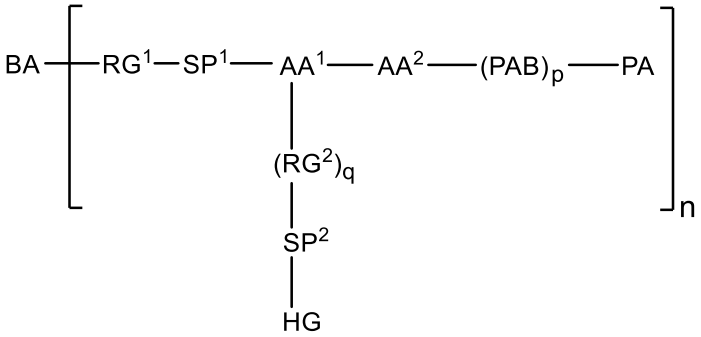
[05a] In one aspect, set forth herein is a compound, or pharmaceutically acceptable salt, solvate, triazole linkage regioisomer, mixture of triazole linkage regioisomers, or stereoisomer thereof,

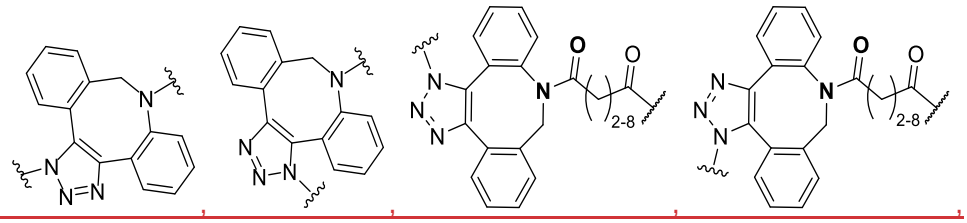
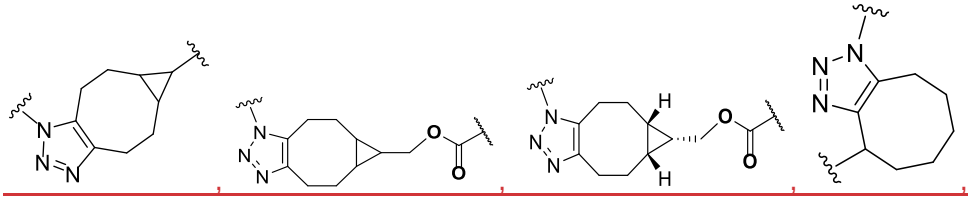
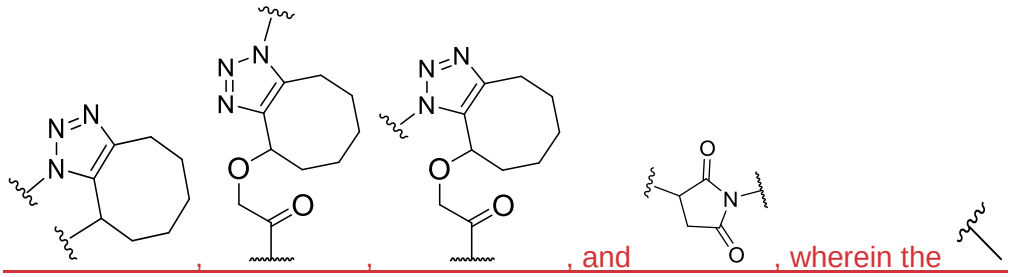
wherein the compound has a structure according to Formula (**IV**):



(**IV**)

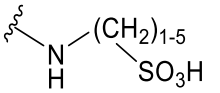
wherein:

BA is an antibody or antigen binding fragment thereof~~a binding agent~~;

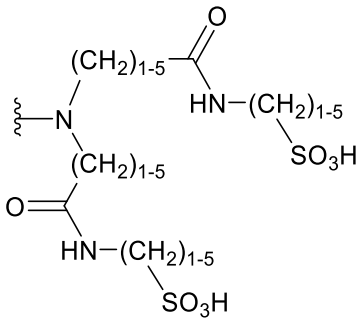
RG¹ and **RG²** are reactive group residuesindependently selected from the group consisting of  ,  ,  , and , wherein the indicates the atom through which the RG^1 or RG^2 is bonded to the adjacent groups in the formula;

SP[1] and **SP[2]** are independently, in each instance, absent, or a spacer group residue selected from the group consisting of C_{1-6}alkylene, -NH-, -C(O)-, -$(CH_2$-CH_2-$O)_e$, -NH-$(CH_2$-CH_2-$O)_e$-CH_2-CH_2-C(O)-, -C(O)-$(CH_2)_u$-C(O)-, -C(O)-NH-$(CH_2)_v$-, and combinations thereof wherein subscript e is an integer from 0 to 6, subscript u is an integer from 1 to 8, and subscript v is an integer from 1 to 8;

HG is a hydrophilic residue selected from



and

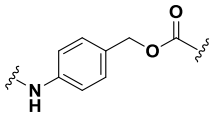


wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula ;

PA is a payload residue;

AA[1] is ~~a trivalent linker comprising~~ an amino acid residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

AA^2 is a dipeptide, tripeptide, or tetrapeptide residue comprising amino acid residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

PAB is  , wherein the  indicates the atom through which the **PAB** is bonded to the adjacent groups in the formula;

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

subscript **p** is 0 or 1; and

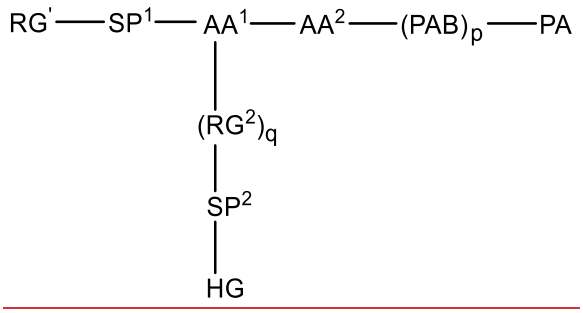
subscript **q** is ~~0 or~~ 1.

[05b] In another aspect, set forth herein, is a pharmaceutical composition comprising a compound as described herein, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

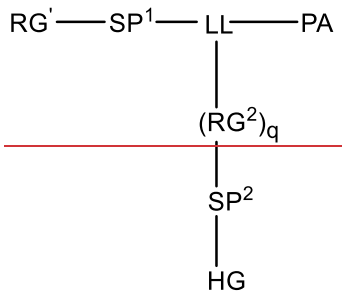
[05c] In another aspect, set forth herein, is a compound as described herein, or a composition as described herein for use in treating a disease or disorder in a patient in need thereof.

[06] In another example, set forth herein, is a compound, including: a reactive group linked to at least one payload moiety and linked to at least one hydrophilic moiety via a covalent linker, wherein said covalent linker is bonded directly or indirectly to each of the reactive group, the payload moiety, and the hydrophilic moiety.

[06a] In another aspect, set forth herein, is a compound or stereoisomeric form, a triazole linkage regioisomer, or mixture of triazole linkage regioisomers thereof, according to Formula (**IX**):~~according to Formula (**VII**):~~



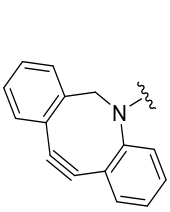
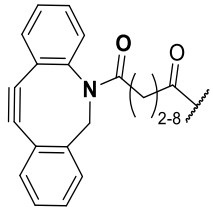
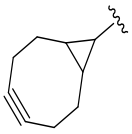
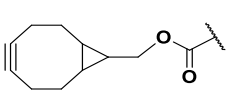
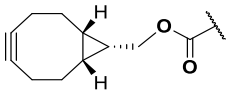
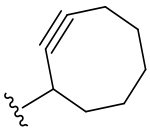
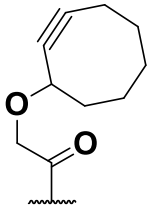
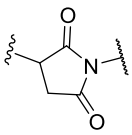
(IX)

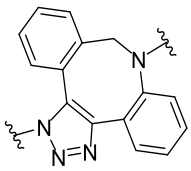
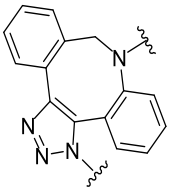
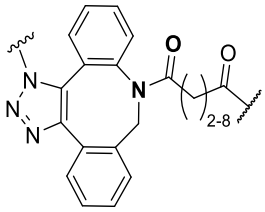
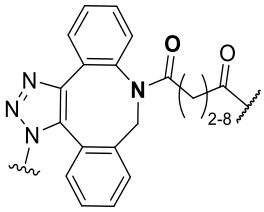
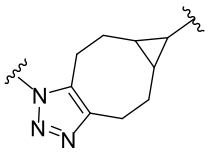
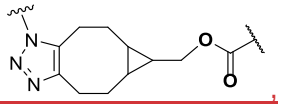
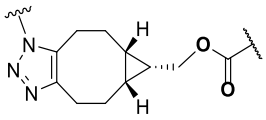
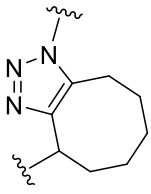
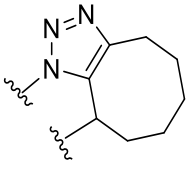
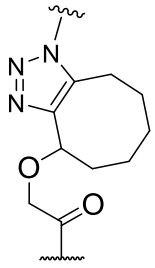
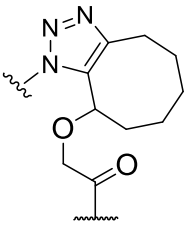
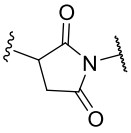


~~(VII)~~

AA1 is an amino acid residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

AA2 is a dipeptide, tripeptide or tetrapeptide residue comprising amino acid residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

RG′ is a reactive group selected from  ,  ,  ,  ,  ,  ,  , and  , wherein the  indicates the atom through which the **RG′** is bonded to the adjacent groups in the formula;

RG² is a reactive group residue selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  , wherein the  indicates the atom through which the RG^1 or RG^2 is bonded to the adjacent groups in the formula;

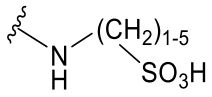
~~**LL** is a trivalent linker;~~

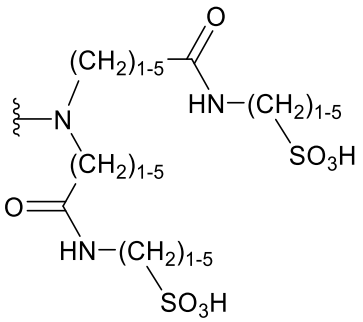
~~**RG′** is a reactive group;~~

~~**RG²** is a reactive group residue;~~

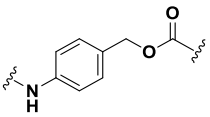
SP¹ and **SP²** are independently, in each instance, absent, or a spacer group residue selected from the group consisting of $C_{1\text{-}6}$alkylene, -NH-, -C(O)-, $-(CH_2\text{-}CH_2\text{-}O)_e$, -NH-

$(CH_2\text{-}CH_2\text{-}O)_e\text{-}CH_2\text{-}CH_2\text{-}C(O)\text{-}$, $\text{-}C(O)\text{-}(CH_2)_u\text{-}C(O)\text{-}$, $\text{-}C(O)\text{-}NH\text{-}(CH_2)_v\text{-}$, and combinations thereof wherein subscript e is an integer from 0 to 6, subscript u is an integer from 1 to 8, and subscript v is an integer from 1 to 8;

HG is a hydrophilic residue selected from  and



;

PAB is  , wherein the  indicates the atom through which the PAB is bonded to the adjacent groups in the formula;

subscript **p** is 0 or 1;

PA is a payload residue; ~~and~~

subscript **q** is ~~0 or~~ 1; and

wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

[07] In another example, set forth herein is an antibody-drug conjugate having a compound, described above and herein, bonded to an antibody or an antigen binding fragment thereof.

[07a] In another aspect, set forth herein is an antibody-drug-conjugate comprising the compound as described herein bonded to an antibody, or an antigen binding fragment thereof.

[08] In another example, set forth herein is a method of treating a disease, condition, or disorder in a patient in need thereof including administering to the patient a compound set forth herein. Also provided is the use of a compound set forth herein for treating a disease, condition, or disorder set forth herein. Further provided is the use of a compound set forth herein for the manufacture of a medicament for treating a disease, condition, or disorder set forth herein. In some examples, the compound is an antibody-drug conjugate.

[08a] In another aspect, set forth herein is a compound or pharmaceutical composition as described herein for use in treating a proliferative disease, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

[08b] In another aspect, set forth herein is a compound or pharmaceutical composition as described herein for use in the treatment of a proliferative disease in a subject.

[08c] In another aspect, set forth herein is a compound or pharmaceutical composition as described herein for use in the treatment of a metabolic disease in a subject.

[08d] In another aspect, set forth herein is a compound or pharmaceutical composition as described herein for use in the treatment of inflammation in a subject.

[08e] In another aspect, set forth herein is a compound or pharmaceutical composition as described herein for use in the treatment of a neurodegenerative disease in a subject.

[08f] In another aspect, set forth herein is use of a compound or pharmaceutical composition as described herein in the manufacture of a medicament for treating a proliferative disease, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

[09] In another example, set forth herein is a method of preparing an antibody-drug conjugate including the step of contacting a binding agent with a linker-payload compound set forth herein under conditions suitable for forming a bond between the binding agent and the linker-payload compound.

[09a] In another aspect, set forth herein is a method of preparing a compound as described herein comprising the step of contacting an antibody or antigen binding fragment thereof ~~binding agent~~ with a compound as described herein, under conditions suitable for forming a bond between the antibody or antigen binding fragment thereof ~~binding agent~~ and the compound.

BRIEF DESCRIPTIONS OF THE DRAWINGS

[010] FIG. 1 shows three different types of payload compounds.

[011] FIG. 2 shows a synthetic process for preparing compounds 1a, 1c, 1e, 1f, 1i, 1j, 1k, 1m, 1q, Ib, Id, Ie-1, If-1, IIb, IIId, IIIe, and IVb.

[012] FIG. 3 shows shows a synthetic process for preparing compounds 1h, 1l, Ig, and Ih-1.

[013] FIG. 4 shows a synthetic process for preparing payloads B and C.

[014] FIG. 5 shows a synthetic process for preparing payload D.

[015] FIG. 6 shows a general synthetic procedure A for preparing intermediates 3a, 3b, 3c, and 3g.

[016] FIG. 7 shows a general synthethic procedure for preparing intermediates 3d, and 3f.

[017] FIG. 8 shows a synthethic process for preparation of intermediate 3e.

[018] FIG. 9 shows a synthethic process for preparation of intermediate 4a.

[019] FIG. 10 shows a synthetic process for preparation of intermediate 4b.

[020] FIG. 11 shows a synthetic process for preparation of intermediates 5a-g.

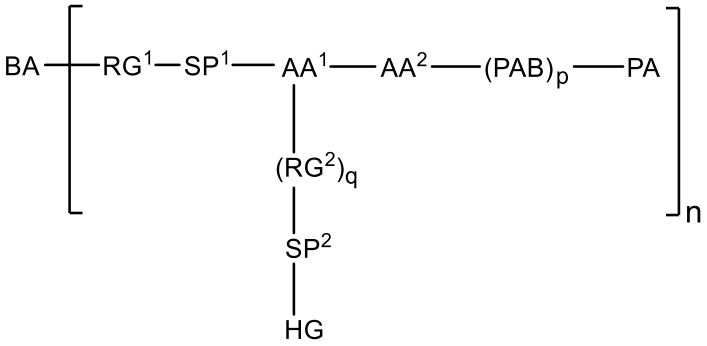
[021] FIG. 11A shows a synthetic process for preparation of intermediate 10a.

CLAIMS

What is claimed is:

1. A compound, or pharmaceutically acceptable salt, solvate, triazole linkage regioisomer, mixture of triazole linkage regioisomers, or stereoisomer thereof,

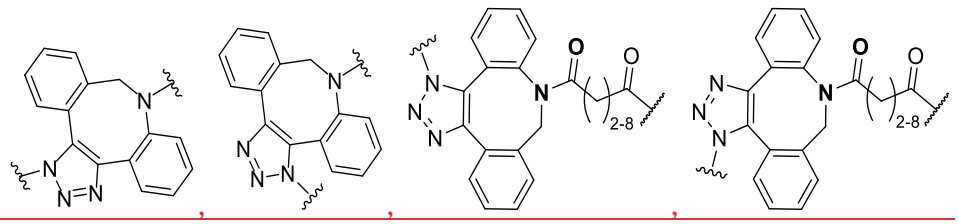
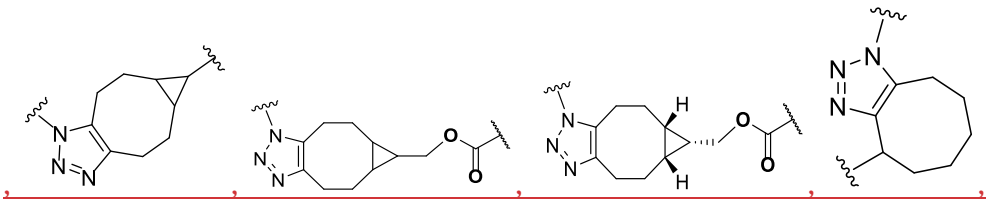
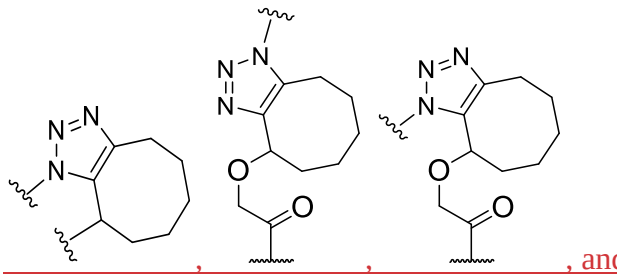
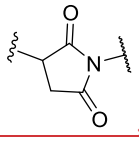
wherein the compound has a structure according to Formula (**IV**):



(**IV**)

wherein:

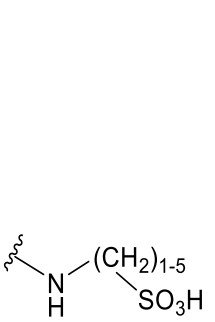
BA is an antibody or antigen binding fragment thereof~~a binding agent~~;

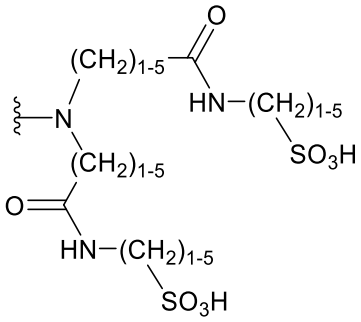
RG^1 and **RG^2** are reactive group residues independently selected from the group consisting of  ,  ,  , and  , wherein the  indicates

the atom through which the RG^1 or RG^2 is bonded to the adjacent groups in the formula;

SP[1] and **SP[2]** are independently, in each instance, absent, or a spacer group residue selected from the group consisting of C_{1-6}alkylene, -NH-, -C(O)-, -$(CH_2$-CH_2-$O)_e$, -NH-$(CH_2$-CH_2-$O)_e$-CH_2-CH_2-C(O)-, -C(O)-$(CH_2)_u$-C(O)-, -C(O)-NH-$(CH_2)_v$-, and combinations thereof wherein subscript e is an integer from 0 to 6, subscript u is an integer from 1 to 8, and subscript v is an integer from 1 to 8;

HG is a hydrophilic residue selected from



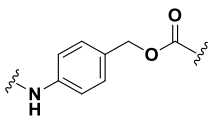
and


wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula;

PA is a payload residue;

AA[1] is ~~a trivalent linker comprising~~ an amino acid residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

AA[2] is a dipeptide, tripeptide, or tetrapeptide residue comprising amino acid residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

PAB is 

, wherein the  indicates the atom through which the **PAB** is bonded to the adjacent groups in the formula;

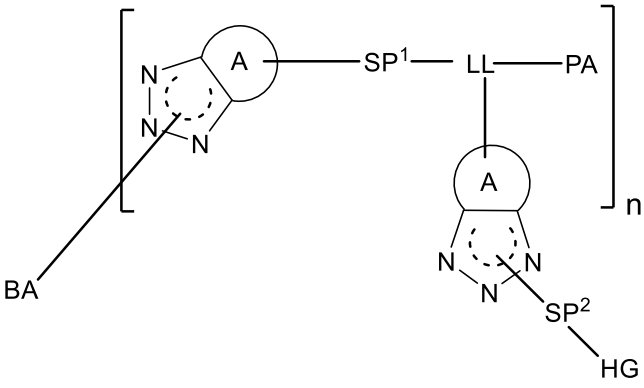
subscript **n** is an integer from 1 to 30;

subscript **p** is 0 or 1; and

subscript **q** is ~~0 or~~ 1~~.~~.

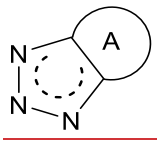
2. The compound of claim 1, wherein subscript **n** is 1, 2, 3 or 4.

3. The compound of claim 1, according to Formula (**III**):

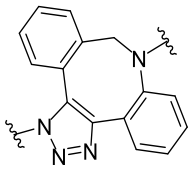


(**III**)

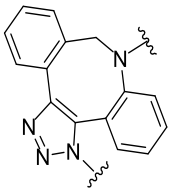
wherein



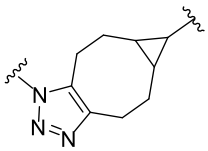
is selected from the group consisting of



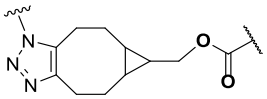
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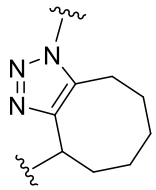
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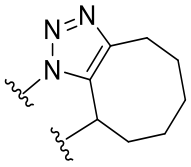
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,



, and

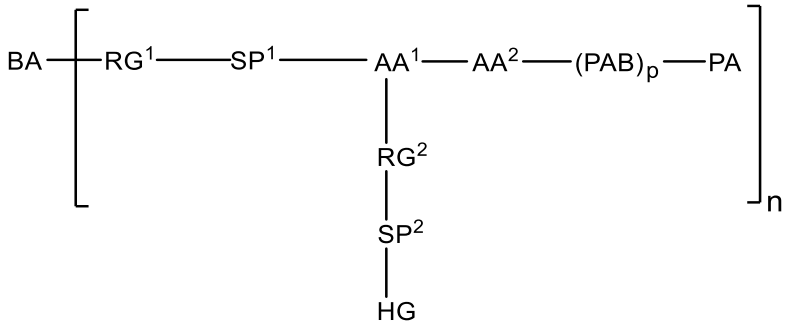


; and

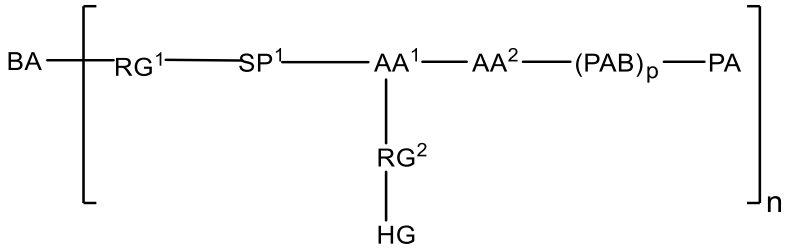
LL is –**AA**^{1}-**AA**^{2}-(**PAB**)$_{p}$-.

~~ring **A** is fused to the triazole and is selected from the group consisting of cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl; wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl are optionally substituted with alkyl, –OH, or –N**R**^{a}**R**^{b}, where each of **R**^{a} and **R**^{b} is alkyl or H.~~

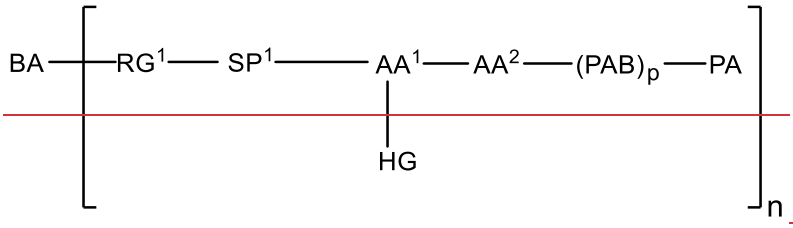
4. The compound of claim 1, according to Formula (**IVa**), or Formula (**IVb**) ~~or Formula (**IVc**)~~:



(IVa),



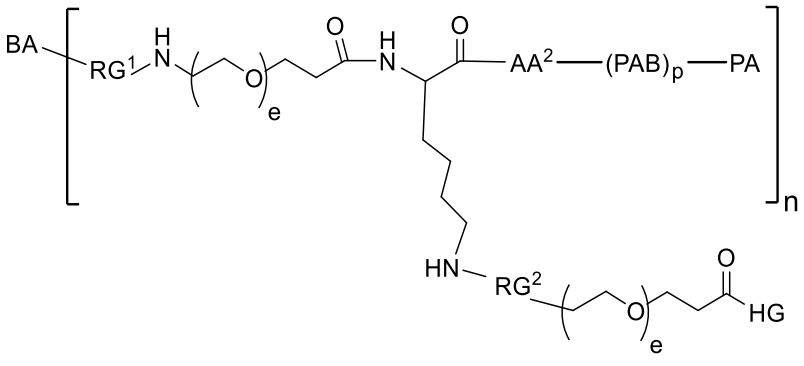
(IVb)~~,~~



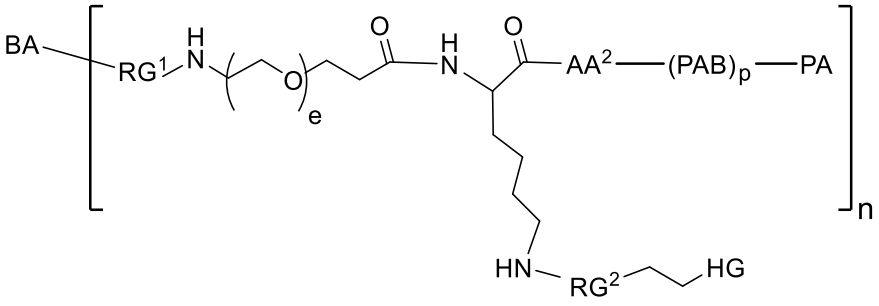
~~**(IVc).**~~

5. The compound of claim 4, wherein **AA^1** is a lysine, glutamine, glutamic acid, or aspartic acid residue.

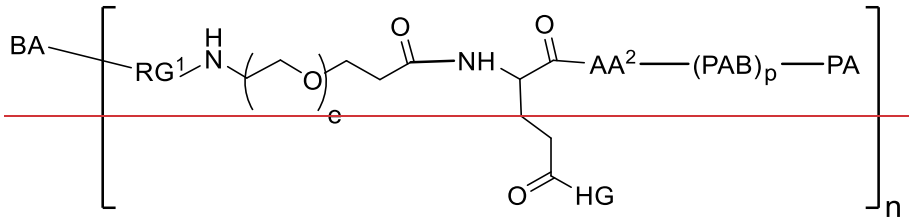
6. The compound of claim 4, according to Formula (**Va**), (**Vb**), ~~(**Vc**)~~ or (**Vd**) respectively:



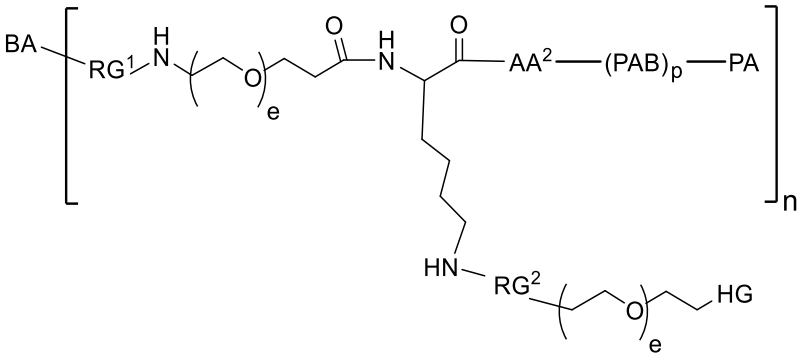
(Va),



(Vb),



~~**(Vc),**~~ or



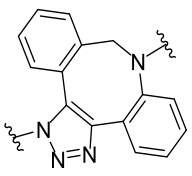
(Vd),

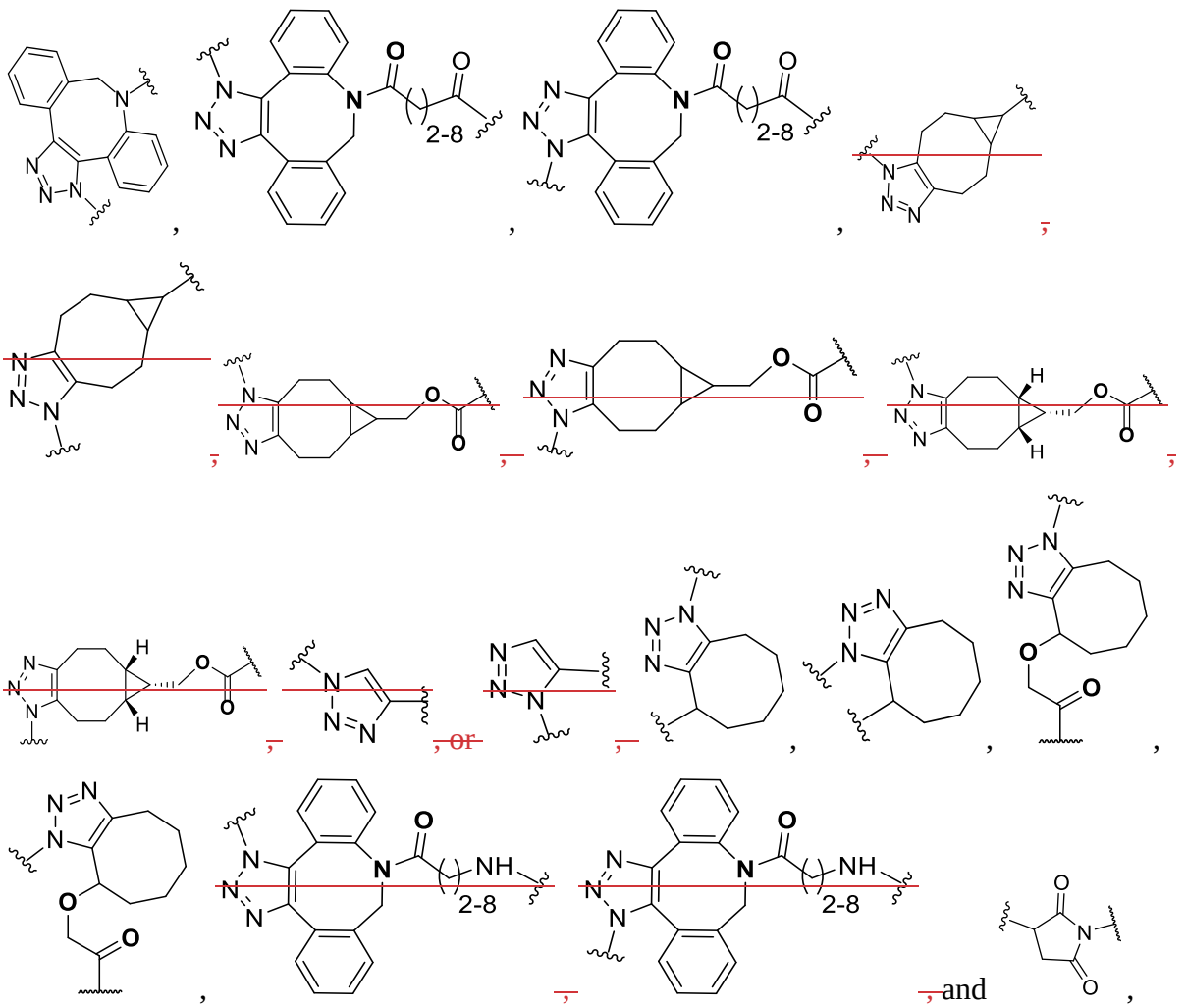
wherein:

subscript **e** is independently, in each instance, an integer from 0 to 6.

~~7. The compound of any one of claims 1 or 4-6, wherein **RG¹** and **RG²** are independently in each instance, a click chemistry residue.~~

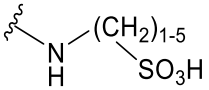
~~8. The compound of any one of claims 1 or 4-6, wherein **RG¹** and **RG²** independently in each instance, comprise a triazaole or a fused triazole.~~

~~9~~7. The compound of any one of claims 1 or 4-~~8~~6, wherein **RG¹** and **RG²** are independently, in each instance, selected from the group consisting of  ,



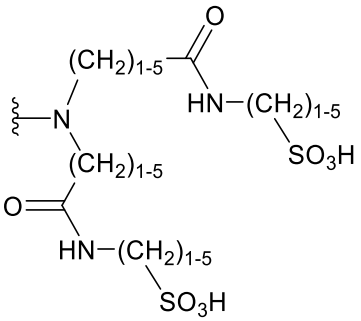
wherein the  indicates the atom through which the **RG**^{1} or **RG**^{2} is bonded to the adjacent groups in the formula.

~~108~~. The compound of any one of claims 1 or 4-~~97~~, wherein **HG** is



wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

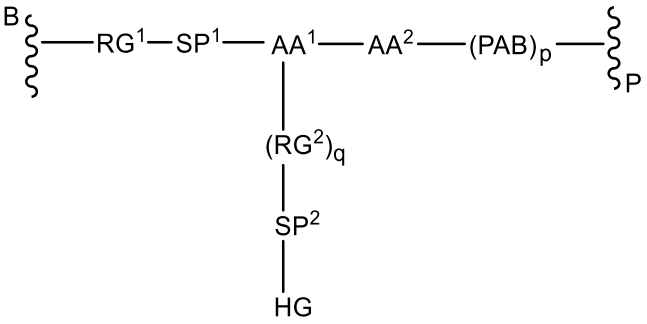
~~11~~9. The compound of any one of claims 1 or 4-~~9~~7, wherein **HG** is



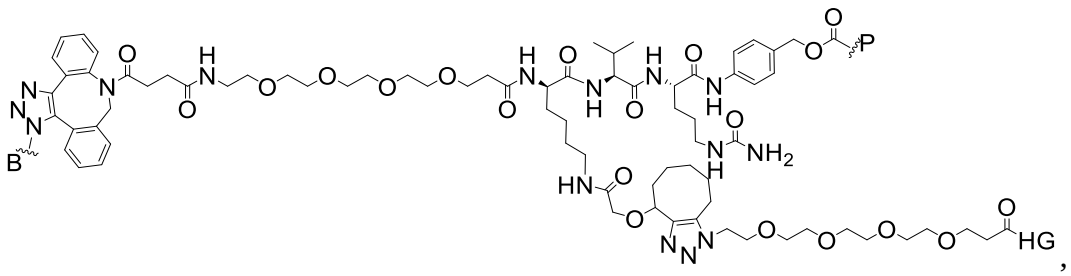
, wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

~~12~~10. The compound of any one of claims 1, 4-5, and 7-~~11~~9, wherein **SP^1** and **SP^2** are independently, in each instance, absent, or selected from the group consisting of ~~C_{1-6} alkylene, -NH-, -C(O)-, (-CH$_2$-CH$_2$-O)$_e$-~~(-CH$_2$-CH$_2$-O)$_e$ and -NH-CH$_2$-CH$_2$-(-O-CH$_2$-CH$_2$)$_e$-C(O)-~~, -C(O)-(CH$_2$)$_u$-C(O)-, -C(O)-NH-(CH$_2$)$_v$-, (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~~.

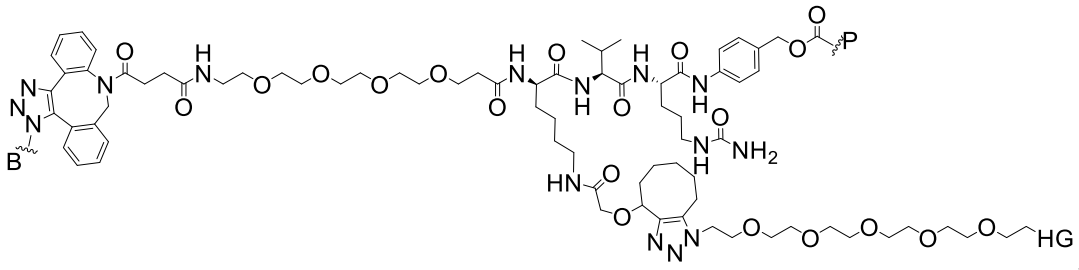
~~13~~11. The compound claim 1, wherein



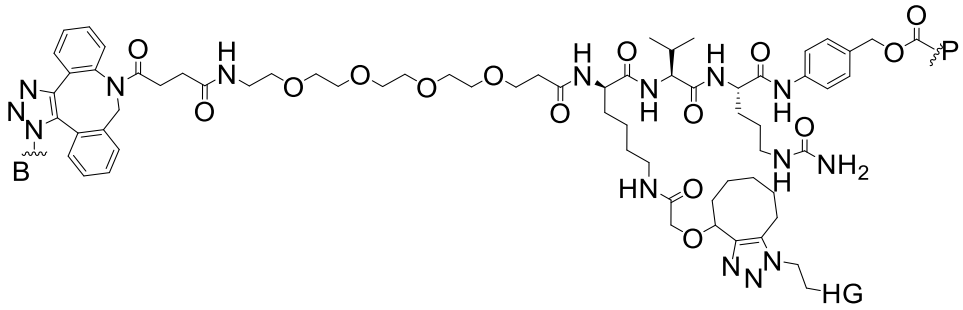
is selected from the group consisting of:



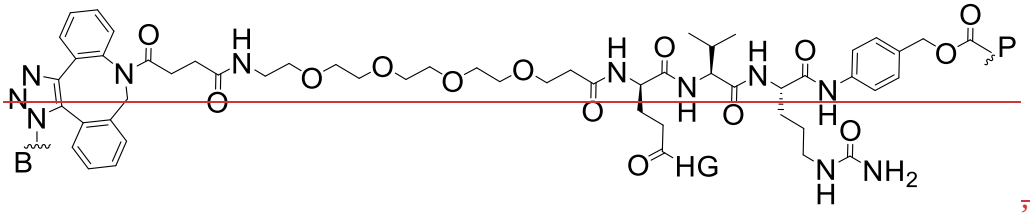
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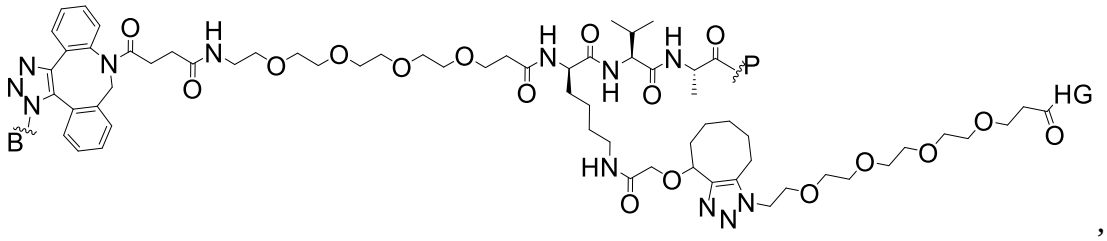
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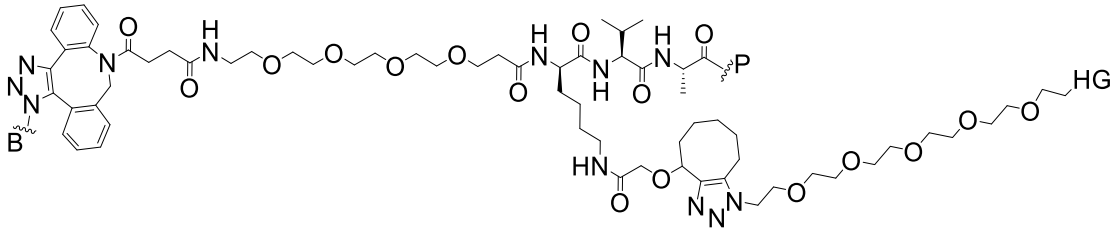
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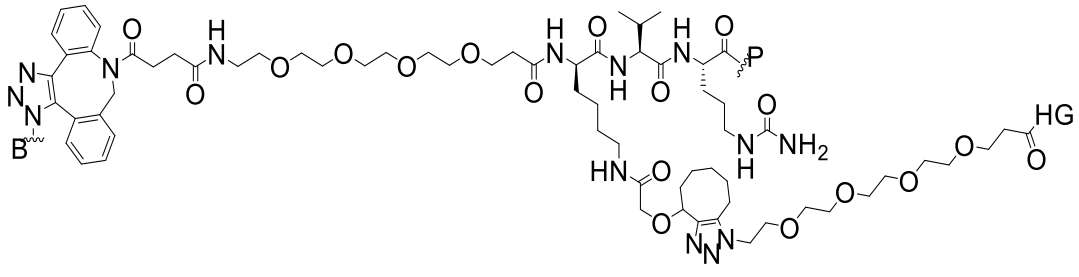
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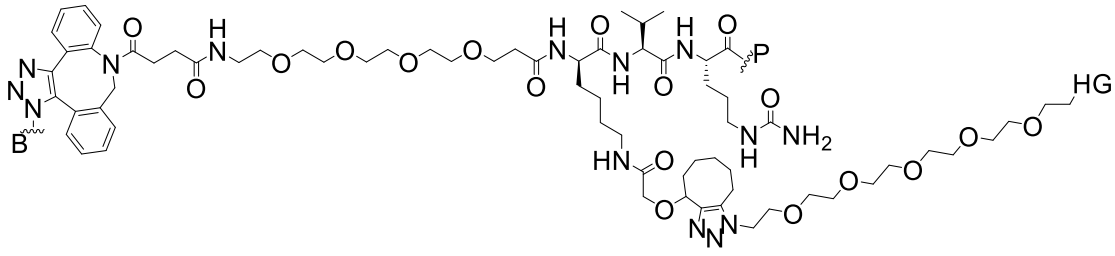
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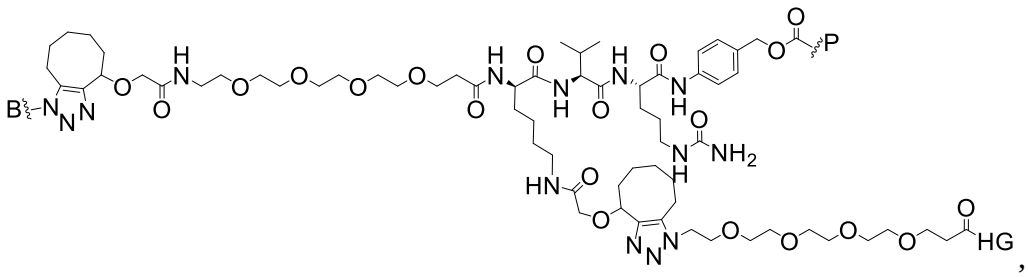
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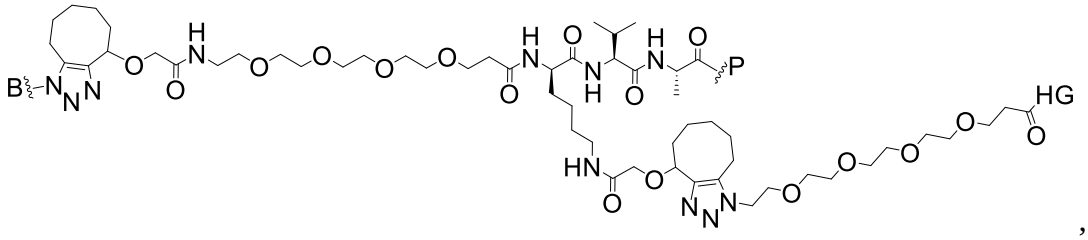
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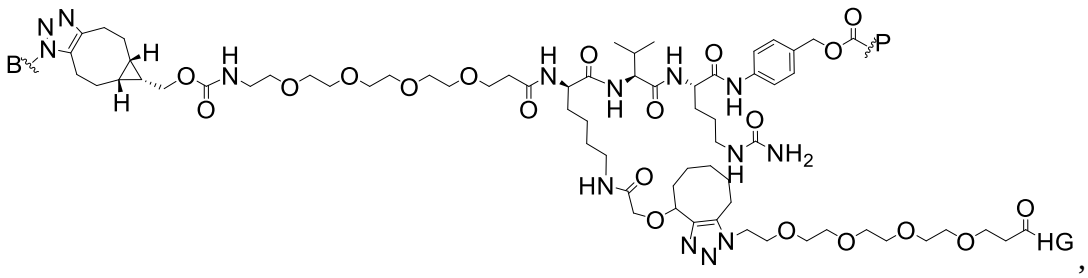
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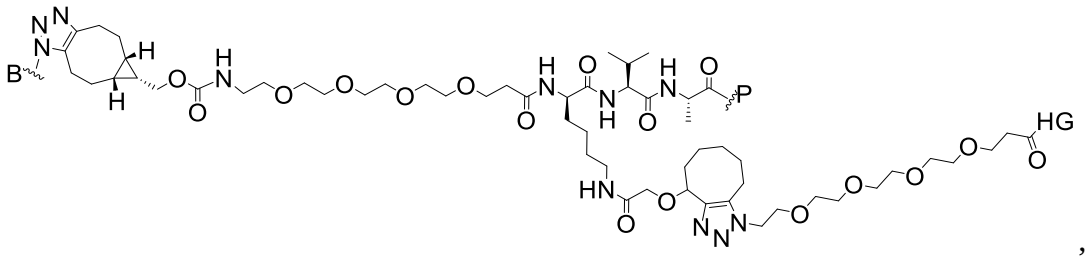


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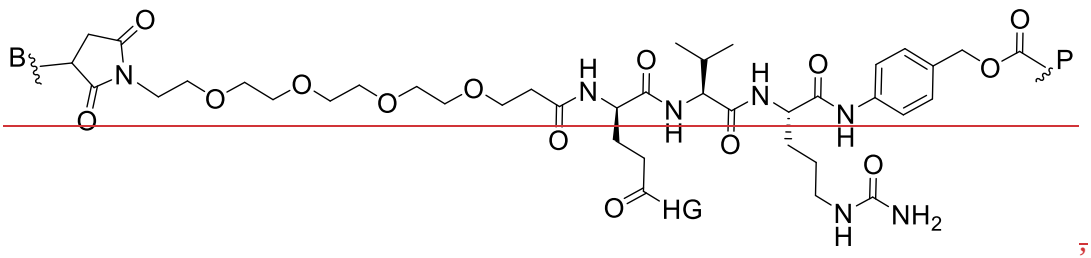


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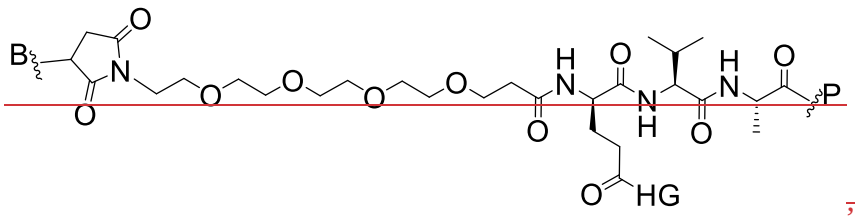


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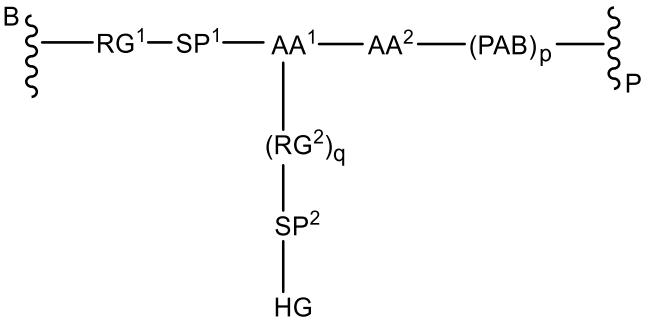
;

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

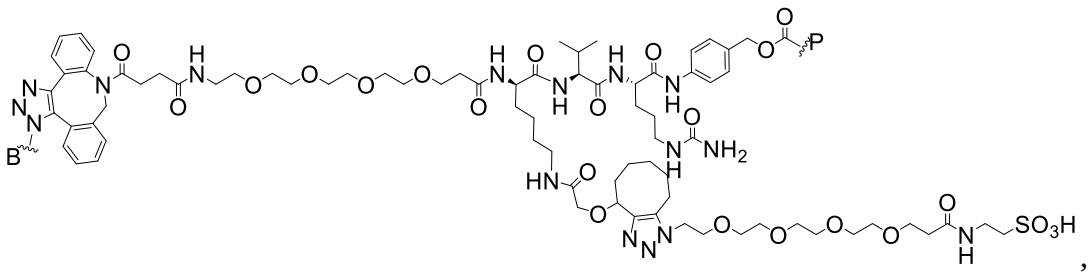
each  is a bond to the antibody or antigen binding fragment thereof~~binding agent~~; and

each  is a bond to the payload residue.

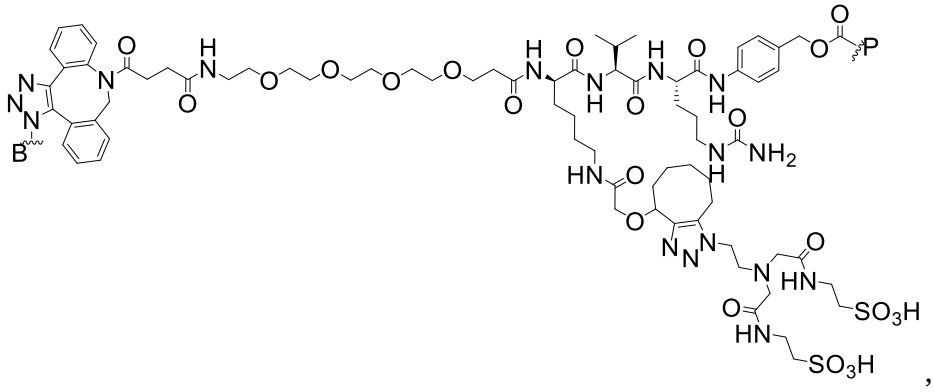
~~14~~12. The compound of claim 1, wherein



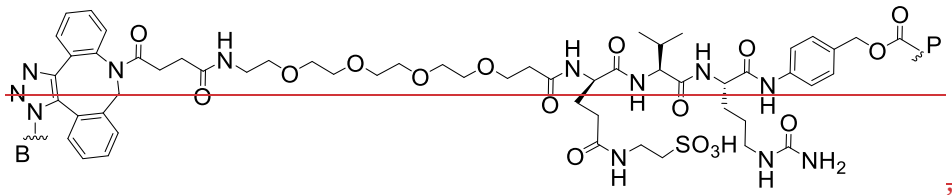
is selected from the group consisting of:



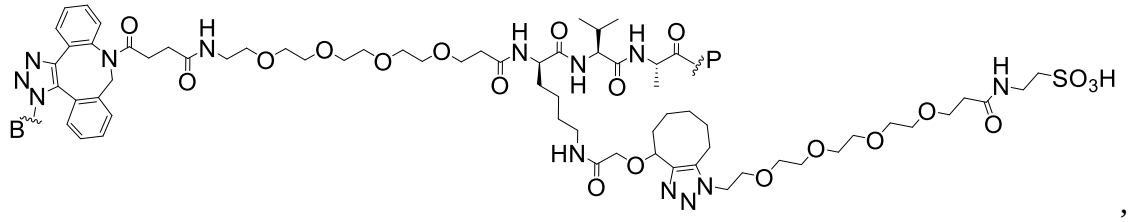
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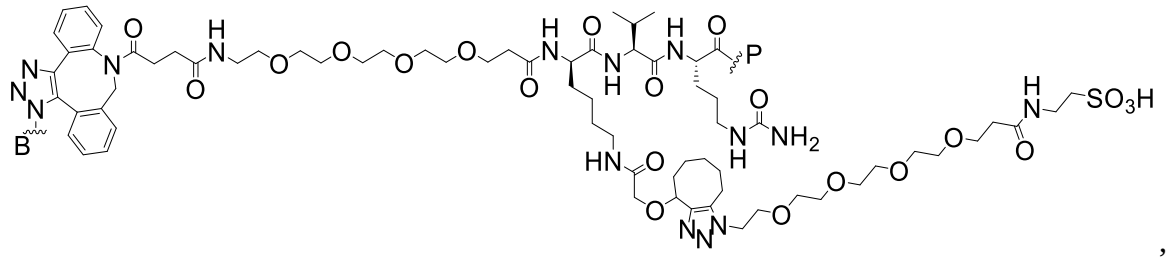


~~, and~~



,

and



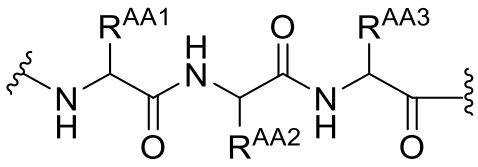
,

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

each  is a bond to the antibody or antigen binding fragment thereof~~binding agent~~; and

each  is a bond to the payload residue.

~~15~~13. The compound of claim 3, wherein **LL** is according to Formula (**LL1**):

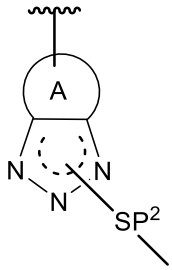


(LL1)

wherein $\mathbf{R^{AA1}}$ is an amino acid sidechain residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline,

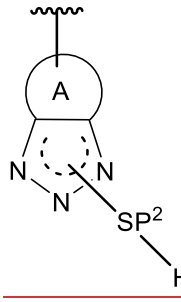
$\mathbf{R^{AA2}}$, and $\mathbf{R^{AA3}}$ are each, independently, amino acid side chain~~s~~ residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine,

proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline; and~~,~~



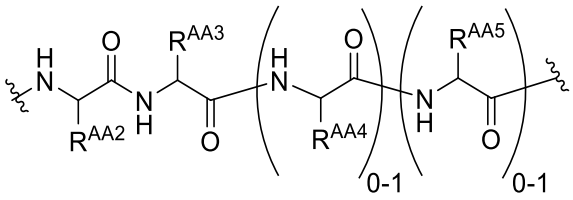
R^AA1 ~~at least one of which~~ is bonded directly ~~or indirectly~~ to ~~–~~ ~~**(RG²)q SP² HG**~~.~~

~~16~~14. The compound of claim ~~15~~13, wherein **R^AA1** is a lysine, glutamine, glutamic acid or aspartic acid side chain residue bonded directly ~~or indirectly~~ to



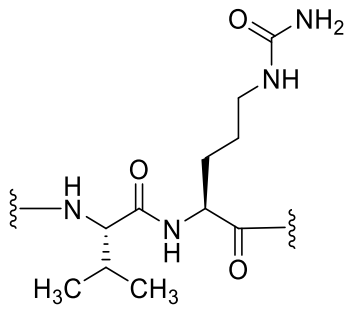
~~**HG**~~, and **R^AA2** and **R^AA3** are either valine and alanine or valine and citrulline sidechain~~s~~ residues respectively.

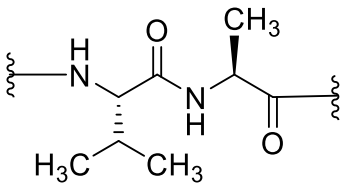
~~17~~15. The compound of any one of claims 1 or 4-6, wherein **AA²** is



wherein **R^AA2**, **R^AA3**, **R^AA4**, and **R^AA5** are each, independently, amino acid side chains selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline, ~~at least one of which is bonded directly or indirectly to **(RG²)q SP² HG**,~~ wherein the  indicates the atom through which **AA²** is bonded to the adjacent groups in the formula.

~~18~~16. The compound of any one of claims 1 or 4-6, wherein **AA²** is



or


,

wherein the  indicates the atom through which **AA²** is bonded to the adjacent groups in the formula.

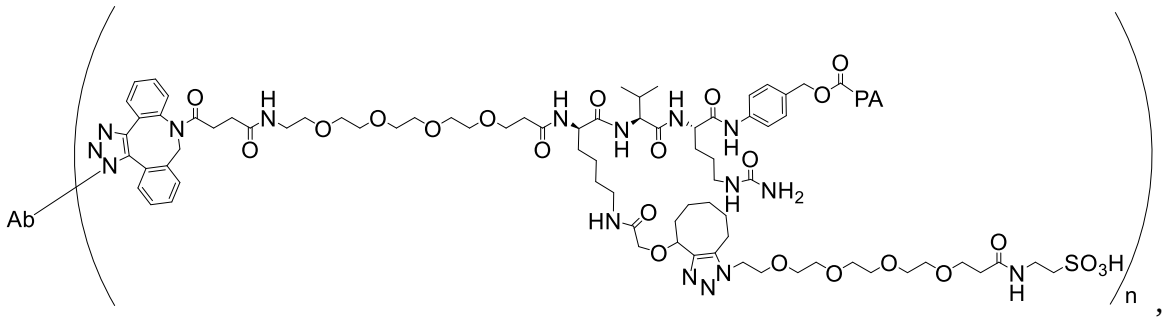
~~19~~17. The compound of any one of claims 6-~~12~~10, wherein subscript e is 4.

~~20~~18. The compound of any one of claims 1-~~19~~17, wherein ~~the binding agent (~~**BA**~~)~~ is an antibody ~~or antigen-binding fragment thereof~~.

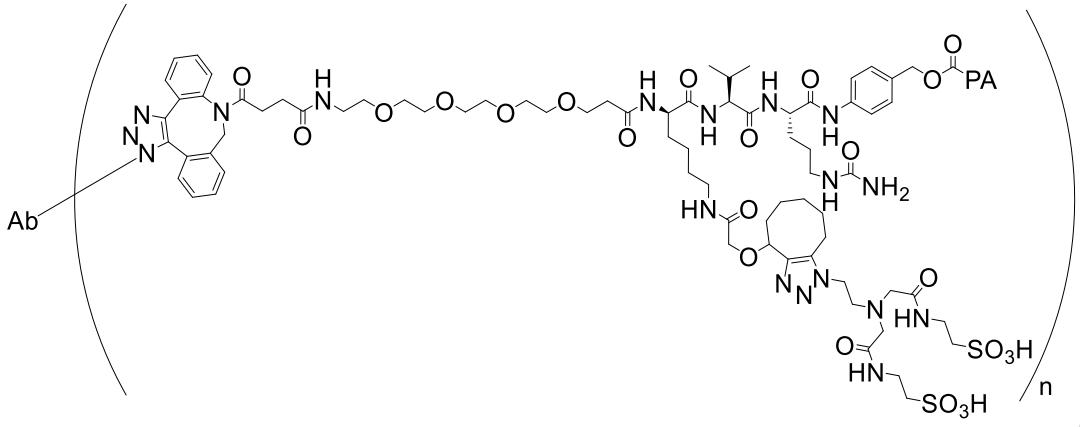
~~21~~19. The compound of any one of claims 1-~~19~~17, wherein ~~the binding agent (~~**BA**~~)~~ is an antibody, or an antigen-binding fragment thereof, selective for an antigen selected from the group consisting of AXL, BAFFR, BCMA, BCR-list components, BDCA2, BDCA4, BTLA, BTNL2, BTNL3, BTNL8, BTNL9, C10 or f54, CCR1, CCR3, CCR4, CCR5, CCR6, CCR7, CCR9, CCR10, CD11c, CD137, CD138, CD14, CD168, CD177, CD19, CD20, CD209, CD209L, CD22, CD226, CD248, CD25, CD27, CD274, CD276, CD28, CD30, CD300A, CD33, CD37, CD38, CD4, CD40, CD44, CD45, CD46, CD48, CD5, CD52, CD55, CD56, CD59, CD62E, CD68, CD69, CD70, CD74, CD79a, CD79b, CD8, CD80, CD86, CD90.2, CD96, CLEC12A, CLEC12B, CLEC7A, CLEC9A, CR1, CR3, CRTAM, CSF1R, CTLA4, CXCR1/2, CXCR4, CXCR5, DDR1, DDR2, DEC-205, DLL4, DR6, FAP, FCamR, FCMR, FcR's, Fire, GITR, HHLA2, HLA class II, HVEM, ICOSLG, IFNLR1, IL10R1, IL10R2, IL12R, IL13RA1, IL13RA2, IL15R, IL17RA, IL17RB, IL17RC, IL17RE, IL20R1, IL20R2, IL21R, IL22R1, IL22RA, IL23R, IL27R, IL29R, IL2Rg, IL31R, IL36R, IL3RA, IL4R, IL6R, IL5R, IL7R, IL9R, Integrins, LAG3, LIFR, MAG/Siglec-4, MMR, MSR1, NCR3LG1, NKG2D, NKp30, NKp46, PDCD1, PROKR1, PVR, PVRIG, PVRL2, PVRL3, RELT, SIGIRR, Siglec-1, Siglec-10, Siglec-5, Siglec-6, Siglec-7, Siglec-8, Siglec-9, SIRPA, SLAMF7, TACI, TCR-list components/assoc, PTCRA, TCRb, CD3z, CD3, TEK, TGFBR1, TGFBR2, TGFBR3, TIGIT, TLR2, TLR4, TROY, TSLPR, TYRO, VLDLR, VSIG4, and VTCN1.

~~22~~20. The compound of any one of claims 1-~~21~~19, wherein **PA** is the residue of a group selected from the group consisting of a dolastatin, an auristatin, a maytansinoid, a plant alkaloid, a taxane, a vinca alkaloid, a steroid, and a liver X receptor (LXR) modulator.

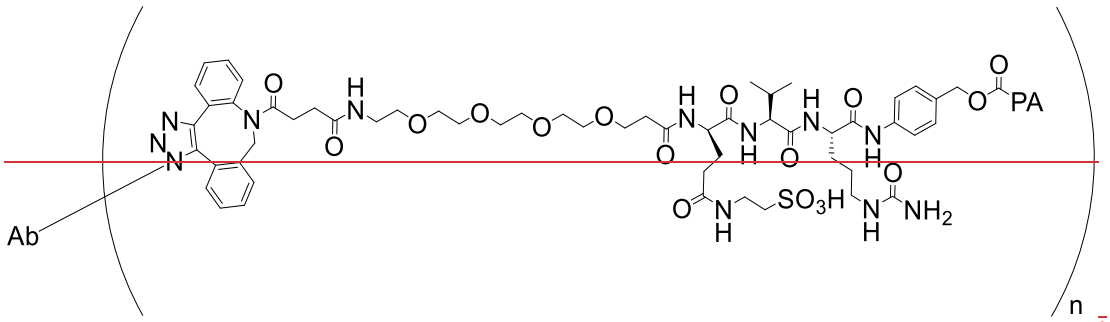
~~23~~21. The compound of any one of claims 1 and ~~20~~18-~~22~~20, selected from the group consisting of:



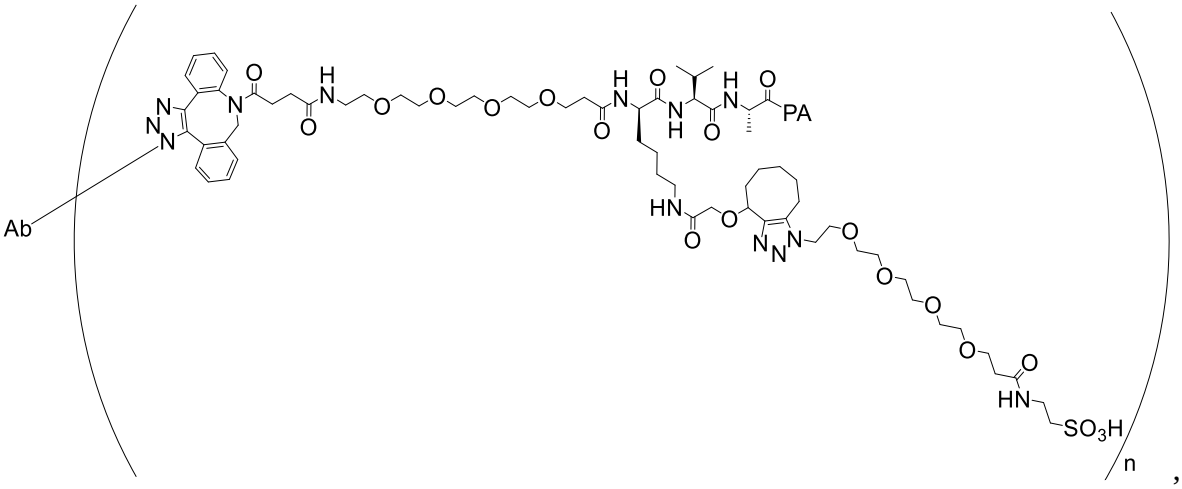
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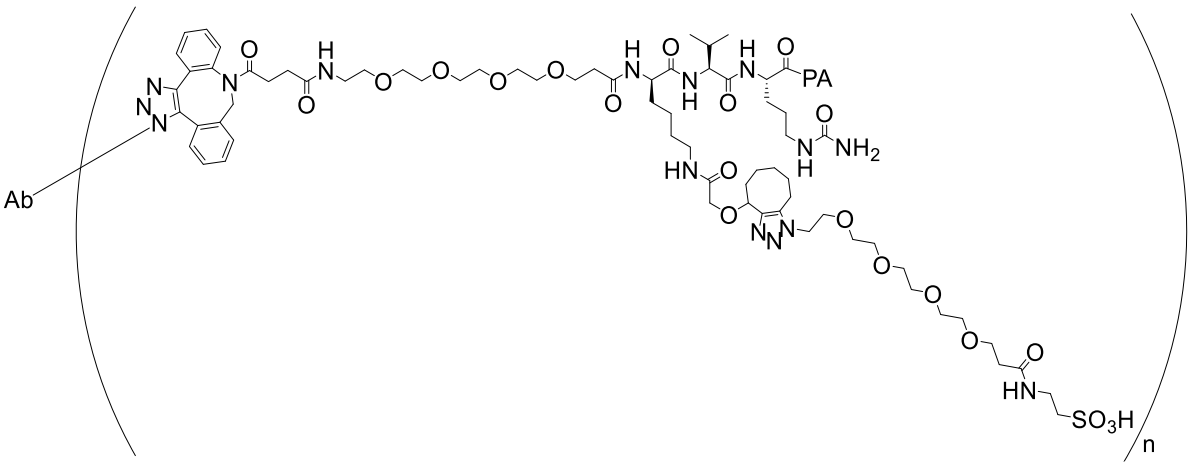
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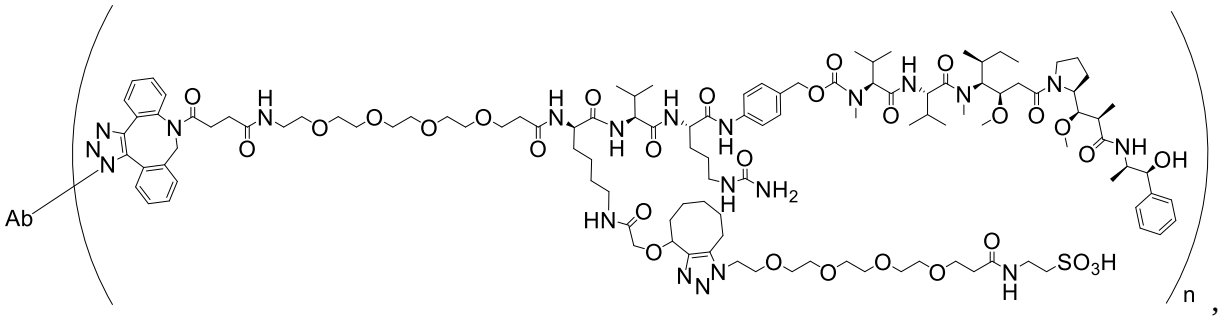
or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof, wherein

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

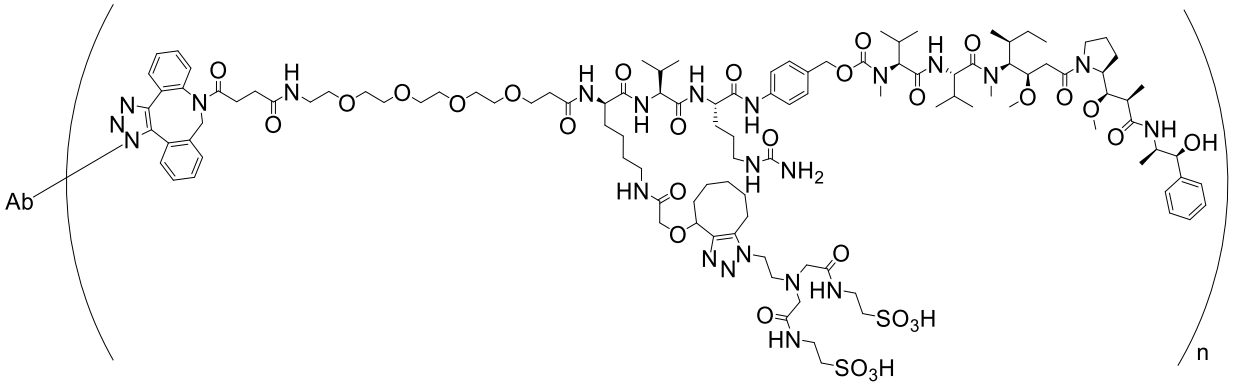
PA is a payload residue; and

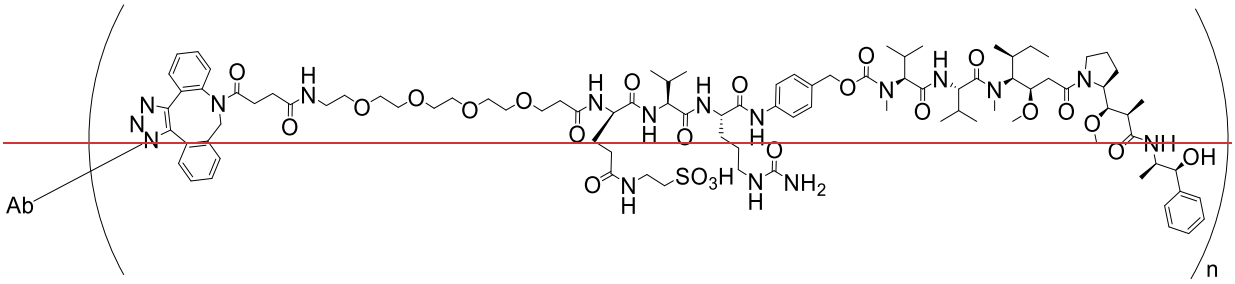
subscript **n** is an integer from 1 to 30.

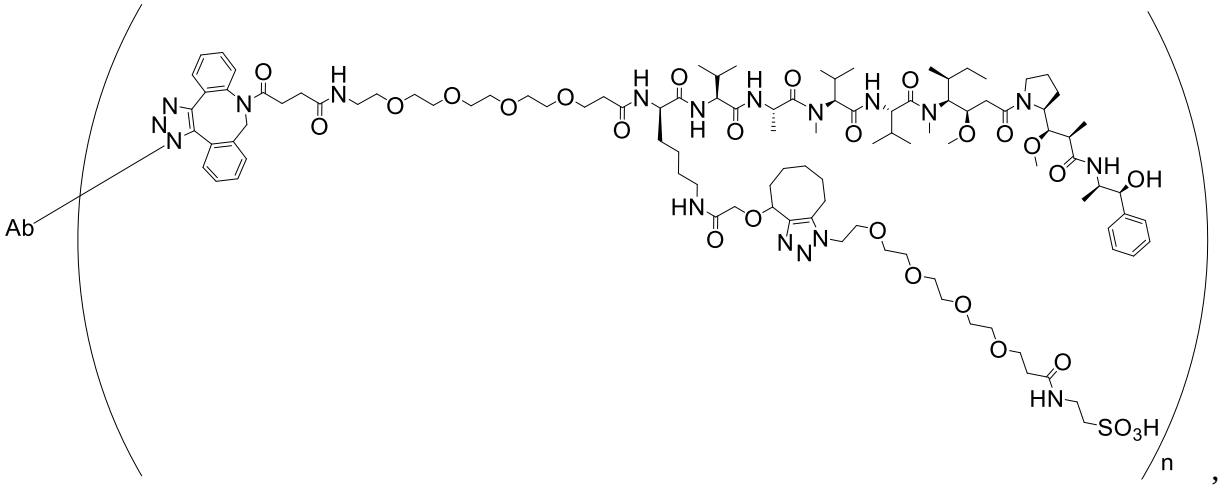
~~24~~22. The compound of any one of claims 1 and ~~20~~18-~~21~~20, selected from the group consisting of:


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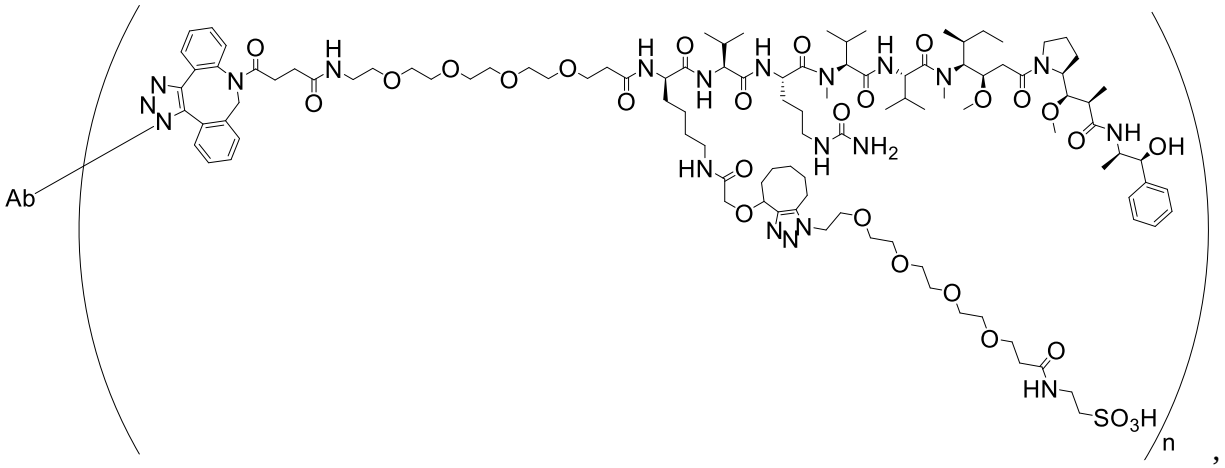
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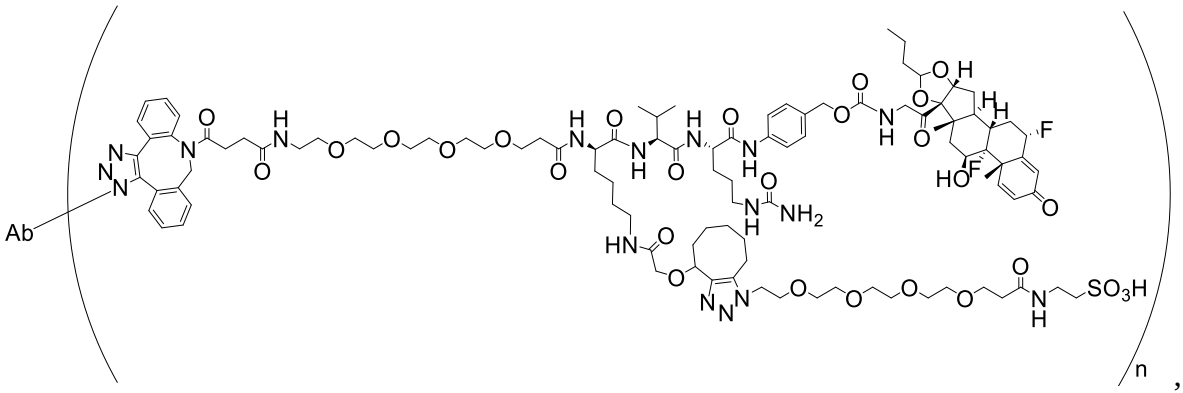

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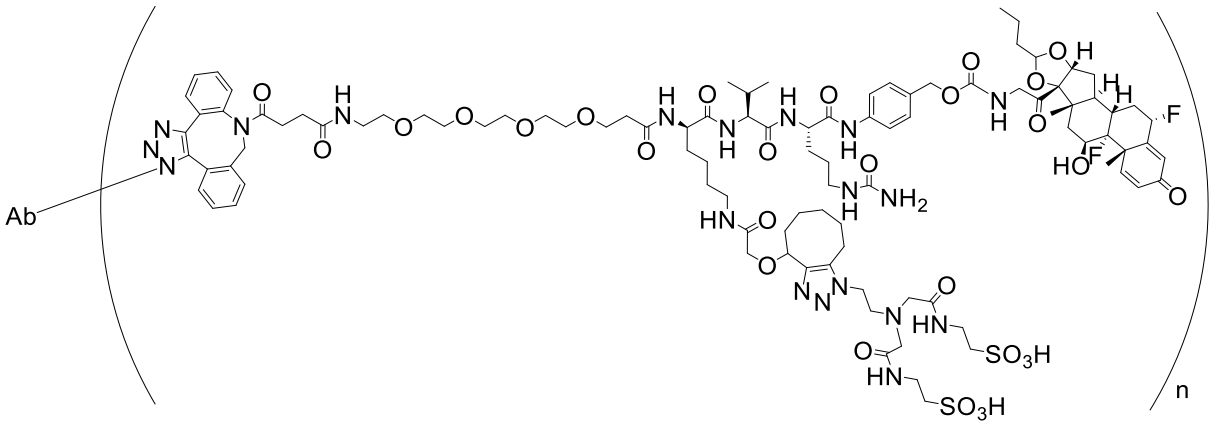
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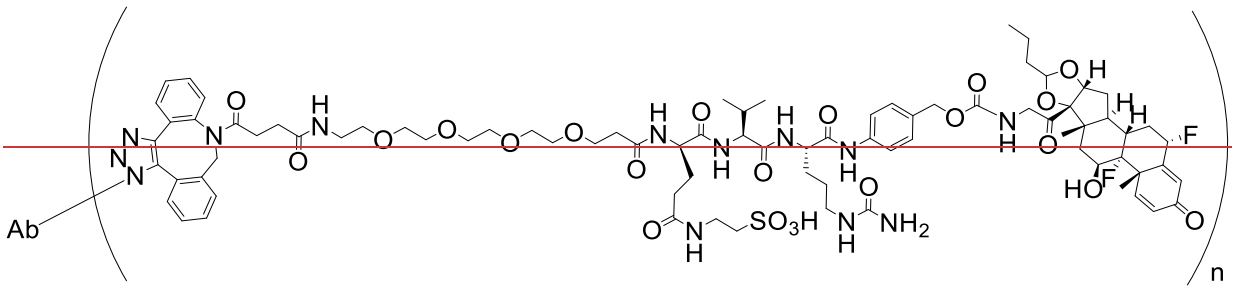
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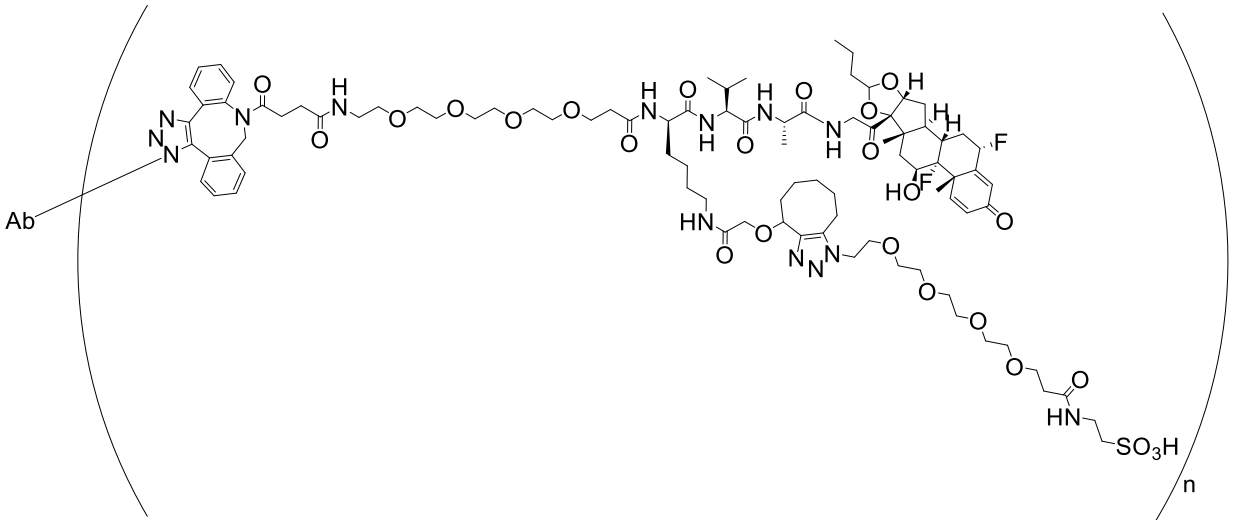


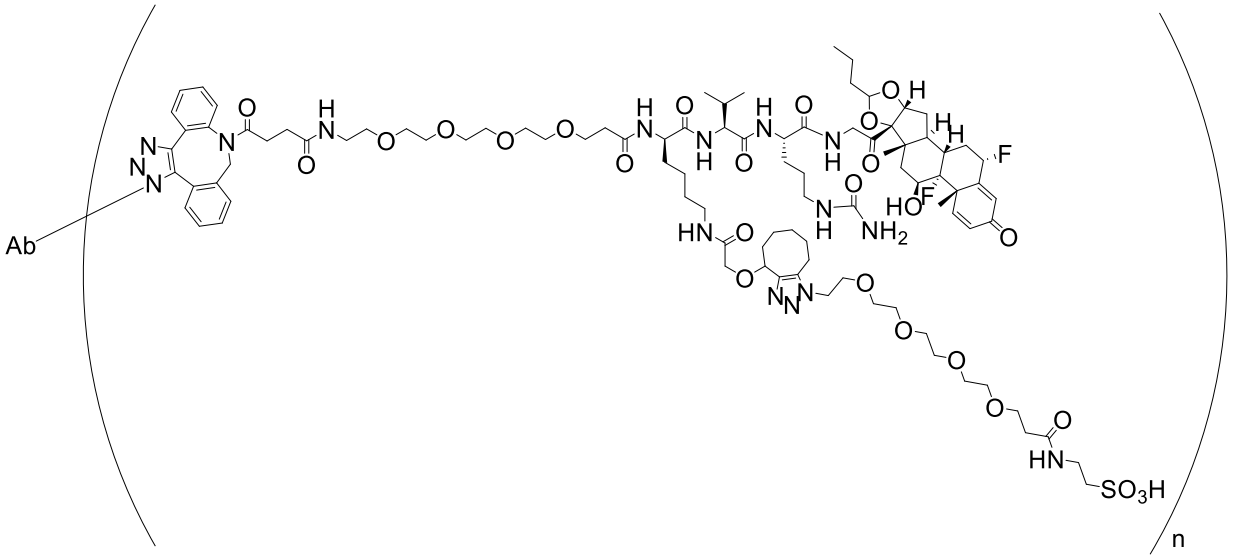
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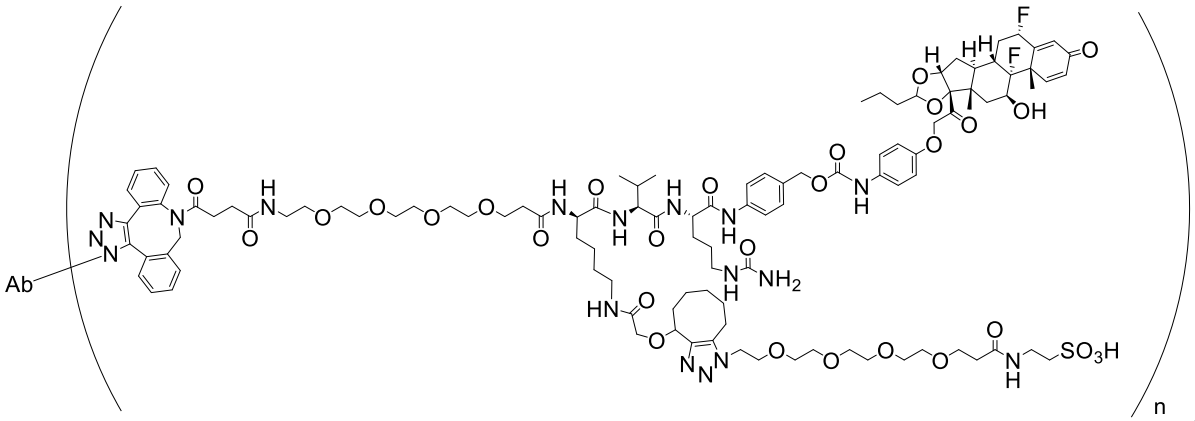


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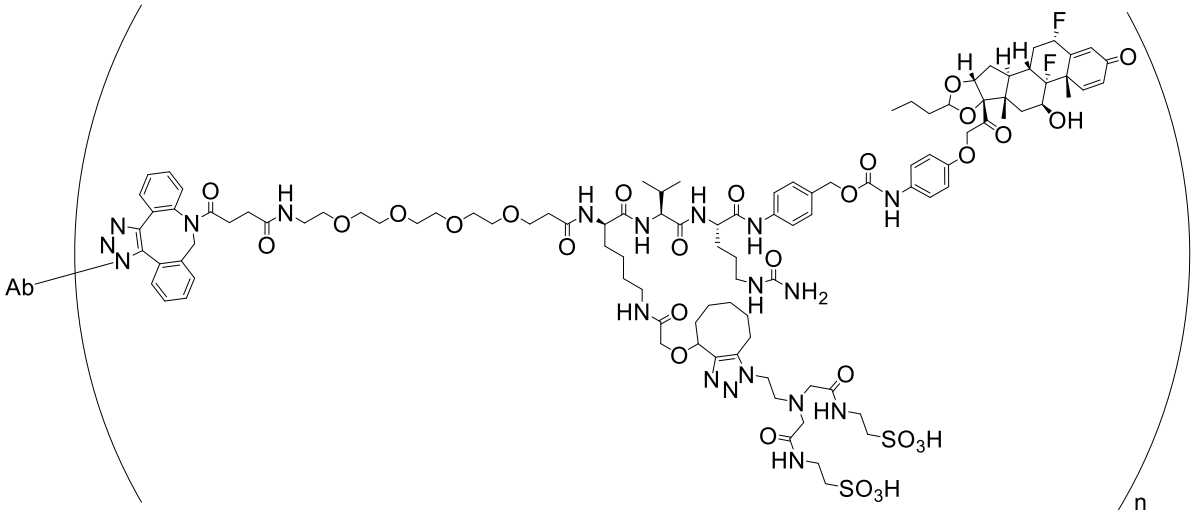


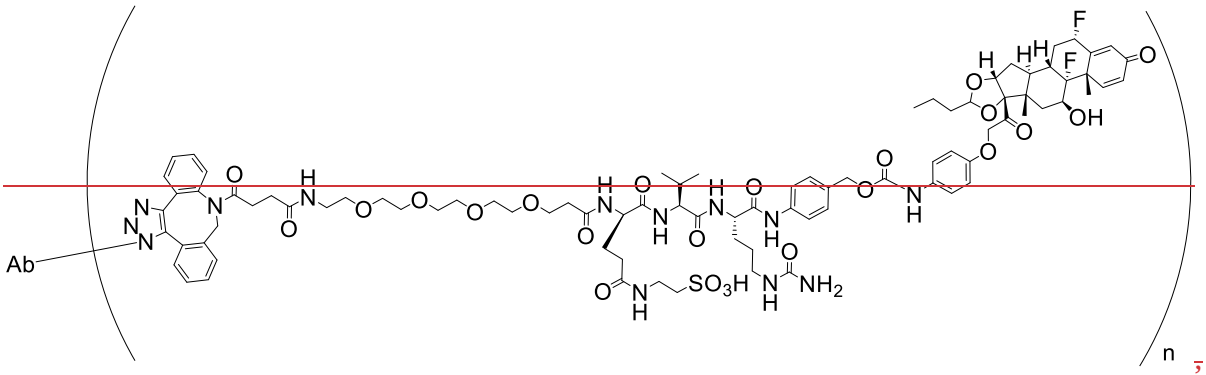


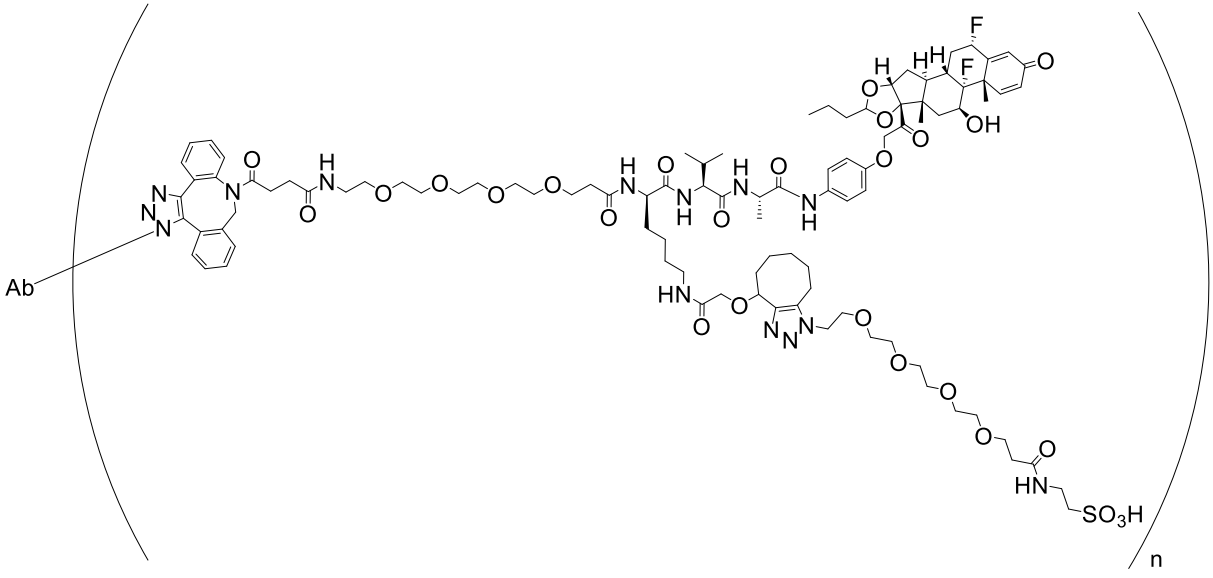


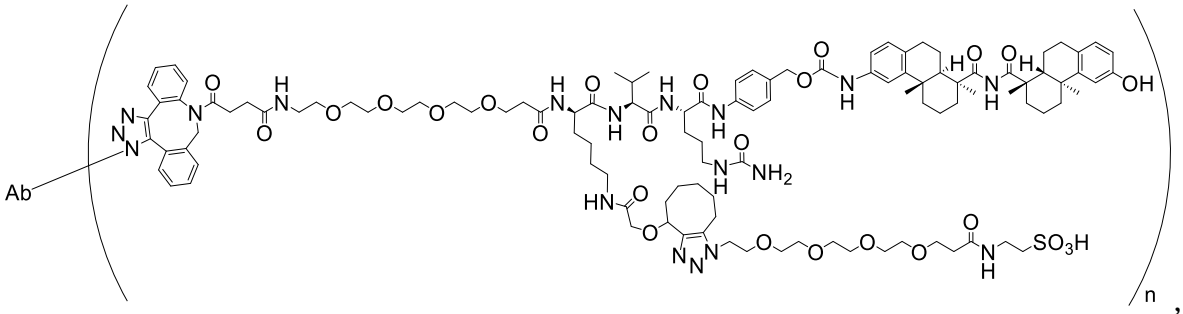


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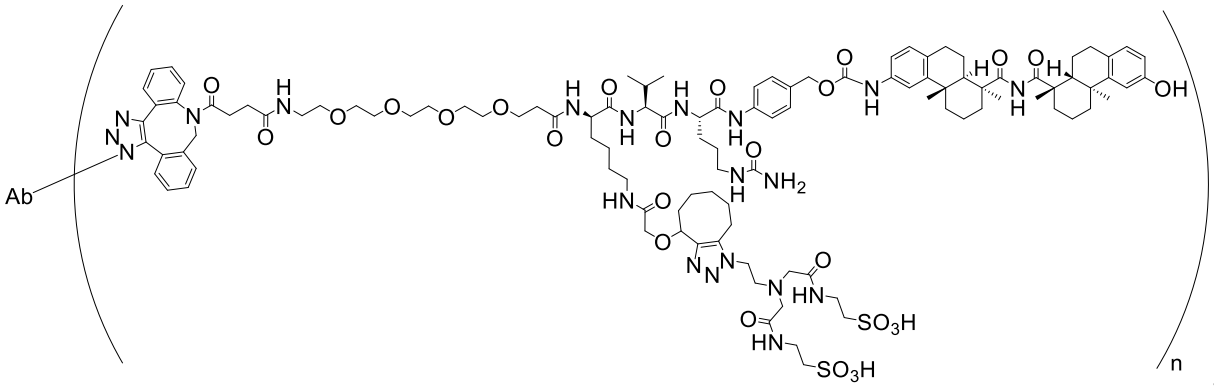




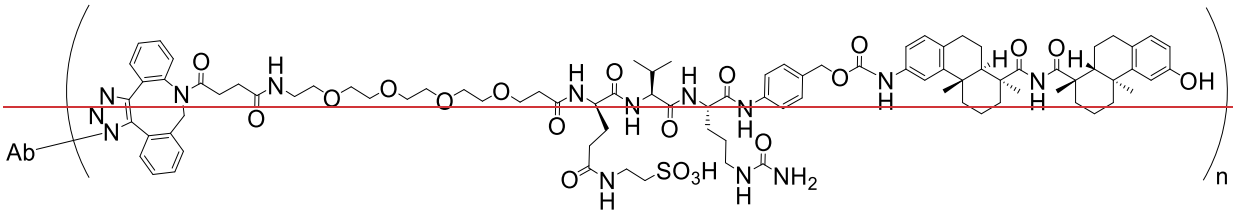


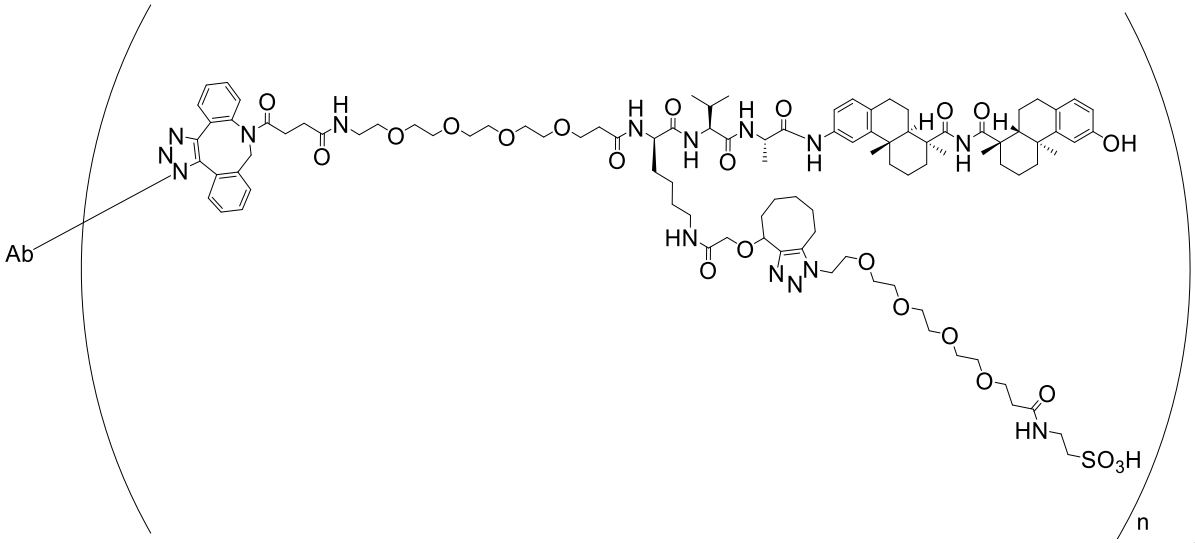

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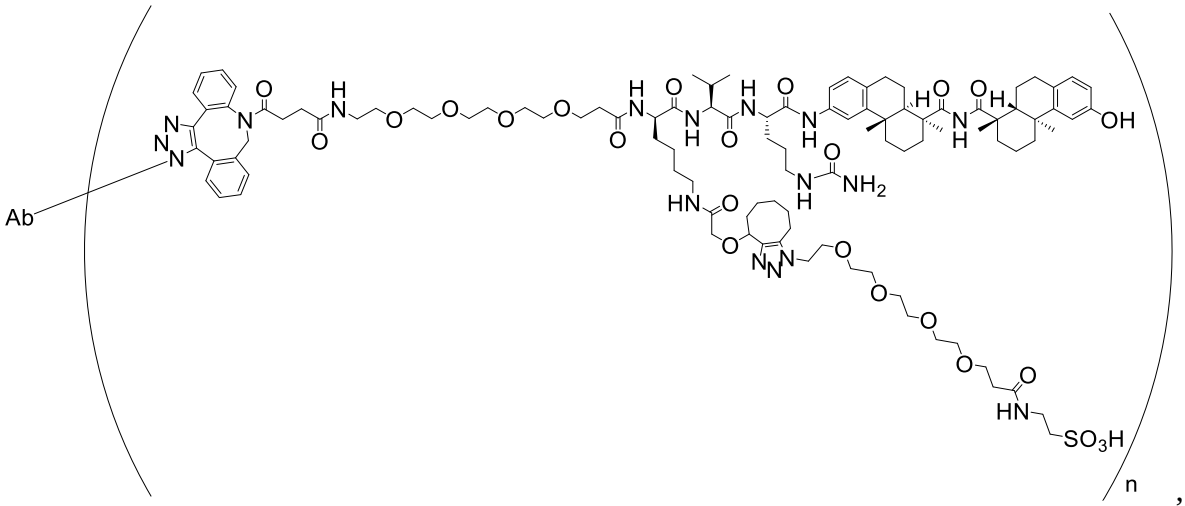

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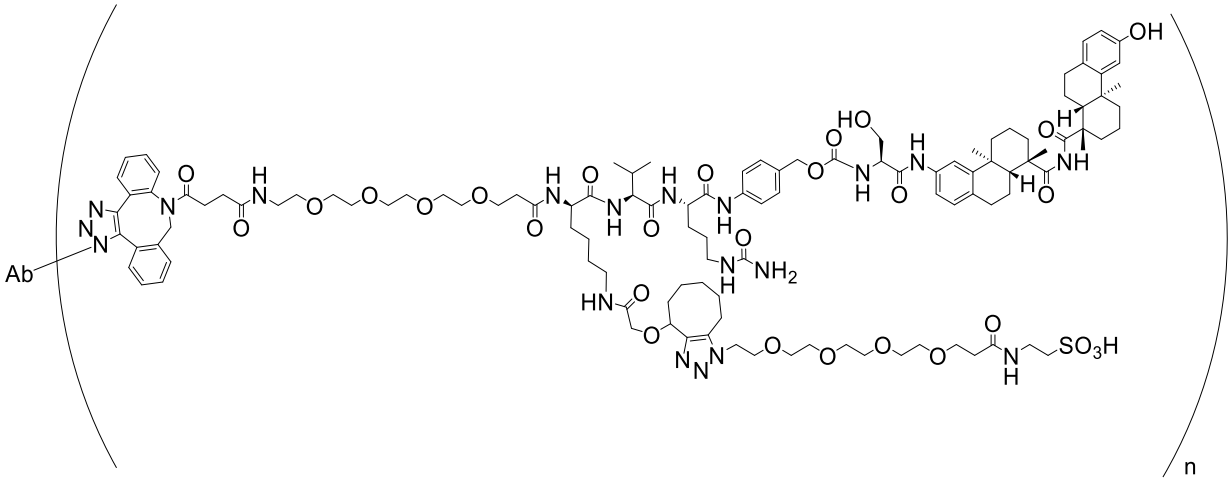

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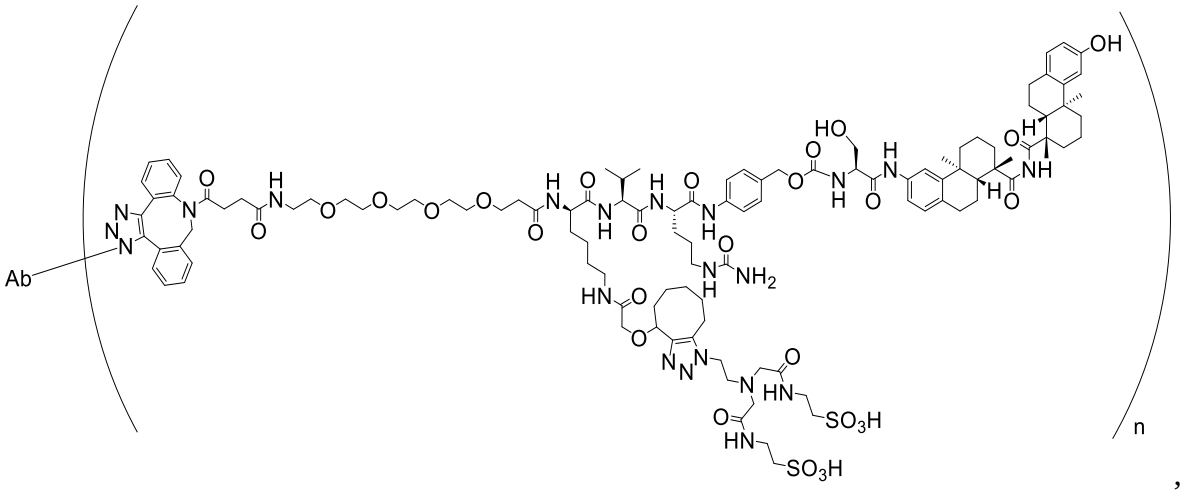

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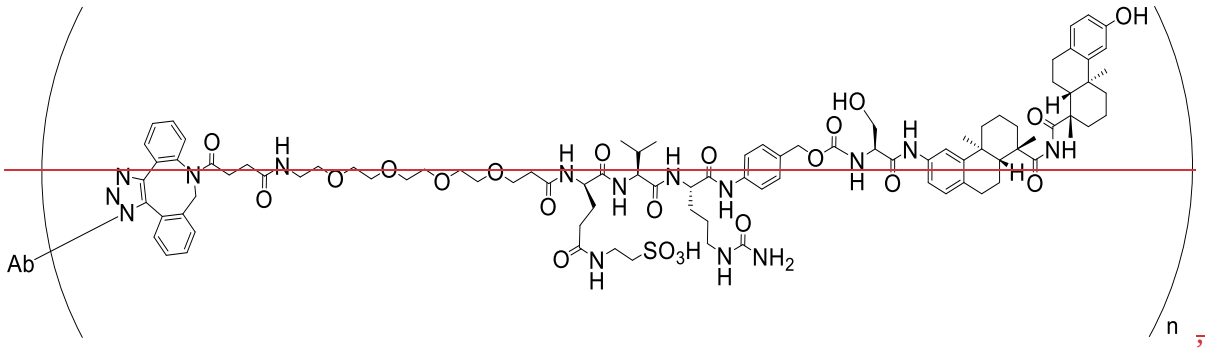

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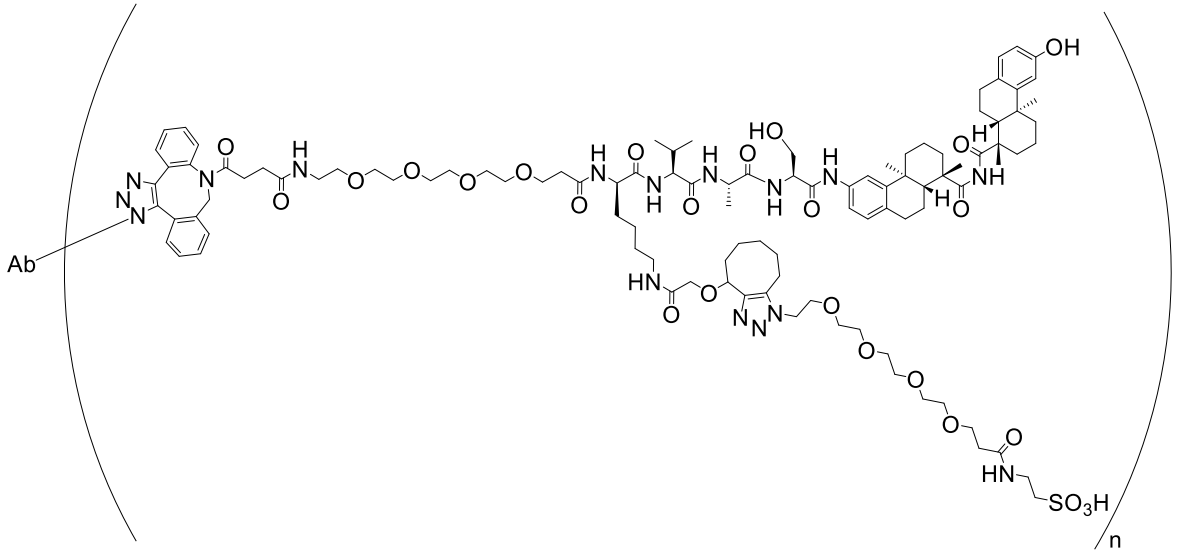

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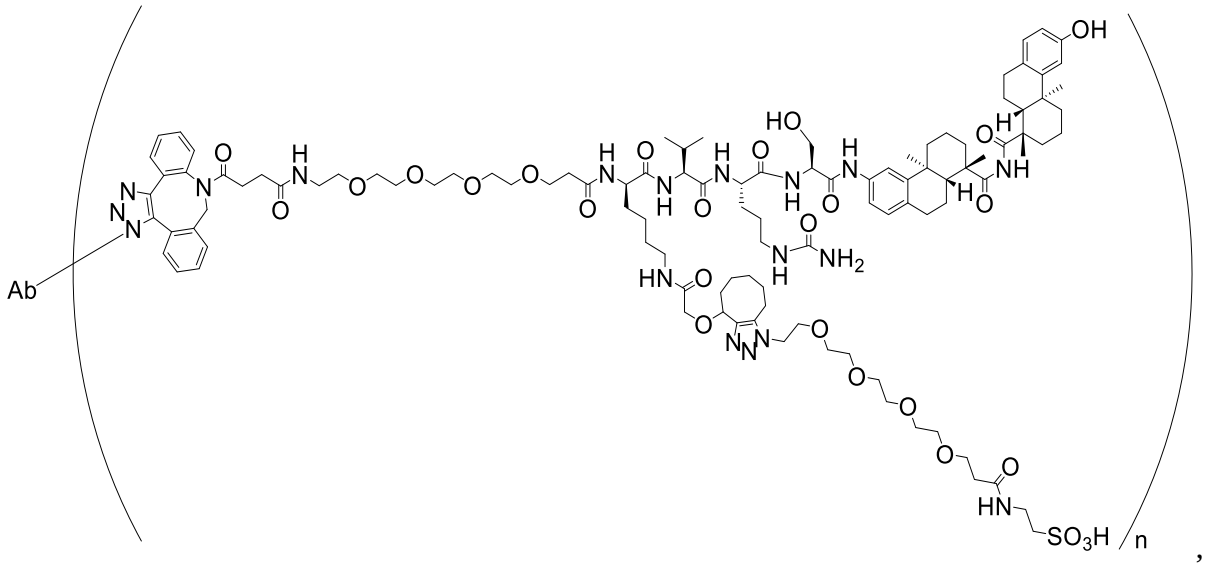


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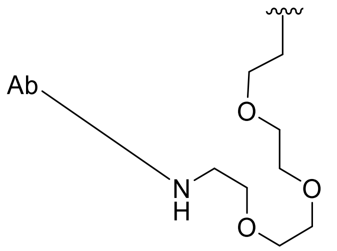
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or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof, wherein

each **Ab** is ~~an~~ the antibody, or an antigen-binding fragment thereof; and

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

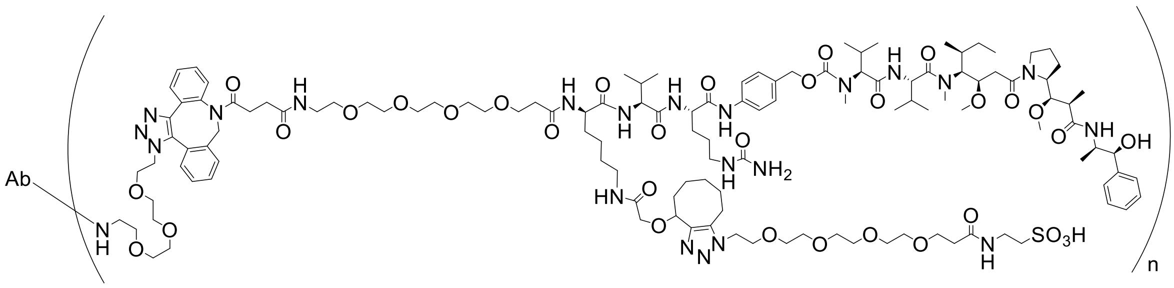
~~25~~23. The compound of any one of claims 1-~~24~~22, wherein **BA** is a modified antibody of formula (**Ab-1**)



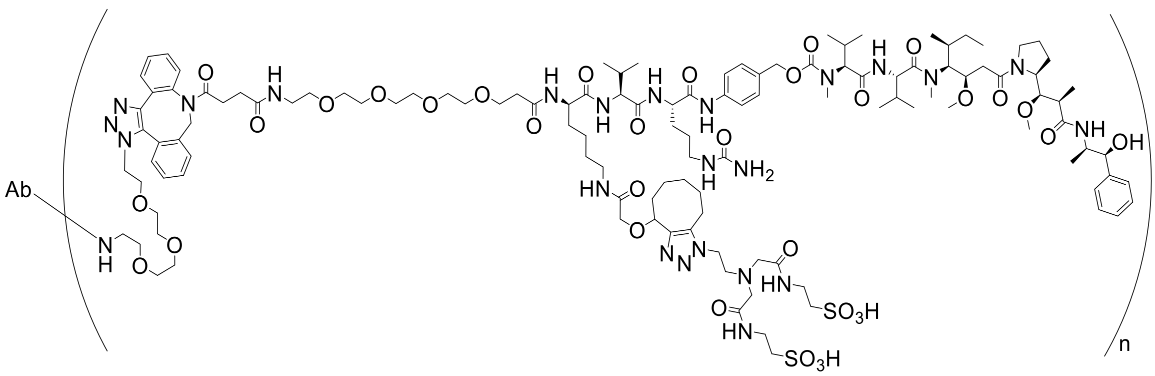
(**Ab-1**)

wherein the  indicates the atom through which **Ab-1** is bonded to the adjacent groups in the formula.

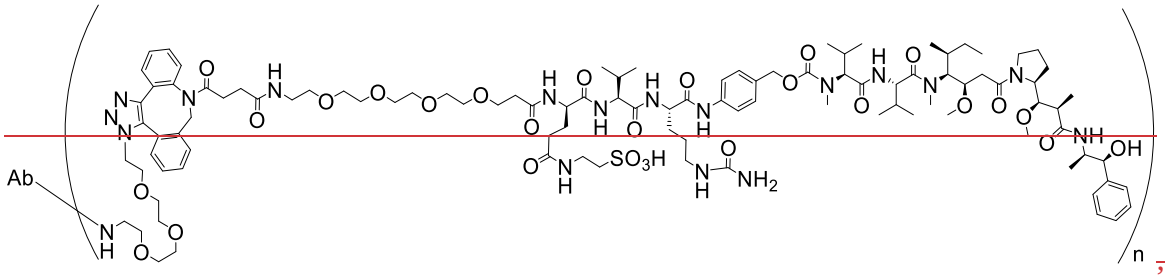
~~26~~24. The compound of claim ~~25~~1, selected from the group consisting of:

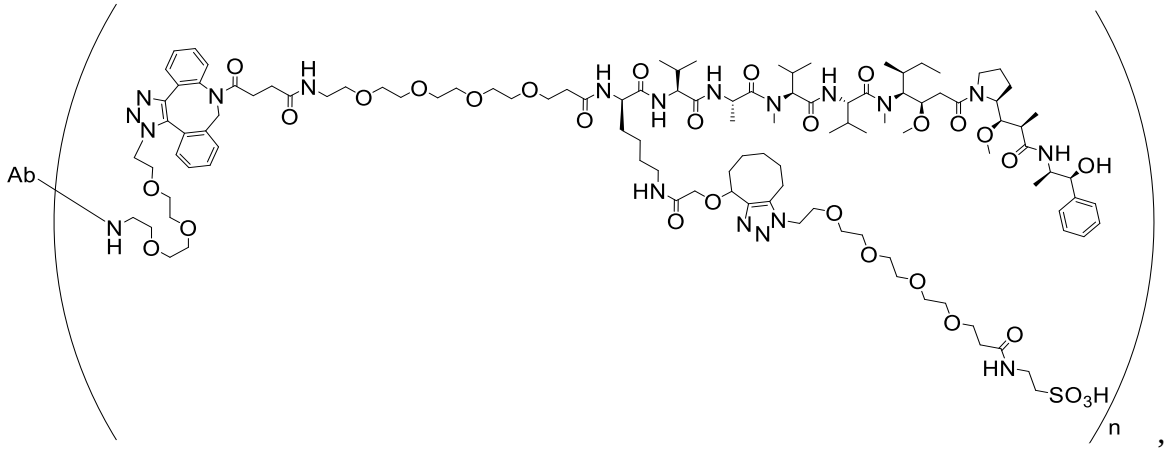


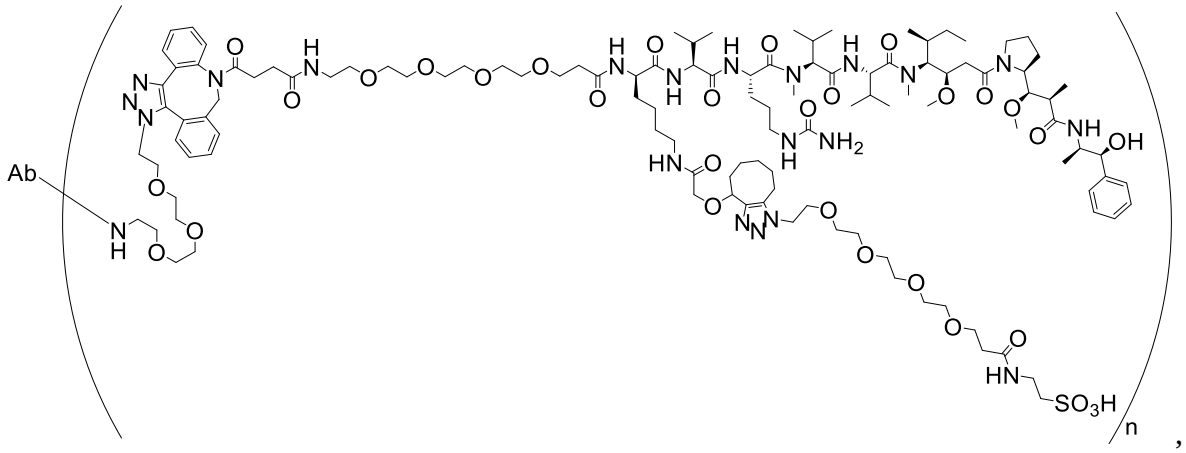
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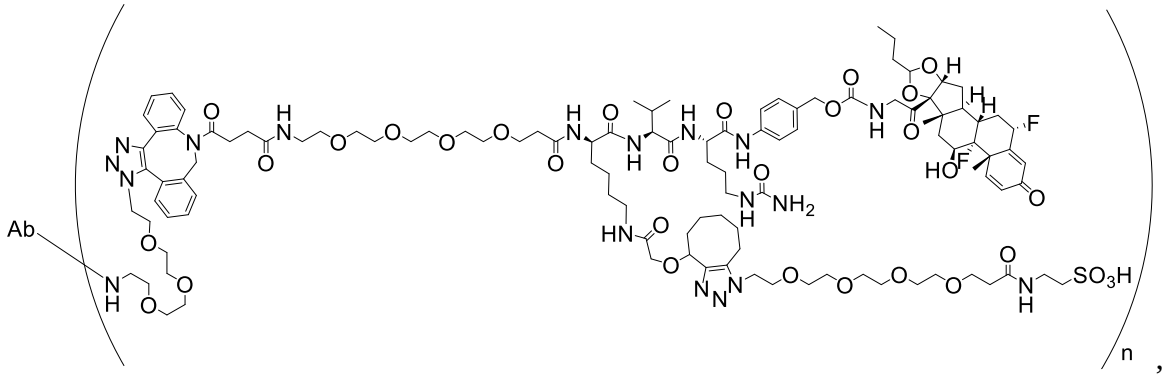


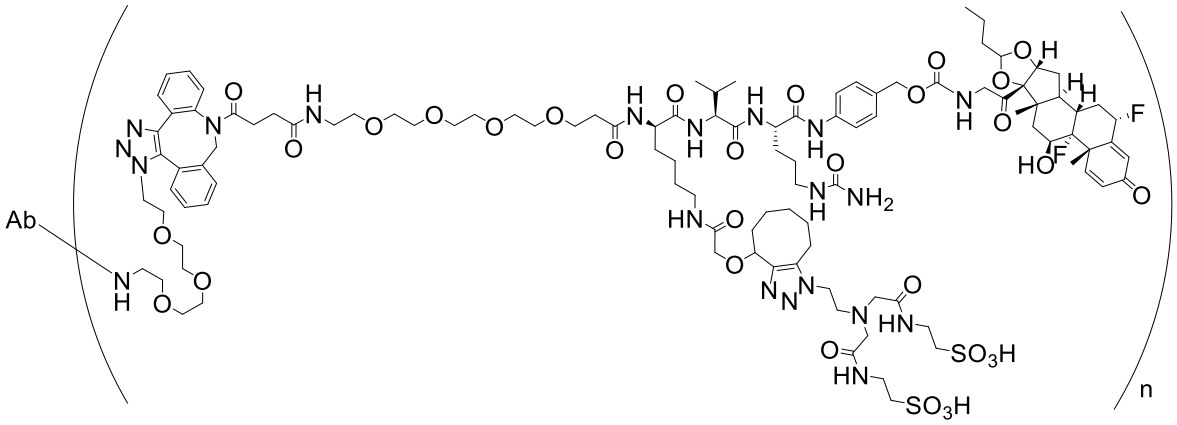
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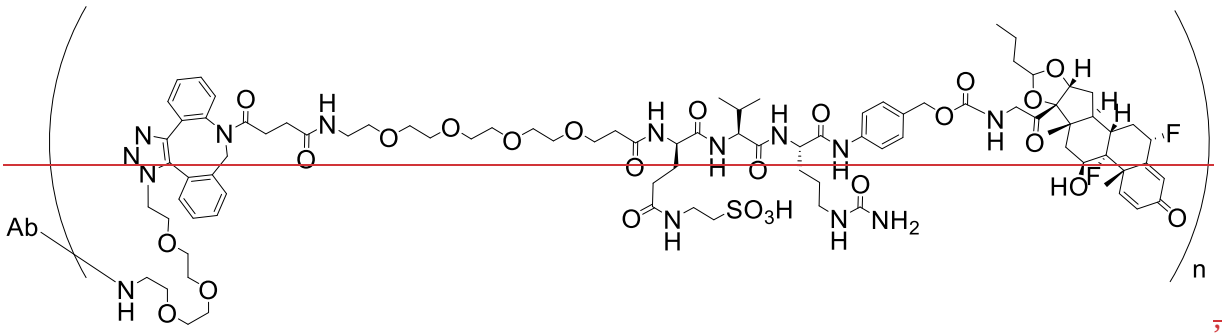




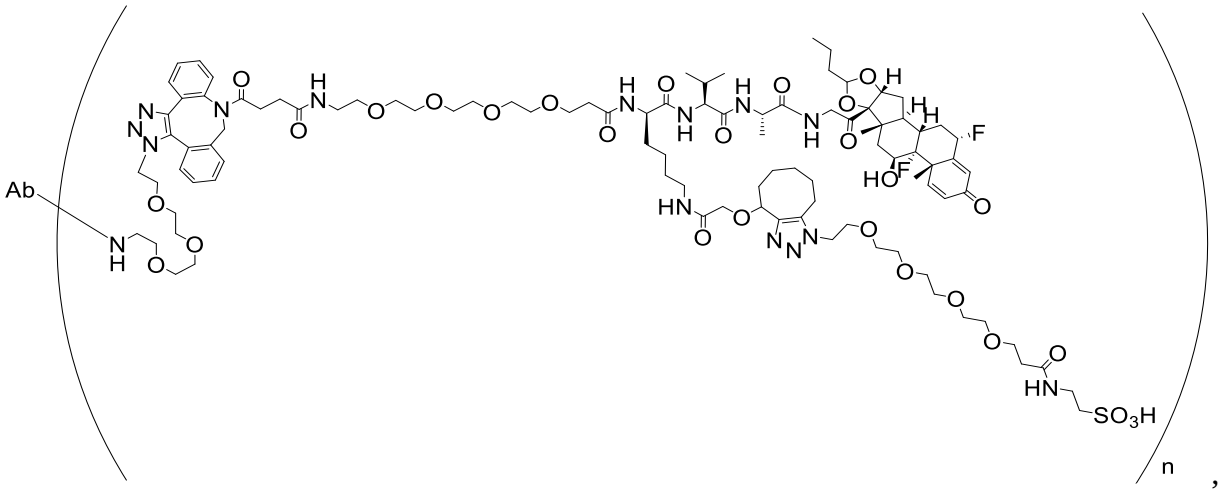



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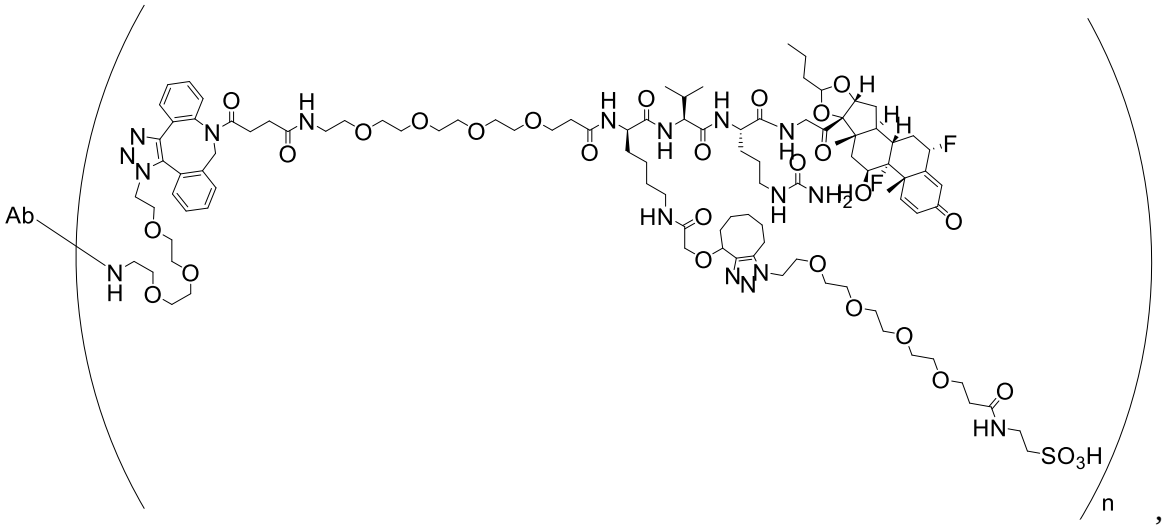
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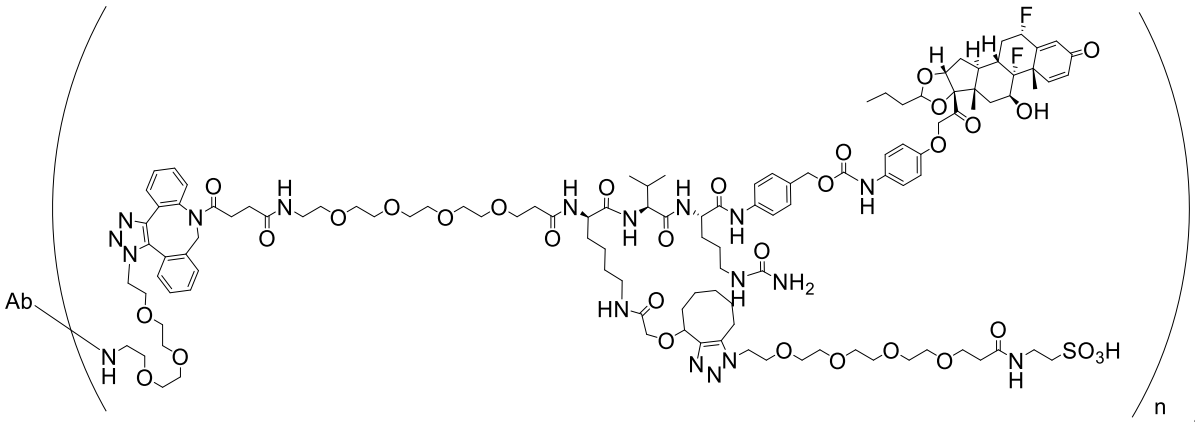
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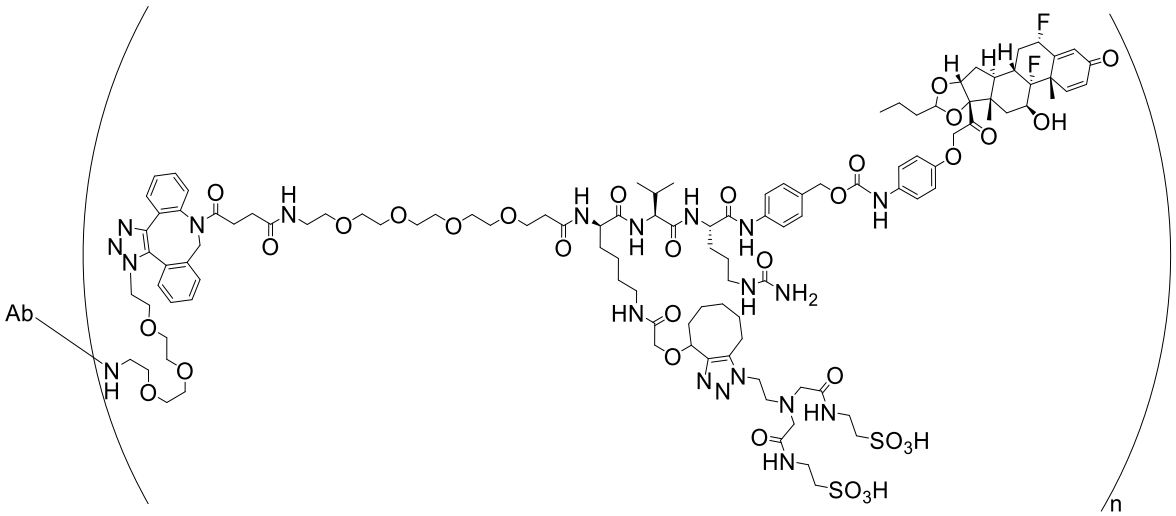
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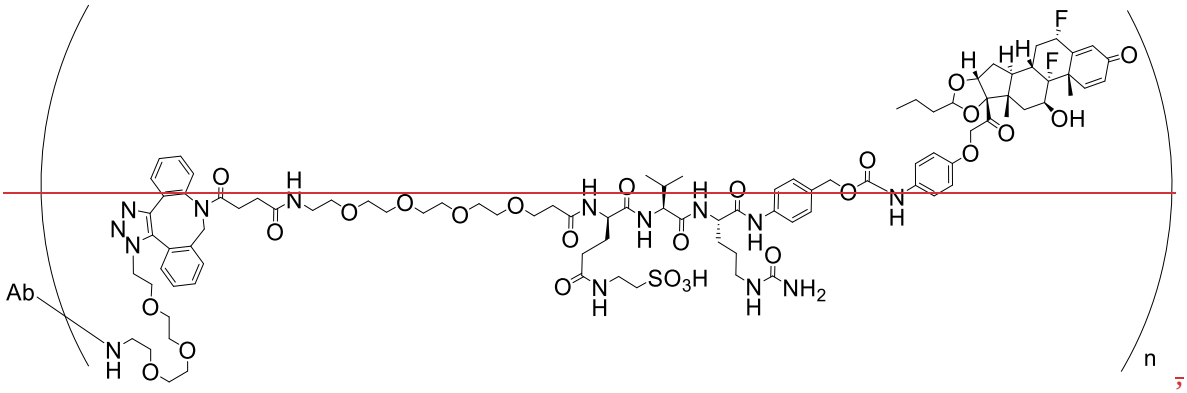
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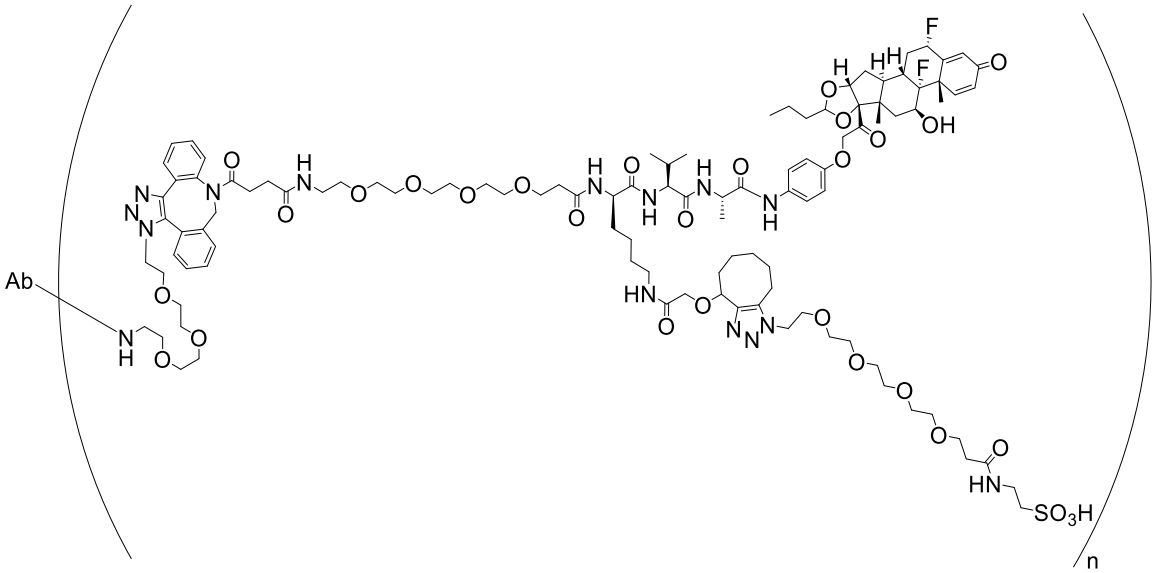


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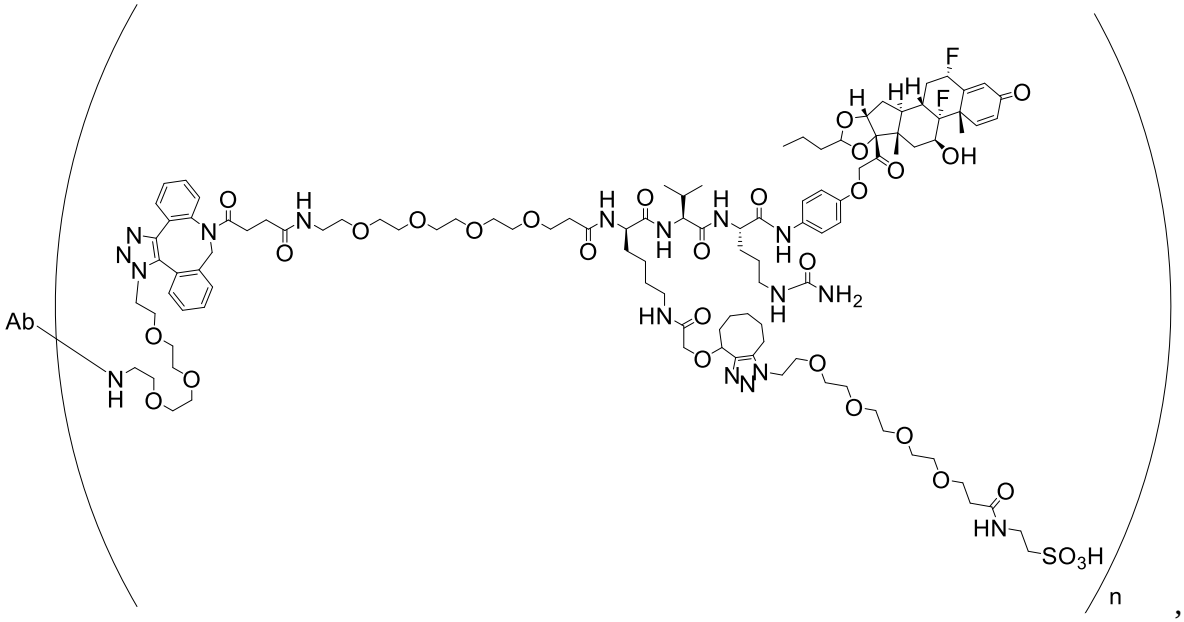


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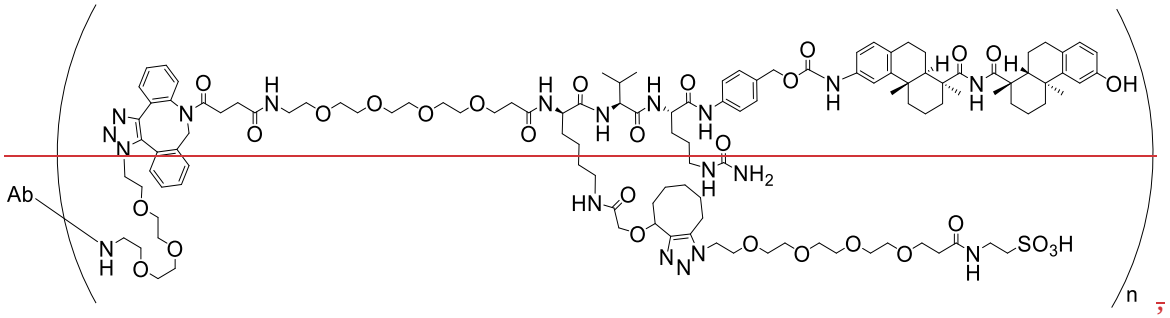


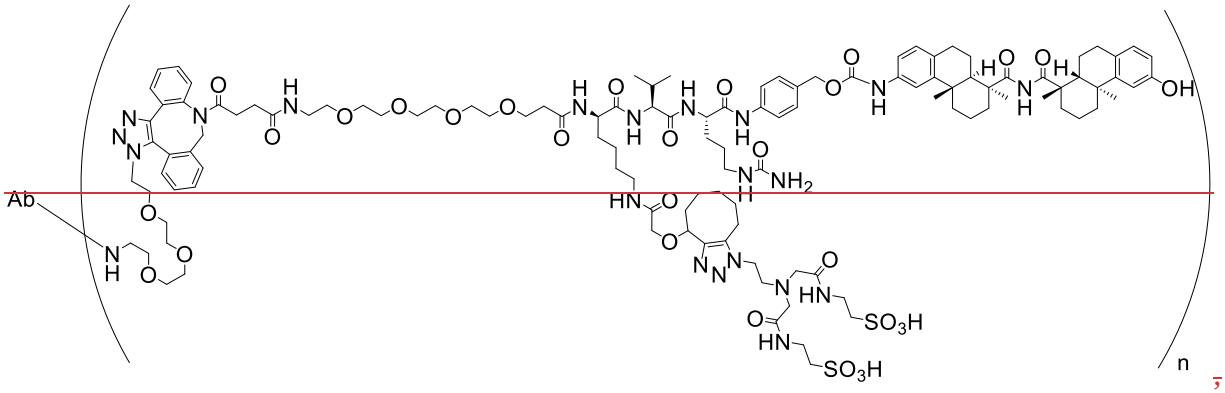


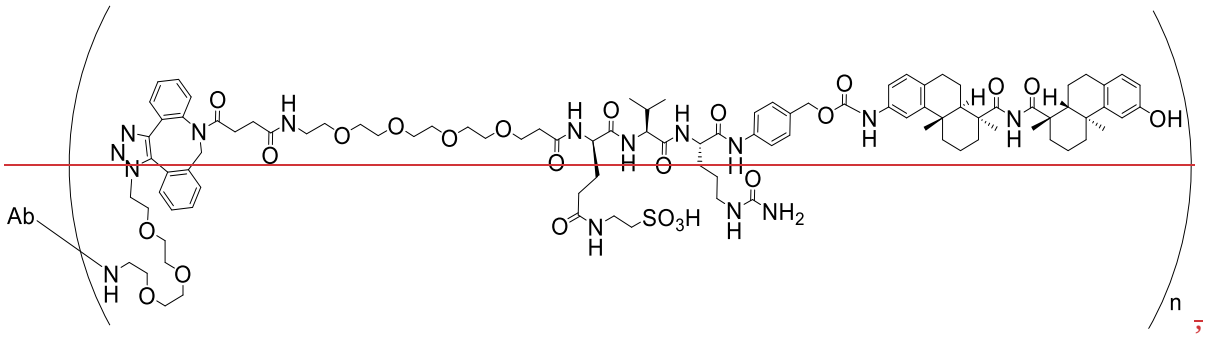
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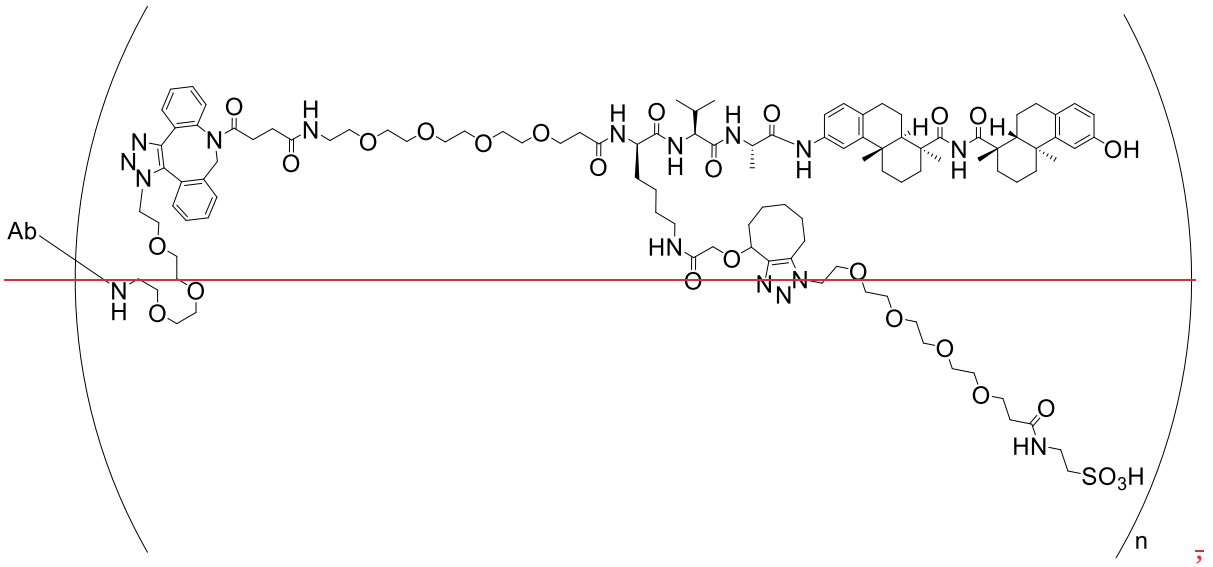


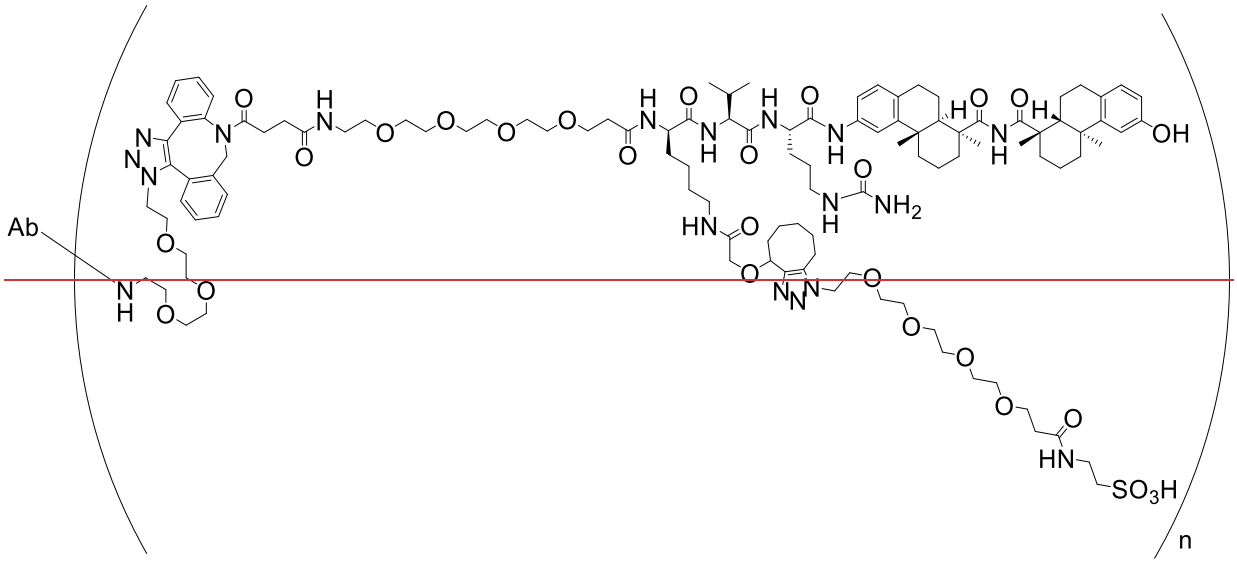
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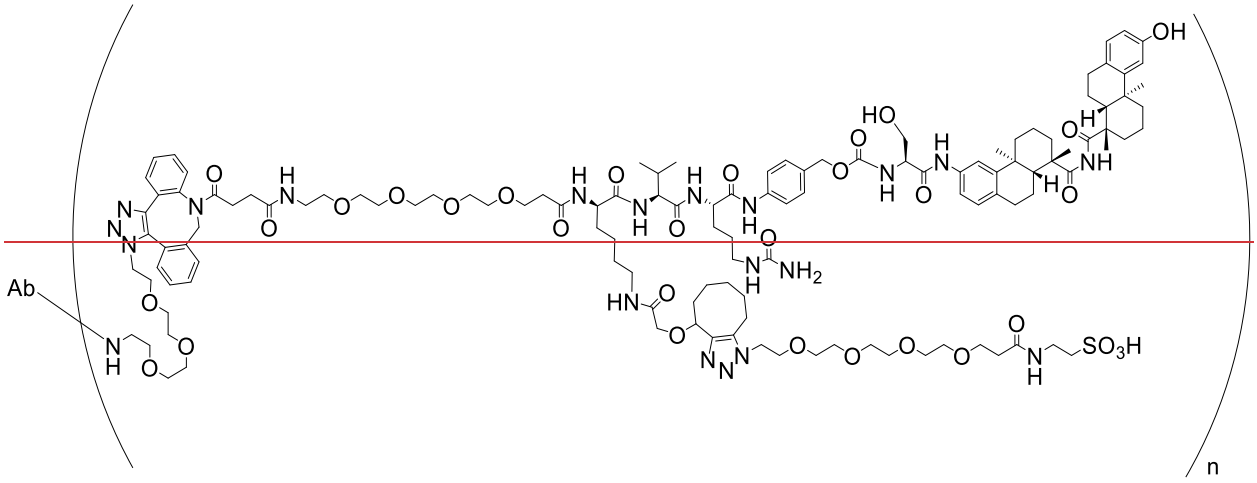

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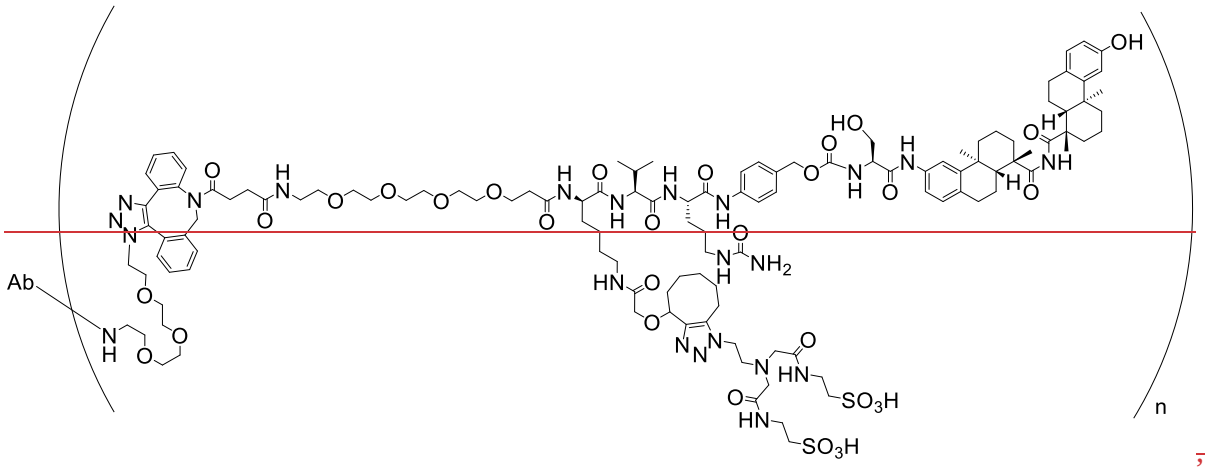

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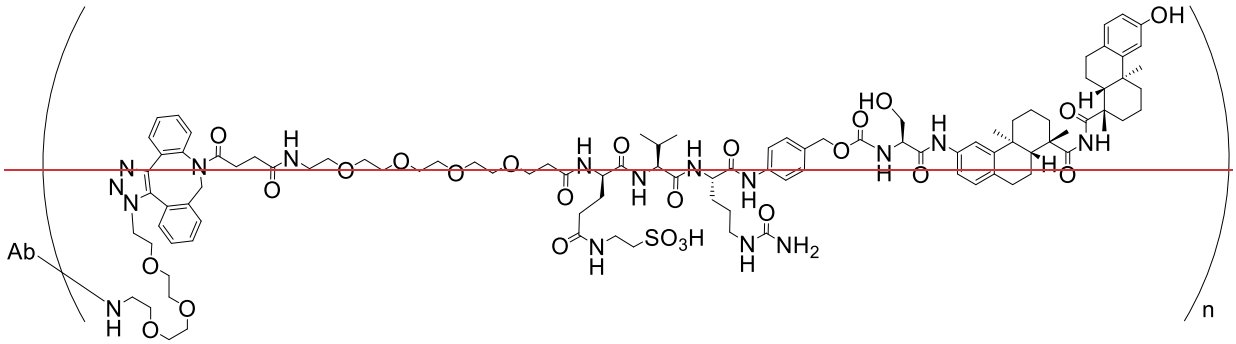

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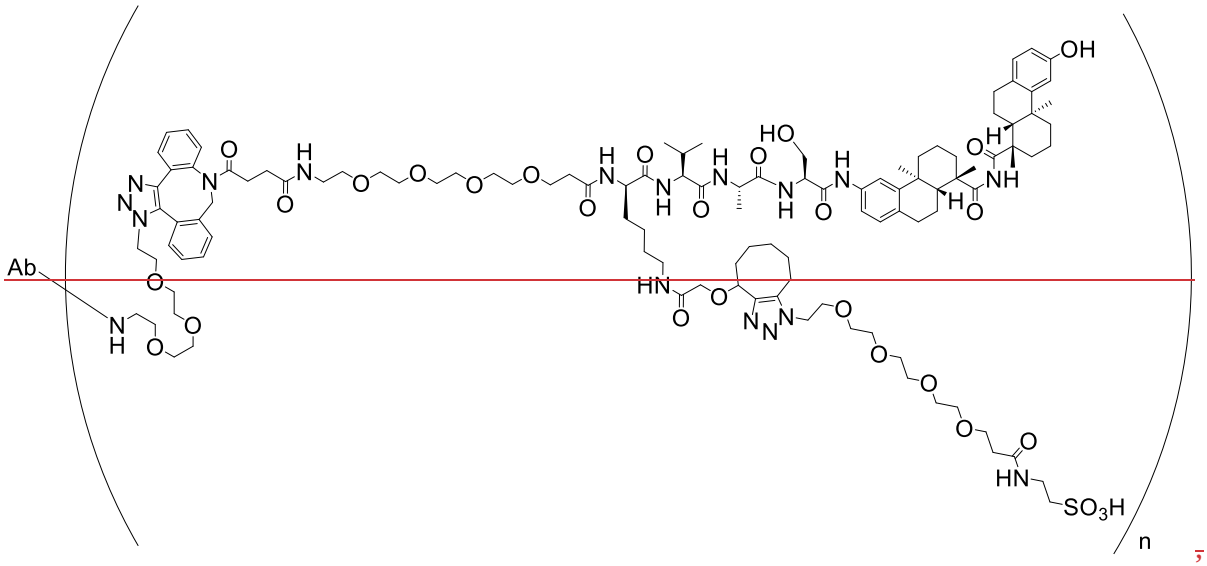

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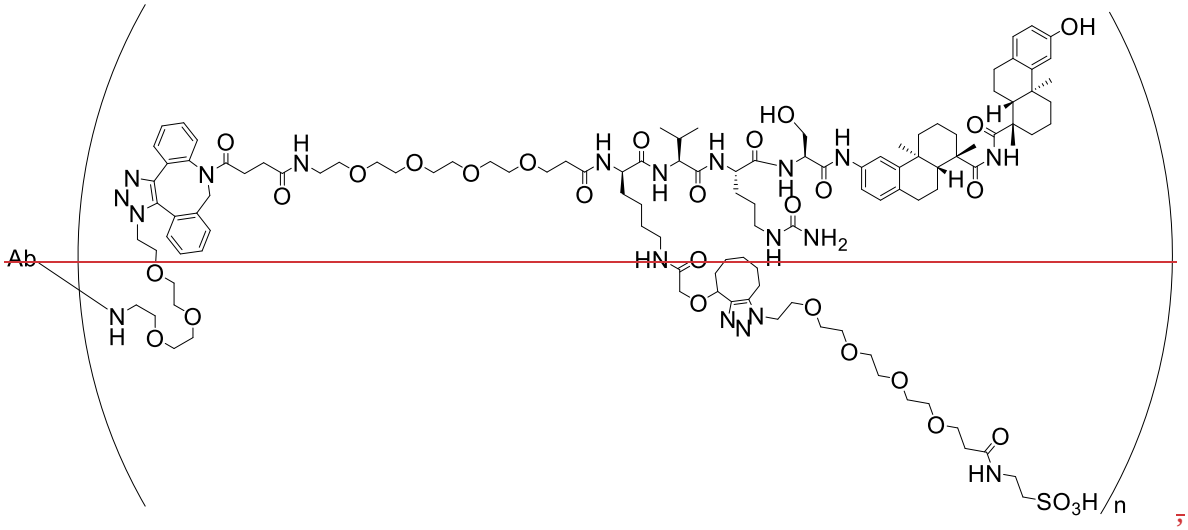

Ab
n


Ab
n





and



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

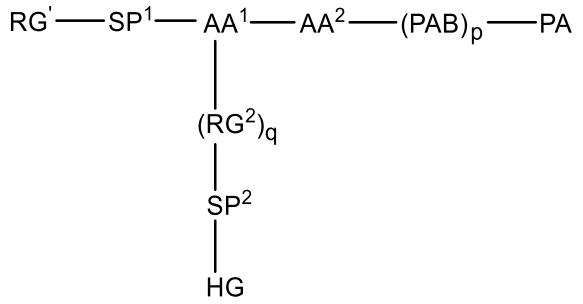
each **Ab** is ~~an~~ the antibody, or an antigen-binding fragment thereof; and

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

~~27~~25. A pharmaceutical composition comprising a compound of any one of claims 1-~~26~~24, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

~~28~~26. A compound of any one of claims 1-~~26~~24, or a composition of claim ~~27~~ 25 for use in treating a disease or disorder in a patient in need thereof.

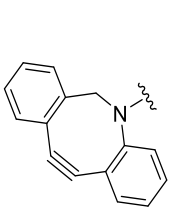
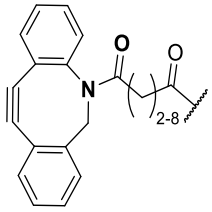
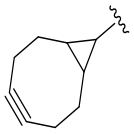
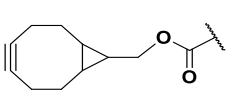
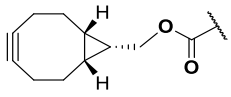
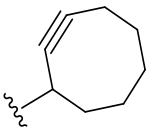
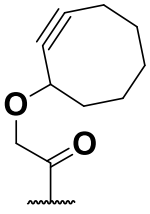
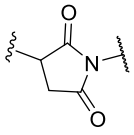
27. A compound or stereoisomeric form, a triazole linkage regioisomer, or mixture of triazole linkage regioisomers thereof, according to Formula (**IX**):

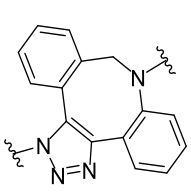
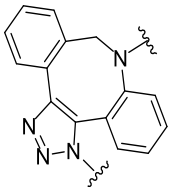
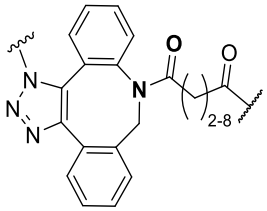
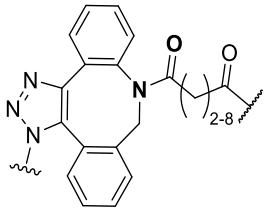
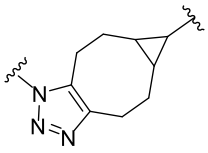
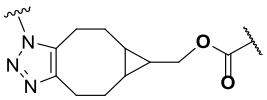
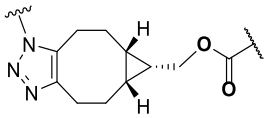
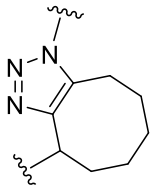
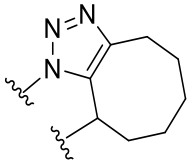
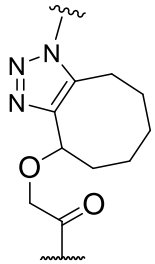
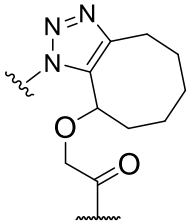
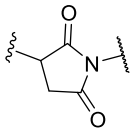


(IX)

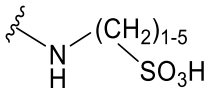
AA1 is an amino acid residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

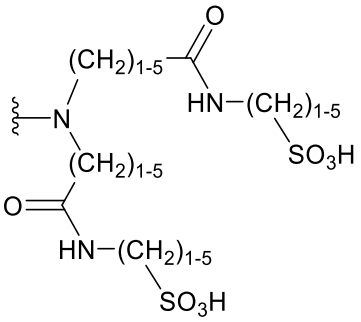
AA2 is a dipeptide, tripeptide or tetrapeptide residue comprising amino acid residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline;

RG′ is a reactive group selected from  ,  ,  ,  ,  ,  ,  , and  , wherein the  indicates the atom through which the **RG′** is bonded to the adjacent groups in the formula;

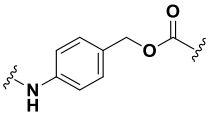
RG² is a reactive group residue selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  , wherein the  indicates the atom through which the RG^1 or RG^2 is bonded to the adjacent groups in the formula;

SP^1 and **SP^2** are independently, in each instance, absent, or a spacer group residue selected from the group consisting of C_{1-6}alkylene, -NH-, -C(O)-, -$(CH_2$-CH_2-O)$_e$, -NH-(CH_2-CH_2-O)$_e$-CH_2-CH_2-C(O)-, -C(O)-(CH_2)$_u$-C(O)-, -C(O)-NH-(CH_2)$_v$-, and combinations thereof wherein subscript e is an integer from 0 to 6, subscript u is an integer from 1 to 8, and subscript v is an integer from 1 to 8;

HG is a hydrophilic residue selected from  and



;

PAB is  , wherein the  indicates the atom through which the PAB is bonded to the adjacent groups in the formula;

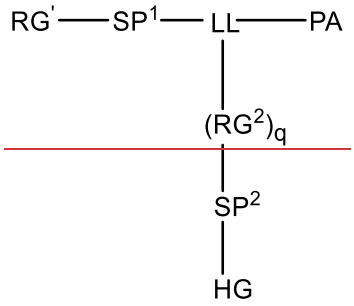
subscript **p** is 0 or 1;

PA is a payload residue;

subscript **q** is 1; and

wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

~~29. A compound according to Formula (VII):~~



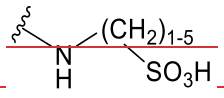
~~(VII)~~

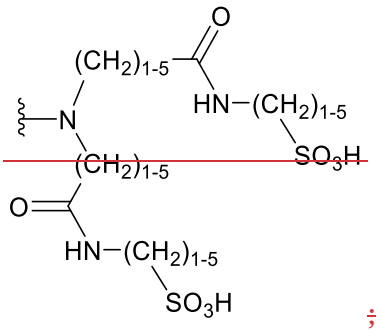
~~**LL** is a trivalent linker;~~

~~**RG′** is a reactive group;~~

~~**RG^2** is a reactive group residue;~~

~~**SP[1]** and **SP[2]** are independently, in each instance, absent, or a spacer group residue;~~

~~**HG** is a hydrophilic residue selected from~~  ~~and~~



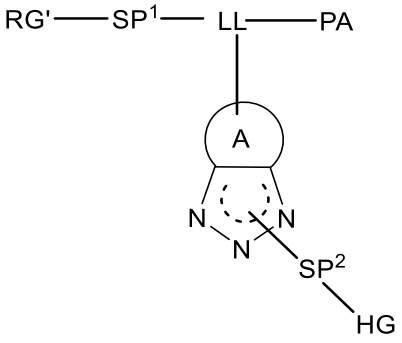
~~;~~

~~**PA** is a payload residue; and~~

~~subscript **q** is 0 or 1;~~

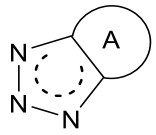
~~wherein the~~  ~~indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.~~

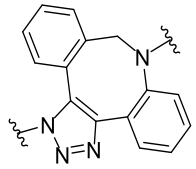
~~30~~28. The compound of claim ~~29~~27, according to Formula (**VIII**):

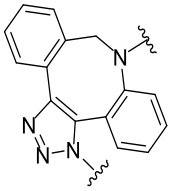


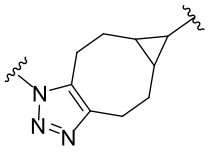
(**VIII**)

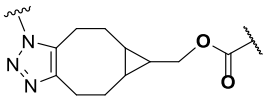
wherein

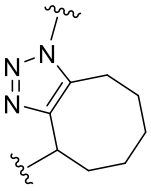


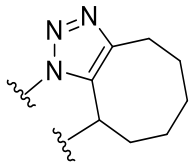
is selected from the groups consisting of 

, 

, 

, 

, 

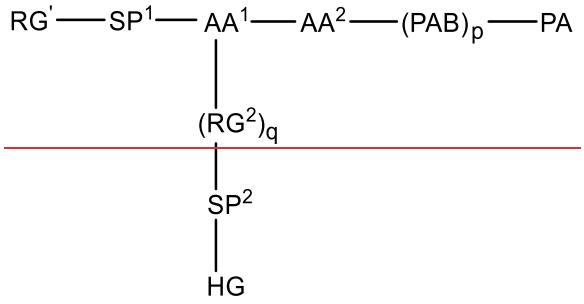
, and 

;

LL is –**AA^1-AA^2-(PAB)$_p$**.~~;~~

~~ring **A** is fused to the triazole and is selected from the group consisting of cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl; wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl are optionally substituted with alkyl, -OH, or -N**R^{a}R^b**, where each of **R^a** and **R^b** is alkyl or -H.~~

~~31. The compound of claim 29, according to Formula (**IX**):~~

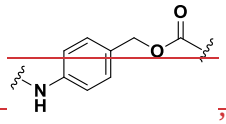


~~(**IX**)~~

~~wherein:~~

~~**AA^1** is a trivalent linker comprising an amino acid residue;~~

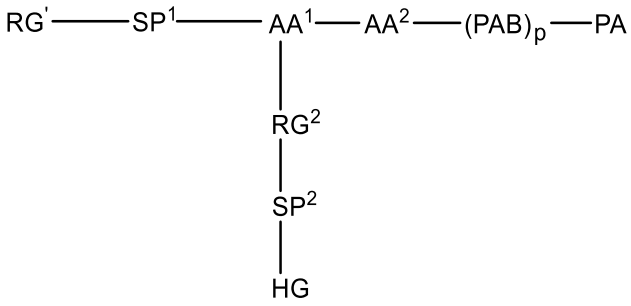
~~**AA^2** is a dipeptide, tripeptide or tetrapeptide residue; and~~

~~**PAB** is~~  ~~, wherein the~~  ~~indicates the atom through which the PAB is bonded to the adjacent groups in the formula;~~

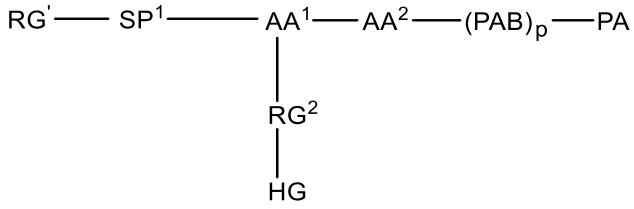
~~subscript **p** is 0 or 1; and~~

~~subscript **q** is 0 or 1.~~

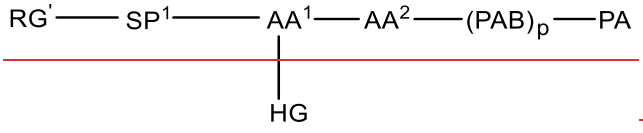
~~32~~29. The compound of claim ~~31~~27, according to Formula (**IXa**)~~,~~ or Formula (**IXb**) ~~or Formula (**IXc**)~~:



(**IXa**),



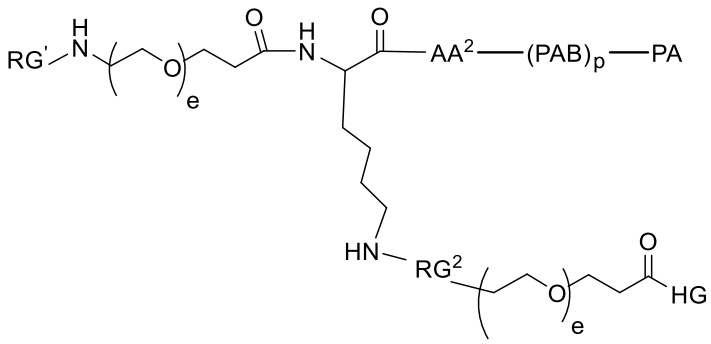
(**IXb**)~~,~~



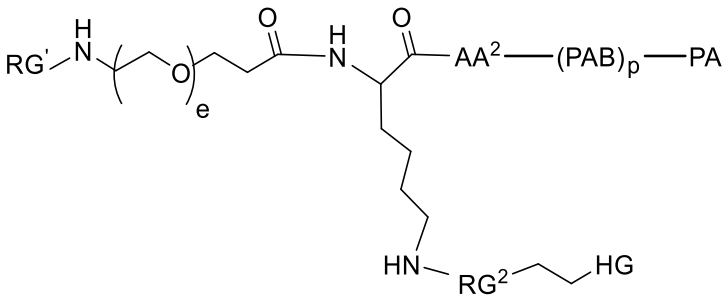
~~(**IXc**)~~.

~~33~~30. The compound according to claim ~~32~~29, wherein **AA^1** is a lysine, glutamine, glutamic acid, or aspartic acid residue.

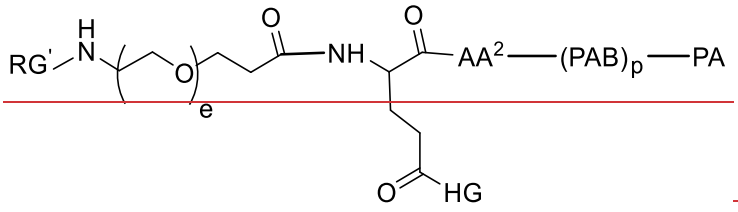
~~34~~31. The compound of claim ~~32~~29, according to Formula (**Xa**), (**Xb**)~~, (**Xc**),~~ or (**Xd**):



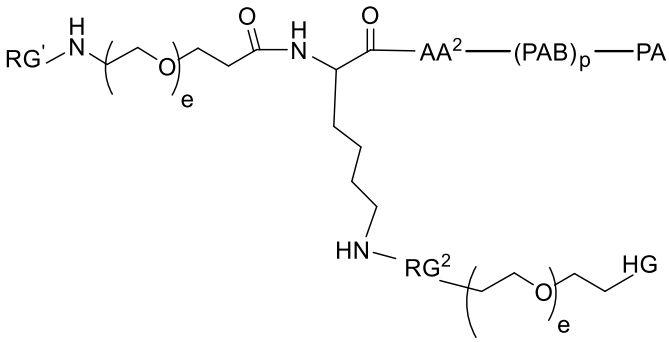
(Xa)



(Xb)



~~**(Xc),**~~ or

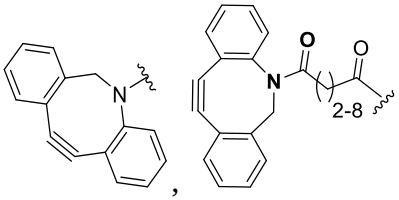


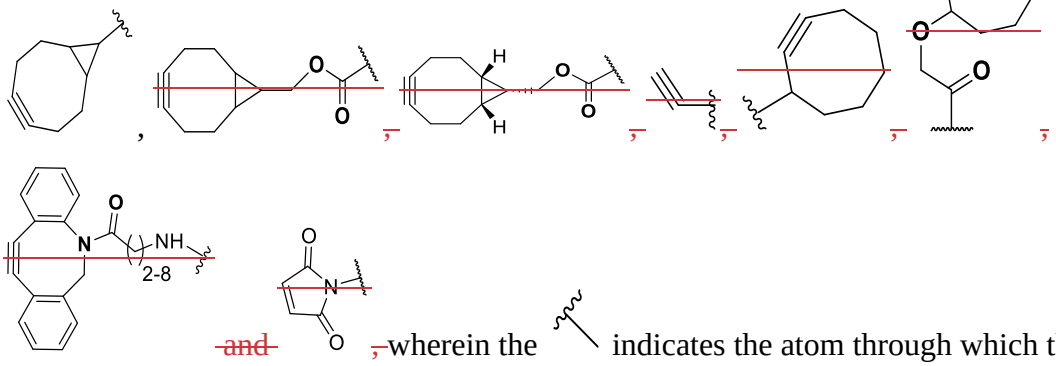
(Xd),

wherein:

subscript **e** is independently, in each instance, an integer from 0 to 6.

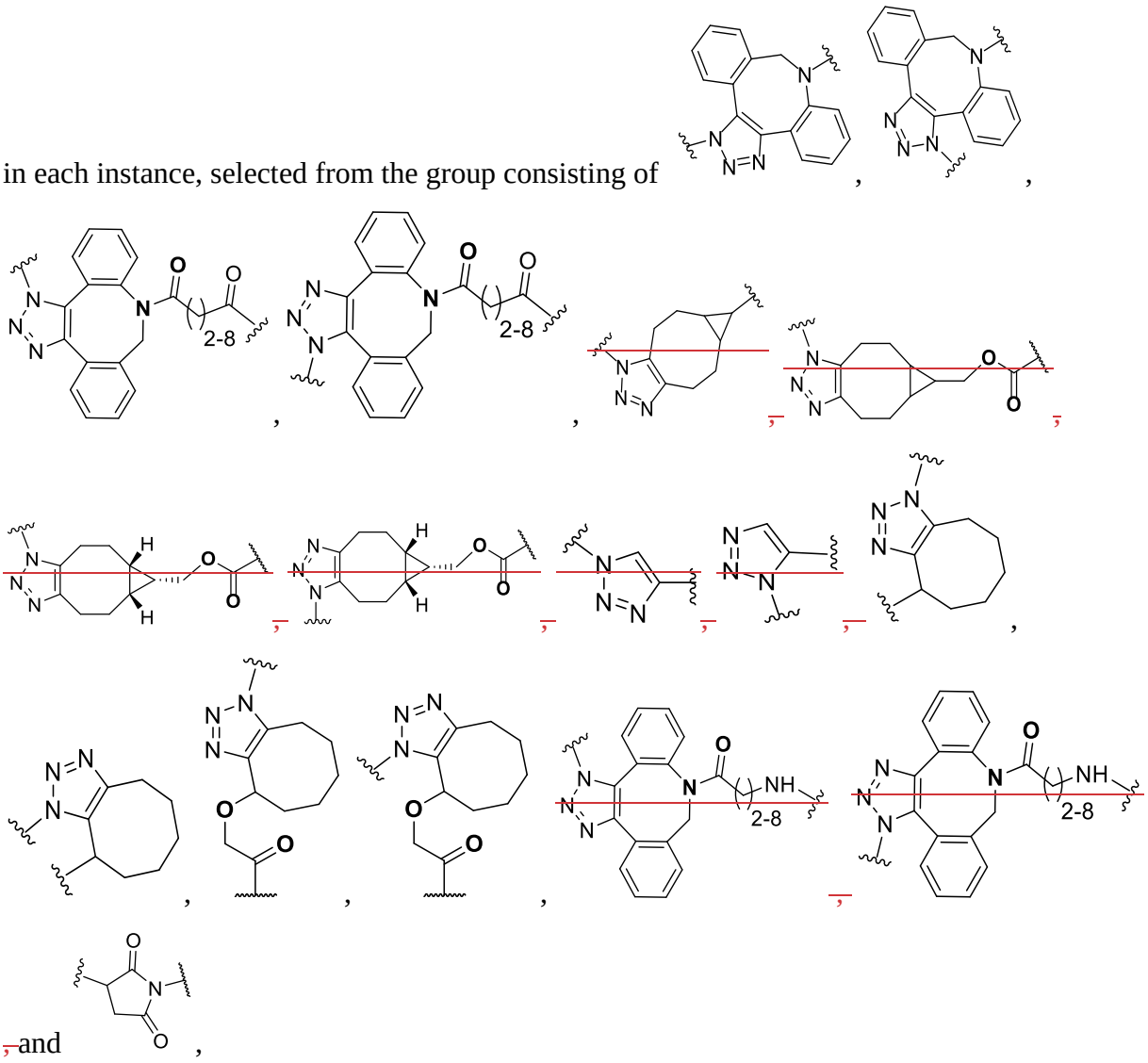
~~35. The compound of any one of claims 30-34, wherein **RG′** is, independently in each instance, a click chemistry residue.~~

~~36~~32. The compound of any one of claims ~~30~~27-~~34~~31, wherein **RG′** is, independently in each instance, selected from the group consisting of  , , and



and , wherein the indicates the atom through which the **RG′** is bonded to the adjacent groups in the formula.

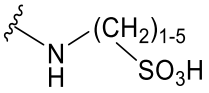
3733. The compound of any one of claims 3027-3632, wherein **RG²** is independently, in each instance, selected from the group consisting of



and

wherein the  indicates the atom through which the **RG²** is bonded to the adjacent groups in the formula.

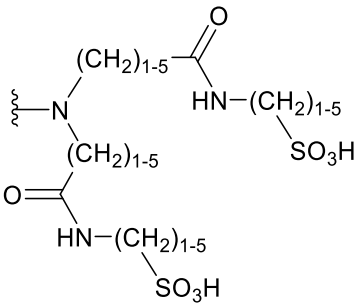
~~38~~34. The compound of any one of claims ~~30~~27-~~37~~33, wherein **HG** is



wherein

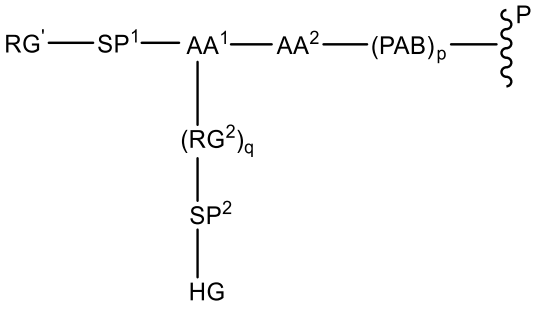
the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

~~39~~35. The compound of any one of claims ~~30~~27-~~37~~34, wherein **HG** is

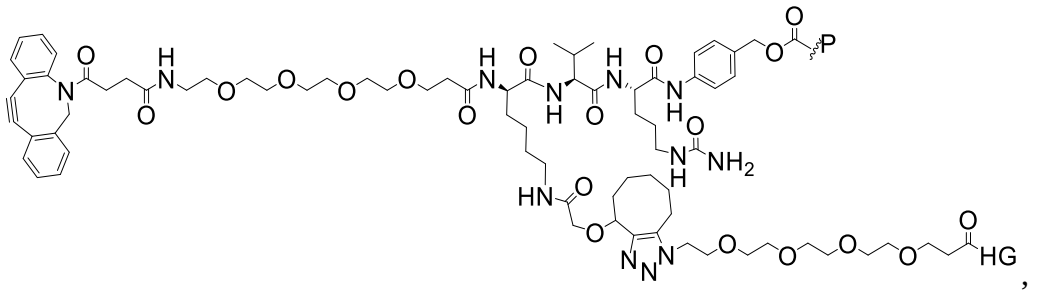
 , wherein the  indicates the atom through which the **HG** is bonded to the adjacent groups in the formula.

~~40~~36. The compound of any one of claims ~~30~~27-~~33~~ 30 and ~~35~~32-~~39~~35, wherein **SP¹** and **SP²** are independently, in each instance, absent, or selected from the group consisting of ~~C_{1-6} alkylene, -NH-, -C(O)-, (-CH_2-CH_2-O)$_e$,~~ -(CH_2-CH_2-O)$_e$ and -NH-CH_2-CH_2-(-O-CH_2-CH_2)$_e$-C(O)-~~., -C(O)-(CH_2)$_u$-C(O)-, -C(O)-NH-(CH_2)$_v$-, (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.~~

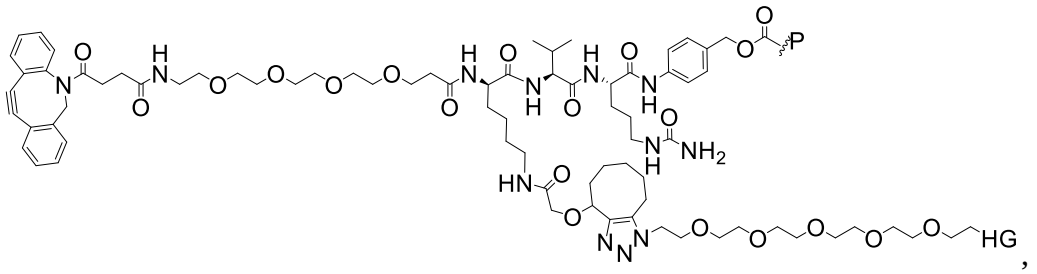
~~41~~37. The compound of claim ~~31~~27, wherein



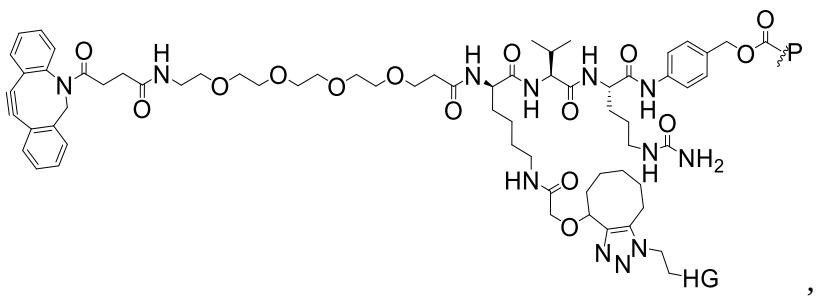
is selected from the group consisting of:



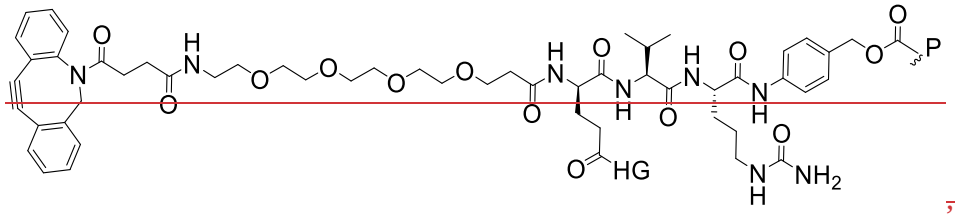
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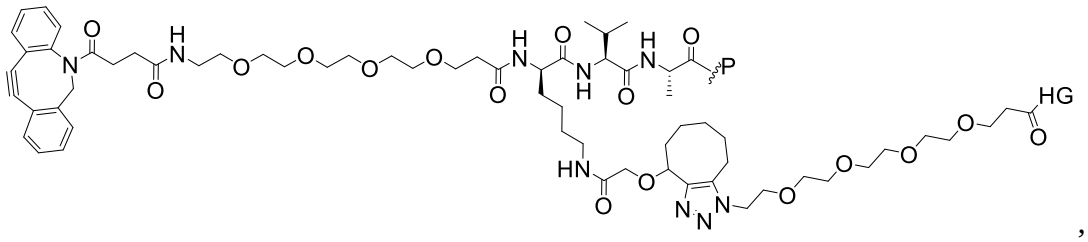
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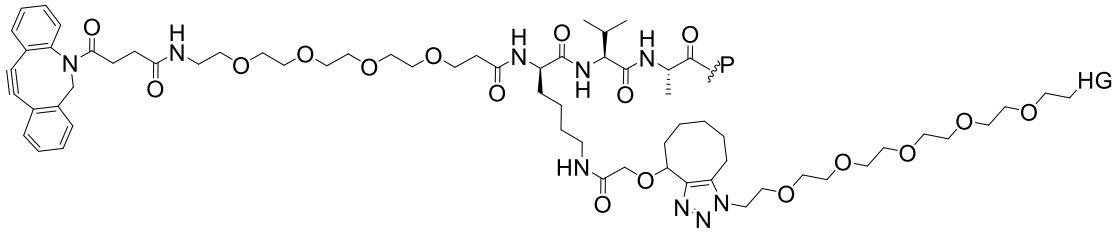
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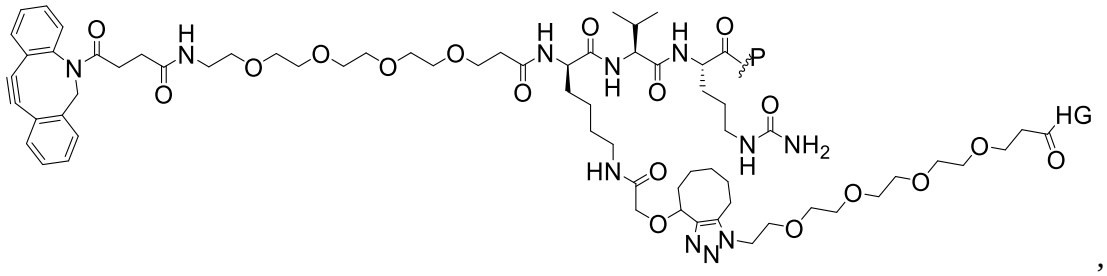
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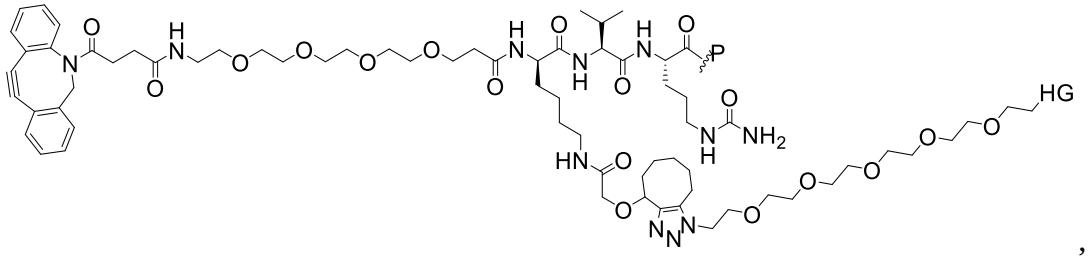
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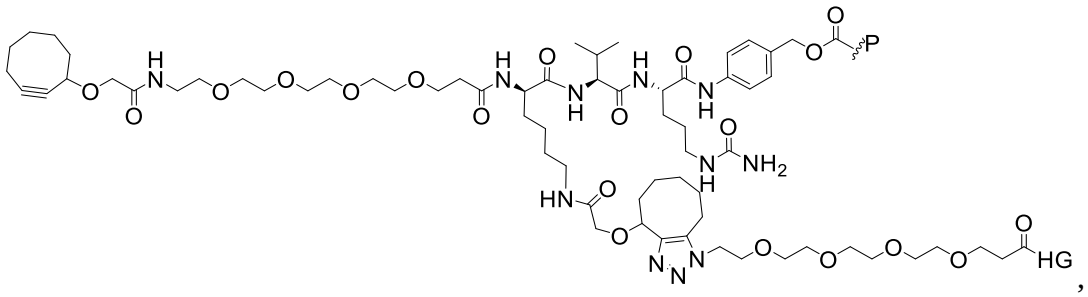
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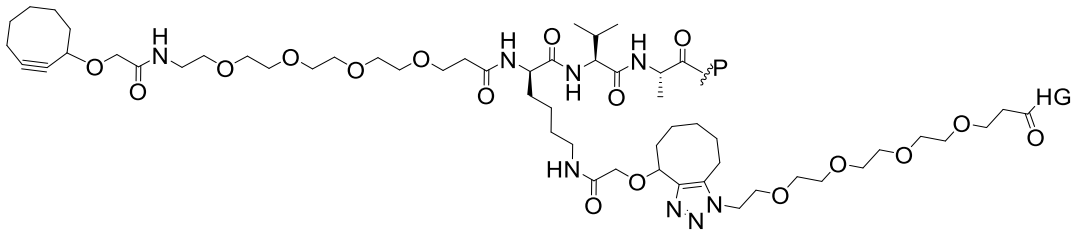
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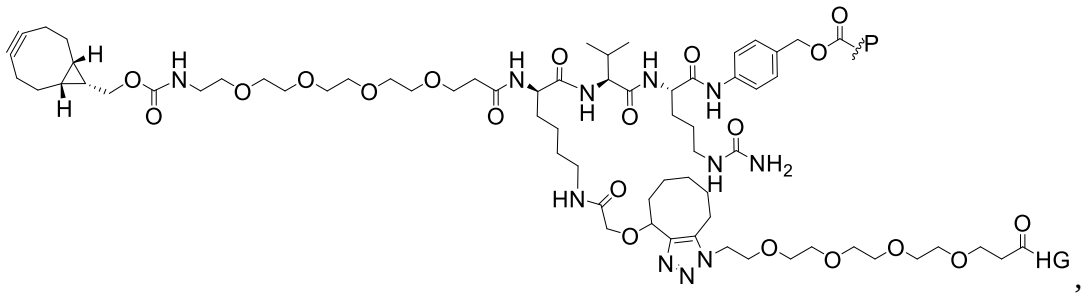
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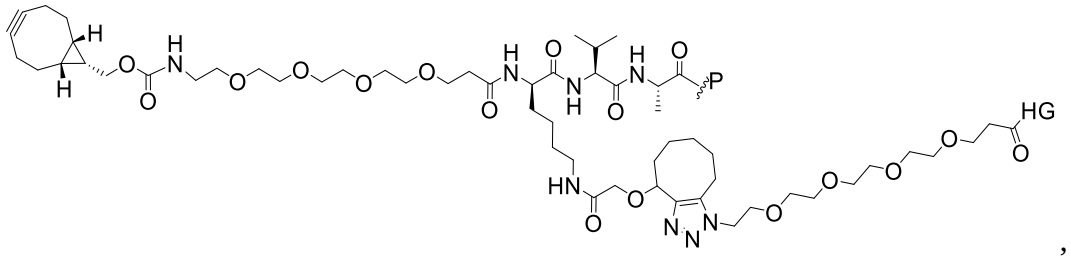


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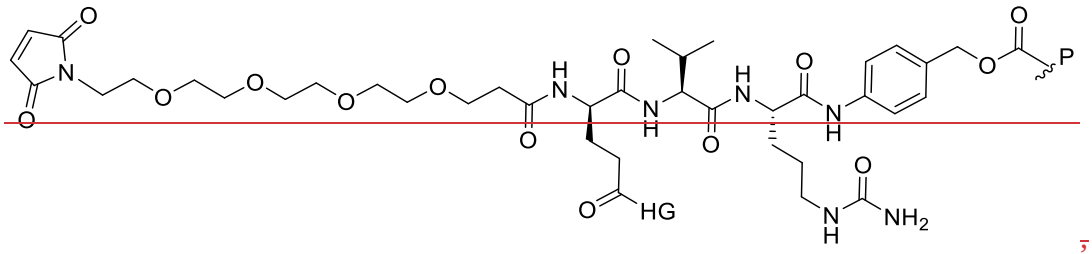


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and

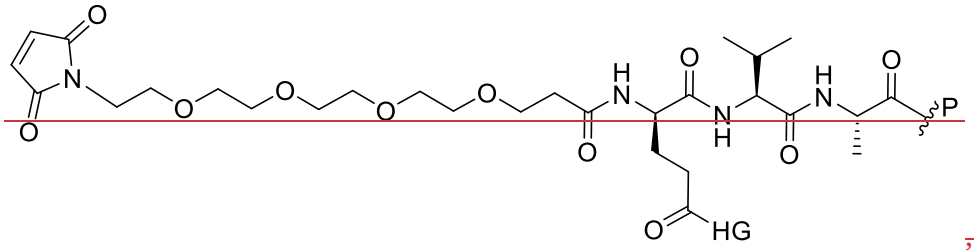


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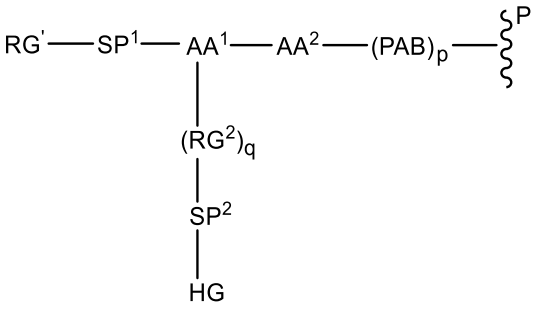


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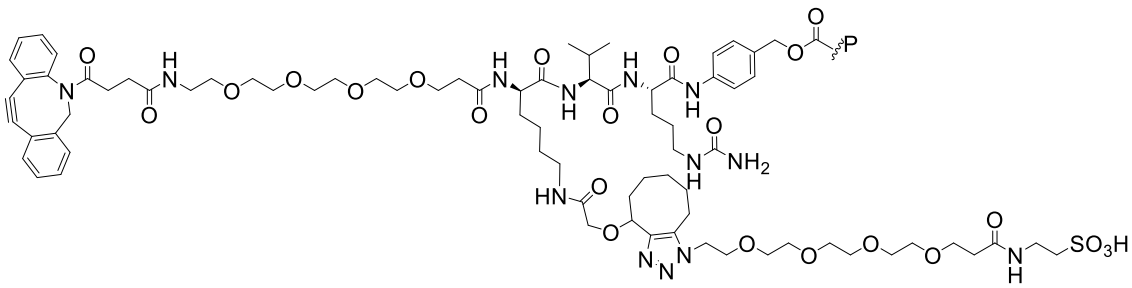
or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof, wherein

each  is a bond to the payload residue.

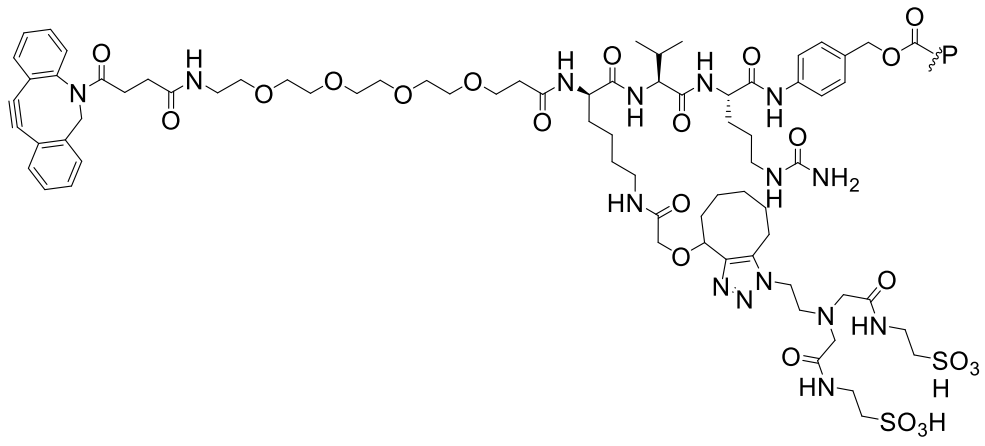
~~42~~38. The compound of claim ~~31~~27, wherein



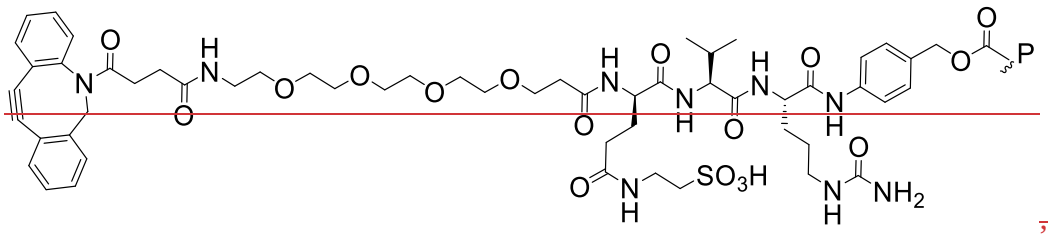
is selected from the group consisting of:



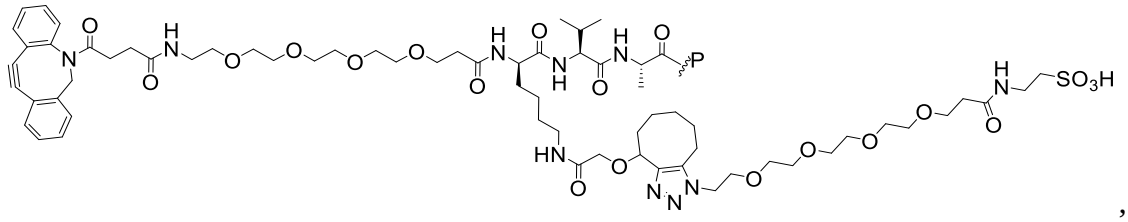
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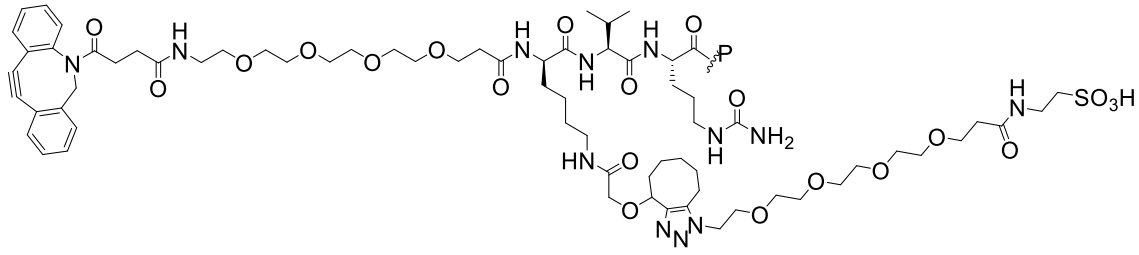


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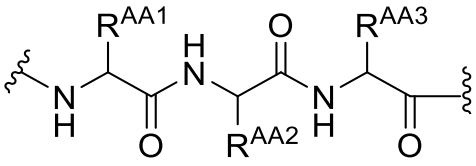


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or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof, wherein

each  is a bond to the payload residue.

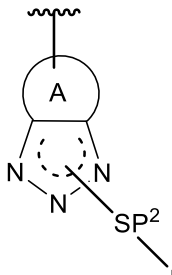
~~43~~39. The compound of claim ~~29~~28, wherein **LL** is according to Formula (**LL1**):



(LL1)

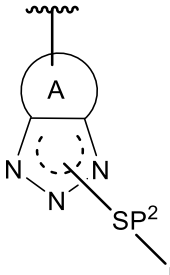
wherein $\mathbf{R^{AA1}}$ is an amino acid sidechain residue selected from tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline,

$\mathbf{R^{AA2}}$, and $\mathbf{R^{AA3}}$ are each, independently, amino acid side chains residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline; and



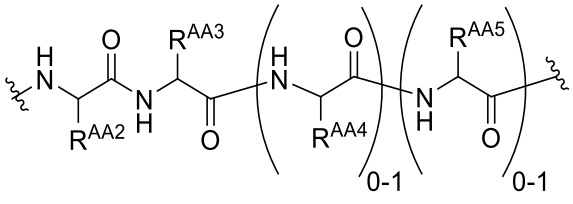
$\mathbf{R^{AA1}}$, at least one of which is bonded directly or indirectly to HG. ~~$\mathbf{(RG^2)_q\text{-}SP^2\text{-}HG}$~~

44~~40~~. The compound of claim 43~~39~~, wherein $\mathbf{R^{AA1}}$ is a lysine, glutamine, glutamic acid



or aspartic acid side chain residue bonded directly or indirectly to HG ~~**HG**~~, and $\mathbf{R^{AA2}}$ and $\mathbf{R^{AA3}}$ are either valine and alanine or valine and citrulline sidechains residues respectively.

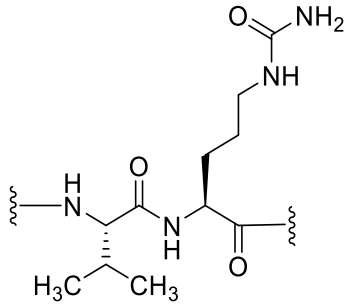
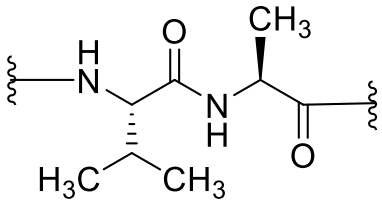
45~~41~~. The compound of any one of claims 27 and 29-36~~31-40~~, wherein $\mathbf{AA^2}$ is



wherein $\mathbf{R^{AA2}}$, $\mathbf{R^{AA3}}$, $\mathbf{R^{AA4}}$, and $\mathbf{R^{AA5}}$ are each, independently, amino acid side chain~~s~~ residues selected from alanine, valine, leucine, isoleucine, methionine, tryptophan, phenylalanine, proline, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, and citrulline~~, at least one of which is bonded directly or indirectly to $-(RG^2)_q-SP^2-HG$~~,

wherein the  indicates the atom through which $\mathbf{AA^2}$ is bonded to the adjacent groups in the formula.

~~46~~42. The compound of any one of claims 27 and 29-36~~31-40~~, wherein $\mathbf{AA^2}$ is

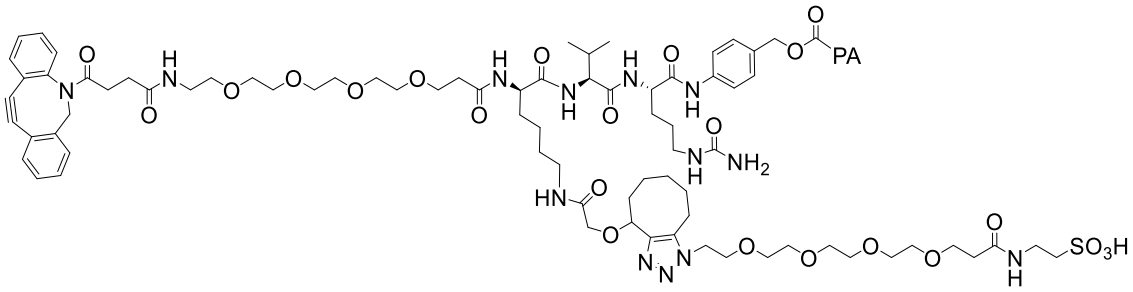
 or  ,

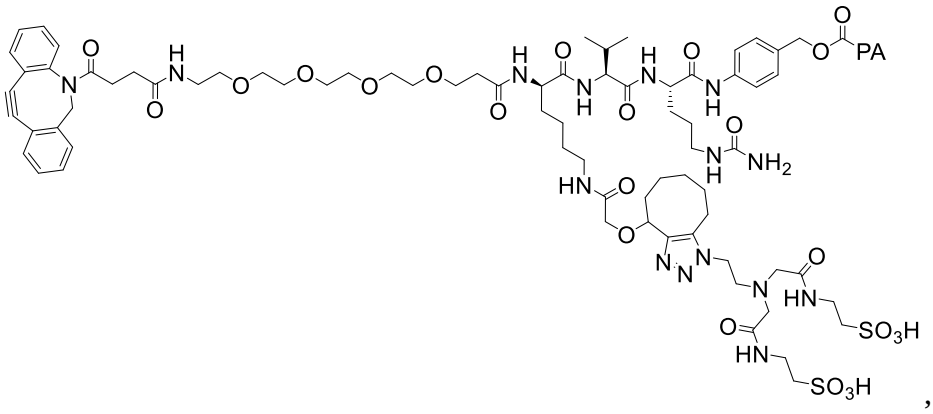
wherein the  indicates the atom through which $\mathbf{AA^2}$ is bonded to the adjacent groups in the formula.

~~47~~43. The compound of any one of claims ~~34~~31-~~40~~36, wherein subscript **e** is 4.

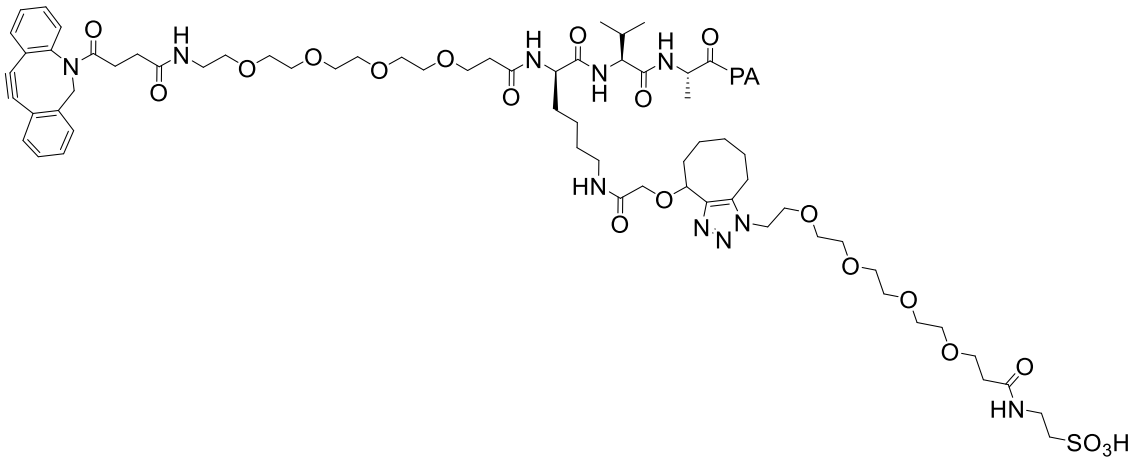
~~48~~44. The compound of any one of claims ~~29~~27-~~47~~43, wherein **PA** is the residue of a group selected from the group consisting of a dolastatin, an auristatin, a maytansinoid, a plant alkaloid, a taxane, a vinca alkaloid, a steroid, and a liver X receptor (LXR) modulator.

~~49~~45. The compound of claim ~~29~~27, selected from the group consisting of:

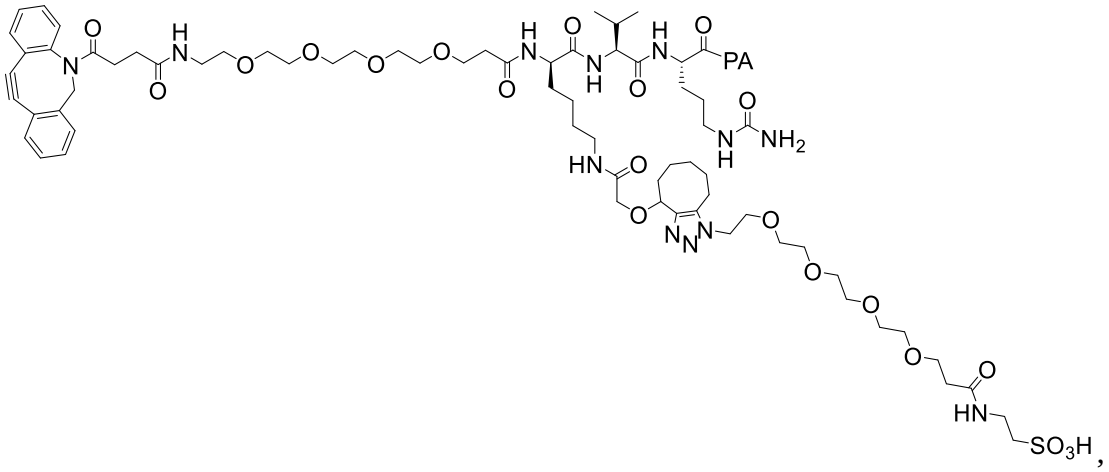




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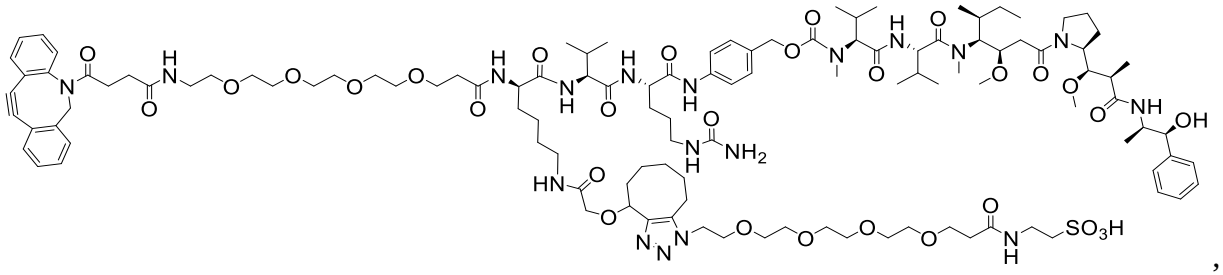


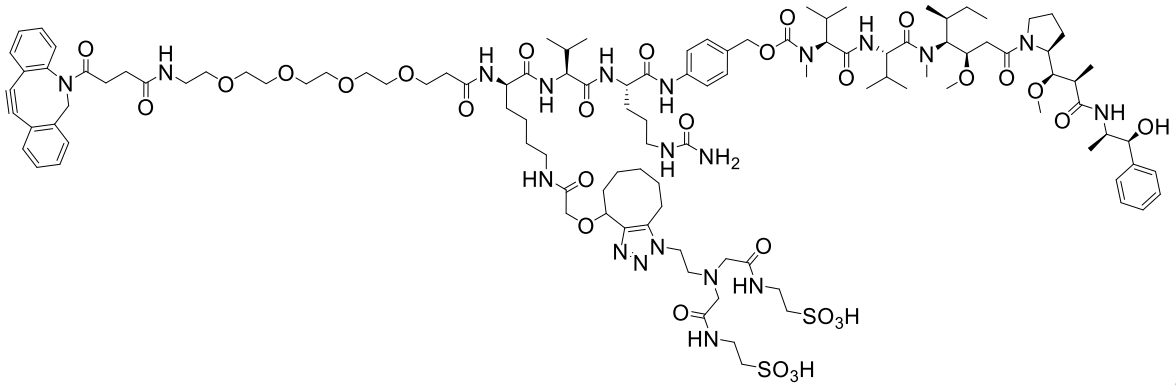
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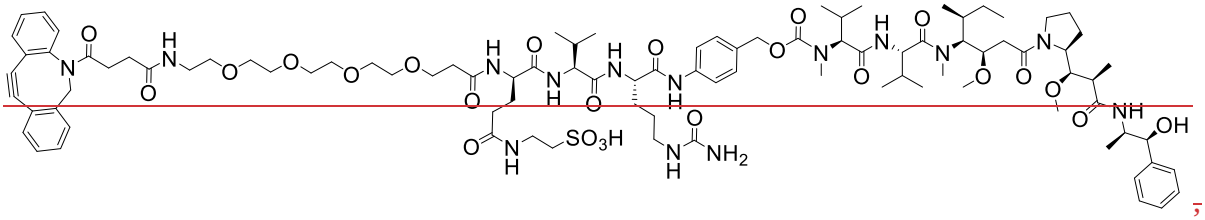
or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof, wherein **PA** is a payload residue.

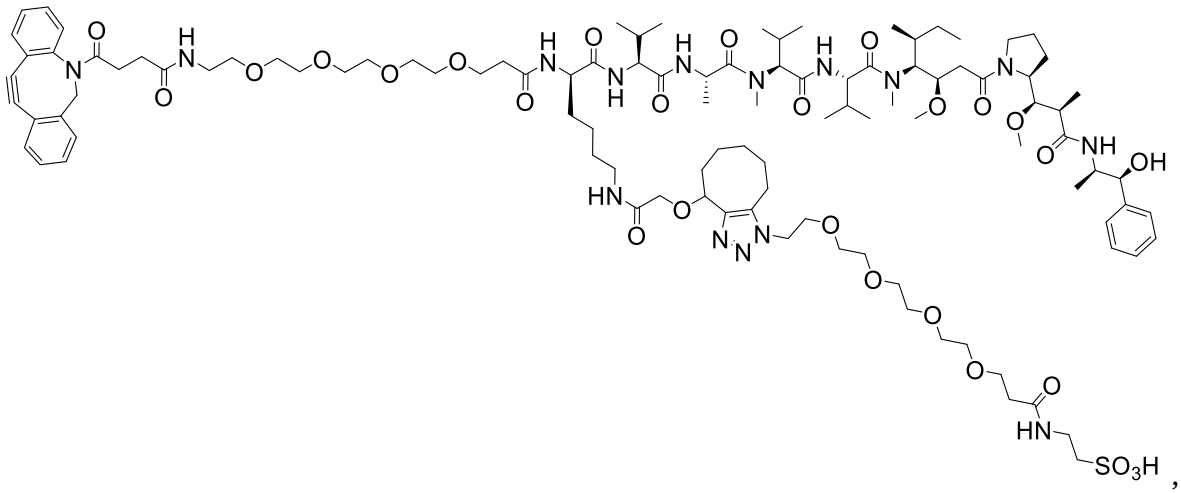
~~50~~46. The compound of claim ~~29~~27, selected from the group consisting of:

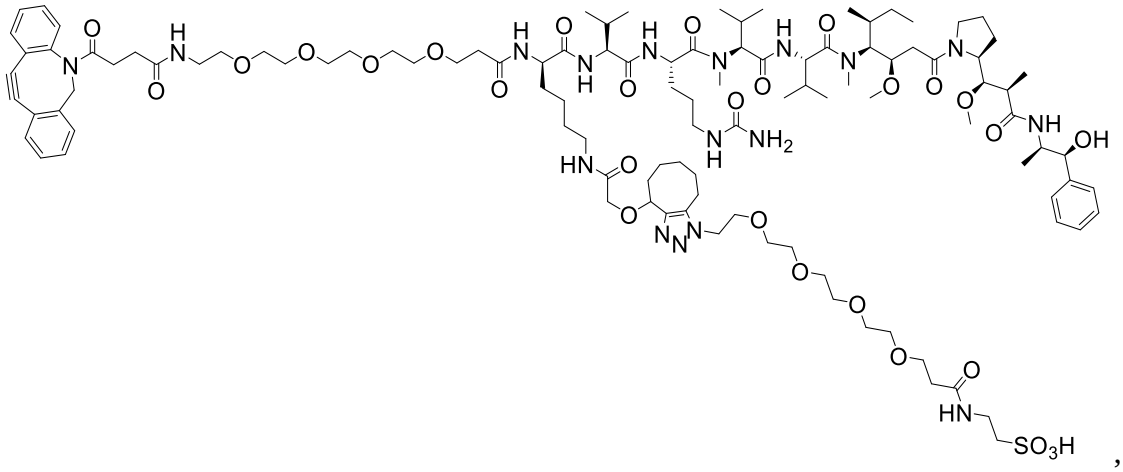
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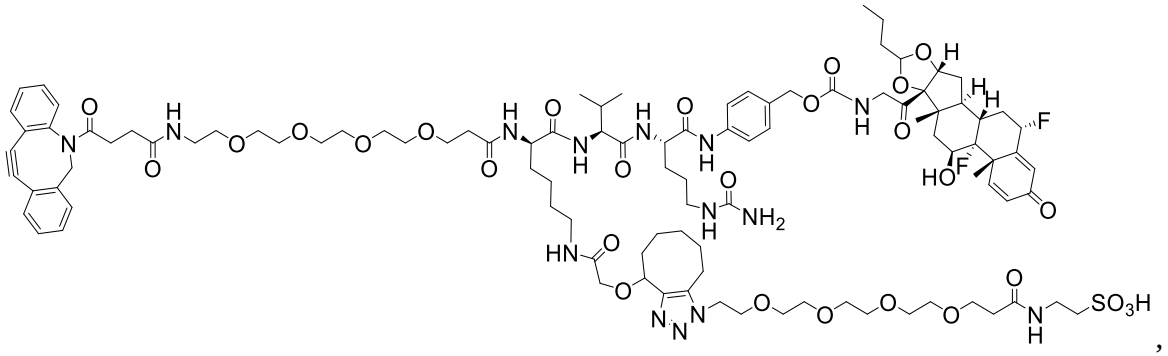

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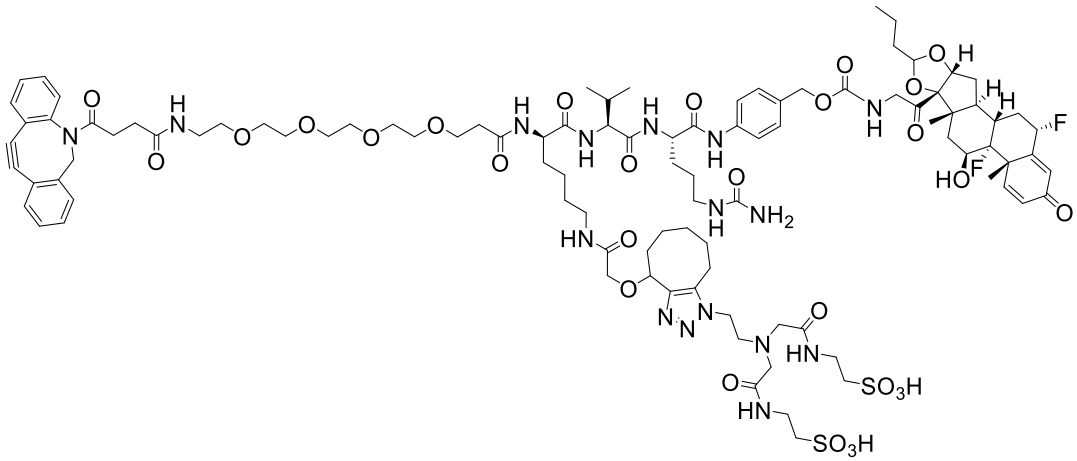

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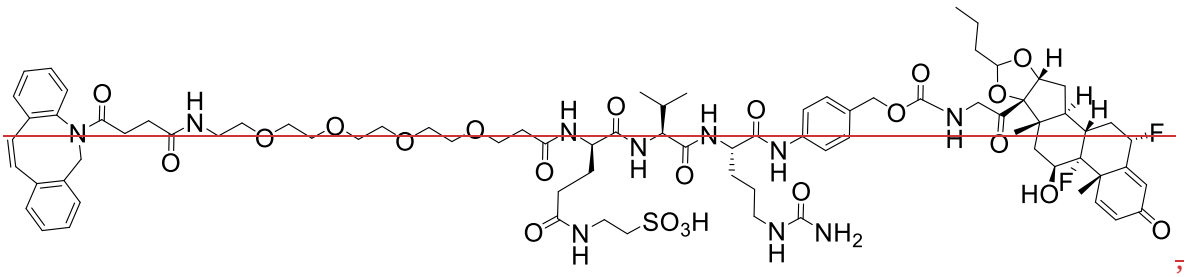
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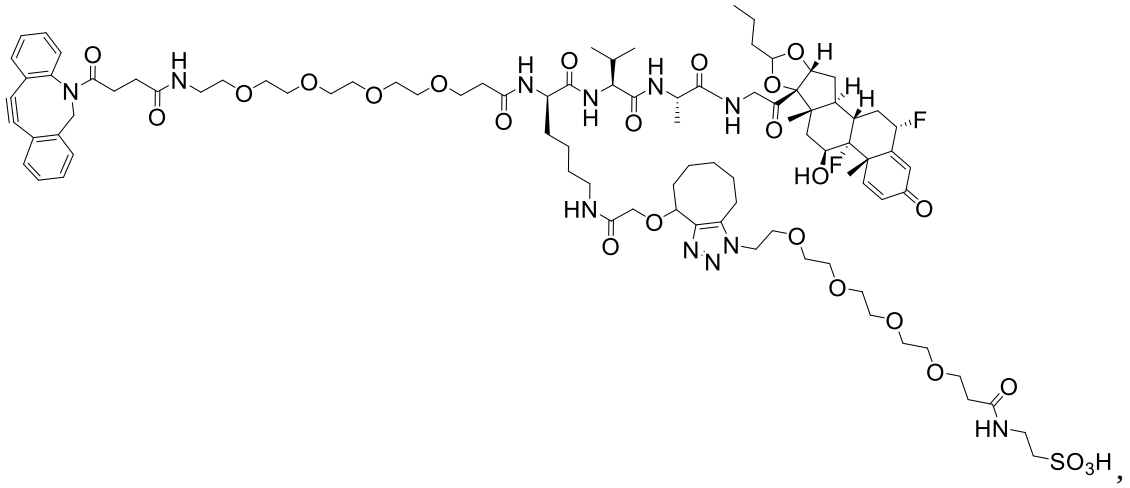
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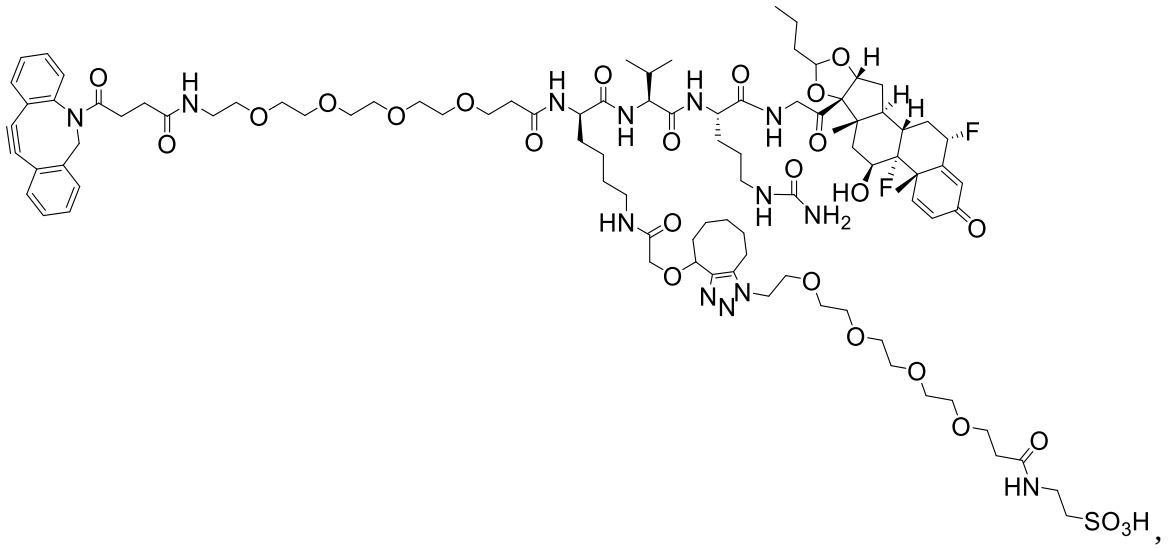


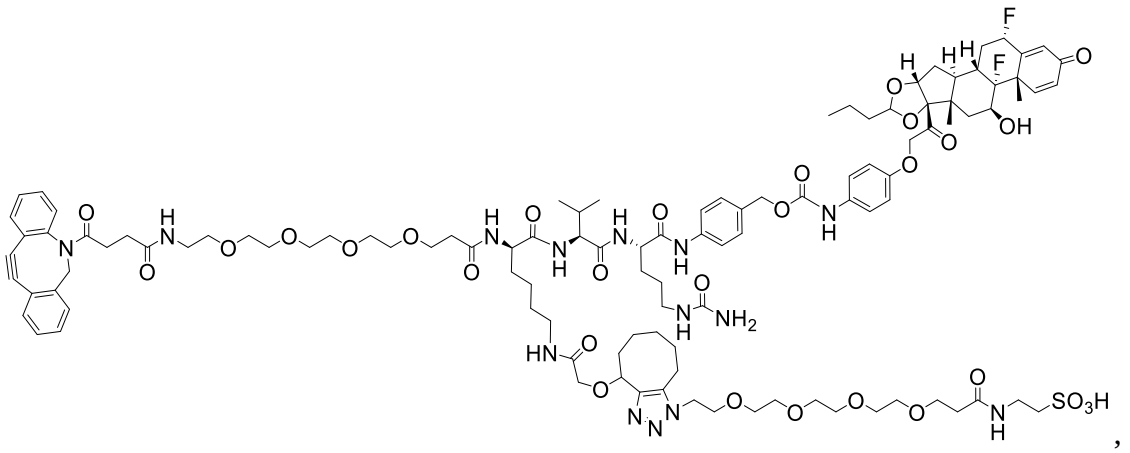
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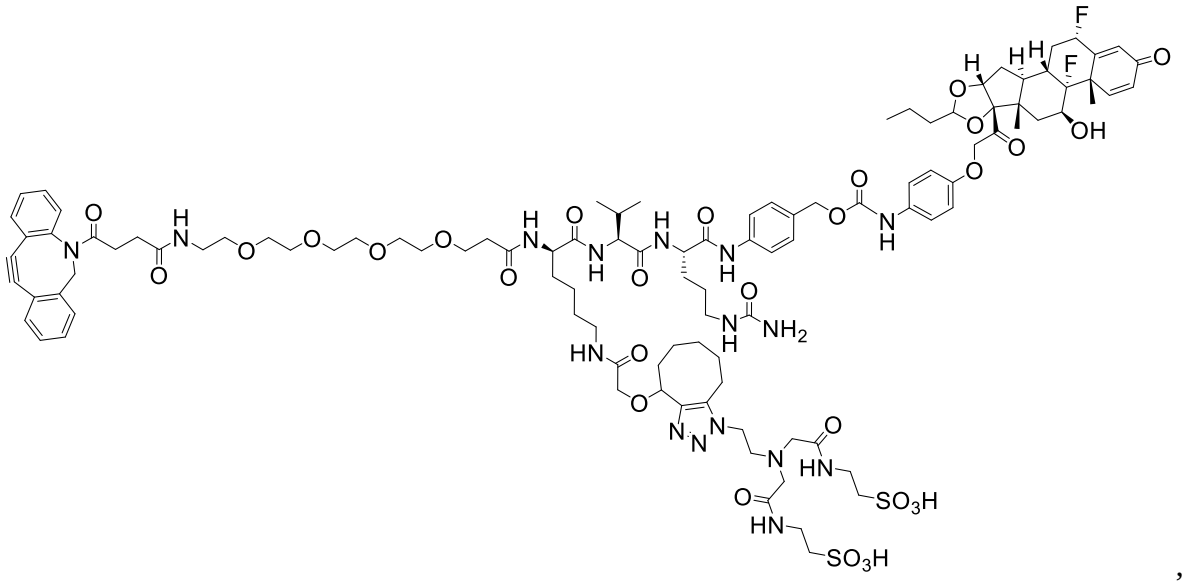


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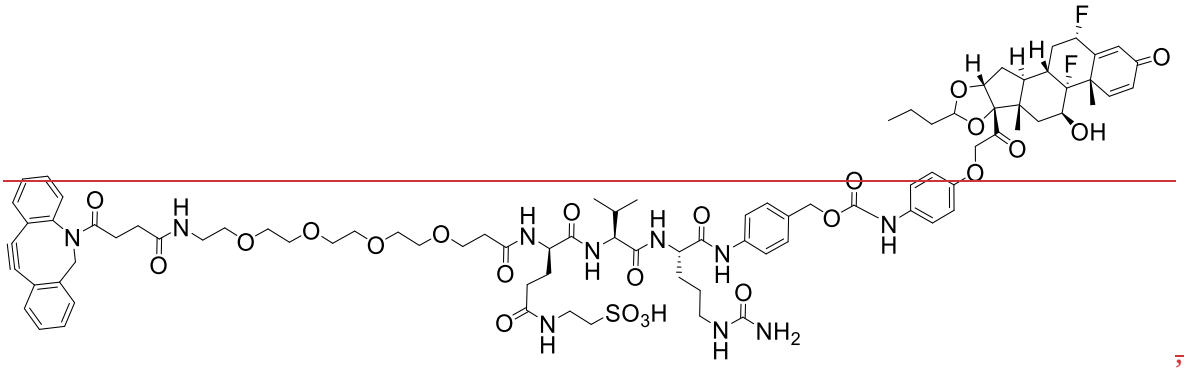




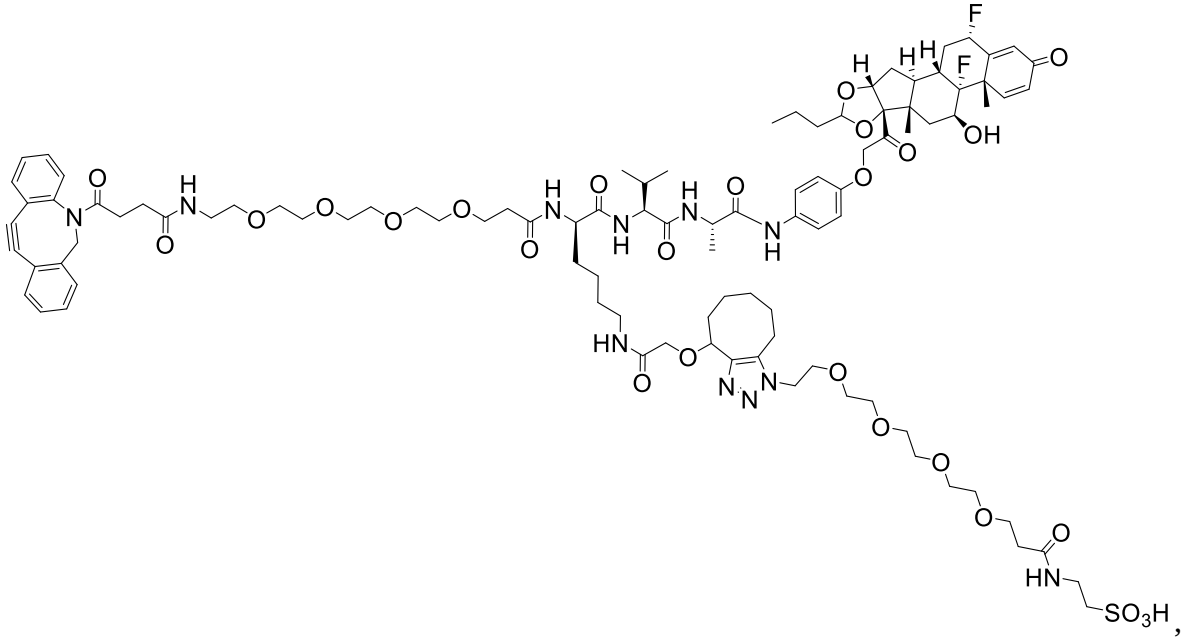




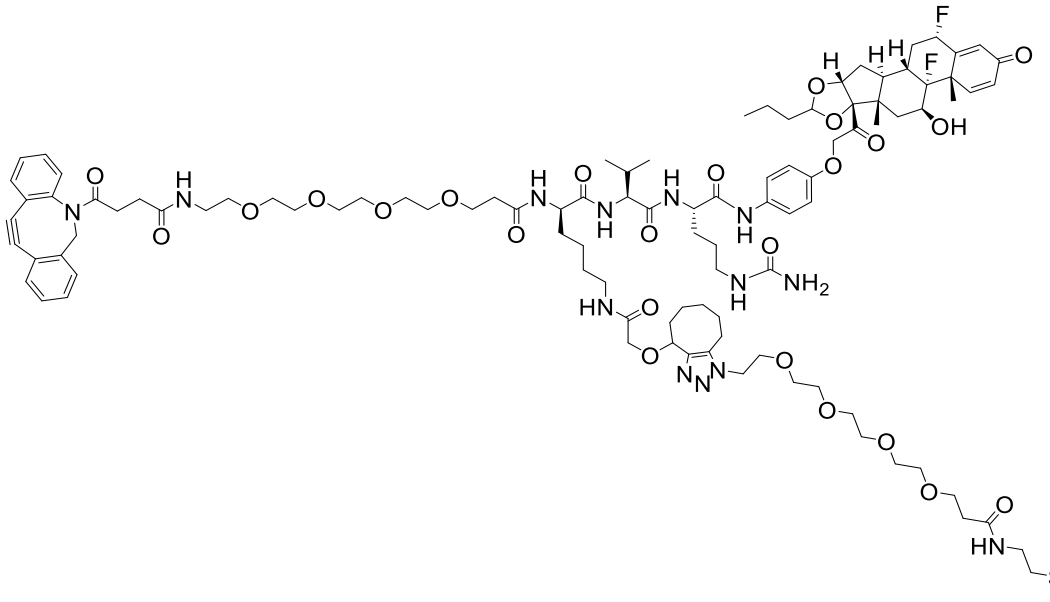
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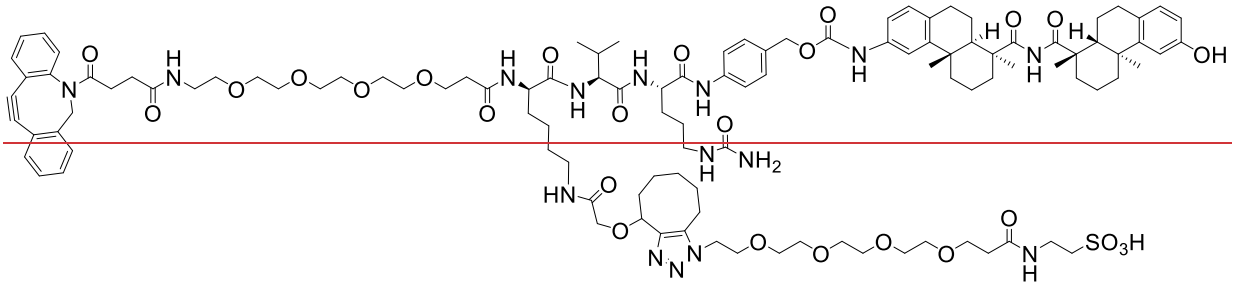
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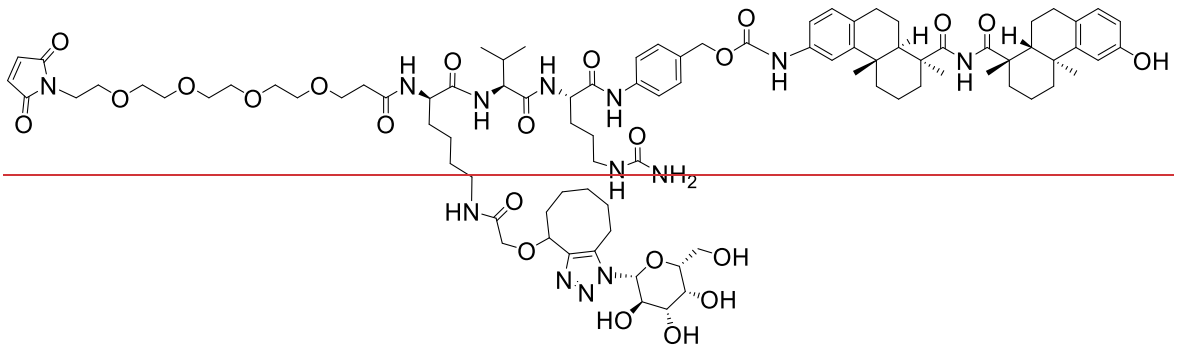
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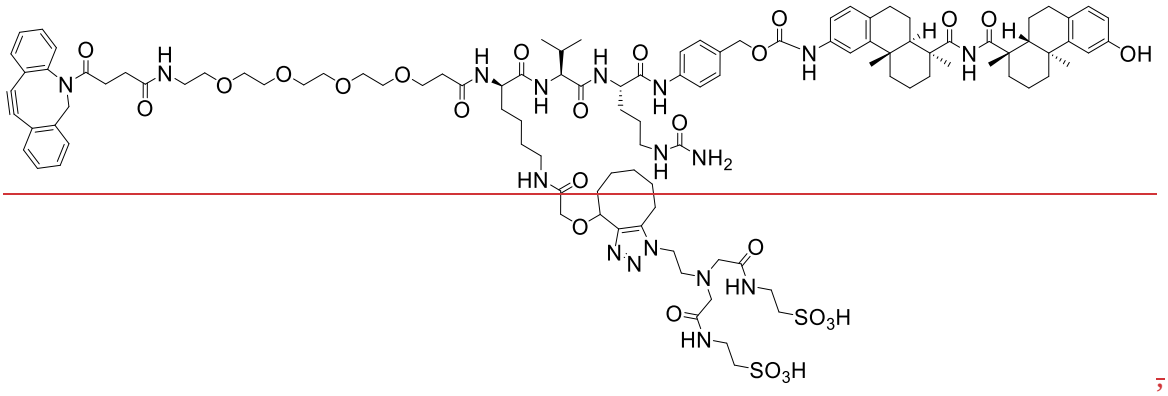
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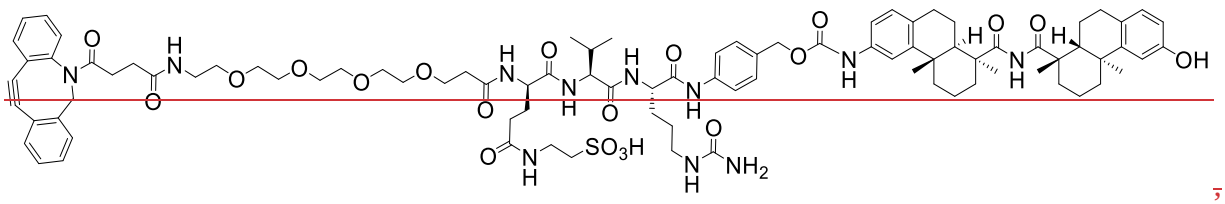
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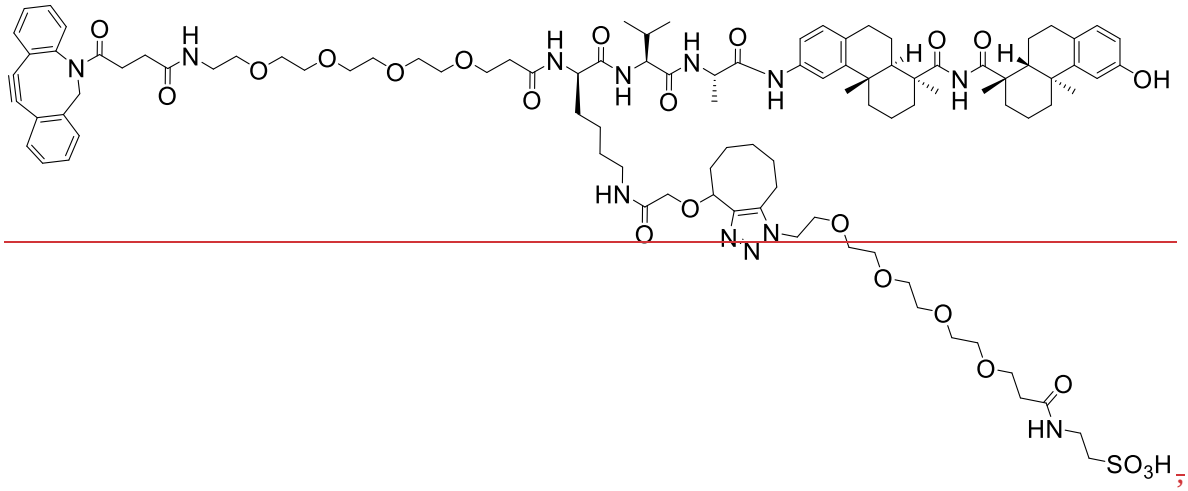


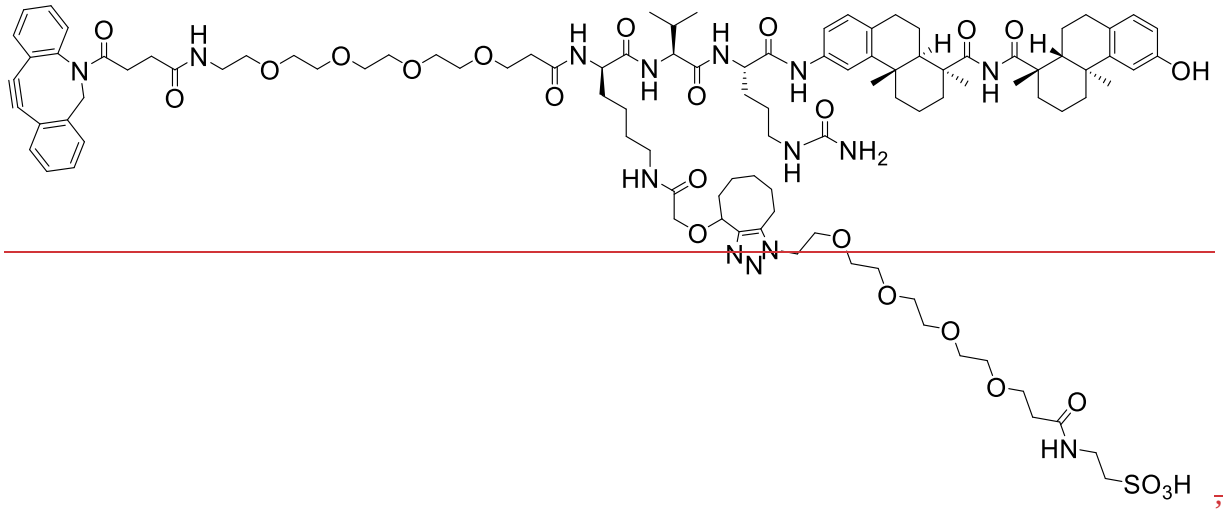
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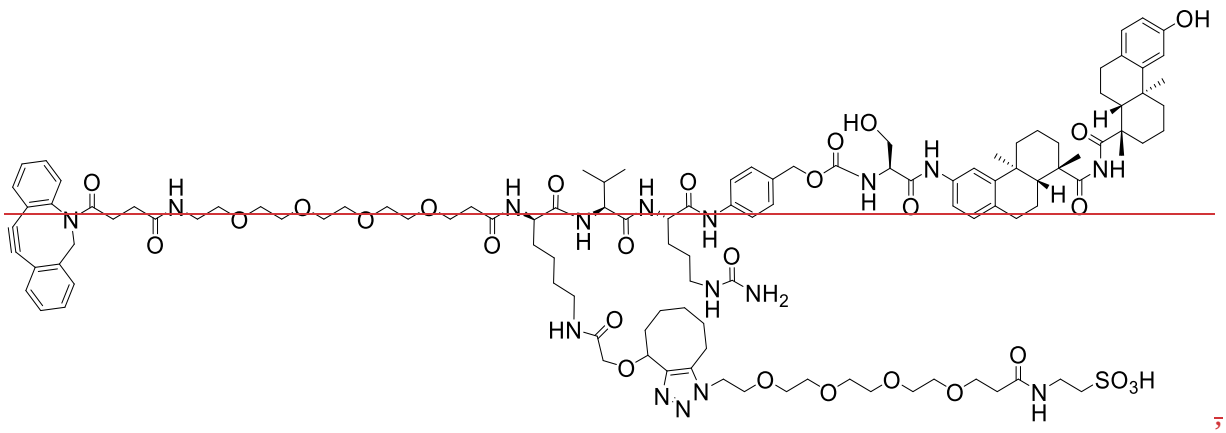


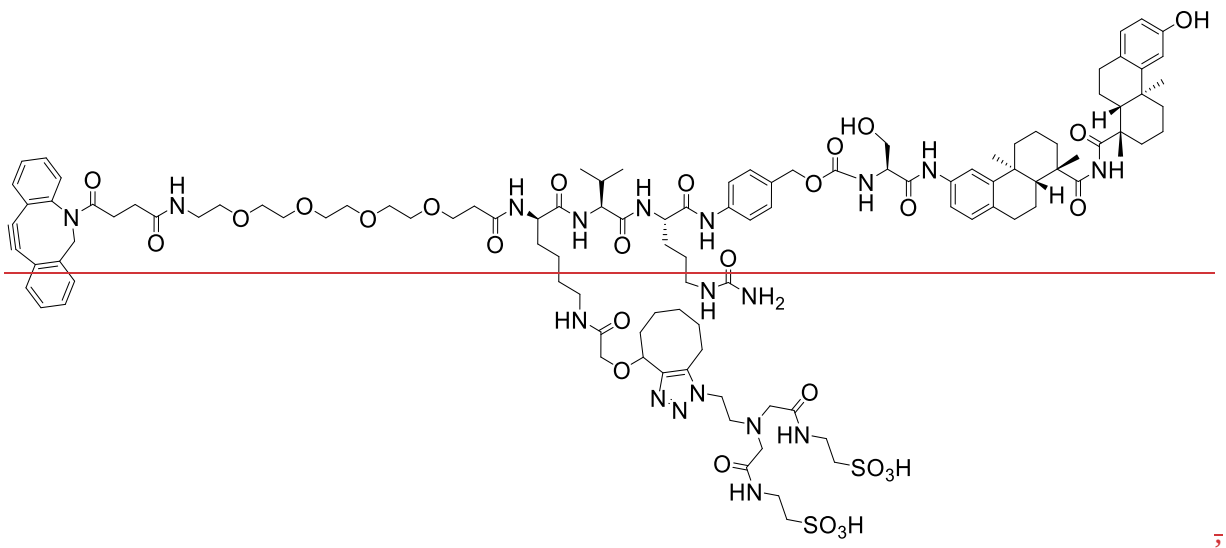
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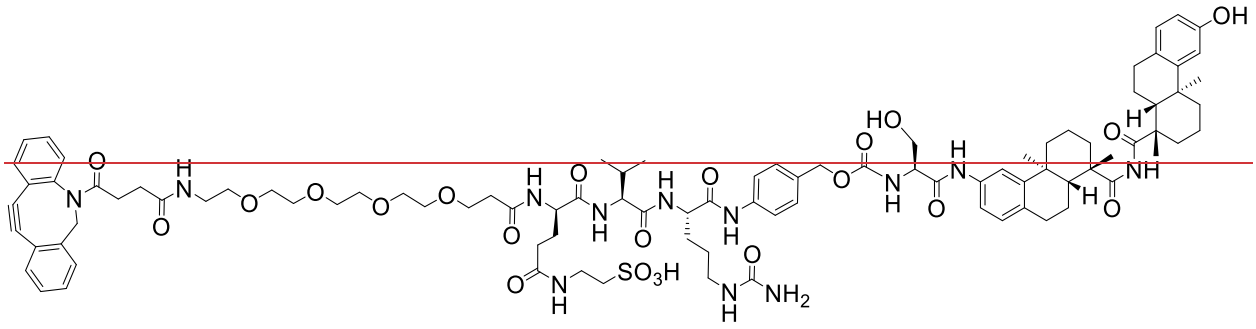




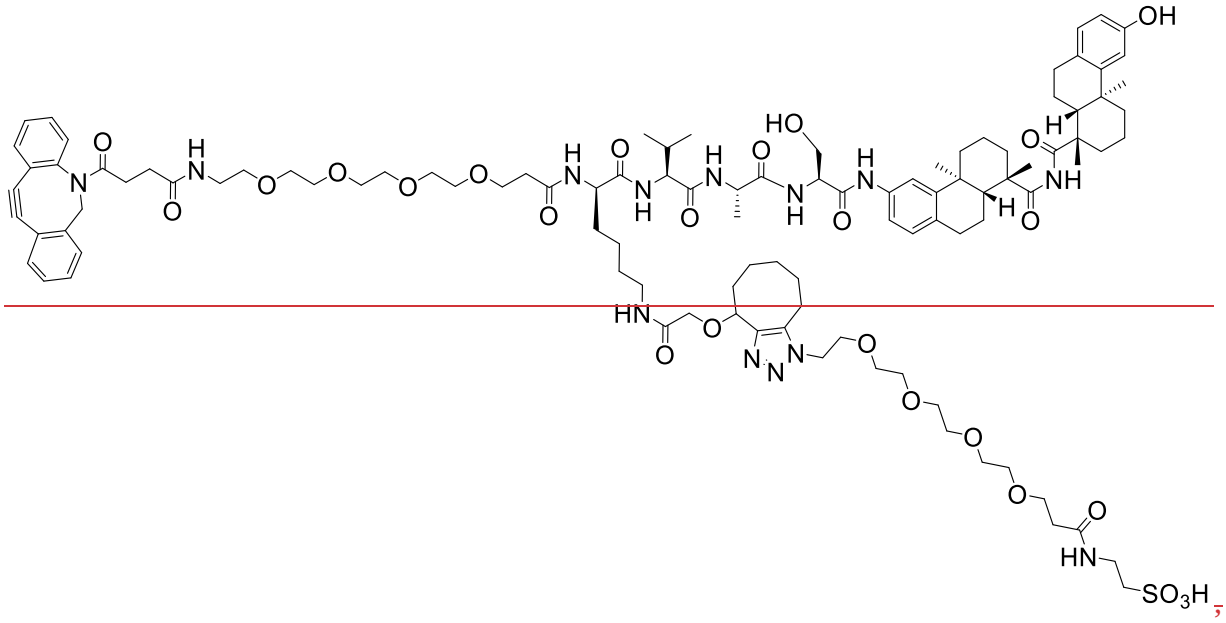




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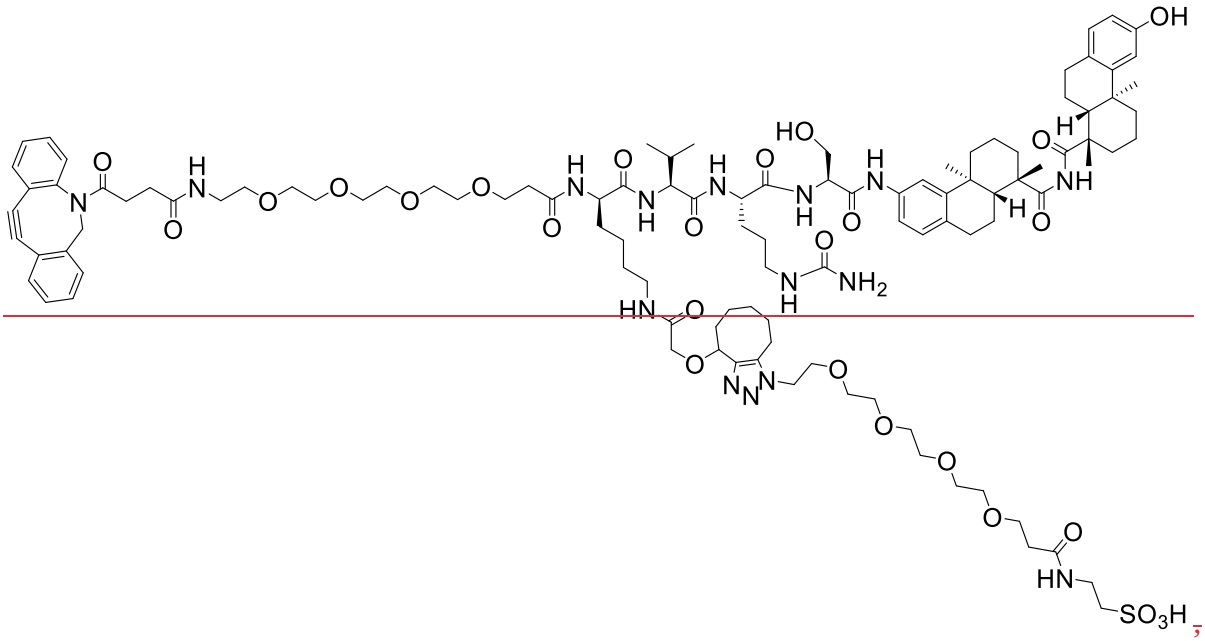


;



;

and



or a stereoisomeric form thereof, or a triazole linkage regioisomer thereof, or a mixture of triazole linkage regioisomers thereof.

~~51~~47. A method of preparing a compound of claim 1 comprising the step of contacting an antibody or antigen binding fragment thereof ~~binding agent~~ with a compound according to any of claims ~~29~~27-~~50~~46, under conditions suitable for forming a bond between the antibody or antigen binding fragment thereof ~~binding agent~~ and the compound.

~~52~~48. The method of claim ~~51~~47, wherein the antibody or antigen binding fragment thereof ~~binding agent~~ is a modified antibody or antigen binding fragment thereof ~~binding agent~~ comprising an azido group () wherein the  indicates the atom through which the azido group is bonded to the adjacent groups in the formula.

~~53~~49. The compound of claim ~~29~~ 28 wherein LL is bonded to an oxygen or a primary or secondary nitrogen of the payload.

~~54~~50. An antibody-drug-conjugate comprising the compound of any of claims ~~29~~27-~~50~~ 46 bonded to an antibody, or an antigen binding fragment thereof.

~~55~~51. A compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 for use in treating a proliferative disease, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

~~56~~52. A compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 for use in the treatment of a proliferative disease in a subject.

~~57~~53. A compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 for use in the treatment of a metabolic disease in a subject.

~~58~~54. A compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 for use in the treatment of inflammation in a subject.

~~59~~55. A compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 for use in the treatment of a neurodegenerative disease in a subject.

~~60~~56. Use of a compound of any one of claims 1-~~28~~ 24 or a pharmaceutical composition of claim ~~29~~ 25 in the manufacture of a medicament for treating a proliferative disease, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.