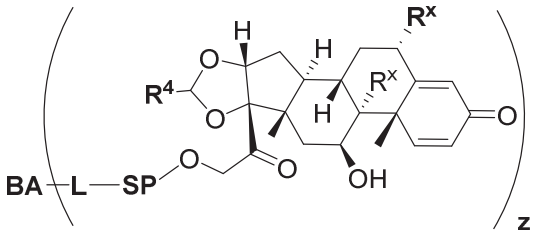
glucocorticoid receptors in non-target cells. The instant disclosure provides solutions to the aforementioned needs as well as other unmet needs in the field to which the instant disclosure pertains. Included in the instant disclosure are antibody-drug conjugates comprising glucocorticoid payloads.

SUMMARY

[0006] Provided herein are compounds and methods useful for the treatment of various diseases, disorders, or conditions.

[0007] A first example is directed to a Compound of Formula (**III**):

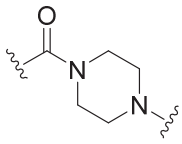
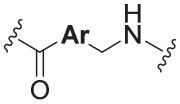


(**III**);

or a pharmaceutically acceptable salt, solvate, stereoisomer, or derivative thereof,

wherein:

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

both $\mathbf{R^x}$ are hydrogen; and **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to **L** in Formula (**III**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where S is attached to **L** in Formula (**III**), -C(O)-N($C_{1\text{-}6}$alkyl)-(C_1-C_{10}-alkylene)-S- where S is attached to **L** in Formula (**III**),  where the point of attachment on the right hand side (*i.e.* at N) is to **L** in Formula (**III**), -CH_2-NH- where the N is attached to **L** in Formula (III),  where the N is attached to **L** in Formula (**III**) and where **Ar** is optionally substituted arylene or optionally substituted heteroarylene, -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$- where

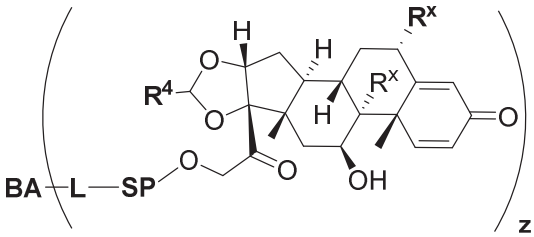
m is 0 or 1;

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

L is a linker; and

BA is a binding agent.

[0007a] One aspect is directed to a Compound of Formula (**III**)

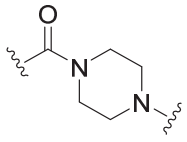
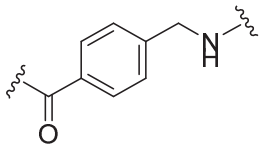


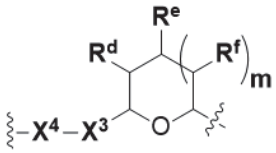
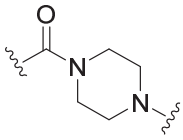
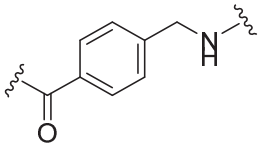
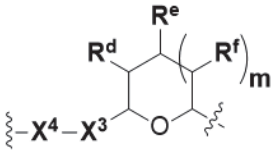
(**III**);

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

both $\mathbf{R^x}$ are hydrogen; and **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to **L** in Formula (**III**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**), -C(O)-N($C_{1\text{-}6}$alkyl)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**),  where the point of attachment at the piperazine nitrogen is attached to **L** in Formula (**III**), -CH_2-NH- where the nitrogen is attached to **L** in Formula (**III**),  where the nitrogen is attached to **L** in Formula (**III**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or

more hydroxy, -C(O)-N(**R**^{5})-C$_{1}$-C$_{10}$-alkylene-C(O)NH-**X**^{2}- where **X**^{2} is attached to **L** in Formula (**III**), or  where **X**^{4} is attached to **L** in Formula (**III**); or both **R**^{x} are fluoro; and **SP** is -C(O)-C$_{1}$-C$_{10}$-alkylene-C(O)-, -C(O)-N(C$_{1-6}$alkyl)-C$_{1}$-C$_{10}$-alkylene-**X**^{1b}- where **X**^{1b} is attached to **L** in Formula (**III**), -C(O)-N(H)-(C$_{1}$-C$_{10}$-alkylene)-**X**^{1b}- where **X**^{1b} is attached to **L** in Formula (**III**),  where the point of attachment at the piperazine nitrogen is attached to **L** in Formula (**III**), -CH$_{2}$-NH- where nitrogen is attached to **L** in Formula (**III**),  where nitrogen is attached to **L** in Formula (**III**), -(C$_{1}$-C$_{10}$-alkylene)-N**R**^{50}C(O)-(C$_{1}$-C$_{10}$-alkylene)-N**R**^{50a}- where the terminal N**R**^{50a} is attached to **L** in Formula (**III**), -C(O)-(C$_{1}$-C$_{10}$-alkylene)-N**R**^{50}C(O)-(C$_{1}$-C$_{10}$-alkylene)-N**R**^{50a}- where the terminal N**R**^{50a} is attached to **L** in Formula (**III**) and where each C$_{1}$-C$_{10}$-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N(**R**^{5})-(C$_{1}$-C$_{10}$-alkylene)-C(O)NH-**X**^{2}- where **X**^{2} is attached to **L** in Formula (**III**), or  where **X**^{4} is attached to **L** in Formula (**III**); and

X^{1} is -N(C$_{1-6}$alkyl)-;

X^{1b} is -S-, -NH-, or -N(C$_{1-6}$alkyl)-;

X^{2} is -NH-;

X^{3} is -CH$_{2}$-, **X**^{3} is -CH$_{2}$-O-(C$_{1}$-C$_{10}$-alkylene)-C(O)- where the C(O) is attached to **X**^{4}, or **X**^{3} is -C(O)-;

X^{4} is -O-;

R^{5} is hydrogen, -OH, -OCH$_{3}$, or C$_{1-6}$alkyl;

R^{50} and **R**^{50a} are independently hydrogen or C$_{1}$-C$_{6}$-alkyl;

R^{d}, **R**^{e}, and **R**^{f} are independently hydrogen, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or -CH$_{2}$O**R**^{g}, where each **R**^{g} is independently -CH$_{2}$C(O)OH or -CH$_{2}$C(O)O(alkyl);

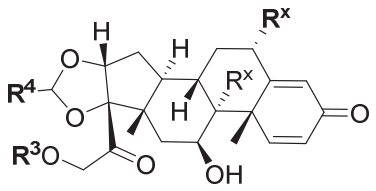
m is zero or one;

z is an integer selected from one to thirty, inclusive;

L is a linker; and

BA is a binding agent.

[0008] A second example is directed to a Compound according to Formula (**I**):



(**I**);

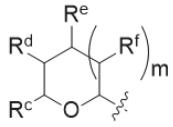
or a pharmaceutically acceptable salt, solvate, stereoisomer, or derivative thereof,

wherein:

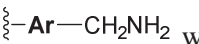
$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

a) both $\mathbf{R^x}$ are hydrogen; and

$\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$; -CH_2NH_2; or



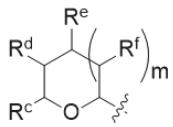
;

$\mathbf{R^Z}$ is -$C_{4\text{-}10}$-alkylene-C(O)OH; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$ where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy;  where where **Ar** is optionally substituted aryl or heteroaryl; or N$\mathbf{R^{15}R^{15a}}$;

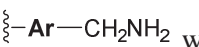
$\mathbf{R^{15}}$ is H or C_1-C_6alkyl and $\mathbf{R^{15a}}$ is -(C_1-C_{10}-alkylene)-SH or -($C_{1\text{-}6}$-alkylene)-C(O)$NHNH_2$;

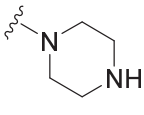
b) both $\mathbf{R^x}$ are fluoro; and

$\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$; -CH_2NH_2; or



;

$\mathbf{R^Z}$ is -$C_{4\text{-}10}$-alkylene-C(O)OH; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$ where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy;  where where **Ar** is optionally substituted aryl or heteroaryl; or N$\mathbf{R^{16}R^{16a}}$;

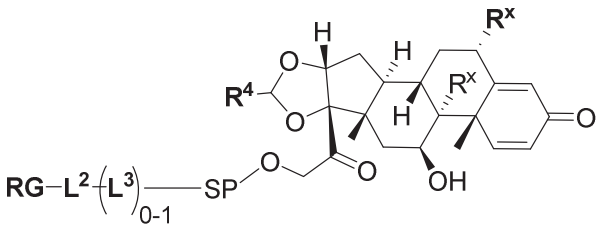
$\mathbf{R^{16}}$ is H or C_1-C_6alkyl and $\mathbf{R^{16a}}$ is -(C_1-C_{10}-alkylene)-SH, -(C_1-C_{10}-alkylene)-NH_2, -(C_1-C_{10}-alkylene)-NH(C_{1-6}alkyl),  , or -(C_{1-6}-alkylene)-C(O)$NHNH_2$; and

each $\mathbf{R^{50}}$, $\mathbf{R^{50a}}$, and $\mathbf{R^{50b}}$ are independently hydrogen or C_1-C_6-alkyl;

one of $\mathbf{R^c}$, $\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ is -$CH_2O\mathbf{R^g}$ and the others are independently -H, -OH, hydroxyalkyl, -C(O)OH, or -$CH_2O\mathbf{R^g}$, where each $\mathbf{R^g}$ is independently -(C_{1-6}-alkylene)-C(O)OH or -(C_{1-6}-alkylene)-C(O)O(alkyl); or one of $\mathbf{R^c}$, $\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ is hydroxyalkyl and the others are -H; and

m is 0 or 1.

[0009] A third example is directed to a Compound of Formula (**II**):

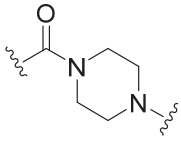
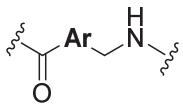


(**II**);

or a pharmaceutically acceptable salt, solvate, stereoisomer, or derivative thereof,

wherein:

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

both $\mathbf{R^x}$ are hydrogen; **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N(C_{1-6}alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where S is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -C(O)-N(C_{1-6}alkyl)-(C_1-C_{10}-alkylene)-S- where S is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**),  where the point of attachment on the right hand side (*i.e.* at N) is to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -CH_2-NH- where the N is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**),  where the N is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**) and where **Ar** is optionally substituted arylene or optionally substituted heteroarylene, -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**) and where each C_1-C_{10}-

$\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ are independently -H, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or $-CH_2O\mathbf{R^g}$, where each $\mathbf{R^g}$ is independently $-CH_2C(O)OH$ or $-CH_2C(O)O(alkyl)$; and

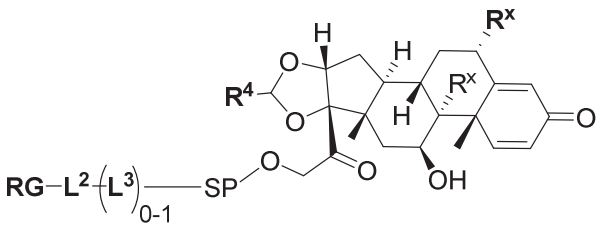
m is 0 or 1;

RG is a reactive group;

$\mathbf{L^2}$ is connecting linker; and

$\mathbf{L^3}$, when present, is a self-immolative linker.

[0009a] Another aspect is directed to a Compound of Formula (**II**)

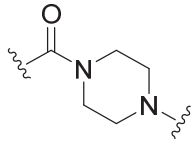
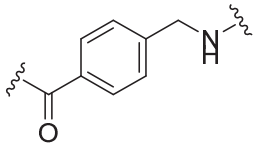


(**II**);

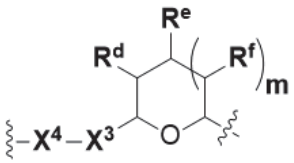
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein

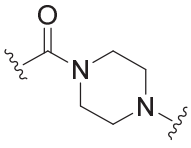
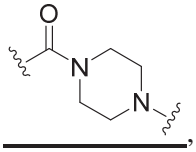
$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

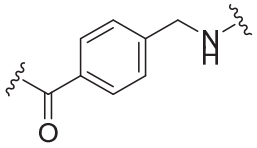
both $\mathbf{R^x}$ are hydrogen; **SP** is $-C(O)-C_1-C_{10}$-alkylene-C(O)-, $-C(O)-N(C_{1-6}alkyl)-C_1-C_{10}$-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), $-C(O)-N(C_{1-6}alkyl)-(C_1-C_{10}$-alkylene)-S- where sulfur is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**),  where the point of attachment at the piperazine nitrogen is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -CH_2-NH- where nitrogen is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**),  where nitrogen is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-$N\mathbf{R^{50}}C(O)-(C_1-C_{10}$-alkylene)-$N\mathbf{R^{50a}}$- where the terminal $N\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-$N\mathbf{R^{50}}C(O)-(C_1-C_{10}$-alkylene)-$N\mathbf{R^{50a}}$- where the terminal $N\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0-1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently

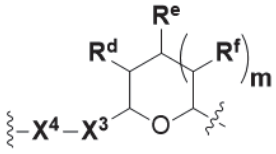
optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$-

where $\mathbf{X^2}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), or  where $\mathbf{X^4}$ is attached to $\mathbf{L^3}$ in Formula (**II**); or

both $\mathbf{R^x}$ are fluoro; **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^{1b}}$- where $\mathbf{X^{1b}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-$\mathbf{X^{1b}}$-

where $\mathbf{X^{1b}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where the point of attachment at the piperazine nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  ,

-CH_2-NH- where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-(C_1-C_{10}-alkylene)-C(O)NH-

$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), or  where $\mathbf{X^4}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**); and

$\mathbf{X^1}$ is -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^{1b}}$ is -S-, -NH-, or -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^2}$ is -NH-;

$\mathbf{X^3}$ is -CH_2-, $\mathbf{X^3}$ is -CH_2-O-(C_1-C_{10}-alkylene)-C(O)- where the C(O) is attached to $\mathbf{X^4}$, or $\mathbf{X^3}$ is -C(O)-;

$\mathbf{X^4}$ is -O-;

R^5 is hydrogen, -OH, $-OCH_3$, or C_{1-6}alkyl;

R^{50} and **R^{50a}** are independently hydrogen or C_1-C_6-alkyl;

R^d, **R^e**, and **R^f** are independently hydrogen, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or $-CH_2OR^g$, where each **R^g** is independently $-CH_2C(O)OH$ or $-CH_2C(O)O$(alkyl);

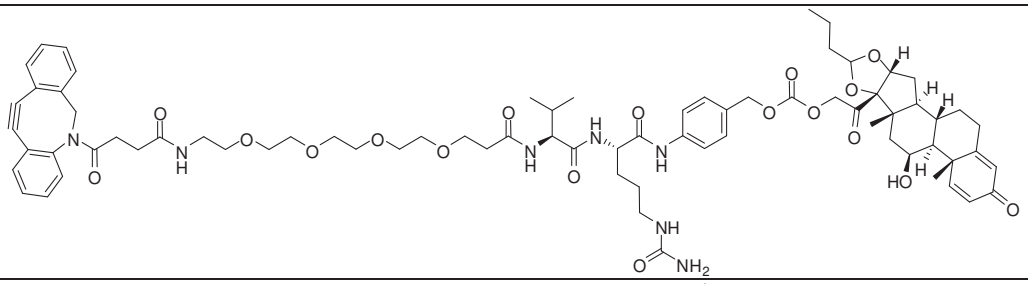
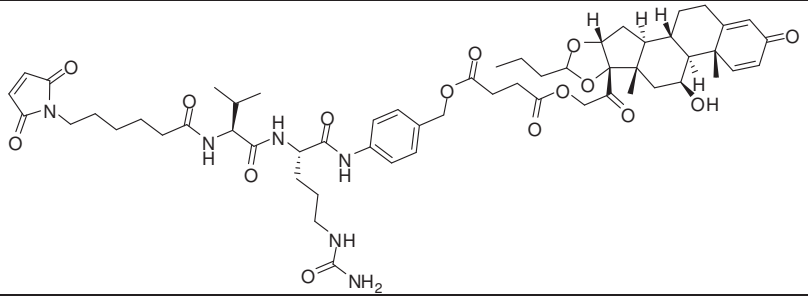
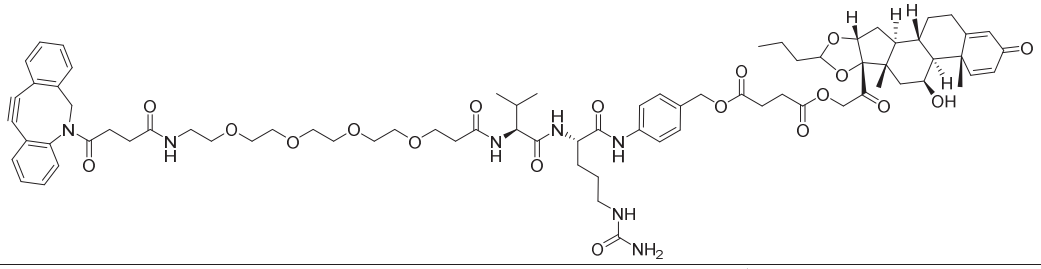
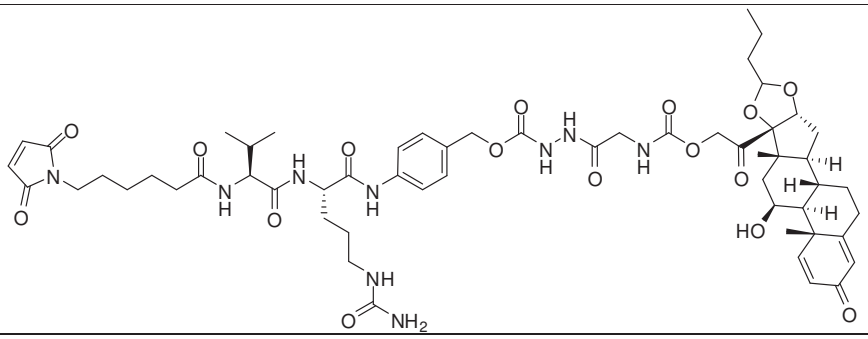
m is zero or one;

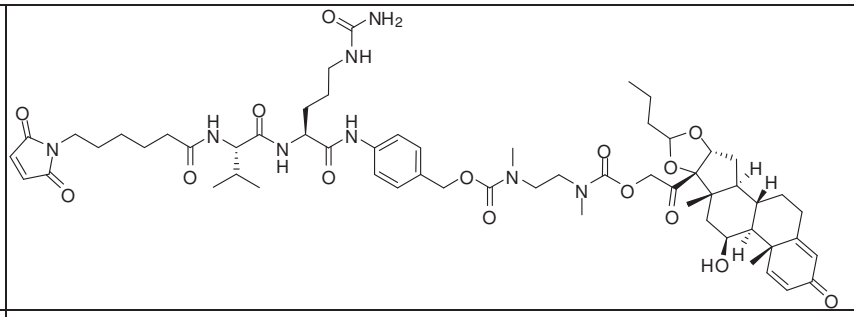
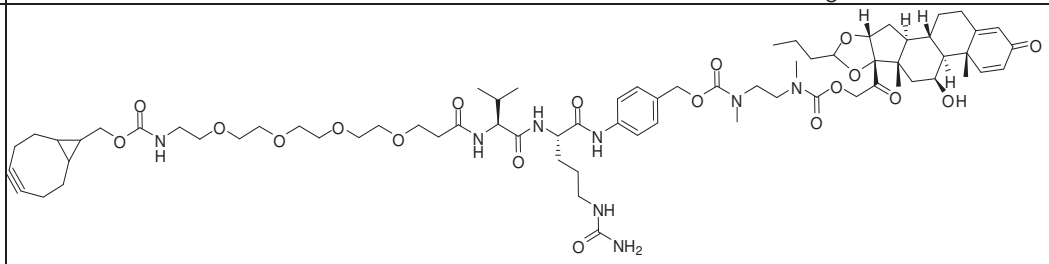
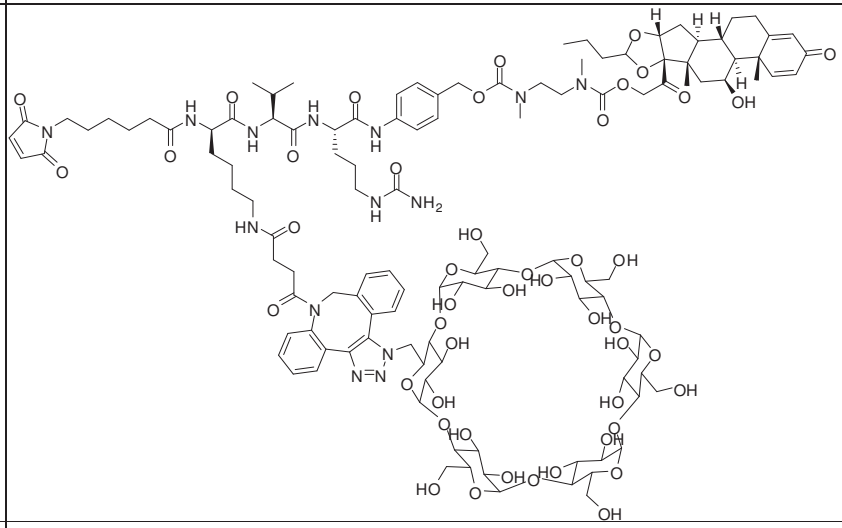
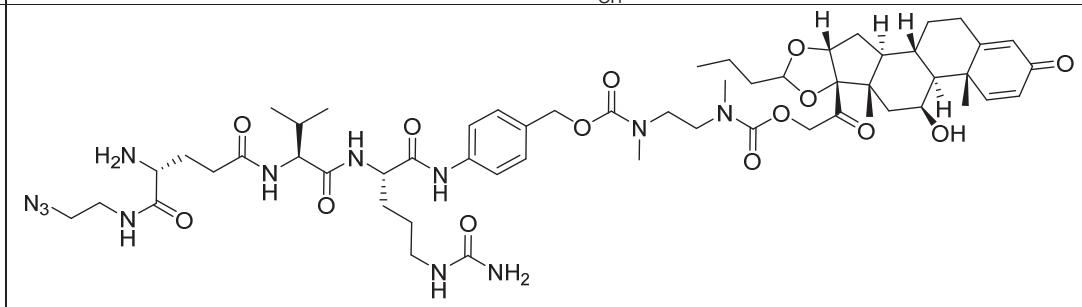
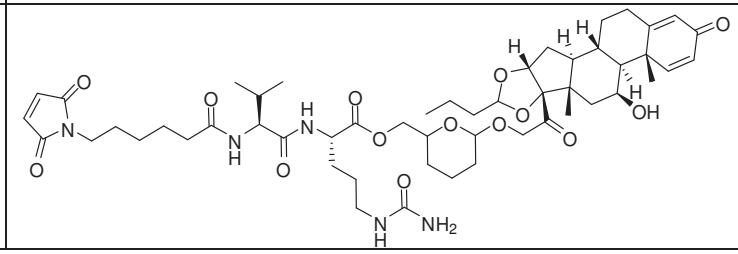
RG is a reactive group;

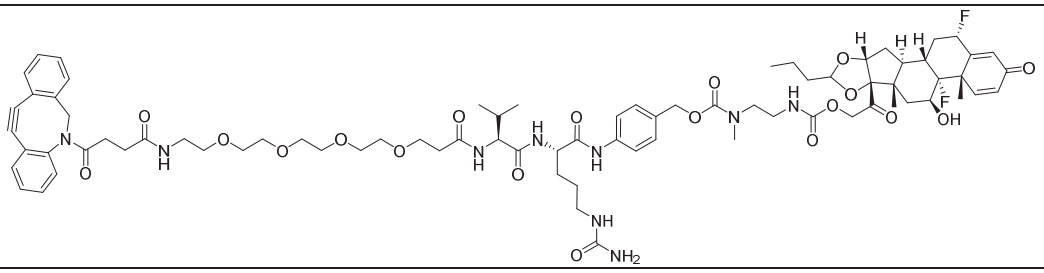
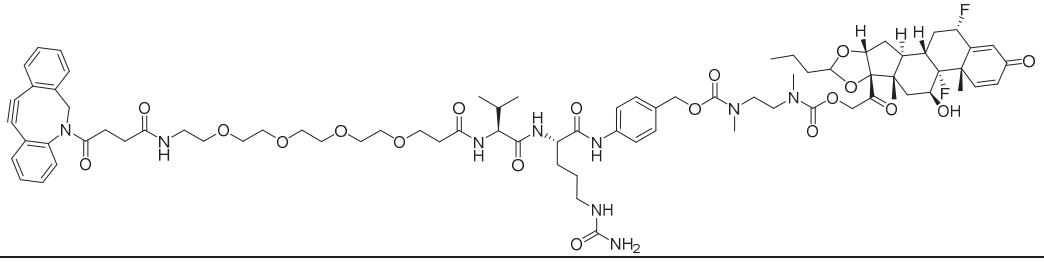
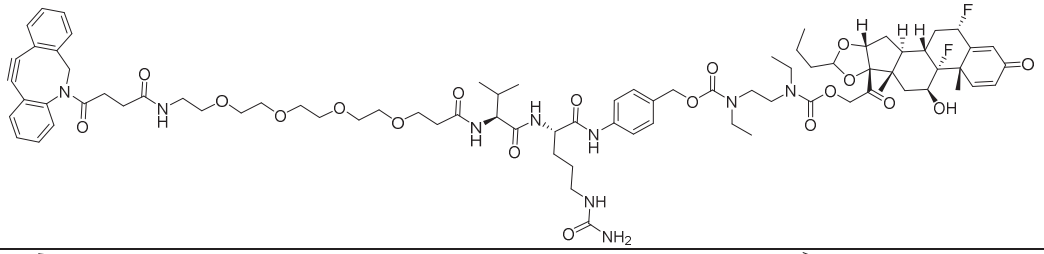
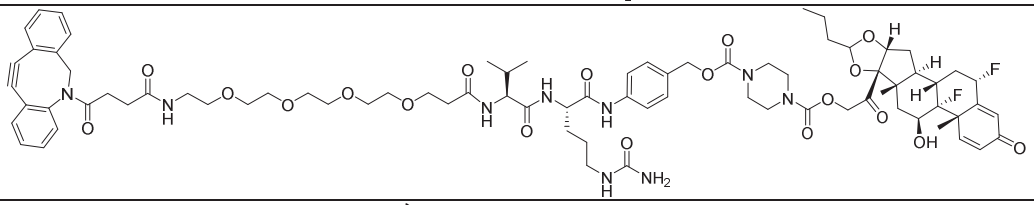
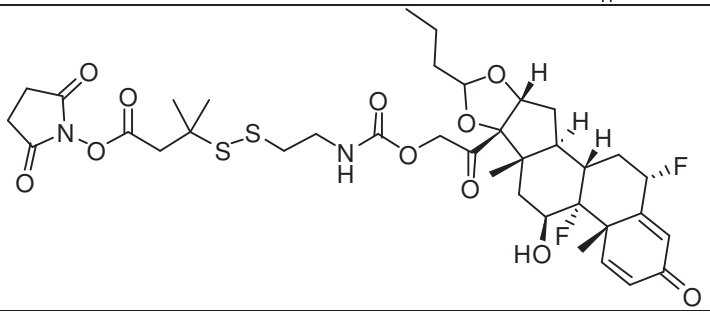
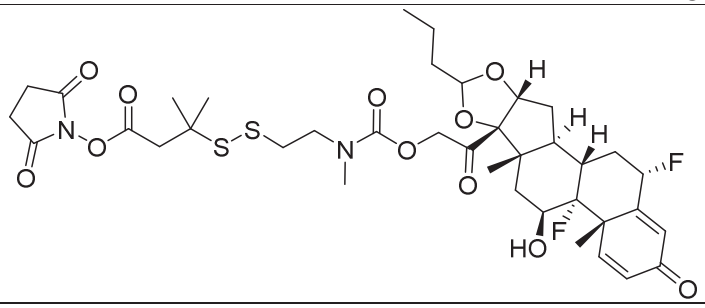
L^2 is a connecting linker; and

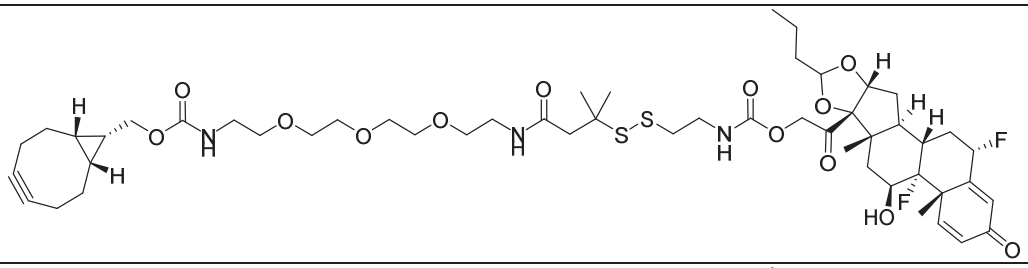
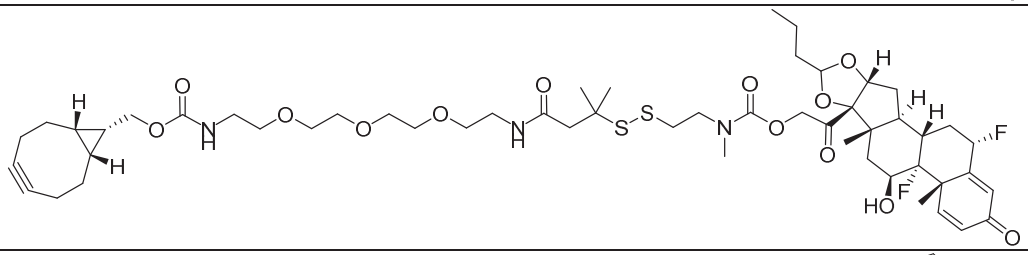
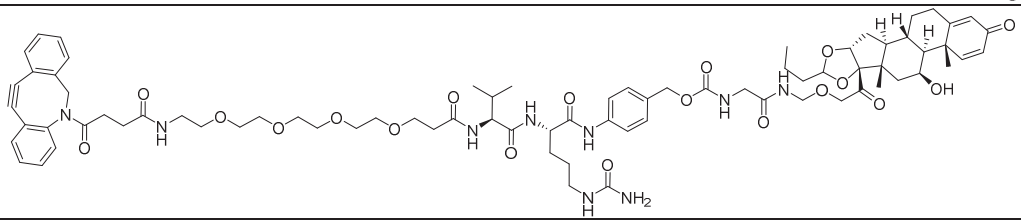
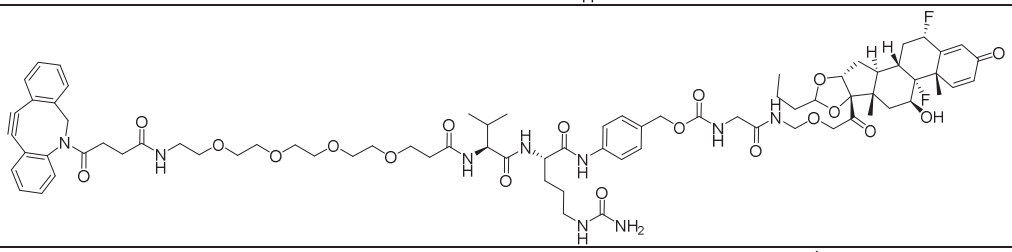
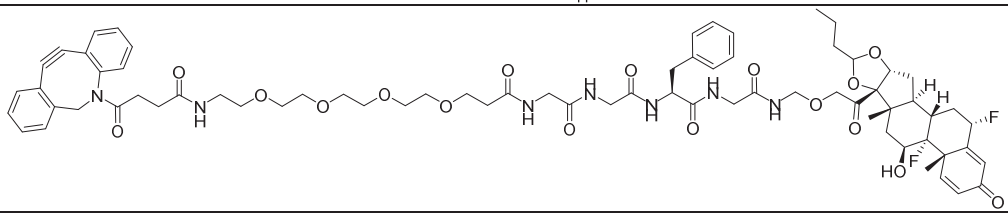
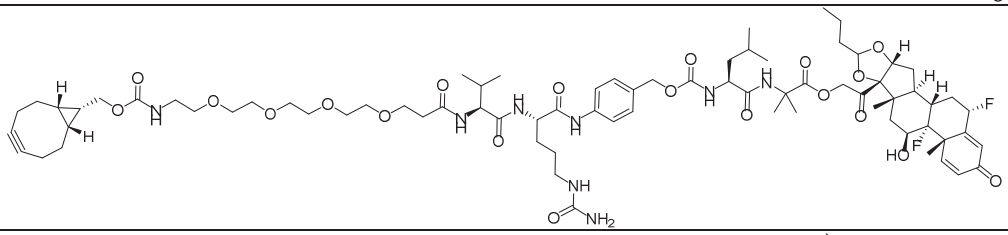
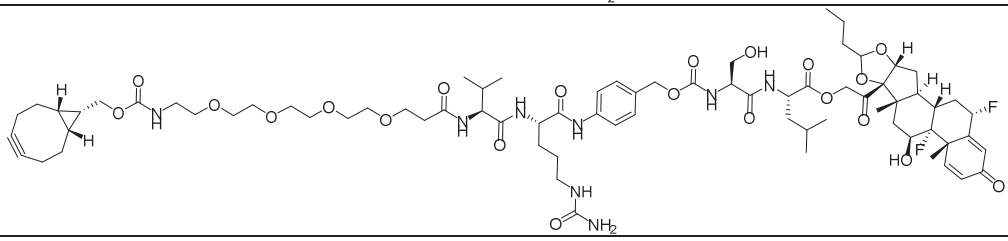
L^3, when present, is a self-immolative linker.

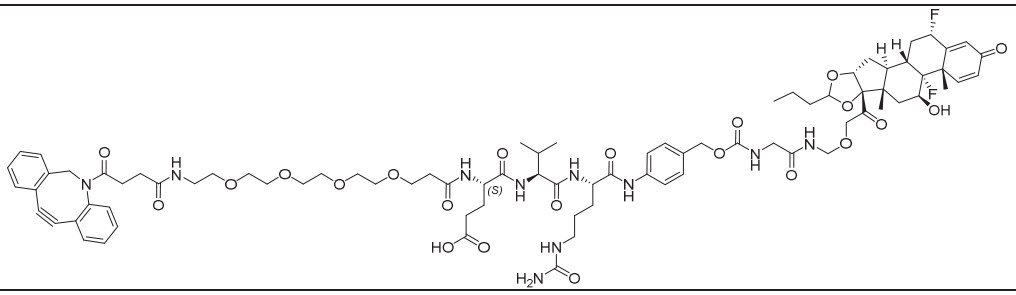
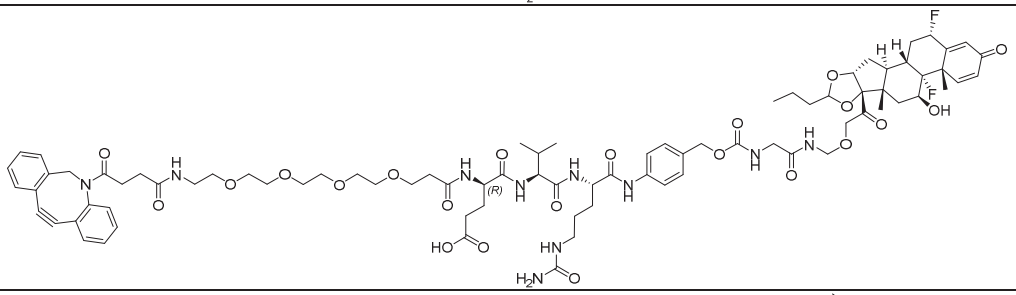
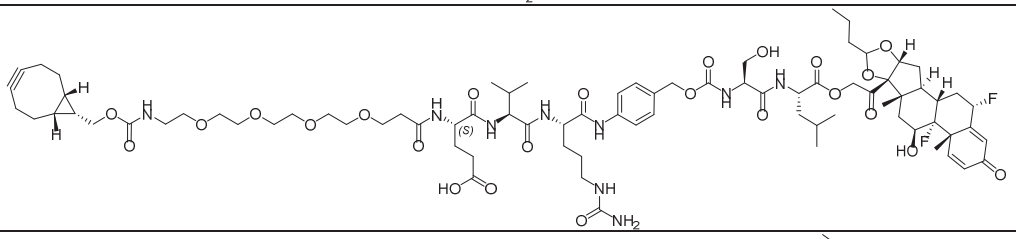
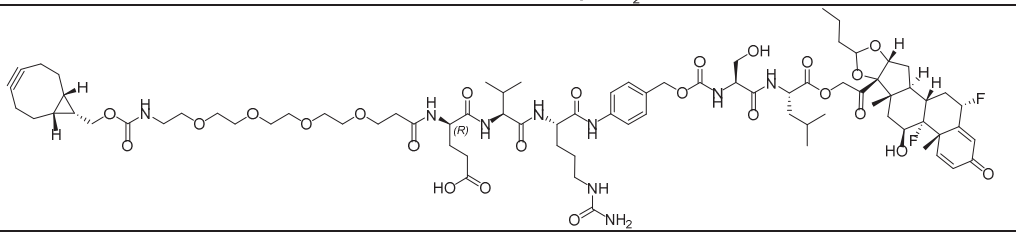
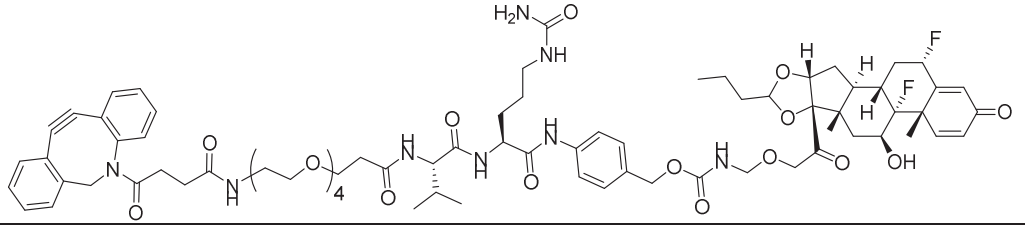
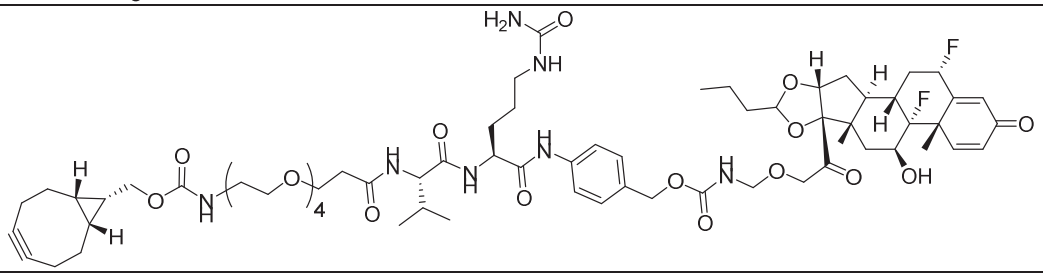
[0009b] Another aspect is directed to a compound selected from the group consisting of

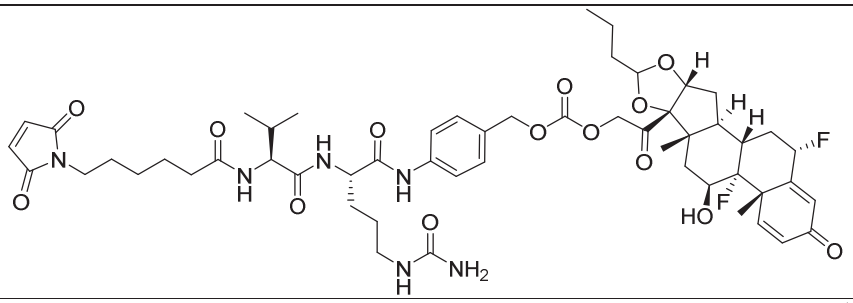
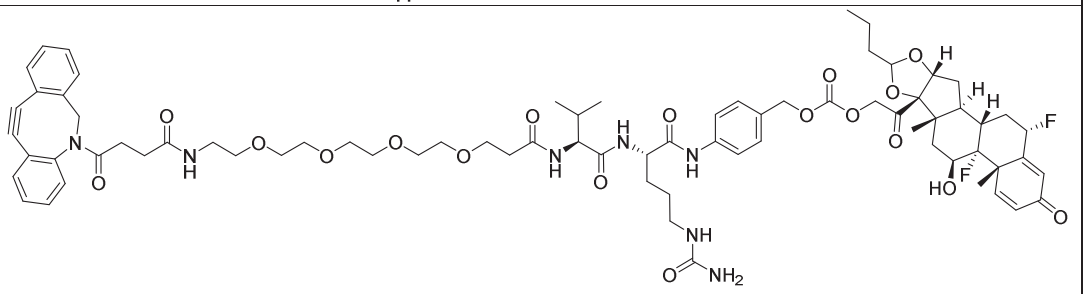
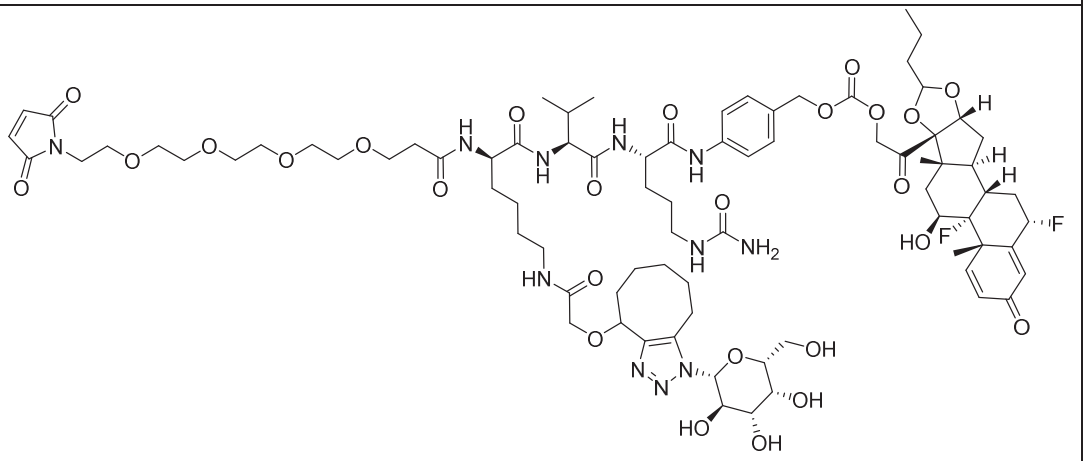
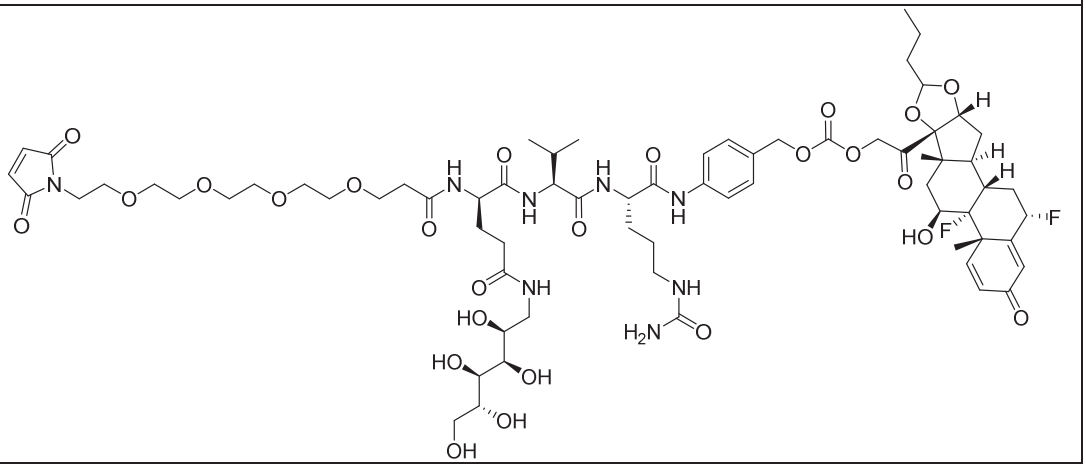
2b	
2f	
2g	
2j	

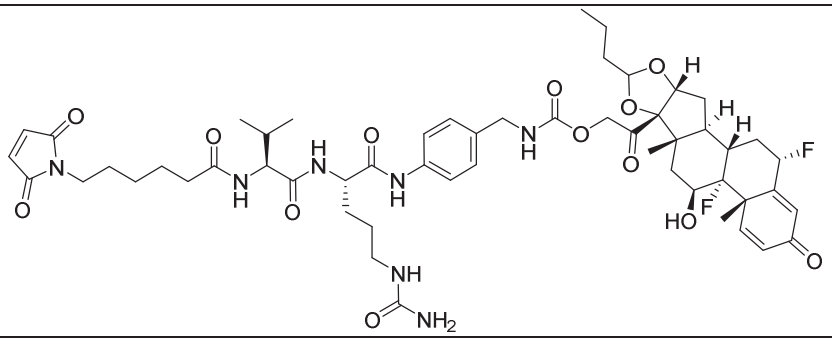
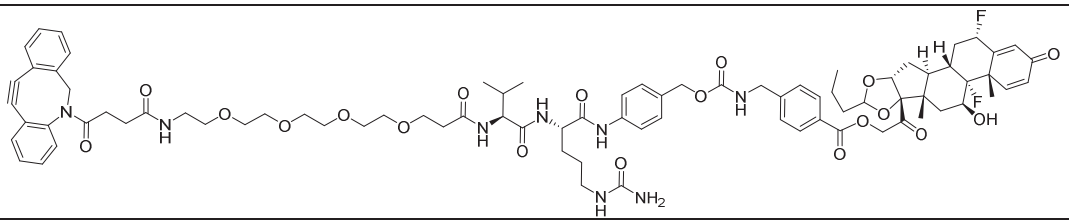
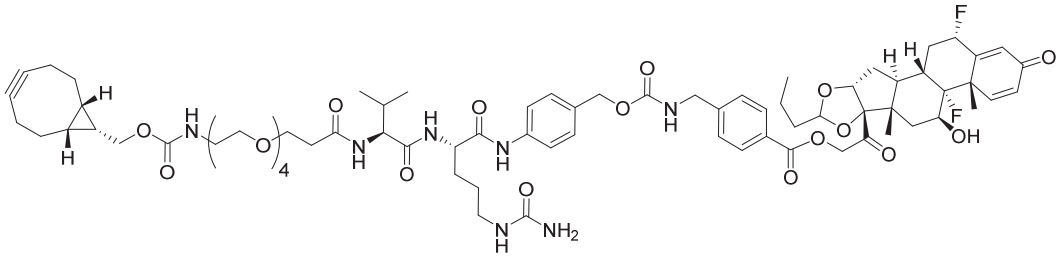
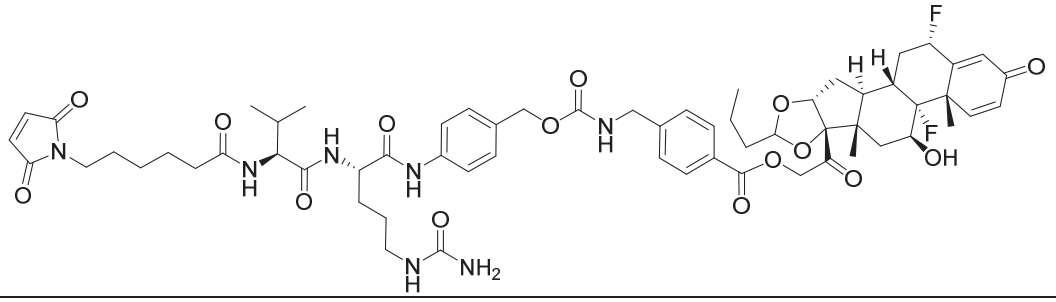
2k	
2l	
2m	
2n	 or a mixture thereof
2q	

LP1	
LP2	
LP3	
LP4	
LP5	
LP6	

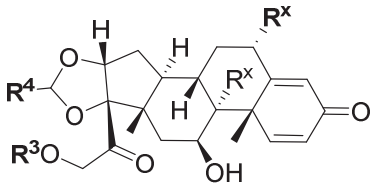
LP7	
LP8	
LP9	
LP10	
LP11	
LP12	
LP13	

LP18	
LP19	
LP20	
LP21	
LP22	
LP23	

LP24	
LP25	
LP26	
LP27	

LP28	
LP29	
LP30	 and
LP31	

[0009c] Another aspect is directed to a Compound according to Formula (**I**)



(**I**);

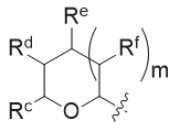
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

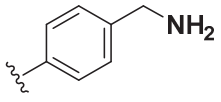
wherein

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

a) both $\mathbf{R^x}$ are hydrogen; and

R³ is -C(O)**R^Z**; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}**; -CH_2NH_2; or

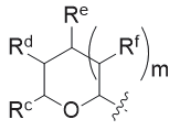

;

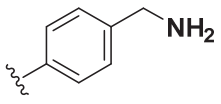
R^Z is -C₄₋₁₀-alkylene-C(O)OH; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}** where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy;  ; or N**R^{15}R^{15a}**;

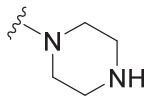
R¹⁵ is hydrogen or C₁-C₆alkyl and **R^{15a}** is -(C₁-C₁₀-alkylene)-SH or -(C₁₋₆-alkylene)-C(O)$NHNH_2$; or

b) both **R^x** are fluoro; and

R³ is -C(O)**R^Z**; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}**; -CH_2NH_2; or


;

R^Z is -C₄₋₁₀-alkylene-C(O)OH; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}** where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy;  ; or N**R^{16}R^{16a}**;

R¹⁶ is hydrogen or C₁-C₆alkyl and **R^{16a}** is -(C₁-C₁₀-alkylene)-SH, -(C₁-C₁₀-alkylene)-NH_2, -(C₁-C₁₀-alkylene)-NH(C₁₋₆alkyl),  , or -(C₁₋₆-alkylene)-C(O)$NHNH_2$; and

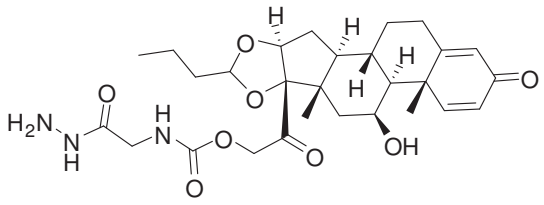
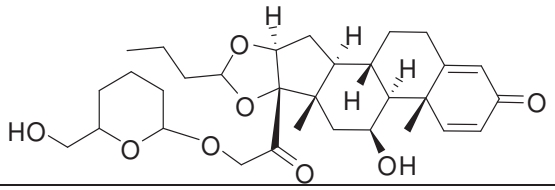
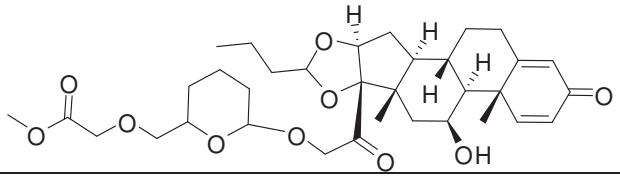
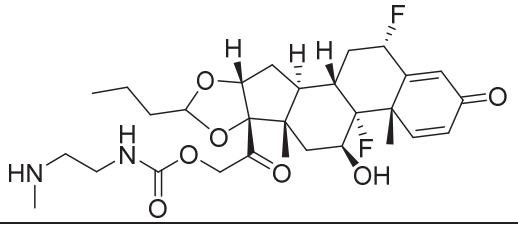
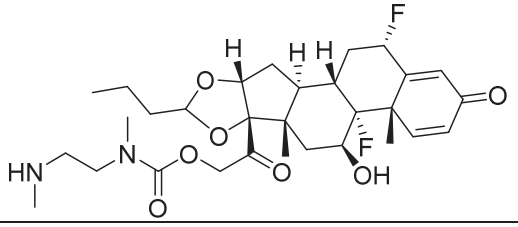
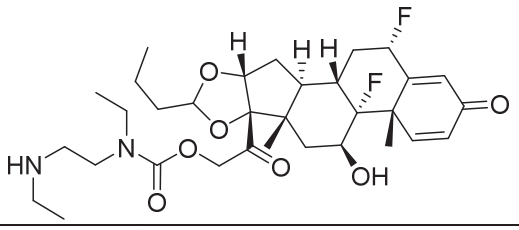
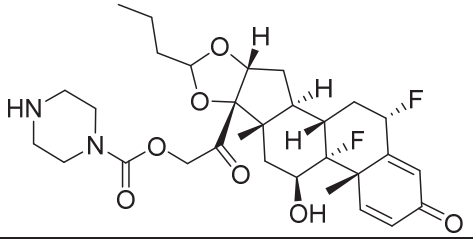
each **R⁵⁰**, **R^{50a}**, and **R^{50b}** are independently hydrogen or C₁-C₆-alkyl;

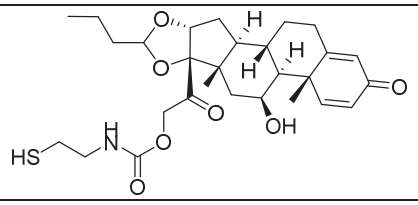
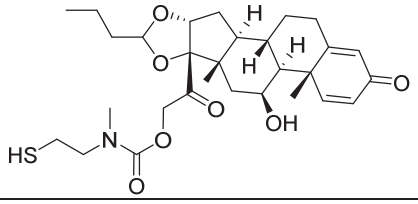
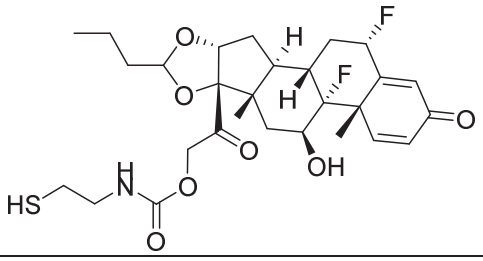
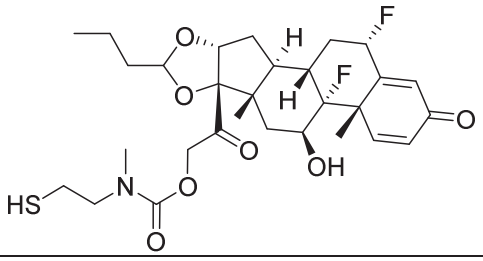
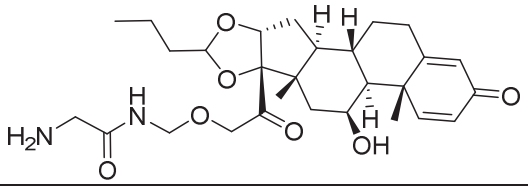
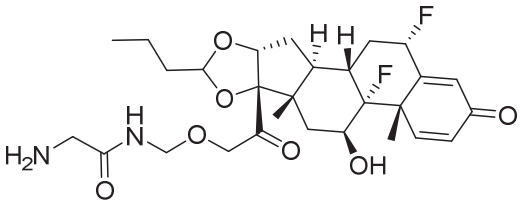
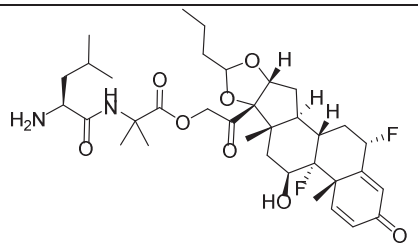
one of **R^c**, **R^d**, **R^e**, and **R^f** is -CH_2O**R^g** and the others are independently hydrogen, -OH, hydroxyalkyl,

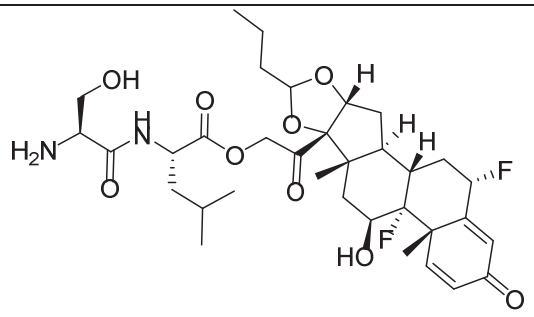
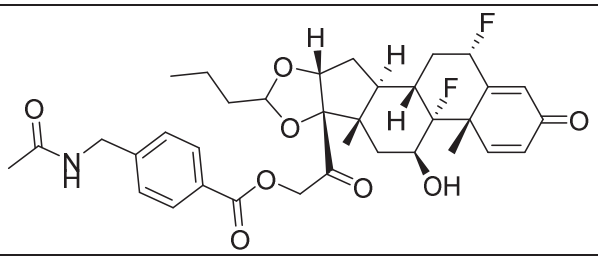
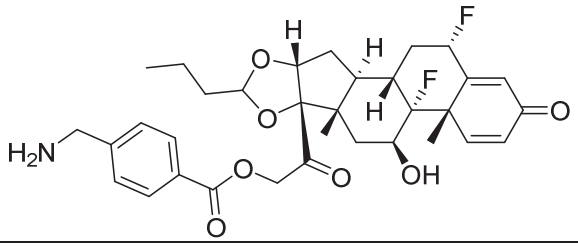
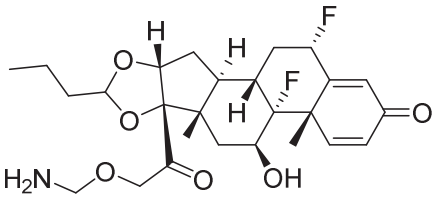
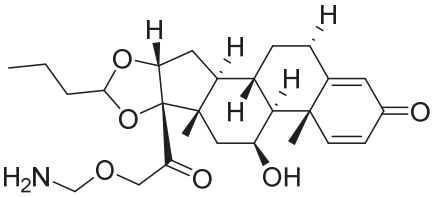
-C(O)OH, or -CH_2O**R^g**, where each **R^g** is independently -(C₁₋₆-alkylene)-C(O)OH or -(C₁₋₆-alkylene)-C(O)O(alkyl); or one of **R^c**, **R^d**, **R^e**, and **R^f** is hydroxyalkyl and the others are hydrogen; and

m is zero to one.

[0009d] Another aspect is directed to a compound selected from the group consisting of

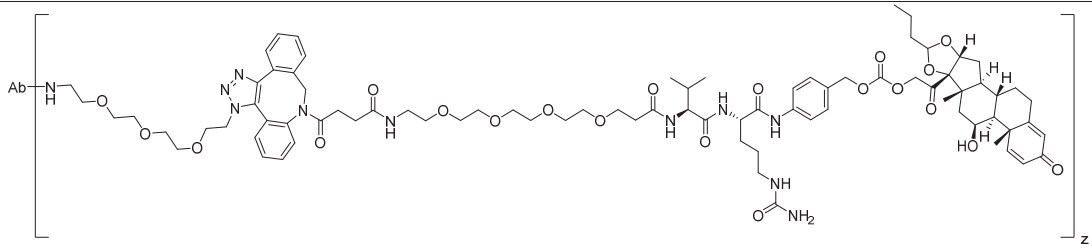
1e	
1g	
1h	
101a	
101b	
101c	
101d	

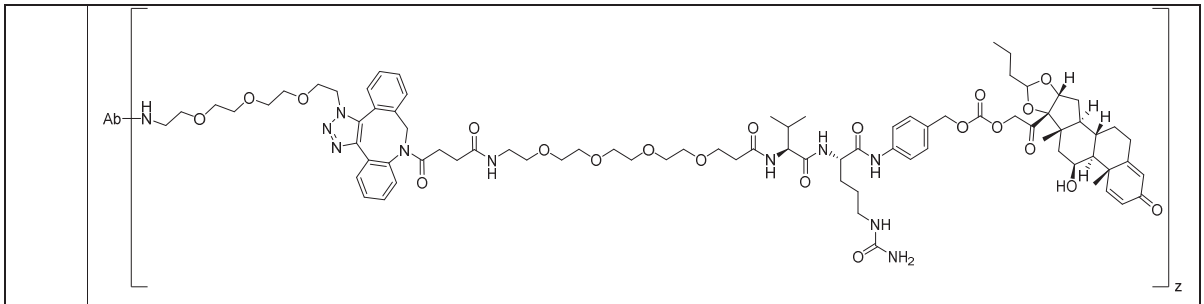
102c	
102d	
102e	
102f	
103a	
103b	
104a	

104b	
105a	
105b	
106a	 and
107a	 ; or

a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

[0009e] Another aspect is directed to a Compound selected from the group consisting of

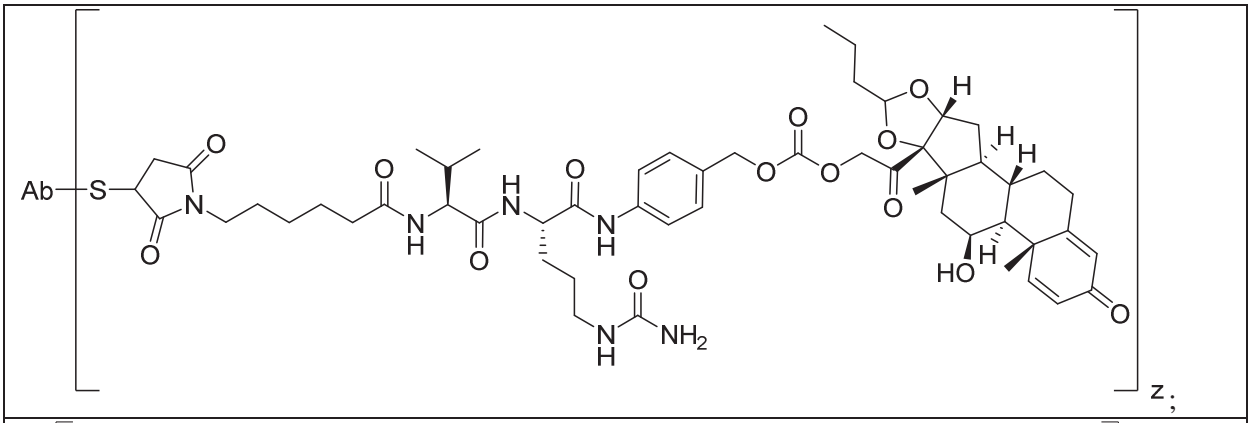
	 , and

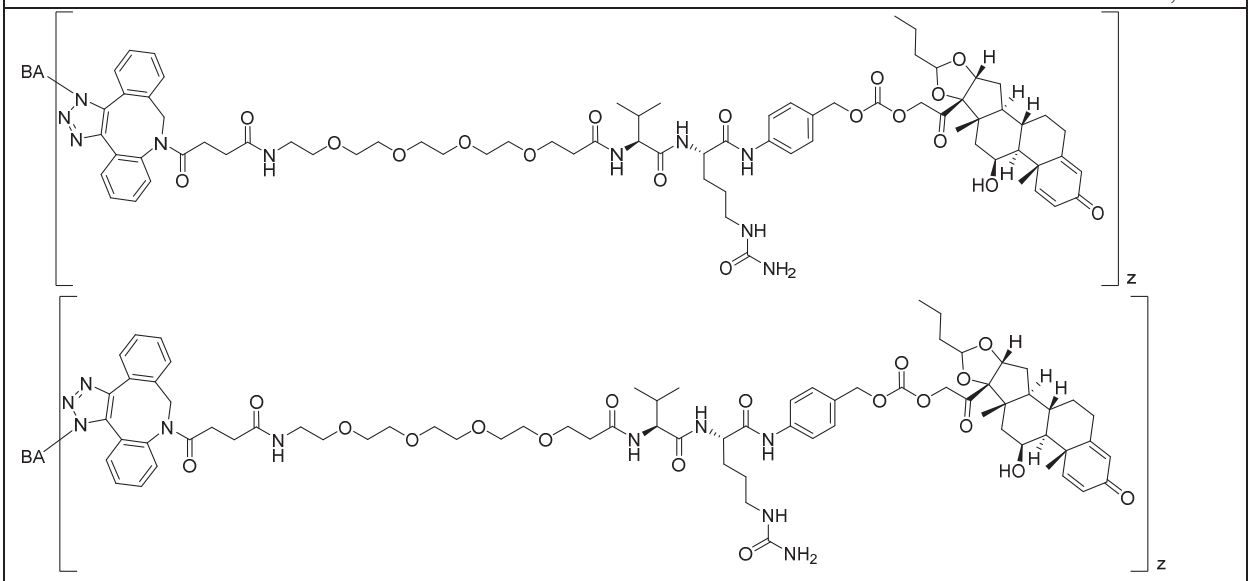


or a mixture thereof;

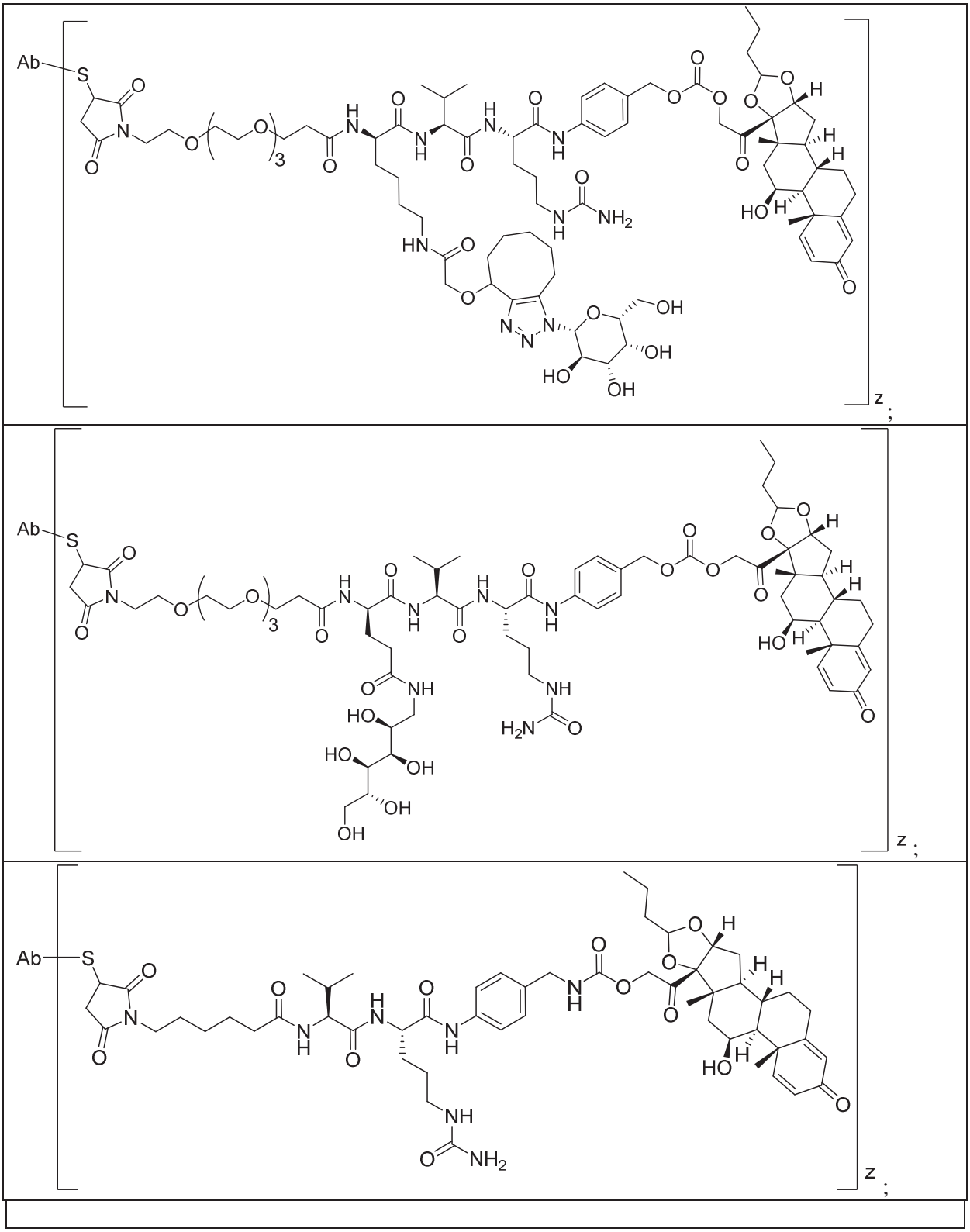
where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof

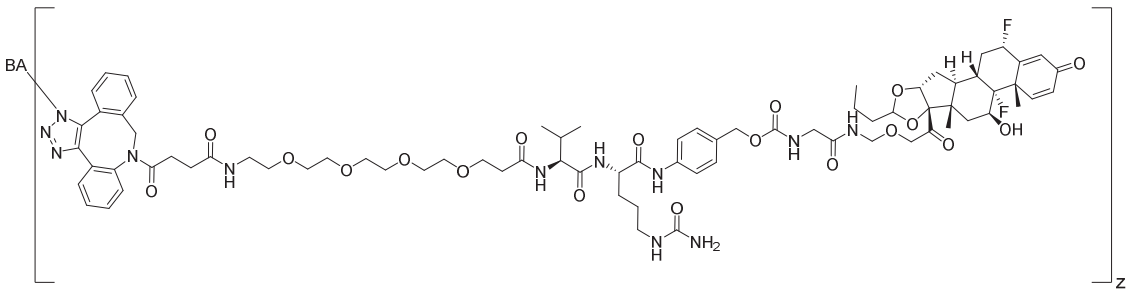
[0009f] Another aspect is directed to a Compound according to one of the following formulae

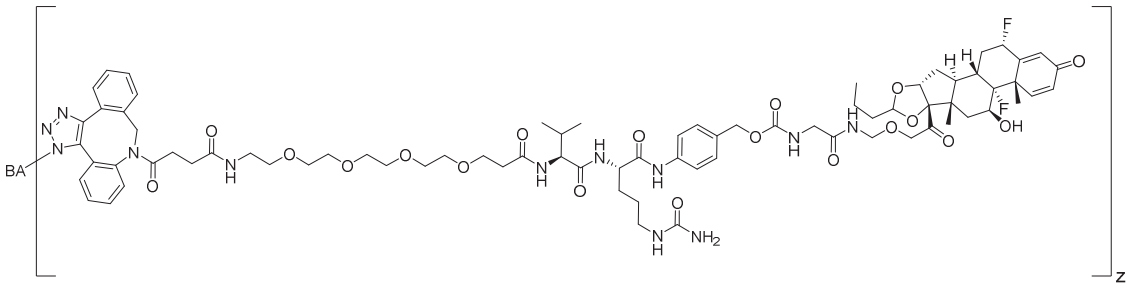




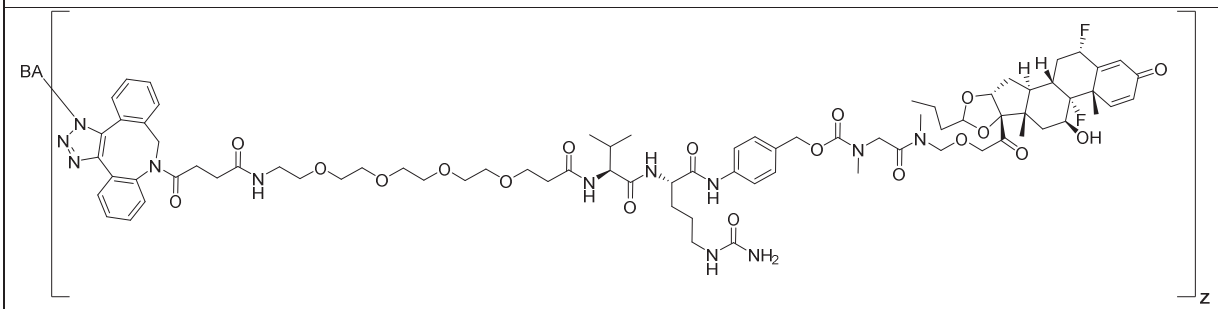
or a mixture thereof;

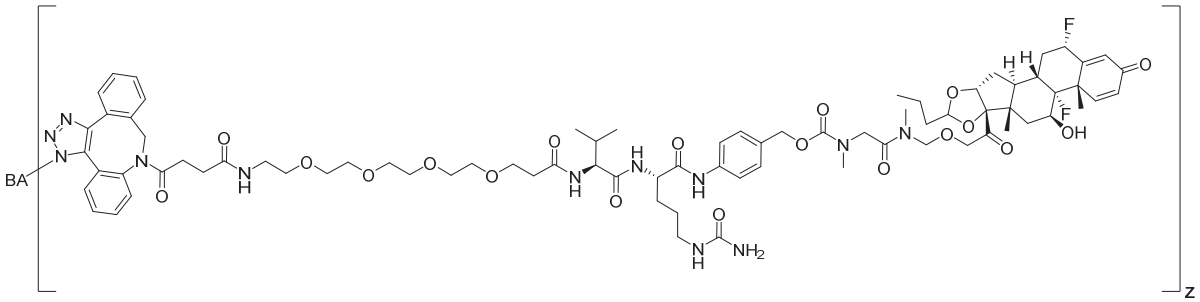




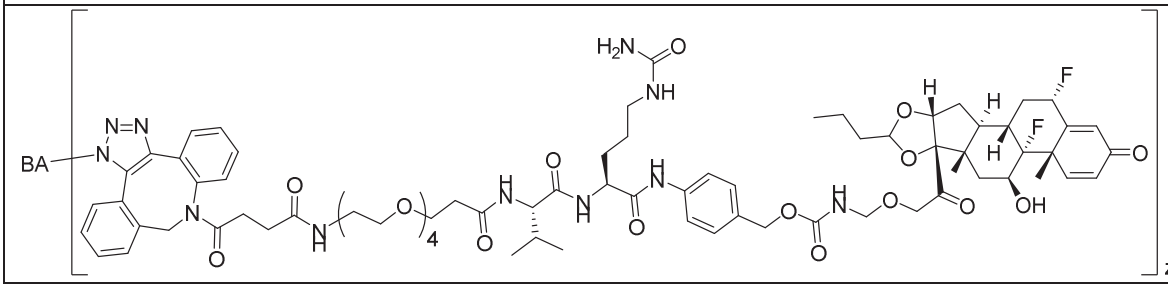


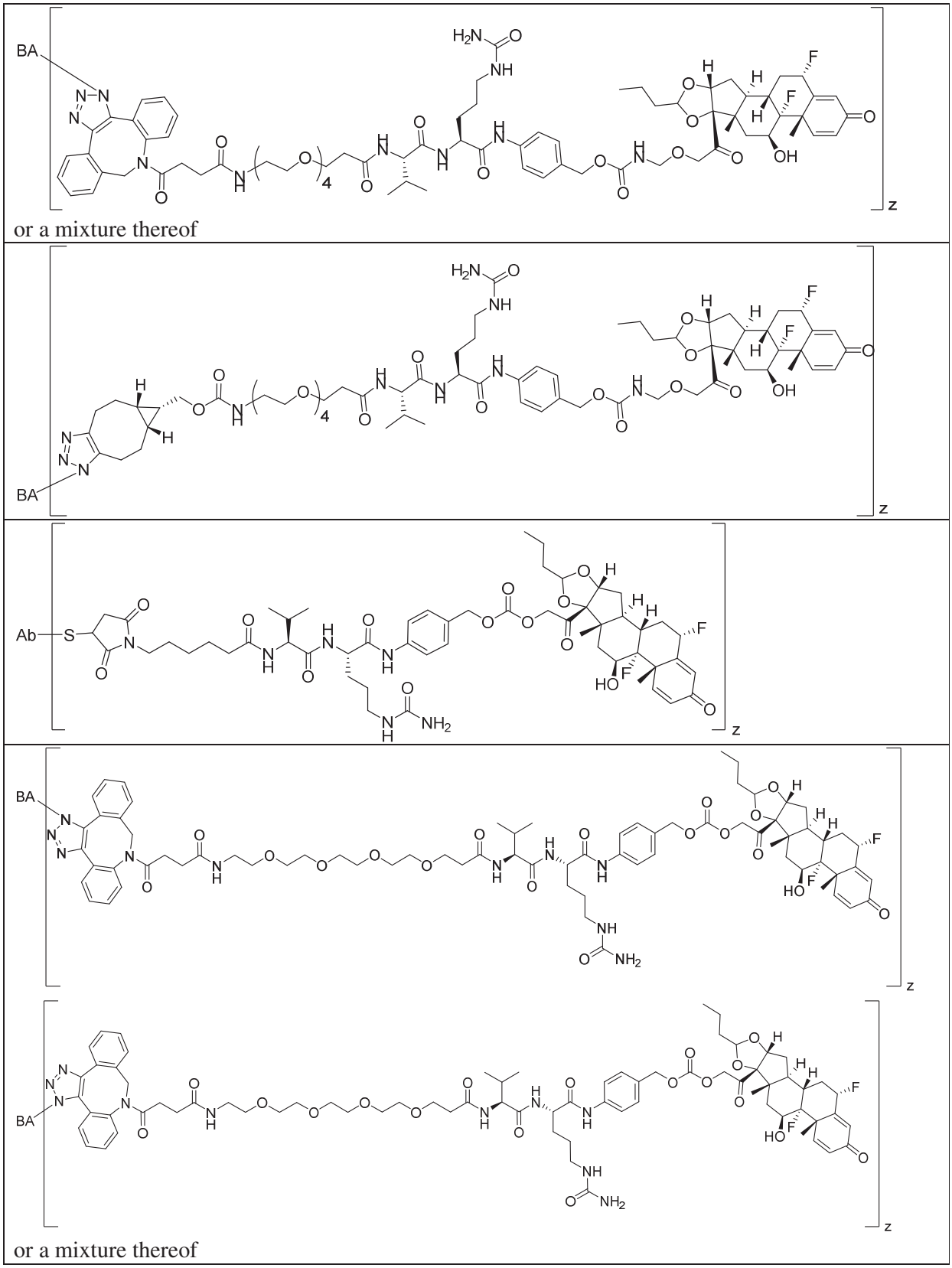
or a mixture thereof;



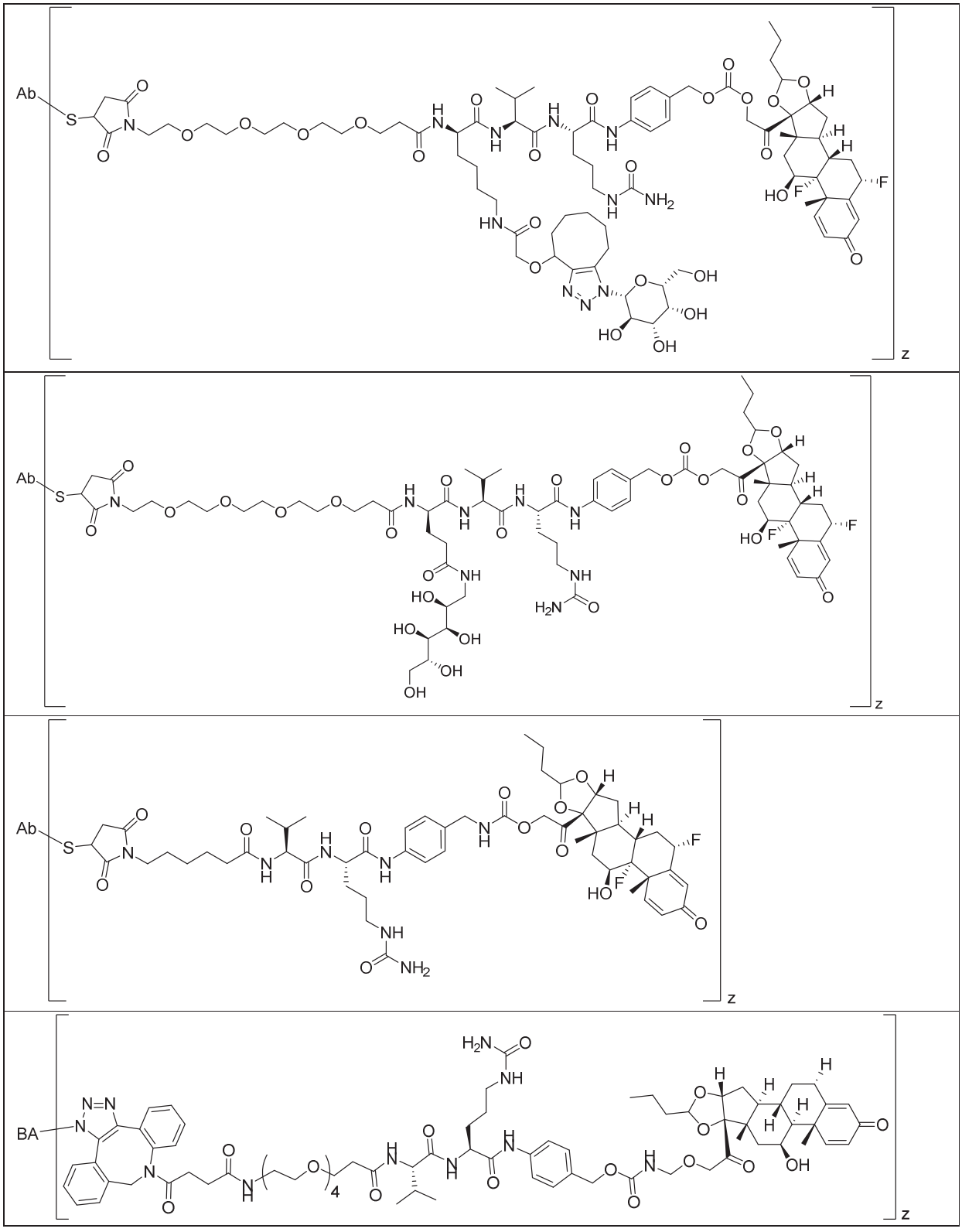


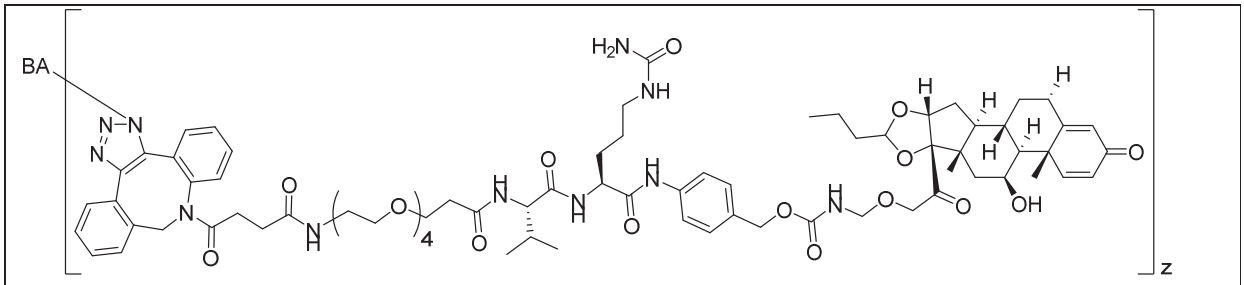
or a mixture thereof



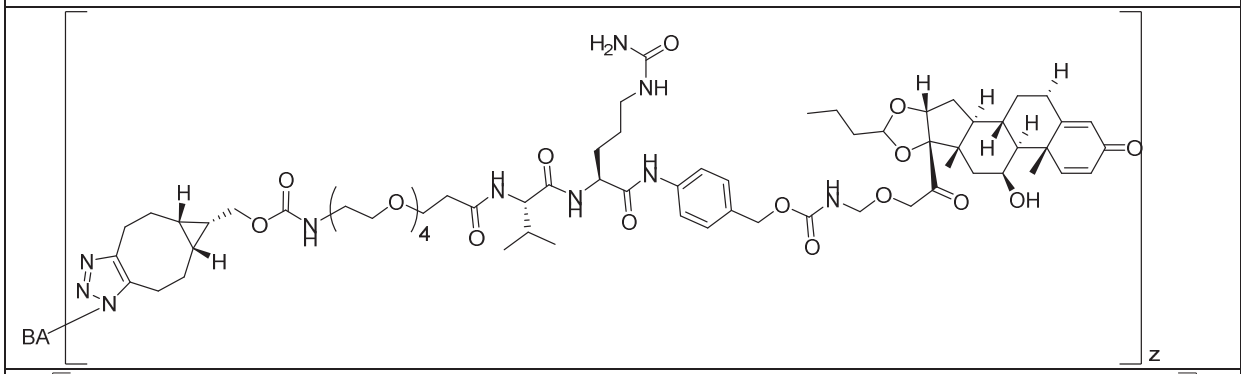


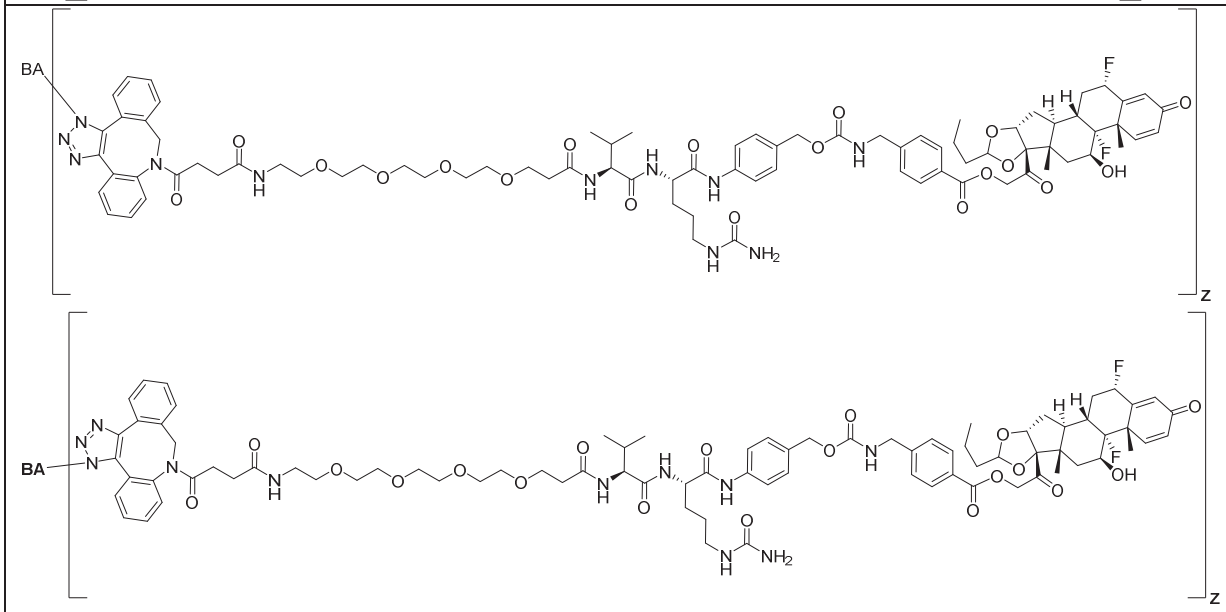
or a mixture thereof



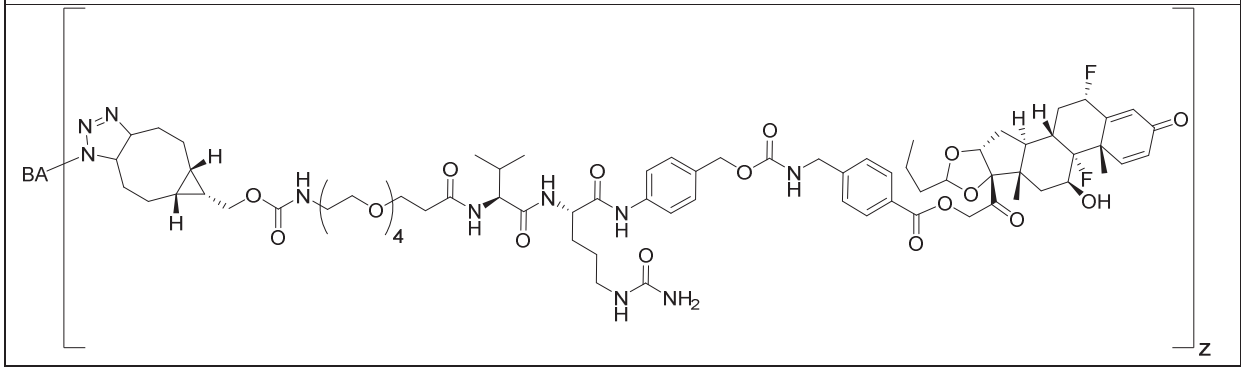


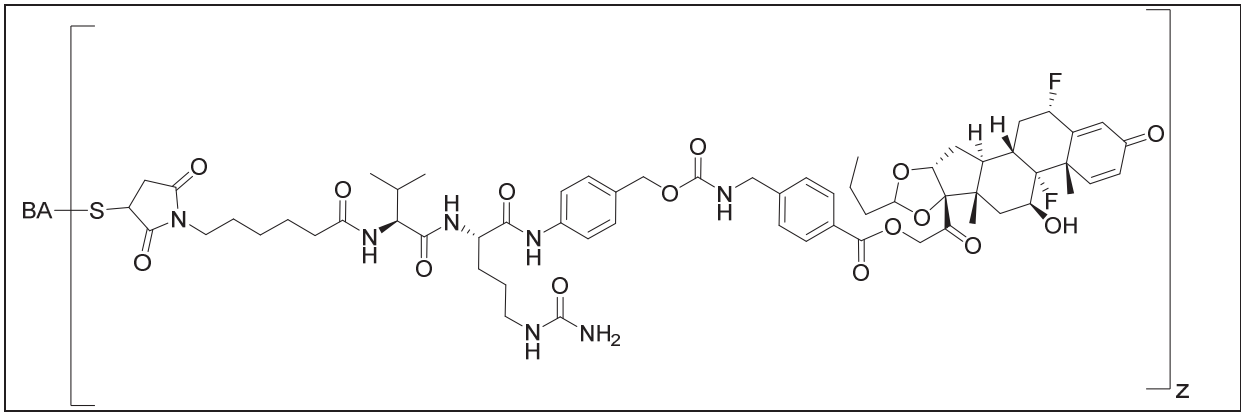
or a mixture thereof



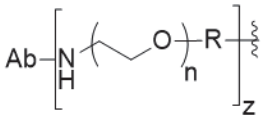


or a mixture thereof





where **BA** comprises an antibody or antigen binding fragment having the following structure



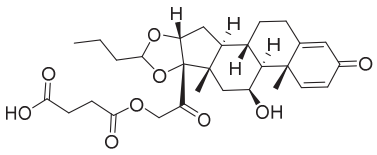
where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; **R** is C_{2-4}-alkylene; and **n** is an integer selected from two to four, inclusive.

[00010] Another example is directed to pharmaceutical compositions comprising the Compound of Formula (**I**), Formula I-P, Formula I-P-1, Formula (**III**-P), Formula III-P-1, Formula (3000), or Formula (**III**) and a pharmaceutically acceptable carrier, diluent, and/or excipient.

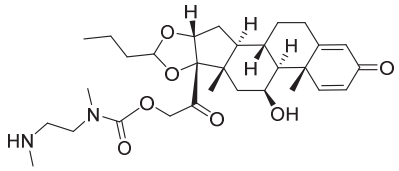
[00011] Another example is directed to methods useful for the treatment of various diseases, disorders, or conditions comprising administering a Compound of Formula I, Formula I-P, Formula I-P-1, Formula (**III**-P), Formula III-P-1, Formula (3000), or Formula (**III**) or administering a pharmaceutical composition comprising a Compound of Formula I, Formula I-P, Formula I-P-1, Formula (**III**-P), Formula III-P-1, Formula (3000), or Formula (**III**) and a pharmaceutically acceptable carrier, diluent, and/or excipient.

[0011a] Another aspect is directed to use of a compound of Formula (III) as defined herein, or the compound as defined herein in the manufacture of a medicament for the treatment of a disease, disorder, or condition associated with glucocorticoid receptor signaling.

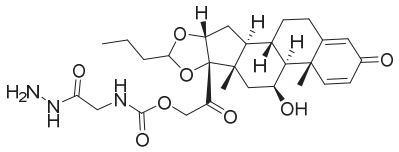
[0011b] Another aspect is directed to a Compound selected from the group consisting of



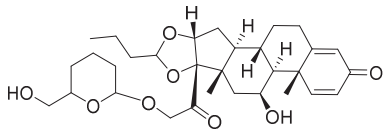
1c



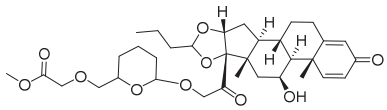
1d



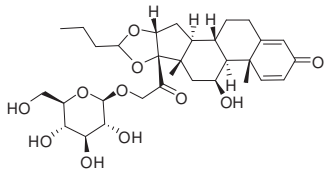
1e



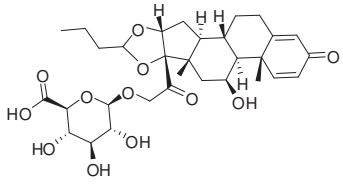
1g



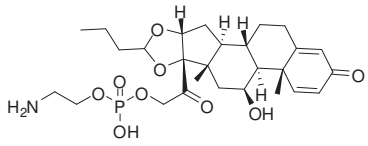
1h



1i



1j



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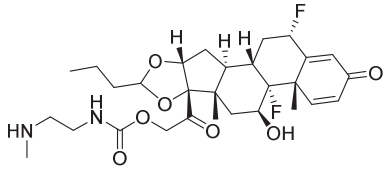
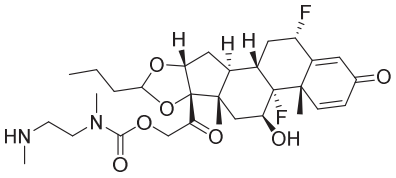
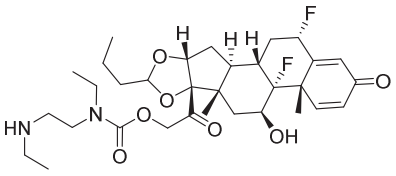


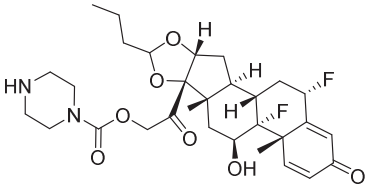
101a



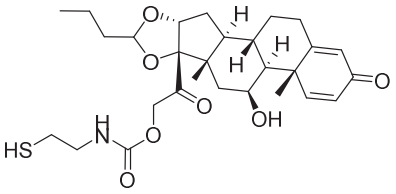
101b



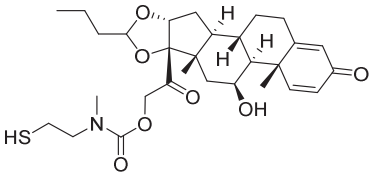
101c



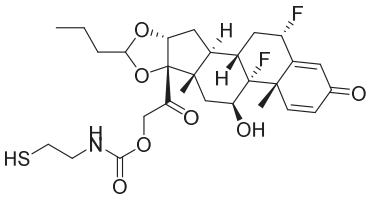
101d



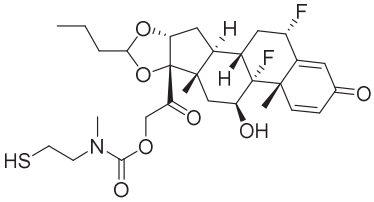
102c



102d



102e



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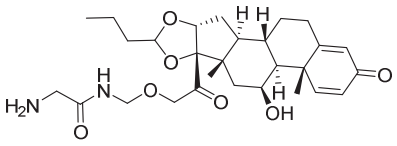
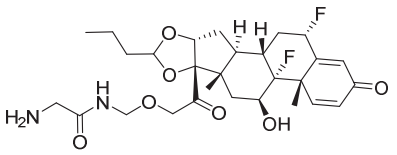
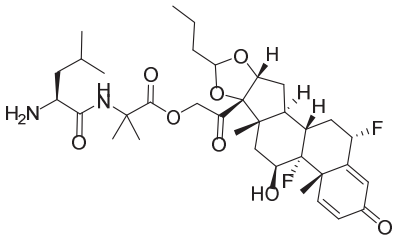


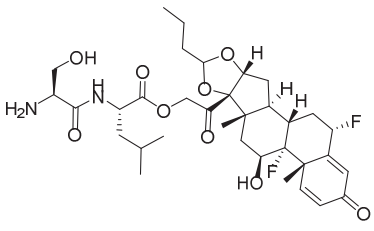
103a



103b



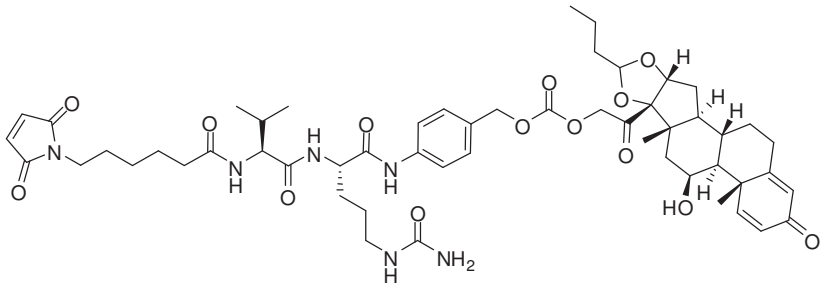
104a and



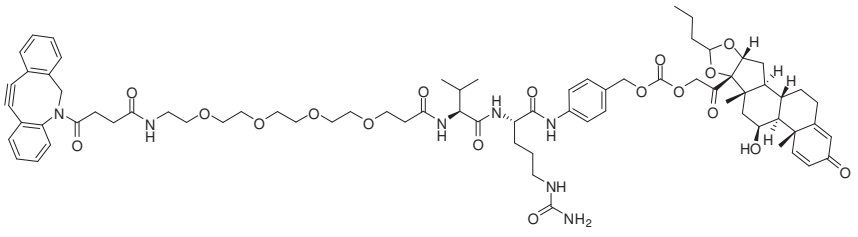
104b

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

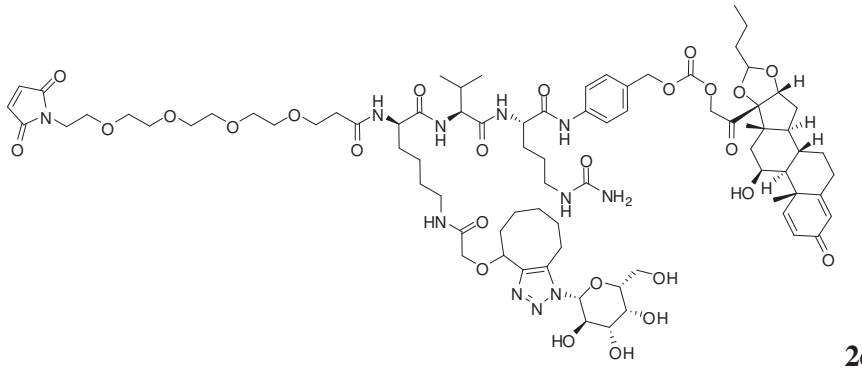
[0011c] Another aspect is directed to a Compound selected from the group consisting of



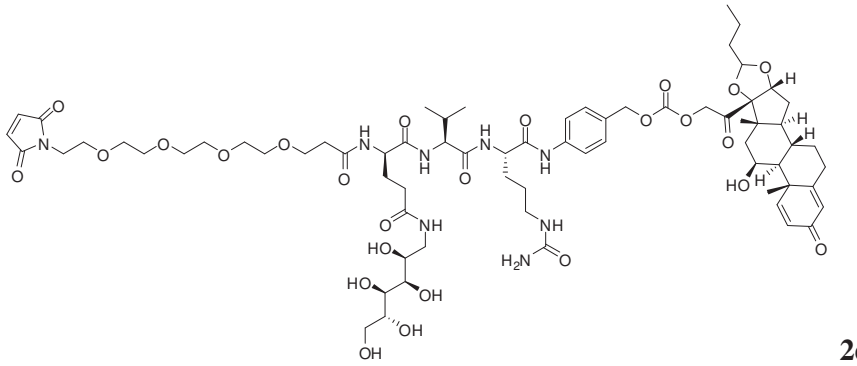
2a



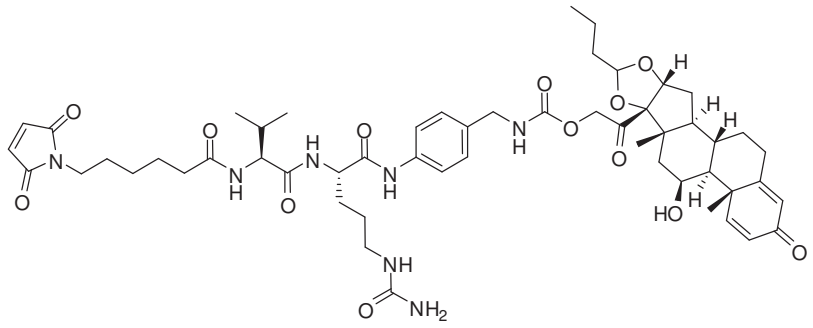
2b



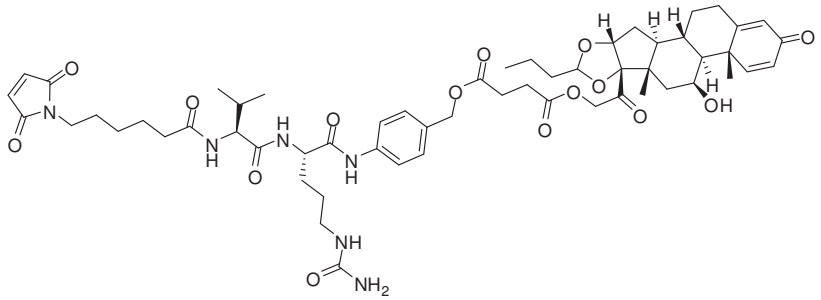
2c



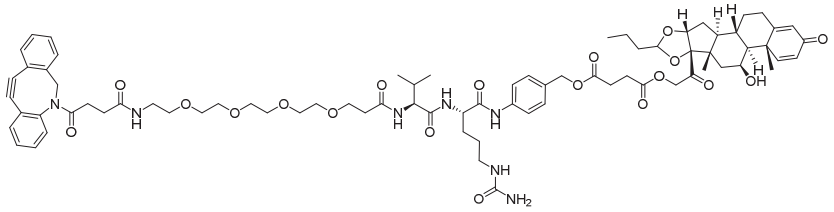
2d



2e



2f



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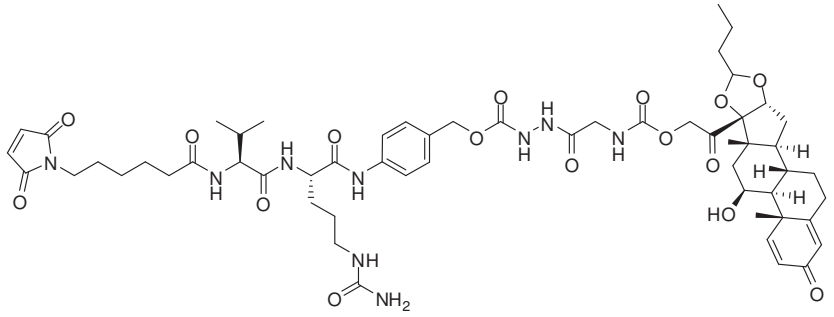

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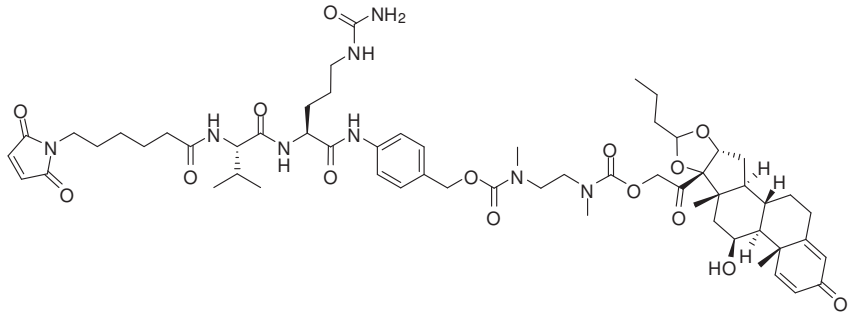

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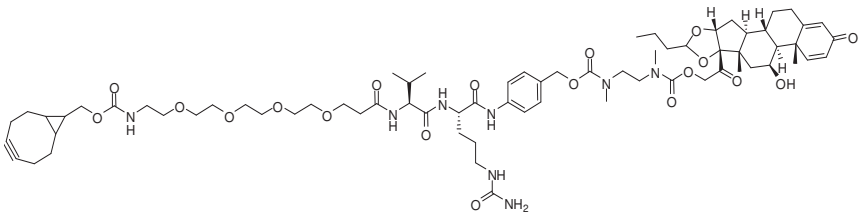

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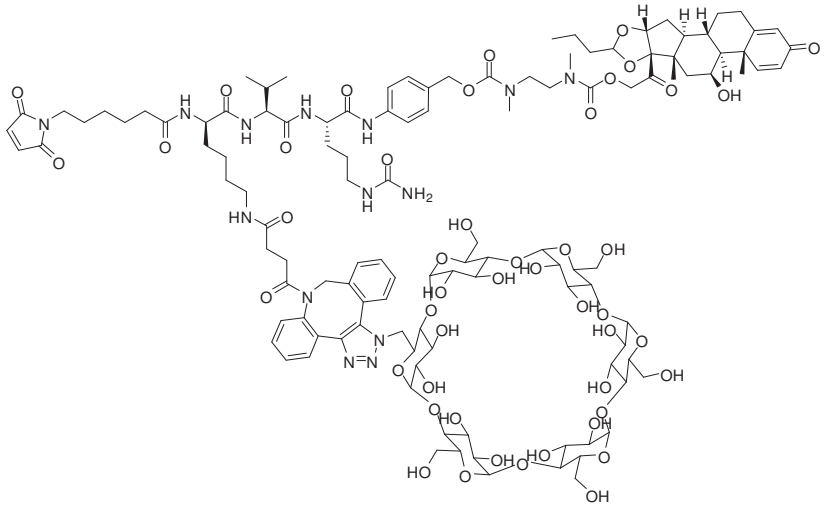

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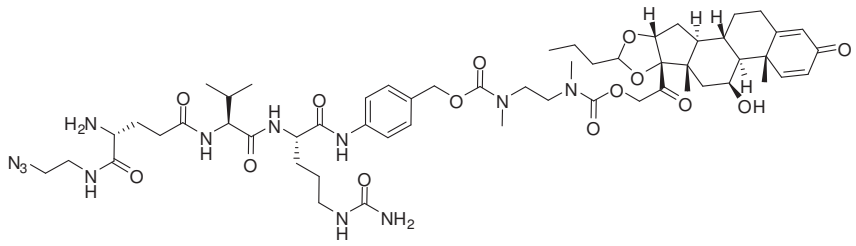

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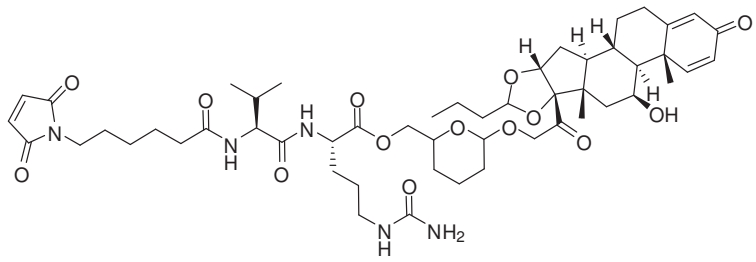

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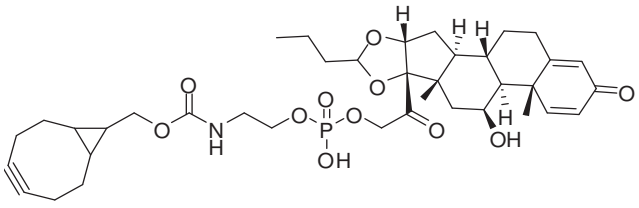

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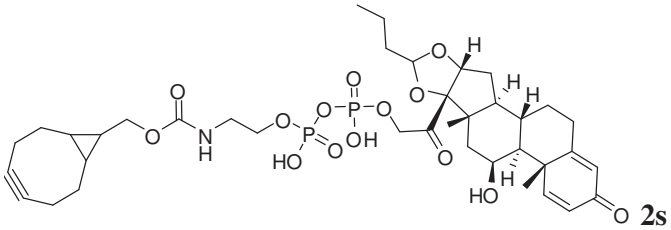

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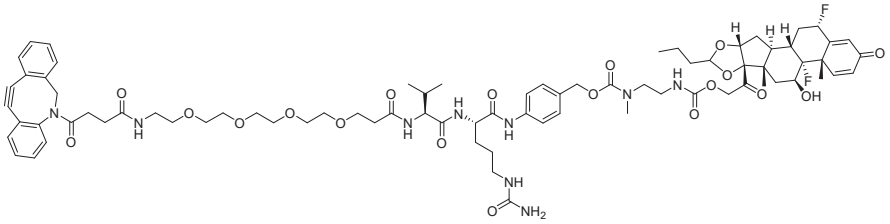

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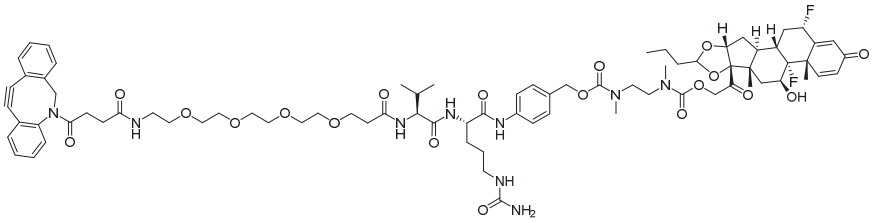

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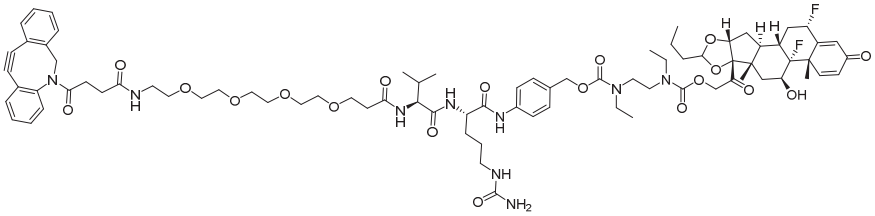

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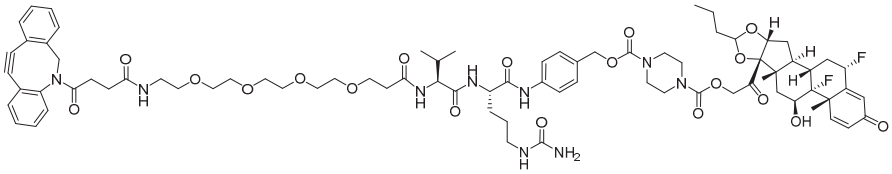

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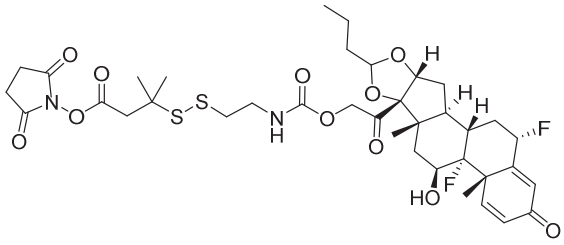

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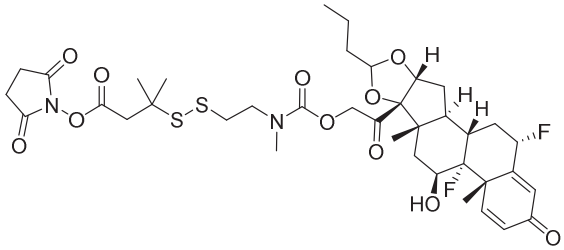

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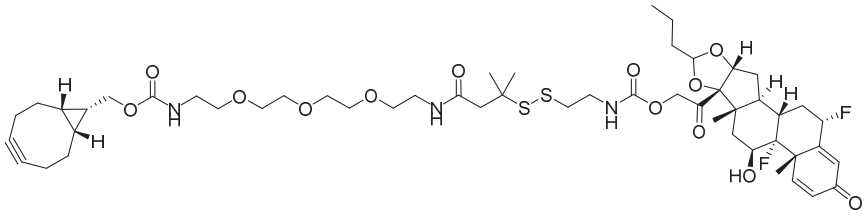

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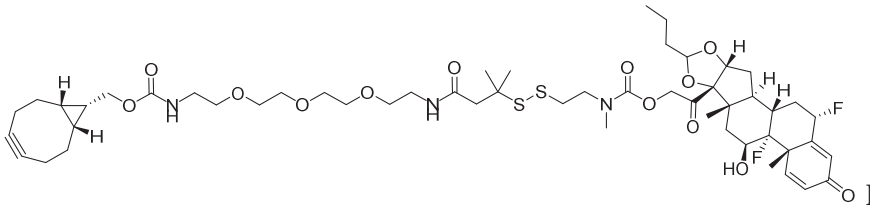

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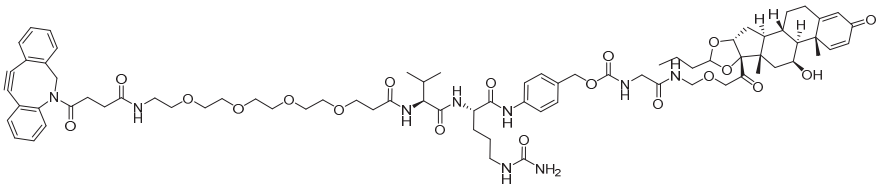

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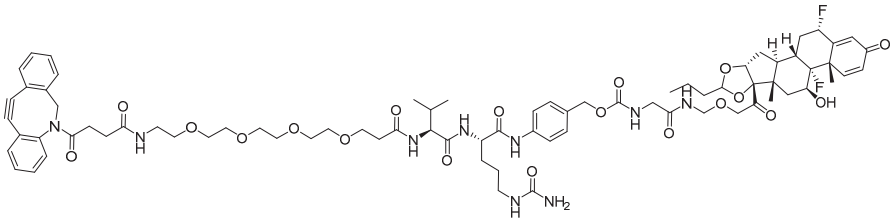

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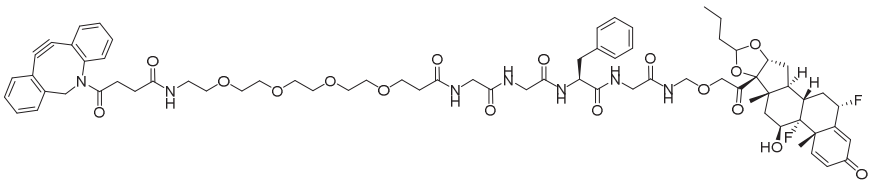

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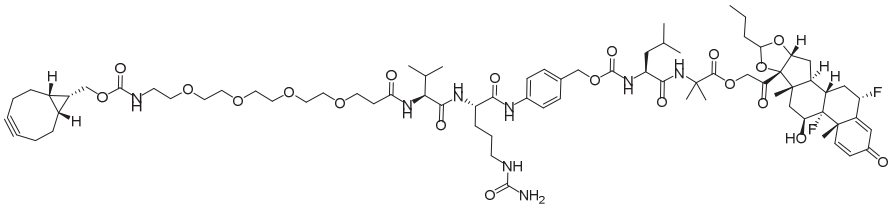

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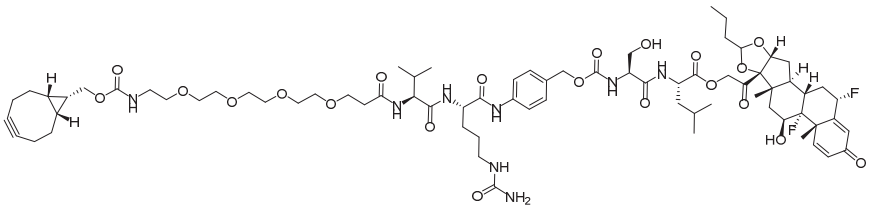

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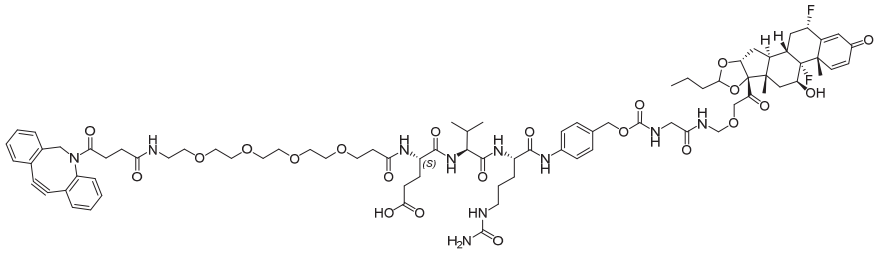

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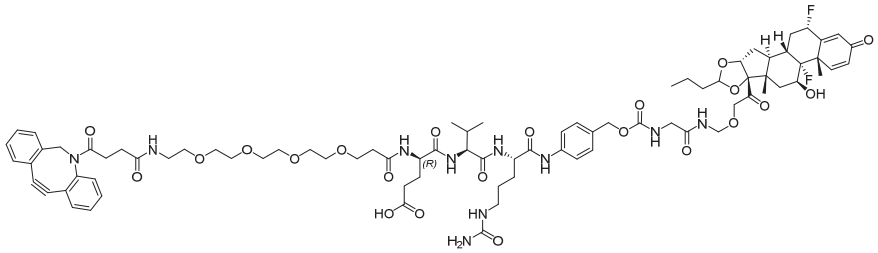

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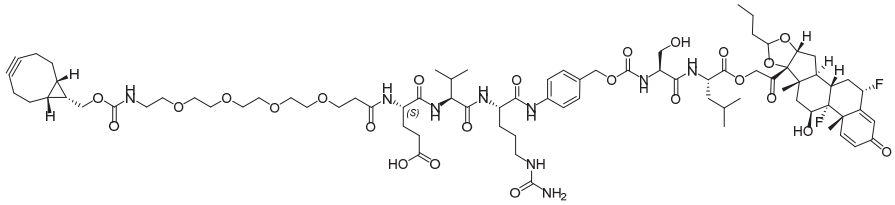
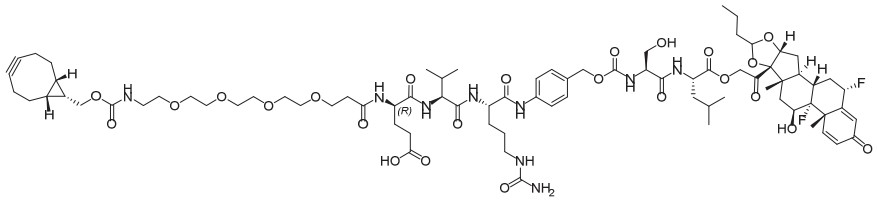


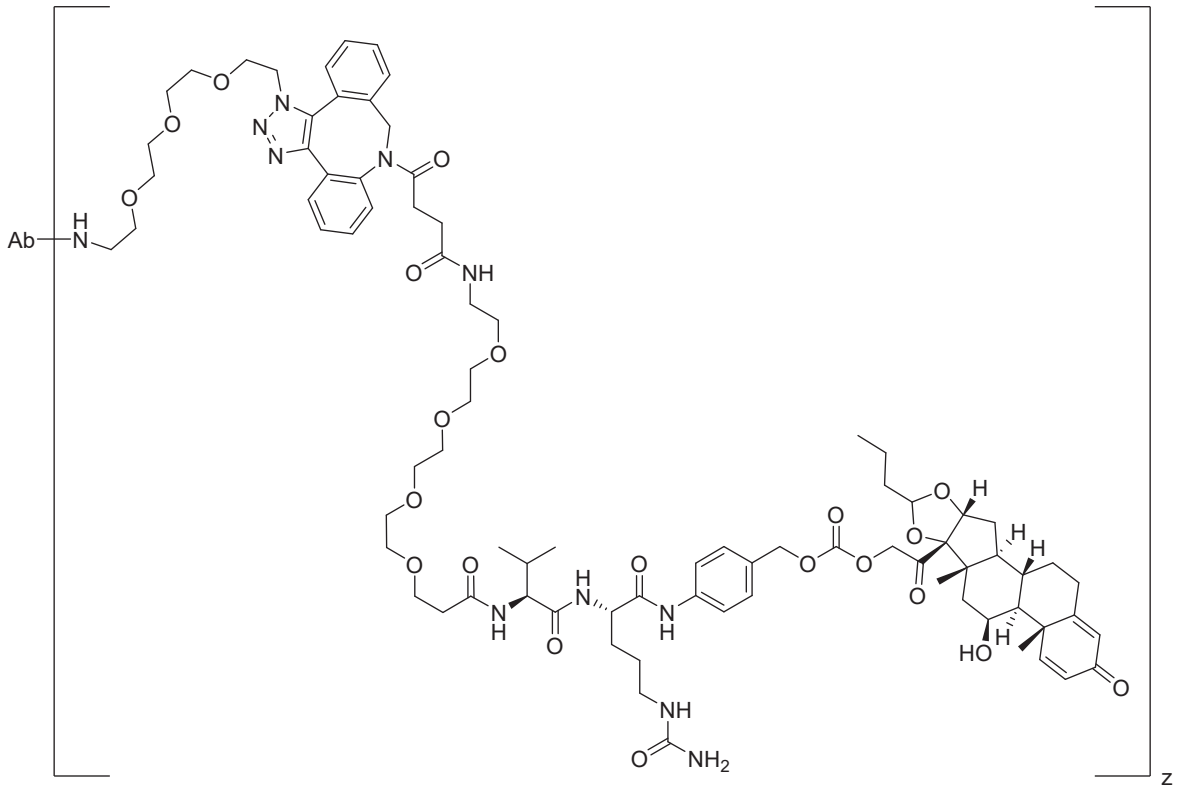
LP20 and

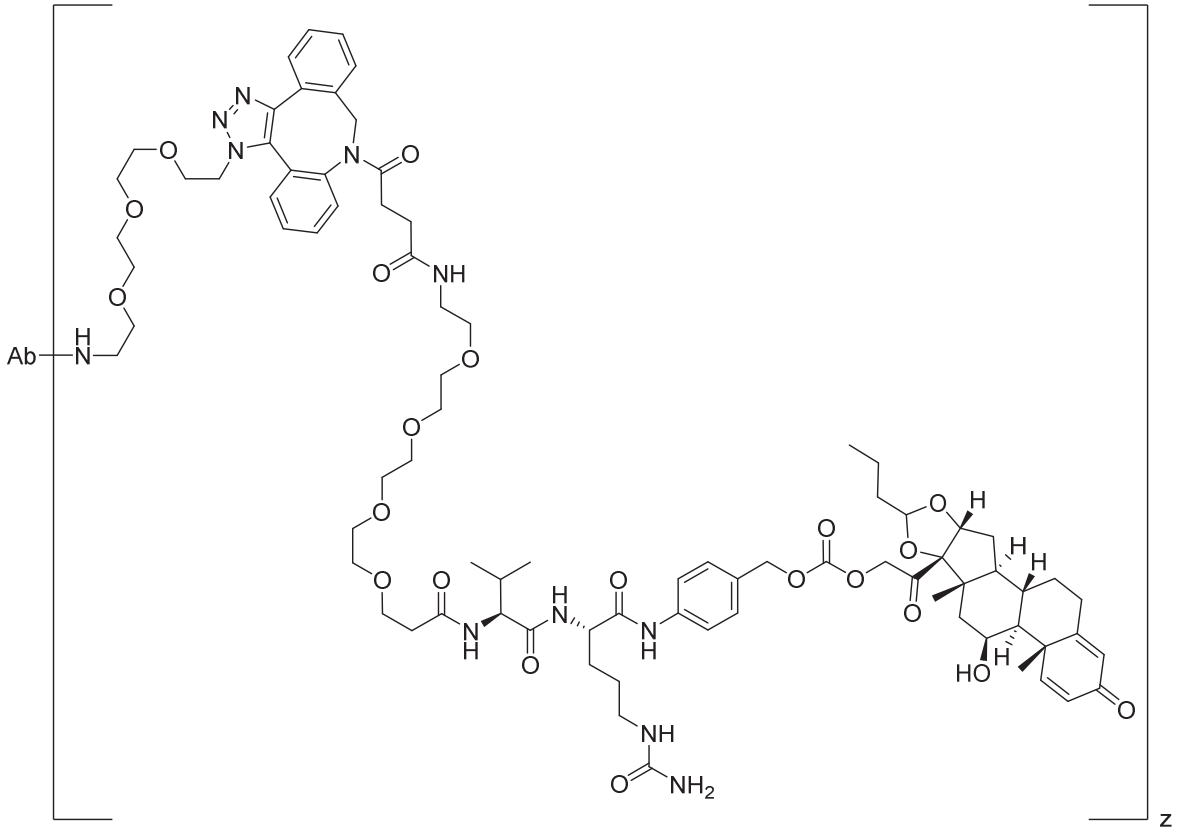


LP21

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

[0011d] Another aspect is directed to a Compound selected from the group consisting of





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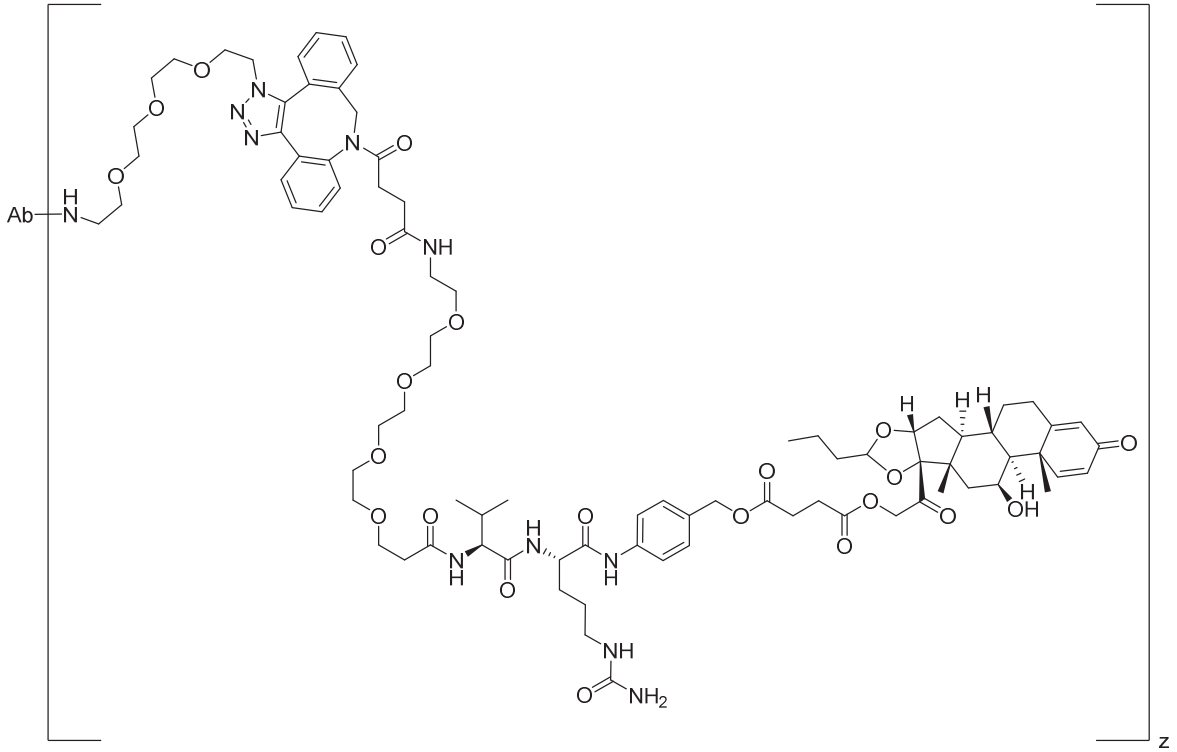

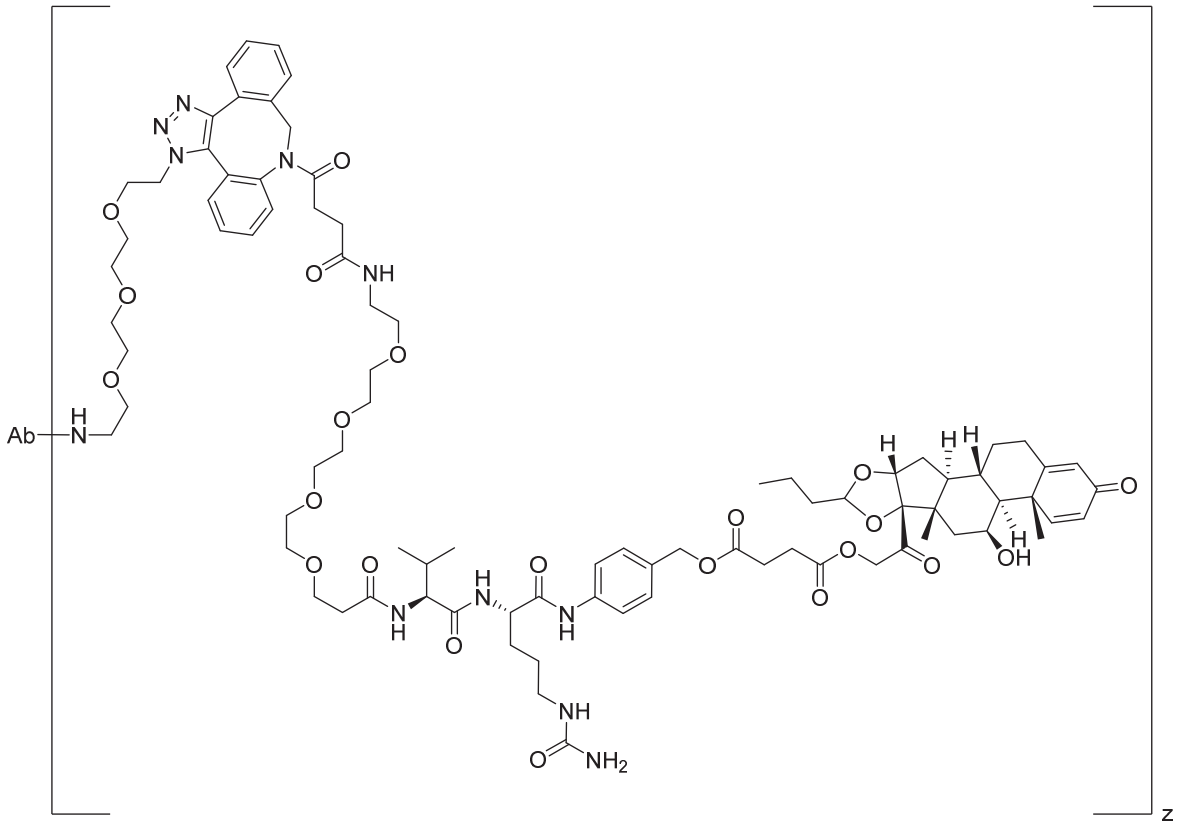

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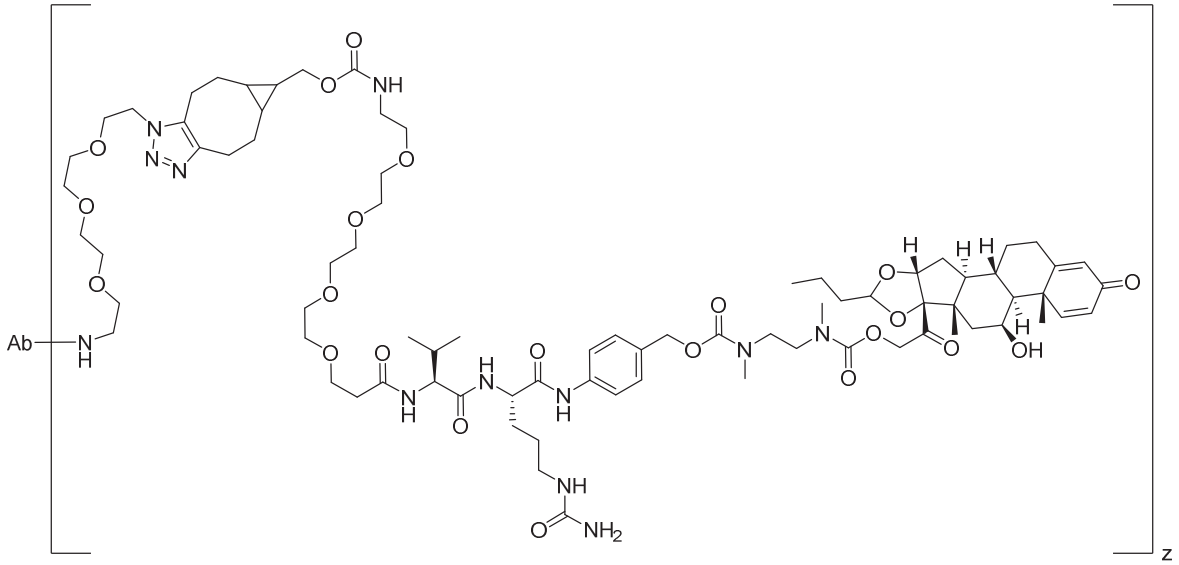

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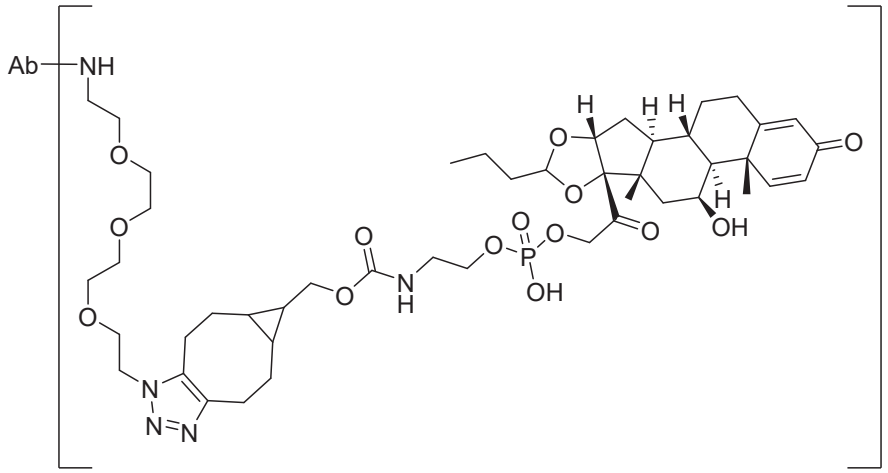
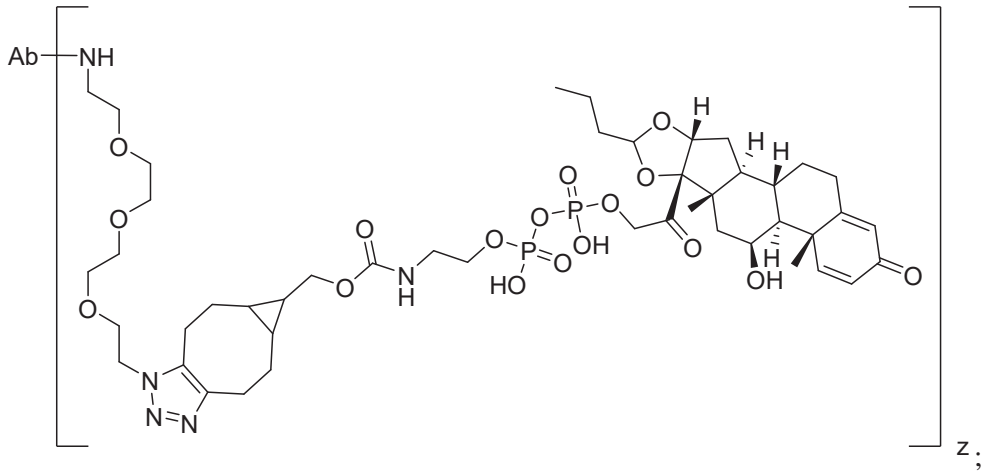


; and

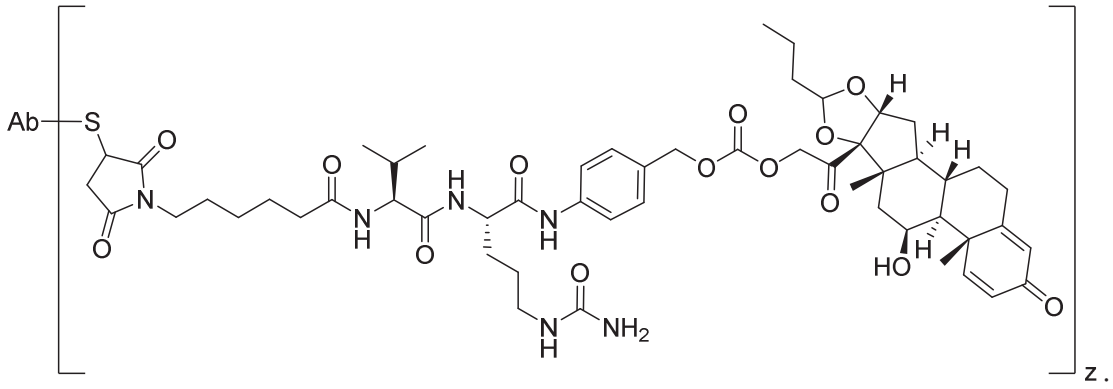


;

wherein **Ab** is an antibody or an antigen binding fragment thereof; and

z is an integer from one to four.

[0011e] Another aspect is directed to a Compound selected from the group consisting of



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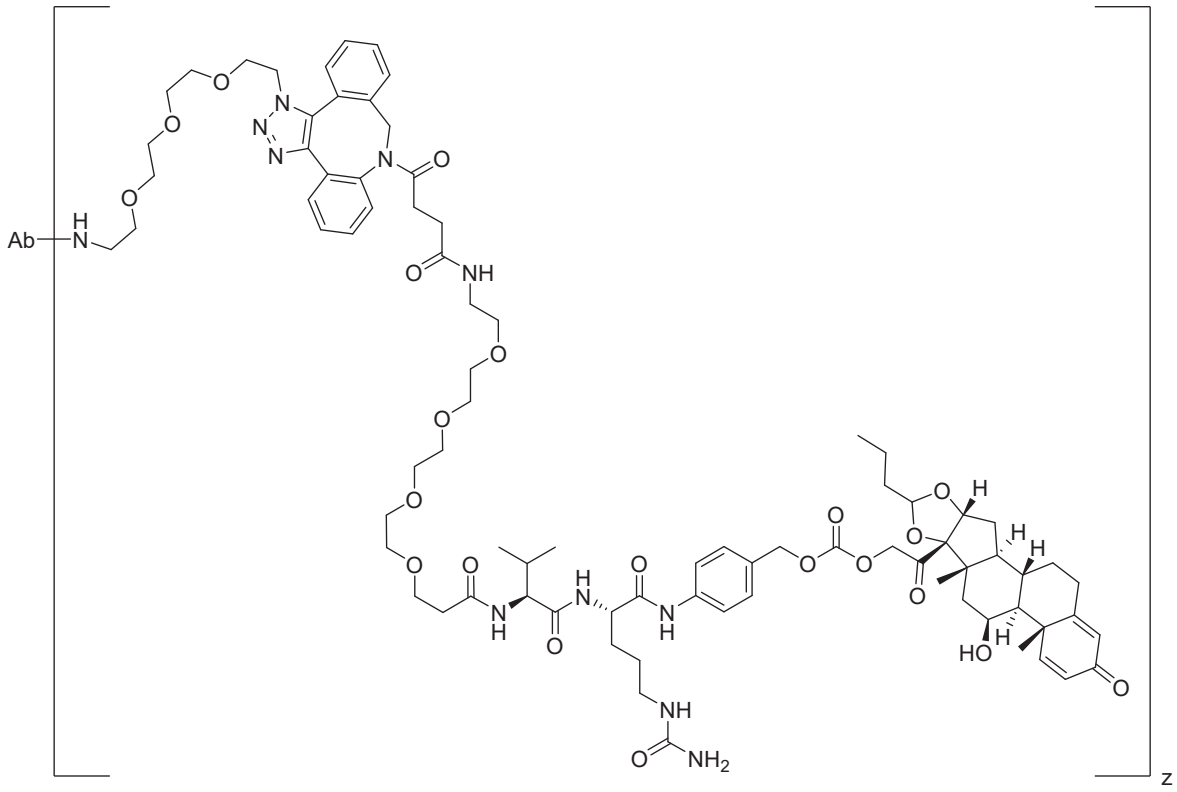
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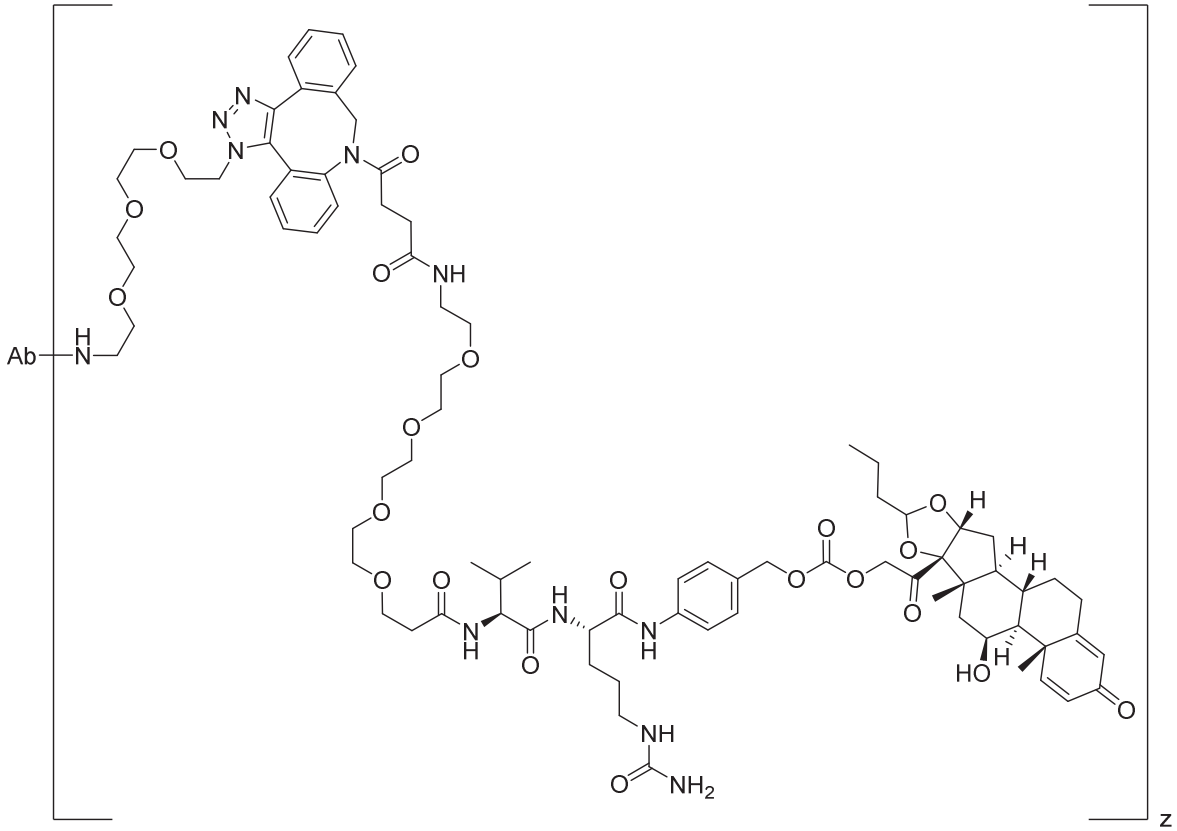

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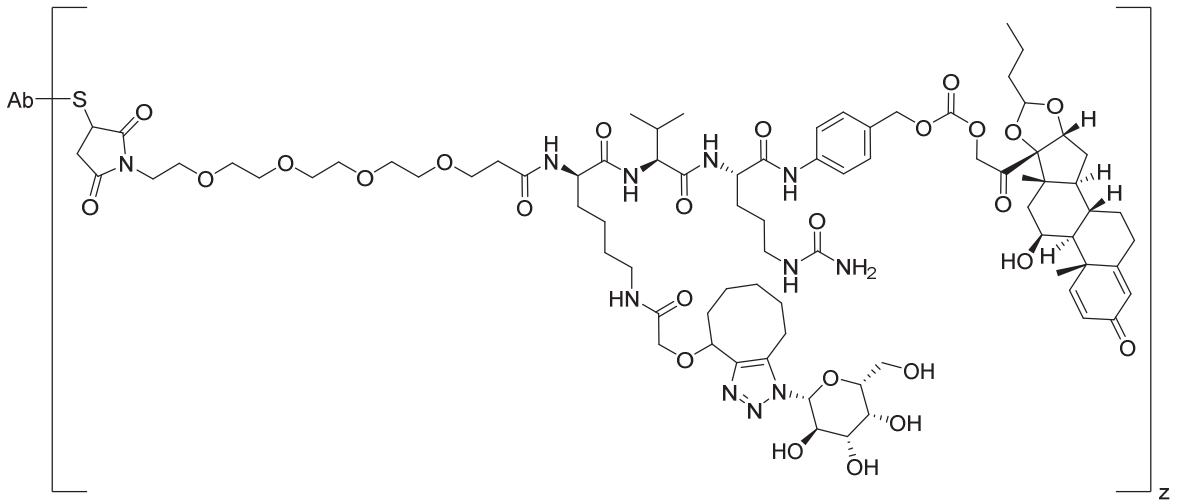

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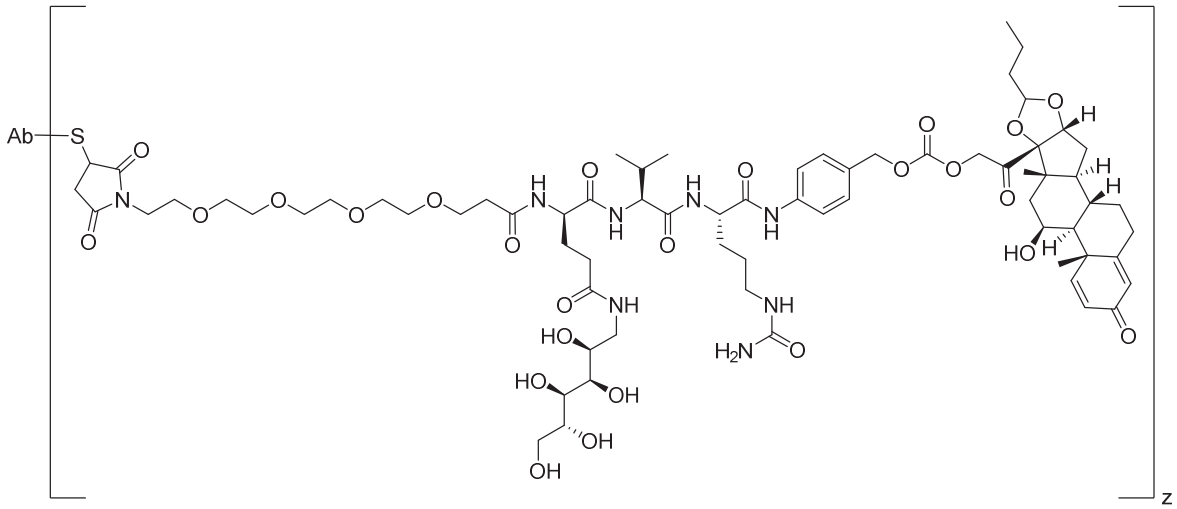

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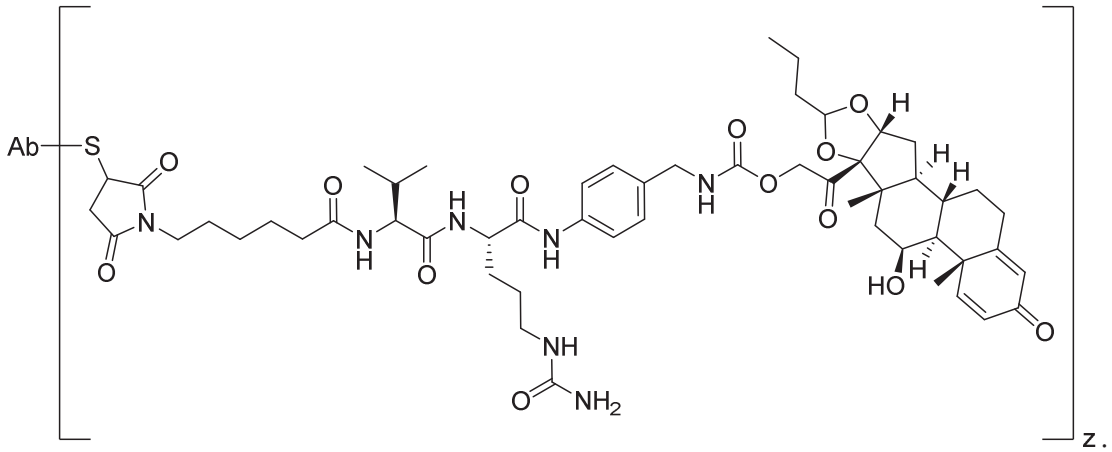

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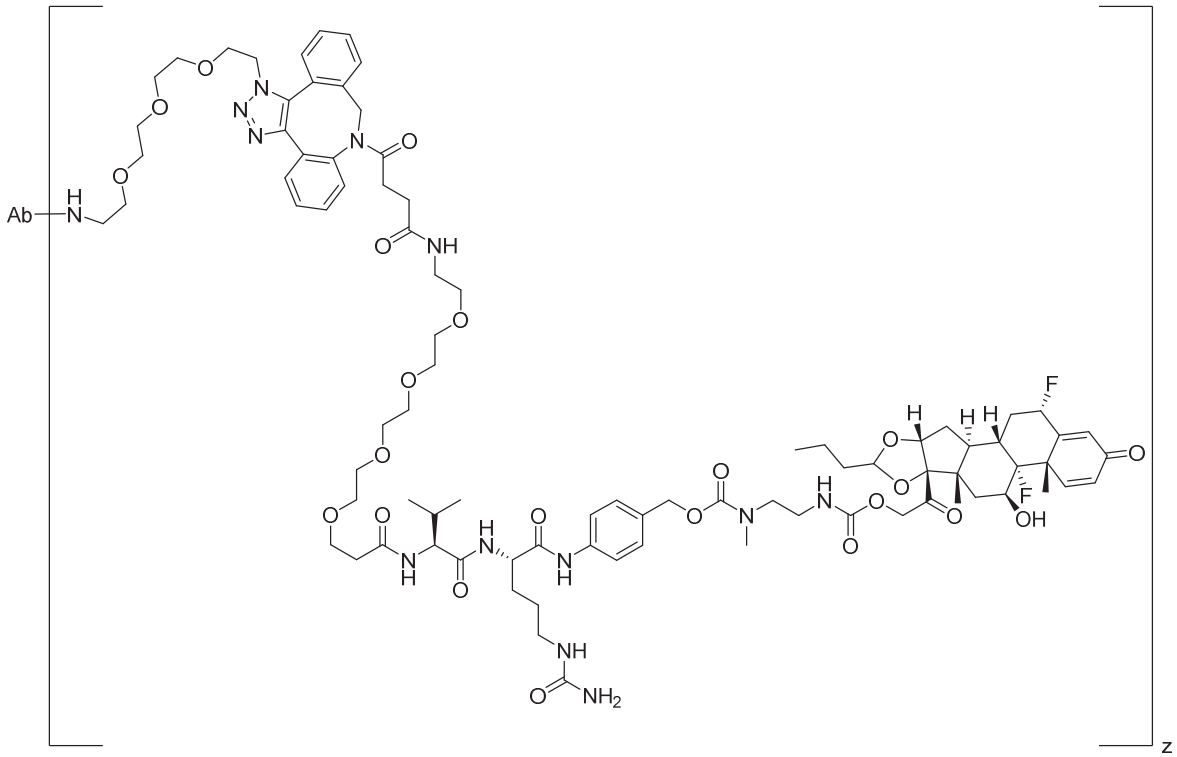
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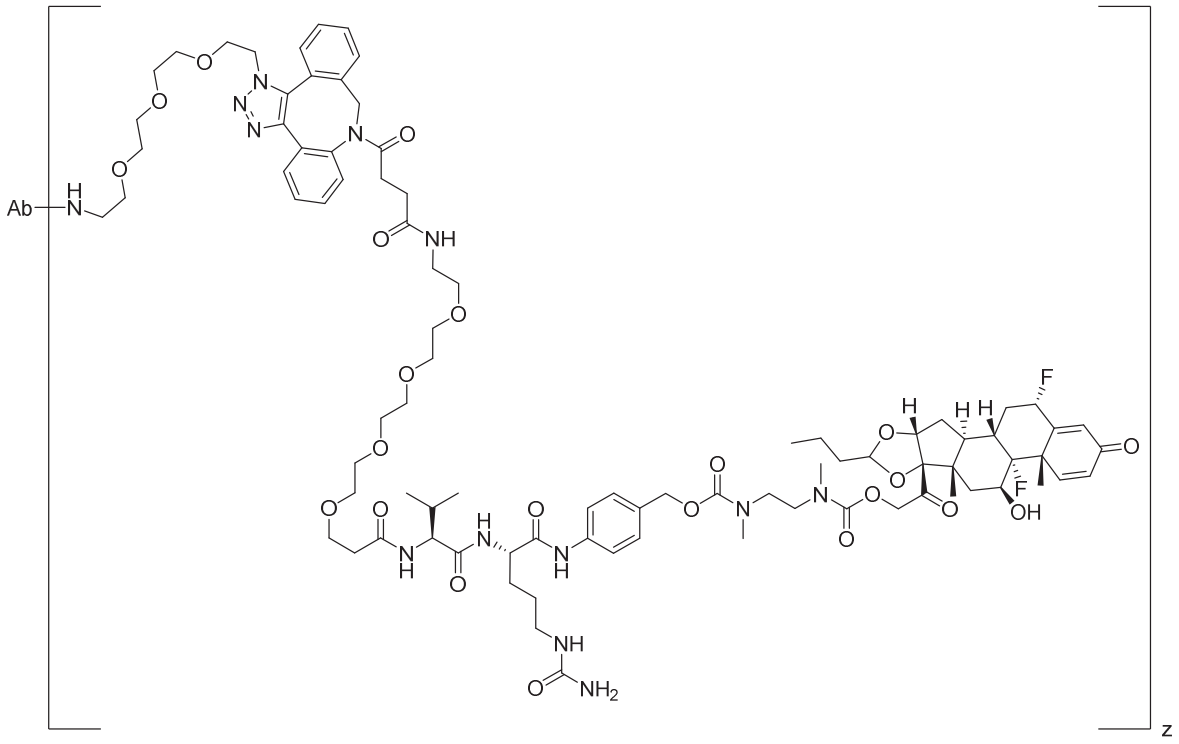

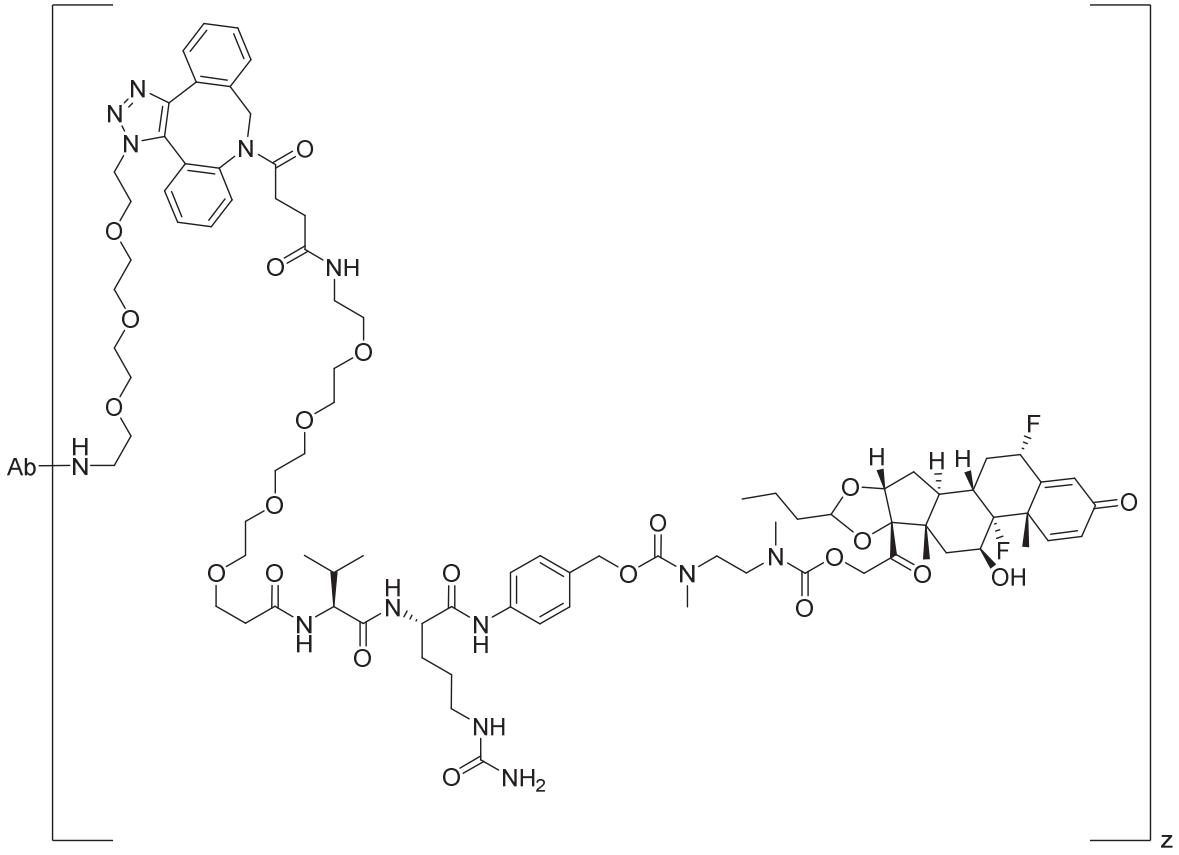

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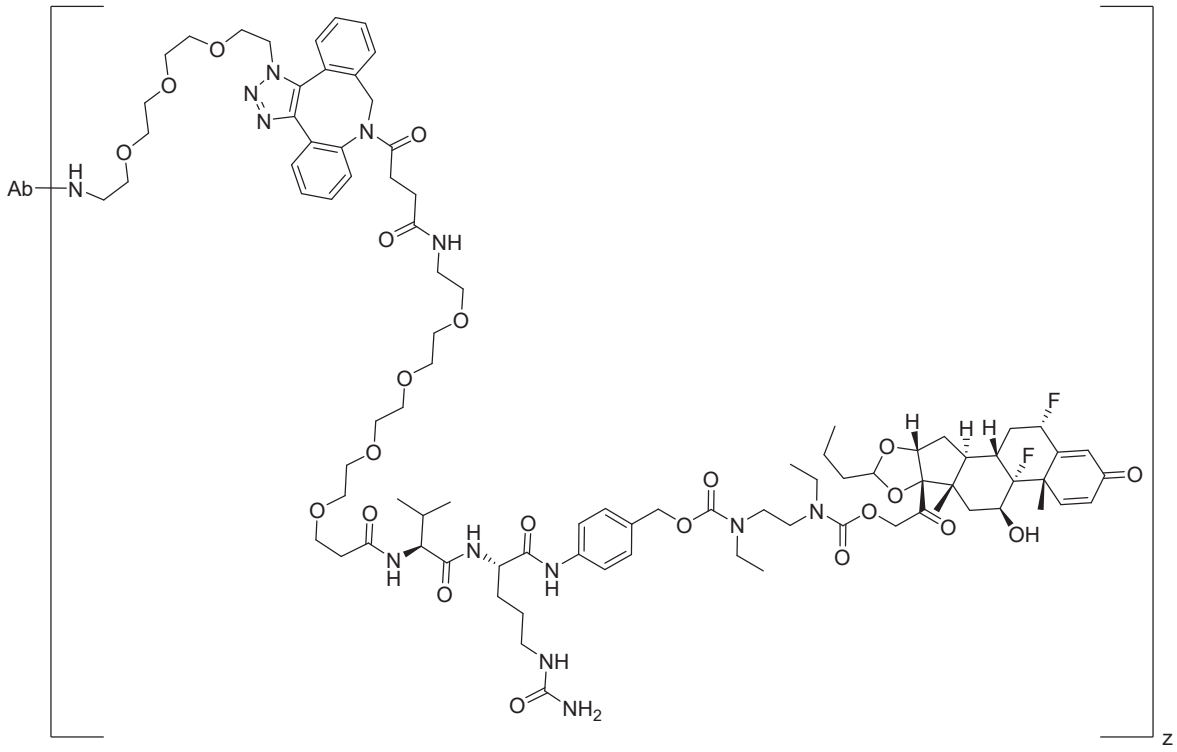
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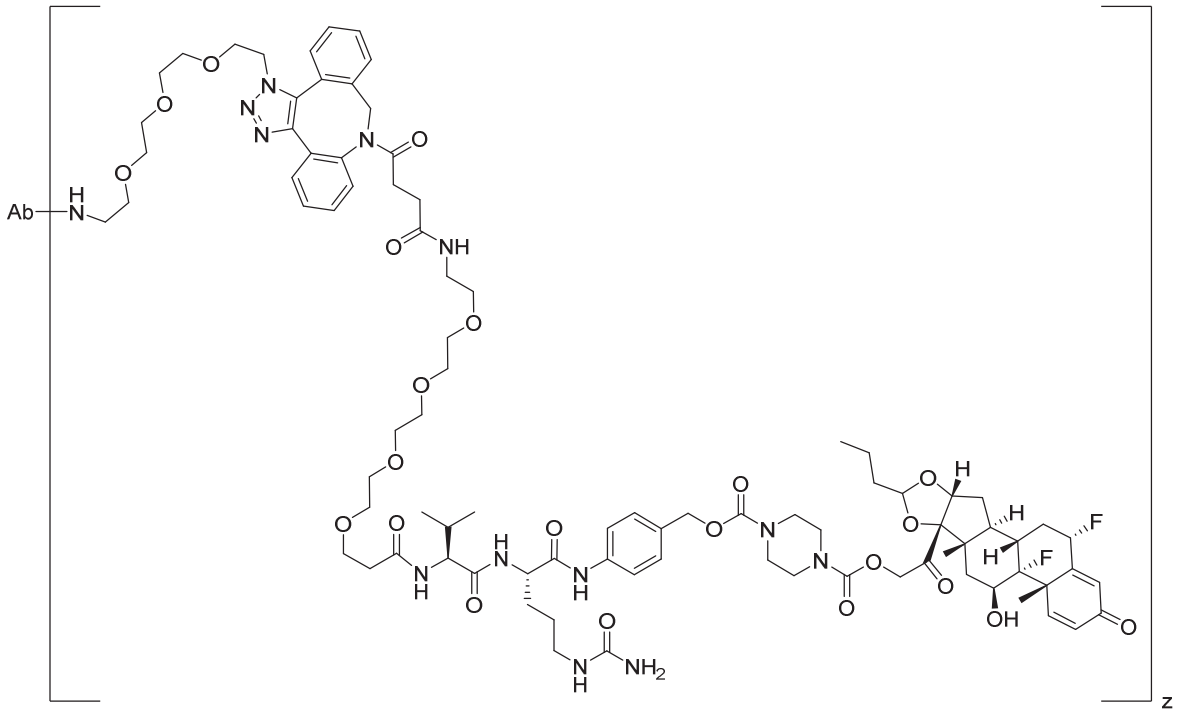

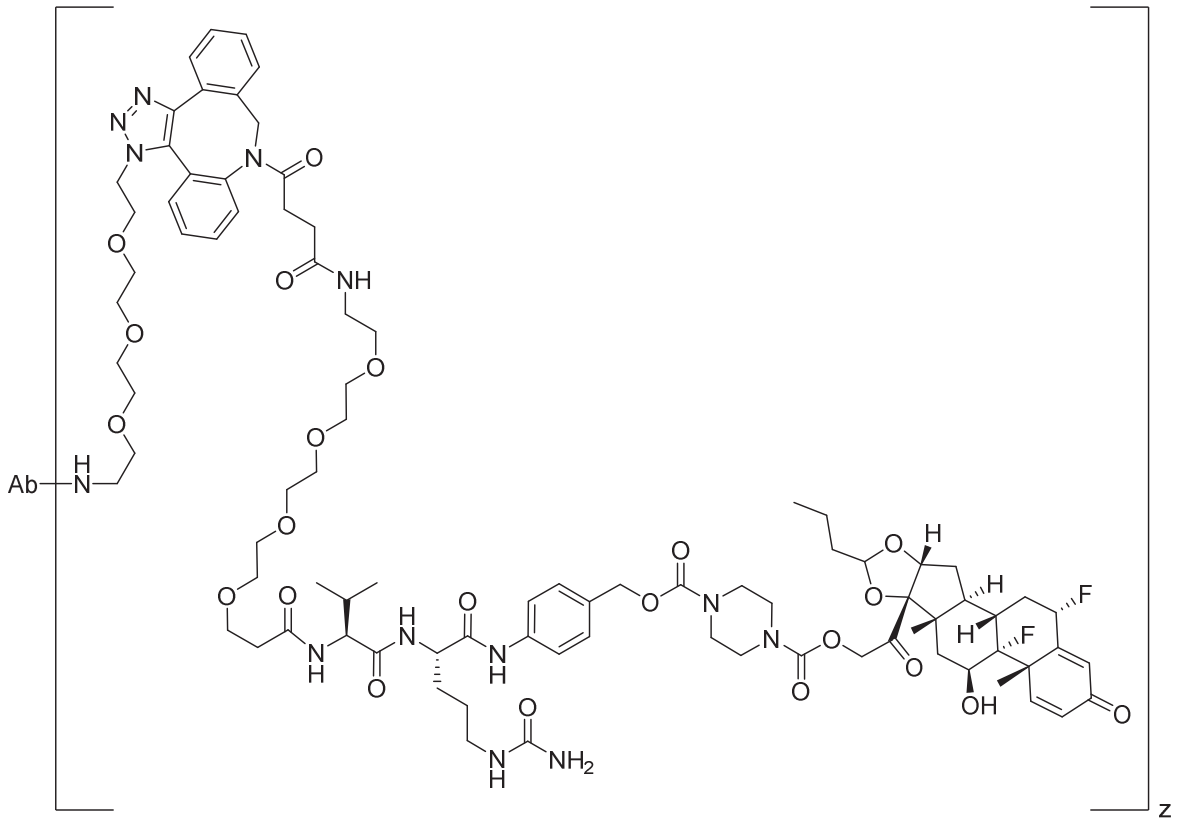

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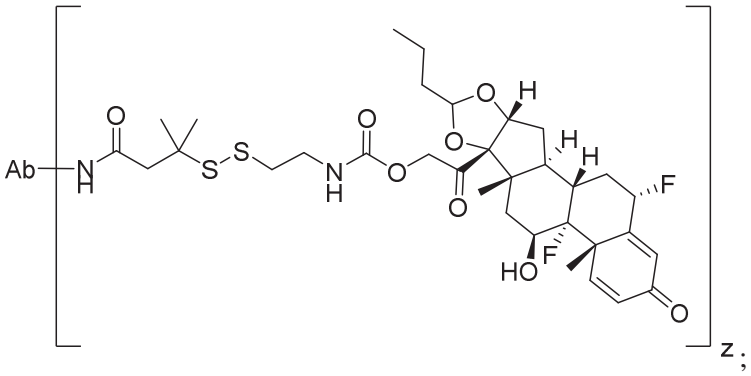

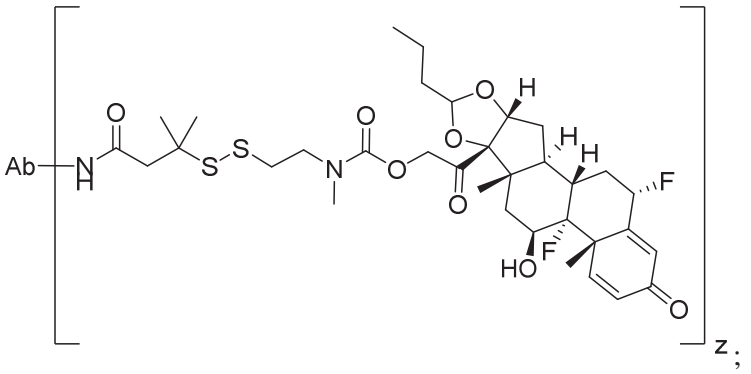

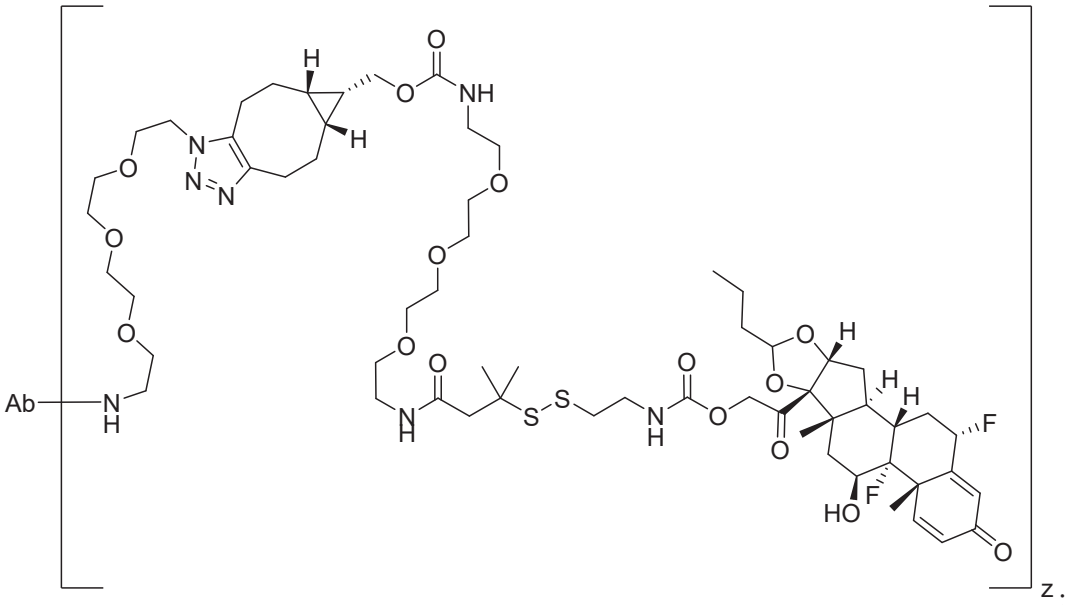

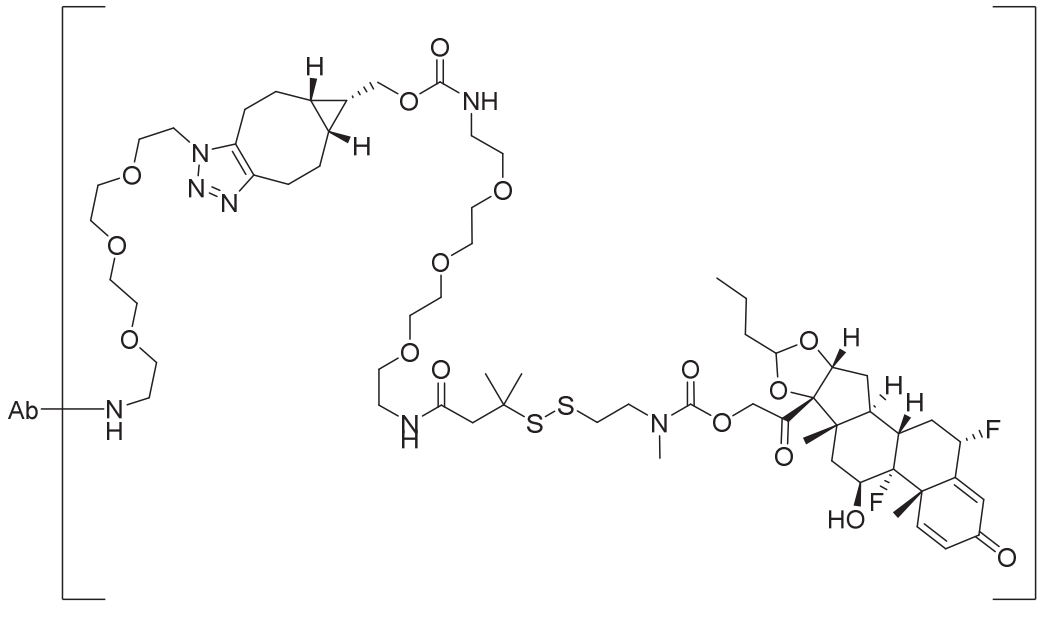
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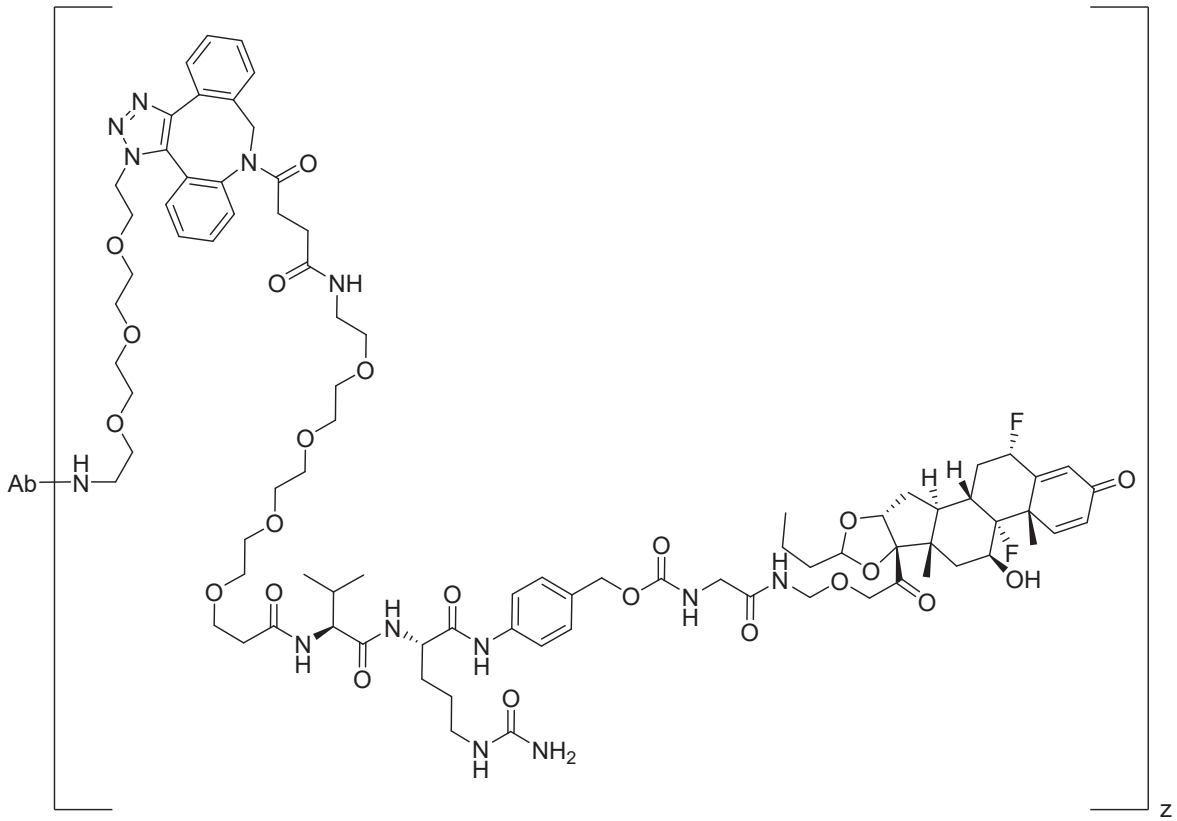
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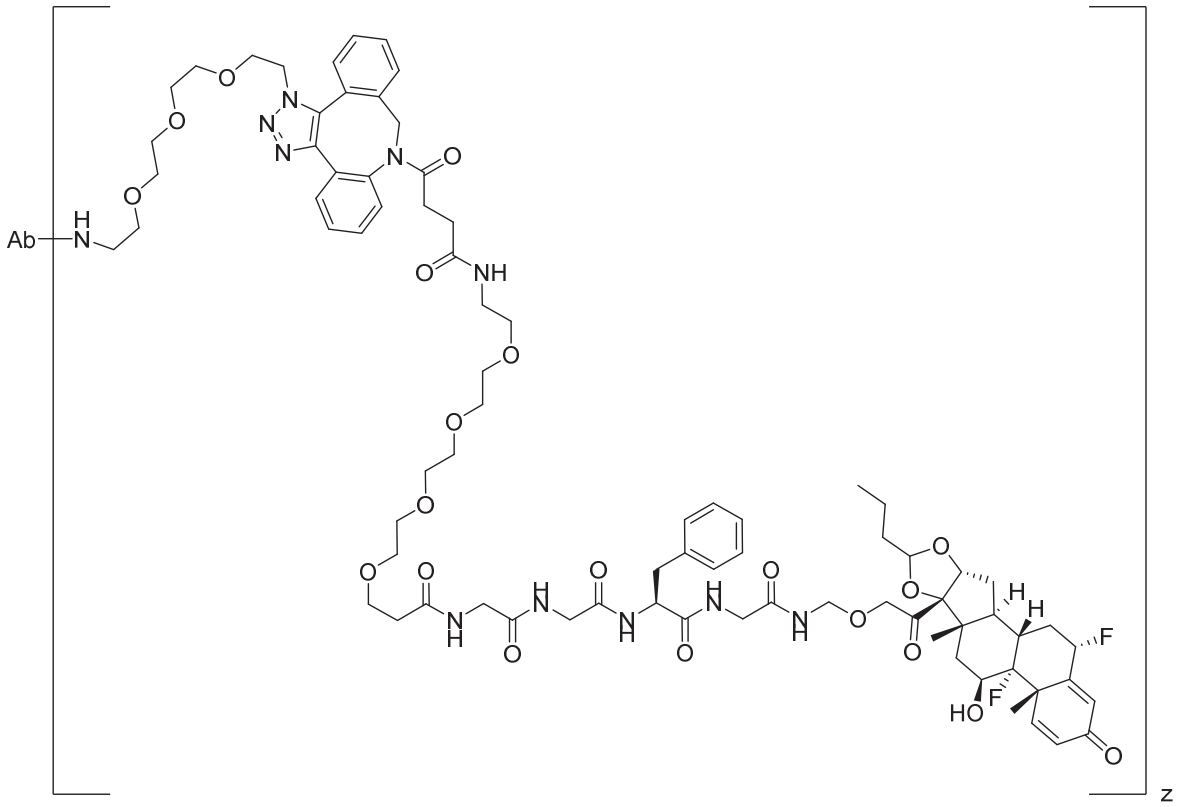
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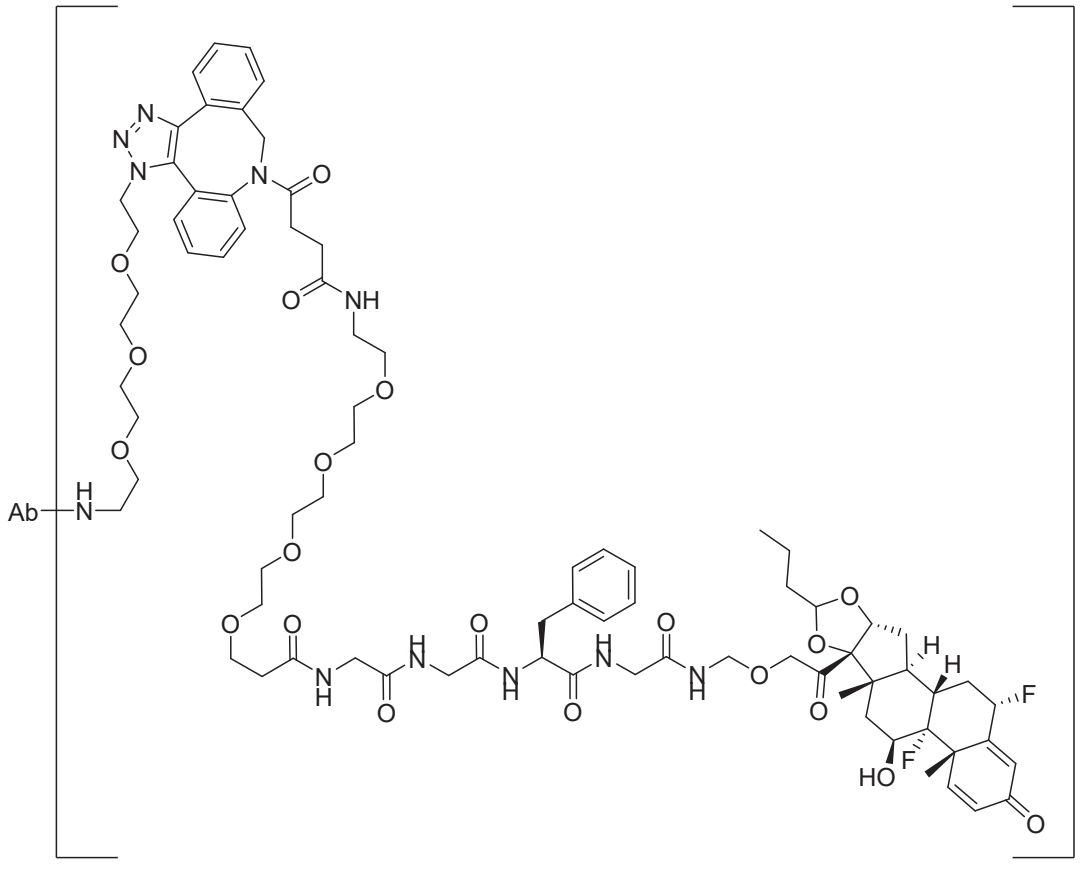

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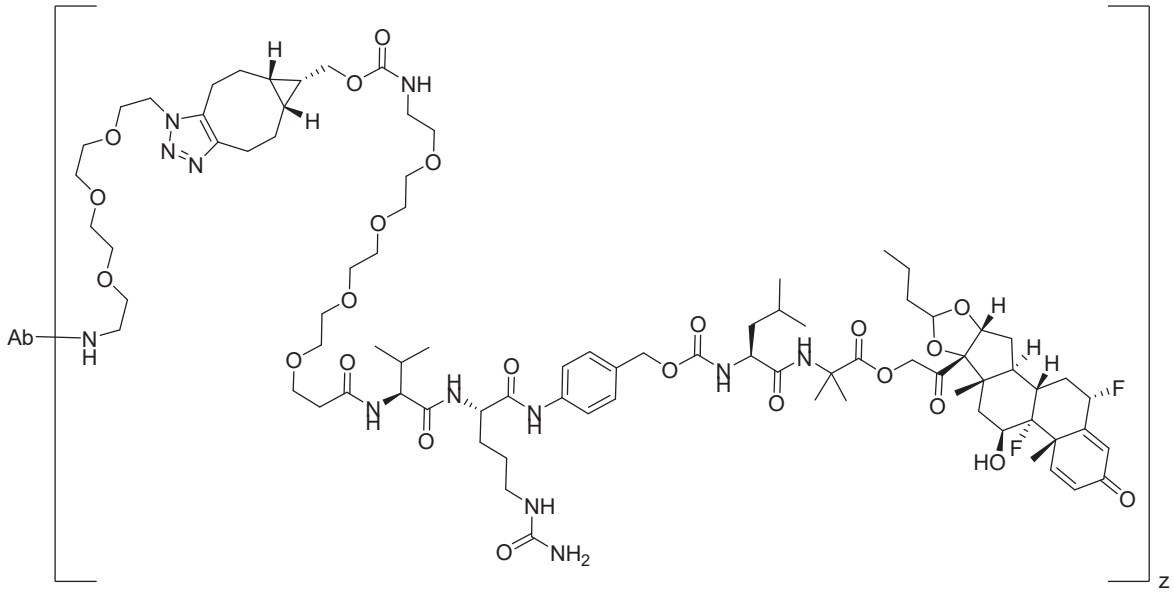

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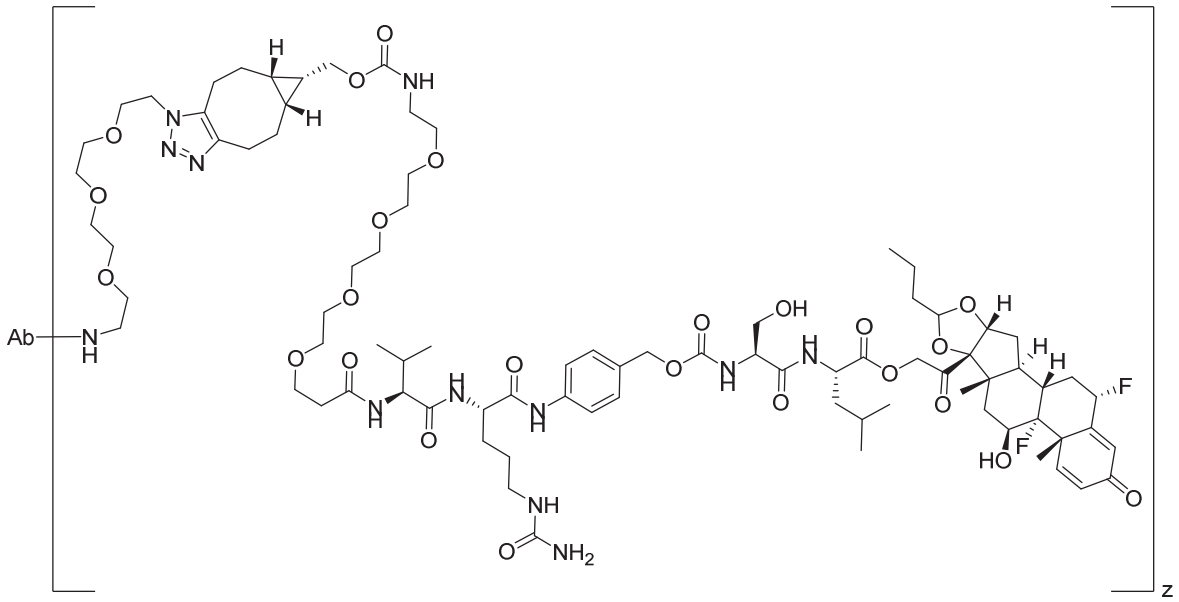

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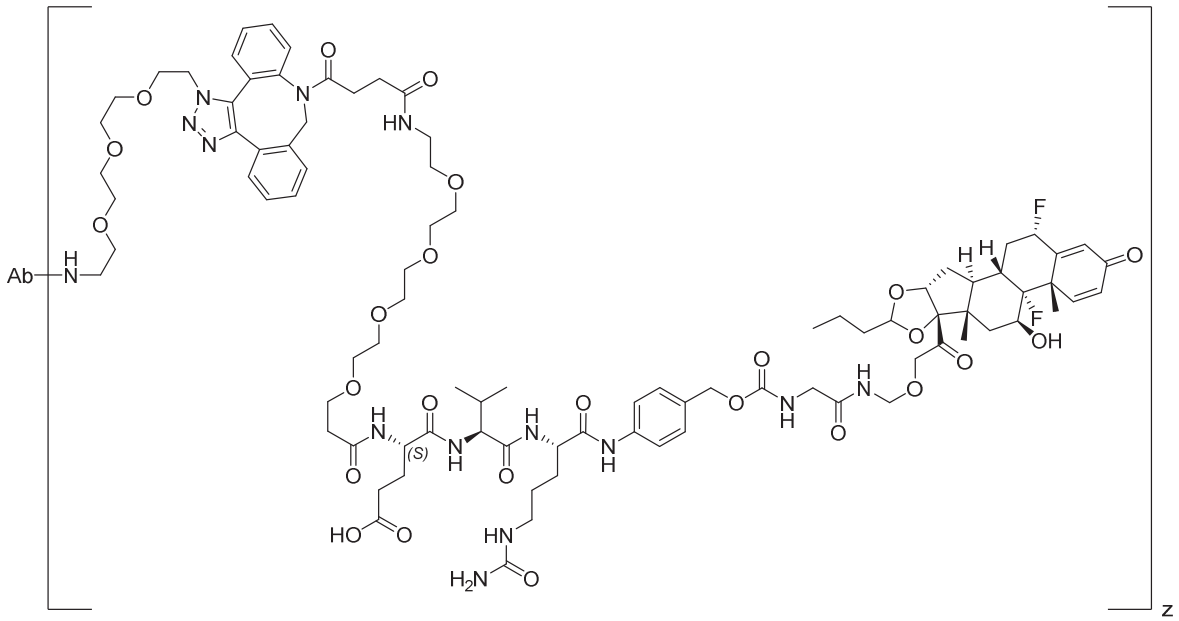

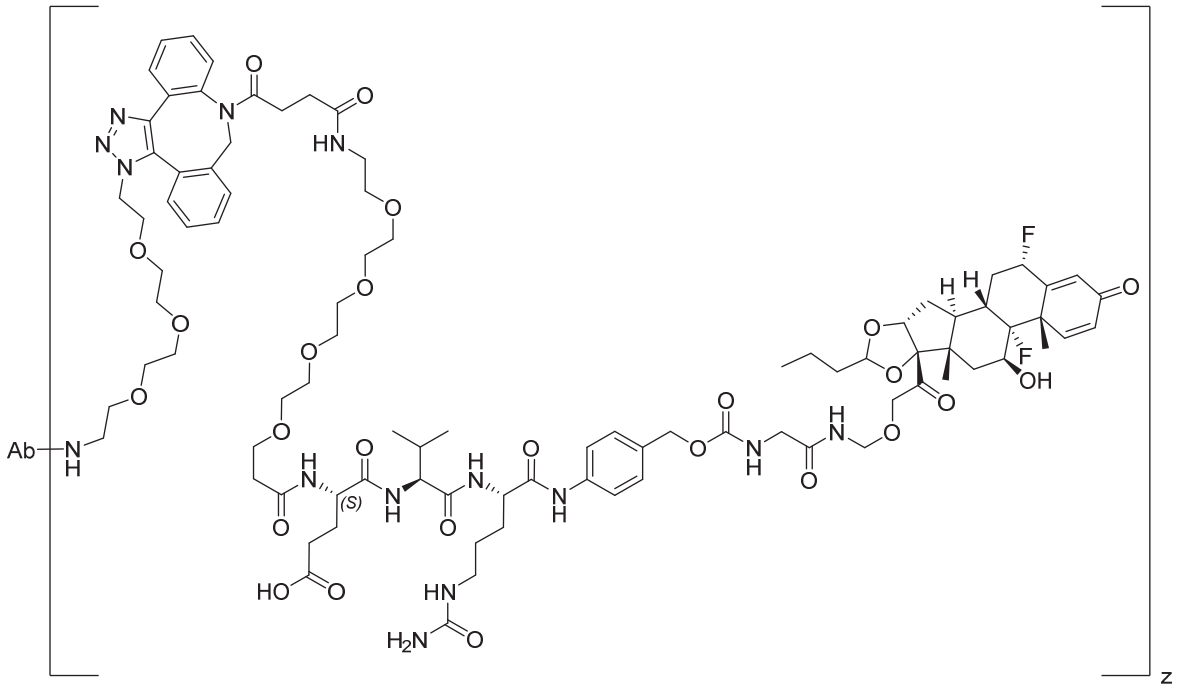

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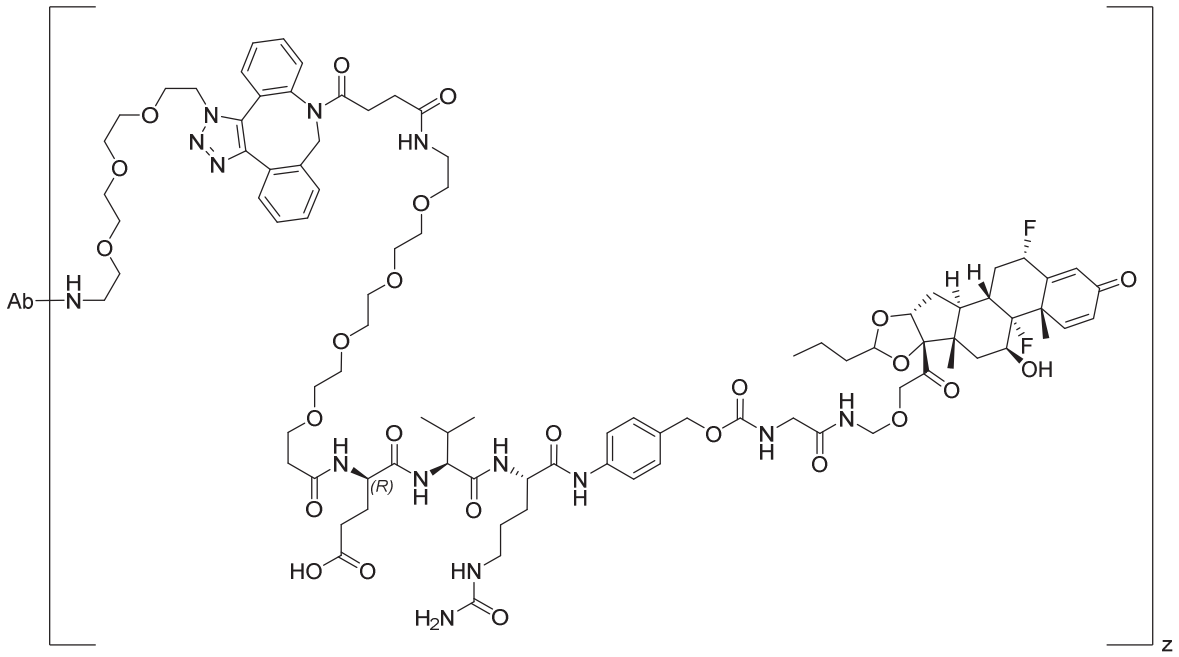
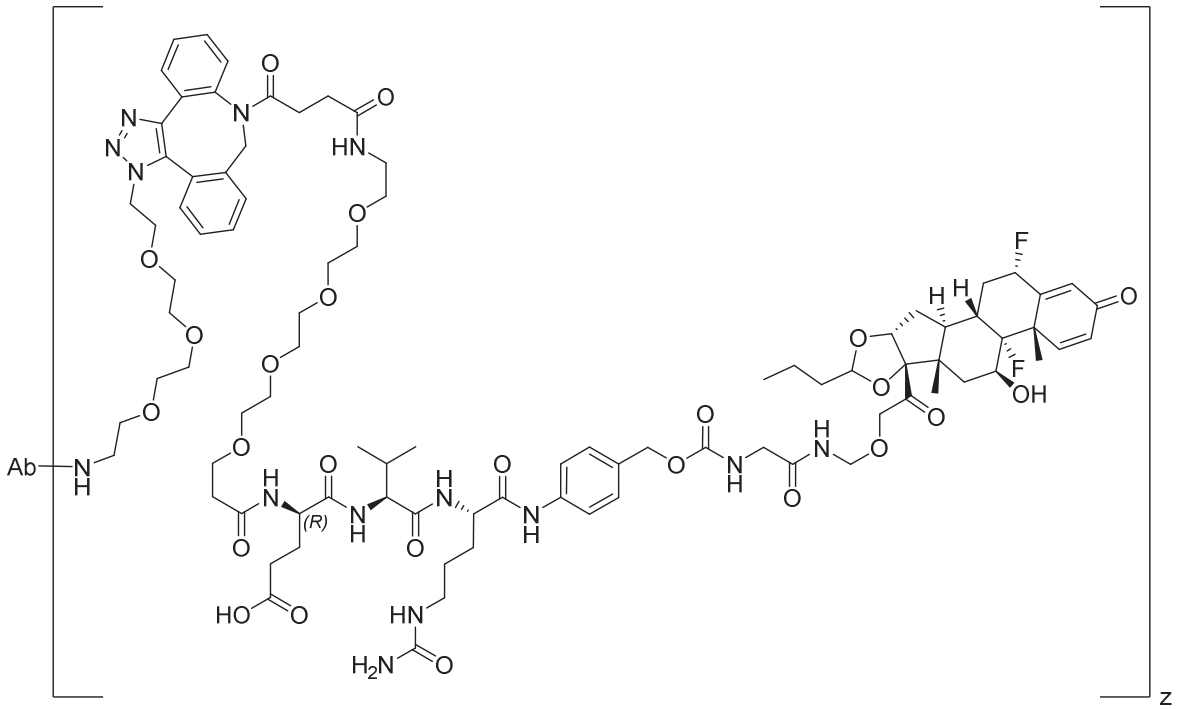
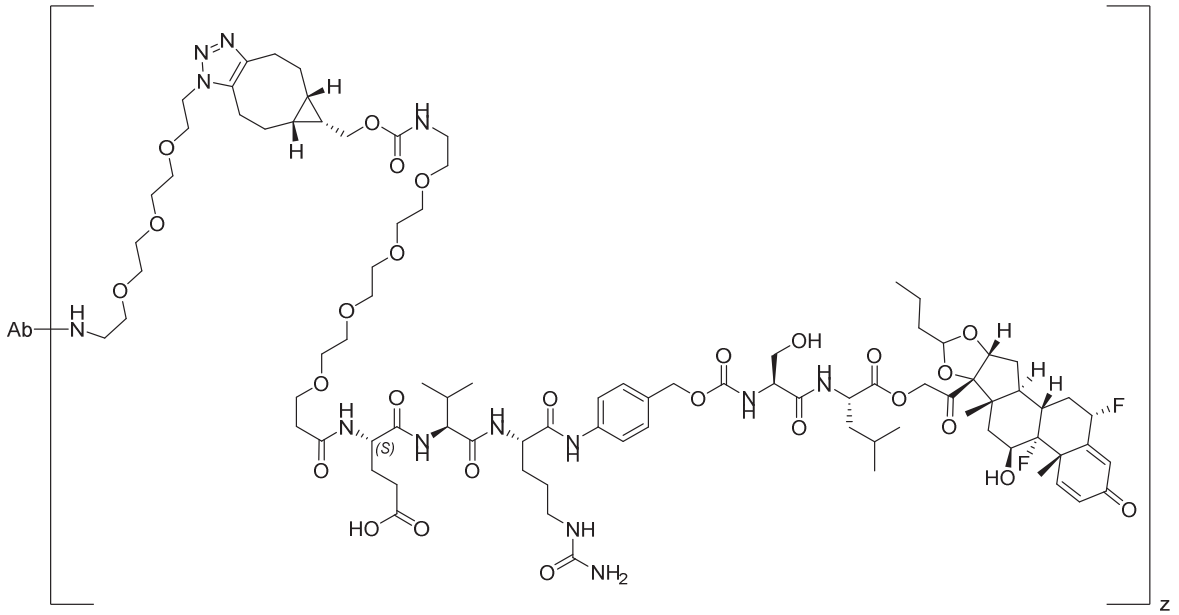
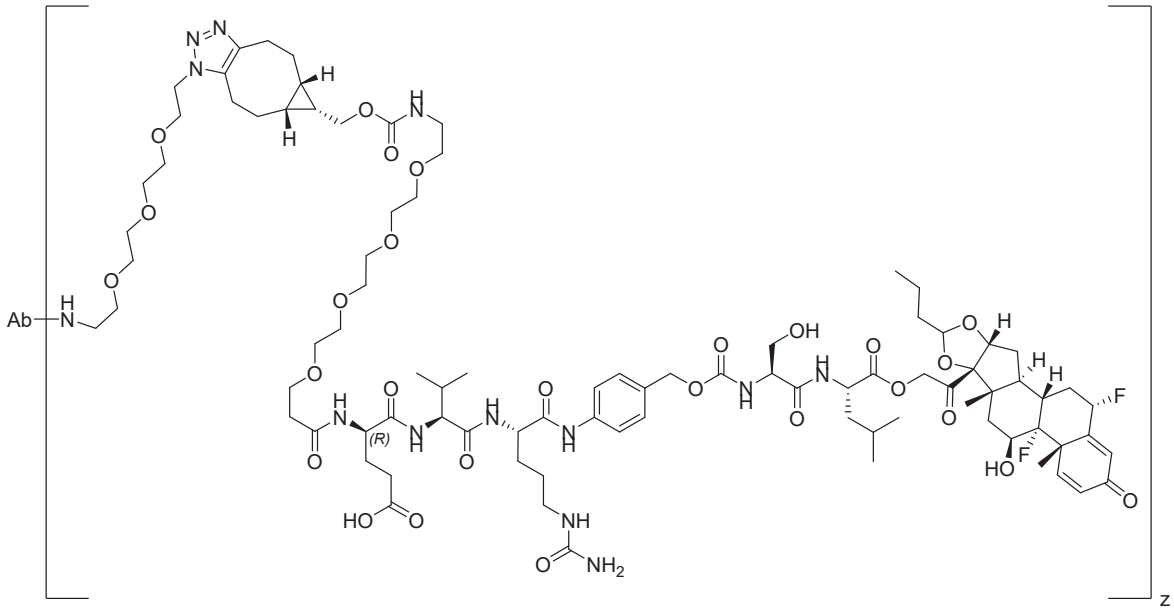




;



; and



wherein **Ab** is an antibody or an antigen binding fragment thereof; and

z is an integer from one to four.

BRIEF DESCRIPTIONS OF THE DRAWINGS

[0010] FIGS. 1A, 1B, and 1C, and 2 show GR activation of steroid-ADCs as tested inExample 7.

[0011] FIG. 3 shows Scheme 1. Synthesis of Spacer-Budesonide 1c-1e, 1g-1i, and 1j-1l.

DETAILED DESCRIPTION

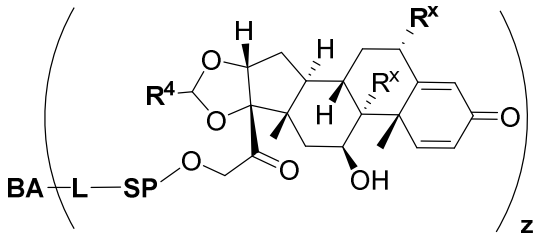
A. DEFINITIONS

[0012] As used herein, "alkyl" refers to a monovalent and saturated hydrocarbon radical moiety. Unless specified otherwise, Alkyl is unsubstituted and can be linear, branched, or cyclic, *i.e.*, cycloalkyl. Alkyl includes, but is not limited to, those having 1–20 carbon atoms, *i.e.*, $C_{1–20}$ alkyl; 1–12 carbon atoms, *i.e.*, $C_{1–12}$ alkyl; 1–8 carbon atoms, *i.e.*, $C_{1–8}$ alkyl; 1–6 carbon atoms, *i.e.*, $C_{1–6}$ alkyl; and 1–3 carbon atoms, *i.e.*, $C_{1–3}$ alkyl. Cycloalkyl, which is a subset of alkyl includes, but is not limited to, groups having 3–20 carbon atoms, *i.e.*, $C_{3–20}$ alkyl; 3–12 carbon atoms, *i.e.*, $C_{3–12}$ alkyl; 3-10 carbon atoms, *i.e.*, $C_{3–10}$ alkyl; 3–8 carbon

CLAIMS

What is claimed is:

1. A Compound of Formula (**III**)

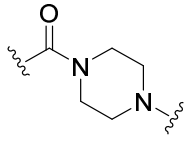
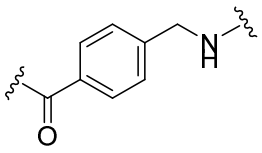
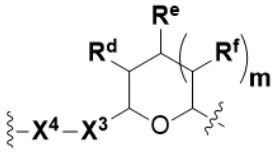


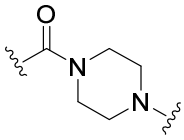
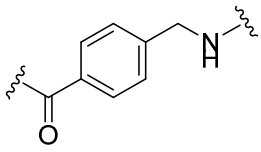
(**III**);

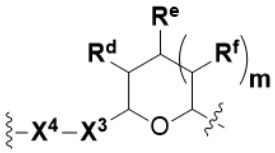
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

both $\mathbf{R^x}$ are hydrogen; and **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to **L** in Formula (**III**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**), -C(O)-N($C_{1\text{-}6}$alkyl)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**),  where the point of attachment at the piperazine nitrogen is attached to **L** in Formula (**III**), -CH_2-NH- where the nitrogen is attached to **L** in Formula (**III**),  where the nitrogen is attached to **L** in Formula (**III**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to **L** in Formula (**III**), or  where $\mathbf{X^4}$ is attached to **L** in Formula (**III**); or

both $\mathbf{R^x}$ are fluoro; and **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^{1b}}$- where $\mathbf{X^{1b}}$ is attached to **L** in Formula (**III**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-$\mathbf{X^{1b}}$- where $\mathbf{X^{1b}}$ is attached to **L** in Formula (**III**),  where the point of attachment at the piperazine nitrogen is attached to **L** in Formula (**III**), -CH_2-NH- where nitrogen is attached to **L** in Formula (**III**),  where nitrogen is attached to **L** in Formula (**III**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to **L** in Formula (**III**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-(C_1-C_{10}-alkylene)-C(O)NH-$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to **L** in Formula (**III**), or

 where $\mathbf{X^4}$ is attached to **L** in Formula (**III**); and

$\mathbf{X^1}$ is -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^{1b}}$ is -S-, -NH-, or -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^2}$ is -NH-;

$\mathbf{X^3}$ is -CH_2-, $\mathbf{X^3}$ is -CH_2-O-(C_1-C_{10}-alkylene)-C(O)- where the C(O) is attached to $\mathbf{X^4}$, or $\mathbf{X^3}$ is -C(O)-;

$\mathbf{X^4}$ is -O-;

$\mathbf{R^5}$ is hydrogen, -OH, -OCH_3, or $C_{1\text{-}6}$alkyl;

$\mathbf{R^{50}}$ and $\mathbf{R^{50a}}$ are independently hydrogen or C_1-C_6-alkyl;

$\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ are independently hydrogen, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or -$CH_2O\mathbf{R^g}$, where each $\mathbf{R^g}$ is independently -CH_2C(O)OH or -CH_2C(O)O(alkyl);

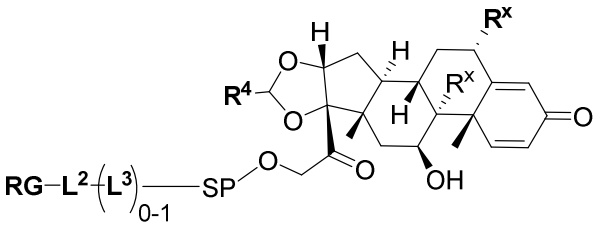
m is zero or one;

z is an integer selected from one to thirty, inclusive;

L is a linker; and

BA is a binding agent.

2. A Compound of Formula (**II**)

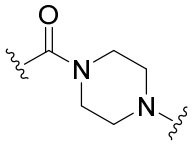
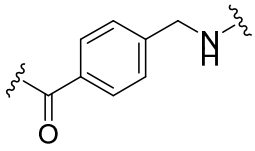
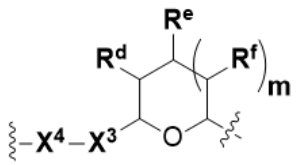


(**II**);

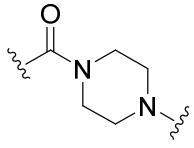
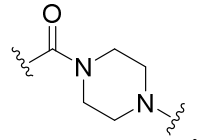
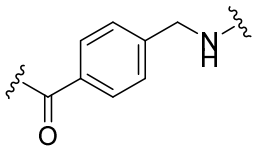
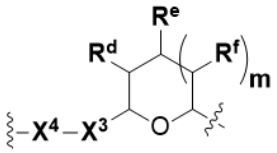
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

both $\mathbf{R^x}$ are hydrogen; **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$- where $\mathbf{X^1}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-N($C_{1\text{-}6}$alkyl)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where the point of attachment at the piperazine nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -CH_2-NH- where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), or  where $\mathbf{X^4}$ is attached to $\mathbf{L^3}$ in Formula (**II**); or

both $\mathbf{R^x}$ are fluoro; **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N($C_{1\text{-}6}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^{1b}}$- where $\mathbf{X^{1b}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-$\mathbf{X^{1b}}$-

where $\mathbf{X^{1b}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where the point of attachment at the piperazine nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  , -CH_2-NH- where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**),  where nitrogen is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where the terminal N$\mathbf{R^{50a}}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N($\mathbf{R^5}$)-(C_1-C_{10}-alkylene)-C(O)NH-$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**), or  where $\mathbf{X^4}$ is attached to $(\mathbf{L^3})_{0\text{-}1}$ in Formula (**II**); and

$\mathbf{X^1}$ is -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^{1b}}$ is -S-, -NH-, or -N($C_{1\text{-}6}$alkyl)-;

$\mathbf{X^2}$ is -NH-;

$\mathbf{X^3}$ is -CH_2-, $\mathbf{X^3}$ is -CH_2-O-(C_1-C_{10}-alkylene)-C(O)- where the C(O) is attached to $\mathbf{X^4}$, or $\mathbf{X^3}$ is -C(O)-;

$\mathbf{X^4}$ is -O-;

$\mathbf{R^5}$ is hydrogen, -OH, -OCH_3, or $C_{1\text{-}6}$alkyl;

$\mathbf{R^{50}}$ and $\mathbf{R^{50a}}$ are independently hydrogen or C_1-C_6-alkyl;

$\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ are independently hydrogen, -OH, hydroxyalkyl, alkoxycarbonyl, -C(O)OH, or -CH_2O$\mathbf{R^g}$, where each $\mathbf{R^g}$ is independently -CH_2C(O)OH or -CH_2C(O)O(alkyl);

m is zero or one;

RG is a reactive group;

$\mathbf{L^2}$ is a connecting linker; and

$\mathbf{L^3}$, when present, is a self-immolative linker.

3. The Compound of Claim 1 or 2, where **R^4** is linear or branched alkyl.

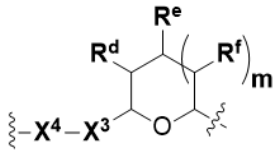
4. The Compound of Claim 1 or 2, where **R^4** is aryl.

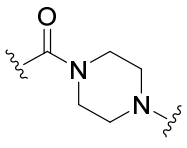
5. The Compound of Claim 1 or 2, where **R^4** is arylalkyl.

6. The Compound of Claim 1 or 2, where **R^4** is N-containing heterocycloalkyl.

7. The Compound of any one of Claims 1-6, where R^4 is in the (*R*)-configuration.

8. The Compound of any one of Claims 1-7, where

both **R^x** are hydrogen; and **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-, -C(O)-N(C_{1-6}alkyl)-C_1-C_{10}-alkylene-**X^1**- where **X^1** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -C(O)-N(C_{1-6}alkyl)-(C_1-C_{10}-alkylene)-S- where sulfur is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-N**R^{50}**C(O)-(C_1-C_{10}-alkylene)-N**R^{50a}**- where the terminal N**R^{50a}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N**R^{50}**C(O)-(C_1-C_{10}-alkylene)-N**R^{50a}**- where the terminal N**R^{50a}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy, -C(O)-N(**R^5**)-C_1-C_{10}-alkylene-C(O)NH-**X^2**- where **X^2** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), or  where **X^4** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**); or

both **R^x** are fluoro; and **SP** is -C(O)-N(C_{1-6}alkyl)-C_1-C_{10}-alkylene-**X^{1b}**- where **X^{1b}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -C(O)-N(H)-(C_1-C_{10}-alkylene)-**X^{1b}**- where **X^{1b}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**),  where the point of attachment at the piperazine nitrogen is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -(C_1-C_{10}-alkylene)-N**R^{50}**C(O)-(C_1-C_{10}-alkylene)-N**R^{50a}**- where the terminal N**R^{50a}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**), -C(O)-(C_1-C_{10}-alkylene)-N**R^{50}**C(O)-(C_1-C_{10}-alkylene)-N**R^{50a}**- where the terminal N**R^{50a}** is attached to **L** in Formula (**III**) or (**L^3**)$_{0-1}$ in Formula (**II**) and where each C_1-C_{10}-alkylene is independently optionally

substituted with one or more hydroxy, or -C(O)-N($\mathbf{R^5}$)-(C_1-C_{10}-alkylene)-C(O)NH-$\mathbf{X^2}$- where $\mathbf{X^2}$ is attached to **L** in Formula (**III**) or ($\mathbf{L^3}$)$_{0\text{-}1}$ in Formula (**II**).

9. The Compound of any one of Claims 1-8, where **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-.

10. The Compound of any one of Claims 1-9, where **SP** is -C(O)-C_2-C_5-alkylene-C(O)-.

11. The Compound of any one of Claims 1-10, where **SP** is -C(O)-CH_2CH_2-C(O)-.

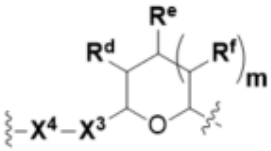
12. The Compound of any one of Claims 1-8, where **SP** is -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$-.

13. The Compound of any one of Claims 1-8 or 12, where **SP** is -C(O)-N($\mathbf{R^5}$)-C_1-C_5-alkylene-C(O)NH-NH-.

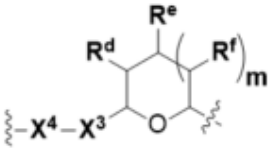
14. The Compound of any one of Claims 1-8, 12, or 13, where **SP** is -C(O)-N($\mathbf{R^5}$)-CH_2-C(O)NH-NH-.

15. The Compound of any one of Claims 1-8 or 12-14, where $\mathbf{R^5}$ is hydrogen or $C_{1\text{-}6}$alkyl.

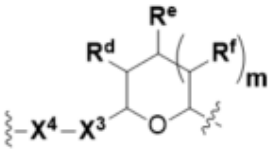
16. The Compound of any one of Claims 1-8 or 12-15, where $\mathbf{R^5}$ is hydrogen or -CH_3.

17. The Compound of any one of Claims 1-8, where **SP** is 

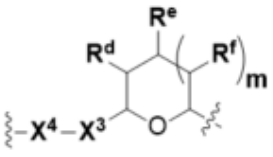
.

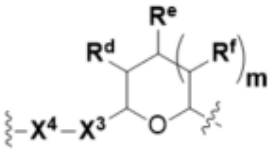
18. The Compound of any one of Claims 1-8, where **SP** is 

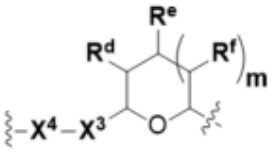
and **m** is one.

19. The Compound of any one of Claims 1-8, where **SP** is 

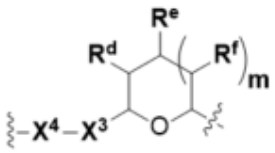
, **m** is one, and $\mathbf{R^f}$ is hydrogen or -OH.

20. The Compound of any one of Claims 1-8, where **SP** is  , **m** is one, and $\mathbf{R^f}$ is hydrogen.

21. The Compound of any one of Claims 1-8, where **SP** is  , **m** is one, and $\mathbf{R^f}$ is –OH.

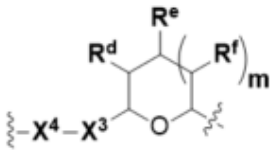
22. The Compound of any one of Claims 1-8, where **SP** is  and **m** is zero.

23. The Compound of any one of Claims 1-8 or 17-22, where **SP** is



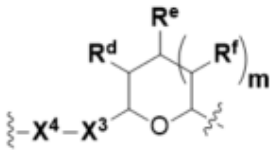
and $\mathbf{X^3}$ is -CH_2-**.**

24. The Compound of any one of Claims 1-8 or 17-22, where **SP** is



and $\mathbf{X^3}$ is -CH_2-O-(C_1-C_{10}-alkylene)-C(O)-.

25. The Compound of any one of Claims 1-8 or 17-22, where **SP** is



and $\mathbf{X^3}$ is -C(O)-.

26. The Compound of any one of Claims 1-8 or 17-25, where $\mathbf{R^d}$ and $\mathbf{R^e}$ are independently hydrogen or –OH.

27. The Compound of any one of Claims 1-8 or 17-25, where $\mathbf{R^d}$ and $\mathbf{R^e}$ are hydrogen.

28. The Compound of any one of Claims 1-8 or 17-25, where $\mathbf{R^d}$ and $\mathbf{R^e}$ are -OH.

29. The Compound of any one of Claims 1-8, where **SP** is -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$-.

30. The Compound of any one of Claims 1-8, where **SP** is -(linear C_1-C_3-alkylene)-N$\mathbf{R^{50}}$C(O)-(linear C_1-C_3-alkylene)-N$\mathbf{R^{50a}}$-.

31. The Compound of any one of Claims 1-8, where **SP** is -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- and where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy.

32. The Compound of any one of Claims 1-8, where **SP** is -(branched C_1-C_6-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_6-hydroxy-alkylene)-N$\mathbf{R^{50a}}$.

33. The Compound of any one of Claims 1-8 or 29-32, where $\mathbf{R^{50}}$ and $\mathbf{R^{50a}}$ are independently hydrogen or methyl.

34. The Compound of any one of Claims 1-8 or 29-32, where $\mathbf{R^{50}}$ and $\mathbf{R^{50a}}$ are each hydrogen.

35. The Compound of any one of Claims 1-8 or 29-32, where $\mathbf{R^{50}}$ and $\mathbf{R^{50a}}$ are each methyl.

36. The Compound of any one of Claims 1-35, where both $\mathbf{R^x}$ are hydrogen.

37. The Compound of any one of Claims 1-8, where both $\mathbf{R^x}$ are hydrogen and **SP** is -C(O)-N(H)-(C_1-C_{10}-alkylene)-S- or -C(O)-N($C_{1\text{-}6}$alkyl)-(C_1-C_{10}-alkylene)-S-.

38. The Compound of any one of Claims 1-8, where both $\mathbf{R^x}$ are hydrogen and **SP** is -C(O)-N($C_{1\text{-}3}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$-.

39. The Compound of any one of Claims 1-8 or 38, where both $\mathbf{R^x}$ are hydrogen and **SP** is -C(O)-N($C_{1\text{-}3}$alkyl)-C_2-C_5-alkylene-$\mathbf{X^1}$-.

40. The Compound of any one of Claims 1-8, 38, or 39, where both $\mathbf{R^x}$ are hydrogen and **SP** is -C(O)-N($C_{1\text{-}3}$alkyl)-CH_2CH_2-$\mathbf{X^1}$-.

41. The Compound of any one of Claims 1-8, 38, or 39, where both **R^x** are hydrogen and **SP** is -C(O)-N(CH_3)-C_2-C_5-alkylene-N(CH_3)-.

42. The Compound of any one of Claims 1-8 or 38-41 where both **R^x** are hydrogen and **SP** is -C(O)-N(CH_3)-CH_2CH_2-N(CH_3)-.

43. The Compound of any one of Claims 1-35, where both **R^x** are fluoro.

44. The Compound of any one of Claims 1-8, where both **R^x** are fluoro and **SP** is -C(O)-N(H)-(C_1-C_{10}-alkylene)-**X^{1b}**- or -C(O)-N(C_{1-6}alkyl)-(C_1-C_{10}-alkylene)-**X^{1b}**-.

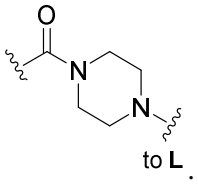
45. The Compound of Claim 44, where **SP** is -C(O)-N(H)-(C_1-C_6-alkylene)-**X^{1b}**- or -C(O)-N(C_{1-6}alkyl)-(C_1-C_6-alkylene)-**X^{1b}**-.

46. The Compound of Claim 44 or 45, where **X^{1b}** is sulfur.

47. The Compound of Claim 44 or 45, where **X^{1b}** is -NH- or -N(C_{1-6}-alkyl)-.

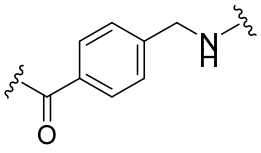
48. The Compound of Claim 44 or 45, where **X^{1b}** is -NH- or -N(CH_3)-.

49. The Compound of any one of Claims 1-8, where both **R^x** are fluoro and **SP** is

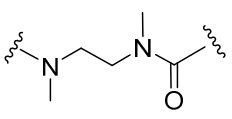


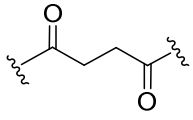
.

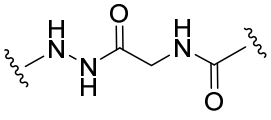
50. The Compound of any one of Claims 1-7, where **SP** is -CH_2-NH-.

51. The Compound of any one of Claims 1-7, where **SP** is 

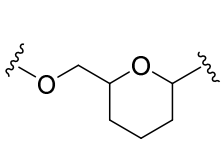
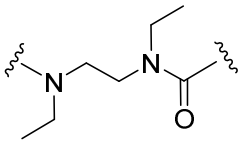
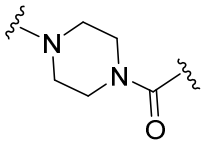
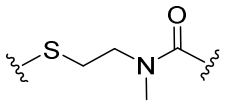
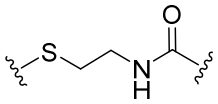
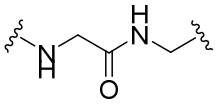
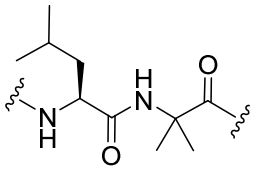
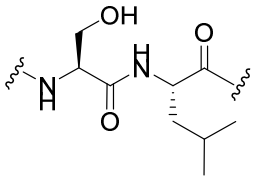
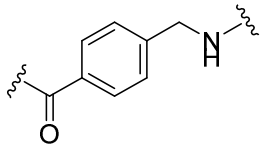
.

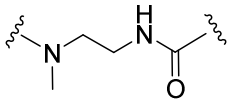
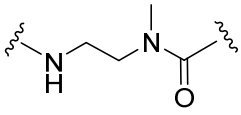
52. The Compound of any one of Claims 1-7, where both **R^x** are hydrogen or both **R^x** are fluoro and **SP** is 

, 

, 

,

 ,  ,  ,  ,  ,  ,  ,  , -CH_2-NH-, or  ;

or both $\mathbf{R^x}$ are fluoro and **SP** is  or  ;

and where the left side point of attachment in the above **SP** structures is attached to **L** or $(\mathbf{L^3})_{0\text{-}1}$.

53. The Compound of Formula (**III**) of any one of Claims 1 or 3-52, where **z** is selected from one to ten, inclusive.

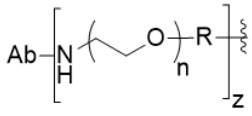
54. The Compound of Formula (**III**) of any one of Claims 1 or 3-53, where **z** is selected from two to four, inclusive.

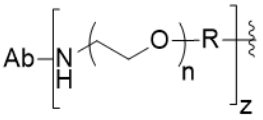
55. The Compound of Formula (**III**) of any one of Claims 1 or 3-54, where **z** is four.

56. The Compound of Formula (**III**) of any one of Claims 1 or 3-54, where **z** is two.

57. The Compound of Formula (**III**) of any one of Claims 1 or 3-56, where **BA** comprises an antibody, an antibody fragment, or an antigen binding fragment thereof.

58. The Compound of Formula (**III**) of any one of Claims 1 or 3-57, where **BA** comprises an antibody or antigen binding fragment thereof having the following structure

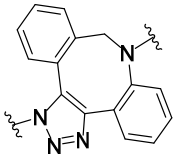
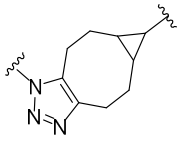
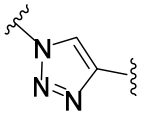
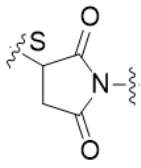
 where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; **R** is $C_{2\text{-}4}$-alkylene, **n** is an integer selected from one to ten, inclusive, and **z** is an integer selected from one to ten, inclusive.

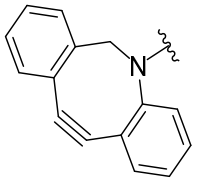
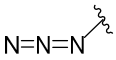
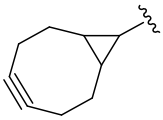
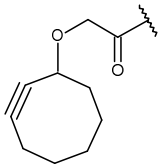
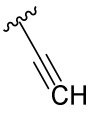
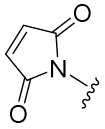
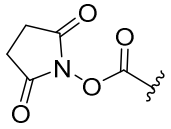
59. The Compound of Formula (**III**) of any one of Claims 1 or 3-59, where **BA** comprises an antibody or antigen binding fragment having the following structure 
where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; **R** is C_{2-4}-alkylene; and **n** is an integer selected from two to four, inclusive.

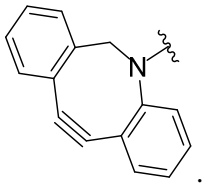
60. The Compound of Formula (**III**) of any one of Claims 1 or 3-59, where **BA** comprises an antibody or antigen binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1).

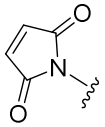
61. The Compound of Formula (**III**) of any one of Claims 1 or 3-60, where **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-($\mathbf{L^3}$)$_{0-1}$-, where $\mathbf{L^1}$ is attached to **BA** and $\mathbf{L^3}$ is attached to **SP**; and where $\mathbf{L^1}$ is a reactive group residue; $\mathbf{L^2}$ is connecting linker; and $\mathbf{L^3}$, when present, is a self-immolative linker.

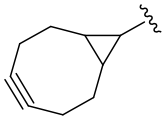
62. The Compound of Formula (**III**) of any one of Claims 1 or 3-61, where **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$-.

63. The Compound of Formula (**III**) of Claim 61 or 62 where $\mathbf{L^1}$ is selected from  or a regioisomer or mixture of isomers thereof;  ;  or  a regioisomer or mixture of isomers thereof; or a stereoisomer or mixture of stereoisomers thereof, where S refers to the sulfur atom on a cysteine residue through which the reactive group residue is attached to **BA**; and  where N refers to the nitrogen atom on a lysine residue through which the reactive group residue is attached to **BA**.

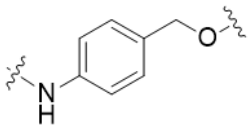
64. The Compound of Formula (**II**) of any one of Claims 2-52, where **RG** is selected from the group consisting of  ,  ,  ,  ,  ,  , and  .

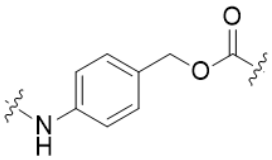
65. The Compound of Formula (**II**) of any one of Claims 2-52, where **RG** is  .

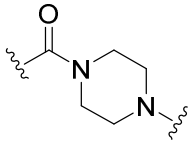
66. The Compound of Formula (**II**) of any one of Claims 2-52, where **RG** is  .

67. The Compound of Formula (**II**) of any one of Claims 2-52, where **RG** is  .

68. The Compound of any one of claims 1-67, where for the Compound of Formula (**III**) **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0\text{-}1}$-; and where

$\mathbf{L^3}$ in the Compound of Formula (**II**) or (**III**) is  where the -NH-group is attached to $\mathbf{L^2}$, when **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-; or

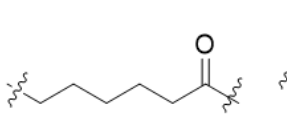
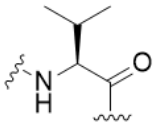
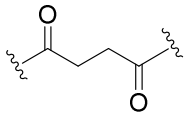
$\mathbf{L^3}$ in the Compound of Formula (**II**) or (**III**) is  where the -NH- group is attached to $\mathbf{L^2}$, when **SP** is -C(O)-N($C_{1\text{-}3}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^1}$-, -C(O)-N($C_{1\text{-}3}$alkyl)-C_1-C_{10}-alkylene-$\mathbf{X^{1b}}$- where $\mathbf{X^{1b}}$ is -NH- or -N($C_{1\text{-}6}$alkyl)-, -C(O)-N(H)-(C_1-C_{10}-alkylene)-$\mathbf{X^{1b}}$-

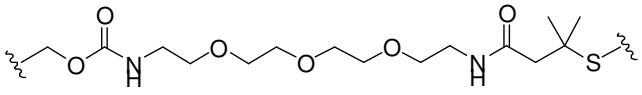
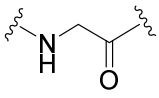
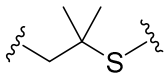
where $\mathbf{X^{1b}}$ is -NH- or -N(C_{1-6}alkyl)-,  , -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$-, -C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}}$- where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxyl or -C(O)-N($\mathbf{R^5}$)-C_1-C_{10}-alkylene-C(O)NH-$\mathbf{X^2}$-; or

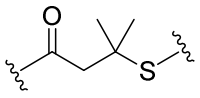
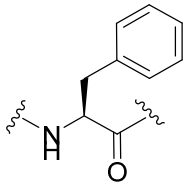
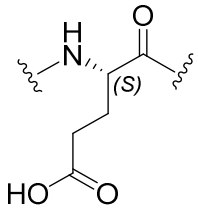
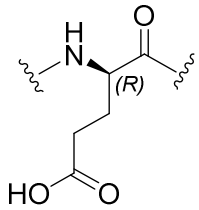
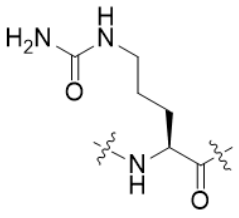
$\mathbf{L^3}$ in the Compound of Formula (**II**) or (**III**) is absent.

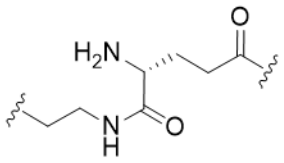
69. The Compound of any one of claims 1-68, where for the Compound of Formula (**III**) **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0-1}$-; and where $\mathbf{L^2}$ in the Compound of Formula (**II**) or (**III**) comprises PEG, a di-peptide residue, a tripeptide residue, a tetrapeptide residue, a pentapeptide residue, -C(O)CH_2CH_2C(O)-, a cyclodextrin (CD) residue, or -$CH_2CH_2CH_2CH_2CH_2$C(O)-, or any combination thereof.

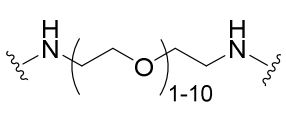
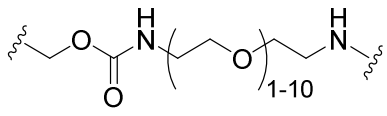
70. The Compound of any one of claims 1-68, where for the Compound of Formula (**III**) **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0-1}$-; and where $\mathbf{L^2}$ in the Compound of Formula (**II**) or (**III**) comprises

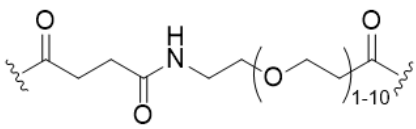
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,  ,  ,

 ,

-C(O)CH_2CH_2C(O)NH-,  ,  ,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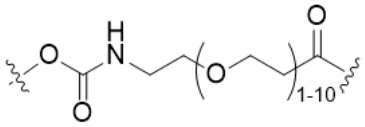
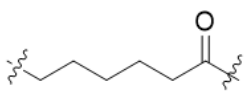

, or a cyclodextrin residue (**CD**); or any combination thereof.

71. The Compound of any one of claims 1-68, where for the Compound of Formula (**III**) **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0\text{-}1}$-; and where $\mathbf{L^2}$ in the Compound of Formula (**II**) or (**III**) comprises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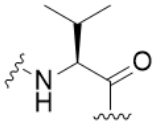
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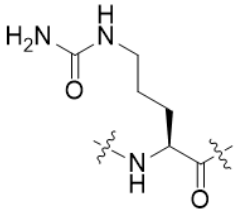
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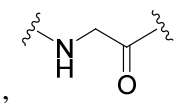
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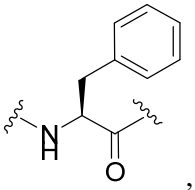
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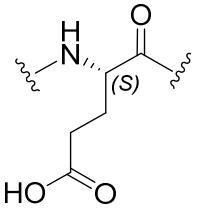
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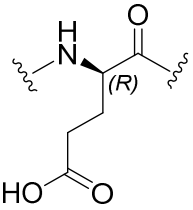
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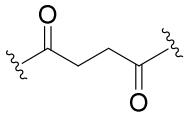
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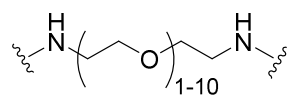
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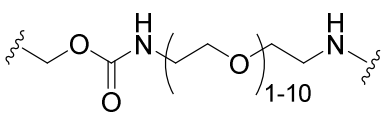
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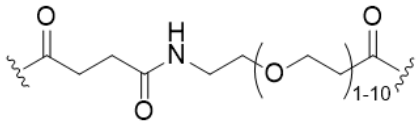
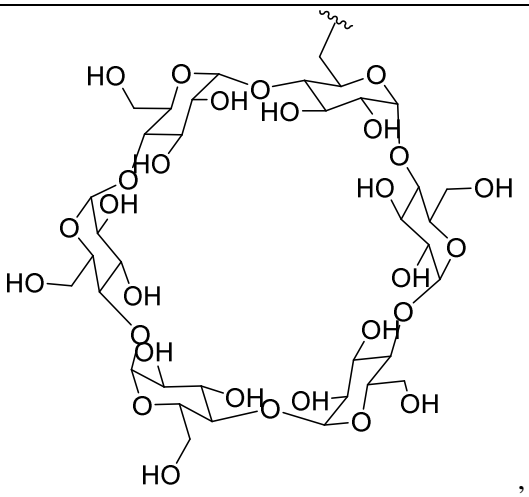

or a **CD** residue, or any combination thereof.

72. The compound of any one of claims 69-71, wherein **CD** is selected from the group consisting of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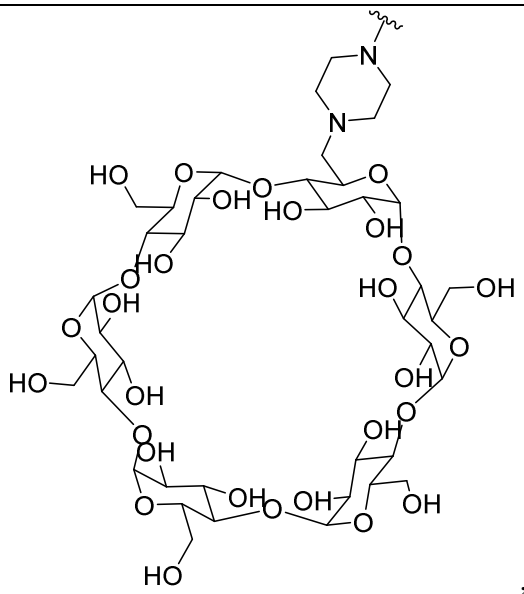
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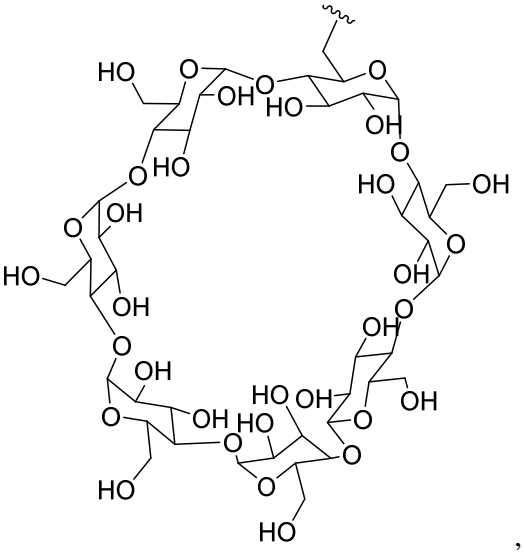
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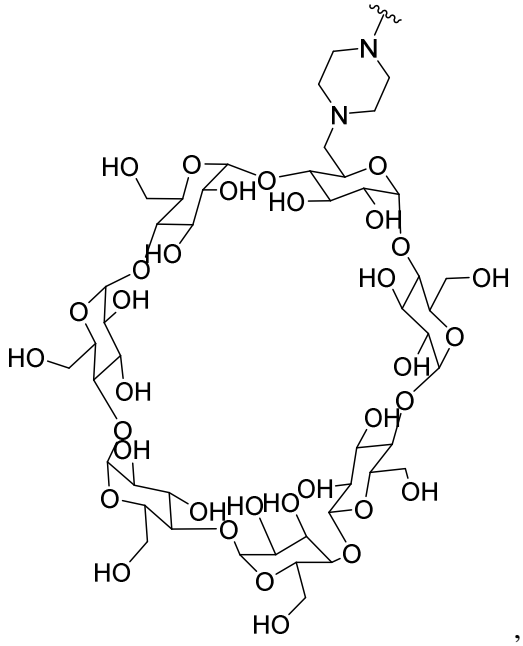
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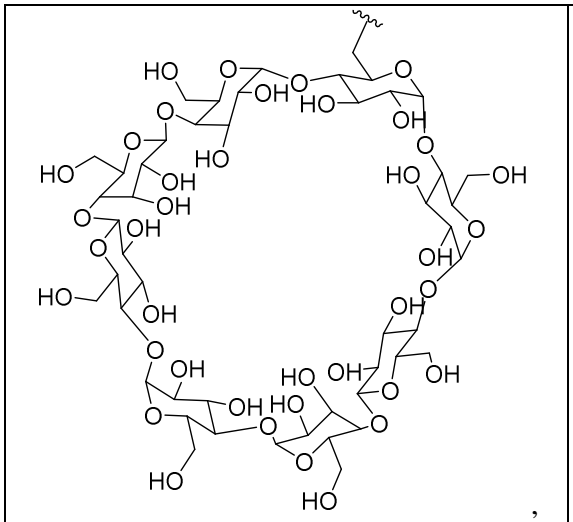

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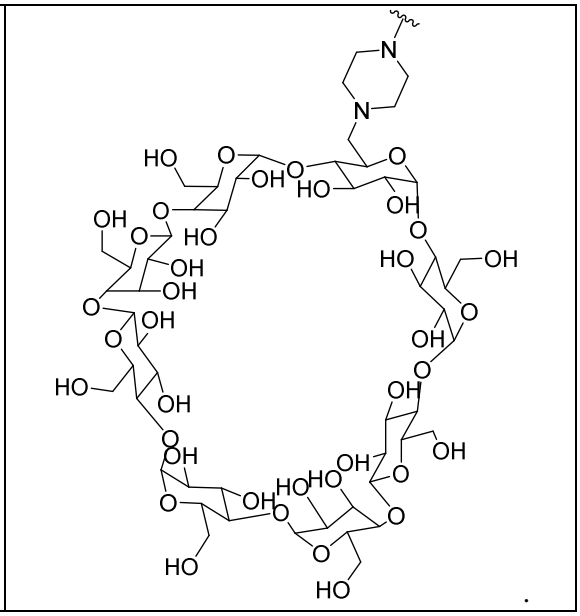
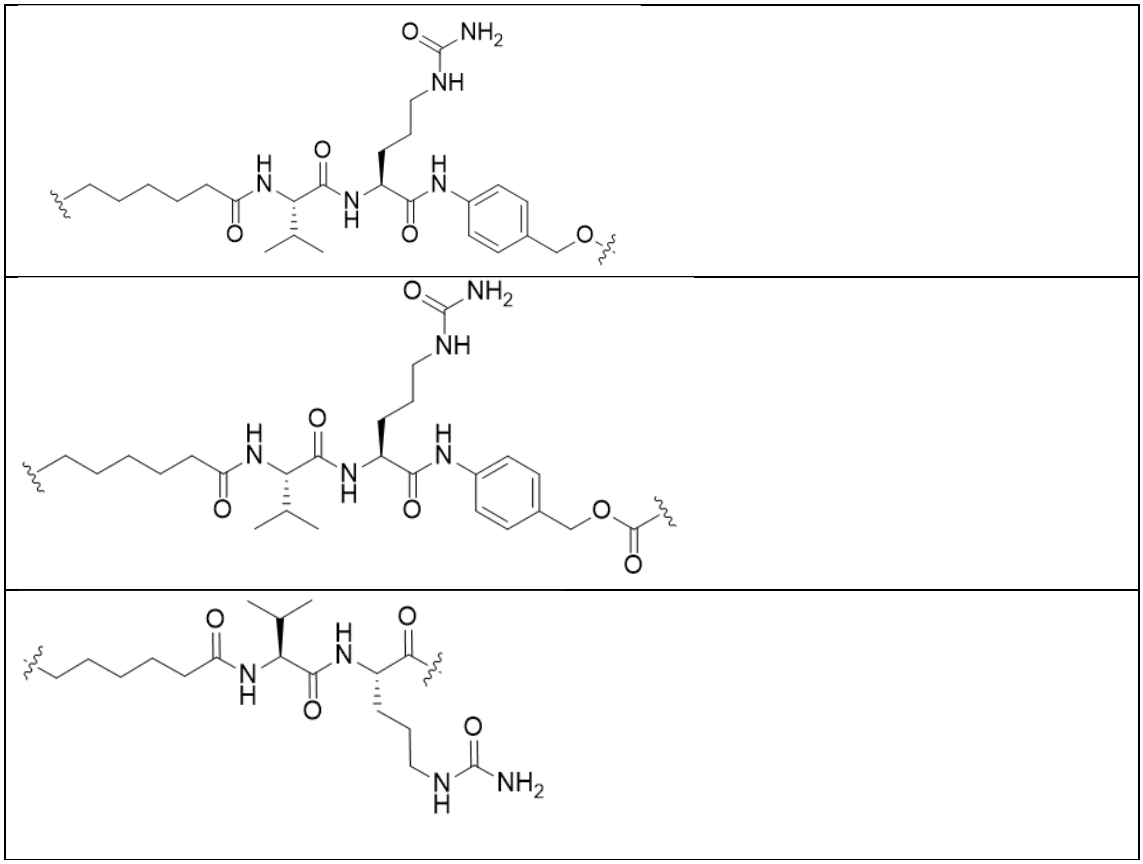
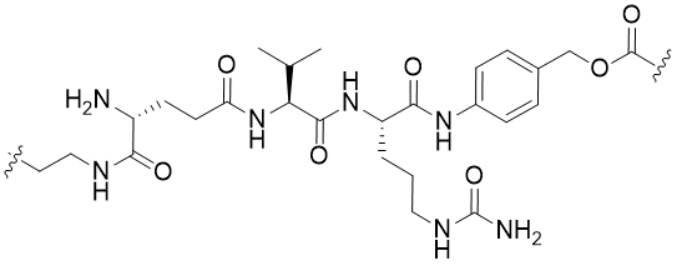
and

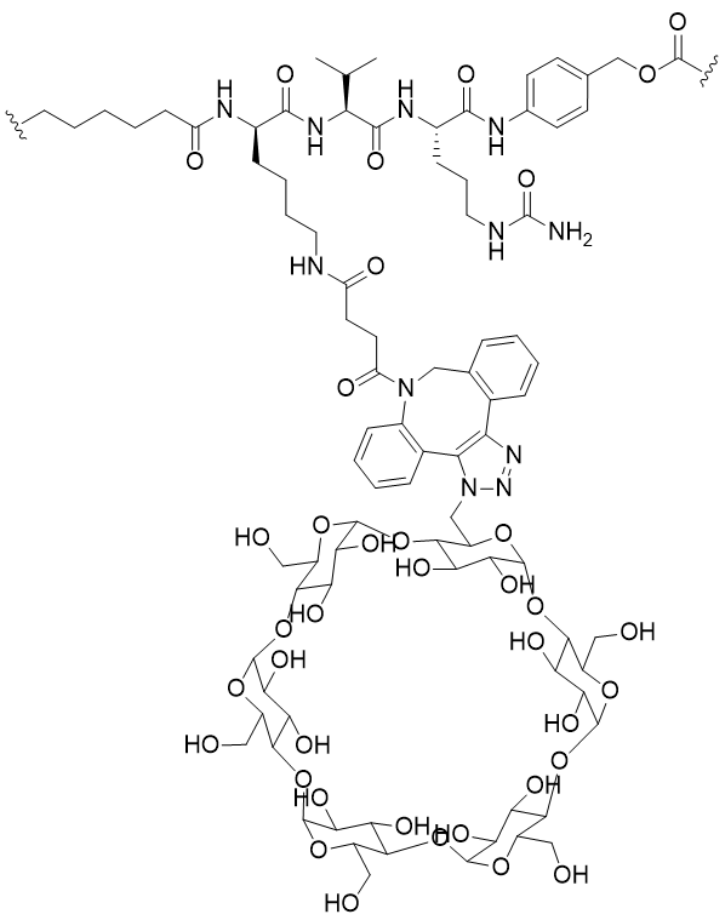


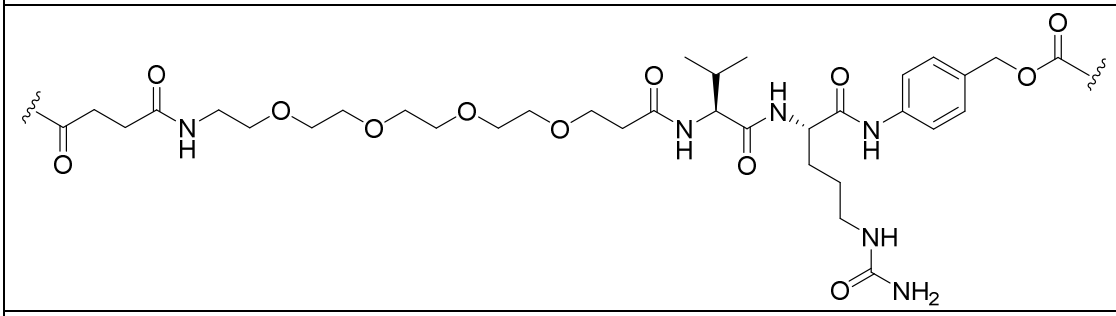
.

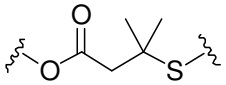
73. The Compound of any one of Claims 1-67, where for the Compound of Formula (**III**) **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0\text{-}1}$-; and where -$\mathbf{L^2}$-($\mathbf{L^3}$)$_{0\text{-}1}$- in the Compound of Formula (**II**) or (**III**) comprise

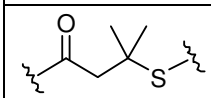


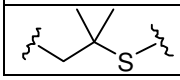


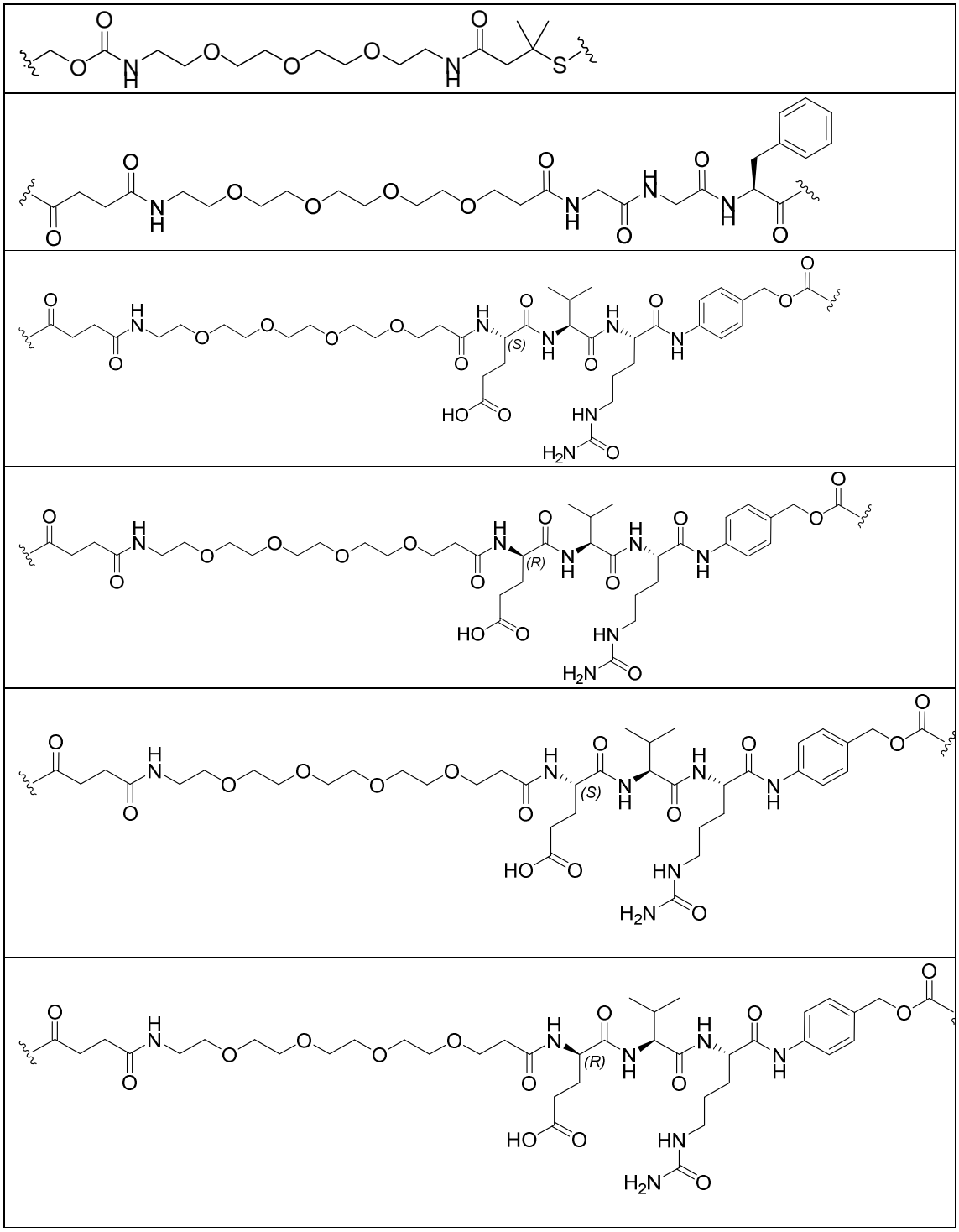


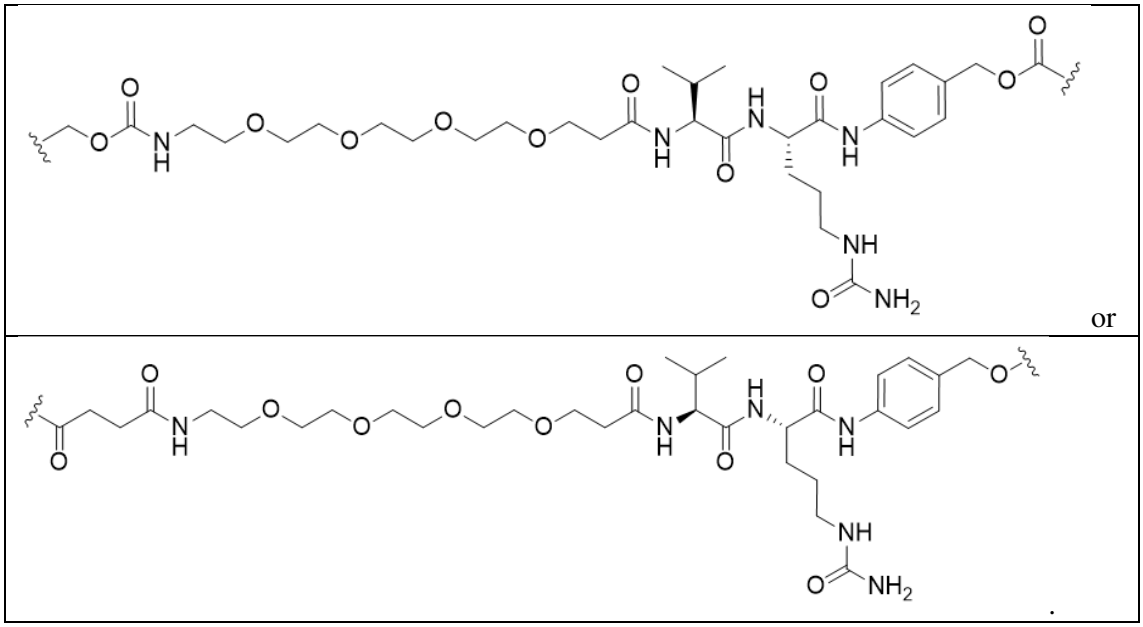






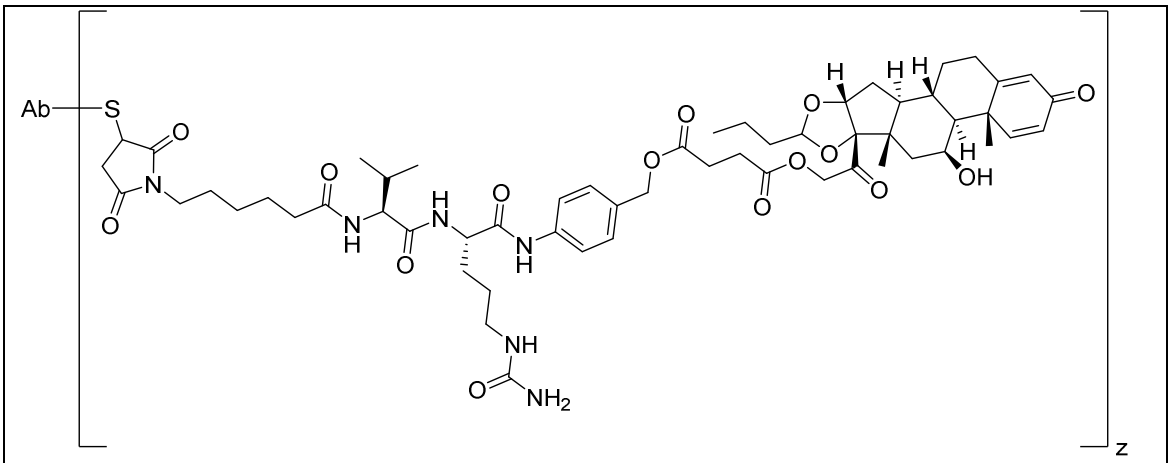




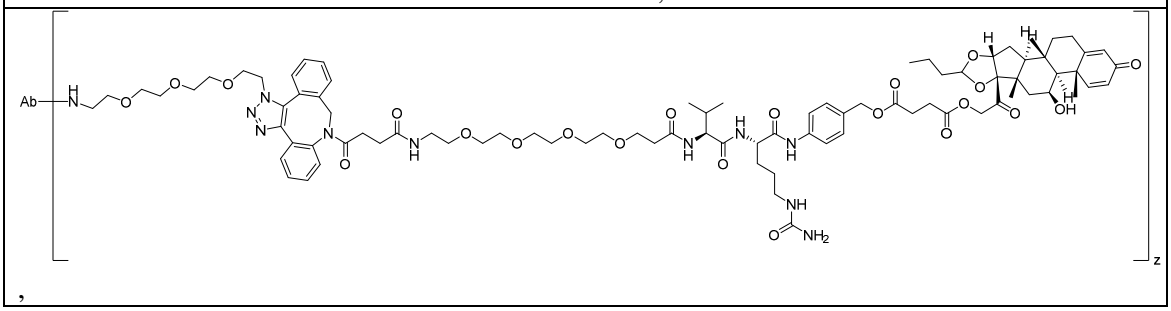


or

74. The compound of claim 1, wherein the compound is



or a stereoisomer or mixture of stereoisomers thereof;



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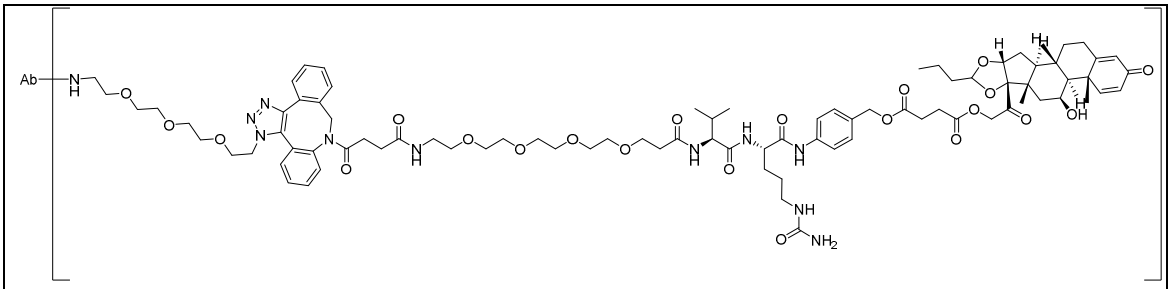
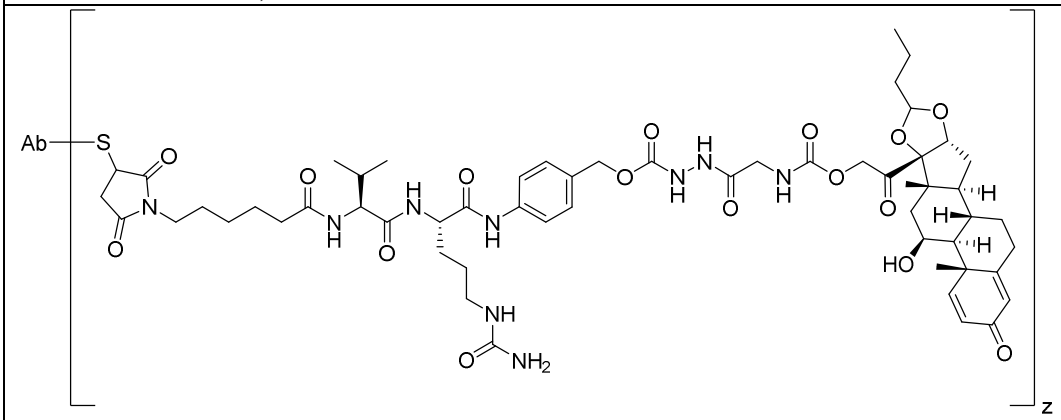
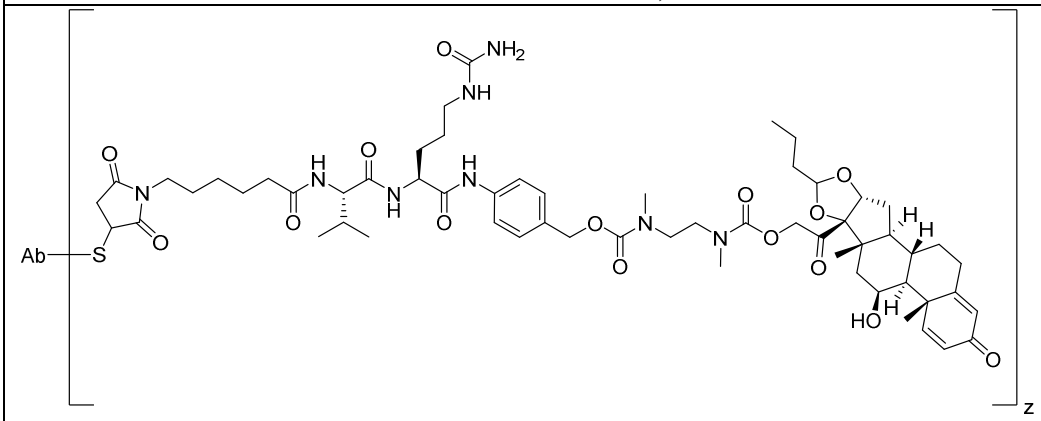


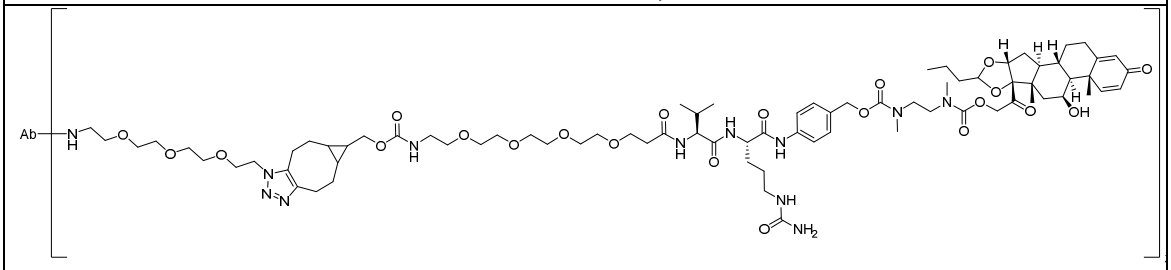
or a mixture thereof;

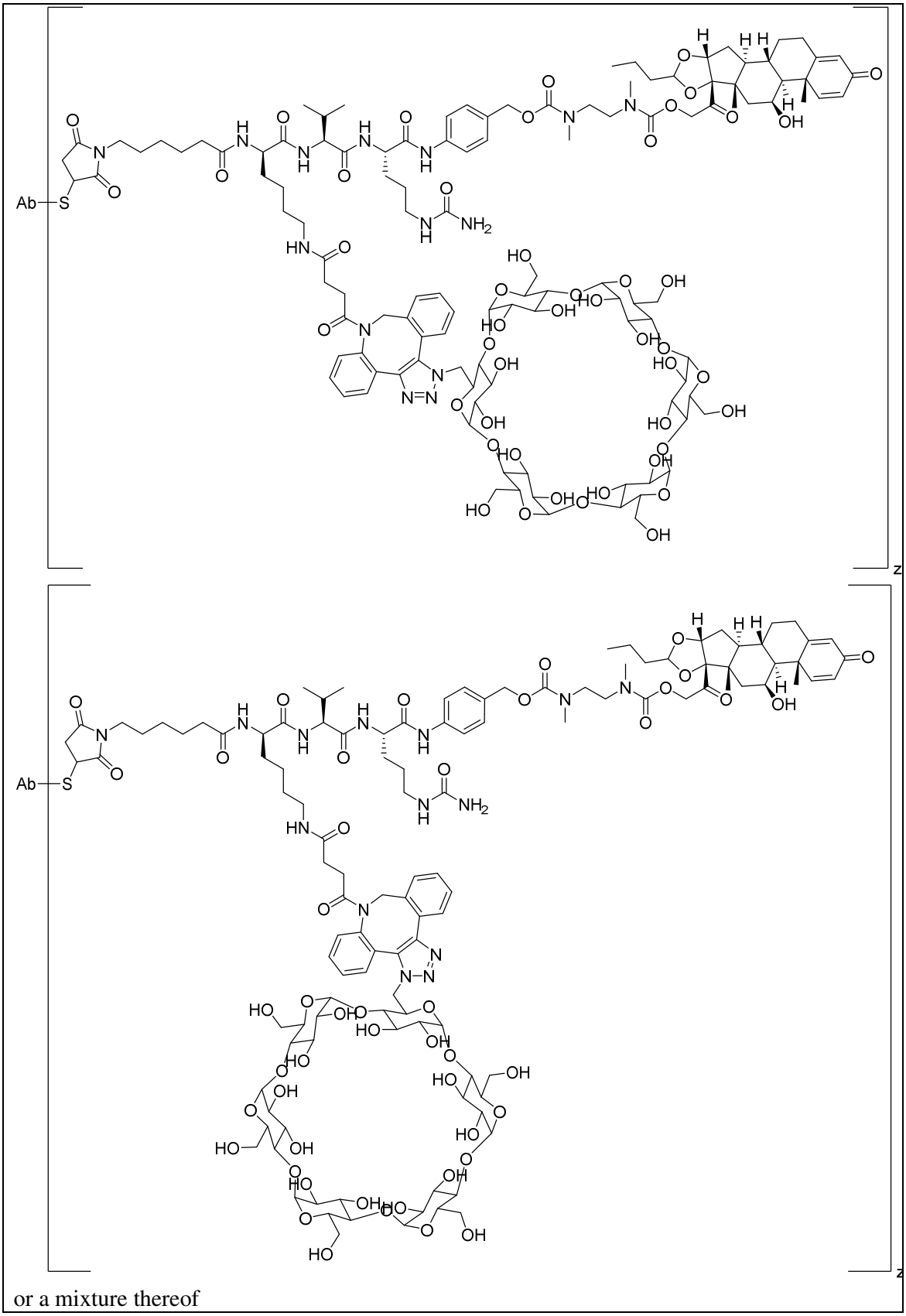


or a stereoisomer or mixture of stereoisomers thereof;

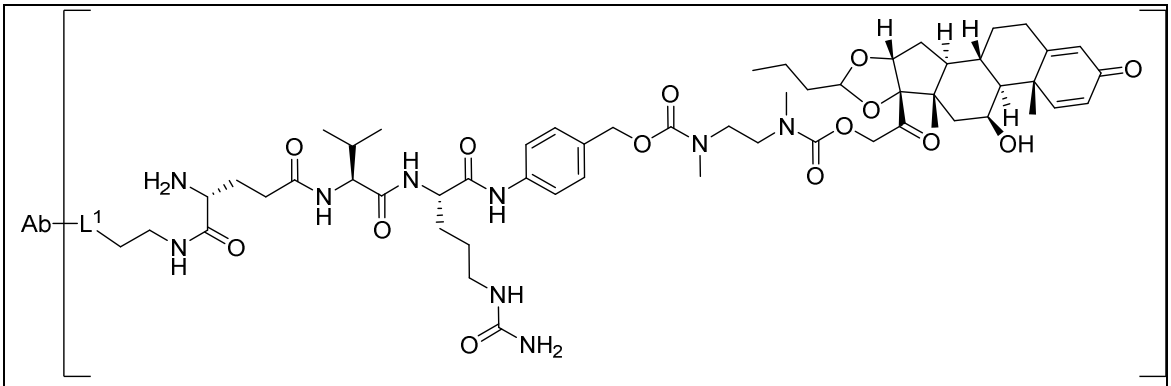


or a stereoisomer or mixture of stereoisomers thereof;

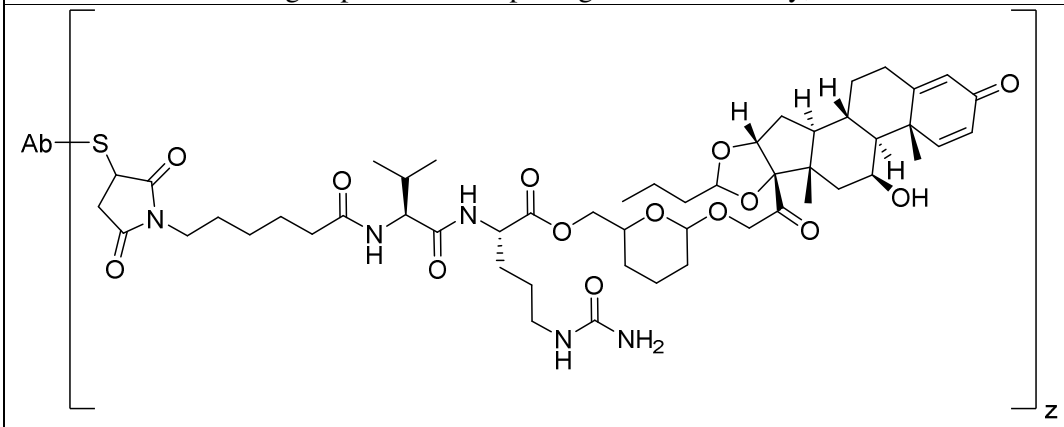




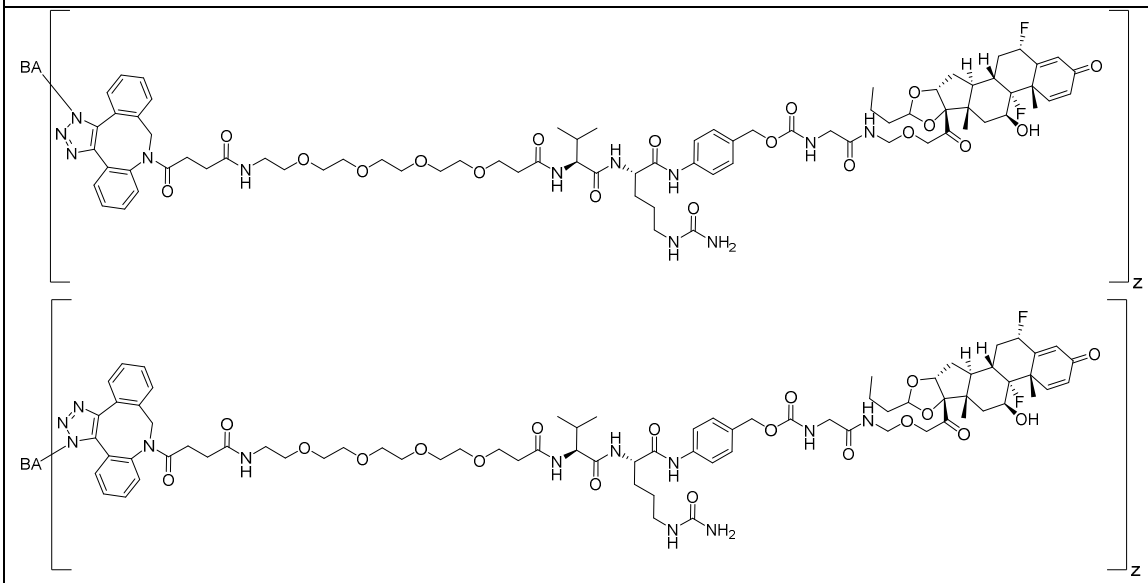
or a mixture thereof



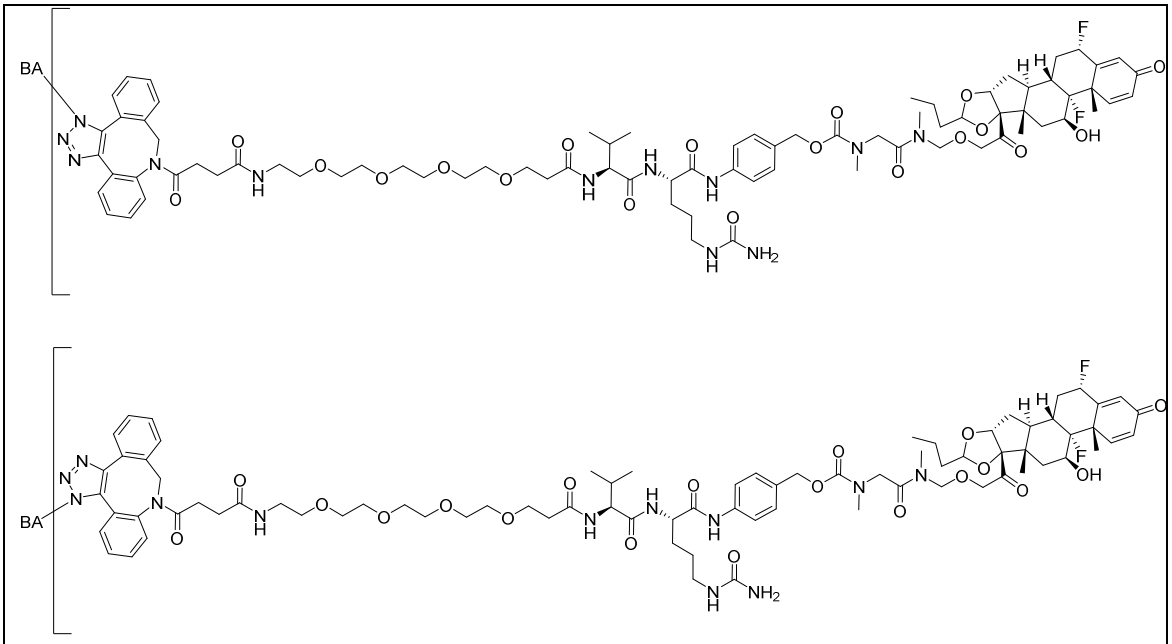
where L^1 is a reactive group residue comprising a triazole moiety;



or a stereoisomer or mixture of stereoisomers thereof

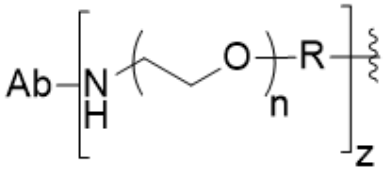


or a mixture thereof



or a mixture thereof

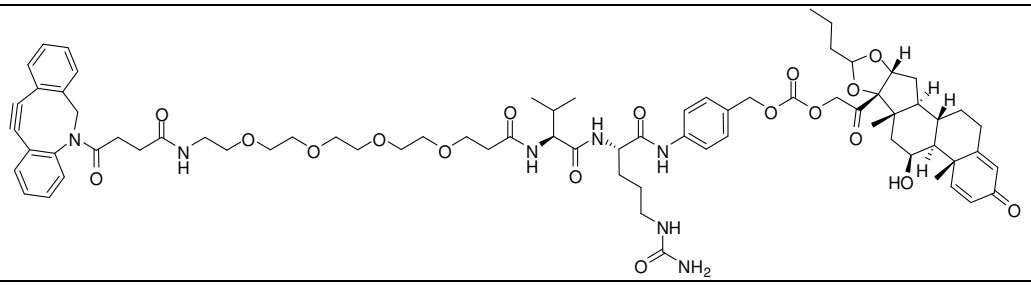
where **BA** comprises an antibody or antigen binding fragment having the following structure

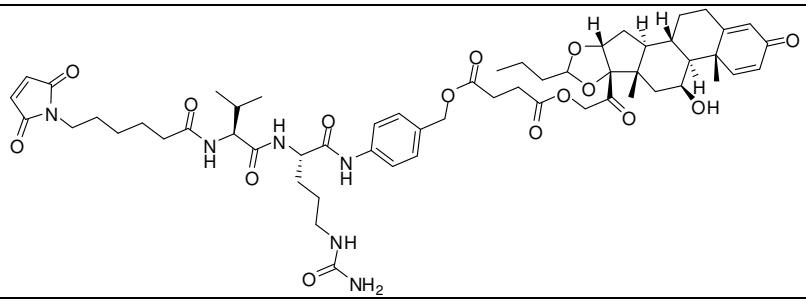
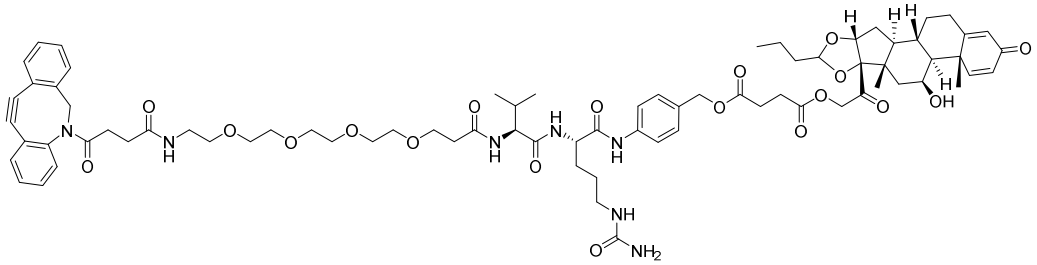
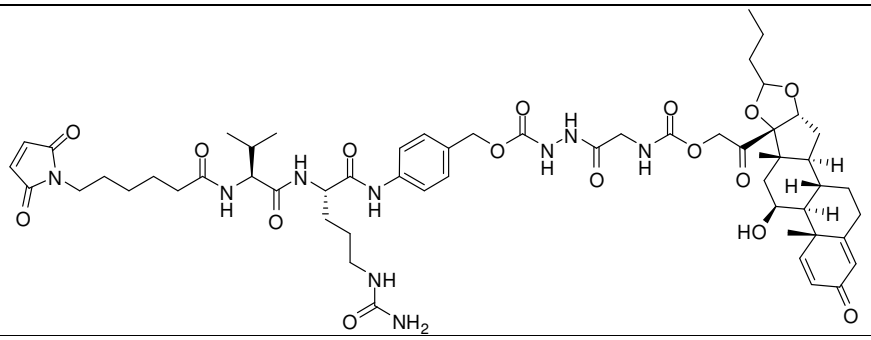
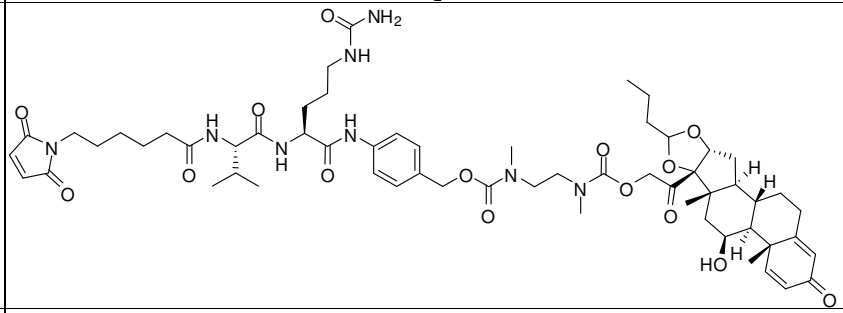
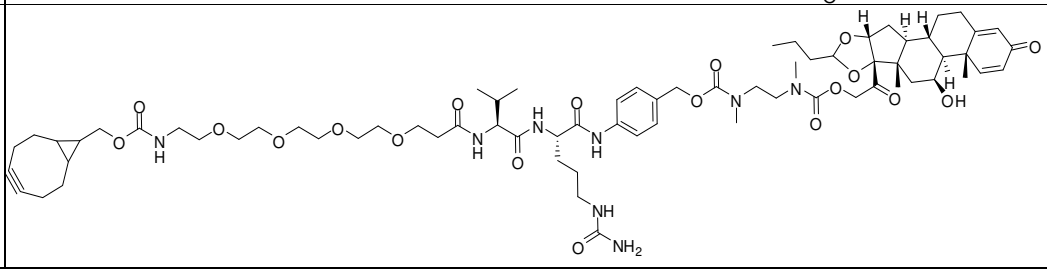


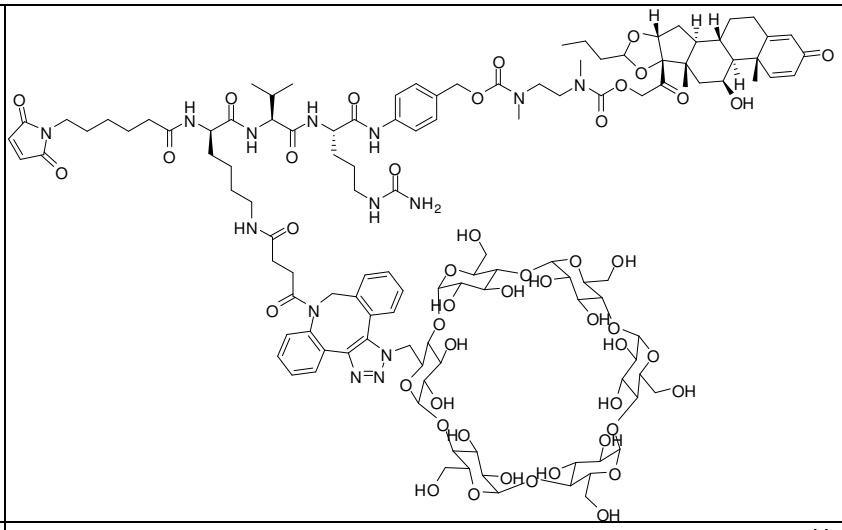
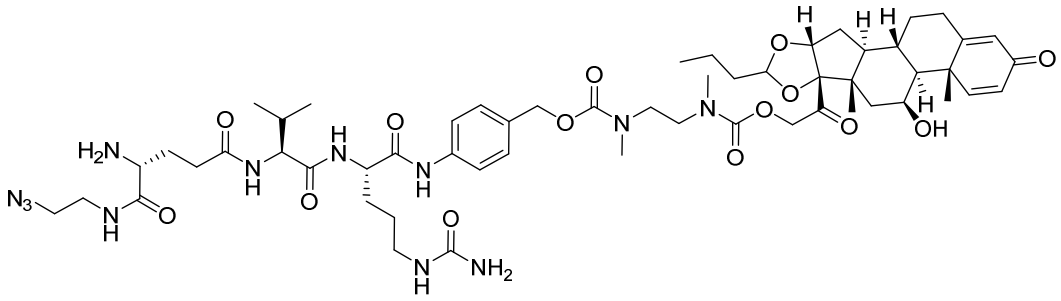
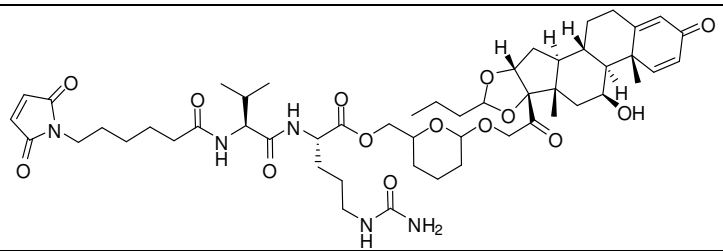
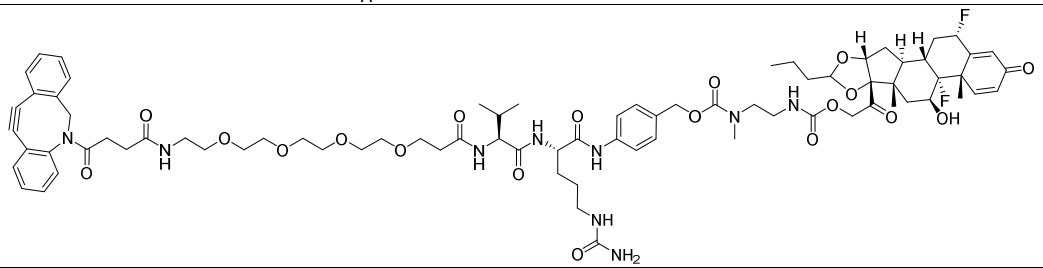
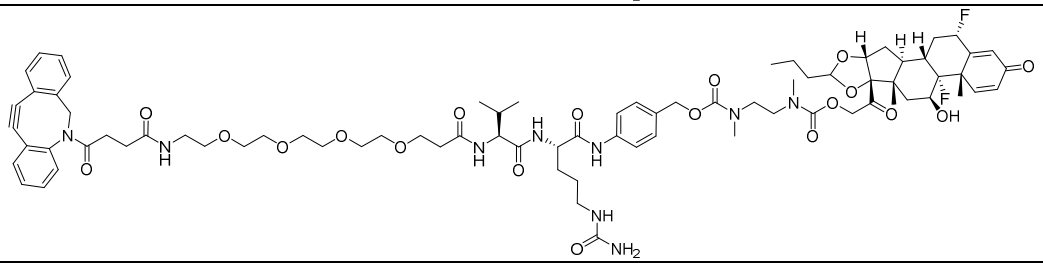
where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; **R** is C_{2-4}-alkylene; and **n** is an integer selected from two to four, inclusive.

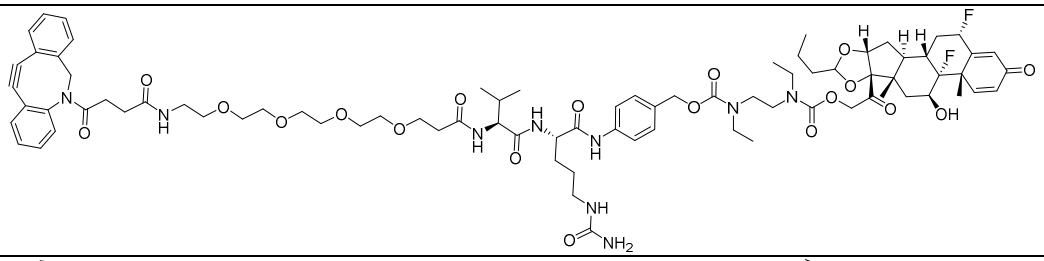
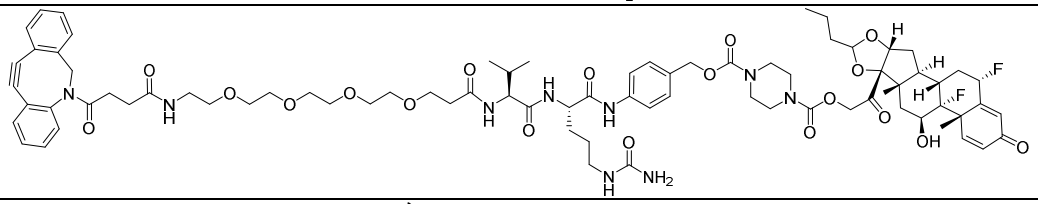
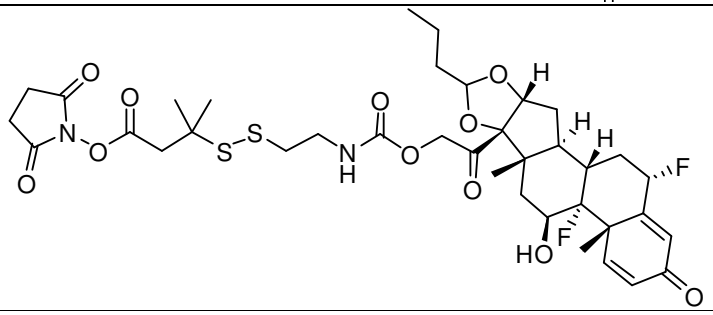
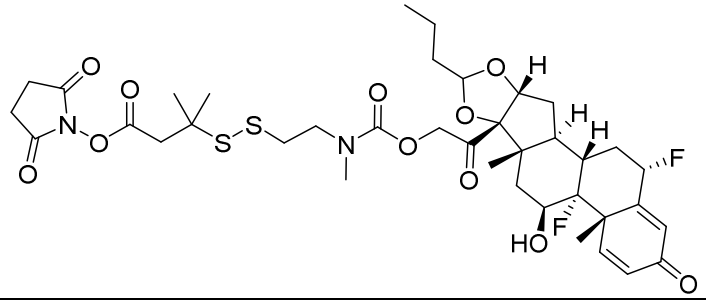
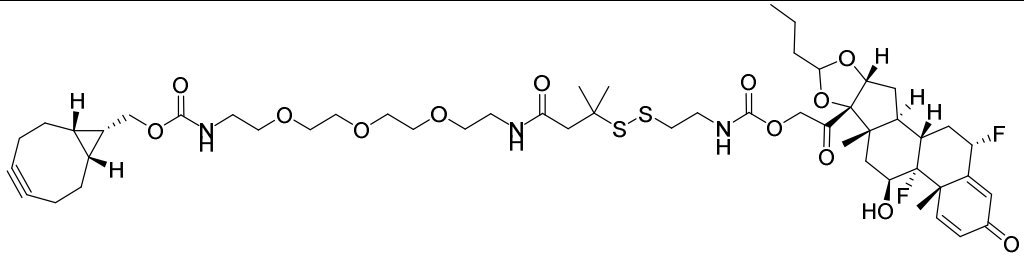
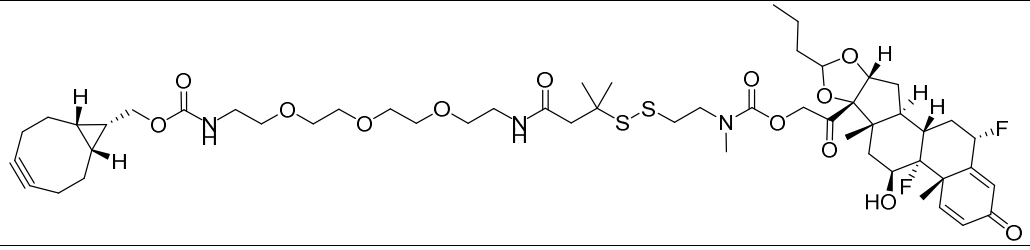
75. The compound of claim 74, wherein **Ab** is an antibody or antigen binding fragment thereof that binds macrophage scavenger receptor 1 (MSR1).

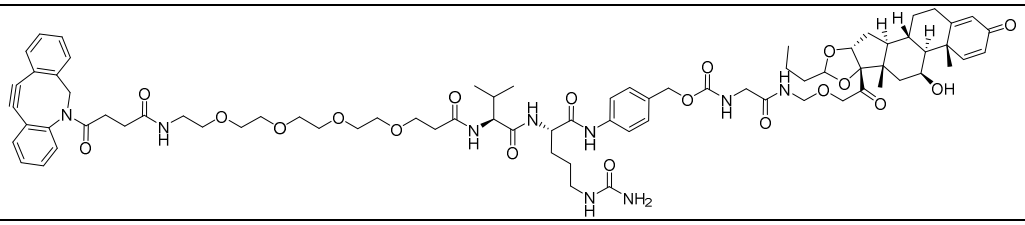
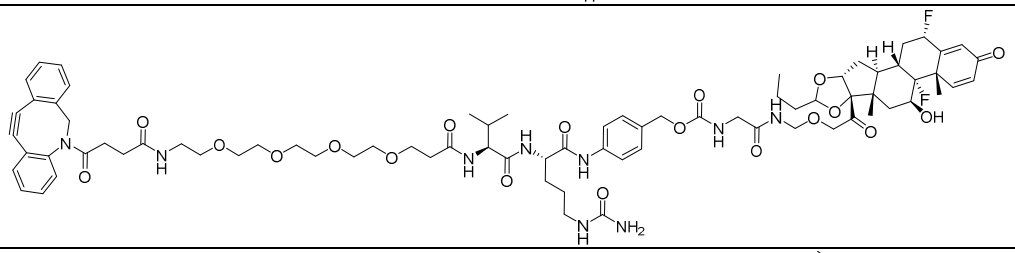
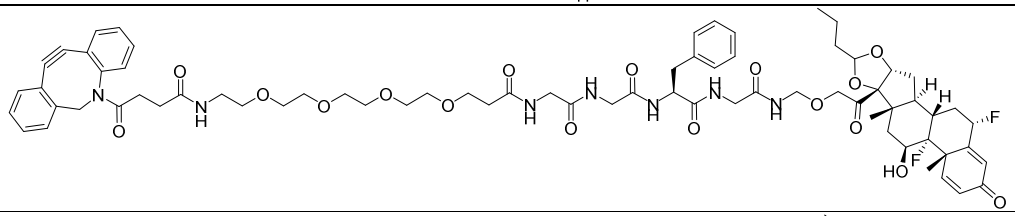
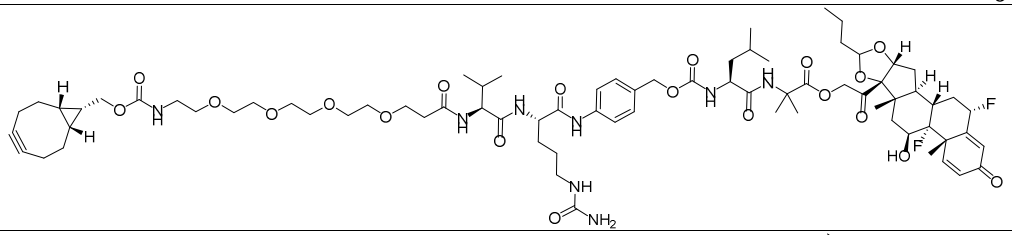
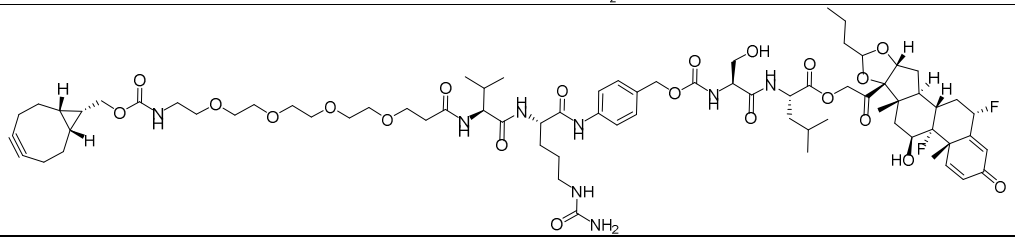
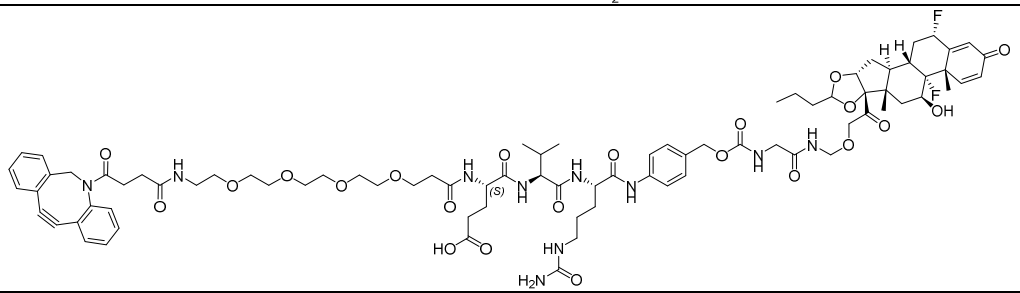
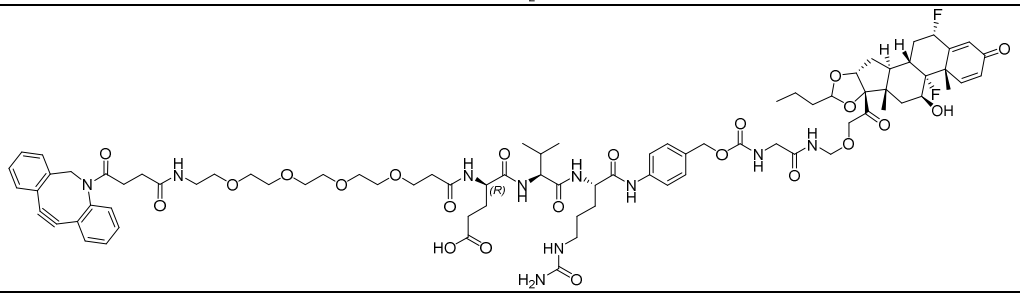
76. A compound selected from the group consisting of

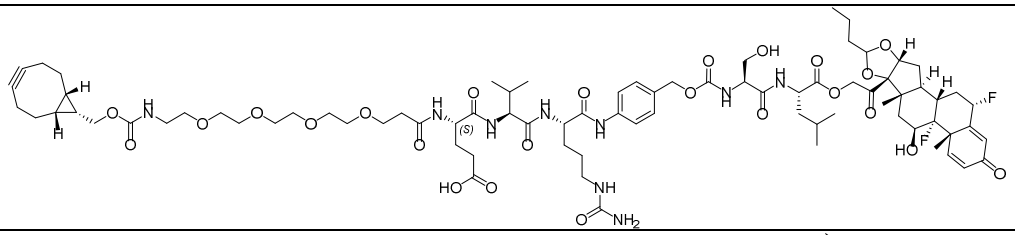
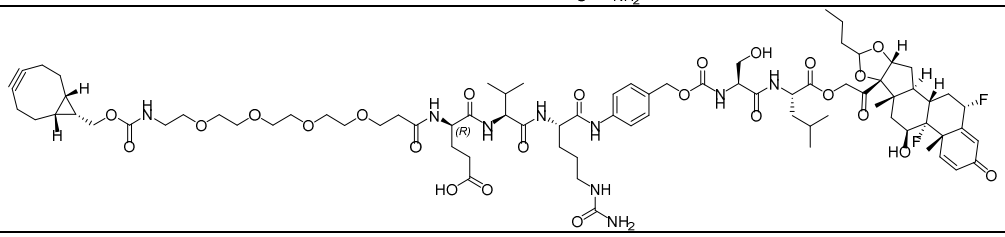
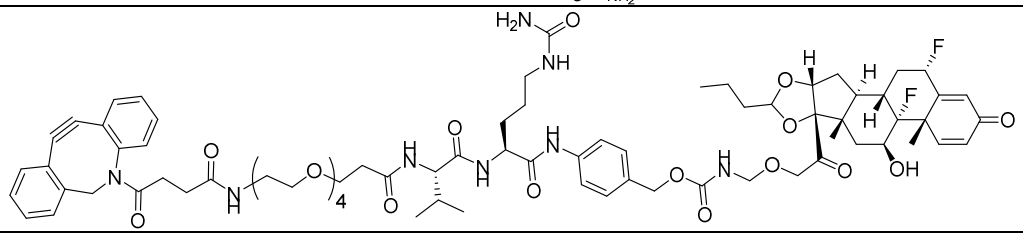
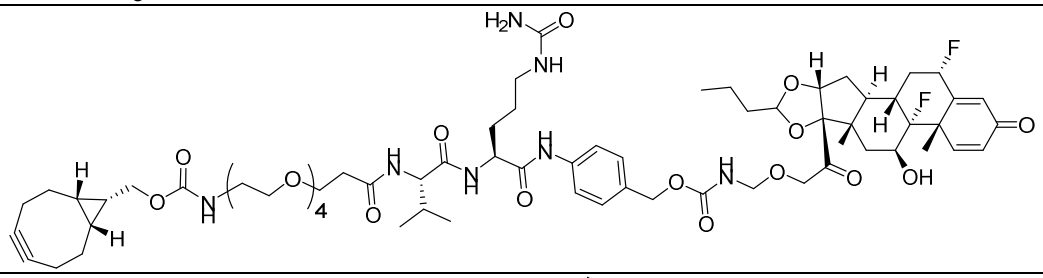
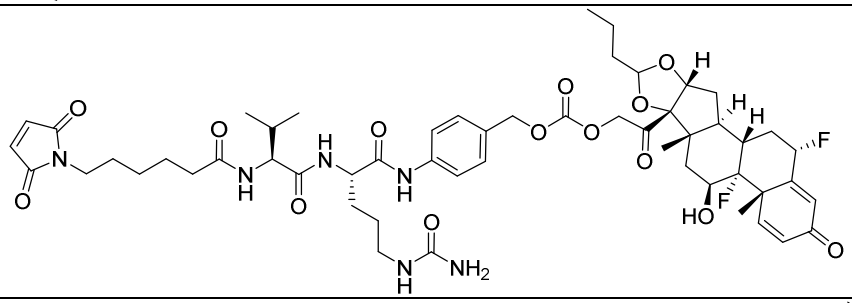
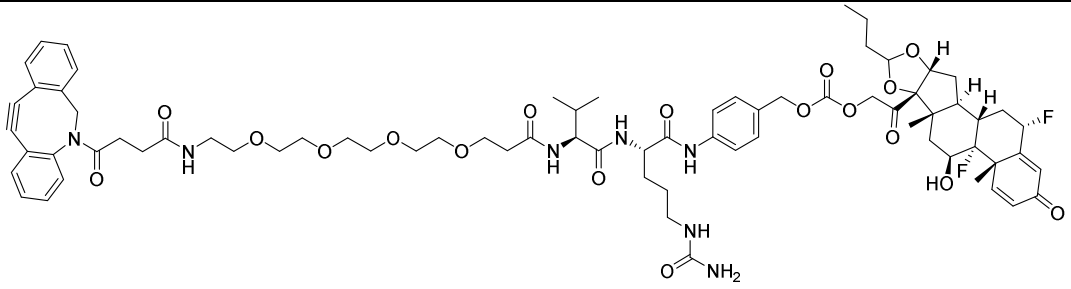
2b	

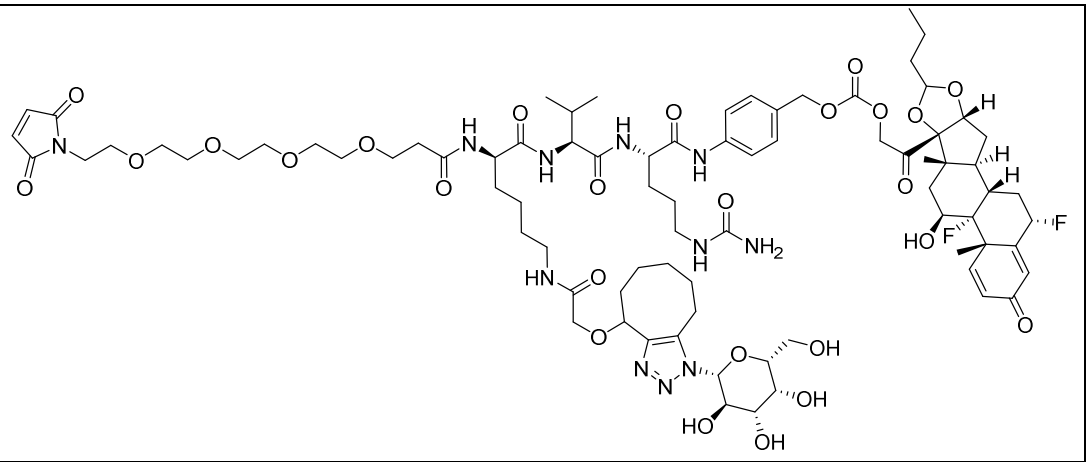
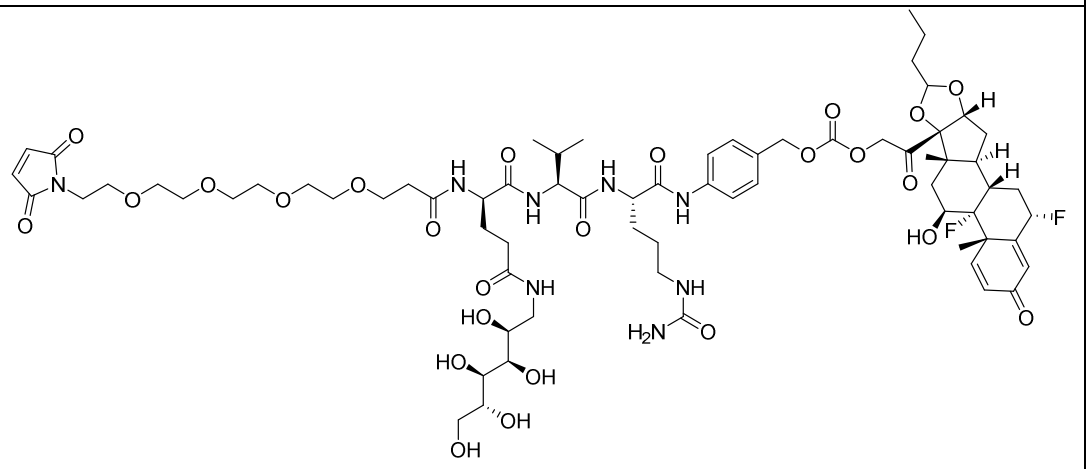
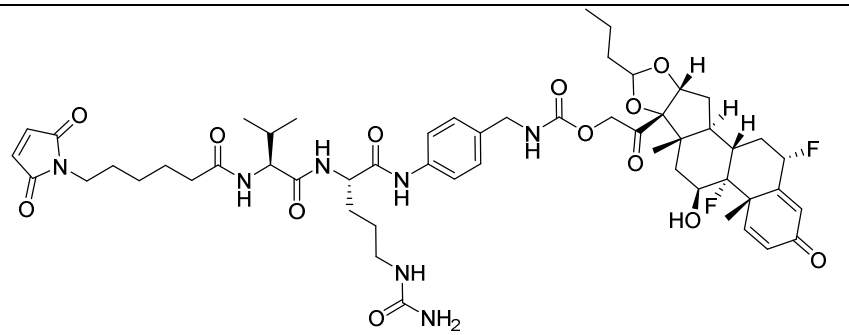
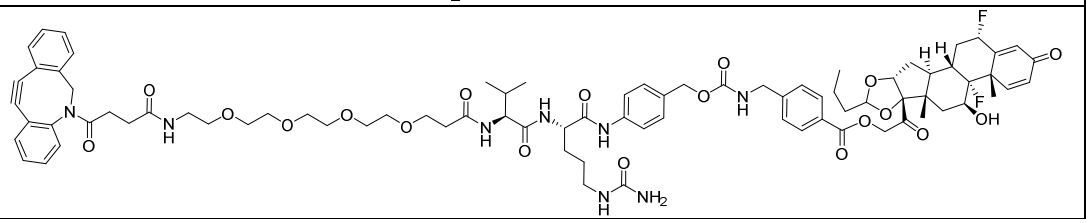
2f	
2g	
2j	
2k	
2l	

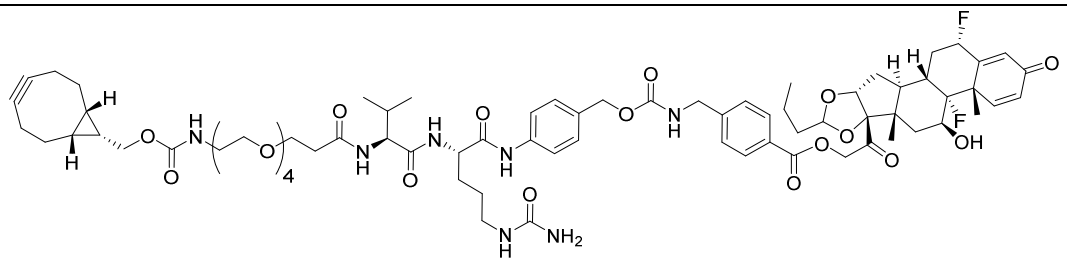
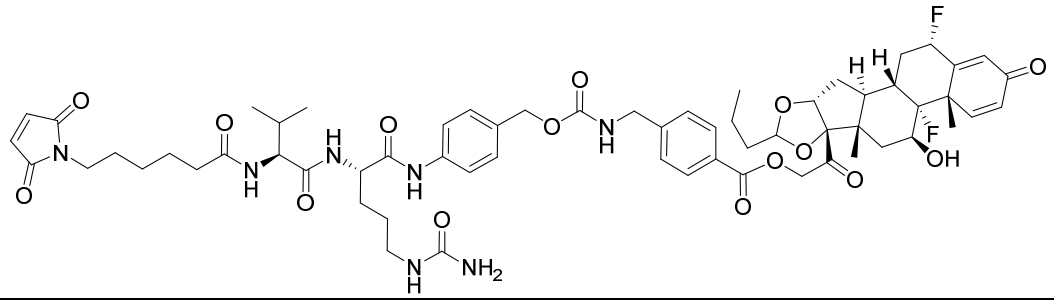
2m	
2n	 or a mixture thereof
2q	
LP1	
LP2	

LP3	
LP4	
LP5	
LP6	
LP7	
LP8	

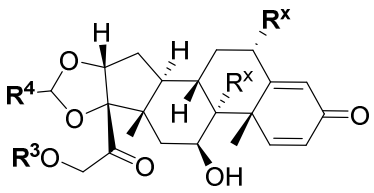
LP9	
LP10	
LP11	
LP12	
LP13	
LP18	
LP19	

LP20	
LP21	
LP22	
LP23	
LP24	
LP25	

LP26	
LP27	
LP28	
LP29	

LP30	 and
LP31	

77. A Compound according to Formula (**I**)



(**I**);

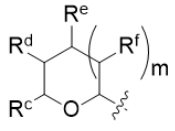
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

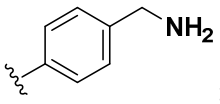
wherein

$\mathbf{R^4}$ is alkyl, aryl, arylalkyl, or an N-containing heterocycloalkyl;

a) both $\mathbf{R^x}$ are hydrogen; and

$\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$; -CH_2NH_2; or

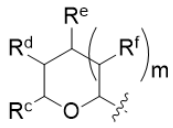
 ;

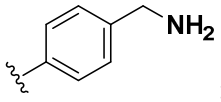
$\mathbf{R^Z}$ is -$C_{4\text{-}10}$-alkylene-C(O)OH; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$ where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy;  ; or N$\mathbf{R^{15}R^{15a}}$;

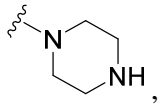
$\mathbf{R^{15}}$ is hydrogen or C_1-C_6alkyl and $\mathbf{R^{15a}}$ is -(C_1-C_{10}-alkylene)-SH or -($C_{1\text{-}6}$-alkylene)-C(O)$NHNH_2$; or

b) both $\mathbf{R^x}$ are fluoro; and

R³ is -C(O)**R^Z**; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}**; -CH_2NH_2; or


;

R^Z is -C₄₋₁₀-alkylene-C(O)OH; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}** where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy;  ; or N**R^{16}R^{16a}**;

R¹⁶ is hydrogen or C₁-C₆alkyl and **R^{16a}** is -(C₁-C₁₀-alkylene)-SH, -(C₁-C₁₀-alkylene)-NH_2, -(C₁-C₁₀-alkylene)-NH(C₁₋₆alkyl),  , or -(C₁₋₆-alkylene)-C(O)$NHNH_2$; and

each **R⁵⁰**, **R^{50a}**, and **R^{50b}** are independently hydrogen or C₁-C₆-alkyl;

one of **R^c**, **R^d**, **R^e**, and **R^f** is -CH_2O**R^g** and the others are independently hydrogen, -OH, hydroxyalkyl,

-C(O)OH, or -CH_2O**R^g**, where each **R^g** is independently -(C₁₋₆-alkylene)-C(O)OH or -(C₁₋₆-alkylene)-C(O)O(alkyl); or one of **R^c**, **R^d**, **R^e**, and **R^f** is hydroxyalkyl and the others are hydrogen; and

m is zero to one.

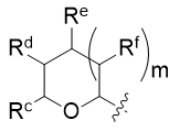
78. The Compound of Claim 77, where **R⁴** is alkyl.

79. The Compound of Claim 77 or 78, where **R⁴** is in the (*R*)-configuration.

80. The Compound of any one of claims 77-79, where

a) both **R^x** are hydrogen; and

R³ is -C(O)**R^Z**; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}**; or

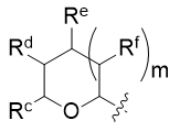

;

R^Z is -C₄₋₁₀-alkylene-C(O)OH; -(C₁-C₁₀-alkylene)-N**R⁵⁰**C(O)-(C₁-C₁₀-alkylene)-N**R^{50a}R^{50b}** where each C₁-C₁₀-alkylene is independently optionally substituted with one or more hydroxy; or N**R^{15}R^{15a}**;

R¹⁵ is hydrogen or C₁-C₆alkyl and **R^{15a}** is -(C₁-C₁₀-alkylene)-SH or -(C₁₋₆-alkylene)-C(O)$NHNH_2$; or

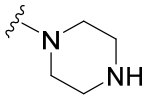
b) both $\mathbf{R^x}$ are fluoro; and

$\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$; or



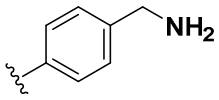
;

$\mathbf{R^Z}$ is -C_{4-10}-alkylene-C(O)OH; -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$ where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy; or N$\mathbf{R^{16}R^{16a}}$;

$\mathbf{R^{16}}$ is hydrogen or C_1-C_6alkyl and $\mathbf{R^{16a}}$ is -(C_1-C_{10}-alkylene)-SH, -(C_1-C_{10}-alkylene)-NH_2, -(C_1-C_{10}-alkylene)-NH(C_{1-6}alkyl), 

, or -(C_{1-6}-alkylene)-C(O)$NHNH_2$.

81. The Compound of any one of Claims 77-79, where $\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$ and R^Z is

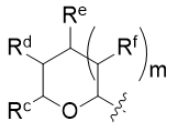


or -CH_2NH_2.

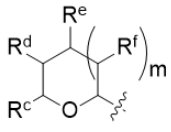
82. The Compound of any one of Claims 77-80, where $\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$.

83. The Compound of Claim 82, wherein $\mathbf{R^Z}$ is -C_{4-10}-alkylene-C(O)OH.

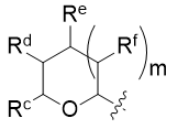
84. The Compound of Claim 82, wherein $\mathbf{R^Z}$ is -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$ where each C_1-C_{10}-alkylene is independently optionally substituted with one or more hydroxy.

85. The Compound of any one of Claims 77-80, where $\mathbf{R^3}$ is 

where **m** is one.

86. The Compound of any one of Claims 77-80, where $\mathbf{R^3}$ is 

, **m** is one, and one of $\mathbf{R^c}$, $\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ is -$CH_2O\mathbf{R^g}$ and the others are independently hydrogen, -OH, or hydroxyalkyl.

87. The Compound of any one of Claims 77-80, where $\mathbf{R^3}$ is  , **m** is one, and one of $\mathbf{R^c}$, $\mathbf{R^d}$, $\mathbf{R^e}$, and $\mathbf{R^f}$ is hydroxyalkyl and the others are hydrogen.

88. The Compound of any one of Claims 77-80, where $\mathbf{R^3}$ is -(C_1-C_{10}-alkylene)-N$\mathbf{R^{50}}$C(O)-(C_1-C_{10}-alkylene)-N$\mathbf{R^{50a}R^{50b}}$.

89. The compound of any one of Claims 77-88, where both $\mathbf{R^x}$ are hydrogen.

90. The compound of any one of Claims 77-88, where both $\mathbf{R^x}$ are fluoro.

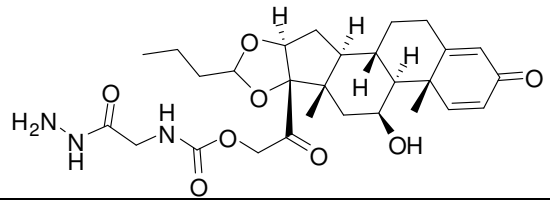
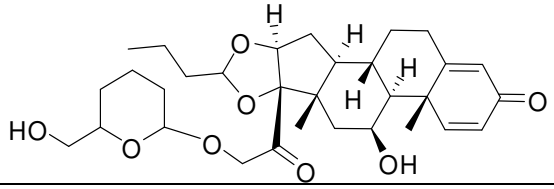
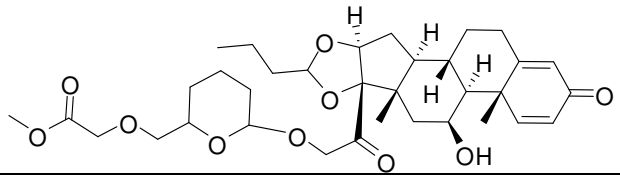
91. The Compound of any one of Claims 77-80, wherein both $\mathbf{R^x}$ are hydrogen, $\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$ and $\mathbf{R^Z}$ is N$\mathbf{R^{15}R^{15a}}$.

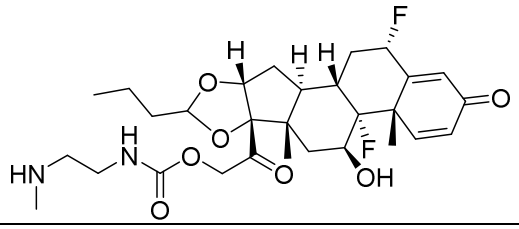
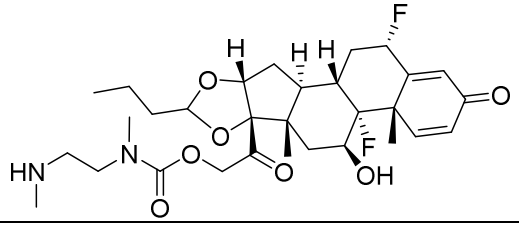
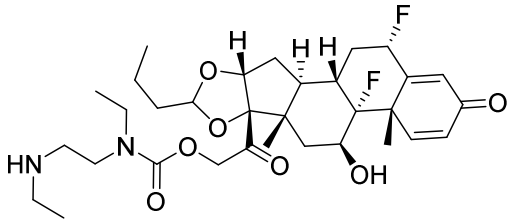
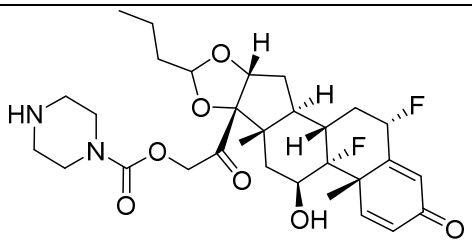
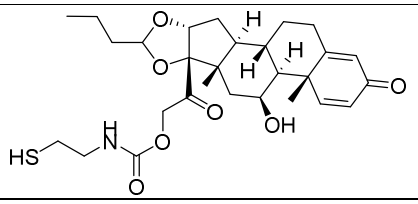
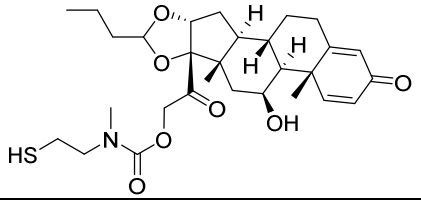
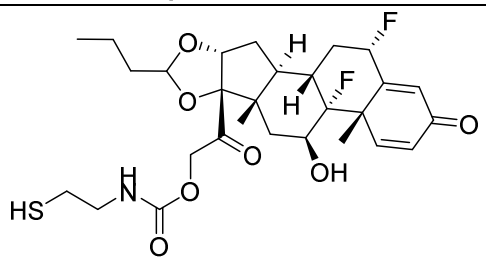
92. The Compound of Claim 91, where $\mathbf{R^{15}}$ is hydrogen.

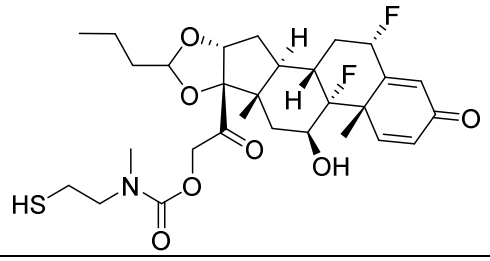
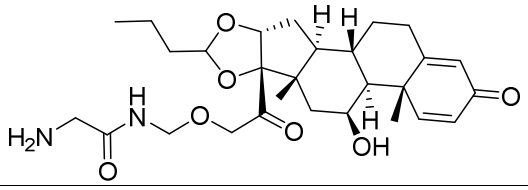
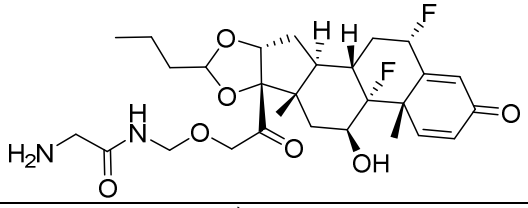
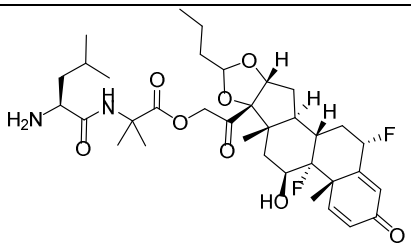
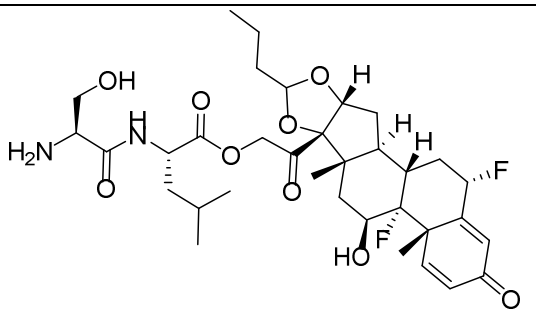
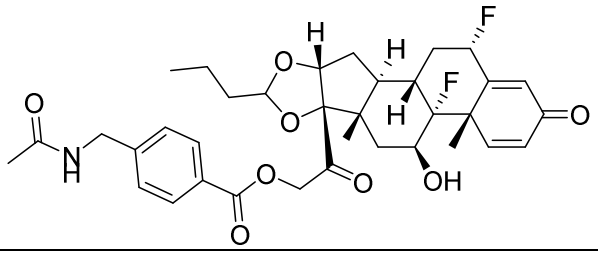
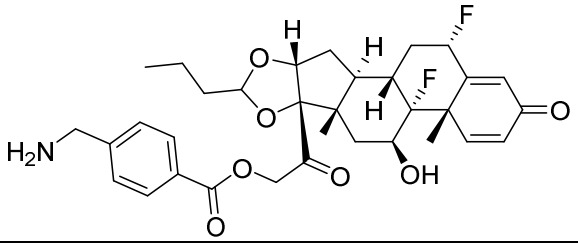
93. The Compound of any one of Claims 77-80, where both $\mathbf{R^x}$ are fluoro, $\mathbf{R^3}$ is -C(O)$\mathbf{R^Z}$ and $\mathbf{R^Z}$ is N$\mathbf{R^{16}R^{16a}}$.

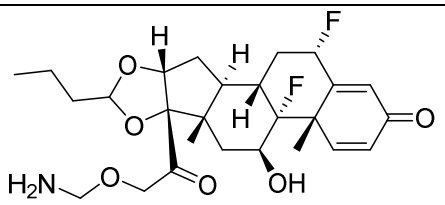
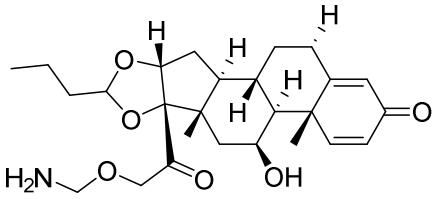
94. The Compound of Claim 93, where $\mathbf{R^{16}}$ is hydrogen.

95. A compound selected from the group consisting of

1e	
1g	
1h	

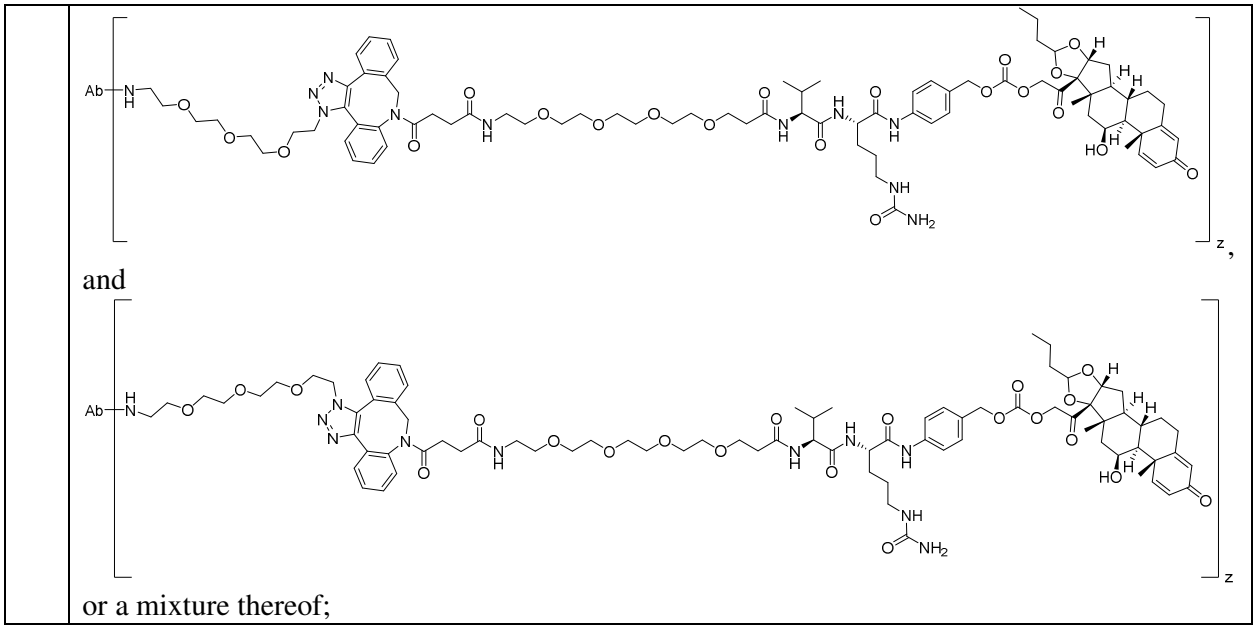
101a	
101b	
101c	
101d	
102c	
102d	
102e	

102f	
103a	
103b	
104a	
104b	
105a	
105b	

106a	 and
107a	 ; or

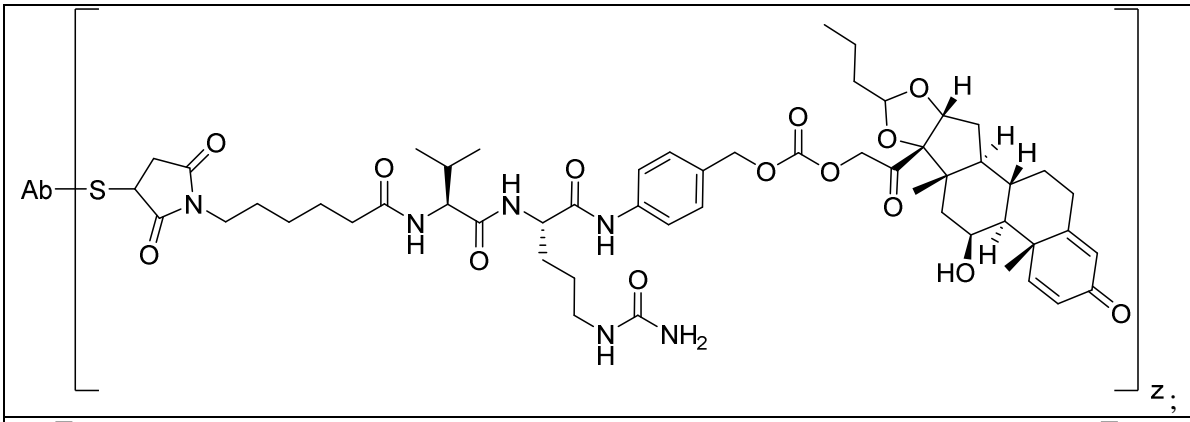
a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

96. A Compound selected from the group consisting of



where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

97. A Compound according to one of the following formulae



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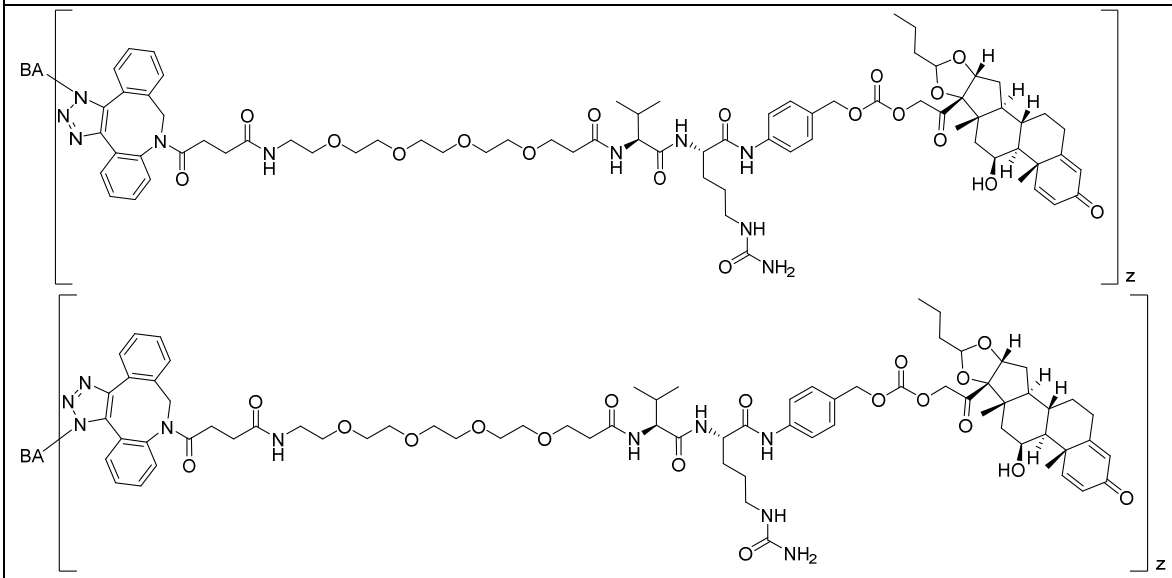
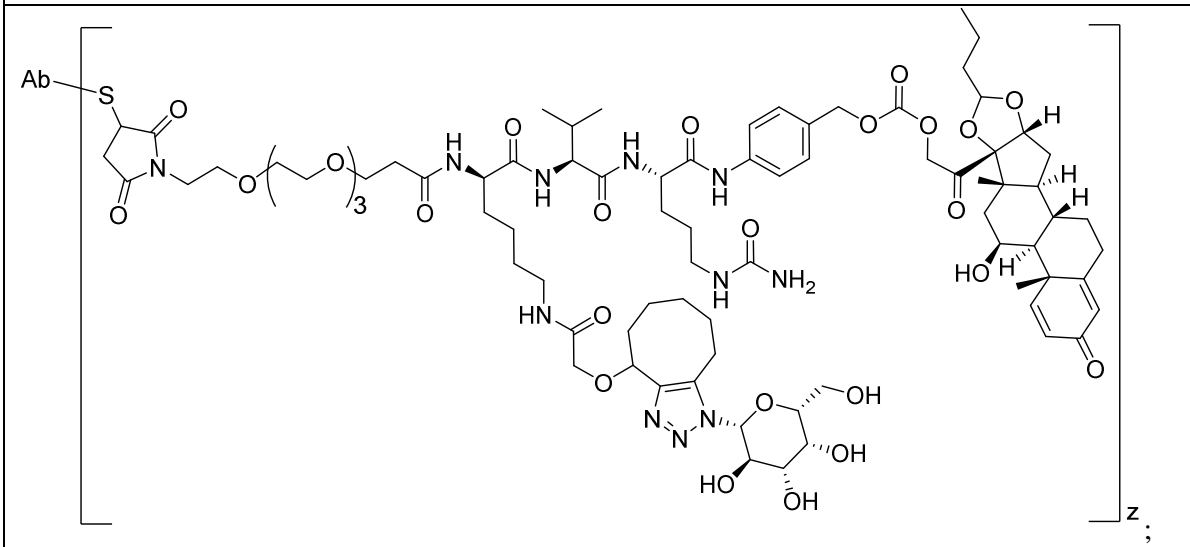


or a mixture thereof;



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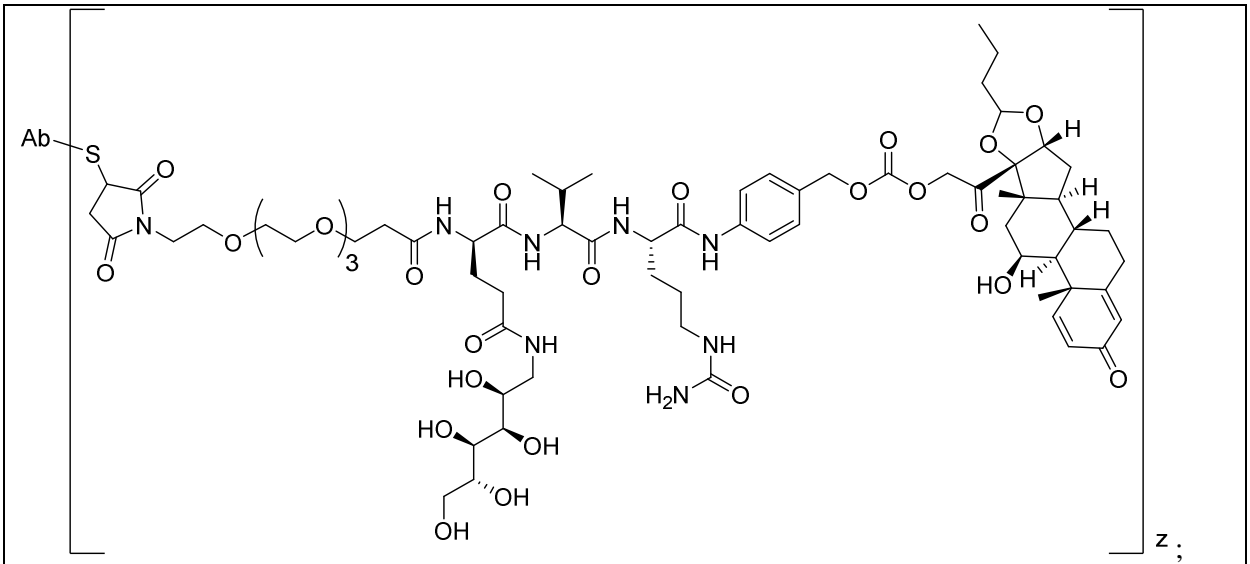
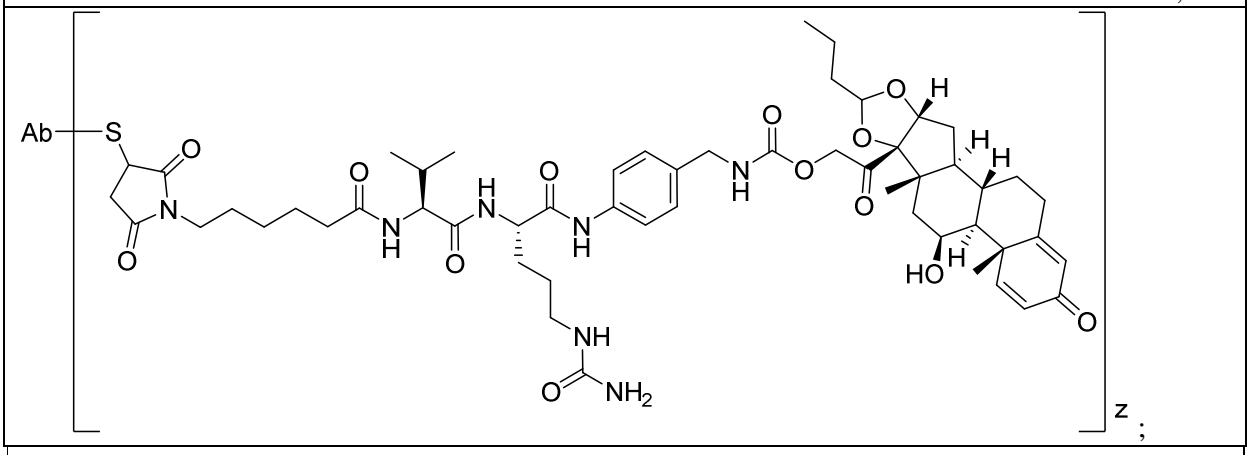
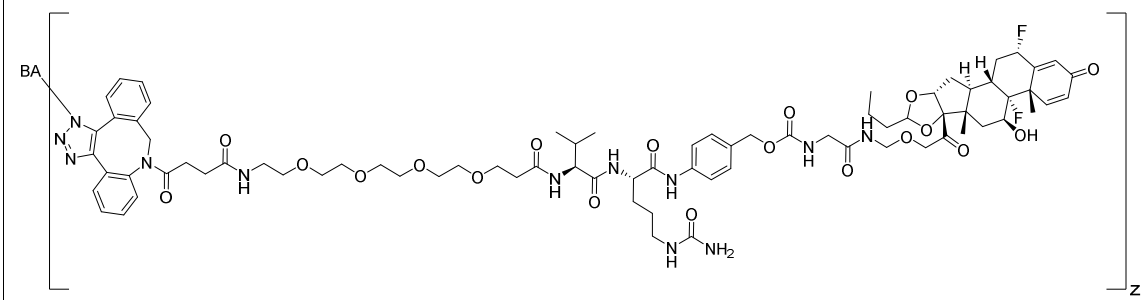
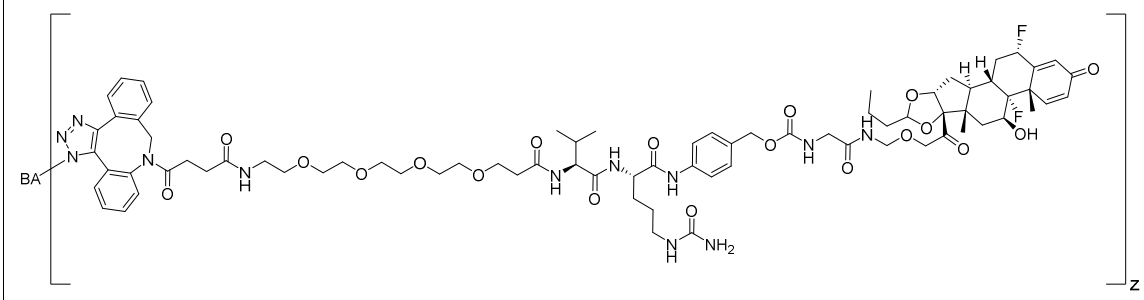
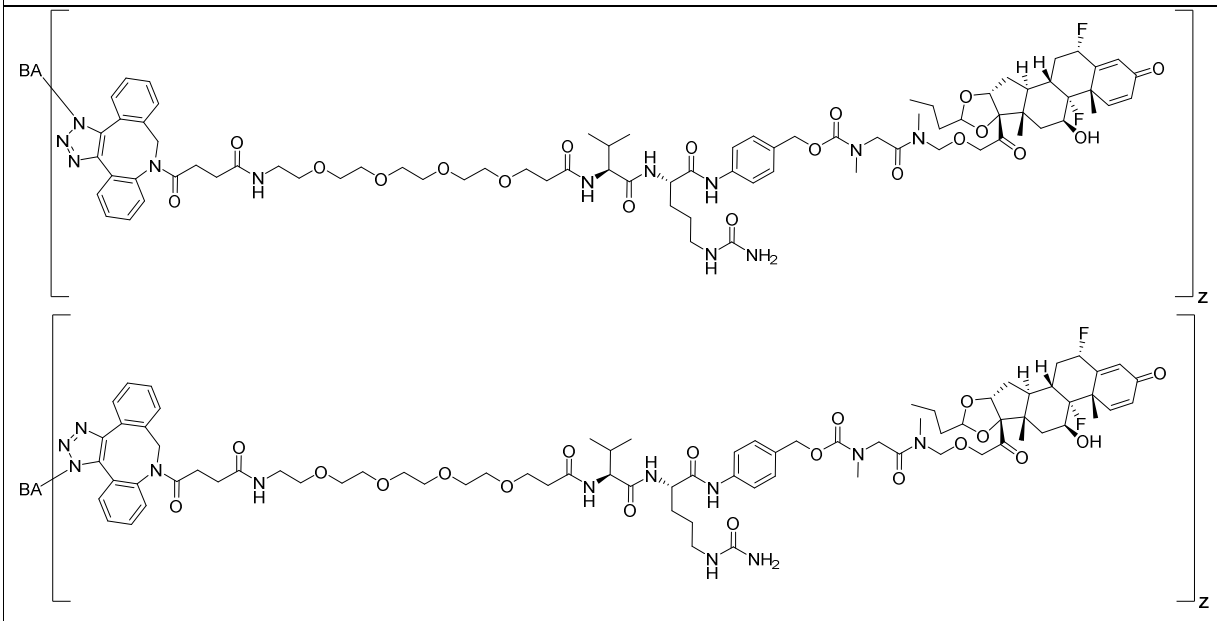




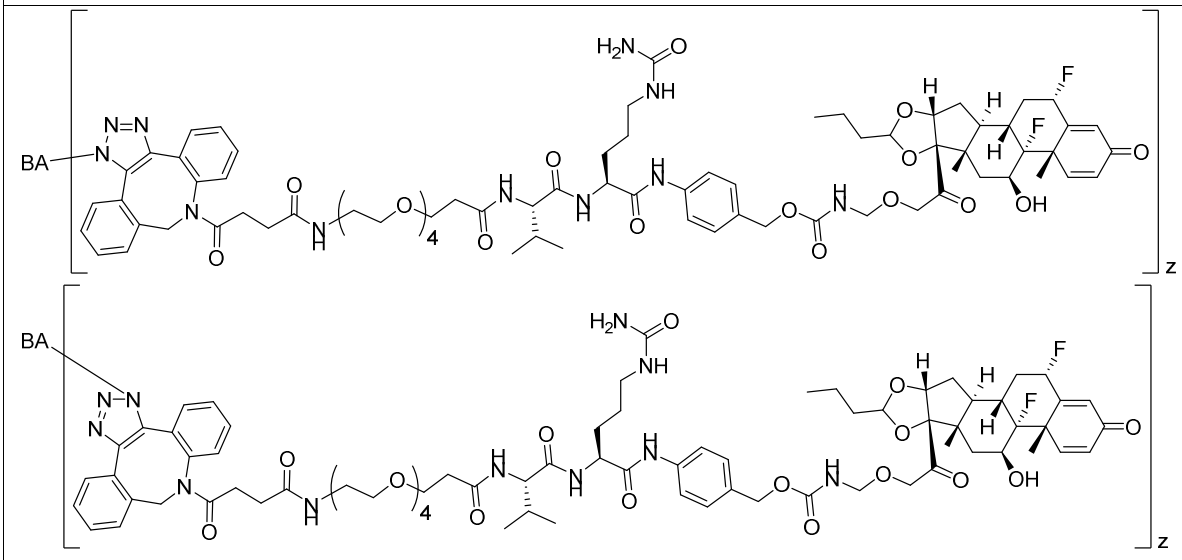




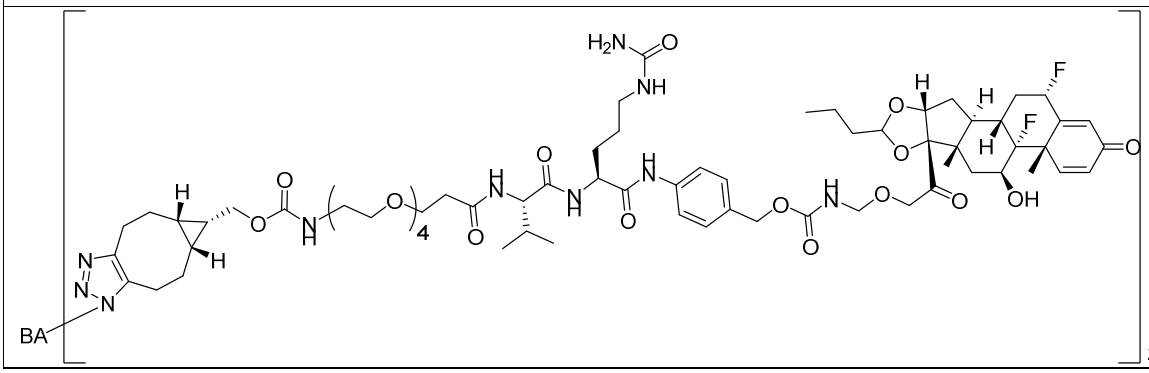
or a mixture thereof;

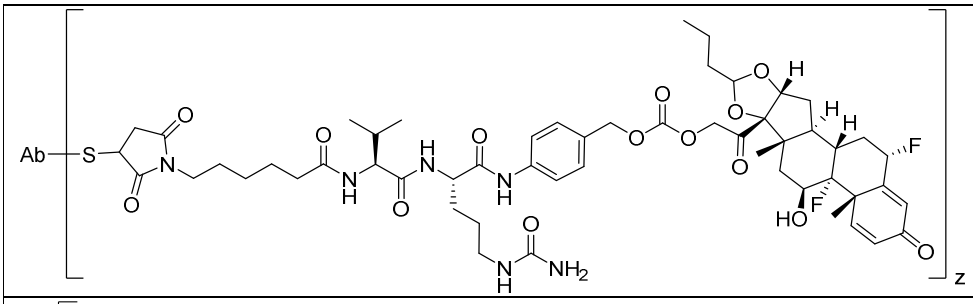


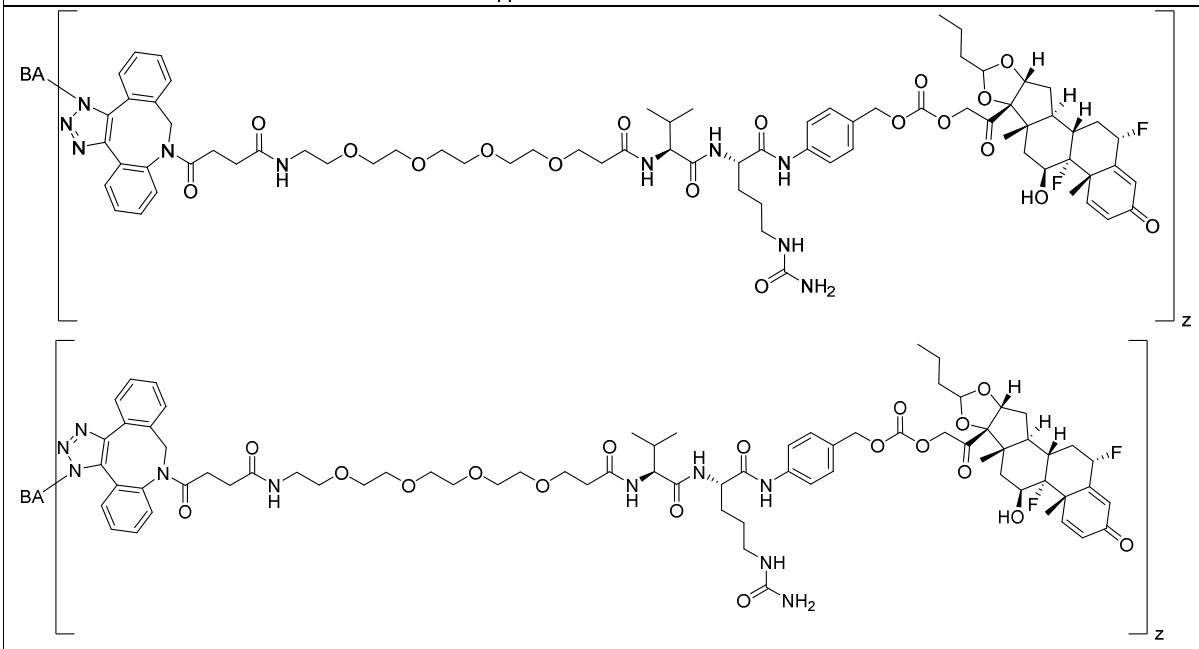
or a mixture thereof



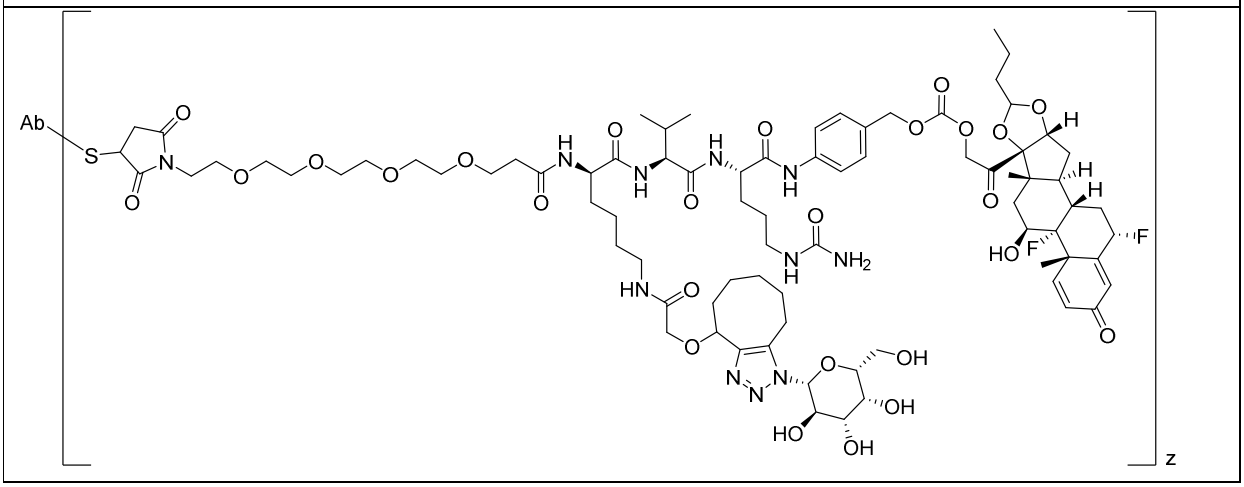
or a mixture thereof

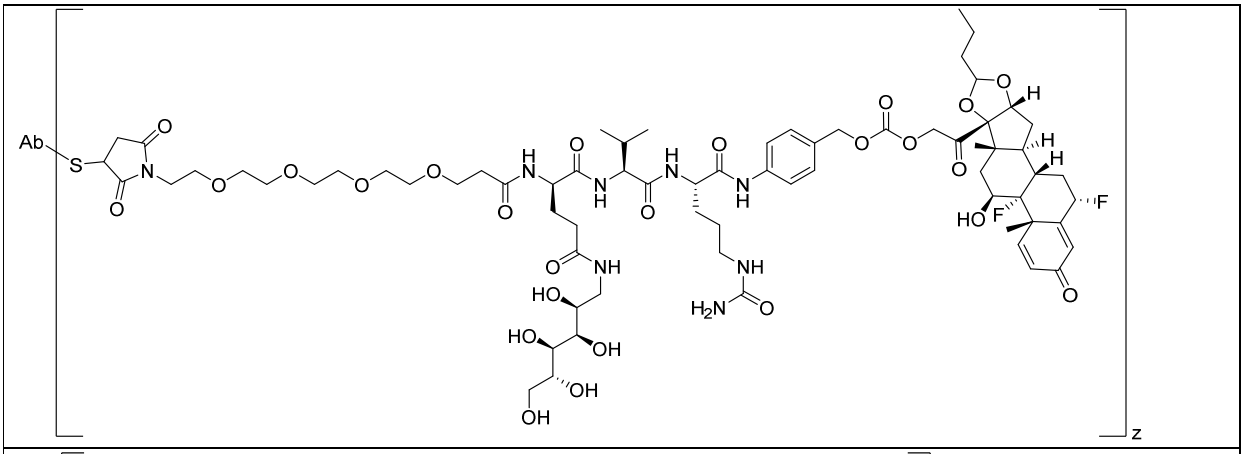


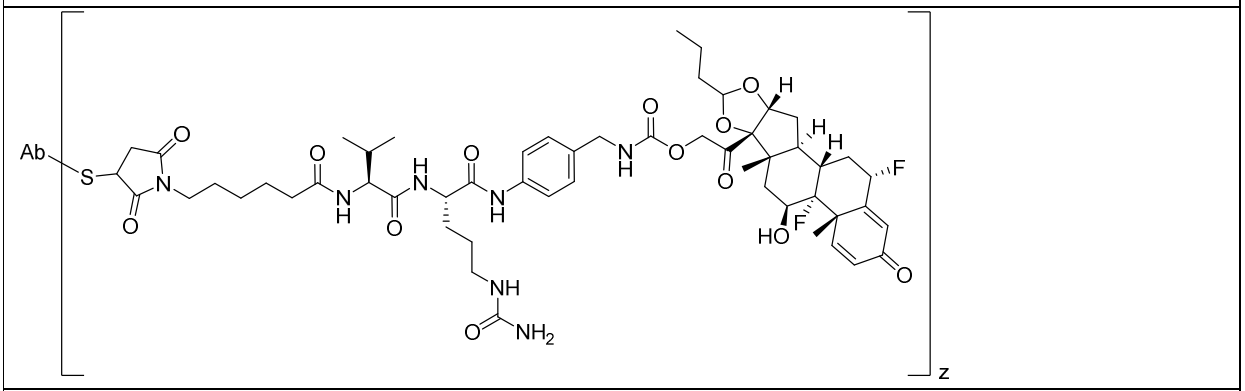


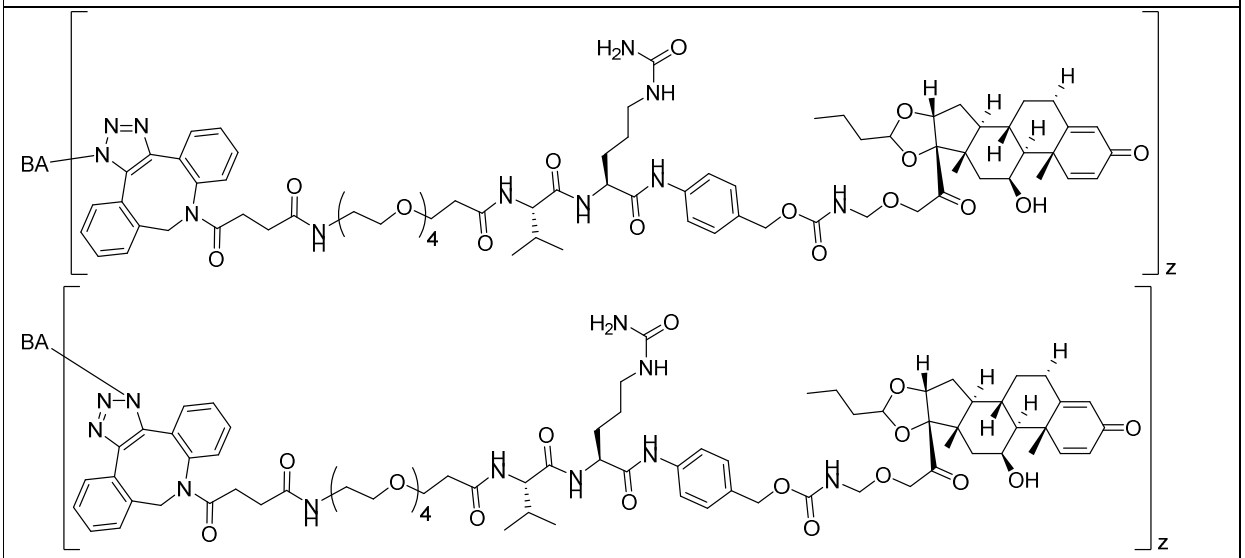


or a mixture thereof

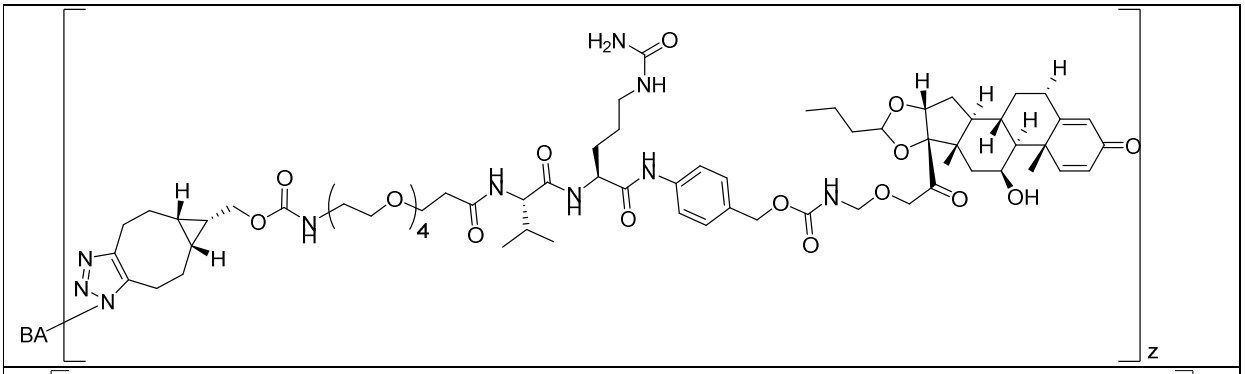


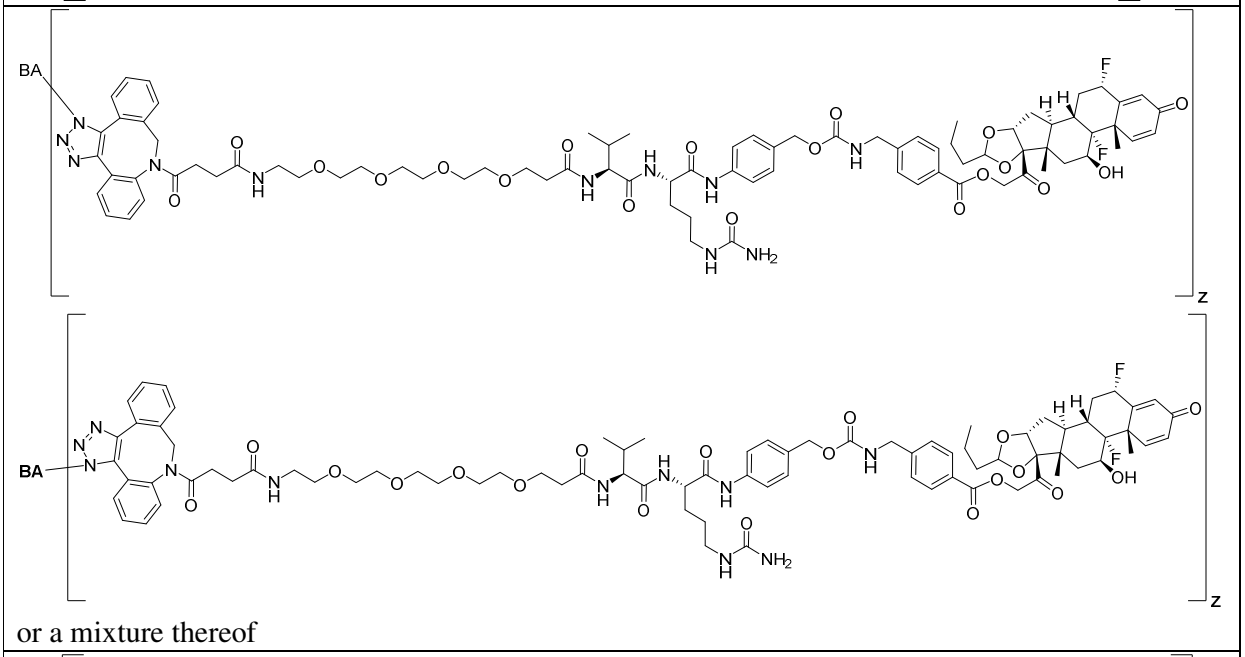




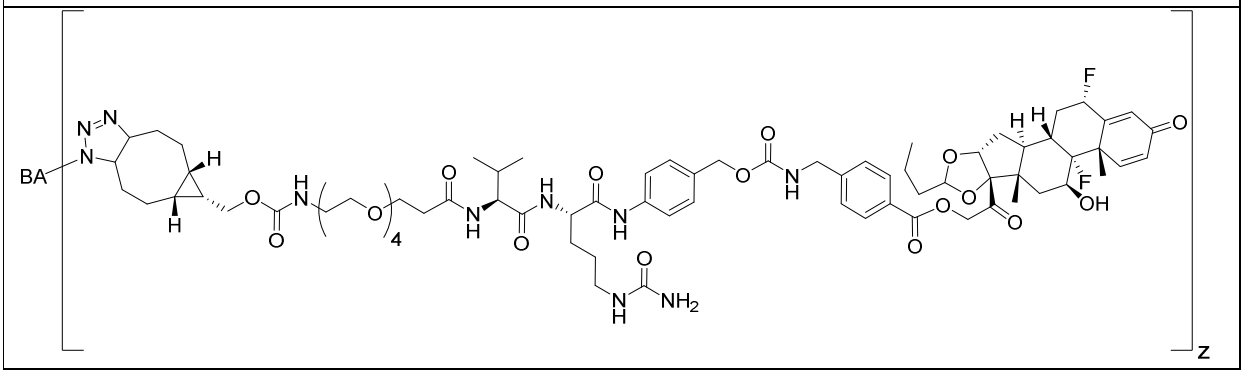


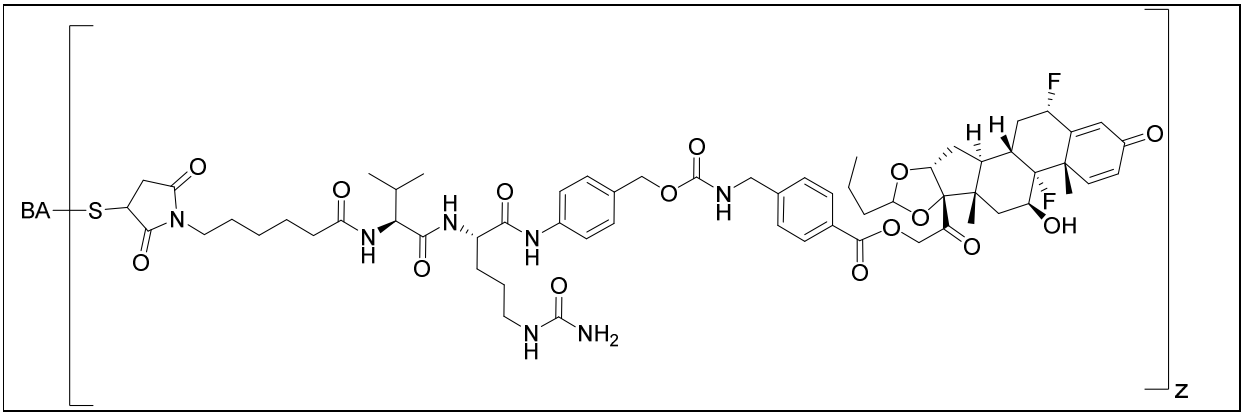
or a mixture thereof



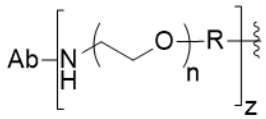


or a mixture thereof





where **BA** comprises an antibody or antigen binding fragment having the following structure

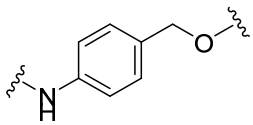
 where **Ab** is a monoclonal antibody, polyclonal antibody, antibody fragment, or bispecific antibody; **R** is C_{2-4}-alkylene; and **n** is an integer selected from two to four, inclusive.

98. The compound of claim 96 or 97, wherein **Ab** or **BA** is an antibody or antigen binding fragment that binds macrophage receptor 1 (MSR1).

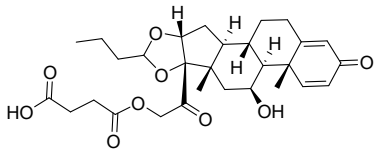
99. Use of a compound of Formula (III) of any one of claims 1, 63, or 68-75, or the compound of any one of claims 96-98 in the manufacture of a medicament for the treatment of a disease, disorder, or condition associated with glucocorticoid receptor signaling.

100. The use of claim 99, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

101. The use of claim 99 or 100, wherein side effects associated with administration of an unconjugated steroid payload of said compound are reduced.

102. The Compound of claim 1, wherein for the Compound of Formula (**III**), **L** is -$\mathbf{L^1}$-$\mathbf{L^2}$-$\mathbf{L^3}$)$_{0-1}$-; **SP** is -C(O)-C_1-C_{10}-alkylene-C(O)-; and $\mathbf{L^3}$ is  where the -NH- group is attached to $\mathbf{L^2}$.

103. A Compound selected from the group consisting of



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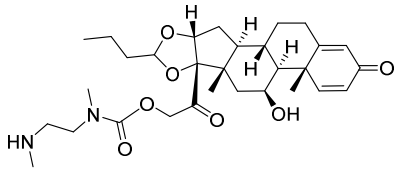
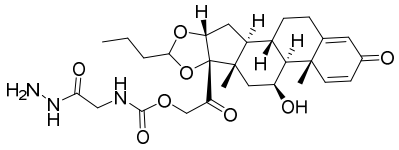


1d



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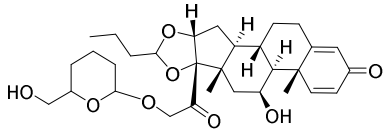
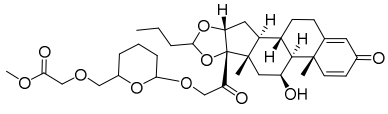


1g



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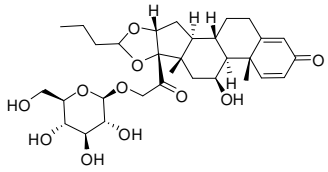

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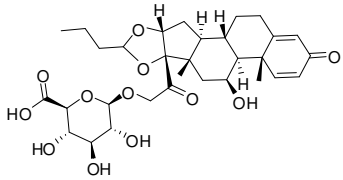
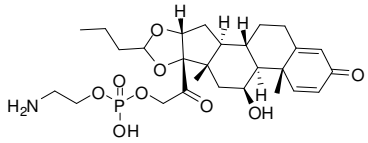


1j



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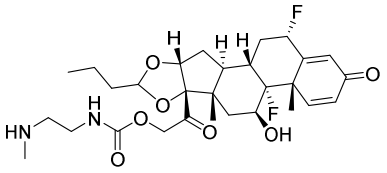
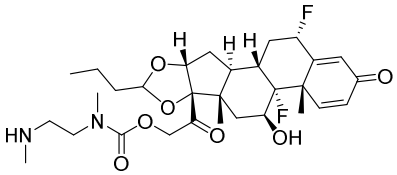


101a



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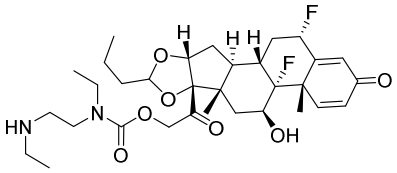

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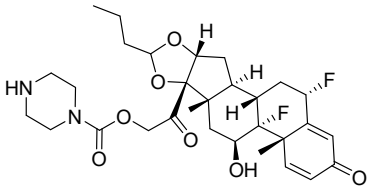

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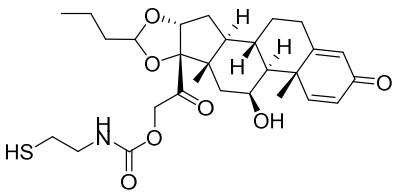

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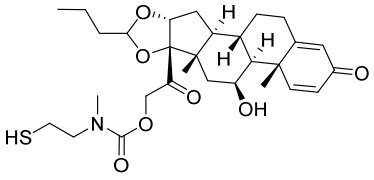

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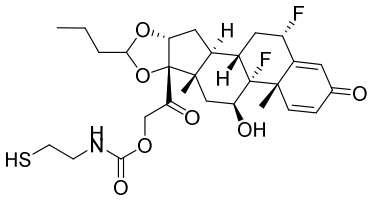

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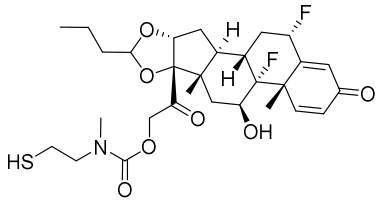

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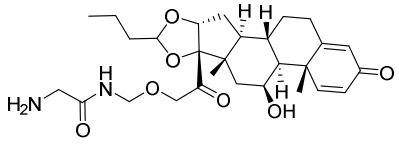
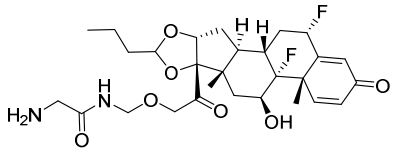
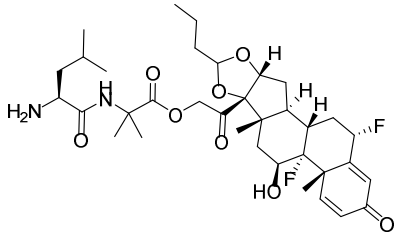


103a



103b



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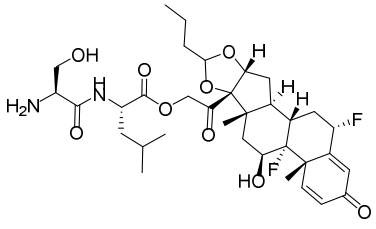
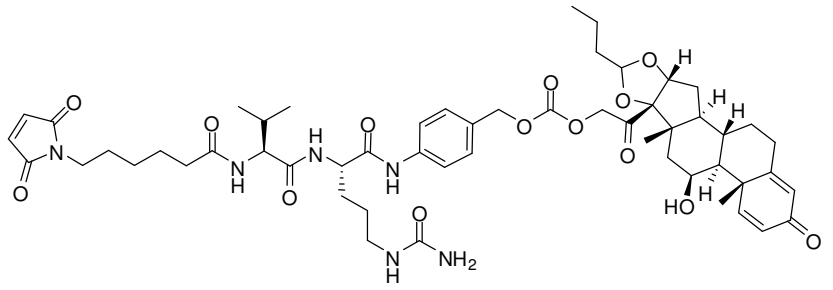


104b

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

104. A Compound selected from the group consisting of



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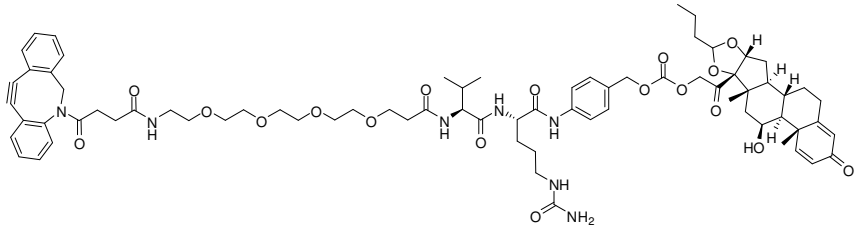

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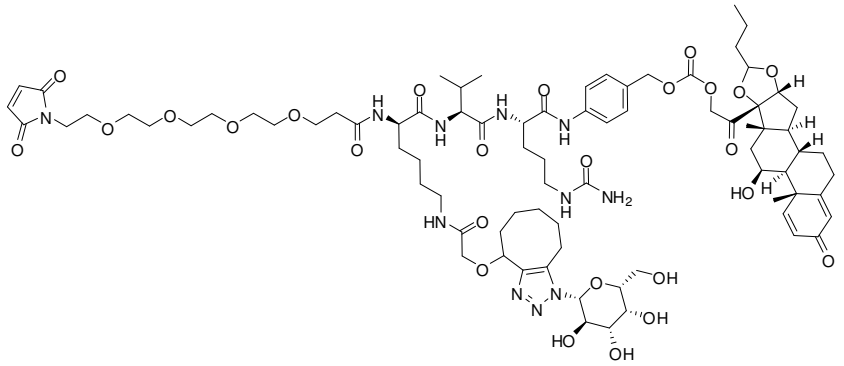

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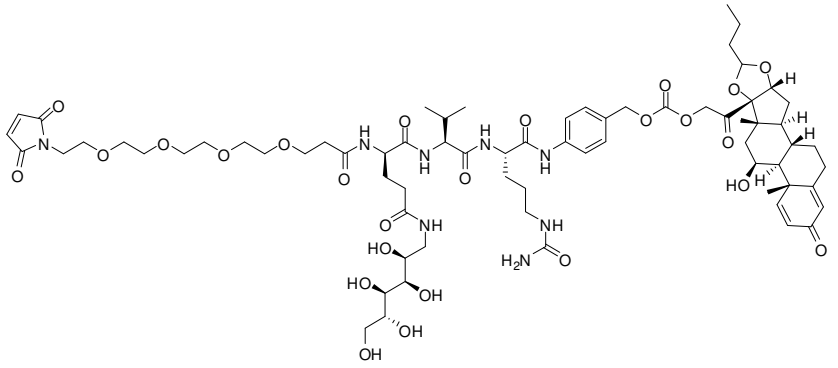

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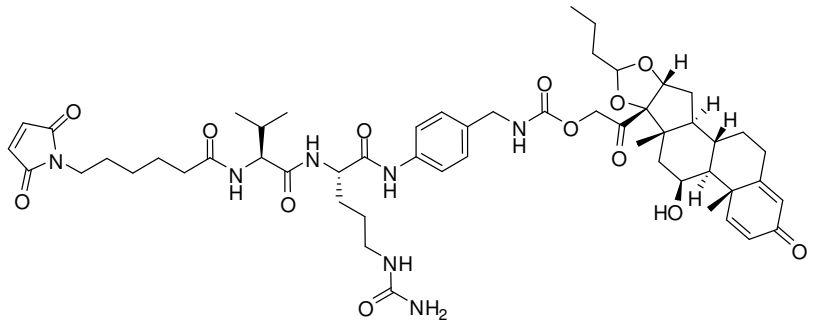

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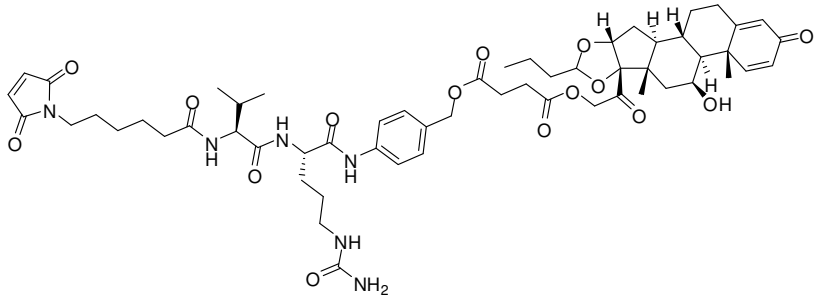

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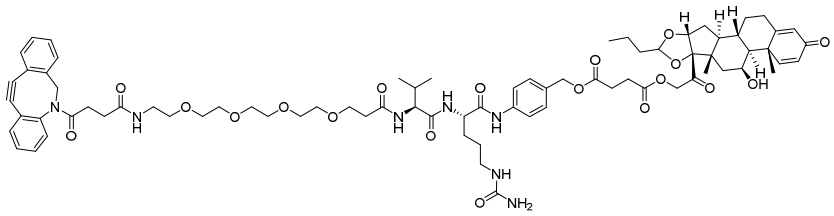

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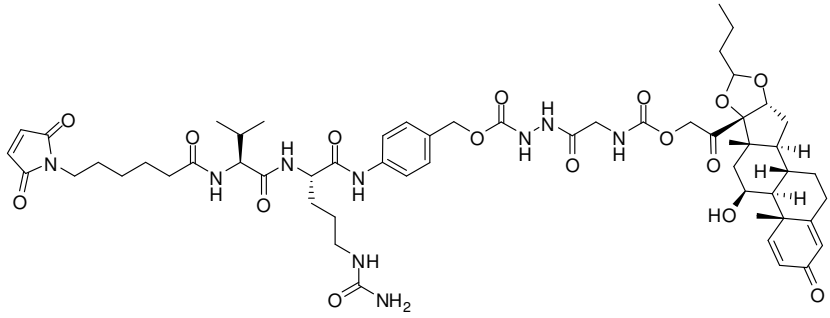

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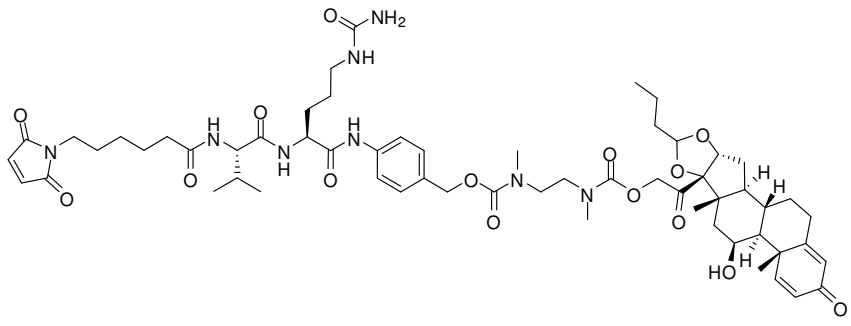

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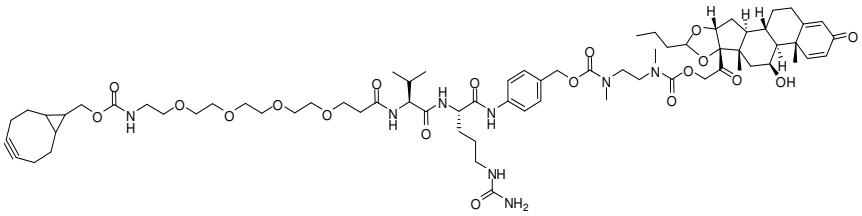

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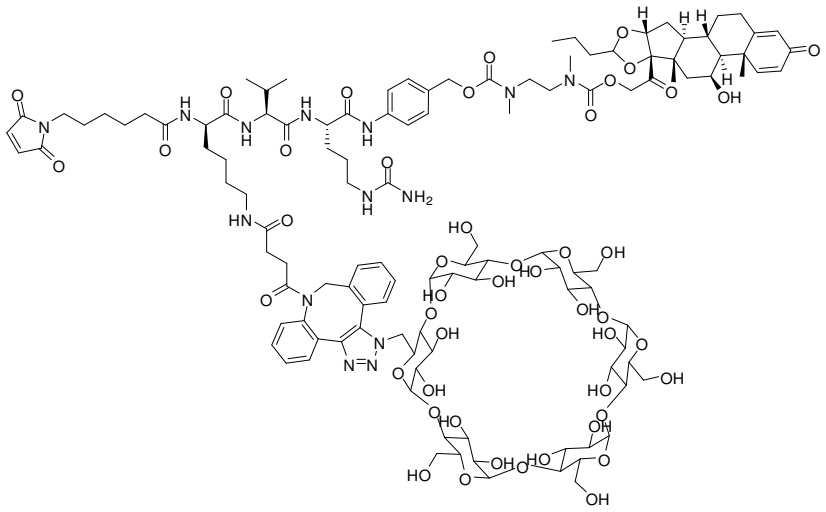

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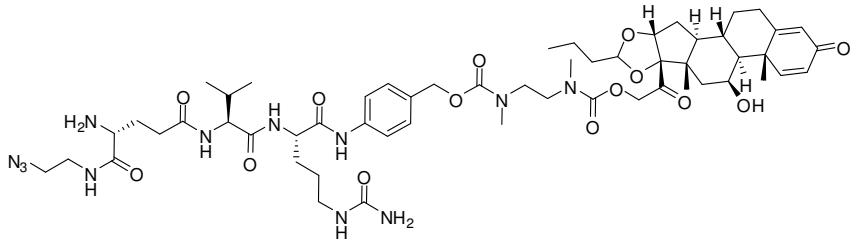

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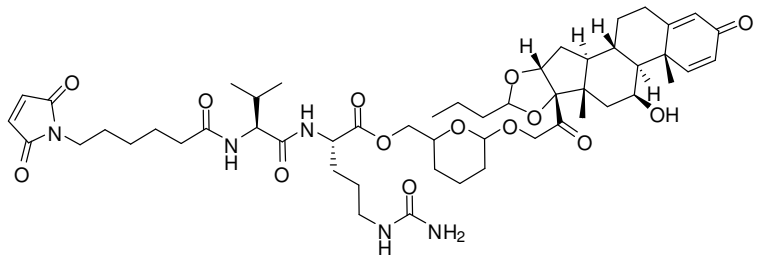

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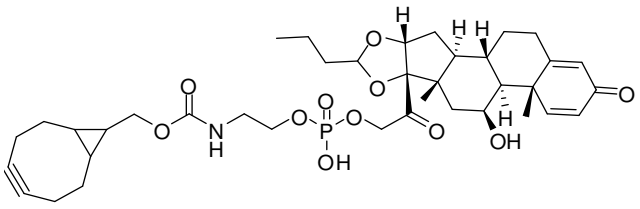

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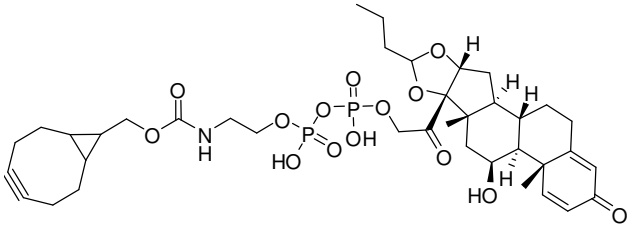

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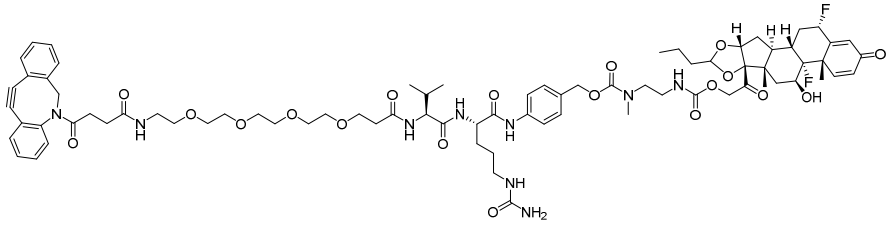
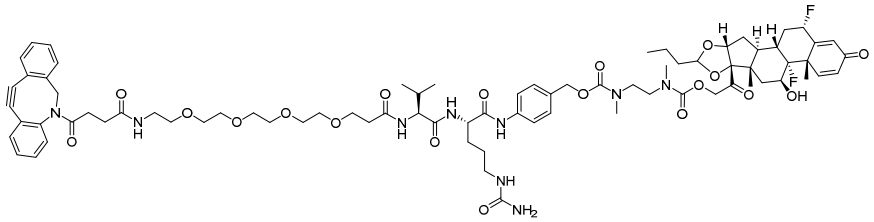


LP1



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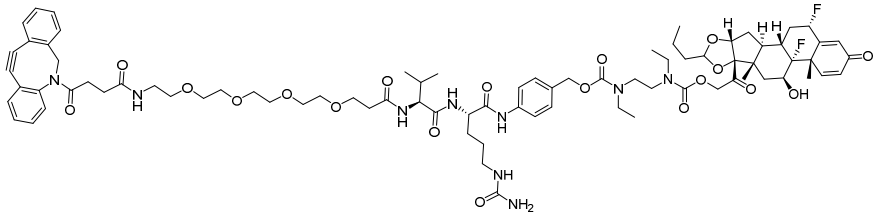

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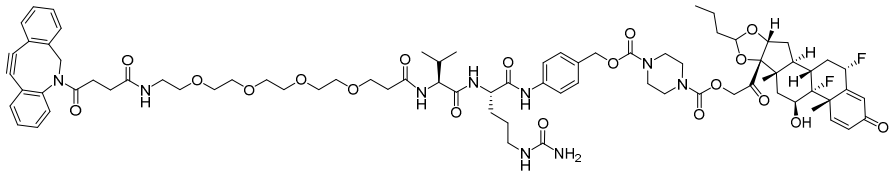

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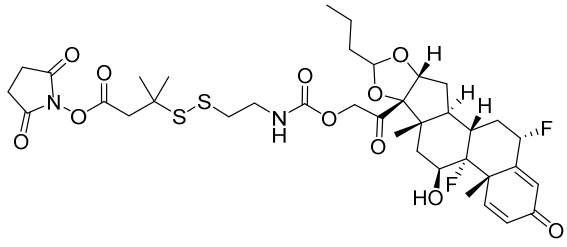
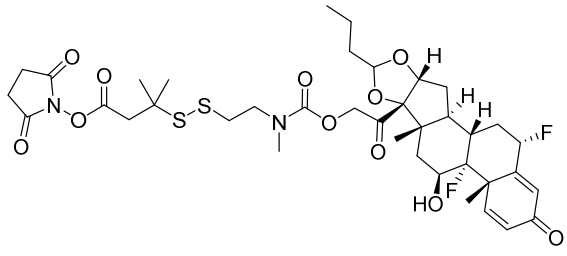


LP5



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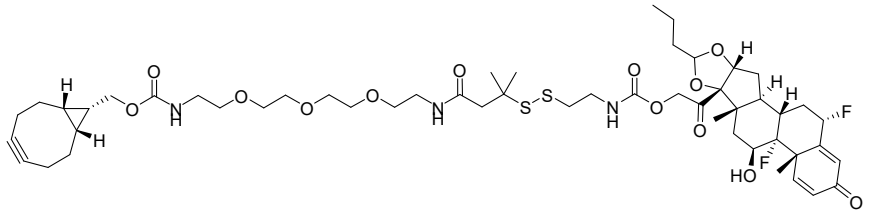

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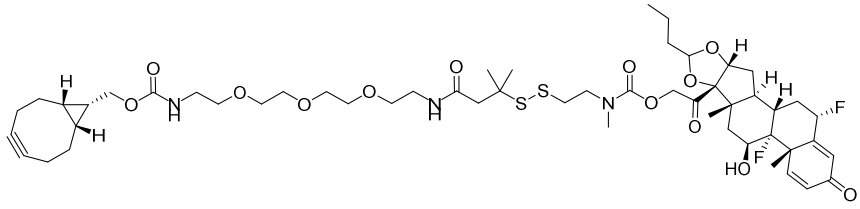
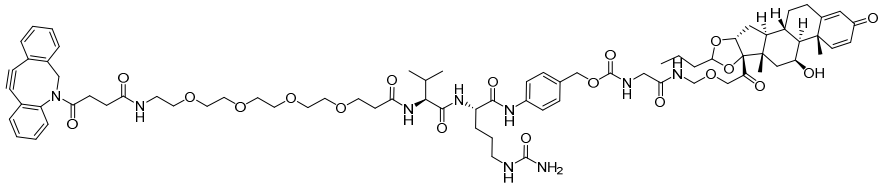
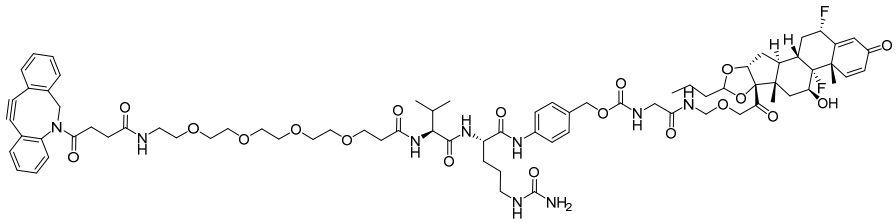


LP8



LP9



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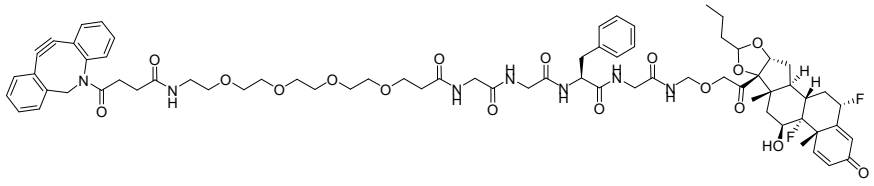

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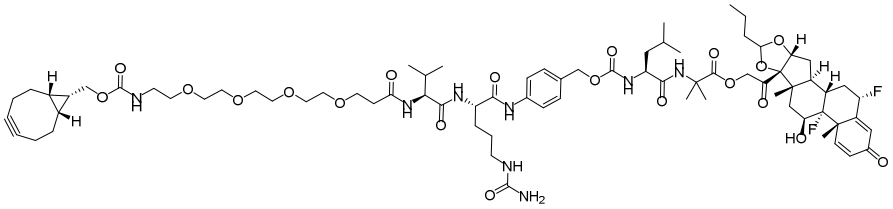

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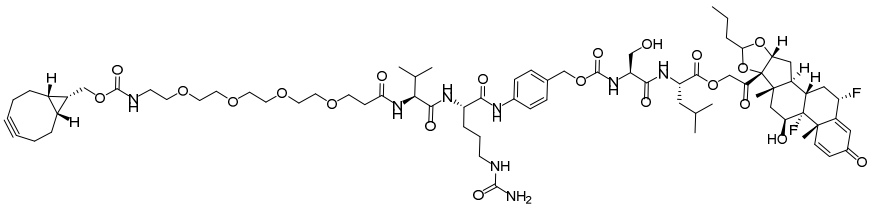

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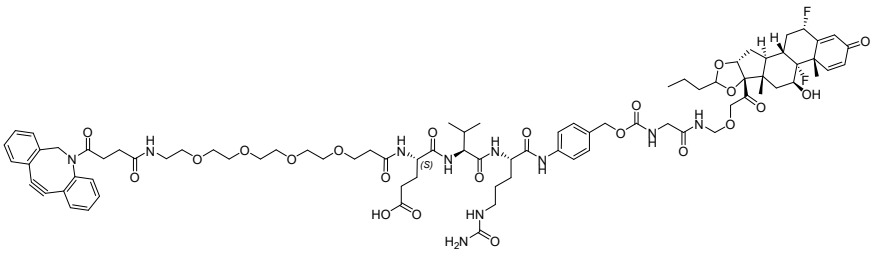

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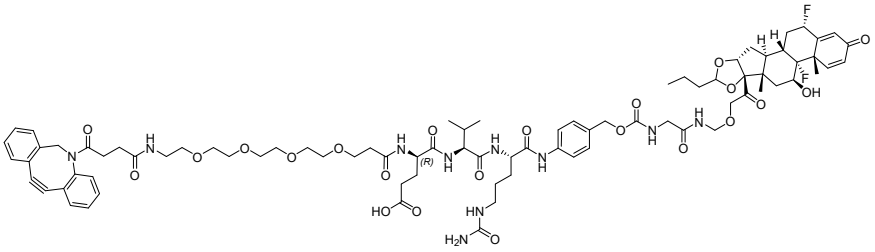

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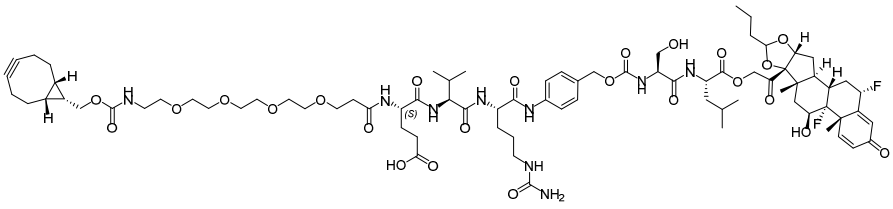
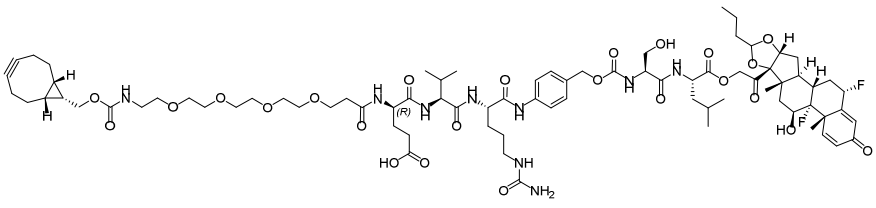


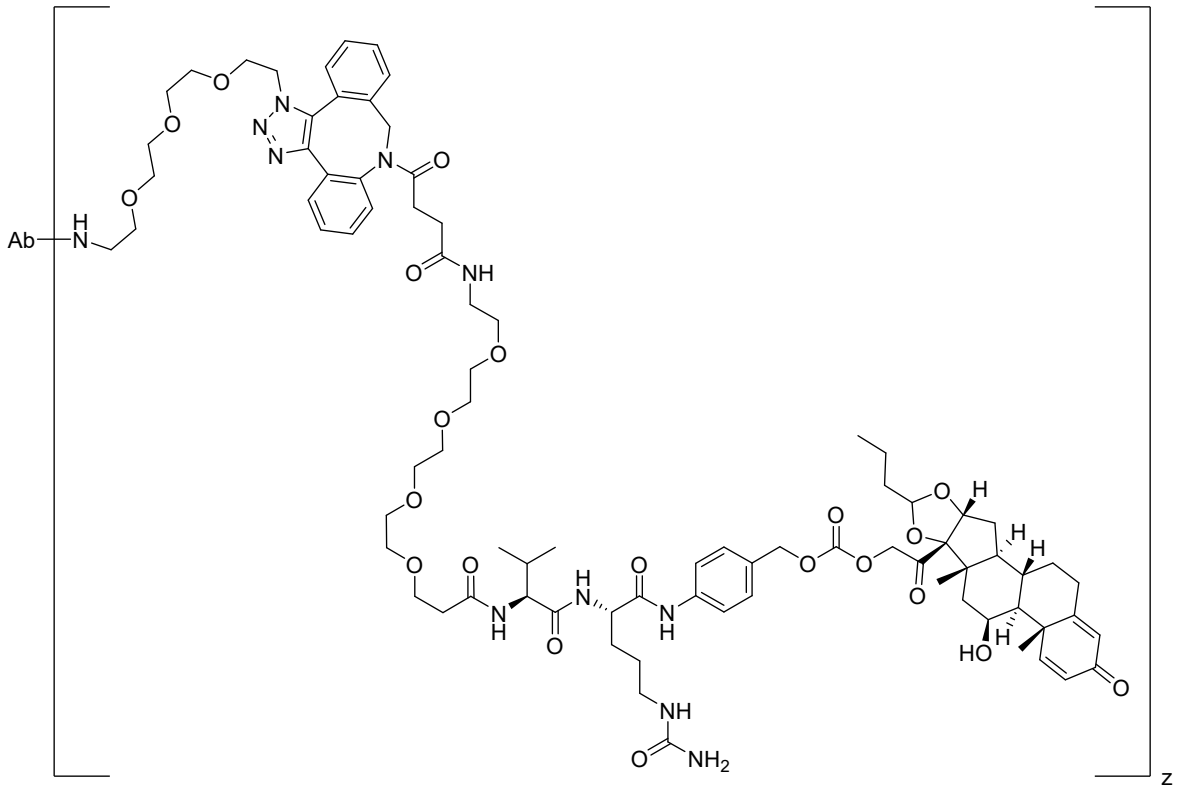
LP20 and

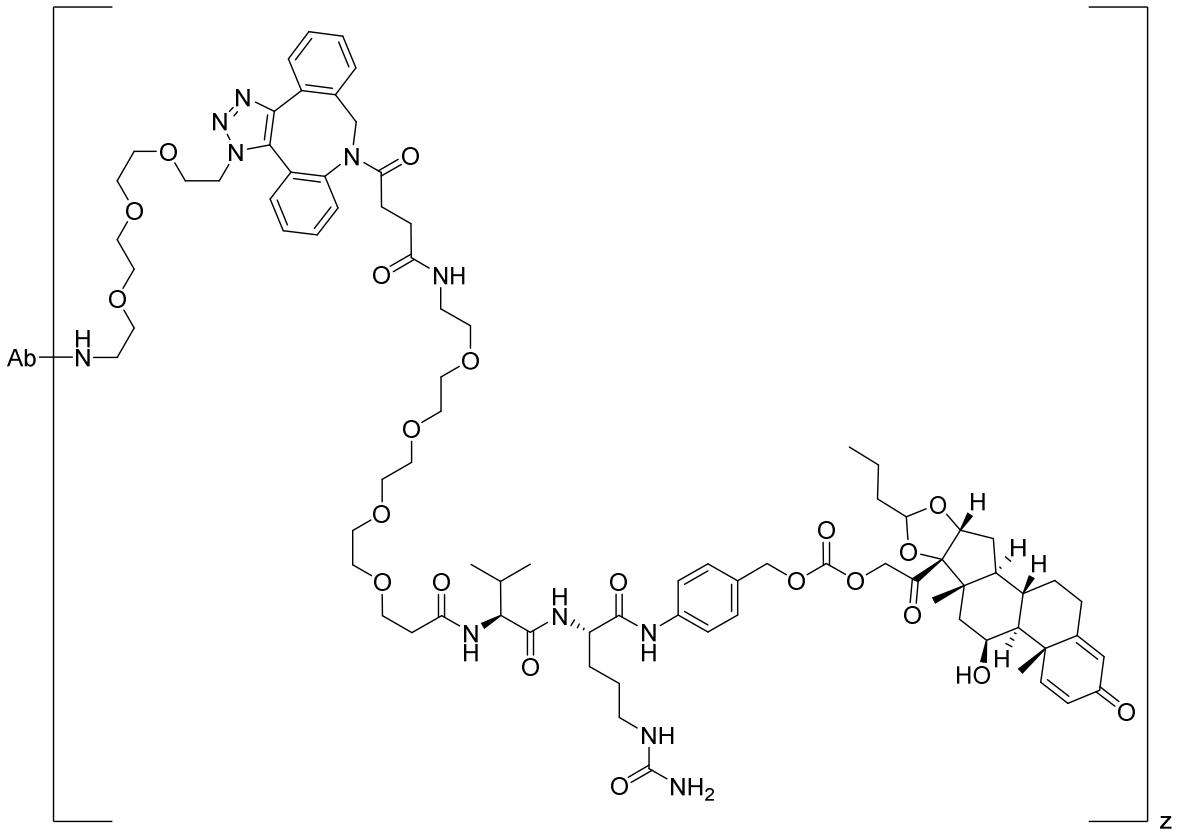


LP21

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

105. A Compound selected from the group consisting of





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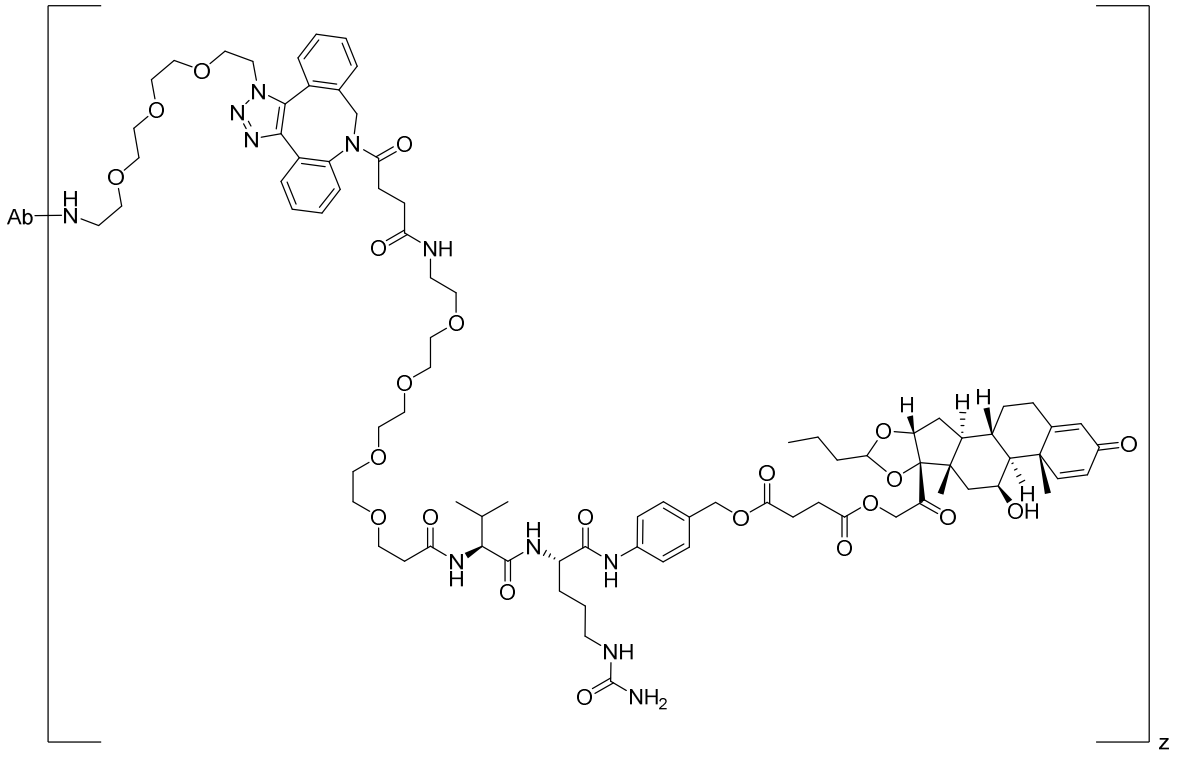

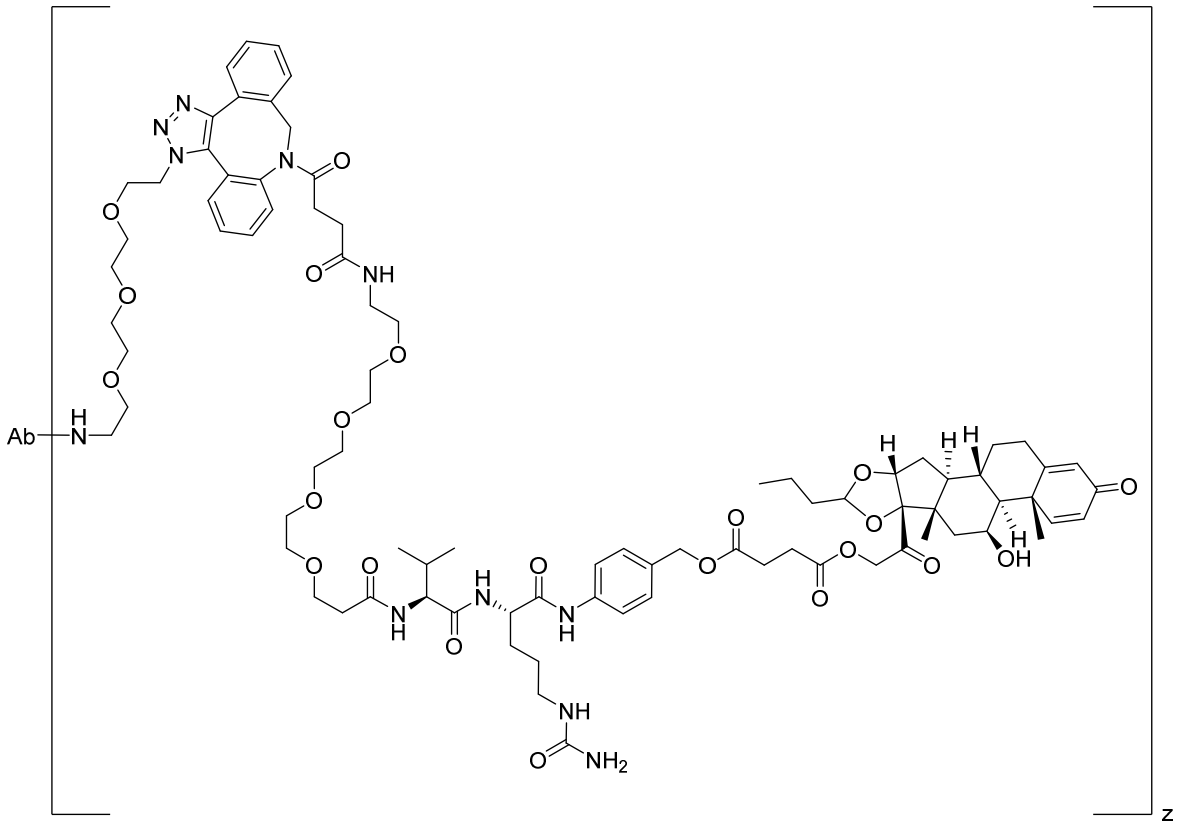

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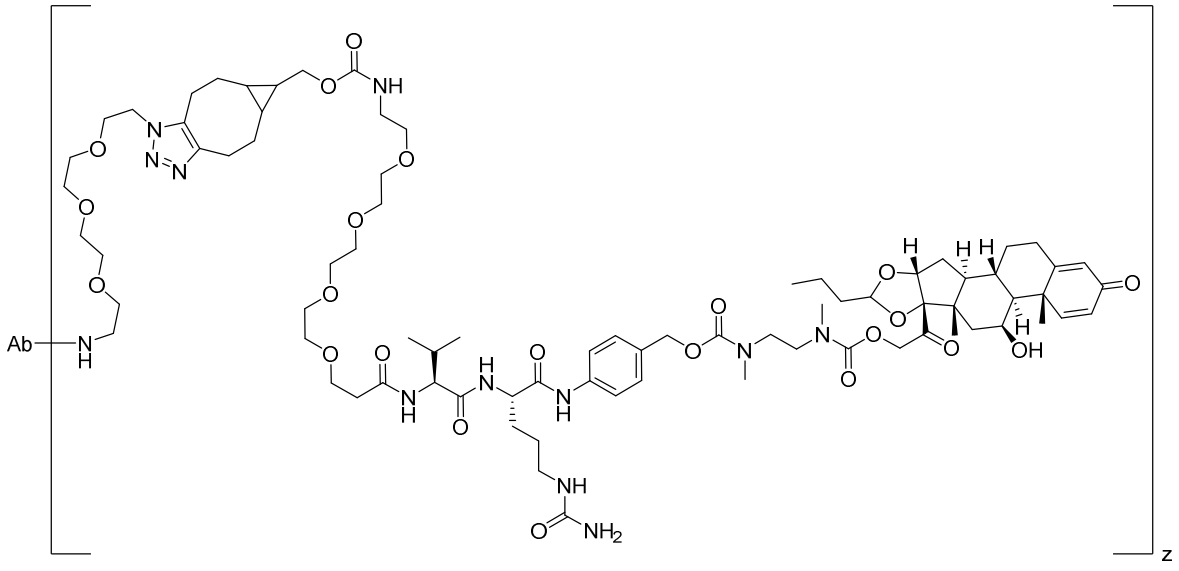

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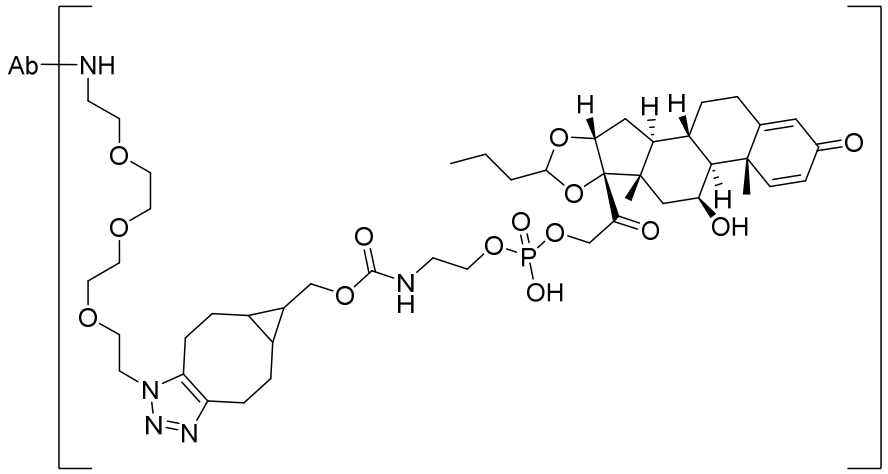
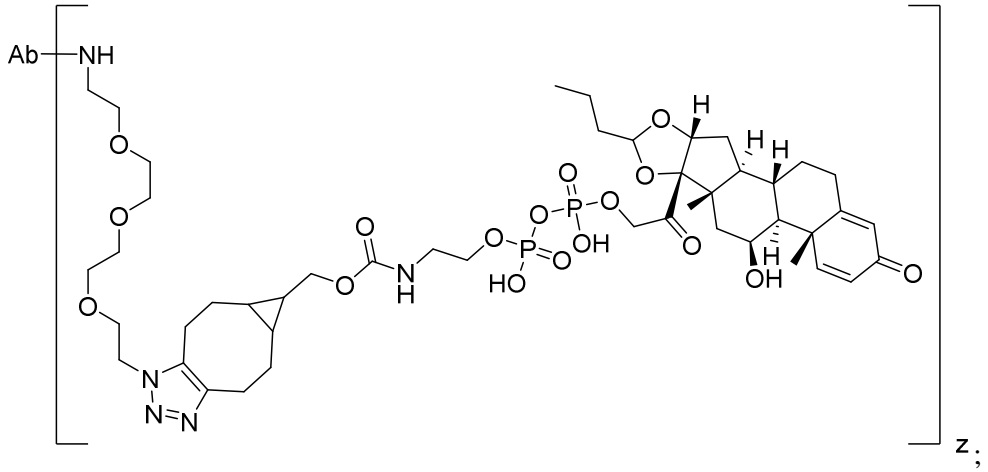


; and

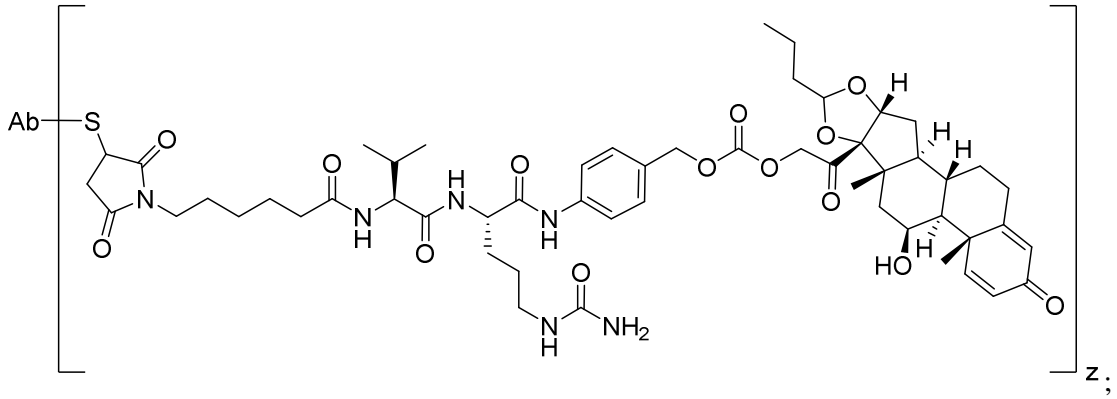


;

wherein **Ab** is an antibody or an antigen binding fragment thereof; and

z is an integer from one to four.

106. A Compound selected from the group consisting of



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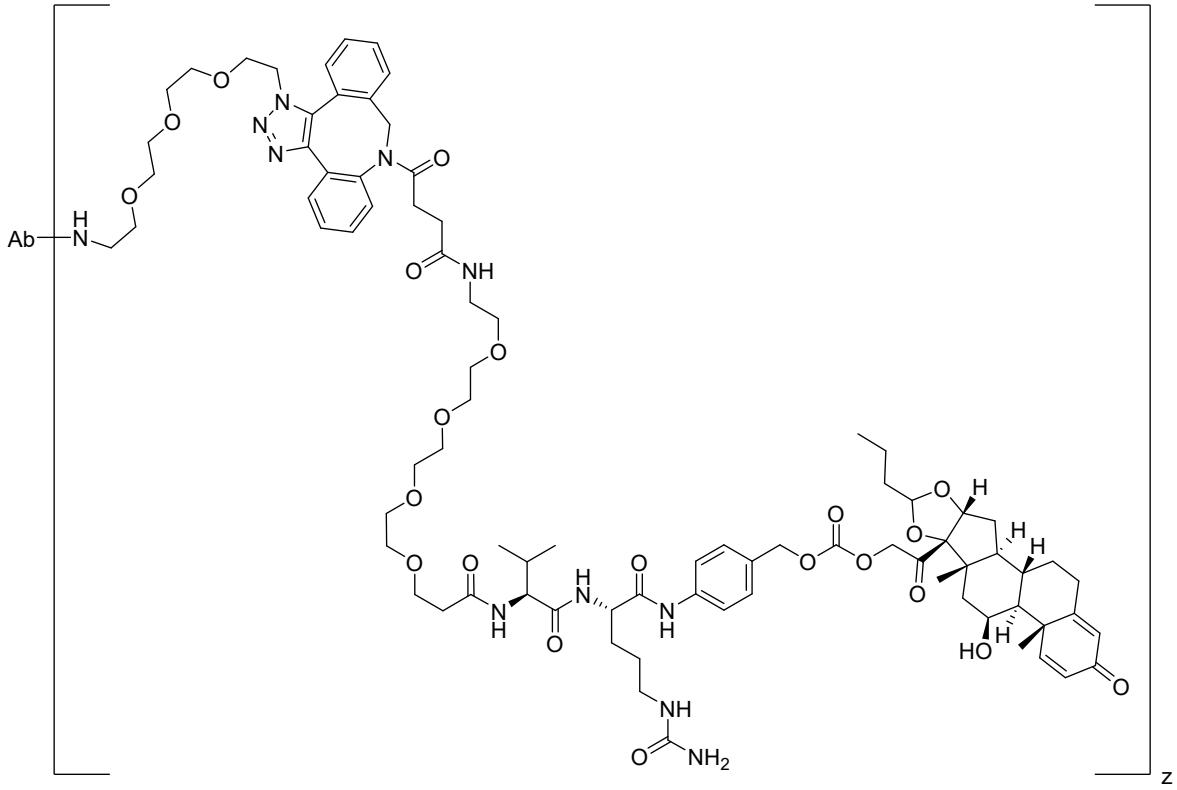

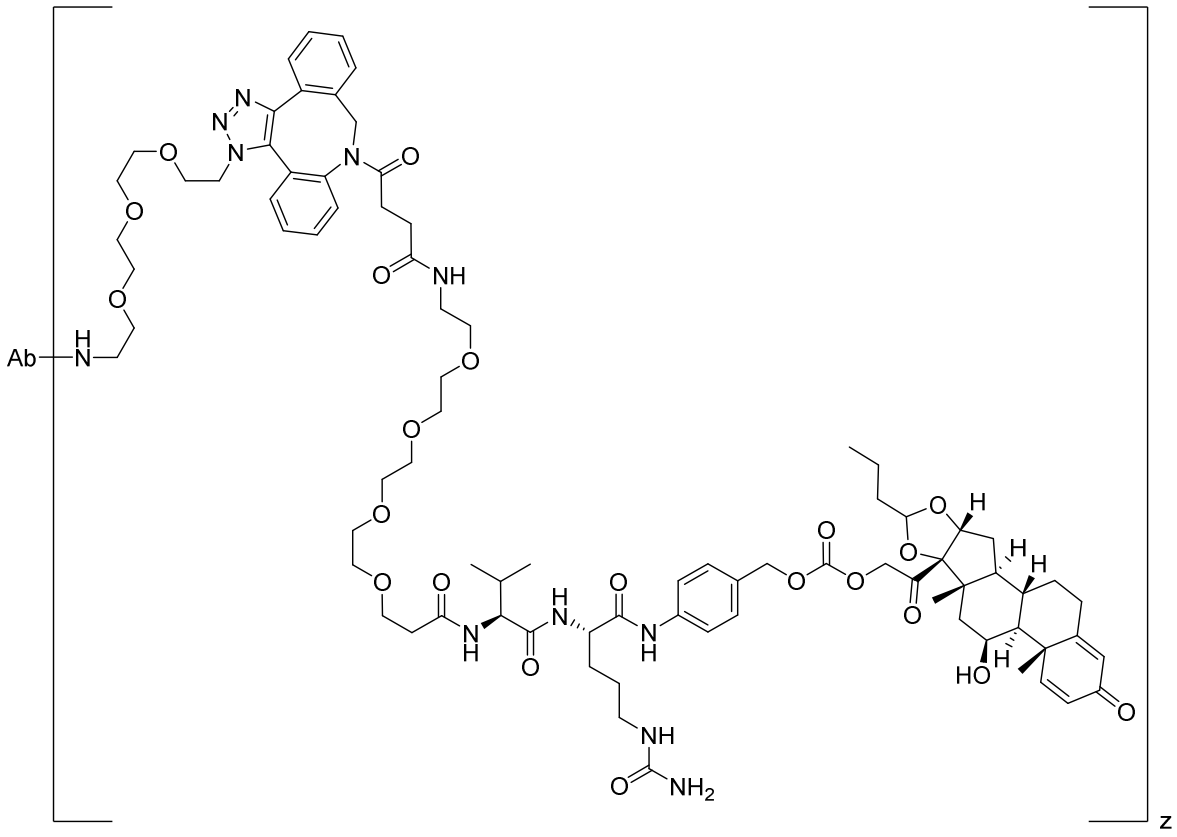

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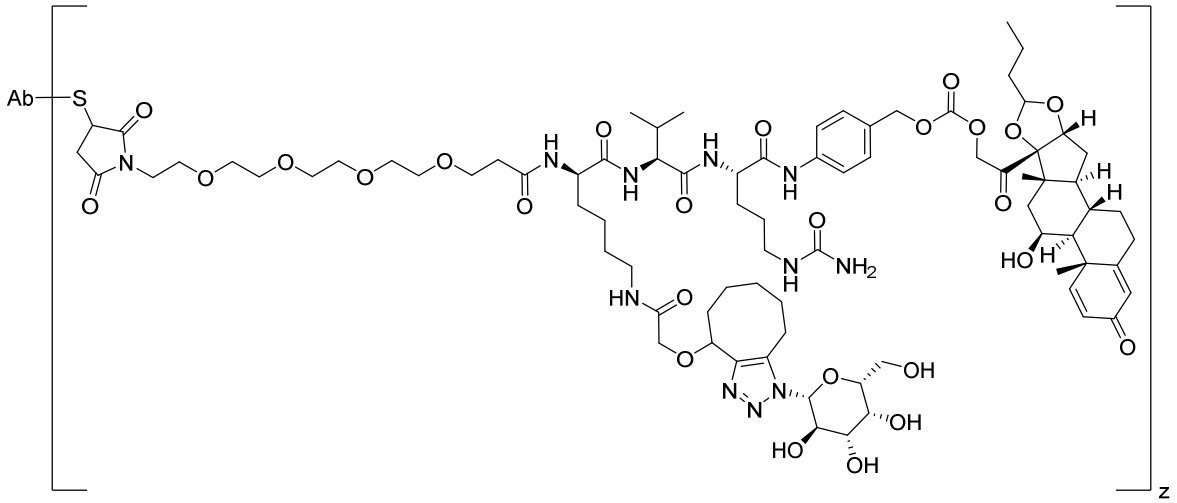

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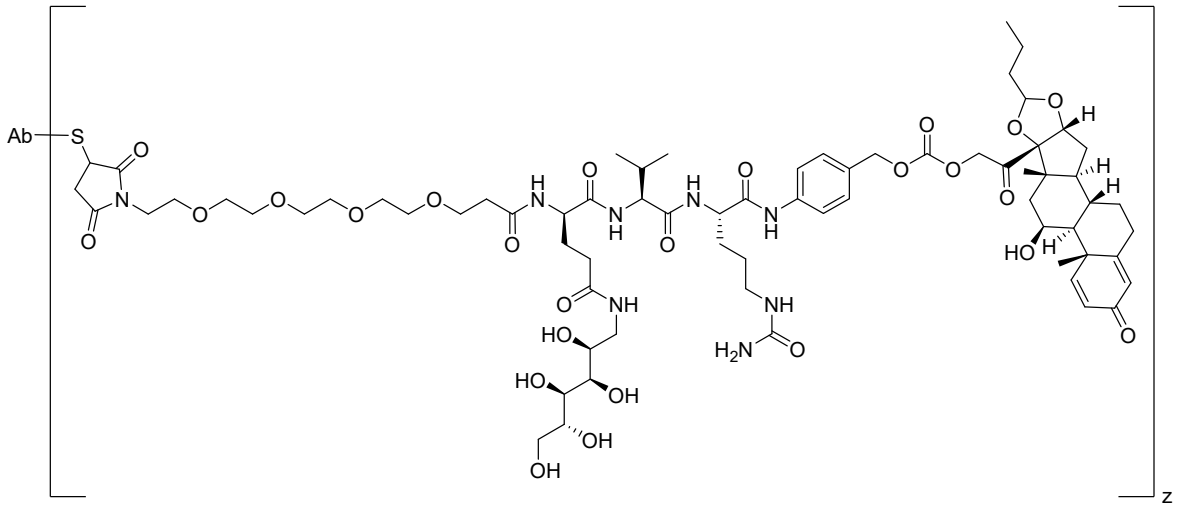

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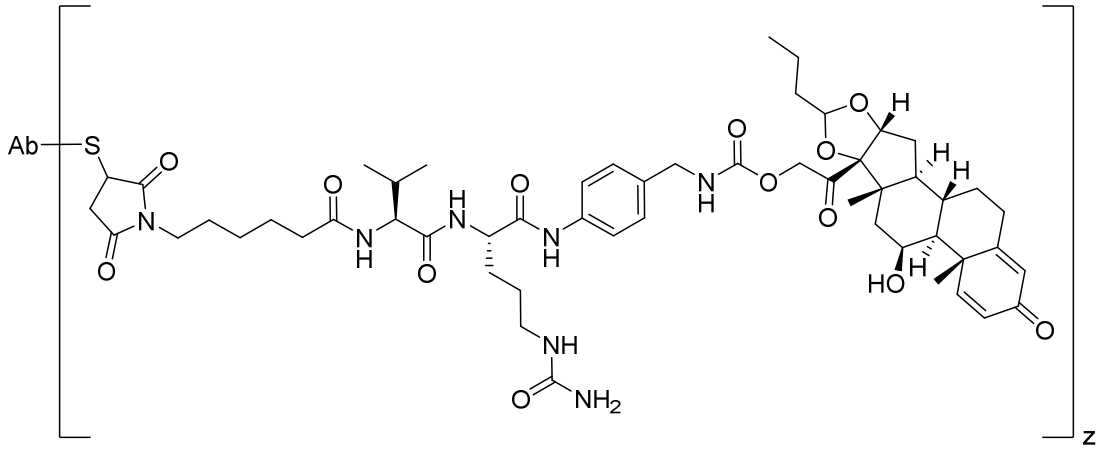

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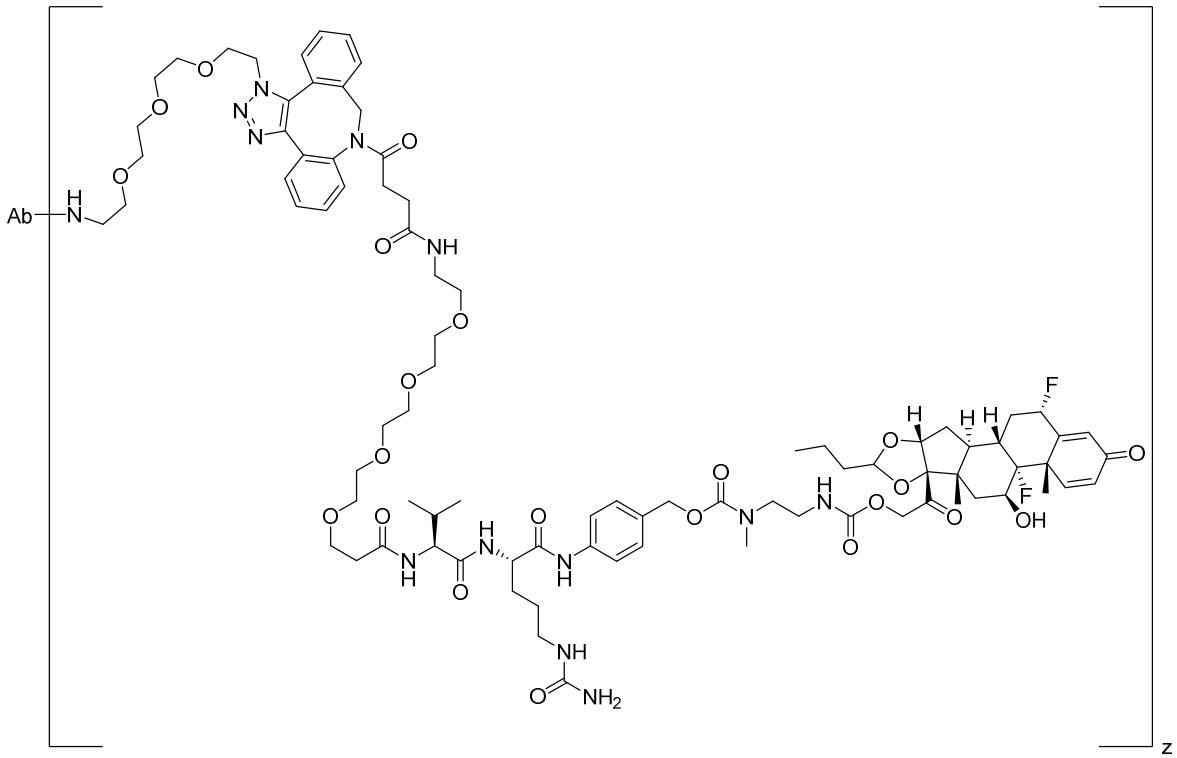

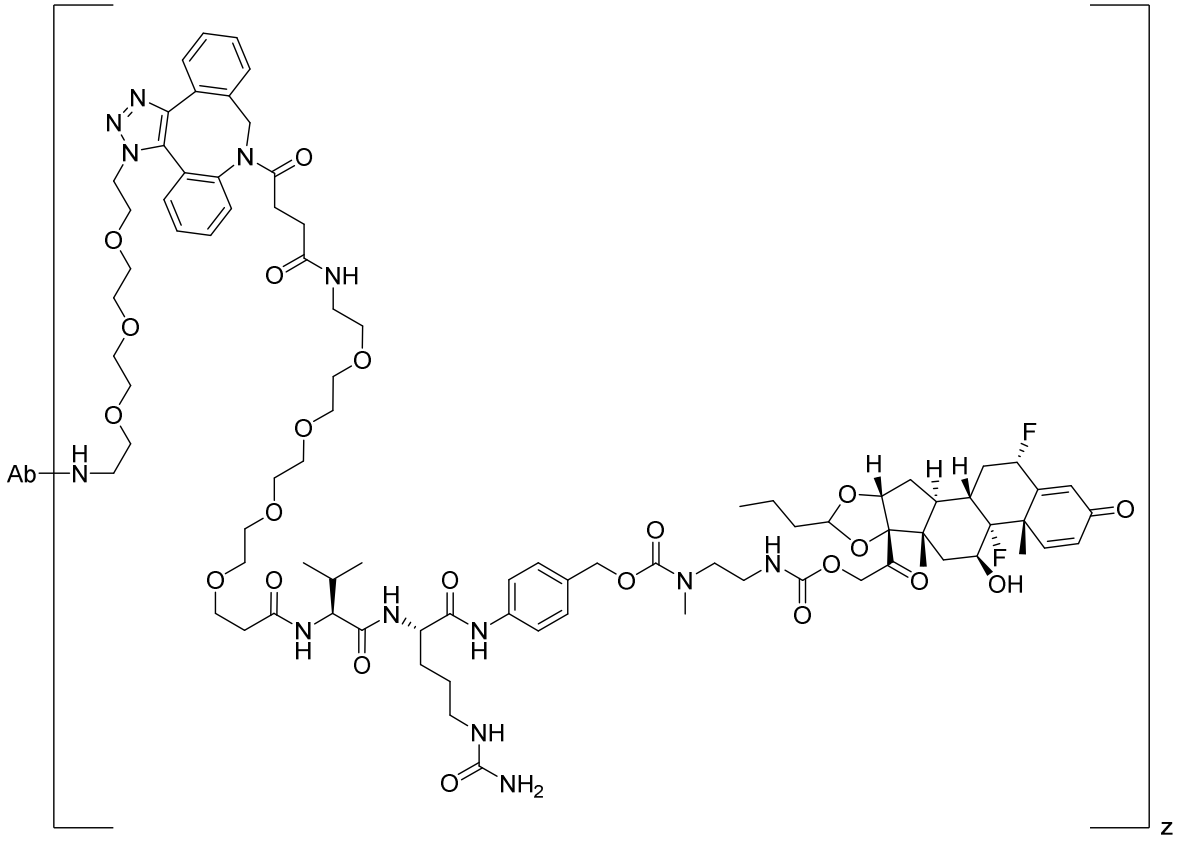
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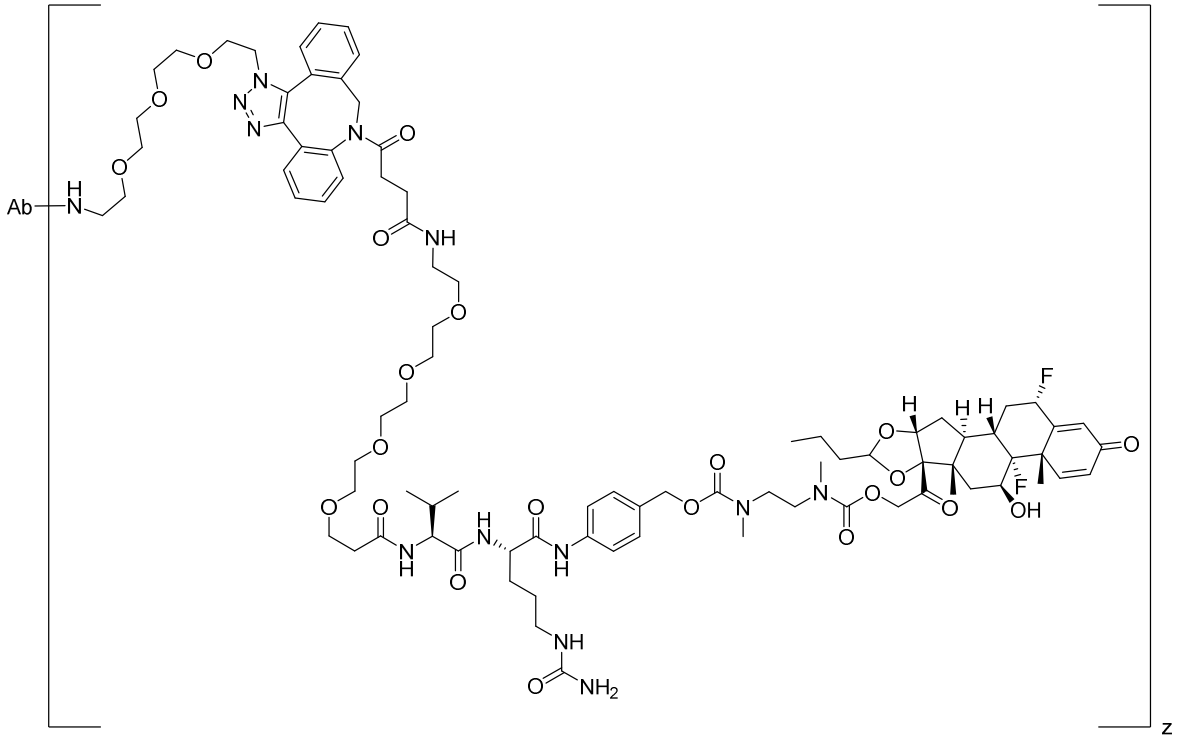
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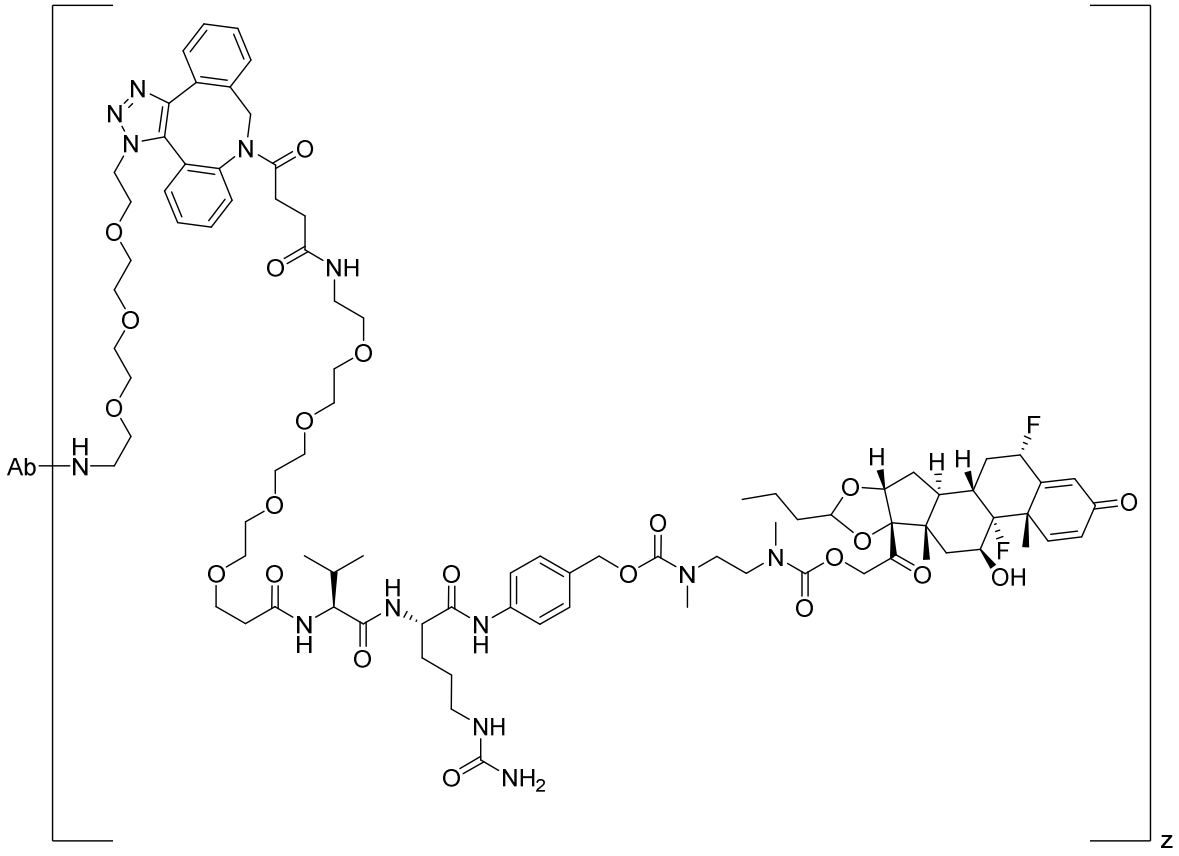
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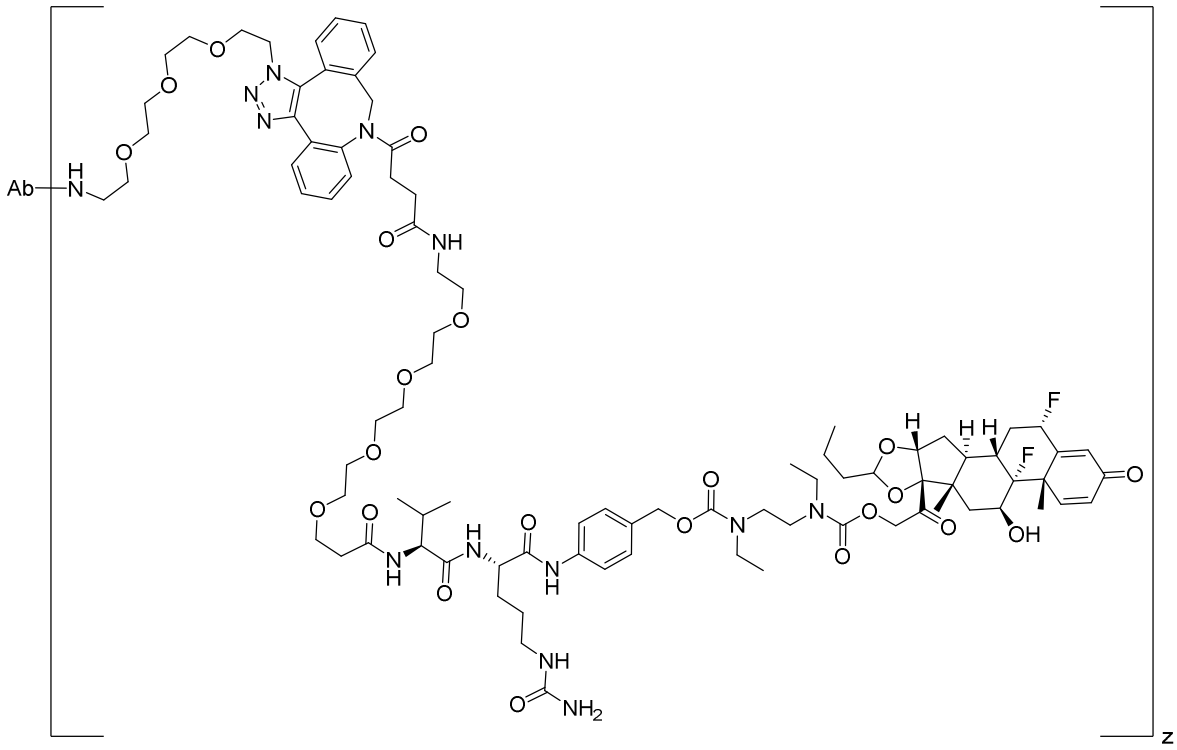

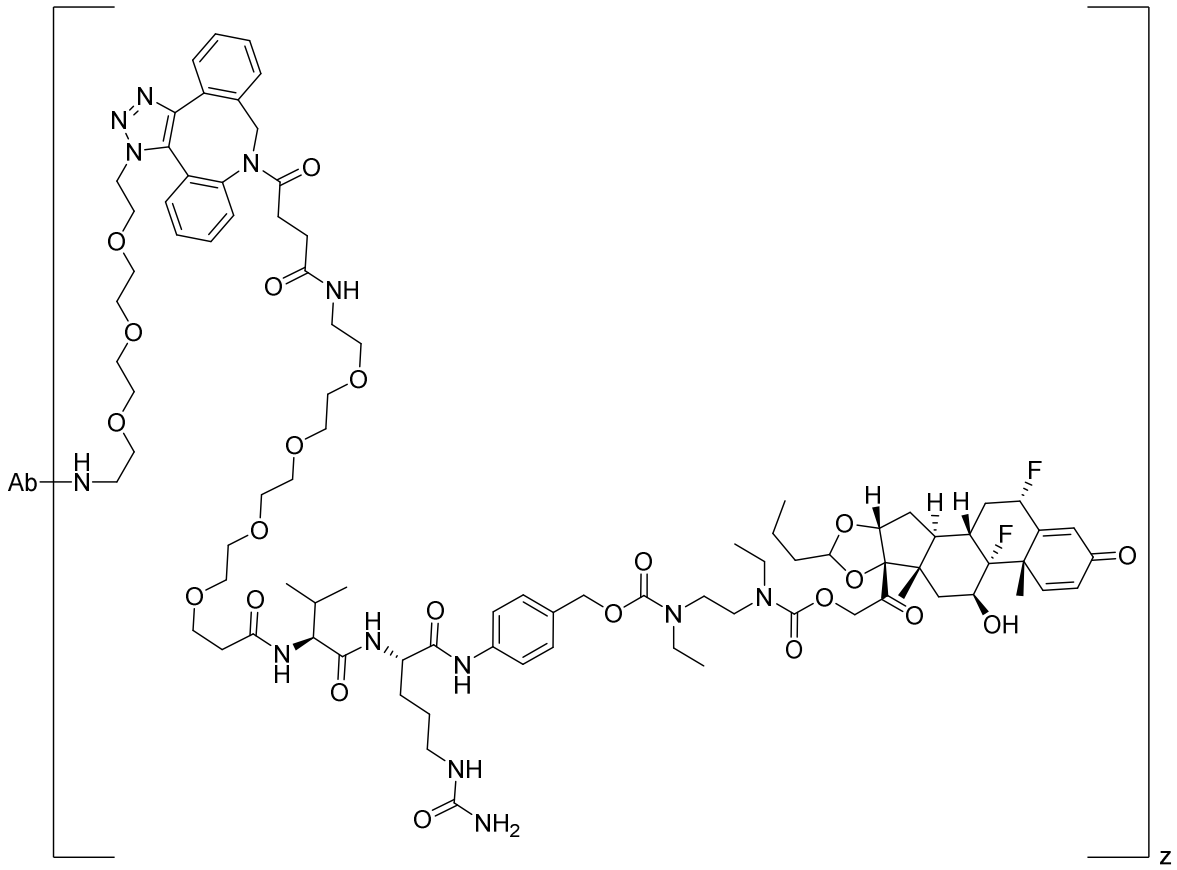

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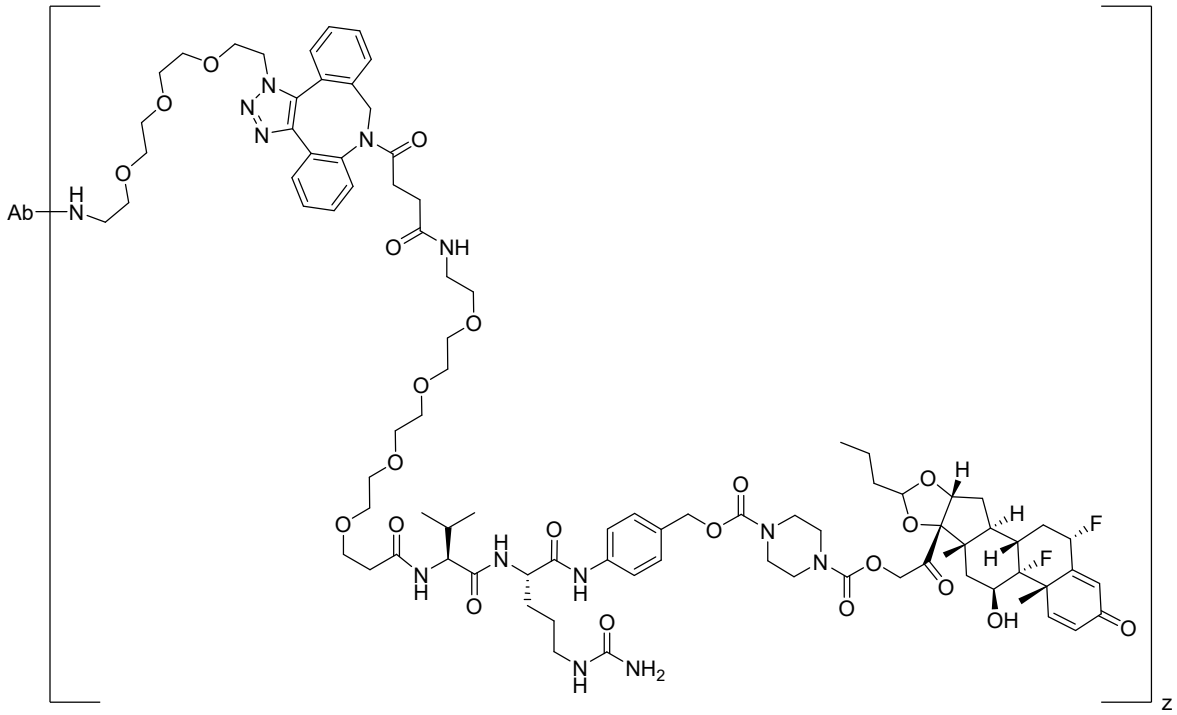

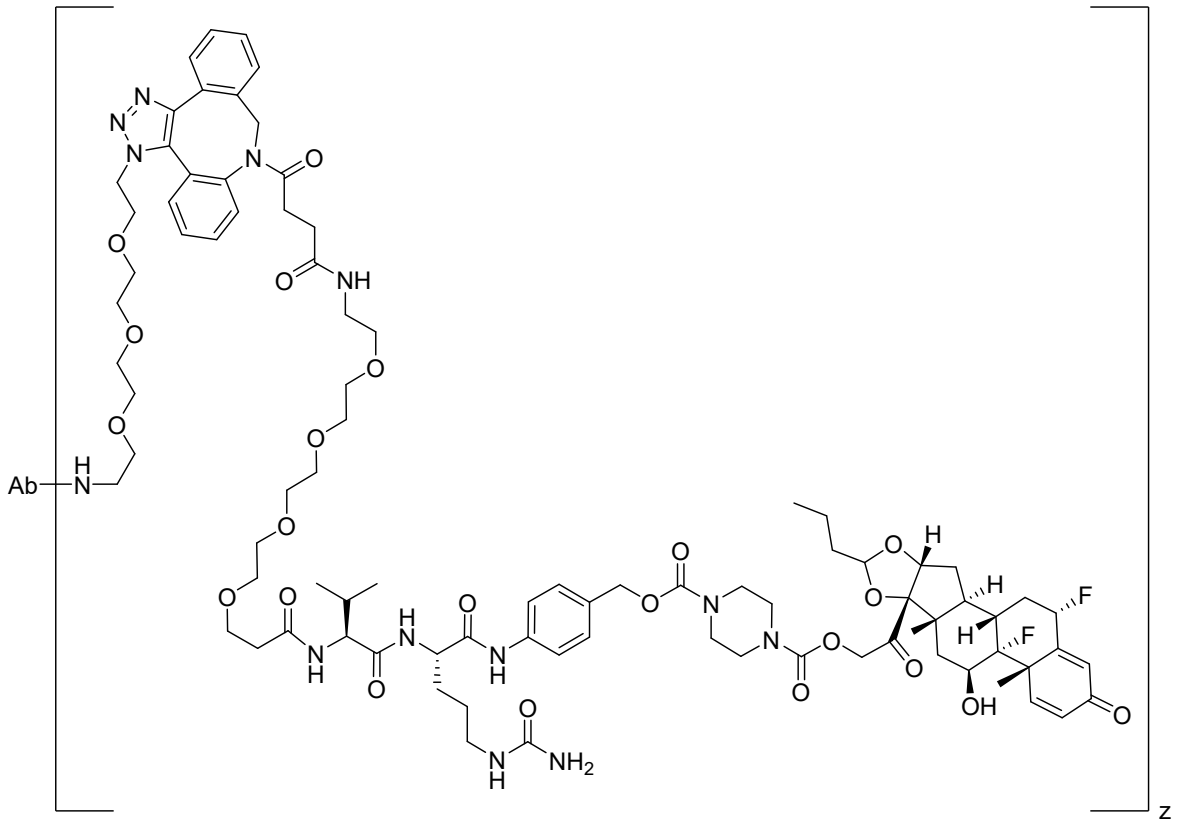

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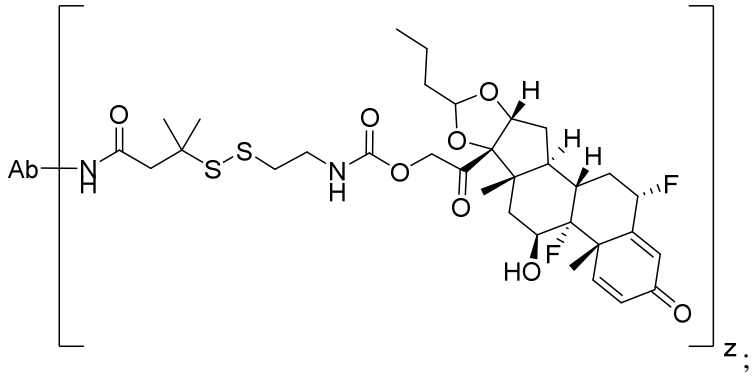

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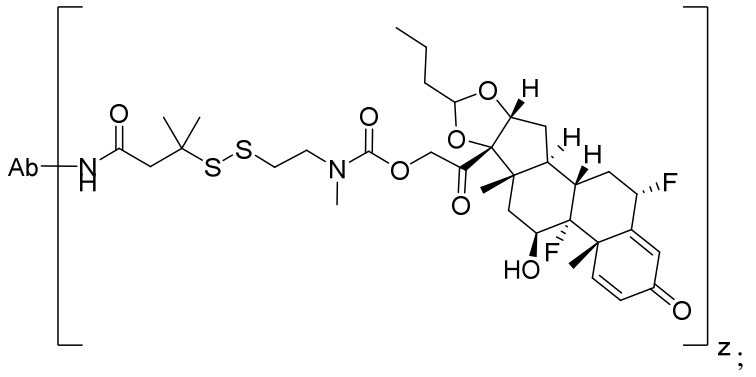

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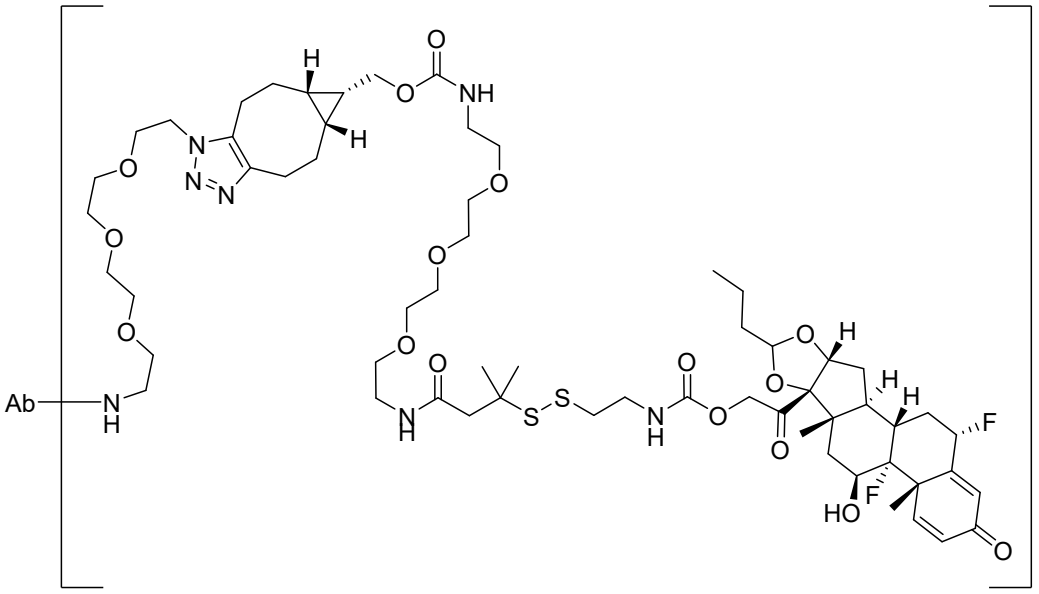

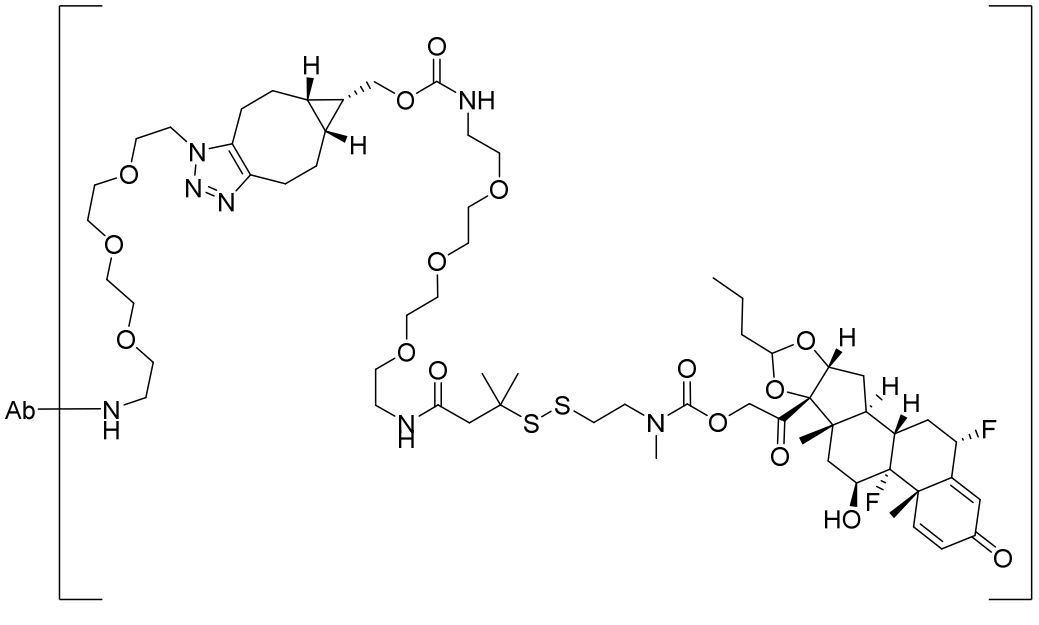

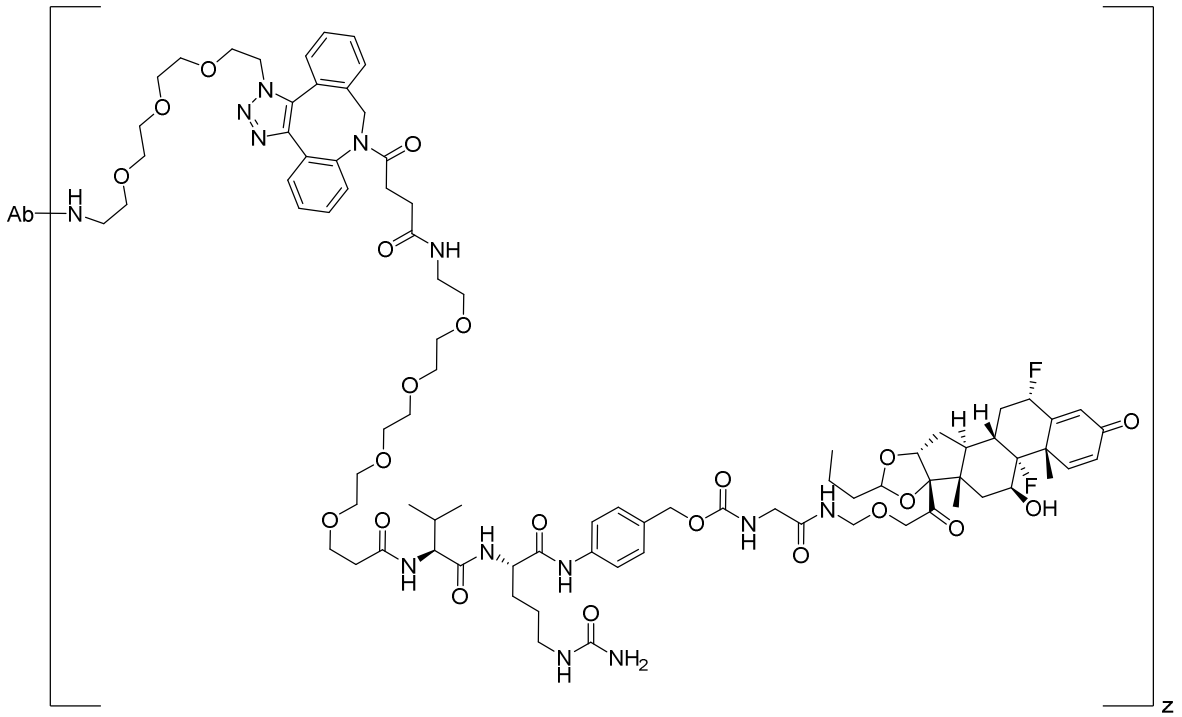

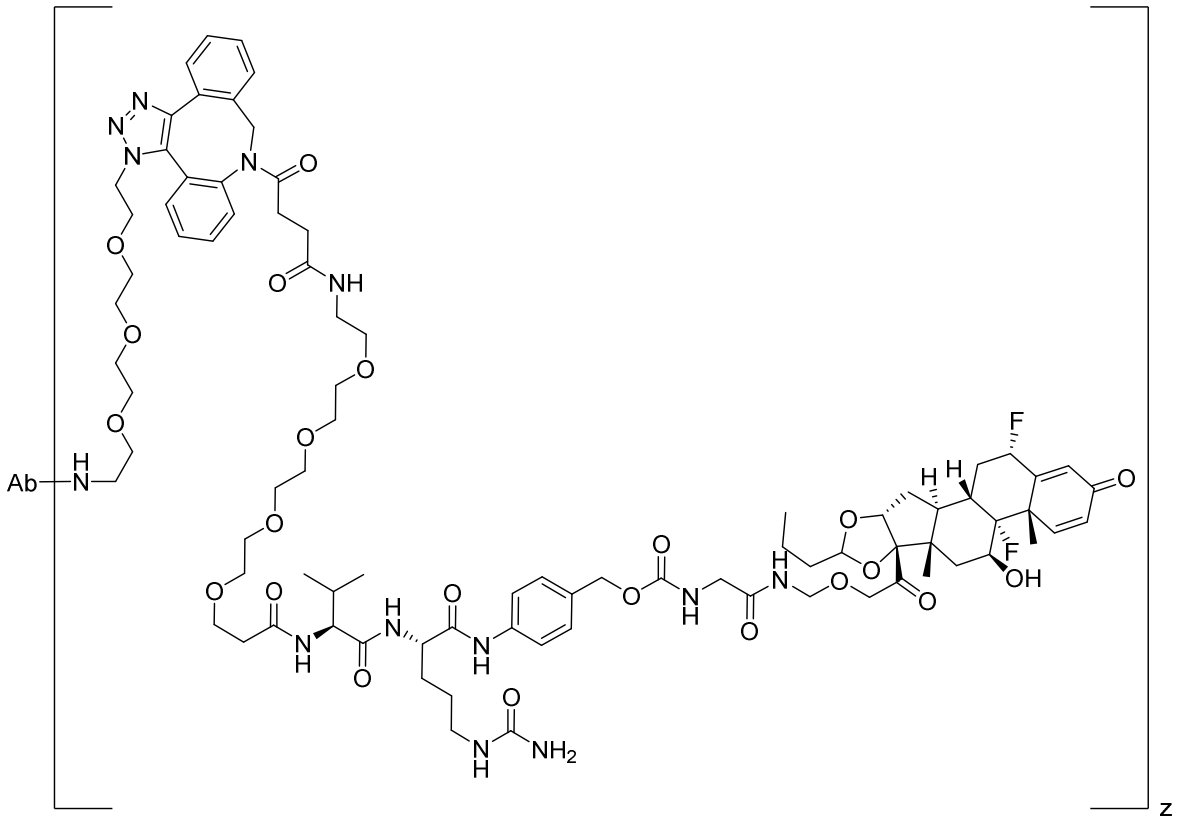

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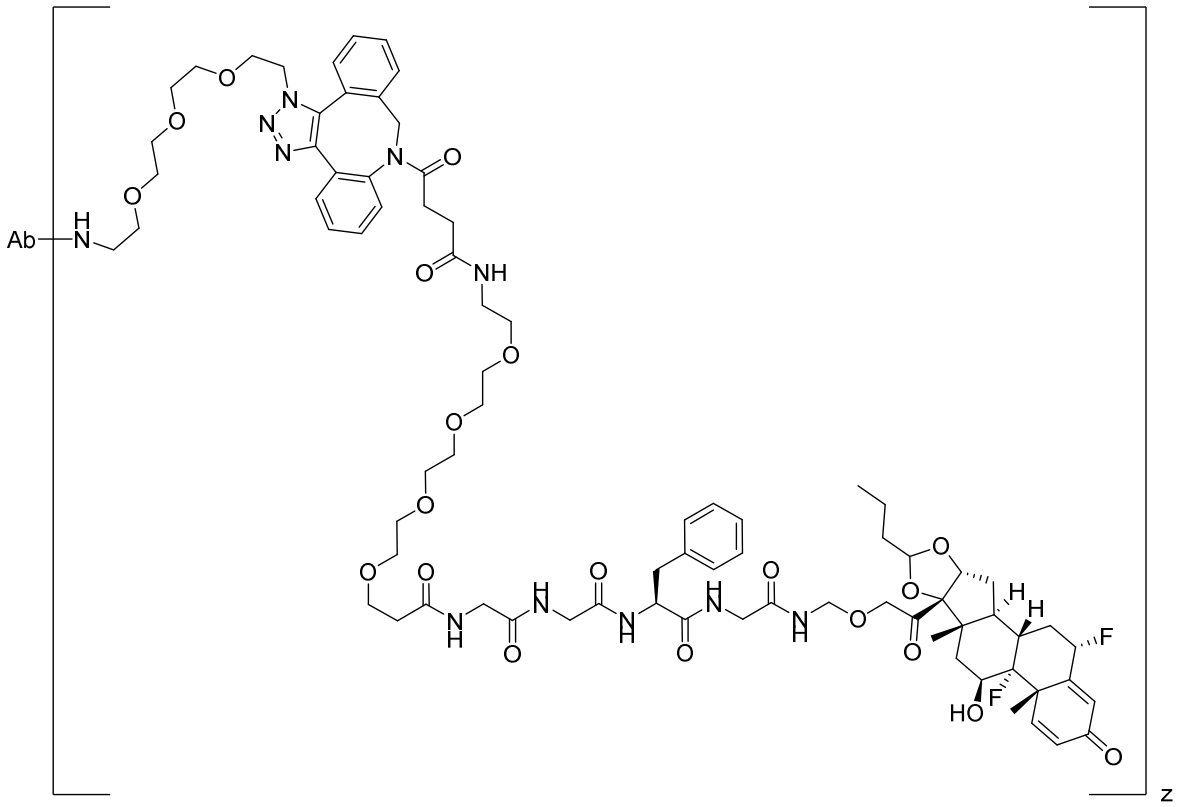
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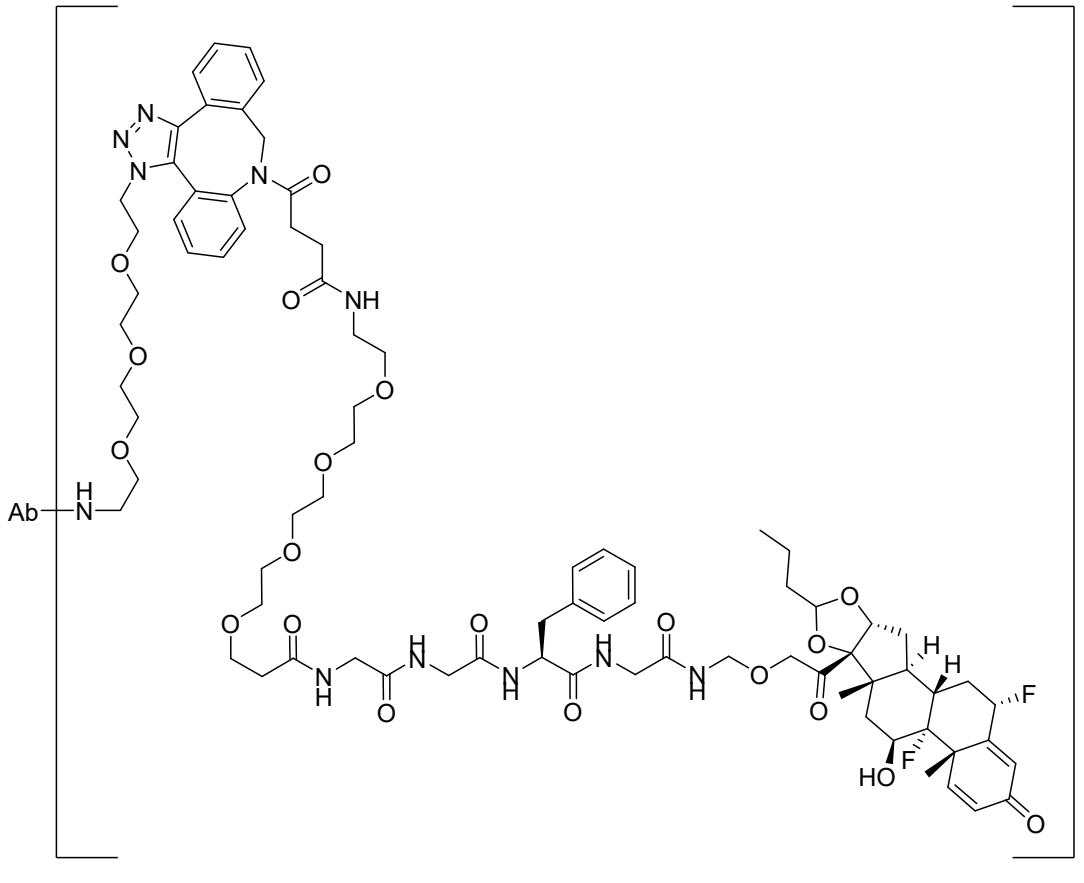

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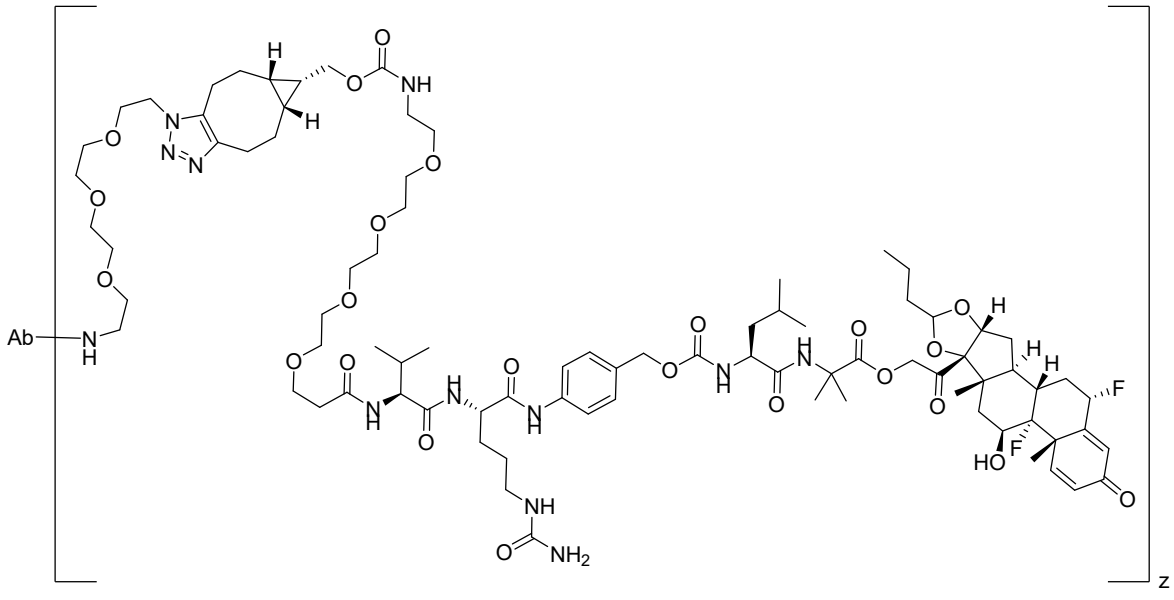

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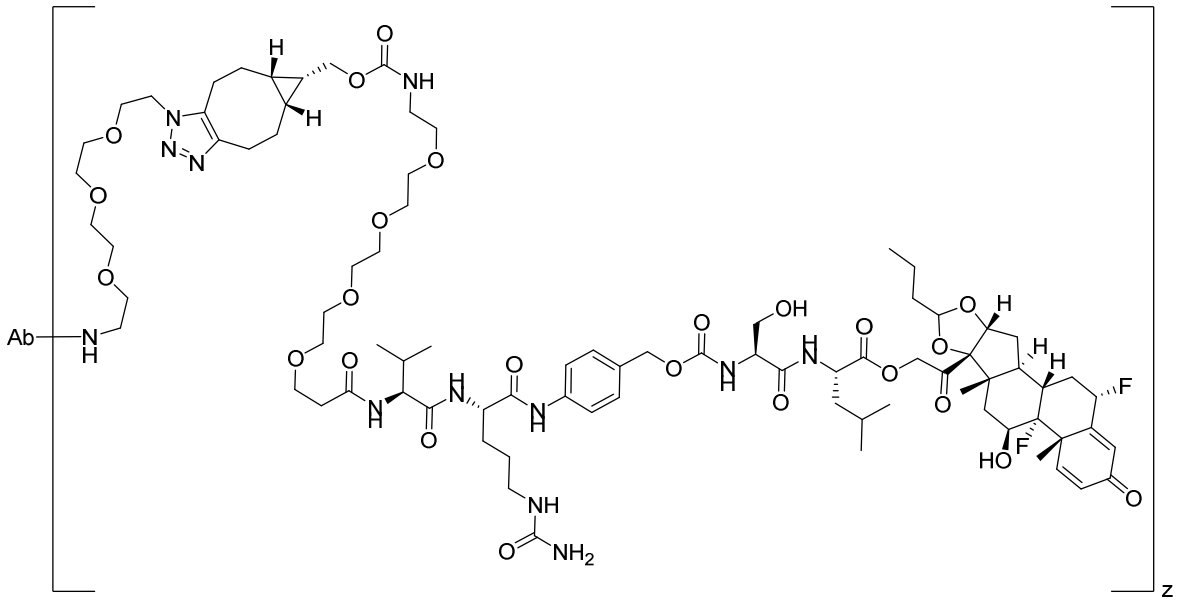

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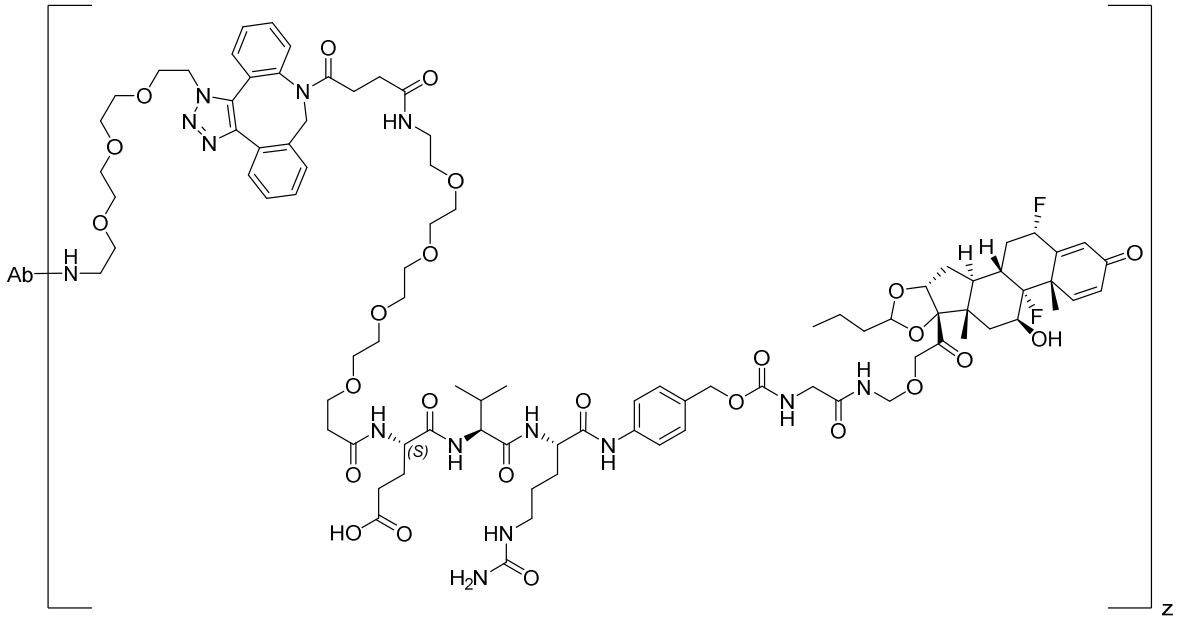

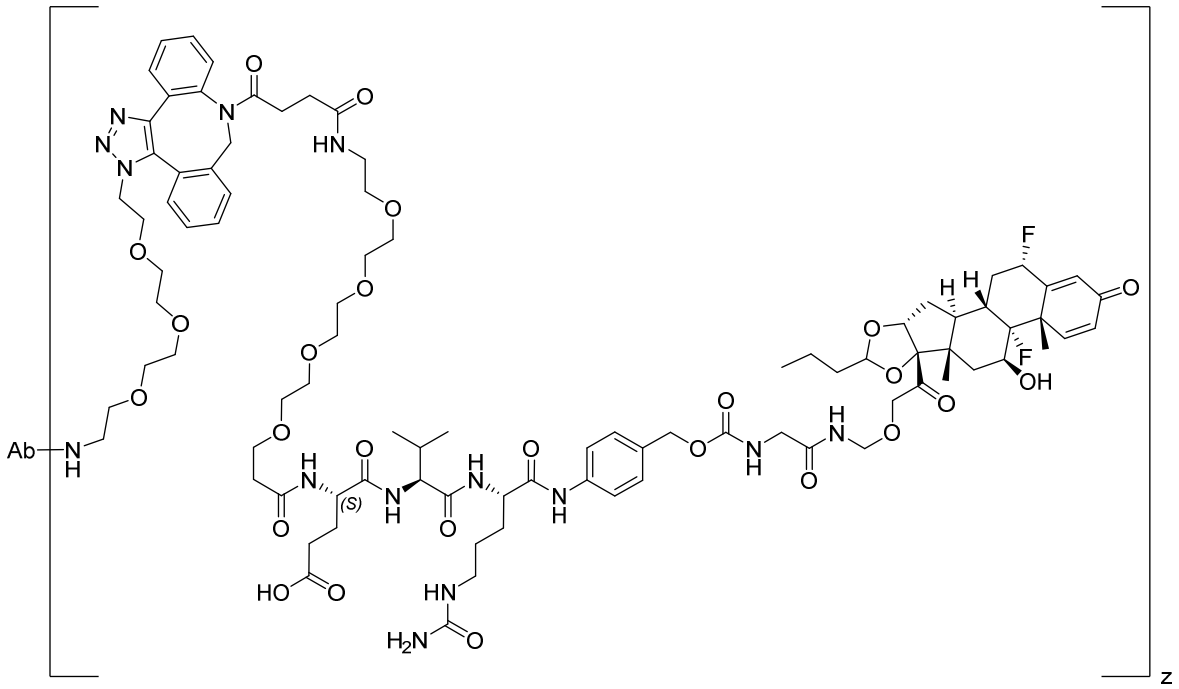
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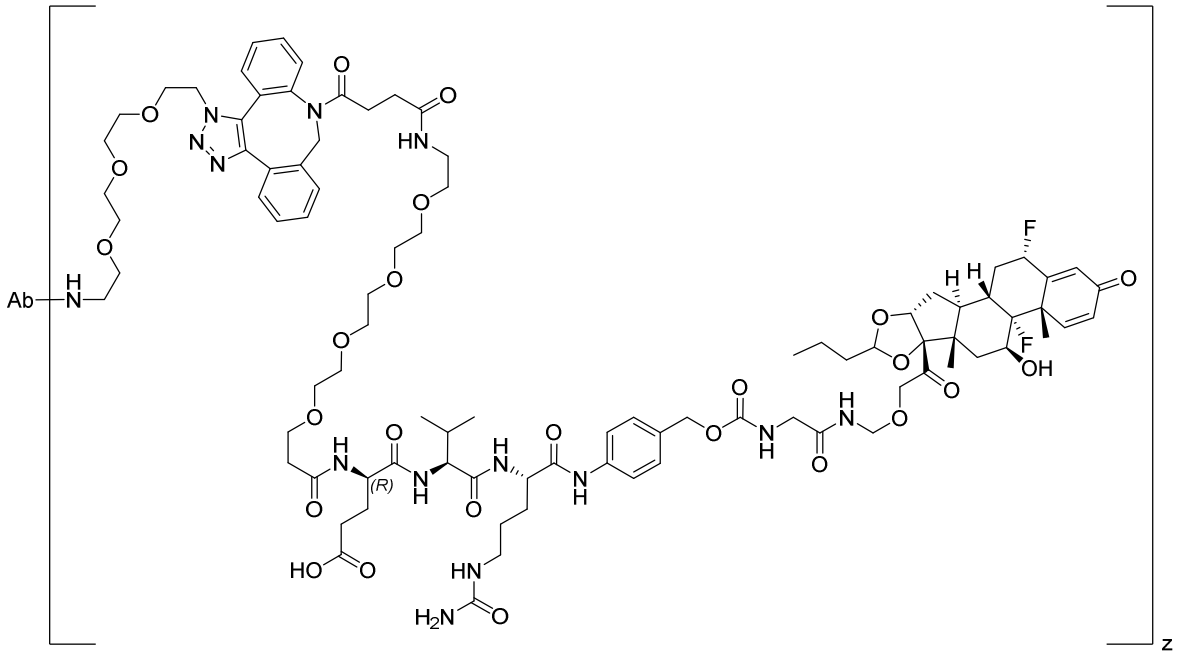
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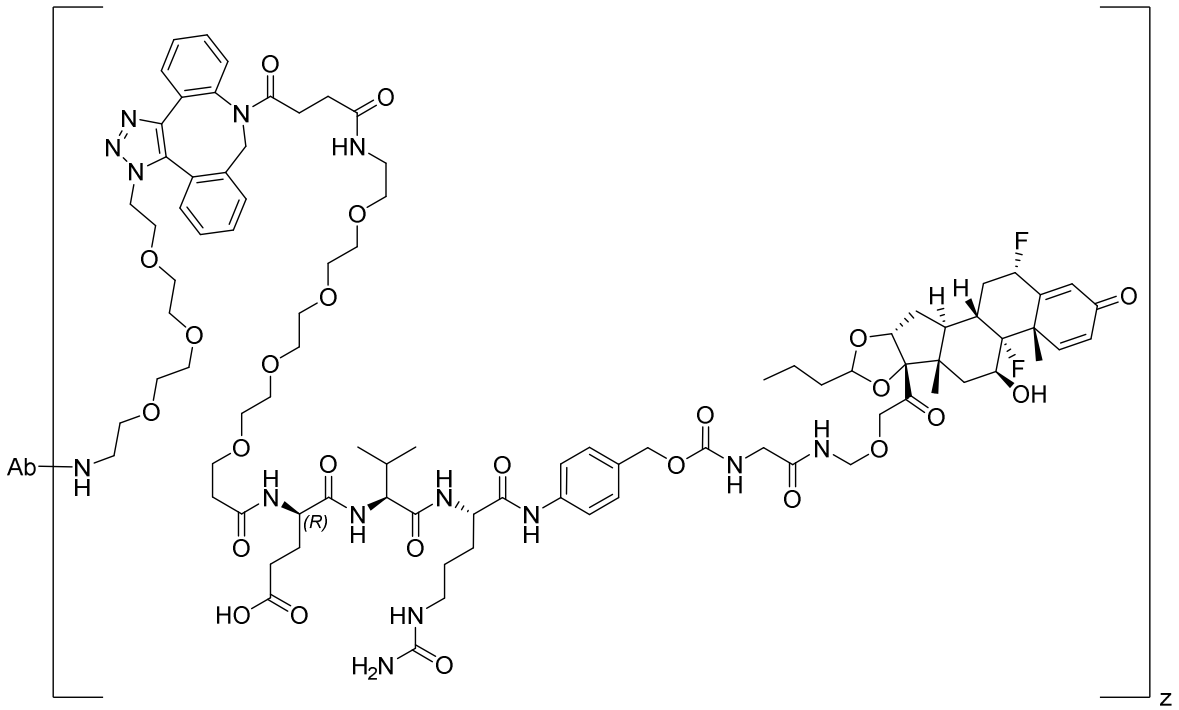

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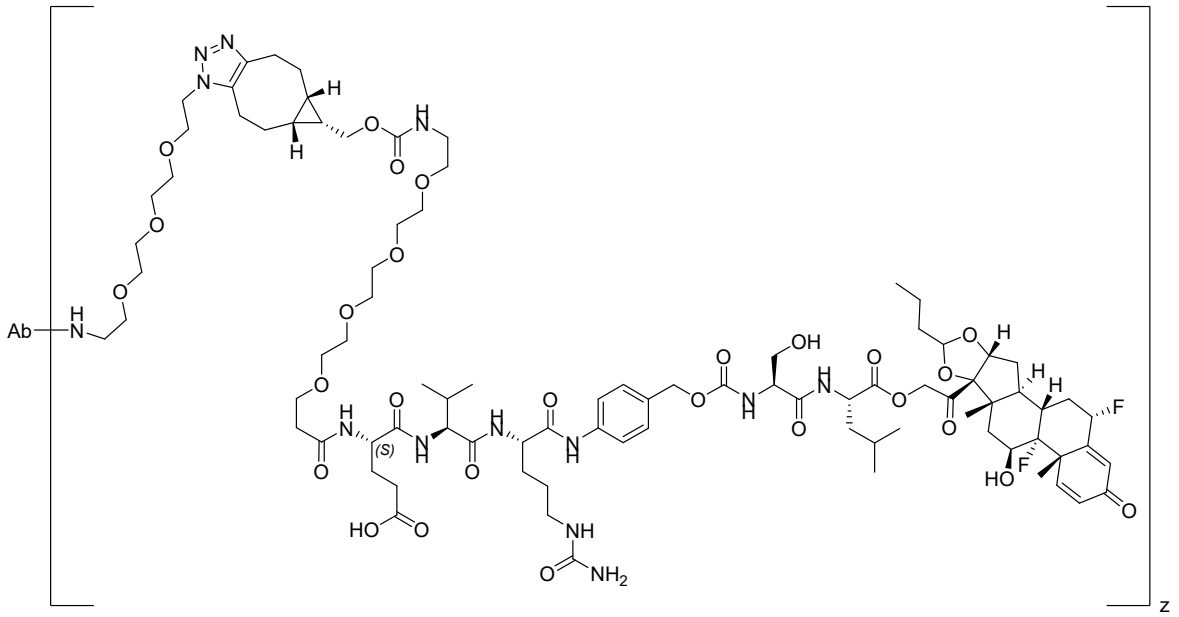

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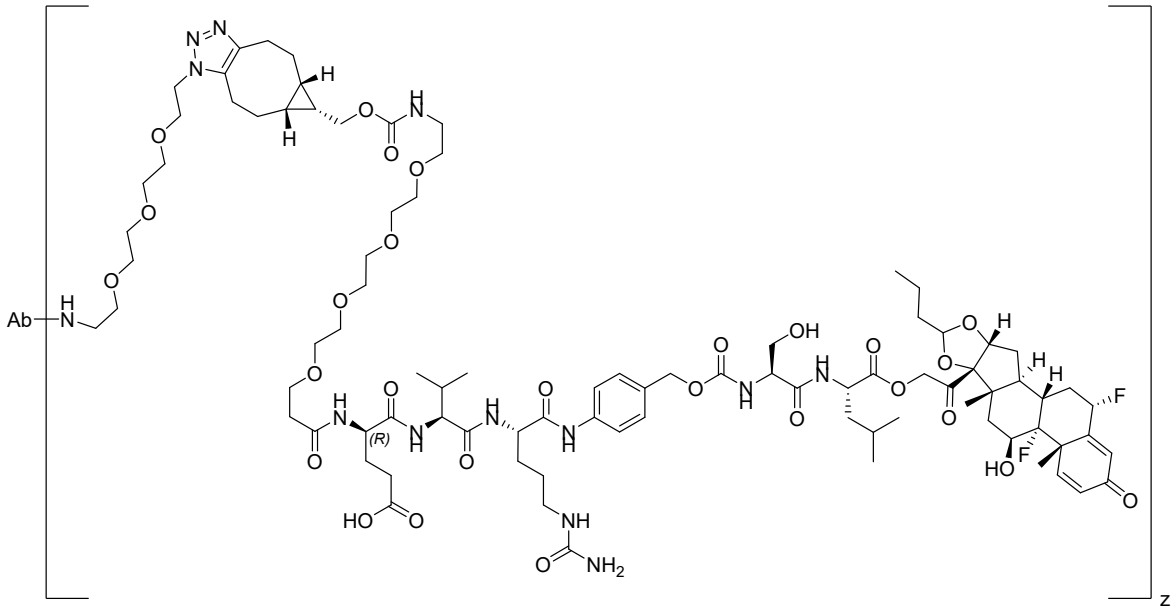

wherein **Ab** is an antibody or an antigen binding fragment thereof; and

z is an integer from one to four.