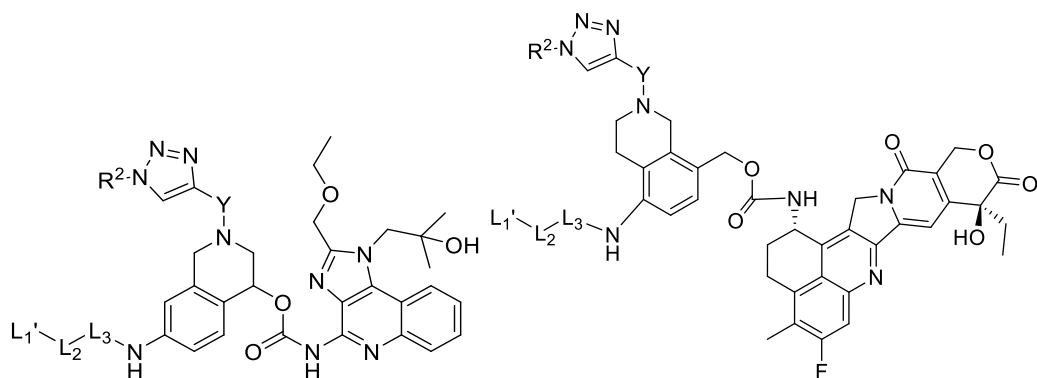
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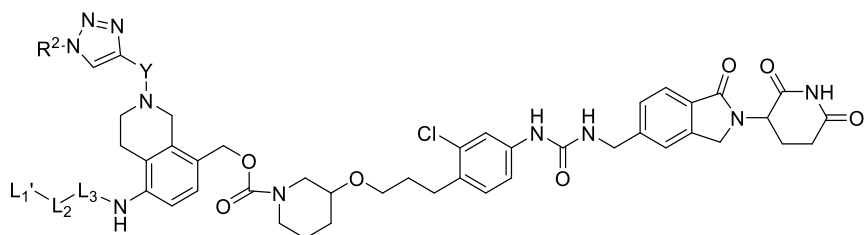
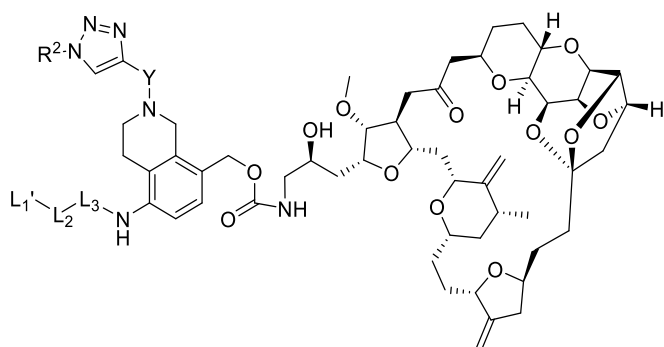
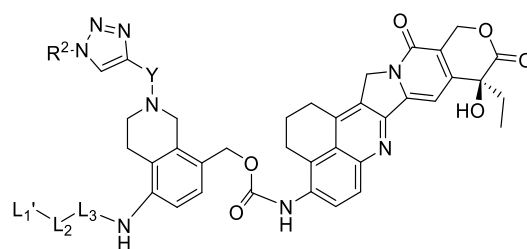
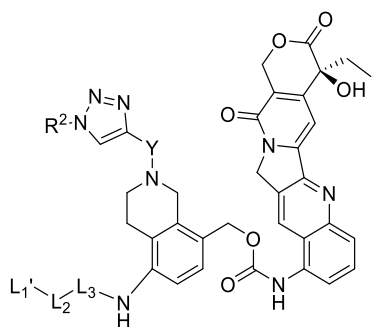
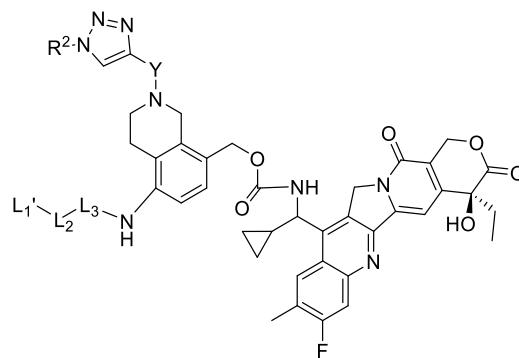
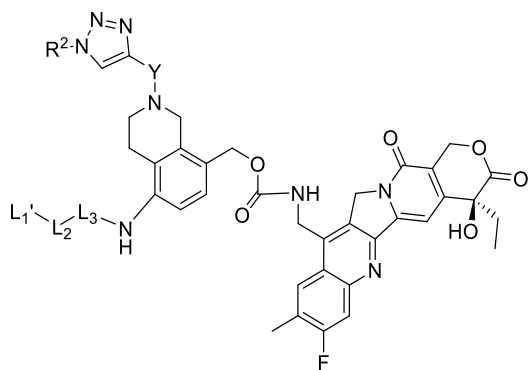
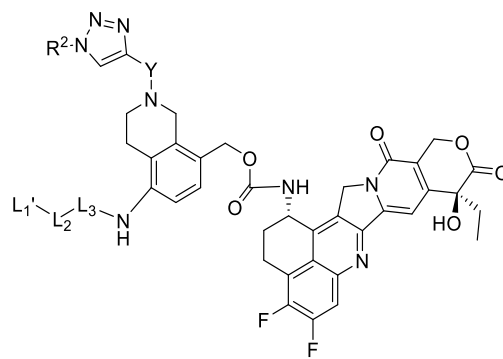
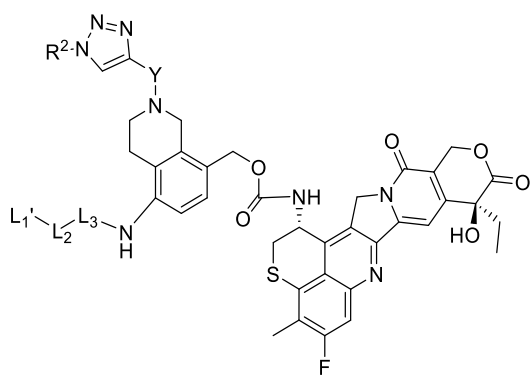


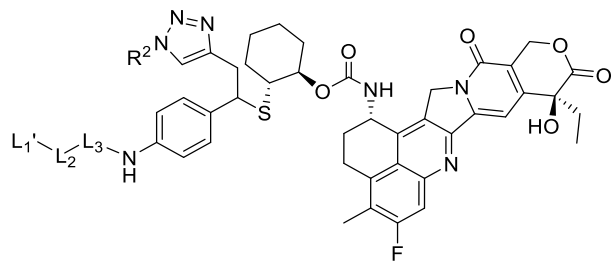
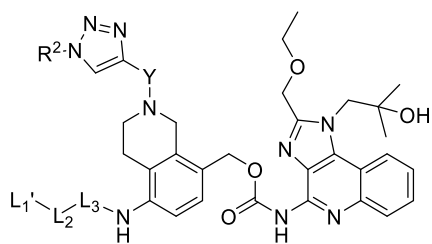
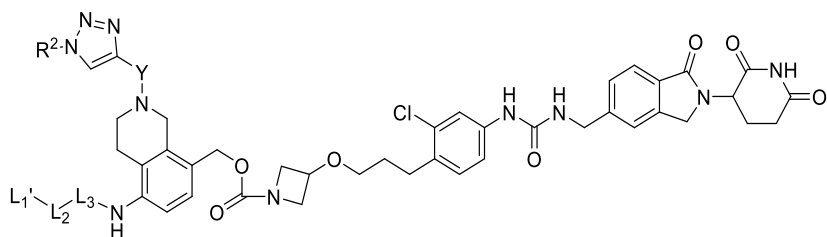
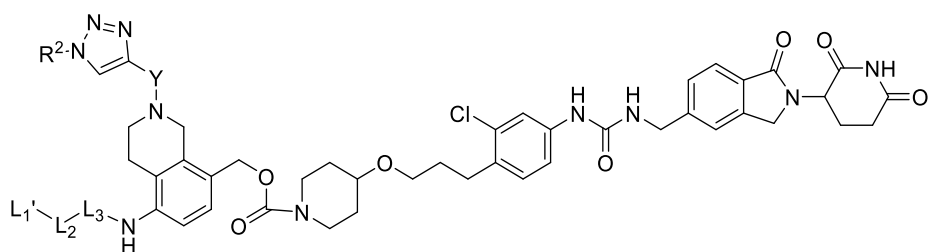
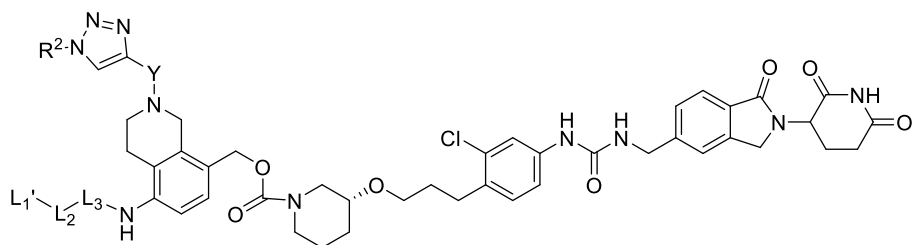
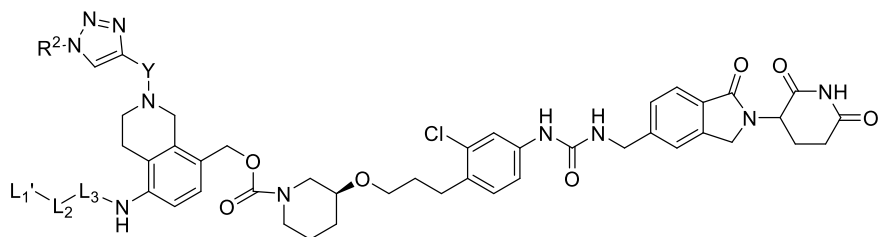




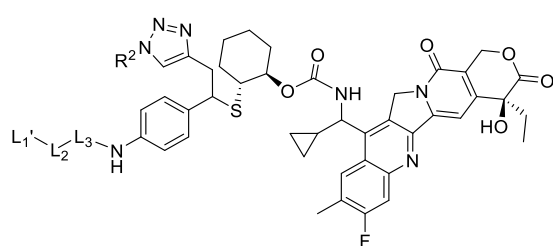
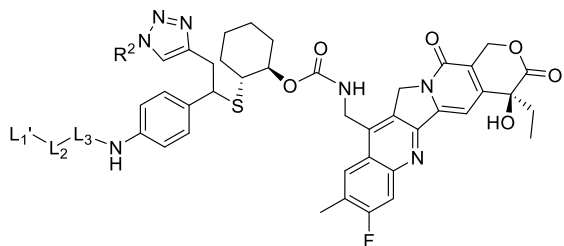
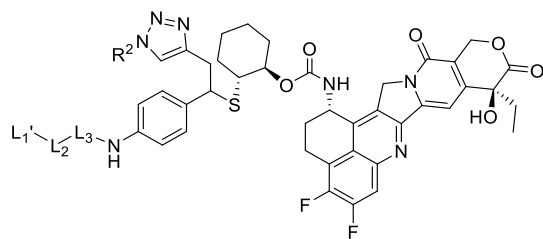
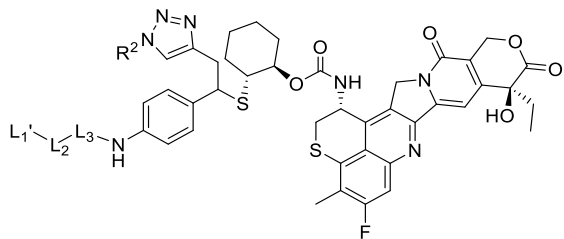
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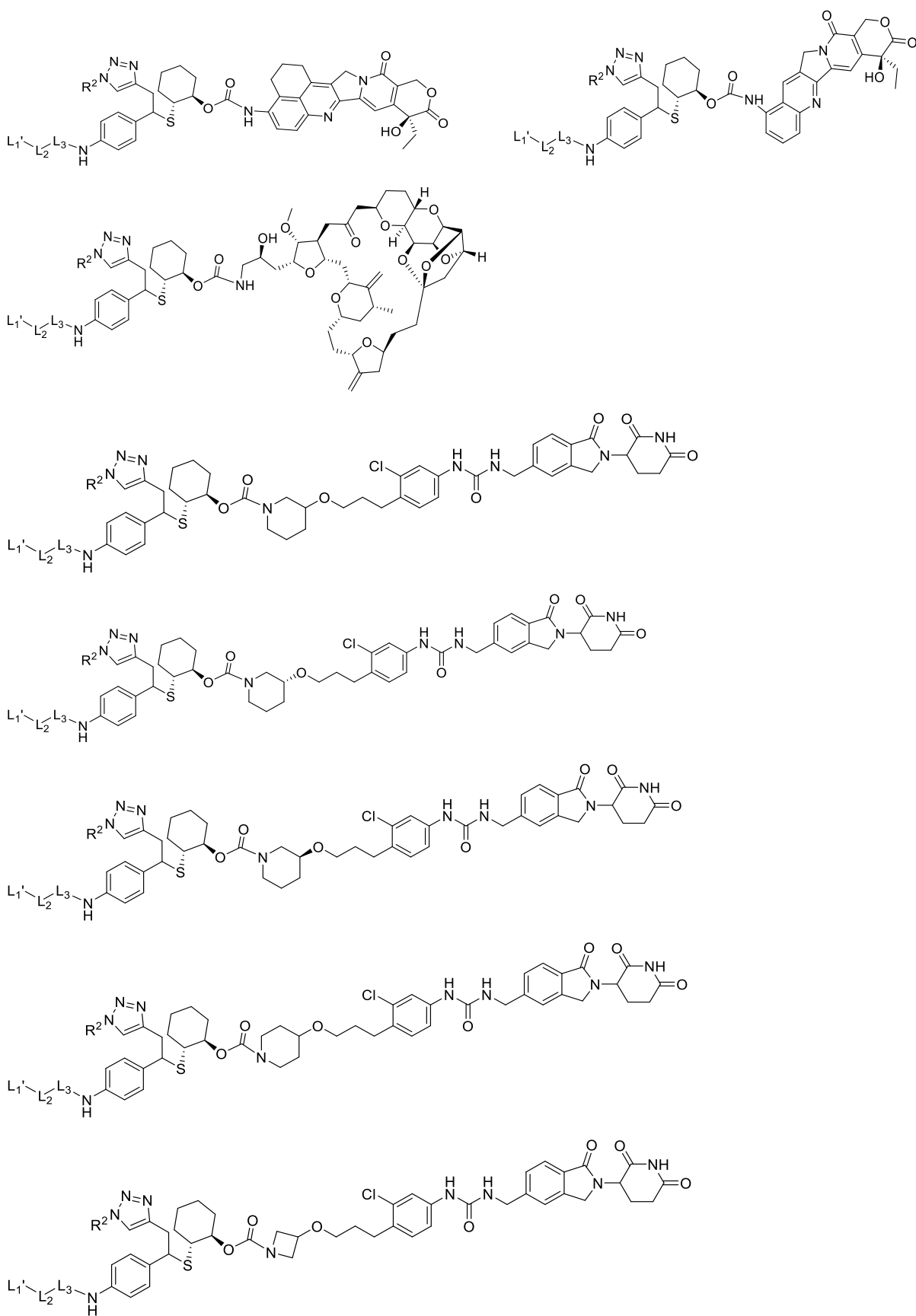


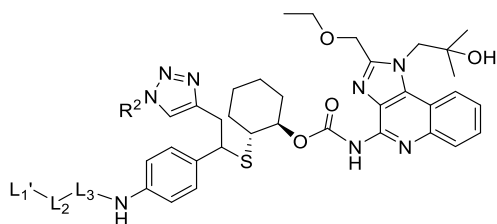




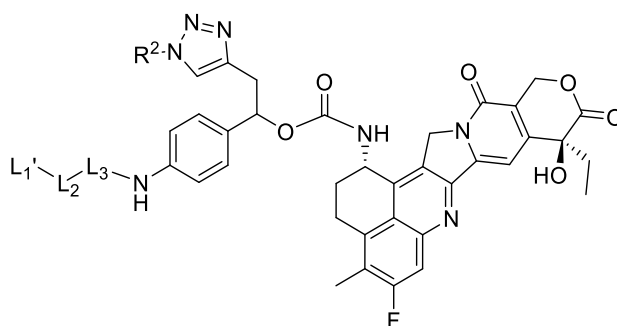
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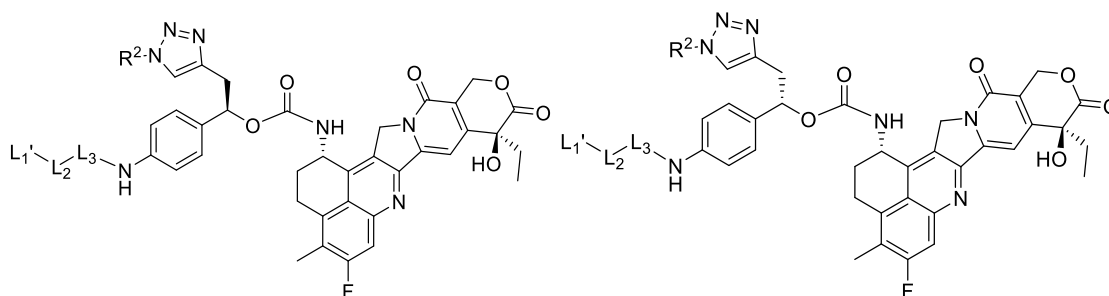




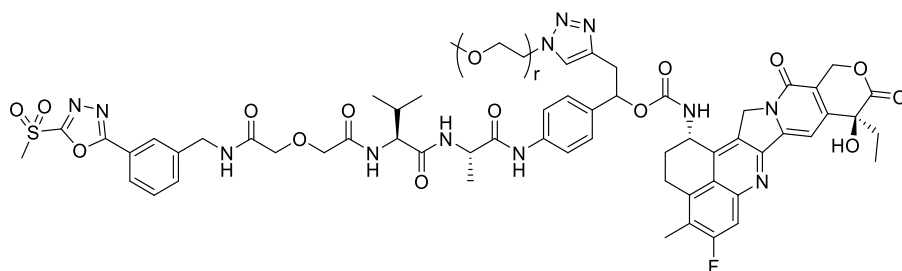
In some embodiments, the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof have a structure shown as follows:

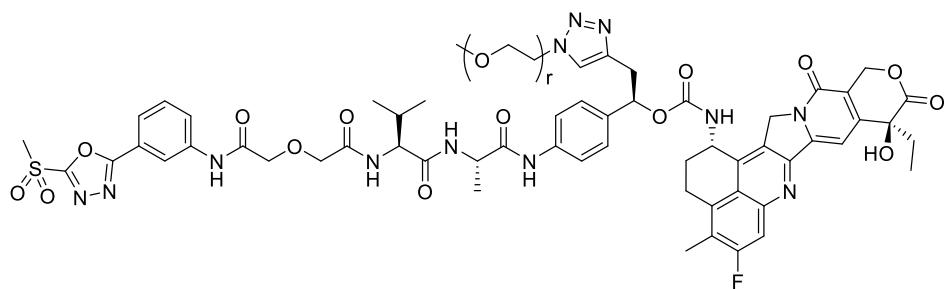
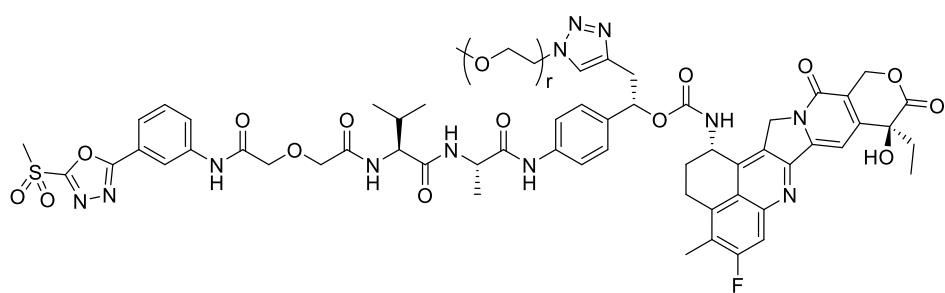
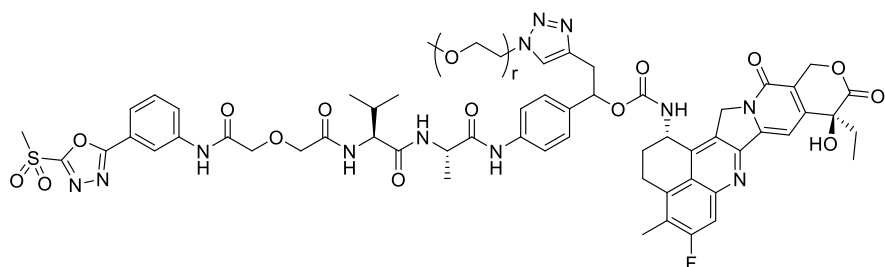
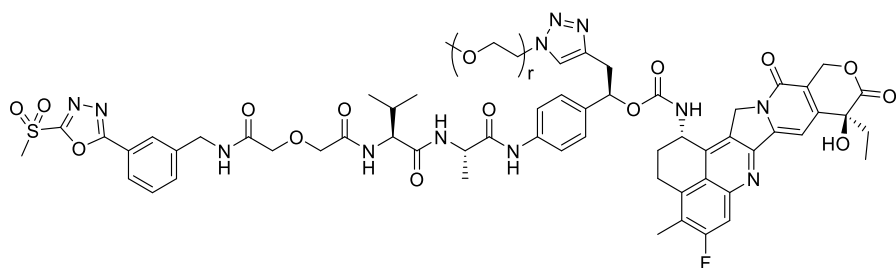
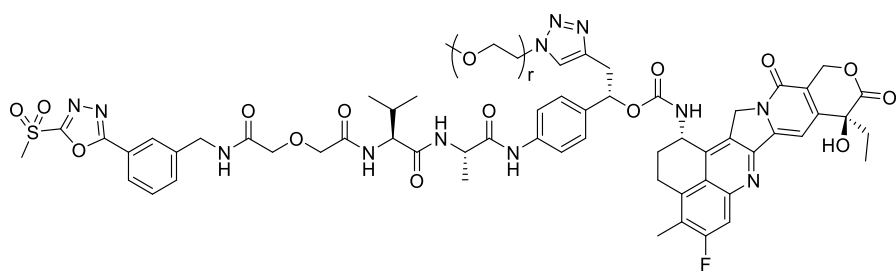


In some embodiments, the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof have a structure shown as follows:

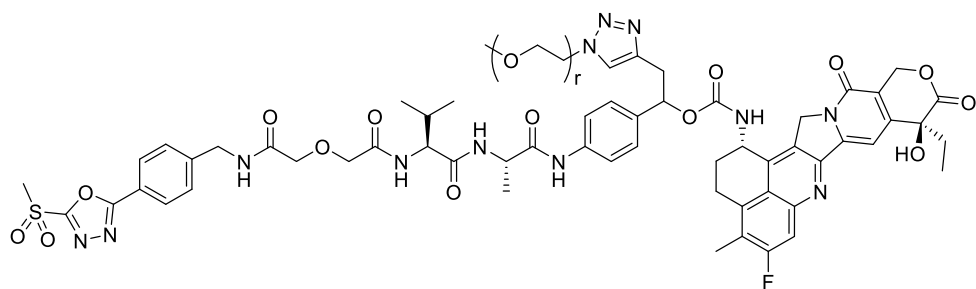


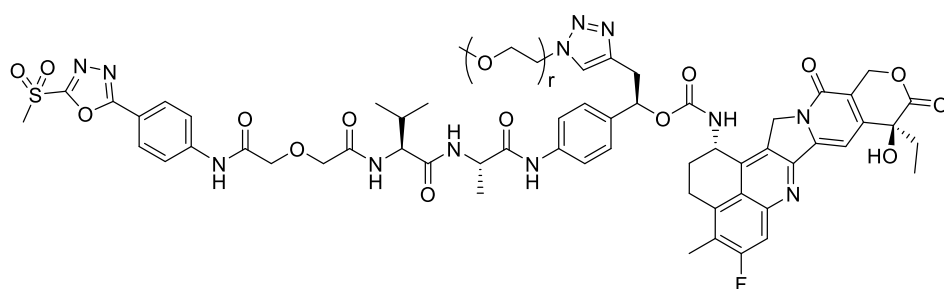
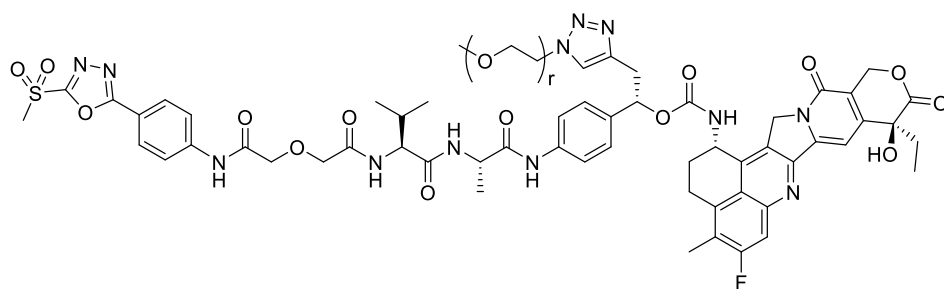
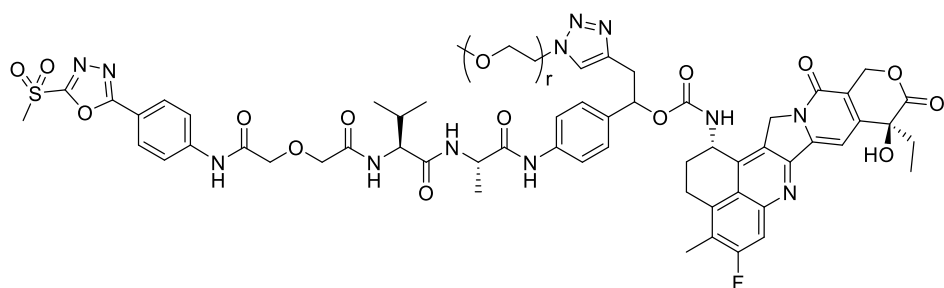
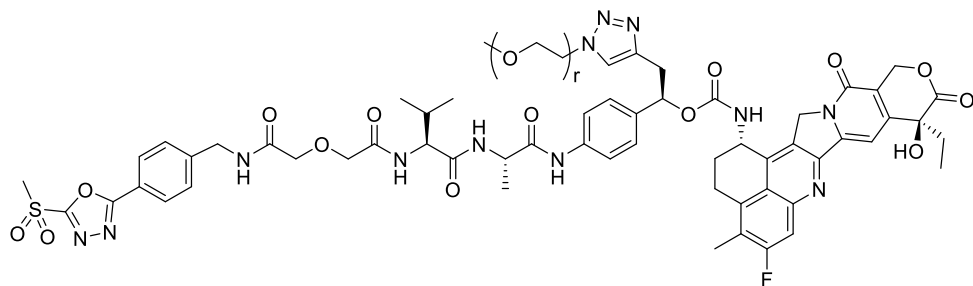
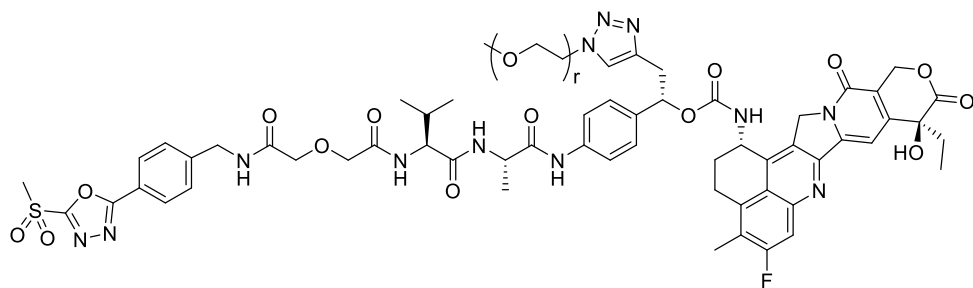
In some embodiments, the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof have a structure shown as follows:



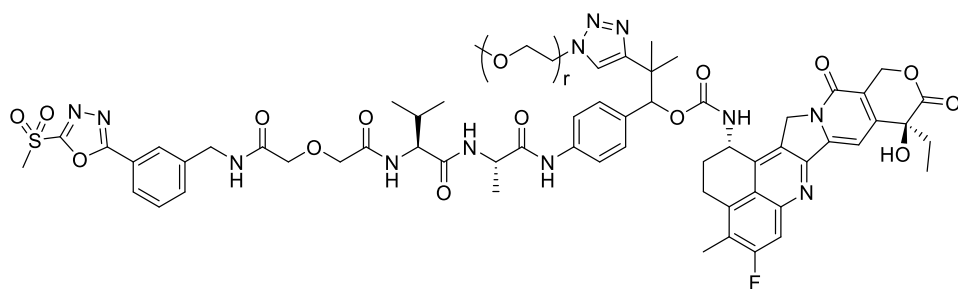


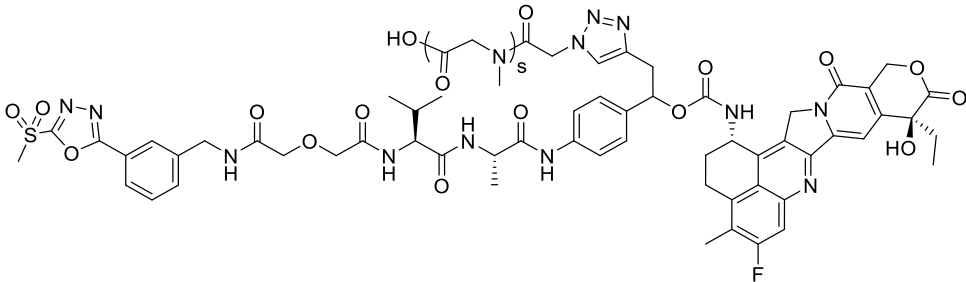
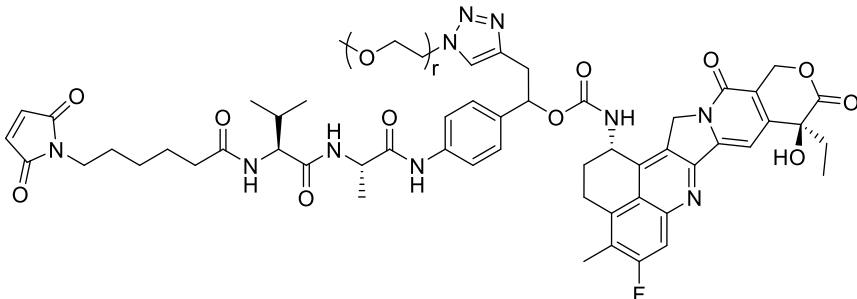
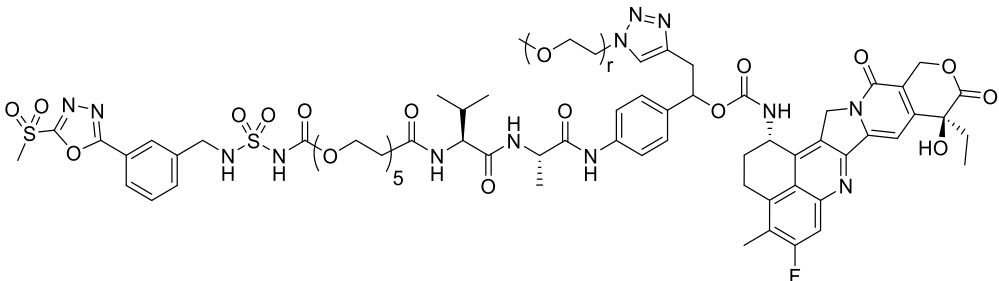
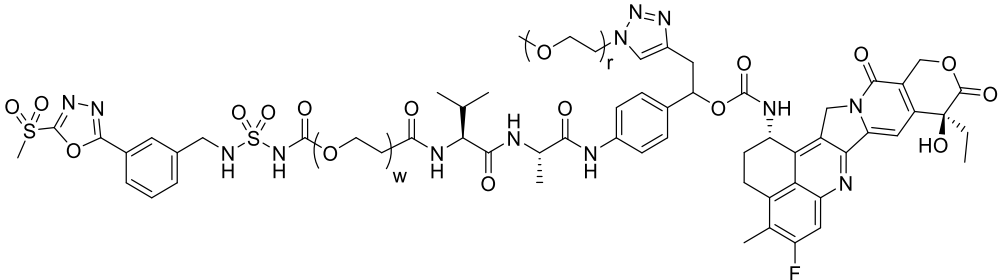
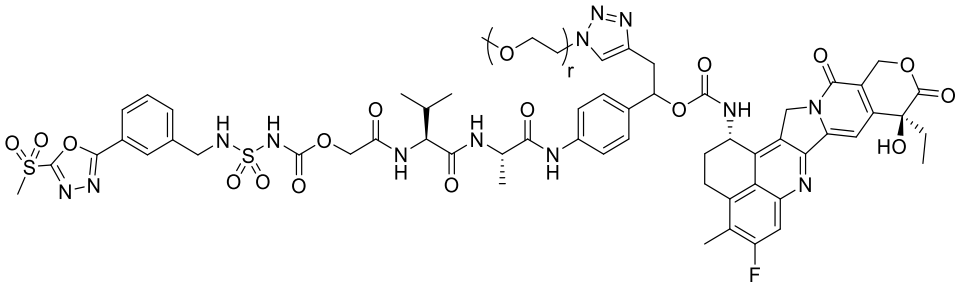
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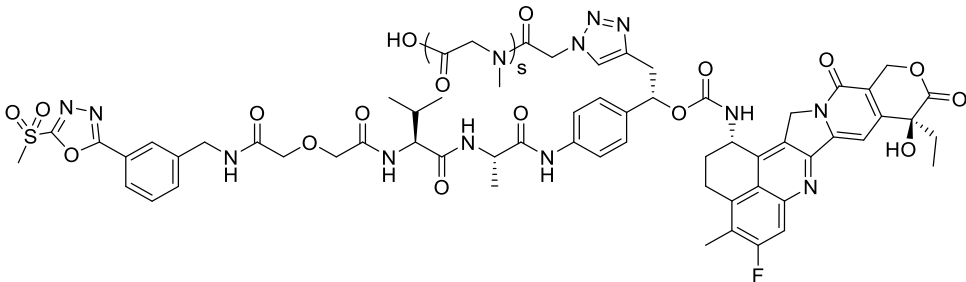


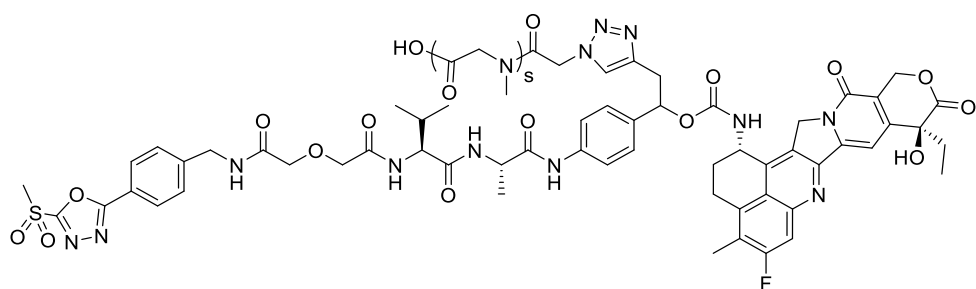
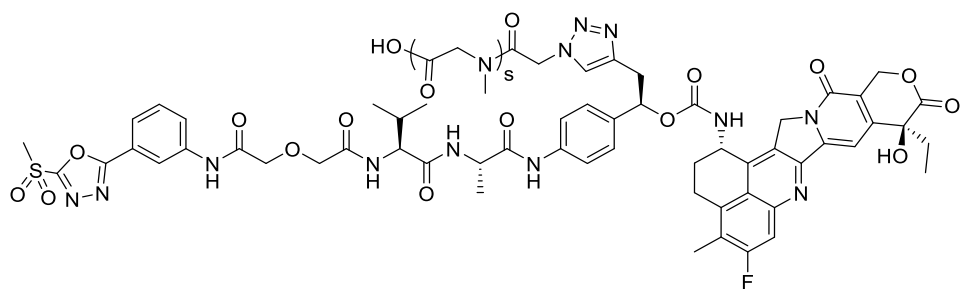
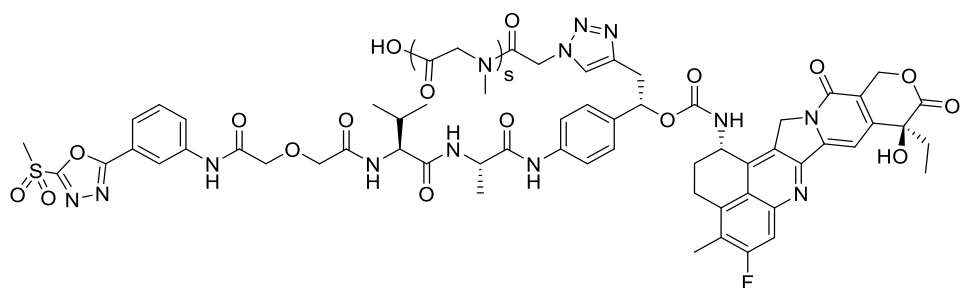
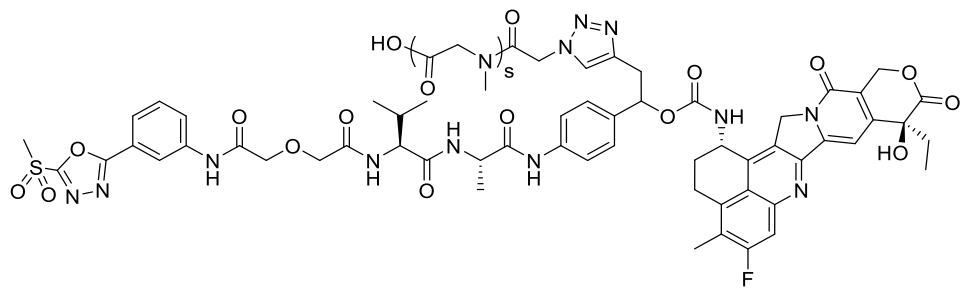
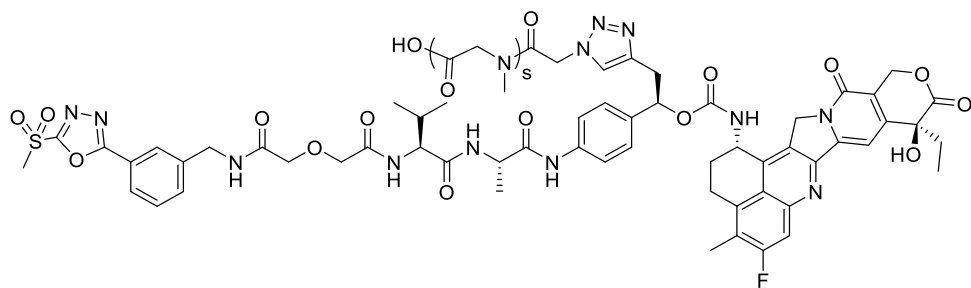
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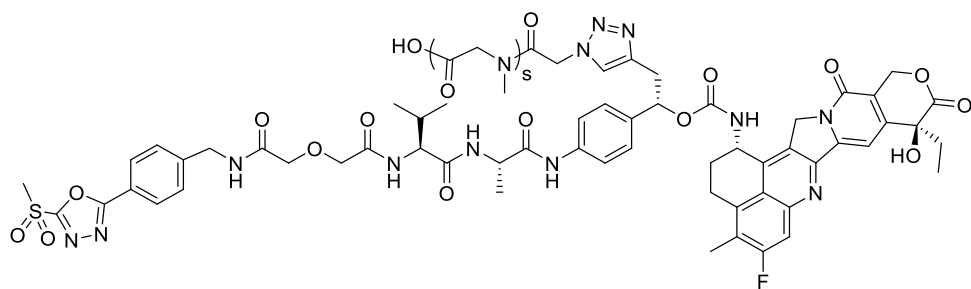


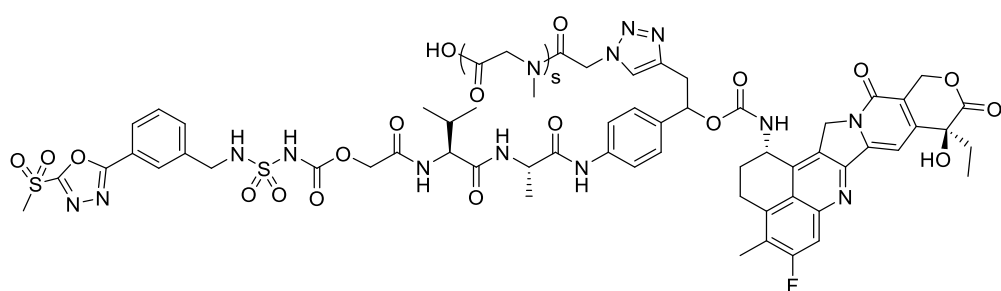
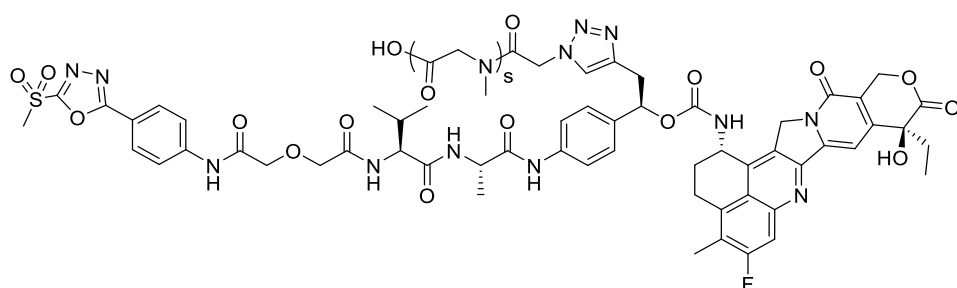
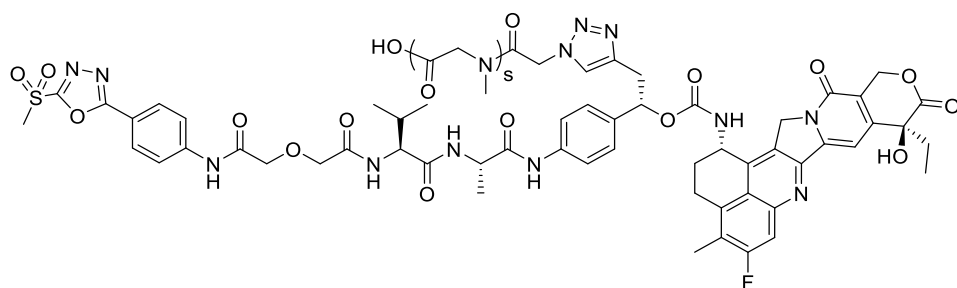
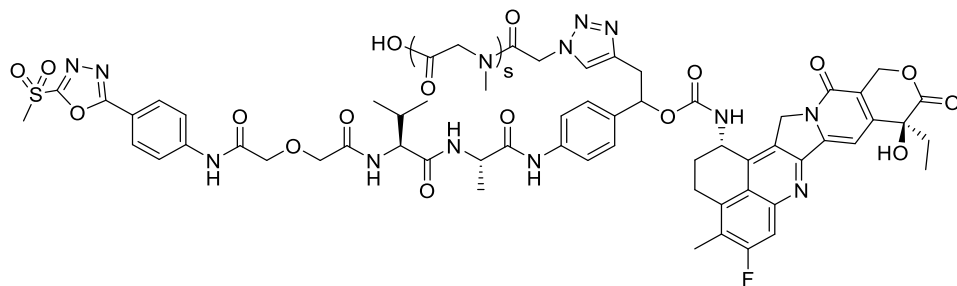
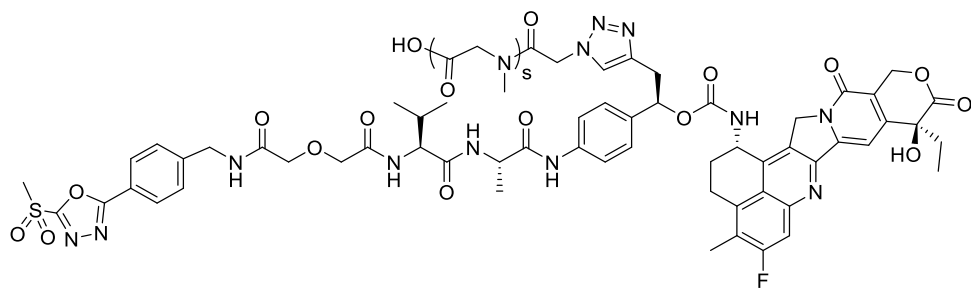
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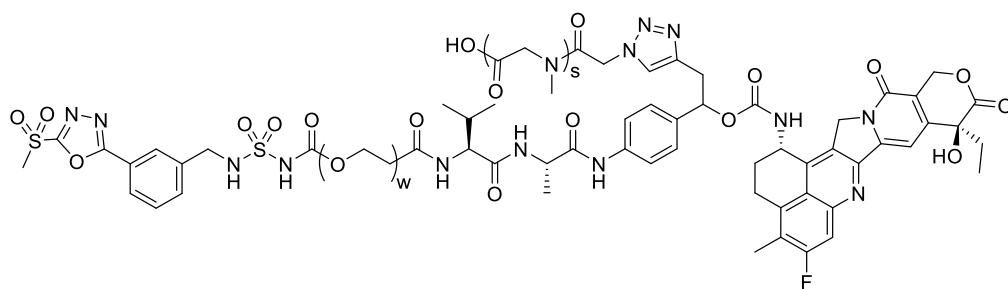


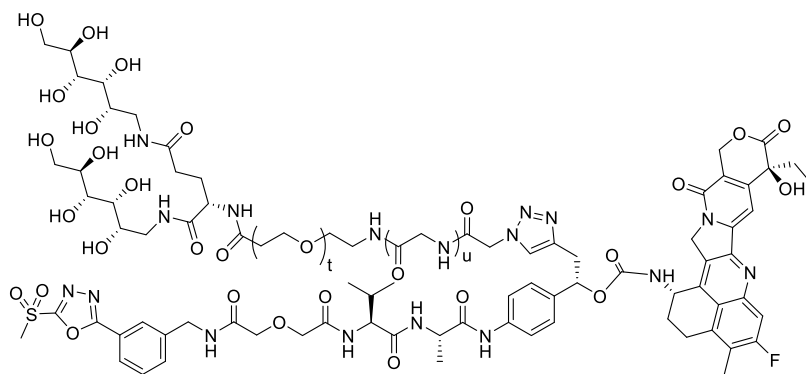
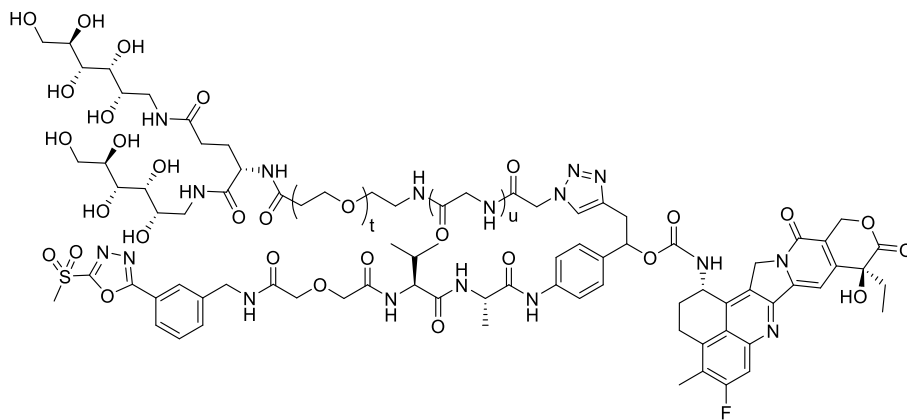
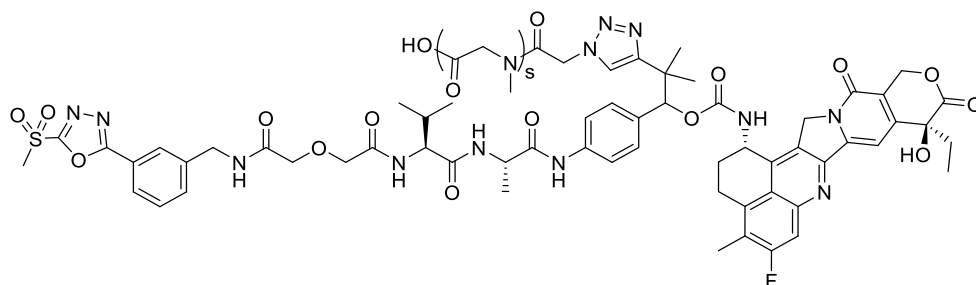
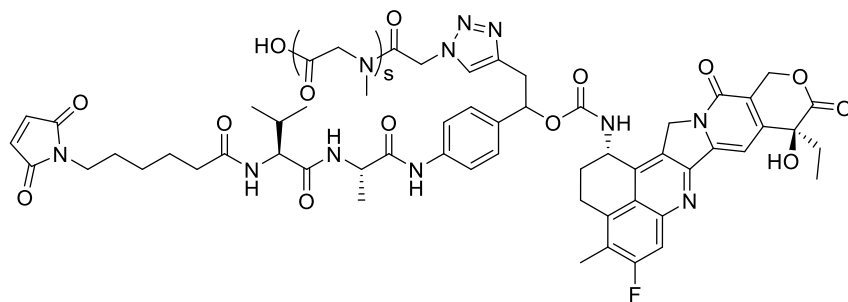
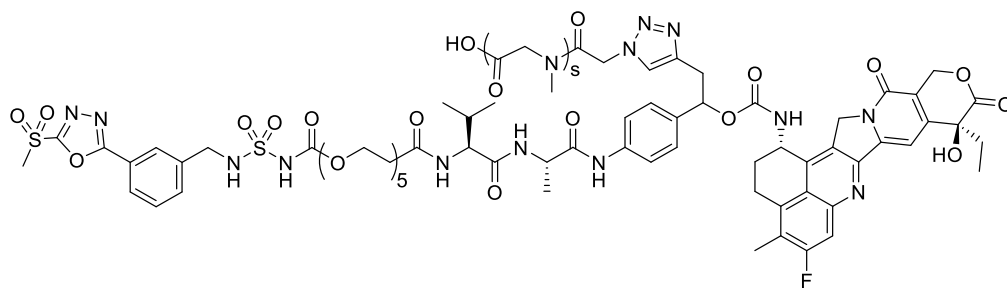
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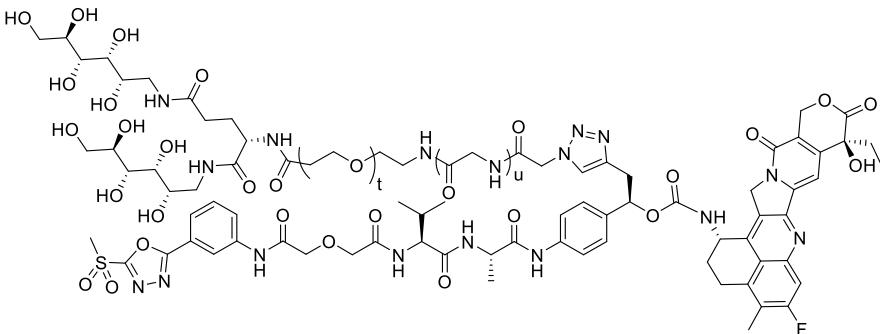
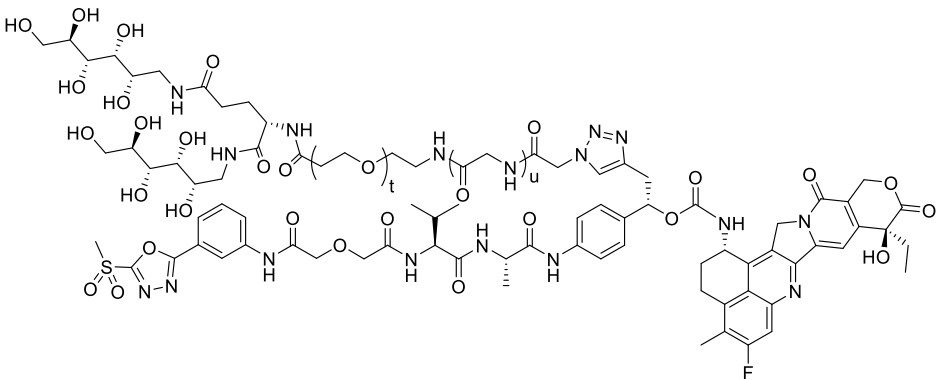
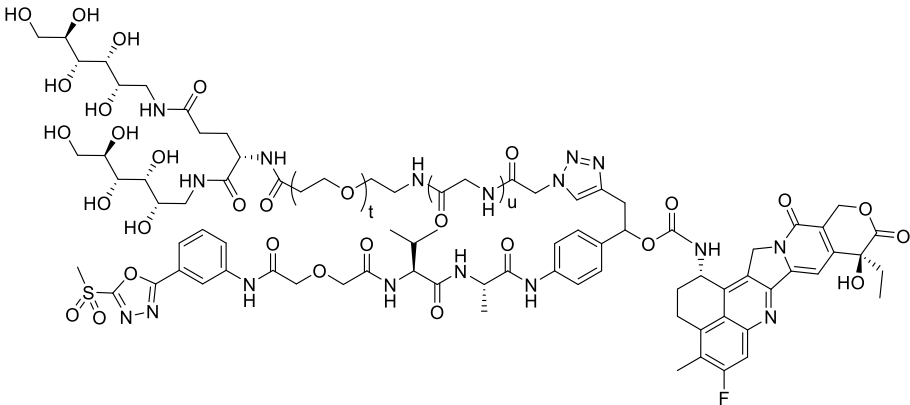
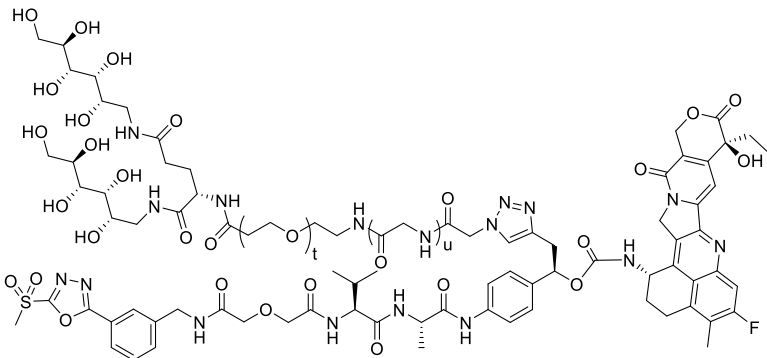


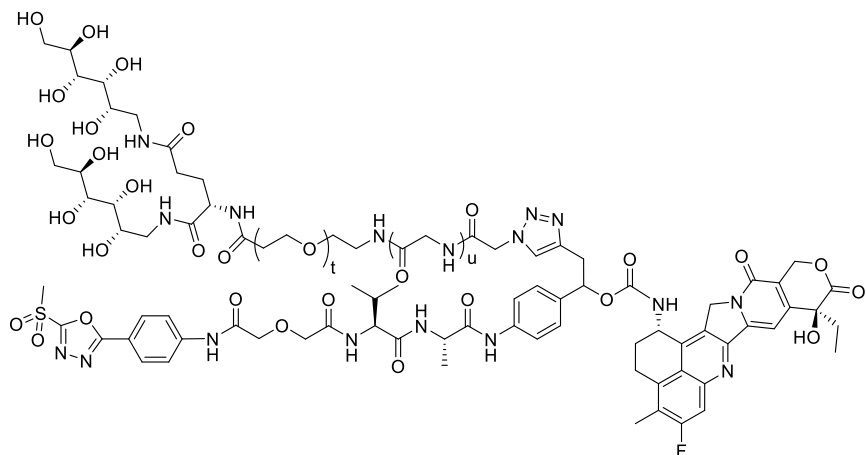
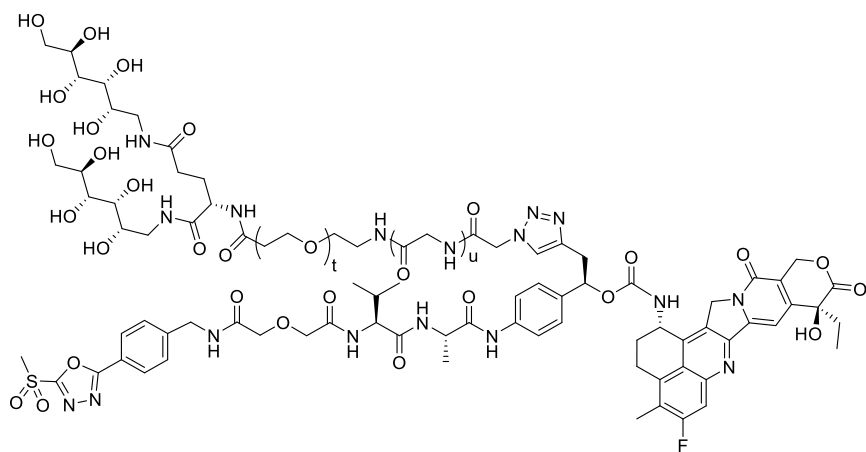
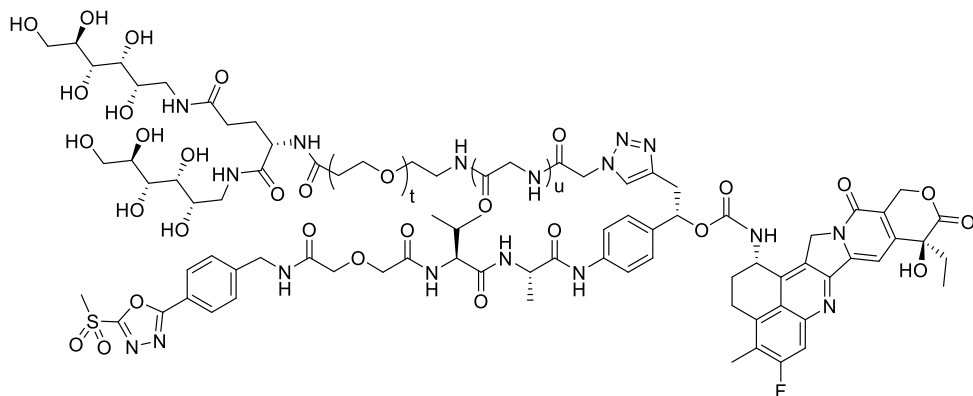
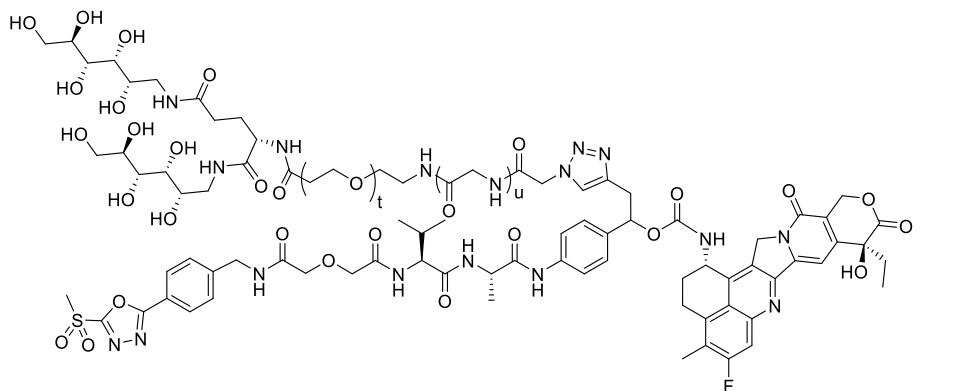


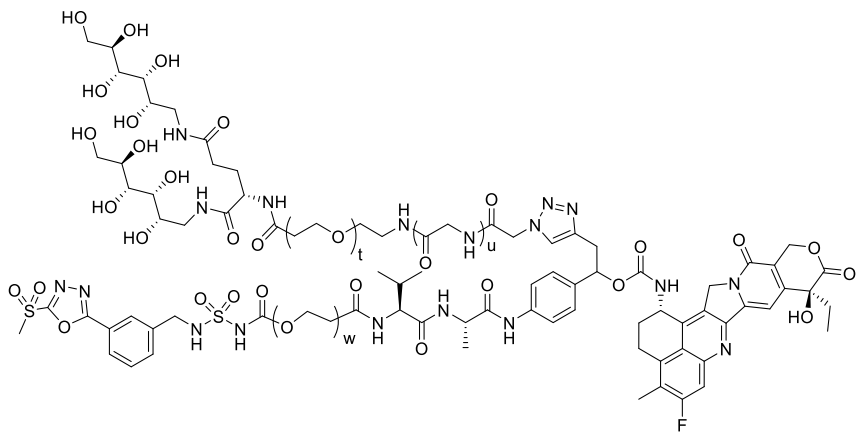
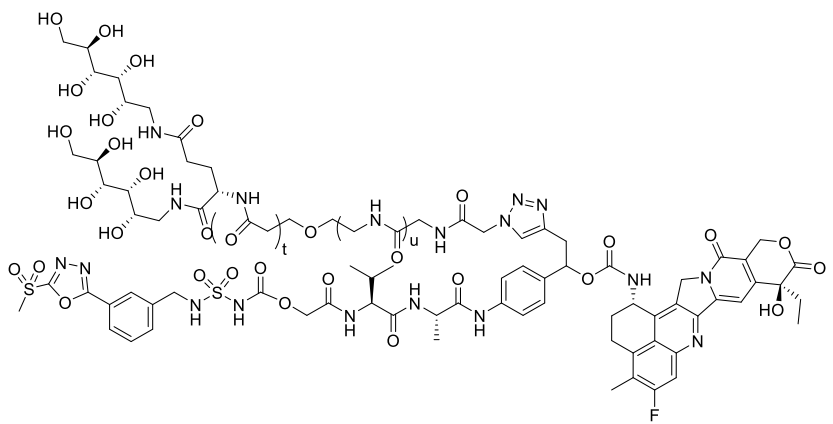
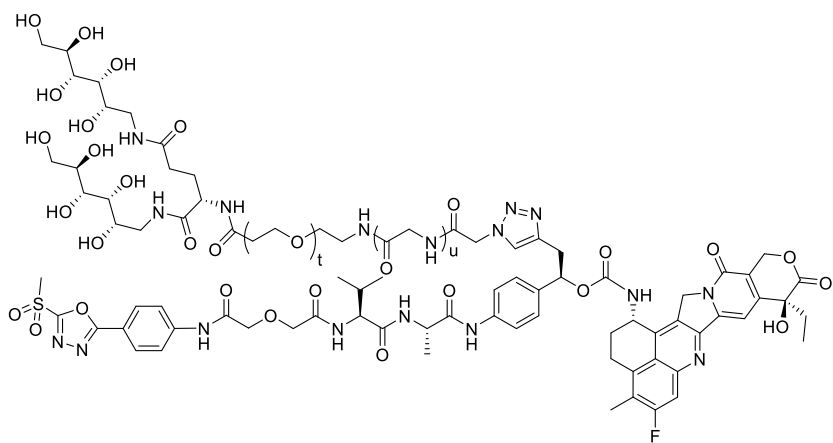
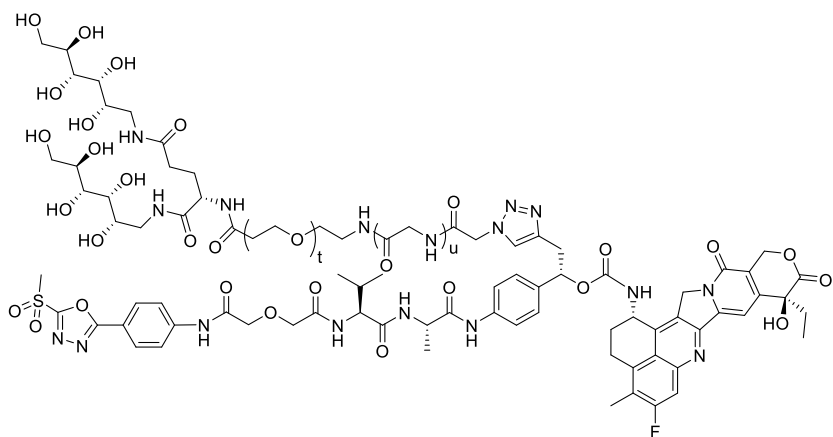
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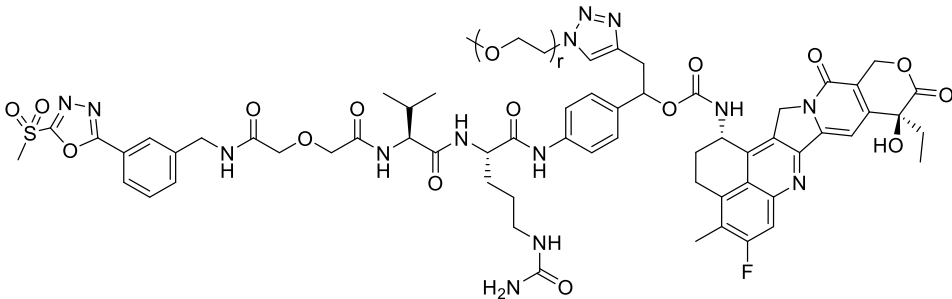
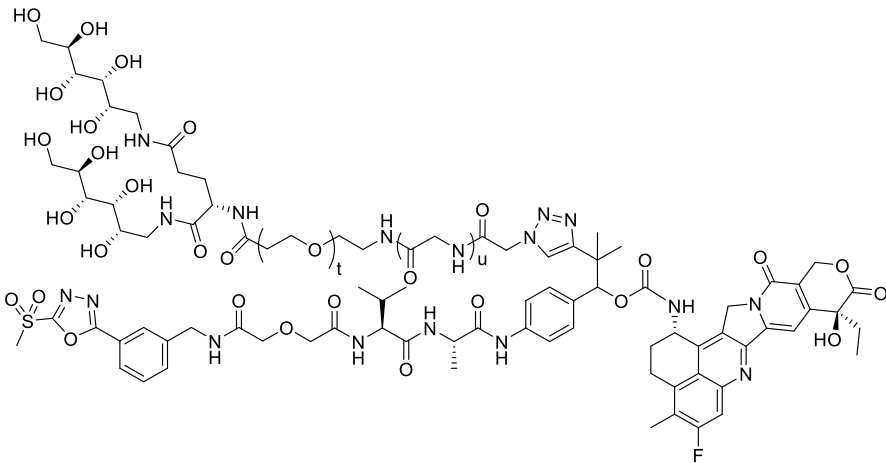
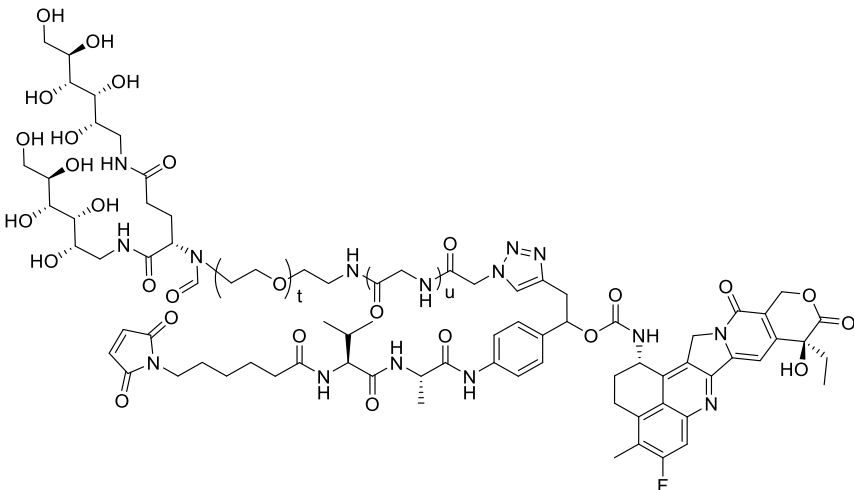
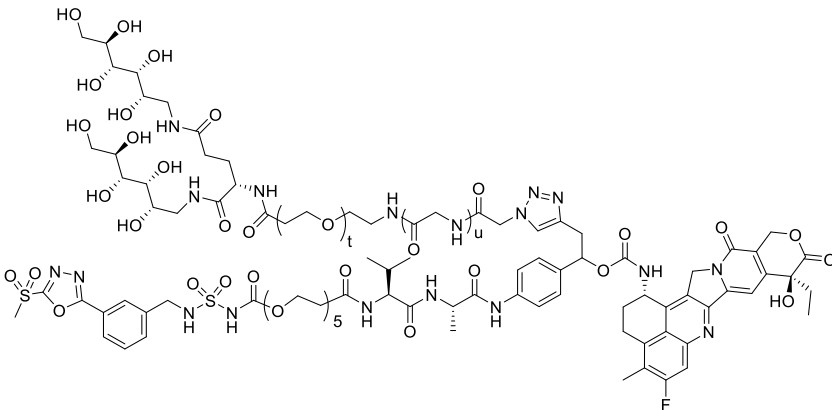


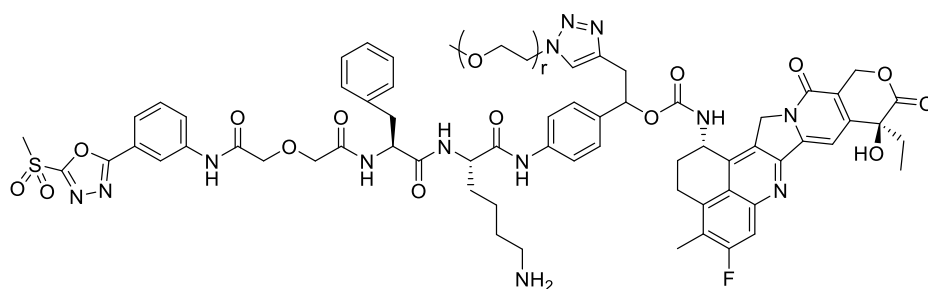
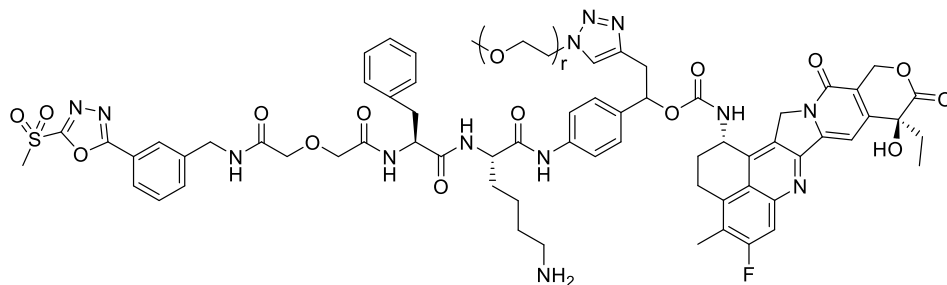
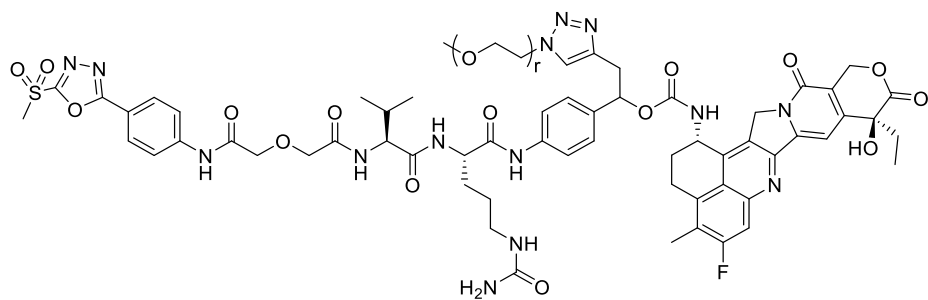
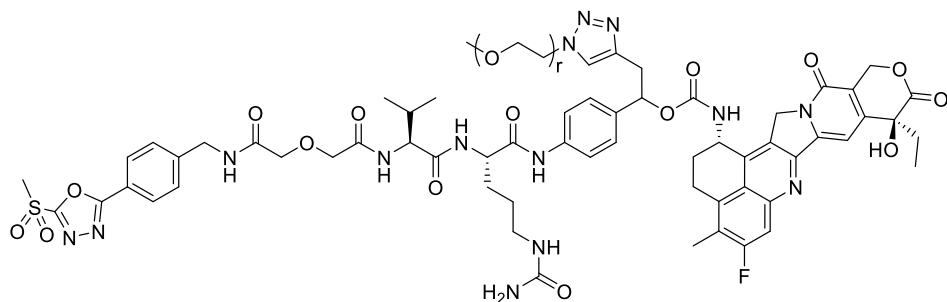
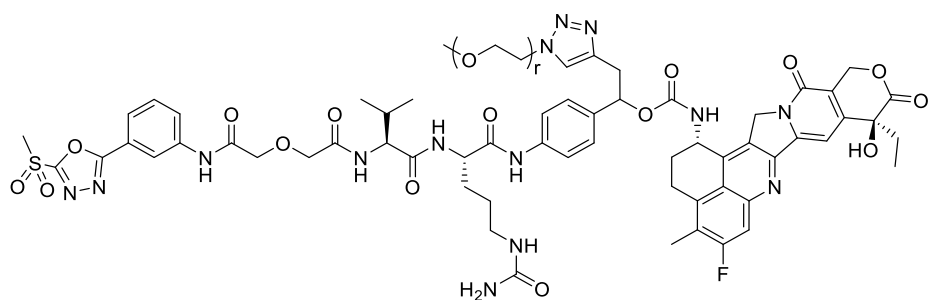




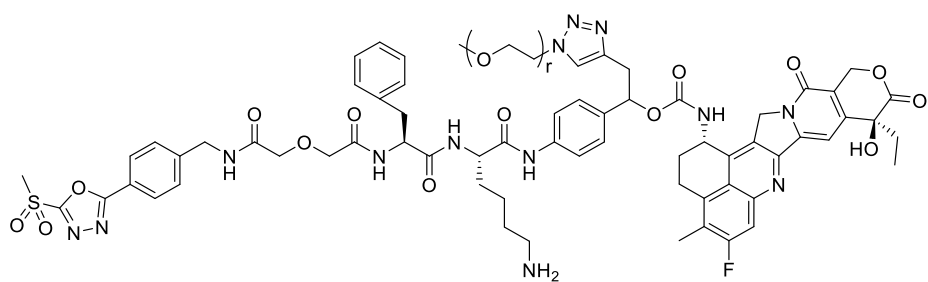


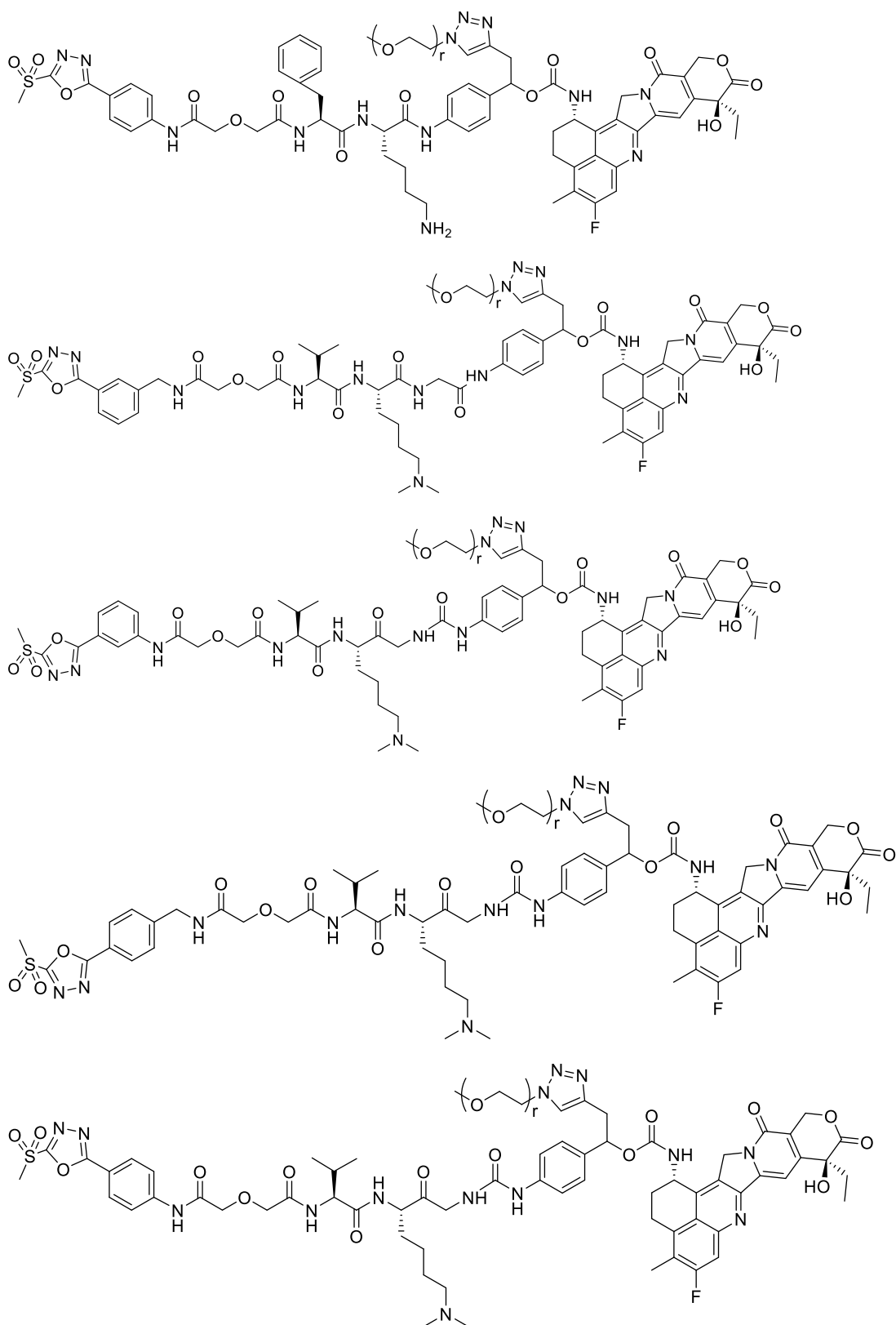


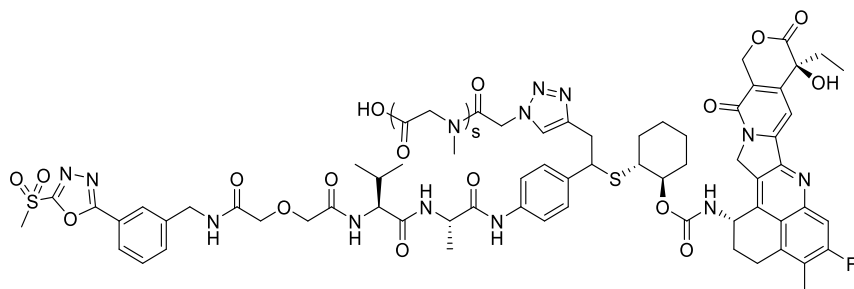
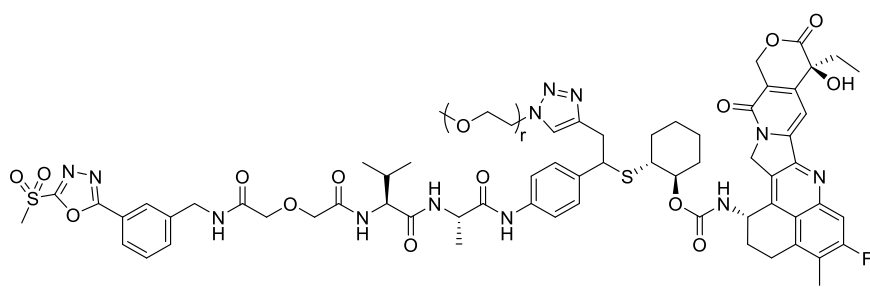
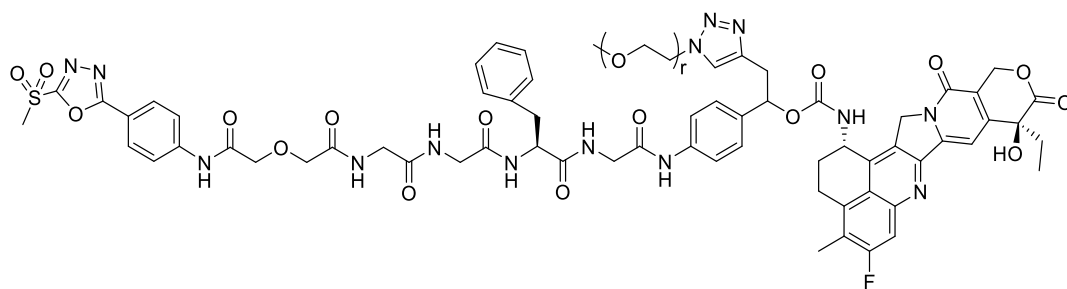
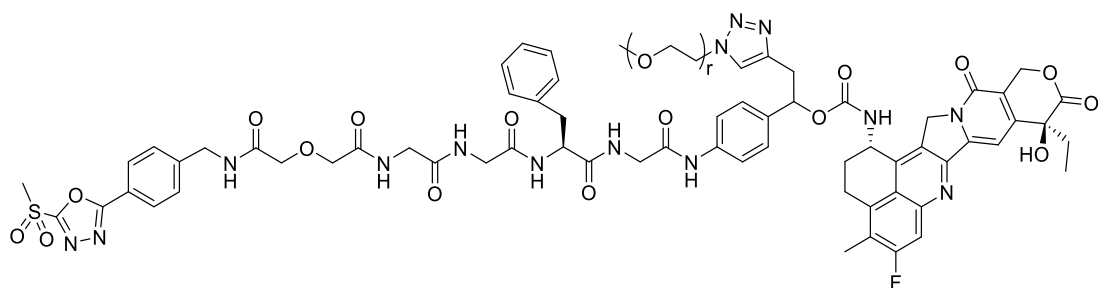
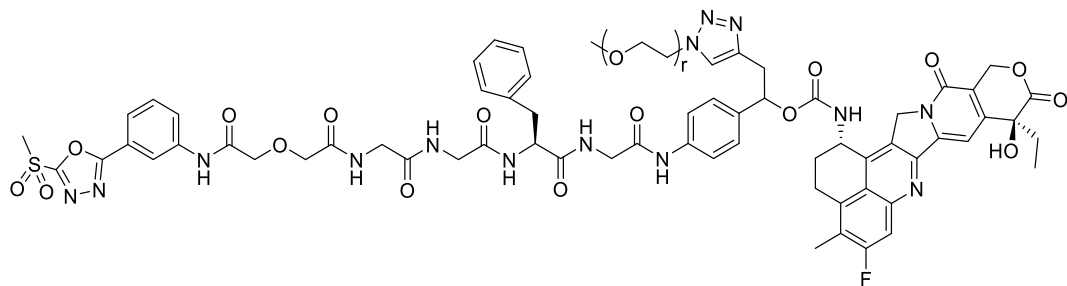
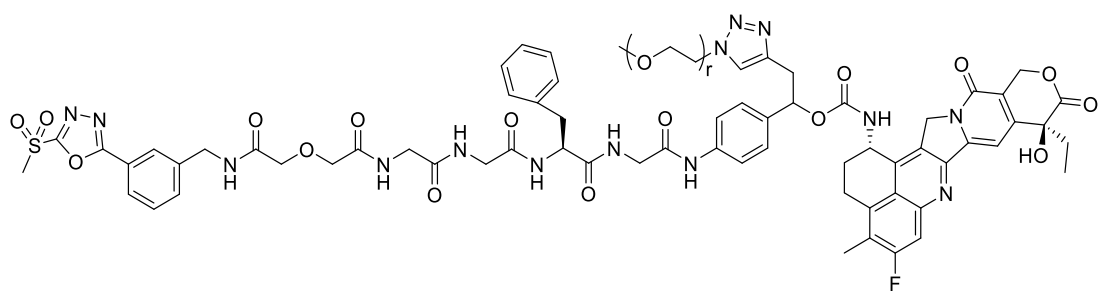


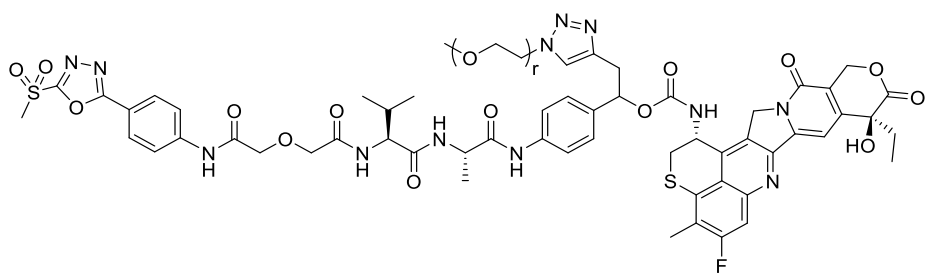
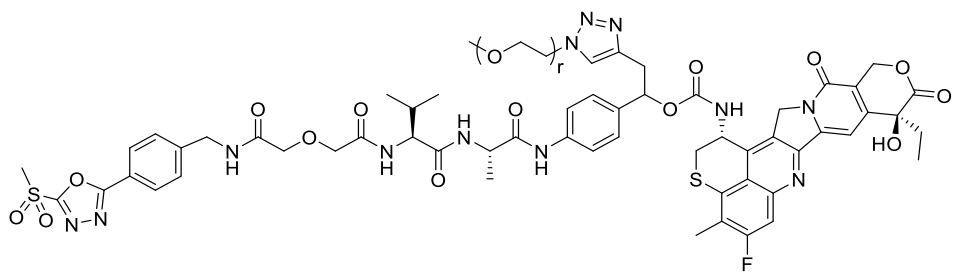
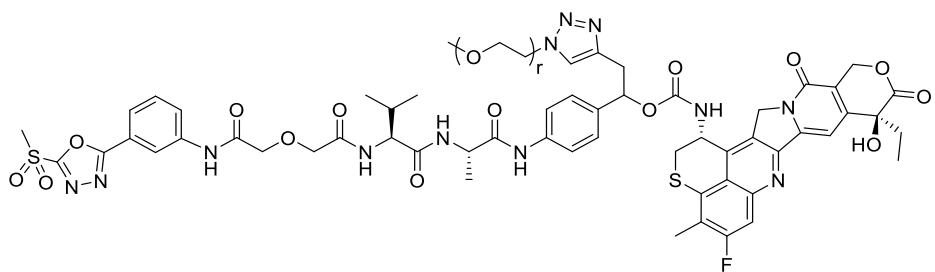
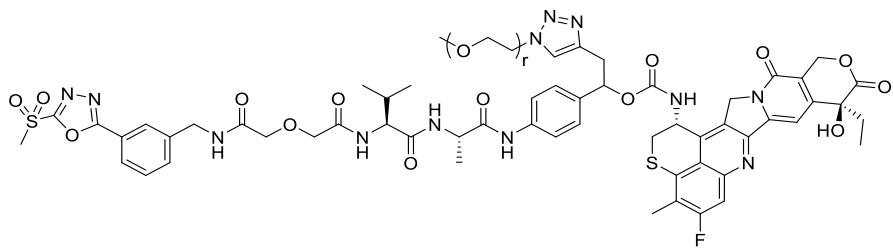
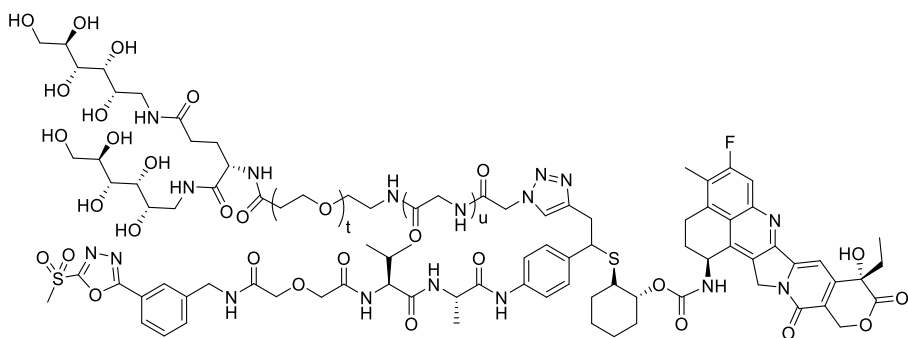


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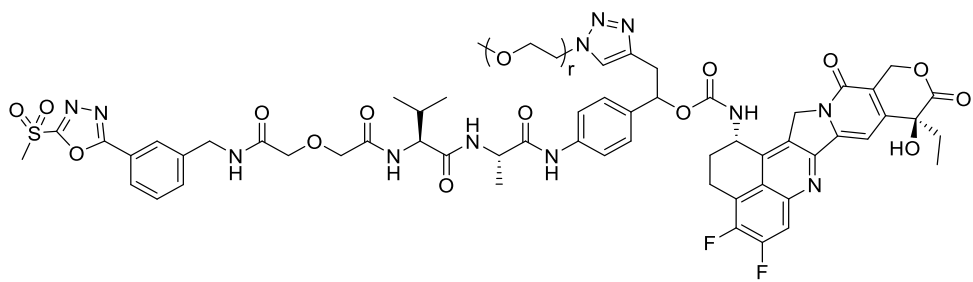


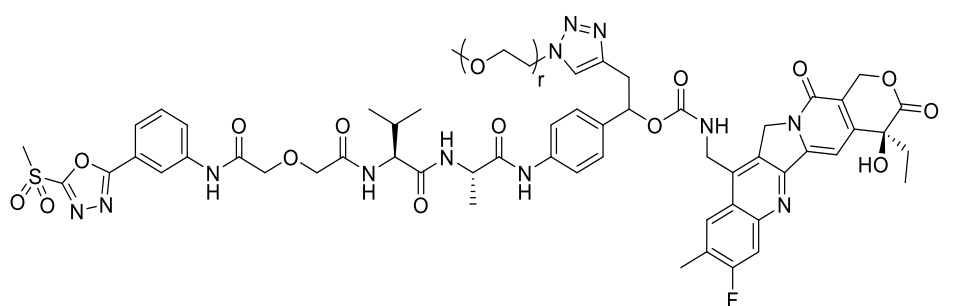
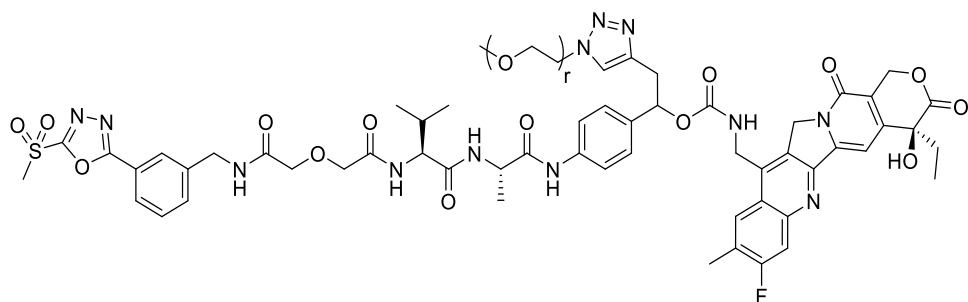
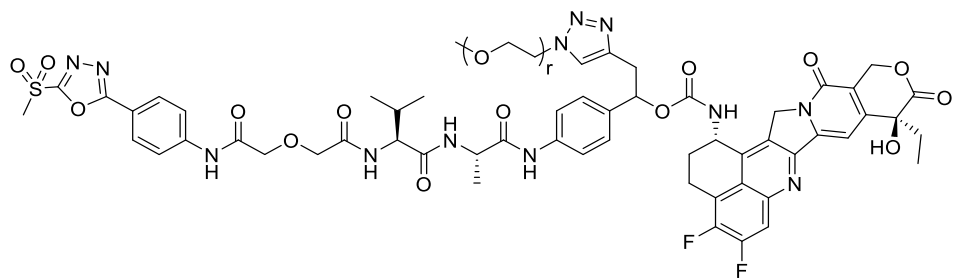
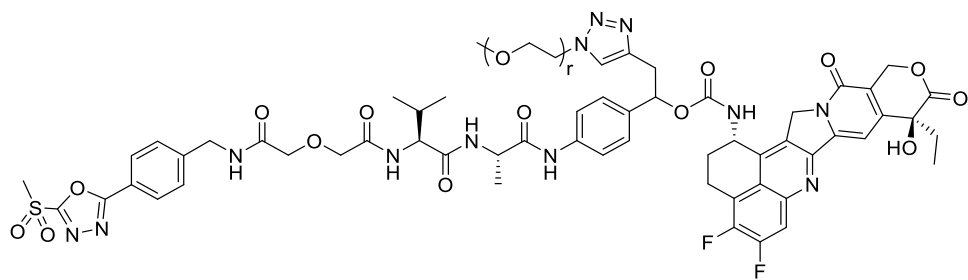
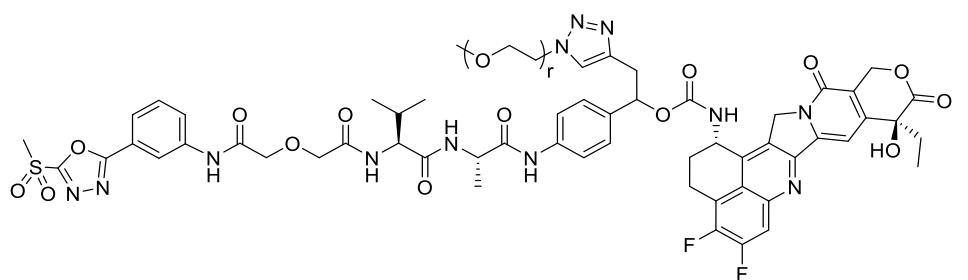




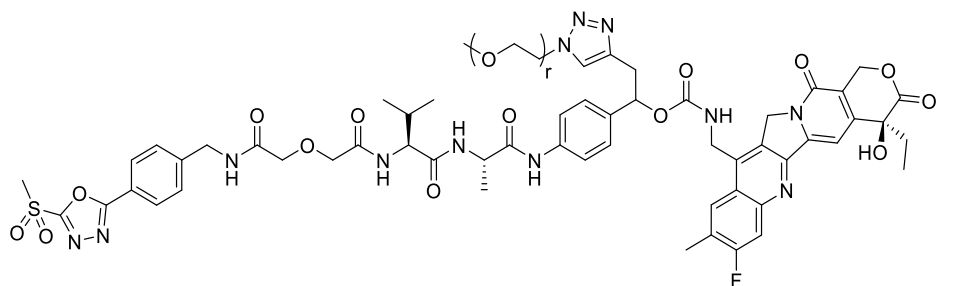


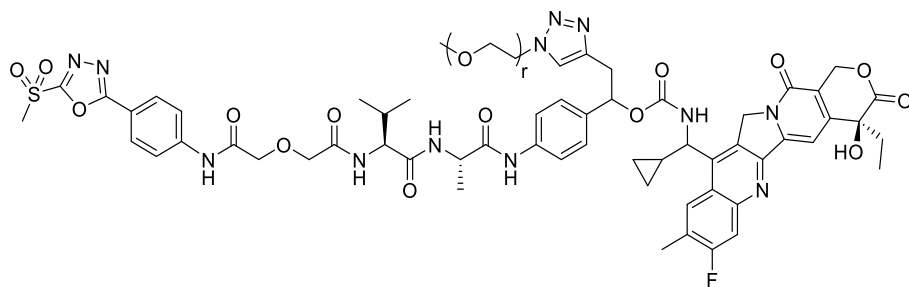
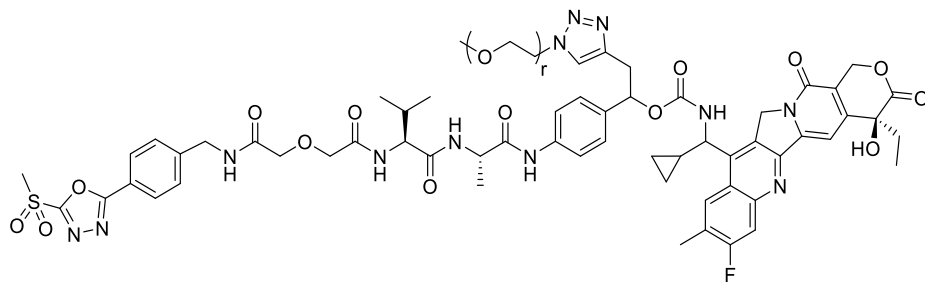
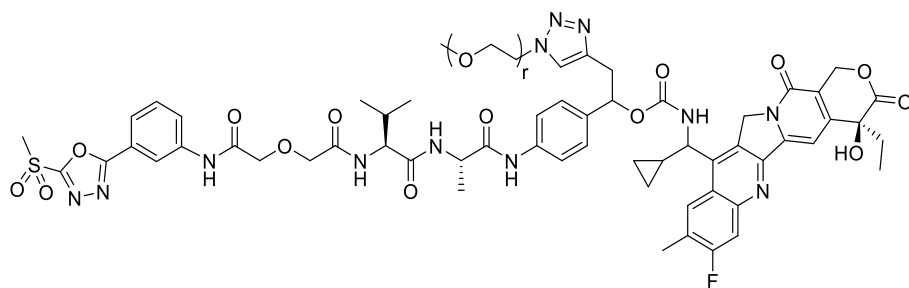
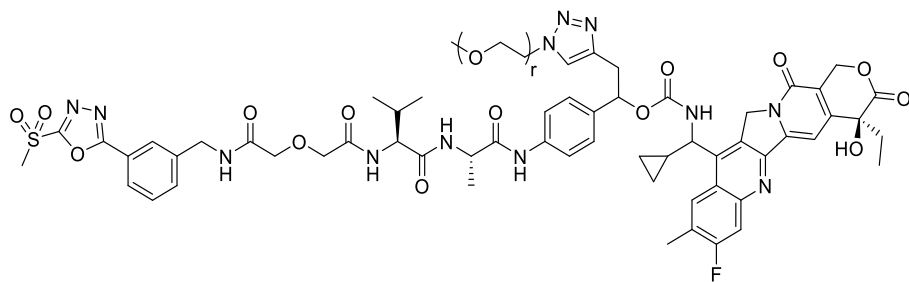
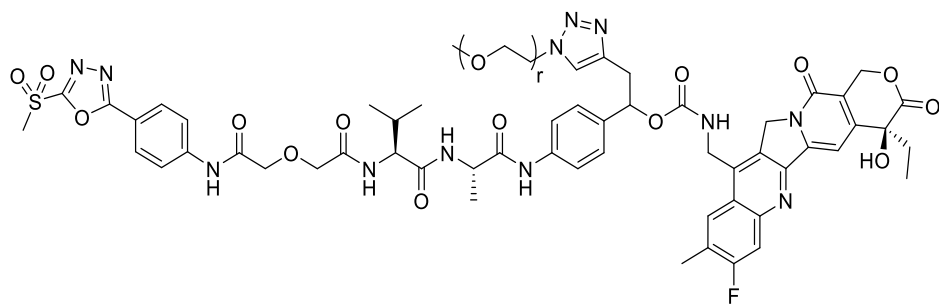
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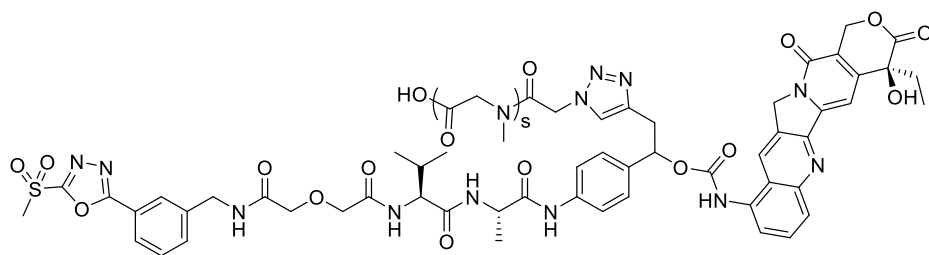


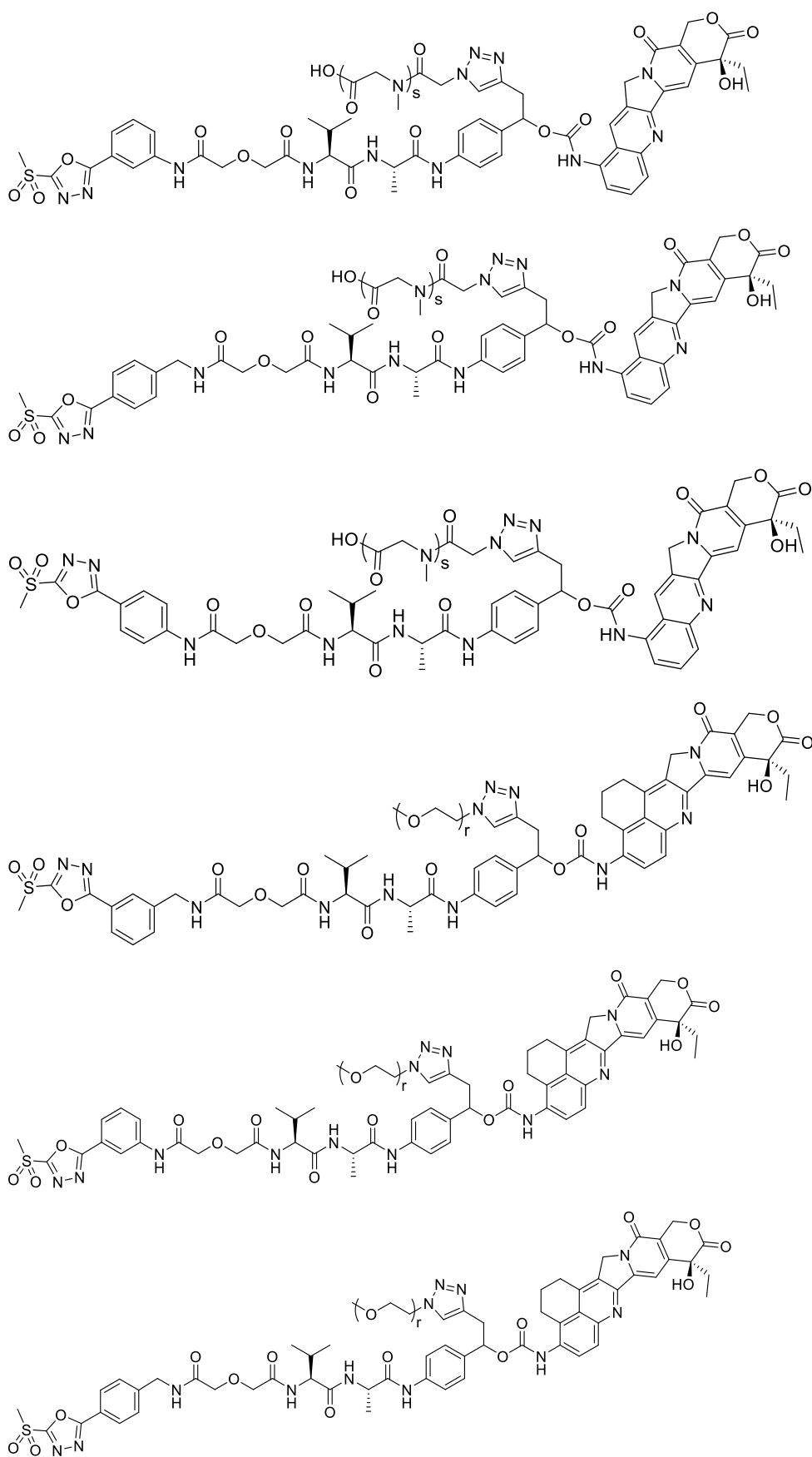
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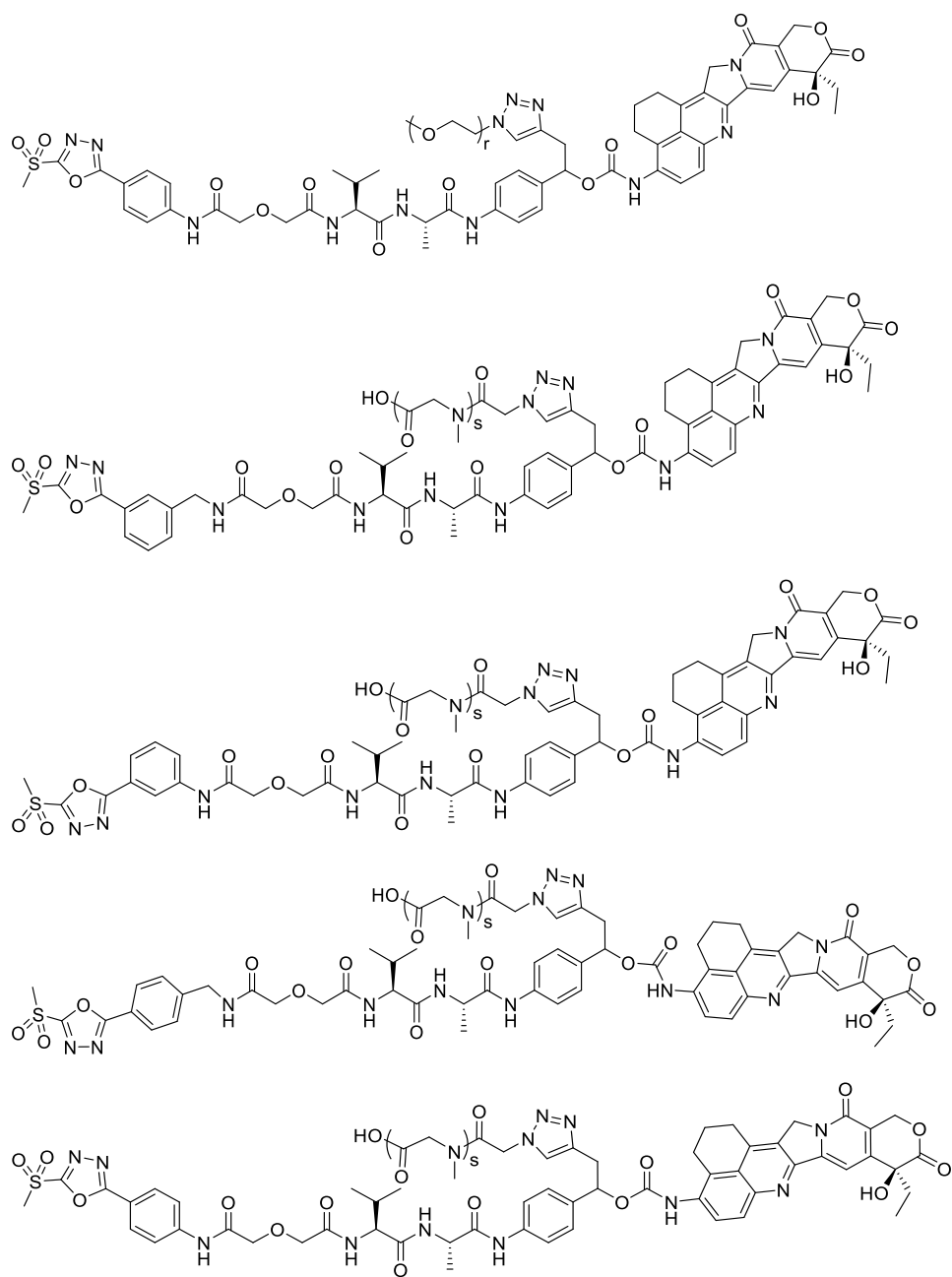




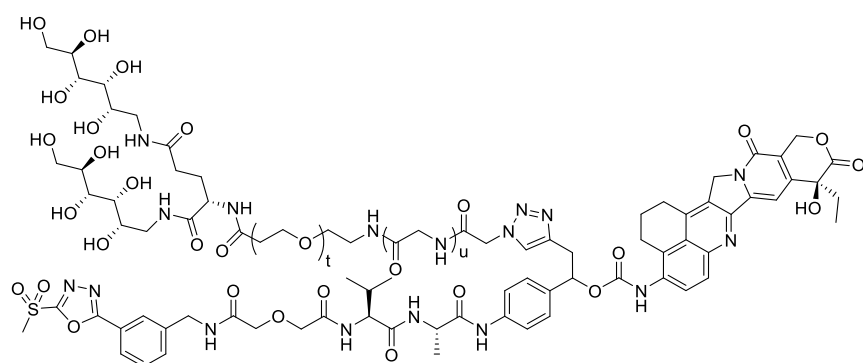
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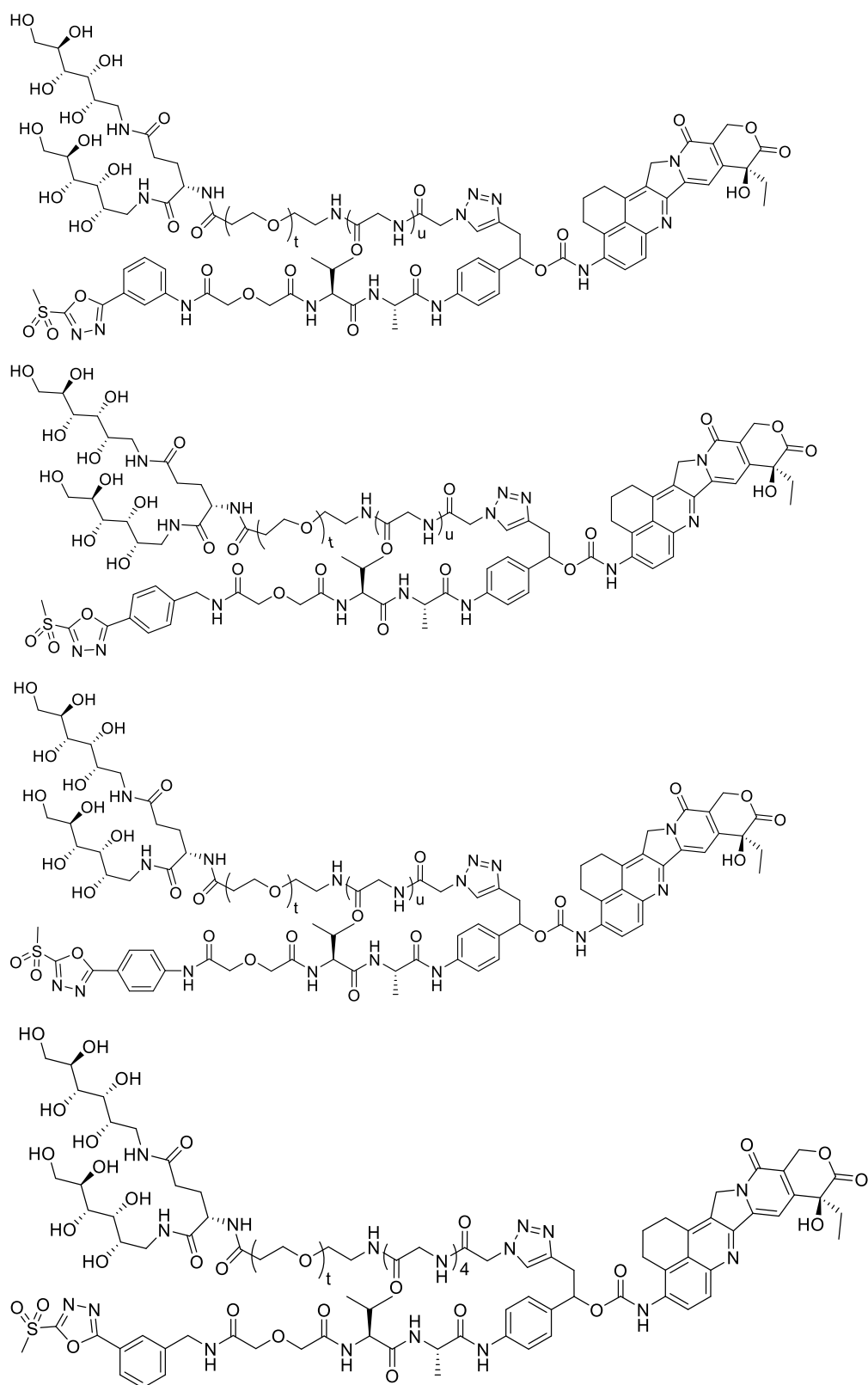


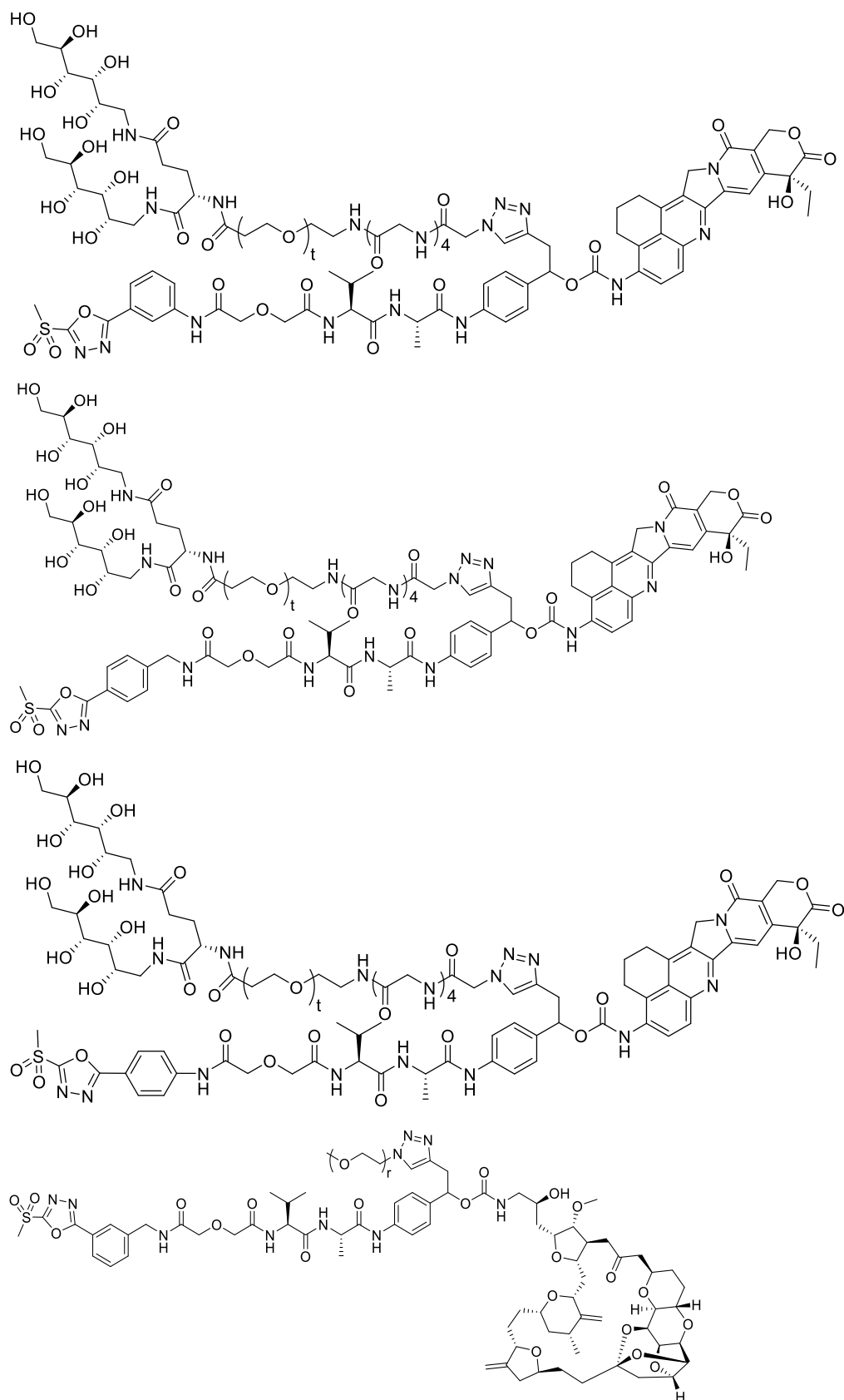


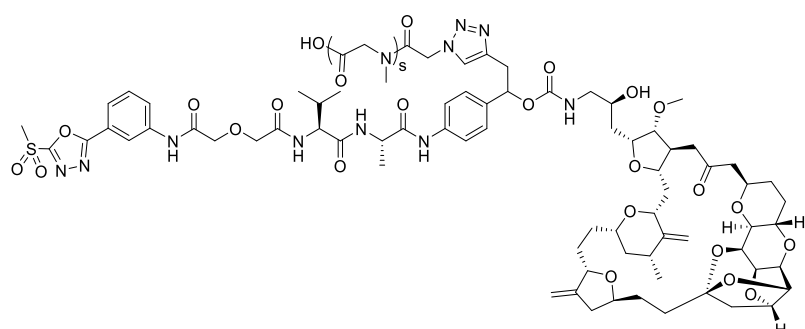
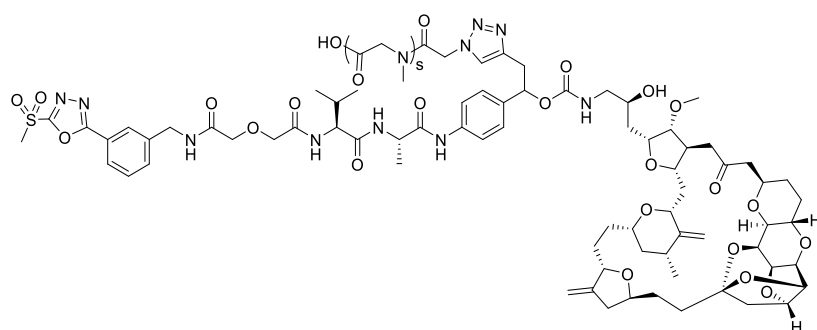
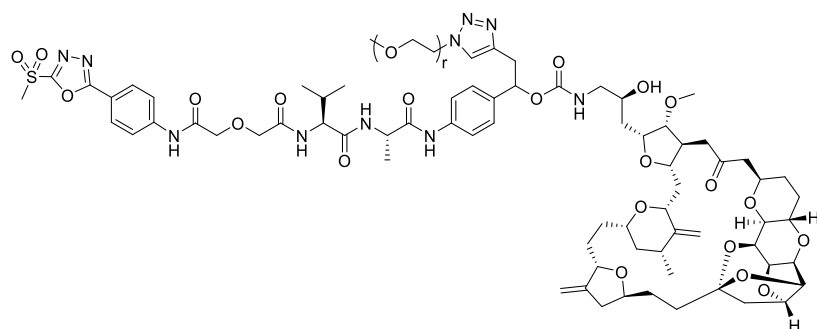
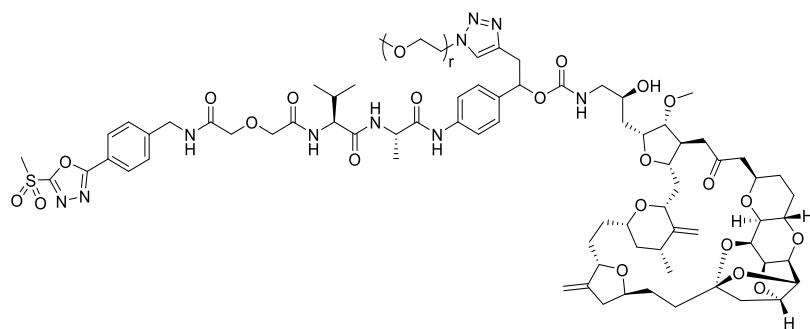
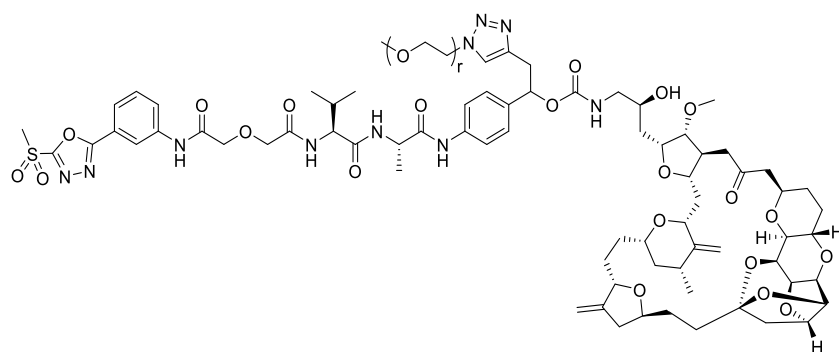


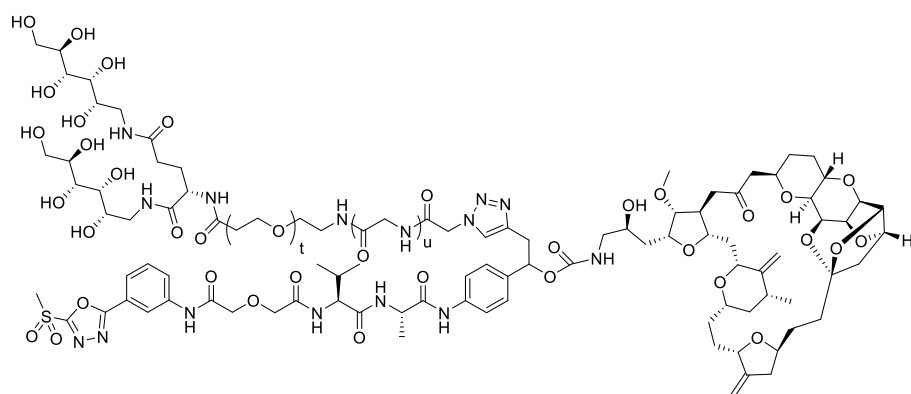
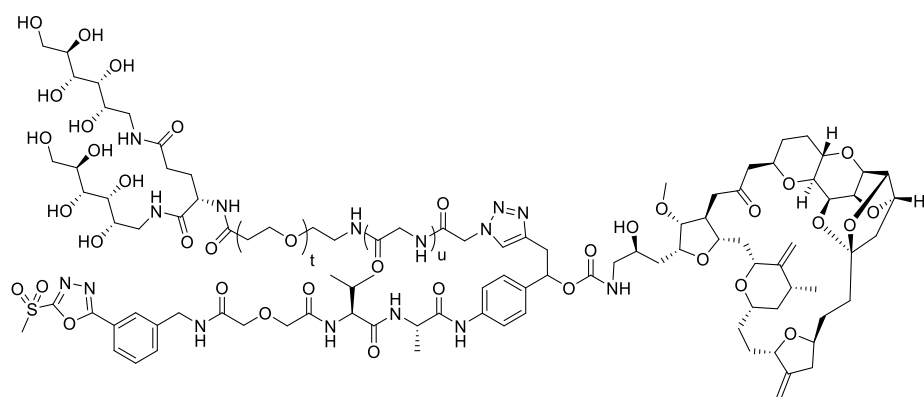
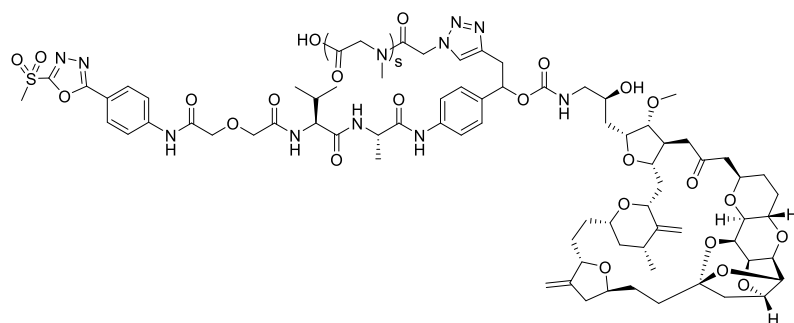
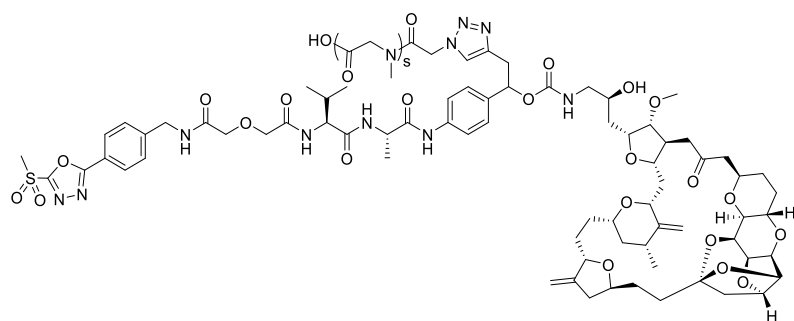
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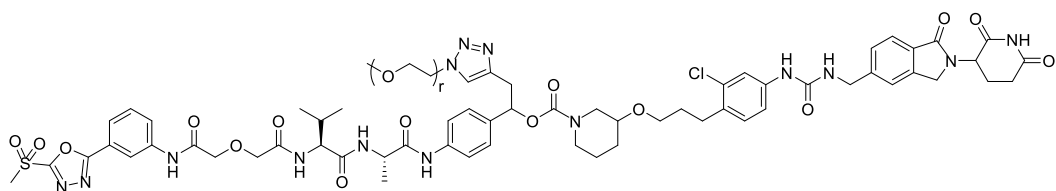
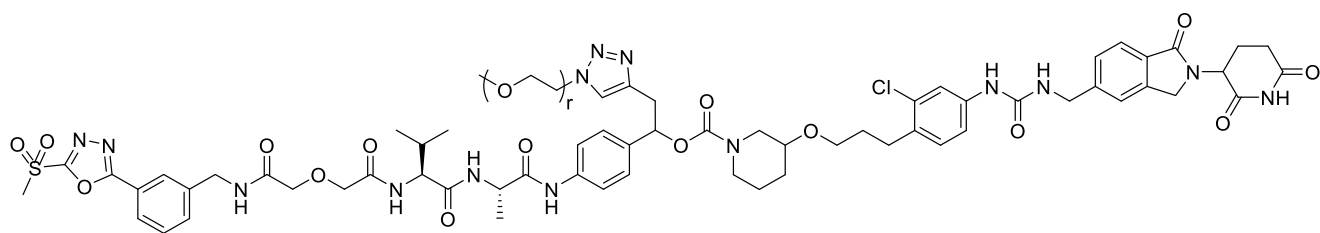
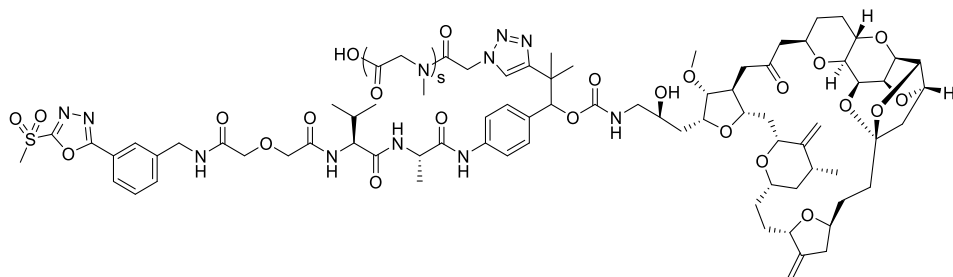
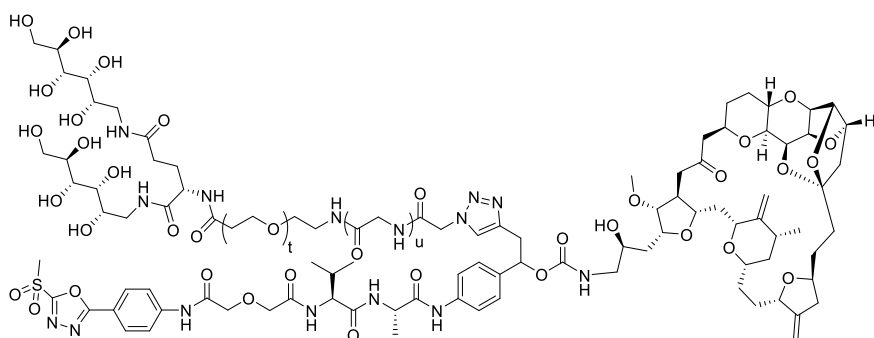
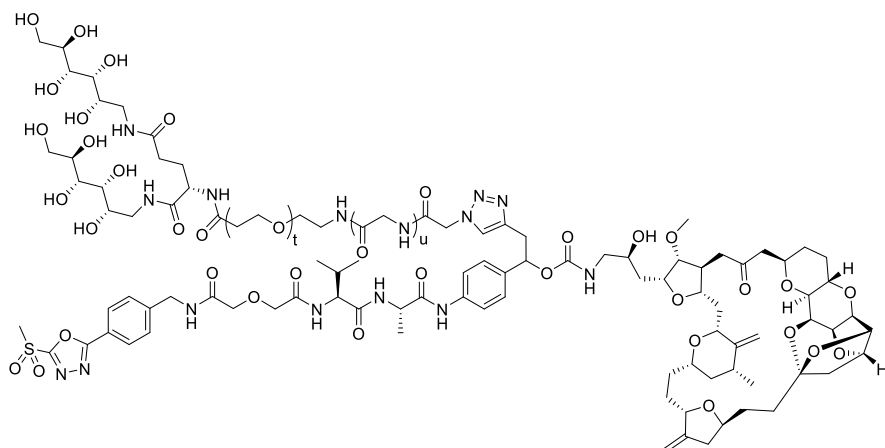




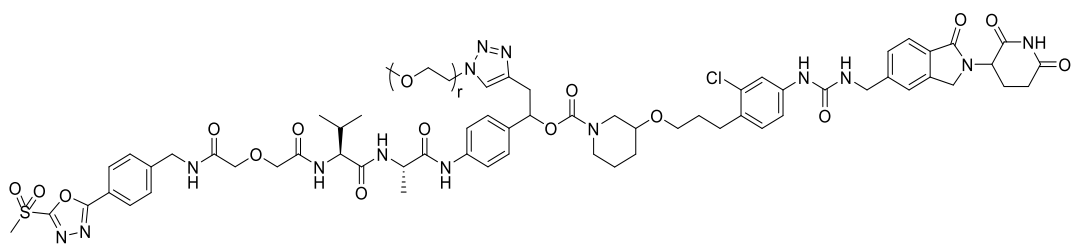


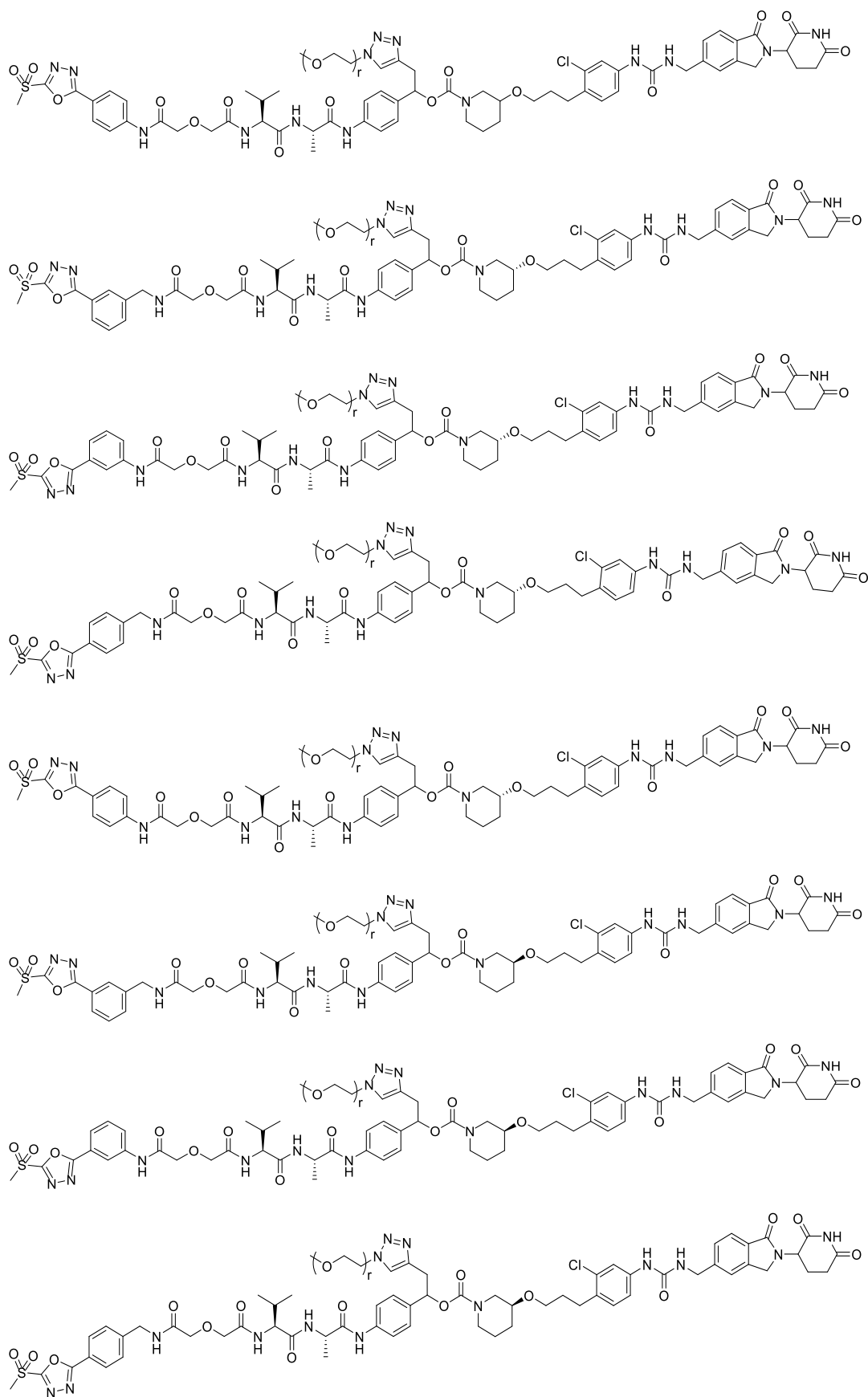


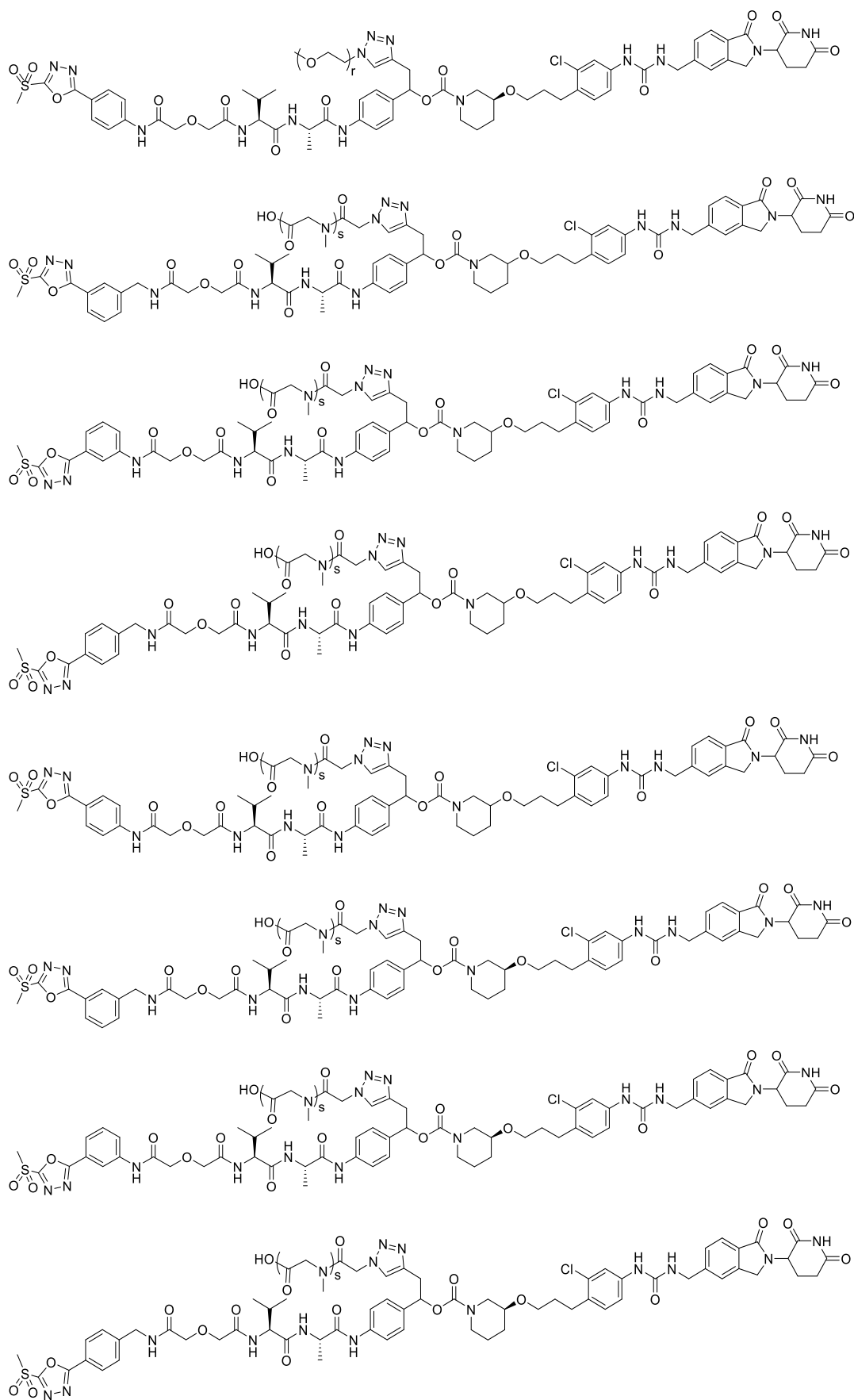


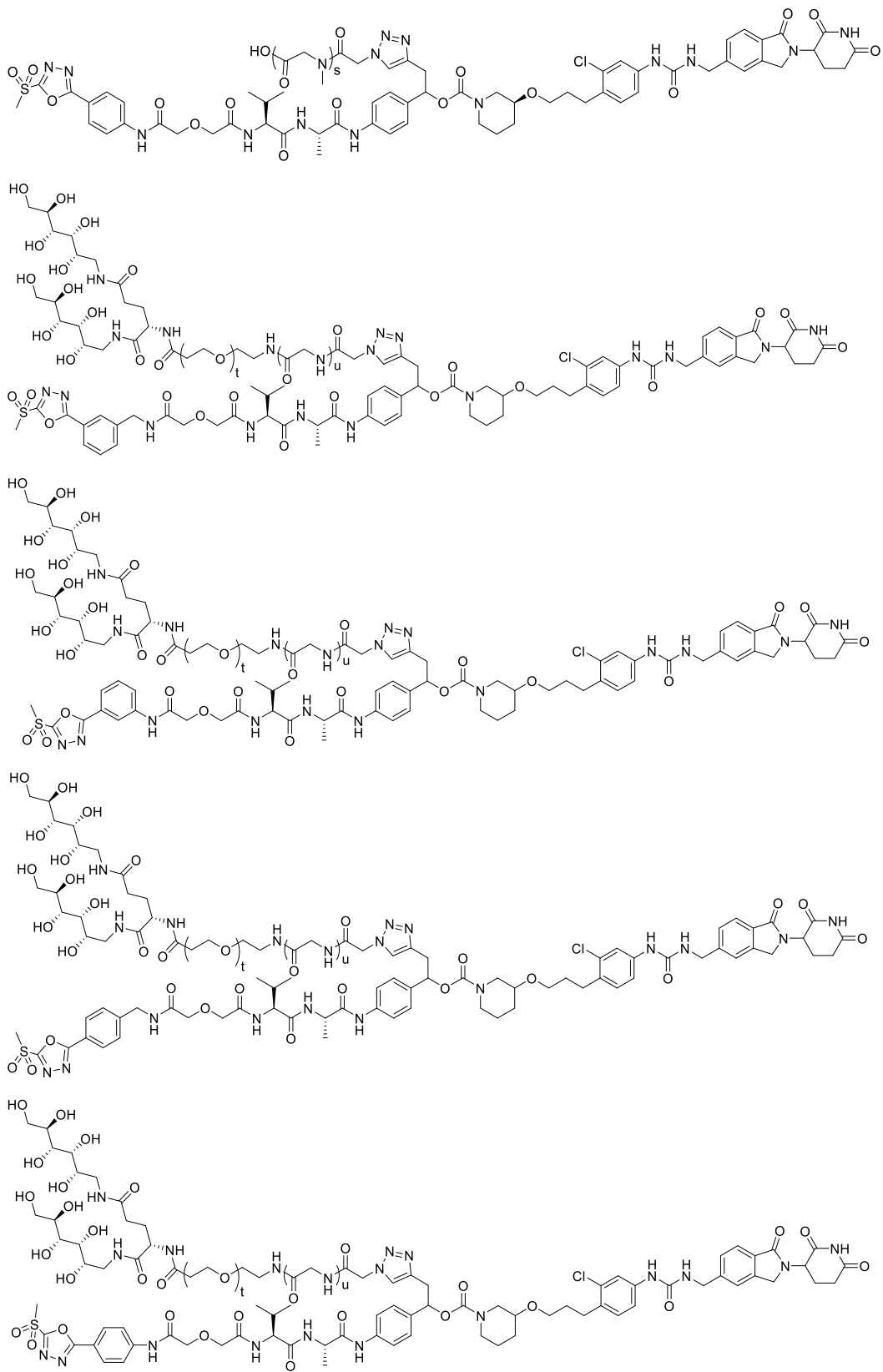


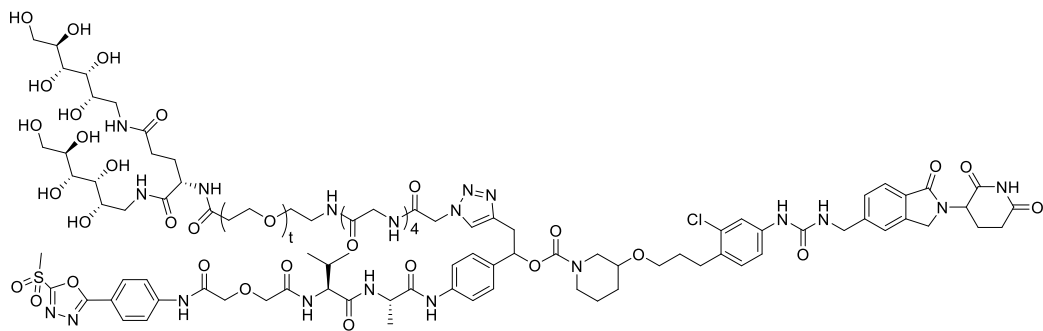
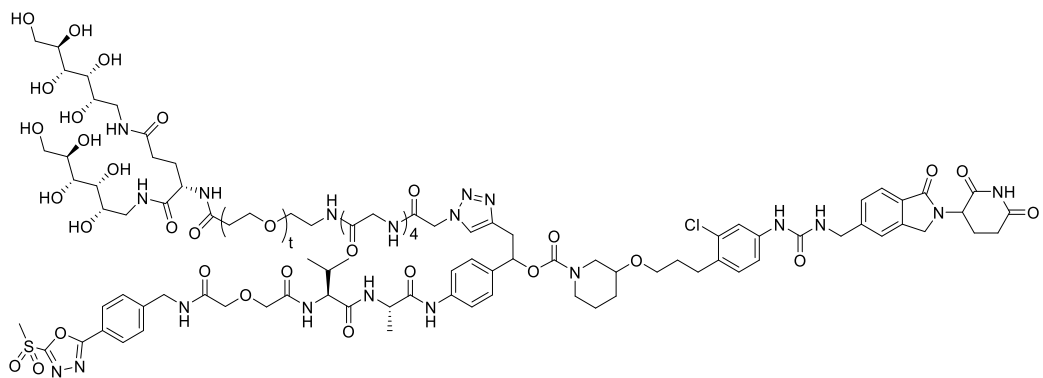
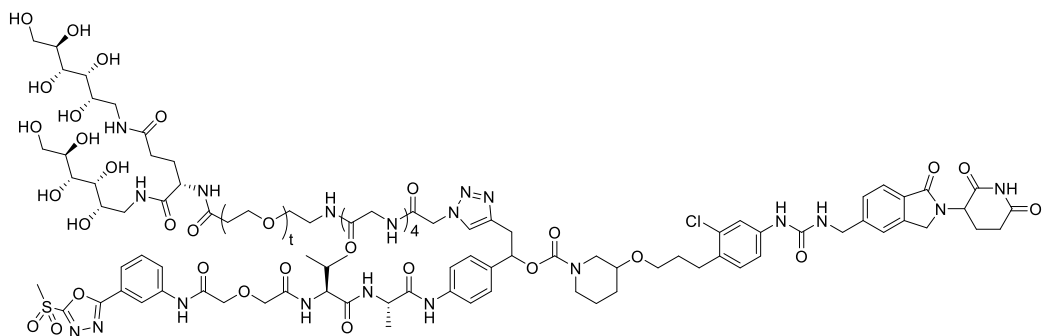
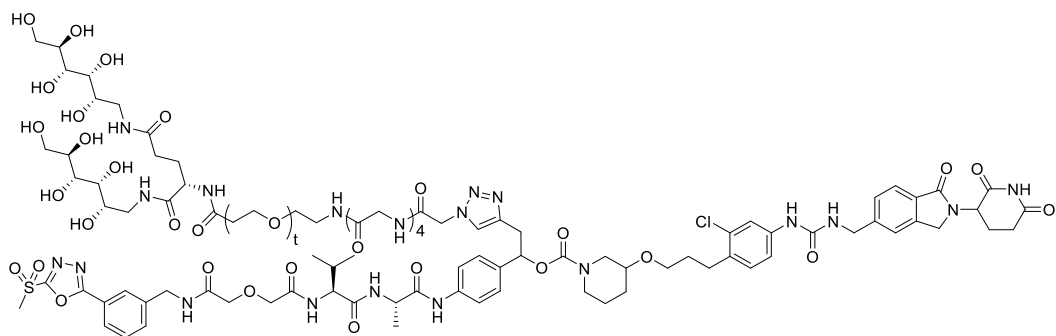
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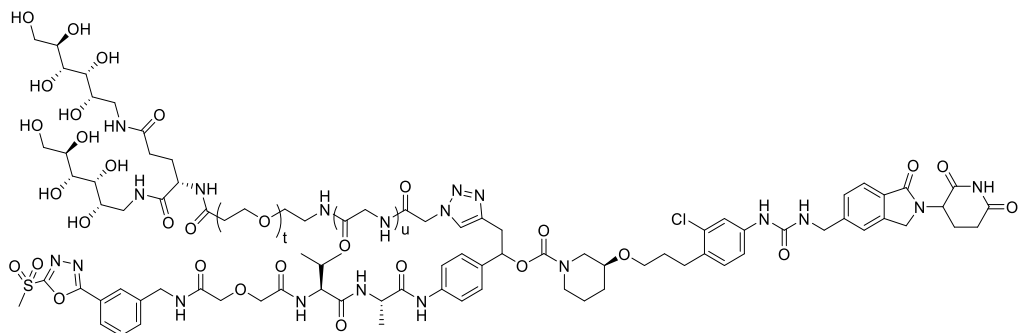


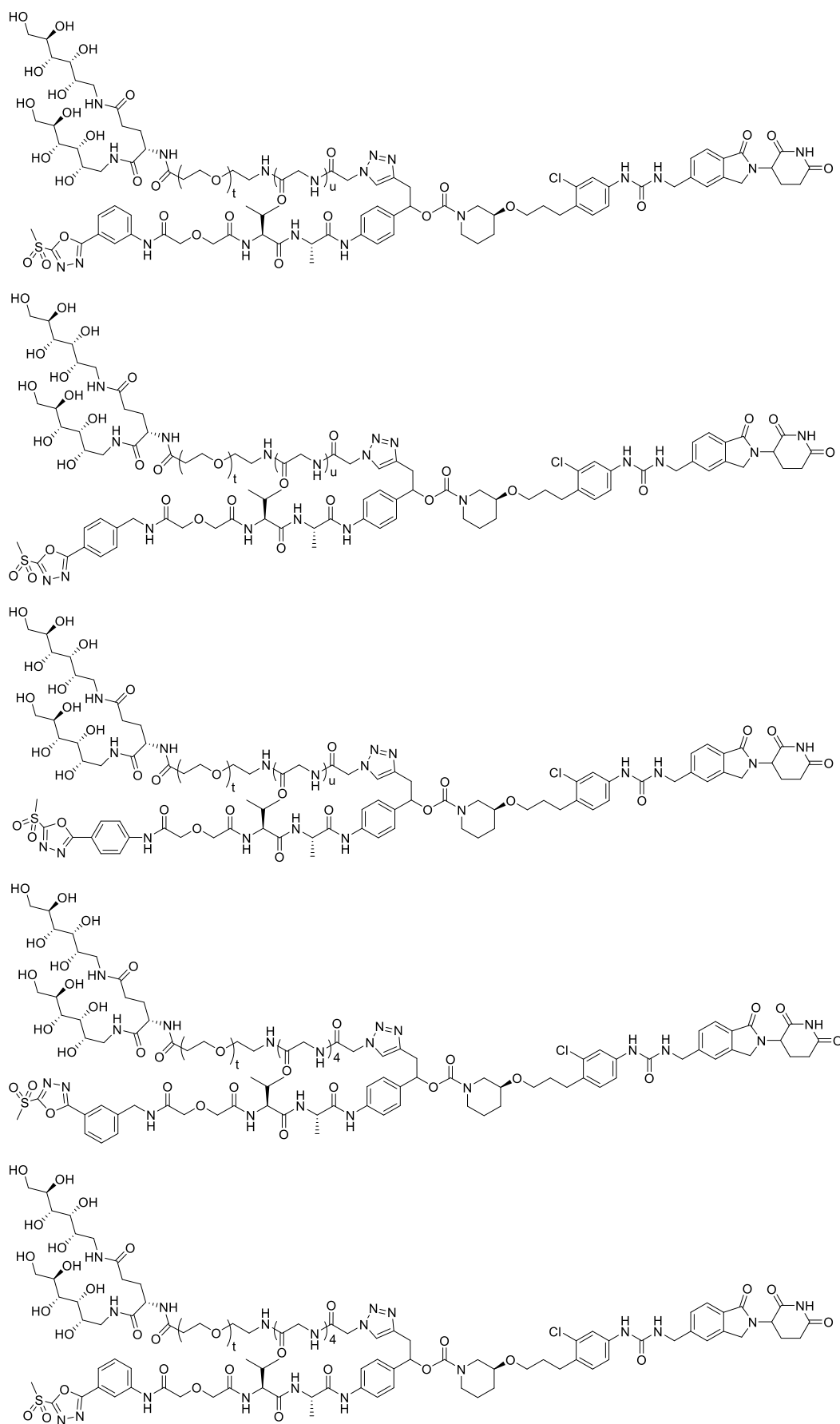


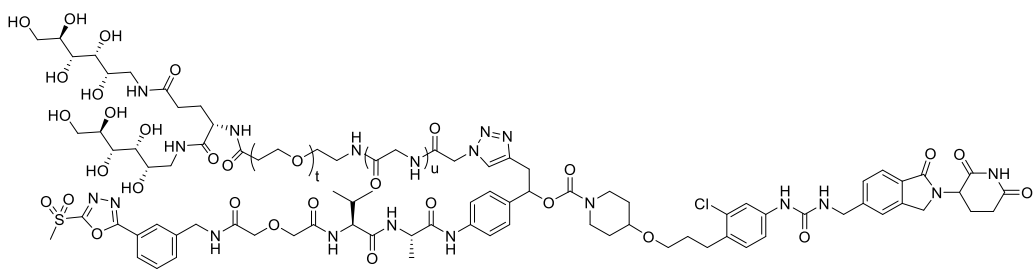
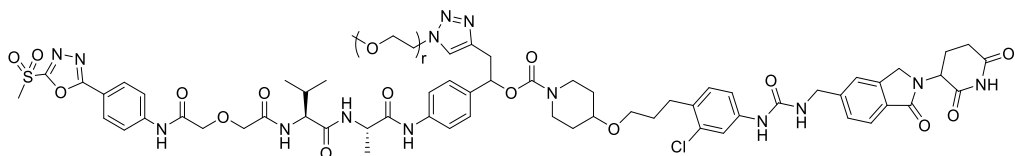
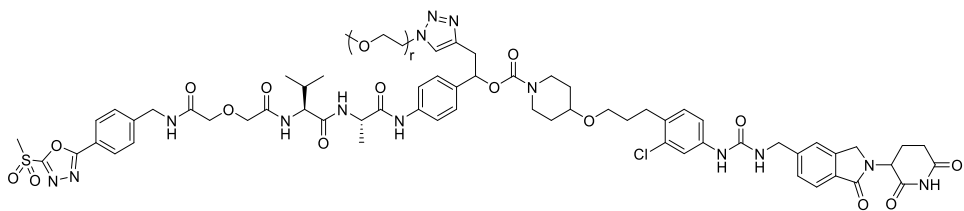
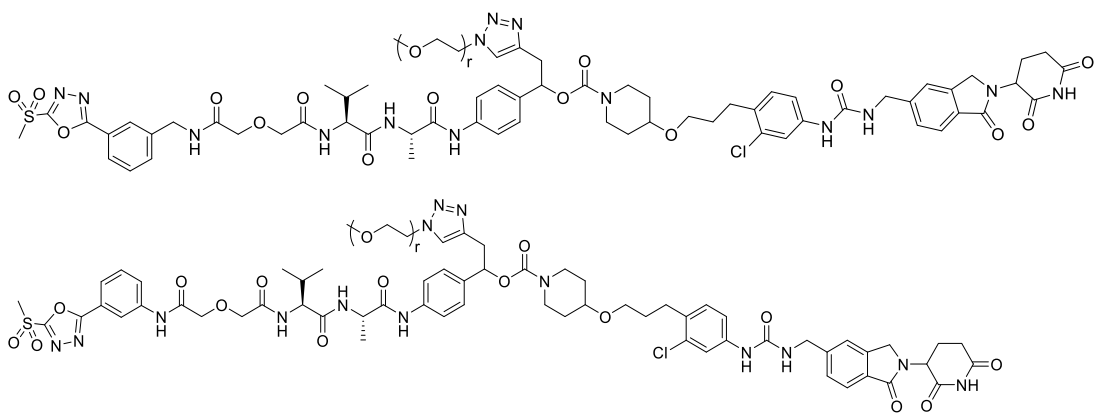
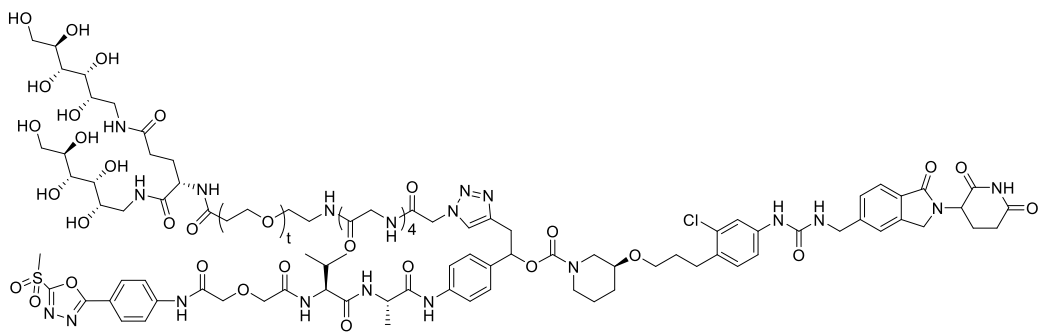
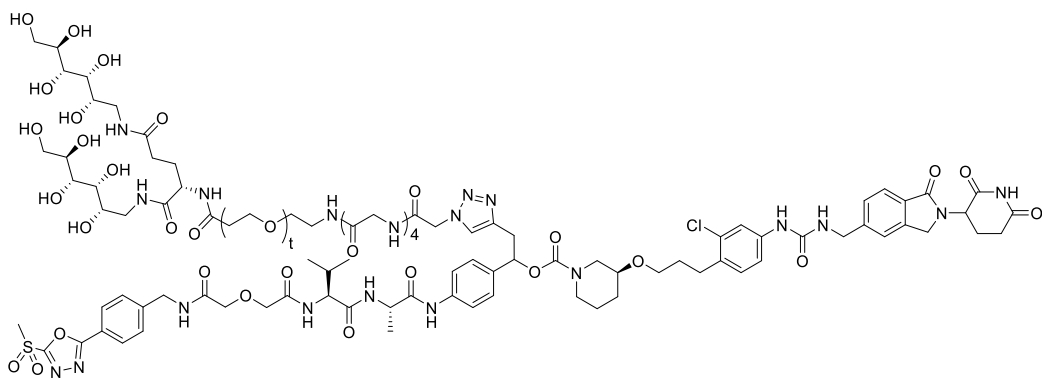




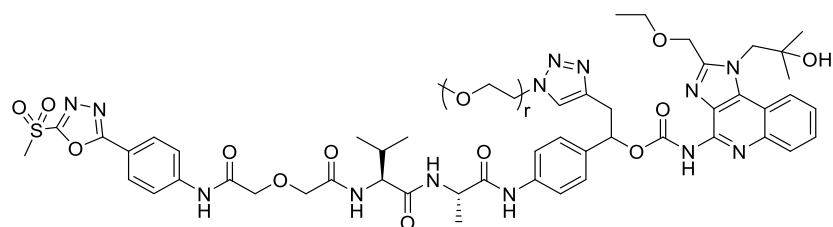
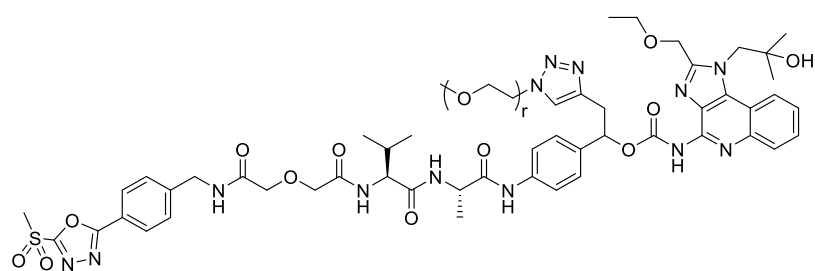
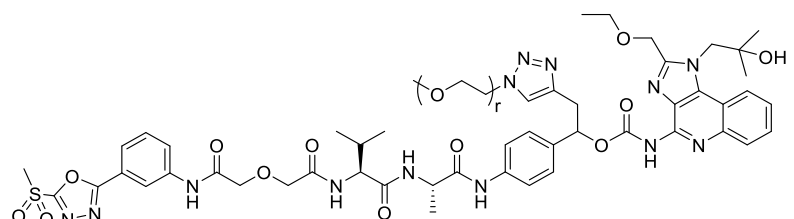
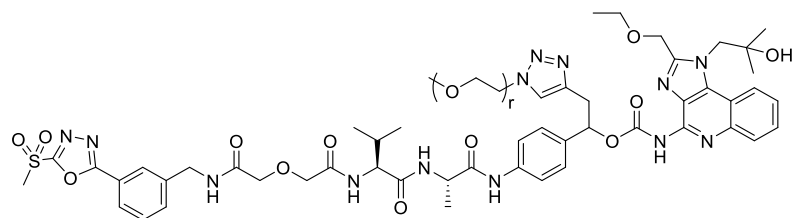
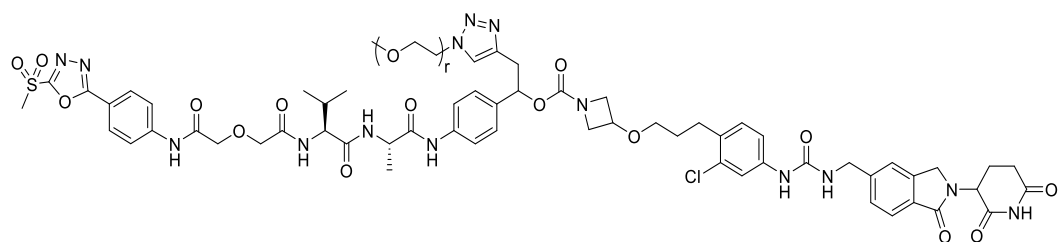
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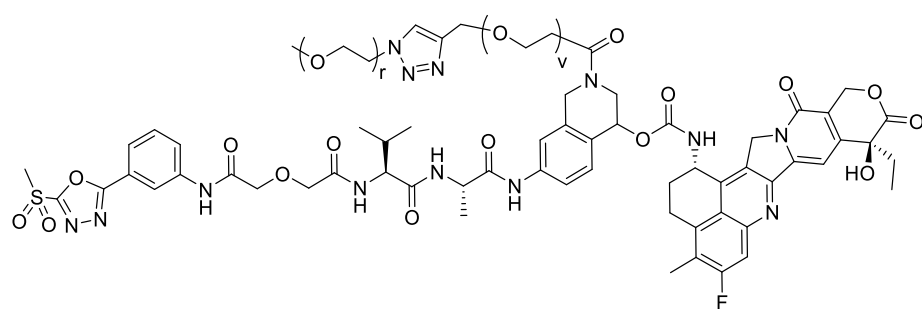
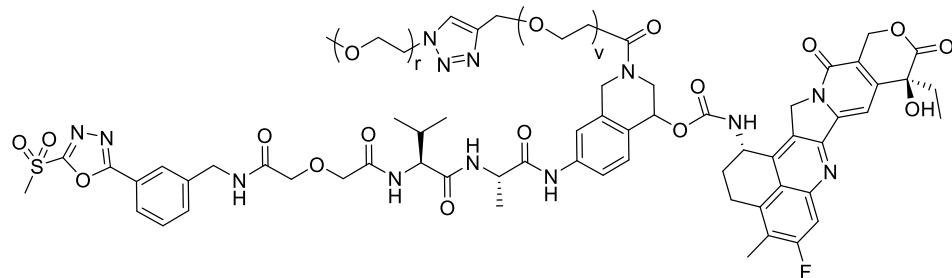


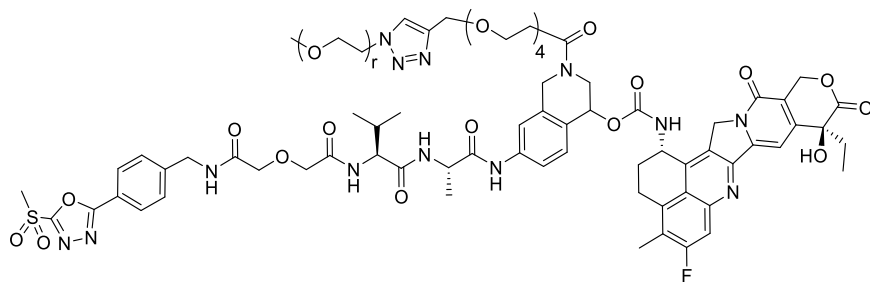
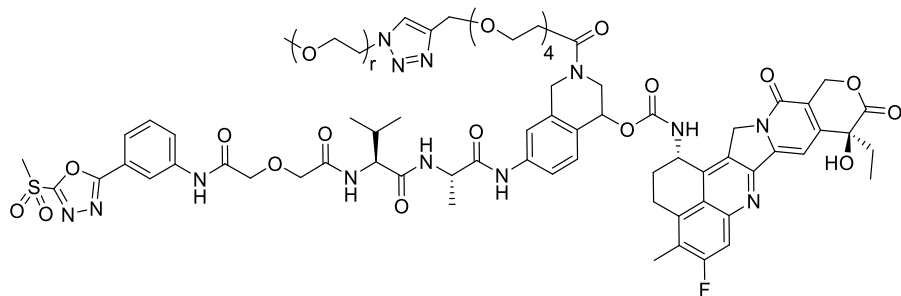
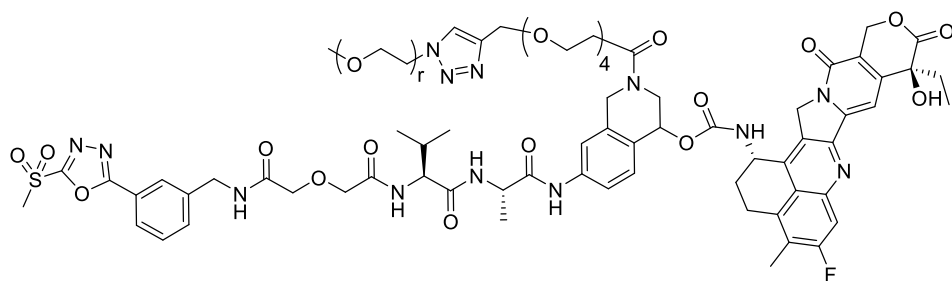
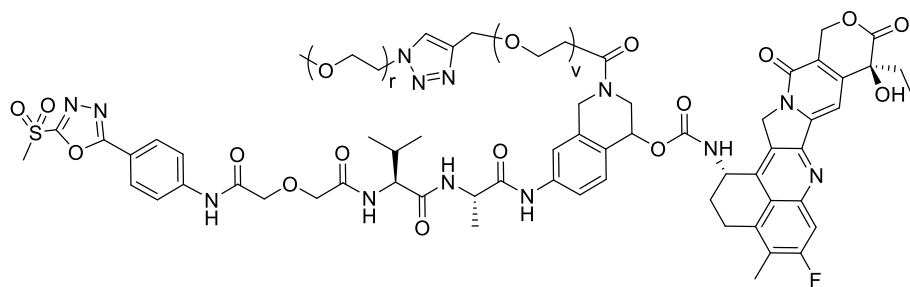
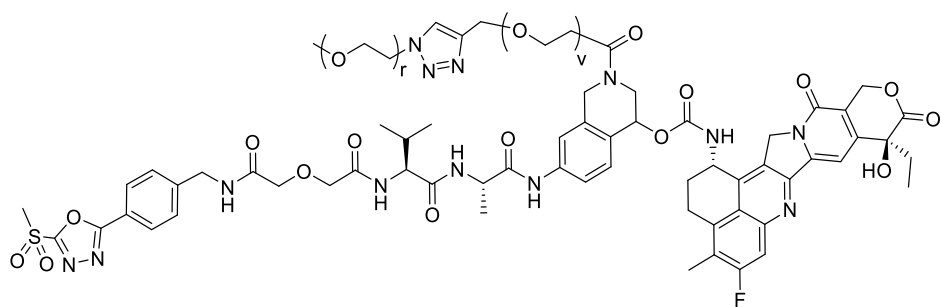


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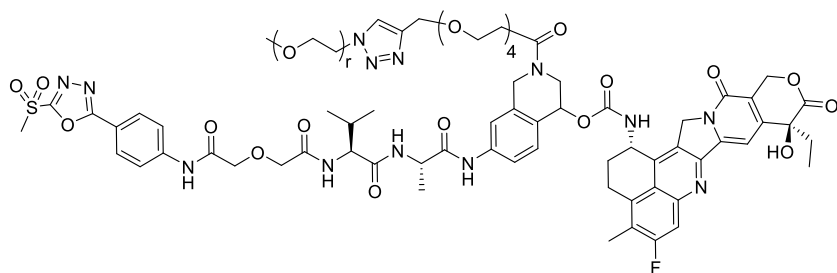


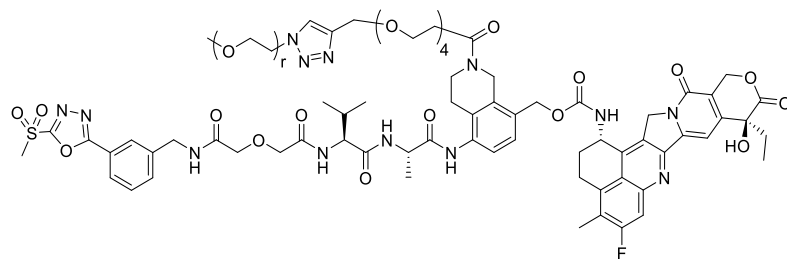
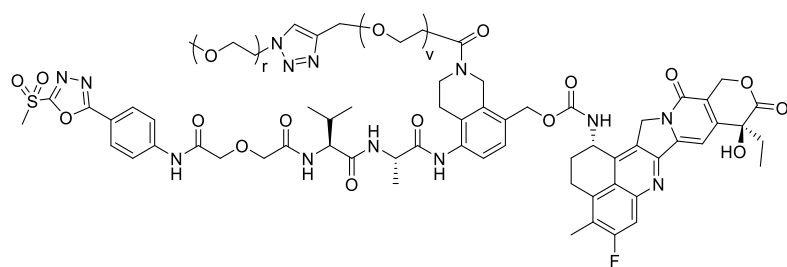
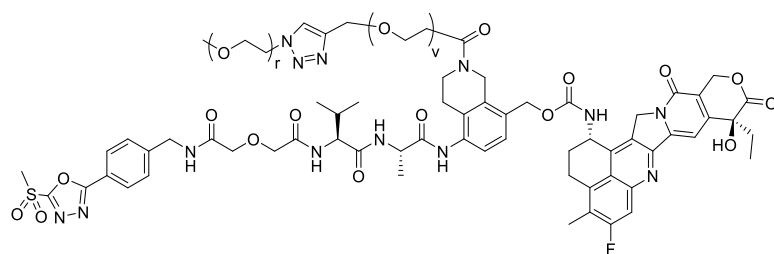
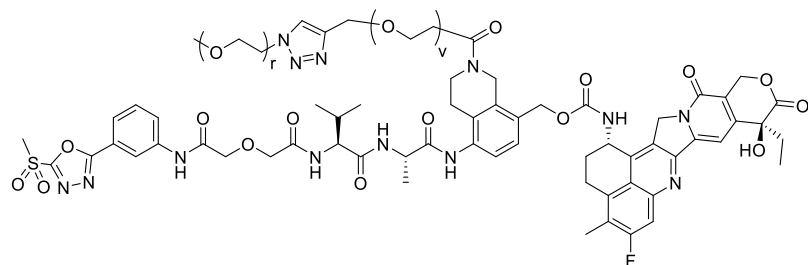
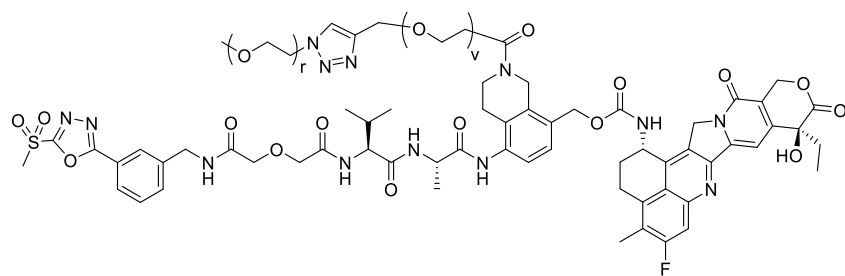
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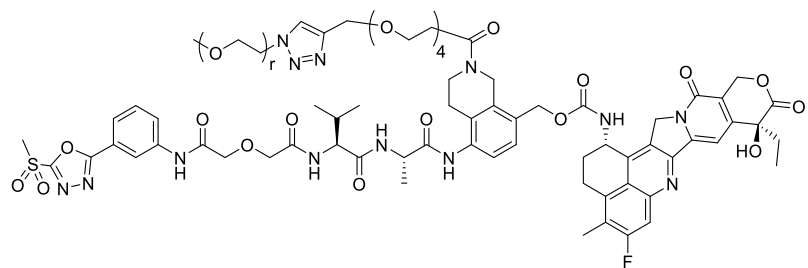


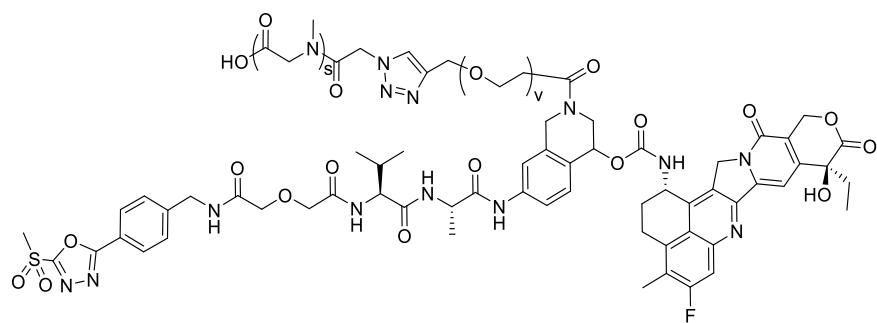
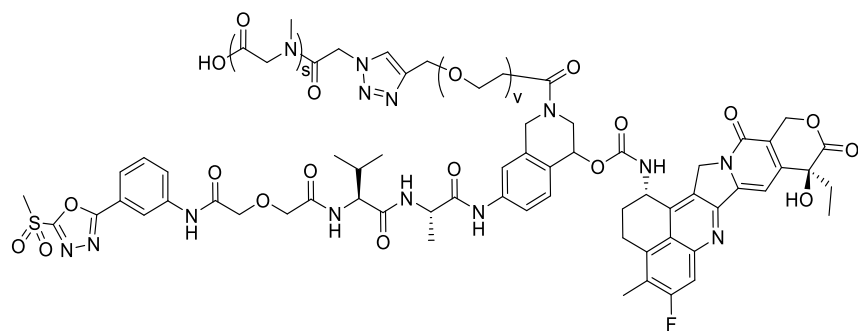
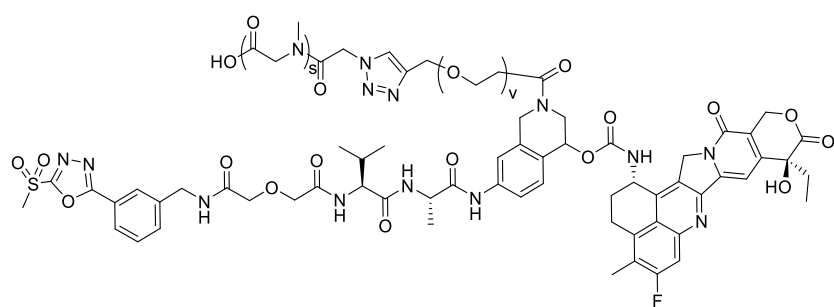
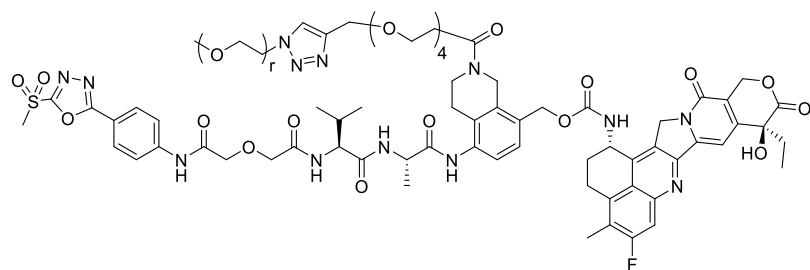
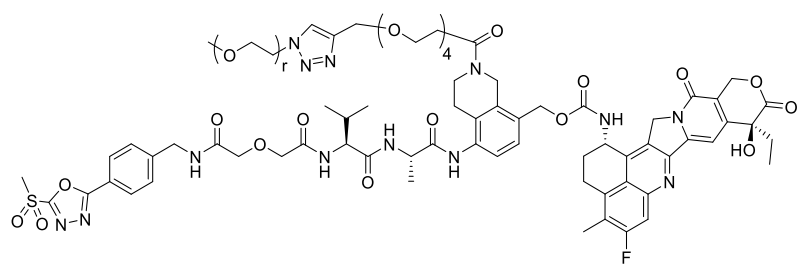
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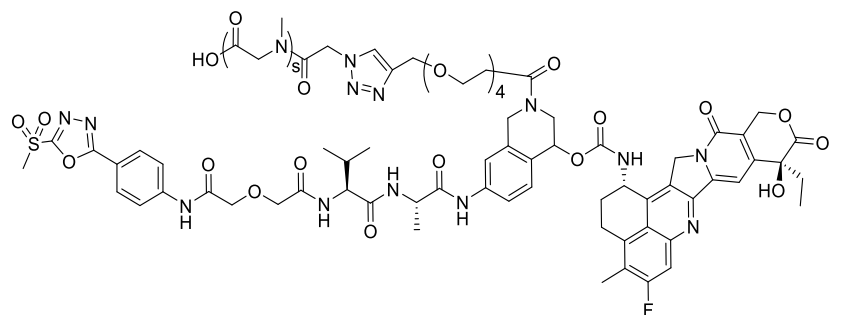
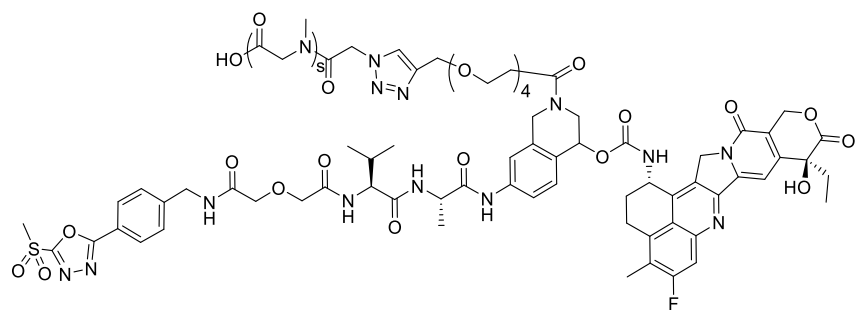
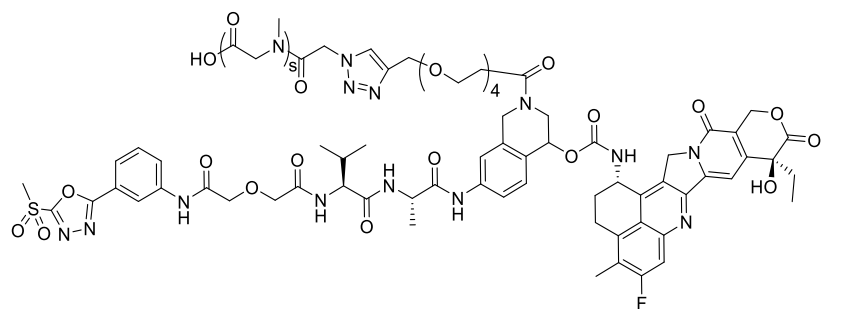
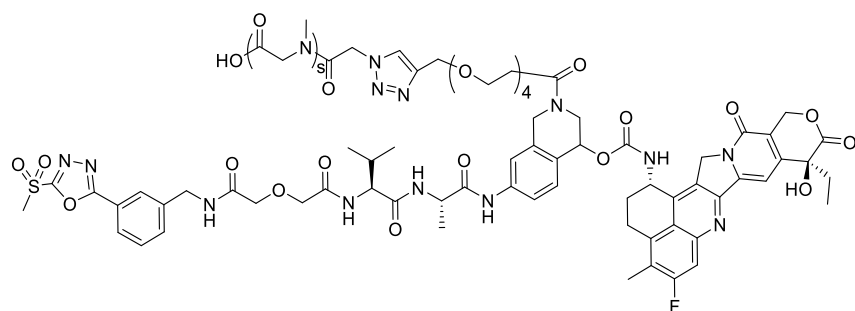
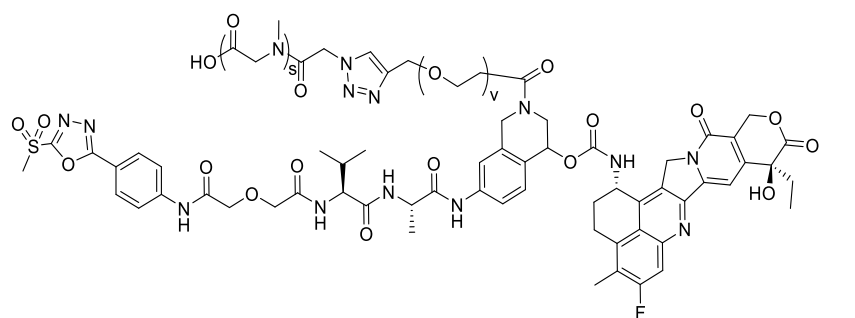


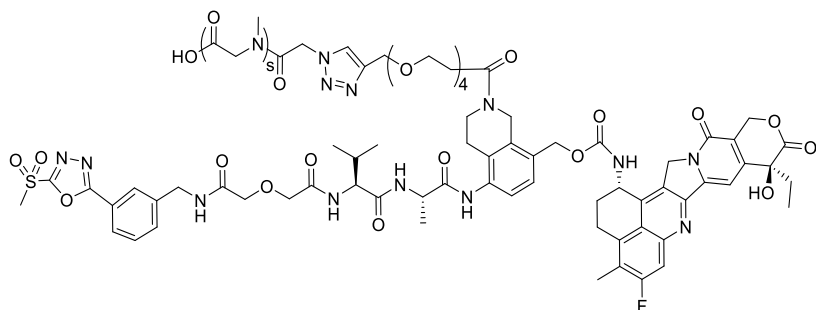
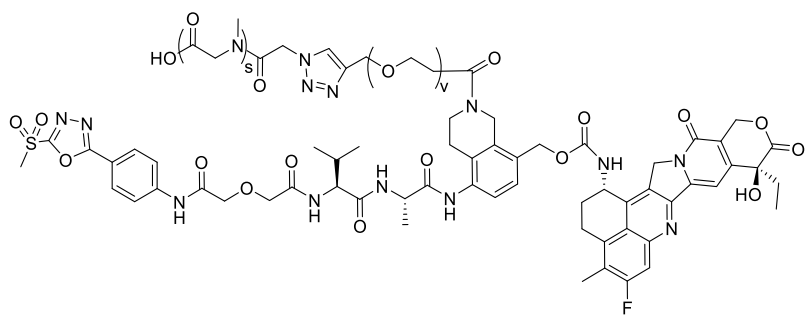
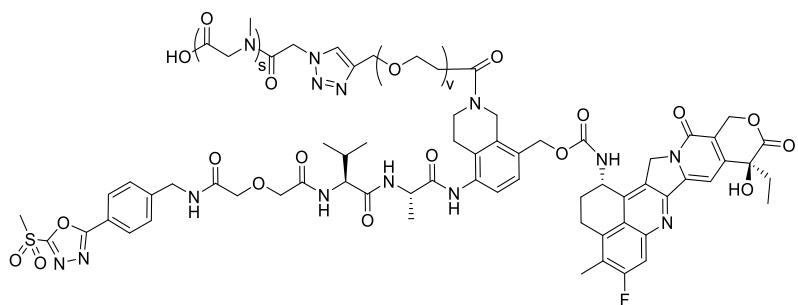
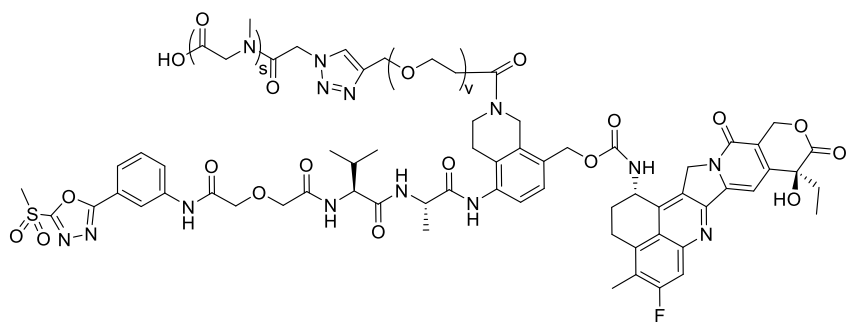
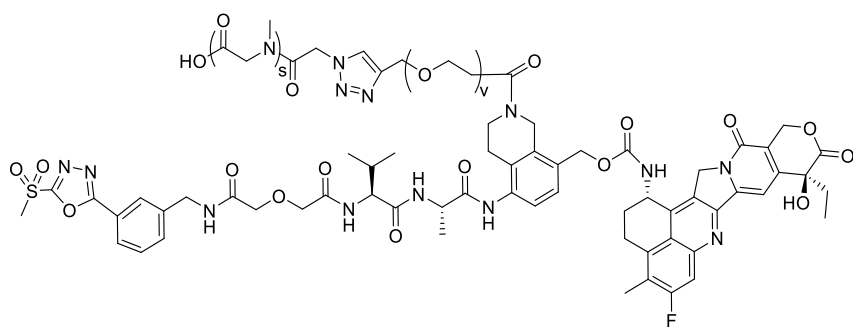


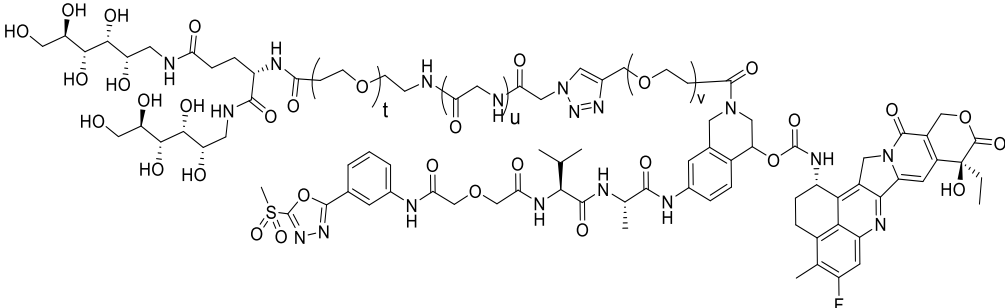
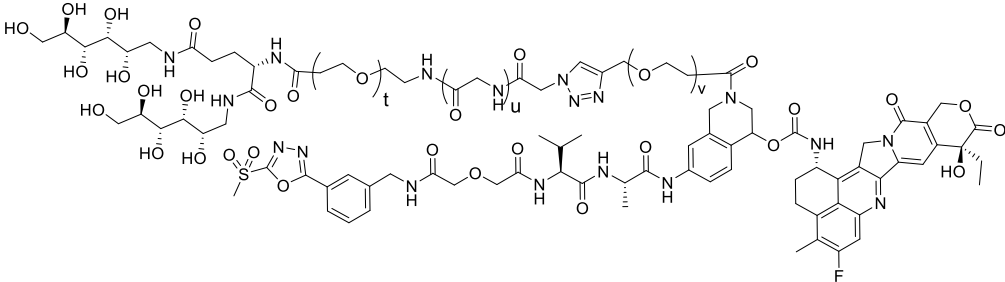
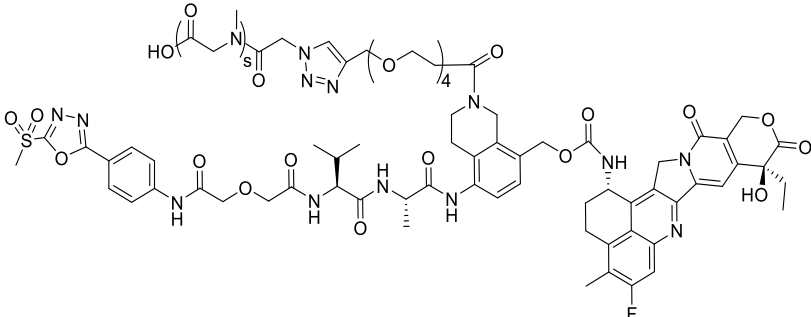
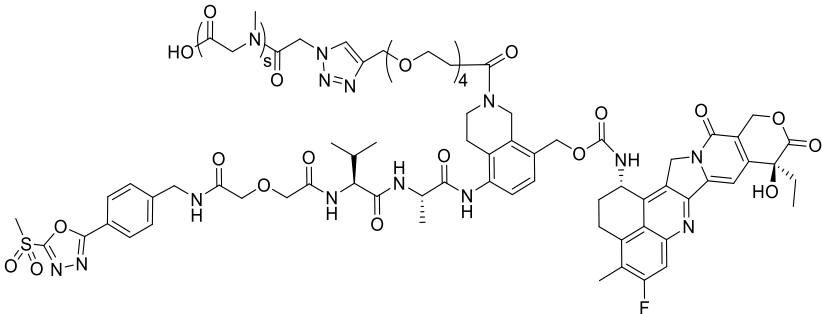
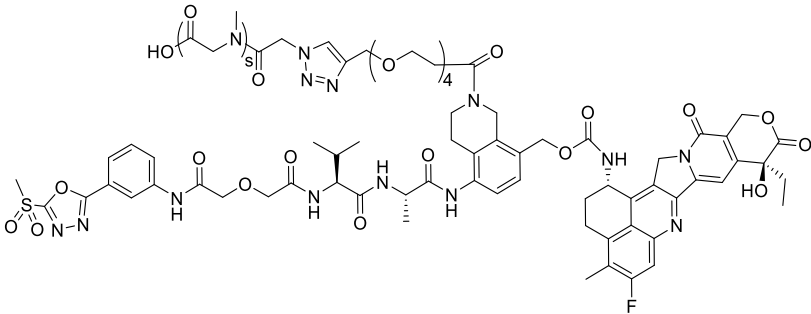
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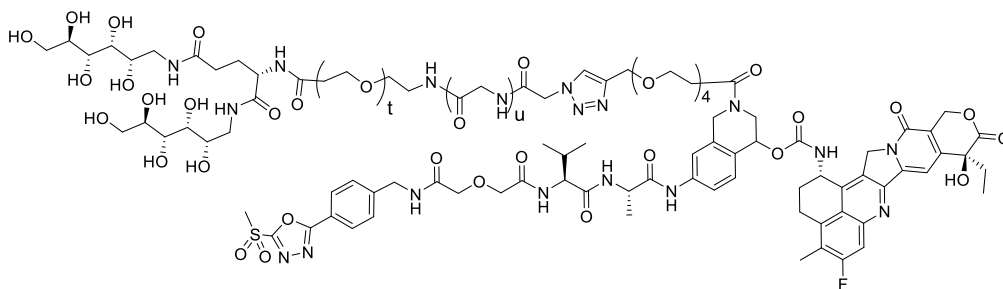
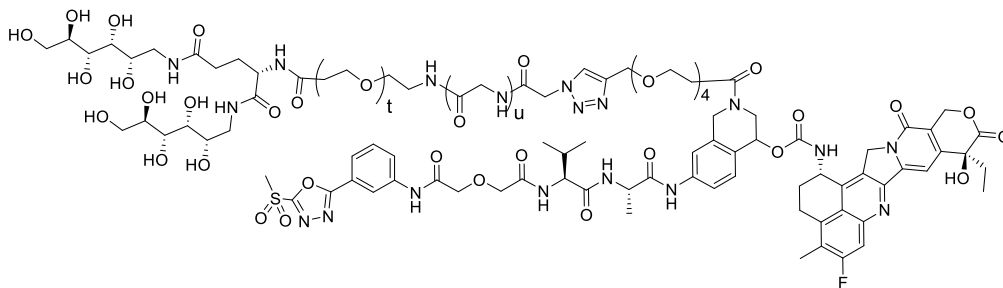
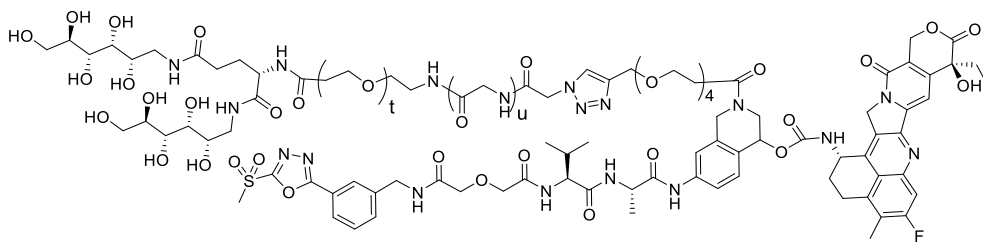
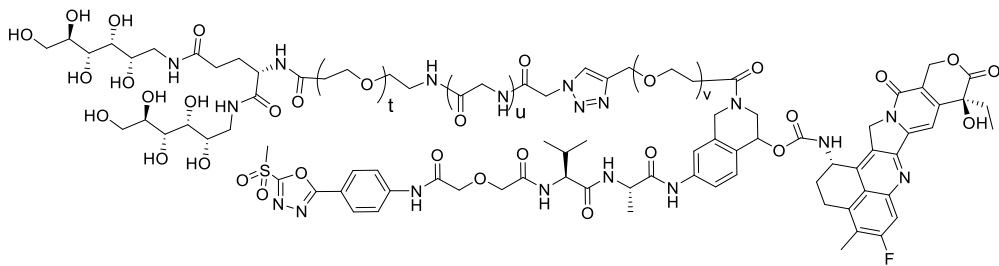
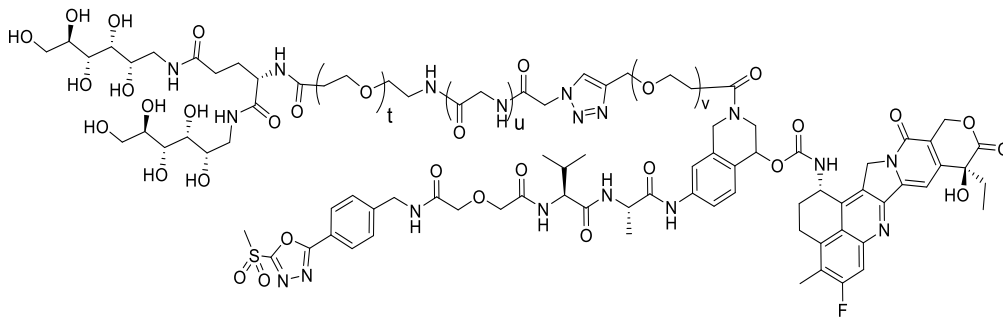




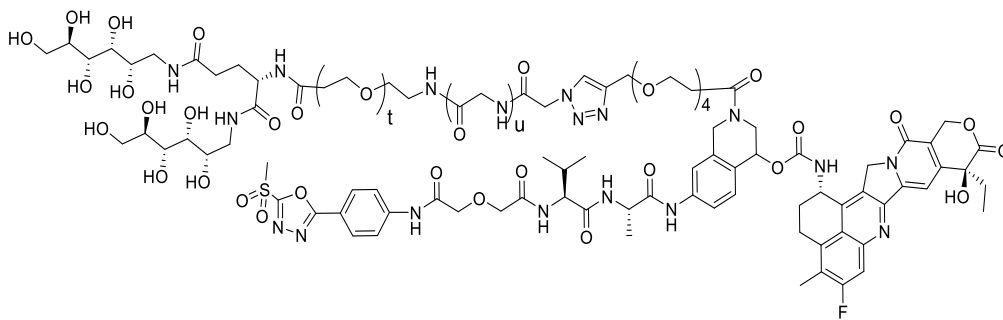


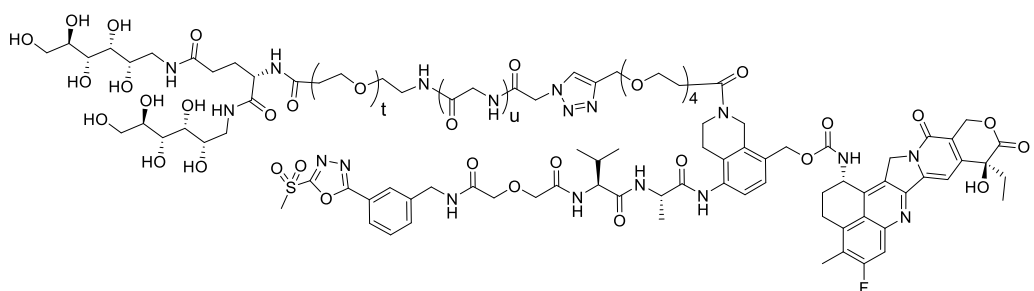
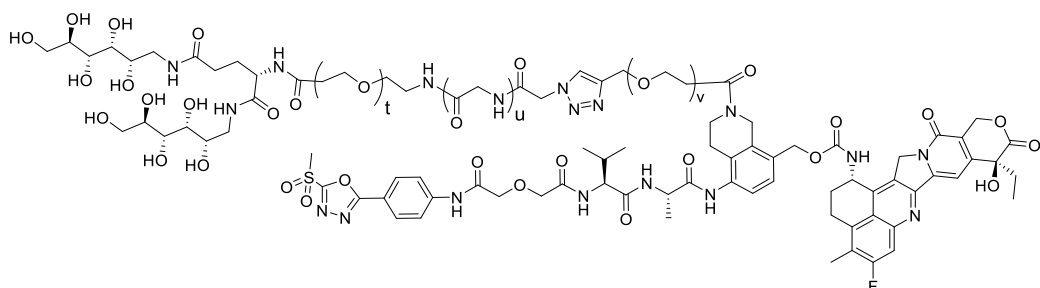
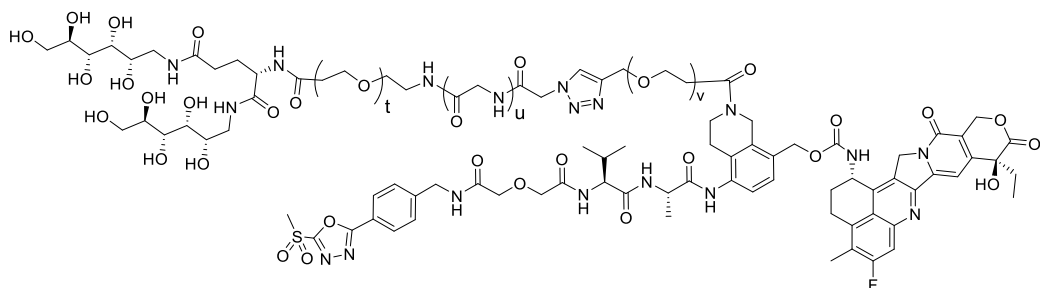
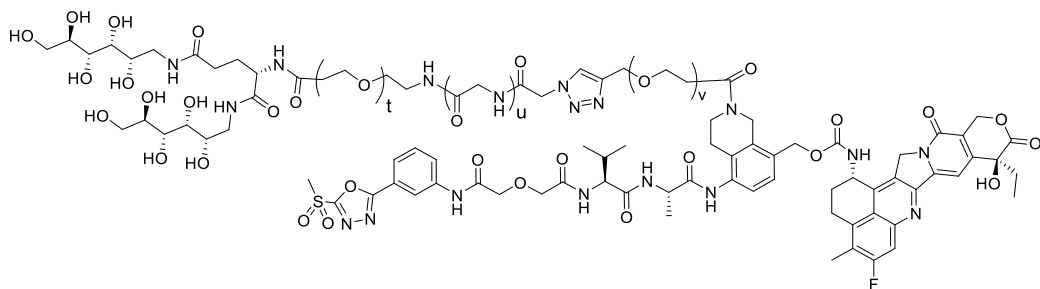
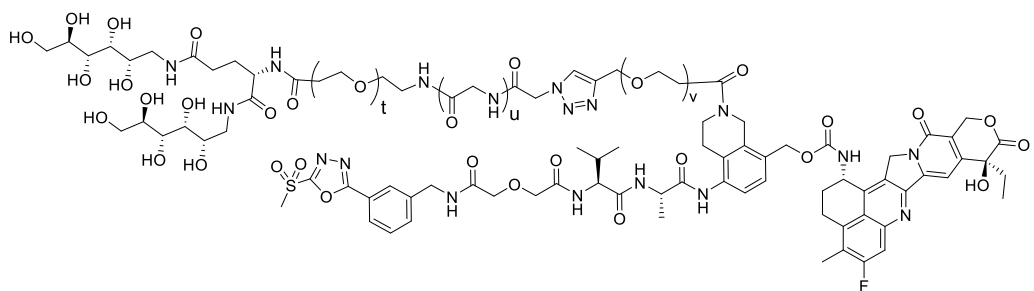




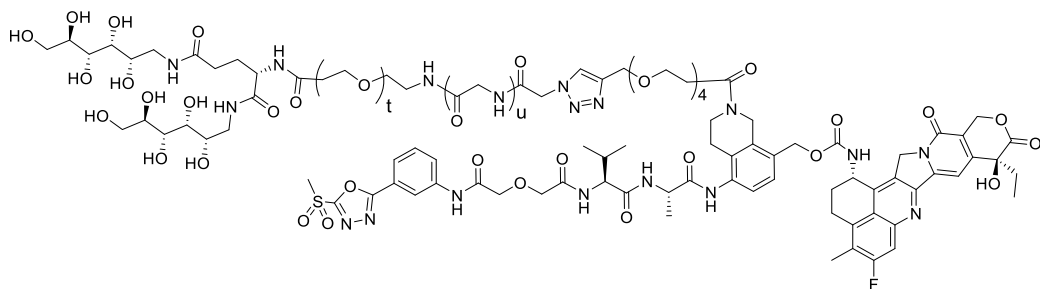


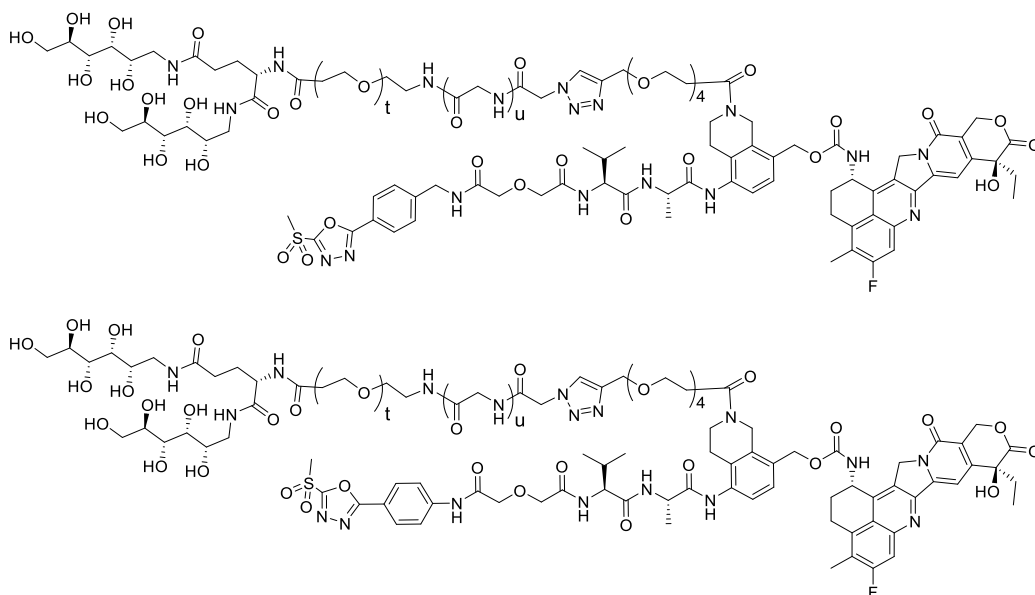
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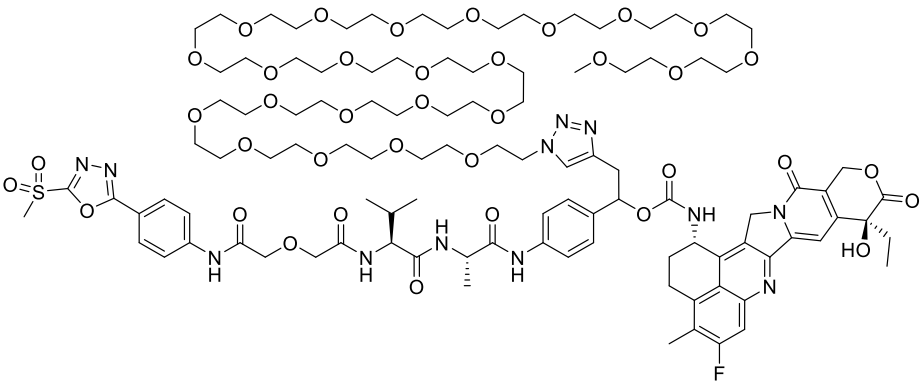
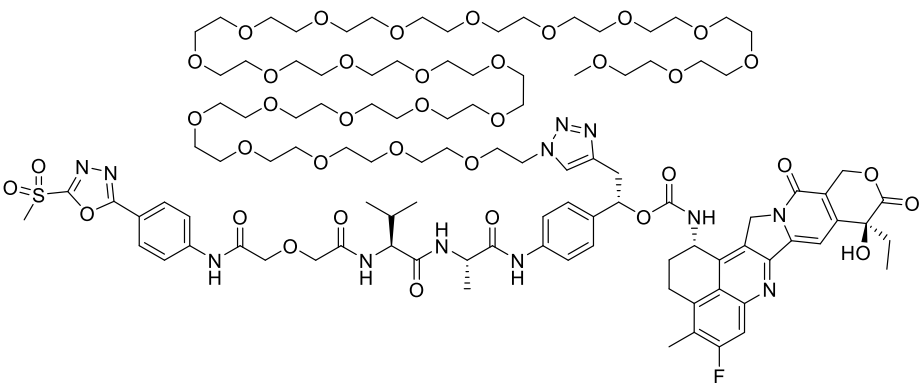
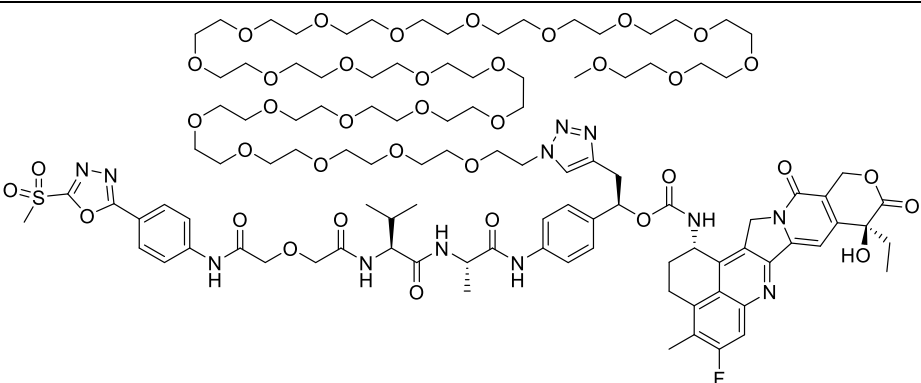
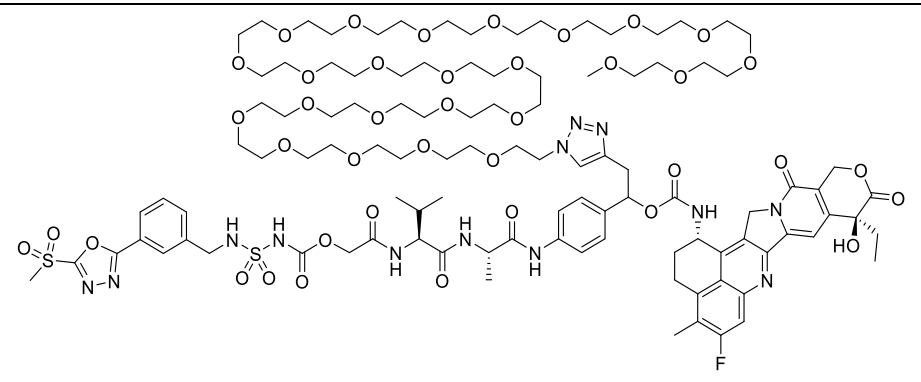


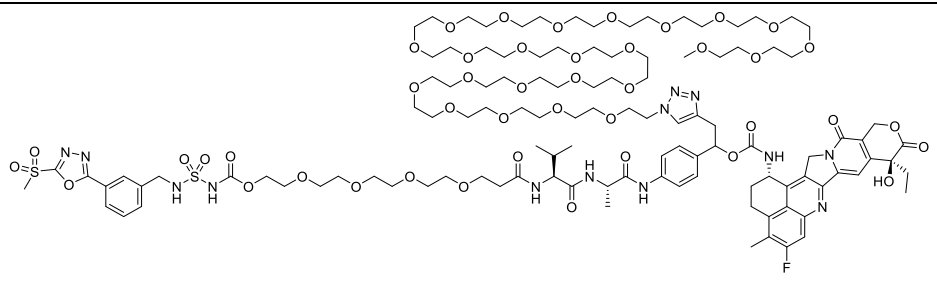
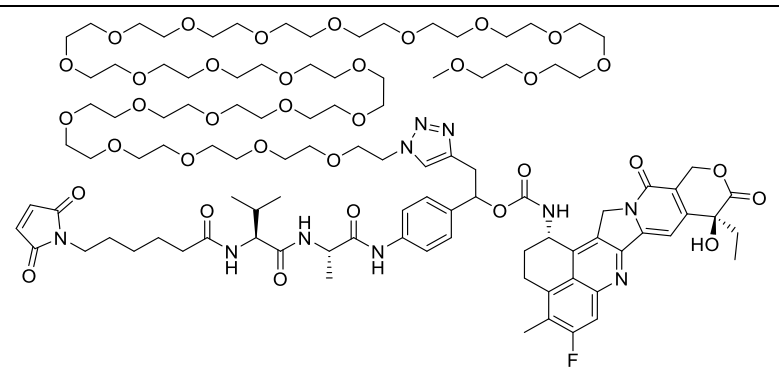
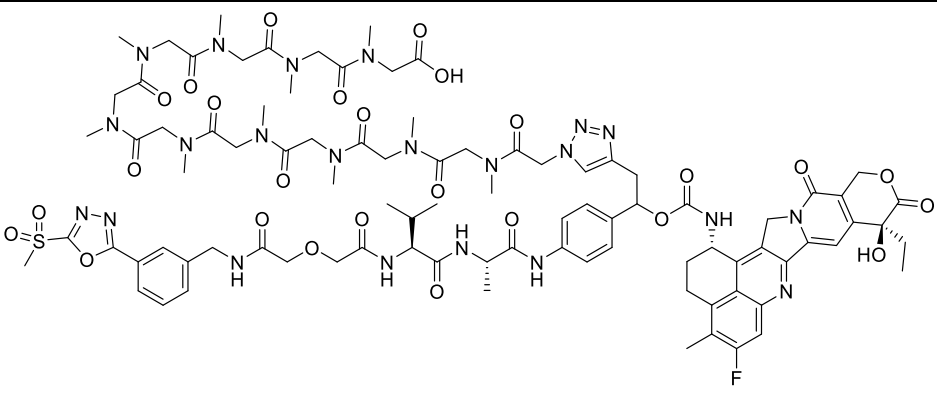
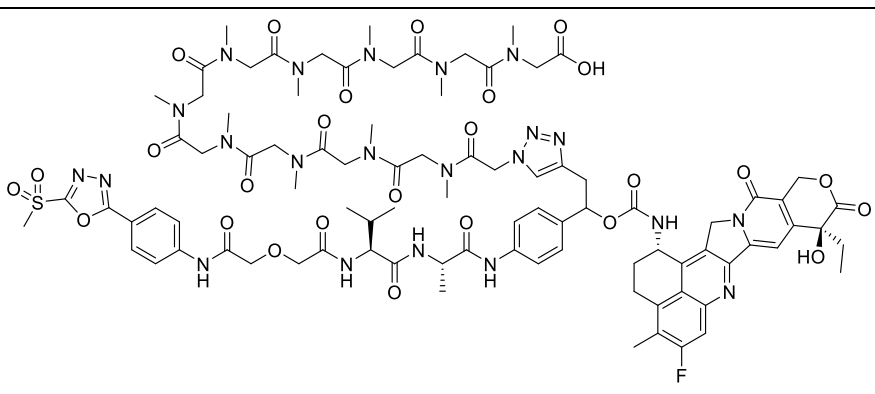


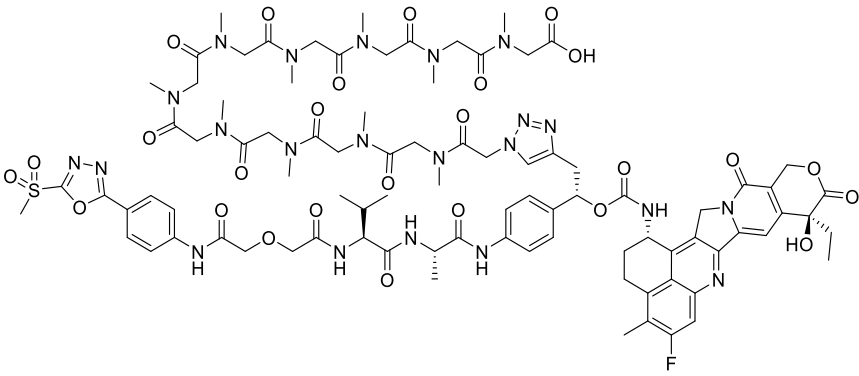
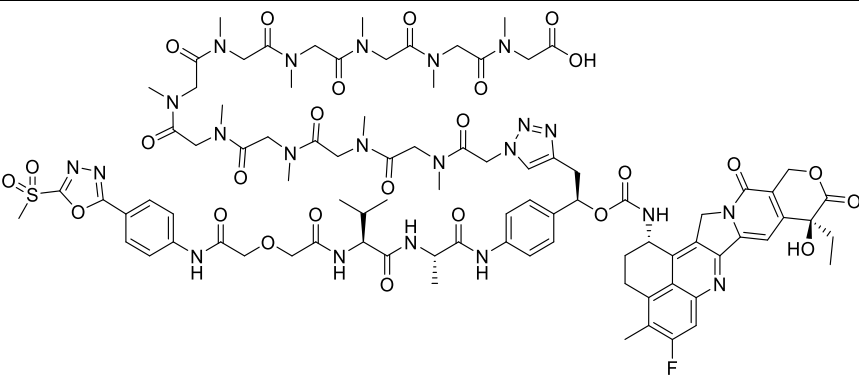
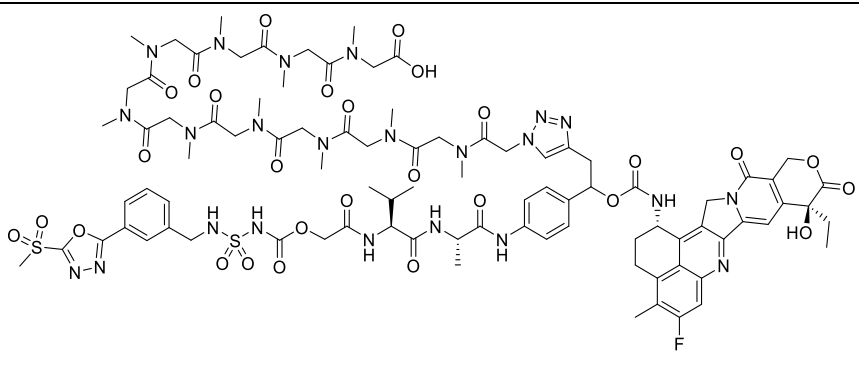
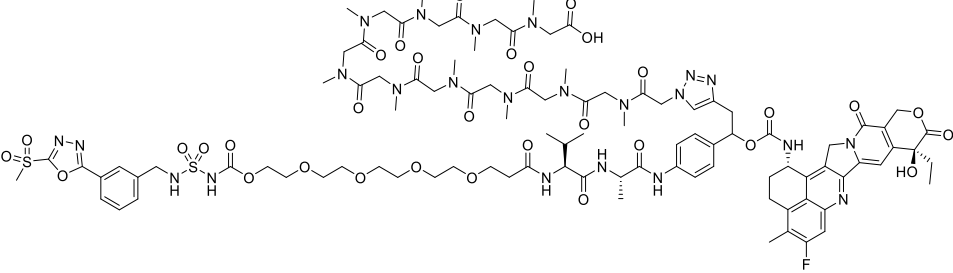
wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50), and v and w are each independently an integer selected from 1-12 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12).

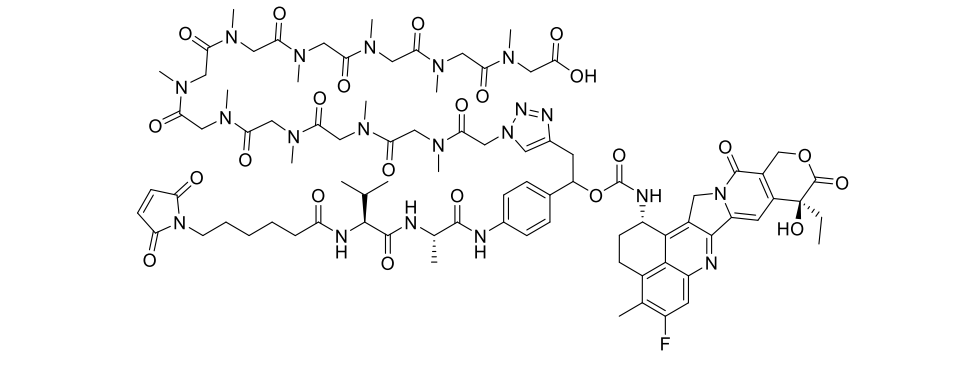
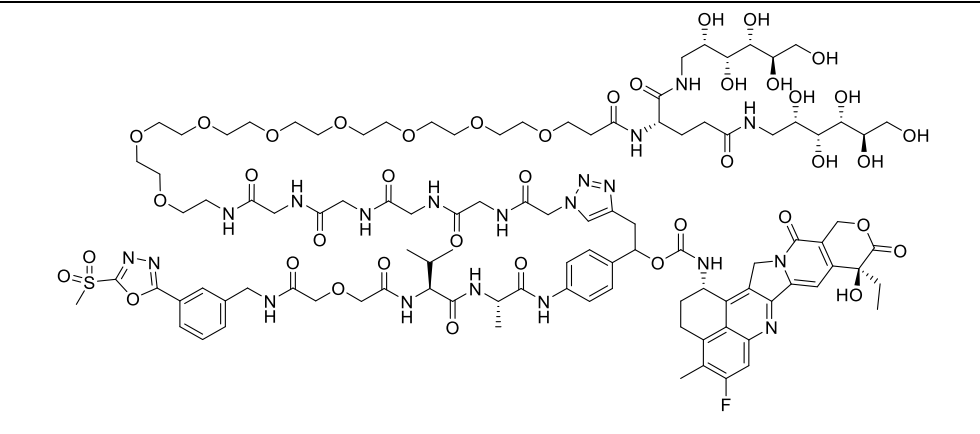
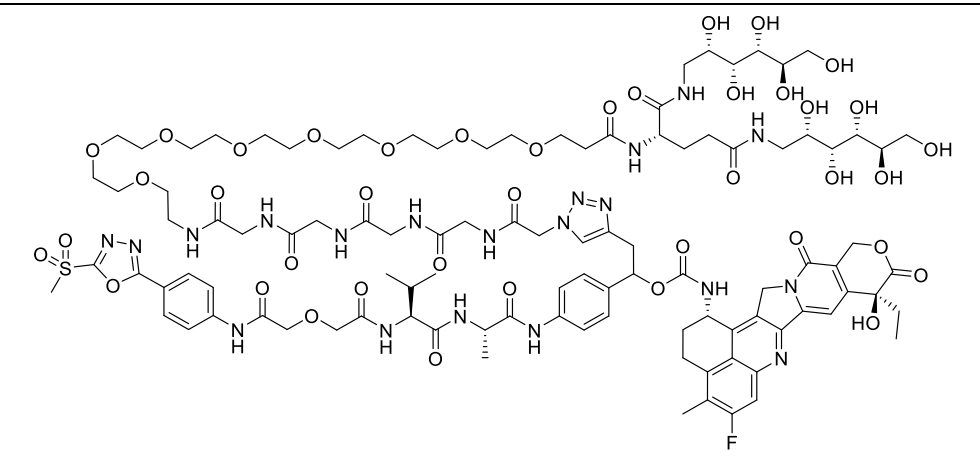
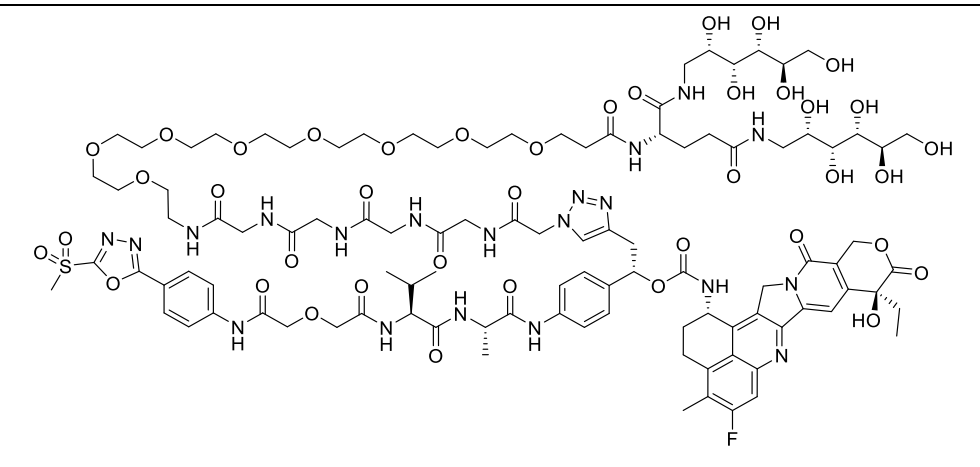
In some embodiments, the linker-drug compound represented by formula (II), or the tautomer, the mesomer, the racemate, the enantiomer or the diastereoisomer thereof, and the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof have a structure shown as follows:

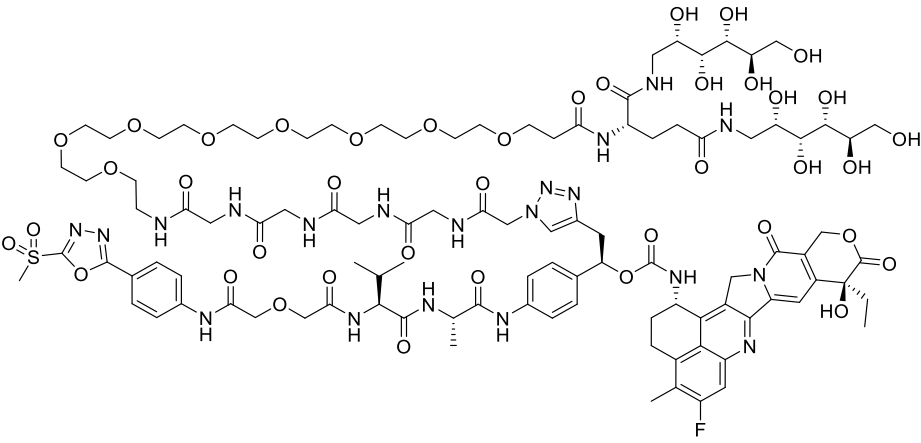
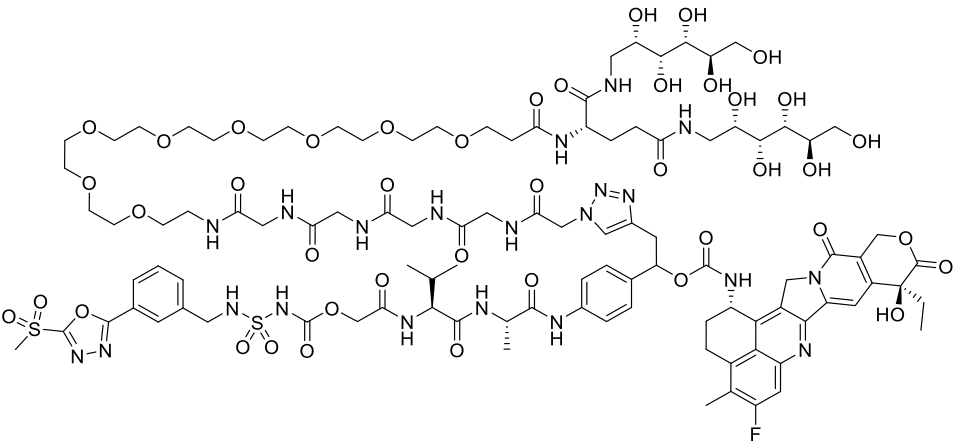
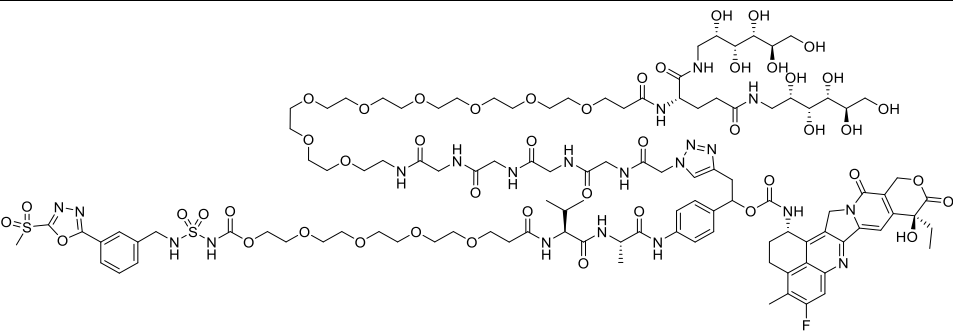
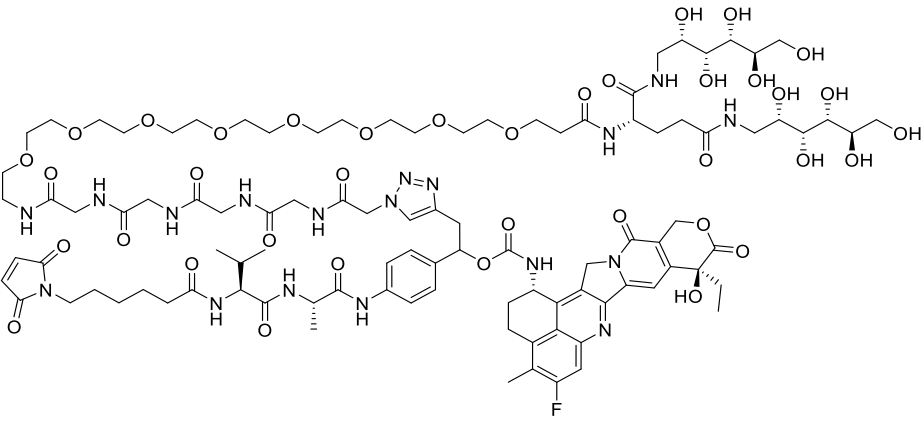
No.	Structure
LD1	The structure of LD1 is a complex molecule featuring a sulfonamide group, a triazole ring, a fluorinated quinoline system, and a hydroxyl group. It is connected via a linker to a complex polycyclic system. The structure is labeled 'LD1'.

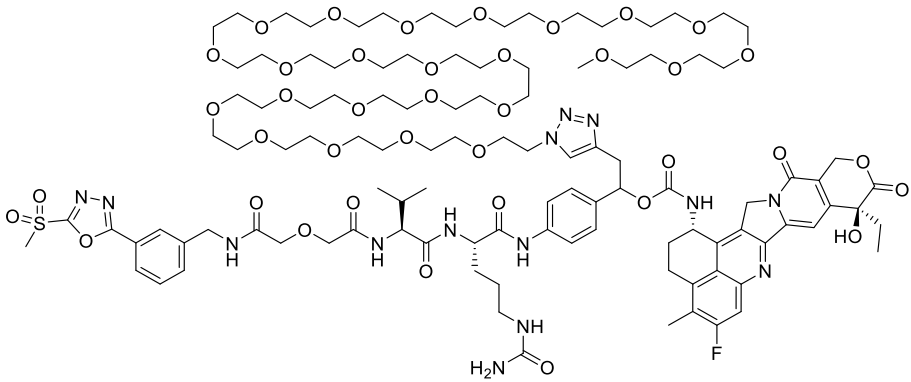
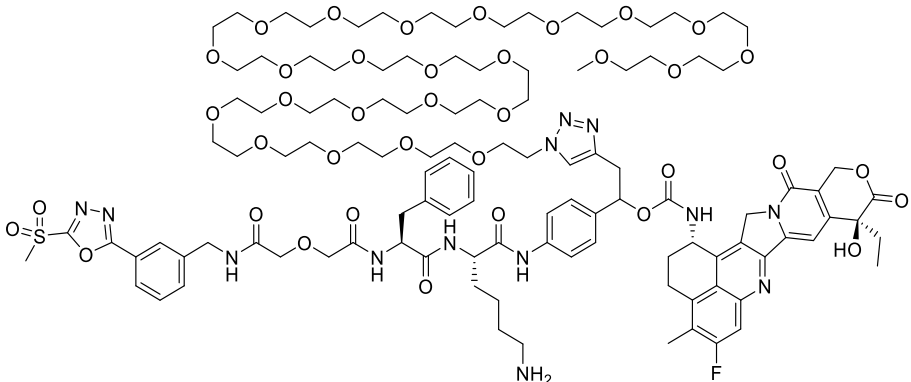
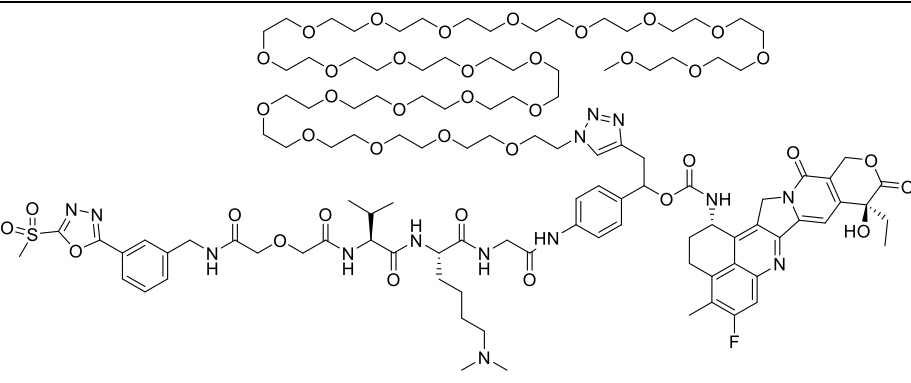
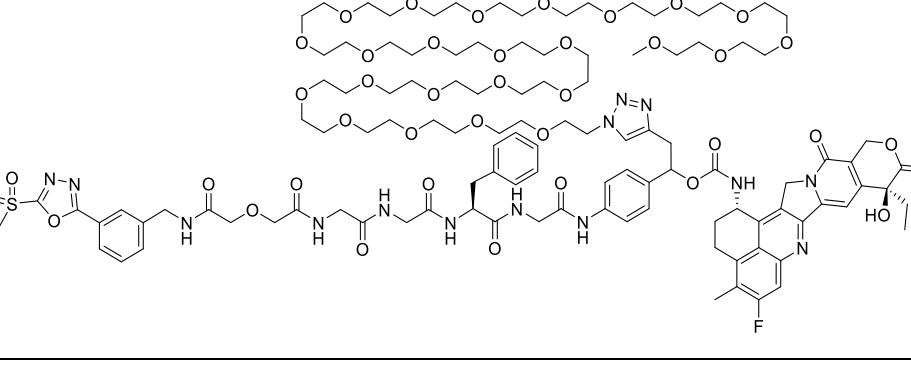
LD2	 Chemical structure of LD2. It features a long, flexible polyether chain (top) connected via a triazole ring to a central linker. The linker consists of a benzene ring substituted with a sulfonamide group (left) and a complex amide chain (right). The amide chain includes a chiral center (methyl group) and a fluorinated quinoline moiety (right).
LD2-1	 Chemical structure of LD2-1. It is identical to LD2, but the stereochemistry at the chiral center (methyl group) is inverted (dashed bond instead of wedge bond).
LD2-2	 Chemical structure of LD2-2. It is identical to LD2, but the stereochemistry at the chiral center (methyl group) is inverted (dashed bond instead of wedge bond).
LD3	 Chemical structure of LD3. It features a long, flexible polyether chain (top) connected via a triazole ring to a central linker. The linker consists of a benzene ring substituted with a sulfonamide group (left) and a complex amide chain (right). The amide chain includes a chiral center (methyl group) and a fluorinated quinoline moiety (right).

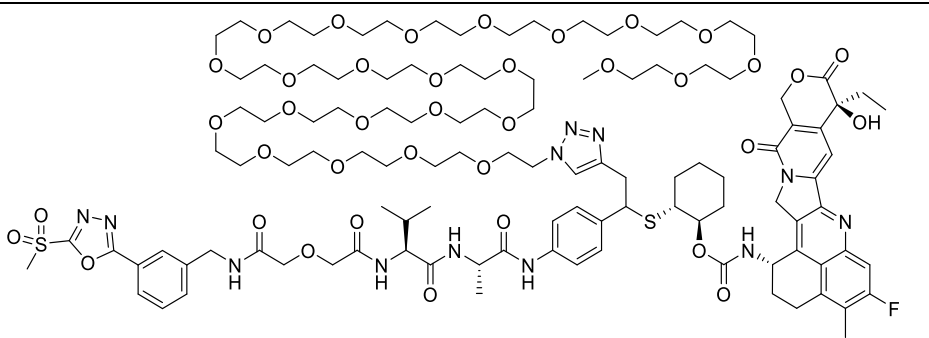
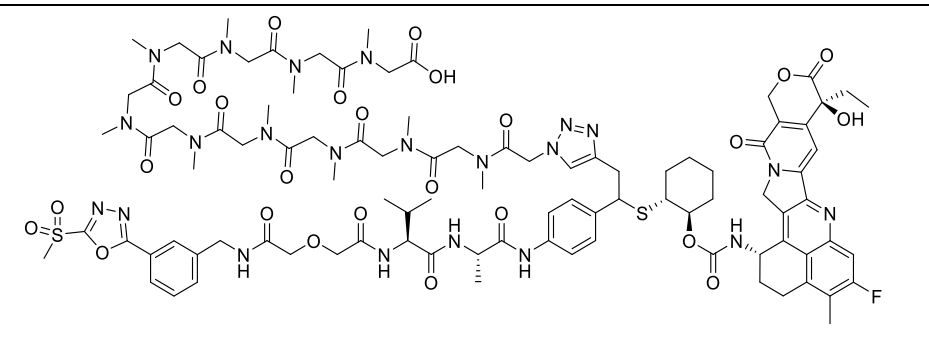
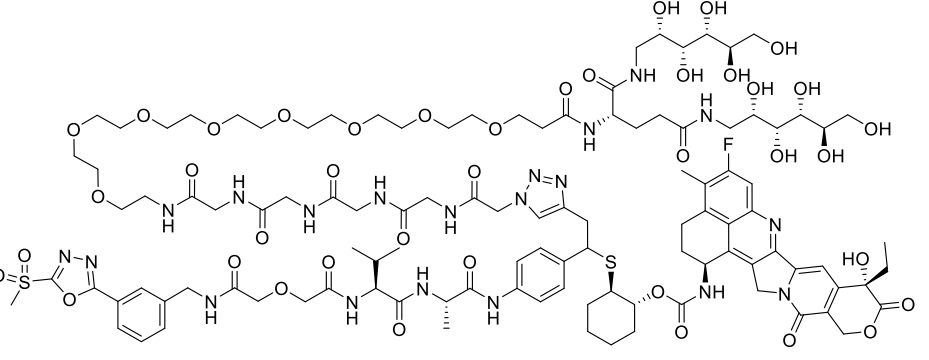
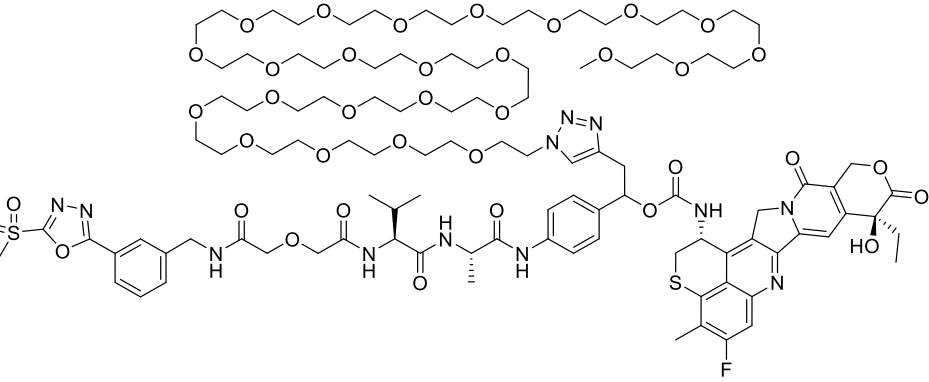
LD4	 Chemical structure of LD4: A complex molecule featuring a central core with a fluorinated benzene ring, a pyrazole ring, and a sulfonamide group. The structure is highly branched and includes multiple ether linkages and a long aliphatic chain.
LD5	 Chemical structure of LD5: A complex molecule featuring a central core with a fluorinated benzene ring, a pyrazole ring, and a sulfonamide group. The structure is highly branched and includes multiple ether linkages and a long aliphatic chain.
LD6	 Chemical structure of LD6: A complex molecule featuring a central core with a fluorinated benzene ring, a pyrazole ring, and a sulfonamide group. The structure is highly branched and includes multiple ether linkages and a long aliphatic chain.
LD7	 Chemical structure of LD7: A complex molecule featuring a central core with a fluorinated benzene ring, a pyrazole ring, and a sulfonamide group. The structure is highly branched and includes multiple ether linkages and a long aliphatic chain.

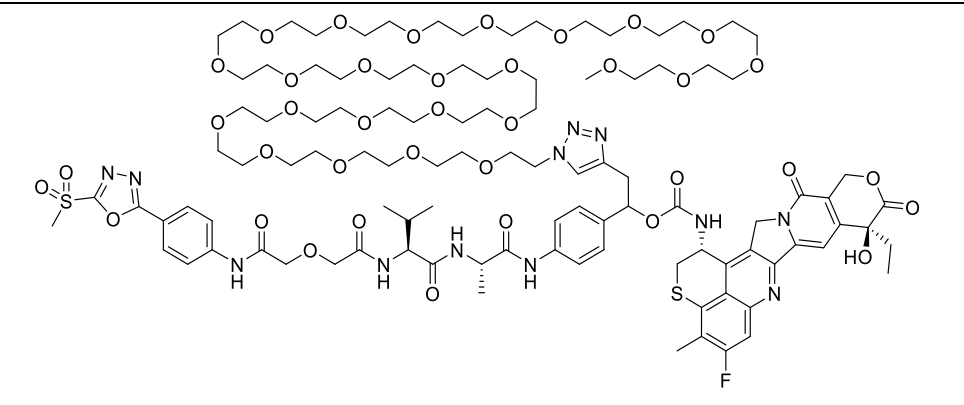
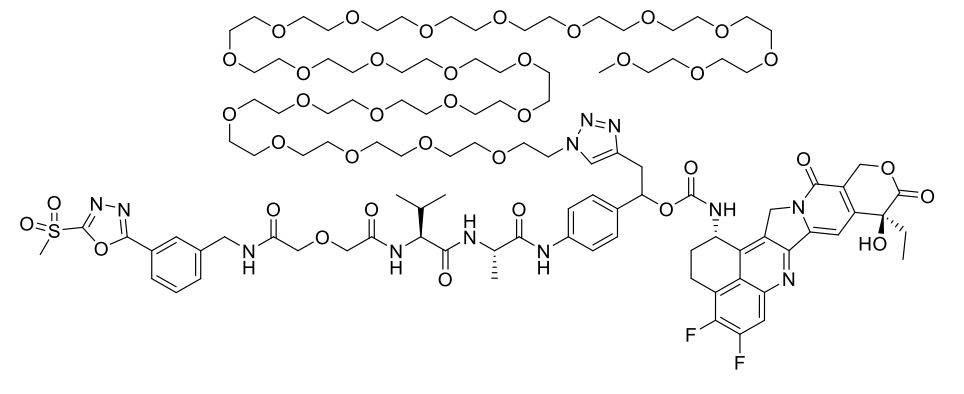
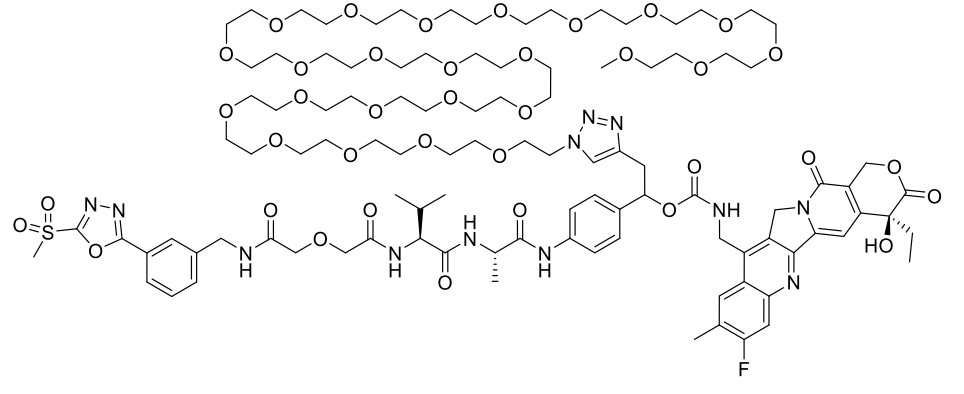
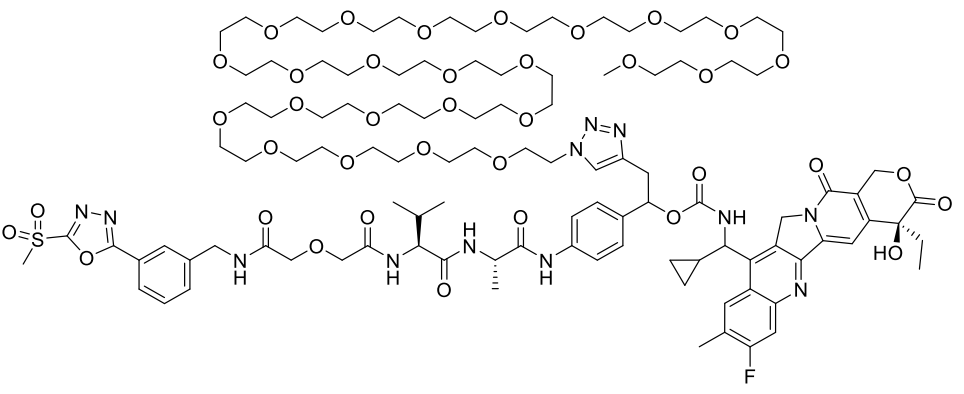
LD7-1	 Chemical structure of LD7-1: A complex molecule featuring a long, branched polyamide chain. The chain is terminated by a carboxylic acid group (COOH) and a sulfonamide group (SO₂NH₂). The chain is linked to a benzimidazole moiety, which is further connected to a fluorinated benzimidazole derivative. The structure includes a hydroxyl group (OH) and a methyl group (CH₃).
LD7-2	 Chemical structure of LD7-2: A complex molecule featuring a long, branched polyamide chain. The chain is terminated by a carboxylic acid group (COOH) and a sulfonamide group (SO₂NH₂). The chain is linked to a benzimidazole moiety, which is further connected to a fluorinated benzimidazole derivative. The structure includes a hydroxyl group (OH) and a methyl group (CH₃).
LD8	 Chemical structure of LD8: A complex molecule featuring a long, branched polyamide chain. The chain is terminated by a carboxylic acid group (COOH) and a sulfonamide group (SO₂NH₂). The chain is linked to a benzimidazole moiety, which is further connected to a fluorinated benzimidazole derivative. The structure includes a hydroxyl group (OH) and a methyl group (CH₃).
LD9	 Chemical structure of LD9: A complex molecule featuring a long, branched polyamide chain. The chain is terminated by a carboxylic acid group (COOH) and a sulfonamide group (SO₂NH₂). The chain is linked to a benzimidazole moiety, which is further connected to a fluorinated benzimidazole derivative. The structure includes a hydroxyl group (OH) and a methyl group (CH₃).

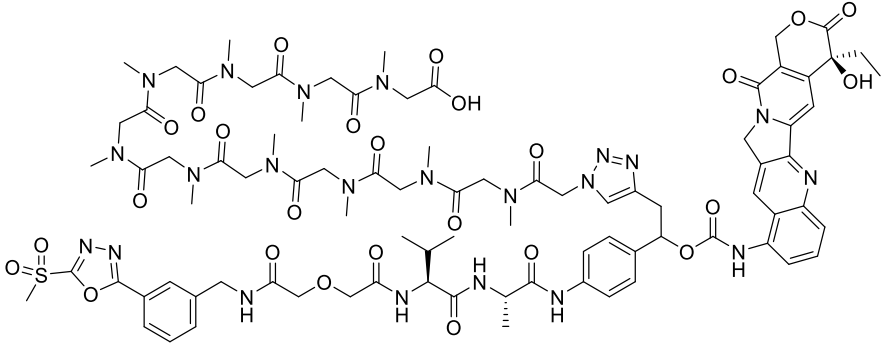
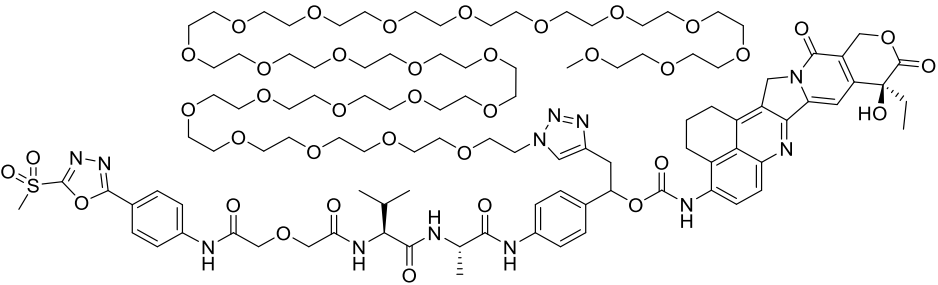
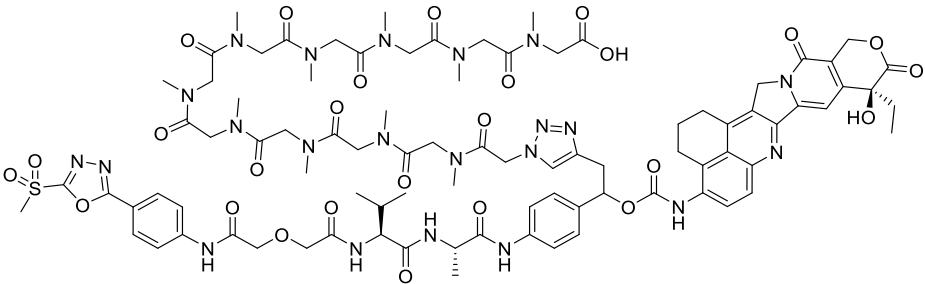
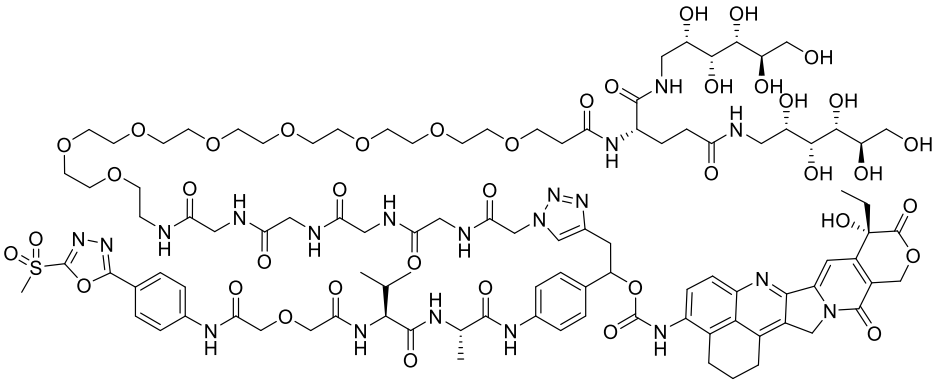
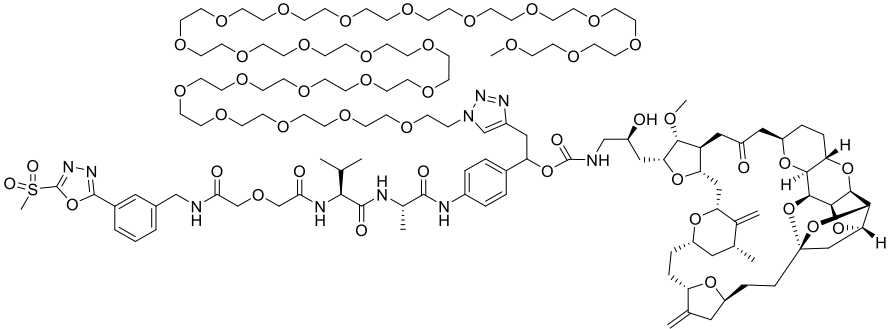
LD10	 Chemical structure of LD10, a complex molecule featuring a long chain of repeating units, including amide bonds, a pyridine ring, and a fluorinated benzene ring, terminating in a carboxylic acid group.
LD11	 Chemical structure of LD11, a complex molecule featuring a long chain of repeating units, including amide bonds, a pyridine ring, and a fluorinated benzene ring, terminating in a carboxylic acid group. It also includes a sulfonamide group and a polyether chain.
LD12	 Chemical structure of LD12, a complex molecule featuring a long chain of repeating units, including amide bonds, a pyridine ring, and a fluorinated benzene ring, terminating in a carboxylic acid group. It also includes a sulfonamide group and a polyether chain.
LD12-1	 Chemical structure of LD12-1, a complex molecule featuring a long chain of repeating units, including amide bonds, a pyridine ring, and a fluorinated benzene ring, terminating in a carboxylic acid group. It also includes a sulfonamide group and a polyether chain.

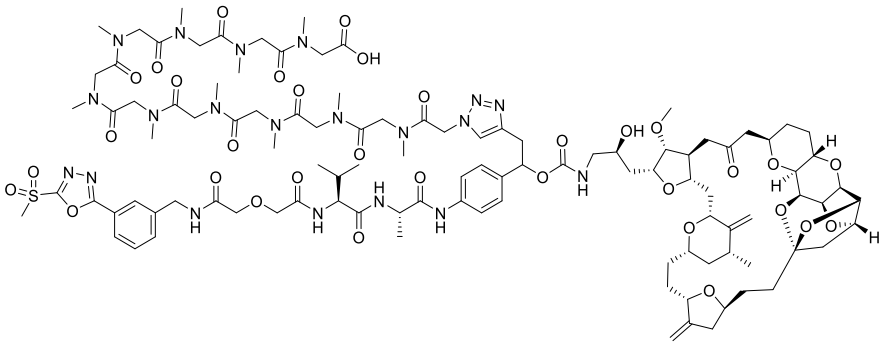
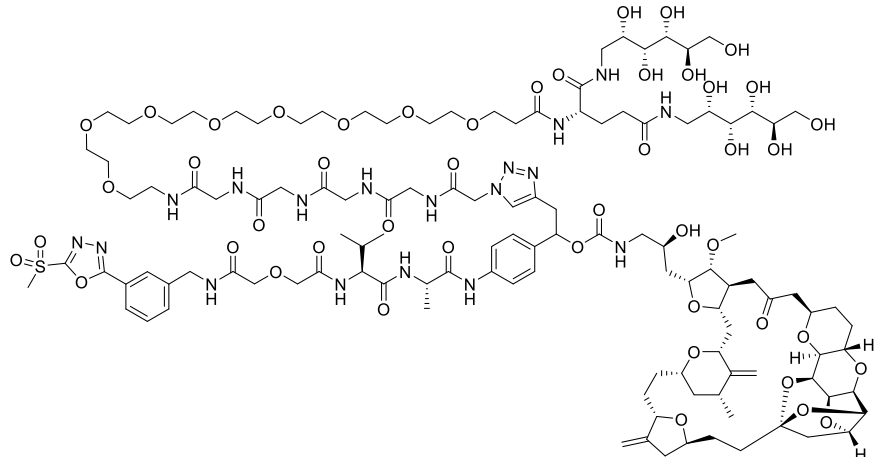
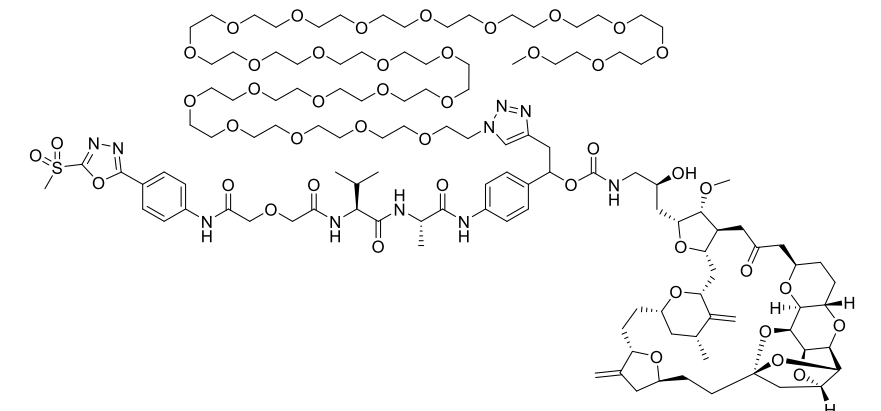
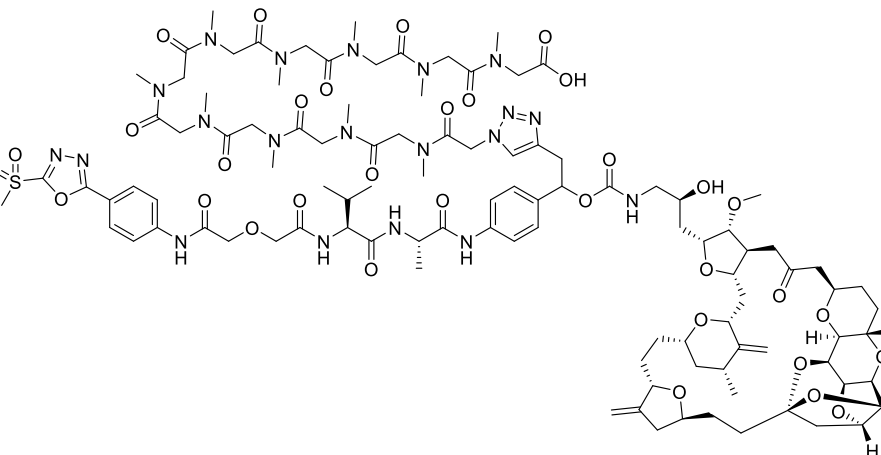
LD12- 2	 Chemical structure of LD12-2, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a fluorinated benzimidazole moiety.
LD13	 Chemical structure of LD13, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a fluorinated benzimidazole moiety.
LD14	 Chemical structure of LD14, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a fluorinated benzimidazole moiety.
LD15	 Chemical structure of LD15, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a fluorinated benzimidazole moiety.

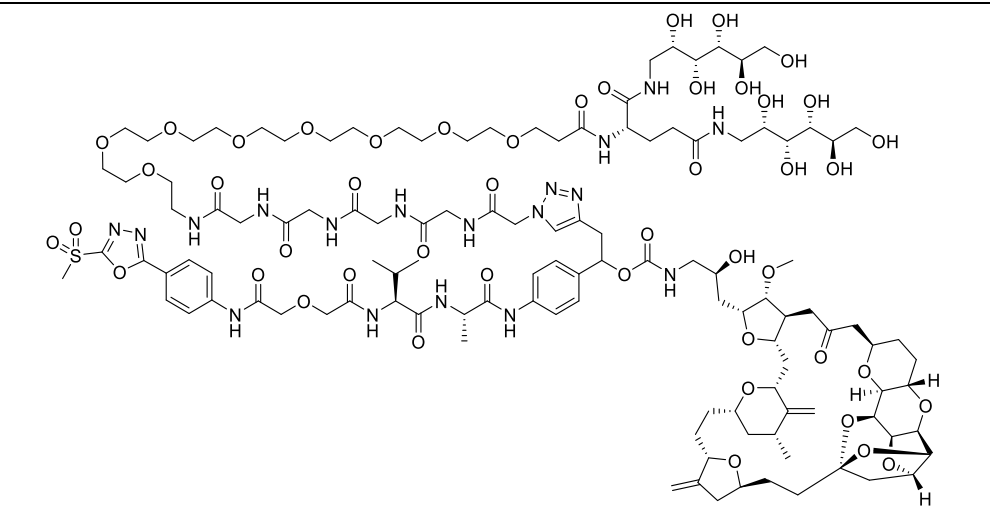
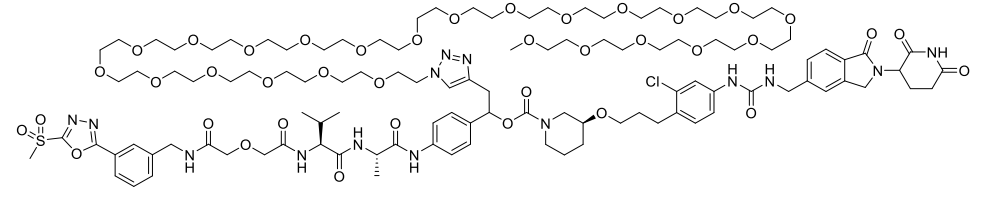
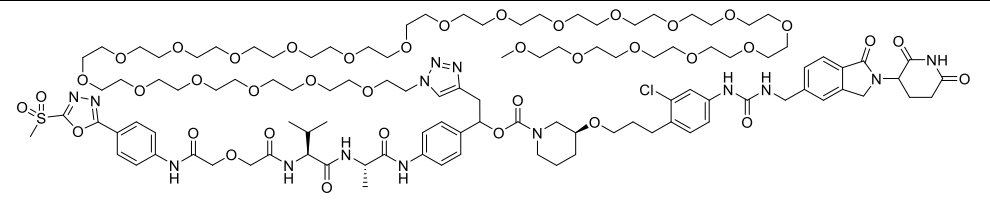
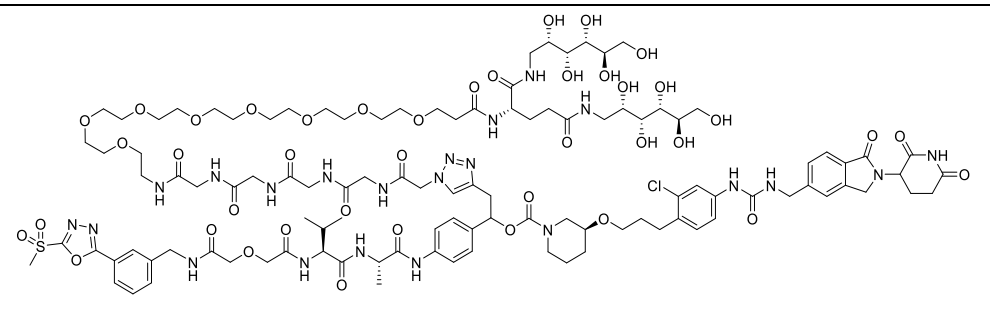
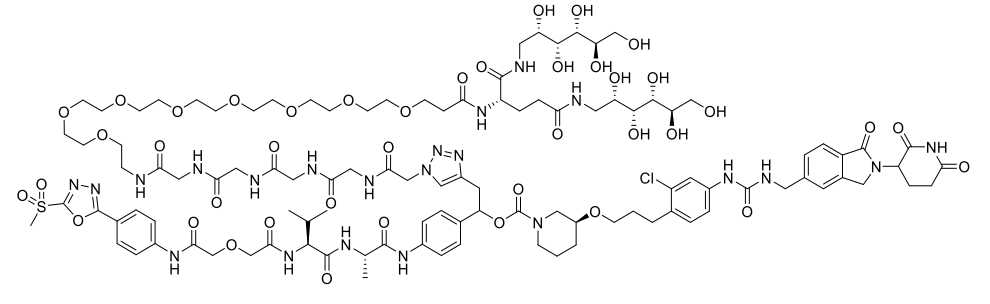
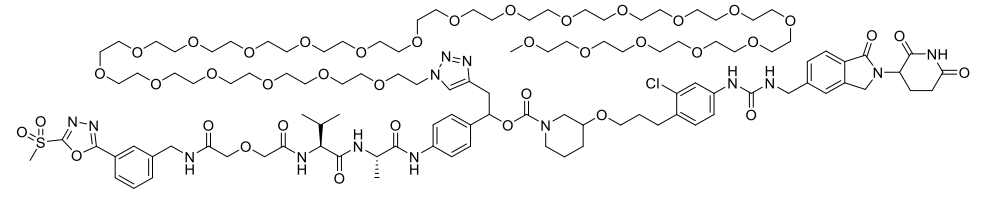
LD16	 Chemical structure of LD16, a complex molecule featuring a long polyether chain (top), a sulfonamide group (left), a peptide backbone (center), and a fluorinated indole derivative (right). The molecule includes a terminal amide group (H₂N-C(=O)-) and a hydroxyl group (HO-).
LD17	 Chemical structure of LD17, similar to LD16, but with a different peptide backbone and a terminal amine group (NH₂).
LD18	 Chemical structure of LD18, featuring a long polyether chain (top), a sulfonamide group (left), a peptide backbone (center), and a fluorinated indole derivative (right). The molecule includes a terminal amide group (H₂N-C(=O)-) and a hydroxyl group (HO-).
LD19	 Chemical structure of LD19, featuring a long polyether chain (top), a sulfonamide group (left), a peptide backbone (center), and a fluorinated indole derivative (right). The molecule includes a terminal amide group (H₂N-C(=O)-) and a hydroxyl group (HO-).

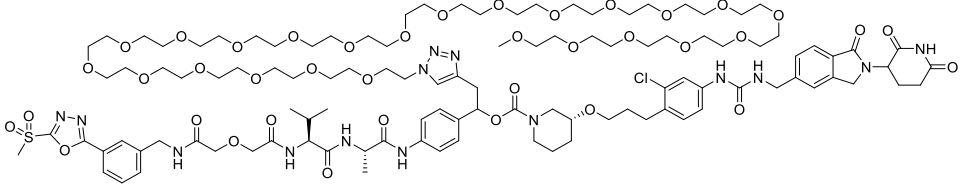
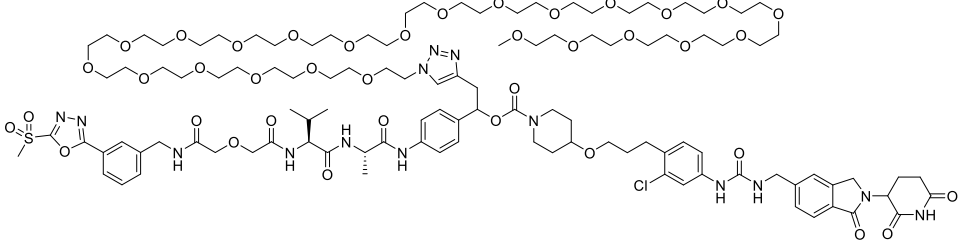
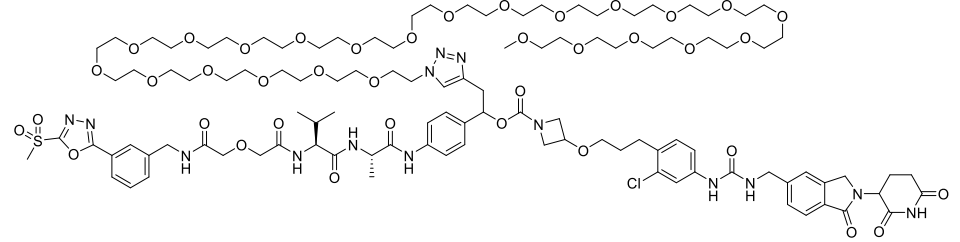
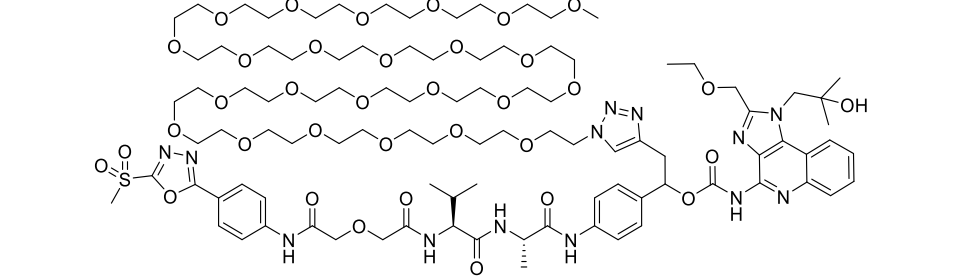
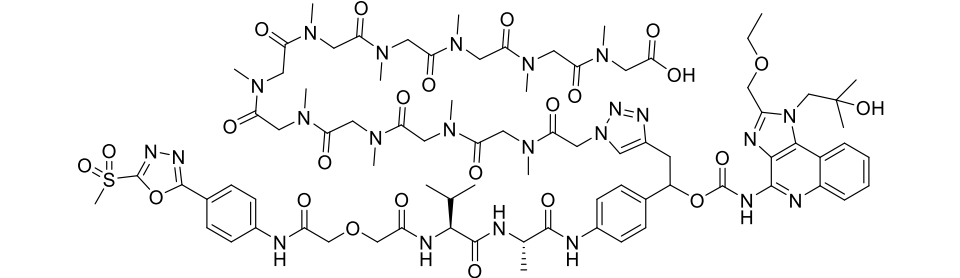
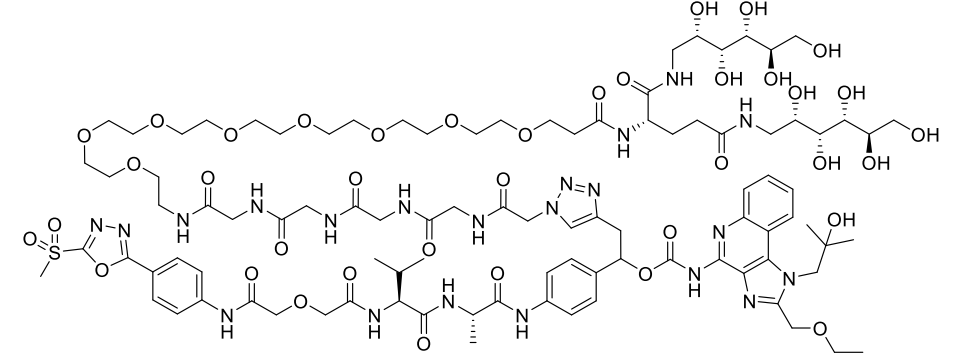
LD20	 Chemical structure of LD20: A complex molecule featuring a long polyether chain (top) connected via a triazole ring to a central core. The core includes a benzene ring with a sulfonamide group, a chiral amide, and a cyclohexyl group. The right side of the molecule contains a fluorinated quinoline system with a hydroxyl group and a carbonyl.
LD21	 Chemical structure of LD21: Similar to LD20, but the polyether chain is replaced by a long, branched amide chain. The rest of the molecule, including the sulfonamide, chiral amide, cyclohexyl group, and fluorinated quinoline system, remains the same.
LD22	 Chemical structure of LD22: The molecule features a long polyether chain (top) and a complex amide chain (middle) that includes a fluorinated quinoline system. The right side of the molecule contains a fluorinated quinoline system with a hydroxyl group and a carbonyl.
LD23	 Chemical structure of LD23: Similar to LD20, but the polyether chain is replaced by a long, branched amide chain. The rest of the molecule, including the sulfonamide, chiral amide, cyclohexyl group, and fluorinated quinoline system, remains the same.

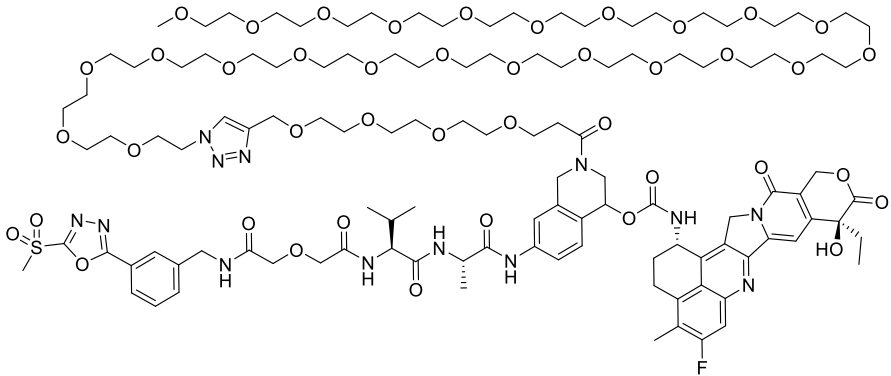
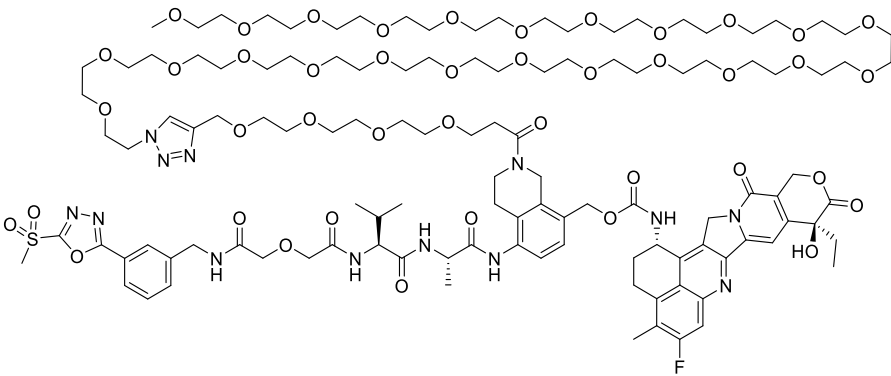
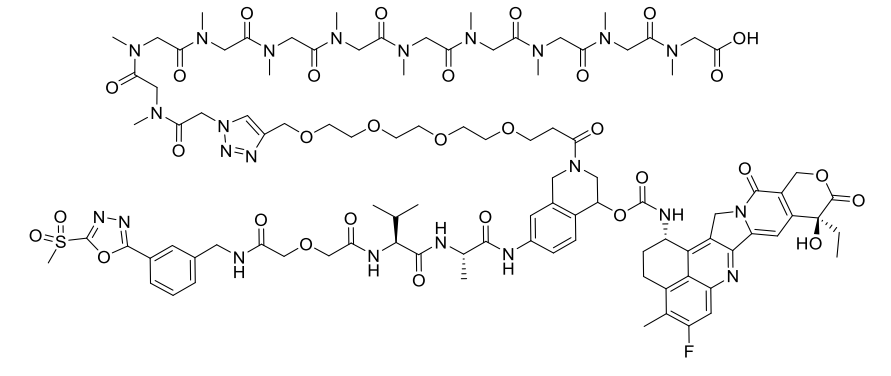
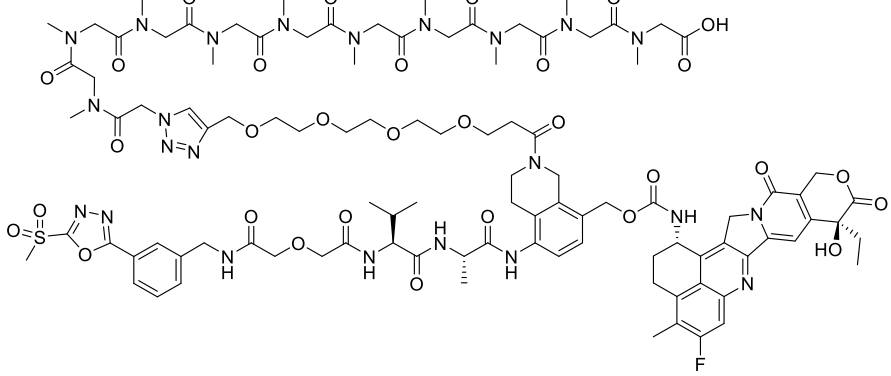
LD24	 Chemical structure of LD24: A complex molecule featuring a long polyether chain (top) connected via a diazo group to a benzyl group. This benzyl group is linked to a peptide backbone containing a chiral center (isopropyl group). The peptide is further connected to a benzyl group, which is linked to a thiazine ring system. The thiazine ring is substituted with a fluorine atom and a hydroxyl group.
LD25	 Chemical structure of LD25: Similar to LD24, but the thiazine ring system is substituted with two fluorine atoms and a hydroxyl group.
LD26	 Chemical structure of LD26: Similar to LD24, but the thiazine ring system is substituted with a fluorine atom and a hydroxyl group, and the benzyl group is linked to a different part of the thiazine ring.
LD27	 Chemical structure of LD27: Similar to LD24, but the thiazine ring system is substituted with a fluorine atom and a hydroxyl group, and the benzyl group is linked to a different part of the thiazine ring.

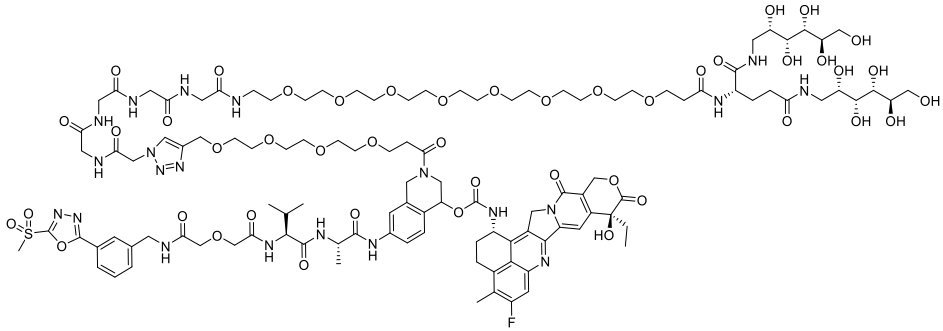
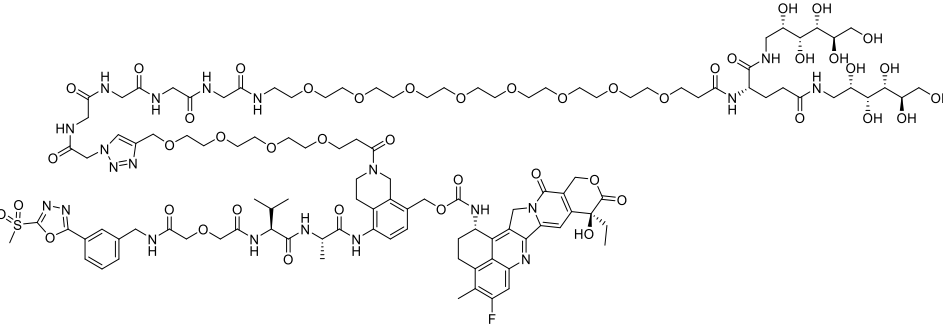
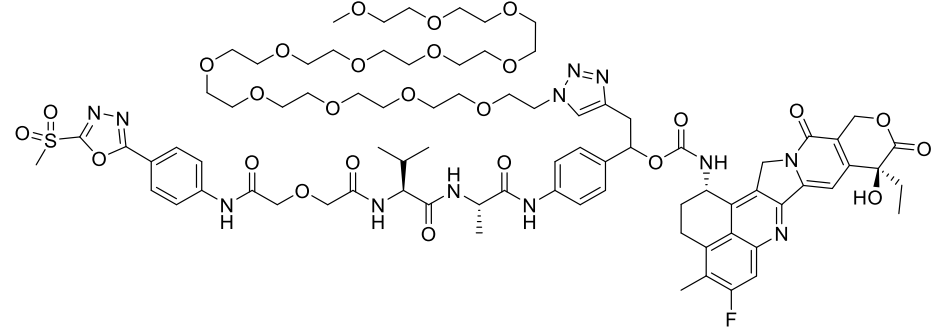
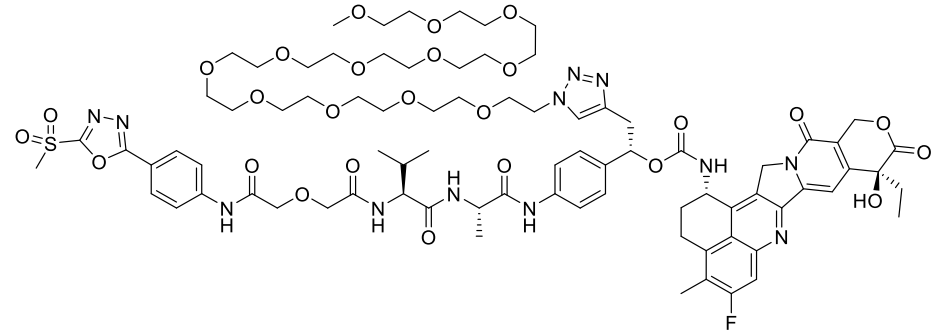
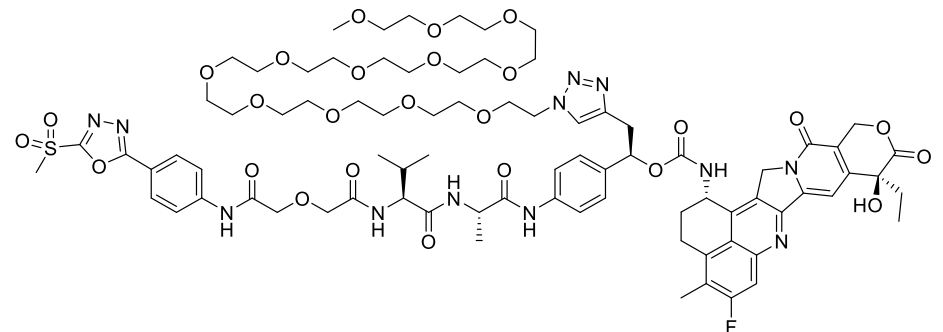
LD28	 Chemical structure of LD28, a complex molecule featuring a long chain of repeating amide and ester linkages, a sulfonamide group, a triazole ring, and a complex polycyclic aromatic system with a carboxylic acid and a hydroxyl group.
LD29	 Chemical structure of LD29, a complex molecule featuring a long chain of repeating amide and ester linkages, a sulfonamide group, a triazole ring, and a complex polycyclic aromatic system with a carboxylic acid and a hydroxyl group.
LD30	 Chemical structure of LD30, a complex molecule featuring a long chain of repeating amide and ester linkages, a sulfonamide group, a triazole ring, and a complex polycyclic aromatic system with a carboxylic acid and a hydroxyl group.
LD31	 Chemical structure of LD31, a complex molecule featuring a long chain of repeating amide and ester linkages, a sulfonamide group, a triazole ring, and a complex polycyclic aromatic system with a carboxylic acid and a hydroxyl group.
LD32	 Chemical structure of LD32, a complex molecule featuring a long chain of repeating amide and ester linkages, a sulfonamide group, a triazole ring, and a complex polycyclic aromatic system with a carboxylic acid and a hydroxyl group.

LD33	 Chemical structure of LD33, a complex molecule featuring a long chain of repeating amide units (N-methyl-L-glutamate) linked to a triazole ring, which is further connected to a complex polycyclic system containing multiple hydroxyl groups and a sulfonamide group.
LD34	 Chemical structure of LD34, a complex molecule featuring a long chain of repeating amide units (N-methyl-L-glutamate) linked to a triazole ring, which is further connected to a complex polycyclic system containing multiple hydroxyl groups and a sulfonamide group. The structure is similar to LD33 but includes a different linker between the amide chain and the polycyclic system.
LD35	 Chemical structure of LD35, a complex molecule featuring a long chain of repeating amide units (N-methyl-L-glutamate) linked to a triazole ring, which is further connected to a complex polycyclic system containing multiple hydroxyl groups and a sulfonamide group. The structure is similar to LD33 but includes a different linker between the amide chain and the polycyclic system.
LD36	 Chemical structure of LD36, a complex molecule featuring a long chain of repeating amide units (N-methyl-L-glutamate) linked to a triazole ring, which is further connected to a complex polycyclic system containing multiple hydroxyl groups and a sulfonamide group. The structure is similar to LD33 but includes a different linker between the amide chain and the polycyclic system.

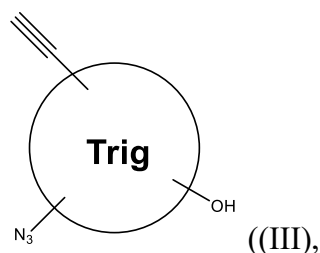
LD37	 Chemical structure of LD37, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.
LD38	 Chemical structure of LD38, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.
LD39	 Chemical structure of LD39, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.
LD40	 Chemical structure of LD40, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.
LD41	 Chemical structure of LD41, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.
LD42	 Chemical structure of LD42, a complex molecule featuring a long polyether chain, a sulfonamide group, a triazole ring, and a complex polycyclic system with multiple hydroxyl groups.

LD43	
LD44	
LD45	
LD46	
LD47	
LD48	

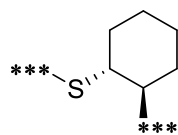
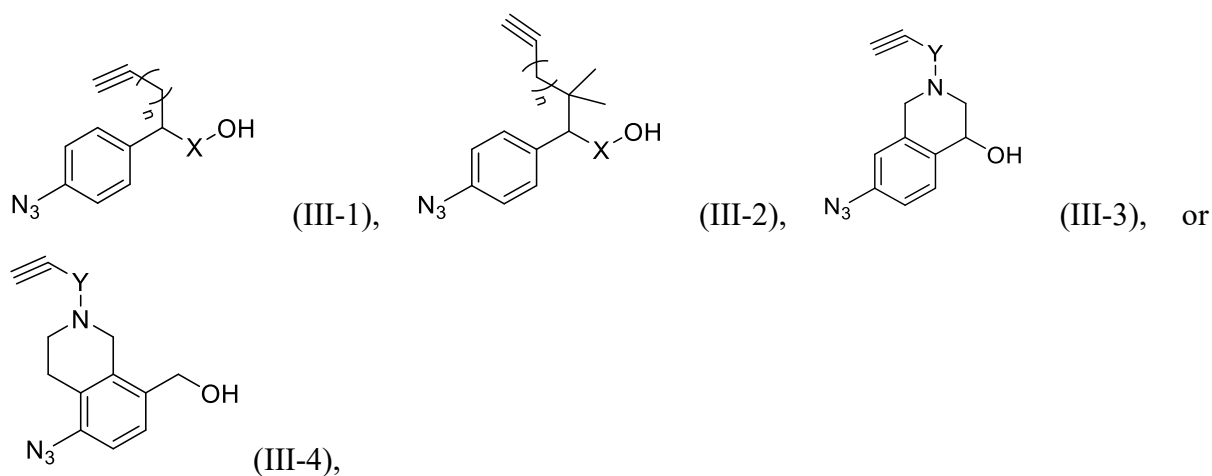
LD49	 Chemical structure of LD49: A complex molecule featuring a long poly(ether) chain (top) connected via a triazole ring to a linker containing a sulfonamide group, a benzene ring, and a carbamate group. This linker is connected to a peptide chain (middle) which is further linked to a pyridine ring (bottom left) and a complex polycyclic system (bottom right) containing a fluorine atom and a hydroxyl group.
LD50	 Chemical structure of LD50: Similar to LD49, but the poly(ether) chain is shorter and the linker contains a different arrangement of functional groups, including a sulfonamide and a carbamate.
LD51	 Chemical structure of LD51: Similar to LD49, but the poly(ether) chain is replaced by a poly(amide) chain, and the linker contains a different arrangement of functional groups, including a sulfonamide and a carbamate.
LD52	 Chemical structure of LD52: Similar to LD51, but the poly(amide) chain is shorter and the linker contains a different arrangement of functional groups, including a sulfonamide and a carbamate.

LD53	 Chemical structure of LD53, featuring a long polyether chain (1,3-bis(2-methoxyethoxy)propane) linked to a 1,2,4-triazole ring, which is further connected to a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group. The structure also includes a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group and a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group.
LD54	 Chemical structure of LD54, featuring a long polyether chain (1,3-bis(2-methoxyethoxy)propane) linked to a 1,2,4-triazole ring, which is further connected to a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group. The structure also includes a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group and a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group.
LD55	 Chemical structure of LD55, featuring a long polyether chain (1,3-bis(2-methoxyethoxy)propane) linked to a 1,2,4-triazole ring, which is further connected to a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group. The structure also includes a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group and a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group.
LD55-1	 Chemical structure of LD55-1, featuring a long polyether chain (1,3-bis(2-methoxyethoxy)propane) linked to a 1,2,4-triazole ring, which is further connected to a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group. The structure also includes a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group and a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group.
LD55-2	 Chemical structure of LD55-2, featuring a long polyether chain (1,3-bis(2-methoxyethoxy)propane) linked to a 1,2,4-triazole ring, which is further connected to a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group. The structure also includes a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group and a 4-((4-methylphenyl)hydrazono)-2-methyl-1,3,4-oxadiazole-5-sulfonyl group.

The present disclosure further provides a compound of formula (III), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:

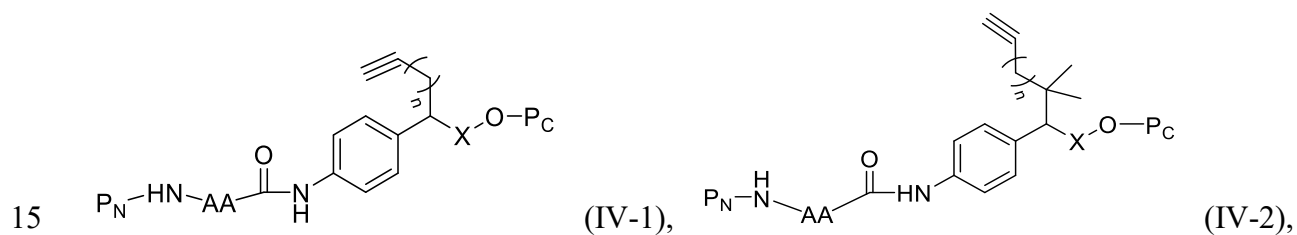


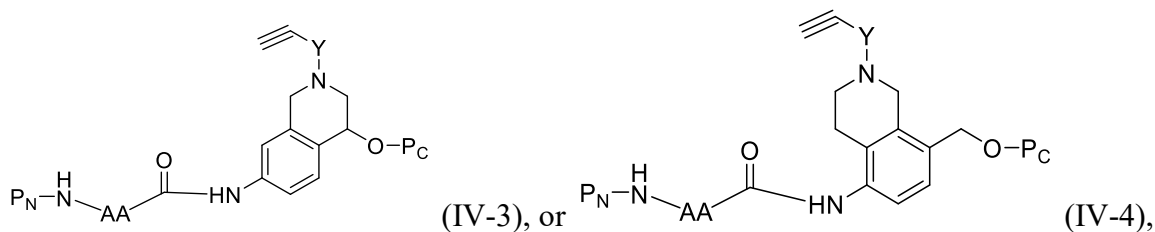
5 wherein formula (III) has the following structure:



wherein X is absent or represents linkage to a carbon atom, and **** represents linkage to an oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6.

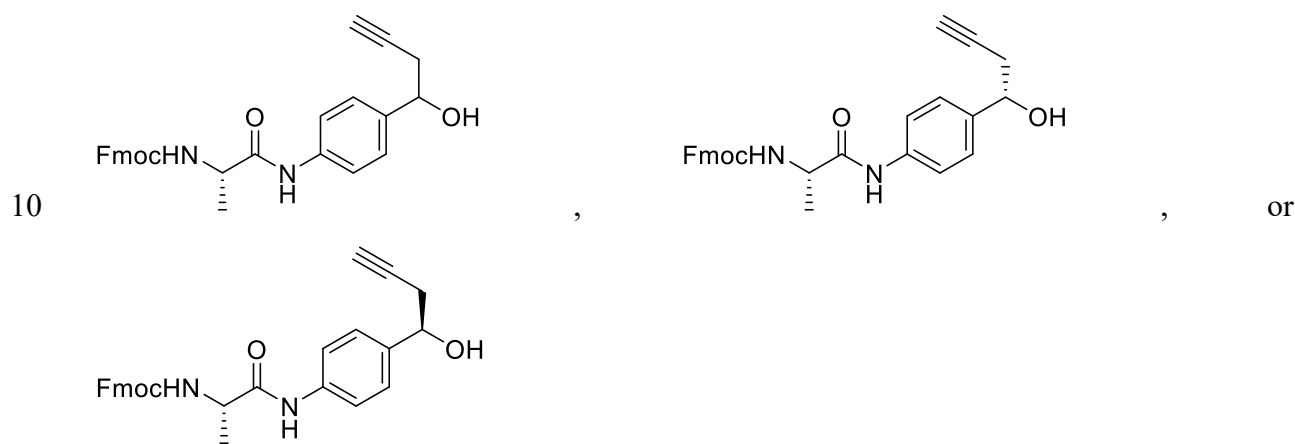
The present disclosure further provides a compound of formula (IV), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:





wherein X is absent or
 ****, *** represents linkage to a carbon atom, and ****
 represents linkage to an oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆
 alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0
 5 to 6;

wherein AA is L₃ or a sub-fragment consisting of the first 1, 2, or more amino acids from the
 C-terminus of L₃, P_N is H or an amino protecting group such as Boc or Fmoc, and P_C is H, a
 hydroxyl protecting group, or a carbonate active ester group such as *p*-nitrophenyl carbonate;
 the compound of formula (IV) is preferably:



Abbreviations and Definitions

Unless otherwise stated, the following terms used in the present application have the following
 meanings.

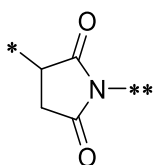
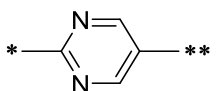
- 15 When a trade name is used in the present application, the trade name includes the product
 formula, generic drug, and active pharmaceutical ingredient of the product under the trade
 name, unless otherwise indicated in the context.

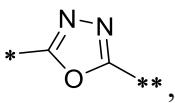
The term “antibody-drug conjugate” or “ADC” means that a targeting ligand such as an
 antibody (e.g., a monoclonal antibody) or an antibody fragment is linked to a bioactive
 20 molecule with biological activity via a stable chemical linker compound.

The term “linker-drug compound” or “linker-drug” refers to a partial structure in an “antibody-
 drug conjugate” consisting of a linker compound and a bioactive compound.

The term “linker” refers to a chemical structural fragment, represented by L, which is linked to an antibody at one end and to a cytotoxic drug at the other end. It is formed by an “linker compound” connecting an antibody and a bioactive compound. In certain embodiments of the present disclosure, one part of the linker compound is first linked to the antibody and the other part is linked to the bioactive compound, and then the “linker” is formed through chemical reactions between different portions of the linker. The linker in the present disclosure comprises a linking moiety to the antibody, a spacer, a polypeptide sequence, and a self-immolative fragment.

The linker-drug compound in the present disclosure is linked to the antibody by conventional conjugation methods in the art, including: lysine conjugation, reductive disulfide bond conjugation between heavy and light chains, and site-specific conjugation (Beck A, Reichert JM. Antibody-drug conjugates: Present and future. *MAbs*, 2014, 6: 15-17; McCombs JR, Owen S C. Antibody drug conjugates: design and selection of linker, payload and conjugation chemistry. *The AAPS journal*, 2015, 17: 339-351). The present disclosure preferably provides conjugation via reductive disulfide bonds between the light and heavy chains, i.e., linkage via a reaction with thiol groups (sulfur atoms of cysteine residues) formed by reduction of one or more of disulfide bond sites between the light and heavy chains (two sites between the heavy chains and two sites between the heavy and light chains). In the present disclosure, the linking moiety of the linker L to the antibody is represented by L₁, which is formed by the reaction of

the L₁' group in the linker compound with the antibody, e.g.,  ,  ,

or  , wherein * represents linkage to a sulfhydryl group of the antibody, and ** represents linkage to a spacer.

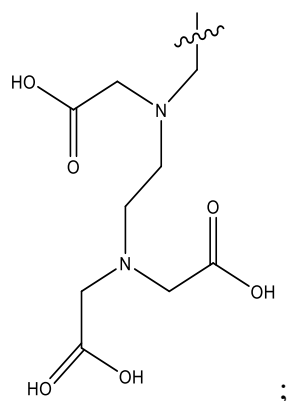
The term “spacer” refers to a linking group between the linking moiety of the linker L to the antibody and the polypeptide sequence, which may be any divalent organic group, such as a chemical bond, C₁₋₁₀ alkylene, C₂₋₁₀ alkenylene, C₂₋₁₀ alkynylene, C₃₋₁₀ cycloalkyl, C₆₋₁₂ aryl, 5- to 12-membered heteroaryl, 5- to 12-membered heterocyclyl, or a combination of two or more thereof; the C₁₋₁₀ alkylene, C₂₋₁₀ alkenylene, C₂₋₁₀ alkynylene, C₃₋₁₀ cycloalkyl, C₆₋₁₂ aryl, 5- to 12-membered heteroaryl, 5- to 12-membered heterocyclyl, or the combination of two or more thereof is optionally interrupted by a carbonyl group or an O, S or N atom; the

heteroaryl, or 5- to 12-membered heterocyclyl may be optionally substituted with C₁₋₆ alkyl, C₃₋₆ cycloalkyl, halogen, or halogenated C₁₋₆ alkyl; preferably, as defined in L₂.

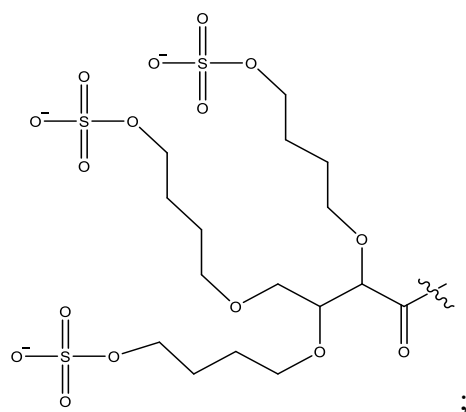
The term “polypeptide sequence” is well known in the art and is selected from a divalent peptide group comprising 2 to 8 optionally substituted natural or unnatural, L-type or D-type amino acid residues, wherein each of the amino acid residues is identical or different and is independently selected from residues of the following amino acids: alanine (Ala), cysteine (Cys), aspartic acid (Asp), glutamic acid (Glu), phenylalanine (Phe), glycine (Gly), histidine (His), isoleucine (Ile), lysine (Lys), leucine (Leu), methionine (Met), asparagine (Asn), proline (Pro), glutamine (Gln), arginine (Arg), serine (Ser), threonine (Thr), valine (Val), tryptophan (Trp), tyrosine (Tyr), citrulline (Cit), norvaline (Nva), norleucine (Nle), and analogs of the amino acids described above.

The term “self-immolative fragment” is well known in the art, such as the *p*-aminobenzyl alcohol carbonate fragment conventionally used in the art. In specific embodiments of the present disclosure, the “self-immolative fragment” of the linker of the present disclosure comprises a modification with a “hydrophilic fragment”.

The term “hydrophilic fragment” is well known in the art, and the hydrophilic fragment may comprise a polyethylene glycol group, such as a polyethylene glycol group terminated with a methoxy group, or may be further linked to other hydrophilic fragments via the polyethylene glycol group. The hydrophilic fragment may also include a polyamino acid fragment, such as polyglycine or polysarcosine; the polyamino acid fragment may be combined with a polyethylene glycol group. The hydrophilic fragment may also be a monosaccharide, a disaccharide, or an oligosaccharide; the monosaccharide, the disaccharide, or the oligosaccharide may be a saccharide of a chain-form molecule or a cyclic molecule, and may comprise a glycosylamine, a sugar acid, or a phosphorylated sugar. Preferably, the saccharide group is combined with a polyethylene glycol fragment or a polyamino acid fragment; also preferably, at least two saccharide groups are introduced by polyvalent linking groups, such as aspartic acid-, glutamic acid- or lysine-based linking groups. The hydrophilic fragment may also comprise a polycarboxylic acid group, a polysulfonic acid group, a chelating group, etc.; the structure of the polycarboxylic acid group is, for example:



the structure of the polysulfonic acid group is, for example:



the chelating group may be, for example, a DOTA group or a NOTA group.

- 5 The term “solvate” means a physical association of the compound of the present disclosure with one or more solvent molecules (whether organic or inorganic). The physical association includes hydrogen bonding. In certain cases, the solvate can be isolated, for example, when one or more solvent molecules are incorporated into the crystal lattice of a crystalline solid. The solvent molecules in the solvate may be present in a regular arrangement and/or a
- 10 disordered arrangement. The solvate may contain a stoichiometric or non-stoichiometric amount of solvent molecules. The “solvate” encompasses both solution phase and isolatable solvates. Exemplary solvates include, but are not limited to, hydrates, ethanlates, methanlates, and isopropanolates. Solvation methods are well known in the art.

- The term “stereoisomer” refers to compounds having the same chemical constitution but
- 15 different spatial arrangements of the atoms or groups. Stereoisomers include enantiomers, diastereoisomers, conformational isomers (rotamers), geometric isomers (cis/trans isomers), atropisomers, etc. Any resulting mixture of stereoisomers may be separated into pure or substantially pure geometric isomers, enantiomers, or diastereoisomers depending on differences in the physicochemical properties of the components, for example, by
- 20 chromatography and/or fractional crystallization.

The term “tautomer” refers to isomers having different energies that are interconvertible by a low energy barrier. If tautomerism is possible (e.g., in a solution), the chemical equilibrium of the tautomers can be achieved. For example, proton tautomers (also known as prototropic tautomers) include tautomers that undergo interconversion by proton migration, such as keto-enol isomerization and imine-enamine isomerization. Valence tautomers include tautomers that

The “more” in the term “one or more” includes two or more (e.g., 3, 4, 5, etc.).

The term “heteroatom” refers to a nitrogen, oxygen, sulfur, or halogen atom.

The term “C_m-C_n” means that the moiety has an integer number of carbon atoms ranging from m to n. For example, the “C₁-C₃” means that the group may have 1 carbon atom, 2 carbon atoms, or 3 carbon atoms.

The term “-(CH₂)_n-” means that the moiety has a group in which n -CH₂- are linked. For example, when the number of a linking group is 0, such as “-(CH)₀-”, it means that the linking group is a covalent bond.

The term “alkyl” refers to a monovalent saturated aliphatic hydrocarbyl group, i.e., a linear or branched group containing 1-20 carbon atoms, preferably containing 1-10 carbon atoms (i.e., C₁₋₁₀ alkyl), further preferably containing 1-8 carbon atoms (C₁₋₈ alkyl), and more preferably containing 1-6 carbon atoms (i.e., C₁₋₆ alkyl). For example, “C₁₋₆ alkyl” means that the group is alkyl and the number of carbon atoms on the carbon chain is between 1 and 6 (specifically 1, 2, 3, 4, 5, or 6), and examples thereof include, but are not limited to, methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *tert*-butyl, *sec*-butyl, *n*-pentyl, neopentyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, 1-ethylpropyl, 2-methylbutyl, 3-methylbutyl, *n*-hexyl, etc.

The term “alkoxy” refers to -O-alkyl, wherein the alkyl is as defined above, i.e., the alkyl contains 1-20 carbon atoms, preferably 1-10 carbon atoms, more preferably 1-8 carbon atoms, and further more preferably 1-6 (specifically 1, 2, 3, 4, 5, or 6) carbon atoms. Representative examples of the alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy, butoxy, 1-methylpropoxy, 2-methylpropoxy, *tert*-butoxy, pentyloxy, 1-methylbutoxy, 2-methylbutoxy, 3-methylbutoxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 2,2-dimethylpropoxy, 1-ethylpropoxy, etc.

The term “halogen”, “halogenated”, or “halo” refers to F, Cl, Br, or I.

The term “haloalkyl” refers to alkyl as defined above in which one, two, or more hydrogen atoms or all hydrogen atoms are replaced by halogen. Representative examples of the haloalkyl include CCl₃, CHCl₂, CH₂Cl, CF₃, CHF₂, CH₂F, CBr₃, CHBr₂, CH₂Br, Cl₃, CHI₂, CH₂I,

CH₂CF₃, CF₂CF₃, etc.

The term “aryl” refers to a monocyclic, bicyclic, or tricyclic aromatic carbocyclic system containing 6-16 carbon atoms, or 6-14 carbon atoms, or 6-12 carbon atoms, or 6-10 carbon atoms, preferably 6-10 carbon atoms. Examples of the aryl group may include, but are not limited to, phenyl, naphthyl, anthryl, phenanthryl, pyrenyl, etc. The term “heteroaryl” refers to an aromatic monocyclic or polycyclic ring system containing a 5- to 14-membered structure, or preferably a 5- to 10-membered structure or a 5- to 8-membered structure, and more preferably a 5- to 6-membered structure, wherein 1, 2, 3, or more ring atoms are heteroatoms and the remaining atoms are carbon, the heteroatoms are independently selected from O, N, and S, and the number of the heteroatoms is preferably 1, 2, or 3. Examples of the heteroaryl include, but are not limited to, furanyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiadiazolyl, triazinyl, phthalazinyl, quinolinyl, isoquinolinyl, pteridinyl, purinyl, indolyl, isoindolyl, indazolyl, benzofuranyl, benzothienyl, benzopyridinyl, benzopyrimidinyl, benzopyrazinyl, benzimidazolyl, benzophthalazinyl, pyrrolo[2,3-*b*]pyridinyl, imidazo[1,2-*a*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, [1,2,4]triazolo[4,3-*b*]pyridazinyl, [1,2,4]triazolo[1,5-*a*]pyrimidinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, etc.

The term “cycloalkyl” refers to a fully saturated carbocyclic ring that may exist as a monocyclic, bridged cyclic, or spiro cyclic structure. Preferably, the cycloalkyl contains 3-12 carbon atoms (i.e., C₃-12 cycloalkyl), more preferably 3-10 carbon atoms (C₃-10 cycloalkyl), and further preferably 3-7 carbon atoms (C₃-7 cycloalkyl), 4-6 carbon atoms (C₄-6 cycloalkyl), or 5-6 carbon atoms (C₅-6 cycloalkyl). Examples of the cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, methylcyclopropyl, 2-ethylcyclopentyl, dimethylcyclobutyl, norbornyl (bicyclo[2.2.1]heptyl), bicyclo[2.2.2]octyl, adamantyl, etc.

The term “-alkyl-” or “alkylene” refers to saturated linear or branched divalent hydrocarbyl. For example, C₁-C₈ alkylene refers to linear or branched alkylene having 1-8 carbon atoms.

The term “heterocyclyl” refers to a fully saturated or partially unsaturated (non-fully unsaturated heteroaromatic) nonaromatic ring that may exist as a monocyclic, bridged cyclic, or spiro cyclic structure. Unless otherwise specified, the heterocycle is generally a 3- to 7-membered ring containing 1 to 3 heteroatoms independently selected from sulfur, oxygen, and/or nitrogen (preferably 1 or 2 heteroatoms, but excluding -O-O-, -O-S-, or -S-S- moieties). Non-limiting examples of the heterocyclyl include, but are not limited to, oxiranyl,

tetrahydrofuranyl, dihydrofuranyl, pyrrolidinyl, *N*-methylpyrrolidinyl, dihydropyrrolyl, piperidinyl, piperazinyl, pyrazolidinyl, 4*H*-pyranyl, morpholinyl, thiomorpholinyl, tetrahydrothienyl, etc.

The term “heteroalkyl”, by itself or in combination with another term, refers to a stable linear or branched alkyl atomic group or a composition thereof, consisting of a certain number of carbon atoms and at least one heteroatom. The number of the carbon atoms may be 1-50 (preferably 1-20, more preferably 1-12, and most preferably 1-8), such as 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50. The heteroalkyl may optionally contain one, two, or more (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12) heteroatoms selected from N, O, and S (or may be construed as optional insertion of heteroatoms into alkyl at any C-C bond or C-H bond). The heteroatoms O, N, and S may be located at any internal position of the heteroalkyl or at the position where the alkyl is attached to the rest of the molecule. Examples of the heteroalkyl include, but are not limited to, -CH₂-CH₂-O-CH₃, -CH₂-CH₂-NH-CH₃, -CH₂-CH₂-N(CH₃)-CH₃, -CH₂-S-CH₂-CH₃, -CH₂-CH₂-S(O)-CH₃, and -CH₂-CH₂-S(O)₂-CH₃. Up to two heteroatoms may be consecutive, such as -CH₂-NH-OCH₃.

Unless otherwise indicated, the definitions of the terms herein are also applicable to groups containing the term; for example, the definition of C1-6 alkyl is also applicable to C1-6 alkyloxy.

In various sections of the present disclosure, linking substituents are described. When a linking group is clearly required by the structure, the Markush variables listed for the group should be understood as linking groups. For example, if a linking group is required by the structure and “heteroalkyl”, “aryl”, and the like are listed for the Markush group definition of the variable, it should be understood that the “heteroalkyl” or “aryl” respectively represents a linked heteroalkylene group or arylene group. Moreover, it should also be understood that when a Markush variable listed for a group is to be understood as a linking group, regardless of whether it is defined as “alkylene” or “heteroalkylene”, the scope of definitions applicable to both is identical. Therefore, for example, the definitions of the terms “alkylene”, “cycloalkylene”, “arylene”, “heteroalkylene”, “heteroarylene”, and “heterocyclylene” herein are equivalent to or referenced as the “alkyl”, “cycloalkyl”, “aryl”, “heteroalkyl”, “heteroaryl”, and “heterocyclyl” as defined above.

The term “derivative” refers to a compound formed by replacing an atom or atomic group in the molecule of a parent compound with another atom or atomic group, which is referred to as a derivative of the parent compound.

The term “pharmaceutically acceptable salt” refers to a pharmaceutically acceptable organic or inorganic salt of a compound (e.g., a drug, a drug-linker, or an antibody-linker-drug conjugate). The compound may contain at least one amino, imino, hydroxyl, or carboxyl group, and thus may form addition salts with the corresponding acids or bases. Exemplary salts include, but are not limited to: sulfate, trifluoroacetate, citrate, acetate, oxalate, hydrochloride, hydrobromide, hydroiodide, nitrate, bisulfate, phosphate, acidic phosphate ($-\text{H}_2\text{PO}_4$), phosphite, isonicotinate, lactate, salicylate, acidic citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, potassium salts, sodium salts, ammonium salts, calcium salts, etc. In addition, the pharmaceutically acceptable salt has more than one charged atom in the structure. Examples in which multiple charged atoms are part of the pharmaceutically acceptable salt can have multiple counter ions. For example, the pharmaceutically acceptable salt has one or more charged atoms and/or one or more counter atoms.

The term “amino acid” refers to a naturally occurring amino acid or a non-naturally occurring amino acid, represented by $\text{NH}_2\text{-C(R'R'')-C(=O)OH}$, wherein R' and R'' are each independently hydrogen, optionally substituted linear, branched, or cyclic alkyl, alkenyl, or alkynyl having 1 to 10 carbon atoms, aryl, heteroaryl, or heterocyclyl, or R' and the N-terminal nitrogen atom may be combined to form a heterocyclic ring, for example, proline.

The term “amino acid residue” refers to the corresponding residue obtained after a hydrogen atom is removed from the amine of an amino acid and/or a hydroxyl group is removed from the carboxyl terminus, for example, $-\text{NH-C(R'R'')-C(O)-}$.

The term “peptide” refers to a short chain of amino acid monomers linked by peptide (amide) bonds.

The term “tumor” refers to a neoplasm formed by clonal abnormal proliferation of a certain cell in a local tissue due to the loss of normal regulation of its growth at the genetic level under the action of various carcinogenic factors in the body.

Broadly, the term “antibody” refers to an immunoglobulin molecule that recognizes and specifically binds to a target, e.g., a protein, a polypeptide, a peptide, a carbohydrate, a polynucleotide, a lipid, or a combination of the foregoing, via at least one antigen recognition site located in a variable region of the immunoglobulin molecule, represented by A. The term encompasses intact polyclonal antibodies, intact monoclonal antibodies, antibody fragments (e.g., Fab, Fab', F(ab')_2 , and Fv fragments), single-chain Fv (scFv) mutants, multispecific antibodies (e.g., bispecific antibodies, biparatopic antibodies, etc.), multivalent antibodies

(e.g., trivalent, tetravalent, or higher-valency antibodies having three, four, or more antigen-binding sites), chimeric antibodies, humanized antibodies, human antibodies, fusion proteins containing an antigen determination portion of an antibody, and any other modified immunoglobulin molecule containing an antigen recognition site, so long as the antibody exhibit the desired biological activity. When “antibody” and “antigen-binding fragment/antigen-binding portion” are presented in the same context, the “antibody” may be understood as being the intact body relative to the “antigen-binding fragment/antigen-binding portion”, both collectively corresponding to the broad concept of an antibody.

10 BRIEF DESCRIPTION OF THE DRAWING

FIG. 1 is a single crystal diffraction pattern of compound 82.

DETAILED DESCRIPTION

The present application is further illustrated by examples, which, however, are not intended to limit the scope of the present application. Experimental procedures without specified conditions in the following examples are generally conducted according to conventional conditions or according to conditions recommended by the manufacturers. Unless otherwise stated, all percentages, proportions, ratios, or parts are by weight.

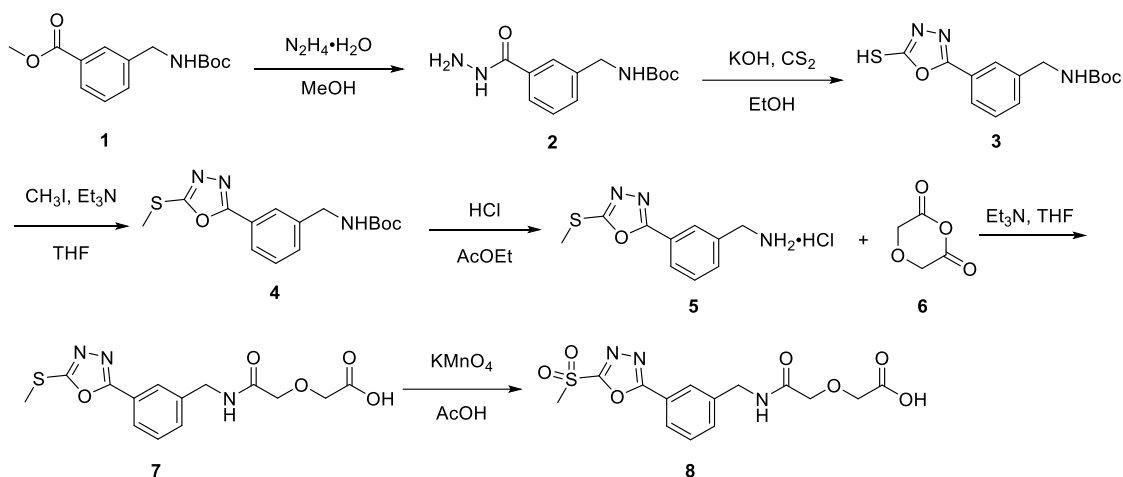
Description of abbreviations

Table 1

DMF	<i>N,N</i> -Dimethylformamide	TBAF	Tetrabutylammonium fluoride
TEA	Triethylamine	DMSO	Dimethylsulfoxide
THF	Tetrahydrofuran	DIBAL-H	Diisobutylaluminium hydride
DIPEA	<i>N,N</i> -Diisopropylethylamine	TFAA	Trifluoroacetic anhydride
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene	Boc	<i>tert</i> -Butoxycarbonyl
EEDQ	2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline	Fmoc	9-Fluorenylmethyloxycarbonyl
PPTS	Pyridinium <i>p</i> -toluenesulfonate	TECP	Tris(2-carboxyethyl)phosphine
THPTA	Tris(3-hydroxypropyltriazolylmethyl)amine	DCA	Dichloroacetic acid

EA	Ethyl acetate	Py	Pyridine
EDCI	1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	HOBT	1-Hydroxybenzotriazole
9-BBN	9-Borabicyclo[3.3.1]nonane	NH ₄ FA	Ammonium formate
tBuOH	<i>tert</i> -Butanol	DCM	Dichloromethane
NPCCl	<i>p</i> -Nitrobenzoyl chloride		
ACN	Acetonitrile		

Example 1: Synthesis of Compounds **8-10**



Compound **1** (50 g, 189 mmol) and methanol (250 mL) were added to a reaction flask, and 80% hydrazine hydrate (35.4 g, 567 mmol) was slowly added at room temperature. The mixture was warmed to 70 °C and refluxed for 6 h. After cooling, a white crystal was precipitated, and the mixture was subjected to suction filtration. The remaining solid was washed with methanol (20 mL × 3) to give **2** (50 g, yield: 100%) as a white solid. MS (ESI): (M+H)⁺, calculated 266.1, found 266.2.

Compound **2** (50 g, 189 mmol), potassium hydroxide (12.7 g, 227 mmol), and ethanol (400 mL) were added to a reaction flask, and the mixture was stirred for dissolution at room temperature. Carbon disulfide (17 g, 283 mmol) was slowly added, and the mixture was warmed to 100 °C and refluxed for 5 h. The solvent was removed by concentration under reduced pressure, and water (50 mL) was added. The mixture was adjusted to pH 6 with diluted hydrochloric acid and extracted with dichloromethane (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **3** (54 g, yield: 93%). MS (ESI): (M+H)⁺, calculated 308.1, found 308.2.

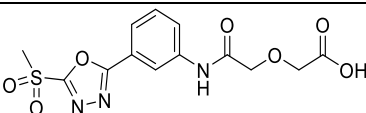
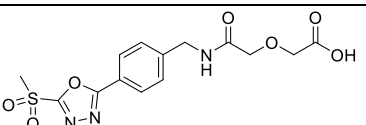
Compound **3** (5 g, 16.3 mmol), triethylamine (2 g, 19.6 mmol), and tetrahydrofuran (30 mL) were added to a reaction flask, and iodomethane (2.5 g, 17.9 mmol) was added to the reaction liquid described above. The reaction was completed after the mixture was stirred for reaction at 25 °C for 1.5 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **4** (3.4 g, yield: 65%). MS (ESI): (M+H)⁺, calculated 322.1, found 322.2.

Compound **4** (3.4 g, 10.6 mmol) and ethyl acetate (20 mL) were added to a reaction flask, and a solution of hydrogen chloride in ethyl acetate (2.7 mL, 4 M) was added dropwise at 25 °C. The mixture was reacted for 6 h, and the solvent was removed by concentration under reduced pressure to give a crude product of **5**, which was directly used in the next step.

The crude product of **5**, diglycolic anhydride **6** (1.35 g, 11.7 mmol), triethylamine (2.14 g, 21.2 mmol), and tetrahydrofuran (30 mL) were added to a reaction flask. The mixture was reacted at 25 °C for 1.5 h, and the solvent was removed by concentration under reduced pressure. Diethyl ether was added to the residue, and the mixture was subjected to suction filtration and then washed with water and diethyl ether to give compound **7** (3.5 g, yield: 99%). MS (ESI): (M+H)⁺, calculated 338.0, found 338.2.

Compound **7** (3.5 g, 10.5 mmol) and glacial acetic acid (20 mL) were added to a reaction flask. After dissolution, potassium permanganate (2.48 g, 15.7 mmol) was added at 0 °C. The mixture was warmed to 25 °C and reacted for 1 h. A saturated sodium sulfite solution was added until the solution became colorless, and then the solution was extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **8** (2.3 g, yield: 60%). MS (ESI): (M+H)⁺, calculated 370.0, found 370.1.

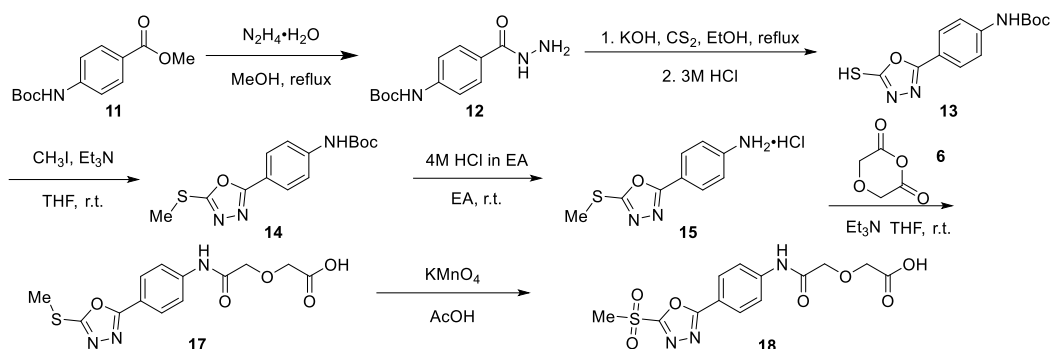
Table 2

No.	Structural formula	MS(ESI) : (M+H) ⁺	
		Calculated	Found
9		356.0	356.1
10		370.0	370.2

The synthesis of compounds **9-10** was carried out with reference to the synthetic route of

compound **8**.

Example 2: Synthesis of Compound **18**



Compound **11** (47.5 g, 189 mmol) and methanol (250 mL) were added to a reaction flask, and 80% hydrazine hydrate (35.4 g, 567 mmol) was slowly added at room temperature. The mixture was warmed to 70 °C and refluxed for 6 h. After cooling, a white crystal was precipitated, and the mixture was subjected to suction filtration. The remaining solid was washed with methanol (20 mL $\times$ 3) to give **12** (47.47 g, yield: 100%) as a white solid. MS (ESI): $(\text{M}+\text{H})^+$, calculated 252.1, found 252.2.

Compound **12** (47.4 g, 189 mmol), potassium hydroxide (12.7 g, 227 mmol), and ethanol (400 mL) were added to a reaction flask, and the mixture was stirred for dissolution at room temperature. Carbon disulfide (17 g, 283 mmol) was slowly added, and the mixture was warmed to 100 °C and refluxed for 5 h. The solvent was removed by concentration under reduced pressure, and then water (50 mL) was added. The mixture was adjusted to pH 6 with diluted hydrochloric acid and extracted with dichloromethane (100 mL $\times$ 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **13** (49.9 g, yield: 90%). MS (ESI): $(\text{M}+\text{H})^+$, calculated 294.1, found 294.3.

Compound **13** (5.86 g, 20 mmol), triethylamine (2.42 g, 24 mmol), and tetrahydrofuran (36 mL) were added to a reaction flask, and iodomethane (3.12 g, 22 mmol) was added to the reaction liquid described above. The reaction was completed after the mixture was stirred for reaction at 25 °C for 1.5 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **14** (4.05 g, yield: 66%). MS (ESI): $(\text{M}+\text{H})^+$, calculated 308.1, found 308.2.

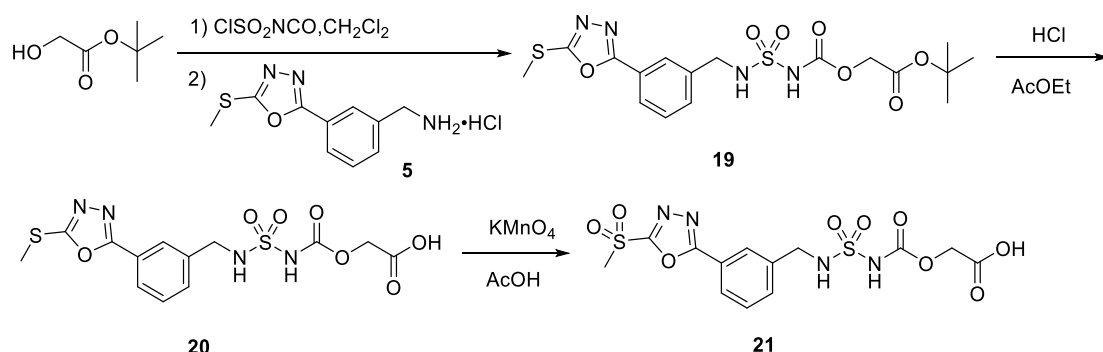
Compound **14** (3.3 g, 10.6 mmol) and ethyl acetate (20 mL) were added to a reaction flask, and a solution of hydrogen chloride in ethyl acetate (2.7 mL, 4 M) was added dropwise at 25 °C. The mixture was then reacted for 6 h, and the solvent was removed by concentration under

reduced pressure to give a crude product of **15**, which was directly used in the next step.

The crude product of **15**, diglycolic anhydride **6** (1.35 g, 11.7 mmol), triethylamine (2.14 g, 21.2 mmol), and tetrahydrofuran (30 mL) were added to a reaction flask. The mixture was reacted at 25 °C for 1.5 h, and the solvent was removed by concentration under reduced pressure. Diethyl ether was added to the residue, and the mixture was subjected to suction filtration and then washed with water and diethyl ether to give compound **17** (3.4 g, yield: 99%). MS (ESI): (M+H)⁺, calculated 324.1, found 324.2.

Compound **17** (3.4 g, 10.5 mmol) and glacial acetic acid (20 mL) were added to a reaction flask. After dissolution, potassium permanganate (2.48 g, 15.7 mmol) was added at 0 °C. The mixture was warmed to 25 °C and reacted for 1 h. A saturated sodium sulfite solution was added until the solution became colorless, and then the solution was extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **18** (2.4 g, yield: 65%). MS (ESI): (M+H)⁺, calculated 356.0, found 356.0.

Example 3: Synthesis of Compound **21**

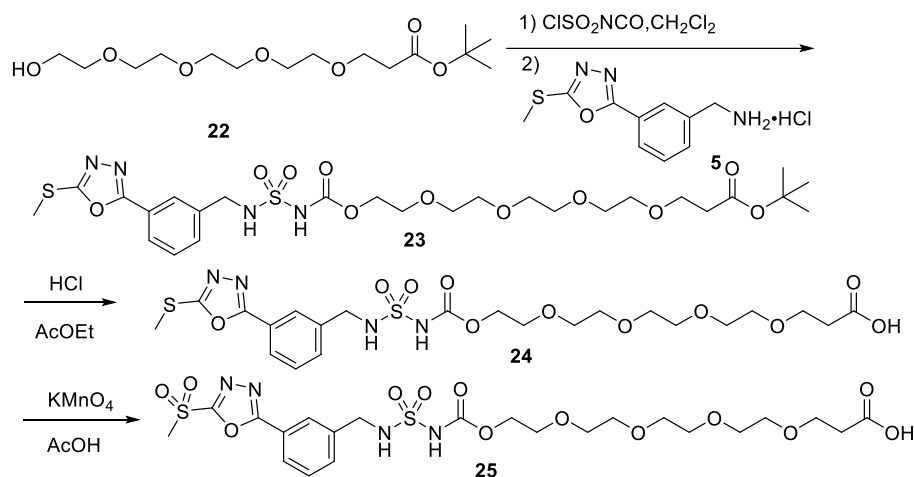


tert-Butyl glycolate (2.57 g, 19.5 mmol) was slowly added dropwise to a solution of chlorosulfonyl isocyanate (2.75 g, 19.5 mmol) in dichloromethane (40 mL) at 0 °C. The mixture was warmed to 25 °C and reacted for 1 h. A solution of compound **5** (5 g, 19.5 mmol) in dichloromethane (10 mL) was added dropwise to the reaction system described above. After 6 h of reaction, water (40 mL) was added, and the mixture was extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **19** (7.68 g, yield: 86%). MS (ESI): (M+H)⁺, calculated 459.1, found 459.0.

Compound **19** (7.68 g, 16.8 mmol) and ethyl acetate (20 mL) were added to a reaction flask,

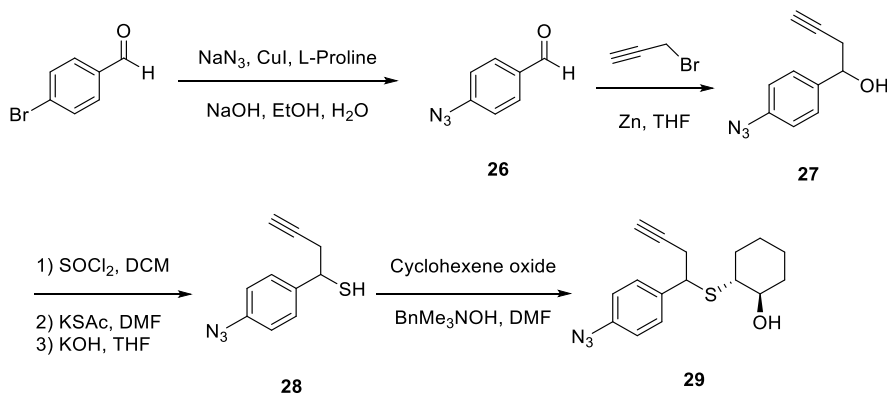
and a solution of hydrogen chloride in ethyl acetate (4.2 mL, 4 M) was added dropwise at 25 °C. The mixture was then reacted for 6 h, and the solvent was removed by concentration under reduced pressure to give a crude product of **20**, which was directly used in the next step. The crude product of **20** and glacial acetic acid (20 mL) were added to a reaction flask. After dissolution, potassium permanganate (4 g, 25.2 mmol) was added at 0 °C. The mixture was warmed to 25 °C and reacted for 1 h. A saturated sodium sulfite solution was added until the solution became colorless, and then the solution was extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **21** (3.28 g, yield: 45%). MS (ESI): (M+H)⁺, calculated 435.0, found 435.1.

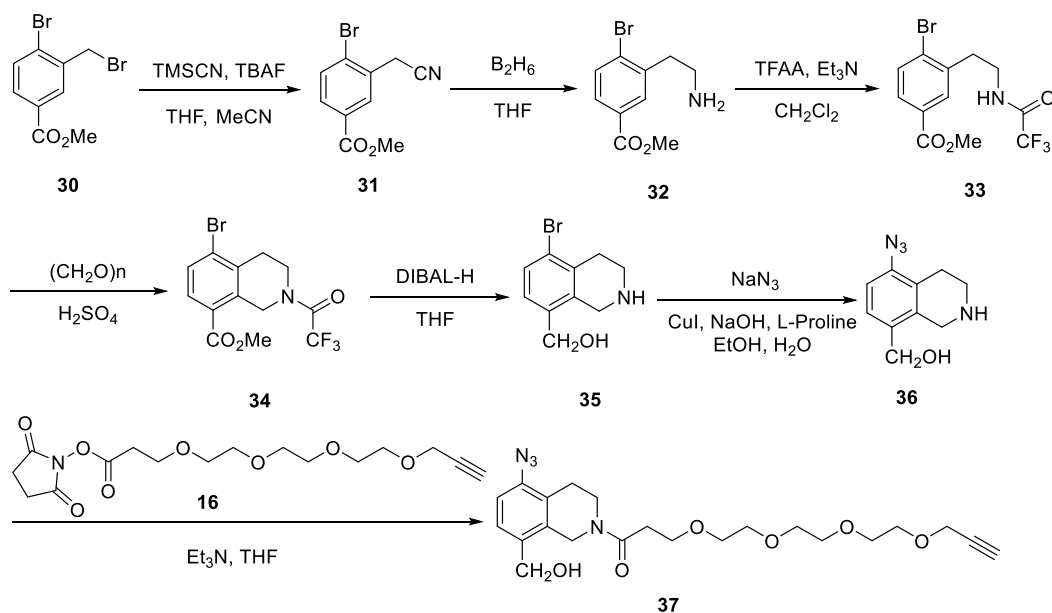
Example 4: Synthesis of Compound **25**



The synthesis of compound **25** was carried out with reference to the synthesis method of compound **21**.

Example 5: Synthesis of Compounds **29** and **37**





p-Bromobenzaldehyde (7.97 g, 43 mmol), sodium azide (5.57 g, 86 mmol), copper(I) iodide (817 mg, 4.3 mmol), L-proline (1.48 g, 12.9 mmol), sodium hydroxide (515 mg, 12.9 mmol), ethanol (70 mL), and water (20 mL) were added to a reaction flask, and the mixture was reacted at 95 °C for 24 h. After the reaction was completed, the mixture was cooled, and water was added. The mixture was extracted with ethyl acetate (100 mL $\times$ 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **26** (5.5 g, yield: 87%). MS (ESI): $(\text{M}+\text{H})^+$, calculated 148.0, found 148.1.

Zinc powder (7.3 g, 113 mmol) and tetrahydrofuran (50 mL) were added to a reaction flask, and a solution of propargyl bromide (14.9 g, 125.5 mmol) in tetrahydrofuran (30 mL) was added dropwise at 10 °C. The mixture was reacted at 10 °C for 2 h, and a solution of **26** (2.75 g, 18.7 mmol) in tetrahydrofuran (30 mL) was slowly added dropwise. The mixture was then stirred for 2 h. The reaction liquid was poured into a 1 N aqueous HCl solution at 0 °C, and the mixture was extracted with ethyl acetate (100 mL $\times$ 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **27** (3.15 g, yield: 90%). MS (ESI): $(\text{M}+\text{H})^+$, calculated 188.0, found 188.1.

Compound **27** (1 g, 5.3 mmol) and dichloromethane (5 mL) were added to a reaction flask, and thionyl chloride (1.9 g, 16 mmol) was added dropwise at 0 °C. After the addition was completed, the mixture was warmed to 25 °C and reacted for 2 h. The solvent and the remaining

thionyl chloride were removed by concentration under reduced pressure, and potassium thioacetate (906 mg, 8 mmol) and *N,N*-dimethylformamide (10 mL) were added. The mixture was reacted at 25 °C for 12 h. Water was then added, and the mixture was extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and a solution of tetrahydrofuran (10 mL) and potassium hydroxide (594 mg, 10.6 mmol) was added. The mixture was reacted at 25 °C for 2 h. Water was then added, and the mixture was extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **28** (612 mg, yield: 56%). MS (ESI): (M+H)⁺, calculated 204.0, found 204.1.

Cyclohexene oxide (1.47 g, 15 mmol) and 40% trimethylbenzylammonium hydroxide (2.5 g, 6 mmol) were added to a reaction flask. Compound **28** (612 mg, 3 mmol) was dissolved in *N,N*-dimethylformamide (6 mL), and the resulting solution was added dropwise to the reaction system described above. The mixture was reacted at 25 °C for 3 h. Water was then added, and the mixture was extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **29** (813 mg, yield: 90%). MS (ESI): (M+H)⁺, calculated 302.1, found 302.1.

Trimethylsilyl cyanide (3.86 g, 39 mmol) was added to tetrahydrofuran (20 mL), and tetrabutylammonium fluoride (35.7 mL, 1 M) was added dropwise to the mixture at 0 °C. After 1 h of reaction, a solution of compound **30** (10 g, 32.5 mmol) in acetonitrile (30 mL) was added to the reaction system described above. The mixture was reacted at 80 °C for 1 h. After cooling, the solvent was removed, and the residue was purified by silica gel chromatography to give compound **31** (5.4 g, yield: 66%). MS (ESI): (M+H)⁺, calculated 254.0, found 254.1.

Compound **31** (5.4 g, 21.5 mmol) was added to tetrahydrofuran, and a solution of borane in tetrahydrofuran (21.5 mL, 1 M) was added dropwise to the mixture at 0 °C. The mixture was then reacted at 25 °C for 16 h. Methanol was added to quench the reaction, and the solvent was removed by concentration under reduced pressure. The residue was purified by silica gel chromatography to give compound **32** (4.1 g, yield: 74%). MS (ESI): (M+H)⁺, calculated 258.0, found 258.1.

Compound **32** (4.1 g, 15.9 mmol) and triethylamine (3.2 g, 31.8 mmol) were added to

dichloromethane (30 mL), and trifluoroacetic anhydride (5 g, 23.8 mmol) was added dropwise to the mixture at 0 °C. The mixture was then reacted at 25 °C for 1 h, added with water for dilution, and extracted with dichloromethane (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **33** (5.6 g, yield: 60%). MS (ESI): (M+H)⁺, calculated 354.0, found 354.1.

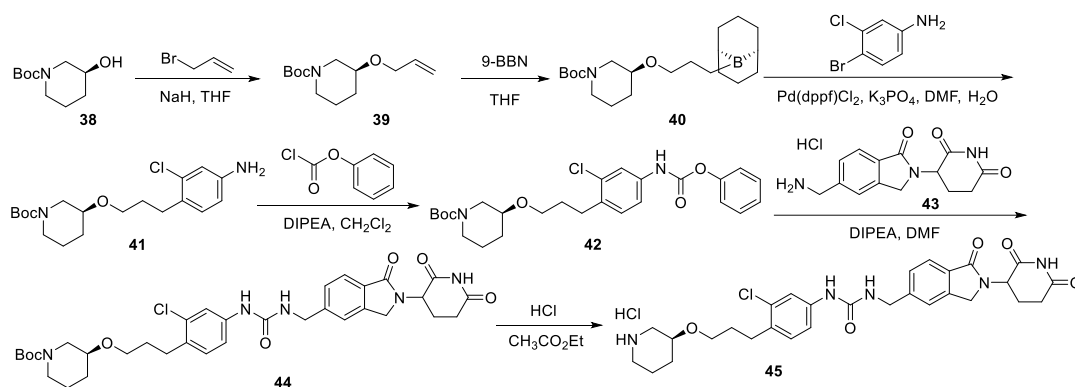
Compound **33** (5.6 g, 9.5 mmol) and paraformaldehyde (0.37 g, 12.4 mmol) were added to sulfuric acid, and the mixture was reacted at 25 °C for 1 h. The reaction liquid was then poured into ice water and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **34** (2.77 g, yield: 80%). MS (ESI): (M+H)⁺, calculated 366.0, found 366.1.

Compound **34** (2.77 g, 7.6 mmol) was added to tetrahydrofuran, and diisobutylaluminium hydride was added dropwise to the mixture at 0 °C. The mixture was then reacted at 25 °C for 2 h. Water was added to quench the reaction, and the mixture was filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **35** (1.65 g, yield: 90%). MS (ESI): (M+H)⁺, calculated 242.0, found 242.1.

Compound **35** (1.65 g, 6.8 mmol), sodium azide (3.5 g, 54.4 mmol), copper(I) iodide (130 mg, 0.68 mmol), L-proline (0.4 g, 2 mmol), and sodium hydroxide (80 mg, 2 mmol) were added to ethanol (20 mL) and water (10 mL), and the mixture was reacted at 95 °C for 24 h. After cooling, water was added, and the mixture was extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **36** (0.97 g, yield: 70%). MS (ESI): (M+H)⁺, calculated 205.1, found 205.1.

Compound **36** (0.97 g, 4.8 mmol), compound **16** (1.8 g, 5.04 mmol), and triethylamine (0.76 g, 7.2 mmol) were added to tetrahydrofuran (10 mL). The mixture was reacted at 25 °C for 12 h, and the solvent was removed by concentration under reduced pressure. The residue was purified by silica gel chromatography to give compound **37** (1.7 g, yield: 80%). MS (ESI): (M+H)⁺, calculated 447.2, found 447.1.

Example 6: Synthesis of Compound **45**



Compound **38** (10 g, 50 mmol) was dissolved in tetrahydrofuran (120 mL), and sodium hydride (4 g, 100 mmol) was added at 0 °C. The mixture was stirred for 0.5 h. Allyl bromide (12.1 g, 100 mmol) was then added, and the mixture was reacted for 2 h. A saturated ammonium chloride solution was added to quench the reaction. The mixture was extracted with ethyl acetate (10 mL × 3). The organic phases were combined, dried over anhydrous sodium sulfate, and then filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by a silica gel column to give compound **39** (4.65 g, yield: 66%). MS (ESI): (M+H)⁺, calculated 142.2, found 142.3.

Compound **39** (4.65 g, 33 mmol) was added to tetrahydrofuran (100 mL), and a solution of 9-borabicyclo[3.3.1]nonane (80 mL, 0.5 M) in tetrahydrofuran was added. The mixture was reacted at 80 °C for 2 h and then cooled to room temperature. The reaction liquid was directly used in the next step.

N,N-Dimethylformamide (100 mL) and an aqueous solution of potassium phosphate (8.7 g, 41 mmol) were added to the reaction liquid of compound **40**, and the mixture was stirred for 10 min. 3-Chloro-4-bromoaniline (6.8 g, 33 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (2.4 g, 3.3 mmol) were added, and the mixture was reacted at 90 °C for 3 h, cooled to room temperature, and extracted with ethyl acetate (10 mL × 3). The organic phases were combined, dried over anhydrous sodium sulfate, and then filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by a silica gel column to give compound **41** (3.7 g, yield: 42%). MS (ESI): (M+H)⁺, calculated 269.1, found 269.1.

Compound **41** (3.7 g, 13.8 mmol) was added to dichloromethane (90 mL), and diisopropylethylamine (3.5 g, 27 mmol) and phenyl chloroformate (2.5 g, 16 mmol) were sequentially added to the solution. The mixture was reacted at 25 °C for 0.5 h. The reaction liquid was then concentrated under reduced pressure, and the residue was purified by a silica gel column to give compound **42** (4.66 g, yield: 89%). MS (ESI): (M+H)⁺, calculated 389.2,

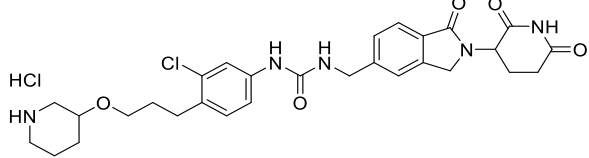
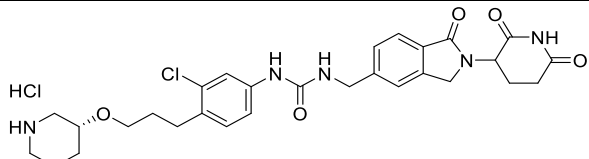
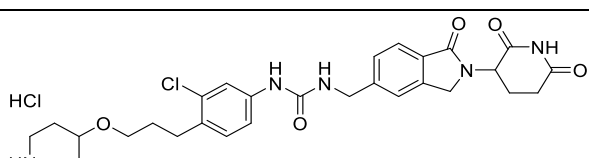
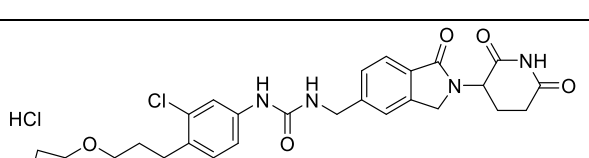
found 389.2.

Compound **42** (4.66 g, 12 mmol) was dissolved in *N,N*-dimethylformamide (50 mL), and then compound **43** (4.08 g, 13.2 mmol) was added. The solid was dispersed in the solution by ultrasonication, and diisopropylethylamine (48 mmol) was then added. The mixture was reacted at 50 °C for 3 h and cooled to room temperature. Water was then added, and the mixture was extracted with ethyl acetate (20 mL × 3). The organic phases were combined, dried over anhydrous sodium sulfate, and then filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by a silica gel column to give compound **44** (6.4 g, yield: 94%). MS (ESI): (M+H)⁺, calculated 568.2, found 568.4.

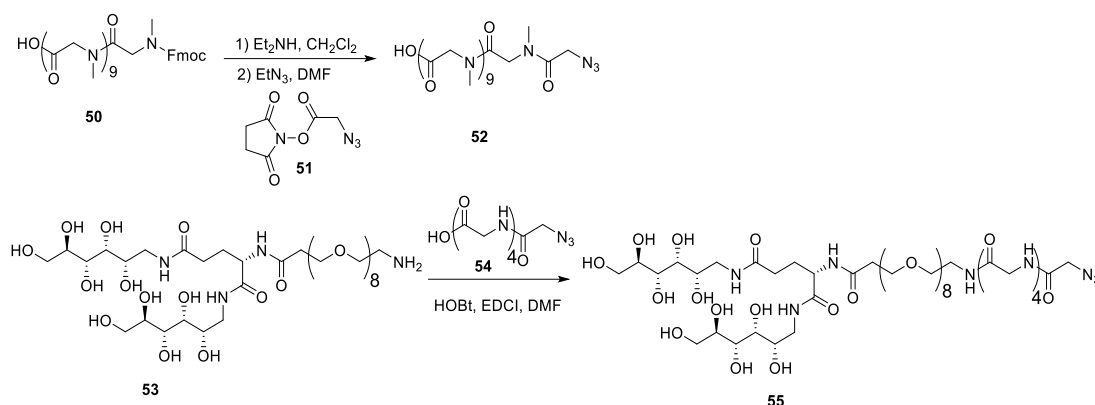
Compound **44** (1.6 g, 2.8 mmol) was added to dichloromethane (19 mL), and a solution of hydrogen chloride in ethyl acetate (11 mL, 4 M) was added dropwise to the mixture at 0 °C. The mixture was then reacted for 2 h, and the solvent was removed by concentration under reduced pressure. The residue was dried under vacuum to give compound **45** (1.6 g, yield: 94%). MS (ESI): (M+H)⁺, calculated 568.2, found 568.3.

Example 7: Synthesis of Compounds **46-49**

Table 3

No	Structural formula	MS(ESI) : (M+H) ⁺	
		Calculated	Found
46		568.2	568.3
47		568.2	568.3
48		568.2	568.4
49		540.2	540.4

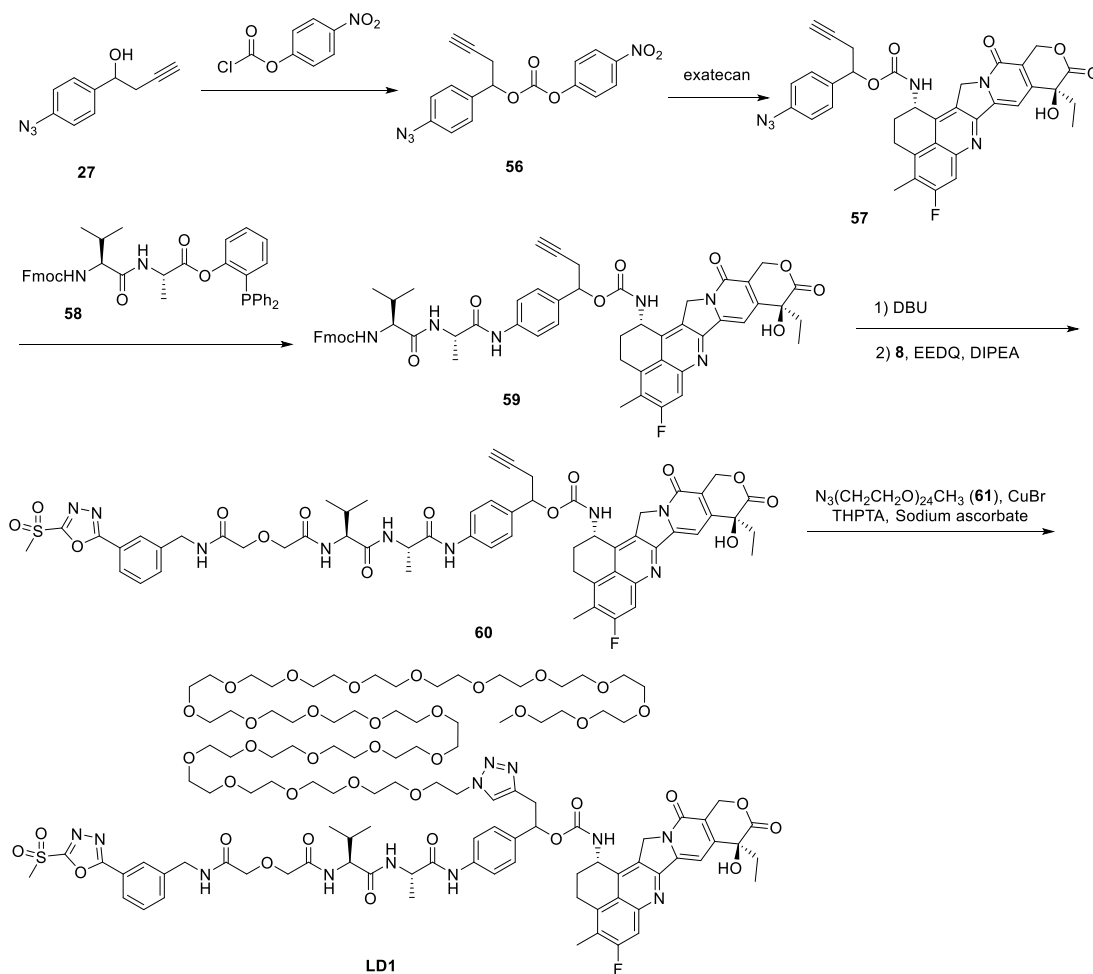
The synthesis of compounds **46-49** was carried out with reference to the synthetic route of compound **45**.

Example 8: Synthesis of Compounds **52** and **55**

Compound **50** (1.1 g, 1.06 mmol, obtained from solid-phase peptide synthesis) and diethylamine (3.89 g, 53.24 mmol) were dissolved in dichloromethane (5 mL), and the reaction liquid was purged 3 times with N₂ and then reacted at 25 °C for 1 h. After the starting materials were completely converted, the reaction liquid was concentrated under reduced pressure to remove the solvent, and then the low-boiling compounds were removed under high vacuum. Compound **51** (3.15 g, 1.6 mmol) and *N,N*-dimethylformamide (4 mL) were then added, and the mixture was stirred. Triethylamine (3.23 g, 3.2 mmol) was added dropwise to the mixture at 25 °C. After 6 h of reaction, no starting material remained as detected by LCMS, and the excess triethylamine was removed by concentration under reduced pressure. The residue was directly separated by reversed-phase chromatography to give compound **52** (810 mg, yield: 10%). MS (ESI): (M+H)⁺, calculated 812.4, found 812.3.

Compound **53** (1.2 g, 1.36 mmol, synthesized with reference to the synthetic route reported in patent CN 111757757 A) and compound **54** (447 mg, 1.36 mmol, obtained from solid-phase peptide synthesis) were added to *N,N*-dimethylformamide (40 mL), and then 1-hydroxybenzotriazole (40 mg, 0.26 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (285 mg, 1.46 mmol) were added. The mixture was stirred for reaction at 25 °C for 16 h. After the reaction was stopped, the solvent was removed by concentration under reduced pressure, and the residue was separated by reversed-phase chromatography to give compound **55** (820 mg, yield: 50%). MS (ESI): (M+H)⁺, calculated 1208.5, found 1208.6.

Example 9: Synthesis of Compound **LD1**



Compound **27** (2.15 g, 11.5 mmol), 4-nitrophenyl chloroformate (3 g, 15 mmol), and *N,N*-dimethylformamide (15 mL) were added to a reaction flask, and the mixture was stirred while triethylamine (2.32 g, 23 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 4 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **56** (4.05 g, yield: 100%).

Compound **56** (176 mg, 0.5 mmol), exatecan mesylate (243 mg, 0.45 mmol), and *N,N*-dimethylformamide (2 mL) were added to a reaction flask, and the mixture was stirred while triethylamine (101 mg, 1 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 6 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **57** (259 mg, yield: 89%). MS (ESI): $(M+H)^+$, calculated 649.2, found 649.1.

Compound **57** (259 mg, 0.4 mmol) and compound **58** (670 mg, 1 mmol, synthesized with reference to the reaction route reported in patent WO 2021252708 A1) were added to a reaction flask, and the mixture was purged three times with nitrogen. Tetrahydrofuran (10 mL) and water (4 mL) were added, and the mixture was reacted at 25 °C for 24 h, added with water (10 mL) for dilution, and extracted with ethyl acetate (20 mL $\times$ 3). The organic phases were

combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **59** (239 mg, yield: 59%). MS (ESI): (M+H)⁺, calculated 1015.4, found 1015.3.

- 5 Compound **59** (239 mg, 0.24 mmol) and *N,N*-dimethylformamide (2 mL) were added to a reaction flask, and 1,8-diazabicyclo[5.4.0]undec-7-ene (18 mg, 0.12 mmol) was added dropwise. The mixture was reacted at 25 °C for 0.5 h. Compound **8** (107 mg, 0.29 mmol), 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (890 mg, 0.36 mmol), diisopropylethylamine (48 mg, 0.48 mmol), and *N,N*-dimethylformamide (10 mL) were added to the reaction system
- 10 described above. The mixture was reacted at 25 °C for 24 h, added with water (20 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **60** (192 mg, yield: 70%). MS (ESI): (M+H)⁺, calculated
- 15 1144.4, found 1144.3.

- Compound **60** (192 mg, 0.168 mmol), compound **61** (280 mg, 0.252 mmol), sodium ascorbate (7 mg, 0.034 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (15 mg, 0.034 mmol), and copper(I) bromide (5 mg, 0.034 mmol) were added to a reaction flask, and the mixture was
- 20 purged three times with nitrogen. *tert*-Butanol (4 mL) and water (1 mL) were added, and the mixture was reacted at 25 °C for 12 h, added with water (10 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **LD1** (220 mg, yield: 62%). MS (ESI): (M+H)⁺, calculated 2258.0, found 2258.2.

25 Example 10: Synthesis of Compounds **LD2-19**, **LD23-28**, and **LD32-54**

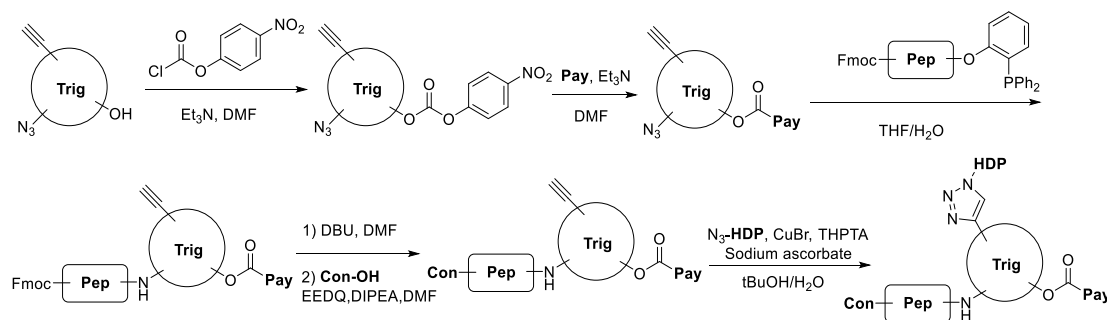


Table 4

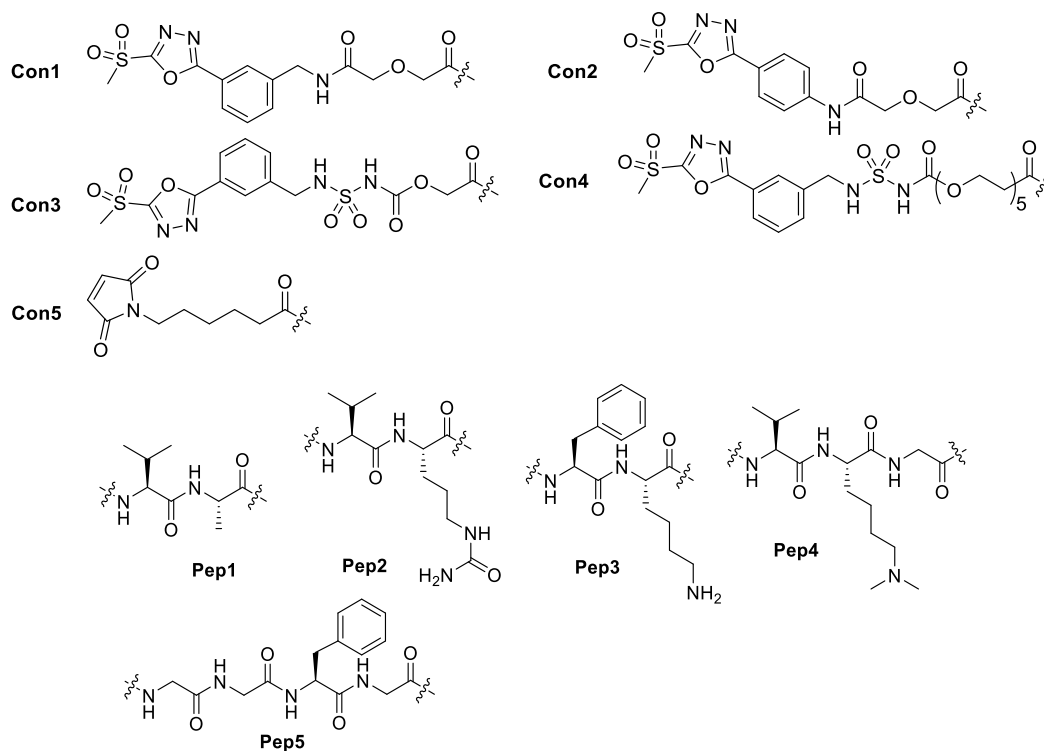
No.	Con	Pep	Trig	HDP	Pay	MS(ESI):(M+H) ⁺
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						Calculated	Found
LD2	Con2	Pep1	Trig1	HDP1	Pay1	2244.0	2244.1
LD3	Con3	Pep1	Trig1	HDP1	Pay1	2323.0	2323.1
LD4	Con4	Pep1	Trig1	HDP1	Pay1	2513.1	2513.0
LD5	Con5	Pep1	Trig1	HDP1	Pay1	2100.0	2100.2
LD6	Con1	Pep1	Trig1	HDP2	Pay1	1955.8	1955.9
LD7	Con2	Pep1	Trig1	HDP2	Pay1	1941.8	1941.8
LD8	Con3	Pep1	Trig1	HDP2	Pay1	2020.7	2020.6
LD9	Con4	Pep1	Trig1	HDP2	Pay1	2210.8	2210.9
LD10	Con5	Pep1	Trig1	HDP2	Pay1	1797.8	1797.8
LD11	Con1	Pep1	Trig1	HDP3	Pay1	2351.9	2352.0
LD12	Con2	Pep1	Trig1	HDP3	Pay1	2337.9	2338.0
LD13	Con3	Pep1	Trig1	HDP3	Pay1	2416.9	2416.9
LD14	Con4	Pep1	Trig1	HDP3	Pay1	2607.0	2607.1
LD15	Con5	Pep1	Trig1	HDP3	Pay1	2194.0	2194.1
LD16	Con1	Pep2	Trig1	HDP1	Pay1	2344.1	2344.1
LD17	Con1	Pep3	Trig1	HDP1	Pay1	2363.1	2363.2
LD18	Con1	Pep4	Trig1	HDP1	Pay1	2391.1	2391.2
LD19	Con1	Pep5	Trig1	HDP1	Pay1	2406.0	2406.1
LD23	Con1	Pep1	Trig1	HDP1	Pay2	2276.0	2276.0
LD24	Con2	Pep1	Trig1	HDP1	Pay2	2262.0	2262.1
LD25	Con1	Pep1	Trig1	HDP1	Pay3	2262.0	2262.1
LD26	Con1	Pep1	Trig1	HDP1	Pay4	2232.0	2232.1
LD27	Con1	Pep1	Trig1	HDP1	Pay5	2272.0	2272.0
LD28	Con1	Pep1	Trig1	HDP2	Pay6	1883.7	1883.6
LD32	Con1	Pep1	Trig1	HDP1	Pay7	2552.3	2552.4
LD33	Con1	Pep1	Trig1	HDP2	Pay7	2250.0	2250.0
LD34	Con1	Pep1	Trig1	HDP3	Pay7	2646.2	2646.3
LD35	Con2	Pep1	Trig1	HDP1	Pay7	2538.3	2538.5
LD36	Con2	Pep1	Trig1	HDP2	Pay7	2236.0	2236.1
LD37	Con2	Pep1	Trig1	HDP3	Pay7	2632.2	2632.1
LD38	Con1	Pep1	Trig1	HDP1	Pay8	2390.1	2390.1

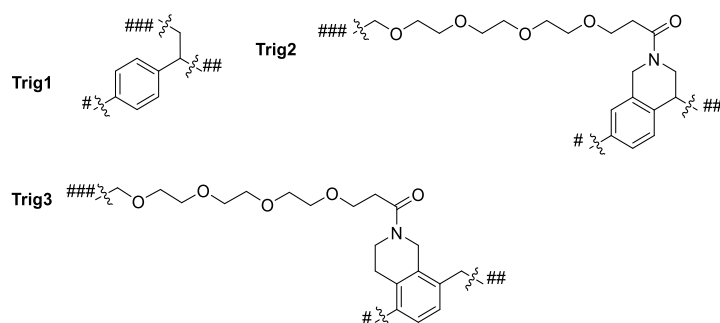
LD39	Con2	Pep1	Trig1	HDP1	Pay8	2376.1	2376.1
LD40	Con1	Pep1	Trig1	HDP3	Pay8	2484.0	2484.0
LD41	Con2	Pep1	Trig1	HDP3	Pay8	2470.0	2470.1
LD42	Con1	Pep1	Trig1	HDP1	Pay9	2390.1	2390.1
LD43	Con1	Pep1	Trig1	HDP1	Pay10	2390.1	2390.1
LD44	Con1	Pep1	Trig1	HDP1	Pay11	2390.1	2390.2
LD45	Con1	Pep1	Trig1	HDP1	Pay12	2362.0	2362.2
LD46	Con2	Pep1	Trig1	HDP1	Pay13	2123.0	2123.1
LD47	Con2	Pep1	Trig1	HDP2	Pay13	1820.8	1820.9
LD48	Con2	Pep1	Trig1	HDP3	Pay13	2216.9	2216.8
LD49	Con1	Pep1	Trig2	HDP1	Pay1	2503.2	2503.1
LD50	Con1	Pep1	Trig3	HDP1	Pay1	2517.2	2517.3
LD51	Con1	Pep1	Trig2	HDP2	Pay1	2200.9	2201.0
LD52	Con1	Pep1	Trig3	HDP2	Pay1	2214.9	2214.9
LD53	Con1	Pep1	Trig2	HDP3	Pay1	2597.0	2597.1
LD54	Con1	Pep1	Trig3	HDP3	Pay1	2611.1	2611.0

For the synthetic routes of compounds **LD2-19**, **LD23-28**, and **LD32-54**, reference was made to the synthesis of compound **LD1**.

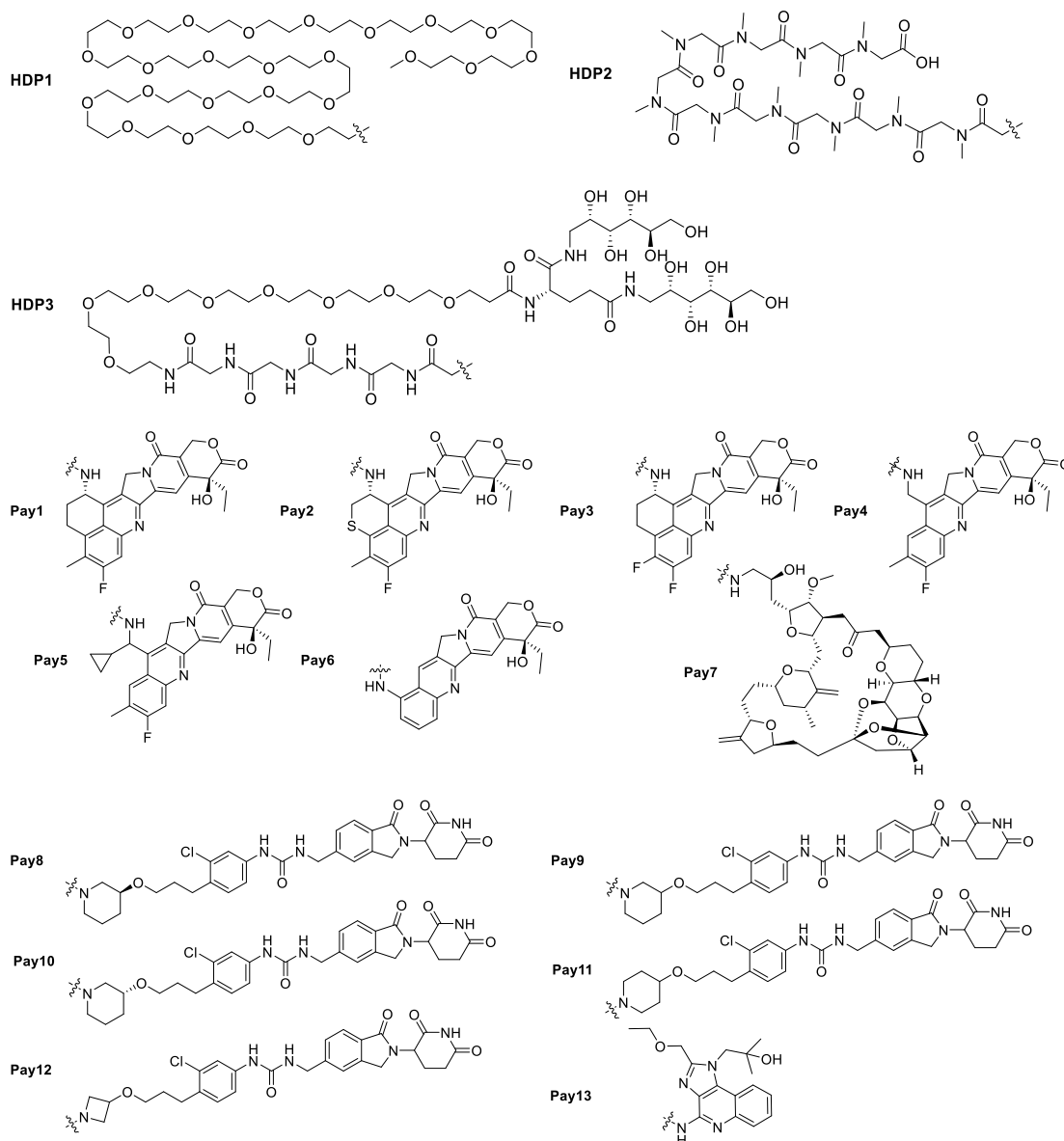
Con1-5, **Pep1-5**, **Trig1-3**, **HDP1-3**, and **Pay1-13** have structures shown as follows:



wherein the N-terminus is linked to Fmoc.



wherein position # is linked to -N₃, position ## is linked to -OH, and position ### is linked to alkynyl.



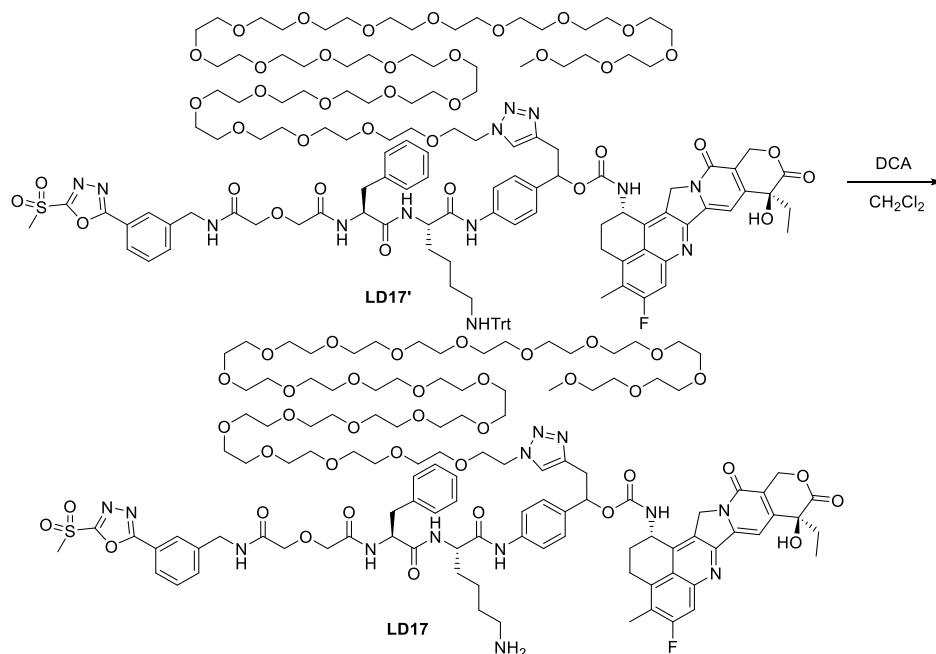
Synthesis of compound **LD17**

Compound **LD17'** was synthesized with reference to the synthetic route of compound **LD1**.

10 Compound **LD17'** (130 mg, 0.05 mmol) was dissolved in dichloromethane (2 mL), and

dichloroacetic acid (2 mL) and a small amount of triethylsilane were added to the reaction system described above at 0 °C. The reaction was completed after 3 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **LD17** (70 mg, yield: 60%). MS (ESI): (M+H)⁺, calculated

5 2363.1, found 2363.2.



Example 11: Synthesis of Compounds **LD20-22**

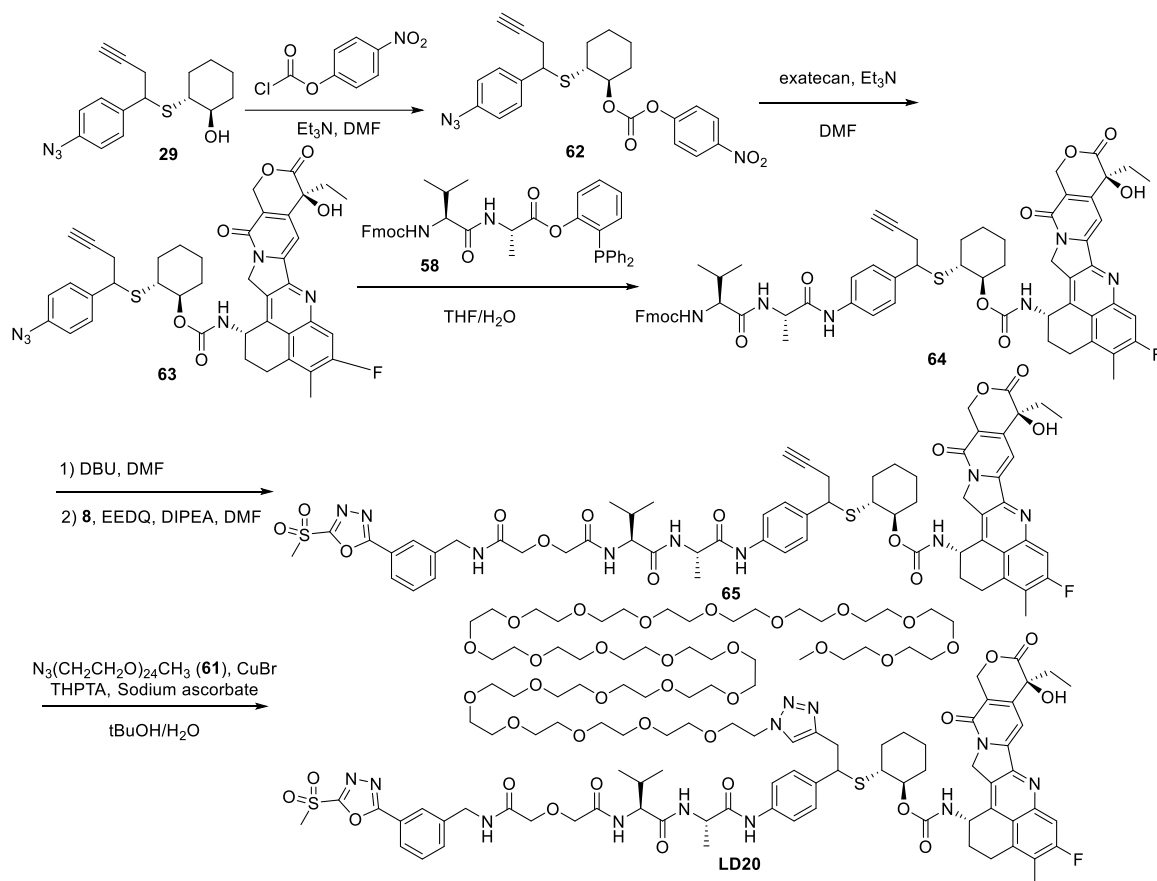
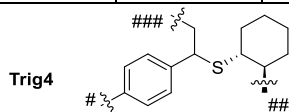


Table 5

No.	Con	Pep	Trig	HDP	Pay	MS(ESI): (M+H) ⁺	
						Calculated	Found
LD20	Con1	Pep1	Trig4	HDP1	Pay1	2372.1	2372.2
LD21	Con1	Pep1	Trig4	HDP2	Pay1	2069.8	2069.9
LD22	Con1	Pep1	Trig4	HDP3	Pay1	2466.0	2466.0



wherein position # is linked to -N₃, position ## is linked to -OH, and position ### is linked to alkynyl.

Compound **29** (3 g, 10 mmol), 4-nitrophenyl chloroformate (3 g, 15 mmol), and *N,N*-dimethylformamide (12 mL) were added to a reaction flask, and the mixture was stirred while triethylamine (2 g, 20 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 4 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **62** (4.5 g, yield: 96%).

Compound **62** (233 mg, 0.5 mmol), exatecan mesylate (243 mg, 0.45 mmol), and *N,N*-dimethylformamide (2 mL) were added to a reaction flask, and the mixture was stirred while

triethylamine (101 mg, 1 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 6 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography to give compound **63** (343 mg, yield: 90%). MS (ESI): (M+H)⁺, calculated 763.2, found 763.3.

- 5 Compound **63** (343 mg, 0.45 mmol) and compound **58** (670 mg, 1 mmol, synthesized with reference to the reaction route reported in patent WO 2021252708 A1) were added to a reaction flask, and the mixture was purged three times with nitrogen. Tetrahydrofuran (10 mL) and water (4 mL) were added, and the mixture was reacted at 25 °C for 24 h, added with water (10 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were
10 combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **64** (304 mg, yield: 60%). MS (ESI): (M+H)⁺, calculated 1129.4, found 1129.3.

- Compound **64** (304 mg, 0.27 mmol) and *N,N*-dimethylformamide (2 mL) were added to a
15 reaction flask, and 1,8-diazabicyclo[5.4.0]undec-7-ene (18 mg, 0.13 mmol) was added dropwise. The mixture was reacted at 25 °C for 0.5 h. Compound **8** (107 mg, 0.3 mmol), 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (890 mg, 0.36 mmol), diisopropylethylamine (54 mg, 0.54 mmol), and *N,N*-dimethylformamide (10 mL) were added to the reaction system described above. The mixture was reacted at 25 °C for 24 h, added with water (20 mL) for
20 dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **65** (170 mg, yield: 50%). MS (ESI): (M+H)⁺, calculated 1258.4, found 1258.3.

- 25 Compound **65** (170 mg, 0.135 mmol), compound **61** (235 mg, 0.21 mmol), sodium ascorbate (6 mg, 0.027 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (11 mg, 0.027 mmol), and copper(I) bromide (4 mg, 0.027 mmol) were added to a reaction flask, and the mixture was purged three times with nitrogen. *tert*-Butanol (4 mL) and water (1 mL) were added, and the mixture was reacted at 25 °C for 12 h, added with water (10 mL) for dilution, and extracted
30 with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **LD20** (180 mg, yield: 56%). MS (ESI): (M+H)⁺, calculated 2372.1, found 2372.2. For the synthetic routes of compounds **LD21-22**, reference was made to the synthesis of

compound **LD20**.

Example 12: Synthesis of Compounds **LD29-31**

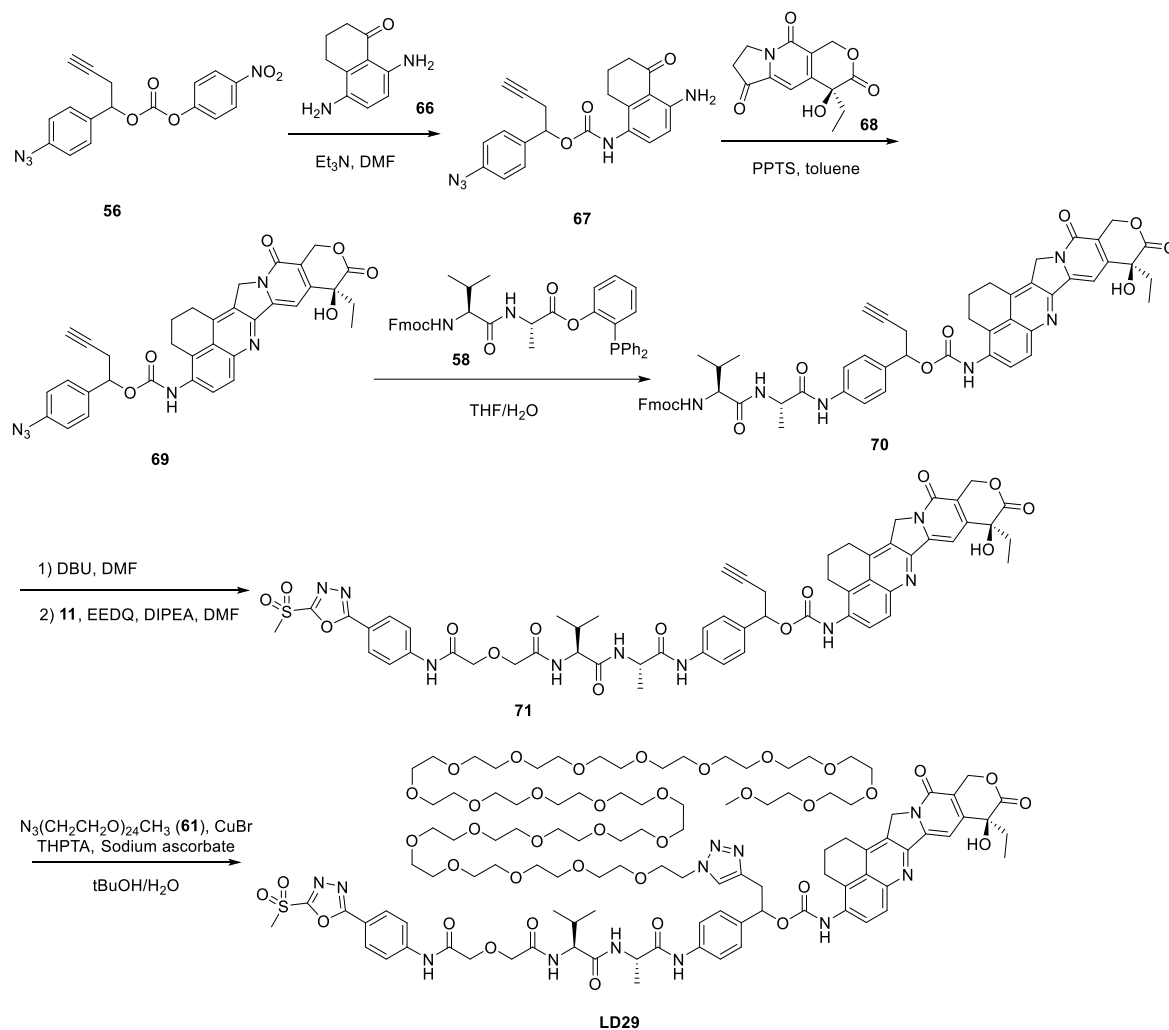
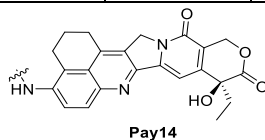


Table 6

No.	Con	Pep	Trig	HDP	Pay	MS(ESI): (M+H) ⁺	
						Calculated	Found
LD29	Con2	Pep1	Trig1	HDP1	Pay14	2212.0	2212.2
LD30	Con2	Pep1	Trig1	HDP2	Pay14	1909.7	1909.8
LD31	Con2	Pep1	Trig1	HDP3	Pay14	2305.9	2306.0



5

Compound **56** (176 mg, 0.5 mmol), compound **66** (88 mg, 0.5 mmol), and *N,N*-dimethylformamide (2 mL) were added to a reaction flask, and the mixture was stirred while triethylamine (101 mg, 1 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 12 h. The solvent was removed by concentration under reduced pressure, and the residue

was purified by silica gel chromatography to give compound **67** (128 mg, yield: 66%). MS (ESI): (M+H)⁺, calculated 390.1, found 390.1.

Compound **67** (128 mg, 0.33 mmol), compound **68** (95 mg, 0.36 mmol), pyridinium *p*-toluenesulfonate (8 mg, 0.03 mmol), and toluene (5 mL) were added to a reaction flask. The mixture was reacted at 100 °C for 12 h and then cooled to room temperature. The mixture was filtered, and the solid was washed with toluene (5 mL) to give compound **69** (185 mg, yield: 90%). MS (ESI): (M+H)⁺, calculated 617.2, found 617.3.

Compound **69** (185 mg, 0.3 mmol) and compound **58** (503 mg, 0.75 mmol, synthesized with reference to the reaction route reported in patent WO 2021252708 A1) were added to a reaction flask, and the mixture was purged three times with nitrogen. Tetrahydrofuran (10 mL) and water (4 mL) were added, and the mixture was reacted at 25 °C for 24 h, added with water (10 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **70** (177 mg, yield: 60%). MS (ESI): (M+H)⁺, calculated 983.4, found 983.3.

Compound **70** (177 mg, 0.18 mmol) and *N,N*-dimethylformamide (2 mL) were added to a reaction flask, and 1,8-diazabicyclo[5.4.0]undec-7-ene (14 mg, 0.09 mmol) was added dropwise. The mixture was reacted at 25 °C for 0.5 h. Compound **11** (82 mg, 0.22 mmol), 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (666 mg, 0.27 mmol), diisopropylethylamine (36 mg, 0.36 mmol), and *N,N*-dimethylformamide (10 mL) were added to the reaction system described above. The mixture was reacted at 25 °C for 24 h, added with water (20 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give compound **71** (150 mg, yield: 75%). MS (ESI): (M+H)⁺, calculated 1112.4, found 1112.3.

Compound **71** (150 mg, 0.135 mmol), compound **61** (224 mg, 0.202 mmol), sodium ascorbate (5 mg, 0.027 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (12 mg, 0.027 mmol), and copper(I) bromide (4 mg, 0.027 mmol) were added to a reaction flask, and the mixture was purged three times with nitrogen. *tert*-Butanol (4 mL) and water (1 mL) were added, and the mixture was reacted at 25 °C for 12 h, added with water (10 mL) for dilution, and extracted with ethyl acetate (20 mL × 3). The organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was then concentrated

under reduced pressure, and the residue was purified by silica gel chromatography to give compound **LD29** (155 mg, yield: 60%). MS (ESI): (M+H)⁺, calculated 2212.0, found 2212.2. For the synthetic routes of compounds **LD30-31**, reference was made to the synthesis of compound **LD29**.

- 5 With reference to the aforementioned examples, the compounds shown in Table 7 (where the final products containing the **Pep3** structure were obtained by acid treatment with reference to **LD17**) can also be synthesized.

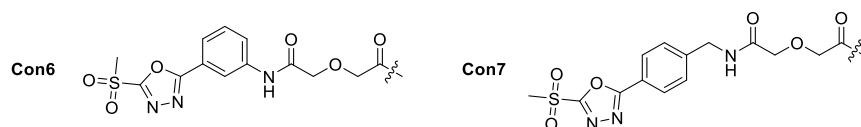
Table 7

No.	Con	Pep	Trig	HDP	Pay
LD56	Con5	Pep1	Trig1	HDP3	Pay1
LD57	Con6	Pep1	Trig1	HDP3	Pay1
LD58	Con5	Pep2	Trig1	HDP3	Pay1
LD59	Con6	Pep2	Trig1	HDP3	Pay1
LD60	Con5	Pep3	Trig1	HDP3	Pay1
LD61	Con6	Pep3	Trig1	HDP3	Pay1
LD62	Con5	Pep4	Trig1	HDP3	Pay1
LD63	Con6	Pep4	Trig1	HDP3	Pay1
LD64	Con5	Pep5	Trig1	HDP3	Pay1
LD65	Con6	Pep5	Trig1	HDP3	Pay1
LD66	Con5	Pep1	Trig2	HDP3	Pay1
LD67	Con6	Pep1	Trig2	HDP3	Pay1
LD68	Con5	Pep2	Trig2	HDP3	Pay1
LD69	Con6	Pep2	Trig2	HDP3	Pay1
LD70	Con5	Pep3	Trig2	HDP3	Pay1
LD71	Con6	Pep3	Trig2	HDP3	Pay1
LD72	Con5	Pep4	Trig2	HDP3	Pay1
LD73	Con6	Pep4	Trig2	HDP3	Pay1
LD74	Con5	Pep5	Trig2	HDP3	Pay1
LD75	Con6	Pep5	Trig2	HDP3	Pay1
LD76	Con5	Pep1	Trig3	HDP3	Pay1
LD77	Con6	Pep1	Trig3	HDP3	Pay1
LD78	Con5	Pep2	Trig3	HDP3	Pay1
LD79	Con6	Pep2	Trig3	HDP3	Pay1

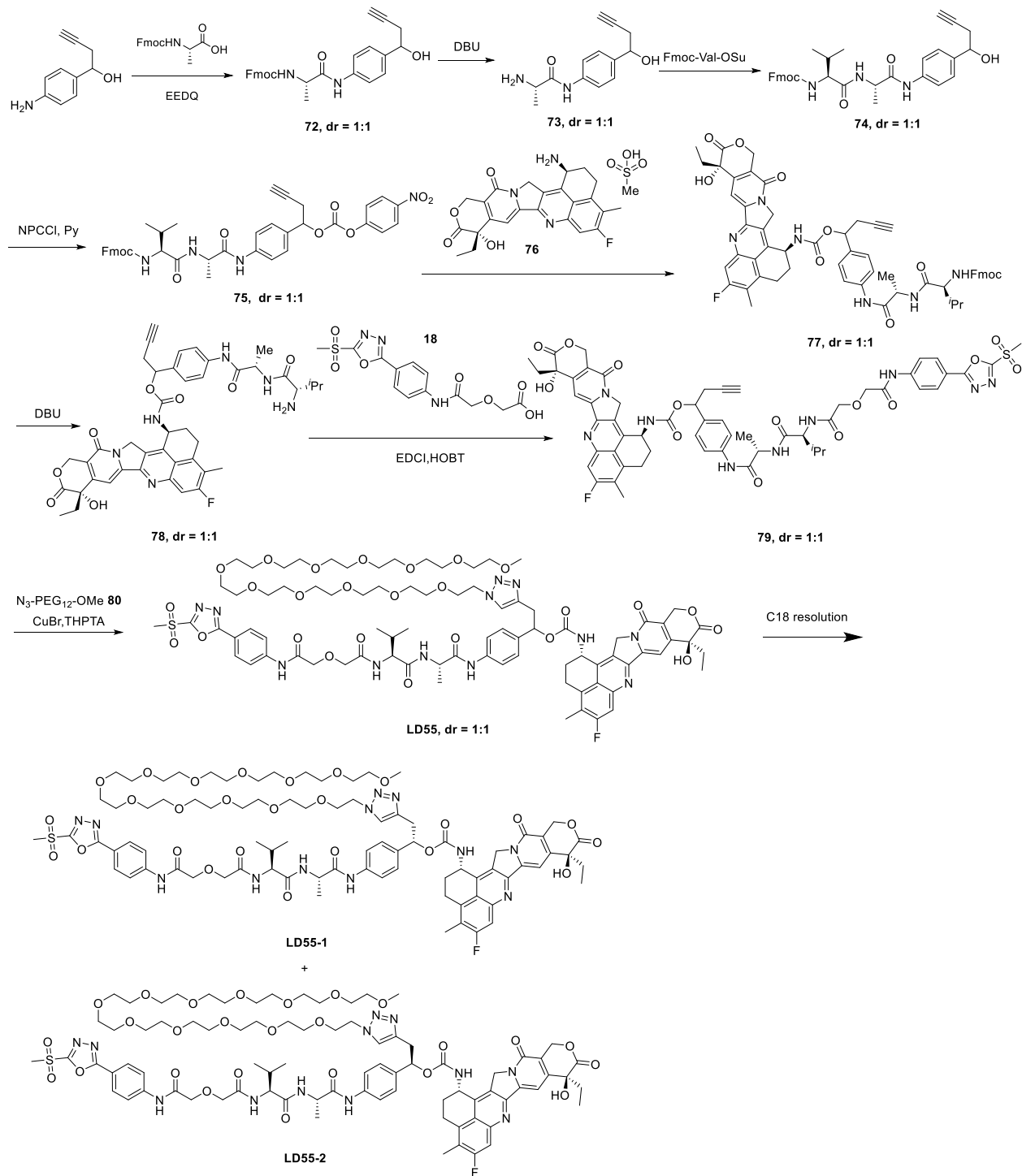
LD80	Con5	Pep3	Trig3	HDP3	Pay1
LD81	Con6	Pep3	Trig3	HDP3	Pay1
LD82	Con5	Pep4	Trig3	HDP3	Pay1
LD83	Con6	Pep4	Trig3	HDP3	Pay1
LD84	Con5	Pep5	Trig3	HDP3	Pay1
LD85	Con6	Pep5	Trig3	HDP3	Pay1
LD86	Con5	Pep1	Trig1	HDP3	Pay2
LD87	Con6	Pep1	Trig1	HDP3	Pay2
LD88	Con5	Pep2	Trig1	HDP3	Pay2
LD89	Con6	Pep2	Trig1	HDP3	Pay2
LD90	Con5	Pep3	Trig1	HDP3	Pay2
LD91	Con6	Pep3	Trig1	HDP3	Pay2
LD92	Con5	Pep4	Trig1	HDP3	Pay2
LD93	Con6	Pep4	Trig1	HDP3	Pay2
LD94	Con5	Pep5	Trig1	HDP3	Pay2
LD95	Con6	Pep5	Trig1	HDP3	Pay2
LD96	Con5	Pep1	Trig2	HDP3	Pay2
LD97	Con6	Pep1	Trig2	HDP3	Pay2
LD98	Con5	Pep2	Trig2	HDP3	Pay2
LD99	Con6	Pep2	Trig2	HDP3	Pay2
LD100	Con5	Pep3	Trig2	HDP3	Pay2
LD101	Con6	Pep3	Trig2	HDP3	Pay2
LD102	Con5	Pep4	Trig2	HDP3	Pay2
LD103	Con6	Pep4	Trig2	HDP3	Pay2
LD104	Con5	Pep5	Trig2	HDP3	Pay2
LD105	Con6	Pep5	Trig2	HDP3	Pay2
LD106	Con5	Pep1	Trig3	HDP3	Pay2
LD107	Con6	Pep1	Trig3	HDP3	Pay2
LD108	Con5	Pep2	Trig3	HDP3	Pay2
LD109	Con6	Pep2	Trig3	HDP3	Pay2
LD110	Con5	Pep3	Trig3	HDP3	Pay2
LD111	Con6	Pep3	Trig3	HDP3	Pay2

LD112	Con5	Pep4	Trig3	HDP3	Pay2
LD113	Con6	Pep4	Trig3	HDP3	Pay2
LD114	Con5	Pep5	Trig3	HDP3	Pay2
LD115	Con6	Pep5	Trig3	HDP3	Pay2
LD116	Con5	Pep1	Trig1	HDP3	Pay7
LD117	Con6	Pep1	Trig1	HDP3	Pay7
LD118	Con5	Pep2	Trig1	HDP3	Pay7
LD119	Con6	Pep2	Trig1	HDP3	Pay7
LD120	Con5	Pep3	Trig1	HDP3	Pay7
LD121	Con6	Pep3	Trig1	HDP3	Pay7
LD122	Con5	Pep4	Trig1	HDP3	Pay7
LD123	Con6	Pep4	Trig1	HDP3	Pay7
LD124	Con5	Pep5	Trig1	HDP3	Pay7
LD125	Con6	Pep5	Trig1	HDP3	Pay7
LD126	Con5	Pep1	Trig2	HDP3	Pay7
LD127	Con6	Pep1	Trig2	HDP3	Pay7
LD128	Con5	Pep2	Trig2	HDP3	Pay7
LD129	Con6	Pep2	Trig2	HDP3	Pay7
LD130	Con5	Pep3	Trig2	HDP3	Pay7
LD131	Con6	Pep3	Trig2	HDP3	Pay7
LD132	Con5	Pep4	Trig2	HDP3	Pay7
LD133	Con6	Pep4	Trig2	HDP3	Pay7
LD134	Con5	Pep5	Trig2	HDP3	Pay7
LD135	Con6	Pep5	Trig2	HDP3	Pay7
LD136	Con5	Pep1	Trig3	HDP3	Pay7
LD137	Con6	Pep1	Trig3	HDP3	Pay7
LD138	Con5	Pep2	Trig3	HDP3	Pay7
LD139	Con6	Pep2	Trig3	HDP3	Pay7
LD140	Con5	Pep3	Trig3	HDP3	Pay7
LD141	Con6	Pep3	Trig3	HDP3	Pay7
LD142	Con5	Pep4	Trig3	HDP3	Pay7
LD143	Con6	Pep4	Trig3	HDP3	Pay7

LD144	Con5	Pep5	Trig3	HDP3	Pay7
LD145	Con6	Pep5	Trig3	HDP3	Pay7



Example 13: Synthesis of Compound **LD55** and Resolution into **LD55-1** and **LD55-2**



1-(4-Aminophenyl)-3-butyn-1-ol (4997 mg, 31 mmol), Fmoc-Ala-OH (9651 mg, 31 mmol), EEDQ (11498 mg, 46.5 mmol), and extra-dry DCM (90 mL) were added to a reaction flask at 0 °C. After 3 h of reaction, the solvent was removed by concentration under reduced pressure, and the residue was added with MTBE (500 mL) for slurring to give compound **72** (9007 mg, yield: 64%, *dr* = 1:1). MS (ESI): (M+H)⁺, calculated 455.2, found 455.2.

72 (4000 mg, 8.8 mmol, *dr* = 1:1) and 100 mL of THF (commercially available) were added to a reaction flask at 0 °C. The mixture was stirred while DBU (1337 mg, 8.8 mmol) was slowly added. After half an hour of reaction, the mixture was warmed to room temperature. After the starting materials disappeared as monitored by TLC, the solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH 95:5) to give compound **73** (1776 mg, yield: 87%, *dr* = 1:1). MS (ESI): (M+H)⁺, calculated 233.1, found 233.2.

Compound **73** (1624 mg, 7 mmol, *dr* = 1:1), Fmoc-Val-OSu (362 mg, 8.4 mmol, CASRN: 688585-20-8), and *N,N*-dimethylformamide (150 mL) were added to a reaction flask. The mixture was stirred while DIEA (1158 µL, 7 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 12 h. The solvent was removed by concentration under reduced pressure, and 50 mL of EA and 50 mL of PE were added for slurring, resulting in the precipitation of a white solid. The procedures were repeated three times to give compound **74** (*dr* = 1:1). MS (ESI): (M+H)⁺, calculated 554.3, found 554.4.

Compound **74** (1303 mg, 2.4 mmol, *dr* = 1:1), 4-nitrophenyl chloroformate (964.8 mg, 4.8 mmol), and THF (120 mL) were added to a reaction flask, and the mixture was stirred while Py (382.8 µL, 4.8 mmol) was added dropwise. The mixture was reacted at 65 °C for 1 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH 98:2) to give compound **75** (1430 mg, yield: 83%, *dr* = 1:1). MS (ESI): (M+Na)⁺, calculated 741.3, found 741.5.

Compound **75** (1554 mg, 2.2 mmol, *dr* = 1:1), exatecan mesylate **76** (520 mg, 1.8 mmol), and *N,N*-dimethylformamide (80 mL) were added to a reaction flask, and the mixture was stirred while DIEA (740 µL, 4.5 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 20 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH 95:5) to give compound **77** (1442 mg, yield: 79%, *dr* = 1:1). MS (ESI): (M+H)⁺, calculated 1015.4, found 1015.1.

77 (1400 mg, 1.37 mmol, *dr* = 1:1) and 35 mL of THF (commercially available) were added to a reaction flask at 0 °C. The mixture was stirred while DBU (209 mg, 1.37 mmol) was slowly

added. After half an hour of reaction, the mixture was warmed to room temperature and then reacted for 40 min until the starting materials disappeared as detected by TLC. The reaction liquid was concentrated under vacuum to remove THF, and the residue was added with DCM/PE (20 mL/200 mL) for slurring. The mixture was filtered through a suction funnel to give **78** (1032 mg, yield: 95%, $dr = 1:1$). MS (ESI): $(M+H)^+$, calculated 793.3, found 793.6.

Compound **78** (793 mg, 1 mmol, $dr = 1:1$), **18** (426 mg, 1.2 mmol), EDCI (382 mg, 2 mmol), HOBT (202 mg, 1.5 mmol), and *N,N*-dimethylformamide (10 mL) were added to a reaction flask. The mixture was reacted at 25 °C for 1 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by C18 (60% ACN/0.05% formic acid in H₂O) and lyophilized to give compound **79** (960 mg, yield: 85%, $dr = 1:1$). MS (ESI): $(M+H)^+$, calculated 1130.4, found 1130.7.

Compound **79** (903 mg, 0.8 mmol), compound **80** (702 mg, 1.2 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (34.7 mg, 0.08 mmol), and copper(I) bromide (11.4 mg, 0.08 mmol) were added to a reaction flask. The mixture was purged three times with nitrogen, and a mixture of THF/DMF/H₂O (3.5 mL:0.6 mL:0.4 mL) was added. The resulting mixture was reacted at 25 °C for 0.5 h. The residue was purified by preparative C18 (62% ACN/0.05% formic acid in H₂O) to give compound **LD55** (1180 mg, yield: 86%, $dr = 1:1$). MS (ESI): $(M+H)^+$, calculated 1715.7, found 1716.2.

LD55 (1180 mg, $dr = 1:1$) was separated by preparative chromatography on a preparative column (Welch Xtimate C18 30 × 250 mm × 10 μm) using ACN/H₂O (0.05% formic acid) to give **LD55-1** (550 mg, HPLC retention time: 18.397 min) and **LD55-2** (520 mg, HPLC retention time: 18.163 min).

Note: HPLC instrument information: Thermo liquid chromatograph (ADC-U3000-01); chromatographic column: Hypersil GOLD™ (4.6 × 250 mm, 5 μm); column temperature: 30 °C; sample tray temperature: 10 °C; mobile phase: A: water + 0.05% TFA; B: ACN; flow rate: 1.0 mL/min; detection wavelength: 254 nm; sample injection volume: 10 μL.

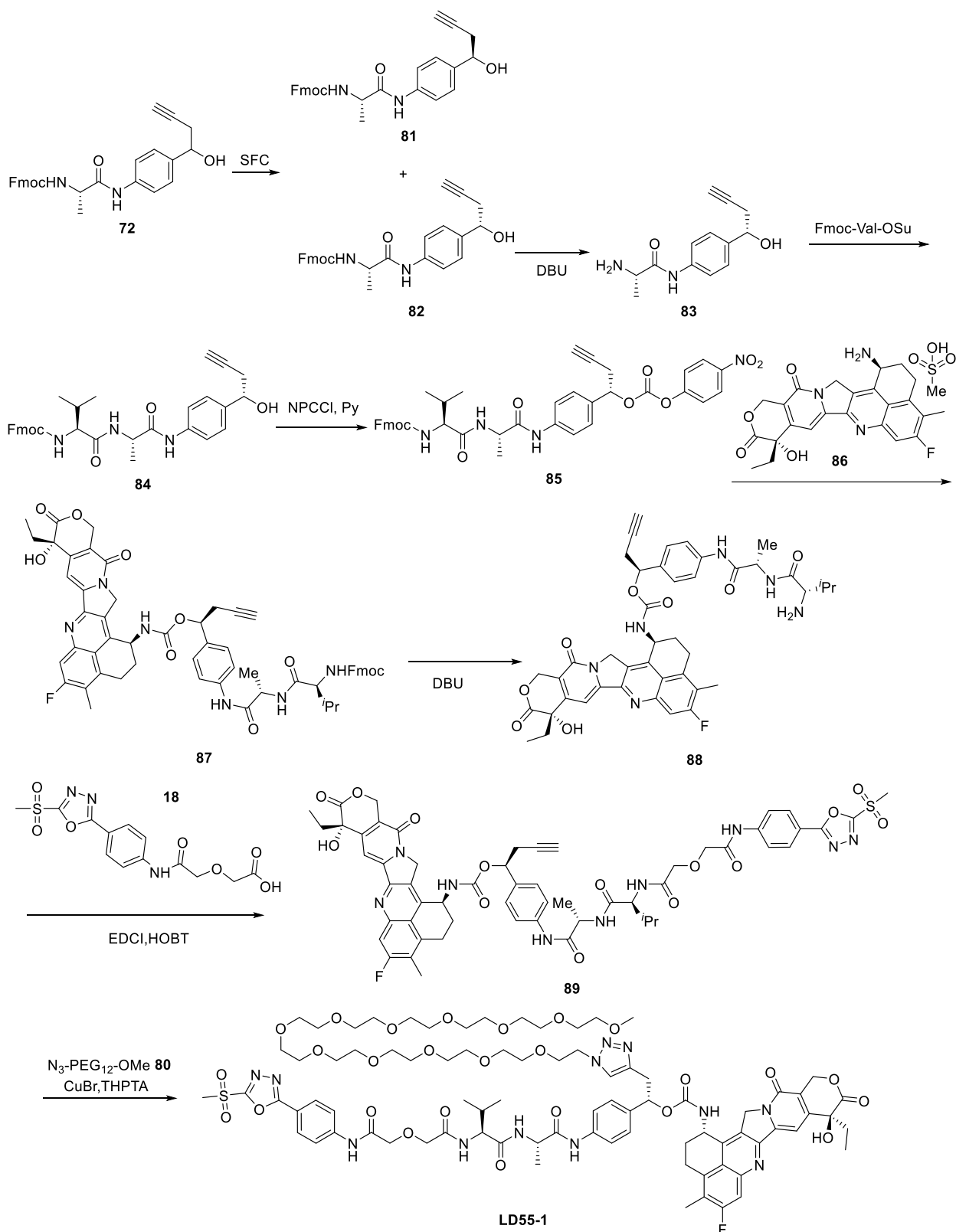
Gradient conditions:

Time (min)	A%	B%
0.000	95.0	5.0
2.000	95.0	5.0
5.000	70.0	30.0

9.000	70.0	30.0
14.000	50.0	50.0
18.000	40.0	60.0
20.000	5.0	95.0
22.000	5.0	95.0
22.100	95.0	5.0
25.000	95.0	5.0

Compounds **LD1-LD54**, **LD56-LD144**, **LD2-1**, **LD2-2**, **LD7-1**, **LD7-2**, **LD12-1**, and **LD12-2** can also be synthesized with reference to the same method.

Example 14: Synthesis of **LD55-1** From Chiral Starting Material **82** Obtained by Resolution of Racemic Starting Material **72**



Chiral resolution of intermediate **72**: Compound **72** (50 g) was resolved by SFC to give **81** (19 g, retention time: 13.55 min) and **82** (20 g, retention time: 16.29 min). SFC resolution method: column model: DAICEL CHIRALCEL OD (250 mm-50 mm, 10 μ m); mobile phase: A: CO₂, B: CO₂-ACN/*i*-PrOH (0.1% NH₃H₂O); isocratic elution: B in A for 50%; flow rate: 200

mL/min; detector: PDA; column temperature: 25 °C; back pressure: 100 Bar.

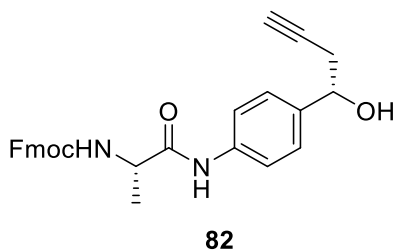
HPLC method: instrument information: Thermo liquid chromatograph (ADC-U3000-01); chromatographic column: CHIRALPAK®ID (4.6 × 150 mm, 5 μm); column temperature: 25 °C; sample tray temperature: 25 °C; mobile phase: A: 10 mM NH₄FA; B: ACN; flow rate:

5 0.8 mL/min; detection wavelength: 254 nm; sample injection volume: 2 μL.

Gradient conditions:

Time (min)	A%	B%
0	40.0	60.0
30.000	40.0	60.0

The structure and configuration of compound **82**, confirmed by X-RAY, are as follows, and its single crystal diffraction pattern is shown in FIG. 1:



10 **82** (3632 mg, 8 mmol) and 90 mL of THF (commercially available) were added to a reaction flask at 0 °C. The mixture was stirred while DBU (1215 mg, 8 mmol) was slowly added. After half an hour of reaction, the mixture was warmed to room temperature. After the starting materials disappeared as monitored by TLC, the solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH
15 95:5) to give compound **83** (1707 mg, yield: 92%). MS (ESI): (M+H)⁺, calculated 233.1, found 233.2.

Compound **83** (1624 mg, 7 mmol), Fmoc-Val-OSu (362 mg, 8.4 mmol), and *N,N*-dimethylformamide (150 mL) were added to a reaction flask. The mixture was stirred while DIEA (1158 μL, 7 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for
20 12 h. The solvent was removed by concentration under reduced pressure, and 50 mL of EA and 50 mL of PE were added for slurring, resulting in the precipitation of a white solid. The procedures were repeated three times to give compound **84**. MS (ESI): (M+H)⁺, calculated 554.3, found 554.4.

Compound **84** (1661 mg, 3 mmol), 4-nitrophenyl chloroformate (1206 mg, 6 mmol), and THF
25 (150 mL) were added to a reaction flask, and the mixture was stirred while Py (474 μL, 6 mmol)

was added dropwise. The mixture was reacted at 65 °C for 1 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH 98:2) to give compound **85** (1831 mg, yield: 85%). MS (ESI): (M+H)⁺, calculated 719.8, found 719.9.

- 5 Compound **85** (1436 mg, 2 mmol), exatecan mesylate **86** (1168.2 mg, 2.2 mmol), and *N,N*-dimethylformamide (100 mL) were added to a reaction flask, and the mixture was stirred while DIEA (695 µL, 4 mmol) was slowly added dropwise. The mixture was reacted at 25 °C for 20 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by silica gel chromatography (DCM/MeOH 95:5) to give compound **87** (1664 mg, yield: 82%). MS (ESI): (M+H)⁺, calculated 1015.4, found 1015.1.

- 10 **87** (1522 mg, 1.5 mmol) and 40 mL of THF (commercially available) were added to a reaction flask at 0 °C. The mixture was stirred while DBU (228 mg, 1.5 mmol) was slowly added. After half an hour of reaction, the mixture was warmed to room temperature and then reacted for 40 min until the starting materials disappeared as detected by TLC. The reaction liquid was concentrated under vacuum to remove THF, and 15 mL of DCM and 300 mL of PE were added, yielding a large amount of yellowish-green solid. The solid **88** (1177 mg, yield: 99%) was obtained by filtration through a Buchner funnel. MS (ESI): (M+H)⁺, calculated 793.3, found 793.6.

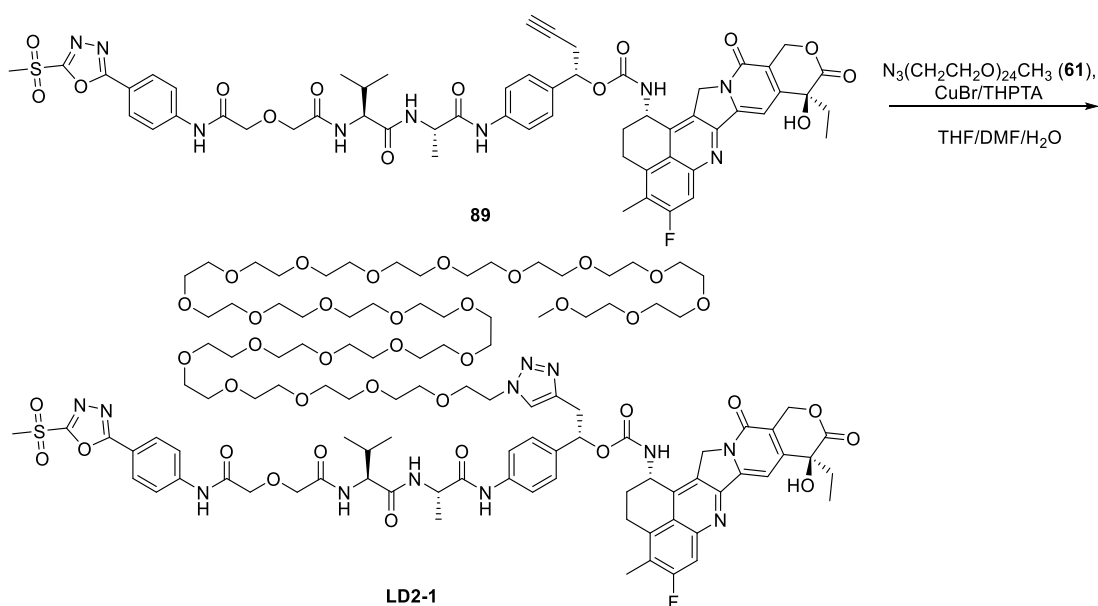
- 15 Compound **88** (1031 mg, 1.3 mmol), **18** (554 mg, 1.56 mmol), EDCI (498 mg, 2.6 mmol), HOBT (263 mg, 1.95 mmol), and *N,N*-dimethylformamide (20 mL) were added to a reaction flask. The mixture was reacted at 25 °C for 1 h. The solvent was removed by concentration under reduced pressure, and the residue was purified by C18 (60% ACN/0.05% formic acid in H₂O) and lyophilized to give compound **89** (1322 mg, yield: 90%). MS (ESI): (M+H)⁺, calculated 1130.4, found 1130.7.

- 25 Compound **89** (903 mg, 0.8 mmol), compound **80** (702 mg, 1.2 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (34.7 mg, 0.08 mmol), and copper(I) bromide (11.4 mg, 0.08 mmol) were added to a reaction flask. The mixture was purged three times with nitrogen, and a mixture of THF/DMF/H₂O (3.5 mL:0.6 mL:0.4 mL) was added. The resulting mixture was reacted at 25 °C for 0.5 h. The residue was purified by preparative C18 (62% ACN/0.05% formic acid in H₂O) to give compound **LD55-1** (1276 mg, yield: 93%). MS (ESI): (M+H)⁺, calculated 1715.7, found 1716.2. ¹H NMR (600 MHz, DMSO) δ 10.71 (s, 1H), 10.08 (s, 1H), 8.48 (d, *J* = 6.7 Hz, 1H), 8.17 (d, *J* = 8.6 Hz, 3H), 8.09 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.89 (s, 1H), 7.81 (d, *J* = 10.8 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.36 (m, 3H), 6.61 (s, 1H), 6.02 (t, *J* = 6.8 Hz, 1H), 5.55 (s, 2H), 5.38 – 5.26 (m, 3H), 4.55 – 4.47 (m, 3H), 4.46 –
- 30

4.41 (m, 1H), 4.36 (q, $J = 15.6$ Hz, 2H), 4.28 (s, 2H), 3.80 (s, 5H), 3.62 – 3.55 (m, 36H), 3.52 – 3.47 (m, 9H), 3.44 – 3.36 (m, 2H), 3.30 – 2.29 (m, 1H), 3.19 – 3.09 (m, 1H), 2.42 (s, 3H), 2.28 – 2.19 (m, 1H), 2.17 (s, 3H), 2.17 – 2.10 (m, 1H), 2.04 – 1.89 (m, 2H), 1.42 (d, $J = 7.0$ Hz, 3H), 1.02 (d, $J = 6.7$ Hz, 3H), 0.98 (t, $J = 7.2$ Hz, 6H).

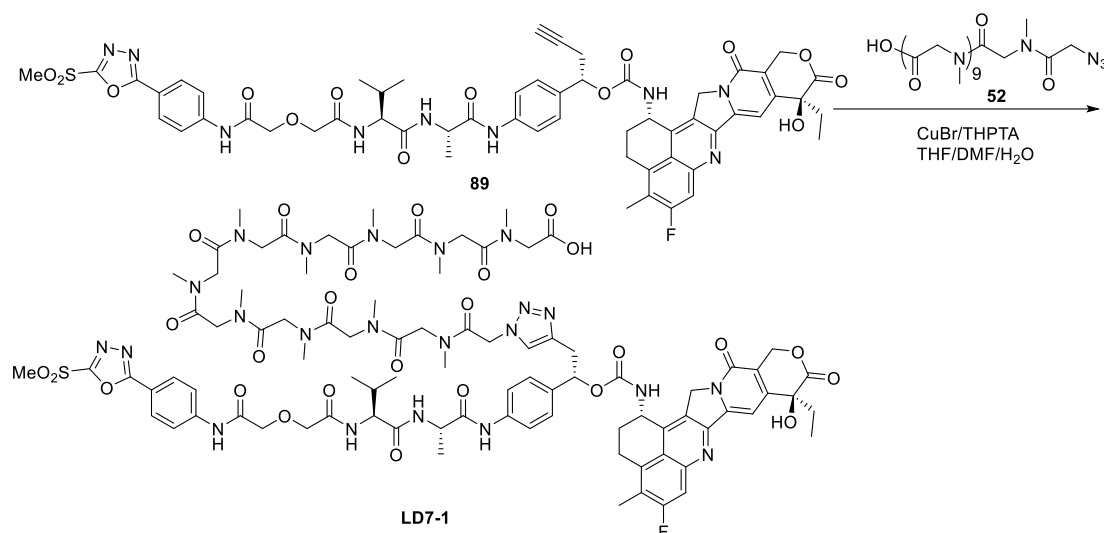
- 5 By comparison with the HPLC method for **LD55-1** in Example 13, it was determined that the retention time of the separated product **LD55-1** in this step was consistent with that of **LD55-1** in Example 13.

Example 15: Synthesis of **LD2-1**



- 10 Compound **89** (113 mg, 0.1 mmol), compound **61** (134 mg, 0.12 mmol), tris(3-hydroxypropyl)triazolylmethylamine (4.3 mg, 0.01 mmol), and copper(I) bromide (14 mg, 0.01 mmol) were added to a reaction flask. The mixture was purged three times with nitrogen, and a mixture of THF/DMF/H₂O (1 mL:0.2 mL:0.2 mL) was added. The resulting mixture was reacted at 25 °C for 0.5 h. The residue was purified by preparative C18 (60% ACN/0.05% formic acid in H₂O) to give compound **LD2-1** (199.7 mg, yield: 89%). MS (ESI): (1/2 M+H)⁺, calculated 1123.0, found 1123.0.
- 15

Example 16: Synthesis of **LD7-1**



Compound **89** (113 mg, 0.1 mmol), compound **52** (99.3 mg, 0.12 mmol), tris(3-hydroxypropyltriazolylmethyl)amine (4.3 mg, 0.01 mmol), and copper(I) bromide (14 mg, 0.01 mmol) were added to a reaction flask. The mixture was purged three times with nitrogen, and a mixture of THF/DMF/H₂O (1 mL:0.2 mL:0.2 mL) was added. The resulting mixture was reacted at 25 °C for 0.5 h. The residue was purified by preparative C18 (55% ACN/0.05% formic acid in H₂O) to give compound **LD7-1** (180 mg, yield: 93%). $(1/2 \text{ M}+\text{H})^+$, calculated 971.4, found 971.5.

Example 17: Synthesis of **LD12-1**

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Example 18: General Method for ADC Sample Preparation and DAR Determination

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room temperature for 1-1.5 h. The reduced intermediate state of the antibody could be monitored by CE-SDS. After the antibody was completely reduced, an appropriate amount of a saturated citric acid solution was first added to adjust the pH to about 6.5, and then an excess of a solution of the linker-drug in DMSO was added to make the equivalents of the linker-drug 15-20 times those of the antibody. The conjugation reaction was performed at room temperature for about 30 min. After the conjugation was completed, the reaction liquid was first filtered, and then subjected to buffer exchange by ultrafiltration using a centrifugal concentration tube to remove excess linker-drug and other small-molecule impurities. After the purification was completed, the resulting sample was subjected to DAR determination by reversed-phase chromatography.

Preparation method for T-ADCs

The concentration of the antibody trastuzumab was adjusted to 10 g/L using a phosphate buffer solution (pH 7.0), and the antibody solution after buffer exchange was placed into a centrifuge tube, followed by the addition of 8.0 equivalents of 5 mM TCEP (Adamas-beta, Ltd.). The mixture was reacted at room temperature for 1 h to reduce the interchain disulfide bond of the antibody to sulfhydryl. Subsequently, a 20 mM solution of linker-drug in DMSO (15 equivalents of toxin per antibody) was added. The mixture was reacted at 10 °C for 1 h. After conjugation, the solution was purified via an ultrafiltration membrane cassette (Cobetter, Ltd.) to remove the residual linker-toxin, followed by storage in PBS at pH 7.4. The average drug loading per antibody was determined by reversed-phase chromatography.

Preparation method for F-ADCs and FS-ADCs

The concentration of the antibody farletuzumab or farletuzumab FcS was adjusted to 10 g/L using a phosphate buffer solution (pH 7.0), and the antibody solution after buffer exchange was placed into a centrifuge tube, followed by the addition of 7.0 equivalents of 5 mM TCEP (Adamas-beta, Ltd.). The mixture was reacted at 37 °C for 1 h to reduce the interchain disulfide bond of the antibody to sulfhydryl. Subsequently, a 20 mM solution of linker-drug in DMSO (10 equivalents of toxin per antibody) was added. The mixture was reacted at 10 °C for 1 h. After conjugation, the solution was purified via an ultrafiltration tube to remove the residual linker-toxin, followed by storage in PBS at pH 7.4. The average drug loading per antibody was determined by reversed-phase chromatography.

Preparation method for D-ADCs

The concentration of the antibody 33B was adjusted to 10 g/L using a phosphate buffer solution (pH 7.0), and the antibody solution after buffer exchange was placed into a centrifuge tube, followed by the addition of 10.0 equivalents of 5 mM TCEP (Adamas-beta, Ltd.). The mixture

was reacted at 37 °C for 1 h to reduce the interchain disulfide bond of the antibody to sulfhydryl. Subsequently, a 20 mM solution of linker-drug in DMSO (12 equivalents of toxin per antibody) was added. The mixture was reacted at 25 °C for 1 h. After conjugation, the solution was purified via an ultrafiltration membrane cassette (Cobetter, Ltd.) to remove the residual linker-toxin, followed by storage in PBS at pH 7.4. The average drug loading per antibody was determined by reversed-phase chromatography.

Preparation method for B-ADCs

The concentration of the antibody 43B was adjusted to 10 g/L using a phosphate buffer solution (pH 7.0), and the antibody solution after buffer exchange was placed into a double-layer glass reaction kettle, followed by the addition of 12.0 equivalents of 100 mM TCEP (Adamas-beta, Ltd.). The mixture was reacted at 37 °C for 3 h to reduce the interchain disulfide bond of the antibody to sulfhydryl. Subsequently, a 10 mM solution of linker-drug in DMSO (10 equivalents of toxin per antibody) was added at room temperature. The mixture was reacted at 25 °C for 30 min. After conjugation, the solution was purified via protein A to remove the residual linker-toxin, followed by storage in PBS at pH 7.4. The average drug loading per antibody was determined by reversed-phase chromatography.

ADCs with different Dar values can be obtained by adjusting the amounts of TCEP and linker-drug used.

The statistical data for all ADC samples are shown in the table below.

Table 8

ADC drug No.	Linker-drug No.	Antibody A (target)	DAR
ADC01	LD1	Trastuzumab (HER2)	7.7
ADC02	LD2	Trastuzumab (HER2)	7.8
ADC03	LD3	Trastuzumab (HER2)	7.6
ADC04	LD4	Trastuzumab (HER2)	7.9
ADC05	LD5	Trastuzumab (HER2)	7.8
ADC06	LD6	Trastuzumab (HER2)	7.8
ADC07	LD7	Trastuzumab (HER2)	7.9
ADC08	LD8	Trastuzumab (HER2)	7.6
ADC09	LD9	Trastuzumab (HER2)	7.7
ADC10	LD10	Trastuzumab (HER2)	7.6
ADC11	LD11	Trastuzumab (HER2)	7.8
ADC12	LD12	Trastuzumab (HER2)	7.6

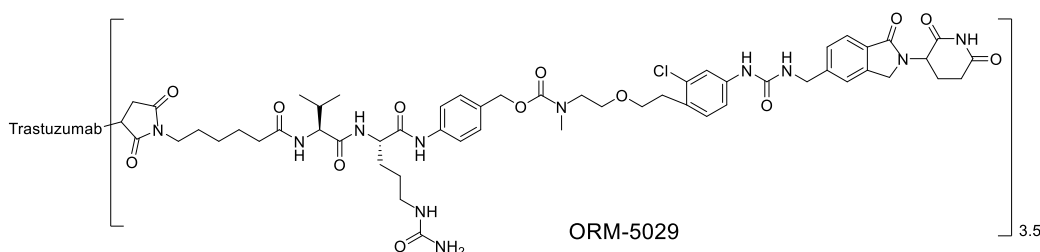
ADC13	LD13	Trastuzumab (HER2)	7.9
ADC14	LD14	Trastuzumab (HER2)	7.5
ADC15	LD15	Trastuzumab (HER2)	7.8
ADC16	LD16	Trastuzumab (HER2)	7.7
ADC17	LD17	Trastuzumab (HER2)	7.9
ADC18	LD18	Trastuzumab (HER2)	7.9
ADC19	LD19	Trastuzumab (HER2)	7.6
ADC20	LD20	Trastuzumab (HER2)	7.8
ADC21	LD21	Trastuzumab (HER2)	7.8
ADC22	LD22	Trastuzumab (HER2)	7.6
ADC23	LD23	Trastuzumab (HER2)	7.7
ADC24	LD24	Trastuzumab (HER2)	7.8
ADC25	LD25	Trastuzumab (HER2)	7.6
ADC26	LD26	Trastuzumab (HER2)	7.9
ADC27	LD27	Trastuzumab (HER2)	7.6
ADC28	LD28	Trastuzumab (HER2)	7.6
ADC29	LD29	Trastuzumab (HER2)	7.8
ADC30	LD30	Trastuzumab (HER2)	7.7
ADC31	LD31	Trastuzumab (HER2)	7.9
ADC32	LD32	Trastuzumab (HER2)	7.5
ADC33	LD33	Trastuzumab (HER2)	7.7
ADC34	LD34	Trastuzumab (HER2)	7.6
ADC35	LD35	Trastuzumab (HER2)	7.8
ADC36	LD36	Trastuzumab (HER2)	7.9
ADC37	LD37	Trastuzumab (HER2)	7.7
ADC38	LD38	Trastuzumab (HER2)	7.6
ADC39	LD39	Trastuzumab (HER2)	7.8
ADC40	LD40	Trastuzumab (HER2)	7.7
ADC41	LD41	Trastuzumab (HER2)	7.9
ADC42	LD42	Trastuzumab (HER2)	7.6
ADC43	LD43	Trastuzumab (HER2)	7.5
ADC44	LD44	Trastuzumab (HER2)	7.8

ADC45	LD45	Trastuzumab (HER2)	7.9
ADC46	LD46	Trastuzumab (HER2)	7.7
ADC47	LD47	Trastuzumab (HER2)	7.6
ADC48	LD48	Trastuzumab (HER2)	7.7
ADC49	LD49	Trastuzumab (HER2)	7.9
ADC50	LD50	Trastuzumab (HER2)	7.5
ADC51	LD51	Trastuzumab (HER2)	7.8
ADC52	LD52	Trastuzumab (HER2)	7.9
ADC53	LD53	Trastuzumab (HER2)	7.9
ADC54	LD54	Trastuzumab (HER2)	7.7
T-ADC2-1-8	LD2-1	Trastuzumab (HER2)	7.8
T-ADC7-1-8	LD7-1	Trastuzumab (HER2)	7.9
T-ADC12-1-8	LD12-1	Trastuzumab (HER2)	7.6
F-ADC55-1-8	LD55-1	Farletuzumab (FR α)	7.6
F-ADC55-2-8	LD55-2	Farletuzumab (FR α)	7.8
F-ADC2-1-8	LD2-1	Farletuzumab (FR α)	7.7
F-ADC2-2-8	LD2-2	Farletuzumab (FR α)	7.8
F-ADC12-1-8	LD12-1	Farletuzumab (FR α)	7.7
F-ADC12-2-8	LD12-2	Farletuzumab (FR α)	7.6
F-ADC7-1-8	LD7-1	Farletuzumab (FR α)	7.5
F-ADC7-2-8	LD7-2	Farletuzumab (FR α)	7.7
FS-ADC55-1-8	LD55-1	Farletuzumab-FcS (FR α)	7.9
D-ADC55-1-8	LD55-1	33B(DLL3)	8.0
D-ADC55-2-8	LD55-2	33B(DLL3)	7.7
D-ADC2-1-8	LD2-1	33B(DLL3)	8.0
D-ADC2-2-8	LD2-2	33B(DLL3)	7.9
D-ADC12-1-8	LD12-1	33B(DLL3)	8.0
D-ADC12-2-8	LD12-2	33B(DLL3)	8.0
D-ADC7-1-8	LD7-1	33B(DLL3)	7.9
D-ADC7-2-8	LD7-2	33B(DLL3)	8.0
B-ADC55-1-6	LD55-1	43B(B7H3)	5.7

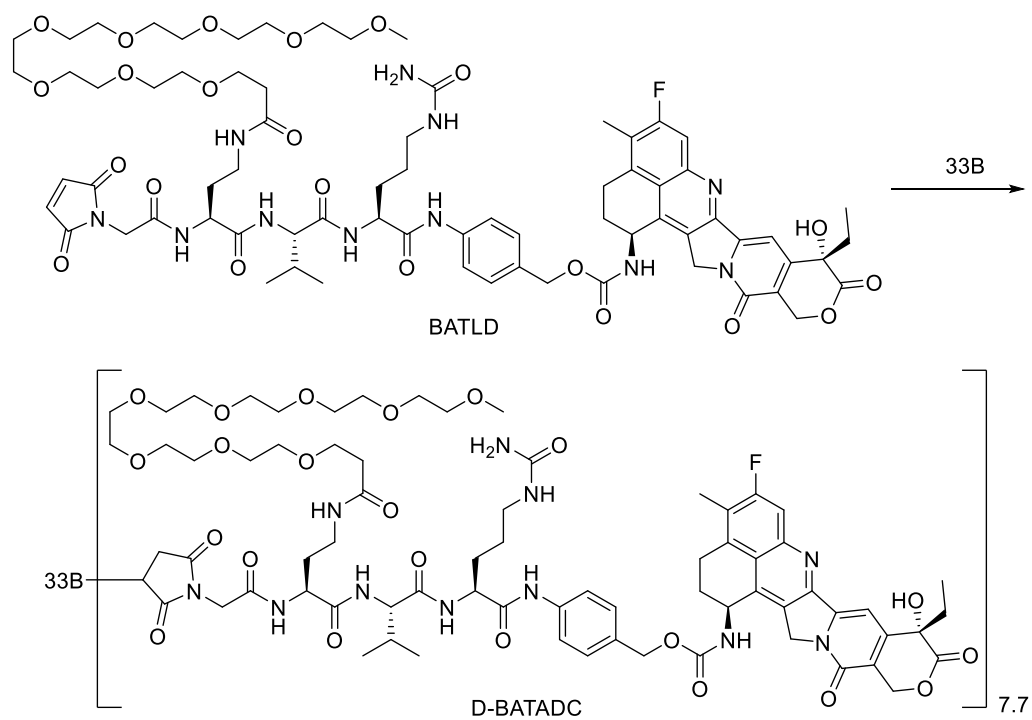
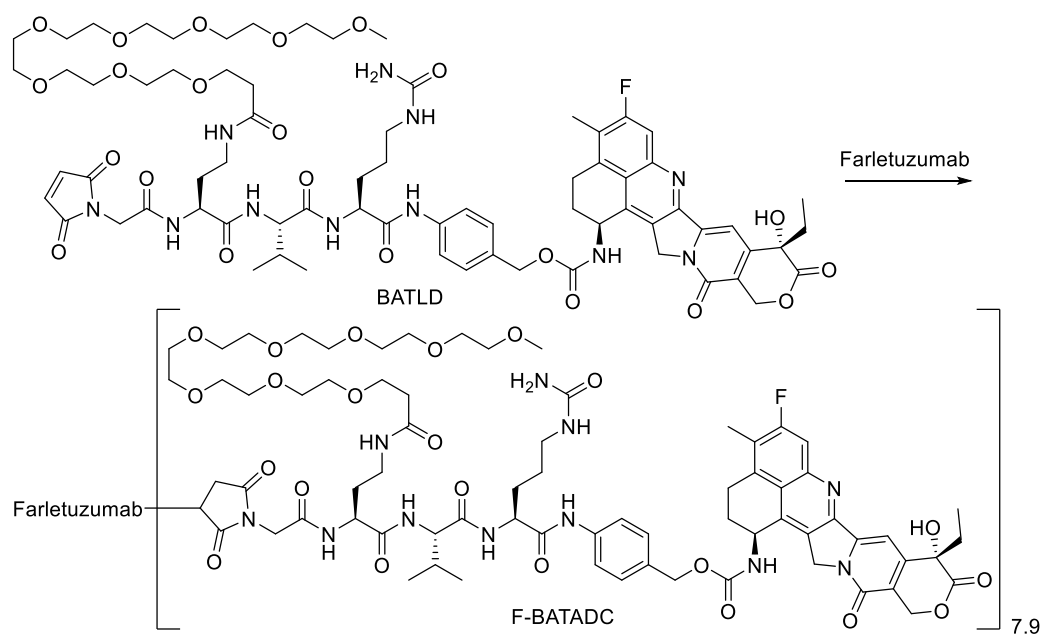
B-ADC55-2-6	LD55-2	43B(B7H3)	5.8
B-ADC2-1-6	LD2-1	43B(B7H3)	5.6
B-ADC2-2-6	LD2-2	43B(B7H3)	6.0
B-ADC12-1-6	LD12-1	43B(B7H3)	6.0
B-ADC12-2-6	LD12-2	43B(B7H3)	5.9
B-ADC7-1-6	LD7-1	43B(B7H3)	5.8
B-ADC7-2-6	LD7-2	43B(B7H3)	5.7
B-ADC-55-1-4	LD55-1	43B(B7H3)	4.0

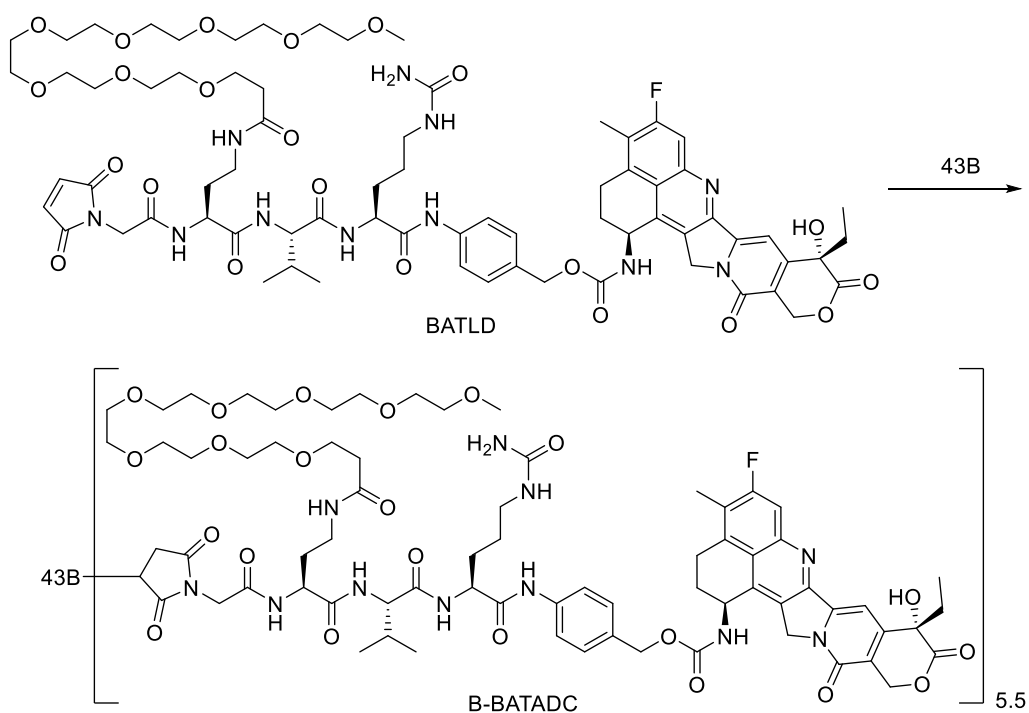
Example 19: Preparation of Control ADC Samples

ORM-5029 was obtained with reference to the method in document WO 2021/198965 A1 to serve as a control example for the HER-2 ADCs, and its DAR was 3.5 as determined by reversed-phase chromatography. Moreover, low-DAR samples of ADC38-ADC44 were obtained under the same conjugation conditions and designated as ADC38-4 to ADC44-4, respectively, and their DARs were also all 3.5 ± 0.1 as determined by LC-MS. In particular, when the linker-drug used in ORM-5029 was employed for antibody conjugation, qualified ADC samples with high Dar values (>7) could not be successfully obtained due to the relatively high aggregate ratio. Enhertu is a commercially available product.

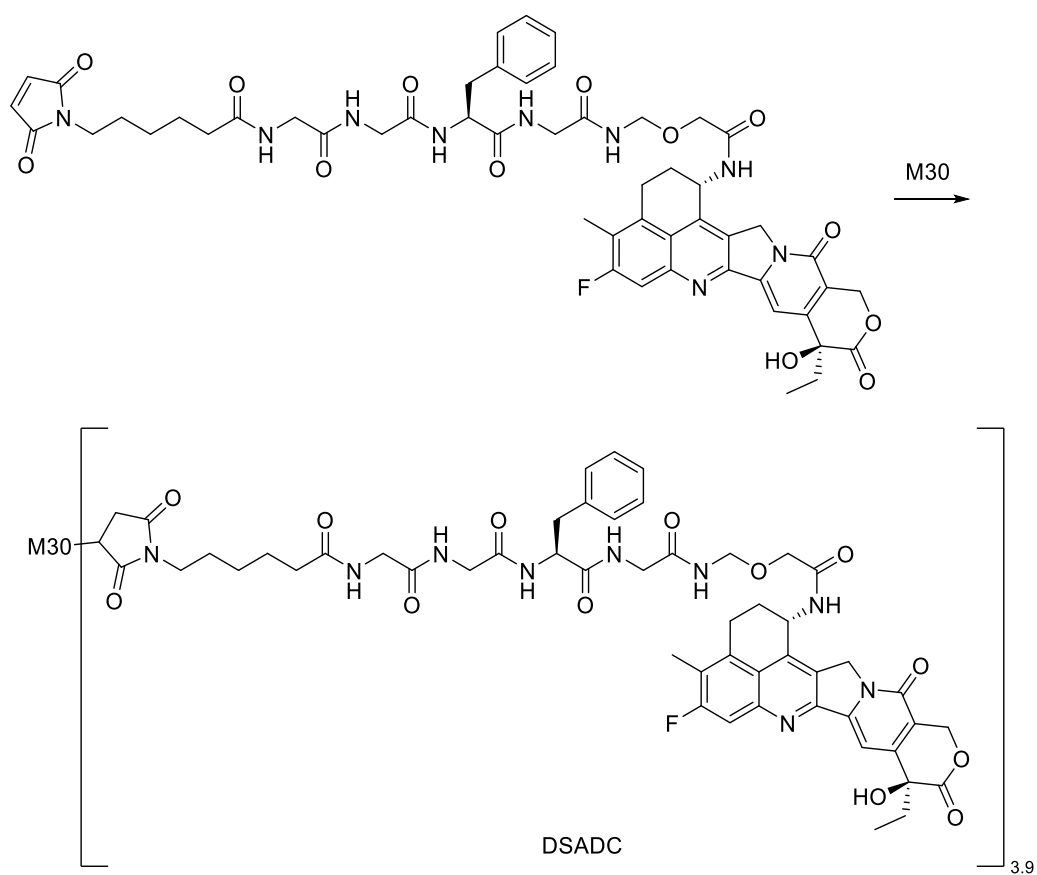


BATLD was synthesized with reference to the method in document CN116333135A. F-BATADC, D-BATADC, and B-BATADC were synthesized using BATLD as a linker-drug and farletuzumab, 33B, and 43B as antibodies with reference to the aforementioned ADC preparation methods, and their DAR values were 7.9, 7.7, and 5.5, respectively, as determined by reversed-phase chromatography.





DSADC was obtained with reference to the method in the document CN104755494A, and its DAR was 3.9 as determined by reversed-phase chromatography.



The sequences of the M30 antibody are as follows:

> M30-H1 (SEQ ID NO: 43)

QVQLVQSGAEVKKPGSSVKVSKASGYTFTNYVMHWVRQAPGQGLEWMGYINPY
 NDDVKYNEKFKGRVTITADESTSTAYMELSSLRSEDNAVYYCARWGYGSPLYYFD
 YWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
 5 LTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC
 DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY
 VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
 KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
 YKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
 10 K

> M30-L4 (SEQ ID NO: 44)

EIVLTQSPATLSLSPGERATLSCRASSRLIYMHWYQQKPGQAPRPLIYATSNLASGIPA
 RFSGSGSGTDFTLTISSELEPEDFAVYYCQQWNSNPPTFGQGTKVEIKRTVAAPSVFIFP
 PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL
 15 SSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC

Efficacy Example 1: Assay for *In Vitro* Activity of ADC Samples

SK-BR-3 cells with high HER2 expression were selected as test cells. The cells were cultured according to the general method and then seeded into a 96-well plate at an appropriate density.

20 After the cell state was observed to be normal, the sample to be tested was added at a concentration gradient of 0-100 nM. After 144 h of culture, the cell viability was determined by the CTG method, and then the IC₅₀ value was calculated.

Table 9

ADC sample No.	IC ₅₀ (pM)
Enhertu	C
ORM-5029	C
ADC38	A
ADC38-4	B
ADC39	A
ADC39-4	B
ADC40	A
ADC40-4	B
ADC41	A

ADC41-4	B
ADC42	A
ADC42-4	B
ADC43	A
ADC43-4	B
ADC44	A
ADC44-4	B

Note: In the table, A represents an IC₅₀ value of <15 pM, B represents an IC₅₀ value between 15 pM and 25 pM, and C represents an IC₅₀ value of >25 pM; Enhertu is a commercially available product.

It can be seen from the activity assay results that the ADCs of the present disclosure exhibited a significant improvement in activity compared to the same-type ADC ORM-5029, and also exhibited a significant improvement in activity compared to Enhertu with the same target.

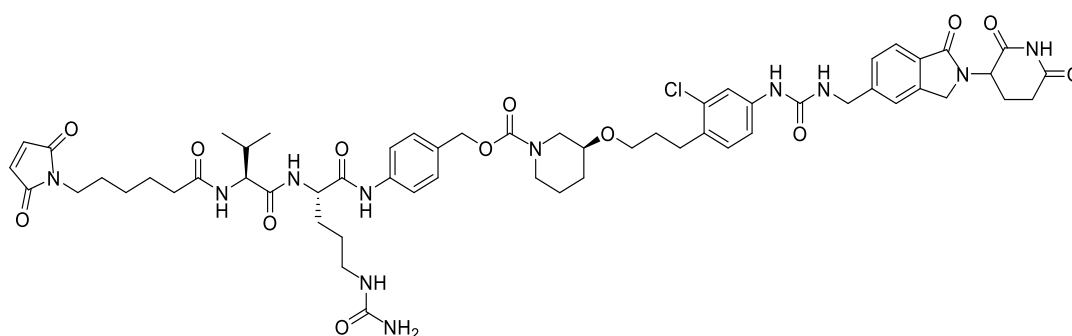
Efficacy Example 2: Assay for *In Vivo* Activity of ADC Samples

JIMT-1 cells with low-to-moderate HER2 expression were selected and inoculated into NUNU mice, and after tumorigenesis, mice with a tumor volume of about 150 mm³ were selected and divided into different groups, with 5 mice in each group. Different drugs were administered via tail vein injection at a preset dose. After administration, the tumor size and mouse body weight were observed and measured periodically. The administration frequency was increased as appropriate. The experiment was terminated when certain conditions were met, the final tumor size and mouse body weight were measured, and the tumor growth inhibition rate was calculated. The assay results are shown in the table below:

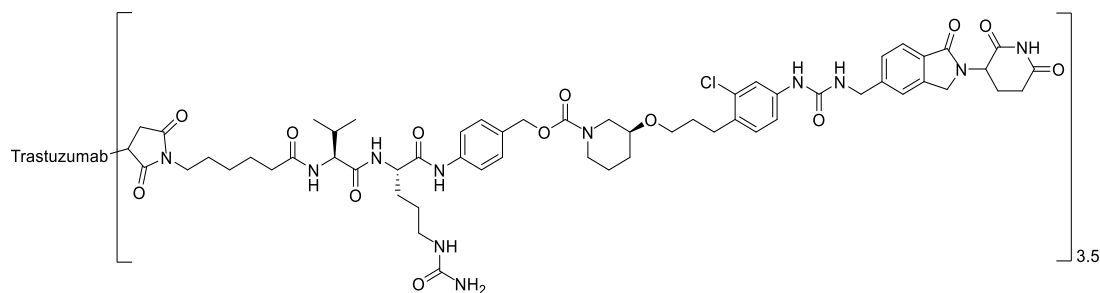
Table 10: *In vivo* efficacy of ADCs with non-hydrophilic linkers

Group	Administration dose (mg/kg)	Administration frequency	TGI%							
			D0	D4	D7	D11	D14	D18	D21	D26
Vehicle	-	D0, D11, D18								
Enhertu	3			44.8	71.9	81.4	95.6	96.0	86.0	74.5
ORM-5029	3			86.8	47.8	24.6	30.8	27.9	23.7	22.4
T-ADC	3			119.8	97.3	61.3	79.3	75.6	69.0	65.0

T-ADC was prepared with reference to the method in the document WO 2021/198965 A1. The following linker-drug compound was first prepared:



which was then conjugated to an antibody to give the target ADC:



T-ADC

5

Table 11: *In vivo* efficacy of ADCs with hydrophilic linkers

Group	Administration dose (mg/kg)	Administration frequency	(1-T/C)% (D13)
Vehicle	-	Single administration	-
Enhertu	5		76.5
ADC38	5		95
ADC40	5		90.1

It can be seen from the *in vivo* efficacy results in Table 10 that among the ADCs using non-hydrophilic linkers, when the linkers were identical, T-ADC exhibited significantly superior efficacy compared to ORM-5029 and slightly lower efficacy compared to Enhertu. It can be seen from the *in vivo* efficacy results in Table 11 that the ADCs using hydrophilic linkers exhibited superior efficacy compared to Enhertu. Based on the results in Tables 10 and 11, it can be concluded that ADCs using hydrophilic linkers exhibit significantly superior efficacy compared to ADCs using non-hydrophilic linkers.

10

Efficacy Example 3: *In Vitro* Cytotoxicity of HER2-ADCs

HER2-ADC-mediated *in vitro* cytotoxicity was evaluated using the HER2-positive cell strain SK-BR-3. Cells were harvested with trypsin, cultured with serially diluted HER2-ADCs, and then incubated at 37 °C. The viability was determined using CTL Plus after 6 days. Readings

15

and analyses were performed on EnVision 2105 (PerkinElmer) to determine IC₅₀ (half-maximal inhibitory concentration) values. SK-BR-3 cells were adjusted to a cell density of 40000 cells/mL with McCoy's 5A + 15% FBS and seeded into a 96-well plate (manufacturer: Corning, Cat. No.: 3599) at 75 µL/well. The plate was left to stand overnight in a Forma™ Steri-Cycle™ i160 CO₂ incubator at 37 °C with 5% CO₂. HER2-ADCs were 5-fold diluted with the medium for the corresponding cells starting at 100 nM to obtain a total of 9 concentration gradients, and then added to the cells at 75 µL/well. The blank control was the medium for the corresponding cells. Two replicate wells were set for each concentration. The SK-BR-3 cells were cultured in a Forma™ Steri-Cycle™ i160 CO₂ incubator at 37 °C with 5% CO₂ for 6 days. After 6 days, 50 µL of CTL Plus (manufacturer: Beyotime, Cat. No.: C0068XL) luminescent reagent was added, and the cells were incubated in the dark at room temperature for 10 min. The chemiluminescence detection was performed on an EnVision 2105 microplate reader. Data analysis and collation: The blank control was taken as a zero-killing control, and the inhibition rate was calculated according to the following formula: inhibition rate (%) = (1 – experimental group/blank control group) × 100. The data were processed and analyzed using GraphPad Prism. The results are shown in the table. The results show that the HER2-ADCs had high *in vitro* cytotoxicity against the HER2-positive cell strain.

Table 12: *In vitro* cytotoxicity of HER2-ADCs

SK-BR-3	IC ₅₀ (nM)
T-ADC2-1-8	0.08855
T-ADC7-1-8	0.0079
T-ADC12-1-8	0.1177

Efficacy Example 4: Determination of ADC Hydrophilicity by Hydrophobic Interaction Chromatography (HIC)

HIC-HPLC conditions: (1) column model: TSKgel Butyl-NPR, 2.5 µm, 4.6 × 100 mm, PN: 0042168; (2) column temperature: 30 °C; (3) UV: 280 nm; (4) mobile phase: A: 1.5 M (NH₄)₂SO₄, 25 mM NaPi, pH 6.73; B: 12.5 mM NaPi (pH 7.28):20% IPA = 80:20 (v:v); (5) flow rate: 0.7 mL/min; (6) elution gradient: 0 min→1.01 min (0% B→20% B), 1.01 min→10 min (20% B→100% B), 10 min→11 min (100% B→100% B), 11 min→11.01 min (100% B→0% B), 11.01 min→17 min (0% B).

Table 13: ADC hydrophilicity

Entry	farletuzumab	F-ADC55-1-8	F-ADC2-1-8	F-ADC12-1-8	F-ADC7-1-8	F-BATADC
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Retention time (min)	4.673	6.123	6.060	4.848	5.087	7.055
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Linkers with high hydrophilicity can not only overcome the problems that many toxins are difficult to conjugate due to poor water solubility, but also reduce the generation of aggregates during the conjugation process, and ensure that ADCs have lower clearance rates and better PK. The data in the table show that different hydrophilic side chains can improve the hydrophilicity of ADCs to different degrees; the naked antibody farletuzumab had the best hydrophilicity, and the ADCs of the present disclosure all exhibited superior hydrophilicity compared to the control F-BATADC.

Efficacy Example 5: Experimental Procedures for Determination of Binding Activity of ADC by Enzyme-Linked Immunosorbent Assay

1. **Antigen coating:** The FOLR1 (manufacturer: Sino Biological, Cat. No.: 11241-H08H) antigen was diluted to 0.1 µg/mL with a coating solution (0.05 mol/L carbonate buffer, pH 9.6) and added to an ELISA-specific polystyrene microplate (manufacturer: Corning, Cat. No.: 3590) at 100 µL/well. The plate was incubated at 4 °C overnight for antigen coating.
2. **Blocking:** The coating solution in the microplate was discarded. The microplate was washed 3 times with a washing solution PBST (PBS containing 0.05% Tween-20 10 mM, pH 7.4), and 300 µL of 2% BSA was added to each well. The plate was incubated at 37 °C for 1 h for blocking.
3. **Washing:** The microplate was washed 3 times with a washing solution. Two replicate wells were set for each sample. ADC samples of F-ADC55-1-8 (11-step gradient dilution with 2% BSA, with a maximum concentration of 1000 nM, each with a volume of 100 µL) were added. The plate was incubated at 37 °C for 2 h.
4. **Secondary antibody:** The FRα primary antibody dilution in the microplate was discarded, and the plate was washed 3 times with a washing solution. A secondary antibody (Goat anti-human IgG (L&H) secondary, HRP) was added to each well, and the plate was incubated at 37 °C for 1 h.
5. **Color development:** The secondary antibody dilution was discarded, and the plate was washed 6 times with a washing solution. Subsequently, 100 µL of a TMB substrate solution was added for color development for 6-8 min, and then 100 µL of 2 M diluted hydrochloric acid was added to terminate the reaction.
6. **Plate reading:** After the reaction was terminated, the absorbance at OD450 was measured on a microplate reader (manufacturer: BioTek; model: Synergy LX).

7. Calculation of EC₅₀

Table 14: ADC binding activity

Sample No.	EC ₅₀ (nM)
Farletuzumab-FS	0.01987
Farletuzumab	0.02606
F-ADC55-1-8	0.03688

Efficacy Example 6: Pharmacodynamic Evaluation in Human Oral Cancer KB Xenograft Tumor Mouse Model

- 5 Cells were taken from the FR α -positive cell strain KB and inoculated into the right forelimb axilla of nu/nu nude mice at 10⁷ cells/mouse (6 mice per group). When the mean tumor volumes of the mice reached about 100 mm³ (groups 1-6) and 145 mm³ (groups 7-8), the mice were randomly grouped and subjected to administration by a single intravenous injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor
- 10 grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm³) = 1/2 $\times$ (a $\times$ b²) (where a represents the long diameter, and b represents the short diameter). The
- 15 pharmacodynamic evaluation of the test drugs is shown in the table below.

Table 15: Efficacy of groups 1-6 in KB xenograft tumor model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 30) ^a	TGI(%) ^b	P value vs control group ^c	CR
1	Vehicle control (normal saline)	-	98.2 $\pm$ 13.4	2,117.3 $\pm$ 257.6	-	-	0
2	F-ADC55-1-8	3	98.6 $\pm$ 10.6	4.4 $\pm$ 7.4	104.7	< 0.0001	4
3	F-BATADC	3	98.4 $\pm$ 10.1	259.4 $\pm$ 259.2	92.0	< 0.0001	0
4	F-ADC2-1-8	3	98.0 $\pm$ 11.0	3.9 $\pm$ 7.2	104.7	< 0.0001	4
5	F-ADC12-2-8	3	98.2 $\pm$ 10.2	5.4 $\pm$ 6.6	104.6	< 0.0001	3
6	F-ADC12-1-8	3	98.0 $\pm$ 10.0	5.7 $\pm$ 6.6	104.6	< 0.0001	3

Note: a. data are expressed as “mean $\pm$ standard error”; b. TGI % = [1 – (Ti – T0)/(Ci – C0)] $\times$ 100%, where T0 and C0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and Ti and Ci are the mean tumor volumes

of the treatment group and vehicle control group on Day 30, respectively; c. comparison is made with the tumor volume of the vehicle control group.

Table 16: Efficacy of groups 7-8 in KB xenograft tumor model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 20) ^a	TGI(%) ^b	<i>P</i> value vs control group ^c
7	Vehicle control (normal saline)	-	145.4±27.2	1,275.0±228.7	-	-
8	F-ADC55-1-8	1.5	145.4±25.9	82.1±85.8	105.6	< 0.0001

- 5 Note: a. data are expressed as “mean ± standard error”; b. $TGI\% = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 20, respectively; c. comparison is made with the tumor volume of the vehicle control group.
- 10 The ADCs of the present disclosure in the 3 mg/kg test groups exhibited significantly superior efficacy compared to the control group F-BATADC (TGI 92.0%); the tumor growth inhibition (TGI) rates for the test groups were 104.7%, 104.7%, 104.6%, and 104.6%, respectively. Within the test groups, 4, 4, 3, and 3 mice achieved CR, respectively. In addition, there was no significant difference in efficacy among the ADCs with linkers of different chiral
- 15 configurations. When the administration dose of F-ADC55-1-8 was reduced to 1.5 mg/kg, the tumor growth inhibition (TGI) rate could still reach 105.6%. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADCs of the present disclosure well during the treatment period. The specific results are shown in the table.
- 20 **Efficacy Example 7: Pharmacodynamic Evaluation of Test Drugs in Human Lung Adenocarcinoma NCI-H441 Xenograft Tumor Mouse Model**
- Cells were taken from the FR α -positive cell strain NCI-H441 and inoculated into the right forelimb axilla of nu/nu nude mice at 10^7 cells/mouse (6 mice per group). When the mean tumor volumes of the mice reached about 100 mm³ (groups 1-6), the mice were randomly
- 25 grouped and subjected to administration by a single intravenous injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment

on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic

5 evaluation of the test drugs is shown in the table below.

Table 17: Efficacy of each group in NCI-H441 xenograft tumor model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 32) ^a	TGI(%) ^b	P value vs control group ^c
1	Vehicle control (normal saline)	-	107.4±19.8	524.9±172.4	-	-
2	F-ADC55-1-8	1	107.1±19.5	33.9±13.0	117.5	< 0.0001
3	F-BATADC	1	107.3±15.2	109.6±20.9	99.5	< 0.0001
4	F-ADC2-1-8	1	107.4±17.9	34.6±20.8	117.4	< 0.0001
5	F-ADC12-1-8	1	107.4±16.4	61.9±33.9	110.9	< 0.0001
6	F-ADC12-2-8	1	107.3±15.5	35.0±21.8	117.3	< 0.0001

Note: a. data are expressed as “mean ± standard error”; b. $\text{TGI \%} = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 32, respectively; c. comparison is made with the tumor volume of the vehicle control group.

Compared to the vehicle control group, the ADCs of the present disclosure in the 1 mg/kg test groups significantly inhibited the tumor growth in the NCI-H441 model, exhibiting significantly superior anti-tumor efficacy compared to the control group F-BATADC. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADCs of the present disclosure well during the treatment period. The specific results are shown in the table.

Efficacy Example 8: Pharmacodynamic Evaluation of Test Drug in Human Colon Cancer SW620 Xenograft Tumor Mouse Model

Cells were taken from the FR α -positive cell strain SW620 and inoculated into the right forelimb axilla of nu/nu nude mice at 10^7 cells/mouse (6 mice per group). When the mean tumor volumes of the mice reached about 130 mm^3 (groups 1-2), the mice were randomly grouped and subjected to administration by a single intravenous injection. The day of grouping was defined

as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects.

- 5 Calculation formula for tumor volume: Tumor volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic evaluation of the test drug is shown in the table below.

Table 18: Efficacy of each group in SW620 xenograft tumor model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 14) ^a	TGI(%) ^b	P value vs control group ^c
1	Vehicle control (normal saline)	-	129.5±19.6	847.0±212.3	-	-
2	F-ADC55-1-8	1.5	130.3±15.3	35.0±18.1	113.3	< 0.0001

- 10 Compared to the vehicle control group, the **ADC** of the present disclosure in the 1.5 mg/kg test group significantly inhibited the tumor growth in the SW620 model. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADC of the present disclosure well during the treatment period. The specific results are shown in the table.

Efficacy Example 9: Pharmacodynamic Evaluation of Test Drugs in Human Ovarian Cancer
15 OV-90 Xenograft Tumor Mouse Model

- Cells were taken from the FR α -positive cell strain OV-90 and inoculated into the right forelimb axilla of NCG and NOD SCID immunodeficient mice aged 4-6 weeks at 10^7 cells/mouse (3 mice per group). When the mean tumor volumes of the mice reached about 180 mm^3 (groups 1-3) and 145 mm^3 (groups 4-5), the mice were randomly grouped and subjected to
20 administration. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor
25 volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic evaluation of the test drugs is shown in the table below.

Table 19: Efficacy of each group in OV-90 xenograft tumor model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 11) ^a	TGI(%) ^b	<i>P</i> value vs control group ^c
1 ^d	Vehicle control (normal saline)	-	182.0±1.8	877.0±47.5	-	-
2 ^d	F-ADC55-1-8	1	180.7±33.8	104.9±30.0	110.9	< 0.0001
3 ^d	F-ADC55-1-8	5	181.4±37.7	37.5±1.3	120.7	< 0.0001
4 ^e	Vehicle control (normal saline)	-	142.3±39.9	587.2±217.8	-	-
5 ^e	F-ADC55-1-8	3	145.2±10.7	29.2±8.4	126.1	< 0.0001

Note: a. data are expressed as “mean ± standard error”; b. $TGI\% = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 11, respectively; c. comparison is made with the tumor volume of the vehicle control group; d. NCG immunodeficient mice; e. NOD SCID immunodeficient mice.

Compared to the vehicle control group, the ADCs of the present disclosure in the 1/3/5 mg/kg groups all significantly inhibited the tumor growth in the OV-90 model, with tumor growth inhibition (TGI) rates of 110.9%, 126.1%, and 120.7%, respectively. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADCs of the present disclosure well during the treatment period. The specific results are shown in the table.

Efficacy Example 10: Determination of Positive Rates of DLL3-Expressing Cells by Flow Cytometry

The binding of DLL3 antibodies to DLL3 on the surface of NCI-H209, SHP77, NCI-H526, NCI-H82, and NCI-H69 cells was determined by flow cytometry.

Experimental procedures: NCI-H209, SHP77, NCI-H526, NCI-H82, and NCI-H69 cells were collected and prepared into cell suspensions at 5×10^5 cells/mL with an FACS buffer (pH 7.4 PBS + 2% FBS), and the cell suspensions were added to 96-well round-bottom plates (manufacturer: Corning, Cat. No.: 3795) at 100 μ L/well. After centrifugation, the supernatants were removed, and then D-ADC55-1-8 diluted with an FACS buffer to different concentrations (final concentration: 15 μ g/mL) was added at 100 μ L/well. The plates were incubated in the dark in a refrigerator at 4 °C for 2 h. After the plates were centrifuged and washed 3 times with

an FACS buffer, the Goat anti-Human IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 488 (manufacturer: Invitrogen, Cat. No.: A11013) at a working concentration was added. The plates were incubated in the dark in a refrigerator at 4 °C for 1 h. The geometric mean fluorescence intensity was measured on a CytoFLEX flow cytometer, and DLL3+ % was calculated.

Table 20: Determination of positive rates of DLL3-expressing cells by flow cytometry

Cell line	DLL3+ %	Experimental well: negative control ratio
NCI-H209	44.42%	7.73
SHP77	35.75%	3.23
NCI-H526	29.15%	3.73
NCI-H82	11.25%	5.02
NCI-H69	5.29%	3.03

Efficacy Example 11: Experiment on Determination of DLL3-ADC Binding Activity by Enzyme-Linked Immunosorbent Assay

- 10 The affinities of the antibodies for recombinant human DLL3 proteins were determined by ELISA. Human DLL3 proteins (Kactus Biosystems, Cat. No.: DLL-HM103) were diluted to a final concentration of 0.1 µg/mL and separately plated on 96-well microplates. The plates were incubated at 4 °C overnight. The next day, the supernatants were discarded, and after the blocking was completed, 4-fold serially diluted antibodies (0-100 nM) were added. The
- 15 mixtures were incubated with a secondary antibody and subjected to color development for 10 min using a TMB substrate solution. After the reaction was terminated by adding 2 M HCl, the absorbance values at 450 nm were measured on a microplate reader, and EC₅₀ was calculated. The results are shown in the table and show that the affinities of the ADCs for human DLL3 proteins were substantially comparable to the binding abilities of the antibodies before
- 20 conjugation.

Table 21: Experiment on determination of DLL3-ADC binding activity by enzyme-linked immunosorbent assay

No.	EC ₅₀ (nM)	E _{max}
33B	0.001873	2.5
D-ADC55-1-8	0.006276	2.5
D-ADC2-1-8	0.004644	2.5
D-ADC12-1-8	0.005843	2.6

D-BATADC	0.005266	2.6
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Efficacy Example 12: *In Vitro* Cytotoxicity of DLL3-ADC

The DLL3-positive cell strains NCI-H82, SHP77, NCI-H526, and NCI-H209 and the DLL3-negative cell strains A431 and NCI-H69 were used to evaluate the *in vitro* cytotoxicity mediated by D-ADC55-1-8. Cells were harvested, cultured with serially diluted D-ADC55-1-8, and then incubated at 37 °C. The viability was determined using CTL Plus after 6 days. Readings and analyses were performed on EnVision 2105 (PerkinElmer) to determine IC₅₀ (half-maximal inhibitory concentration) values.

Experimental procedures: The test cells were adjusted to a cell density of 6.7×10^4 cells/mL and seeded into a 96-well plate at 75 µL/well. The plate was incubated overnight in an incubator at 37 °C with 5% CO₂. 5-fold gradient dilutions of D-ADC55-1-8 (0-100 nM) with a total of 9 concentration gradients were added to the cells at 75 µL/well. The blank control was the medium for the corresponding cells. Two replicate wells were set for each concentration. After the cells were cultured in an incubator at 37 °C with 5% CO₂ for 6 days, 50 µL of CTL Plus (manufacturer: Beyotime, Cat. No.: C0068XL) luminescent reagent was added, and the cells were incubated in the dark at room temperature for 10 min. The chemiluminescence detection was performed on an EnVision 2105 microplate reader. Data analysis and collation: The blank control was taken as a zero-killing control, and the inhibition rate was calculated according to the following formula: inhibition rate (%) = $(1 - \text{test group}/\text{blank control group}) \times 100\%$. The data were processed and analyzed using GraphPad Prism, and IC₅₀ was calculated. The results are shown in the table. The results show that D-ADC55-1-8 exhibited good *in vitro* cytotoxicity against the DLL3-positive cell strains.

Table 22: *In vitro* cytotoxicity of DLL3-ADC

Cell line	IC ₅₀ (nM)
NCI-H82	4.4
SHP77	36.56
NCI-H526	16.71
NCI-H209	1.07
NCI-H69	>100
A431	>100

Efficacy Example 13: Pharmacodynamic Evaluation of Test Drugs in Human Small Cell Lung Cancer SHP77 Xenograft Tumor Mouse Model

Cells were taken from the DLL3-positive cell strain SHP77 and inoculated into the right forelimb axilla of nu/nu nude mice at 10^7 cells/mouse (7 mice per group). When the mean tumor volumes of the mice reached about 100 mm^3 (groups 1-6), the mice were randomly grouped and subjected to administration by a single intravenous injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic evaluation of the test drugs is shown in the table below.

Table 23: Pharmacodynamic evaluation of test drugs in human small cell lung cancer xenograft SHP-77 mouse model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 22) ^a	TGI(%) ^b	P value vs control group ^c
1	Vehicle control (normal saline)	-	104.1±15.0	2932.5±443.9	-	-
2	D-ADC55-1-8	1	104.1±14.5	158.3±82.4	98.1	< 0.0001
3	D-ADC2-1-8	1	104.1±15.6	199.2±166.9	96.6	< 0.0001
4	D-ADC12-1-8	1	104.3±14.7	187.7±63.9	97.1	< 0.0001
5	D-ADC12-2-8	1	104.0±15.2	181.8±52.5	97.3	< 0.0001
6	D-BATADC	1	104.0±13.9	672.8±261.2	79.9	< 0.0001

Note: a. data are expressed as “mean ± standard error”; b. $\text{TGI \%} = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 22, respectively; c. comparison is made with the tumor volume of the vehicle control group.

Compared to the vehicle control group, the ADCs of the present disclosure at the dose of 1 mg/kg all significantly inhibited the tumor growth in the SHP-77 model, with tumor growth inhibition (TGI) rates of 98.1%, 96.6%, 97.1%, and 97.3%, respectively, which were significantly superior to that of the control group D-BATADC (TGI 79.9%). No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in

any treatment group. The mice tolerated the ADCs of the present disclosure well during the treatment period. The specific results are shown in the table.

Efficacy Example 14: Pharmacodynamic Evaluation of Test Drug in Human Small Cell Lung Cancer NCI-H526 Xenograft Tumor Mouse Model

- 5 Cells were taken from the DLL3-positive cell strain NCI-H526 and inoculated into the right forelimb axilla of nu/nu nude mice at 10^7 cells/mouse (3 mice per group). When the mean tumor volumes of the mice reached about 160 mm³ (groups 1-2), the mice were randomly grouped and subjected to administration by a single intravenous injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the
- 10 experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm³) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic
- 15 evaluation of the test drug is shown in the table below.

Table 24: Pharmacodynamic evaluation of test drug in human small cell lung cancer xenograft NCI-H526 mouse model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 21) ^a	TGI(%) ^b
1	Vehicle control (normal saline)	-	160.4±40.5	970.0±589.8	-
2	D-ADC55-1-8	3	162.7±21.1	57.3±49.7	113.0

- Note: a. data are expressed as “mean ± standard error”; b. $TGI\% = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T₀ and C₀ are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 21, respectively.
- 20

Efficacy Example 15: Pharmacodynamic Evaluation of Test Drug in Human Small Cell Lung Cancer NCI-H69 Xenograft Tumor Mouse Model

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Cells were taken from the DLL3-positive cell strain NCI-H69 and inoculated into the right forelimb axilla of nu/nu nude mice at 10^7 cells/mouse (3 mice per group). When the mean tumor volumes of the mice reached about 140 mm³, the mice were randomly grouped and

subjected to administration by a single intravenous injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter). The pharmacodynamic evaluation of the test drug is shown in the table below.

Table 25: Pharmacodynamic evaluation of test drug in human small cell lung cancer xenograft NCI-H69 mouse model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 14) ^a	TGI(%) ^b
1	Vehicle control (normal saline)	-	137.1±59.1	908.4±54.3	-
2	D-ADC55-1-8	3	142.7±53.2	323.7±244.6	76.5

Note: a. data are expressed as “mean ± standard error”; b. $\text{TGI \%} = [1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 21, respectively.

In the NCI-H526 and NCI-H69 models, compared to the vehicle control group, the ADC of the present disclosure at the dose of 3 mg/kg significantly inhibited the tumor growth in the NCI-H526 and NCI-H69 models, with tumor growth inhibition (TGI) rates of 113.0% and 76.5%, respectively. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADC of the present disclosure well during the treatment period. The specific results are shown in the tables.

Efficacy Example 16: Determination of ADC Affinities by FACS

The affinities of B-ADC55-1-6, B-ADC2-1-6, B-ADC12-1-6, and DSADC were determined using the B7H3-positive human melanoma cell strain A375. Each sample was diluted to 15000 ng/mL with a PBS solution containing 2% BSA and then serially diluted across 11 gradients to achieve sample concentrations ranging from 0.014 ng/mL to 15000 ng/mL. A375 cells were taken, centrifuged at $500 \times g$ for 5 min, washed 3 times with a PBS solution containing 2%

BSA, incubated with samples at different dilution concentrations at 4 °C for 2 h, further washed, and then incubated with the goat anti-human Alexa Fluor 488 fluorescent dye at 4 °C for 1 h in the dark. After washing, the cells were resuspended, and the mean fluorescence intensity (MFI) of the cells was measured using an Attune NxT flow cytometer (Thermo Fisher Scientific, Inc.).

Table 26: Determination of affinities of ADCs for B7H3 antigen on A375 surface by flow cytometry

ADC No.	EC ₅₀ (ng/mL)
DSADC	92.52
B-ADC55-1-6	37.78
B-ADC2-1-6	41.61
B-ADC12-1-6	40.01

As can be seen from the data described above, the ADCs of the present disclosure exhibited significantly superior affinities for the B7H3 antigen on the surface of A375 compared to the control group DSADC.

Efficacy Example 17: Pharmacodynamic Evaluation of Test Drugs in Human Liver Cancer Hep3B Xenograft Tumor Mouse Model

Cells were taken from the B7H3-positive cell strain Hep3B and inoculated into the right forelimb axilla of nu/nu nude mice aged 4-6 weeks at 10⁷ cells/mouse (6 mice per group). When the mean tumor volumes of the mice reached about 150 mm³, the mice were randomly grouped and subjected to administration by a single injection. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm³) = 1/2 × (a × b²) (where a represents the long diameter, and b represents the short diameter).

Table 27: Pharmacodynamic evaluation of test drugs in liver cancer xenograft Hep3B mouse model

Group	Treatment group	Dose (mg/kg)	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 22) ^a	TGI(%) ^b	P value vs control group ^c
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1	Vehicle control (normal saline)	-	152.9±46.8	2434.6±529.4	-	-
2	B-ADC55-1-6	2	153.0±57.1	917.5±405.8	66.5	< 0.001
3	B-ADC2-1-6	2	152.5±52.7	1138.2±856.6	56.8	< 0.05
4	B-ADC12-1-6	2	153.0±58.6	847.7±384.0	69.6	< 0.01
5	B-BATADC	2	152.7±54.9	1386.2±869.9	45.9	< 0.05

Note: a. data are expressed as “mean ± standard error”; b. TGI % = $[1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$, where T_0 and C_0 are the mean tumor volumes of the treatment group and vehicle control group on the day of grouping (Day 0), respectively, and T_i and C_i are the mean tumor volumes of the treatment group and vehicle control group on Day 22, respectively; c. comparison is made with the tumor volume of the vehicle control group.

Compared to the vehicle control group, the ADCs of the present disclosure in the 2 mg/kg groups all significantly inhibited the tumor growth in the Hep3B model, and the experimental groups were significantly superior to the control group. No animal died or had significant body weight loss and no significant drug toxicity reactions were observed in any treatment group. The mice tolerated the ADCs of the present disclosure well during the treatment period. The specific results are shown in the table.

Efficacy Example 18: Pharmacodynamic Evaluation of Test Drugs in Human Malignant Melanoma Cell A375 Xenograft Tumor Mouse Model

Cells were taken from the B7H3-positive cell strain A375 and inoculated into the right forelimb axilla of nu/nu nude mice aged 4-6 weeks at 10^7 cells/mouse (7 mice per group). When the mean tumor volumes of the mice reached about 130 mm^3 , the mice were randomly grouped and subjected to administration. The day of grouping was defined as Day 0, and the administration was started on Day 0. After tumor grafting, the experimental animals were routinely monitored for tumor growth and the effect of treatment on the normal behavior, specifically the activity, food and water intake, body weight gain or loss (the body weight was measured twice a week), and abnormalities in eyes, fur, and other aspects. Calculation formula for tumor volume: Tumor volume (mm^3) = $1/2 \times (a \times b^2)$ (where a represents the long diameter, and b represents the short diameter).

Table 28: Grouping and administration regimen

Group	Number of animals	Treatment group	Dose (mg/kg)	Route of administration	Administration schedule
1	7	Vehicle control (normal saline)	-	i.v.	Single administration
2	7	DSADC	2	i.v.	Single administration
3	7	B-ADC55-1-6	2	i.v.	Single administration
4	7	B-ADC2-1-6	2	i.v.	Single administration
5	7	B-ADC12-1-6	2	i.v.	Single administration
6	7	B-BATADC	2	i.v.	Single administration

Table 29: Pharmacodynamic evaluation of test drugs in human malignant melanoma cell xenograft A375 mouse model

Group	Test ADC	Mean tumor volume (Day 0) ^a	Mean tumor volume (Day 26) ^a	<i>P</i> value vs control group ^c
1	Vehicle control (normal saline)	128.7±32.9	-	-
2	DSADC	129.7±35.9	2164.1±851.7	< 0.001
3	B-ADC55-1-6	128.9±39.0	144.6±90.1	< 0.001
4	B-ADC2-1-6	129.8±38.3	346.4±144.3	< 0.001
5	B-ADC12-1-6	128.3±29.1	177.1±132.2	< 0.001
6	B-BATADC	129.9±40.1	1026.8±580.7	< 0.001

Note: a. data are expressed as “mean ± standard error”; b. comparison is made with the tumor volume of the vehicle control group.

The data in the table show that on Day 22, the mean tumor volume of the vehicle control group reached 3000 mm³, and the animals were euthanized according to animal welfare. On Day 26, the efficacy of the control group was significantly inferior to that of the test groups at the same dose. The test groups all showed significant tumor inhibitory efficacy compared to the vehicle control group.

Efficacy Example 19: Anti-Tumor Experiment of Antibody-Drug Conjugate on Human Lung Cancer Calu-6 Xenograft Tumors in Mice

In this experiment, age-appropriate NOD/SCID mice were selected to be inoculated with Calu-6 human lung cancer cells. When the tumor volume reached about 100-200 mm³, animals with good tumor growth were selected and evenly divided into groups according to the tumor

volume. The animal grouping and dosing regimen are shown in the table below.

Table 30: Animal grouping and dosing regimen

Group	Number of animals (mice)	Dose (mg/kg)	Route/frequency of administration
Vehicle group	6	0	Intravenous administration/once every two weeks
B-ADC55-1-4	6	3.0	Intravenous administration/once every two weeks

After grouping was completed, administration was performed, and the mouse body weight was measured. The data were recorded. By measuring the tumor diameters at different time points after administration, the tumor growth was dynamically observed, and the tumor volume was calculated using the following formula:

$$\text{Tumor volume (mm}^3\text{)} = 1/2 \times \text{long diameter (mm)} \times [\text{short diameter (mm)}]^2$$

At the end of the experiment, the test sample group could significantly inhibit the tumor growth compared to the vehicle group.

Table 31: Efficacy of ADC on Calu-6 xenograft tumors in tumor-bearing mice

Group	D0 mean tumor volume (mm ³)	D28 mean tumor volume (mm ³)	Tumor growth inhibition (TGI) rate (%)
Vehicle group	157.7±51.2	3041.5±1395.0	N/A
B-ADC55-1-4	158.5±55.3	276.2±123.7	95.9

Efficacy Example 20: Enzyme Digestion Rate Determination

1. CTB activation:

The cathepsin B lyophilized powder (10 units) was diluted to obtain a 10 UN/mL solution with a total volume of 1 mL using a corresponding storage solution (pH = 5.0, 25 mM acetic acid buffer + 1.0 mM EDTA), and the solution was then aliquoted at 50 µL/vial for storage at -80 °C. For the enzyme digestion reaction, 860 µL of a buffer (pH = 5.0) was added to one vial containing 50 µL of the CTB (10 UN/mL) stock solution, and then 100 µL of a Cys (200 mM) activation solution was added, followed by activation for 15 min. A CTB activation solution with a total volume of 1.0 mL and a final concentration of 0.5 UN/mL was thus obtained.

2. Blocking of substrate stock solutions:

5 μL of a 10 mM solution of LD55-1, LD55-2, LD2-1, or LD2-2 in DMSO was measured and taken, and 5 μL of a 100 mM (5.0 equiv) aqueous cysteine (Cys) solution was added. The mixture was mixed homogeneously and subjected to a blocking reaction for 5-10 min. Blocked substrate stock solutions Cys-LD55-1, Cys-LD55-2, Cys-LD2-1, and Cys-LD2-2 were thus obtained, each with a substrate concentration of 5 mM in 10 μL .

3. Enzyme digestion reaction:

10 The final substrate concentration was 40 μM . 2.0 μL of a 5 mM substrate blocking solution was measured and taken, and 250 μL of the 0.5 UN/mL CTB solution was added. The mixture in a total volume of 0.25 mL was incubated at 37 °C, and sampling and detection were performed at intervals of 30 min for 24 h.

4. Sample detection:

15 At the reaction time point, an appropriate amount of sample was taken and diluted with an equal volume of ice-cold MeOH (HPLC-grade) for precipitation. The mixture was then centrifuged at no less than 10000 rpm in a centrifuge at 4 °C for 10 min, and the supernatant was taken for detection.

5. Data results:

20 The drug peak area detected for the drug without enzyme addition was taken as 1, and the percentage obtained by comparing the drug peak area detected by sampling at the corresponding time point with this reference was the drug release proportion at that point. Table 32 records the remaining amounts of Cys-linker-drug after enzyme digestion for Cys-LD55-1, Cys-LD55-2, Cys-LD2-1, and Cys-LD2-2.

Table 32: Enzyme digestion release experiment

Retention (%)	0 min	30 min	60 min	24 h
Cys-LD55-1	100%	1.31%	-	-
Cys-LD55-2	100%	89.47%	-	3.32%
Cys-LD2-1	100%	12.2%	3.20%	-
Cys-LD2-2	100%	93.05%	-	4.89%

25 It can be seen from the enzyme digestion curves that the configurations of Cys-LD55-1, Cys-55-2, Cys-LD2-1, and Cys-LD2-2 could all be completely digested, Cys-LD55-1 and Cys-LD2-1 required about 30-60 min to be completely digested, and Cys-LD55-2 and Cys-LD2-2

required about 24 h to be completely digested.

Efficacy Example 21: Evaluation of ADC Toxicokinetics and Tolerability in Cynomolgus Monkeys

Cynomolgus monkeys (female, 2 monkeys) were selected, and the ADC was administered intravenously (5 mg/mL; injection was completed within 30 min) at a dose level of 10-50 mg/kg every 2-3 weeks (totaling 3 doses). Parameters evaluated during the study included general observation, body weight, food intake, body temperature, electrocardiogram (lead II), clinical pathology (hematology, blood biochemistry, and coagulation), and macroscopic and microscopic examinations of a large number of tissues. Toxicokinetic samples were collected at 0 h, 24 h, 72 h, 120 h, 336 h, and 504 h after completion of each dose administration. The TK samples were analyzed using the MesoScale Discovery (MSD) electrochemiluminescence platform (total monoclonal antibody and total ADC) and LC-MS/MS (free exatecan). The experiment shows that the ADCs of the present disclosure exhibited good tolerability. During the dose investigation, after ADC injection, no abnormalities were observed in the general observation of cynomolgus monkeys, and no toxicological abnormalities were observed in body weight, body temperature, coagulation, or urinalysis. The ADCs of the present disclosure exhibited good tolerability in cynomolgus monkeys and demonstrated stable pharmacokinetic characteristics.

CLAIMS

1. An antibody-drug conjugate having a structure of formula (I), a tautomer, a mesomer, a racemate, an enantiomer, a diastereoisomer, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:



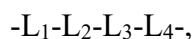
wherein A is a targeting ligand selected from an antibody (e.g., a monoclonal antibody) or an antigen-binding fragment, a small-molecule ligand, and a polypeptide;

L is a linker moiety, with one end linked to the ligand A and the other end linked to a bioactive molecule D;

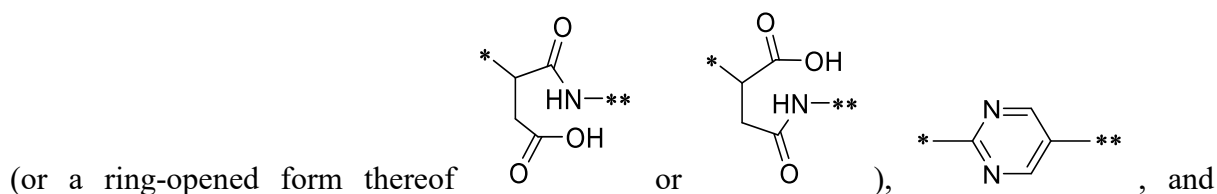
D is an amino-containing bioactive molecule or a tautomer, a mesomer, a racemate, an enantiomer, a diastereoisomer or an isotopically labeled compound thereof, covalently linked to the linker moiety L via the amino group in its molecular structure;

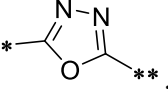
m is an integer or a decimal from 1 to 12;

the linker moiety -L- is represented by the following formula:



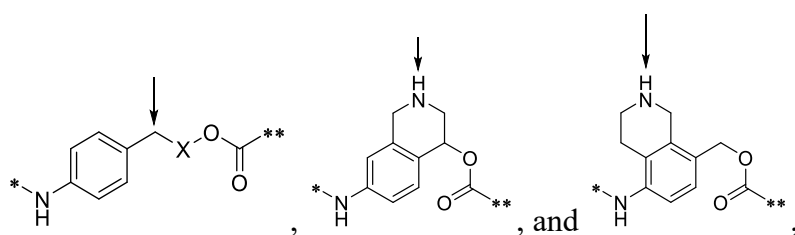
wherein L₁ is a moiety of L linked to the ligand A; preferably, L₁ is selected from



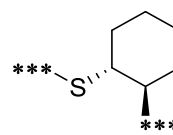
, wherein * represents linkage to a sulfhydryl group of A (e.g., a monoclonal antibody), and ** represents linkage to L₂;

L₂ is a spacer, preferably selected from -L_{2a}-C(O)-, -L_{2a}-L_{2b}-C(O)-, -L_{2a}-NH-C(O)-, -L_{2a}-C(O)-NH-, -L_{2a}-L_{2b}-NH-C(O)-, -L_{2a}-L_{2b}-C(O)-NH-, -L_{2a}-C(O)-NH-L_{2b}-C(O)-, -L_{2a}-NH-C(O)-L_{2b}-C(O)-, -L_{2a}-C(O)-NH-L_{2b}-C(O)-NH-, -L_{2a}-NH-C(O)-L_{2b}-NH-C(O)-, -L_{2a}-NR¹-SO₂-NH-C(O)-O-L_{2b}-C(O)-, and -L_{2a}-NR¹-SO₂-NH-C(O)-O-L_{2b}-NH-C(O)-, wherein L_{2a} is selected from -C₁-C₈ alkylene-, -C₁-C₈ alkylene-C₃-C₈ cycloalkylene-, -C₆-C₁₄ arylene-, -C₆-C₁₄ arylene-C₁-C₈ alkylene-, -(5- to 6-membered heteroarylene)-, -(5- to 6-membered heteroarylene)-C₁-C₈ alkylene-, linear or branched heteroalkylene having 1-50 atoms, and (linear or branched

- heteroalkylene having 1-50 atoms)-(3- to 8-membered heterocyclylene), wherein the alkylene, cycloalkylene, arylene, heteroalkylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 1-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl, the heteroalkylene, heterocyclylene, or heteroalkyl contains 1-12 heteroatoms, and the heteroatom in the heteroalkylene, heterocyclylene, heteroarylene, or heteroalkyl is selected from one or more of N, O, and S; L_{2b} is selected from -C₁-C₈ alkylene- and linear or branched heteroalkylene having 1-50 atoms, and R¹ is selected from hydrogen, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, 3- to 8-membered heterocyclyl, C₁-C₆ haloalkyl, heteroalkyl having 2-8 atoms, C₆-C₁₄ aryl, and 5- to 6-membered heteroaryl, wherein the alkyl, heteroalkyl, aryl, and heteroaryl are each optionally substituted with one or more substituents independently selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, amino, and carboxyl, the heteroalkyl or heteroalkylene contains 1-12 heteroatoms, and the heteroatom in the heteroalkyl, heterocyclyl, heteroaryl, heteroalkylene, or heteroarylene is selected from one or more of N, O, and S;
- L₃ is a polypeptide sequence, preferably selected from a peptide residue consisting of 2-8 natural or unnatural amino acids, wherein optionally, the amino acid is further substituted with one or more substituents selected from C₁-C₆ alkyl, heteroalkyl having 2-6 atoms, C₁-C₆ alkoxy, hydroxyl, amino, carboxyl, and C₃-C₈ cycloalkyl;
- L₄ is a hydrophilic group-modified self-immolative fragment, and the self-immolative fragment is selected from:

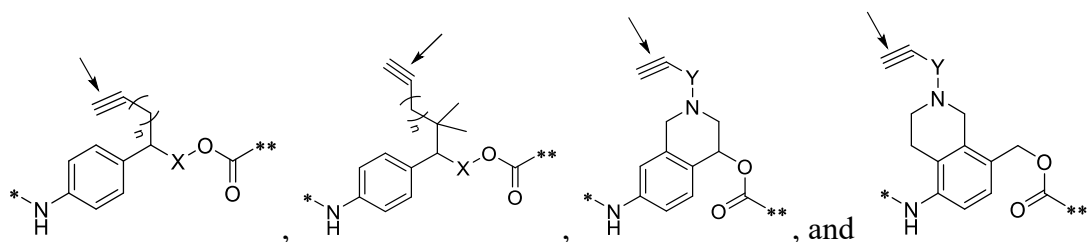


wherein * represents linkage to a carboxyl group of L₃ via an amide bond, ** represents linkage



to the amino group of the bioactive molecule D, X is absent or linkage to a carbon atom, **** represents linkage to an oxygen atom, and the arrow indicates a modification site of the hydrophilic group;

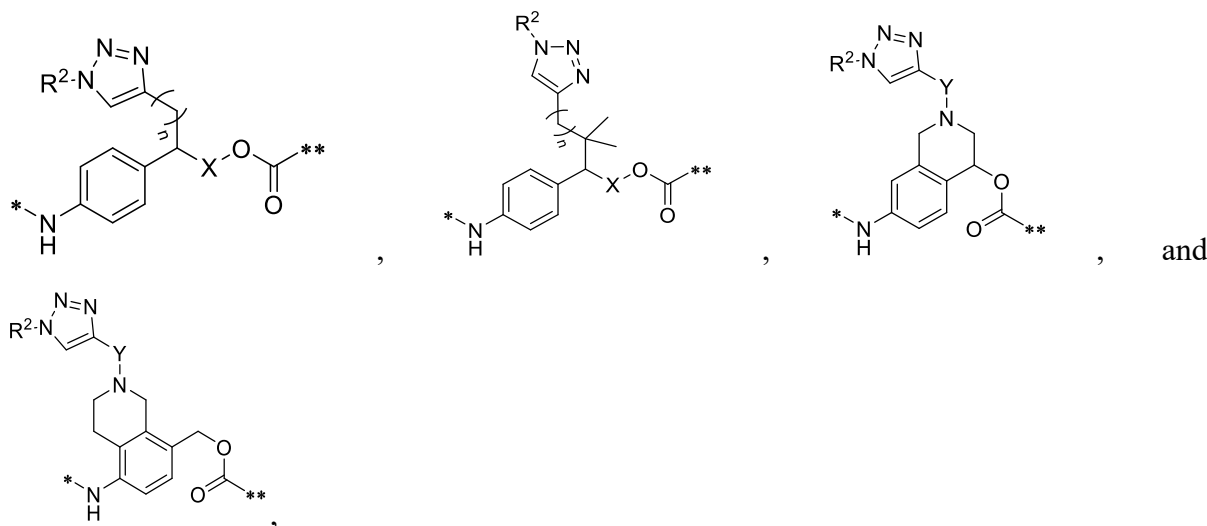
further preferably, the self-immolative fragment, prior to modification by the hydrophilic group, is selected from the following structures:



wherein Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6;

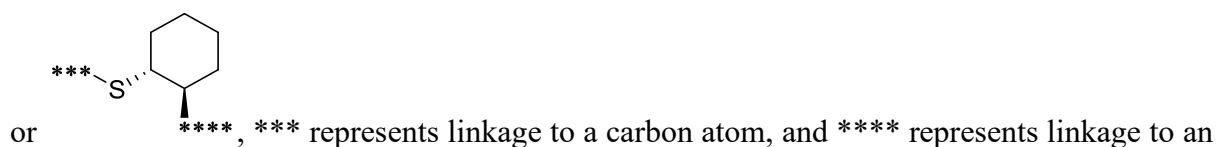
the hydrophilic group has at least one azido group and comprises a polyethylene glycol group, a poly-natural or unnatural amino acid group, a monosaccharide, an oligosaccharide, or a polysaccharide, or a combination thereof;

preferably, L_4 is selected from:



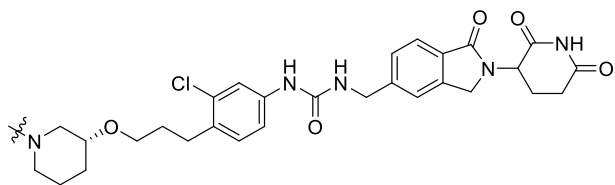
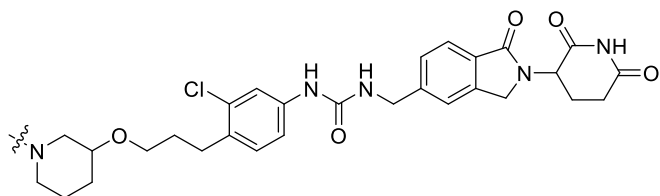
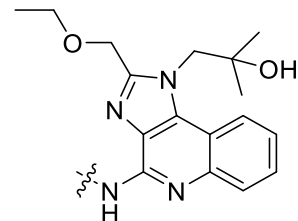
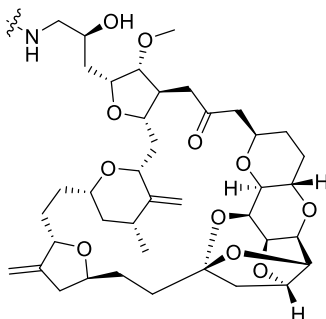
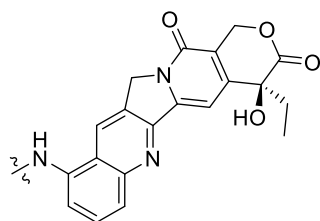
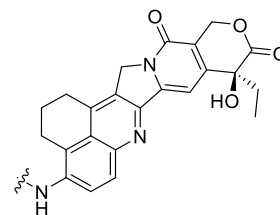
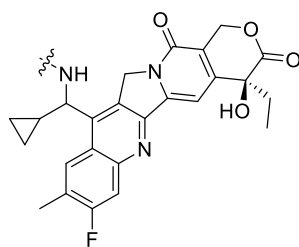
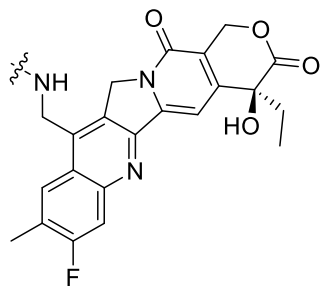
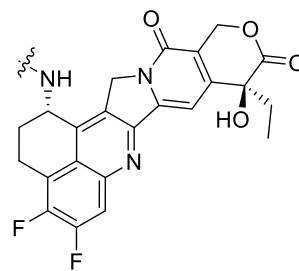
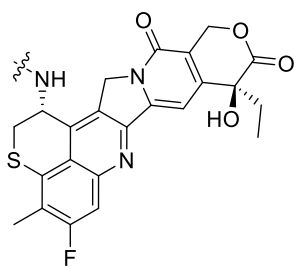
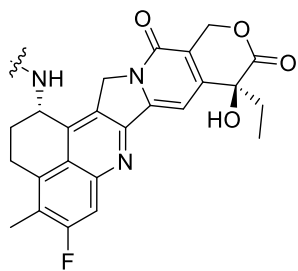
10 wherein * represents linkage to a carboxyl group of L₃ via an amide bond, and ** represents linkage to the amino group of the bioactive molecule D;

R² is a hydrophilic fragment, preferably selected from linear or branched heteroalkyl containing 4-50 (OCH₂CH₂) structural units, a peptide chain containing 4-50 proteinogenic amino acids (e.g., glycines) or non-proteinogenic amino acids (e.g., sarcosines), and linear or branched heteroalkyl containing a monosaccharide, an oligosaccharide, or a polysaccharide; X is absent

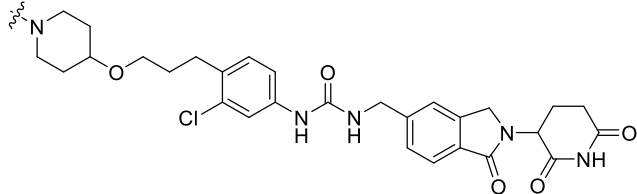
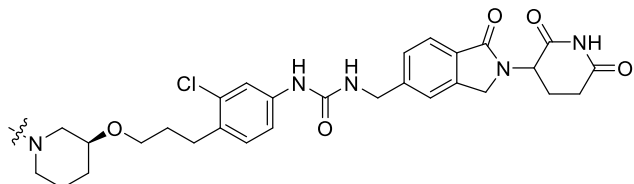


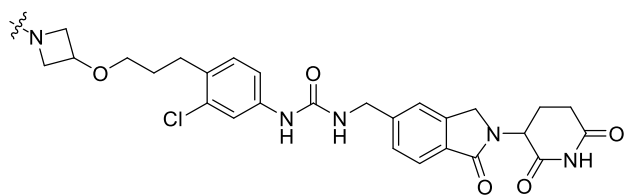
oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6;

D is selected from compounds of the following formulas:



5





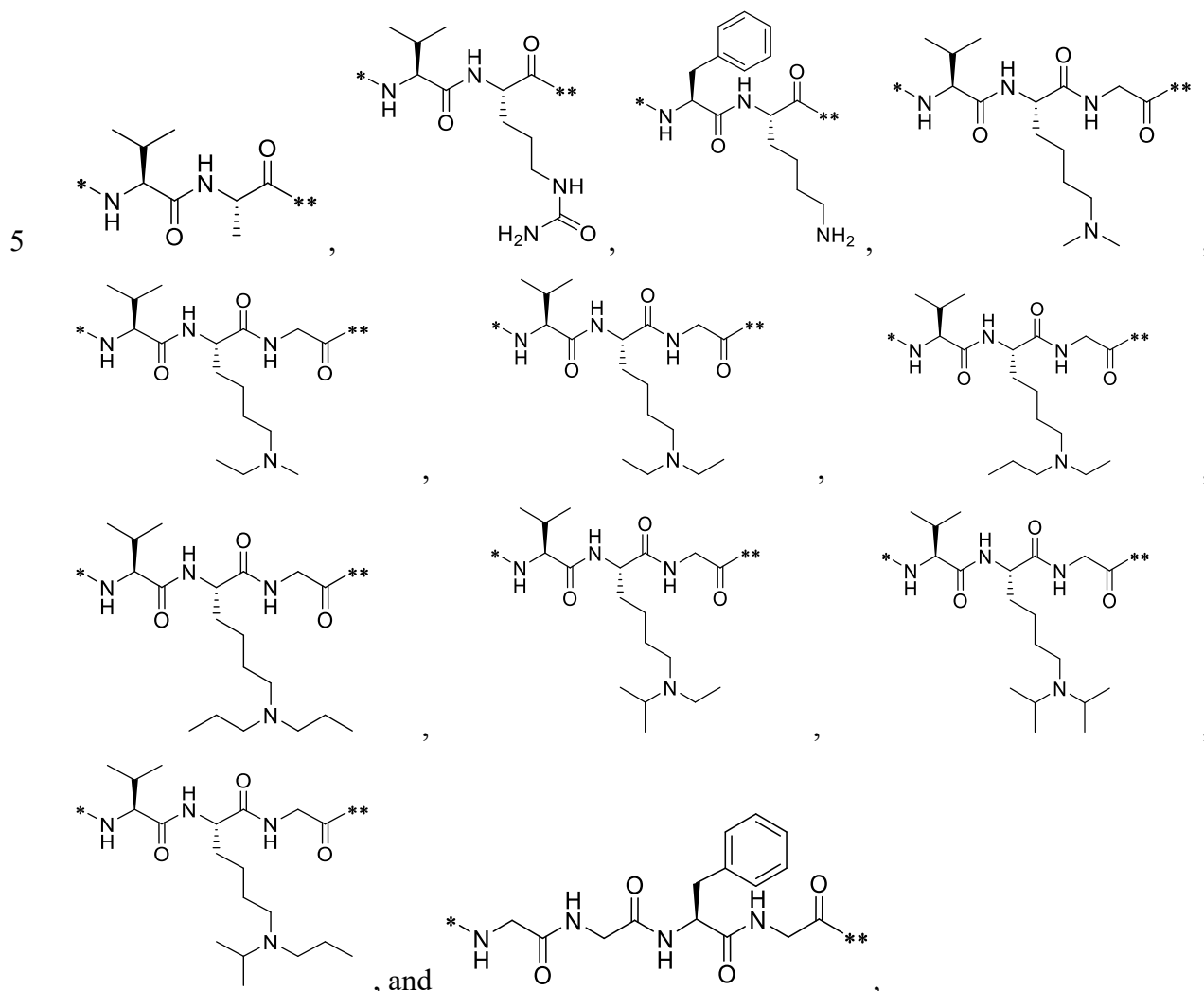
2. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to claim 1, wherein A is selected from an antibody or an antigen-binding fragment thereof targeting HER2 (ErbB2), HER3 (ErbB3), HER4 (ErbB4), EGFR, DLL3, TROP2, B7H3, c-Met, CD20, CD22, CD30, CD33, CD44, CD47, CD56, CD70, CD73, CD79b, CD105, CEA, A33, Cripto, EphA2, G250, MUC1, Lewis Y, VEGFR, VEGF, PD-1, PD-L1, MET, RET, GPNMB, Integrin, PSMA, Tenascin-C, SLC44A4, FR α , or Mesothelin.

3. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-2, wherein L₂ is selected from the following structures:

(1)	(7)
(2)	(8)
(3)	(9)
(4)	(10)
(5)	(11)
(6)	(12)

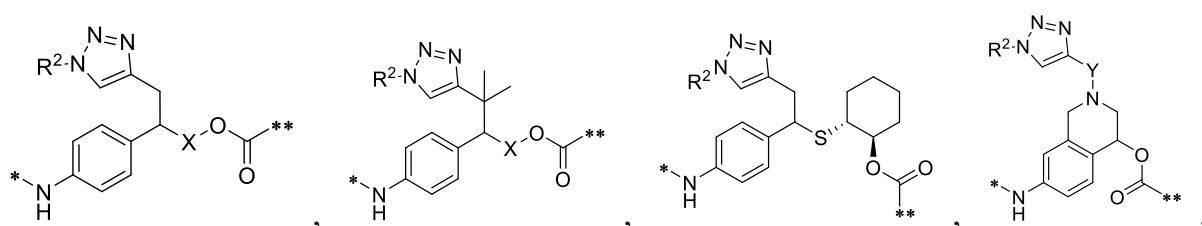
wherein w is an integer selected from 1-12, * represents linkage to L₁, and ** represents linkage to L₃.

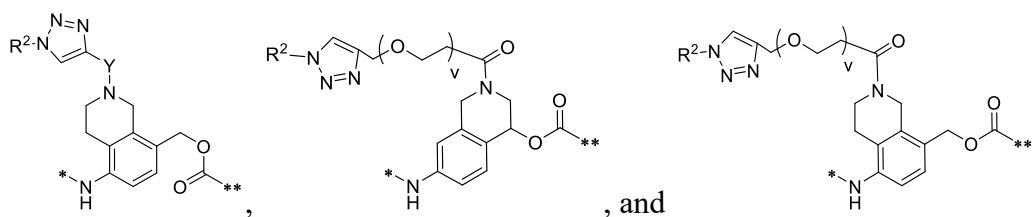
4. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-3, wherein L_3 is selected from the following structures:



wherein * represents linkage to L_2 , and ** represents linkage to L_4 .

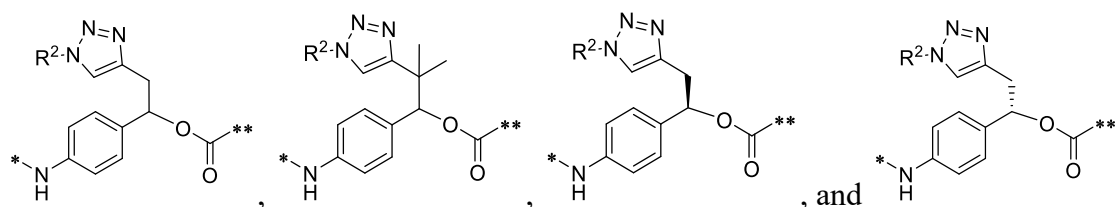
10 5. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-4, wherein L_4 is selected from the following structures:



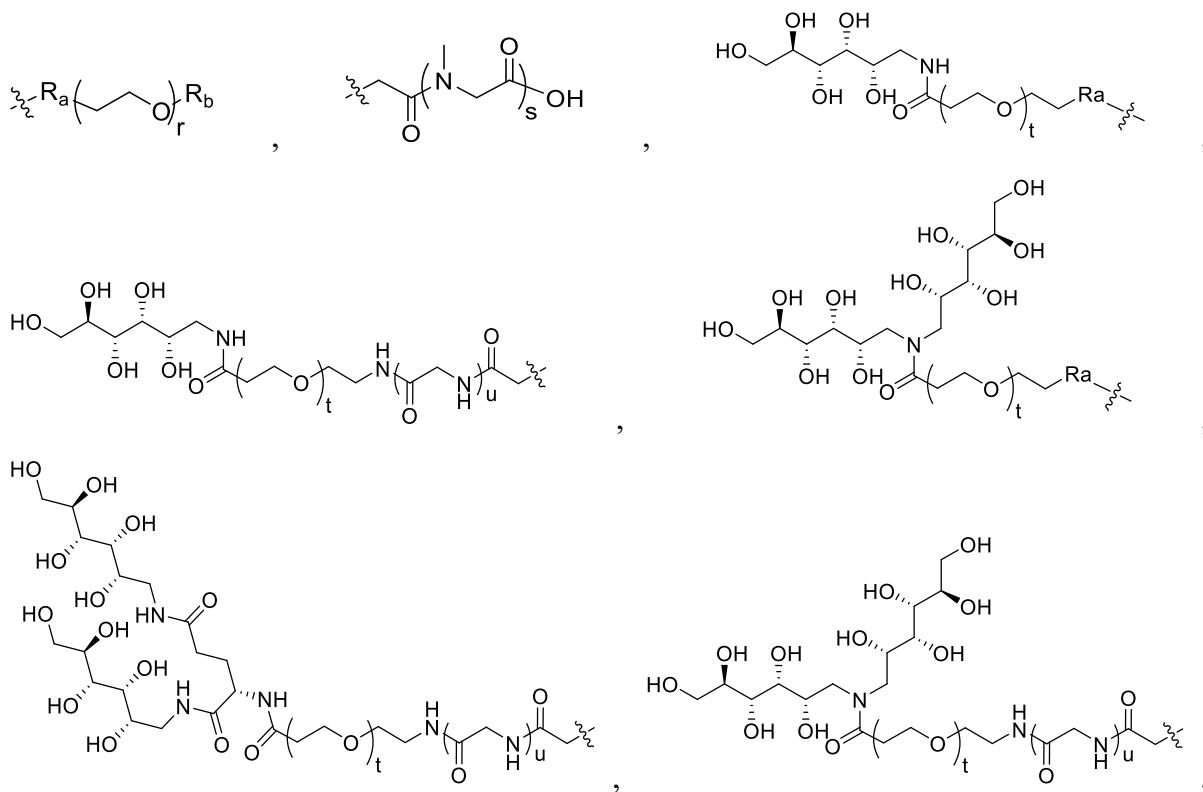


wherein v is an integer selected from 1-12, $*$ represents linkage to a carboxyl group of L_3 via an amide bond, and $**$ represents linkage to the amino group of the bioactive molecule D.

6. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-5, wherein L_4 is selected from the following structures:

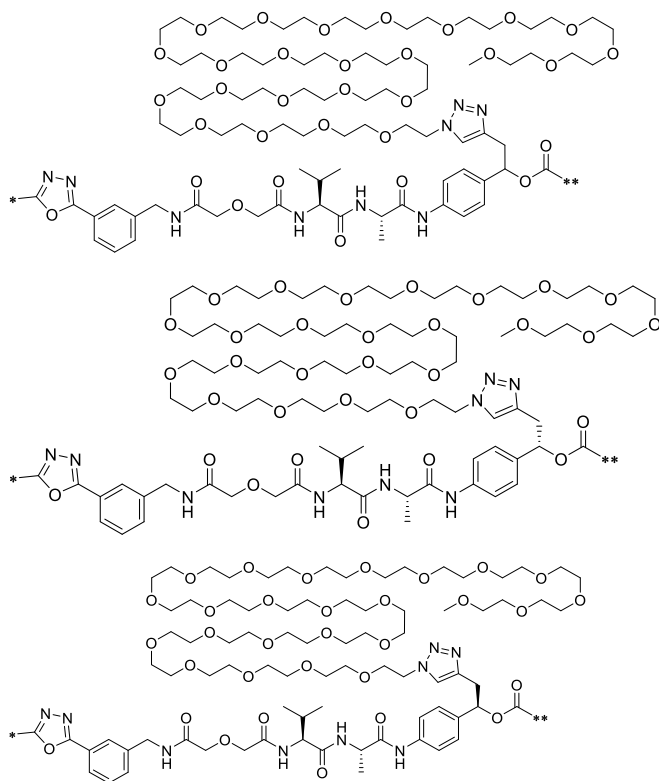


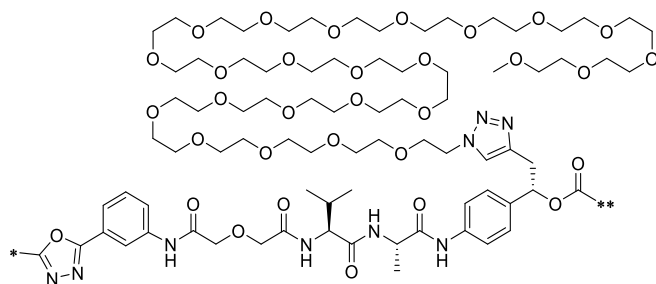
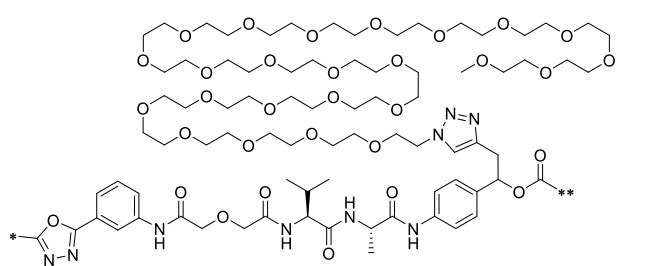
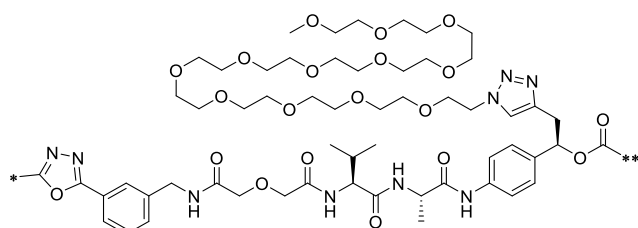
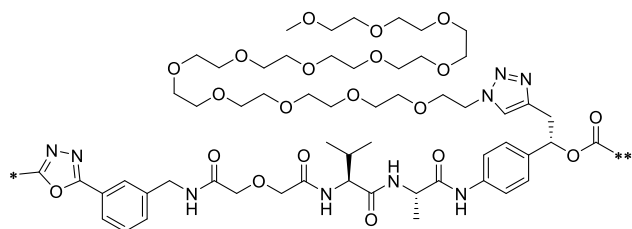
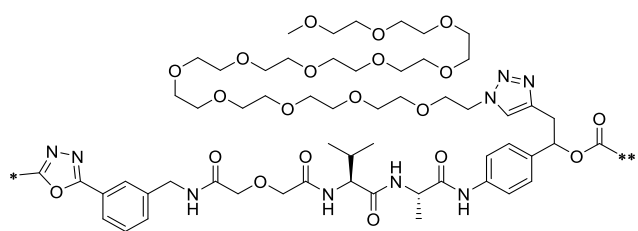
7. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-6, wherein R^2 is selected from the following structures:



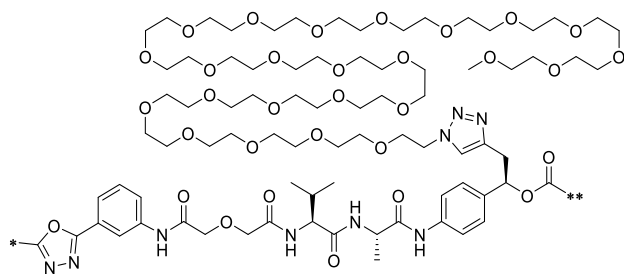
wherein r, s, t, and u are each independently an integer selected from 1-50 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50); R_a is selected from a bond and C₁-C₃ alkylene, such as methylene, ethylidene, *n*-propylidene, or isopropylidene; R_b is selected from C₁-C₃ alkyl, such as methyl, ethyl, *n*-propyl, or isopropyl.

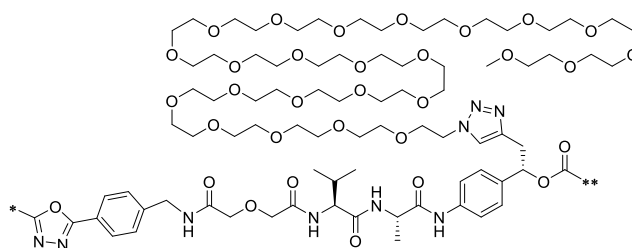
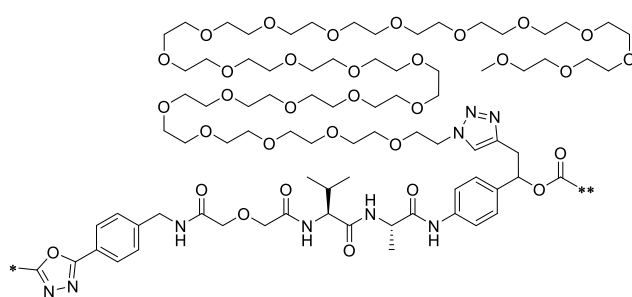
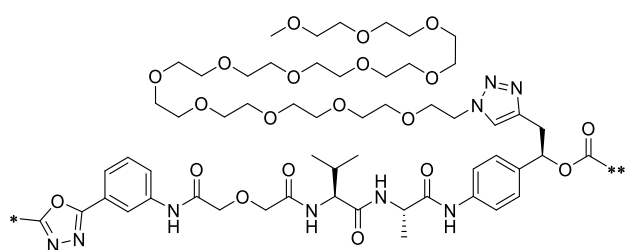
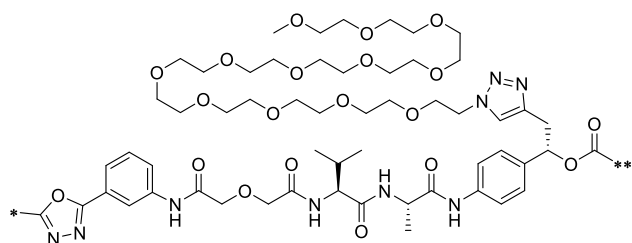
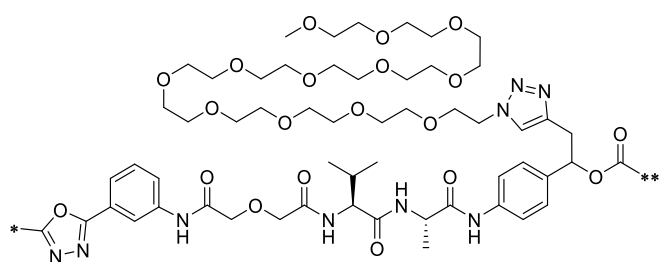
10 of claims 1-7, wherein L is selected from the following structures:



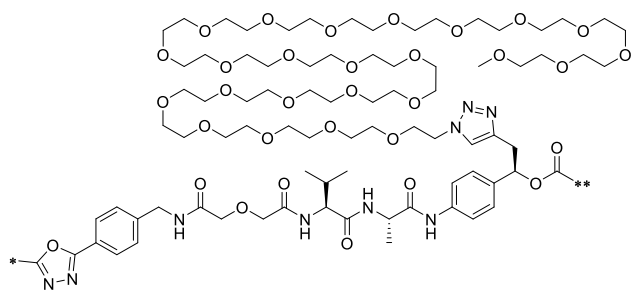


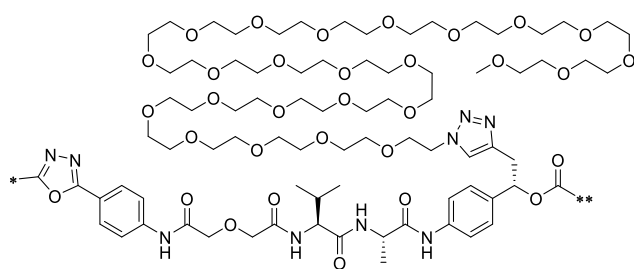
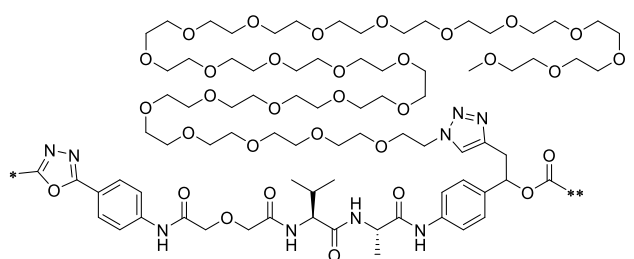
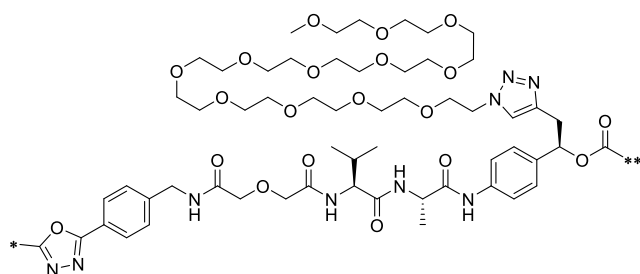
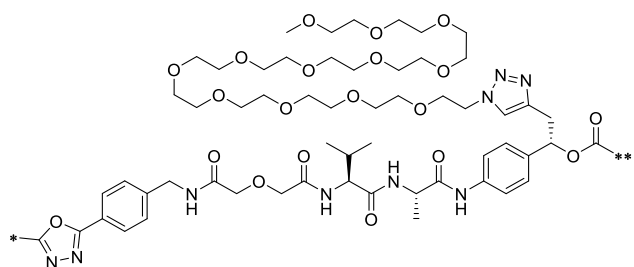
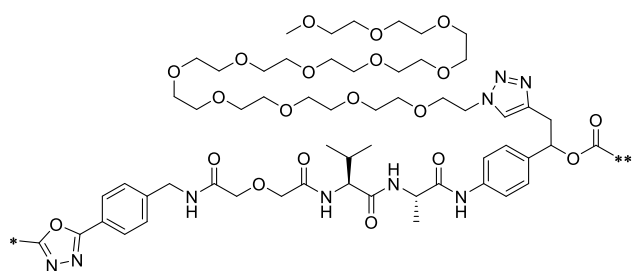
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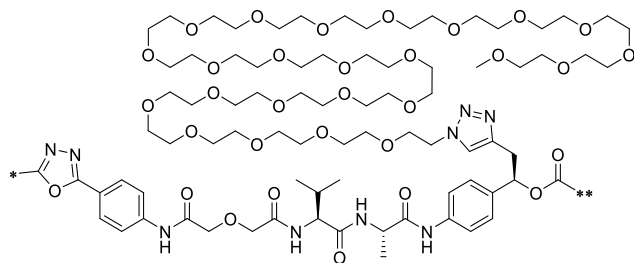


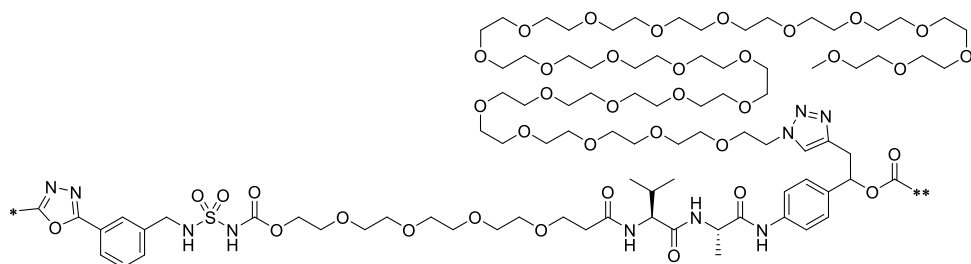
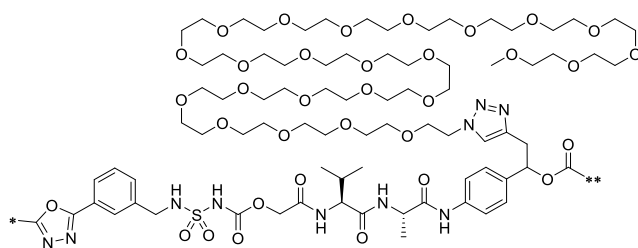
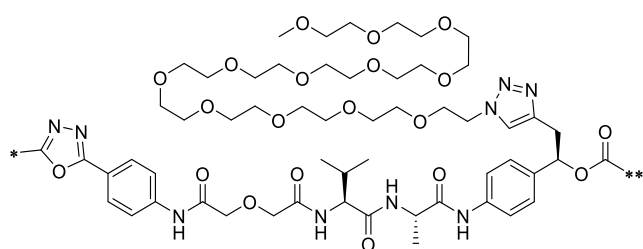
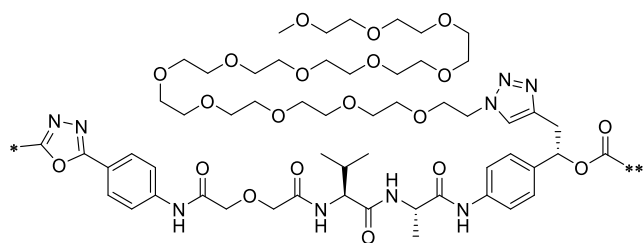
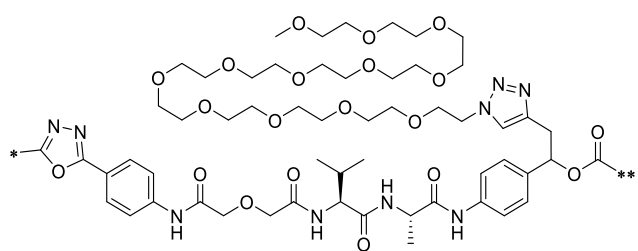
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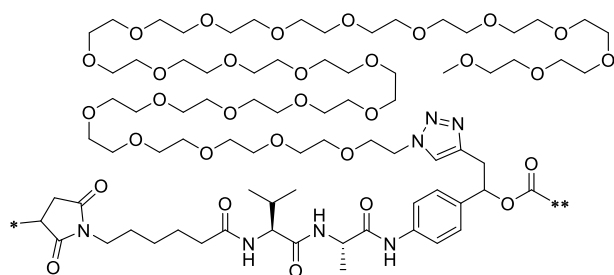


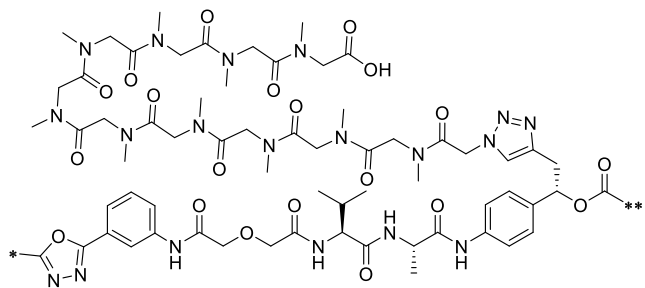
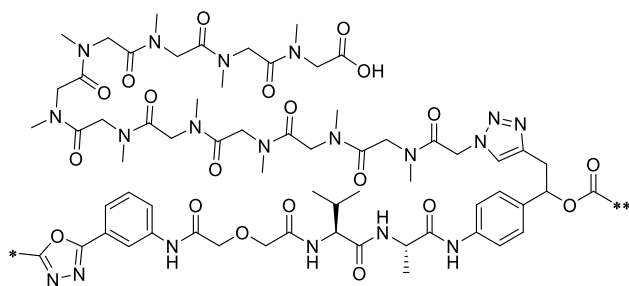
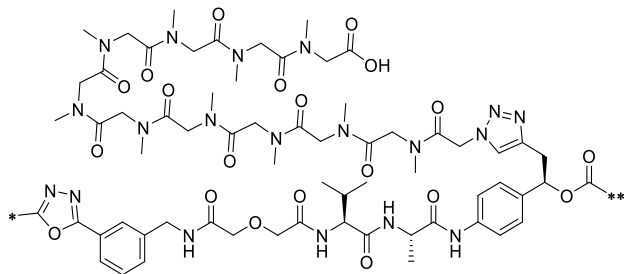
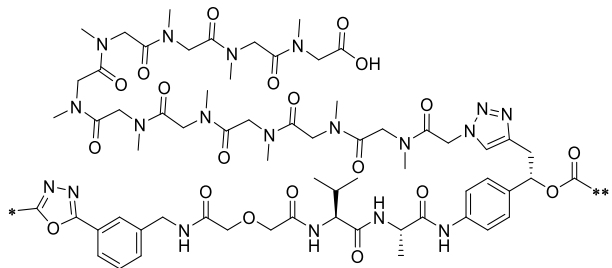
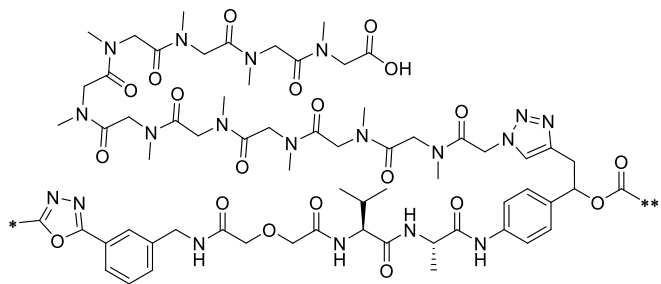
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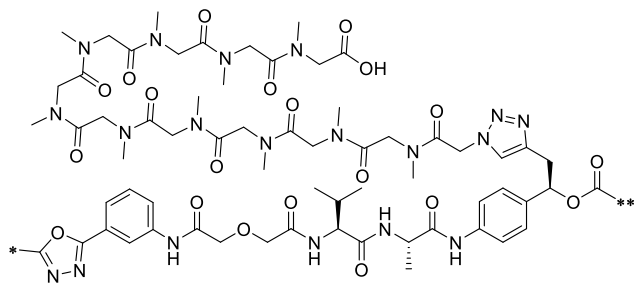


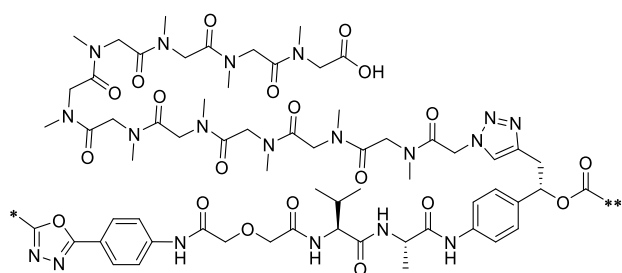
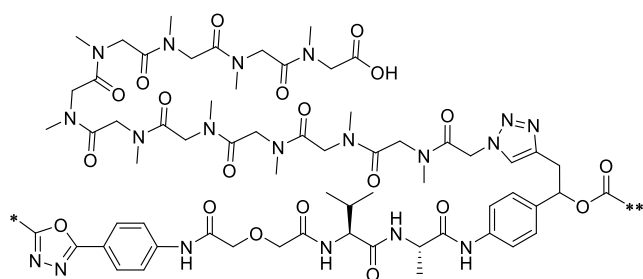
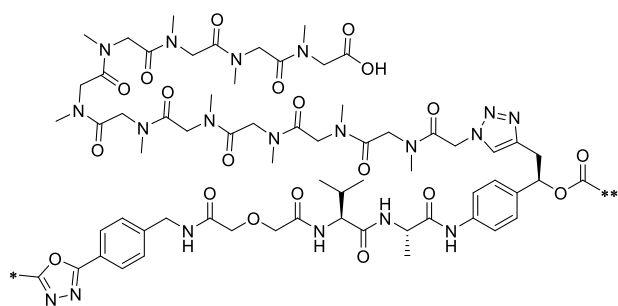
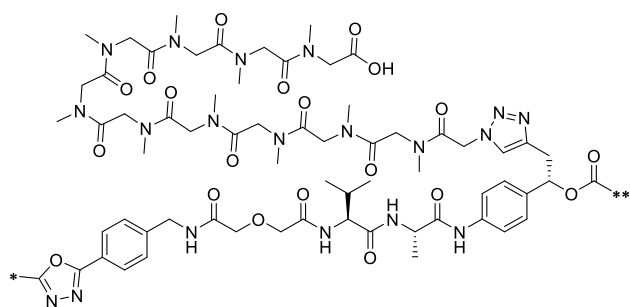
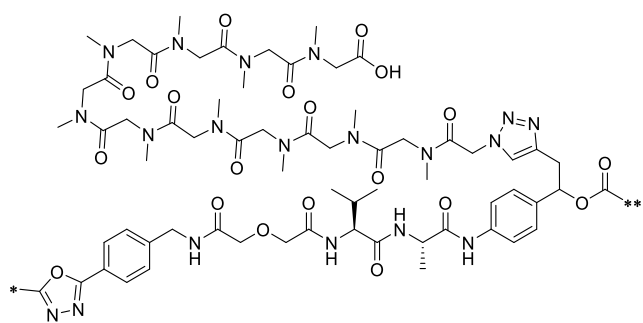
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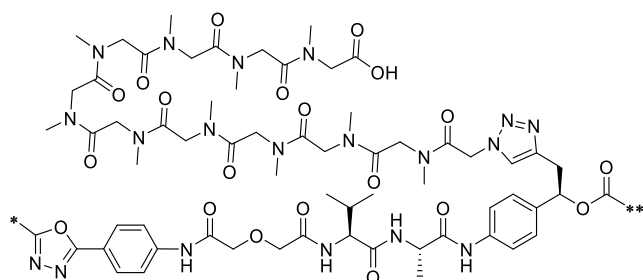


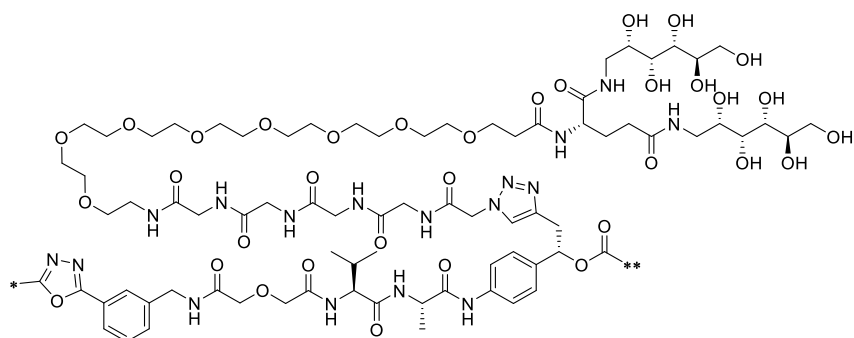
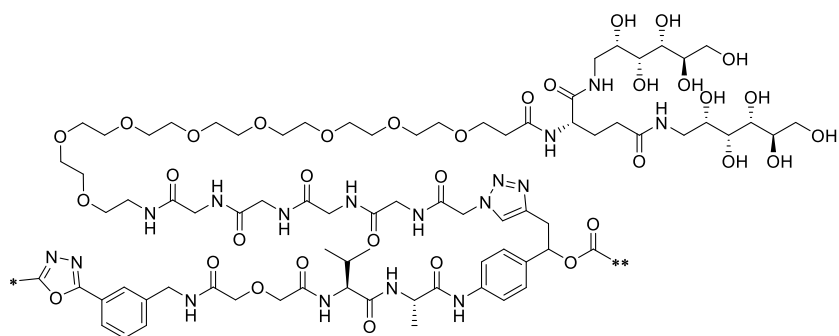
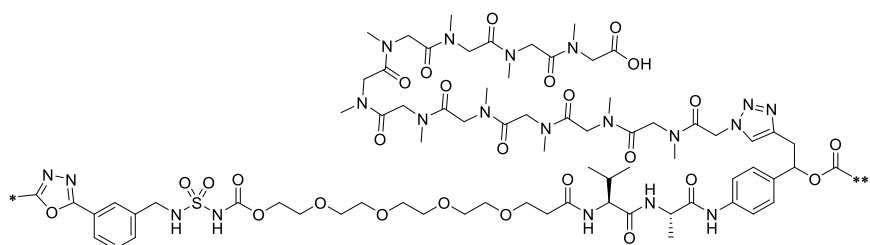
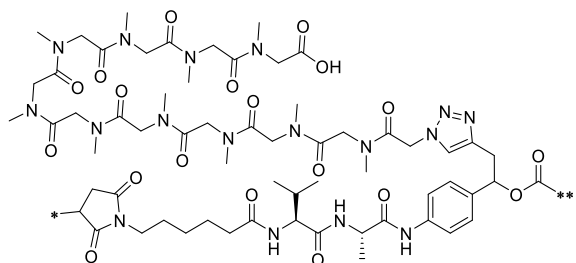
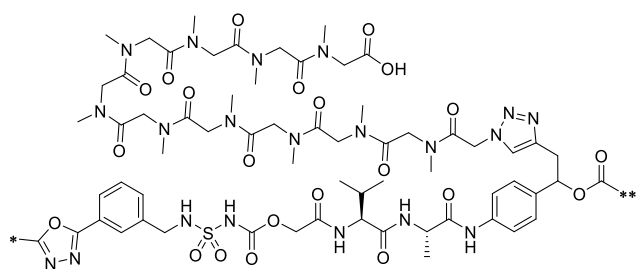
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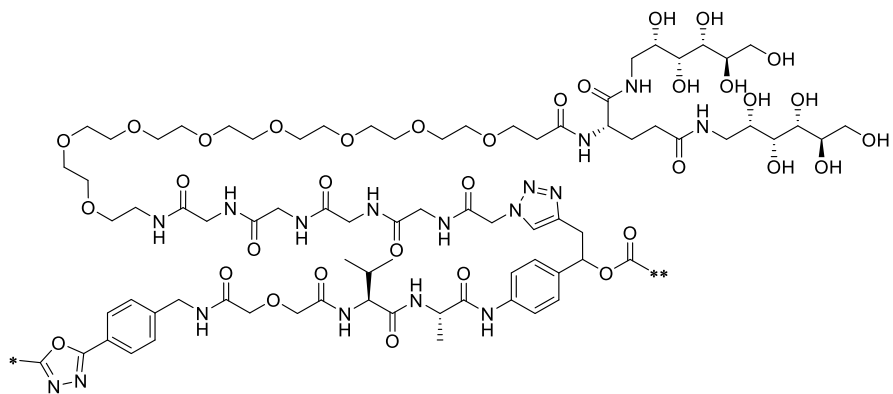
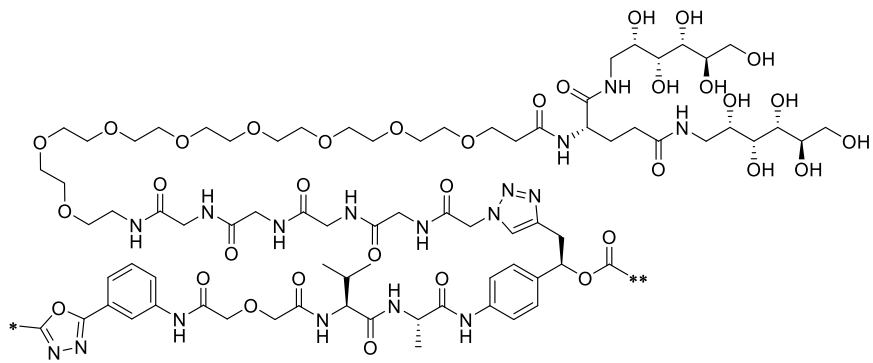
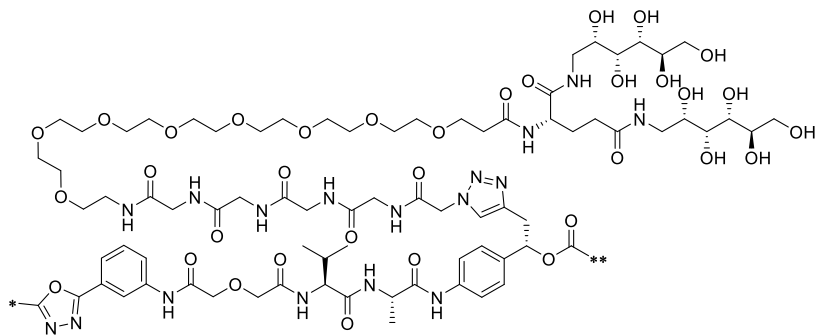
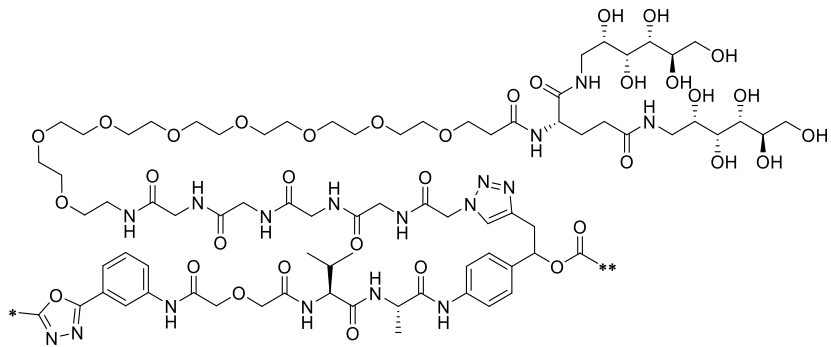
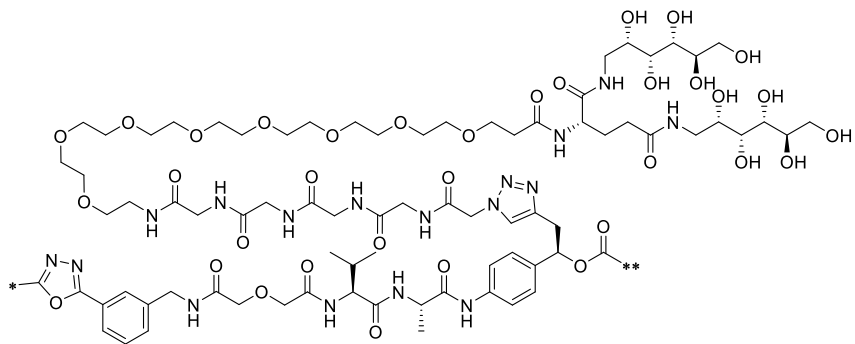


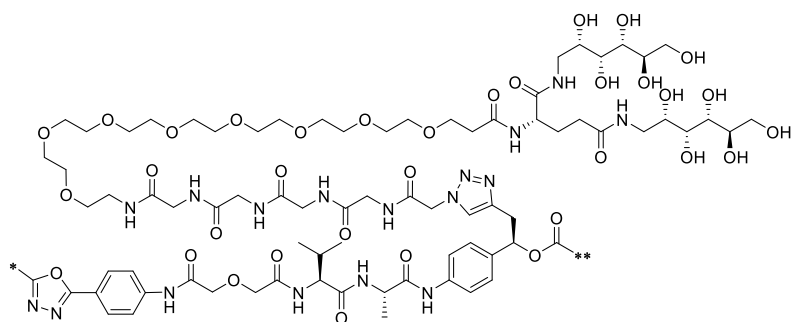
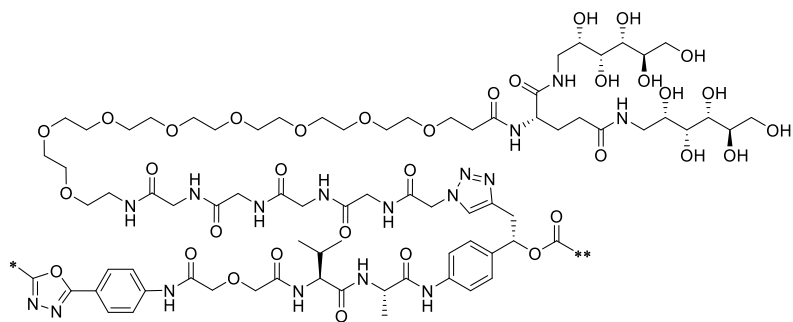
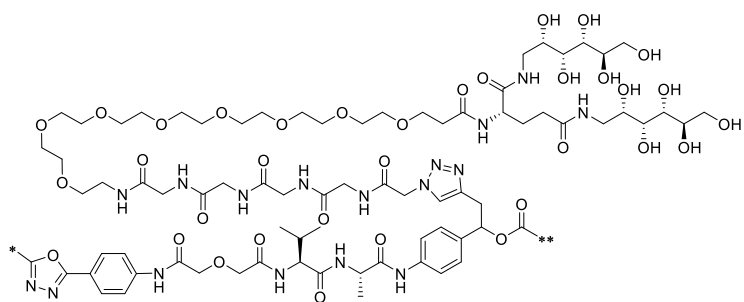
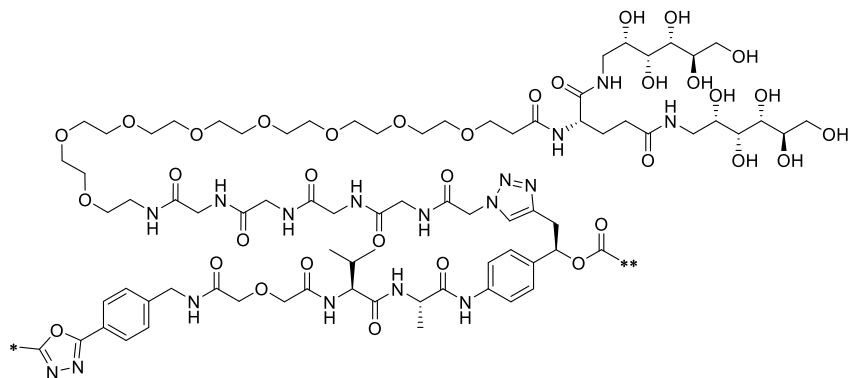
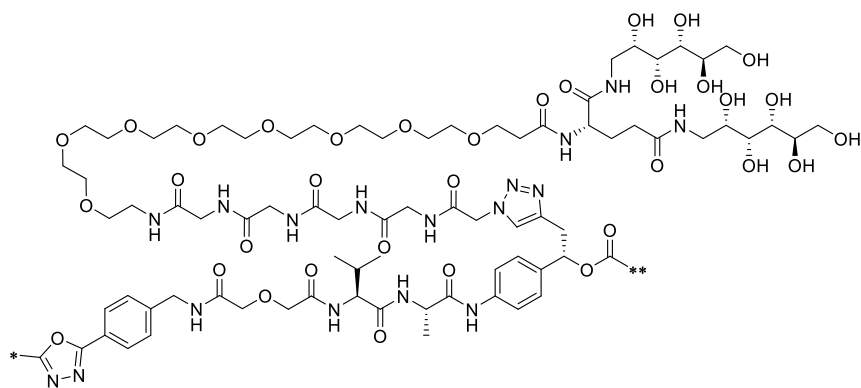


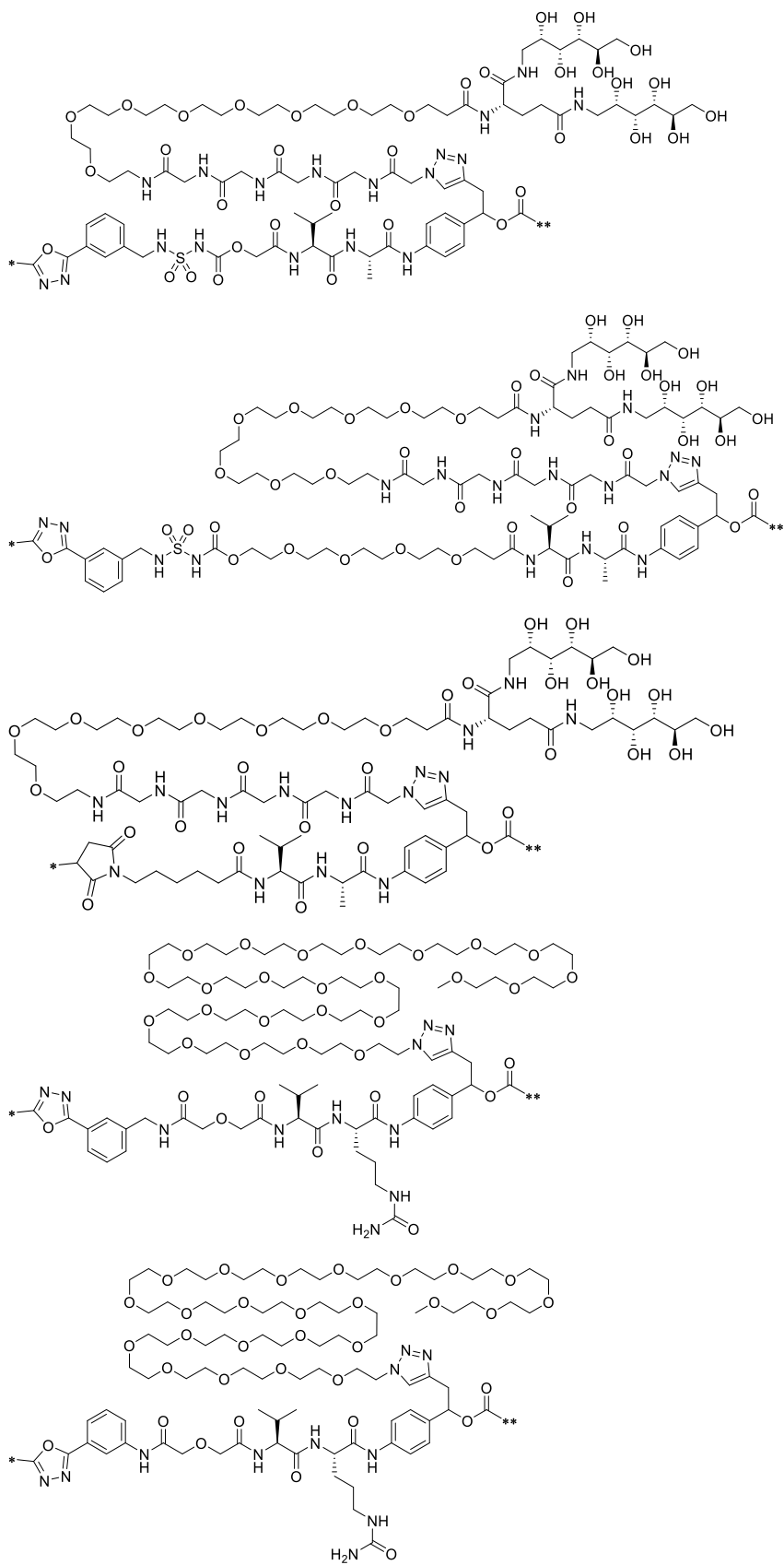
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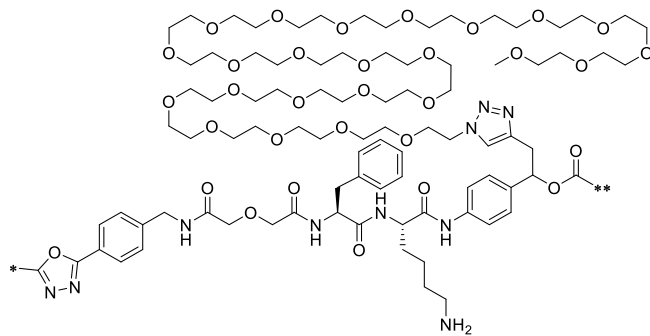
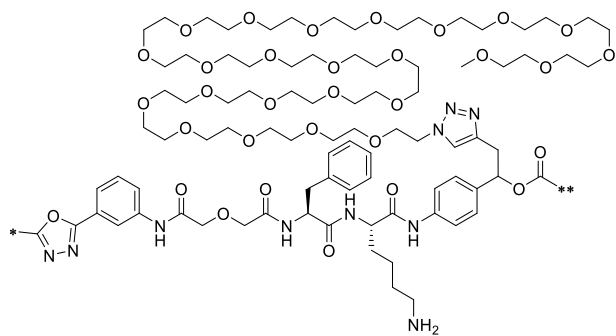
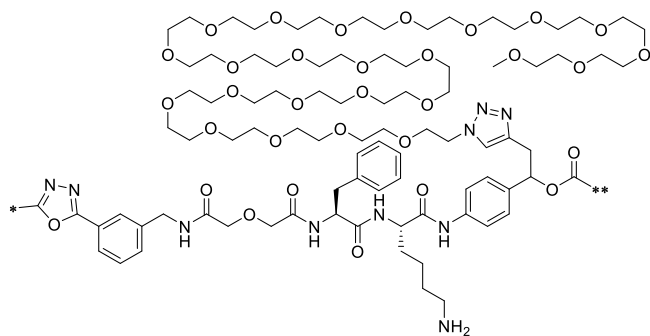
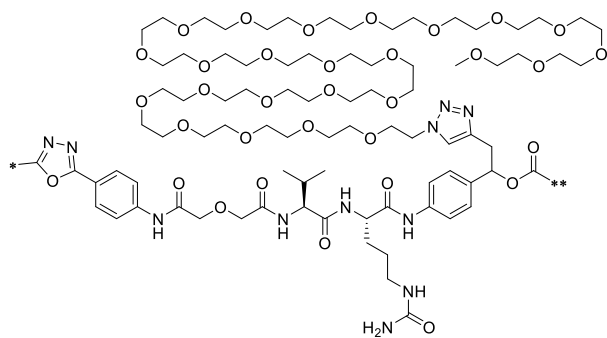
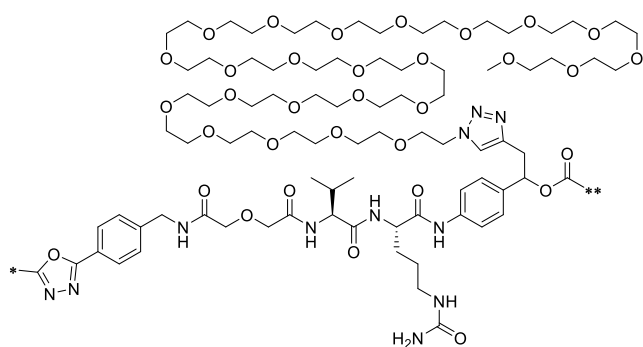


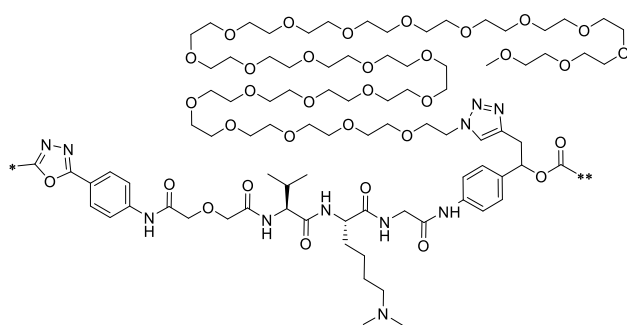
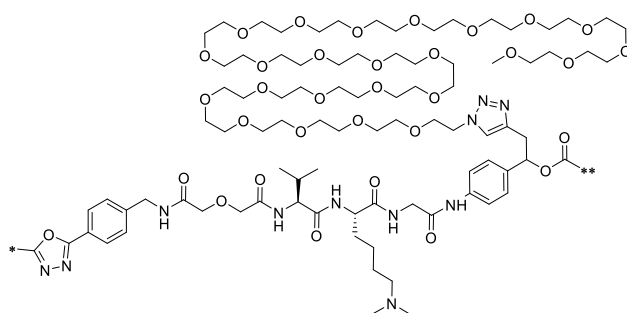
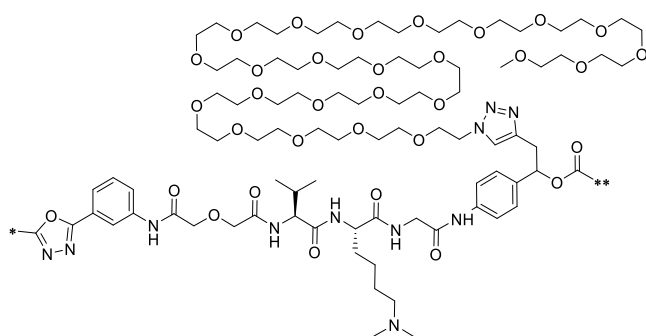
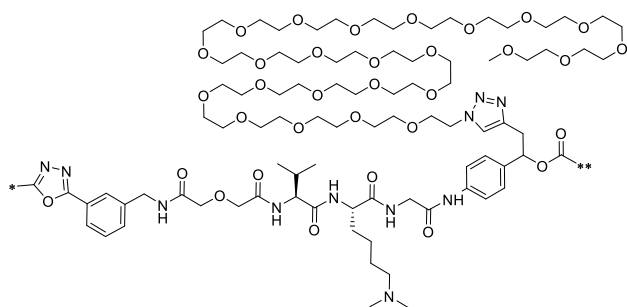
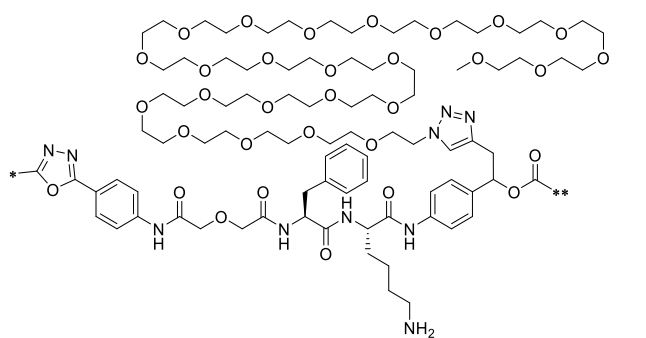


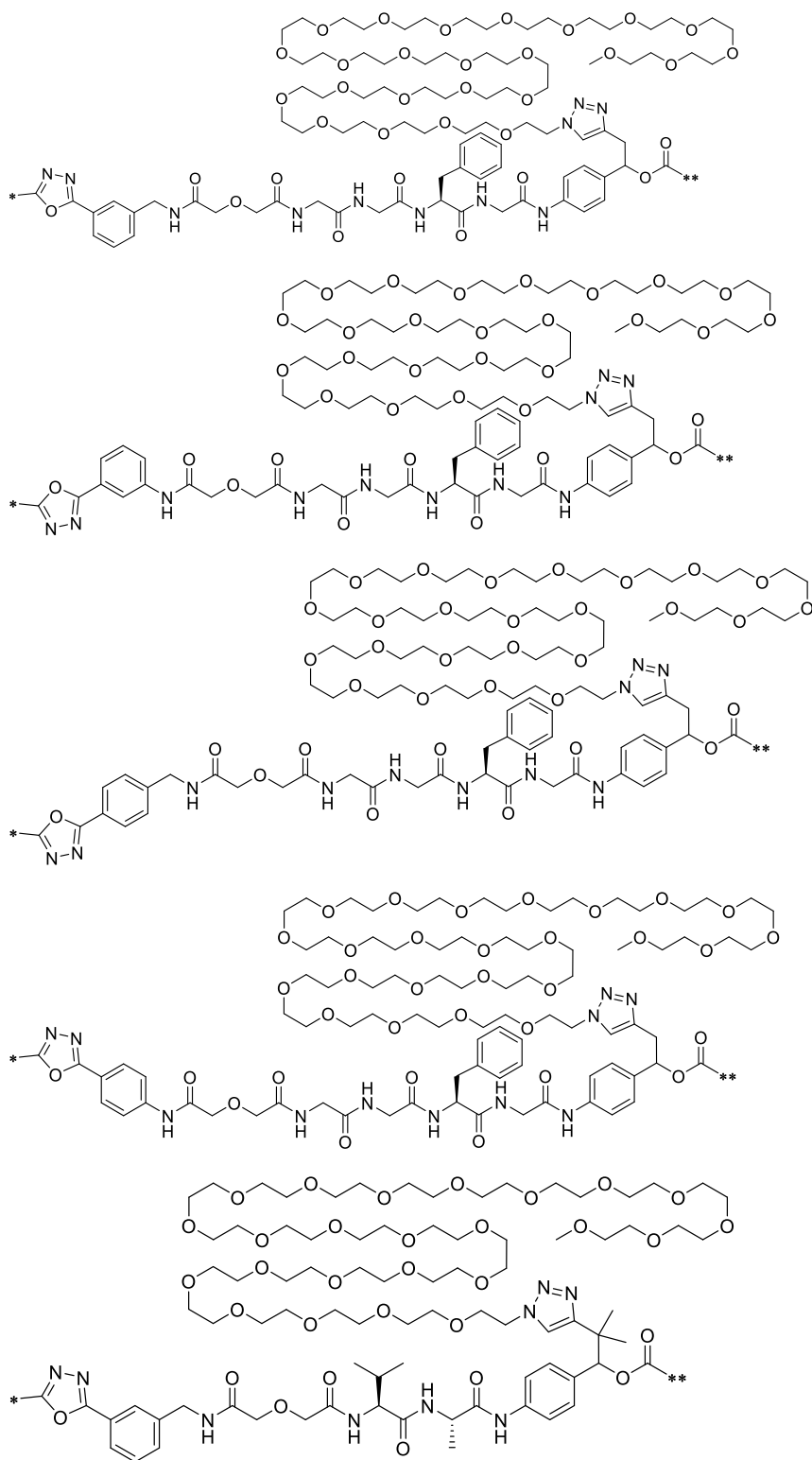


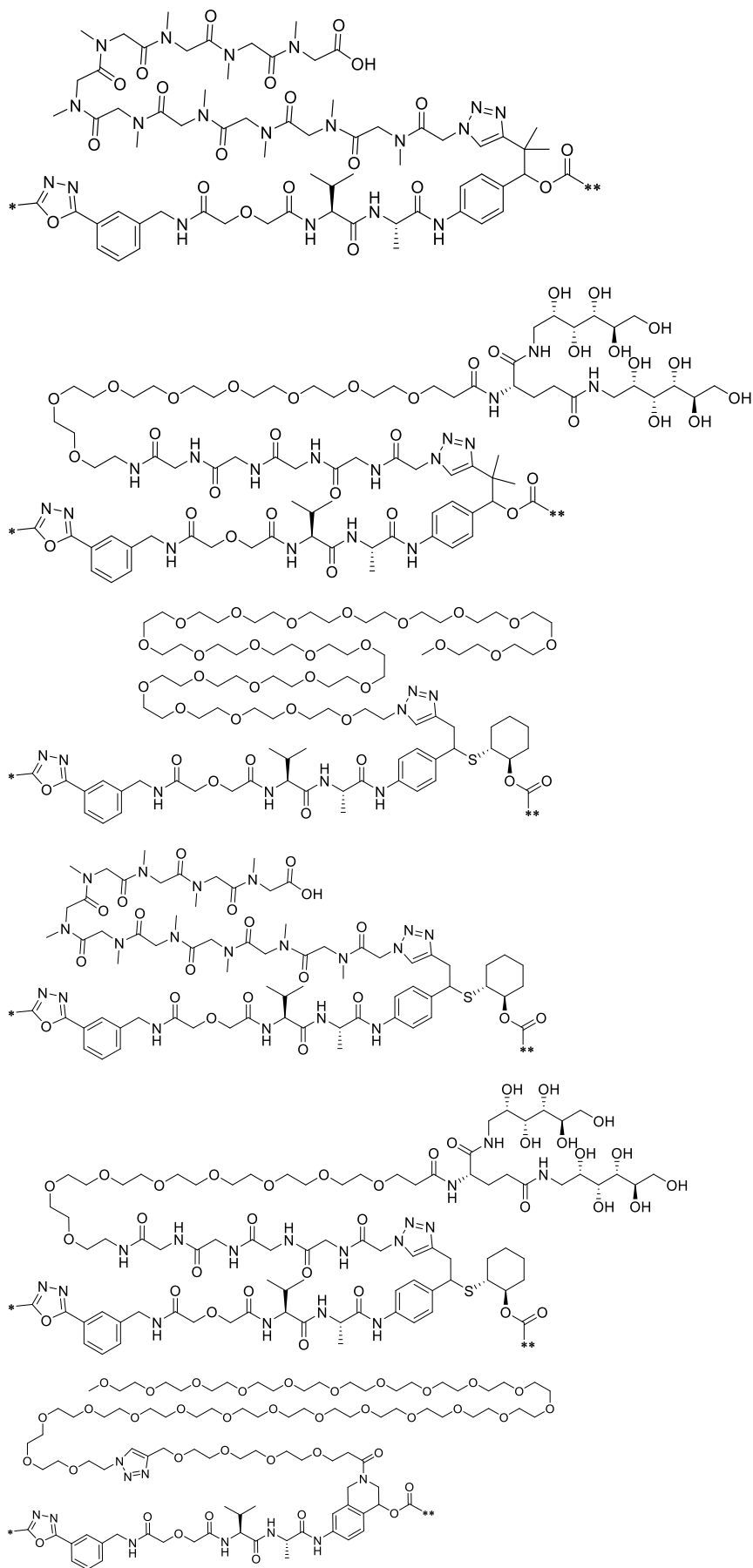


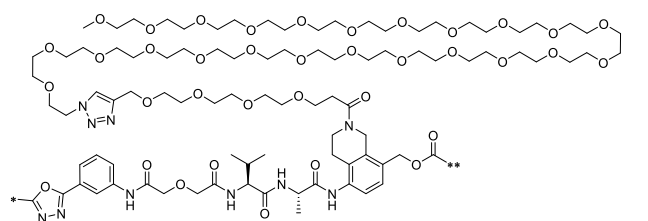
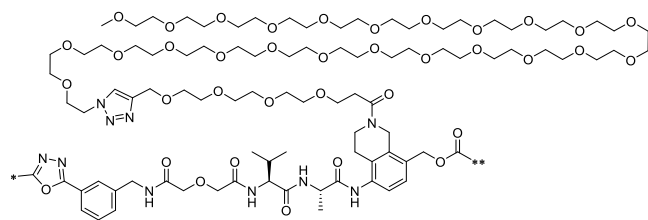
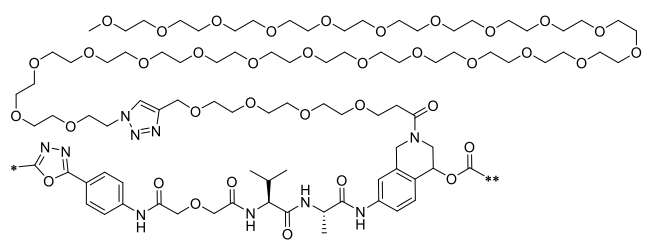
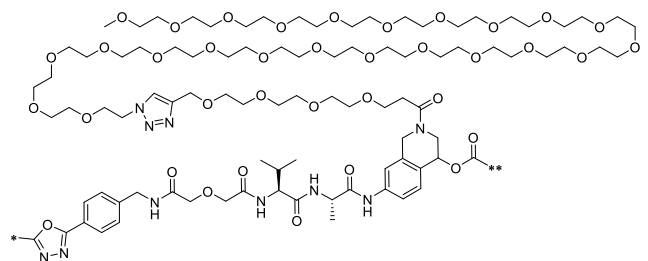
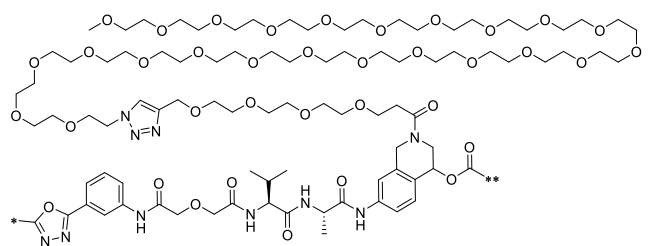




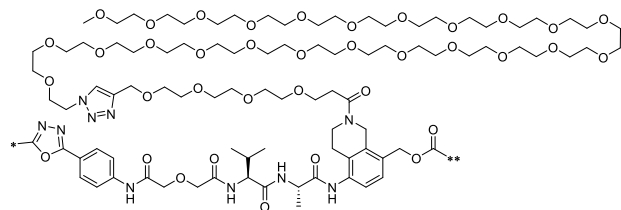
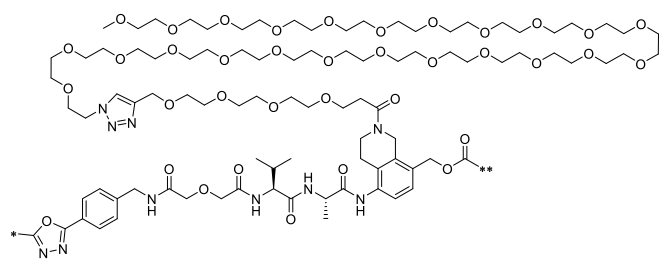


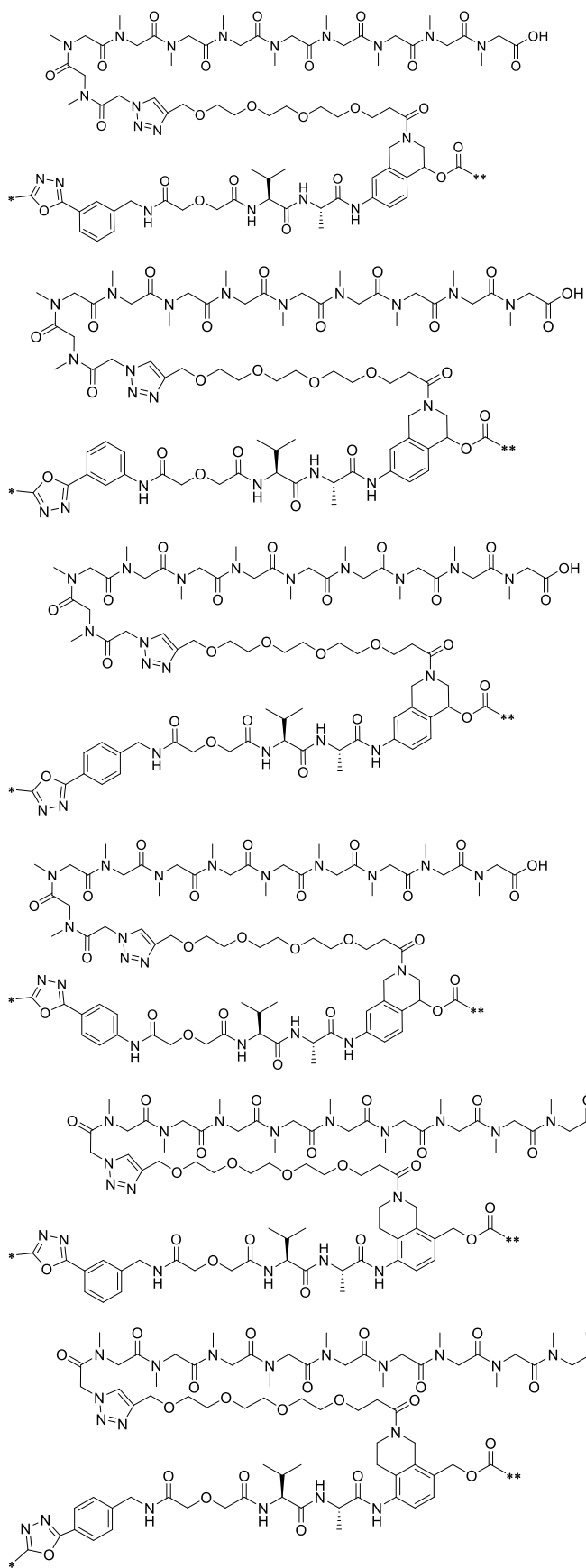


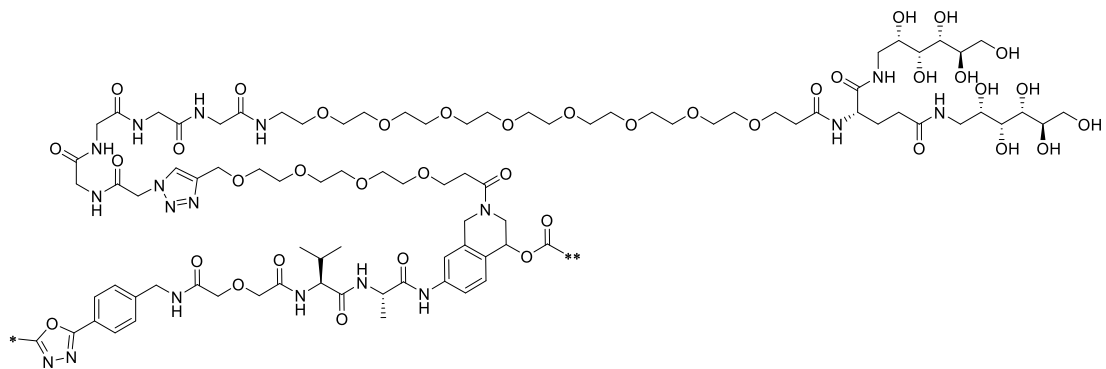
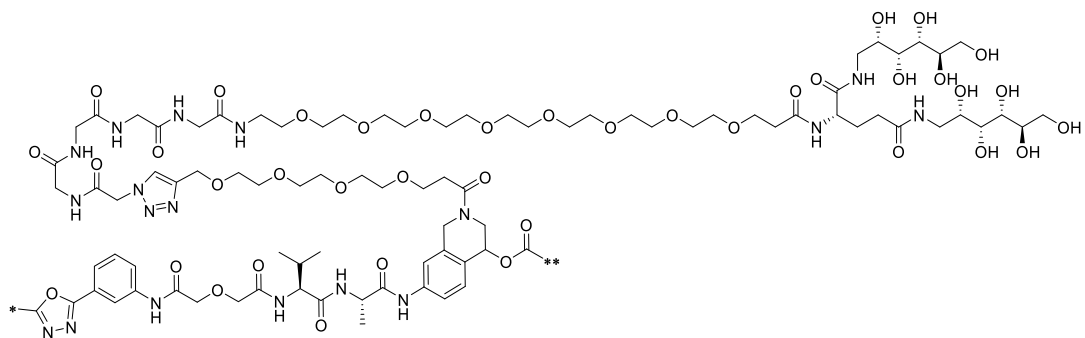
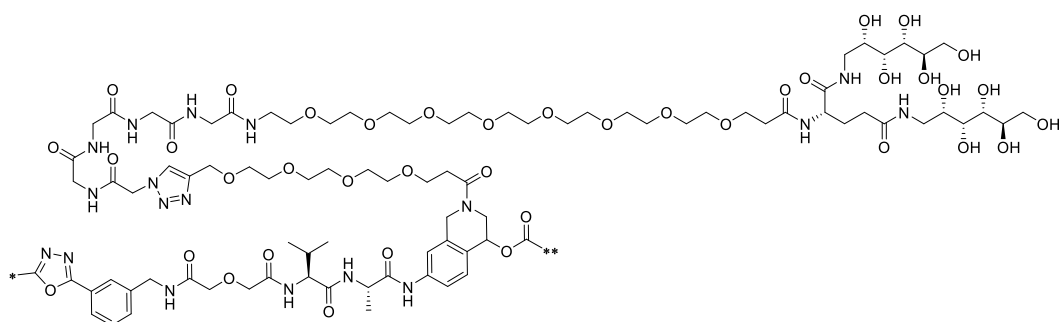
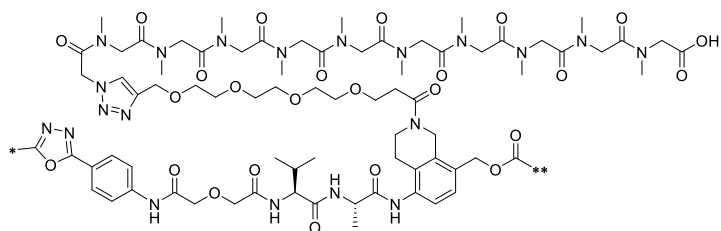
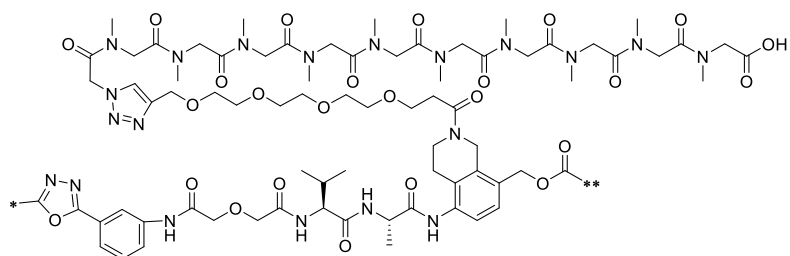


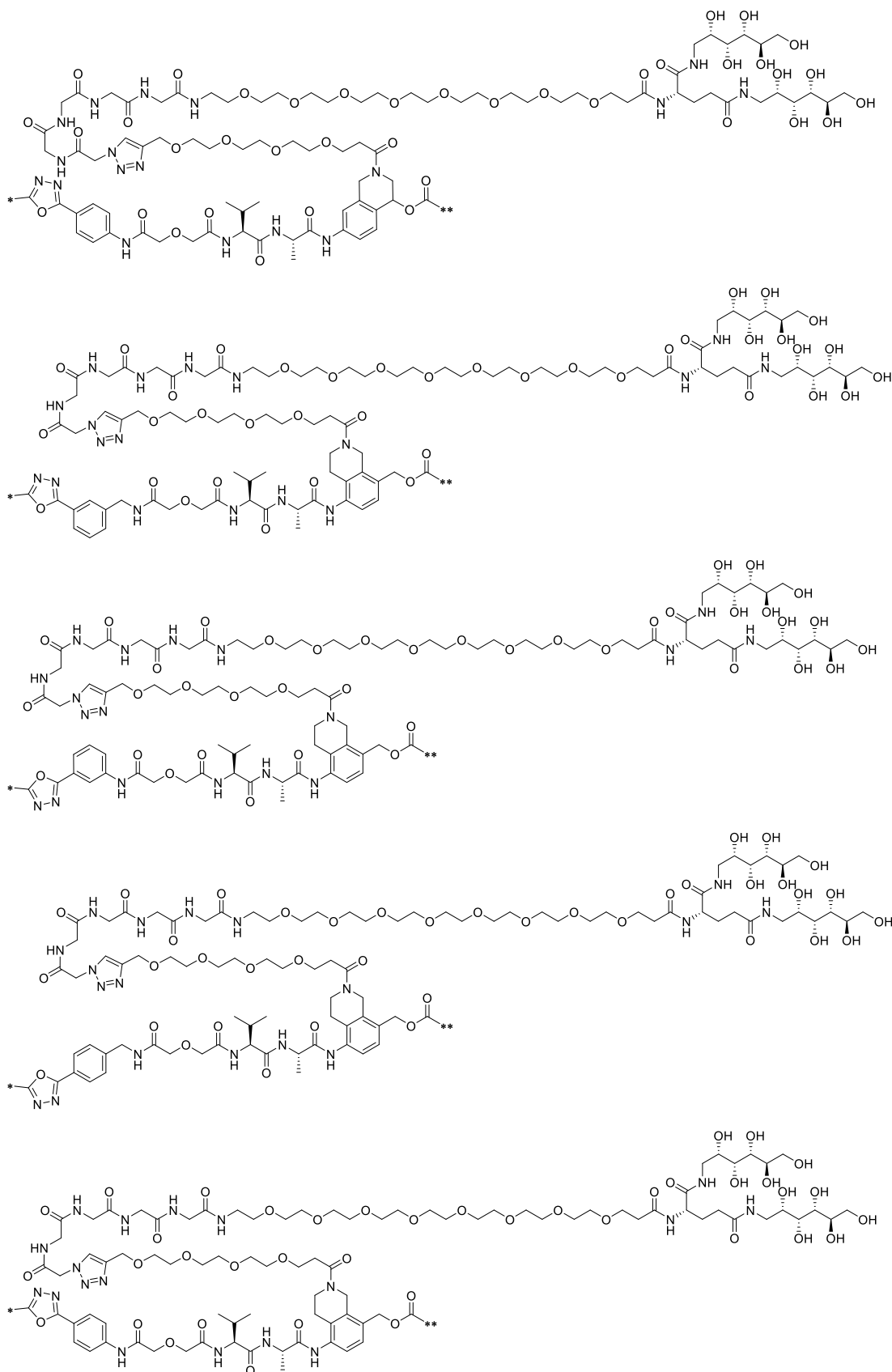


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wherein * represents linkage to a sulfhydryl group of the antibody A, and ** represents linkage to the amino group of the bioactive molecule D.

9. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the

mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-8, wherein A is an antibody or an antigen-binding fragment thereof targeting FR α , DLL3, B7H3, or HER2.

- 5 10. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-9, wherein

A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the antibody
 10 or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 22, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 23, and the amino acid sequence of the heavy
 15 chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 24; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 25, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 26, and the amino acid sequence of the light chain
 20 complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 27, wherein the CDRs are determined according to the Kabat numbering scheme; or

A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the antibody
 or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino
 25 acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 12, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 13, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 14; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid
 30 sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 15, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 16, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 17, wherein the CDRs are determined according to the Kabat numbering scheme; or

A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 1, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 2, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 3; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 4, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 5, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 6, wherein the CDRs are determined according to the Kabat numbering scheme; or

A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the heavy chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the heavy chain complementarity determining region 1 (HCDR1) is set forth in SEQ ID NO: 37, the amino acid sequence of the heavy chain complementarity determining region 2 (HCDR2) is set forth in SEQ ID NO: 38, and the amino acid sequence of the heavy chain complementarity determining region 3 (HCDR3) is set forth in SEQ ID NO: 39; the light chain comprises 3 complementarity determining regions (CDRs), wherein the amino acid sequence of the light chain complementarity determining region 1 (LCDR1) is set forth in SEQ ID NO: 40, the amino acid sequence of the light chain complementarity determining region 2 (LCDR2) is set forth in SEQ ID NO: 41, and the amino acid sequence of the light chain complementarity determining region 3 (LCDR3) is set forth in SEQ ID NO: 42, wherein the CDRs are determined according to the Kabat numbering scheme.

11. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-10, wherein

A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the anti-FR α antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 28, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 29;

or

A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the anti-DLL3 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 18, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 19; or

A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the anti-B7H3 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 7, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 8; or

A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the anti-HER2 antibody or the antigen-binding fragment thereof comprises a heavy chain and/or a light chain, wherein the sequence of a variable region of the heavy chain (HV) is set forth in SEQ ID NO: 35, and the sequence of a variable region of the light chain (LV) is set forth in SEQ ID NO: 36.

12. The antibody-drug conjugate having the structure of formula (I), and the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-11, wherein

A is an antibody or an antigen-binding fragment thereof targeting FR α , wherein the anti-FR α antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 30 or SEQ ID NO: 32, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 31; or

A is an antibody or an antigen-binding fragment thereof targeting DLL3, wherein the anti-DLL3 antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 20, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 21; or

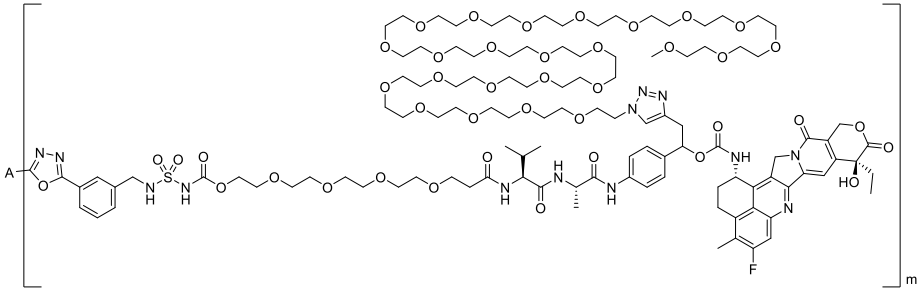
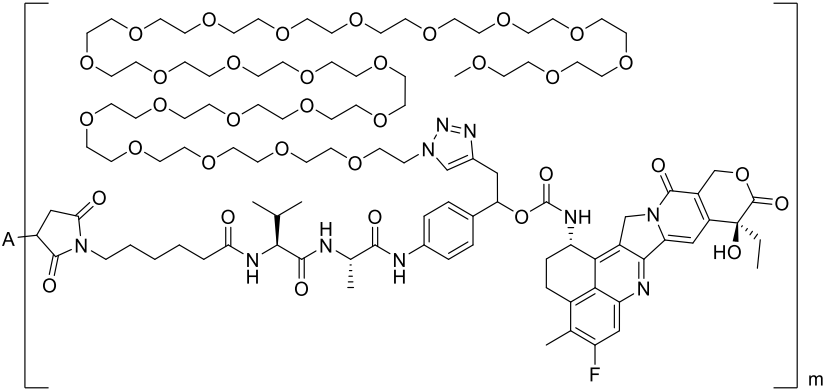
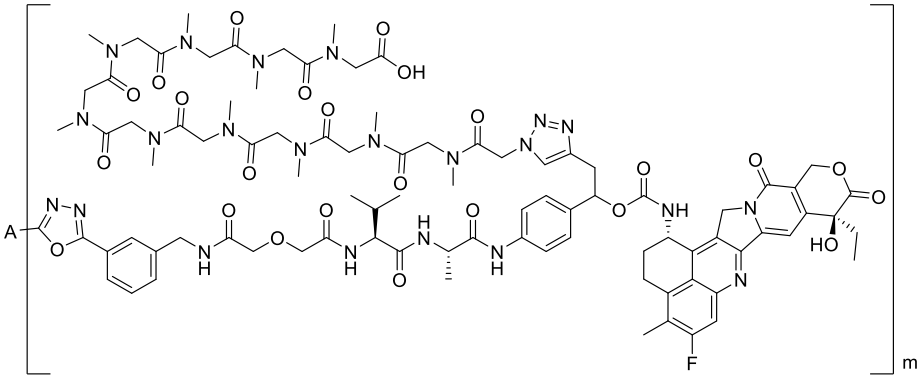
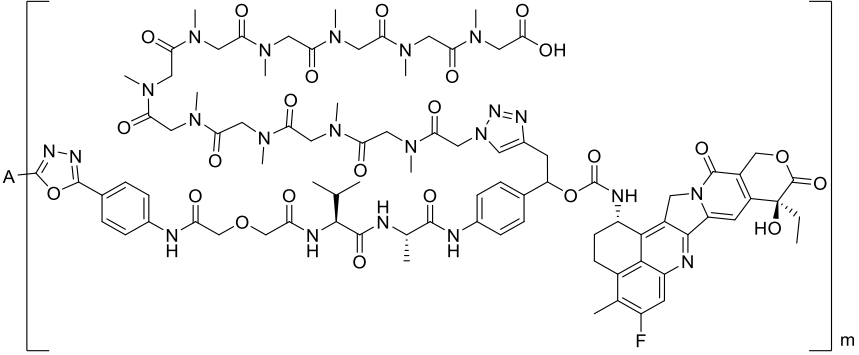
A is an antibody or an antigen-binding fragment thereof targeting B7H3, wherein the anti-B7H3 antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence of the heavy chain is set forth in SEQ ID NO: 9 or SEQ ID NO: 10, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 11; or

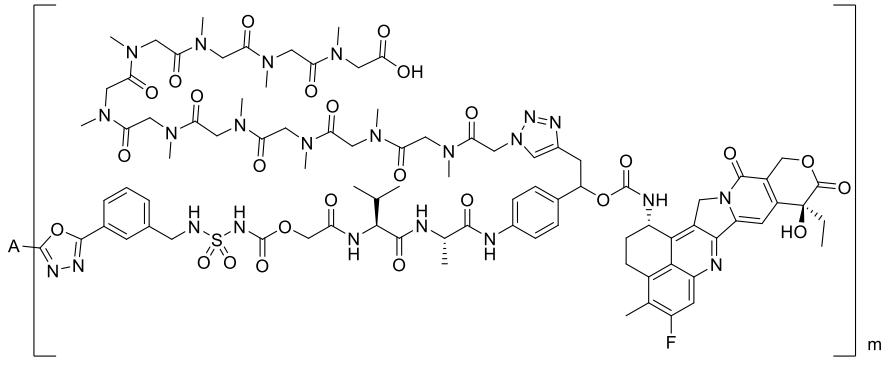
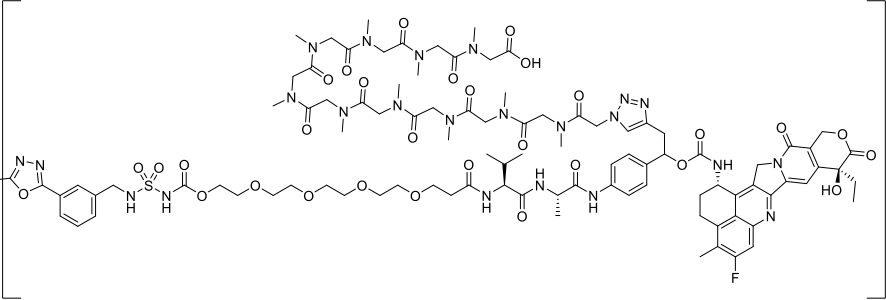
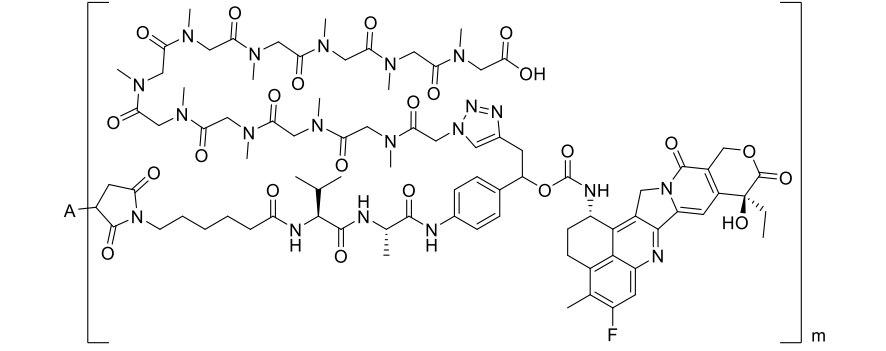
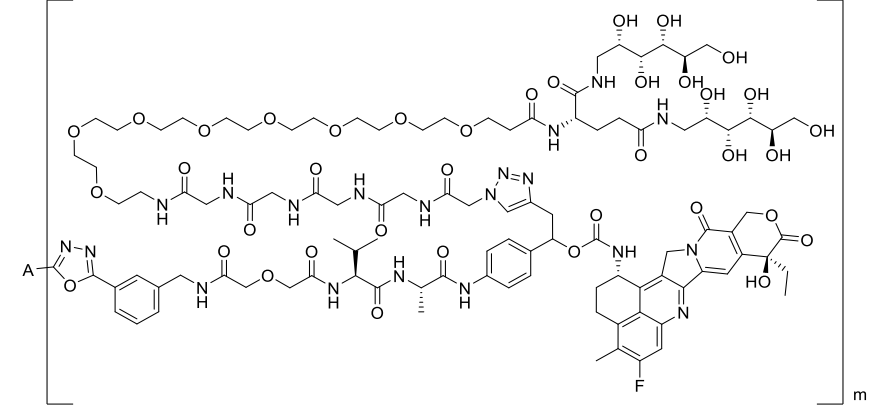
A is an antibody or an antigen-binding fragment thereof targeting HER2, wherein the anti-HER2 antibody comprises a heavy chain and/or a light chain, wherein the amino acid sequence

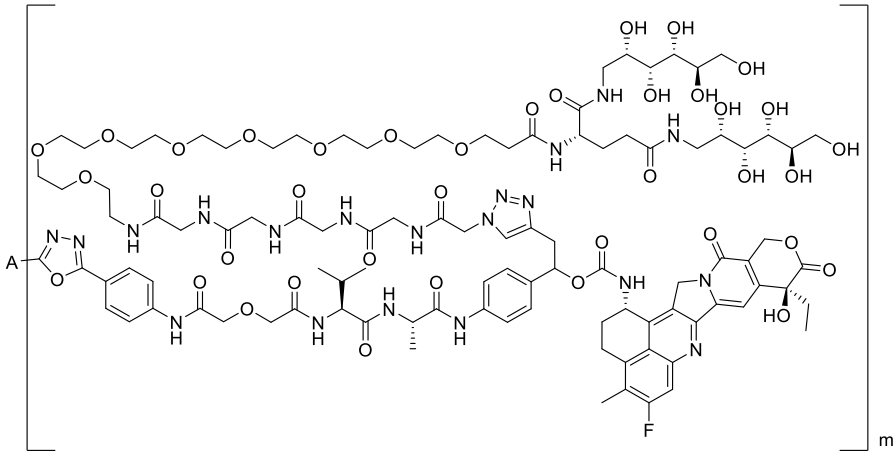
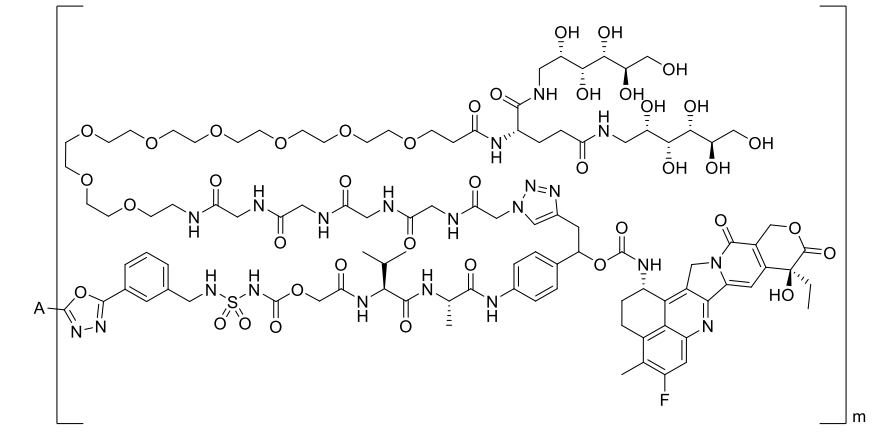
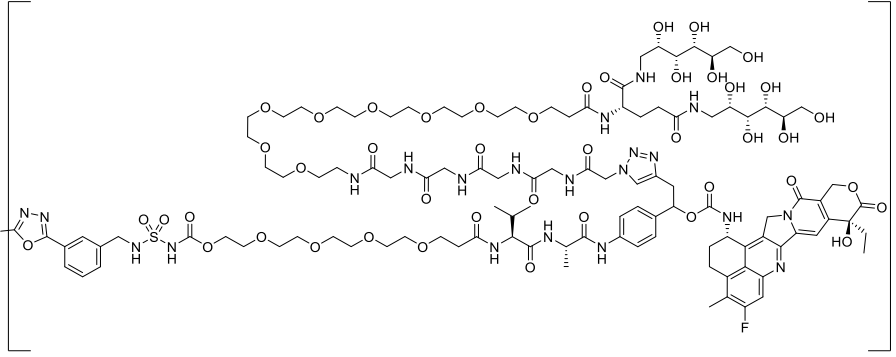
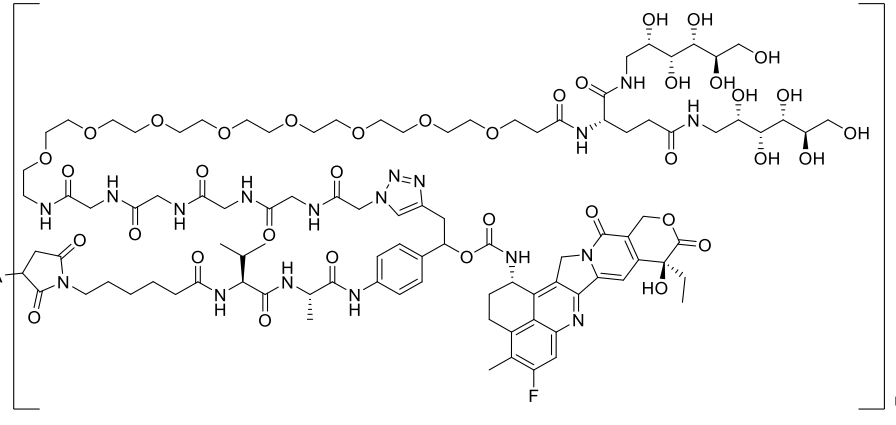
of the heavy chain is set forth in SEQ ID NO: 33, and the amino acid sequence of the light chain is set forth in SEQ ID NO: 34.

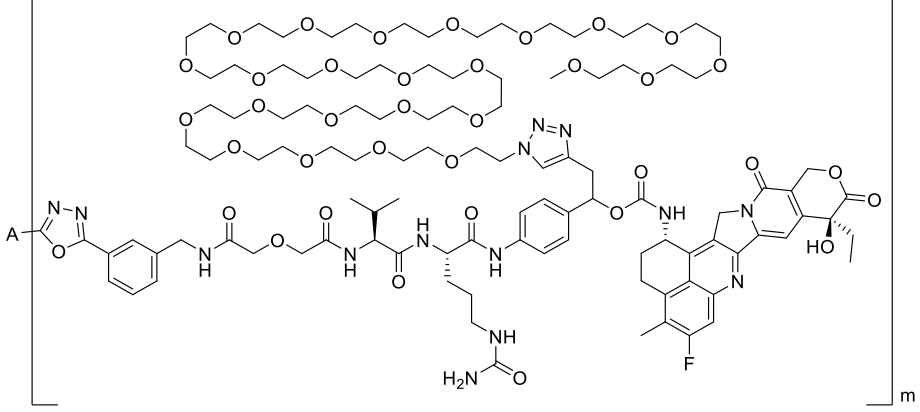
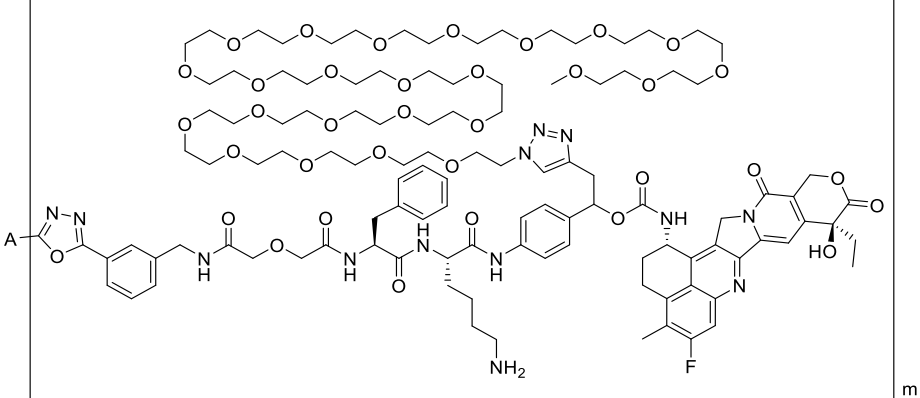
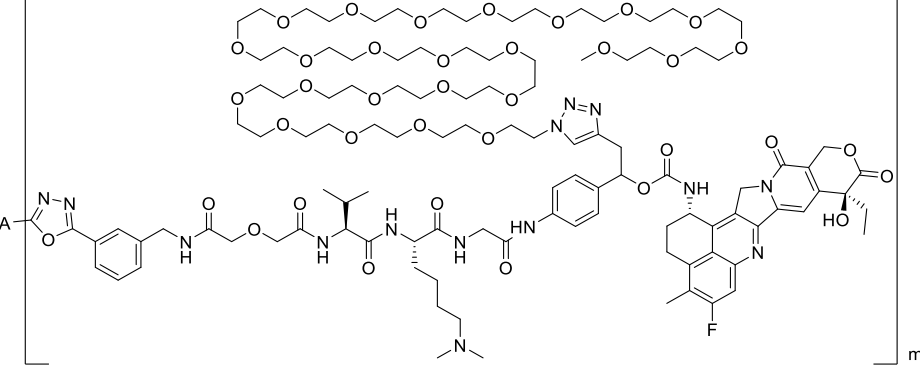
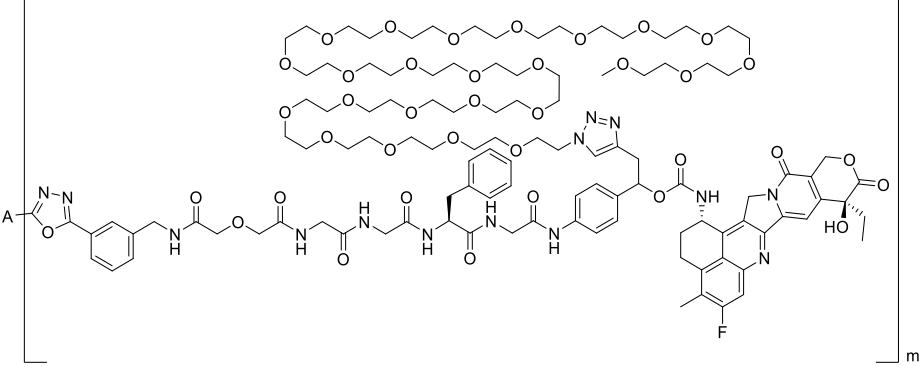
13. The antibody-drug conjugate having the structure of formula (I), the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-12, selected from the following structures:

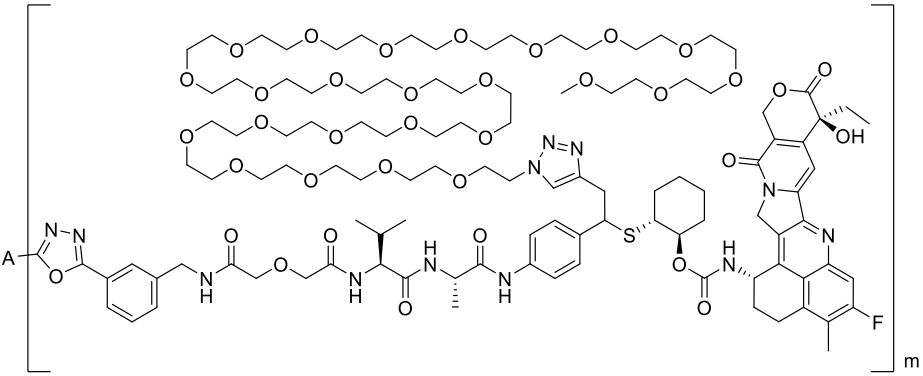
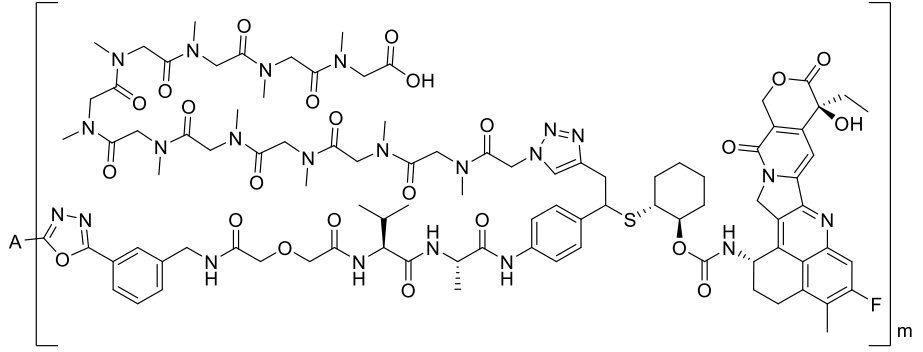
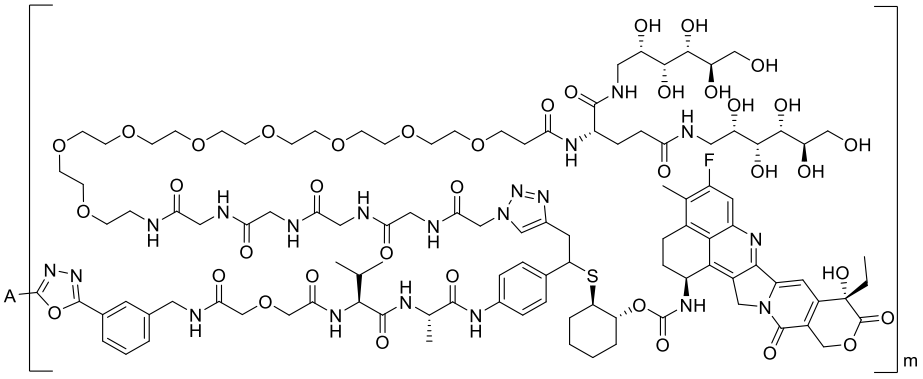
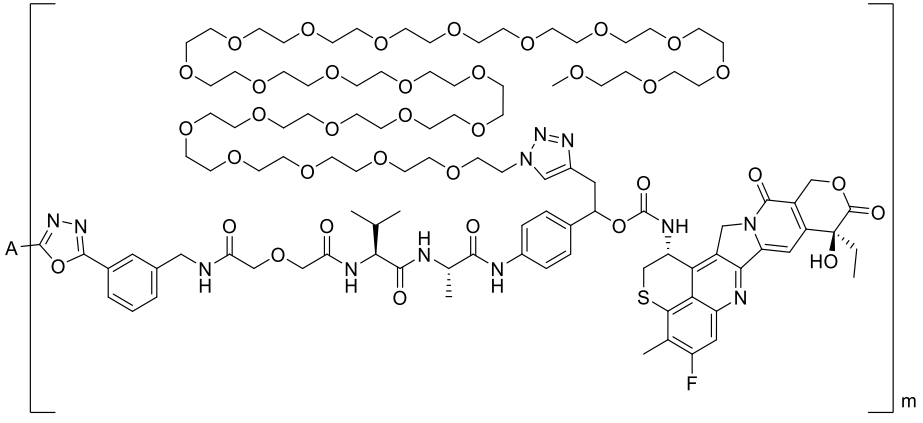
No.	Structure
ADC1	
ADC2	
ADC3	

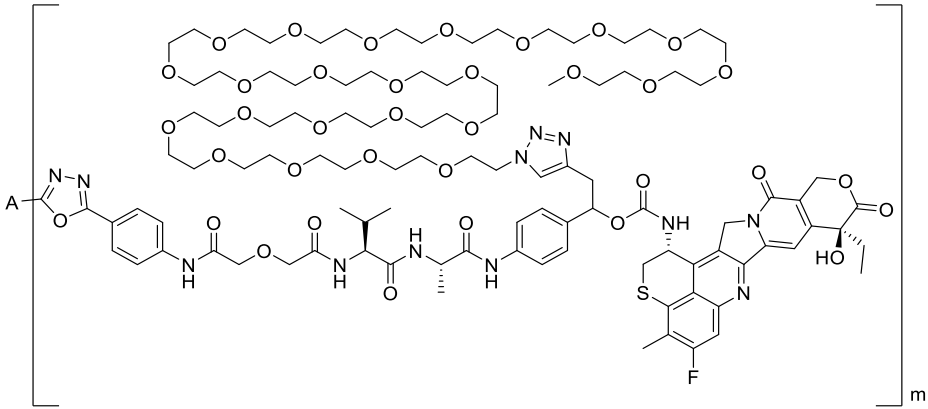
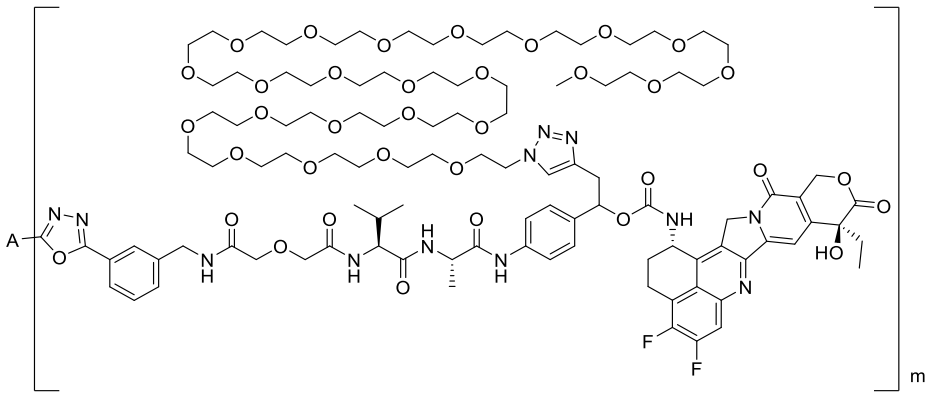
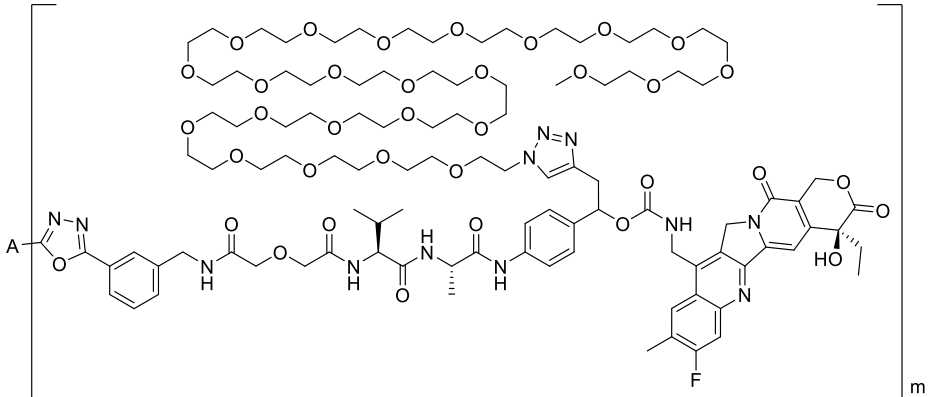
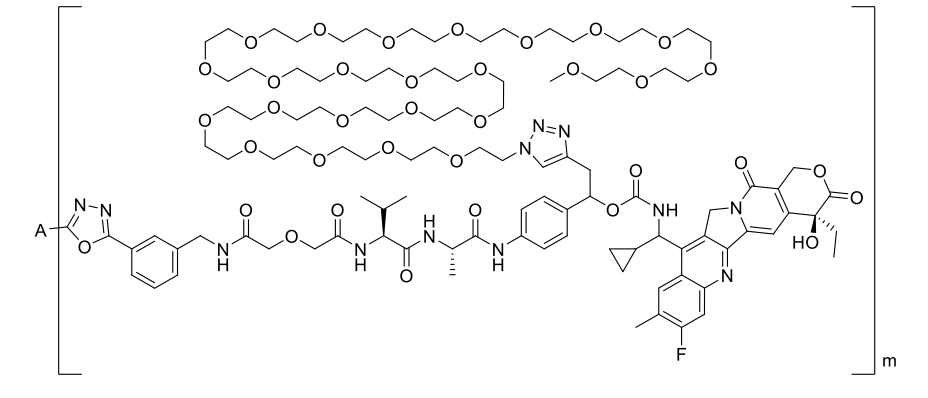
ADC4	 Chemical structure of ADC4, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a sulfonamide group, a poly(ethylene glycol) (PEG) chain, and a triazole ring. The triazole ring is connected to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety. The linker system is attached to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety.
ADC5	 Chemical structure of ADC5, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a sulfonamide group, a poly(ethylene glycol) (PEG) chain, and a triazole ring. The triazole ring is connected to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety. The linker system is attached to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety.
ADC6	 Chemical structure of ADC6, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a sulfonamide group, a poly(ethylene glycol) (PEG) chain, and a triazole ring. The triazole ring is connected to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety. The linker system is attached to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety.
ADC7	 Chemical structure of ADC7, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a sulfonamide group, a poly(ethylene glycol) (PEG) chain, and a triazole ring. The triazole ring is connected to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety. The linker system is attached to a fluorinated quinoline moiety, which is further linked to a fluorinated quinoline moiety.

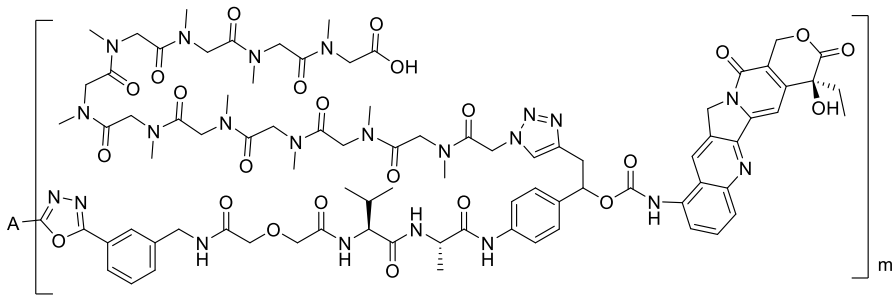
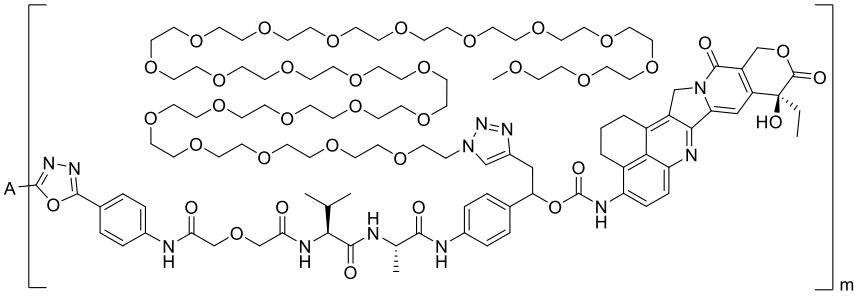
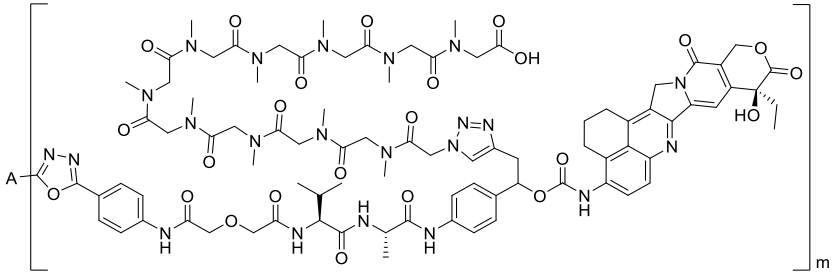
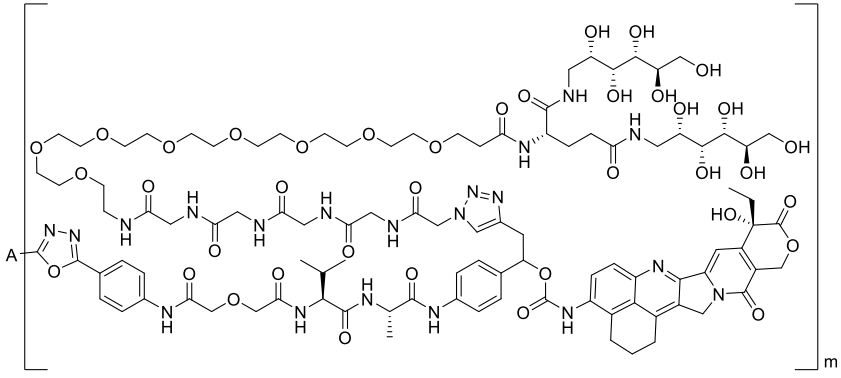
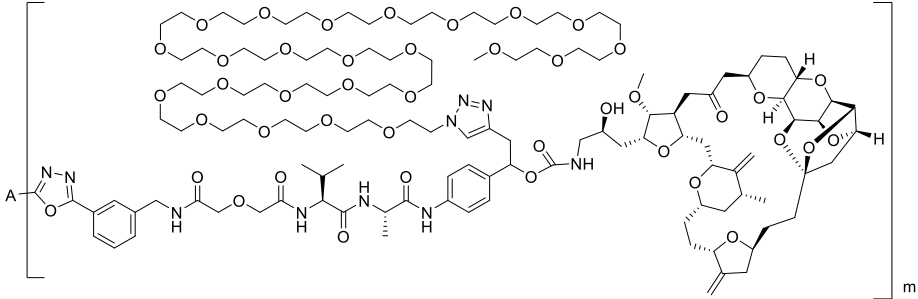
ADC8	 Chemical structure of ADC8, a conjugate consisting of a fluorinated quinoline core linked via an amide bond to a triazole-containing linker, which is further connected to a sulfonamide group and a poly(amide-ester) chain. The structure is enclosed in brackets with a subscript 'm'.
ADC9	 Chemical structure of ADC9, a conjugate consisting of a fluorinated quinoline core linked via an amide bond to a triazole-containing linker, which is further connected to a sulfonamide group and a poly(amide-ester) chain. The structure is enclosed in brackets with a subscript 'm'.
ADC10	 Chemical structure of ADC10, a conjugate consisting of a fluorinated quinoline core linked via an amide bond to a triazole-containing linker, which is further connected to a sulfonamide group and a poly(amide-ester) chain. The structure is enclosed in brackets with a subscript 'm'.
ADC11	 Chemical structure of ADC11, a conjugate consisting of a fluorinated quinoline core linked via an amide bond to a triazole-containing linker, which is further connected to a sulfonamide group and a poly(amide-ester) chain. The structure is enclosed in brackets with a subscript 'm'.

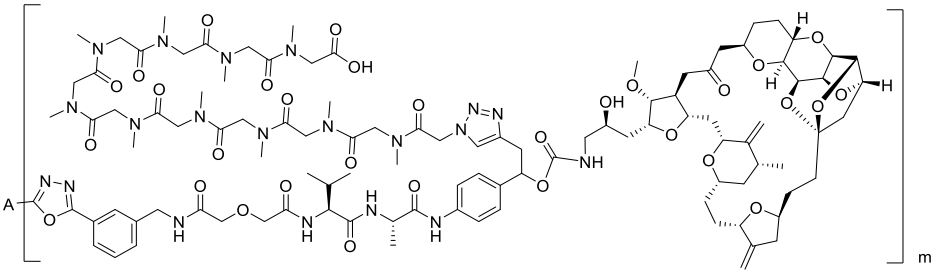
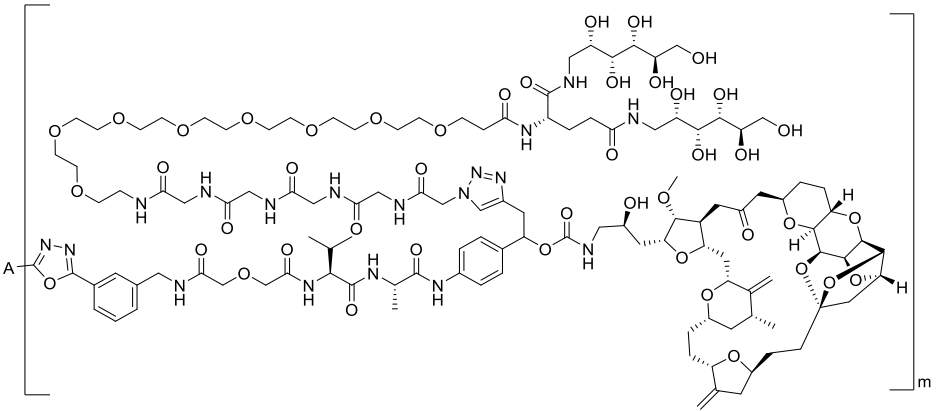
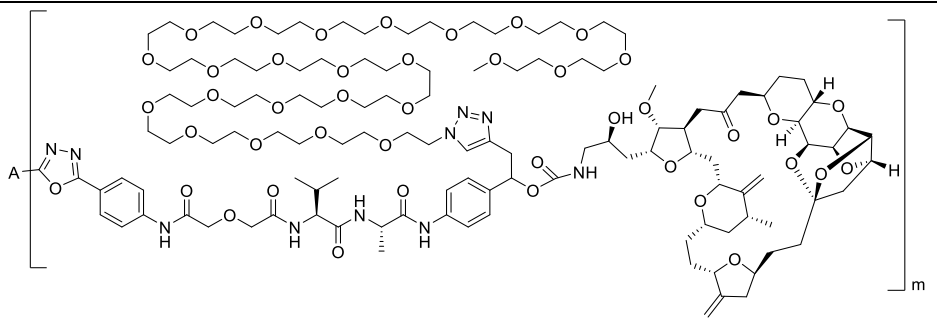
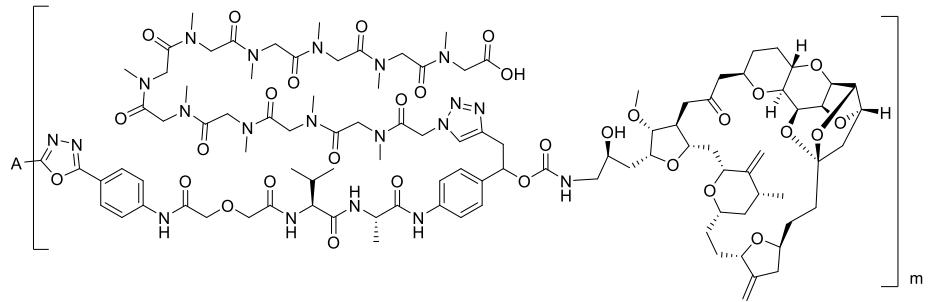
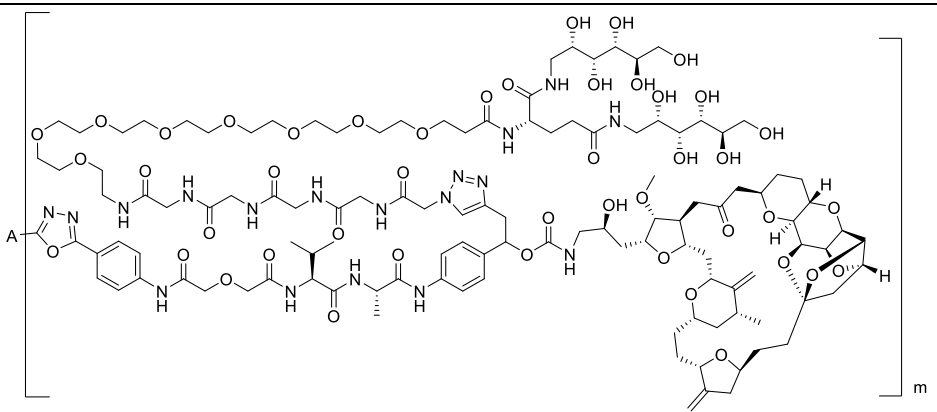
ADC12	 Chemical structure of ADC12, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long poly(ethylene glycol) (PEG) linker chain. The linker is connected to a fluorinated quinoline moiety, which is further linked to a complex peptide chain. The peptide chain includes a triazole ring and a sulfonamide group. The structure also shows a complex sugar moiety with multiple hydroxyl groups.
ADC13	 Chemical structure of ADC13, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long poly(ethylene glycol) (PEG) linker chain. The linker is connected to a fluorinated quinoline moiety, which is further linked to a complex peptide chain. The peptide chain includes a triazole ring and a sulfonamide group. The structure also shows a complex sugar moiety with multiple hydroxyl groups.
ADC14	 Chemical structure of ADC14, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long poly(ethylene glycol) (PEG) linker chain. The linker is connected to a fluorinated quinoline moiety, which is further linked to a complex peptide chain. The peptide chain includes a triazole ring and a sulfonamide group. The structure also shows a complex sugar moiety with multiple hydroxyl groups.
ADC15	 Chemical structure of ADC15, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long poly(ethylene glycol) (PEG) linker chain. The linker is connected to a fluorinated quinoline moiety, which is further linked to a complex peptide chain. The peptide chain includes a triazole ring and a sulfonamide group. The structure also shows a complex sugar moiety with multiple hydroxyl groups.

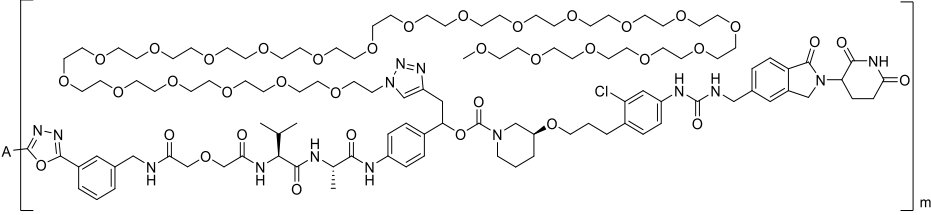
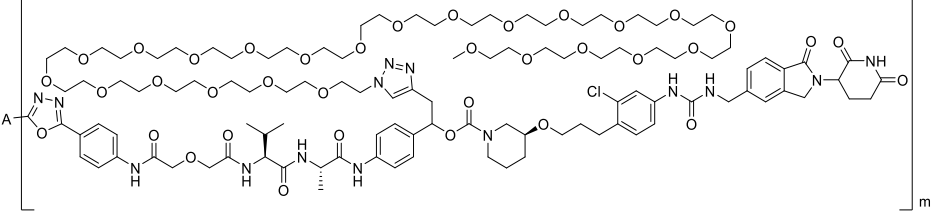
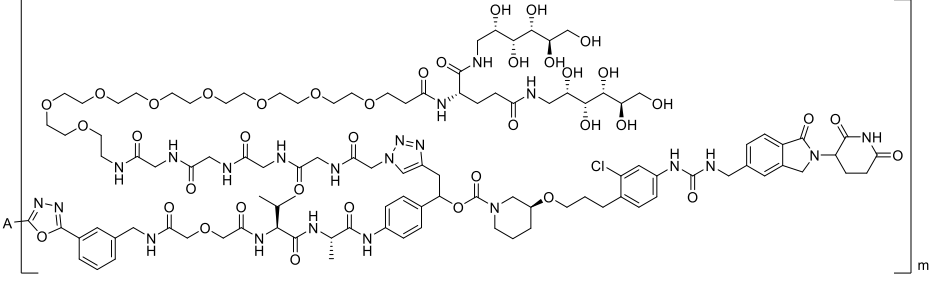
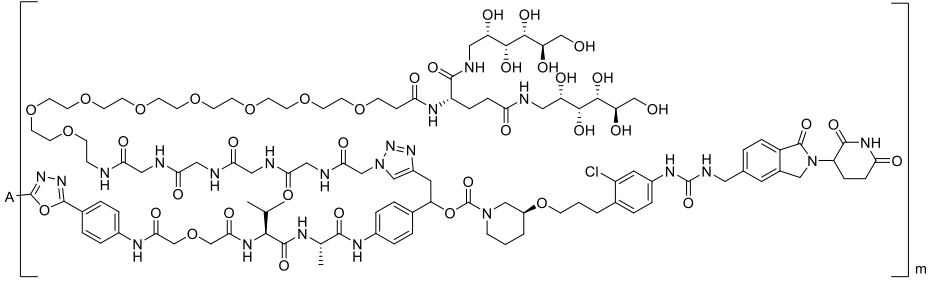
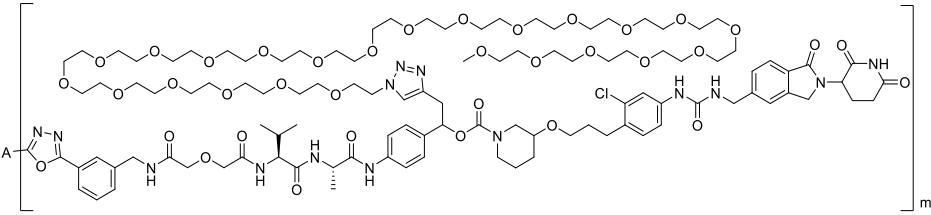
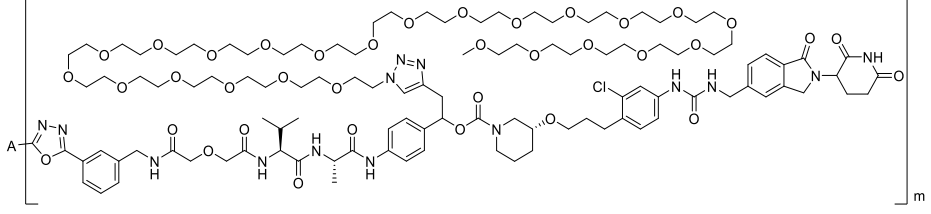
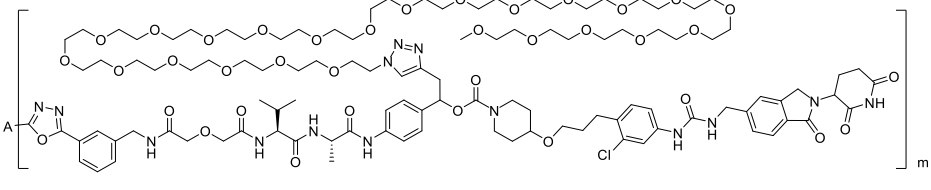
ADC16	 Chemical structure of ADC16, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain includes a hydrophobic residue (isopropyl) and a hydrophilic residue (amino acid). The peptide chain is connected to a fluorinated phenyl ring via an amide linkage. The fluorinated phenyl ring is connected to a complex polycyclic system, which includes a fluorine atom and a hydroxyl group.
ADC17	 Chemical structure of ADC17, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain includes a hydrophobic residue (isopropyl) and a hydrophilic residue (amino acid). The peptide chain is connected to a fluorinated phenyl ring via an amide linkage. The fluorinated phenyl ring is connected to a complex polycyclic system, which includes a fluorine atom and a hydroxyl group.
ADC18	 Chemical structure of ADC18, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain includes a hydrophobic residue (isopropyl) and a hydrophilic residue (amino acid). The peptide chain is connected to a fluorinated phenyl ring via an amide linkage. The fluorinated phenyl ring is connected to a complex polycyclic system, which includes a fluorine atom and a hydroxyl group.
ADC19	 Chemical structure of ADC19, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a long, flexible poly(ethylene glycol) (PEG) linker chain. The linker is connected to a phenyl ring via a triazole linkage. The phenyl ring is further connected to a peptide chain. The peptide chain includes a hydrophobic residue (isopropyl) and a hydrophilic residue (amino acid). The peptide chain is connected to a fluorinated phenyl ring via an amide linkage. The fluorinated phenyl ring is connected to a complex polycyclic system, which includes a fluorine atom and a hydroxyl group.

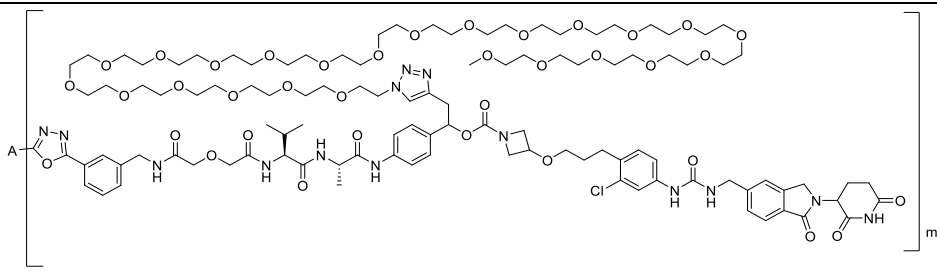
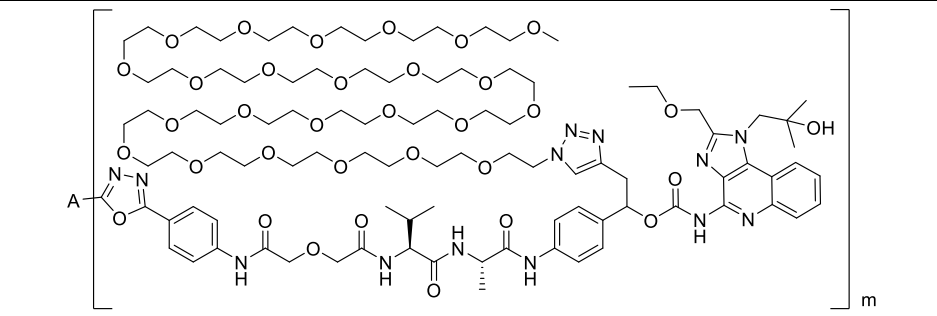
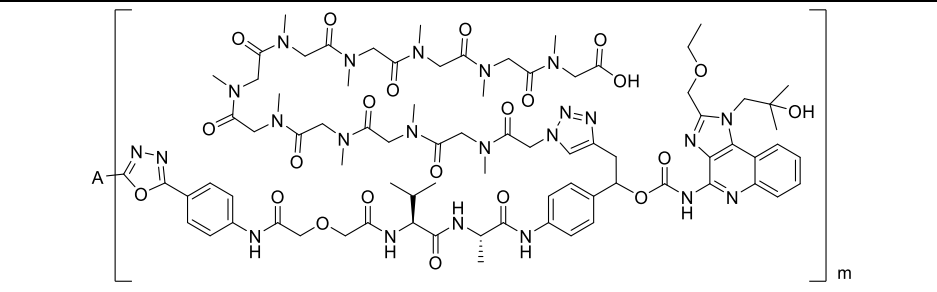
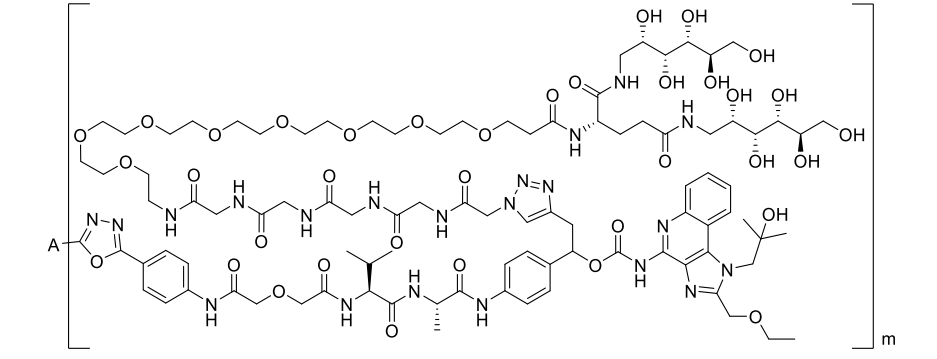
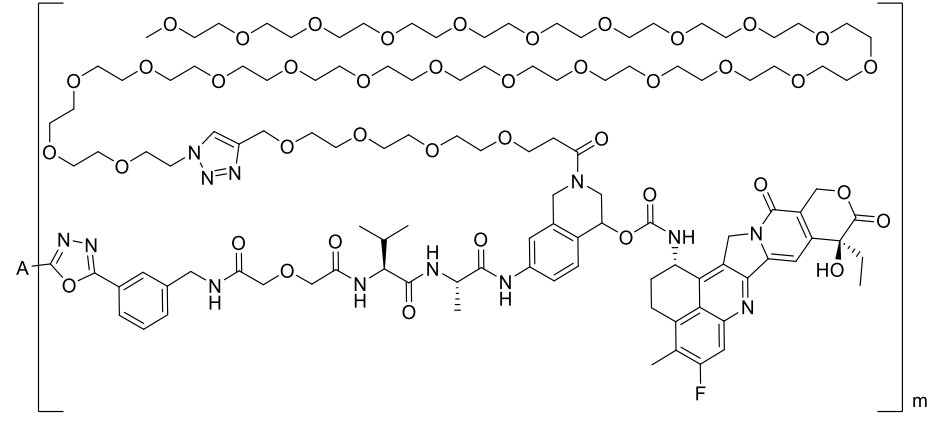
ADC20	 Chemical structure of ADC20, a conjugate consisting of a fluorinated nucleoside derivative linked via a thioether bridge to a triazole-containing linker, which is further connected to a poly(ethylene glycol) (PEG) chain. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC21	 Chemical structure of ADC21, a conjugate consisting of a fluorinated nucleoside derivative linked via a thioether bridge to a triazole-containing linker, which is further connected to a poly(ethylene glycol) (PEG) chain. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC22	 Chemical structure of ADC22, a conjugate consisting of a fluorinated nucleoside derivative linked via a thioether bridge to a triazole-containing linker, which is further connected to a poly(ethylene glycol) (PEG) chain. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC23	 Chemical structure of ADC23, a conjugate consisting of a fluorinated nucleoside derivative linked via a thioether bridge to a triazole-containing linker, which is further connected to a poly(ethylene glycol) (PEG) chain. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.

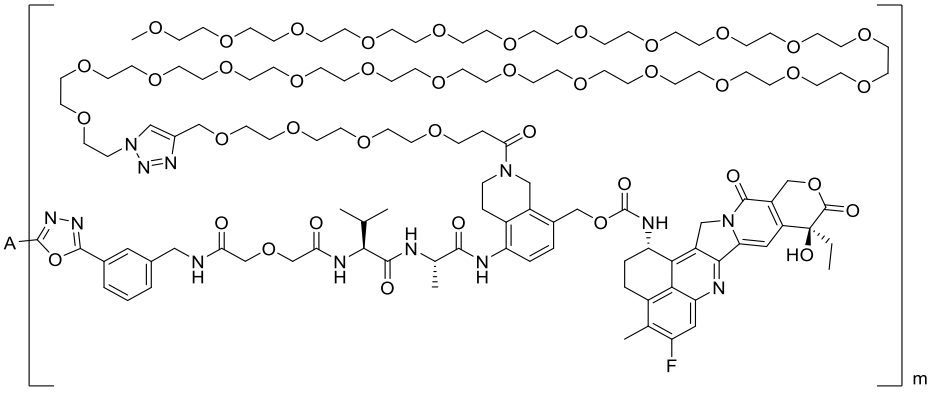
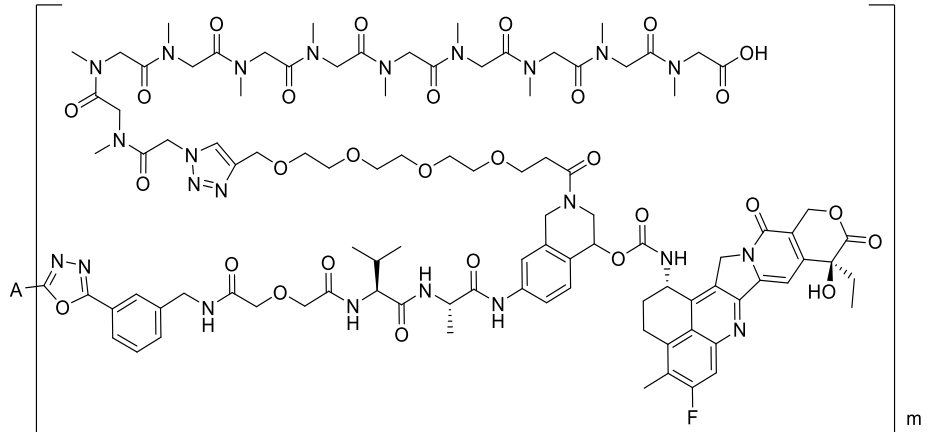
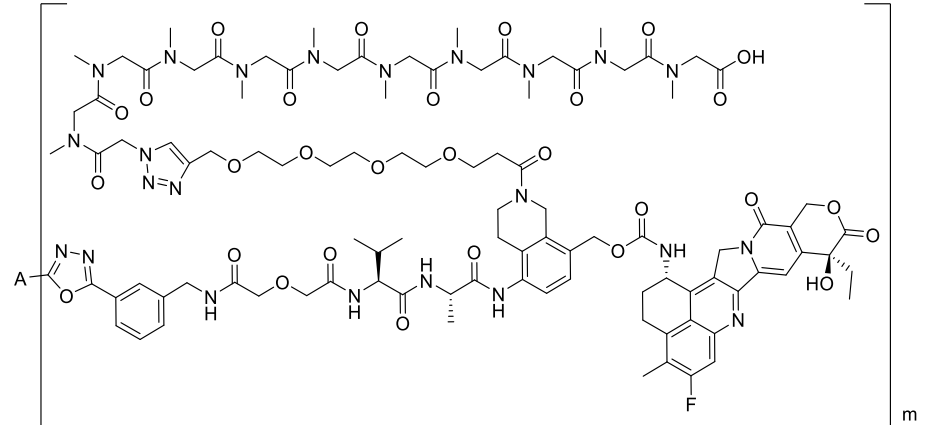
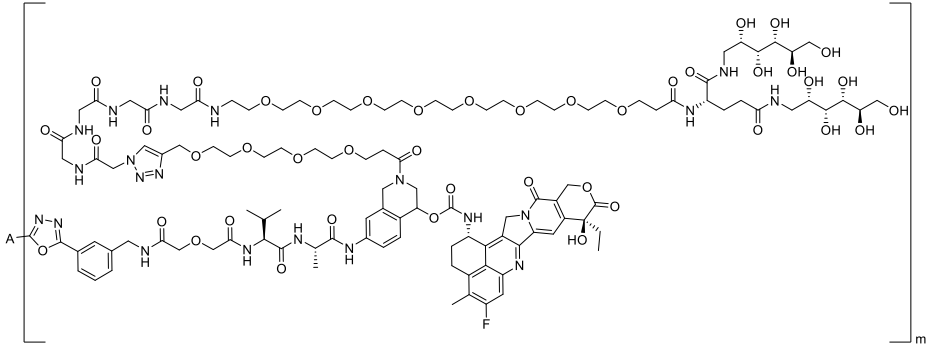
ADC24	 Chemical structure of ADC24, a conjugate consisting of a poly(ethylene glycol) (PEG) chain linked via an azide group to a linker molecule. The linker molecule contains a fluorinated benzimidazole moiety and a hydroxyl group. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC25	 Chemical structure of ADC25, a conjugate consisting of a poly(ethylene glycol) (PEG) chain linked via an azide group to a linker molecule. The linker molecule contains a fluorinated benzimidazole moiety and a hydroxyl group. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC26	 Chemical structure of ADC26, a conjugate consisting of a poly(ethylene glycol) (PEG) chain linked via an azide group to a linker molecule. The linker molecule contains a fluorinated benzimidazole moiety and a hydroxyl group. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.
ADC27	 Chemical structure of ADC27, a conjugate consisting of a poly(ethylene glycol) (PEG) chain linked via an azide group to a linker molecule. The linker molecule contains a fluorinated benzimidazole moiety and a hydroxyl group. The structure is shown within brackets with a subscript 'm' indicating the number of repeating units.

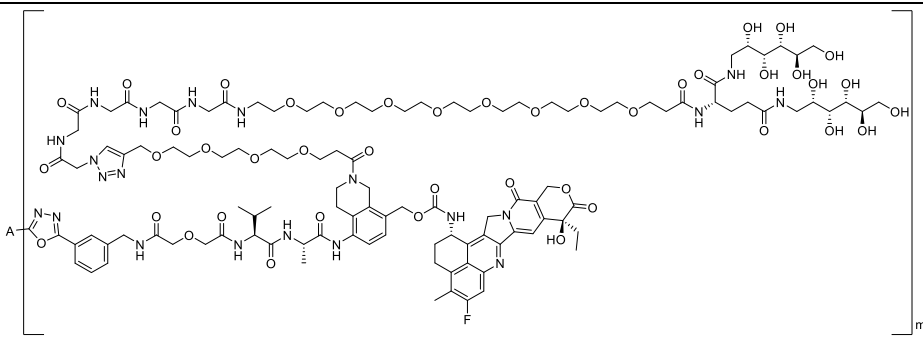
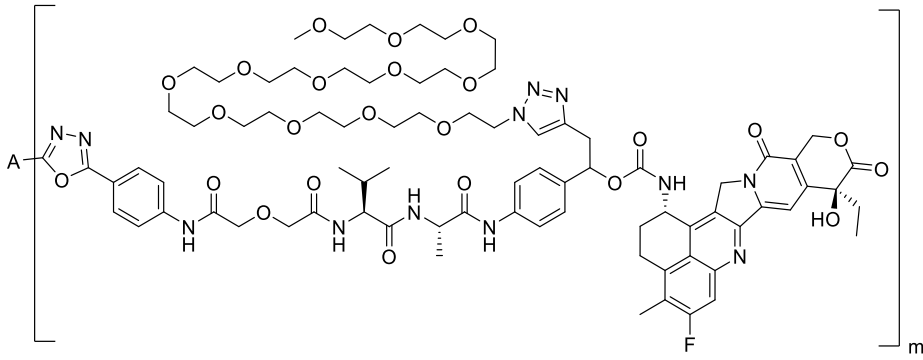
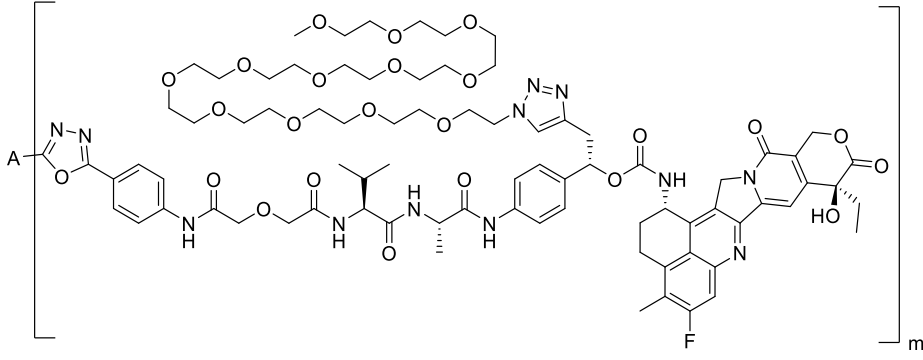
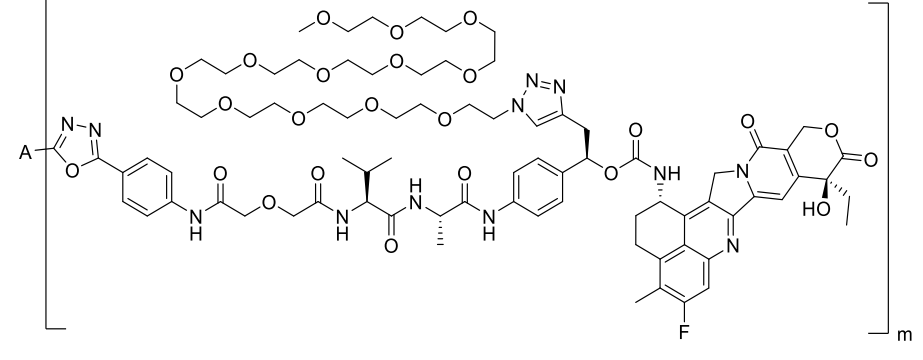
ADC28	 Chemical structure of ADC28, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a poly(amide) chain. The chain terminates in a triazole ring, which is connected to a complex polycyclic aromatic system, including a quinoline derivative.
ADC29	 Chemical structure of ADC29, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a poly(amide) chain. The chain terminates in a triazole ring, which is connected to a complex polycyclic aromatic system, including a quinoline derivative.
ADC30	 Chemical structure of ADC30, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a poly(amide) chain. The chain terminates in a triazole ring, which is connected to a complex polycyclic aromatic system, including a quinoline derivative.
ADC31	 Chemical structure of ADC31, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a poly(amide) chain. The chain terminates in a triazole ring, which is connected to a complex polycyclic aromatic system, including a quinoline derivative.
ADC32	 Chemical structure of ADC32, a conjugate consisting of a linker (A) connected to a phenyl ring, which is further linked to a poly(amide) chain. The chain terminates in a triazole ring, which is connected to a complex polycyclic aromatic system, including a quinoline derivative.

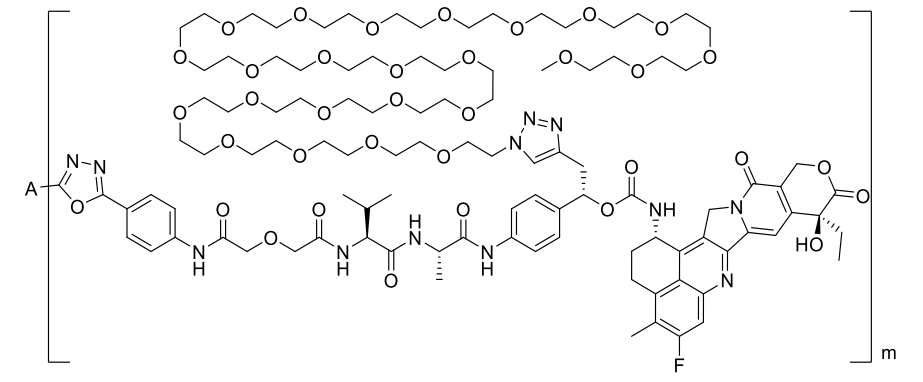
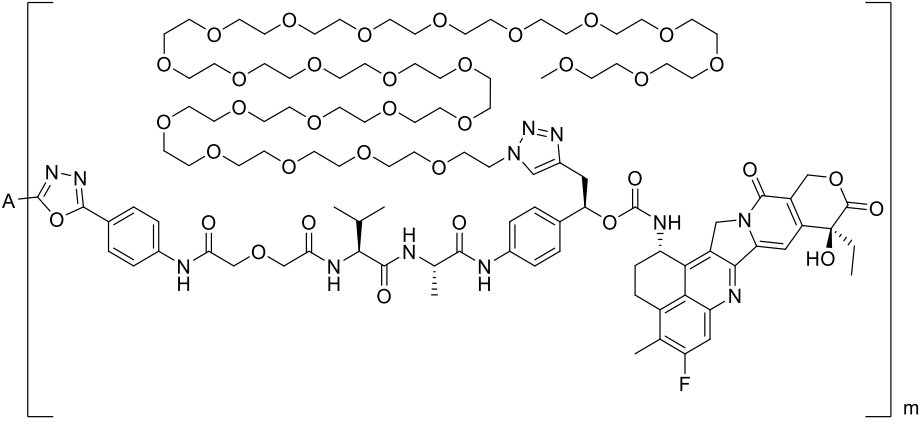
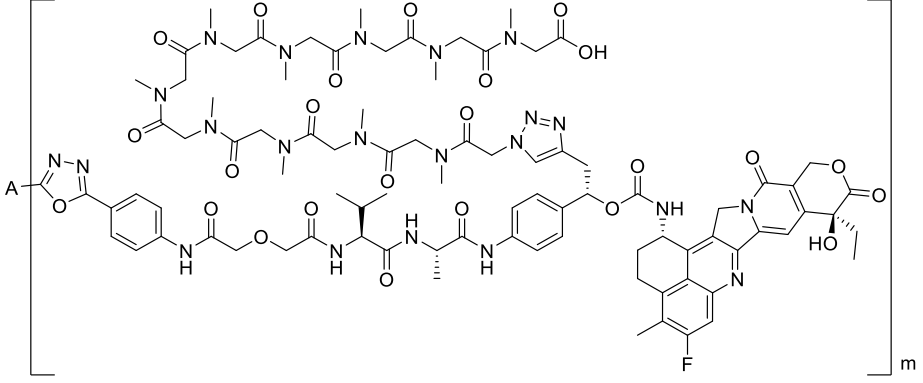
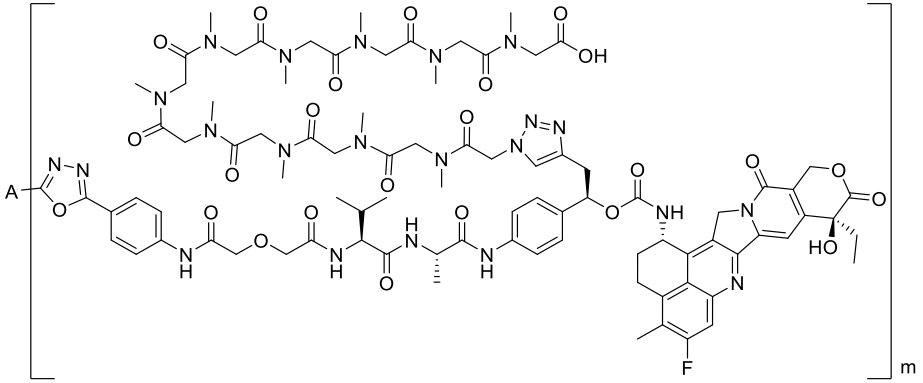
ADC33	 Chemical structure of ADC33, a conjugate consisting of a linker (A) connected to a complex molecule. The linker (A) is a 4-azobenzene derivative. The complex molecule features a long chain of amide bonds, a triazole ring, and a complex polycyclic structure with multiple hydroxyl groups and a terminal carboxylic acid group. The structure is enclosed in brackets with a subscript 'm'.
ADC34	 Chemical structure of ADC34, a conjugate consisting of a linker (A) connected to a complex molecule. The linker (A) is a 4-azobenzene derivative. The complex molecule features a long chain of amide bonds, a triazole ring, and a complex polycyclic structure with multiple hydroxyl groups and a terminal carboxylic acid group. The structure is enclosed in brackets with a subscript 'm'.
ADC35	 Chemical structure of ADC35, a conjugate consisting of a linker (A) connected to a complex molecule. The linker (A) is a 4-azobenzene derivative. The complex molecule features a long chain of amide bonds, a triazole ring, and a complex polycyclic structure with multiple hydroxyl groups and a terminal carboxylic acid group. The structure is enclosed in brackets with a subscript 'm'.
ADC36	 Chemical structure of ADC36, a conjugate consisting of a linker (A) connected to a complex molecule. The linker (A) is a 4-azobenzene derivative. The complex molecule features a long chain of amide bonds, a triazole ring, and a complex polycyclic structure with multiple hydroxyl groups and a terminal carboxylic acid group. The structure is enclosed in brackets with a subscript 'm'.
ADC37	 Chemical structure of ADC37, a conjugate consisting of a linker (A) connected to a complex molecule. The linker (A) is a 4-azobenzene derivative. The complex molecule features a long chain of amide bonds, a triazole ring, and a complex polycyclic structure with multiple hydroxyl groups and a terminal carboxylic acid group. The structure is enclosed in brackets with a subscript 'm'.

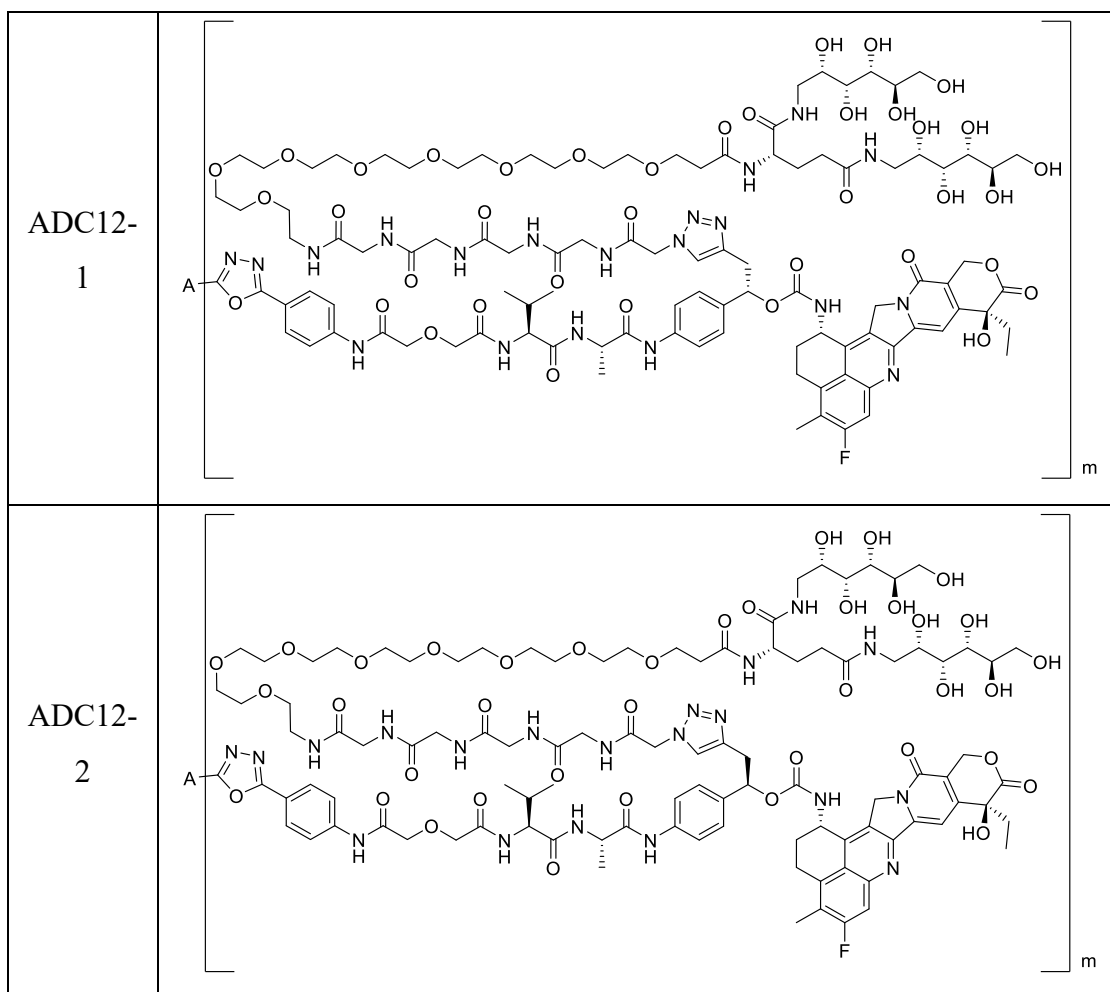
ADC38	
ADC39	
ADC40	
ADC41	
ADC42	
ADC43	
ADC44	

ADC45	
ADC46	
ADC47	
ADC48	
ADC49	

ADC50	 Chemical structure of ADC50, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a linker system. The linker system includes a triazole ring connected to a poly(ethylene glycol) (PEG) chain, which is further connected to a carbamate group. The structure is shown within brackets with a subscript 'm'.
ADC51	 Chemical structure of ADC51, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a linker system. The linker system includes a triazole ring connected to a poly(ethylene glycol) (PEG) chain, which is further connected to a carbamate group. The structure is shown within brackets with a subscript 'm'.
ADC52	 Chemical structure of ADC52, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a linker system. The linker system includes a triazole ring connected to a poly(ethylene glycol) (PEG) chain, which is further connected to a carbamate group. The structure is shown within brackets with a subscript 'm'.
ADC53	 Chemical structure of ADC53, a conjugate consisting of a fluorinated nucleoside derivative linked via a carbamate to a linker system. The linker system includes a triazole ring connected to a poly(ethylene glycol) (PEG) chain, which is further connected to a carbamate group. The structure is shown within brackets with a subscript 'm'.

ADC54	 Chemical structure of ADC54 repeating unit. The structure is enclosed in brackets with a subscript 'm'. It features a central core with a fluorine atom and a hydroxyl group. The core is connected via amide bonds to a long, flexible linker chain consisting of multiple ether and amide groups. The linker chain is terminated by a triazole ring, which is further connected to a phenyl ring and a hydroxyl group.
ADC55	 Chemical structure of ADC55 repeating unit. The structure is enclosed in brackets with a subscript 'm'. It features a central core with a fluorine atom and a hydroxyl group. The core is connected via amide bonds to a long, flexible linker chain consisting of multiple ether and amide groups. The linker chain is terminated by a triazole ring, which is further connected to a phenyl ring and a hydroxyl group.
ADC55-1	 Chemical structure of ADC55-1 repeating unit. The structure is enclosed in brackets with a subscript 'm'. It features a central core with a fluorine atom and a hydroxyl group. The core is connected via amide bonds to a long, flexible linker chain consisting of multiple ether and amide groups. The linker chain is terminated by a triazole ring, which is further connected to a phenyl ring and a hydroxyl group.
ADC55-2	 Chemical structure of ADC55-2 repeating unit. The structure is enclosed in brackets with a subscript 'm'. It features a central core with a fluorine atom and a hydroxyl group. The core is connected via amide bonds to a long, flexible linker chain consisting of multiple ether and amide groups. The linker chain is terminated by a triazole ring, which is further connected to a phenyl ring and a hydroxyl group.

ADC2-1	 Chemical structure of ADC2-1, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl ring, which is further linked to a chain of amide bonds and a fluorinated pyridine ring. The linker is attached to a complex polycyclic aromatic system, which includes a fluorine atom and a hydroxyl group. The linker is also connected to a long, flexible polyether chain (poly(ethylene glycol) derivative) via a triazole ring.
ADC2-2	 Chemical structure of ADC2-2, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl ring, which is further linked to a chain of amide bonds and a fluorinated pyridine ring. The linker is attached to a complex polycyclic aromatic system, which includes a fluorine atom and a hydroxyl group. The linker is also connected to a long, flexible polyether chain (poly(ethylene glycol) derivative) via a triazole ring.
ADC7-1	 Chemical structure of ADC7-1, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl ring, which is further linked to a chain of amide bonds and a fluorinated pyridine ring. The linker is attached to a complex polycyclic aromatic system, which includes a fluorine atom and a hydroxyl group. The linker is also connected to a long, flexible polyether chain (poly(ethylene glycol) derivative) via a triazole ring.
ADC7-2	 Chemical structure of ADC7-2, a conjugated antibody-drug conjugate. The structure is enclosed in brackets with a subscript 'm'. It features a linker system consisting of a triazole ring connected to a phenyl ring, which is further linked to a chain of amide bonds and a fluorinated pyridine ring. The linker is attached to a complex polycyclic aromatic system, which includes a fluorine atom and a hydroxyl group. The linker is also connected to a long, flexible polyether chain (poly(ethylene glycol) derivative) via a triazole ring.



wherein m is an integer or a decimal from 1 to 12, preferably an integer or a decimal from 2 to 8, and further preferably 2, 4, 6, or 8.

14. A pharmaceutical composition, comprising the antibody-drug conjugate having the structure of formula (I), the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-13, and one or more pharmaceutically acceptable auxiliary materials.

15. Use of the antibody-drug conjugate having the structure of formula (I), the tautomer, the mesomer, the racemate, the enantiomer, the diastereoisomer, the pharmaceutically acceptable salt, the hydrate, the solvate or the isotopically labeled compound thereof according to any one of claims 1-13, or the pharmaceutical composition according to claim 14 for the manufacturing of a medicament for the treatment of a cancer.

16. The use according to claim 15, wherein the cancer comprises liver cancer, kidney cancer, lung cancer (e.g., small cell lung cancer and non-small cell lung cancer), gastric cancer, esophageal cancer, oral cancer, urethral cancer, bladder cancer, colon cancer, rectal cancer, prostate cancer, breast cancer, ovarian cancer, pancreatic cancer, melanoma, hematological

tumors or glioblastoma multiforme, lymphoma (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or recurrent anaplastic large cell lymphoma), cervical cancer, uterine cancer, endometrial cancer, salivary gland cancer, glioma, neuroblastoma, sarcoma, colorectal cancer, leukemia (e.g., acute lymphoblastic leukemia, acute myeloid leukemia, acute promyelocytic leukemia, chronic myeloid leukemia, or chronic lymphocytic leukemia), bone cancer, skin cancer, thyroid cancer, etc.

17. A linker-drug compound represented by formula (II), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:

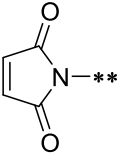
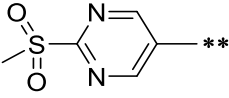
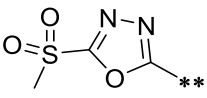
10 L'-D (II)

wherein L' is a linker moiety;

D is an amino-containing bioactive molecule or a pharmaceutically acceptable salt thereof, covalently linked to the linker moiety L' via an amine group in its molecular structure;

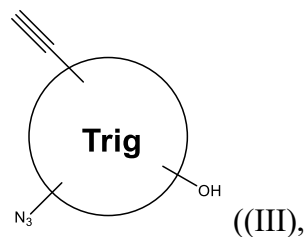
L' is represented by the following formula:

15 L₁'-L₂-L₃-L₄-,

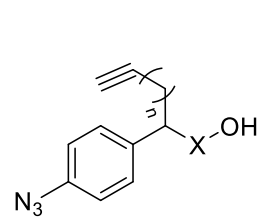
wherein L₁' is selected from , , and , wherein ** represents linkage to L₂;

L₂, L₃, L₄, and D are as defined in claims 1-8.

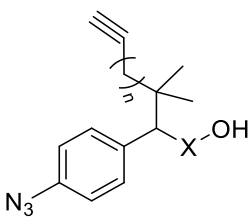
18. A compound of formula (III), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:



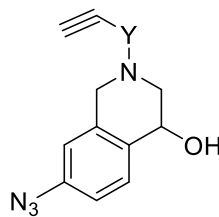
wherein formula (III) has the following structure:



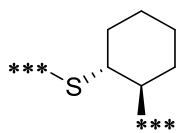
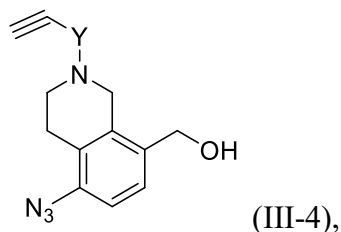
(III-1),

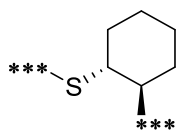


(III-2),

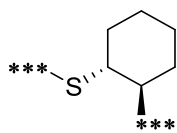
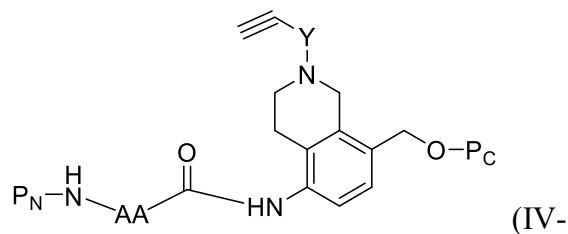
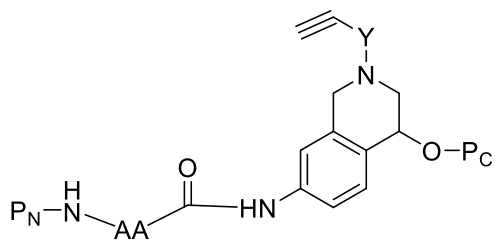
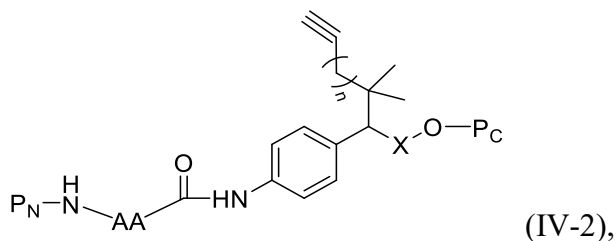
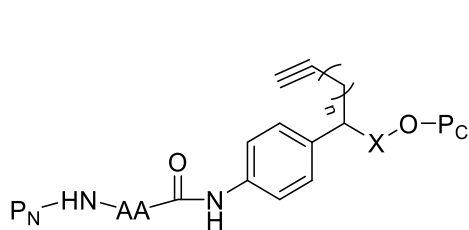


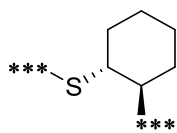
(III-3), or



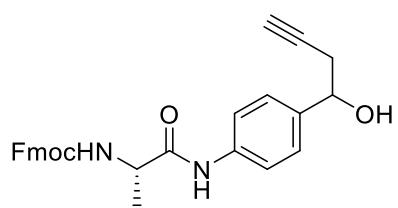
wherein X is absent or , *** represents linkage to a carbon atom, and **** represents linkage to an oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6.

19. A compound of formula (IV), or a tautomer, a mesomer, a racemate, an enantiomer or a diastereoisomer thereof, a pharmaceutically acceptable salt, a hydrate, a solvate or an isotopically labeled compound thereof:

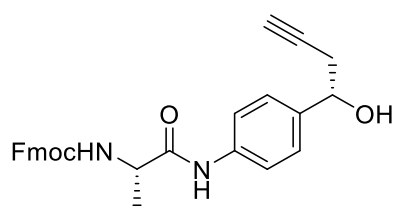


wherein X is absent or , *** represents linkage to a carbon atom, and **** represents linkage to an oxygen atom; Y is C₁-C₆ alkylene or -R³-C(O)-, wherein R³ is C₁-C₆ alkylene or heteroalkylene containing 1-8 -OCH₂CH₂- structural units; n is an integer from 0 to 6;

wherein AA is L₃ or a sub-fragment consisting of the first 1, 2, or more amino acids from the C-terminus of L₃, P_N is H or an amino protecting group such as Boc or Fmoc, and P_C is H, a hydroxyl protecting group, or a carbonate active ester group such as *p*-nitrophenyl carbonate; the compound of formula (IV) is preferably:

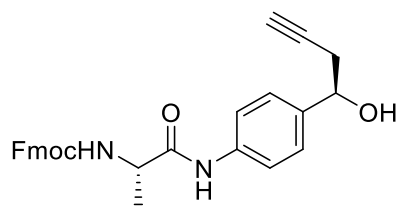


,



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or



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