

[0013] The antibodies disclosed herein can be full-length (for example, an IgG1 or IgG4 antibody) or can comprise only an antigen-binding portion (for example, a Fab, F(ab')₂ or scFv fragment), and may be modified to affect functionality, e.g., to eliminate residual effector functions (Reddy et al., 2000, J. Immunol. 164:1925-1933).

[0014] Examples of anti-MSR1 antibodies disclosed herein are listed in Tables 4 and 5. Table 4 sets forth the amino acid sequence identifiers of the heavy chain variable regions (HCVRs), light chain variable regions (LCVRs), heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3), and light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) of the exemplary anti-MSR1 antibodies. Table 5 sets forth the nucleic acid sequence identifiers of the HCVRs, LCVRs, HCDR1, HCDR2 HCDR3, LCDR1, LCDR2 and LCDR3 of the exemplary anti-MSR1 antibodies.

[0015] Provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising an HCVR comprising an amino acid sequence selected from any of the HCVR amino acid sequences listed in Table 4, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0016] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising an LCVR comprising an amino acid sequence selected from any of the LCVR amino acid sequences listed in Table 4, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0017] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising an HCVR and an LCVR amino acid sequence pair (HCVR/LCVR) comprising any of the HCVR amino acid sequences listed in Table 4 paired with any of the LCVR amino acid sequences listed in Table 4. Certain examples relate to antibodies, or antigen-binding fragments thereof, comprising an HCVR/LCVR amino acid sequence pair contained within any of the exemplary anti-MSR1 antibodies listed in Table 4. In some examples, the HCVR/LCVR amino acid sequence pair is selected from the group consisting of: 2/10, 23/42, 50/58; 90/98, and 282/290.

[0018] Provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a heavy chain CDR1 (HCDR1) comprising an amino acid sequence selected from any of the HCDR1 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0019] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a heavy chain CDR2 (HCDR2) comprising an amino acid

sequence selected from any of the HCDR2 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0020] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a heavy chain CDR3 (HCDR3) comprising an amino acid sequence selected from any of the HCDR3 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0021] Provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a light chain CDR1 (LCDR1) comprising an amino acid sequence selected from any of the LCDR1 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0022] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a light chain CDR2 (LCDR2) comprising an amino acid sequence selected from any of the LCDR2 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0023] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a light chain CDR3 (LCDR3) comprising an amino acid sequence selected from any of the LCDR3 amino acid sequences listed in Table 4 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0024] Also provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising an HCDR3 and an LCDR3 amino acid sequence pair (HCDR3/LCDR3) comprising any of the HCDR3 amino acid sequences listed in Table 4 paired with any of the LCDR3 amino acid sequences listed in Table 4. Certain examples relate to antibodies, or antigen-binding fragments thereof, comprising an HCDR3/LCDR3 amino acid sequence pair contained within any of the exemplary anti-MSR1 antibodies listed in Table 4. In some examples, the HCDR3/LCDR3 amino acid sequence pair is selected from the group consisting of: 8/16, 40/48, 56/64; 96/104, and 288/296.

[0025] Provided herein are antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising a set of six CDRs (*i.e.*, HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3) contained within any of the exemplary anti-MSR1 antibodies listed in Table 4. In certain examples, the HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences set is

selected from the group consisting of: 4-6-8-12-14-16; 36-38-40-44-46-48; 52-54-56-60-62-64; 92-94-96-100-102-104, and 284-286-288-292-294-296.

[0026] In a related example, provided herein are antibodies, or antigen-binding fragments thereof that specifically bind MSR1, comprising a set of six CDRs (*i.e.*, HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3) contained within an HCVR/LCVR amino acid sequence pair as defined by any of the exemplary anti-MSR1 antibodies listed in Table 4. For example, the present disclosure includes antibodies or antigen-binding fragments thereof that specifically bind MSR1, comprising the HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences set contained within an HCVR/LCVR amino acid sequence pair selected from the group consisting of: 2/10, 23/42, 50/58, 90/98, and 282/290. Methods and techniques for identifying CDRs within HCVR and LCVR amino acid sequences are well known in the art and can be used to identify CDRs within the specified HCVR and/or LCVR amino acid sequences disclosed herein. Exemplary conventions that can be used to identify the boundaries of CDRs include, *e.g.*, the Kabat definition, the Chothia definition, and the AbM definition. In general terms, the Kabat definition is based on sequence variability, the Chothia definition is based on the location of the structural loop regions, and the AbM definition is a compromise between the Kabat and Chothia approaches. See, *e.g.*, Kabat, "Sequences of Proteins of Immunological Interest," National Institutes of Health, Bethesda, Md. (1991); Al-Lazikani *et al.*, *J. Mol. Biol.* 273:927-948 (1997); and Martin *et al.*, *Proc. Natl. Acad. Sci. USA* 86:9268-9272 (1989). Public databases are also available for identifying CDR sequences within an antibody.

[0026a] In one aspect, provided herein is an isolated antibody or antigen-binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1), wherein the antibody or antigen-binding fragment thereof exhibits one or more properties selected from the group consisting of: (i) binds human MSR1 at 37°C with a K_D of less than about 1.4 nM as measured by surface plasmon resonance; (ii) binds human MSR1 at 37°C with a $t_{1/2}$ of greater than about 4 minutes as measured by surface plasmon resonance; (iii) exhibits maximum inhibition of modified LDL uptake by human MSR1 of less than about 90% with an IC_{50} of less than about 10 nM as measured by ligand uptake assay; (iv) blocks < 50% of modified LDL binding to human MSR1 as measured by competition ELISA assay; and (v) exhibits binding of human MSR1 and internalization of the bound complex of more than about 10% as assayed by binding in THP-1 cells.

[0026b] In another aspect, provided herein is an isolated antibody or antigen-binding fragment thereof that binds to cell surface-expressed macrophage scavenger receptor 1 (MSR1) and blocks inhibition of modified LDL uptake by MSR1 by less than 80% with an IC_{50} of less than 3.5 nM.

[0026c] In another aspect, provided herein is an isolated antibody or antigen-binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1), wherein the antibody or antigen-binding fragment comprises: (a) the complementarity determining regions (CDRs) of a heavy chain variable region (HCVR) having an amino acid sequence as set forth in Table 4; and (b) the CDRs of a light chain variable region (LCVR) having an amino acid sequence as set forth in Table 4.

[0026d] In another aspect, provided herein is an isolated antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof competes for binding to human MSR1 with a reference antibody comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOS: 2/10, 23/42, 50/58; 90/98, and 282/290.

[0027] Also provided herein are nucleic acid molecules encoding anti-MSR1 antibodies or portions thereof. For example, provided herein are nucleic acid molecules encoding any of the HCVR amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCVR nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0028] Also provided herein are nucleic acid molecules encoding any of the LCVR amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCVR nucleic acid sequences listed in

Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0029] Also provided herein are nucleic acid molecules encoding any of the HCDR1 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR1 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0030] Also provided herein are nucleic acid molecules encoding any of the HCDR2 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR2 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0031] Also provided herein are nucleic acid molecules encoding any of the HCDR3 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR3 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0032] Also provided herein are nucleic acid molecules encoding any of the LCDR1 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR1 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0033] Also provided herein are nucleic acid molecules encoding any of the LCDR2 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR2 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0034] Also provided herein are nucleic acid molecules encoding any of the LCDR3 amino acid sequences listed in Table 4; in certain examples the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR3 nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0035] Also provided herein are nucleic acid molecules encoding an HCVR, wherein the HCVR comprises a set of three CDRs (*i.e.*, HCDR1-HCDR2-HCDR3), wherein the HCDR1-HCDR2-HCDR3 amino acid sequence set is as defined by any of the exemplary anti-MSR1 antibodies listed in Table 4.

[0036] Also provided herein are nucleic acid molecules encoding an LCVR, wherein the LCVR comprises a set of three CDRs (*i.e.*, LCDR1-LCDR2-LCDR3), wherein the LCDR1-LCDR2-LCDR3 amino acid sequence set is as defined by any of the exemplary anti-MSR1 antibodies listed in Table 4.

[0037] Also provided herein are nucleic acid molecules encoding both an HCVR and an LCVR, wherein the HCVR comprises an amino acid sequence of any of the HCVR amino acid sequences listed in Table 4, and wherein the LCVR comprises an amino acid sequence of any of the LCVR amino acid sequences listed in Table 4. In certain examples, the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCVR nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto, and a polynucleotide sequence selected from any of the LCVR nucleic acid sequences listed in Table 5, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto. In certain examples according to this disclosure, the nucleic acid molecule encodes an HCVR and LCVR, wherein the HCVR and LCVR are both derived from the same anti-MSR1 antibody listed in Table 4.

[0038] Also provided herein are recombinant expression vectors capable of expressing a polypeptide comprising a heavy or light chain variable region of an anti-MSR1 antibody. For example, examples include recombinant expression vectors comprising any of the nucleic acid molecules mentioned above, *i.e.*, nucleic acid molecules encoding any of the HCVR, LCVR, and/or CDR sequences as set forth in Table 4. Also included within the scope of the present disclosure are host cells into which such vectors have been introduced, as well as methods of producing the antibodies or portions thereof by culturing the host cells under conditions permitting production of the antibodies or antibody fragments, and recovering the antibodies and antibody fragments so produced.

[0039] Provided herein are anti-MSR1 antibodies having a modified glycosylation pattern. In some examples, modification to remove undesirable glycosylation sites, may be useful for example, to increase antibody dependent cellular cytotoxicity (ADCC) function (see Shield et al. (2002) JBC 277:26733). In some examples, modification to provide an antibody lacking a fucose moiety present on the oligosaccharide chain, may be useful for example, to increase antibody dependent cellular cytotoxicity (ADCC) function. In other applications, modification of galactosylation can be made in order to modify complement dependent cytotoxicity (CDC).

[0040] In another example, provided herein is a pharmaceutical composition comprising a recombinant human antibody or fragment thereof which specifically binds MSR1 and a pharmaceutically acceptable carrier. In a related example, provided herein is a composition

[0040a] In another aspect, provided herein is a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof as described herein, and a pharmaceutically acceptable carrier.

[0041] Also provided herein are antibody-drug conjugates (ADCs) comprising an anti-MSR1 antibody, or an MSR1 antigen-binding fragment thereof, conjugated to a drug or a therapeutic agent. Also provided herein are reactive linker-payloads useful for making the ADCs. Further provided herein are modified anti-MSR1 antibodies and modified MSR1 antigen-binding fragments useful for making the ADCs.

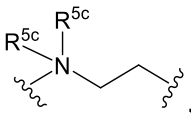
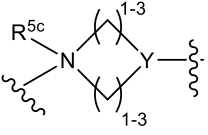
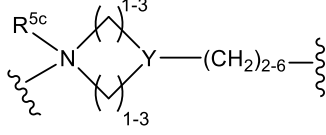
[0041b] In another aspect, provided herein is an antibody-rifamycin analog conjugate having the structure of Formula (7003):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein:

$\mathbf{X}^{1c}$ is selected from $-\text{S}-$; $-\text{O}-$ and $-\text{NR}^{5c}$;

$\mathbf{R}^{1c}$ is , ; or ; wherein $\mathbf{Y}$ is C or N;

$\mathbf{R}^{2c}$, $\mathbf{R}^{3c}$, and $\mathbf{R}^{4c}$ are independently selected from hydrogen, C_{1-6} alkyl, and $-(\text{C}=\text{O})-\mathbf{R}^{5c}$;

$\mathbf{R}^{5c}$ is independently, at each occurrence, absent, or selected from hydrogen; and C_{1-6} alkyl;

each $\mathbf{AA}$ is an independently selected amino acid;

$\mathbf{SP}^1$ is absent, or a spacer;

$\mathbf{RG}^1$ is a reactive group residue;

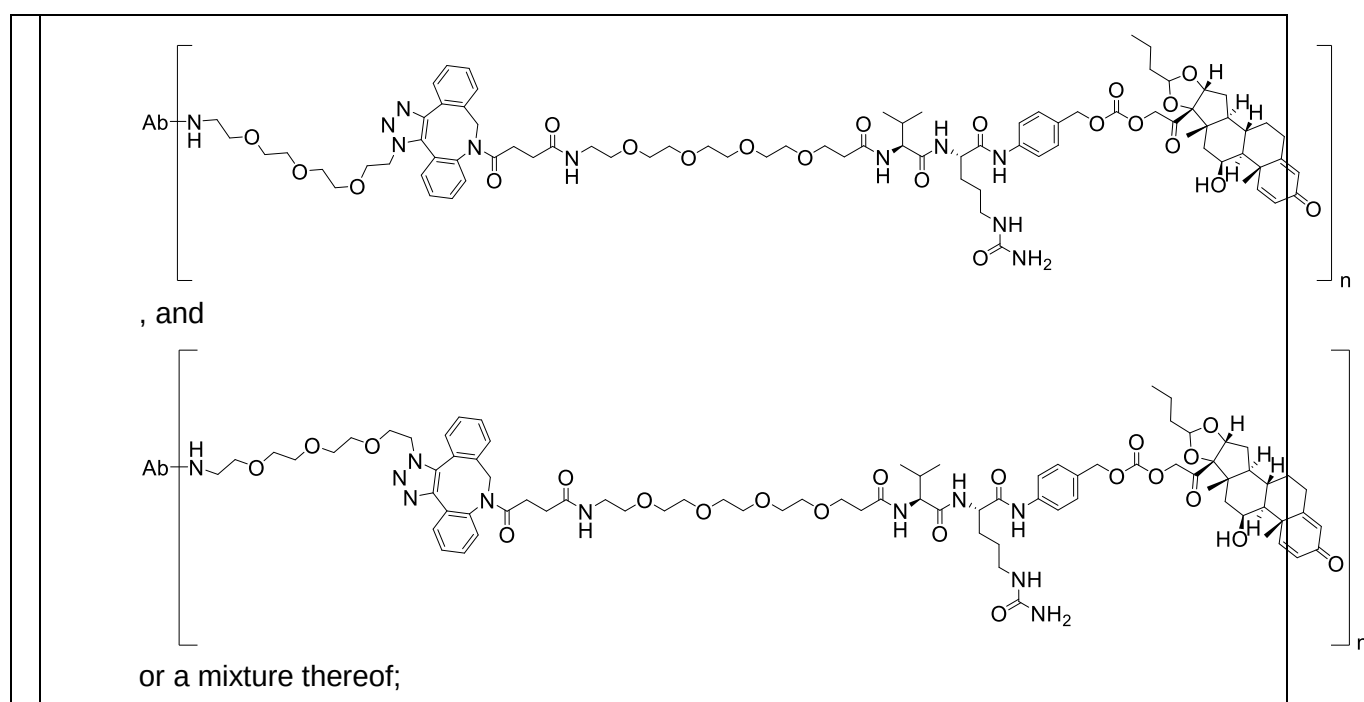
$\mathbf{BA}$ is an anti-MSR1 antibody or antigen binding fragment thereof;

subscript $\mathbf{n}$ is an integer from 1 to 30;

subscript $\mathbf{w}$ is 2, 3, or 4;

wherein $\mathbf{R}^{1c}$ is bonded to the linker via a nitrogen atom as indicated by the wavy line .

[0041c] In another aspect, provided herein is an antibody-drug conjugate selected from

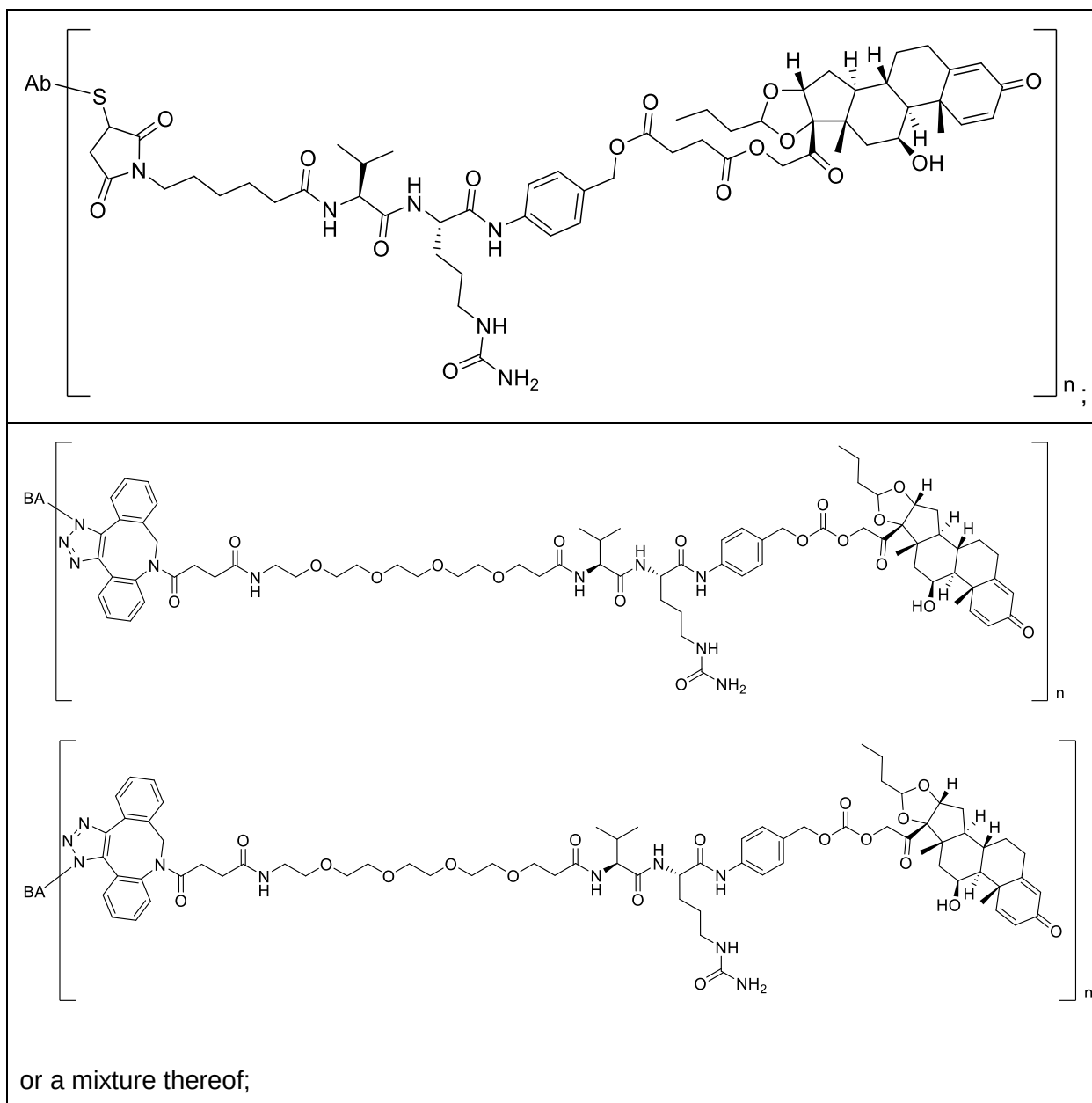


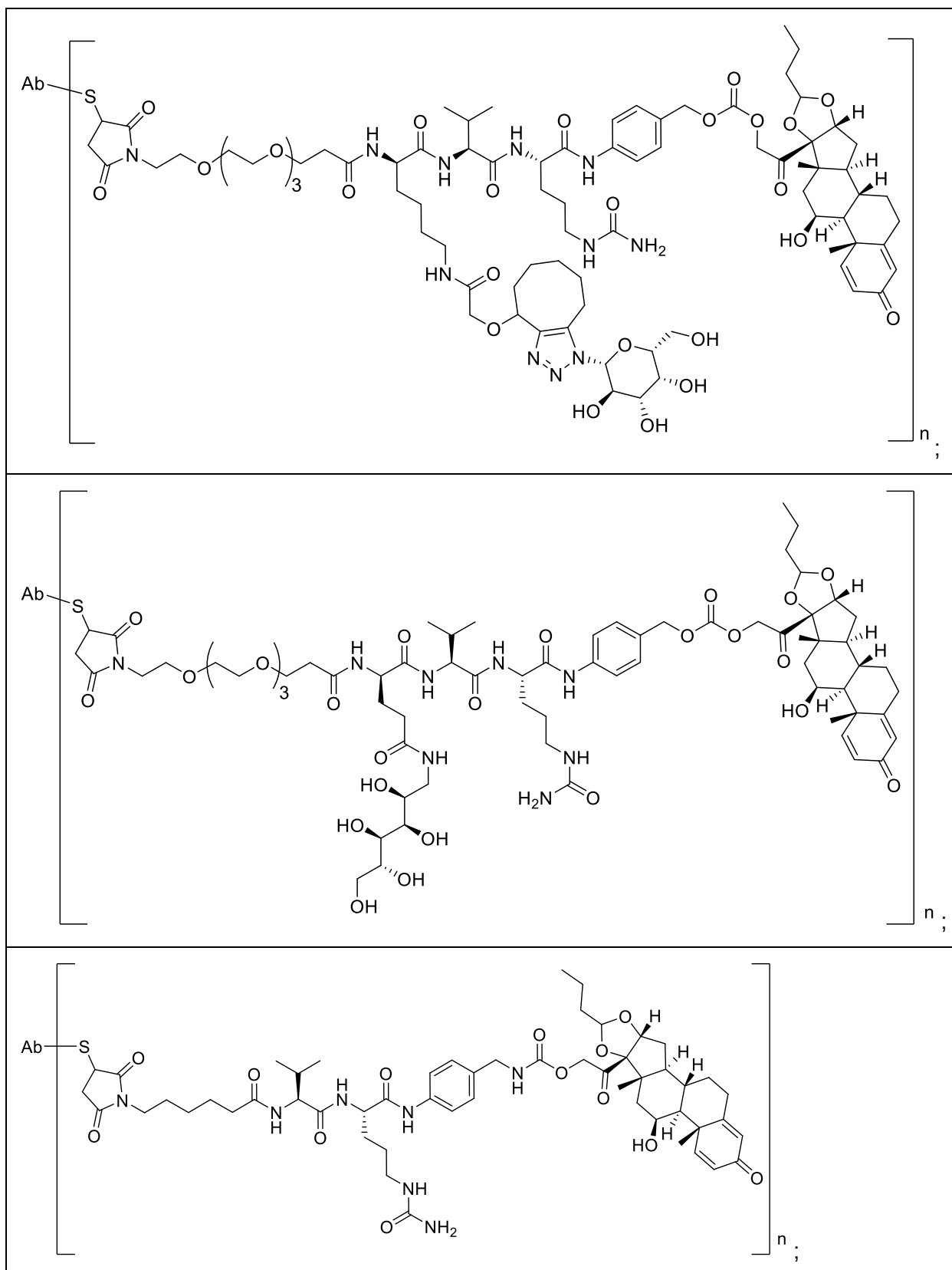
or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, wherein

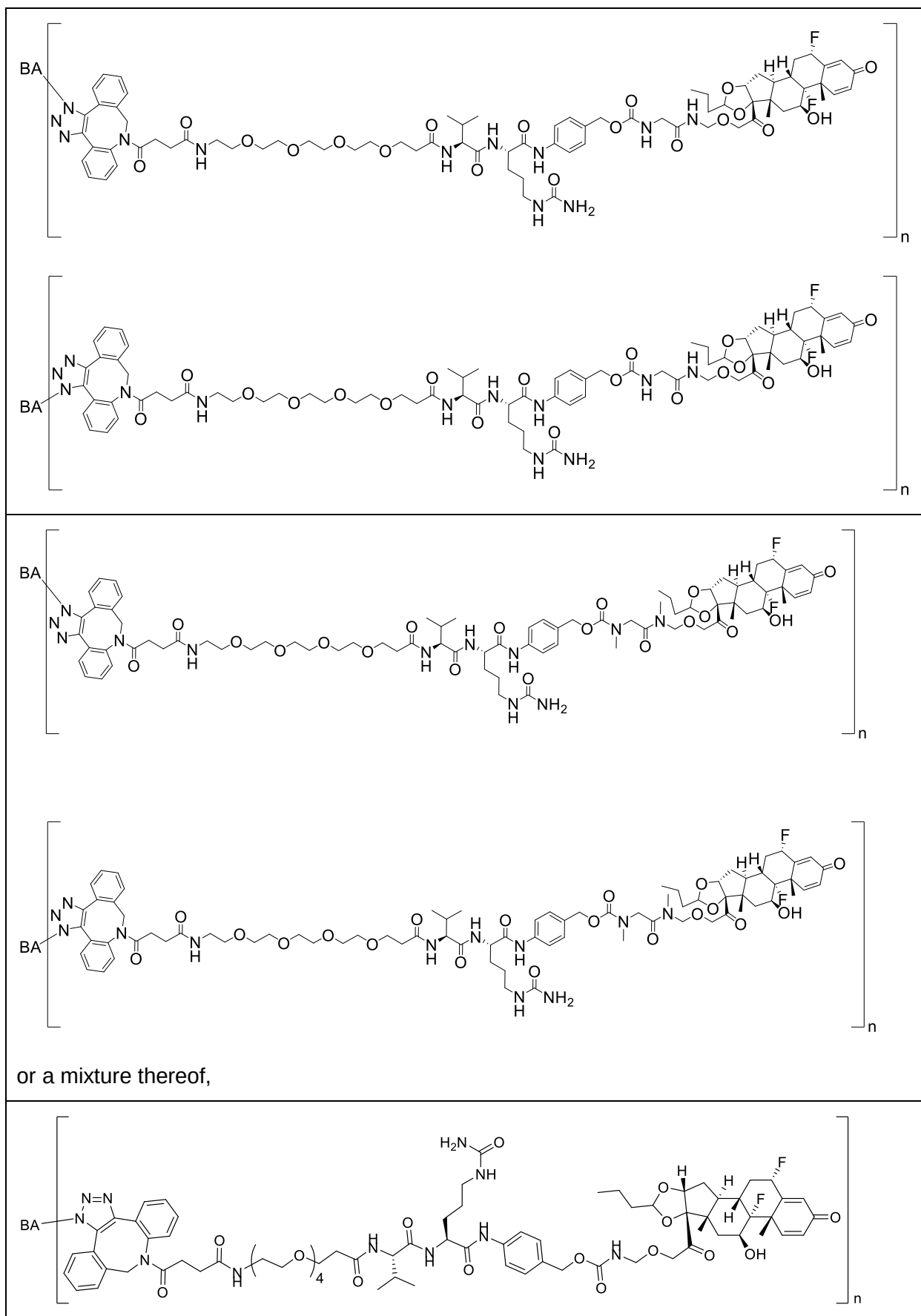
each Ab is an anti-MSR1 antibody, or an antigen binding fragment thereof; and

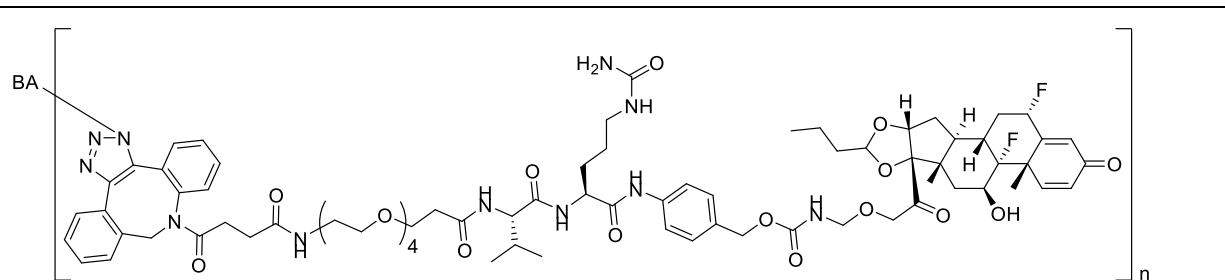
each n is an integer from 1 to 4.

[0041d] In another aspect, provided herein is an antibody-drug conjugate according to one of the following formulas:

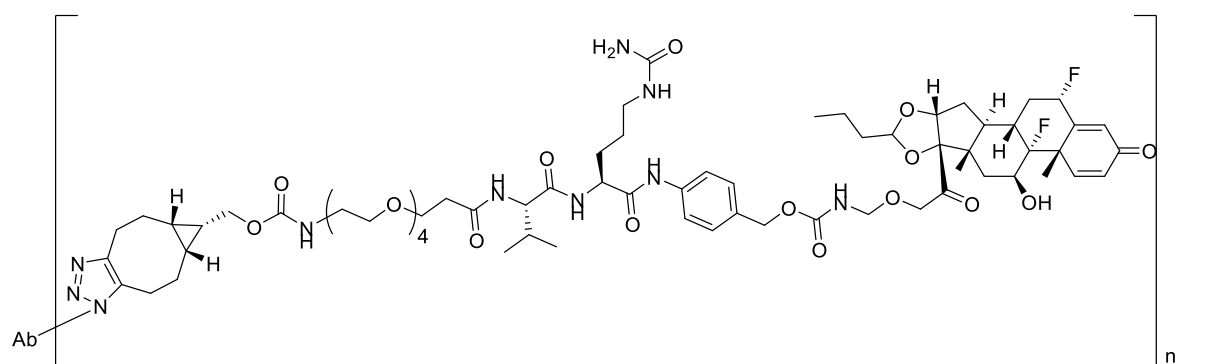
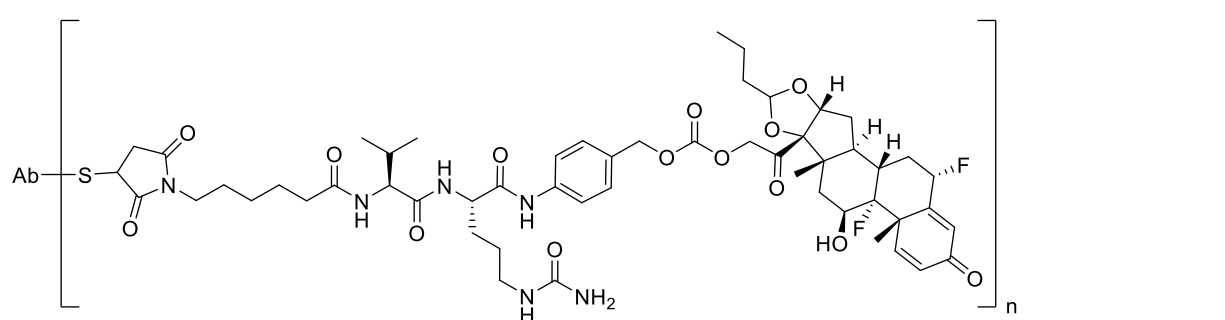
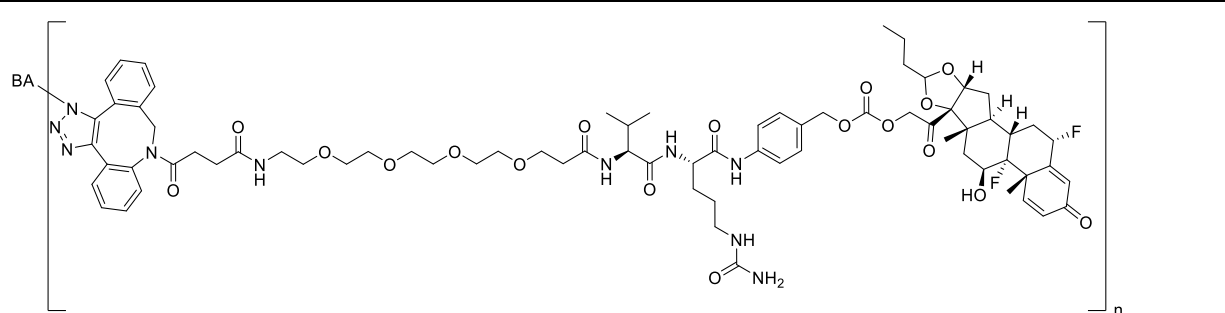
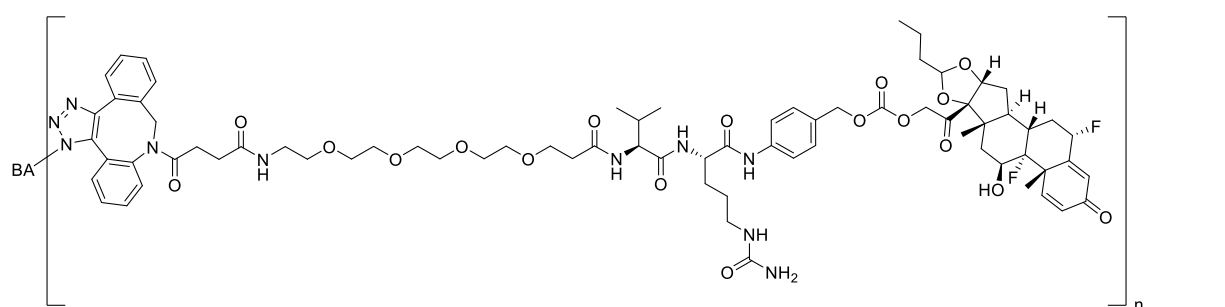




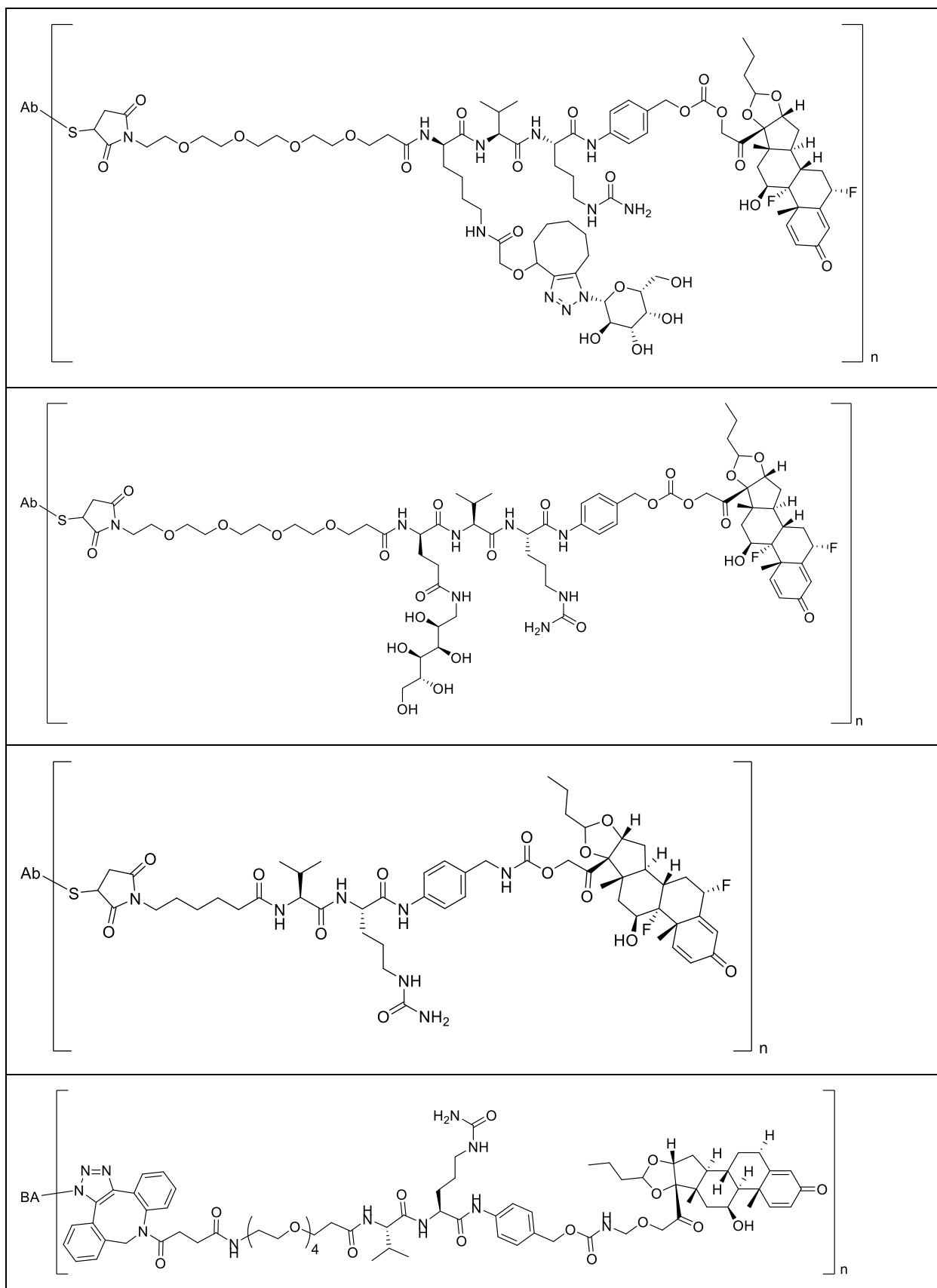


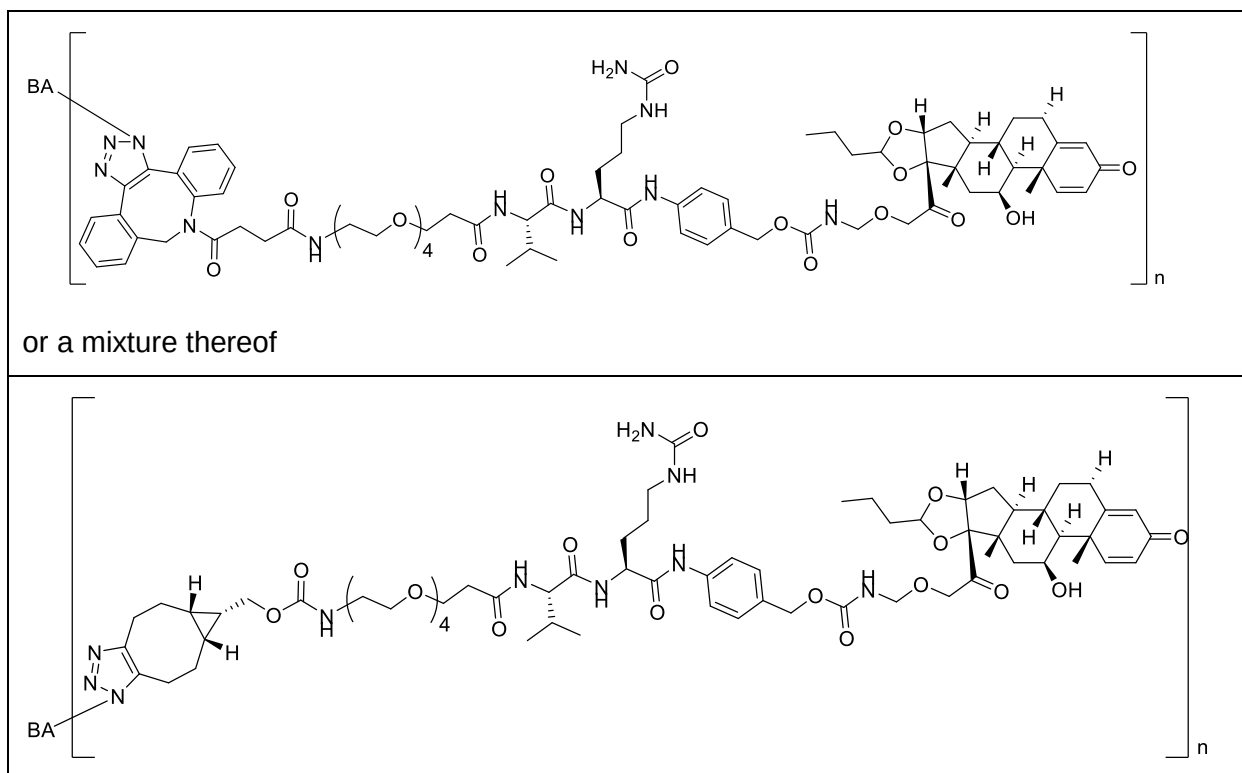


or a mixture thereof



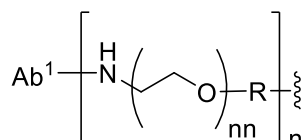
or a mixture thereof





or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, wherein

each **Ab** is an anti-MSR1 antibody, or an antigen binding fragment thereof;

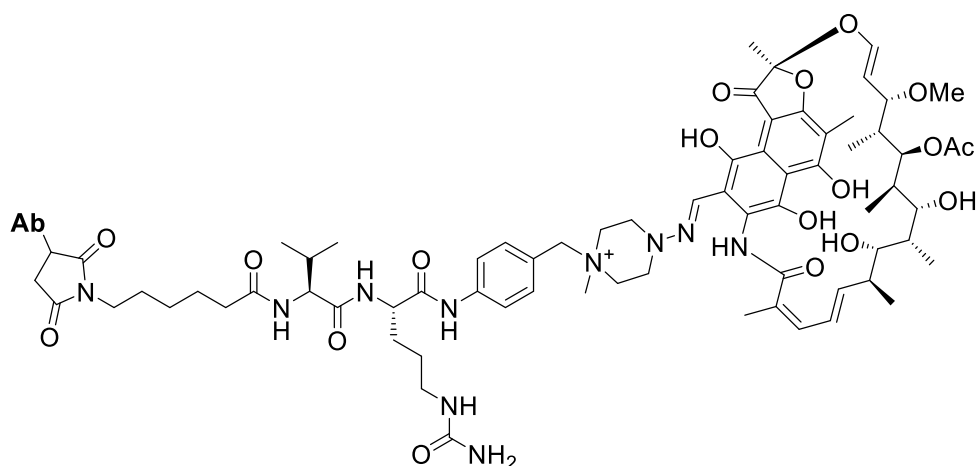


each **BA** is where **Ab¹** is an anti-MSR1 antibody, or an antigen-binding fragment thereof; **R** is C₂₋₄-alkylene; and **nn** is an integer selected from 2 to 4, inclusive.

and

each **n** is an integer from 1 to 4.

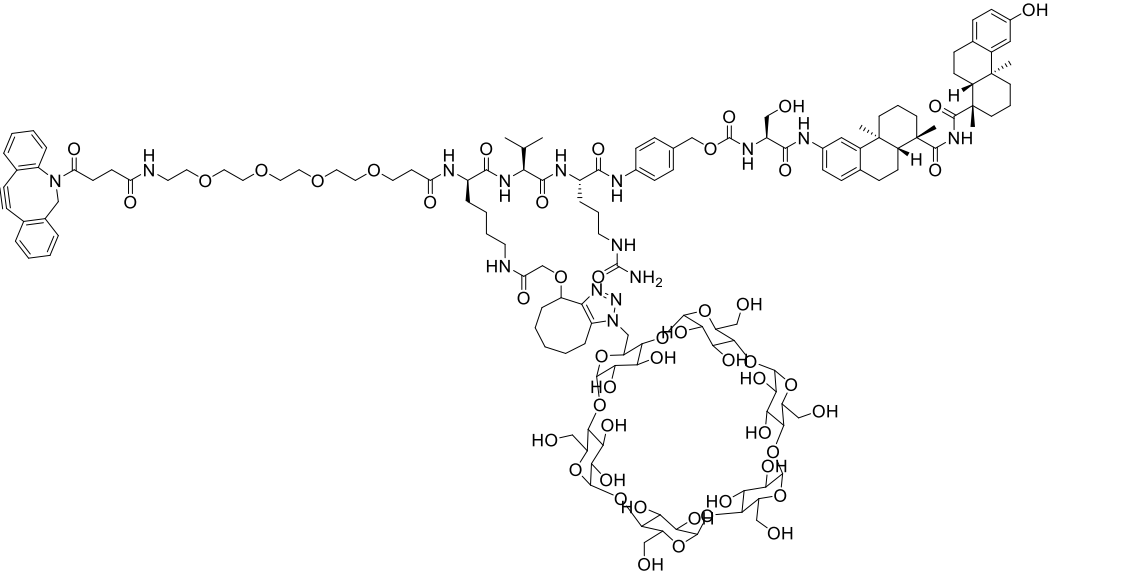
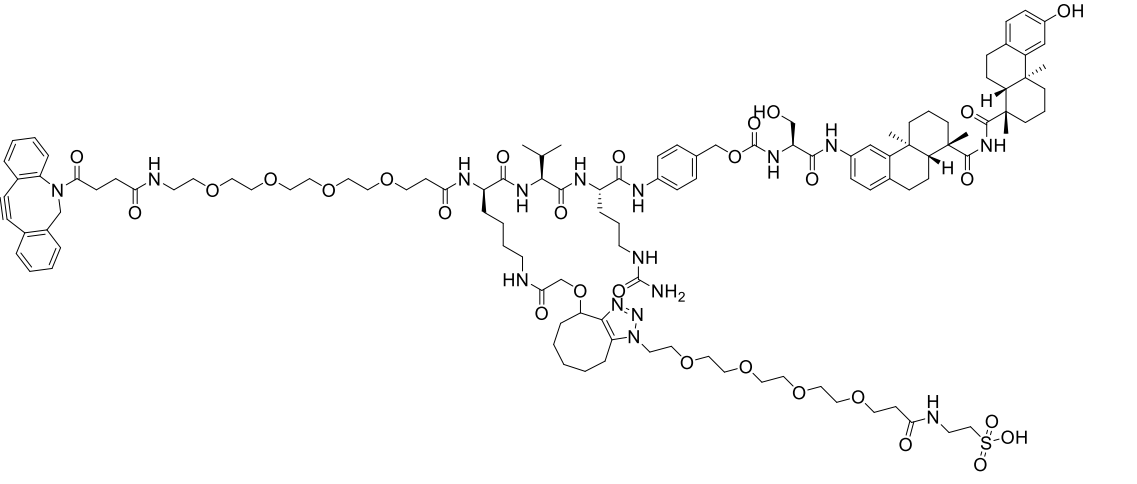
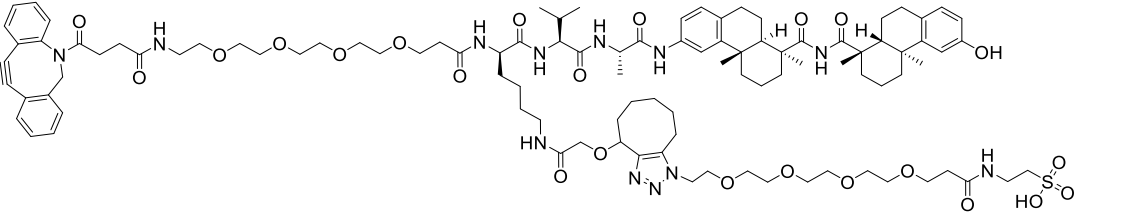
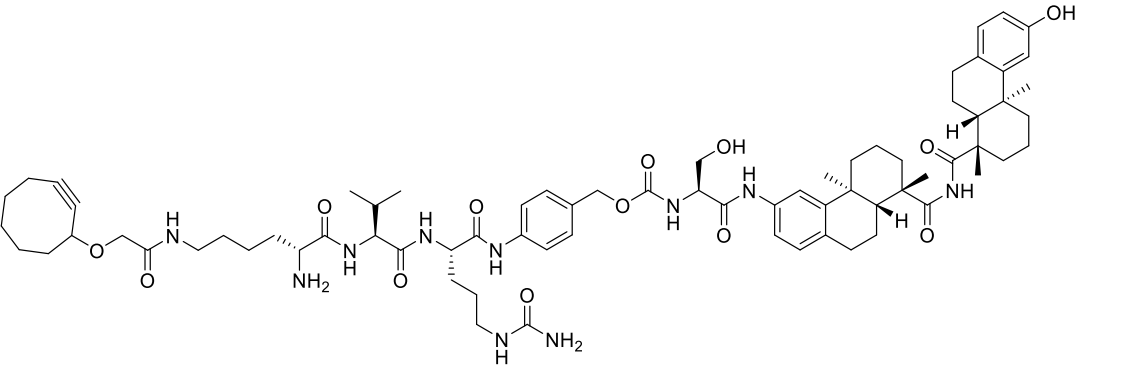
[0041e] In another aspect, provided herein is an antibody-drug conjugate of any one of claims 9-10 and 24, according to Formula (**7004**):

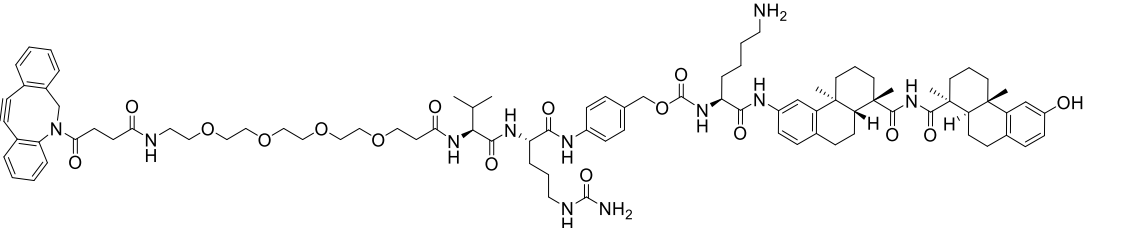
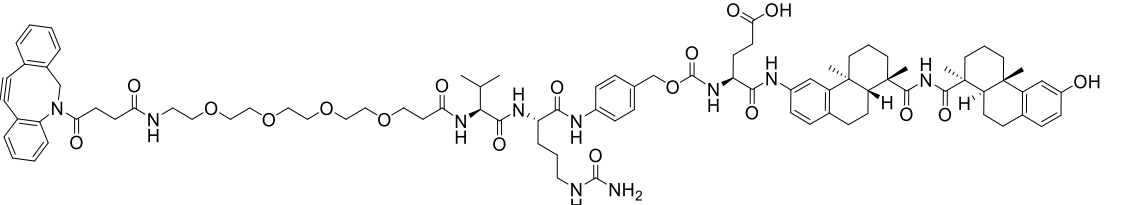
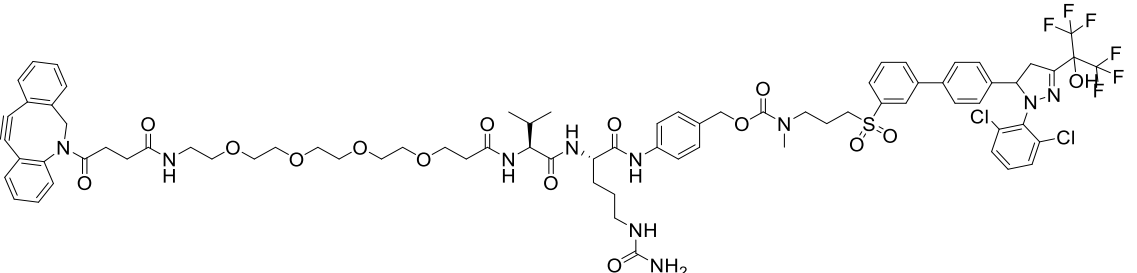
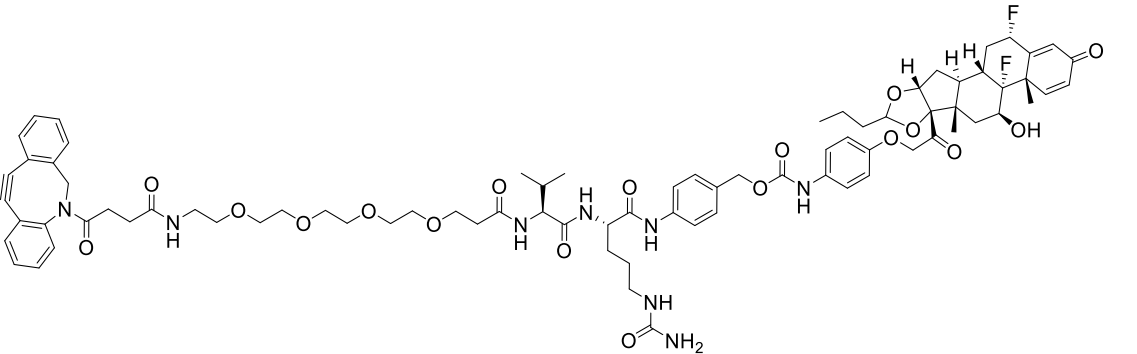
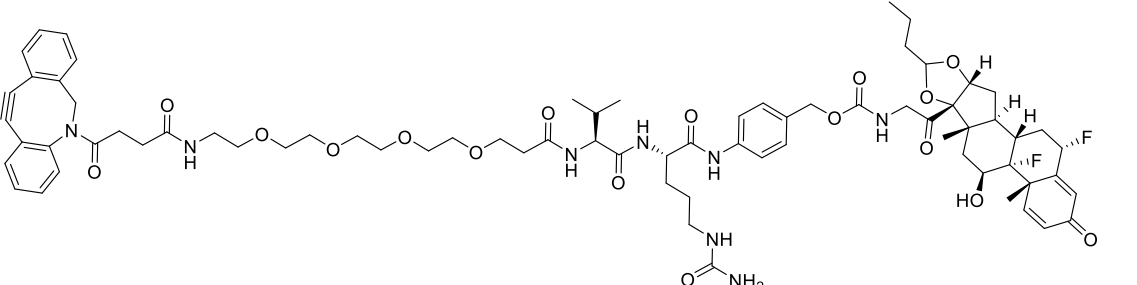


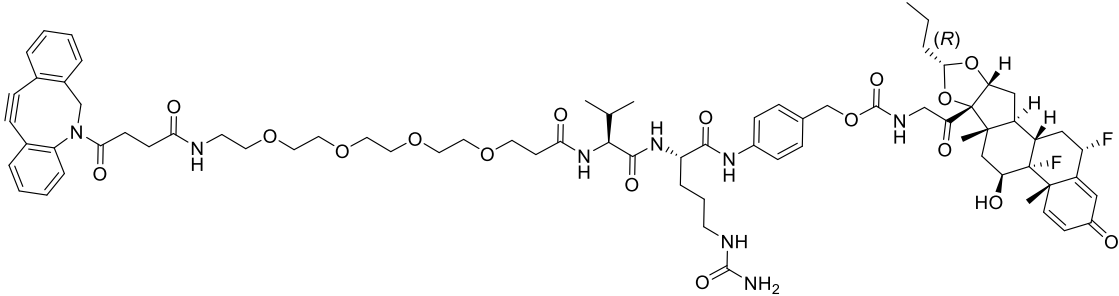
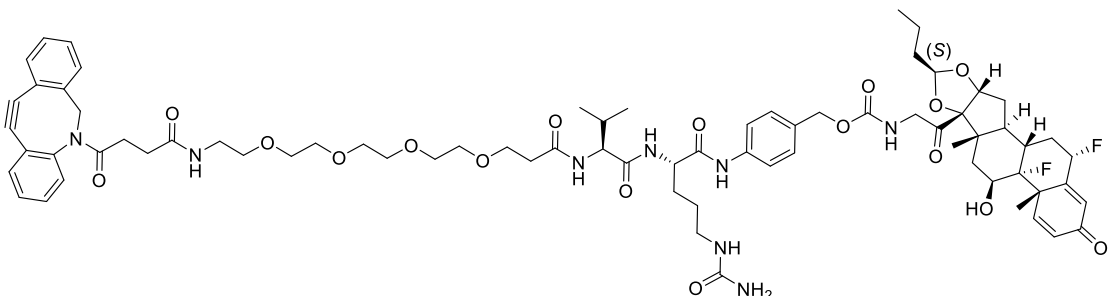
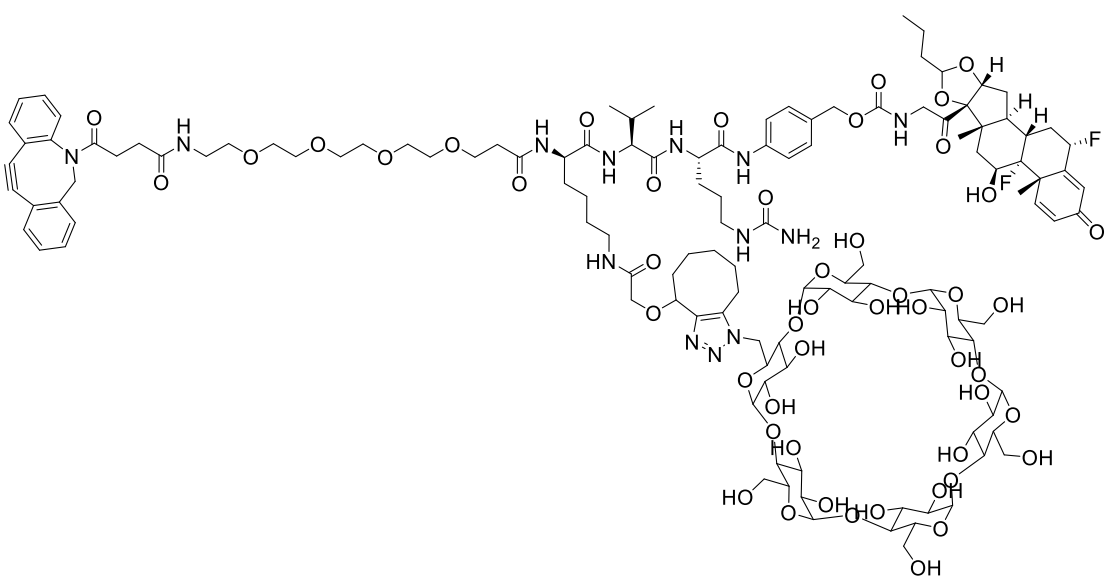
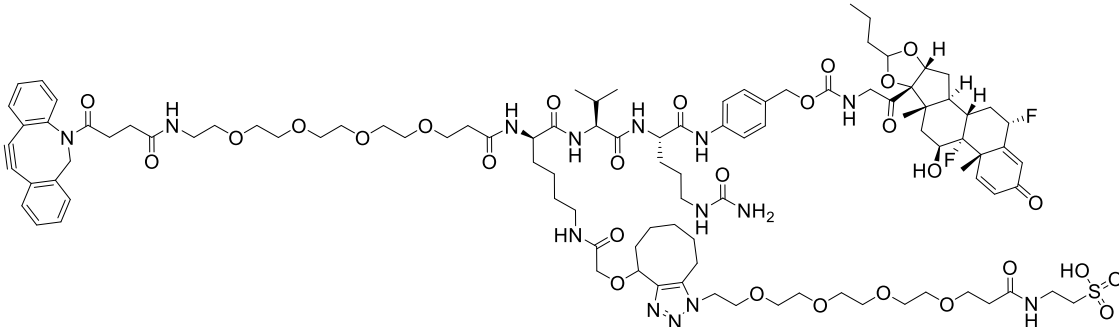
Formula (7004).

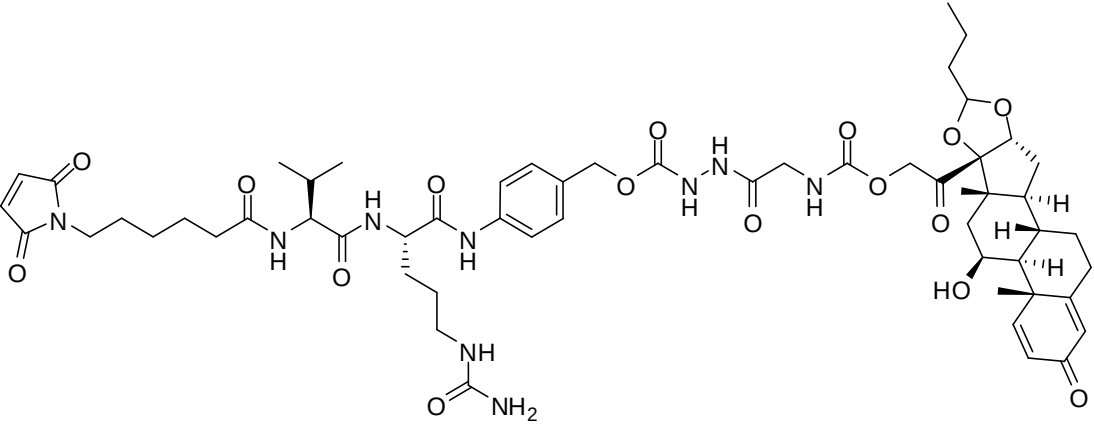
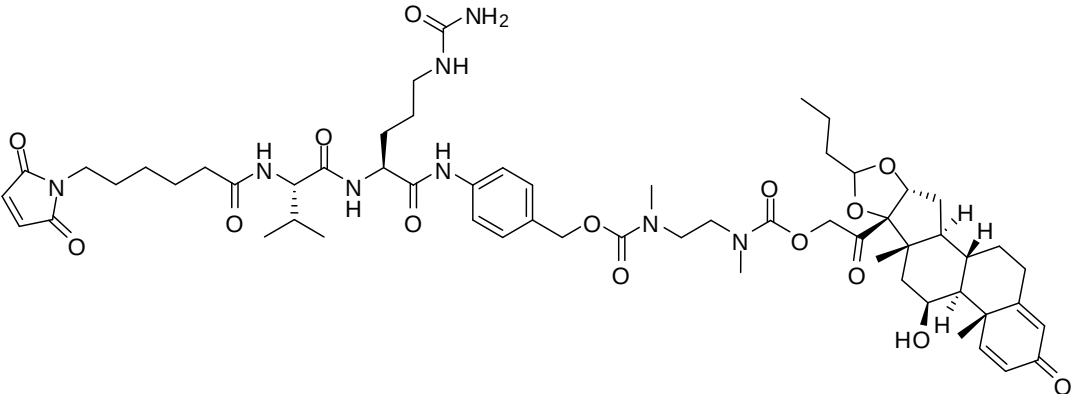
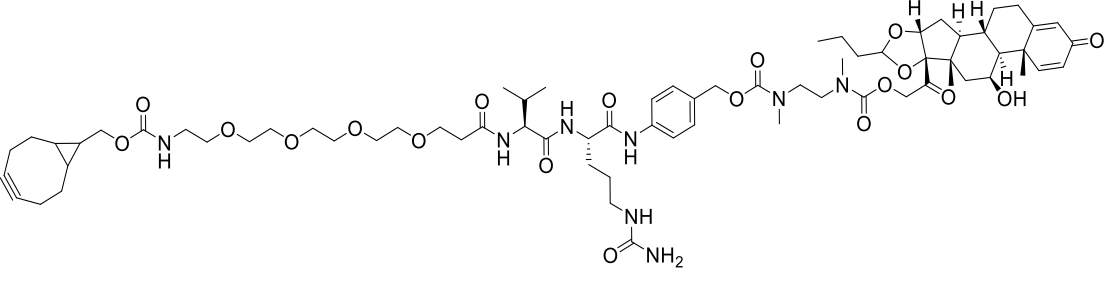
[0041f] In another aspect, provided herein is an antibody drug conjugate prepared by conjugating an anti-MSR1 antibody or a PEG-modified anti-MSR1 antibody, or an antigen binding fragment thereof, with a linker payload, or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, selected from the group consisting of:

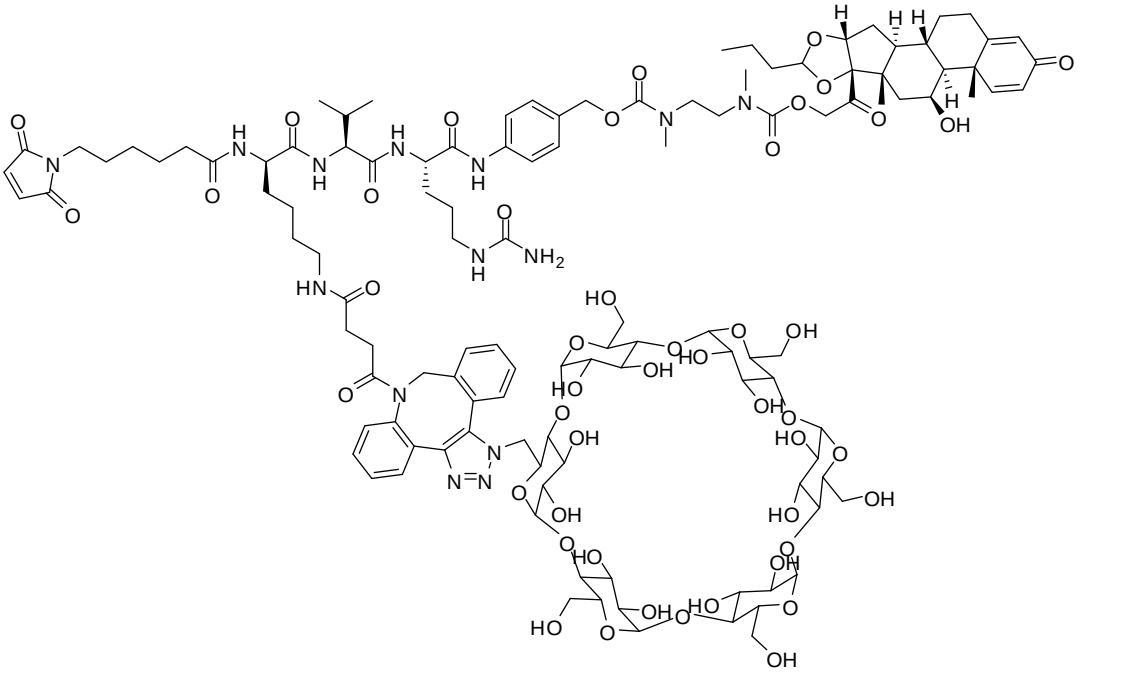
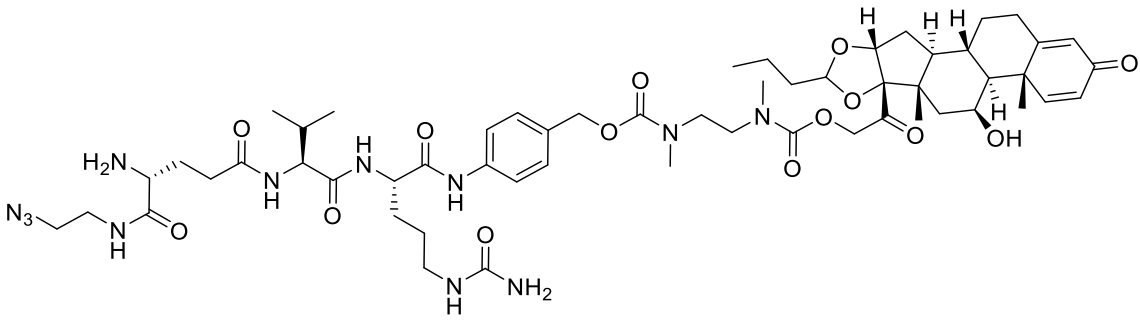
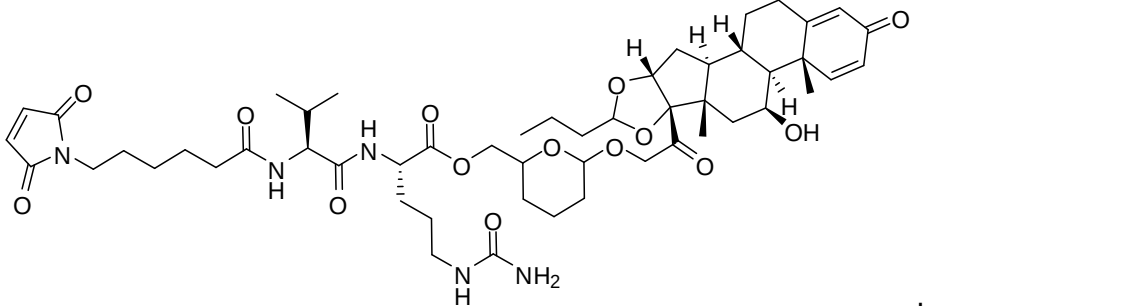
LP1	
LP2	

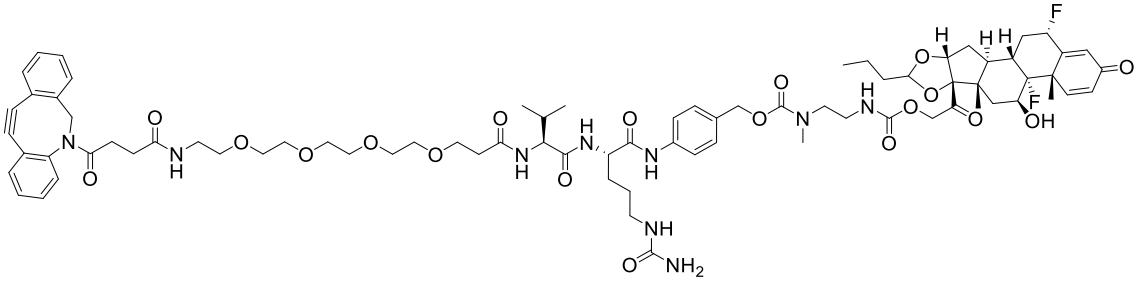
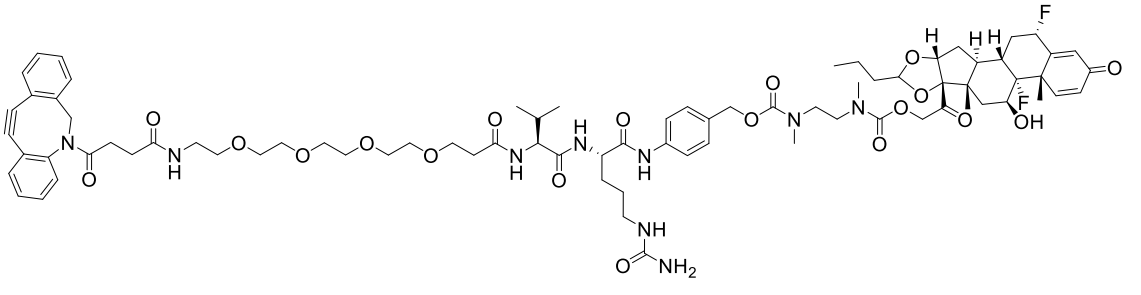
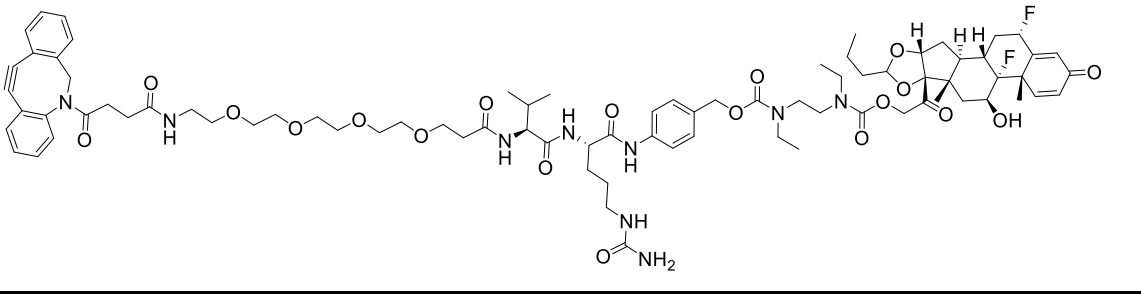
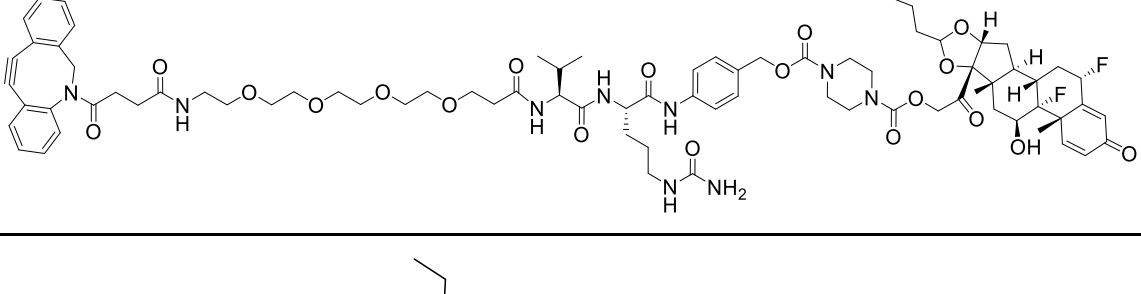
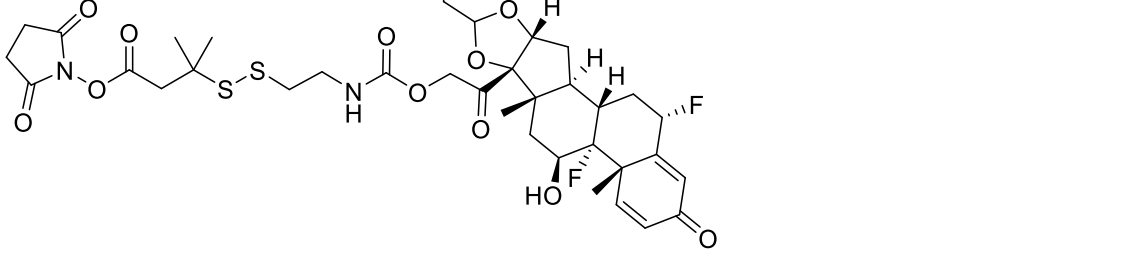
LP5	
LP6	
LP18	
LP4	

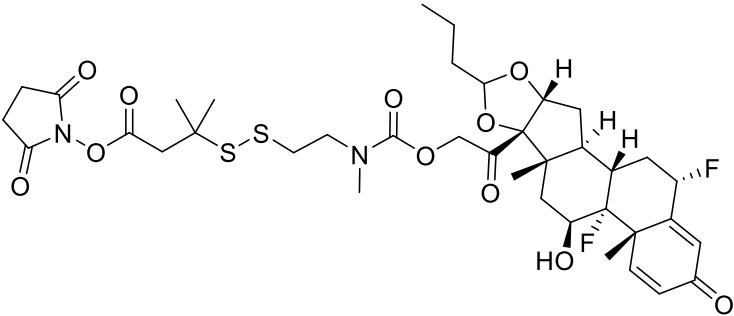
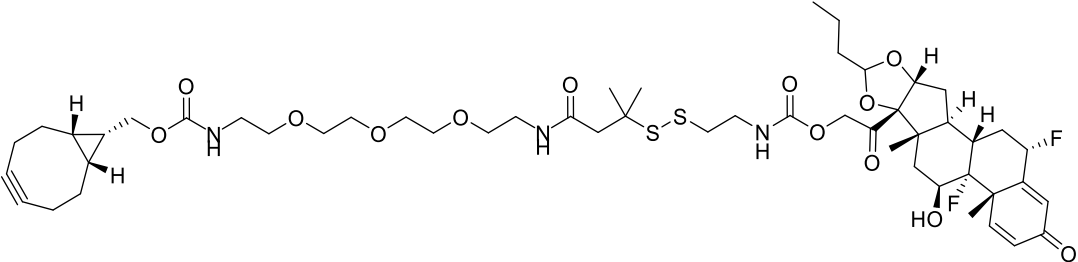
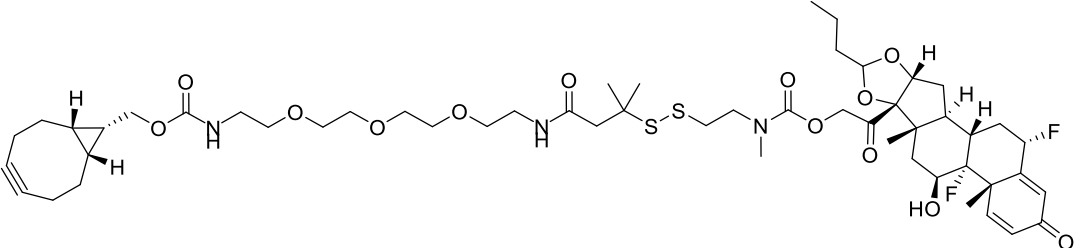
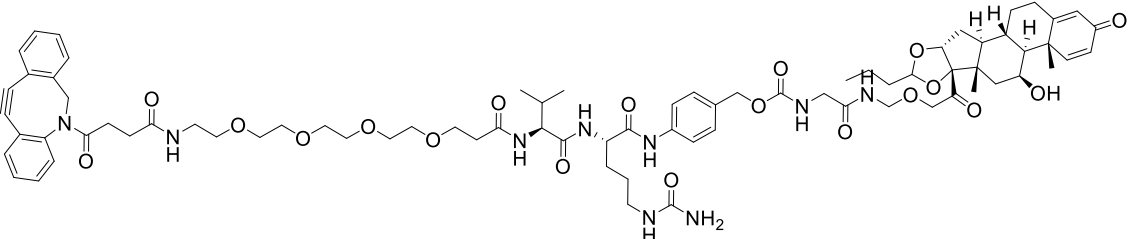
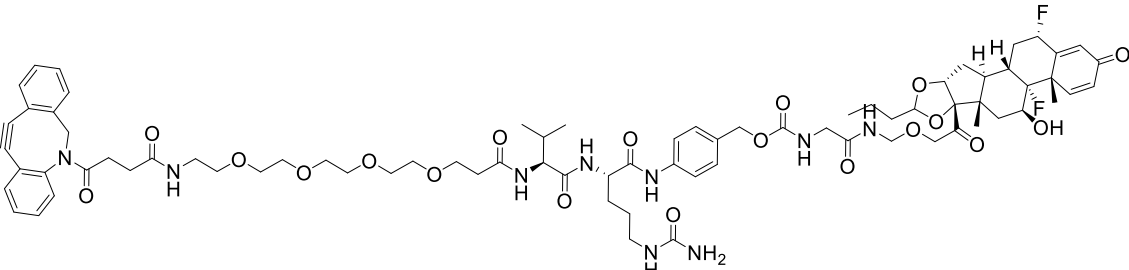
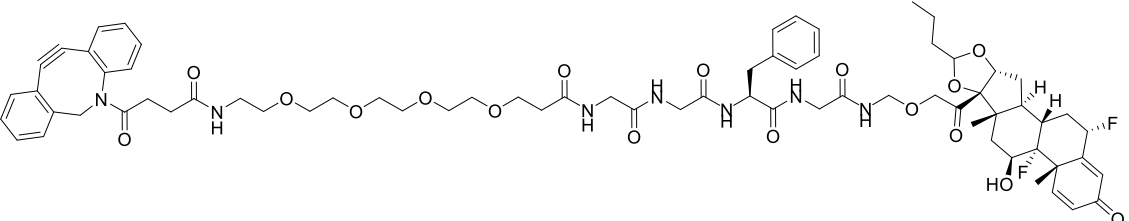
LP11	
LP9	
LP12	
LP3	
LP13	

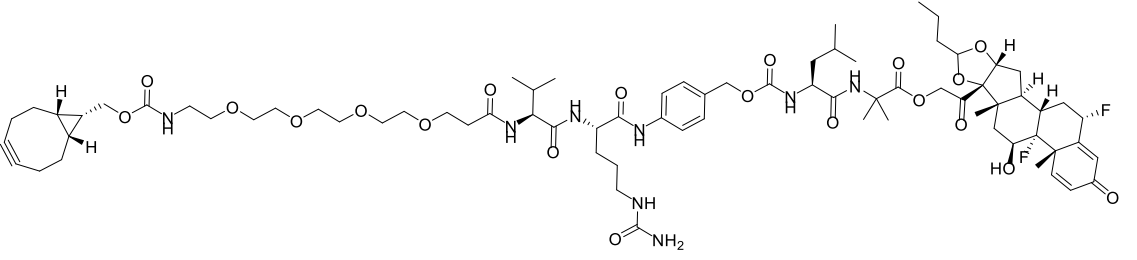
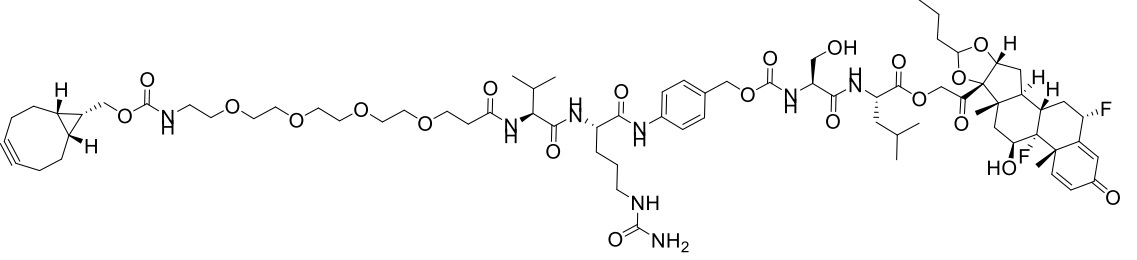
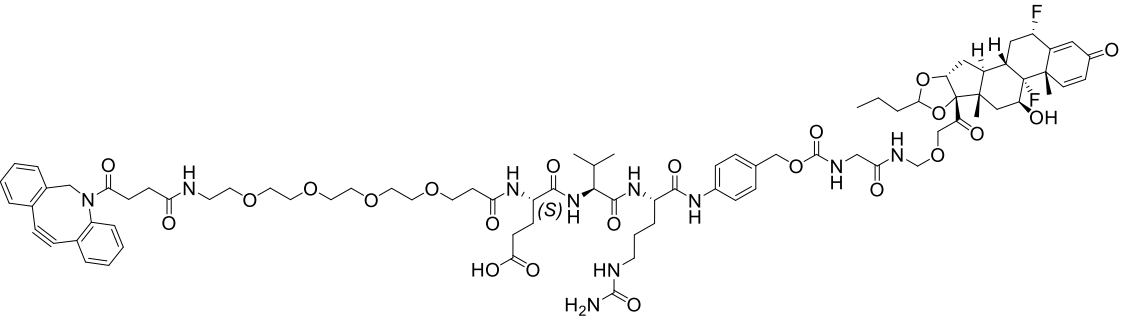
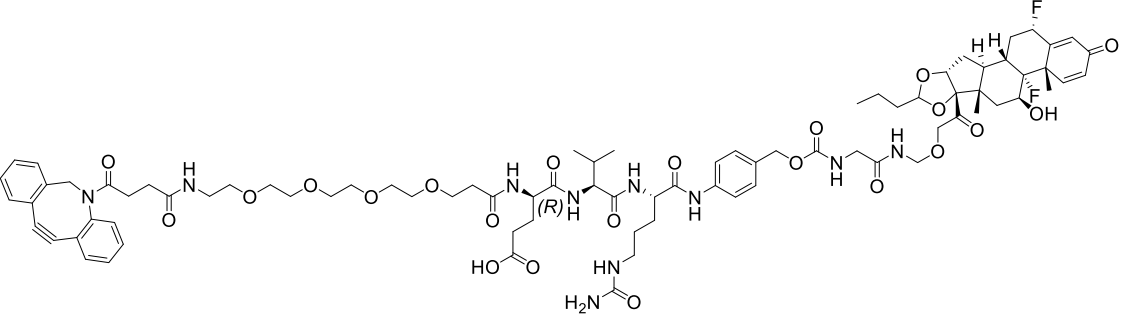
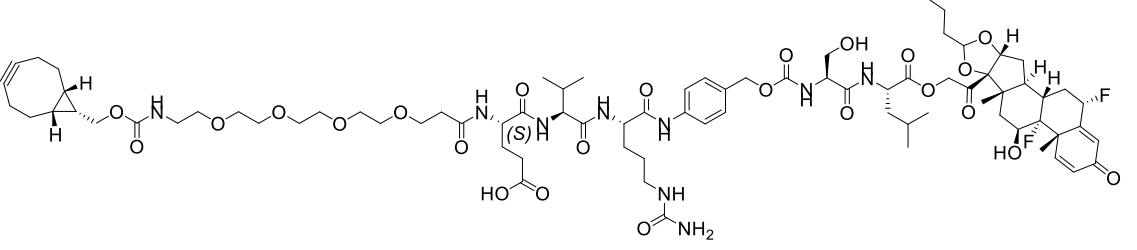
	
	
LP14	
LP15	

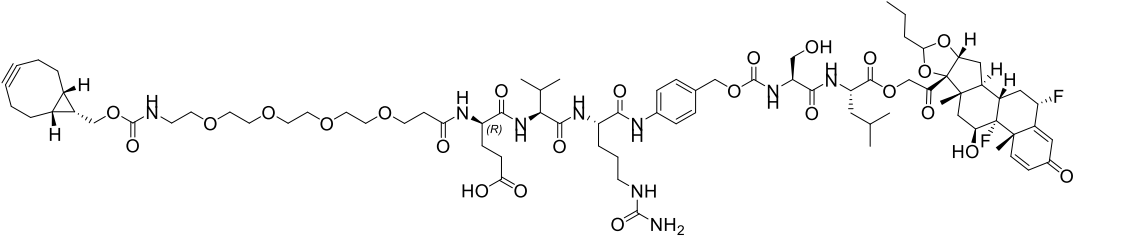
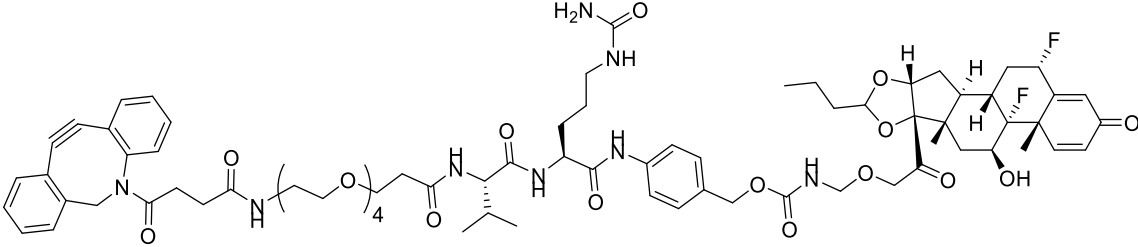
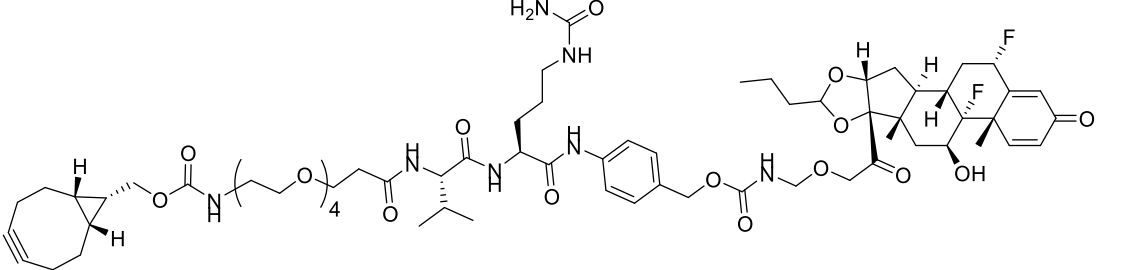
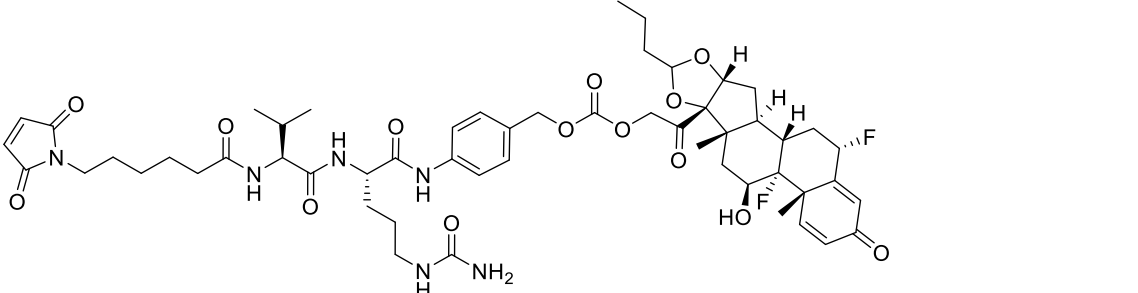
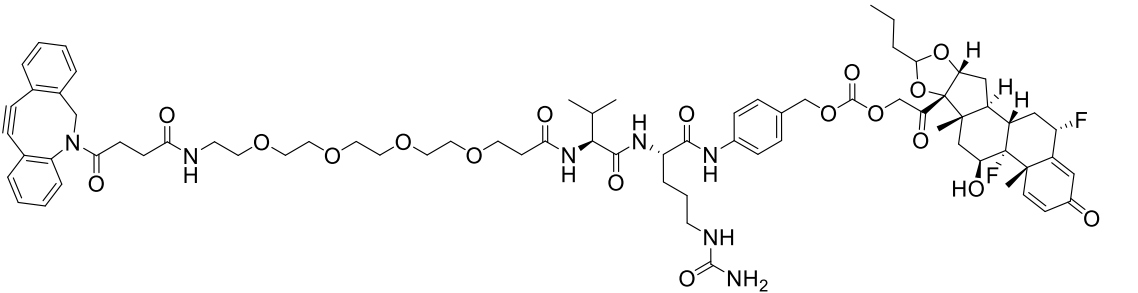
2j	 <p>Chemical structure of compound 2j: A complex molecule featuring a steroid core with a ketone at C3 and a hydroxyl group at C14. The steroid is linked via an ester to a chain containing a hydrazide, a benzamide, a chiral amide, and a succinimide ring.</p>
2k	 <p>Chemical structure of compound 2k: A complex molecule featuring a steroid core with a ketone at C3 and a hydroxyl group at C14. The steroid is linked via an ester to a chain containing a dimethylamino group, a benzamide, a chiral amide, and a succinimide ring.</p>
2l	 <p>Chemical structure of compound 2l: A complex molecule featuring a steroid core with a ketone at C3 and a hydroxyl group at C14. The steroid is linked via an ester to a chain containing a dimethylamino group, a benzamide, a chiral amide, and a succinimide ring. The molecule also includes a long polyether chain and a cyclooctene ring.</p>

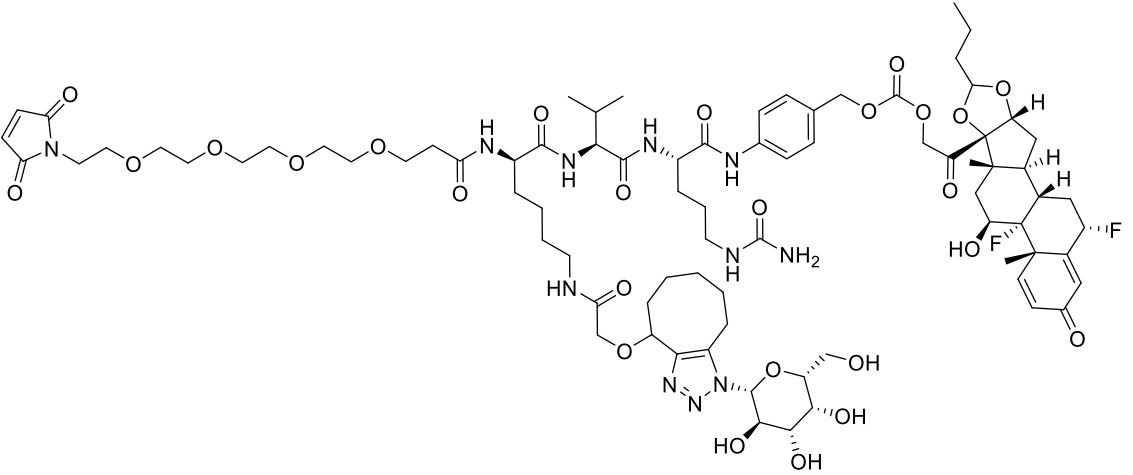
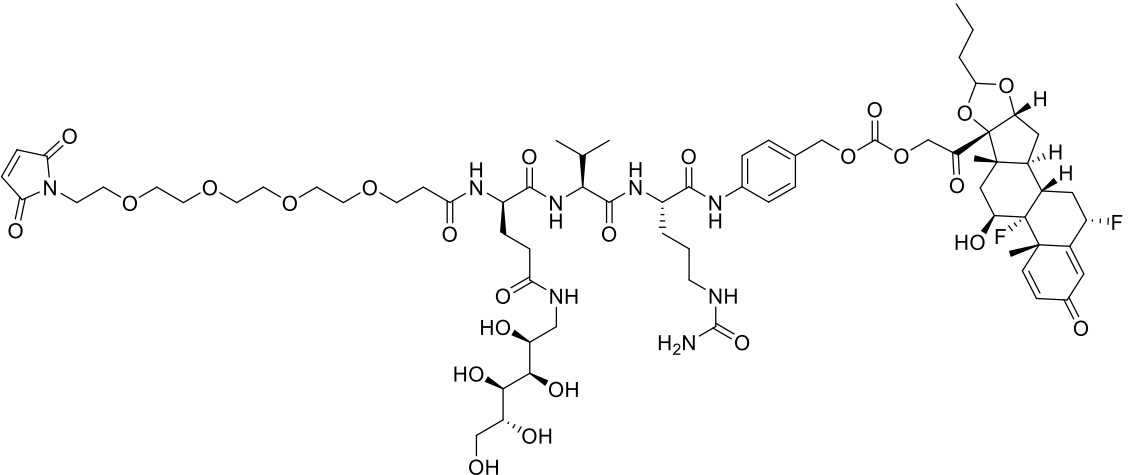
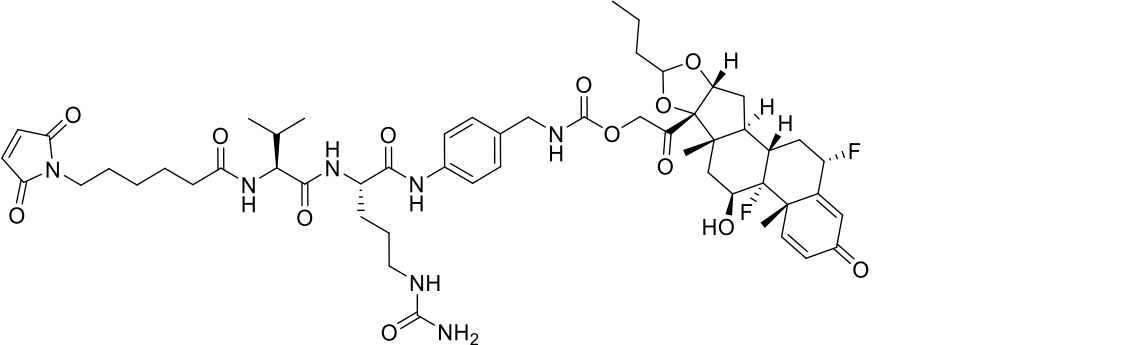
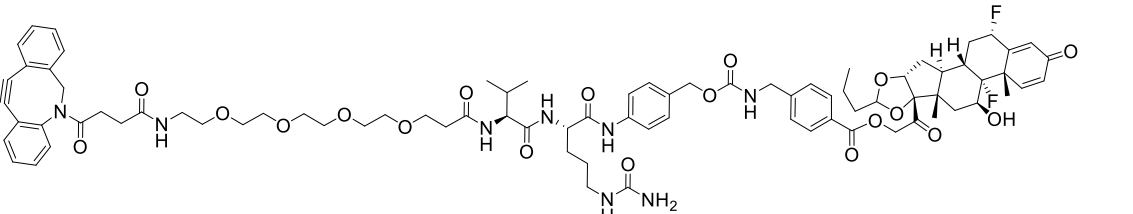
2m	
2n	 <p>or a mixture thereof</p>
2q	

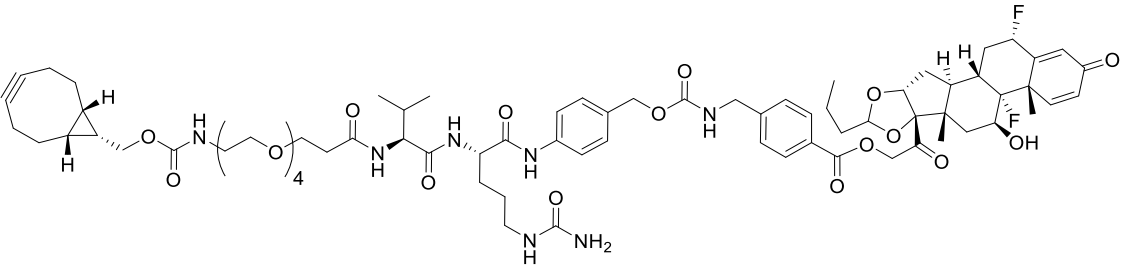
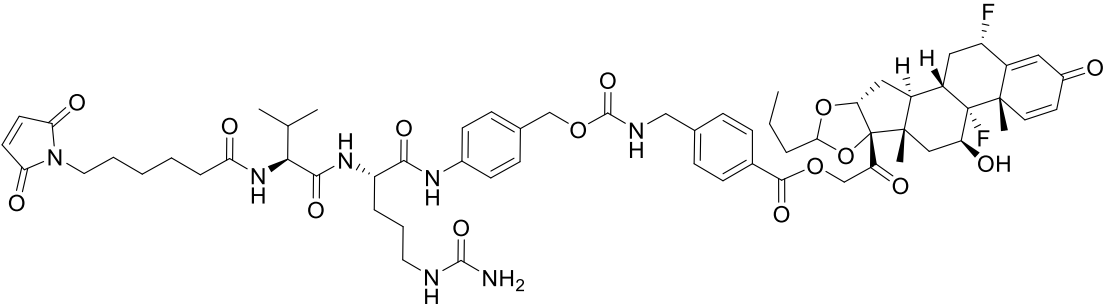
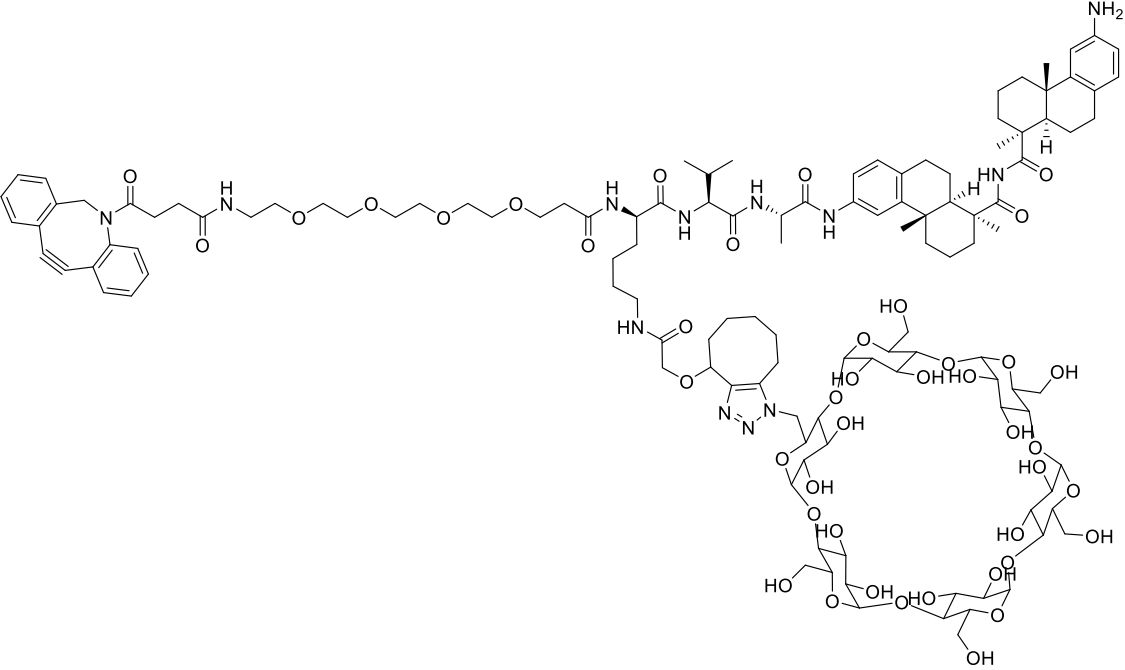
LP1A	
LP2A	
LP3A	
LP4A	
LP5A	

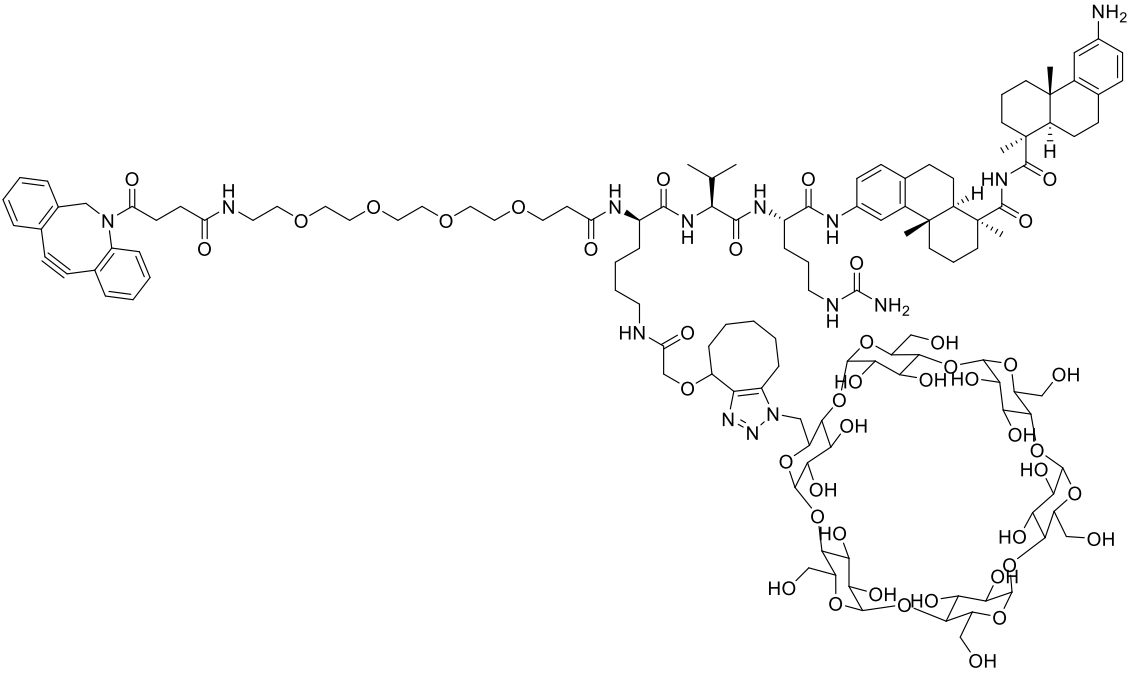
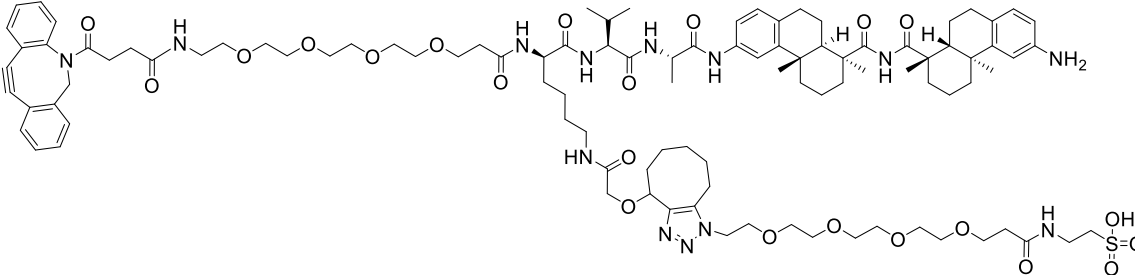
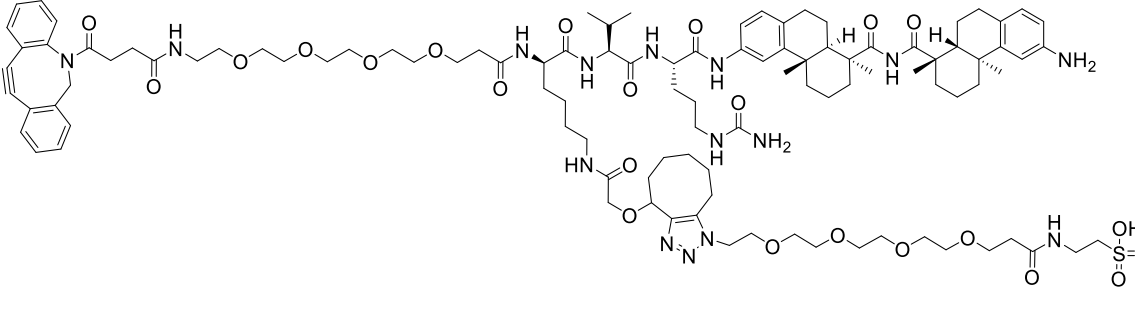
LP6A	
LP7A	
LP8A	
LP9A	
LP10 A	
LP11 A	

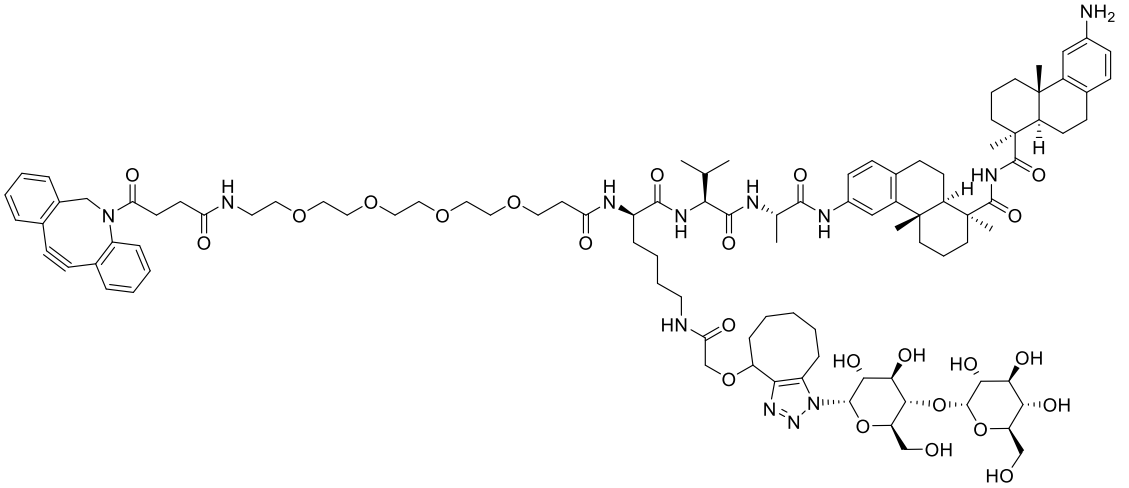
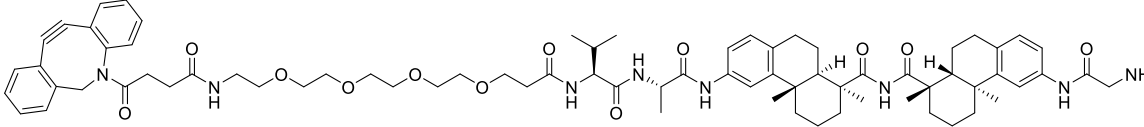
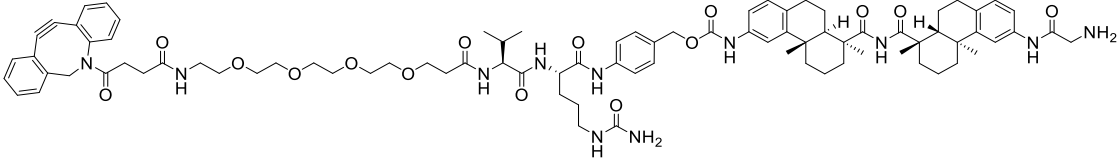
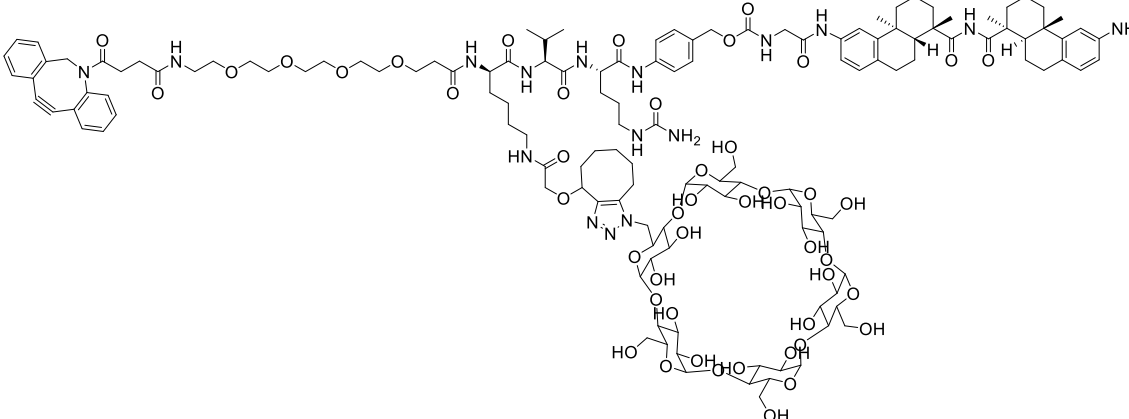
<p>LP12 A</p>	
<p>LP13 A</p>	
<p>LP18 A</p>	
<p>LP19 A</p>	
<p>LP20 A</p>	

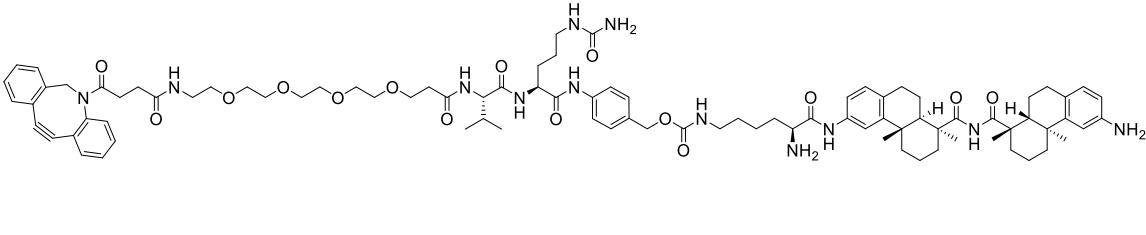
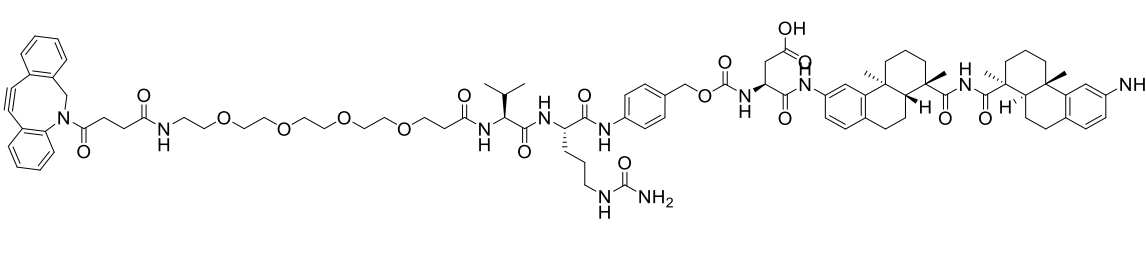
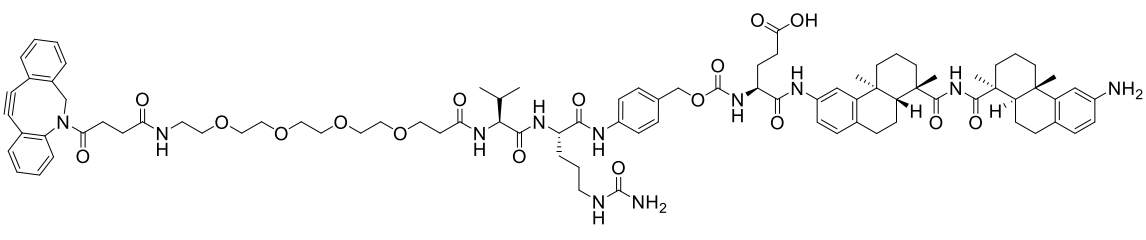
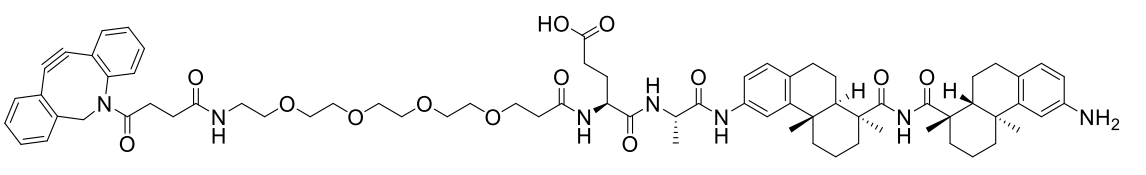
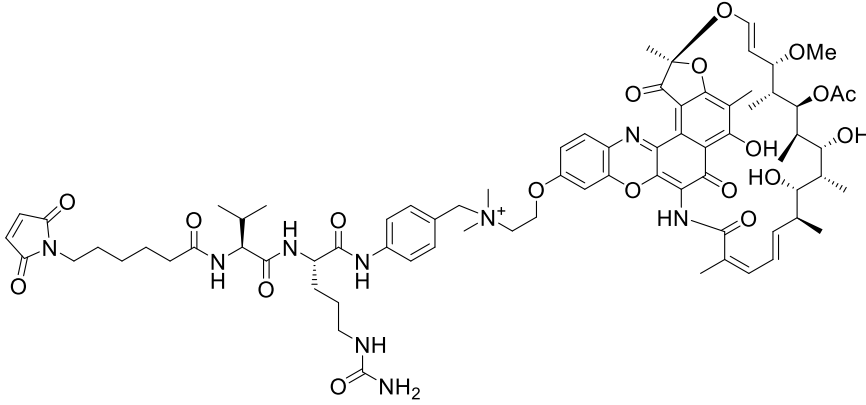
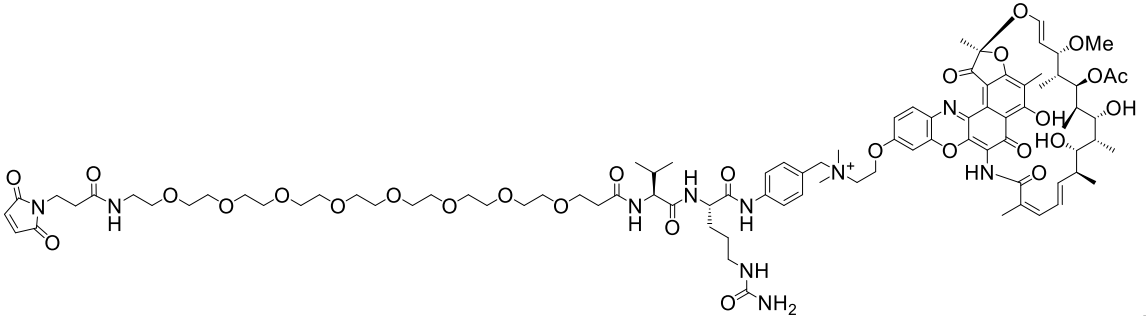
<p>LP21 A</p>	
<p>LP22 A</p>	
<p>LP23 A</p>	
<p>LP24 A</p>	
<p>LP25 A</p>	

<p>LP26 A</p>	 <p>The chemical structure of LP26 A is a complex molecule. It features a long polyether chain on the left, starting with a succinimide ring. This chain is linked via an amide bond to a side chain containing a chiral center with an isopropyl group. Further along, there is a benzamide moiety connected to a steroid-like core. The steroid core has multiple stereocenters, including a fluorine atom and a hydroxyl group. A side chain on the steroid includes a triazole ring and a tetrahydrofuran ring with multiple hydroxyl groups.</p>
<p>LP27 A</p>	 <p>The chemical structure of LP27 A is similar to LP26 A but with a different side chain on the steroid core. It features a long polyether chain, a chiral center with an isopropyl group, and a benzamide moiety. The steroid core has a fluorine atom and a hydroxyl group. The side chain on the steroid includes a primary amide group and a different arrangement of hydroxyl groups compared to LP26 A.</p>
<p>LP28 A</p>	 <p>The chemical structure of LP28 A is a shorter molecule. It features a succinimide ring connected to a polyether chain, which is then linked to a chiral center with an isopropyl group. This is followed by a benzamide moiety and a steroid-like core. The steroid core has a fluorine atom and a hydroxyl group. The side chain on the steroid includes a primary amide group.</p>
<p>LP29 A</p>	 <p>The chemical structure of LP29 A is a complex molecule. It features a fluorenyl group connected to a polyether chain, which is then linked to a chiral center with an isopropyl group. This is followed by a benzamide moiety and a steroid-like core. The steroid core has a fluorine atom and a hydroxyl group. The side chain on the steroid includes a primary amide group.</p>

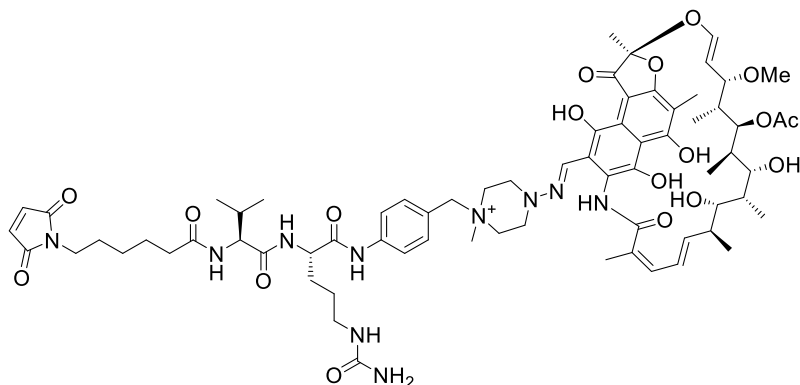
<p>LP30 A</p>	
<p>LP31 A</p>	
<p>LP1B</p>	

LP2B	
LP3B	
LP4B	

LP5B	
LP6B	
LP7B	
LP8B	

LP9B	
LP10 B	
LP11 B	
LP12 B	
R20	 <p style="text-align: right;">and</p>
R25	

[0041g] In another aspect, provided herein is an antibody-drug conjugate of claim 9, prepared by contacting an anti-MSR1 antibody or a PEG-modified anti-MSR1 antibody, or antigen-binding fragment thereof, with a linker payload, or a stereoisomeric form thereof, or a regioisomer thereof, according to Formula (D):



Formula (D).

under conditions suitable for forming a bond between anti-MSR1 antibody, or antigen-binding fragment thereof.

[0042] Also provided herein are therapeutic methods comprising administration of an anti-MSR1 antibody, an antigen-binding portion of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding fragment thereof, to a subject in need thereof. The therapeutic methods comprise administering a therapeutically effective amount of a pharmaceutical composition comprising an anti-MSR1 antibody, an antigen-binding portion of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding fragment thereof to the subject. The disorder treated is any disease or condition which is improved, ameliorated, inhibited or prevented by targeting MSR1. In some examples, the disease or condition is a proliferative disease, a metabolic disease, inflammation, a neurodegenerative disease, or disease, disorder, or condition associated with glucocorticoid receptor signaling. In some examples the disease or condition is atherosclerosis. In some examples, the disease, disorder, or condition associated with glucocorticoid receptor signaling is an inflammatory disease, disorder, or condition. In some of such examples, the side effects associated with administration of the unconjugated steroid payload of said compound are reduced. Also provided herein are therapeutic methods comprising administration an anti-MSR1 antibody, an antigen-binding portion of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding fragment thereof, for the treatment and/or prevention of bacterial infection in a subject.

[0043] Provided herein is the use of an anti-MSR1 antibody, an antigen-binding portion of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding

fragment thereof, described herein, for the treatment of any disease disorder or condition described herein.

[0044] Also provided herein are therapeutic methods for treating, attenuating, or ameliorating atherosclerosis, comprising administration of an anti-MSR1 antibody, an antigen-binding portion

of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding fragment thereof, to a subject in need thereof. The therapeutic methods comprise administering a therapeutically effective amount of a pharmaceutical composition comprising an anti-MSR1 antibody, an antigen-binding portion of an MSR1 antibody, or an ADC comprising an anti-MSR1 antibody of MSR1 antigen-binding fragment thereof to the subject.

[0044a] In another aspect, provided herein is the antibody-drug conjugate as described herein, or the pharmaceutical composition as described herein for use in therapy.

[0044b] In another aspect, provided herein is a use of the antibody-drug conjugate as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating a proliferative disease, a metabolic disease, inflammation, a neurodegenerative disease, or disease, disorder, or condition associated with glucocorticoid receptor signaling.

[0044c] In another aspect, provided herein is a use of the antibody-drug conjugate as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for preventing or treating bacterial infection.

[0044d] In another aspect, provided herein is a use of the antibody-drug conjugate as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for preventing or treating cellulitis, bacteremia, dermonecrosis, eyelid infection, eye infection, neonatal conjunctivitis, osteomyelitis, impetigo, boils, scalded skin syndrome, food poisoning, pneumonia, surgical infection, urinary tract infection, burn infection, meningitis, endocarditis, septicemia, toxic shock syndrome, septic arthritis, mastitis, infection associated with a prosthetic joint, infection associated with a catheter, or infection associated with an implant.

[0044e] In another aspect, provided herein is a use of the antibody-drug conjugate as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for preventing or treating an intracellular bacterial infection.

[0045] Other examples will become apparent from a review of the ensuing detailed description.

BRIEF DESCRIPTION OF THE FIGURES

- [0046] **Figure 1** provides a scheme for the synthesis of **P1** and **P2B**.
- [0047] **Figure 2** provides a scheme for the synthesis of **LP1**.
- [0048] **Figure 3** provides a scheme for the synthesis of **LP2**.
- [0049] **Figure 4** provides a scheme for the synthesis of **LP5**.
- [0050] **Figure 5** provides a scheme for the synthesis of **LP6**.
- [0051] **Figure 6** provides a scheme for the synthesis of **LP18**.
- [0052] **Figure 7** provides a scheme for the synthesis of **LP4**.
- [0053] **Figure 8** provides a scheme for the synthesis of **LP11**.
- [0054] **Figure 9** provides a scheme for the synthesis of **LP9**.
- [0055] **Figure 10** provides a scheme for the synthesis of **LP12**.
- [0056] **Figure 11** provides a scheme for the synthesis of **P3** and **P4**.
- [0057] **Figure 12** provides a scheme for the synthesis of **LP3**.
- [0058] **Figure 13** provides a scheme for the synthesis of **LP13**.
- [0059] **Figure 14** provides a scheme for the synthesis of **LP14**.
- [0060] **Figure 15** provides a scheme for the synthesis of **LP15**.
- [0061] **Figure 16** provides a scheme for the synthesis of antibody-drug conjugates (ADCs).
- [0062] **Figure 17** is a line graph illustrating percentage of dose-dependent cholesterol efflux in THP-1 macrophages for an exemplary MSR1 antibody-LXR conjugate, its unconjugated counterpart, an isotype control-steroid conjugate, and the corresponding free payload.
- [0063] **Figure 18** provides a series of bar graphs illustrating the effect of an exemplary MSR1 antibody-LXR agonist conjugate and its unconjugated counterpart on serum lipid levels in a mouse model of atherosclerosis.

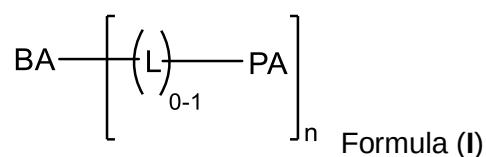
What is claimed is:

1. An isolated antibody or antigen-binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1), wherein the antibody or antigen-binding fragment thereof exhibits one or more properties selected from the group consisting of:
 - (i) binds human MSR1 at 37°C with a K_D of less than about 1.4 nM as measured by surface plasmon resonance;
 - (ii) binds human MSR1 at 37°C with a $t_{1/2}$ of greater than about 4 minutes as measured by surface plasmon resonance;
 - (iii) exhibits maximum inhibition of modified LDL uptake by human MSR1 of less than about 90% with an IC_{50} of less than about 10 nM as measured by ligand uptake assay;
 - (iv) blocks < 50% of modified LDL binding to human MSR1 as measured by competition ELISA assay; and
 - (v) exhibits binding of human MSR1 and internalization of the bound complex of more than about 10% as assayed by binding in THP-1 cells.

2. An isolated antibody or antigen-binding fragment thereof that binds to cell surface-expressed macrophage scavenger receptor 1 (MSR1) and blocks inhibition of modified LDL uptake by MSR1 by less than 80% with an IC₅₀ of less than 3.5 nM.
3. The isolated antibody or antigen-binding fragment of claim 2, wherein the antibody or antigen-binding fragment thereof blocks blocks inhibition of modified LDL uptake by MSR1 by less than 60% with an IC₅₀ of less than 1.5 nM.
4. An isolated antibody or antigen-binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1), wherein the antibody or antigen-binding fragment comprises: (a) the complementarity determining regions (CDRs) of a heavy chain variable region (HCVR) having an amino acid sequence as set forth in Table 4; and (b) the CDRs of a light chain variable region (LCVR) having an amino acid sequence as set forth in Table 4.
5. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment comprises an HCVR having an amino acid sequence as set forth in Table 4 and a LCVR having an amino acid sequence as set forth in Table 4.
6. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment comprises:
 - (i) a HCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 36, 52, 92, and 284;
 - (ii) a HCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 6, 38, 54, 94, and 286;
 - (iii) a HCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 40, 56, 96, and 288;
 - (iv) a LCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 12, 44, 60, 100, and 292;
 - (v) a LCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 46, 62, 102, and 294; and
 - (vi) a LCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 16, 48, 64, 104, and 296.

7. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment comprises:
- (i) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 52; an HCDR2 comprising SEQ ID NO: 54; an HCDR3 comprising SEQ ID NO: 56; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 60; an LCDR2 comprising SEQ ID NO: 62; and an LCDR3 comprising SEQ ID NO: 64;
 - (ii) an HCDR1 comprising SEQ ID NO: 4; an HCDR2 comprising SEQ ID NO: 6; an HCDR3 comprising SEQ ID NO: 8; an LCDR1 comprising SEQ ID NO: 12; an LCDR2 comprising SEQ ID NO: 14; and an LCDR3 comprising SEQ ID NO: 16;
 - (iii) an HCDR1 comprising SEQ ID NO: 36; an HCDR2 comprising SEQ ID NO: 38; an HCDR3 comprising SEQ ID NO: 40; an LCDR1 comprising SEQ ID NO: 44; an LCDR2 comprising SEQ ID NO: 46; and an LCDR3 comprising SEQ ID NO: 48;
 - (iv) an HCDR1 comprising SEQ ID NO: 92; an HCDR2 comprising SEQ ID NO: 94; an HCDR3 comprising SEQ ID NO: 96; an LCDR1 comprising SEQ ID NO: 100; an LCDR2 comprising SEQ ID NO: 102; and an LCDR3 comprising SEQ ID NO: 104;
 - (v) an HCDR1 comprising SEQ ID NO: 284; an HCDR2 comprising SEQ ID NO: 286; an HCDR3 comprising SEQ ID NO: 288; an LCDR1 comprising SEQ ID NO: 292; an LCDR2 comprising SEQ ID NO: 294; and an LCDR3 comprising SEQ ID NO: 296;.

8. An isolated antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof competes for binding to human MSR1 with a reference antibody comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOS: 2/10, 23/42, 50/58; 90/98, and 282/290.
9. An antibody-drug conjugate comprising the antibody, or antigen-binding fragment thereof, of any one of claims 1 to 8 conjugated to a payload residue optionally through a linker or through a linker-spacer.
10. The antibody-drug conjugate of claim 9, having the structure of Formula (I):



or a pharmaceutically acceptable salt, solvate, stereoisomeric form thereof, a regioisomer thereof, or mixtures of regioisomers thereof;

wherein:

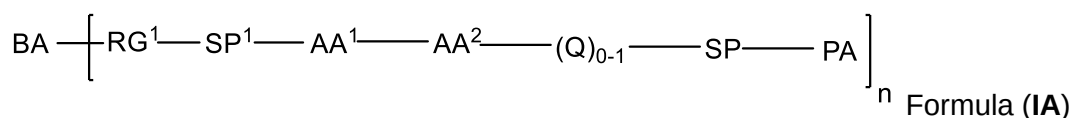
BA is a binding agent;

L is a linker;

PA is a payload moiety selected from the group consisting of a steroid residue, a LXR modulator residue, or a rifamycin analog residue; and

subscript **n** is an integer from 1 to 30.

11. The antibody-drug conjugate of claim 9 or claim 10, having the structure of Formula (IA):



wherein

SP¹ is absent, or a spacer;

RG¹ is a reactive group residue;

AA¹ is absent, or a divalent or trivalent linker comprising an amino acid residue which is optionally bonded directly or indirectly to a group **HG**;

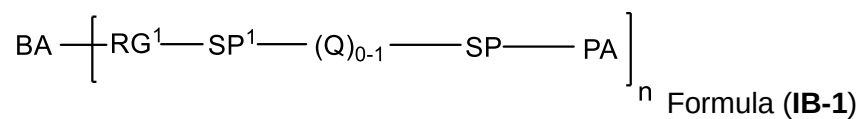
AA² is absent, or a dipeptide, tripeptide, or tetrapeptide residue;

Q, when present, is a connector group residue;

SP is absent, or a spacer; and

HG, when present, is a hydrophilic group.

12. The antibody-drug conjugate of any one of claims 9-11, having the structure of Formula (IB-1):

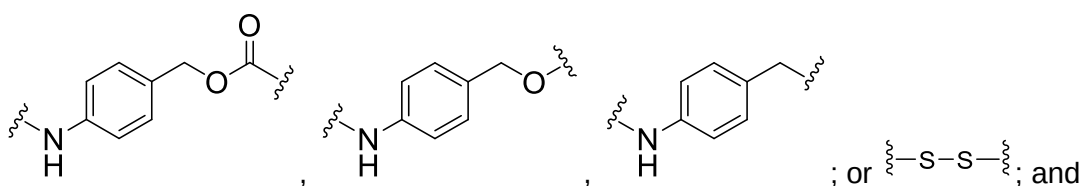


wherein

SP¹ is absent, or a spacer;

RG¹ is a reactive group residue;

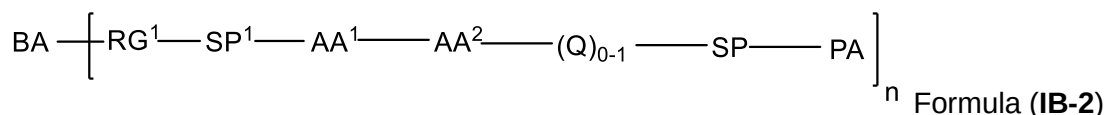
Q, when present, is



SP is absent, or a spacer;

wherein the indicates the atoms through which the referenced group is bonded to the adjacent groups in the formula.

13. The antibody-drug conjugate of any one of claims 9-11, having the structure of Formula (IB-2):



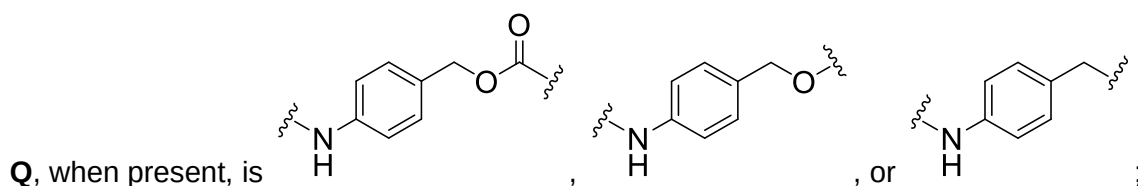
wherein

SP¹ is absent, or a spacer;

RG¹ is a reactive group residue;

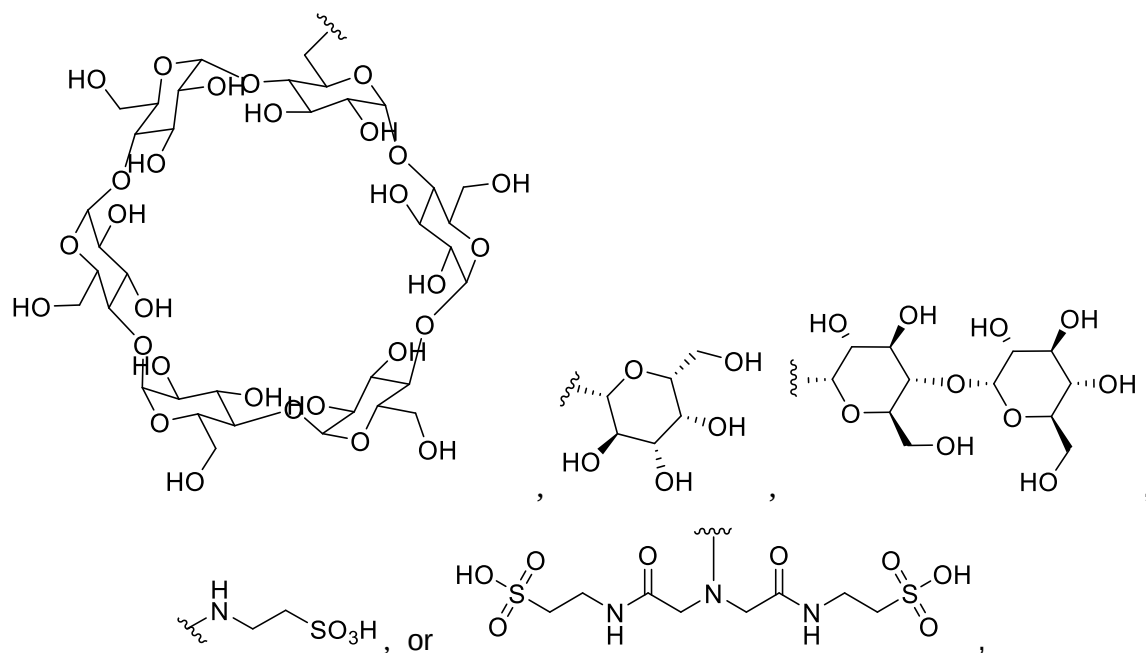
AA¹ is absent, or a divalent or trivalent linker comprising an amino acid residue which is optionally bonded directly or indirectly to a group **HG**;

AA² is absent, or a dipeptide, tripeptide, or tetrapeptide residue;



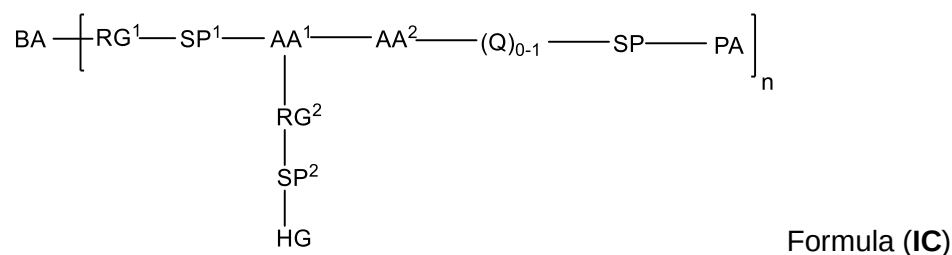
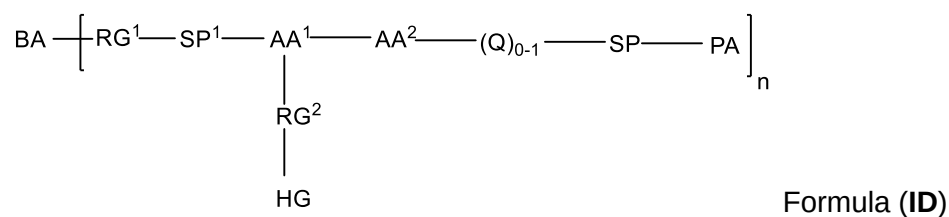
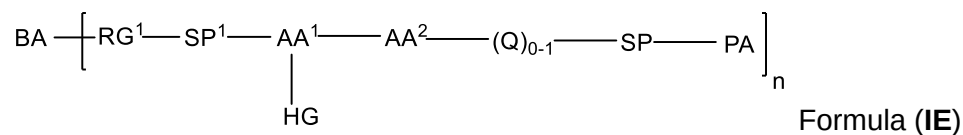
SP is absent, or a spacer; and

HG, when present, is



wherein the  indicates the atoms through which the referenced group is bonded to the adjacent groups in the formula.

14. The antibody-drug conjugate of any one of claims 9-11 and 13, having the structure of Formula (IC), Formula (ID), or Formula (IE):



wherein

SP¹ is absent, or a spacer;

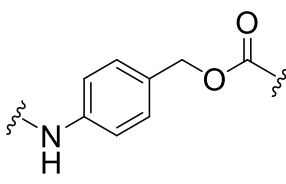
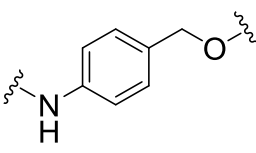
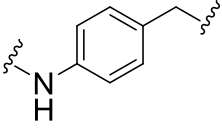
RG¹ is a reactive group residue;

SP² is absent, or a spacer;

RG² is a reactive group residue;

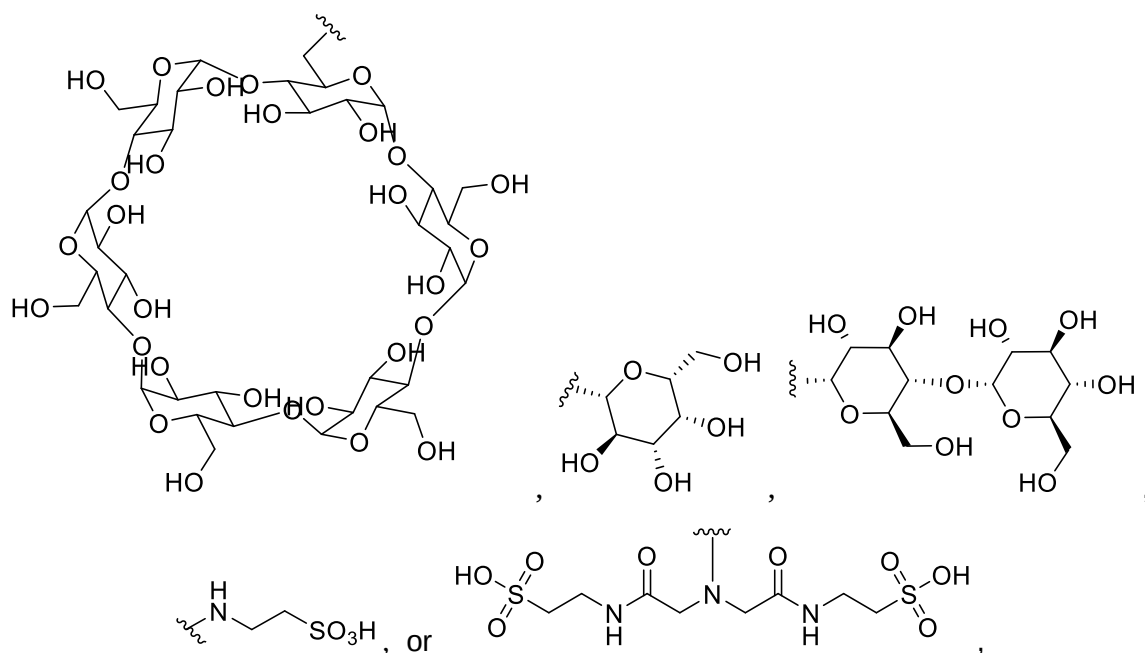
AA¹ is a divalent or trivalent linker comprising an amino acid residue;

AA² is a dipeptide, tripeptide, or tetrapeptide residue;

Q, when present, is , , or ;

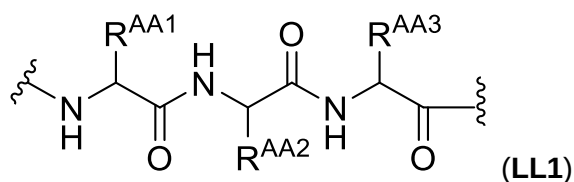
SP is absent, or a spacer; and

HG is



wherein the  indicates the atoms through which the referenced group is bonded to the adjacent groups in the formula.

15. The antibody-drug conjugate of any one of claims 11, and 13-14, wherein **AA¹-AA²** is according to Formula (**LL1**):



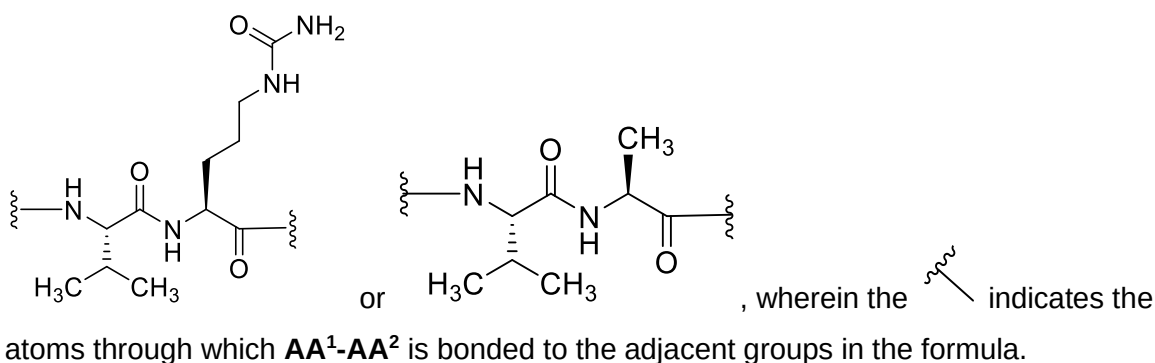
wherein **R^{AA1}**, **R^{AA2}**, and **R^{AA3}** are each, independently, amino acid side chains, at least

one of which is bonded to **-(RG²)-SP²-HG**, **-(RG²)-HG** or **HG**; wherein the 

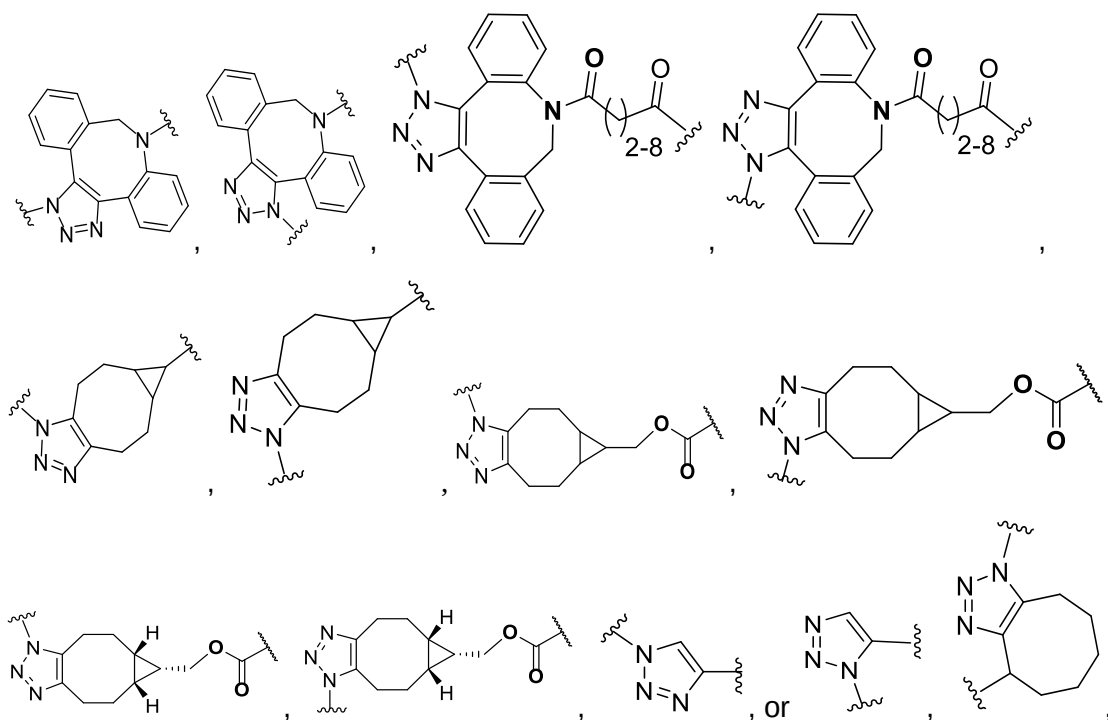
indicates the atoms through which **AA¹-AA²** is bonded to the adjacent groups in the formula.

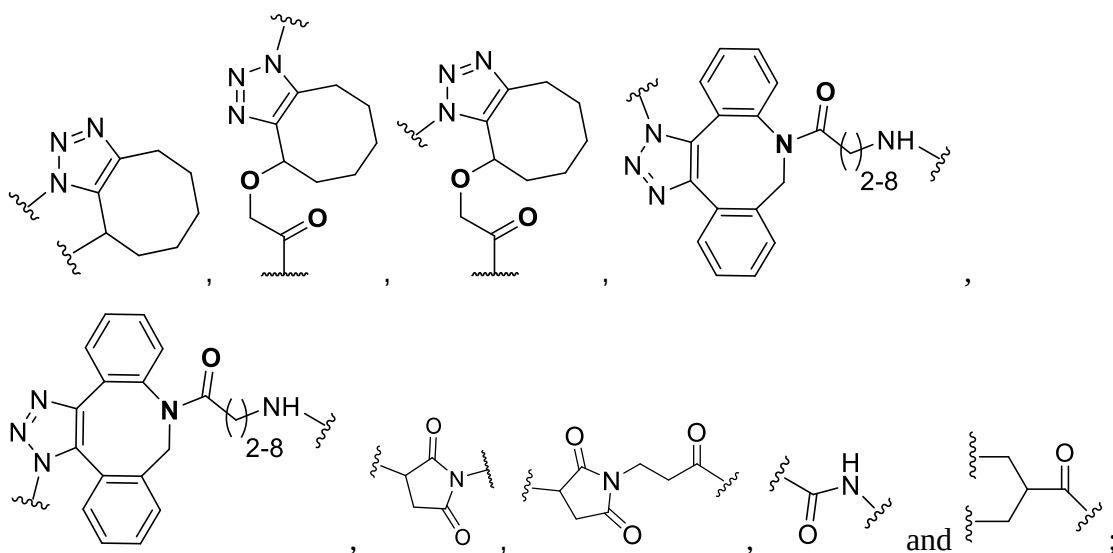
16. The antibody-drug conjugate of claim 15, wherein **R^{AA1}** is a lysine, glutamine, glutamic acid or aspartic acid side chain bonded directly or indirectly to **HG**, and **R^{AA2}** and **R^{AA3}** are either valine and alanine or valine and citrulline sidechains respectively.

17. The antibody-drug conjugate of any one of claims 11, and 13-16, wherein **AA¹-AA²** is



18. The antibody-drug conjugate of any one of claims 11-17, wherein the **RG¹** and **RG²** residues are independently, in each instance, selected from the group consisting of:



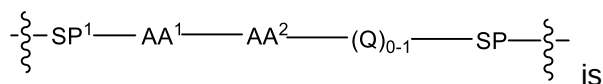
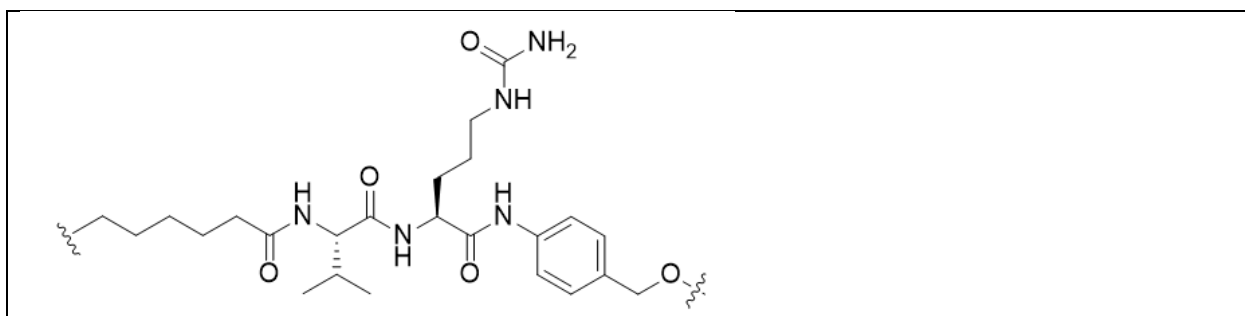


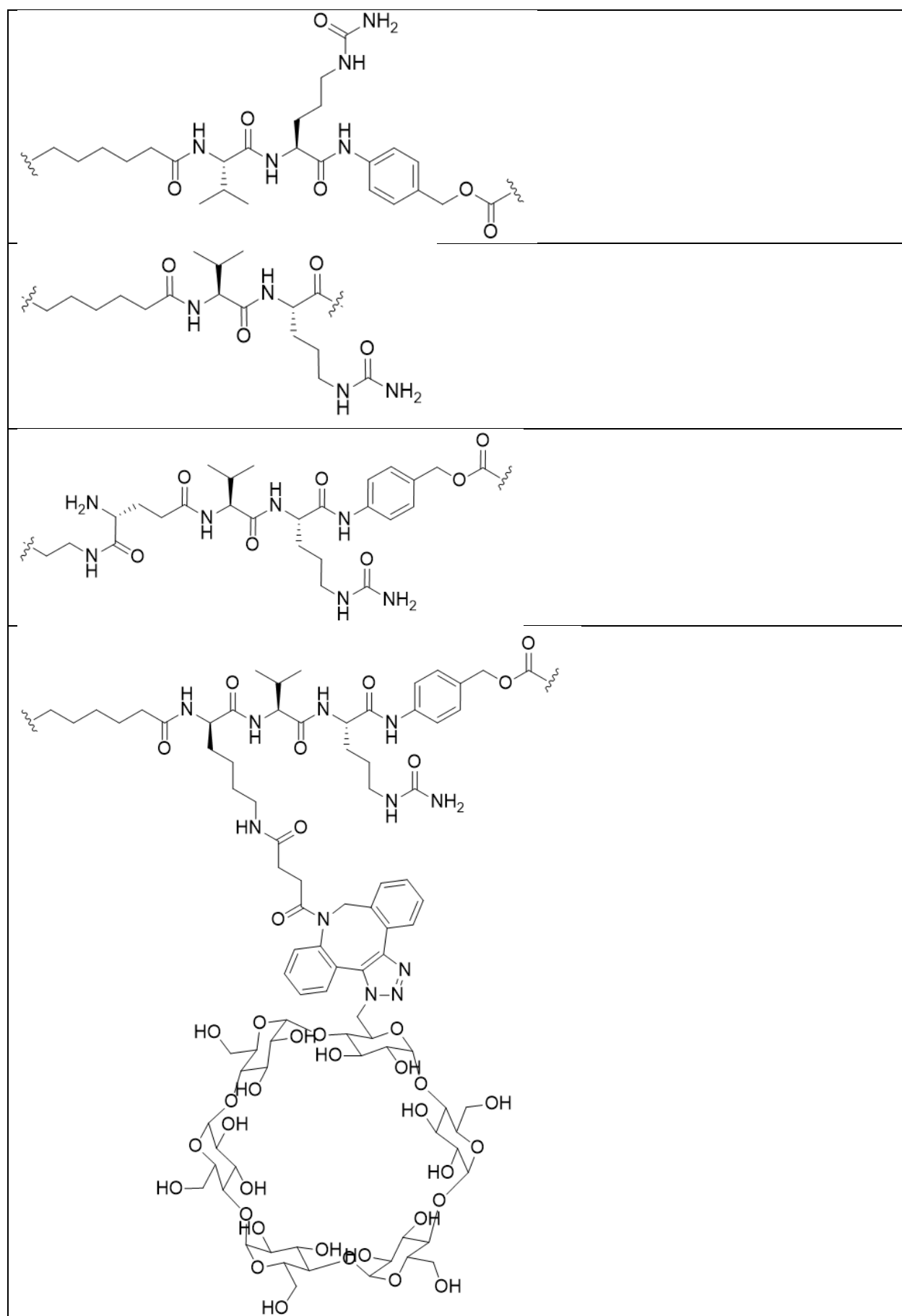
wherein the  indicates the atom through which the **RG**¹ or **RG**² residue is bonded to the adjacent groups in the formula.

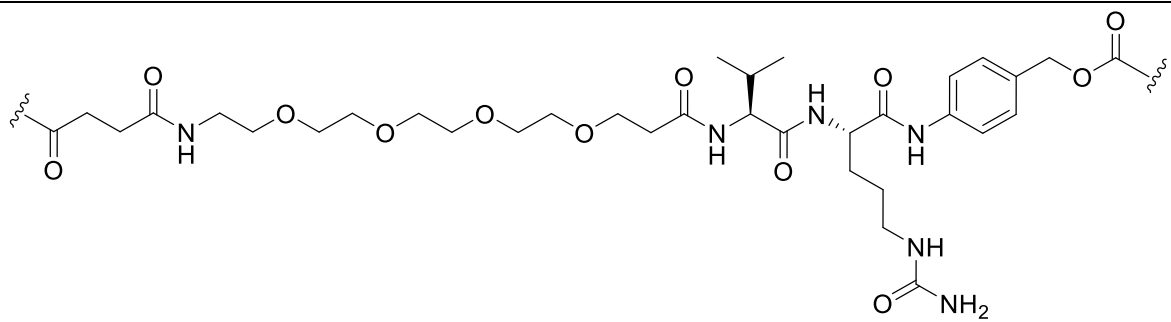
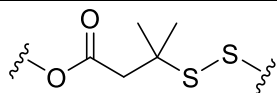
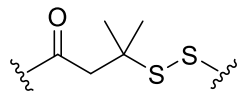
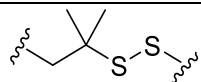
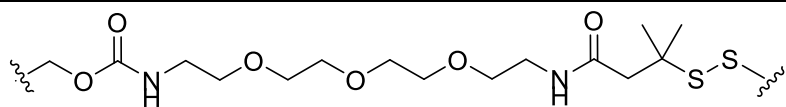
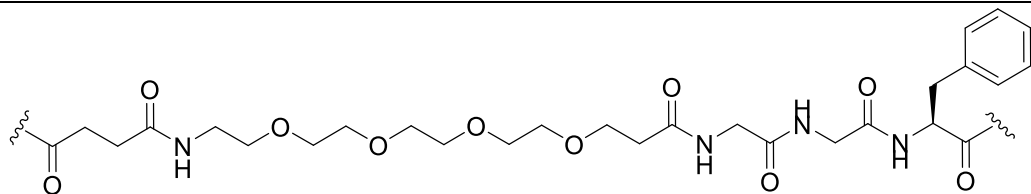
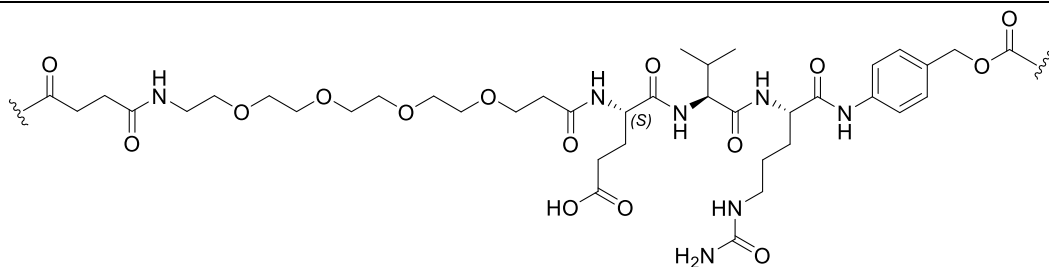
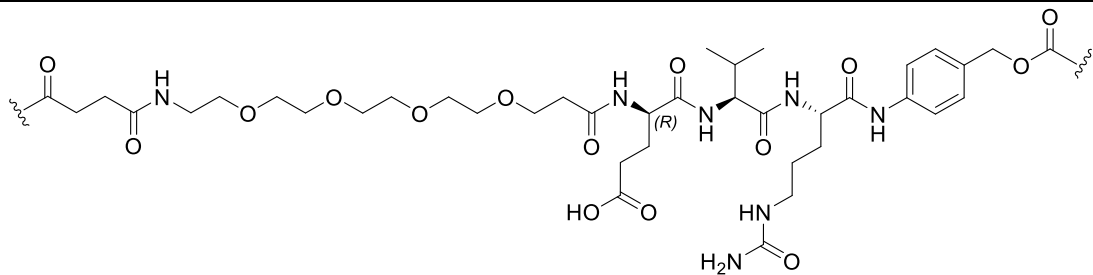
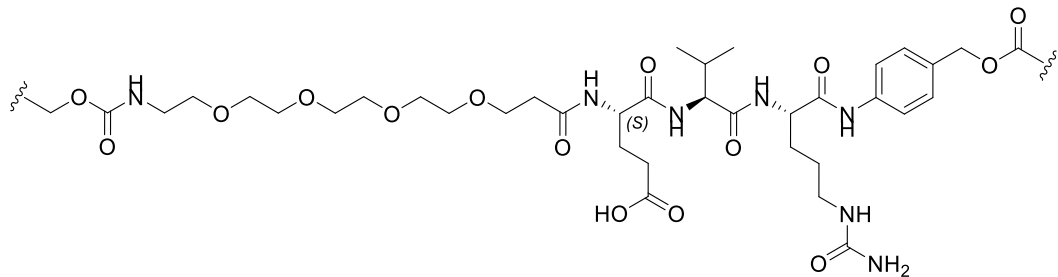
19. The antibody-drug conjugate of any one of claims 11-18, wherein **SP**, **SP**¹ and **SP**² are independently, in each instance, absent, or selected from the group consisting of C₁₋₆ alkylene, -NH-, -S-, -O-, -C(O)-, (-CH₂-CH₂-O)_e, -NH-CH₂-CH₂-(O-CH₂-CH₂)_e-C(O)-, -C(O)-(CH₂)_u-C(O)-, -C(O)-NH-(CH₂)_v-, (glycine)₄-serine, and combinations thereof, wherein subscript **e** is an integer from 0 to 4, subscript **u** is an integer from 1 to 8, and subscript **v** is an integer from 1 to 8.

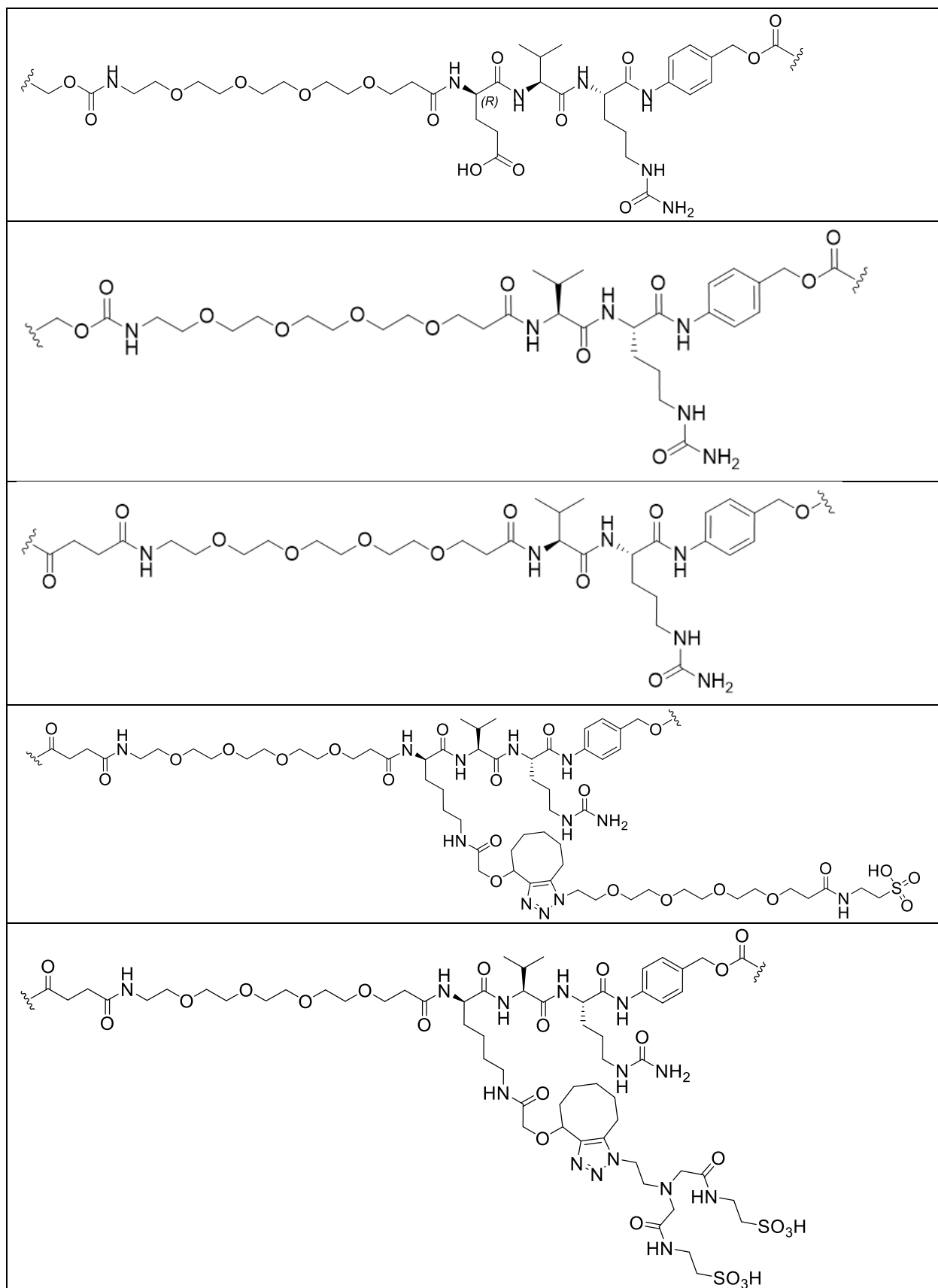
20. The antibody-drug conjugate of any one of claims 9-19, wherein **n** is 1, 2, 3, or 4.

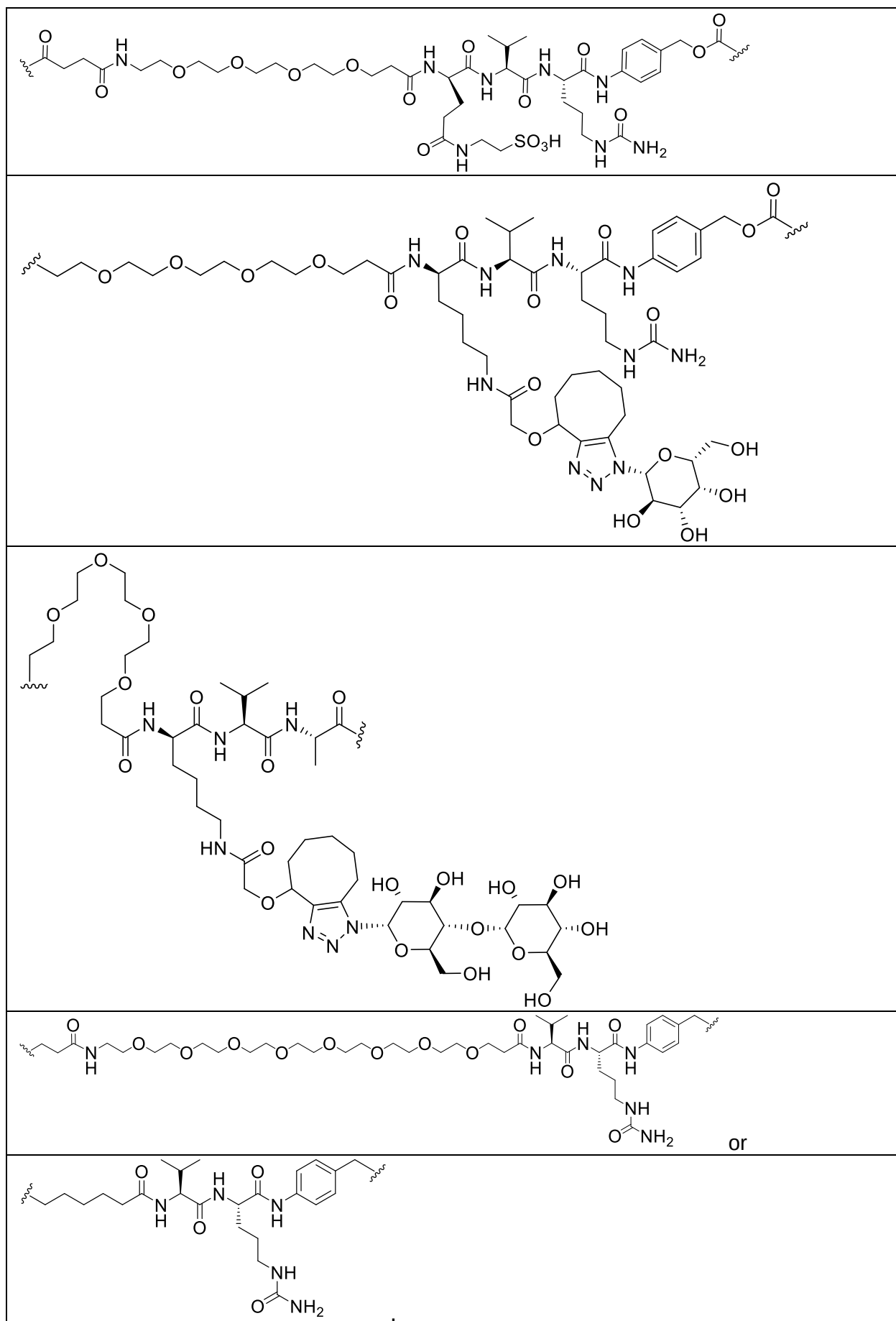
21. The antibody-drug conjugate of any one of claims 11-20, wherein



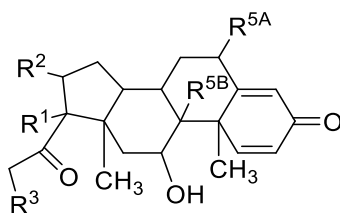








22. The antibody-drug conjugate molecule of claim 9, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a steroid payload through a linker or a linker-spacer.
23. The antibody-drug conjugate molecule of claim 9, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a LXR modulator payload through a linker.
24. The antibody-drug conjugate molecule of claim 9, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a rifamycin analog payload through a linker.
25. The antibody-drug conjugate molecule of claim 22, wherein the steroid conjugated to the antibody, or antigen-binding fragment thereof, through a linker or a linker-spacer is a compound of Formula (A-1)

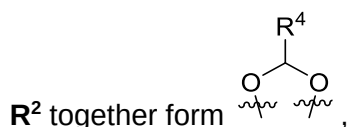


Formula (A-1)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein

R^1 and R^2 are, independently, $-H$, alkyl, alkyl- $C(O)-O-$, $-OH$, or halo; or R^1 and



wherein R^4 is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl,

wherein the alkyl, aryl, arylalkyl, and N-containing heterocycloalkyl are, independently in each instance, optionally substituted with $-NR^{Aa}R^{Ab}$;

R^3 is $-O$, $R^Z-C(O)-X-$, $-heteroalkyl$, $-piperidiny$, $-NR^{Aa}R^{Ab}$, $-oxyaryl-NR^{Aa}R^{Ab}$ or $-Z-A'(R^P)_t$;

R^Z is alkyl;

X is O or NR^{Aa} ;

Z is S , $S(O)$, $S(O)_2$, SO_2NR^{Aa} , O , $C(O)NR^{Aa}$, $C(O)$, or NR^{Aa} ;

A' is aryl, arylalkyl, or heteroaryl;

R^P is, independently in each instance, halo, optionally substituted alkyl, $-OH$,
or $-NR^{Aa}R^{Ab}$;

R^{Aa} and R^{Ab} are, independently in each instance, $-H$, optionally substituted alkyl, or
optionally substituted aryl;

subscript a is an integer from 0-19; and

t is an integer from 1-3;

and

R^{5A} and R^{5B} are each, independently, halo or a hydrogen atom;

wherein the group R^3 or R^4 is bonded to the linker.

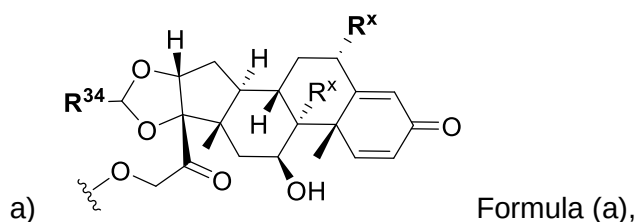
26. The antibody-drug conjugate of claim 22, having the structure of Formula (3000):

BA-(L'-SP-D)_n Formula (3000)

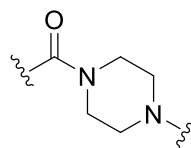
or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein

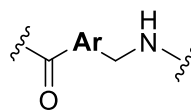
D is selected from



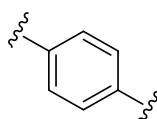
where both R^x in Formula (a) are hydrogen; R^{34} is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl; and **SP** is $-C(O)-C_1-C_{10}$ -alkylene- $C(O)-$, $-C(O)-N(C_{1-6}alkyl)-C_1-C_{10}$ -alkylene- X^1 - where X^1 is attached to **L'** in Formula (3000), $-C(O)-N(H)-(C_1-C_{10}$ -alkylene)-S- where S is attached to **L'** in Formula (3000), $-C(O)-N(C_{1-6}alkyl)-(C_1-C_{10}$ -alkylene)-S-



where S is attached to **L'** in Formula (3000), where the point of attachment on the right hand side (*i.e.* at N) is to **L'** in Formula (3000), $-CH_2-NH-$ where

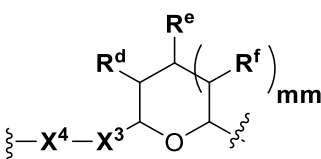


the N is attached to **L'** in Formula (3000), where the N is attached to **L'** in Formula (3000) and where **Ar** is optionally substituted arylene (in some embodiments

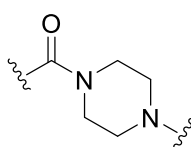


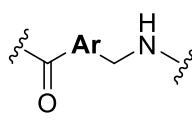
) or optionally substituted heteroarylene, $-(C_1-C_{10}$ -alkylene)- $NR^{50}C(O)-(C_1-$

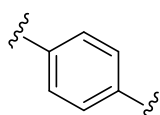
C₁₀-alkylene)-NR^{50a}- where NR^{50a} is attached to L' in Formula (3000), -C(O)-(C₁-C₁₀-alkylene)-NR⁵⁰C(O)-(C₁-C₁₀-alkylene)-NR^{50a}- where NR^{50a} is attached to L' in Formula (3000) and where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N(R³⁵)-C₁-C₁₀-alkylene-C(O)NH-X²- where X² is attached to L' in

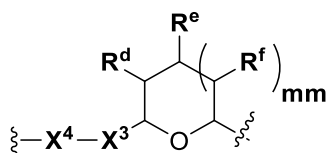
Formula (3000), or  where X⁴ is attached to L' in Formula (3000); or

where both R^x in Formula (a) are fluoro; R³⁴ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl; and SP is -C(O)-C₁-C₁₀-alkylene-C(O)-, -C(O)-N(C₁₋₆alkyl)-C₁-C₁₀-alkylene-X^{1b}- where X^{1b} is attached to L' in Formula (3000), -C(O)-N(H)-(C₁-C₁₀-

alkylene)-X^{1b}- where X^{1b} is attached to L' in Formula (3000),  where the point of attachment on the right hand side (i.e. at N) is to L' in Formula (3000), -CH₂-NH-

where the N is attached to L' in Formula (3000),  where the N is attached to L' in Formula (3000) and where Ar is optionally substituted arylene (in some

embodiments ) or optionally substituted heteroarylene, -(C₁-C₁₀-alkylene)-NR⁵⁰C(O)-(C₁-C₁₀-alkylene)-NR^{50a}- where NR^{50a} is attached to L' in Formula (3000), -C(O)-(C₁-C₁₀-alkylene)-NR⁵⁰C(O)-(C₁-C₁₀-alkylene)-NR^{50a}- where NR^{50a} is attached to L' in Formula (3000) and where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N(R³⁵)-(C₁-C₁₀-alkylene)-C(O)NH-X²- where

X² is attached to L' in Formula (3000), or  where X⁴ is attached to L' in Formula (3000); and/or

b) the compounds in Table A, where the compounds in Table A are linked to BA of the Compound of Formula (III) through the hydroxy of the -C(O)CH₂OH group, or through the hydroxy of Mapracorat;

X¹ is -N(C₁₋₆alkyl)-;

X^{1b} is -S-, -NH-, or -N(C₁₋₆alkyl)-;

X^2 is -NH-;

X^3 is -CH₂-, X^3 is -CH₂-O-(C₁-C₁₀-alkylene)-C(O)- where the C(O) is attached to X^4 , or X^3 is -C(O)-;

X^4 is -O-;

R^{35} is H, -OH, -OCH₃, or C₁₋₆alkyl;

R^{50} and R^{50a} are independently hydrogen or C₁-C₆-alkyl;

R^d , R^e , and R^f are independently -H, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or -CH₂OR^g, where each R^g is independently -CH₂C(O)OH or -CH₂C(O)O(alkyl); and

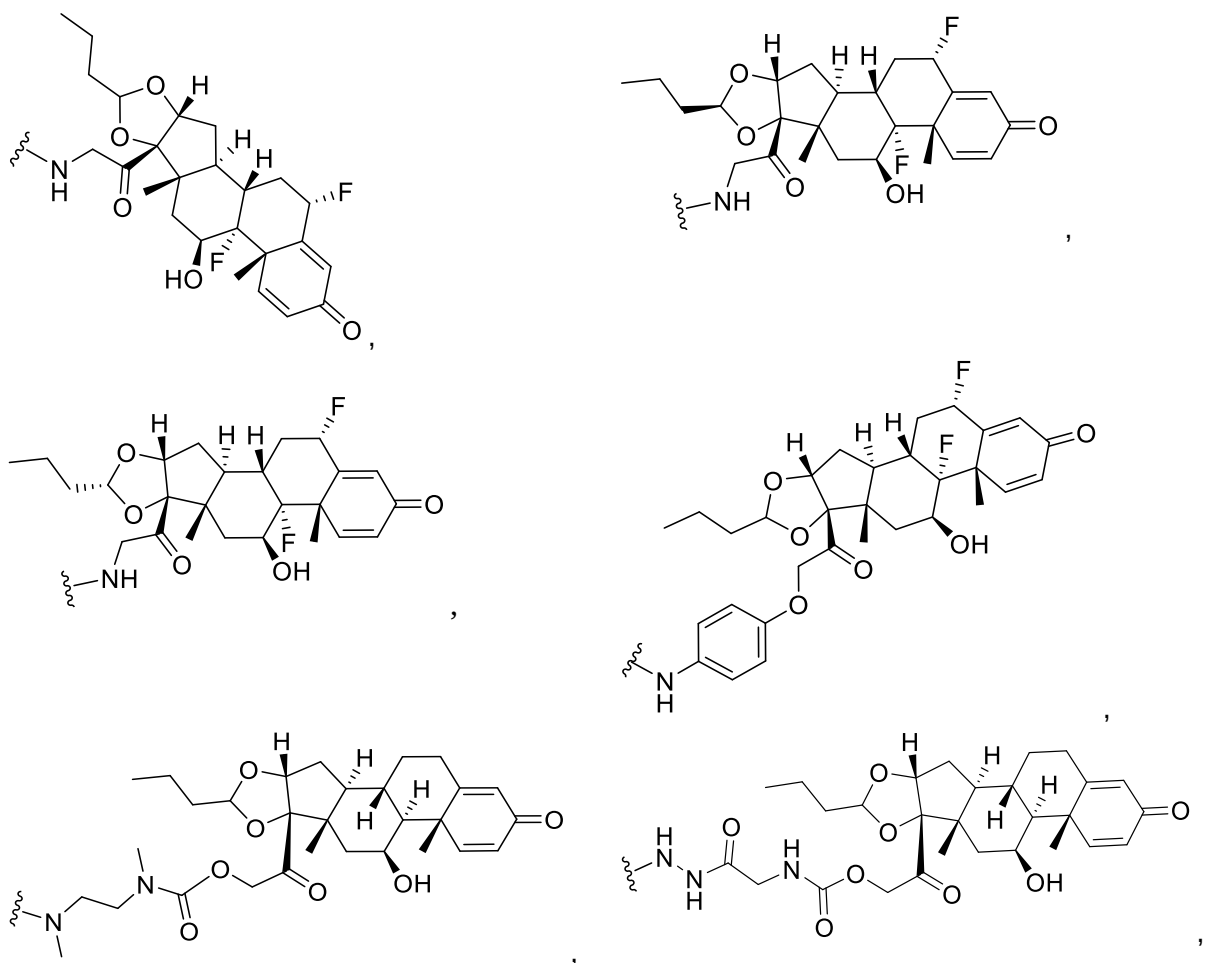
mm is 0 or 1;

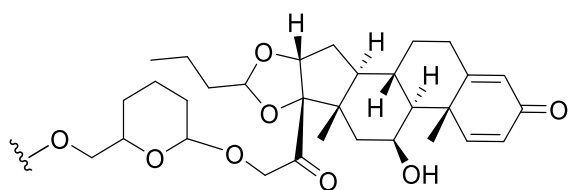
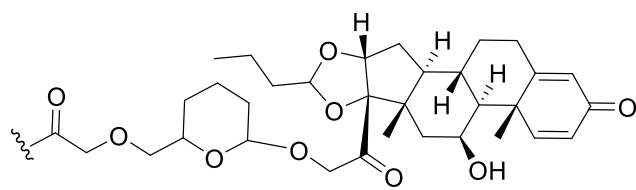
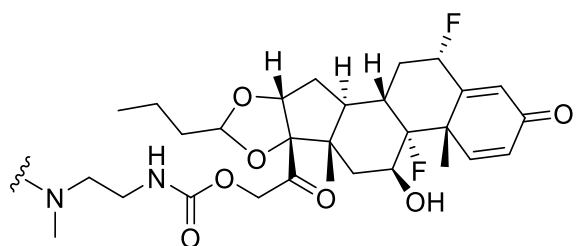
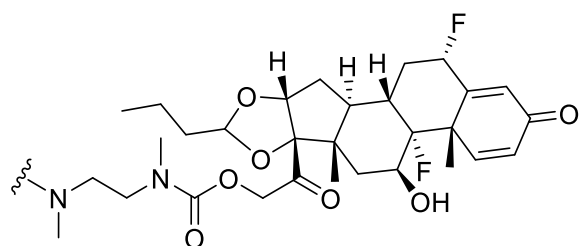
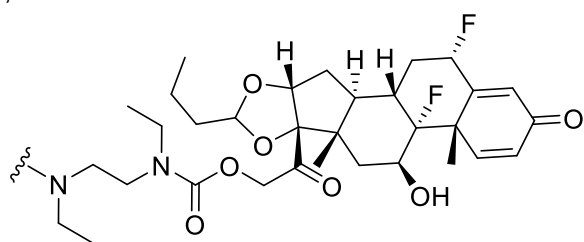
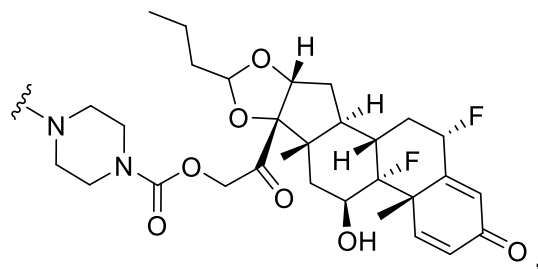
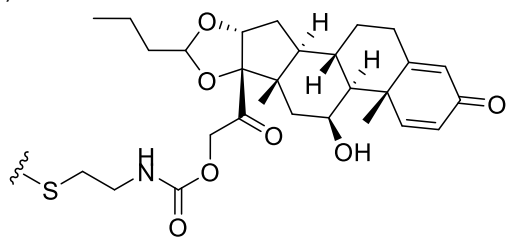
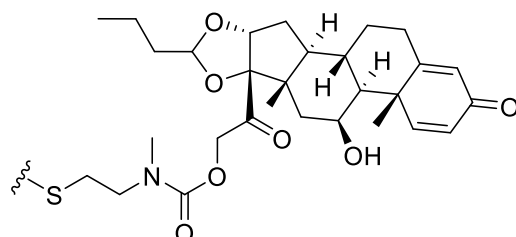
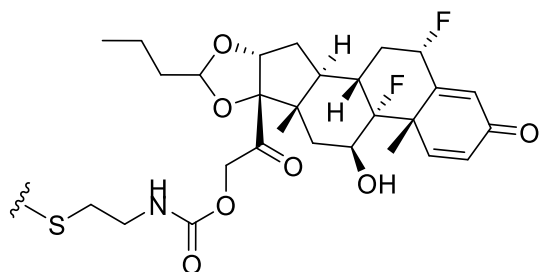
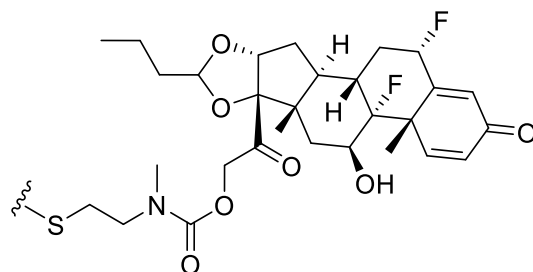
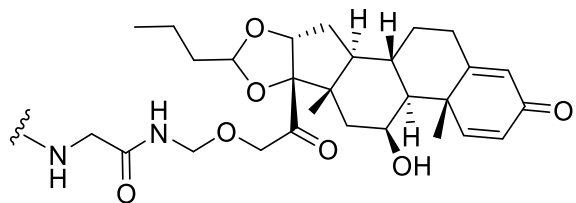
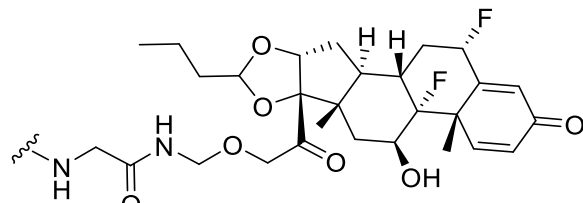
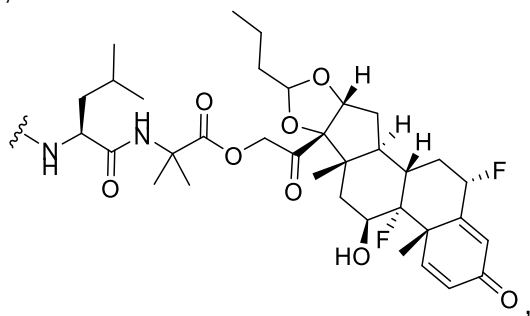
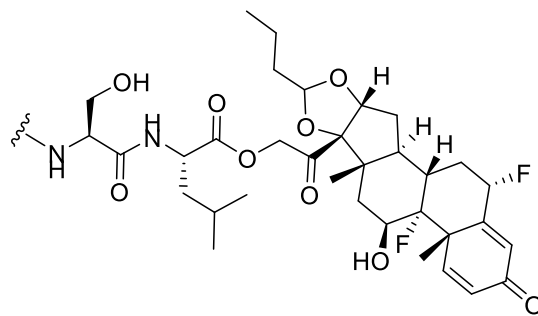
n is an integer selected from 1-30, inclusive;

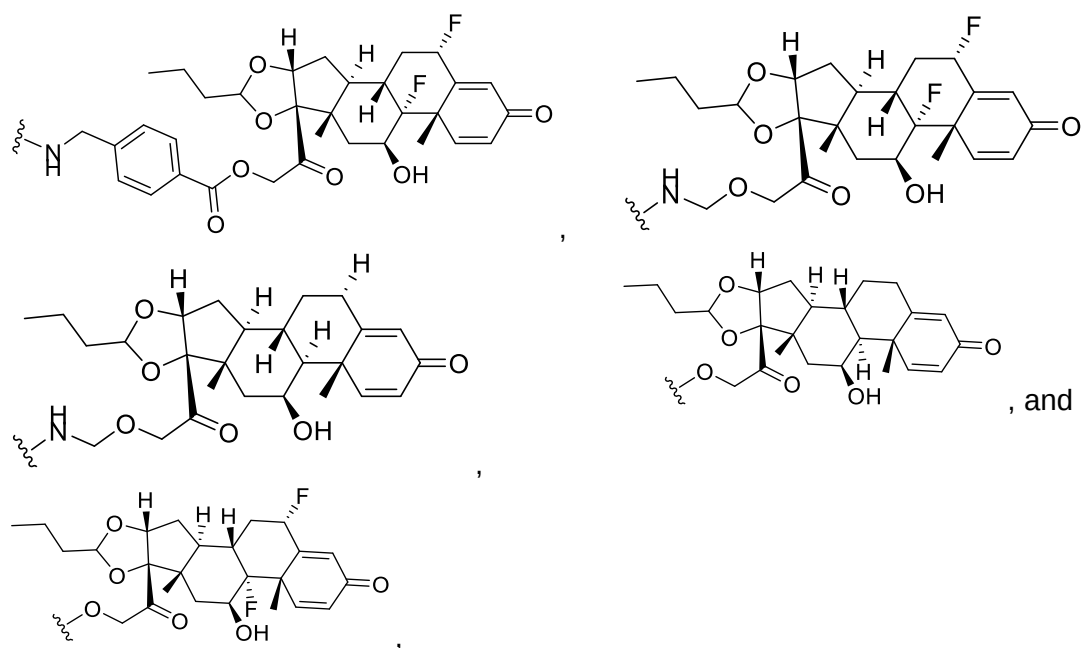
L' is a linker; and

BA is a binding agent.

27. The antibody-drug conjugate of claim 22, wherein the steroid payload is selected from the group consisting of:

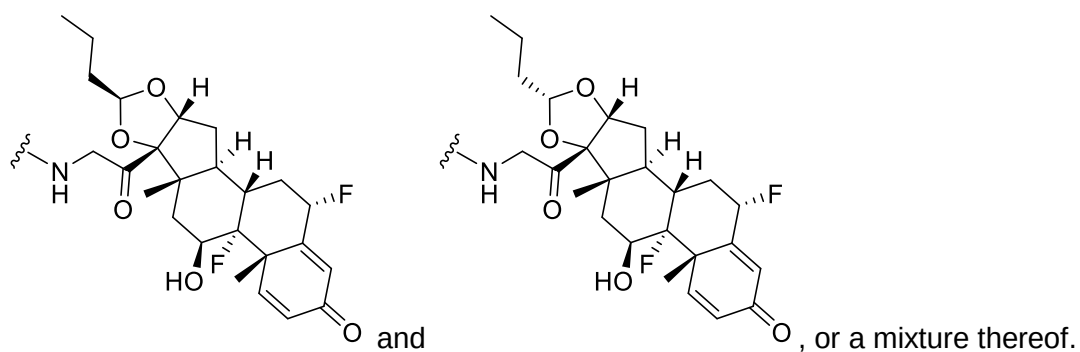




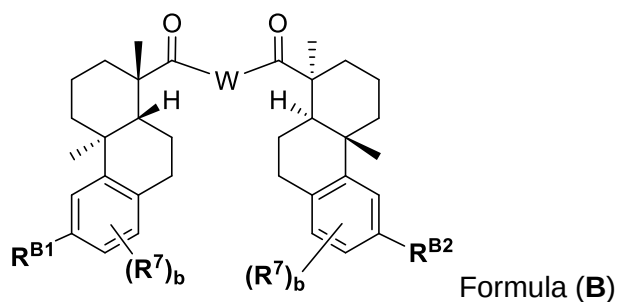


wherein the  is the bond to the linker.

28. The antibody-drug conjugate of claim 22, wherein the steroid payload is selected from the group consisting of:



29. The antibody-drug conjugate of claim 23, wherein the LXR modulator conjugated to the antibody, or antigen-binding fragment thereof, through a linker is a compound of Formula (B):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form, wherein

W is $-\text{CH}_2-$, $-\text{N}(\text{H})-$, or $-\text{O}-$;

R^{B1} is $-H$, $-OH$, $-NH_2$, alkyl, or $-OP(O)(OR^6)_2$;

R^{B2} is $-H$, $-OH$, $-CH_2NH_2$, R^{B3} , R^{B4} , R^{B5} , or $-O-R^{B5}$, wherein R^{B1} and R^{B2} are not simultaneously $-H$;

R^{B3} is $-N(R^6)_2$;

R^{B4} is $-X-Y-Z$;

X is selected from the group consisting of $-O-$ and $-N(H)-$;

Y is selected from the group consisting of alkylene, substituted alkylene (including, without limitation, oxo substitution, i.e., $=O$), heteroalkylene, and substituted heteroalkylene (including, without limitation, oxo substitution (i.e., $=O$));

Z is selected from the group consisting of $-OH$ and $-NH_2$;

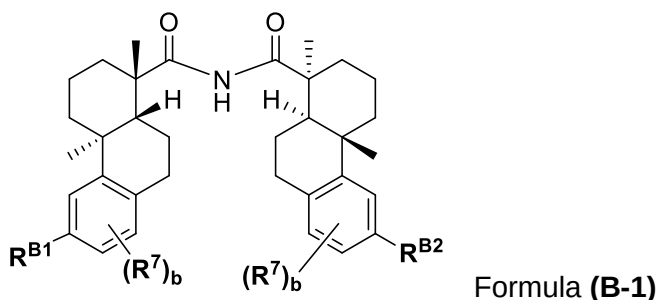
R^{B5} is alkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl includes one, two, or three heteroatoms selected from nitrogen and oxygen, and includes at least one $-OH$ and $-CH_2OH$ substituent, or at least one primary or secondary nitrogen, for instance, O-glucose;

each R^6 is in each instance, $-H$, an amino acid residue, an *N*-alkyl amino acid residue, a peptide, or alkyl; and

each R^7 is, independently, halo, C_{1-6} alkyl, C_{1-6} alkoxy, $-CN$, O-glucose, O-amino acid residue, and O-PEG_b, wherein each subscript **b** is an integer from 0-3;

wherein the group R^{B1} or R^{B2} is bonded to the linker.

30. The antibody-drug conjugate of claim 23, wherein the LXR modulator conjugated to the antibody, or antigen-binding fragment thereof, through a linker is a compound of Formula (B-1):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein:

R^{B1} is $-N(H)R^8$ or $-N(R^9)_2$;

R^{B2} is $-N(H)R^8$;

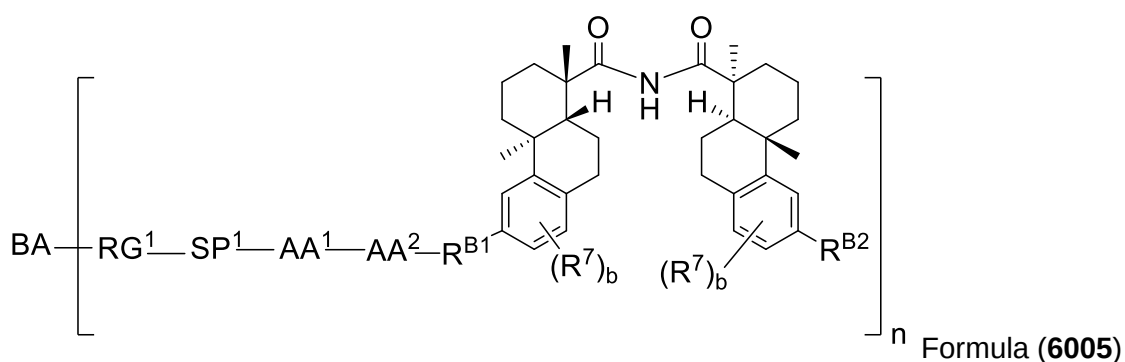
each R^8 is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, or alkyl;

R^9 is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one $-OH$ and $-CH_2OH$, or at least one primary or secondary nitrogen;

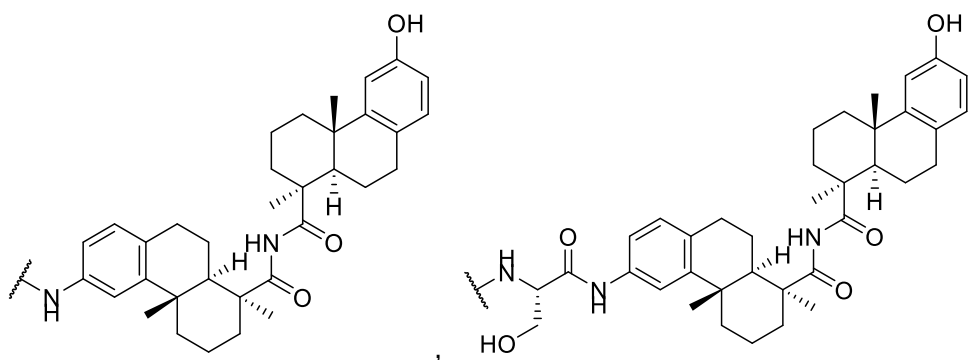
each R^7 is independently halo, C_{1-6} alkyl, C_{1-6} alkoxy, $-CN$, O-glucose, O-amino acid residue, or O-PEG_b, wherein each subscript *b* is an integer from 0-3;

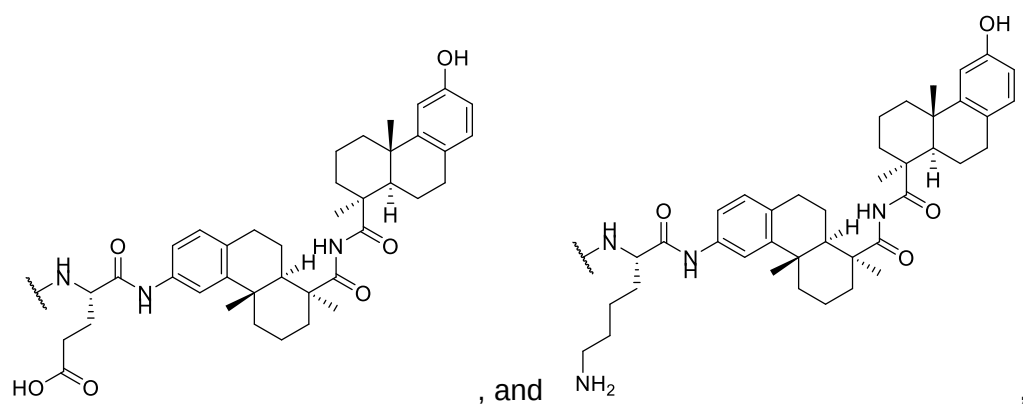
wherein the group R^{B1} or R^{B2} is bonded to the linker.

31. The antibody-drug conjugate of any one of claims 9-21, 23, and 29-30, having the structure of Formula (6005)



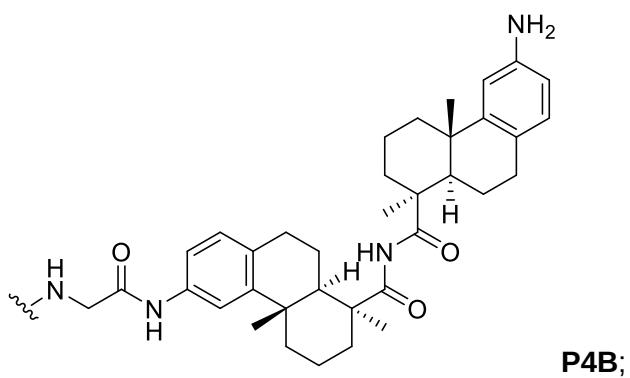
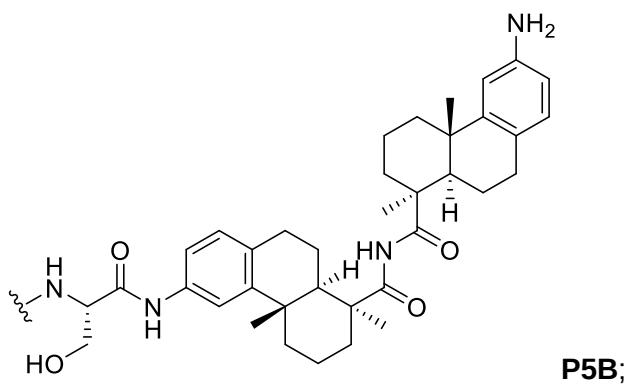
32. The antibody-drug conjugate of claim 23, wherein the LXR modulator is selected from the group consisting of:

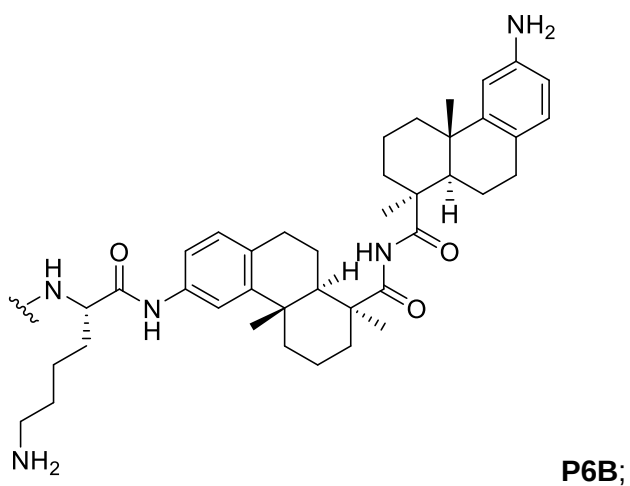
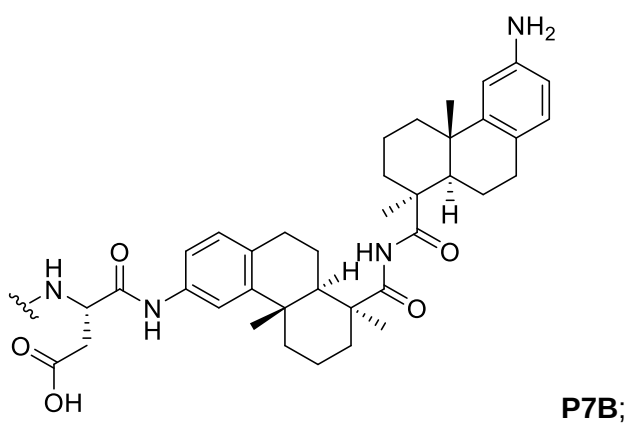
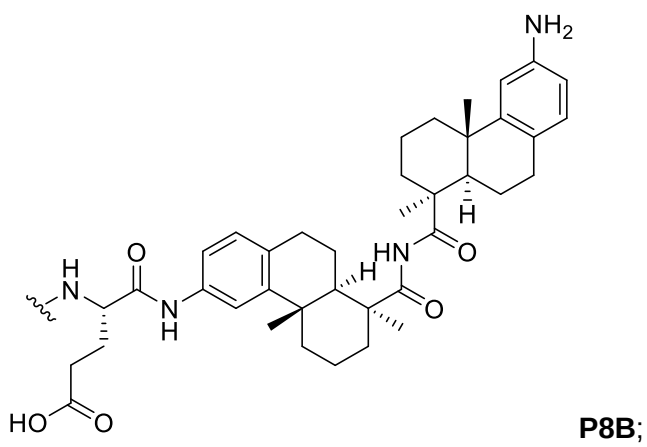
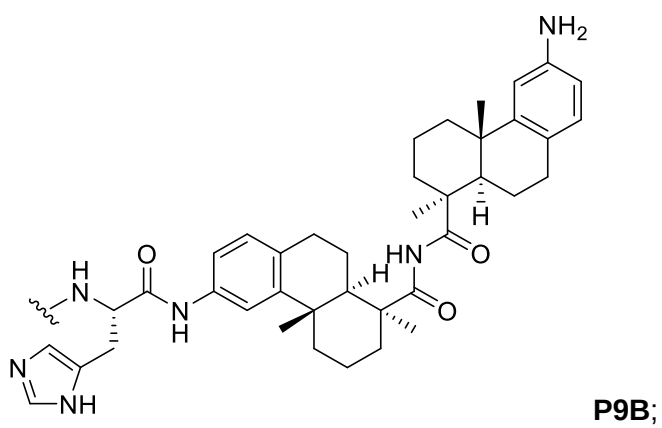


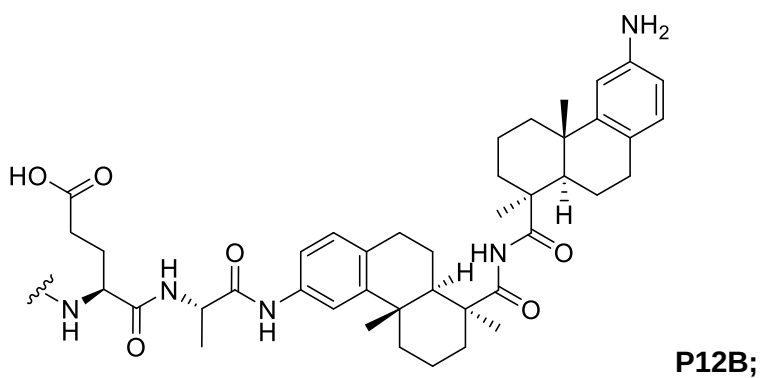
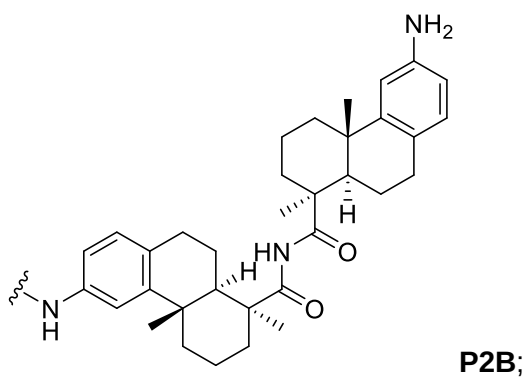
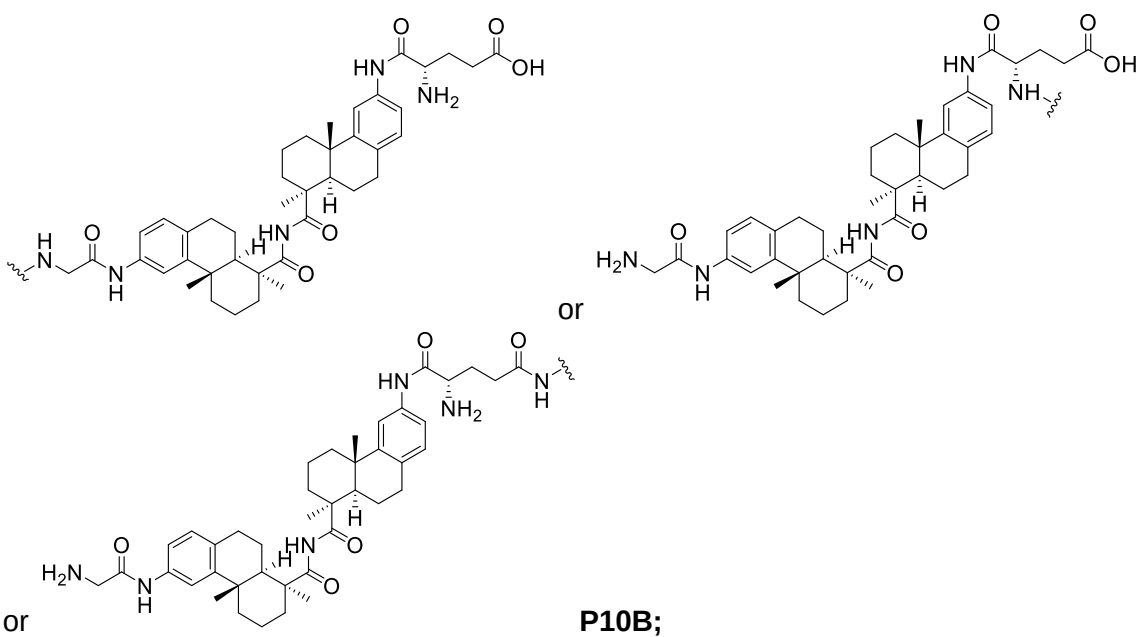
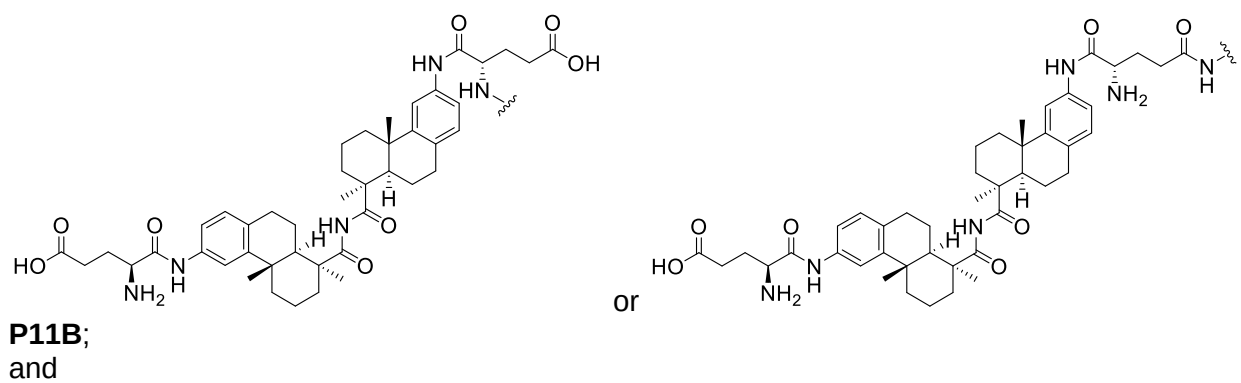


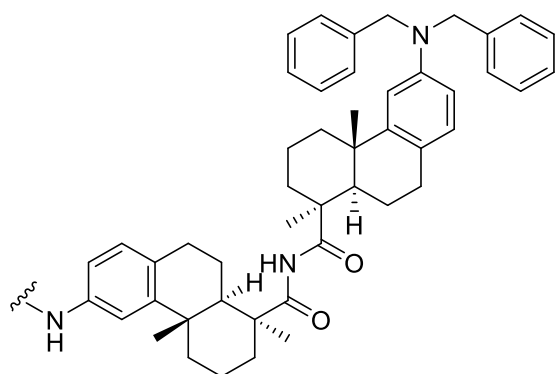
wherein the  is the bond to the linker.

33. The antibody-drug conjugate of claim 23, wherein the LXR modulator is selected from the group consisting of:





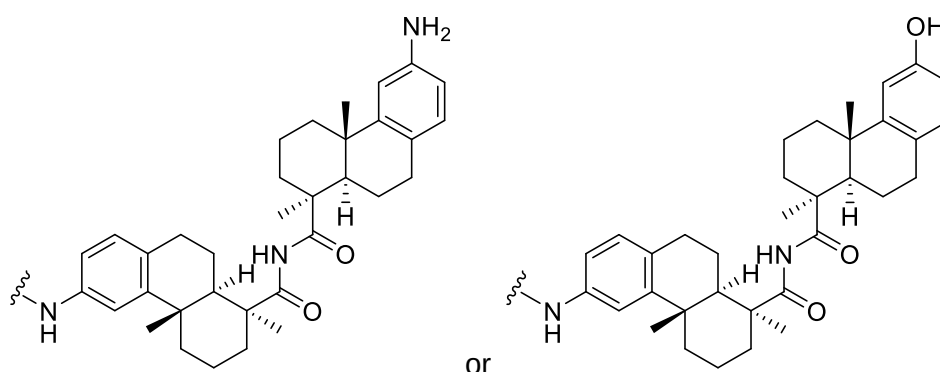




P3B;

wherein the  is the bond to the linker.

34. The antibody-drug conjugate of claim 23, wherein the LXR modulator is

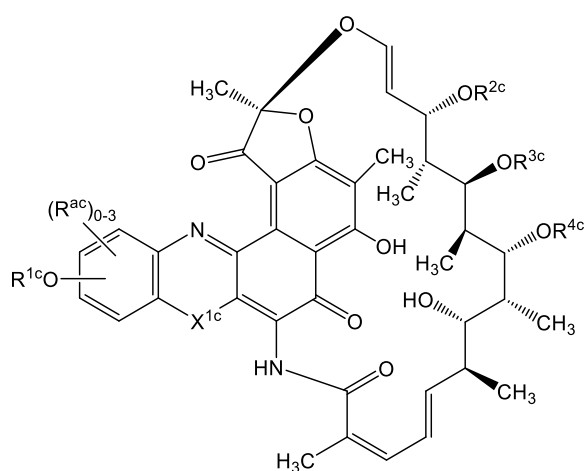


or

;

wherein the  is the bond to the linker.

35. The antibody-drug conjugate of claim 24, wherein the rifamycin analog is a compound of Formula (C-1):



Formula (C-1)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein:

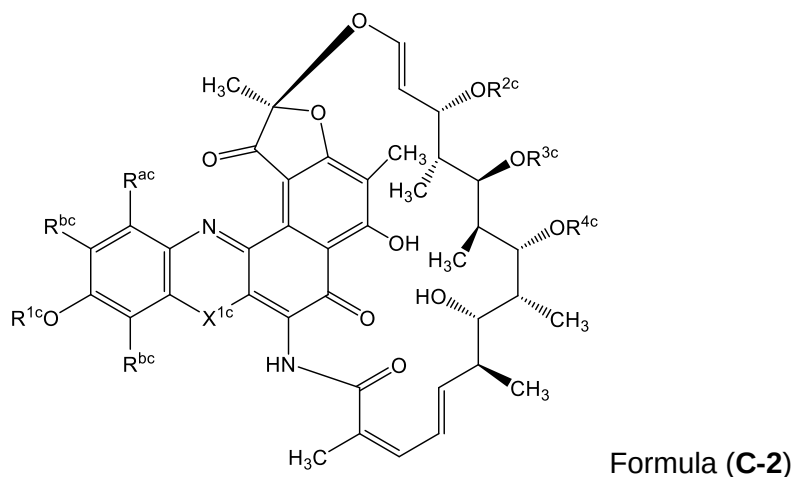
X^{1c} is selected from $-S-$; $-O-$ and $-NR^{5c}$;

R^{1c} is amino-C₁₋₆alkyl; C₁₋₆alkylaminoC₁₋₆alkyl; di-C₁₋₆alkylaminoC₁₋₆alkyl; hydroxy-C₁₋₆alkyl; HS-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-N(**R^{5c}**)-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-O-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-S-C₁₋₆alkyl; heterocycloalkyl or heterocycloalkyl-C₁₋₆alkyl; wherein heterocycloalkyl includes one, two, or three heteroatoms selected from O, N, and S; and wherein heterocycloalkyl is optionally substituted with halo, C₁₋₆alkyl, -OH, =O, or – N(**R^{5c}**)₂;

R^{2c}, **R^{3c}**, and **R^{4c}** are independently selected from hydrogen, C₁₋₆alkyl, and -(C=O)-**R^{5c}**; each **R^{ac}**, when present, is independently selected from -F; -Cl; -Br; -I; -OH; -NH₂; and C₁₋₆alkoxy; and

R^{5c} is independently, at each occurrence, selected from hydrogen; and C₁₋₆alkyl; wherein the group **R^{1c}** is bonded to the linker.

36. The antibody-drug conjugate of claim 24, wherein the rifamycin analog is a compound of Formula (**C-2**):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof; wherein:

X^{1c} is selected from –S–; –O– and –N**R^{5c}**;

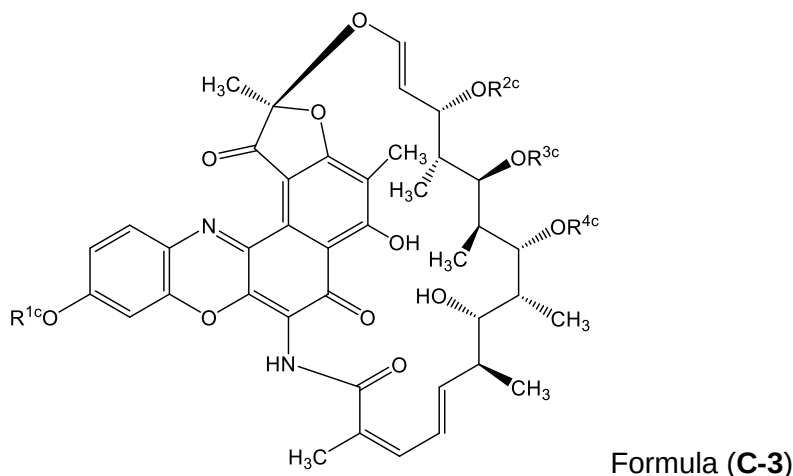
R^{1c} is amino-C₁₋₆alkyl; C₁₋₆alkylaminoC₁₋₆alkyl; di-C₁₋₆alkylaminoC₁₋₆alkyl; hydroxy-C₁₋₆alkyl; HS-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-N(**R^{5c}**)-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-O-C₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-S-C₁₋₆alkyl; heterocycloalkyl or heterocycloalkyl-C₁₋₆alkyl; wherein heterocycloalkyl includes one, two, or three heteroatoms selected from O, N, and S; and wherein heterocycloalkyl is optionally substituted with halo, C₁₋₆alkyl, -OH, =O, or – N(**R^{5c}**)₂;

R^{2c}, **R^{3c}**, and **R^{4c}** are independently selected from hydrogen, C₁₋₆alkyl, and -(C=O)-**R^{5c}**;

R^{ac} and **R^{bc}** are independently selected from -F; -Cl; -Br; -I; -OH; -NH₂; and C₁₋₆alkoxy; and

R^{5c} is independently, at each occurrence, selected from hydrogen; and C₁₋₆alkyl; wherein the group **R^{1c}** is bonded to the linker.

37. The antibody-drug conjugate of claim 24, wherein the rifamycin analog is a compound of Formula (C-3):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;
wherein:

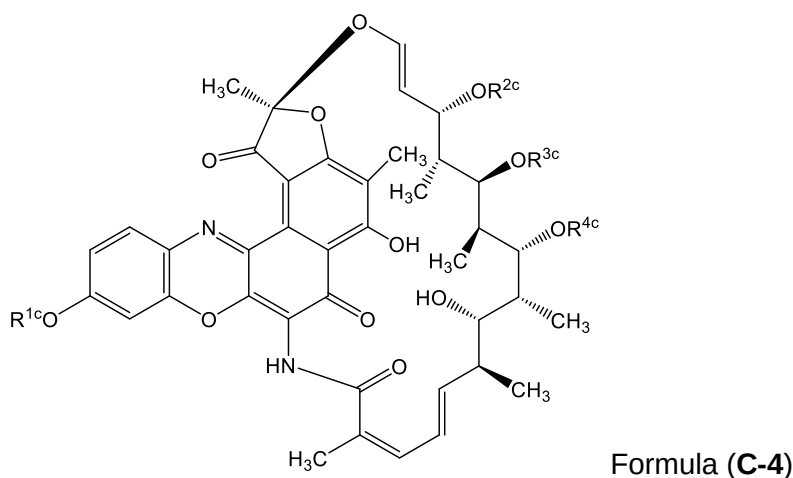
R^{1c} is di-C₁₋₆alkylaminoC₁₋₆alkyl; (**R^{5c}**)₂N-C₁₋₆alkylene-N(**R^{5c}**)-C₁₋₆alkyl; heterocycloalkyl or heterocycloalkyl-C₁₋₆alkyl; wherein heterocycloalkyl includes one, two, or three heteroatoms selected from O, N, and S; and wherein heterocycloalkyl is optionally substituted with halo, C₁₋₆alkyl, -OH, =O, or -N(**R^{5c}**)₂; and

R^{2c}, **R^{3c}**, and **R^{4c}** are independently selected from hydrogen, C₁₋₆alkyl, and -(C=O)-**R^{5c}**;
and

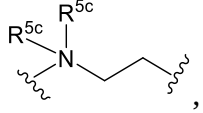
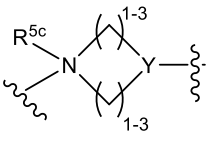
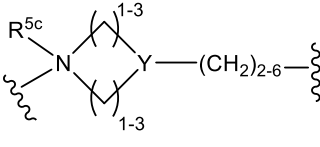
R^{5c} is selected from hydrogen and C₁₋₆alkyl;

wherein the group **R**^{1c} is bonded to the linker.

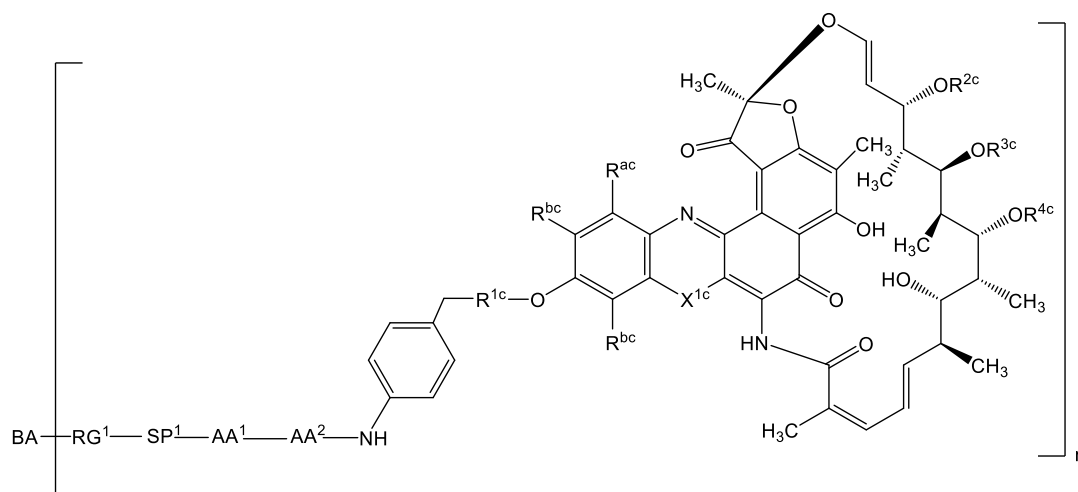
38. The antibody-drug conjugate of claim 24, wherein the rifamycin analog is a compound of Formula (C-4):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;
wherein:

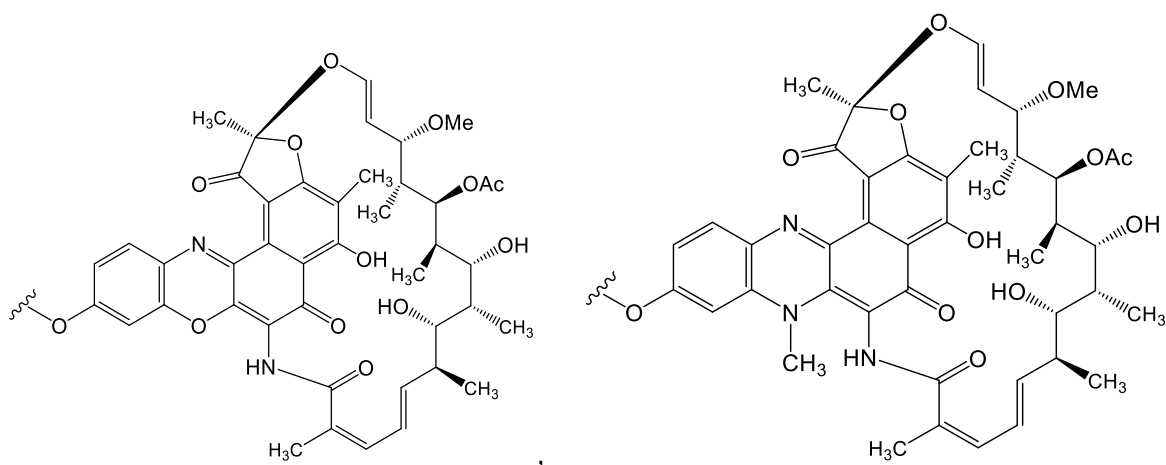
R^{1c} is , ; or ; wherein Y is C or N;
 R^{2c} , R^{3c} , and R^{4c} are independently selected from hydrogen, C_{1-6} alkyl, and $-(C=O)-R^{5c}$;
and
 R^{5c} is independently, at each occurrence, absent, or selected from hydrogen and C_{1-6} alkyl;
wherein the group R^{1c} is bonded to the linker via a nitrogen atom as indicated by the wavy line .

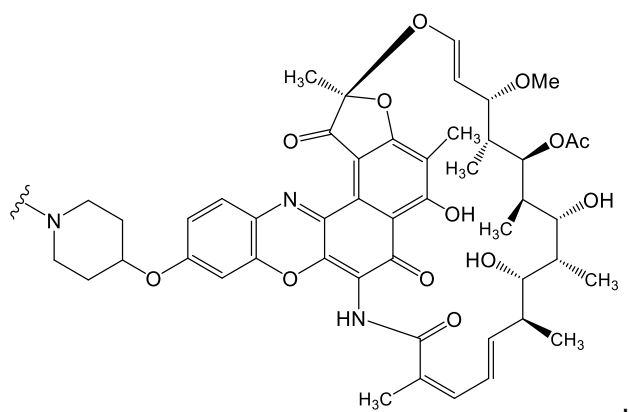
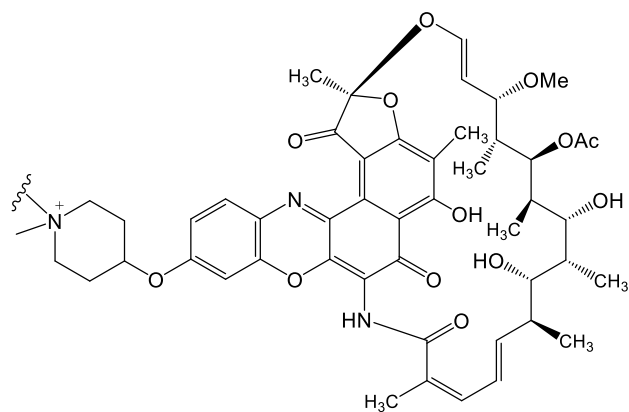
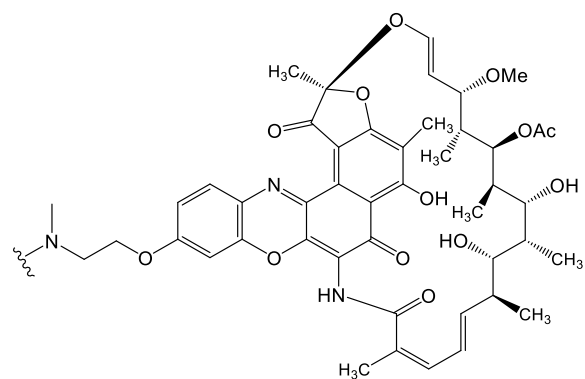
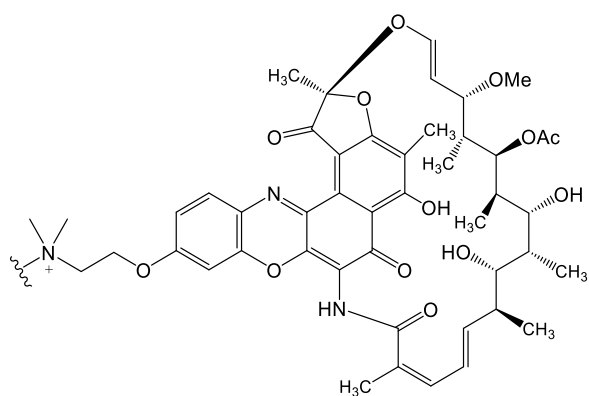
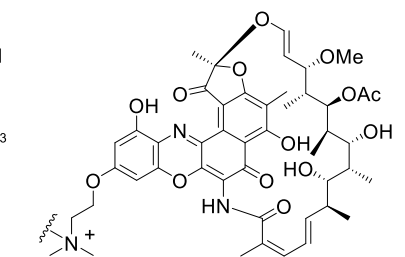
39. The antibody-drug conjugate of any one of claims 9-11, 13, 17-21, 24 and 35-38, having the structure of Formula (7002):

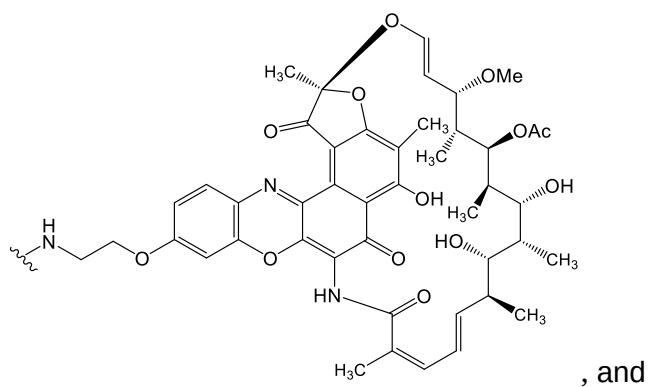
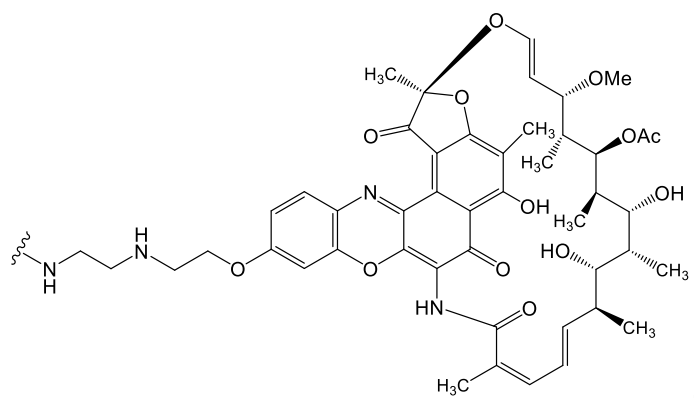


Formula (7002).

40. The antibody-drug conjugate of any one of claims 9-11, 13, 17-21, 24 and 35-39, wherein the rifamycin analog is selected from the group consisting of:

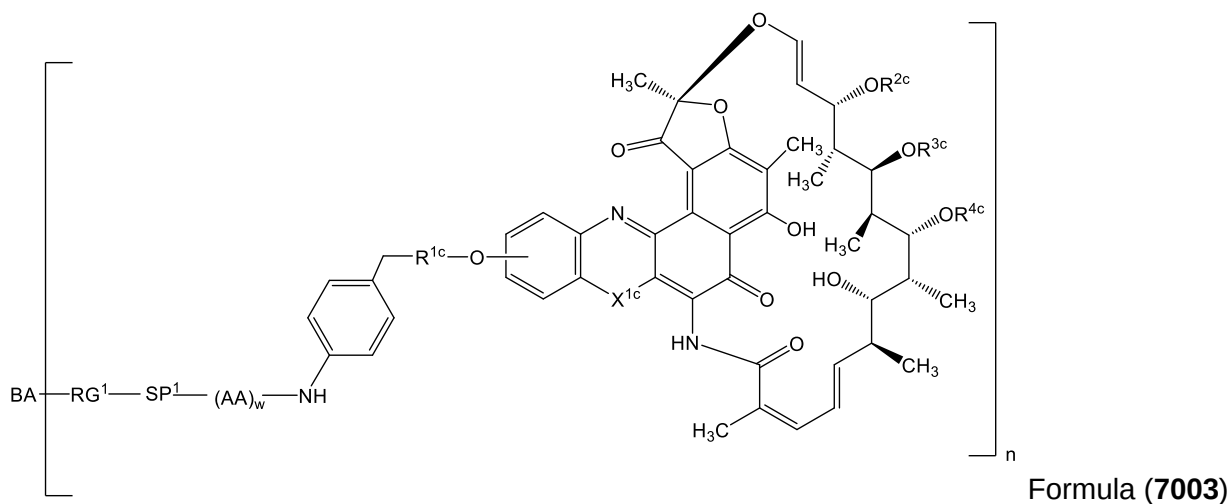






wherein the is the bond to the linker.

41. An antibody-rifamycin analog conjugate having the structure of Formula (7003):



or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof;

wherein:

X^{1c} is selected from $-S-$; $-O-$ and $-NR^{5c}$;

R^{1c} is , , or ; wherein Y is C or N;

R^{2c} , R^{3c} , and R^{4c} are independently selected from hydrogen, C_{1-6} alkyl, and $-(C=O)-R^{5c}$;

R^{5c} is independently, at each occurrence, absent, or selected from hydrogen; and C₁₋₆alkyl;

each **AA** is an independently selected amino acid;

SP¹ is absent, or a spacer;

RG¹ is a reactive group residue;

BA is an anti-MSR1 antibody or antigen binding fragment thereof;

subscript **n** is an integer from 1 to 30;

subscript **w** is 2, 3, or 4;

wherein **R**^{1c} is bonded to the linker via a nitrogen atom as indicated by the wavy line



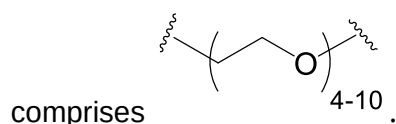
42. The antibody- rifamycin analog conjugate of claim 41, wherein **X**^{1c} is O.

43. The antibody- rifamycin analog conjugate of claim 41 or claim 42, wherein **BA** is an anti-MSR1 antibody or antigen binding fragment thereof; comprising an N297Q mutation.

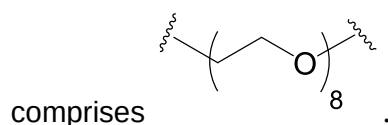
44. The antibody- rifamycin analog conjugate of any one of claims 41-43, wherein subscript **w** is 2.

45. The antibody- rifamycin analog conjugate of any one of claims 41-44, wherein (**AA**)₂ is valine-citrulline.

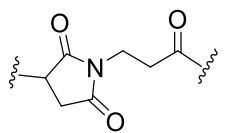
46. The antibody- rifamycin analog conjugate of any one of claims 41-45, wherein **SP**¹



47. The antibody- rifamycin analog conjugate of any one of claims 41-45, wherein **SP**¹

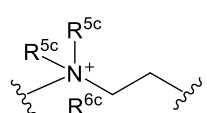
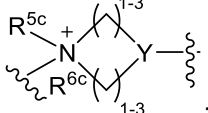
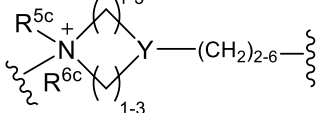


48. The antibody- rifamycin analog conjugate of any one of claims 41-47, wherein **RG**¹ comprises



49. The antibody- rifamycin analog conjugate of any one of claims 41-47, wherein

X^{1c} is O;

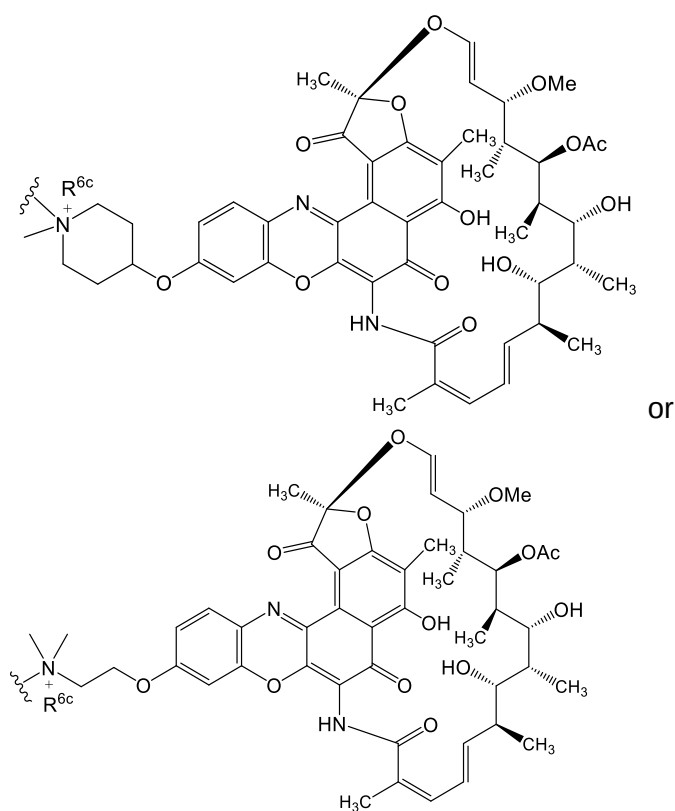
R^{1c} is , ; or ; wherein **Y** is C or N;

wherein R^{1c} is bonded to the linker via the quaternary nitrogen atom of R^{1c} ;

R^{5c} is C_{1-6} alkyl; and

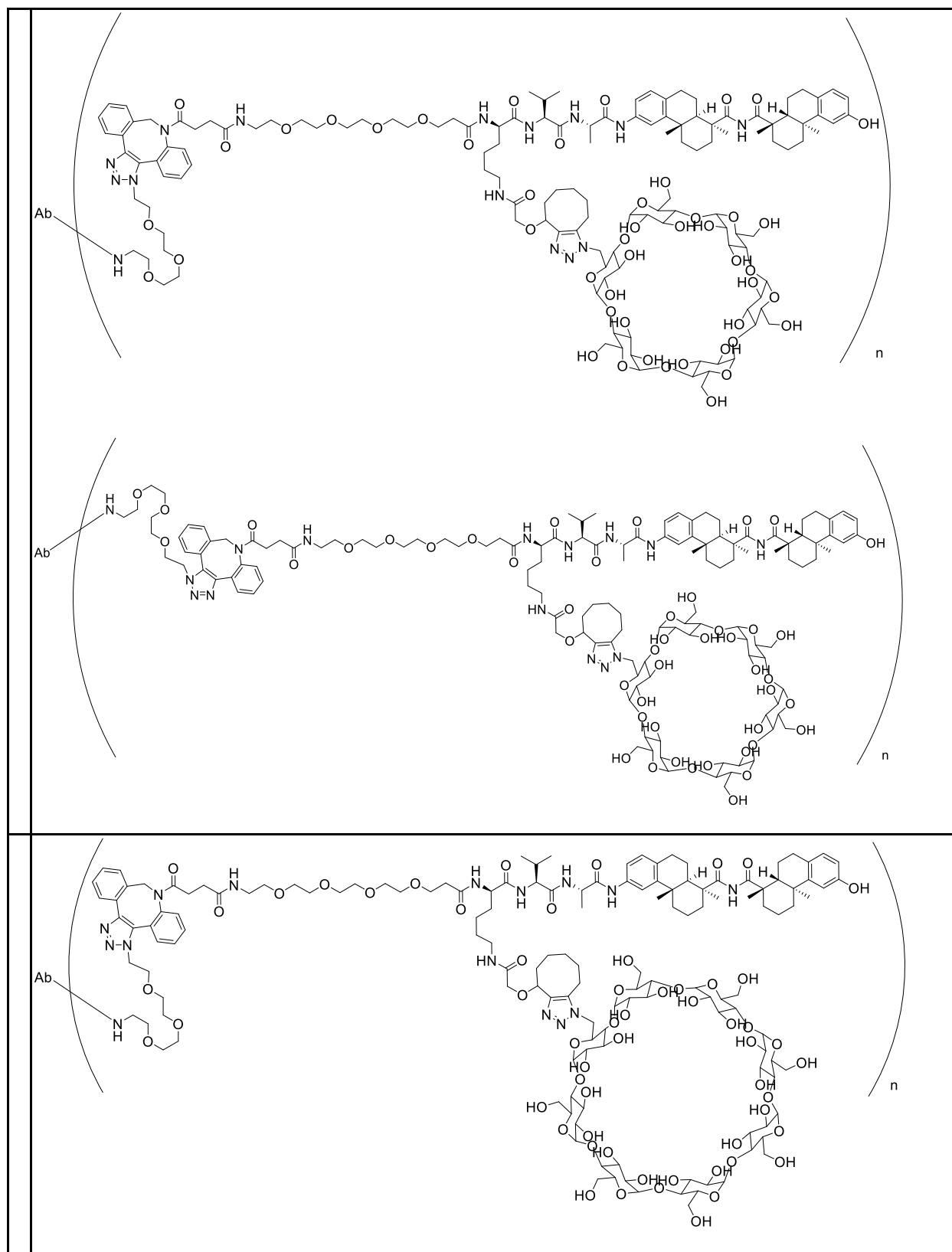
R^{6c} is a counter ion.

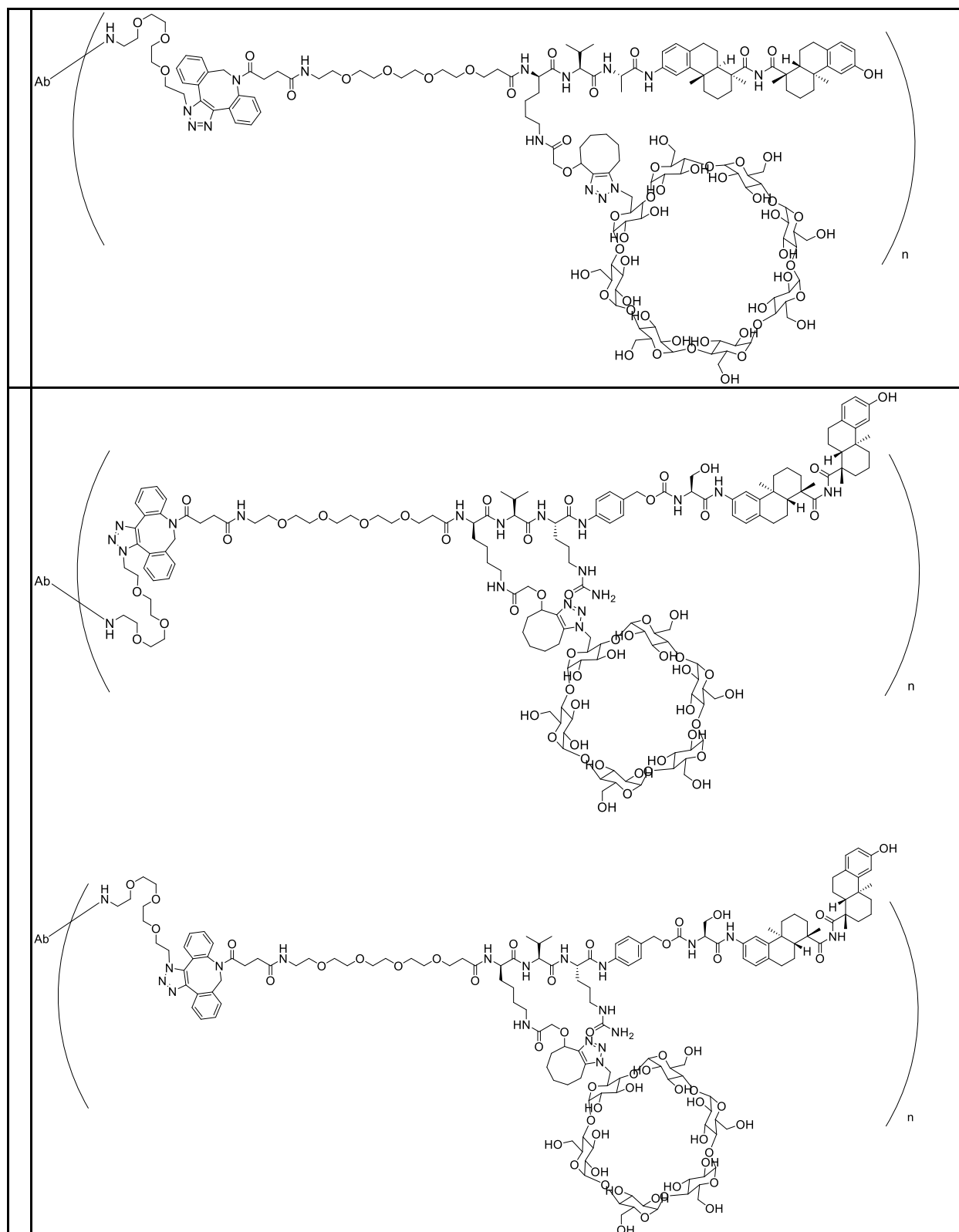
50. The antibody- rifamycin analog conjugate of any one of claims 41-49, wherein the rifamycin analog is:

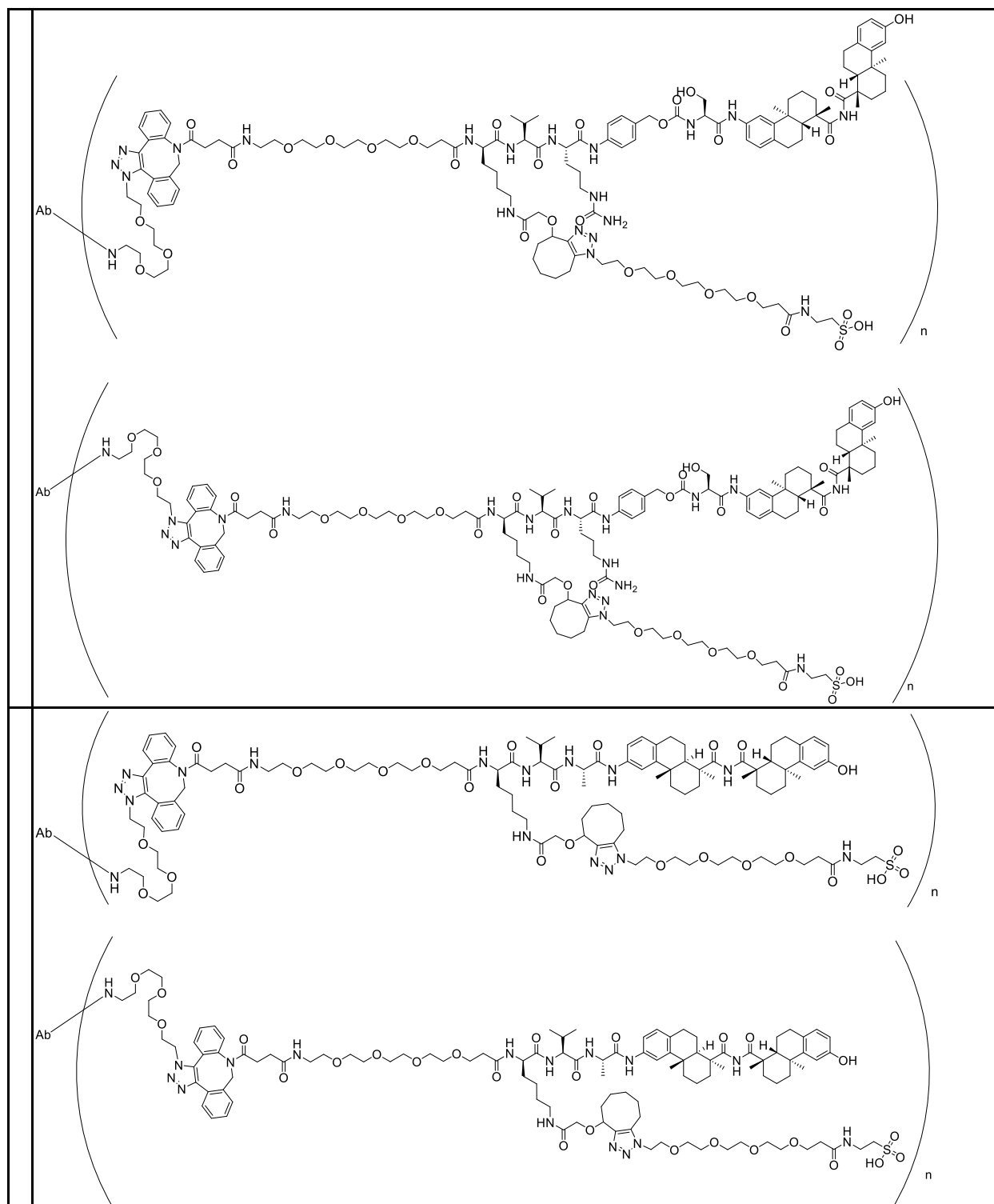


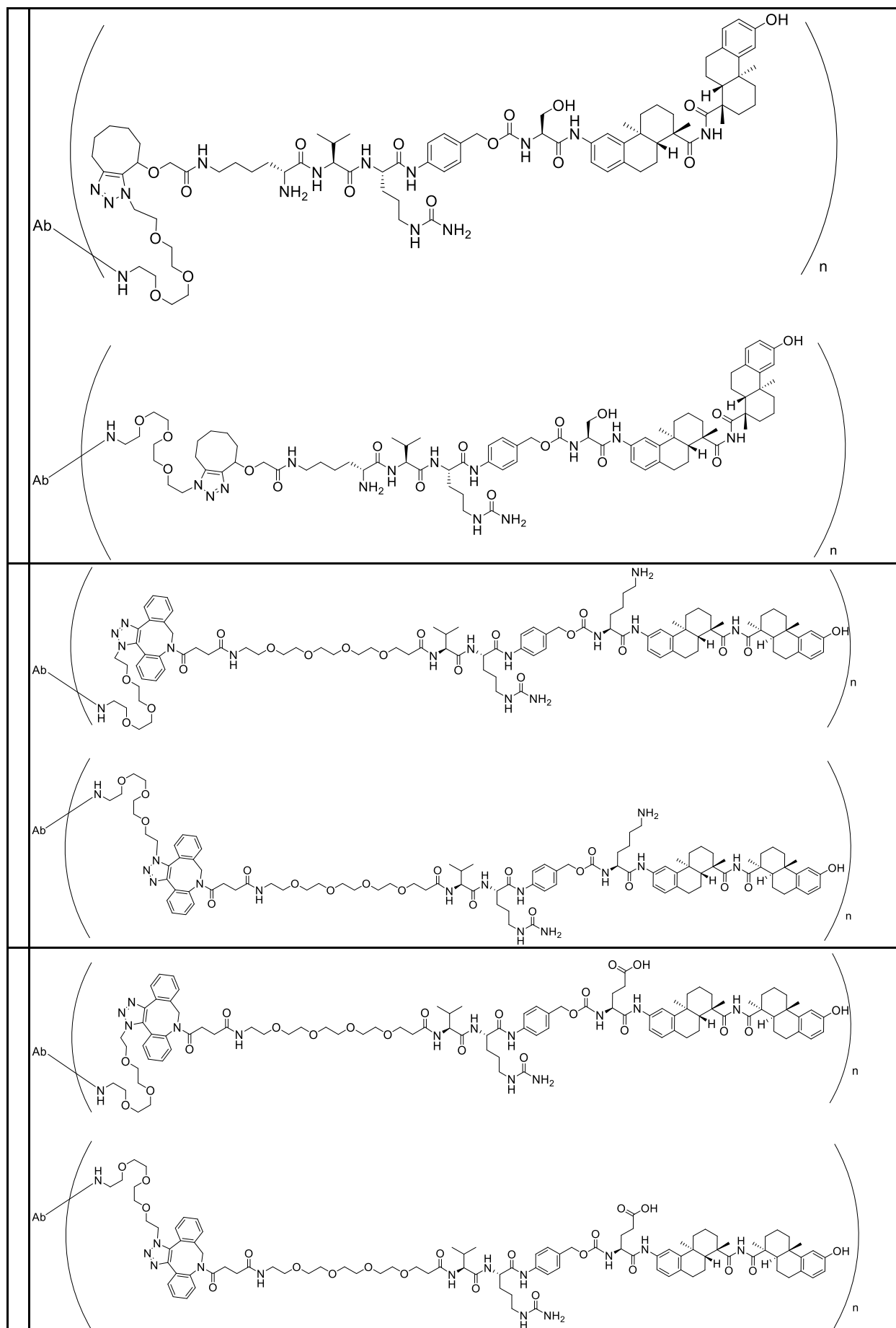
51. The antibody-drug conjugate of any one of claims 9-24, selected from the group consisting of:

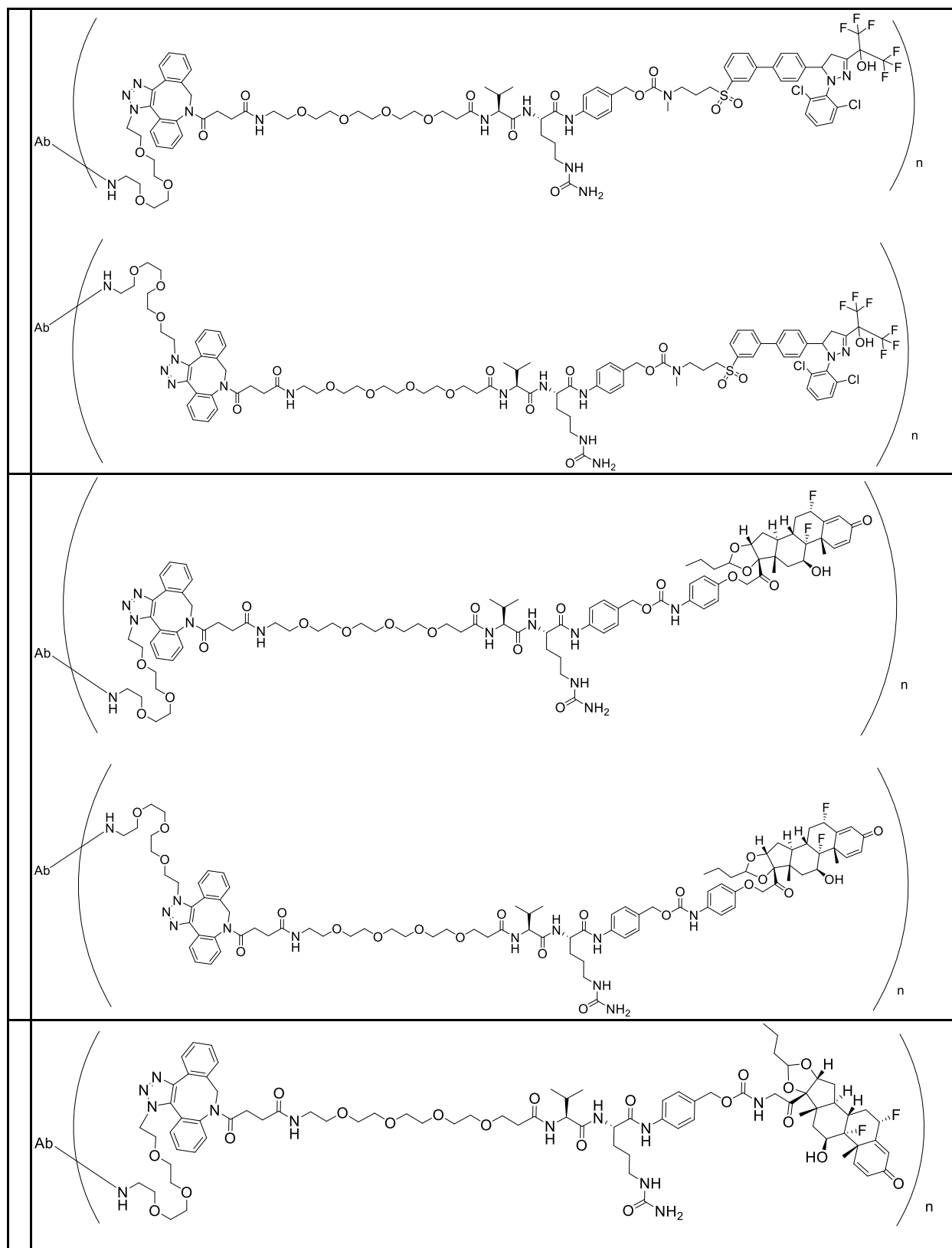
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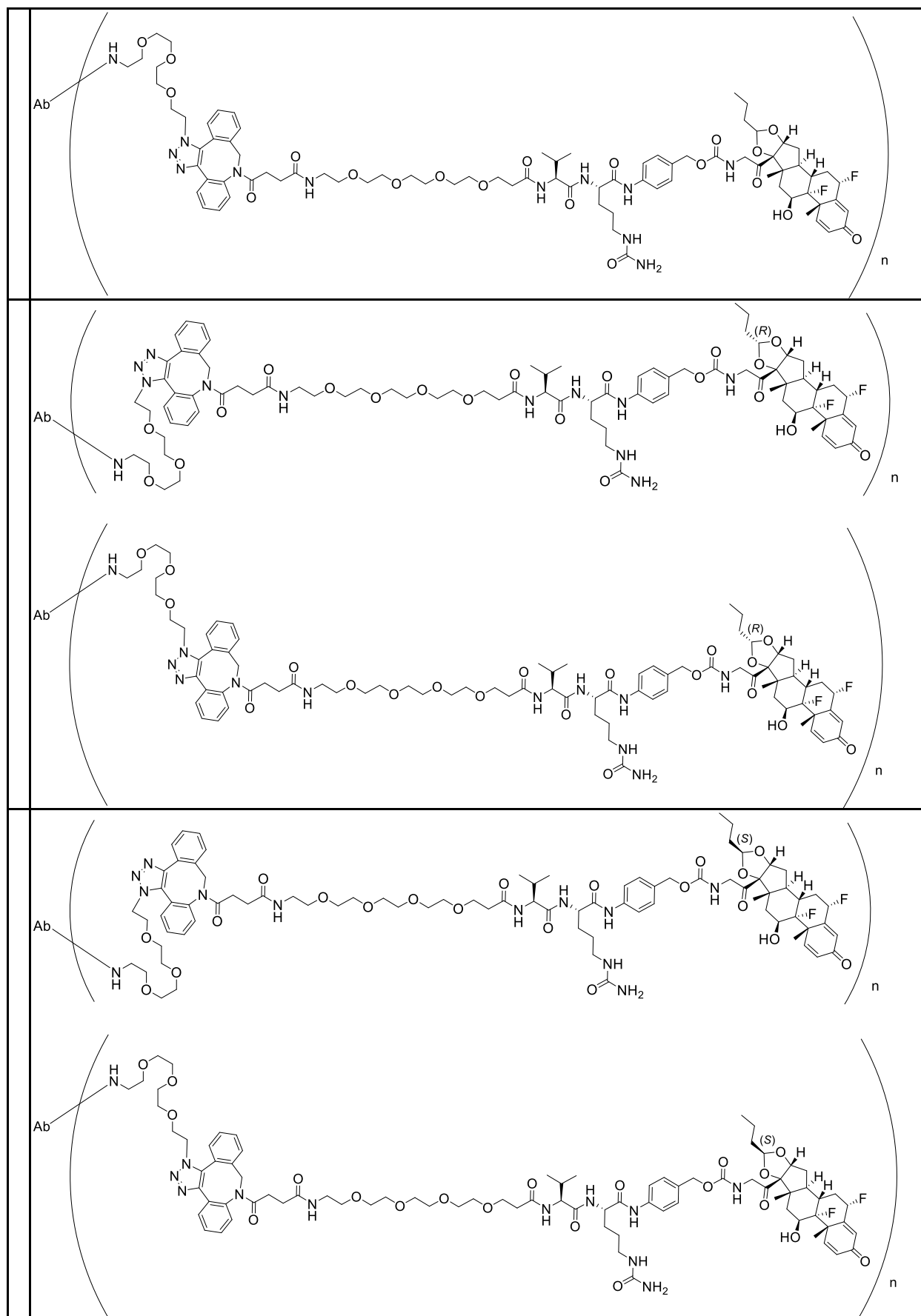


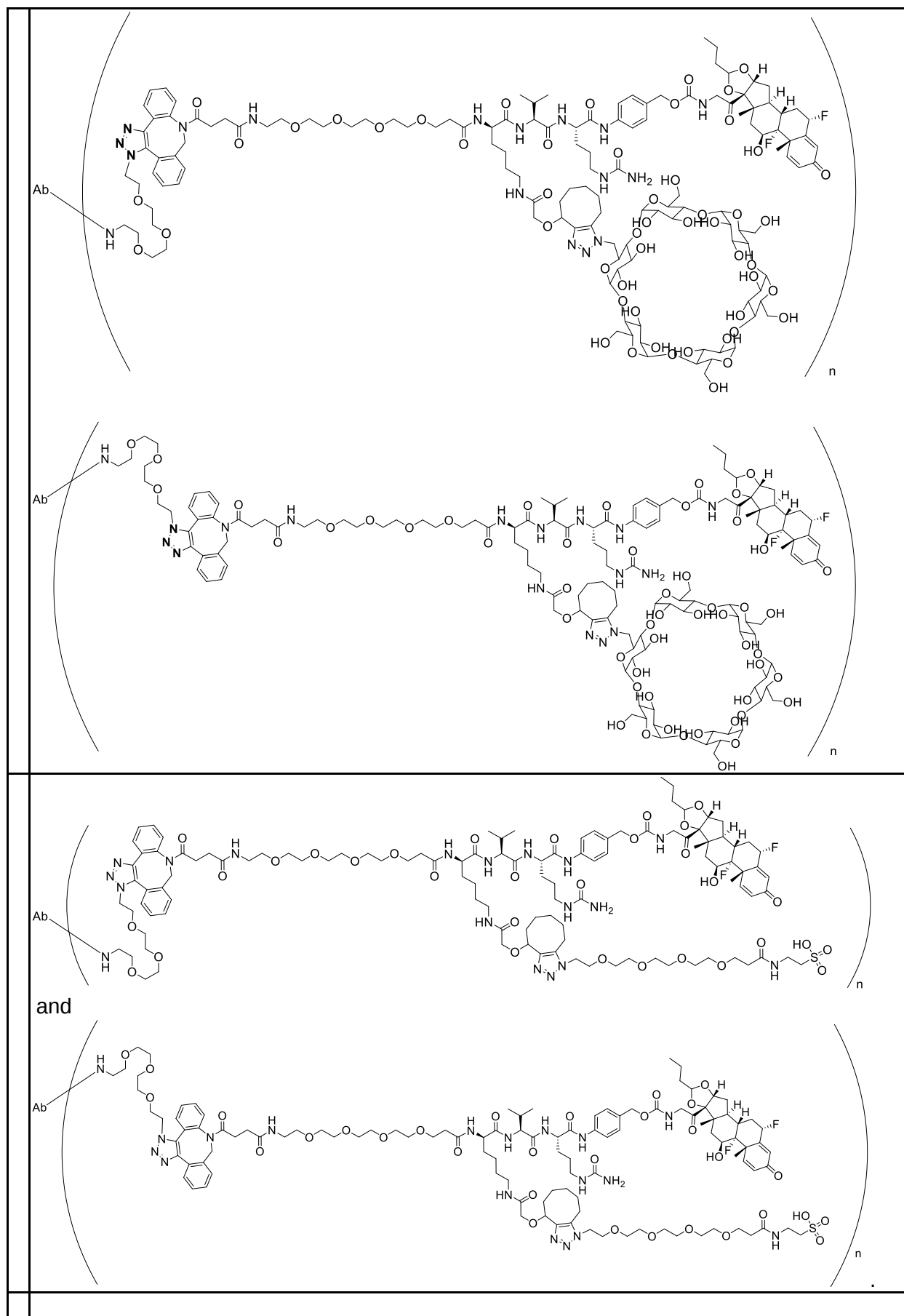


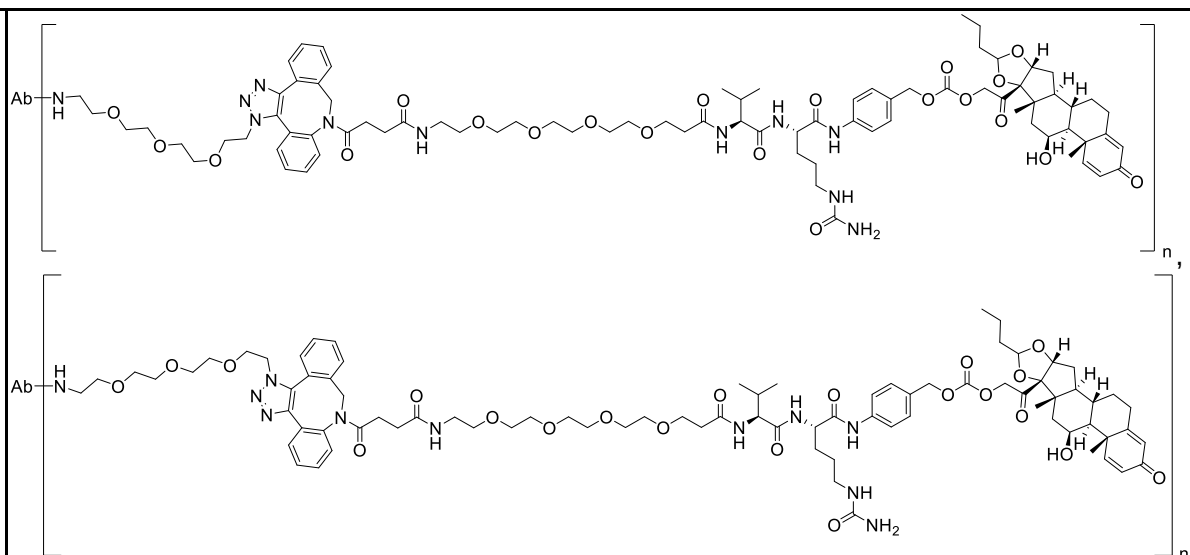




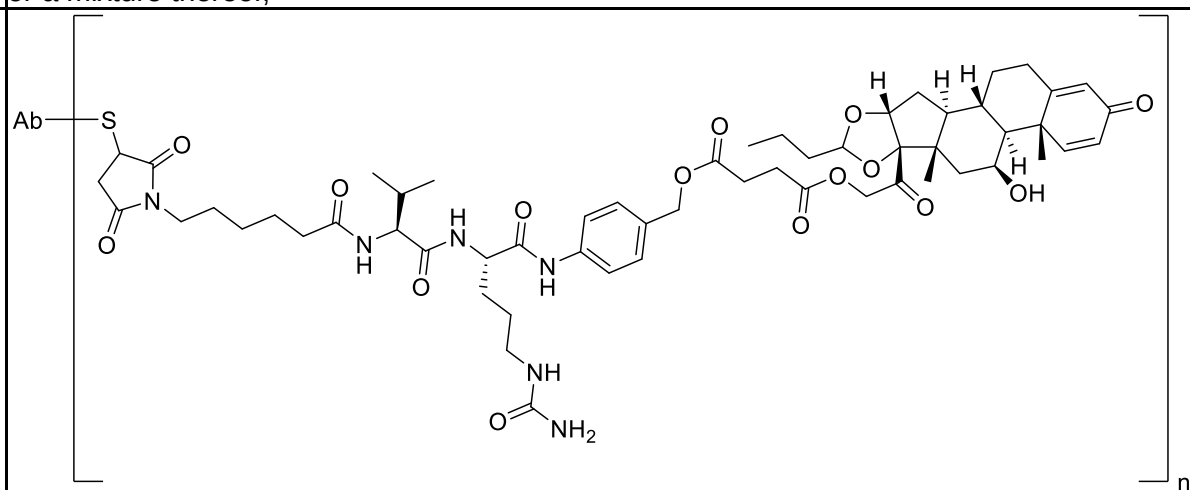




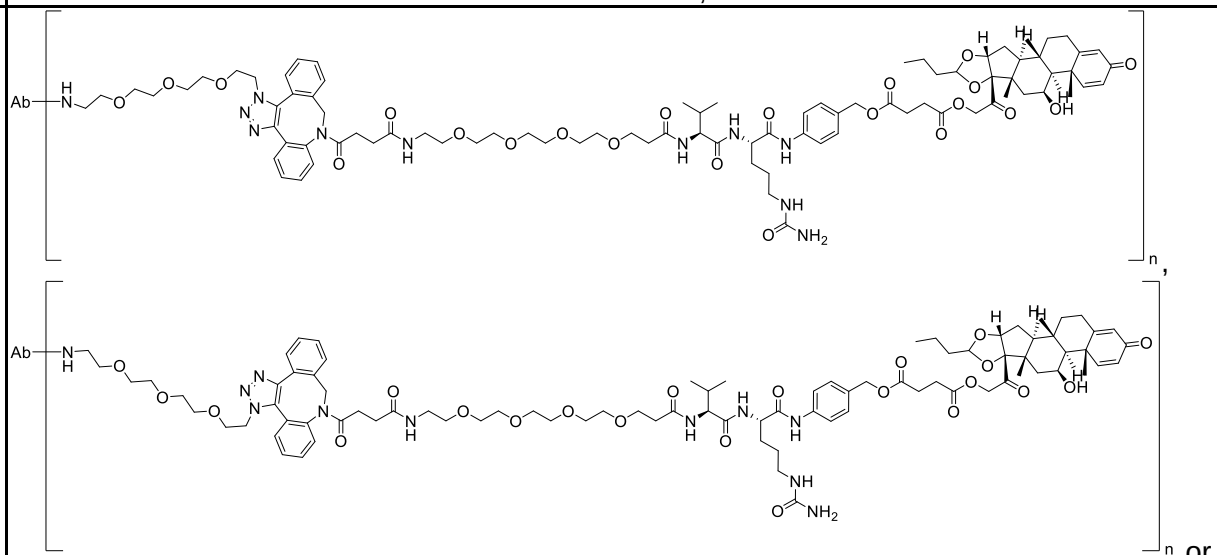




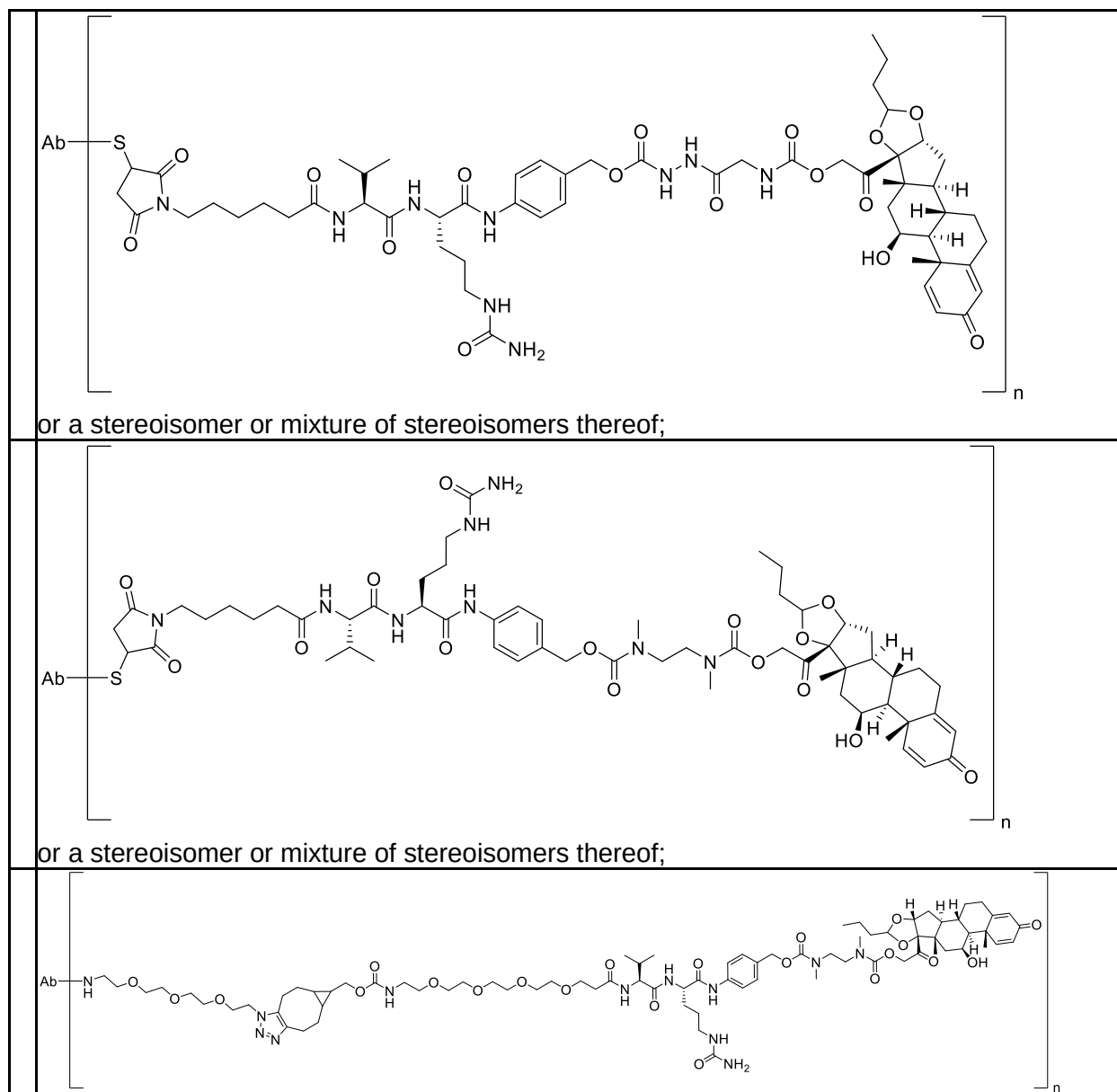
or a mixture thereof;

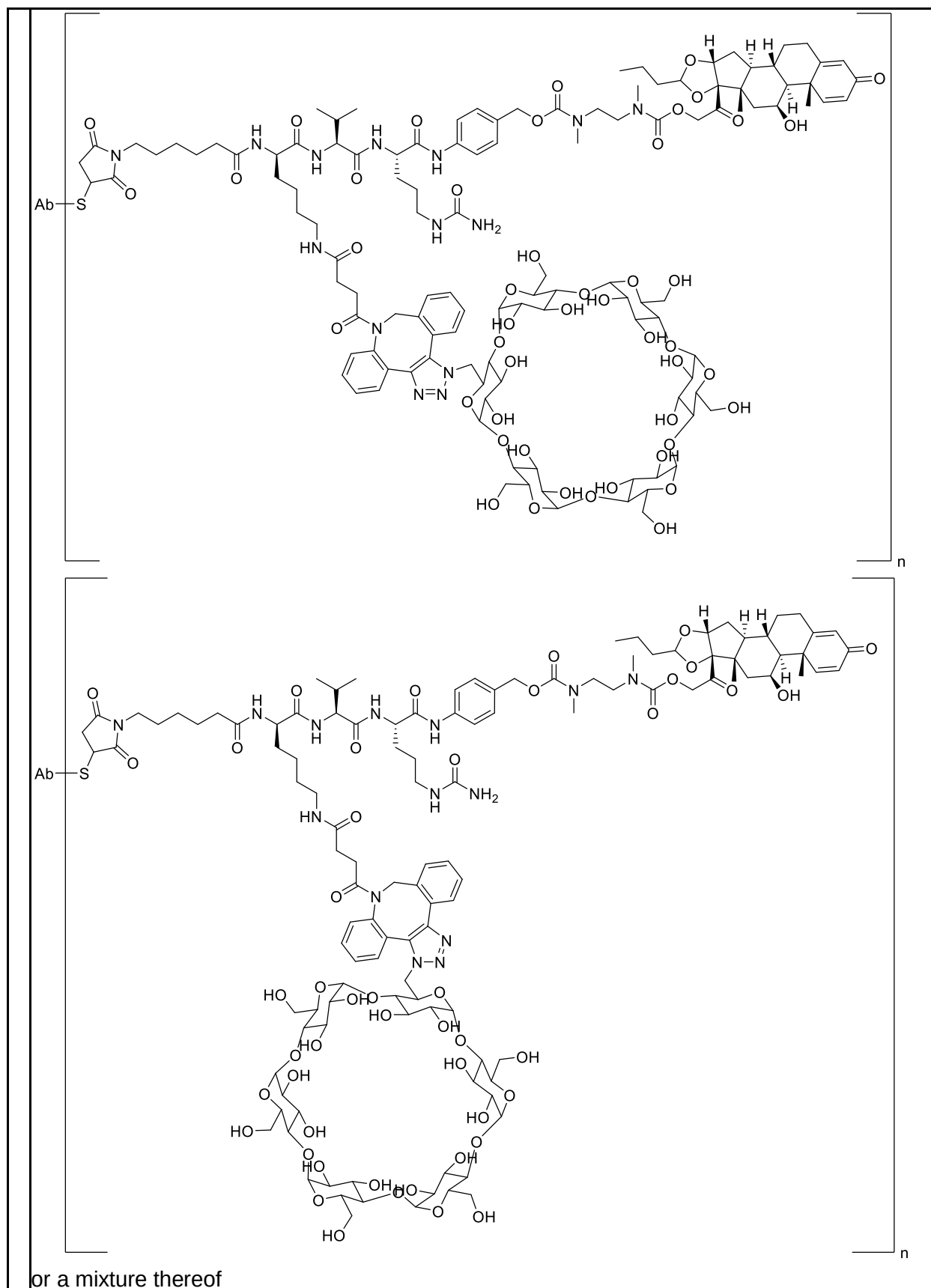


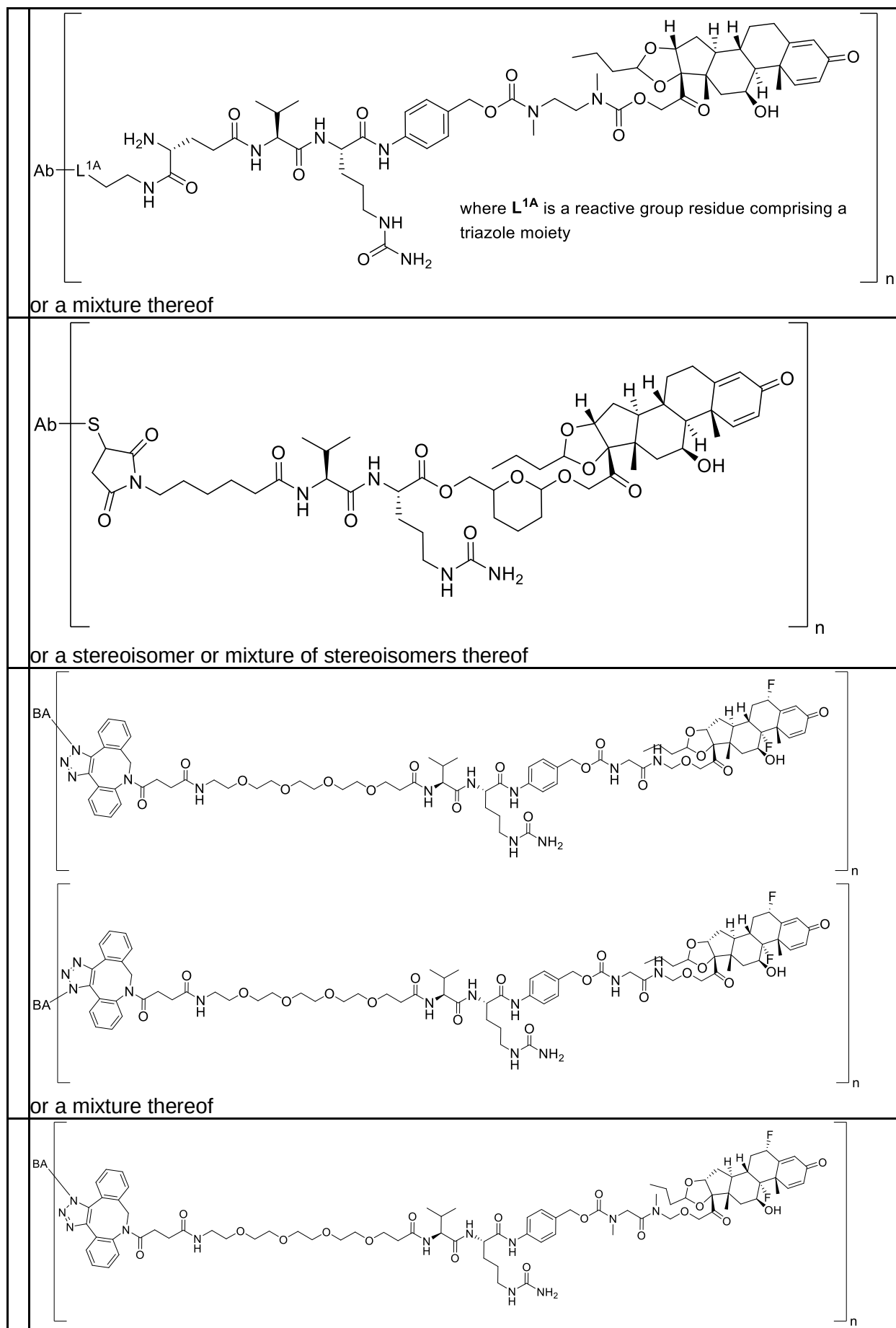
or a stereoisomer or mixture of stereoisomers thereof;

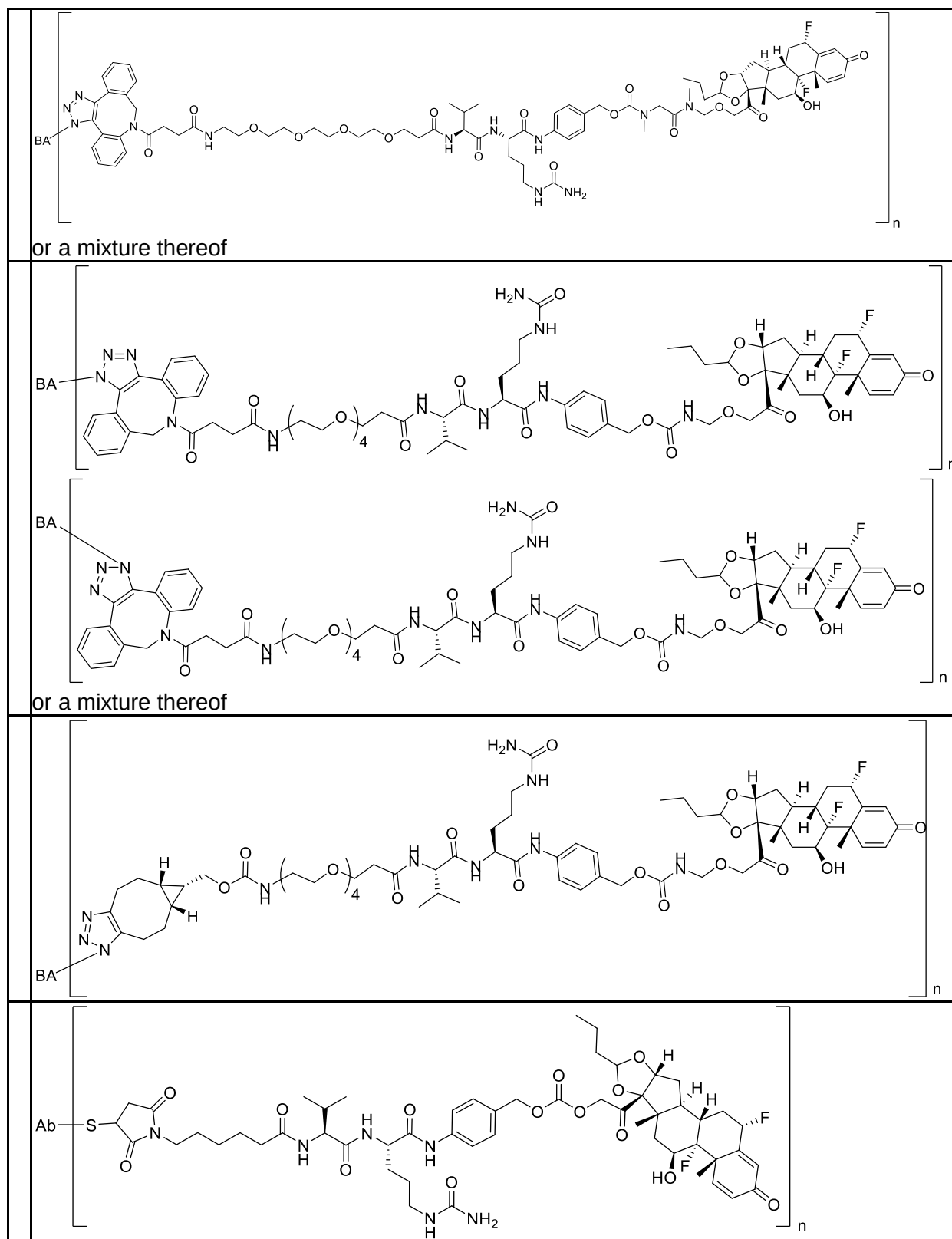


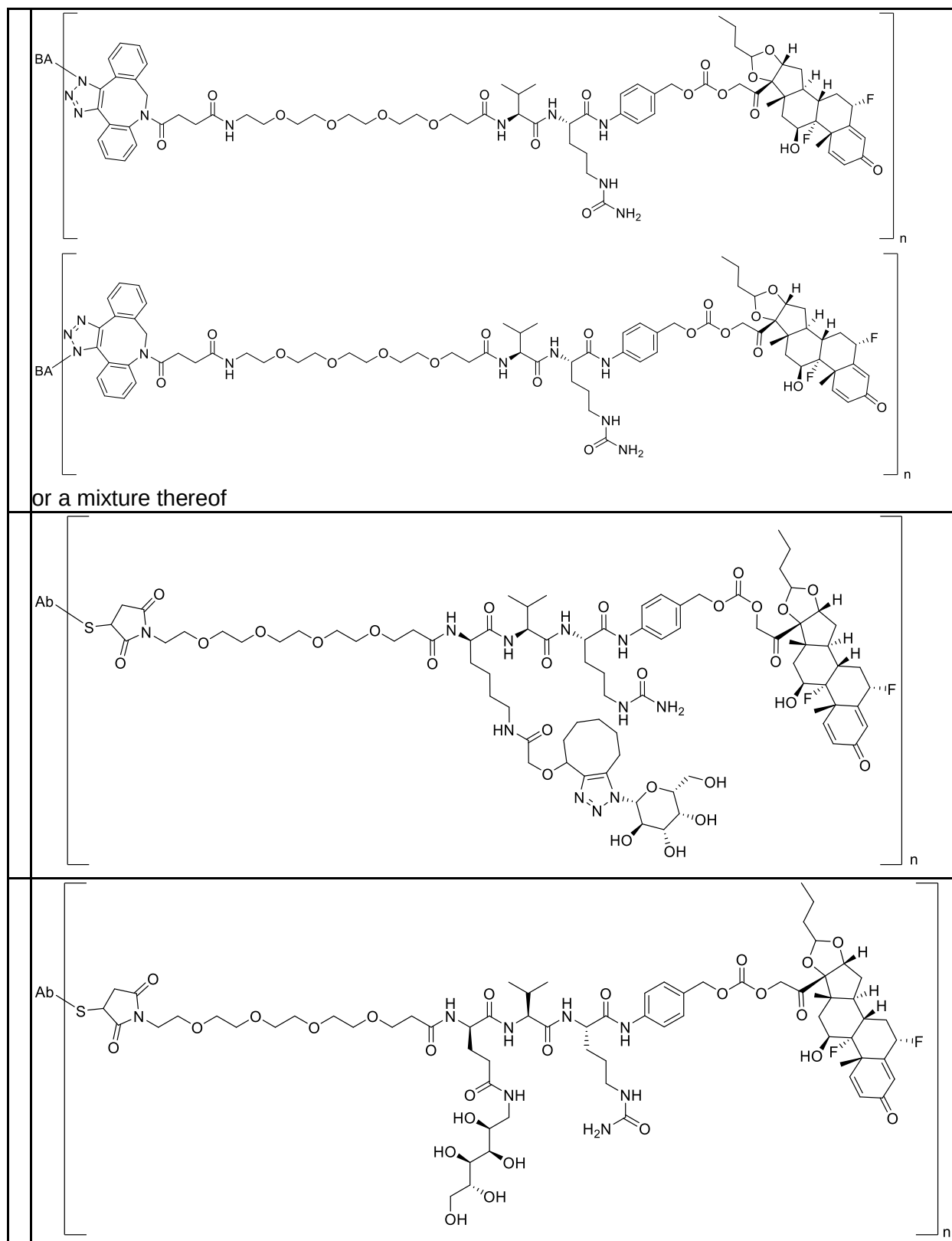
a mixture thereof;

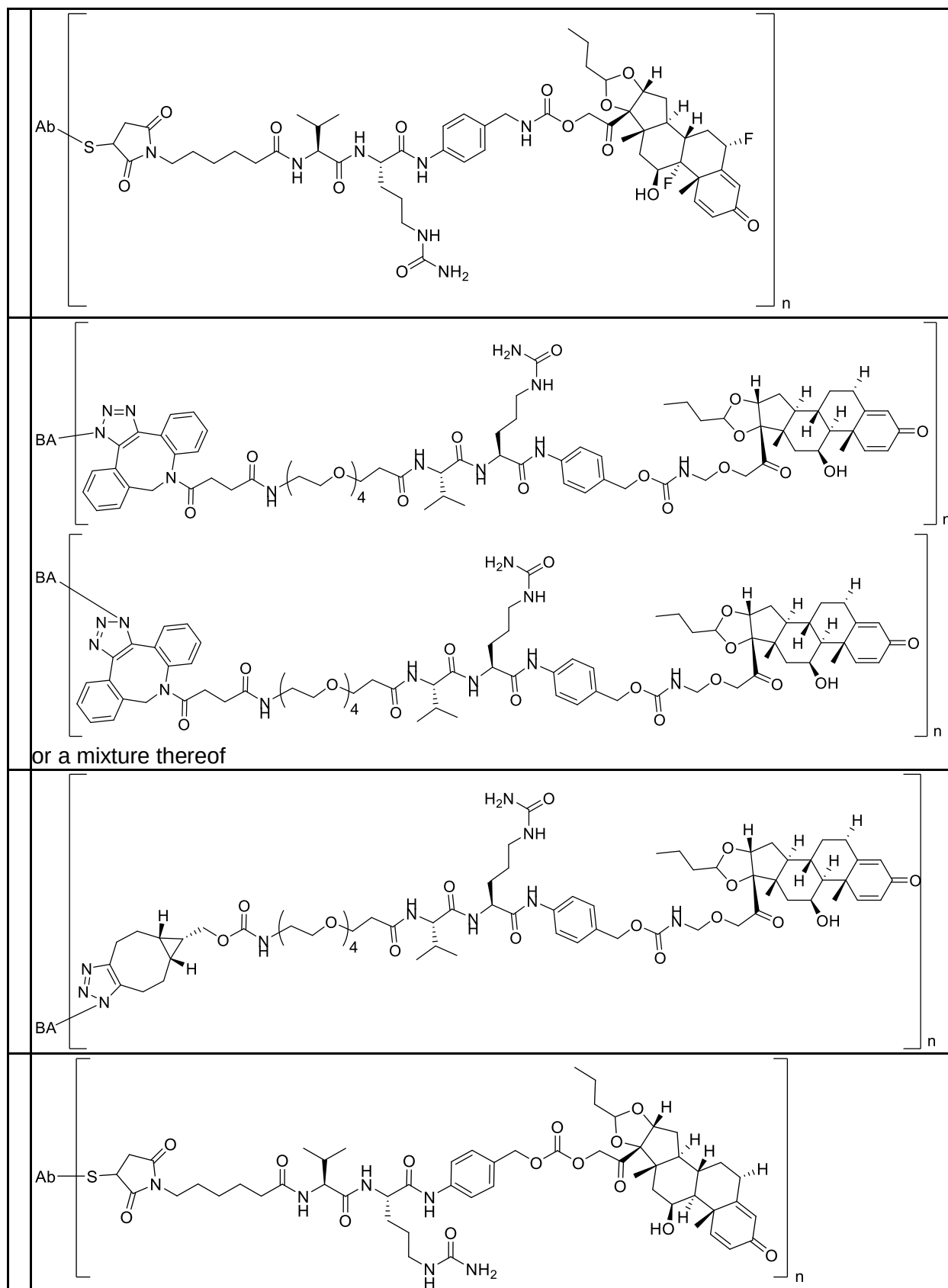


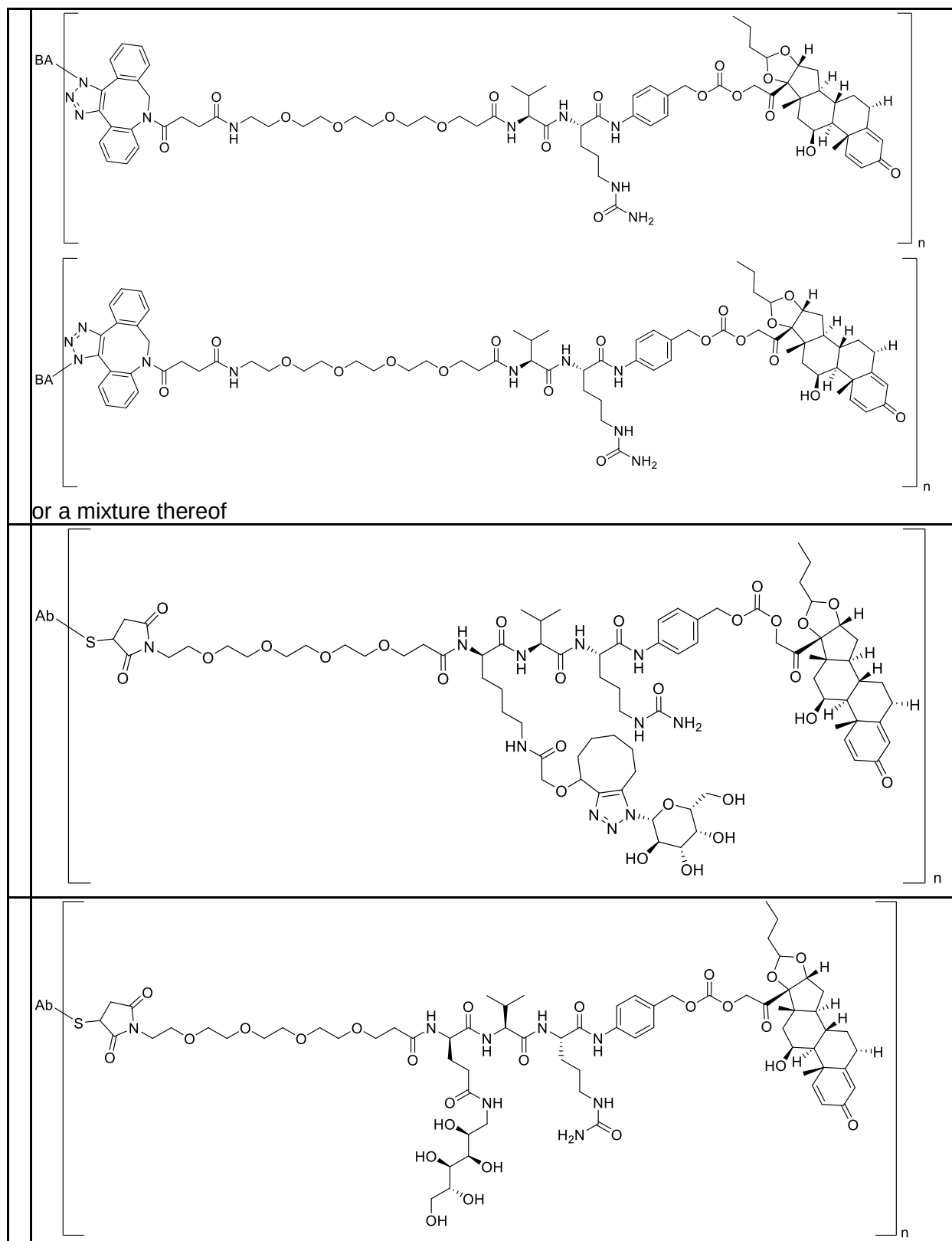


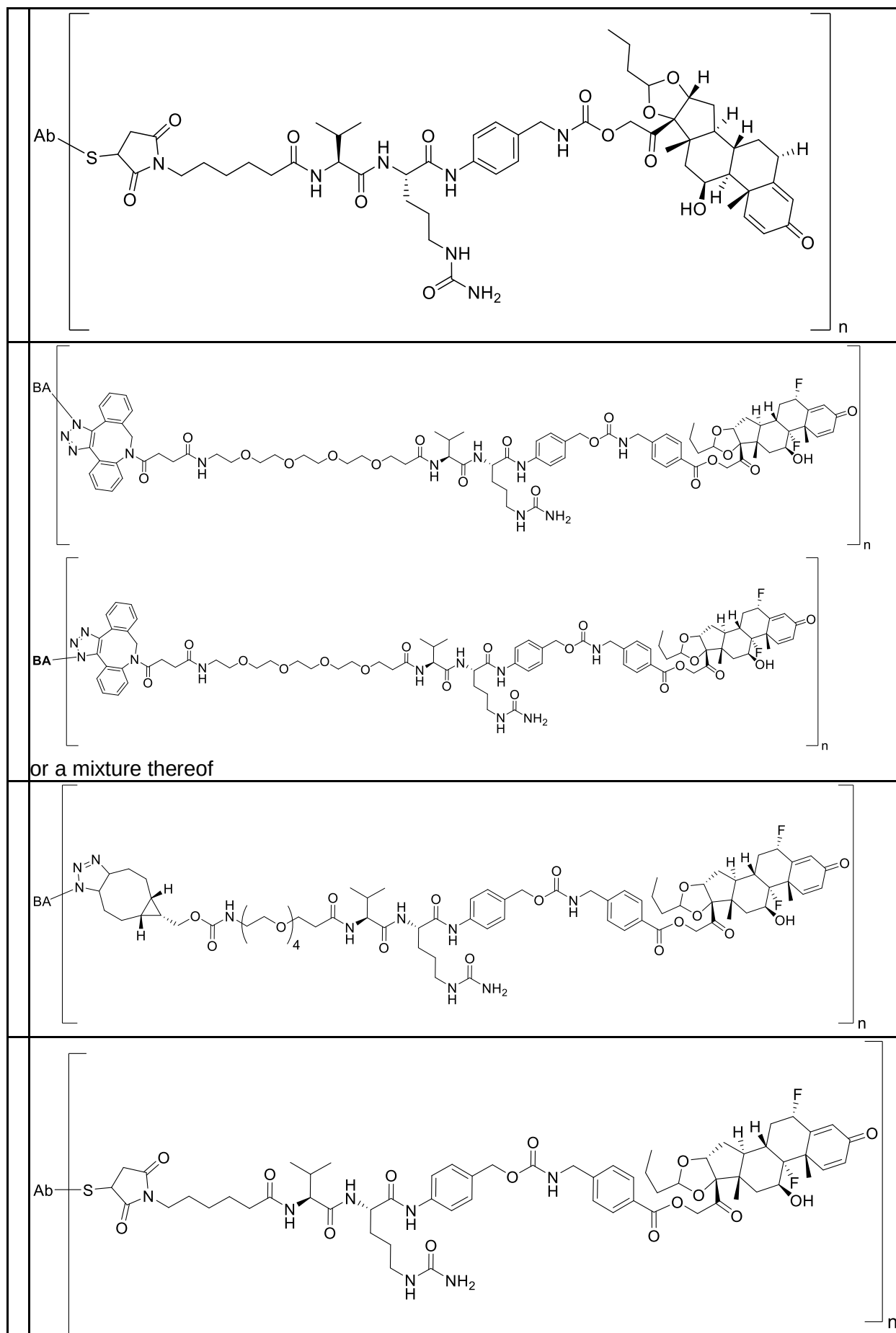


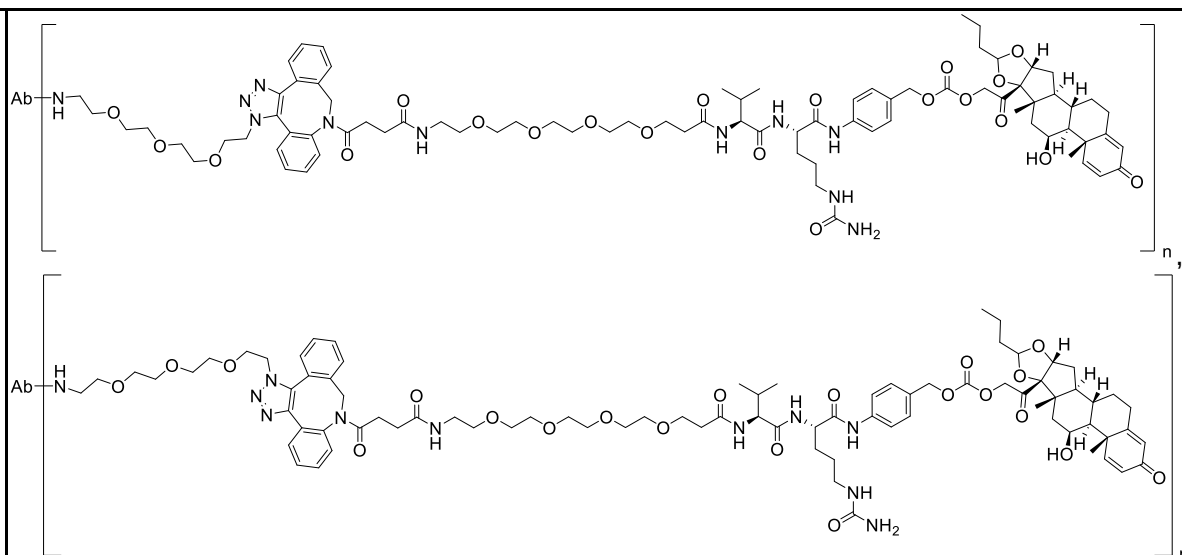




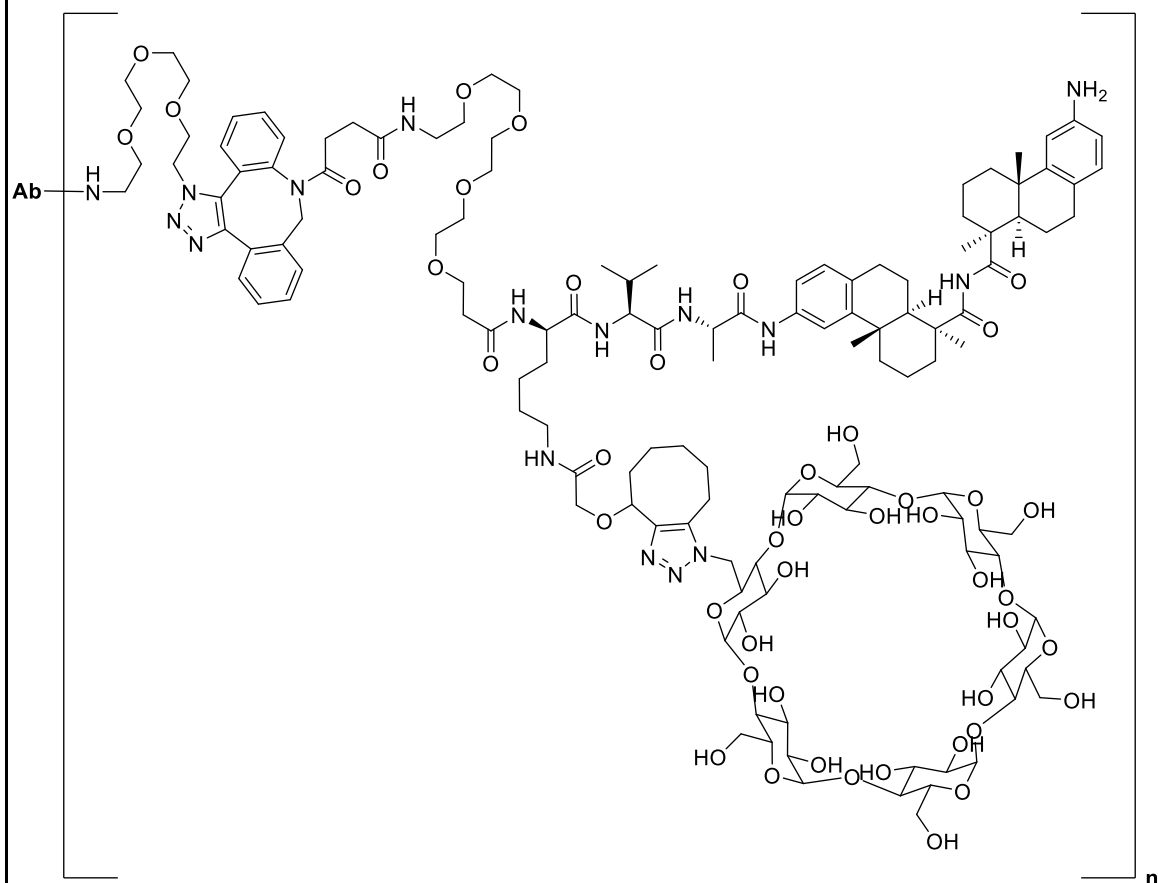


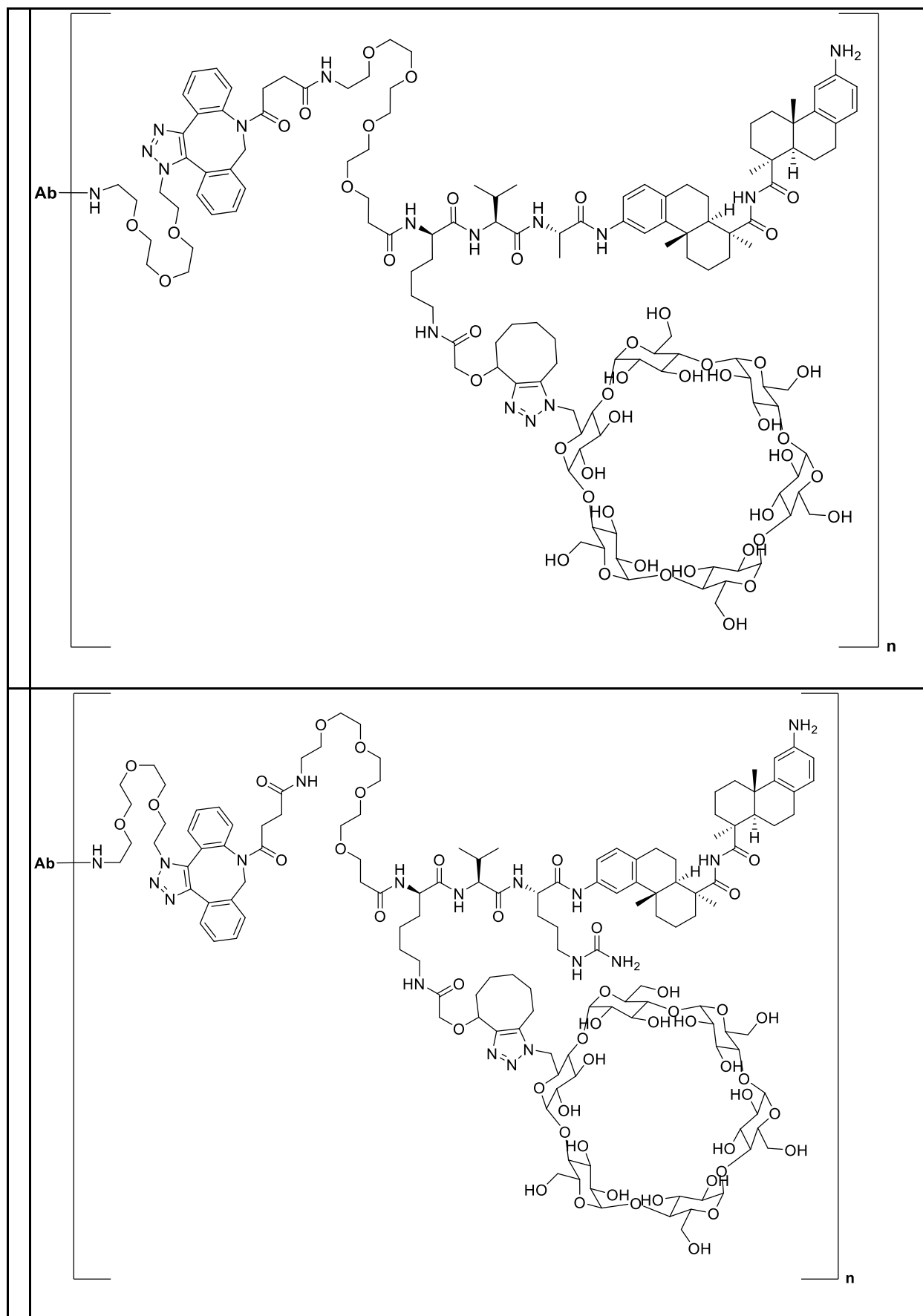


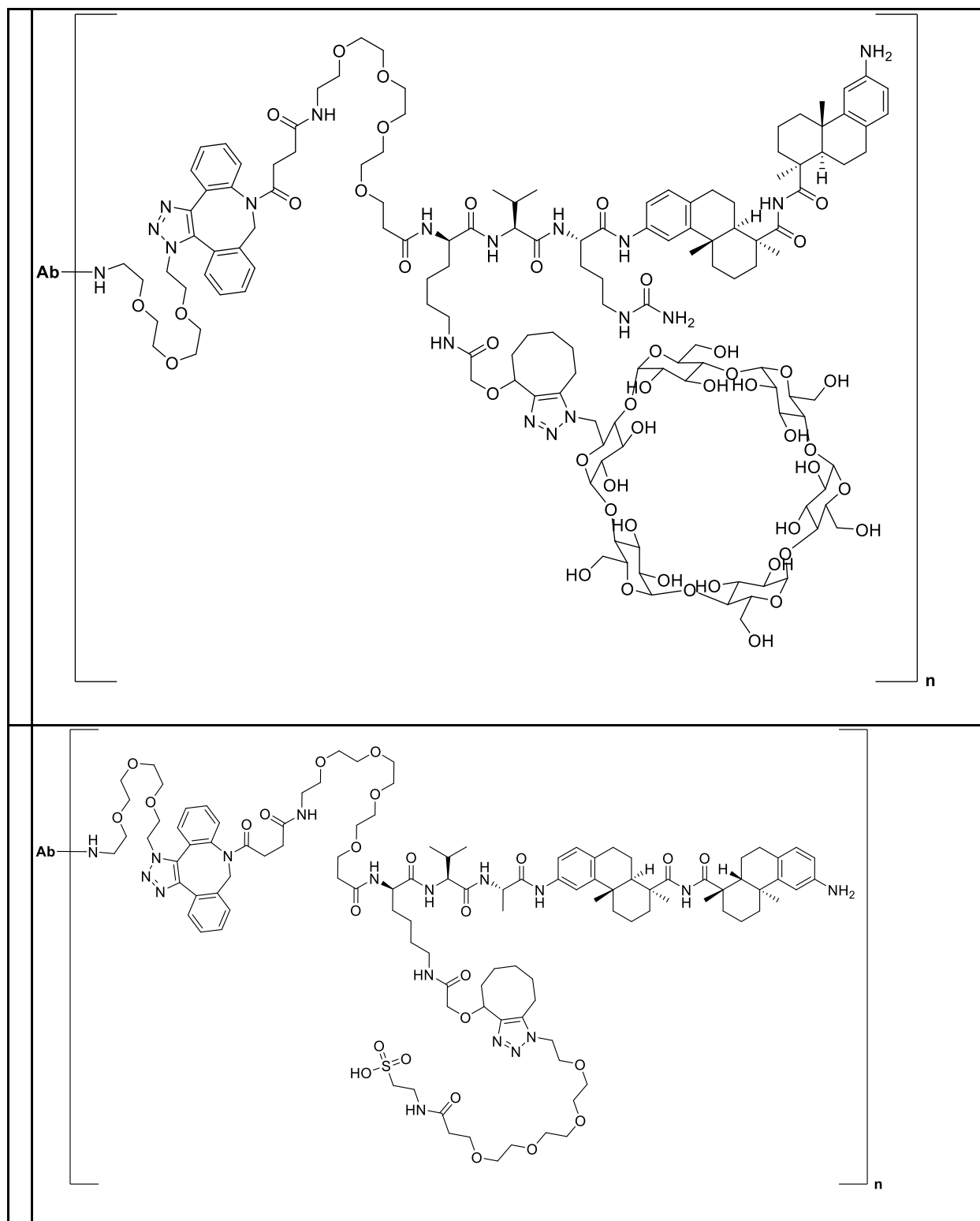


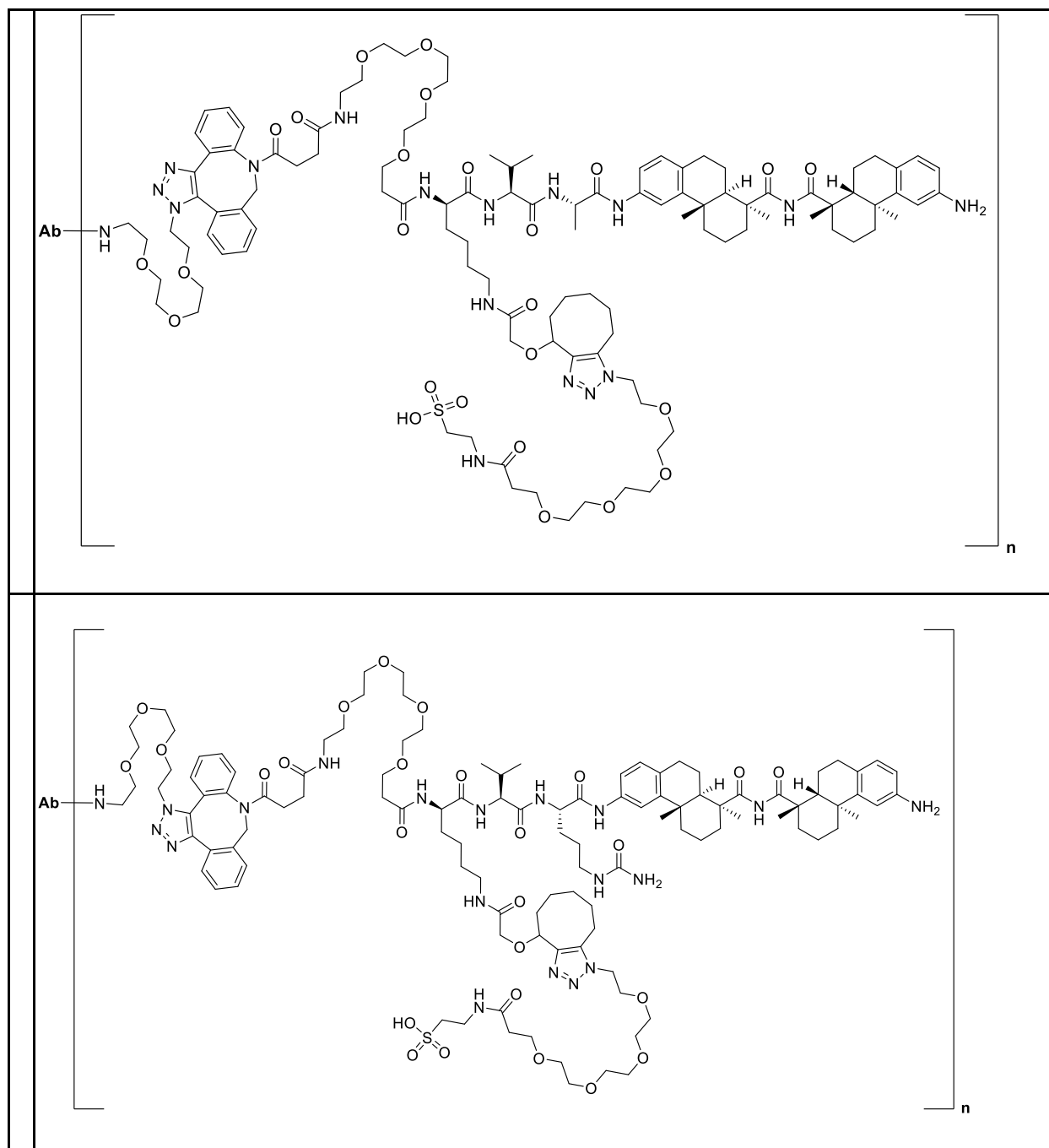


or a mixture thereof;

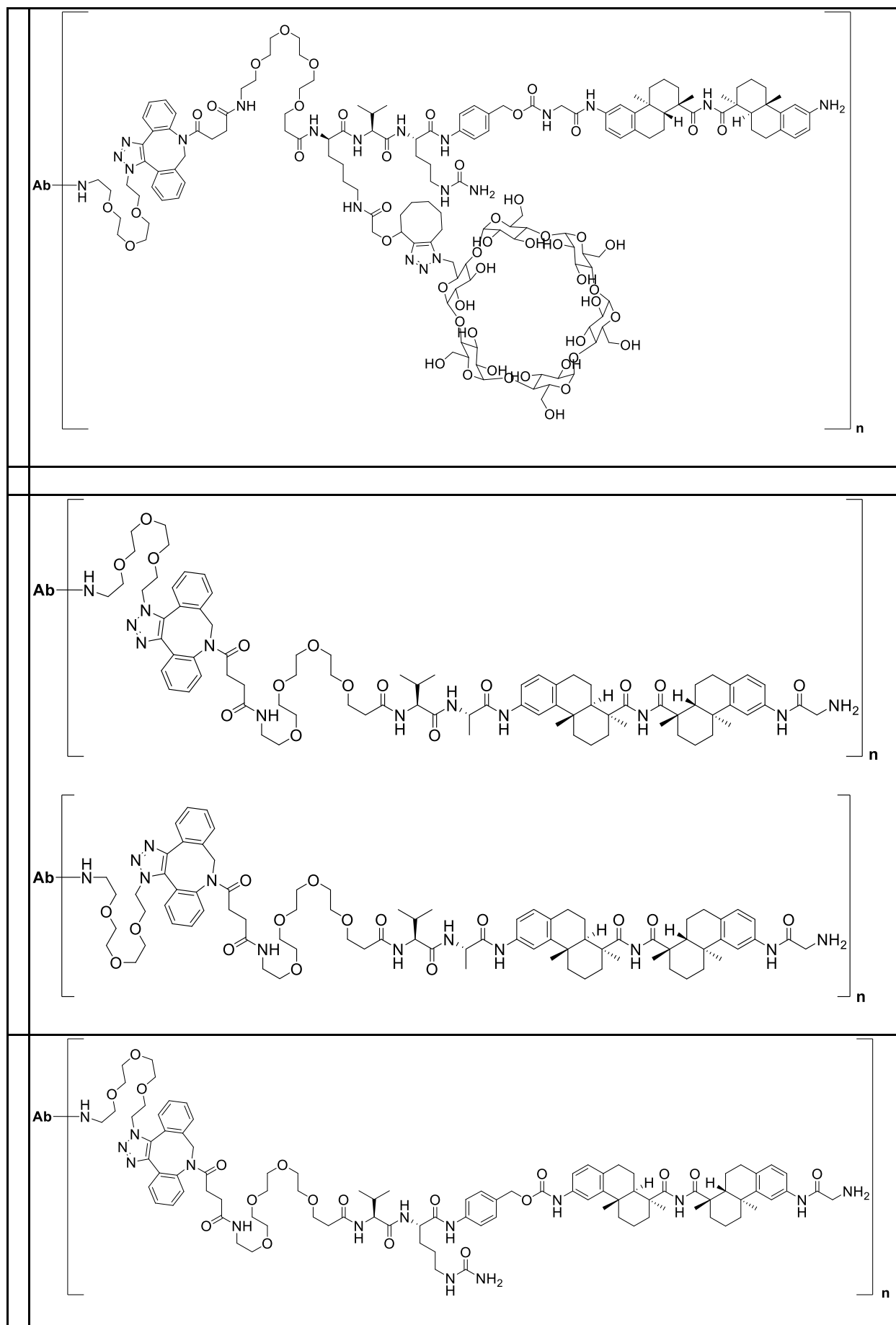


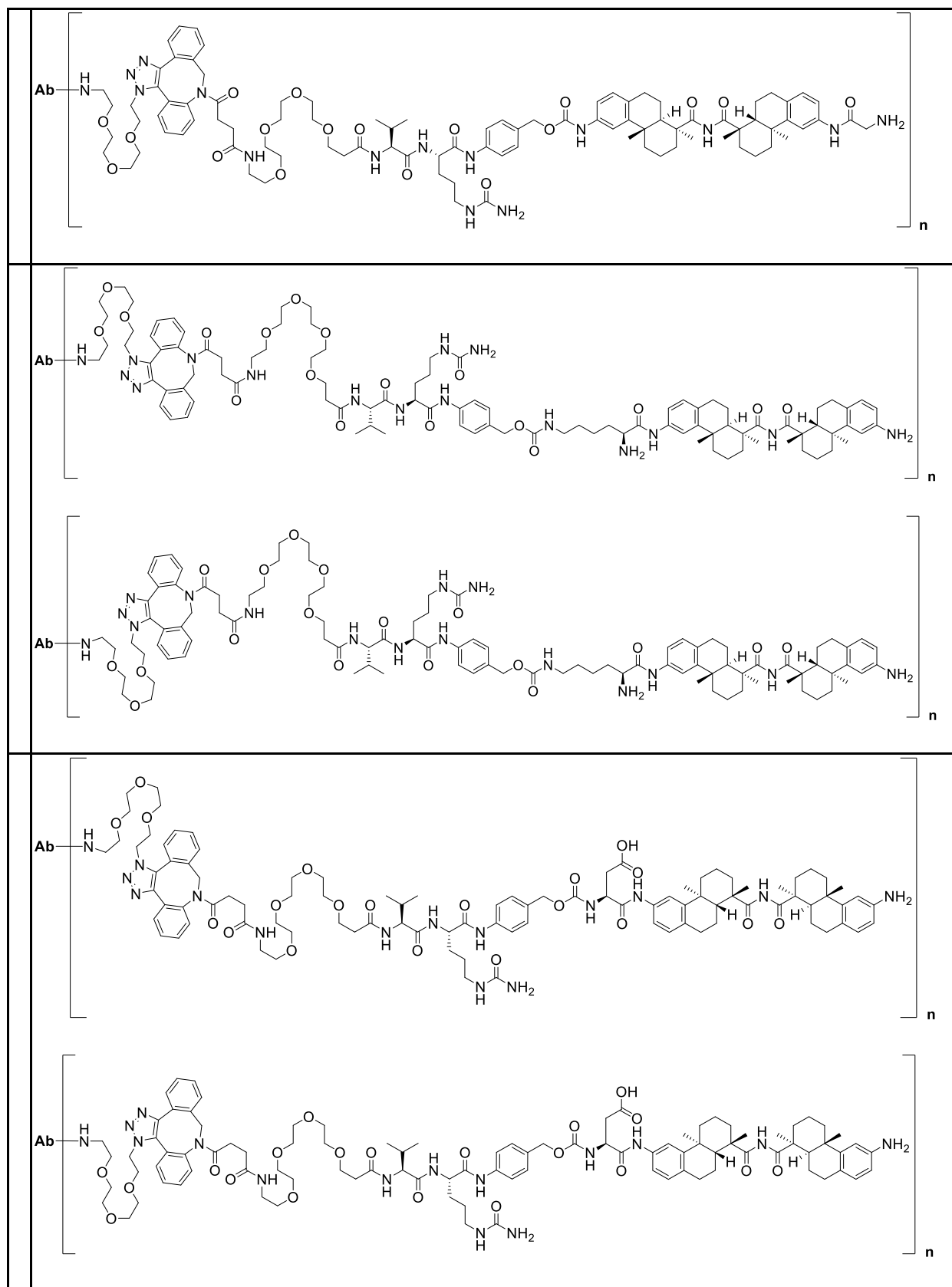


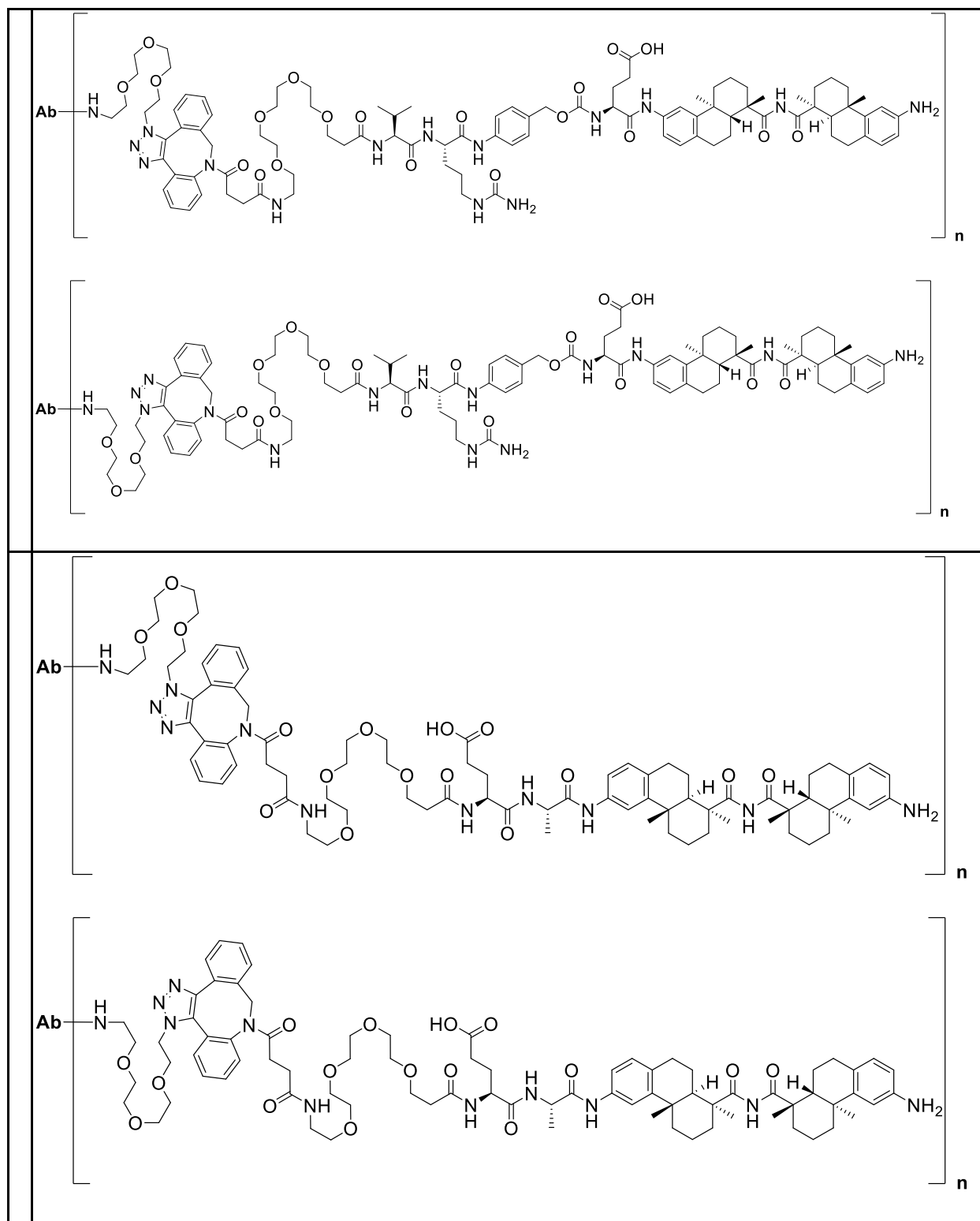


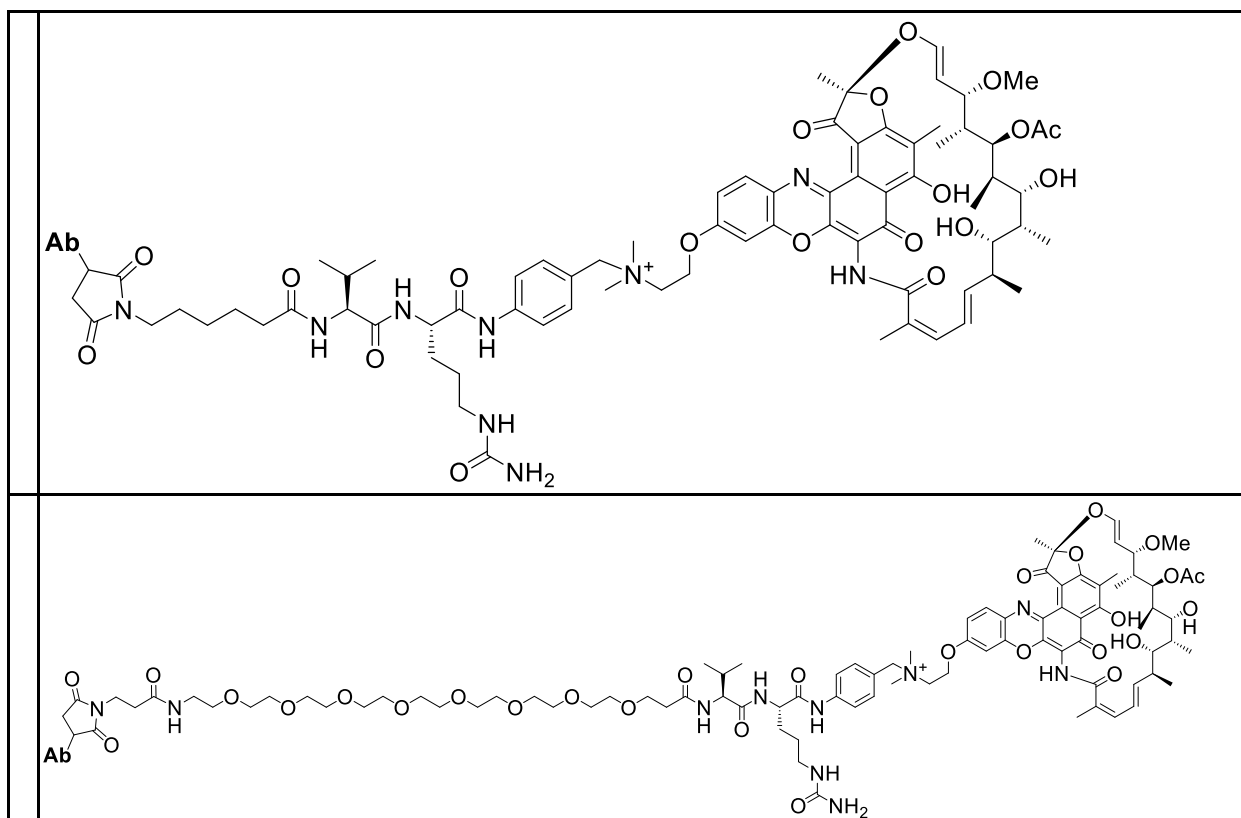






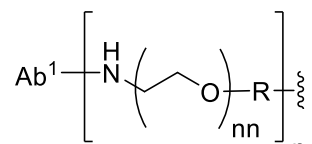






or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, wherein

each **Ab** is an anti-MSR1 antibody, or an antigen binding fragment thereof;

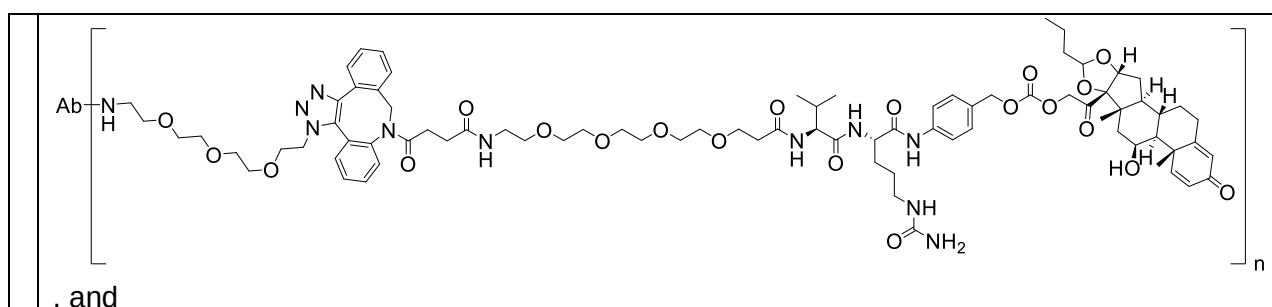


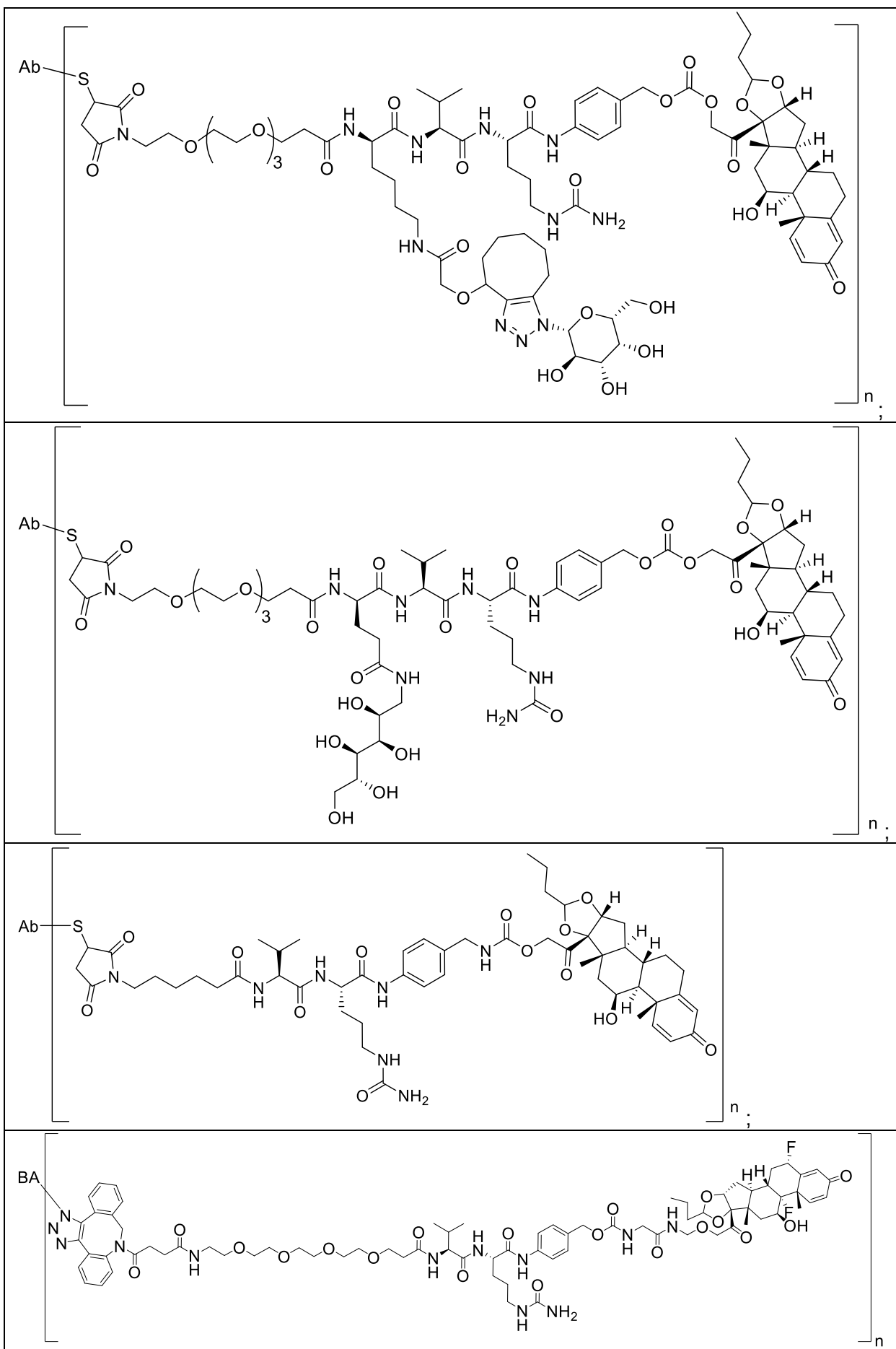
each **BA** is where **Ab¹** is an anti-MSR1 antibody, or an antigen-binding fragment thereof; **R** is C₂₋₄-alkylene; and **nn** is an integer selected from 2 to 4, inclusive.

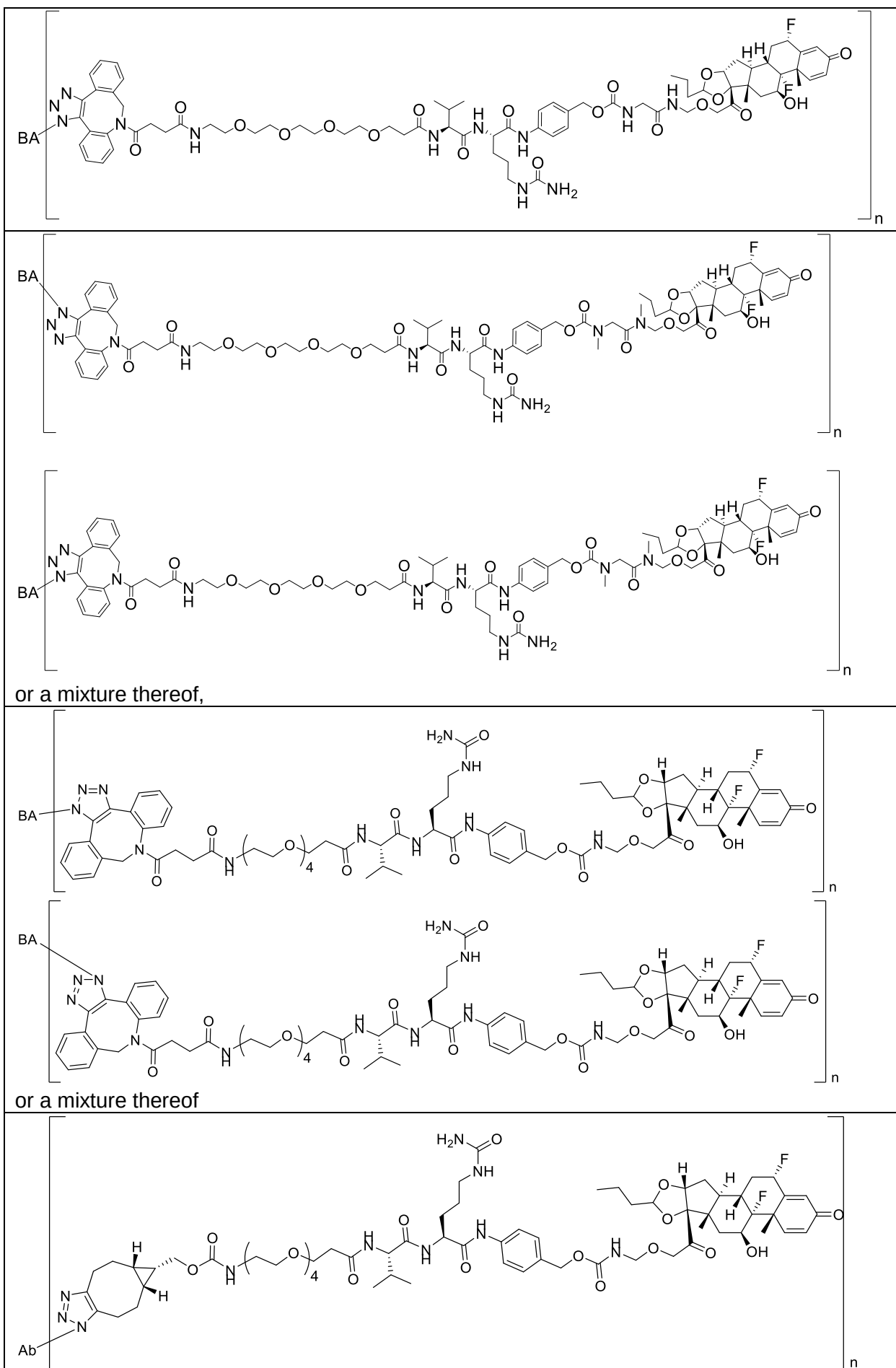
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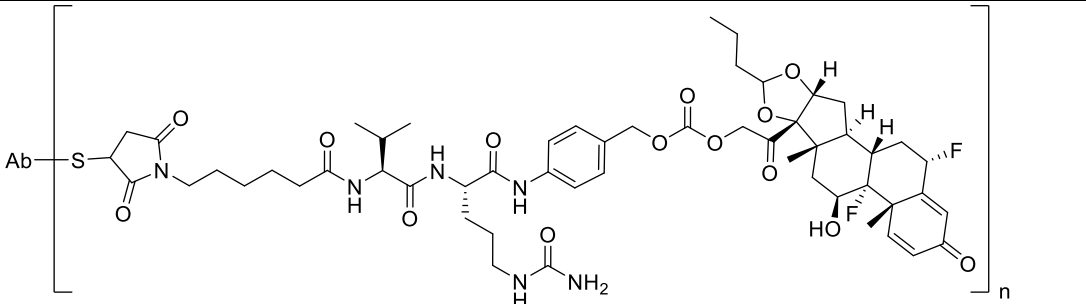
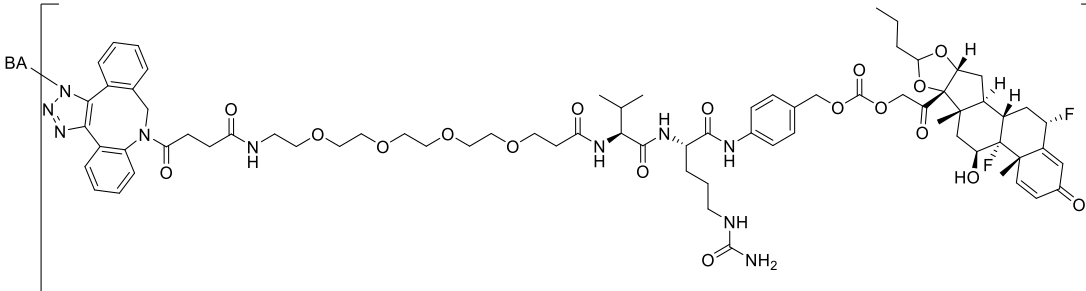
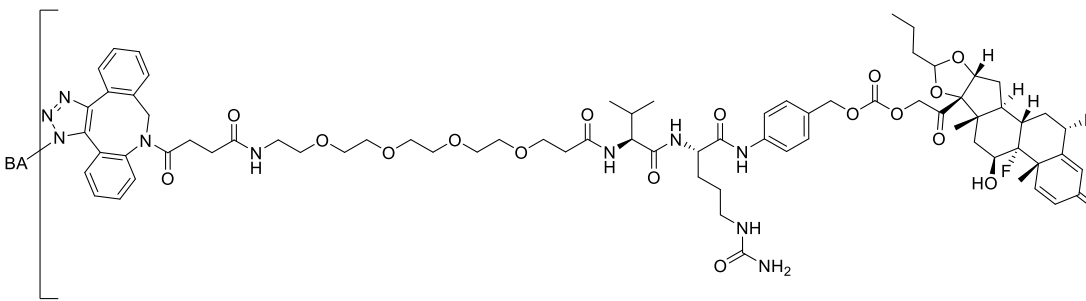
each **n** is an integer from 1 to 4.

52. An antibody-drug conjugate selected from

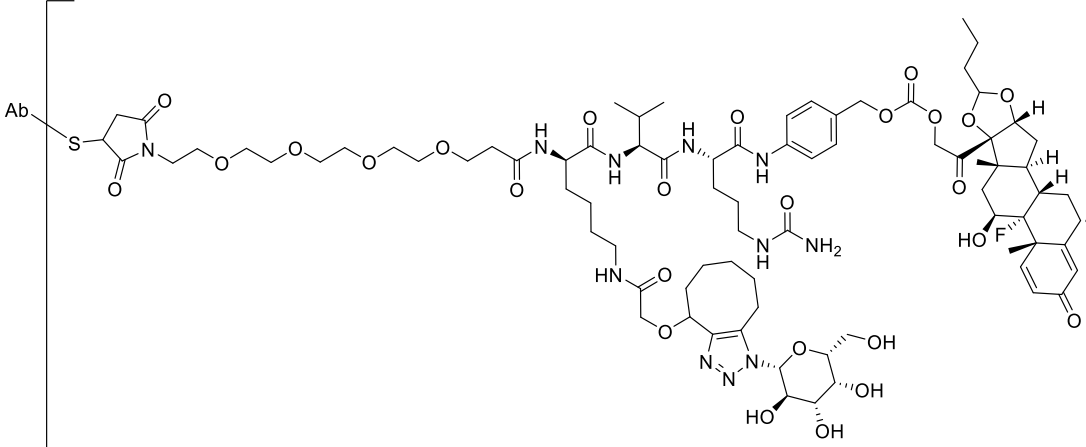
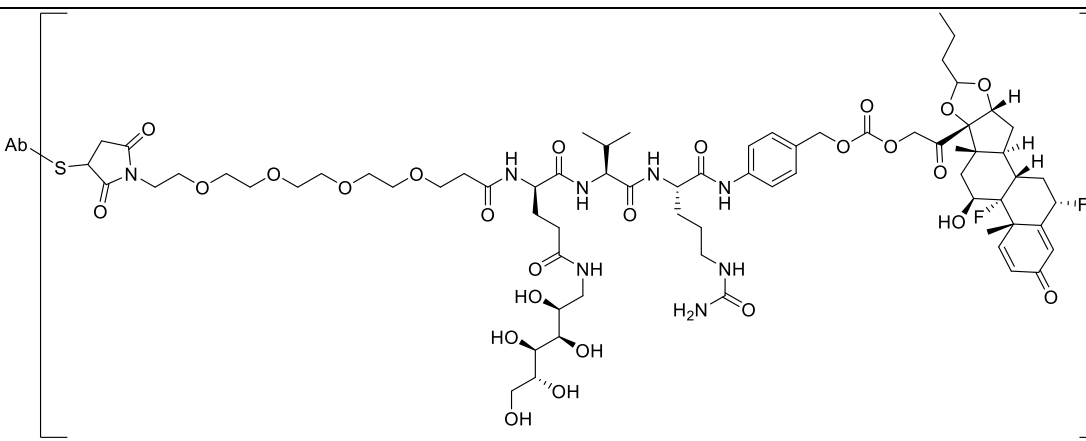


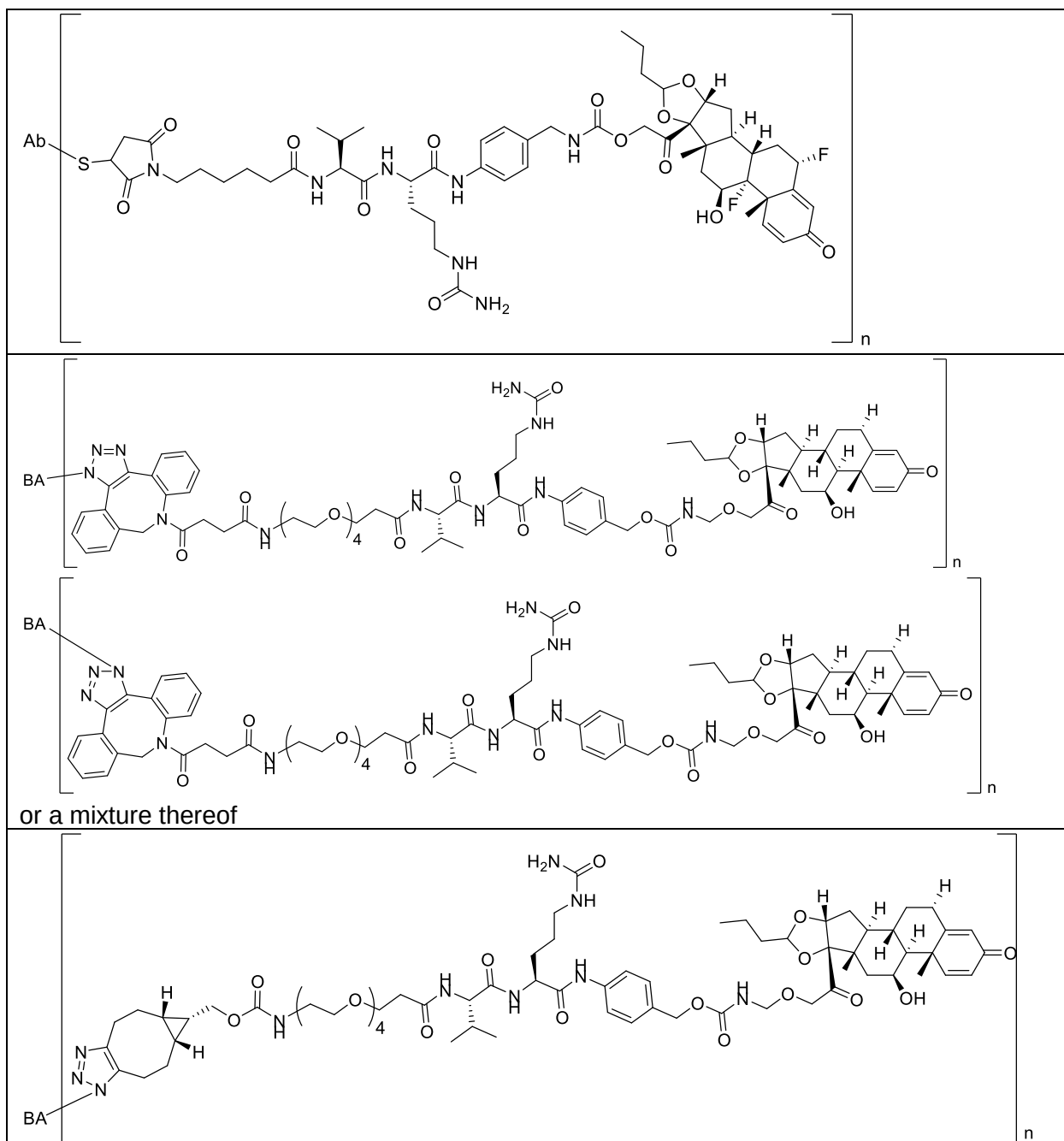






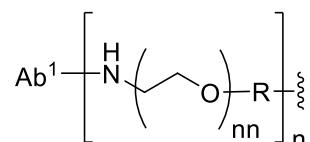
or a mixture thereof





or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, wherein

each **Ab** is an anti-MSR1 antibody, or an antigen binding fragment thereof;

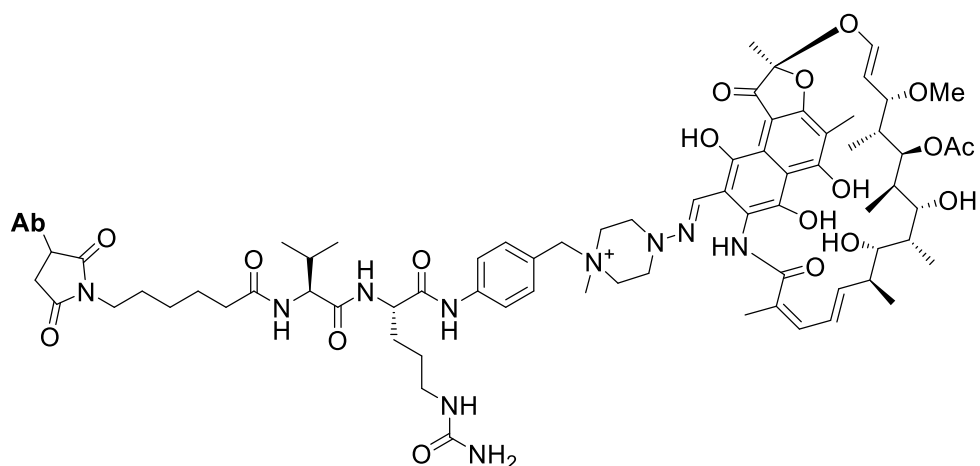


each **BA** is where **Ab**¹ is an anti-MSR1 antibody, or an antigen-binding fragment thereof; **R** is C₂₋₄-alkylene; and **nn** is an integer selected from 2 to 4, inclusive.

and

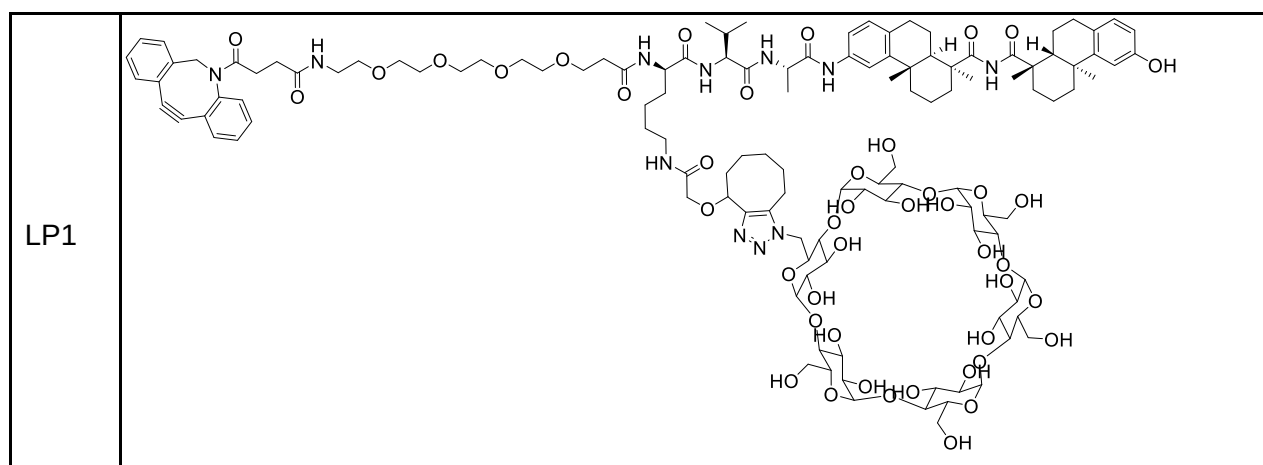
each **n** is an integer from 1 to 4.

54. An antibody-drug conjugate of any one of claims 9-10 and 24, according to Formula (7004):

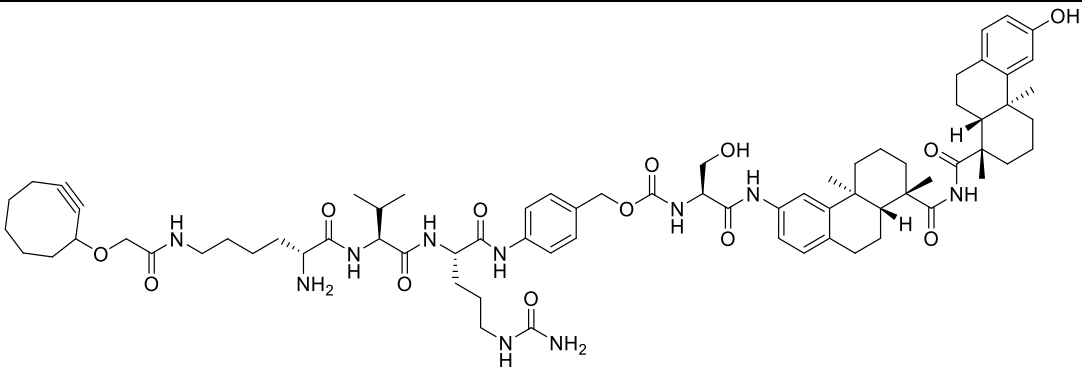
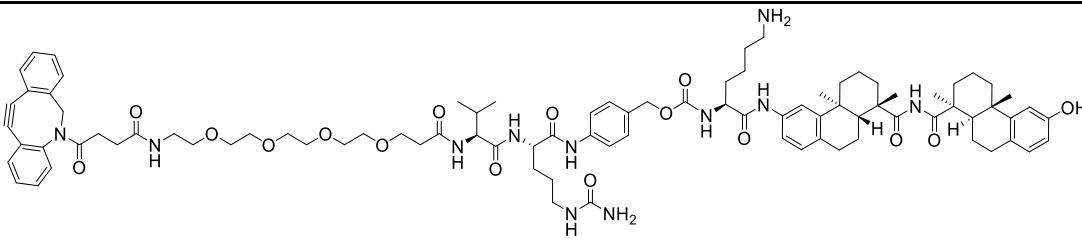
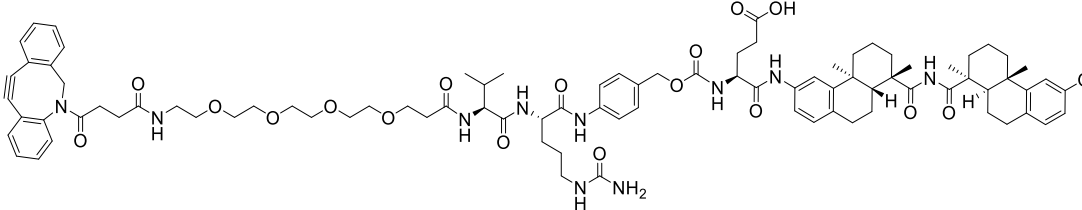
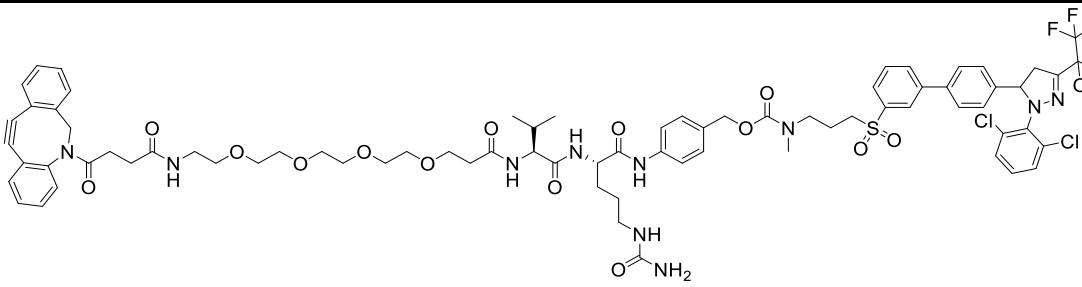
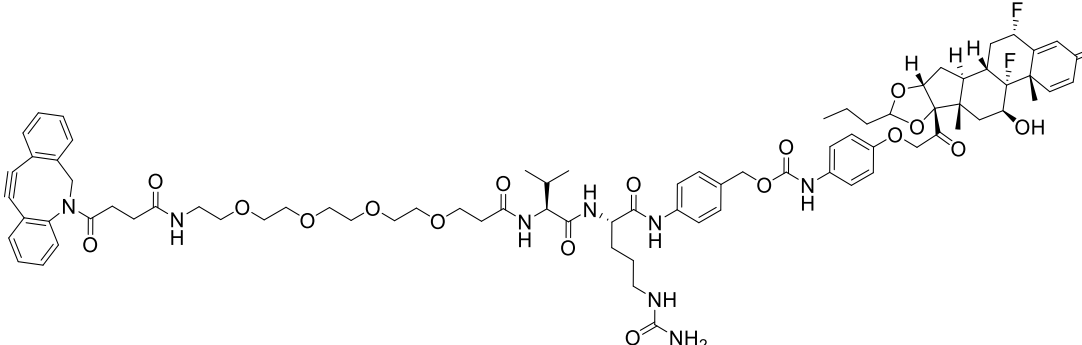
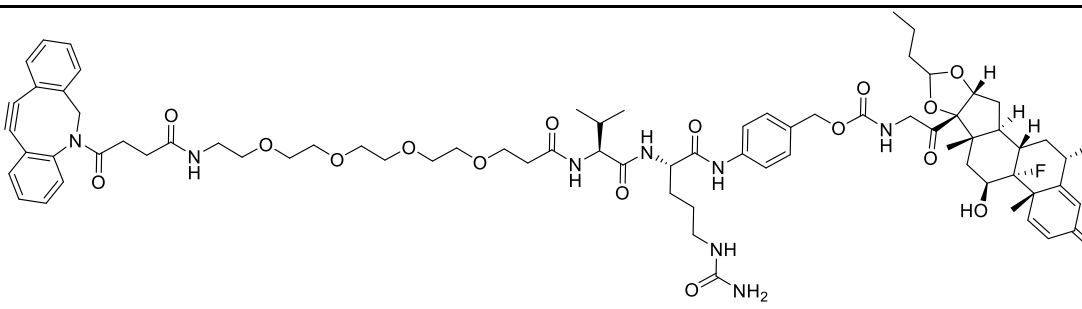


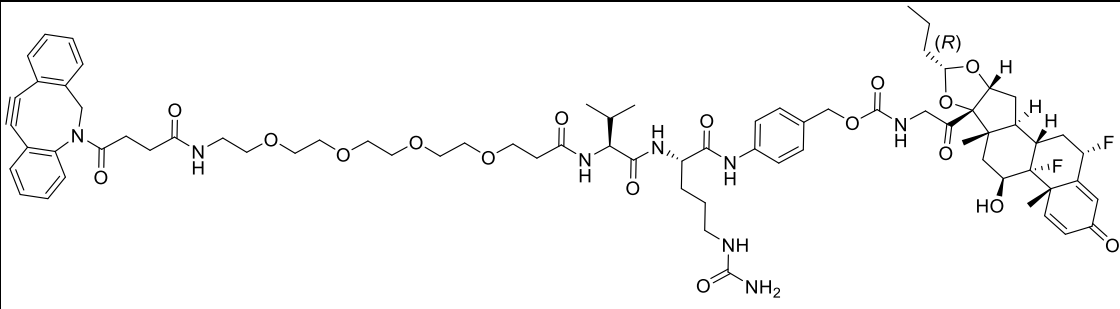
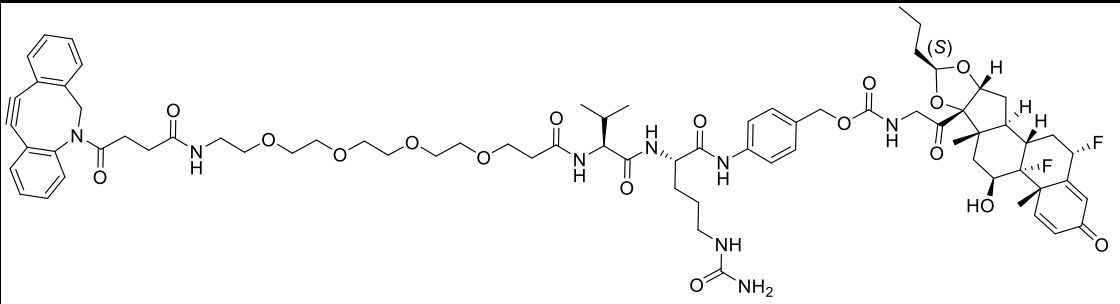
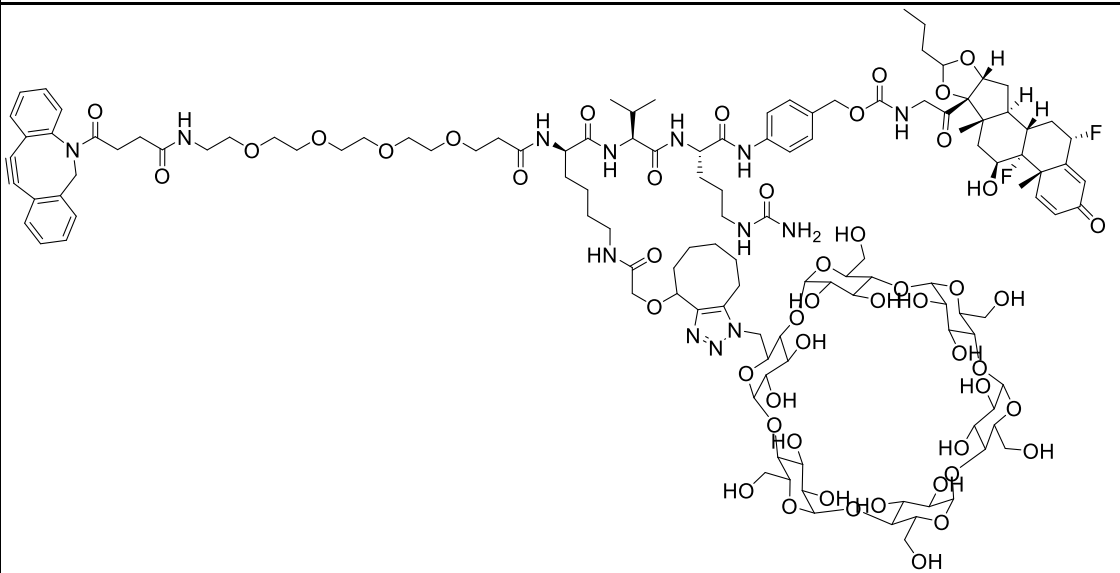
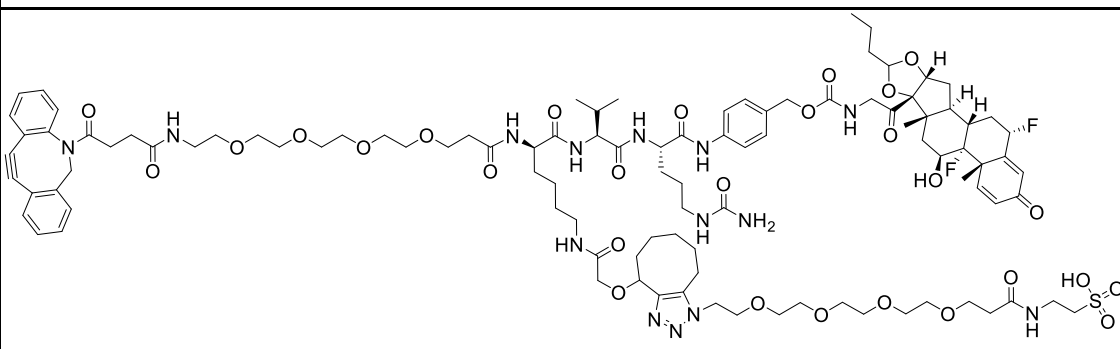
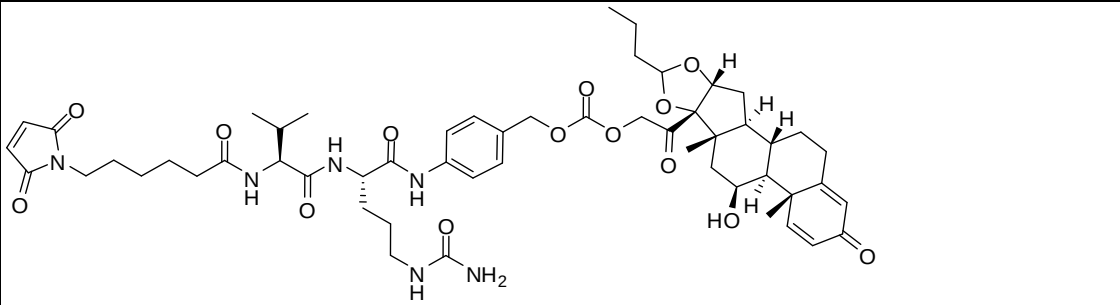
Formula (7004).

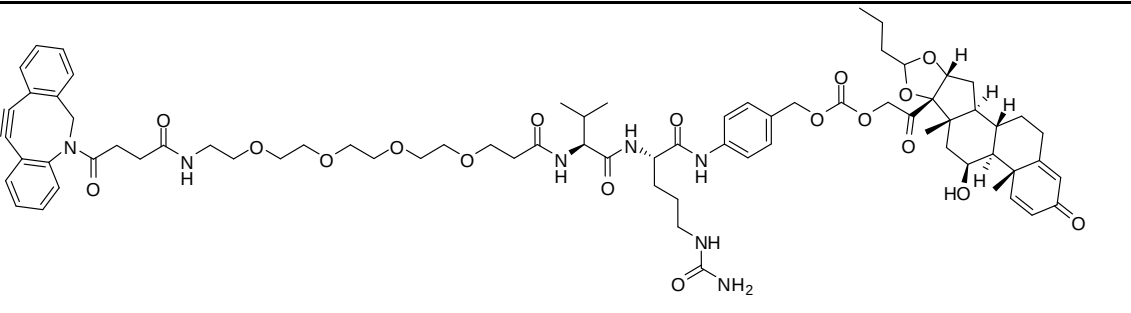
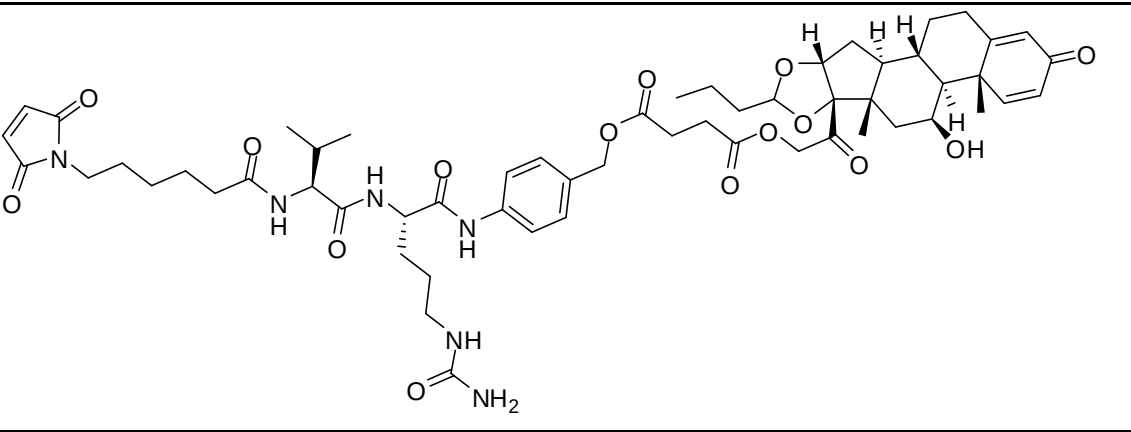
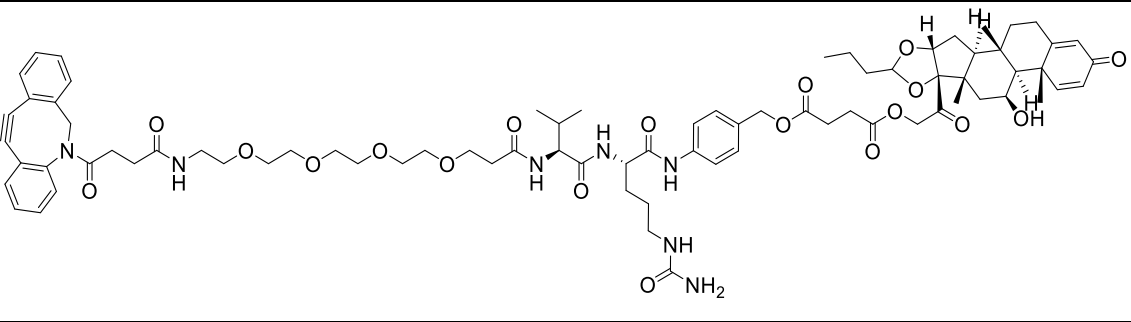
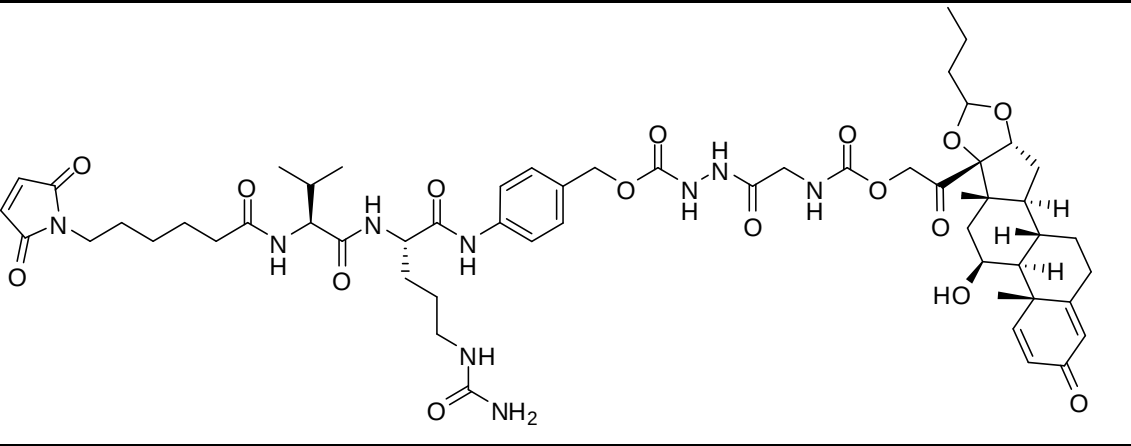
55. An antibody drug conjugate prepared by conjugating an anti-MSR1 antibody or a PEG-modified anti-MSR1 antibody, or an antigen binding fragment thereof, with a linker payload, or a stereoisomeric form thereof, or a regioisomer thereof, or a mixture of regioisomers thereof, selected from the group consisting of:

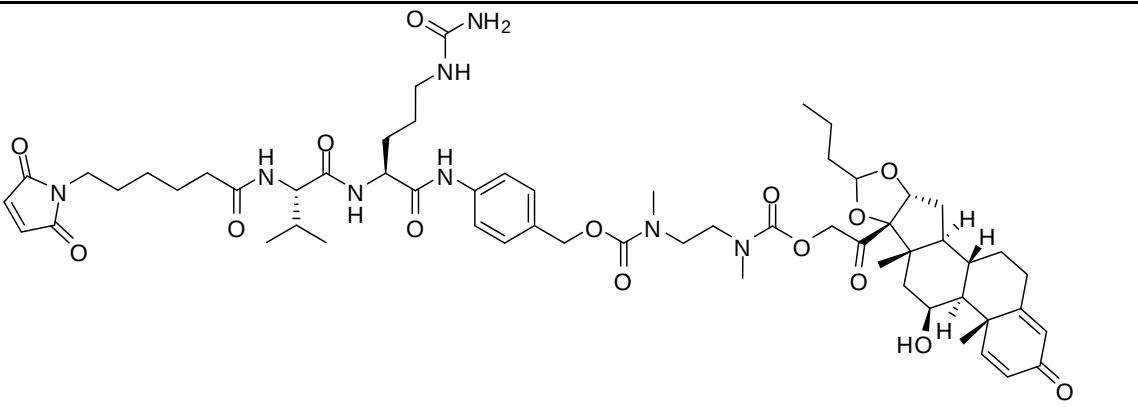
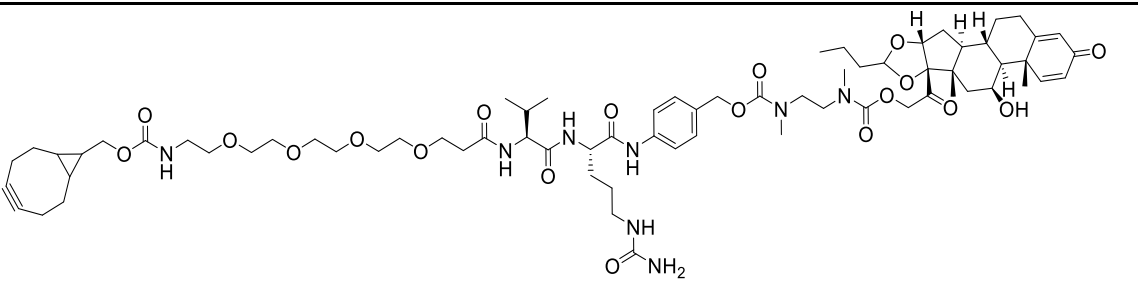
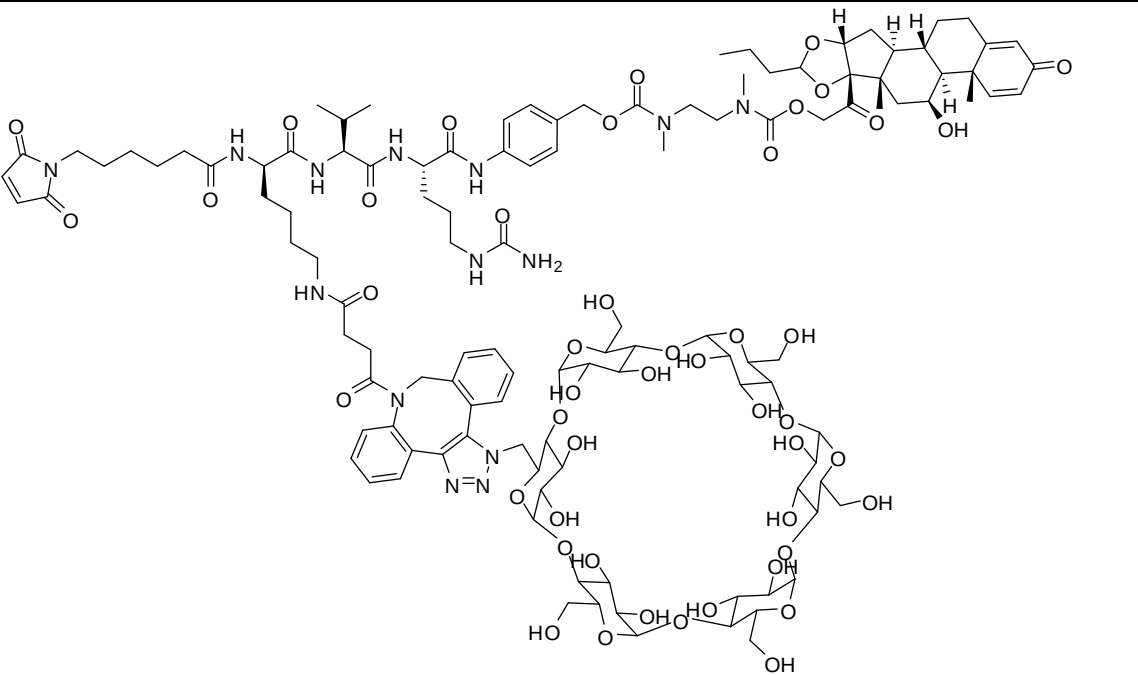
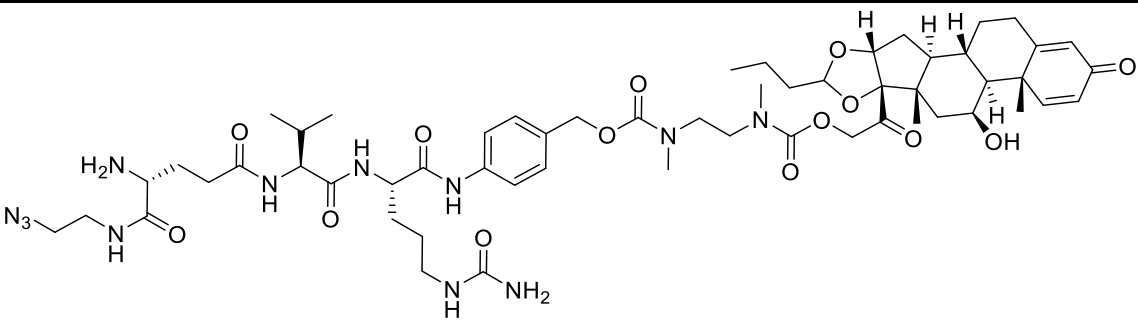


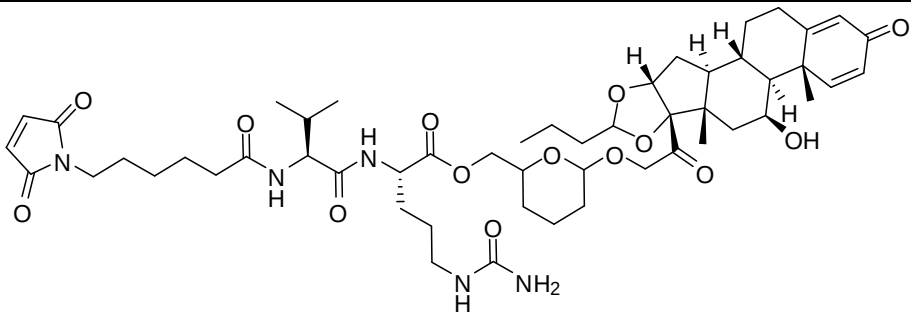
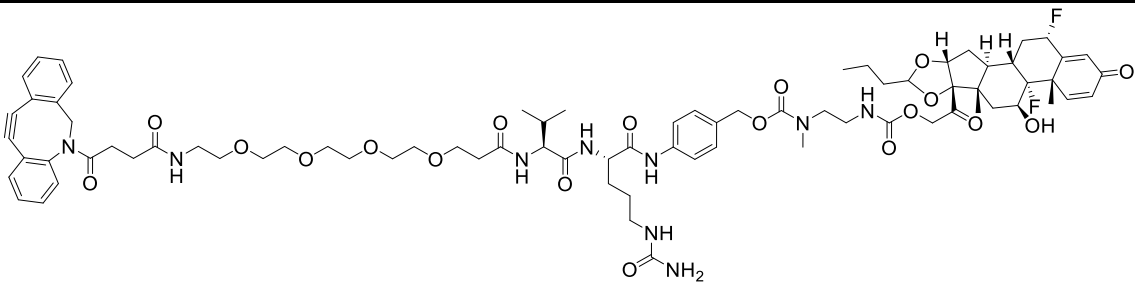
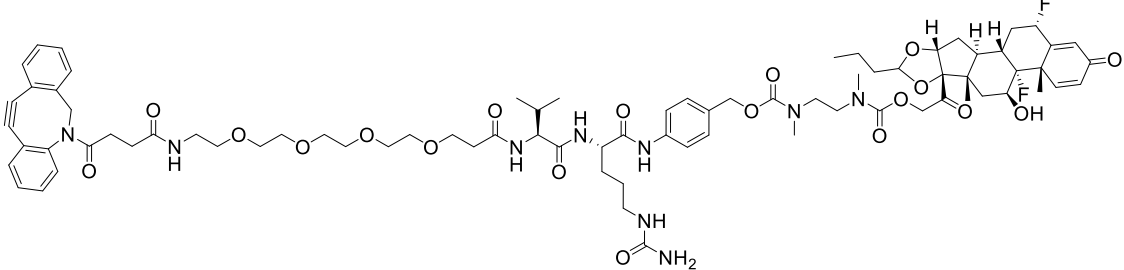
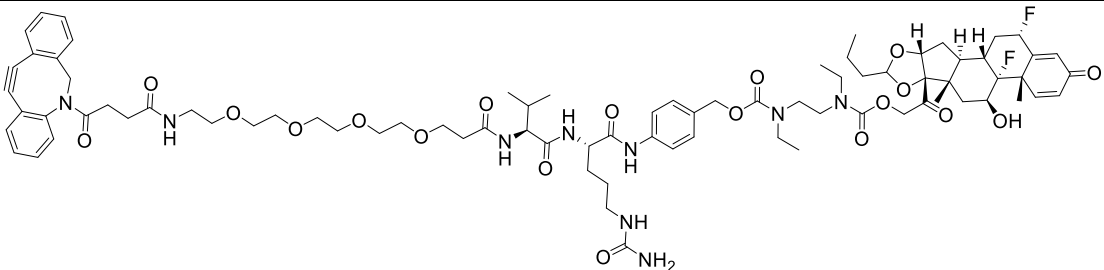
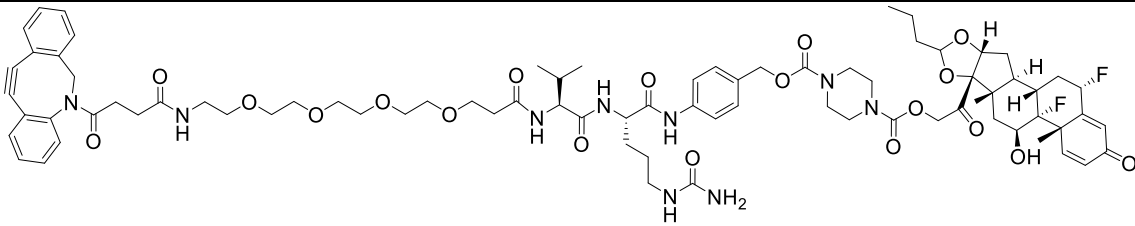
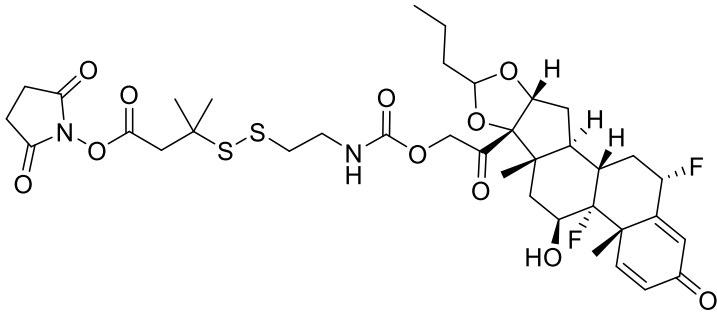
LP2	
LP5	
LP6	
LP18	

LP4	
LP11	
LP9	
LP12	
LP3	
LP13	

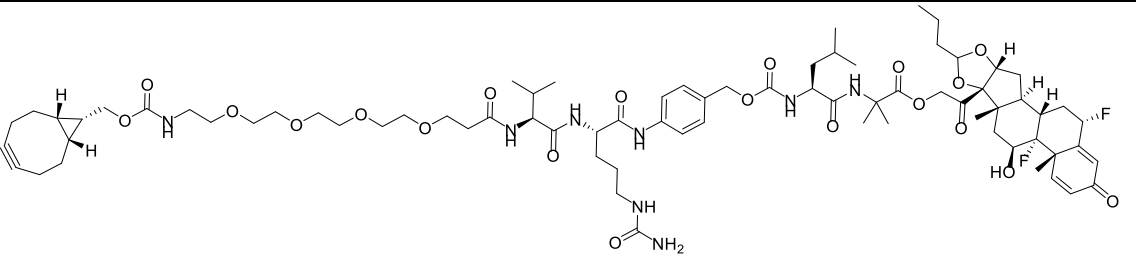
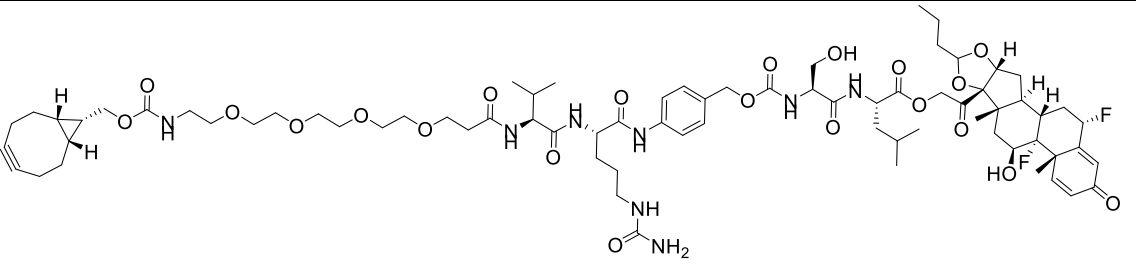
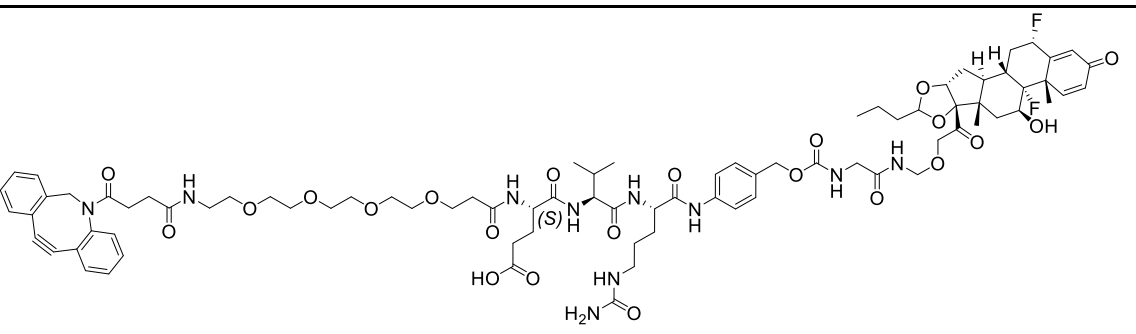
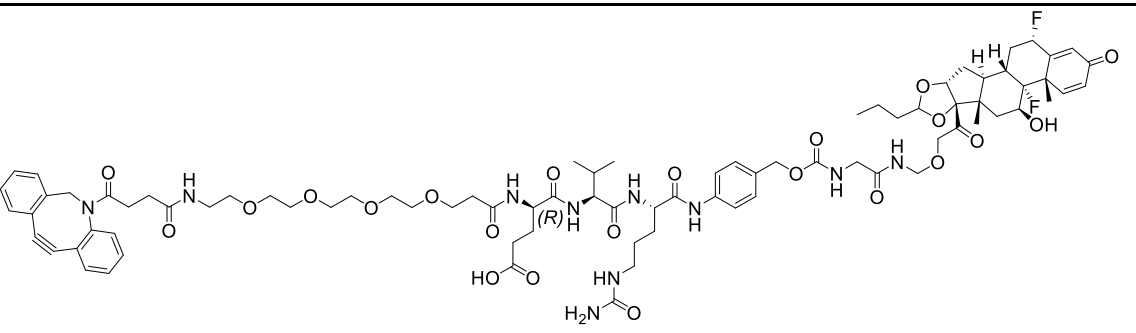
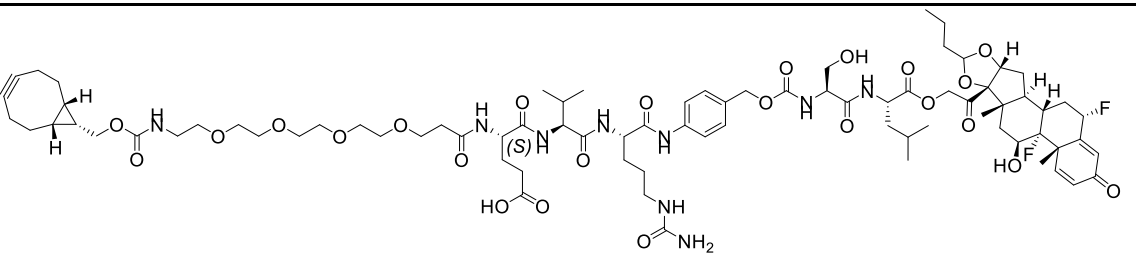
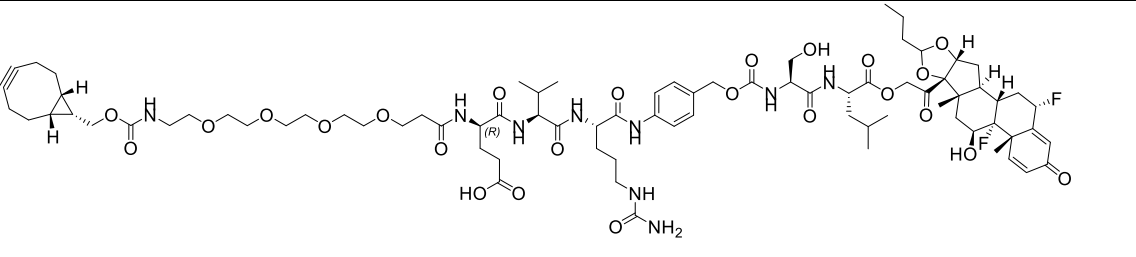
	
	
LP14	
LP15	
2a	

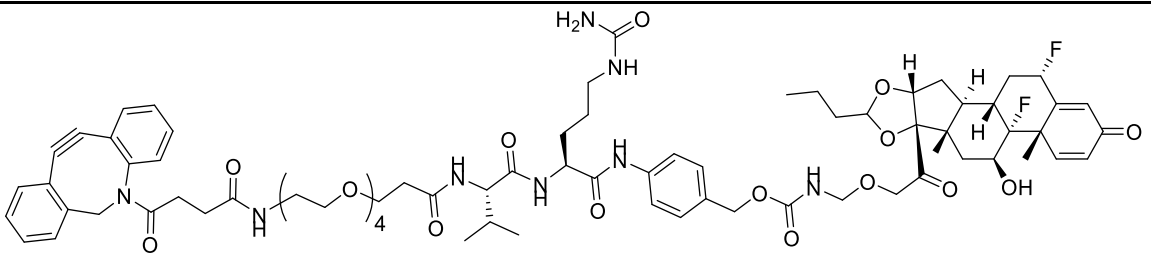
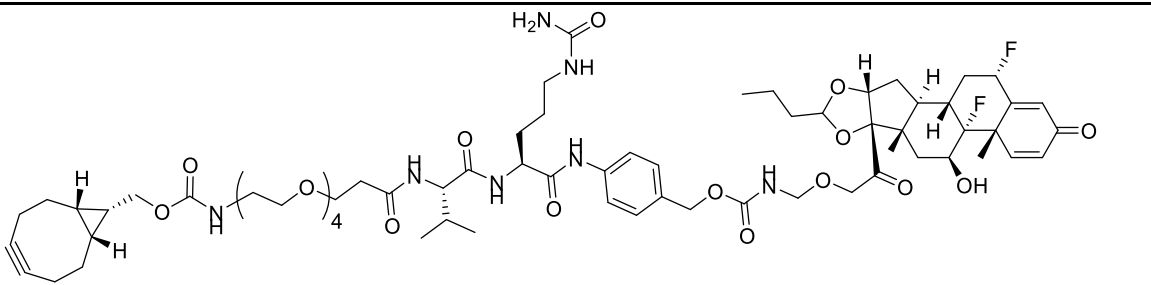
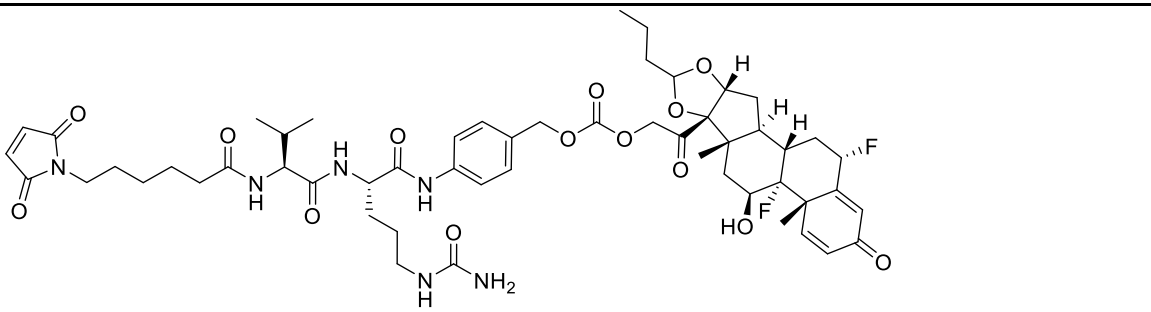
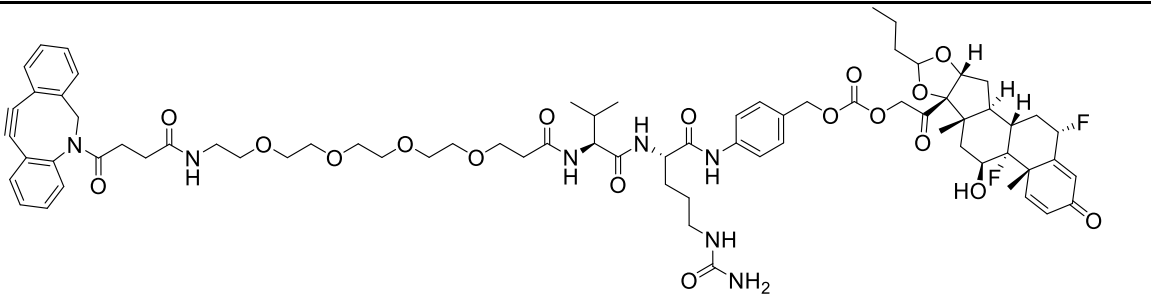
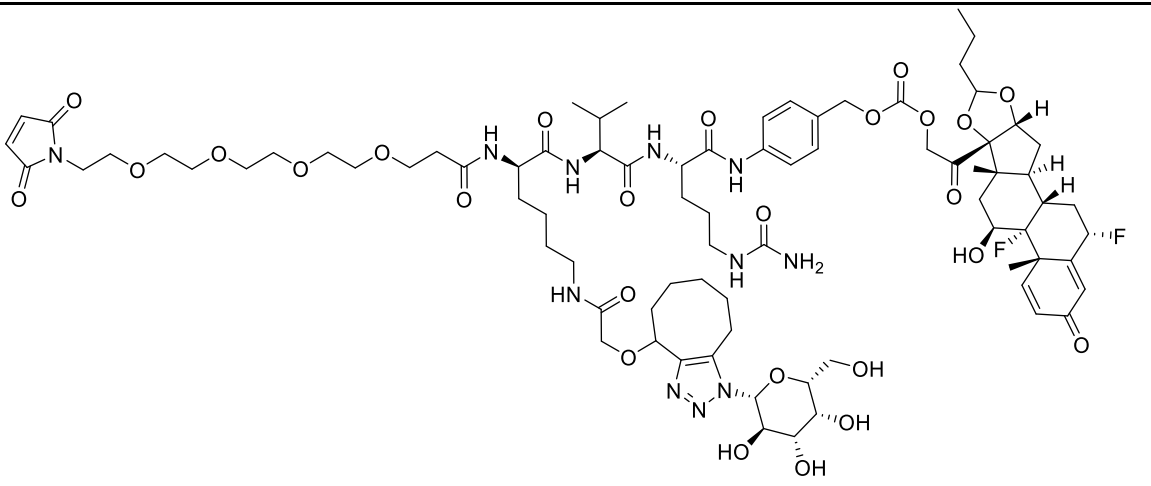
2b	
2f	
2g	
2j	

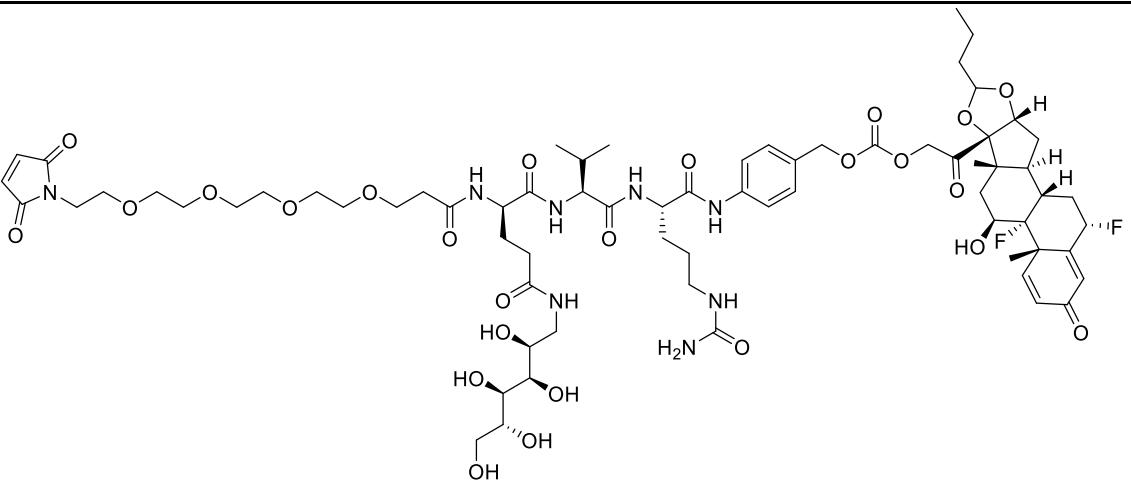
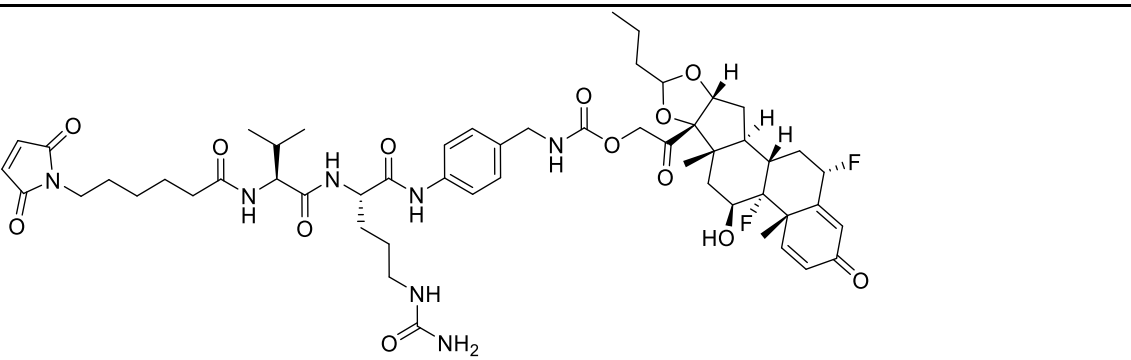
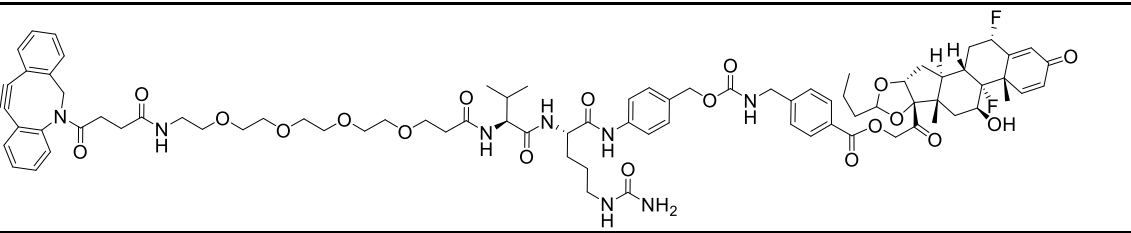
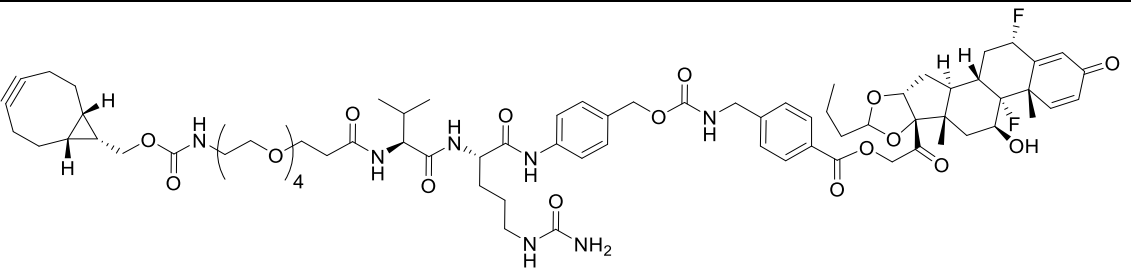
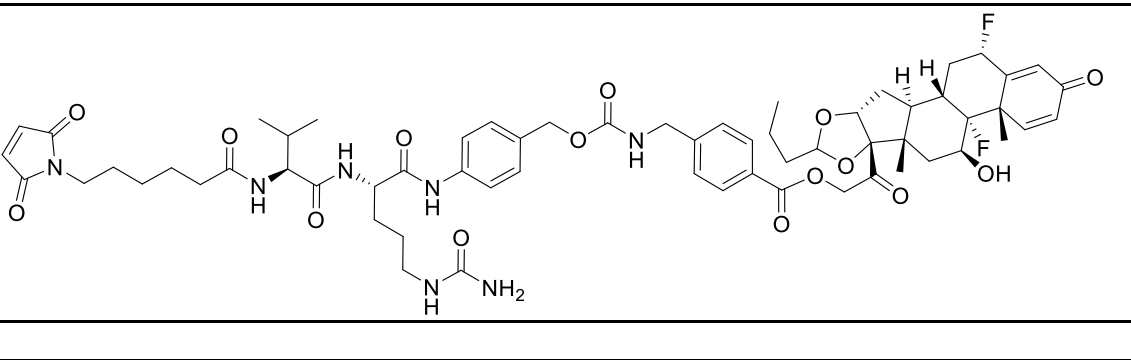
2k	
2l	
2m	
2n	 <p>or a mixture thereof</p>

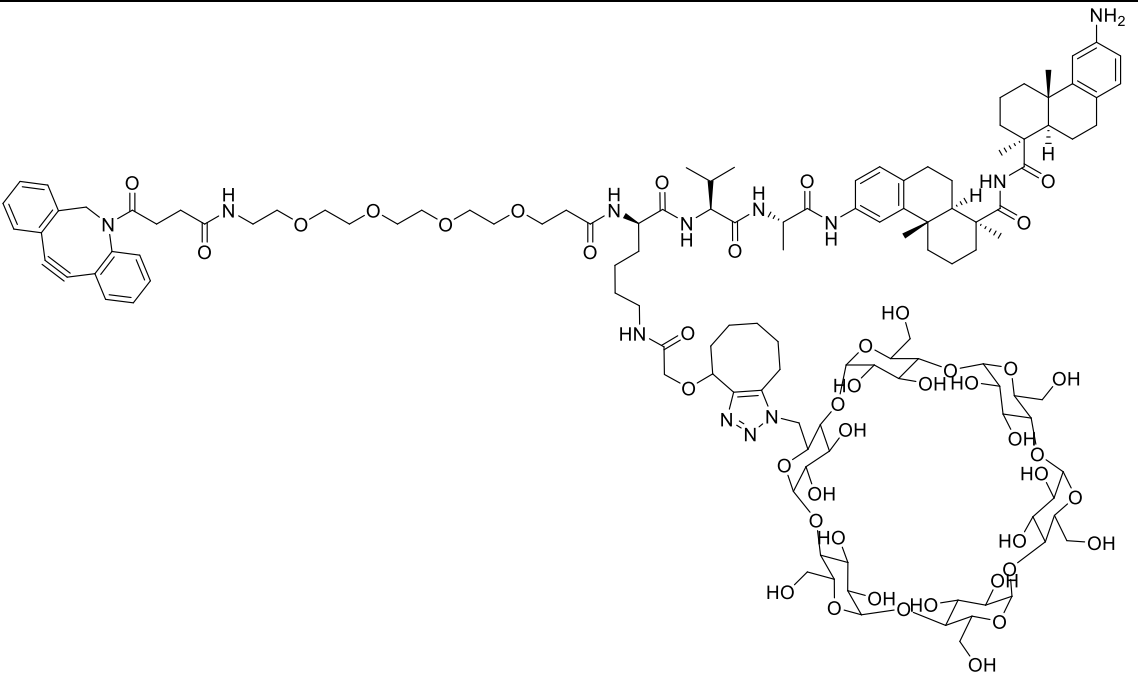
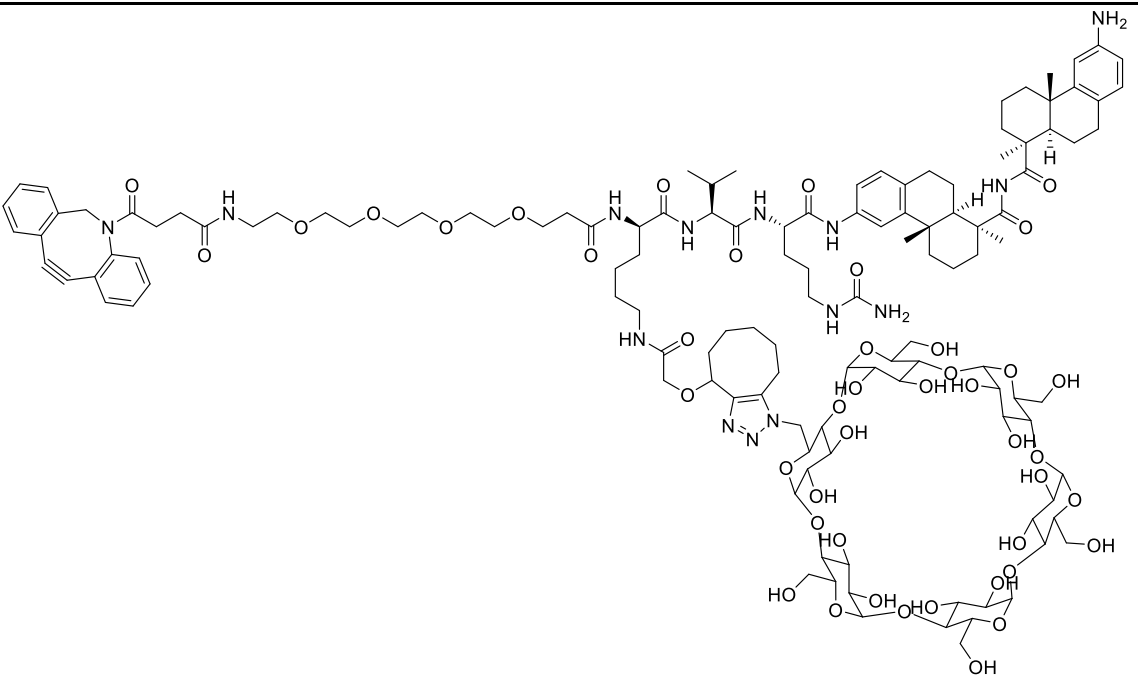
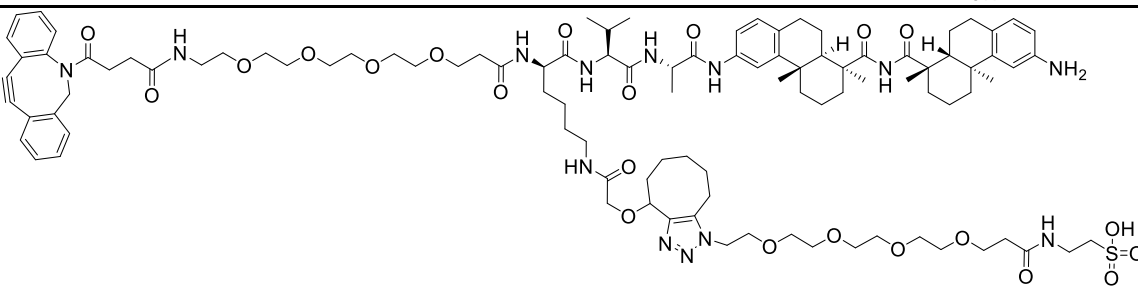
2q	
LP1A	
LP2A	
LP3A	
LP4A	
LP5A	

LP6A	
LP7A	
LP8A	
LP9A	
LP10 A	
LP11 A	

<p>LP12</p> <p>A</p>	
<p>LP13</p> <p>A</p>	
<p>LP18</p> <p>A</p>	
<p>LP19</p> <p>A</p>	
<p>LP20</p> <p>A</p>	
<p>LP21</p> <p>A</p>	

LP22 A	
LP23 A	
LP24 A	
LP25 A	
LP26 A	

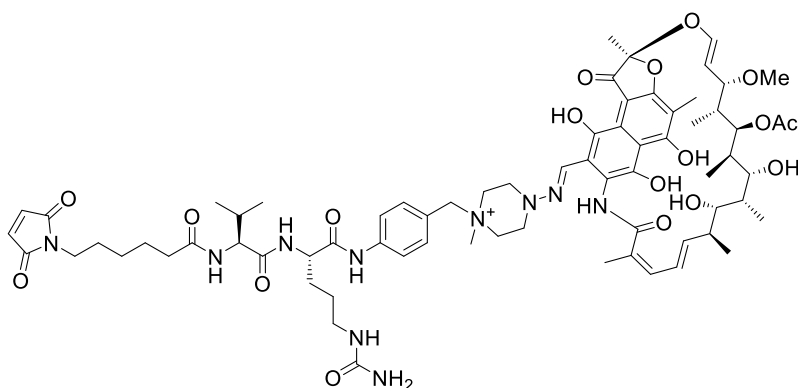
<p>LP27 A</p>	
<p>LP28 A</p>	
<p>LP29 A</p>	
<p>LP30 A</p>	
<p>LP31 A</p>	

LP1B	
LP2B	
LP3B	

LP4B	
LP5B	
LP6B	
LP7B	
LP8B	

LP9B	
LP10 B	
LP11 B	
LP12 B	
R20	<p style="text-align: right;">and</p>
R25	

56. An antibody-drug conjugate of claim 9, prepared by contacting an anti-MSR1 antibody or a PEG-modified anti-MSR1 antibody, or antigen-binding fragment thereof, with a linker payload, or a stereoisomeric form thereof, or a regioisomer thereof, according to Formula (D):



Formula (D).

under conditions suitable for forming a bond between anti-MSR1 antibody, or antigen-binding fragment thereof.

57. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1 to 8, and a pharmaceutically acceptable carrier.
58. A pharmaceutical composition comprising the antibody-drug conjugate of any one of claims 9 to 54, and a pharmaceutically acceptable carrier.
59. The antibody-drug conjugate of any one of claims 1-54, or the pharmaceutical composition of any one of claims 57-58 for use in therapy.
60. Use of the antibody-drug conjugate of any one of claims 1-23, 25-34, 51-53, or the pharmaceutical composition of any one of claims 57-58 in the manufacture of a medicament for treating a proliferative disease, a metabolic disease, inflammation, a neurodegenerative disease, or disease, disorder, or condition associated with glucocorticoid receptor signaling.
61. The use of claim 60, wherein the medicament is for treating atherosclerosis.
62. The use of claim 60, wherein the disease, disorder, or condition associated with glucocorticoid receptor signaling is an inflammatory disease, disorder, or condition.
63. The use of claim 60, wherein the medicament is for treating arthritis.
64. The use of claim 60, wherein side effects associated with administration of the unconjugated steroid payload of said compound are to be reduced.

65. The use of claim 60, wherein the metabolic disease is dyslipidemia.
66. Use of the antibody-drug conjugate of any one of claims 1-21, 24, 35-50, and 54, or the pharmaceutical composition of any one of claims 57-58 in the manufacture of a medicament for preventing or treating bacterial infection.
67. The use of claim 66, wherein the bacterium is a gram positive bacterium, penicillin-resistant bacterium *Staphylococcus aureus*, methicillin resistant *Staphylococcus aureus* (MRSA), methicillin susceptible *Staphylococcus aureus* (MSSA), or vancomycin-resistant *Staphylococcus aureus* (VRSA), or multi-drug resistant *Mycobacterium tuberculosis*.
68. The use of claim 66, wherein the antibody-drug conjugate of any one of claims 1-21, 24, 35-50, and 54, or the pharmaceutical composition of any one of claims 57-58, is to be administered in combination with vancomycin.
69. Use of the antibody-drug conjugate of any one of claims 11-21, 24, 35-50, and 54, or the pharmaceutical composition of any one of claims 57-58 in the manufacture of a medicament for preventing or treating cellulitis, bacteremia, dermonecrosis, eyelid infection, eye infection, neonatal conjunctivitis, osteomyelitis, impetigo, boils, scalded skin syndrome, food poisoning, pneumonia, surgical infection, urinary tract infection, burn infection, meningitis, endocarditis, septicemia, toxic shock syndrome, septic arthritis, mastitis, infection associated with a prosthetic joint, infection associated with a catheter, or infection associated with an implant.
70. Use of the antibody-drug conjugate of any one of claims 11-21, 24, 35-50, and 54, or the pharmaceutical composition of any one of claims 57-58 in the manufacture of a medicament for preventing or treating an intracellular bacterial infection.