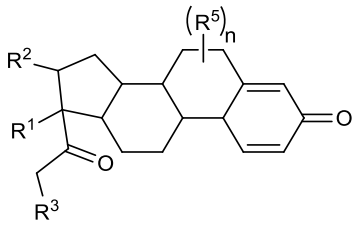
CLAIMS

What is claimed is:

1. A compound of Formula (**A**):



(**A**);

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

wherein:

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

R^1 and R^2 together form ,

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

wherein the alkyl, aryl, arylalkyl, and N-containing heterocycloalkyl are, independently in each instance, optionally substituted with $-NR^aR^b$;

R^3 is $-NR^aR^b$, -oxyaryl-NR^aR^b, or $-Z-A(R^P)_t$,

R^5 is, independently in each instance, -OH, halo, alkyl, or arylalkyl;

Z is O;

A is aryl or heteroaryl;

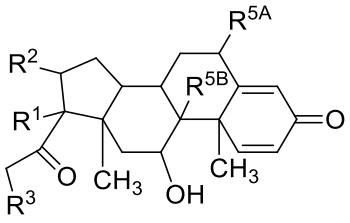
R^P is, independently in each instance, halo, optionally substituted alkyl, -OH, or $-NR^aR^b$; wherein at least one R^P is $-NR^aR^b$;

R^a and R^b are, independently in each instance, -H, optionally substituted alkyl, or optionally substituted aryl;

n is an integer from 0-19; and

t is an integer from 1-3.

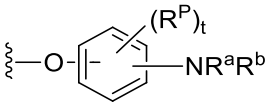
2. The compound of claim 1, wherein the compound of Formula (**A**) has the structure of Formula (**A^1**):



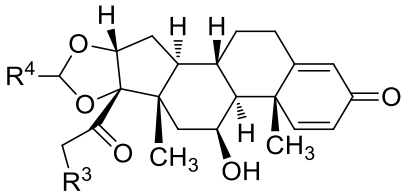
(**A^1**)

wherein R^1-R^3 are as defined above and R^{5A} and R^{5B} are each, independently, halo or a hydrogen atom.

3. The compound of claim 2, wherein R^1 and R^2 together form , wherein R^4 is aryl, arylalkyl, or alkyl, wherein the aryl, arylalkyl, and alkyl are optionally substituted with $-NR^aR^b$.

4. The compound of any of claims 1-3, wherein R^3 is $-NR^aR^b$ or , wherein R^P is halo, t is an integer from 0 to 2, R^a is H, or R^b is H or alkyl.

5. The compound of claim 1 according to Formula (**A^4**):



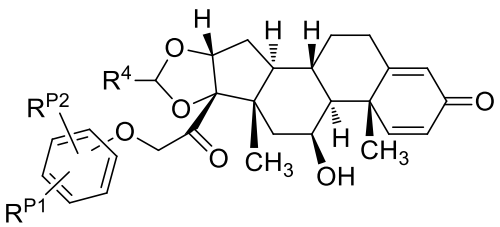
(**A^4**)

wherein R^3 is $–NR^aR^b$ and R^4 is alkyl, wherein R^a and R^b are each, independently, a hydrogen atom or alkyl, or R^a and R^b, taken together form a 3-7 membered ring.

6. The compound of claim 5, wherein R^4 is $C_{1\text{-}4}$ alkyl.

7. The compound of claim 5 or 6, wherein R^3 is $-NH_2$, $-NHCH_3$, or $-N(CH_3)_2$.

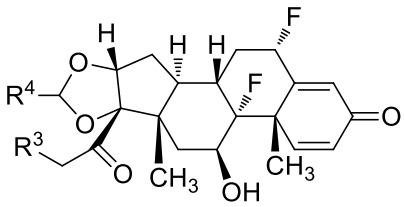
8. The compound of claim 1 according to Formula (**A^5**):



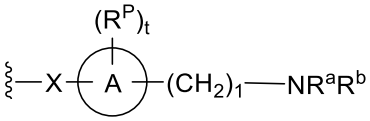
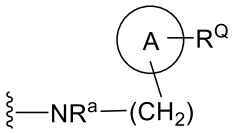
(**A^5**)

wherein R^4 is alkyl, R^{P1} is halo or a hydrogen atom, and R^{P2} is $-NR^aR^b$, wherein R^a and R^b are each, independently, a hydrogen atom or alkyl.

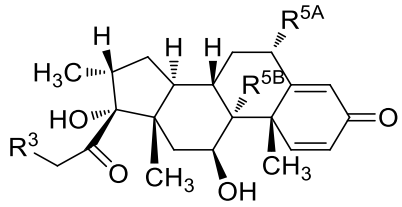
9. The compound of claim 1 according to Formula (**A^6**):



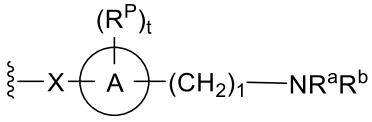
(**A^6**)

wherein R^3 is  ,  or NR^aR^b, wherein X is O or NR^a,  is aryl or heteroaryl, R^P is halo, t is an integer from 0-2, R^a and R^b are each, independently, a hydrogen atom or alkyl, R^Q is alkoxy, and R^4 is alkyl

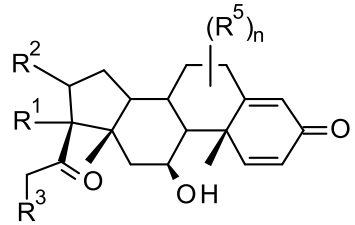
10. The compound of claim 1 according to Formula (**A^7**)



(**A^7**)

wherein R^3 is  ,wherein X is O or NR^a,  is aryl or heteroaryl, R^P is halo, t is an integer from 0-2, R^a and R^b are each, independently, a hydrogen atom or alkyl, R^{5A} is a hydrogen atom or fluoro, and R^{5B} is fluoro.

11. The compound of claim 1 according to Formula **1000**:



1000

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

wherein:

R^1 and R^2 are, independently, selected from the group consisting of -H, -OH, alkyl, -O-C(O)-alkyl, and halo; or

R^1 and R^2 together form ,

either (a), or (b), or (c):

(a) R^3 is selected from the group consisting of -X-arylene-Y-NR^aR^b and -X-heteroarylene-Y-NR^aR^b; wherein X is -O-; wherein Y is absent; and

R^4 is selected from the group consisting of alkyl, aryl, alkylaryl, arylalkyl, heteroaryl, -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, -X-heteroarylene-Y-NR^aR^b, and N-containing heterocycloalkyl; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

or

(b) R^3 is selected from the group consisting of -NR^aR^b, -X-arylene-Y-NR^aR^b, and -X-heteroarylene-Y-NR^aR^b; wherein X is -O-; wherein Y is absent; and

R^4 is selected from the group consisting of -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, -X-heteroarylene-Y-NR^aR^b, and N-containing heterocycloalkyl; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

or

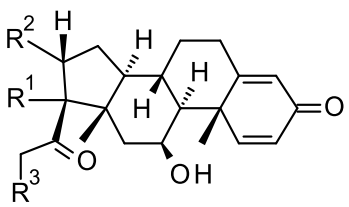
(c) R^3 is -NR^aR^b; and

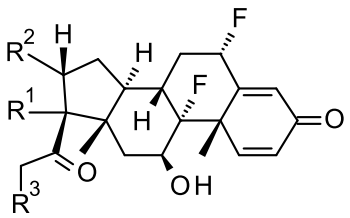
R^4 is alkyl;

R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; n is an integer from 0-19; and each R^5 is positioned on any ring atom;

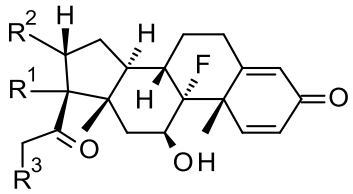
R^a and R^b are, independently in each instance, selected from the group consisting of -H and alkyl; or R^a and R^b cyclize to form cycloheteroalkyl with three to six ring atoms, including one hetero atom, which is the N to which they are attached.

12. The compound of claim 11 according to Formula **1010**, **1020**, **1030**, or **1040**:

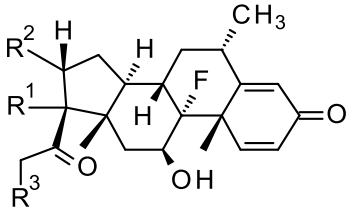




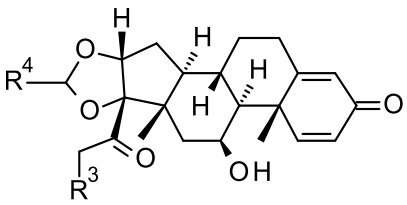
1010



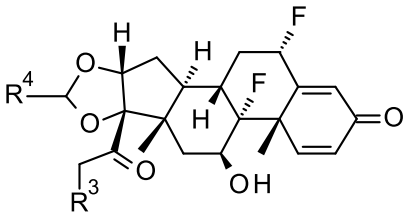
1020



1030



1040



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

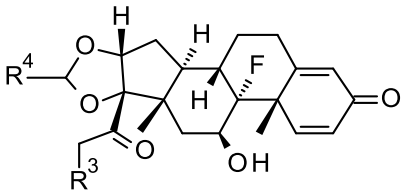
13. The compound of claim 12 wherein R^1 is -OH; R^2 is -H, -CH_3 or -OH; and R^3 is -NH_2.

14. The compound of claim 11 according to Formula **1110**, **1120**, **1130**, or **1140**:

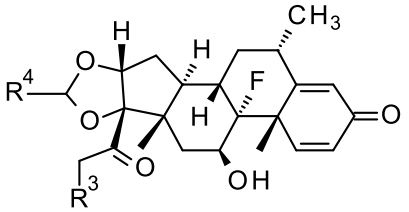
1110

1120

1130



1140



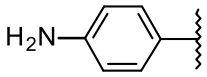
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

15. The compound of claim 14 wherein

R^3 is -NR^aR^b; and

R^4 is n-propyl.

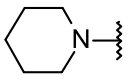
16. The compound of claim 15 according to formula **1120**.

17. The compound of claim 14 wherein R^4 is $H_2NCH_2CH_2$- or .

18. The compound of claim 14 wherein

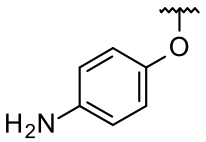
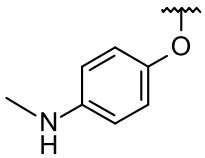
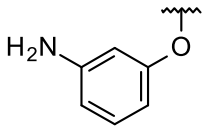
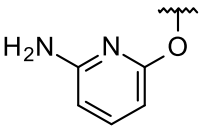
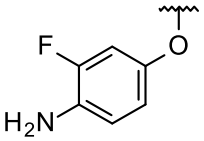
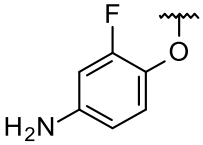
R^3 is -NR^aR^b, -X-arylene-Y-NR^aR^b, or -X-heteroarylene-Y-NR^aR^b; wherein X is -O-; wherein Y is absent; and

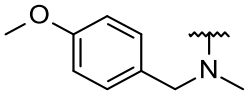
R^4 is alkyl, aryl, alkylaryl, or arylalkyl.

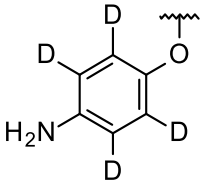
19. The compound of claim 18 wherein R^3 is $-NH_2$, $-N(H)CH_3$, $-N(CH_3)_2$, or .

20. The compound of claim 18 wherein R^3 is -O-arylene-NR^aR^b or -O-heteroarylene-NR^aR^b; wherein aryl or heteroaryl is optionally substituted with halogen, deuterium, hydroxyl, or methoxyl.

21. The compound of claim 18 wherein R^3 is -O-phenyl-NR^aR^b or -O-heteroarylene-NR^aR^b; wherein phenyl or heteroaryl is optionally substituted with halogen or deuterium.

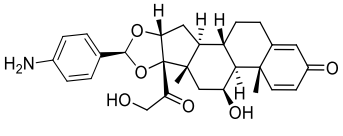
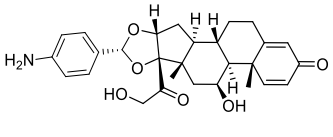
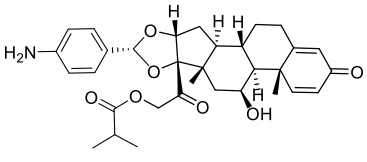
22. The compound of claim 18 wherein R^3 is , , , , , or .

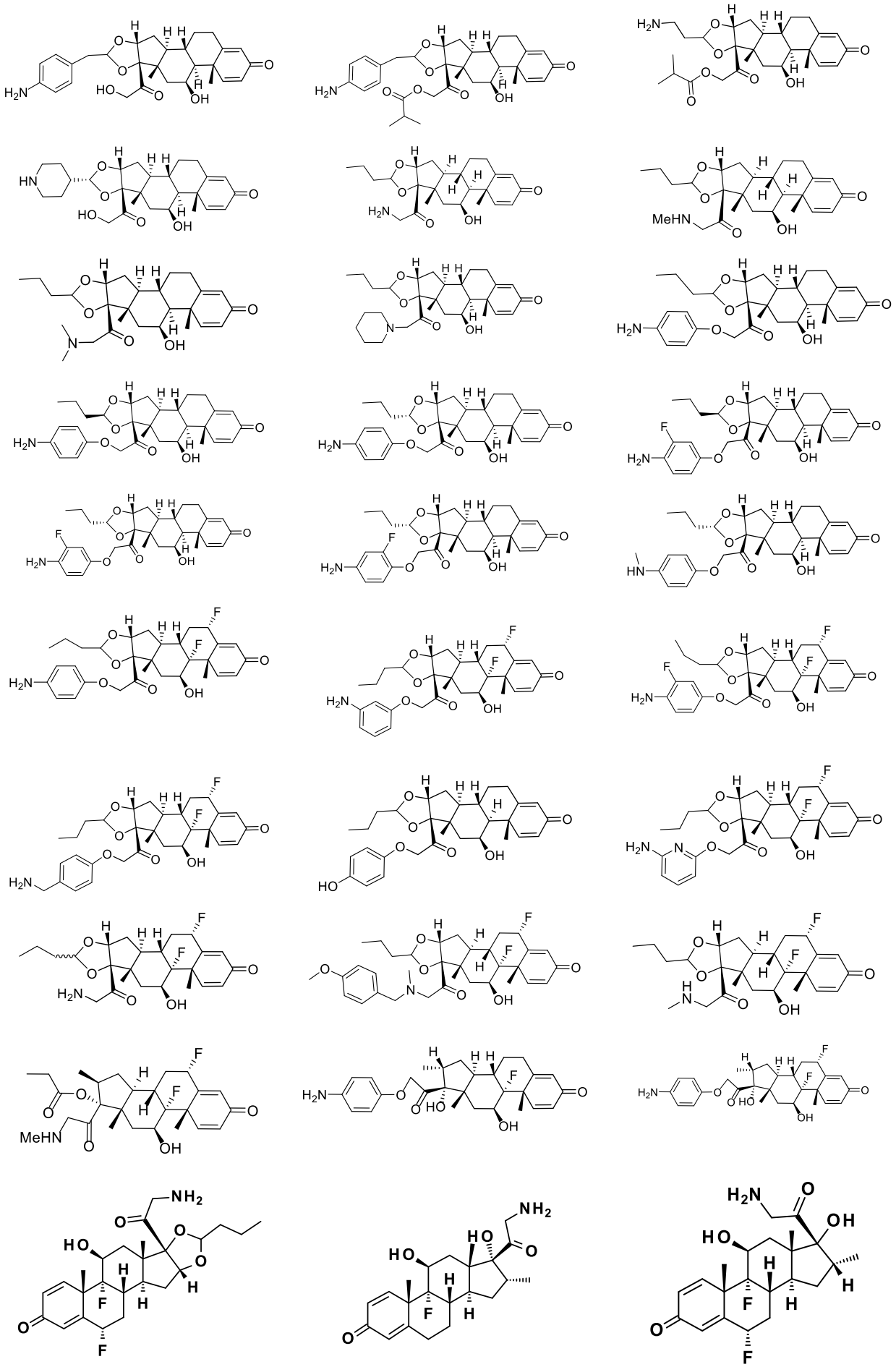
23. The compound of claim 18 wherein R^3 is .

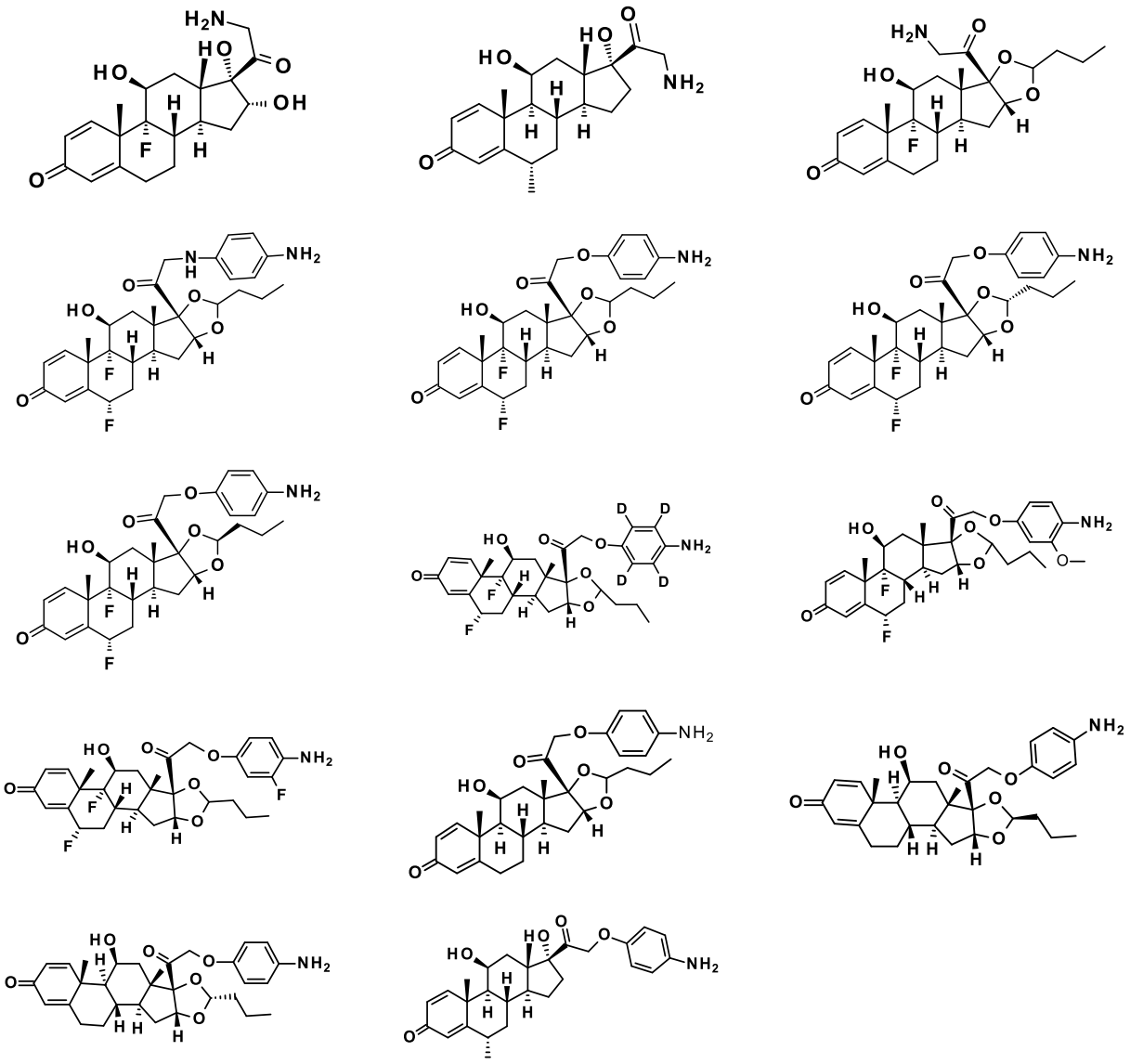
24. The compound of claim 18, wherein R^3 is .

25. The compound of any of claims 18-24, wherein R^4 is n-propyl.

26. The compound of claim 1, wherein the compound is:



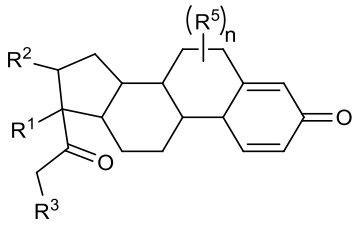


or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

27. A conjugate compound comprising a binding agent conjugated to a compound of any of claims
1-26.

28. A conjugate compound comprising a binding agent conjugated to a compound of any of claims
1-26 and a cyclodextrin (**CD**).

29. A conjugate compound comprising a binding agent conjugated to a compound of Formula (**A'**) and a cyclodextrin (**CD**); wherein the compound of Formula (**A'**) is:



(**A'**);

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

wherein:

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

R^1 and R^2 together form ,

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

wherein the alkyl, aryl, arylalkyl, and N-containing heterocycloalkyl are, independently in each instance, optionally substituted with $-NR^aR^b$;

R^3 is $-NR^aR^b$, -oxyaryl-NR^aR^b, or -Z-A$(R^P)_t$,

R^5 is, independently in each instance, -OH, halo, alkyl, or arylalkyl;

Z is O;

A is aryl or heteroaryl;

R^P is, independently in each instance, halo, optionally substituted alkyl, -OH, or $-NR^aR^b$;

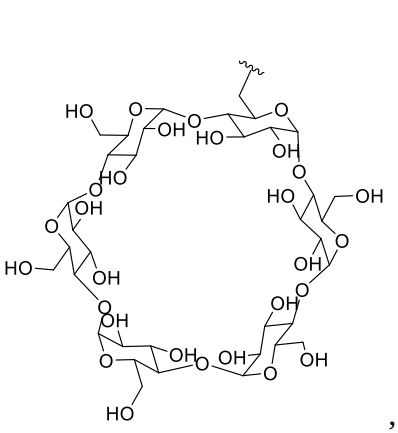
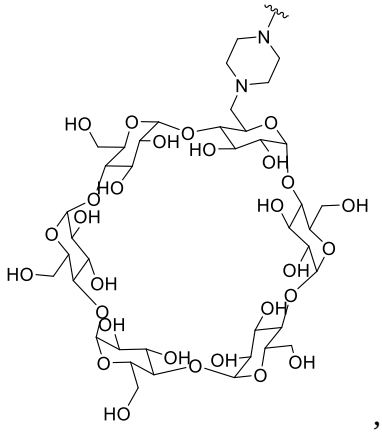
wherein at least one R^P is $-NR^aR^b$;

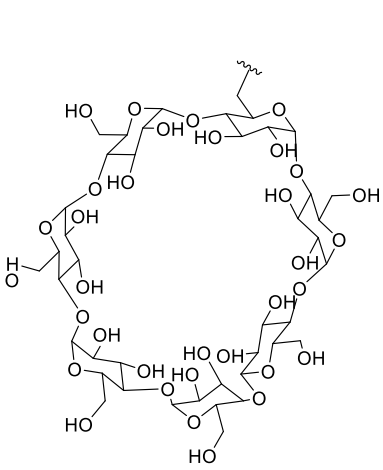
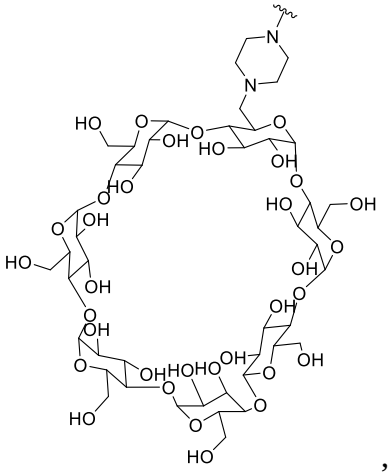
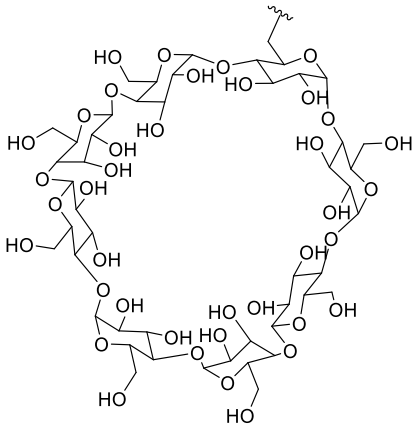
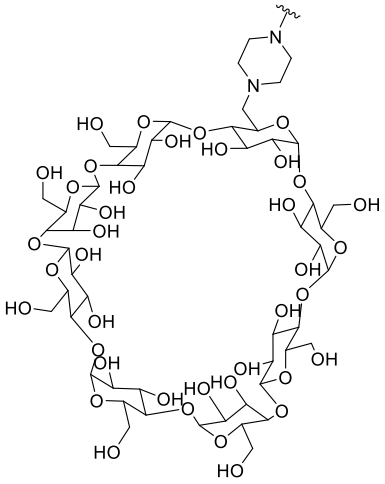
R^a and R^b are, independently in each instance, -H, optionally substituted alkyl, or optionally substituted aryl;

n is an integer from 0-19; and

t is an integer from 1-3.

30. The conjugate compound of claim 28 or 29, wherein **CD** is selected from the group consisting of

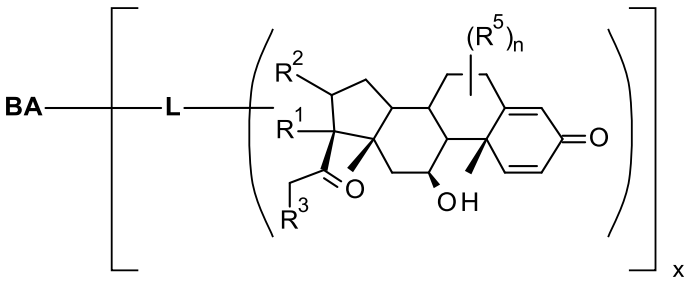
, ,


,

,

, and

, wherein ⁄ indicates the bond through which the CD is linked to the binding agent conjugate.

31. The conjugate compound of any one of claims 27 to 30, wherein the binding agent is an antibody or antigen binding fragment thereof.

32. The conjugate compound of claim 27, wherein the binding agent is an antibody or antigen binding fragment thereof

33. The conjugate compound of claim 27, according to Formula **1200**:



1200

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

wherein:

R^1 and R^2 are, independently, selected from the group consisting of -H, -OH, alkyl, -O-C(O)-alkyl, and halo; or

R^1 and R^2 together form ,

either (a), or (b), or (c):

(a) R^3 is selected from the group consisting of -X-arylene-Y-NR^aR^b or -X-heteroarylene-Y-NR^aR^b; wherein X is -O-; wherein Y is absent; and

R^4 is selected from the group consisting of alkyl, aryl, alkylaryl, arylalkyl, heteroaryl, -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, -X-heteroarylene-Y-NR^aR^b, and N-containing heterocycloalkyl; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

or

(b) R^3 is selected from the group consisting of -NR^aR^b, -X-arylene-Y-NR^aR^b, and -X-heteroarylene-Y-NR^aR^b; wherein X is -O-; wherein Y is absent; and

R^4 is selected from the group consisting of -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, -X-heteroarylene-Y-NR^aR^b, and N-containing heterocycloalkyl; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

or

(c) R^3 is -NR^aR^b; and

R^4 is alkyl;

R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; n is an integer from 0-19; and each R^5 is positioned on any ring atom;

R^a and R^b are, independently in each instance, selected from the group consisting of -H and alkyl; or R^a and R^b cyclize to form cycloheteroalkyl with three to six ring atoms, including one hetero atom, which is the N to which they are attached;

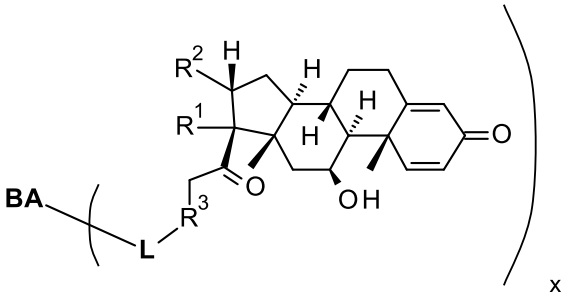
BA is a binding agent;

each L is an optional linker;

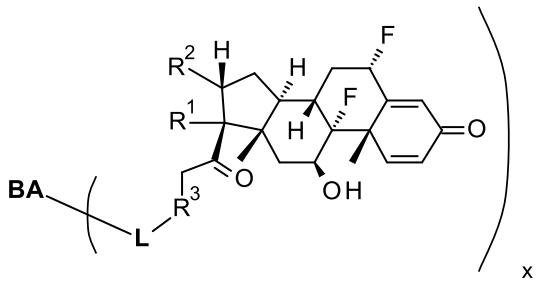
BA or L is covalently bonded to R^3 or R^4; and

x is an integer from 1 to 30.

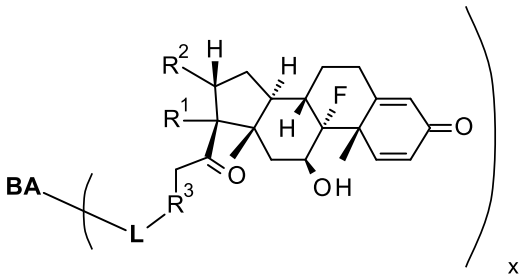
34. The conjugate compound of claim 33 according to Formula **1210**, **1220**, **1230**, or **1240**:



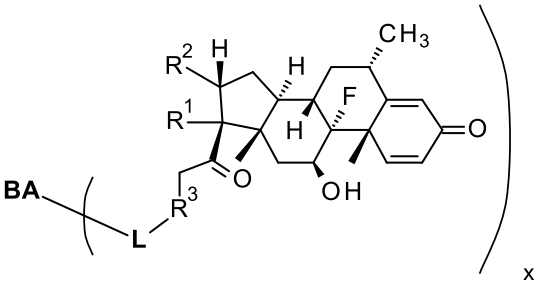
1210



1220



1230

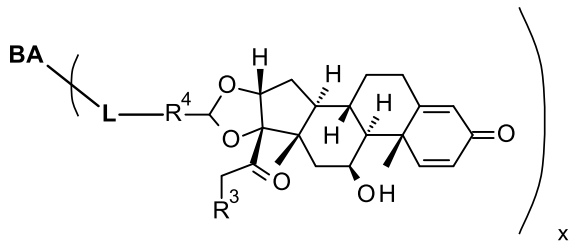


1240

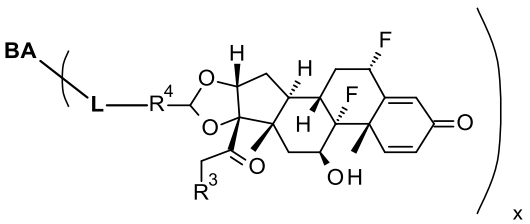
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;

wherein R^3 is covalently bonded to L or BA.

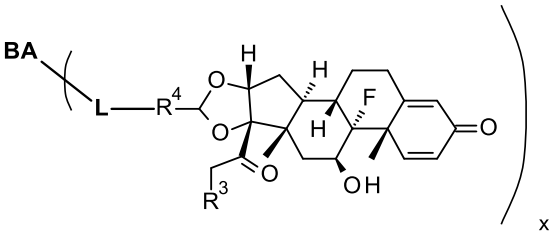
35. The conjugate compound of claim 33 according to Formula **1310**, **1320**, **1330**, or **1340**:



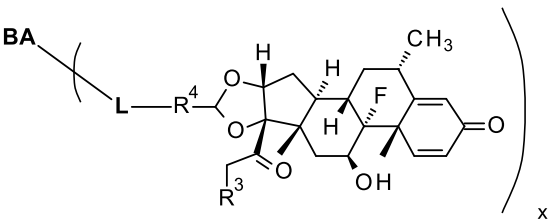
1310



1320



1330

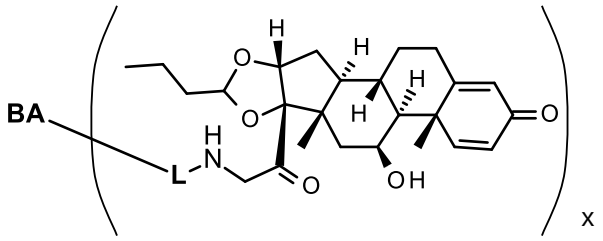


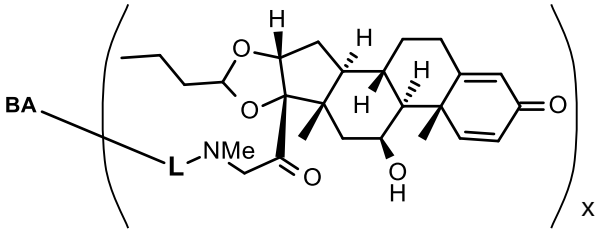
1340

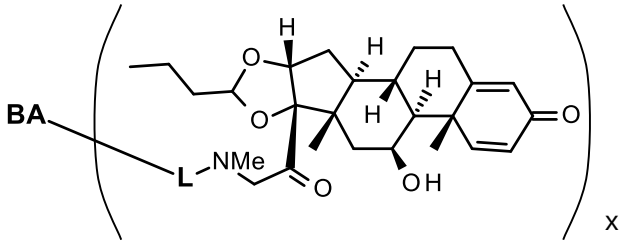
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;

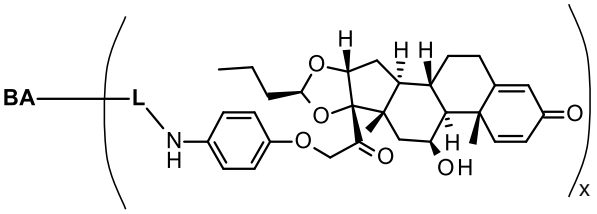
wherein R^4 is covalently bonded to L or BA.

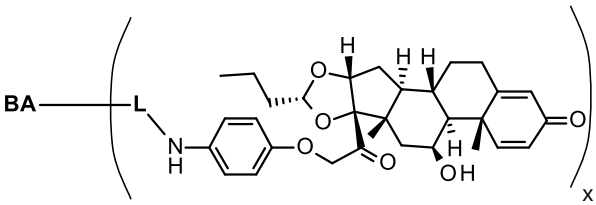
36. The conjugate compound of claim 27 selected from the group consisting of:

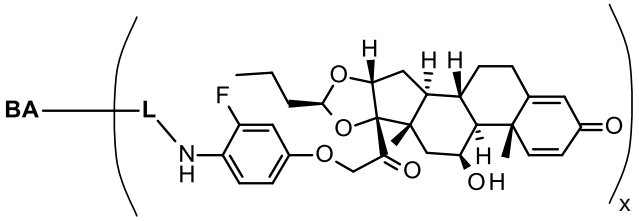


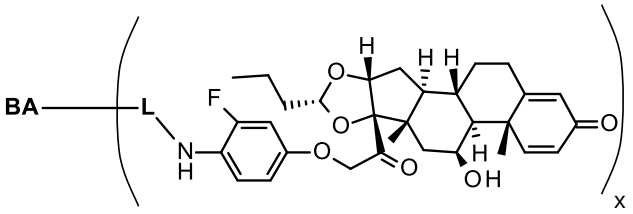


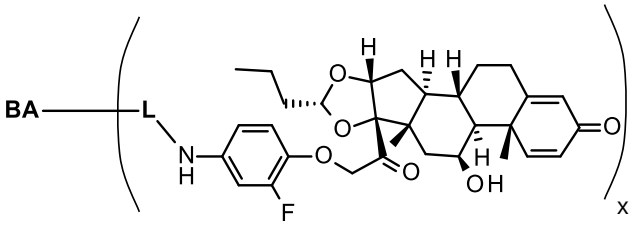


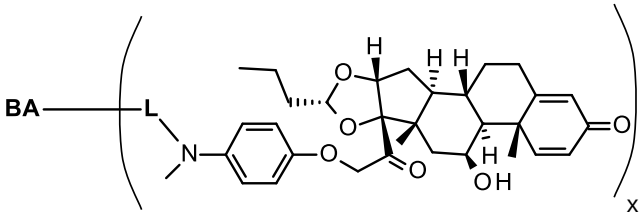


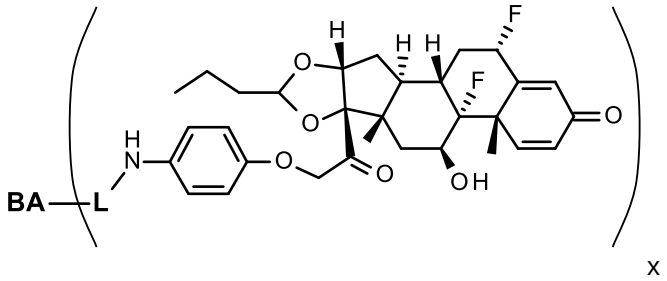


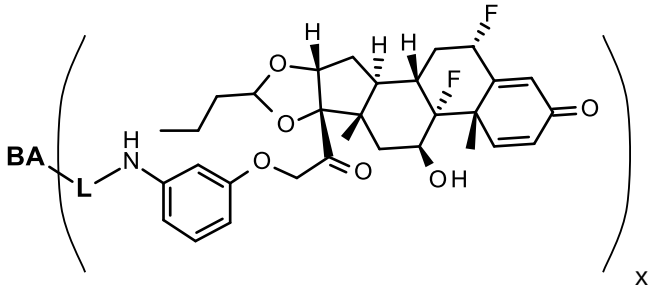


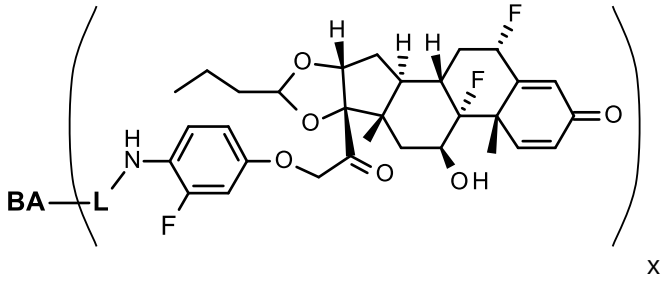


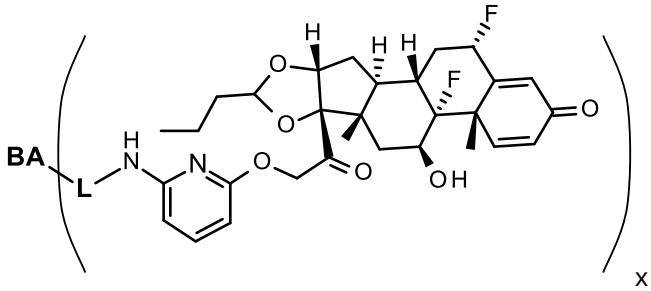


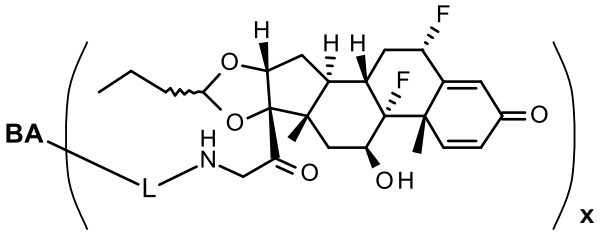


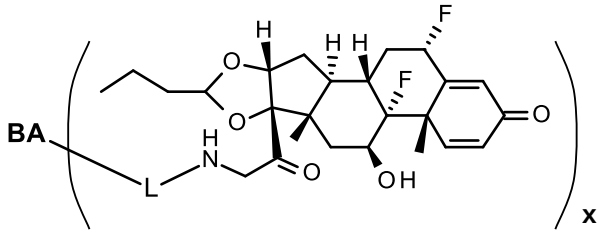


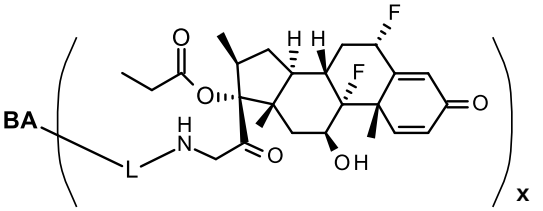


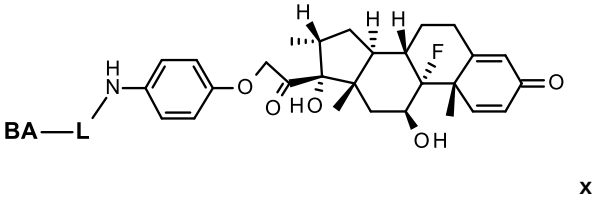


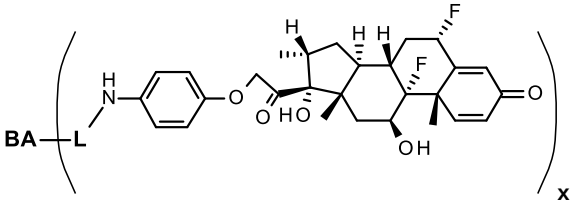


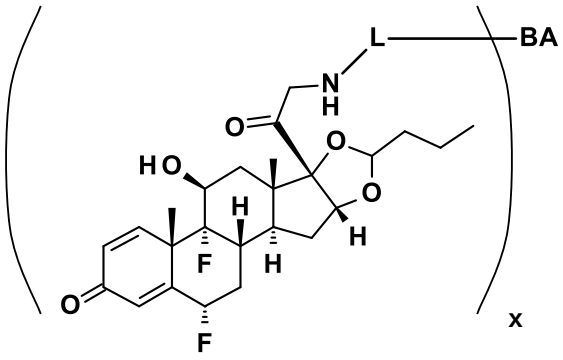


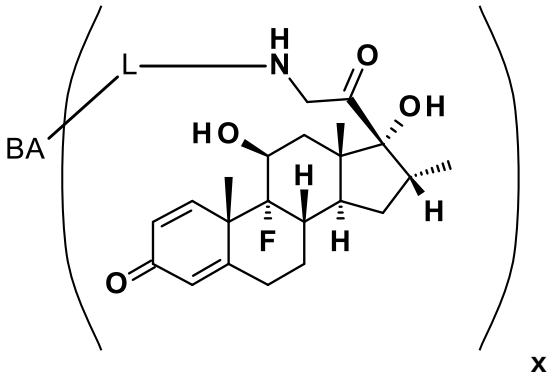


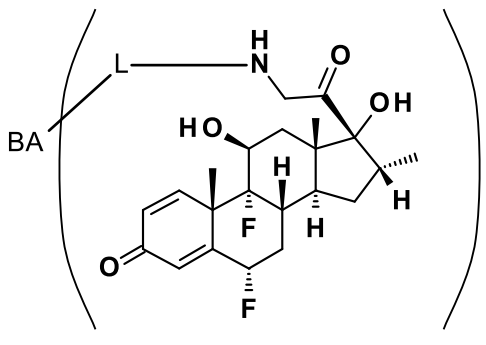


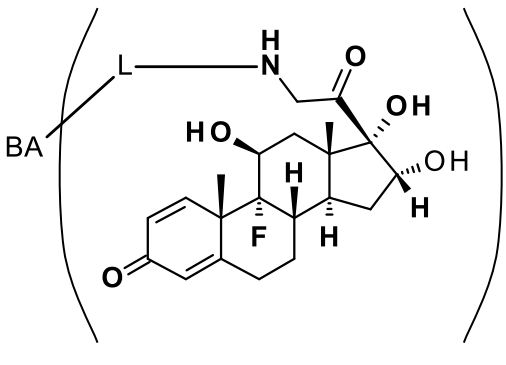


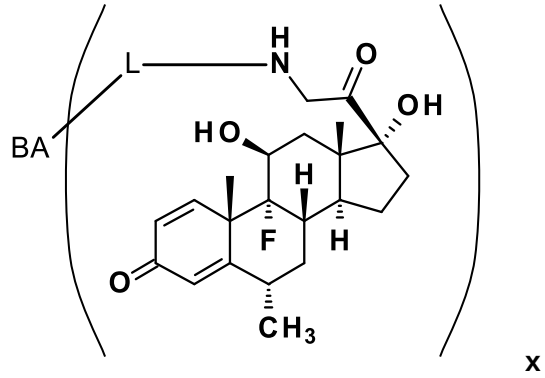


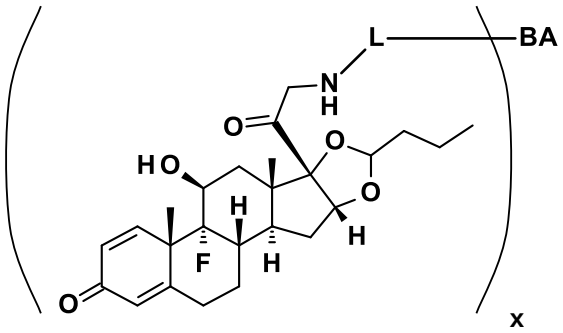


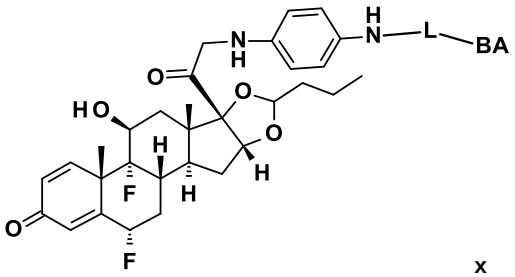


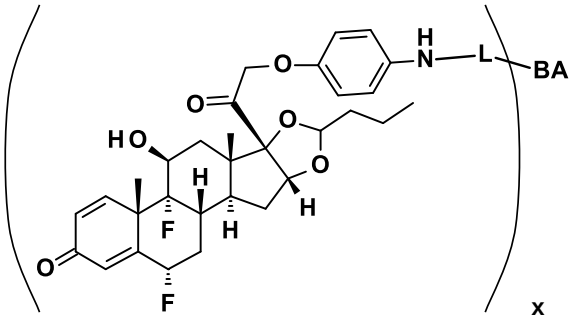


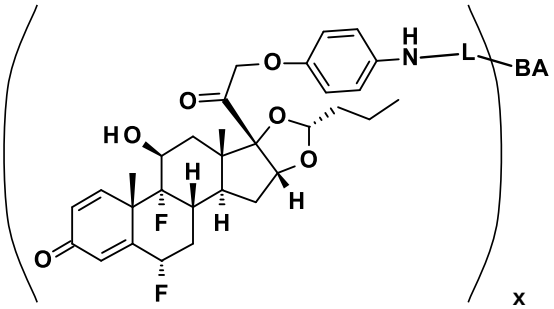


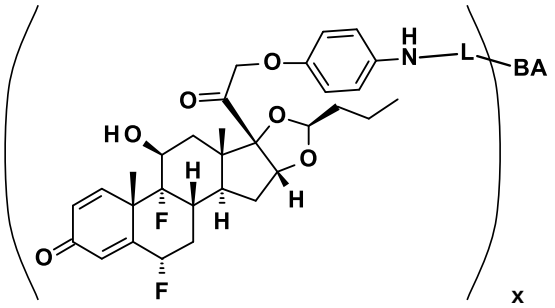


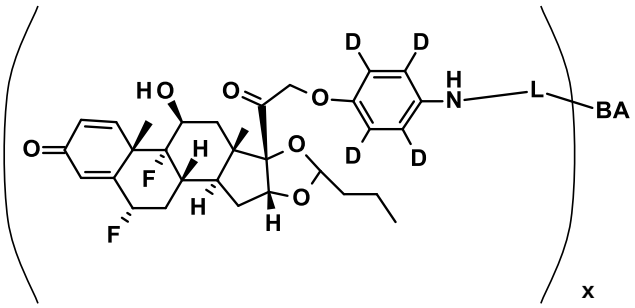


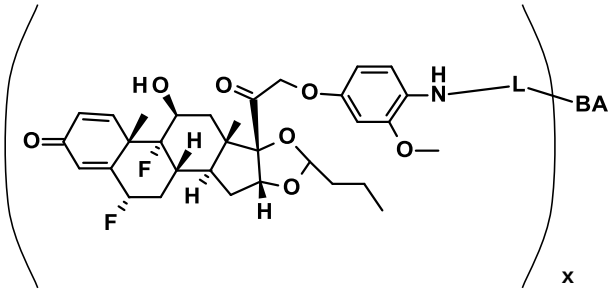


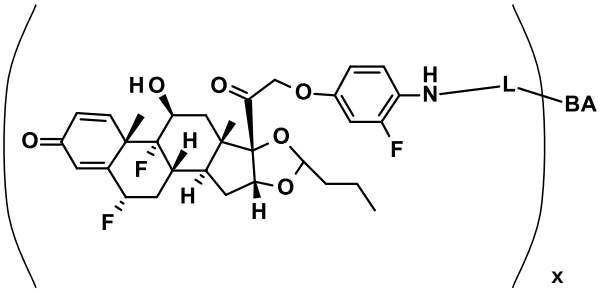


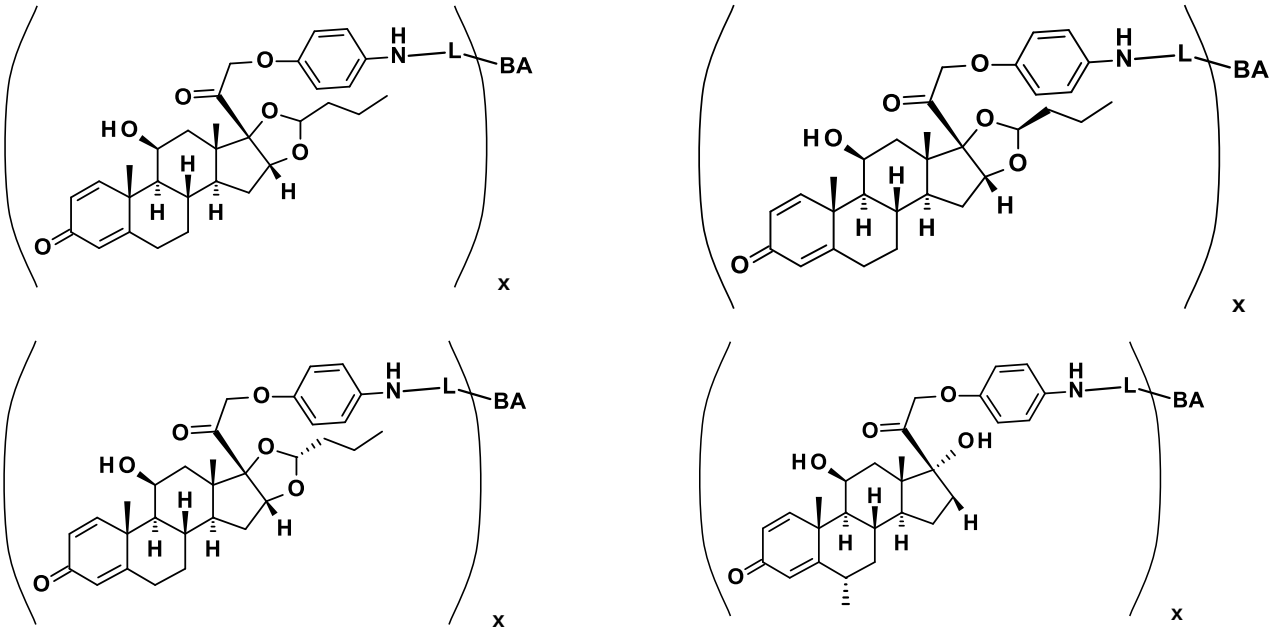












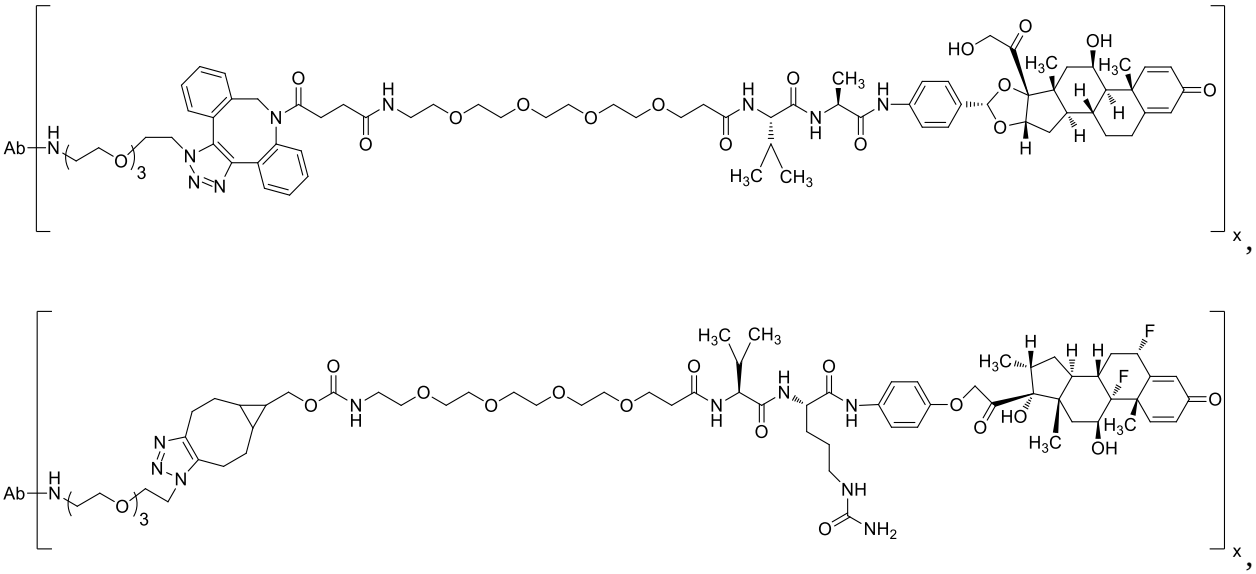
and pharmaceutically acceptable salts, solvates, and stereoisomers thereof;

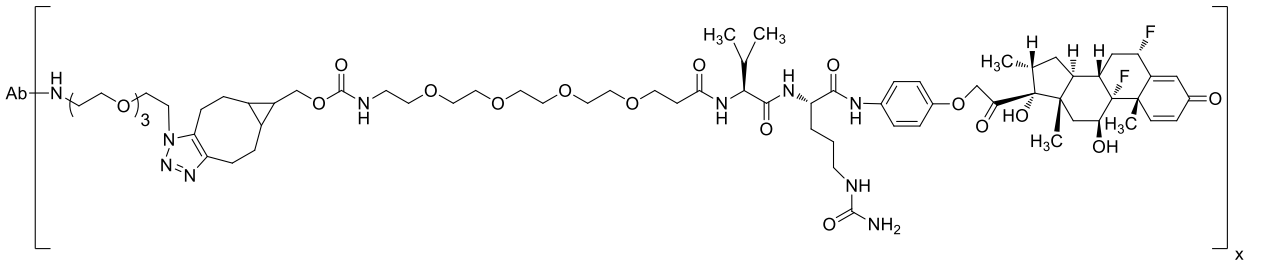
wherein each L is an optional linker;

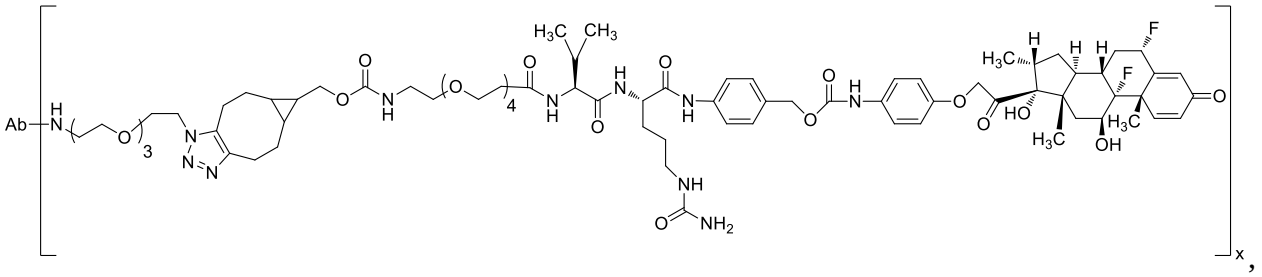
each BA is a binding agent; and

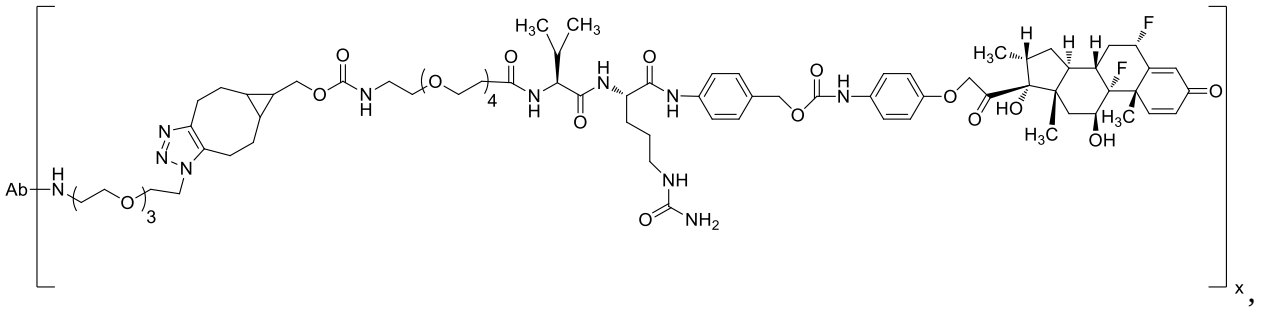
each x is an integer from 1 to 30.

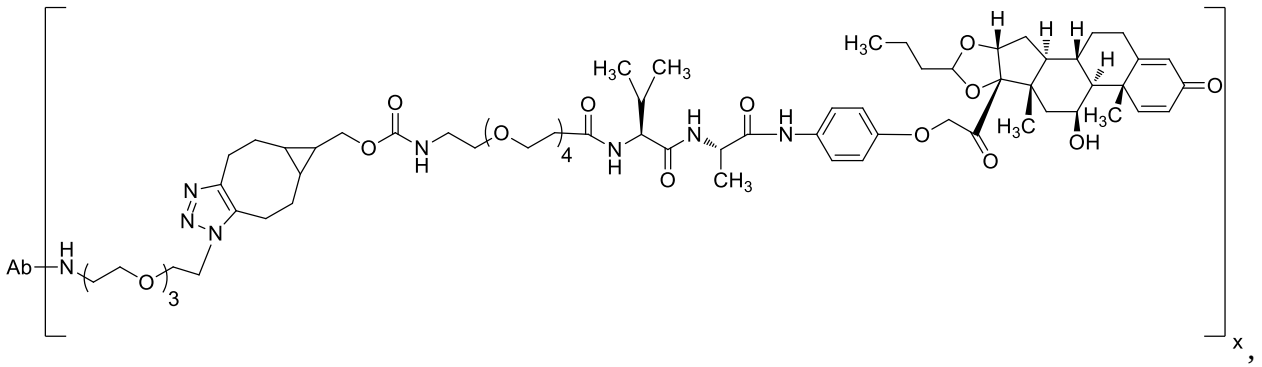
37. The conjugate compound of claim 27 selected from the group consisting of:

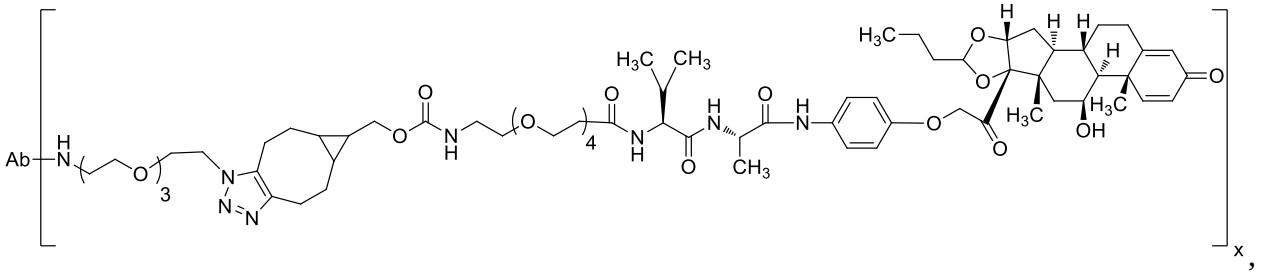


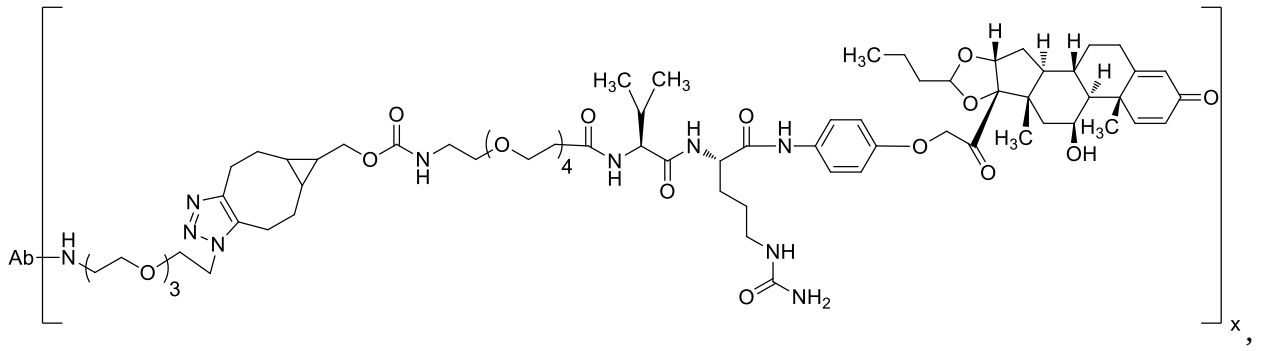


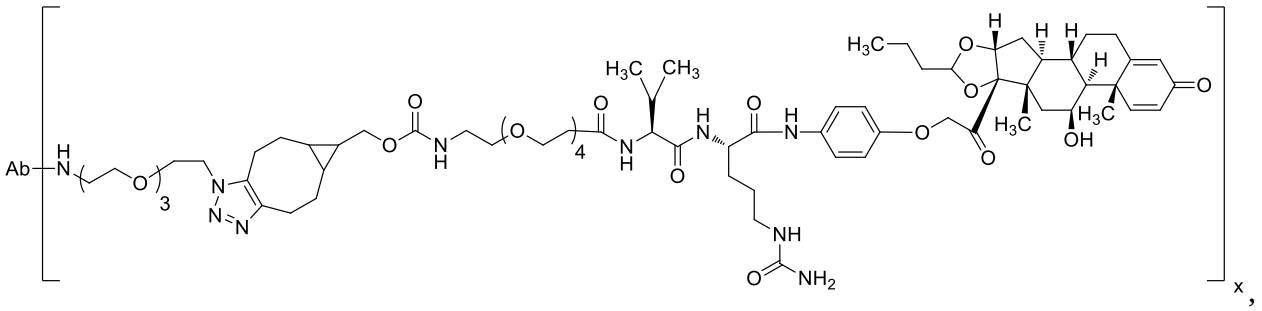


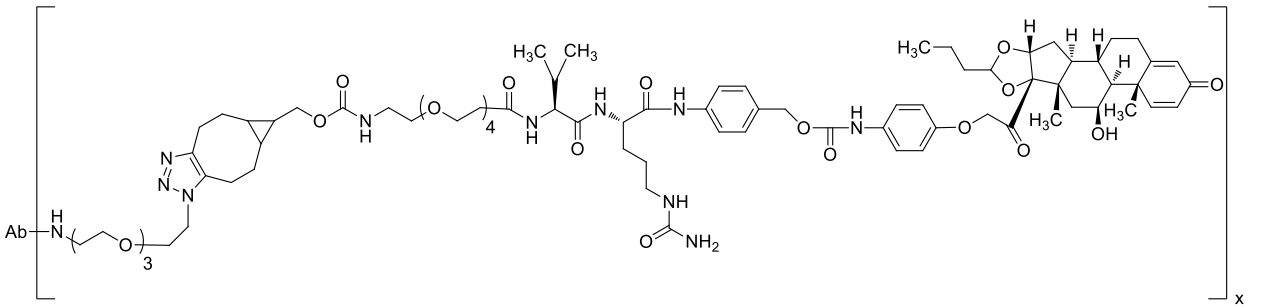


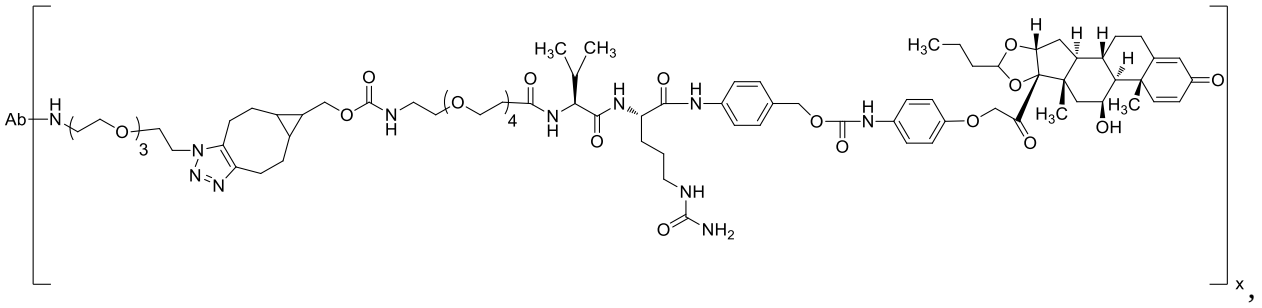


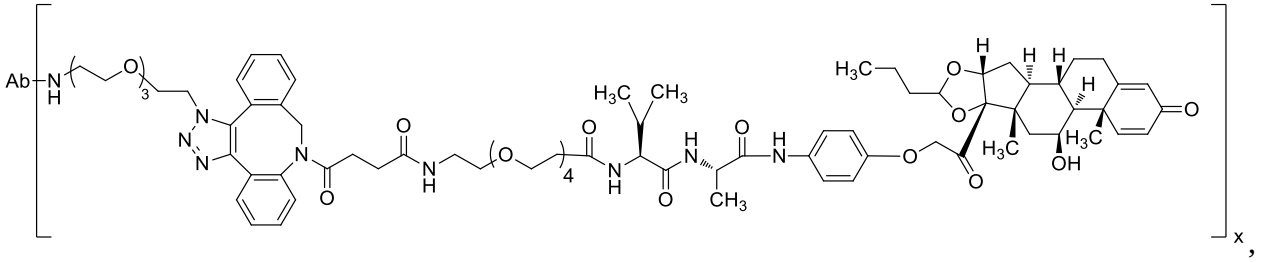


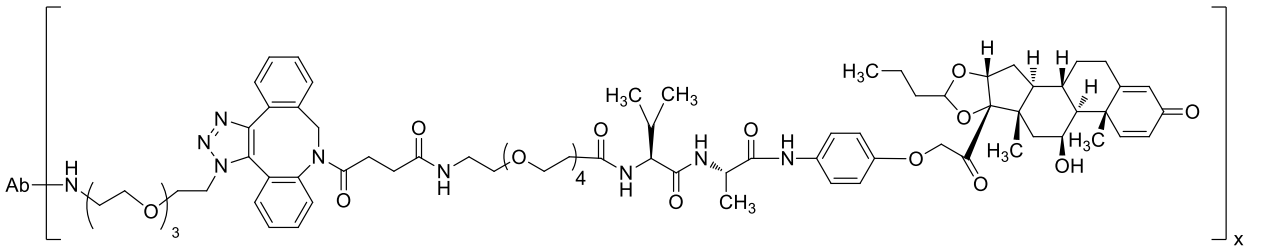


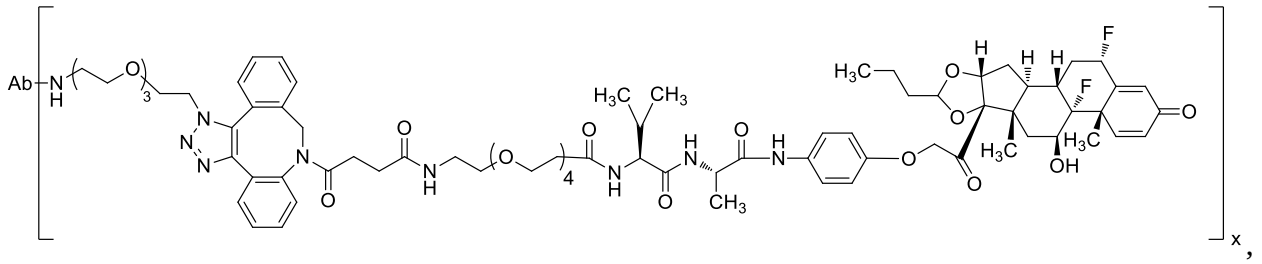


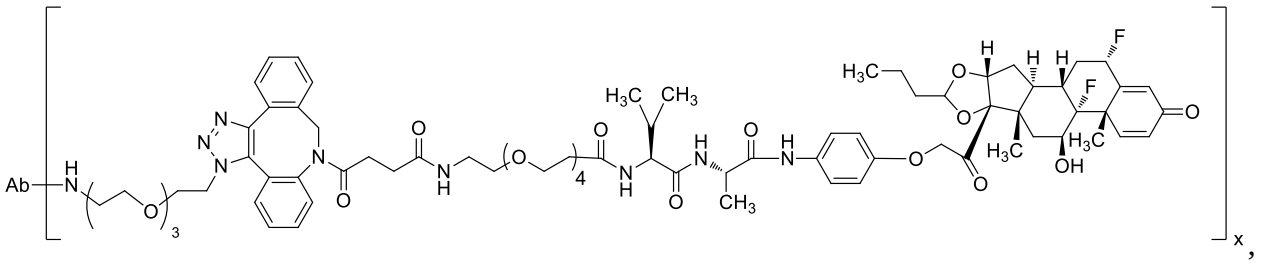


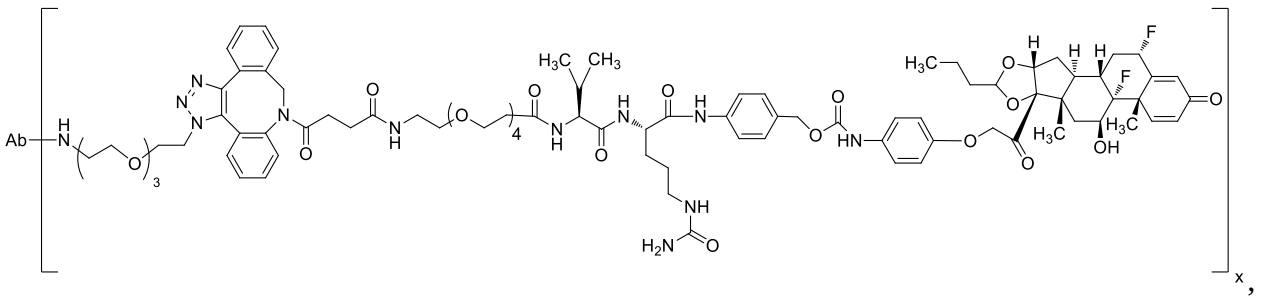


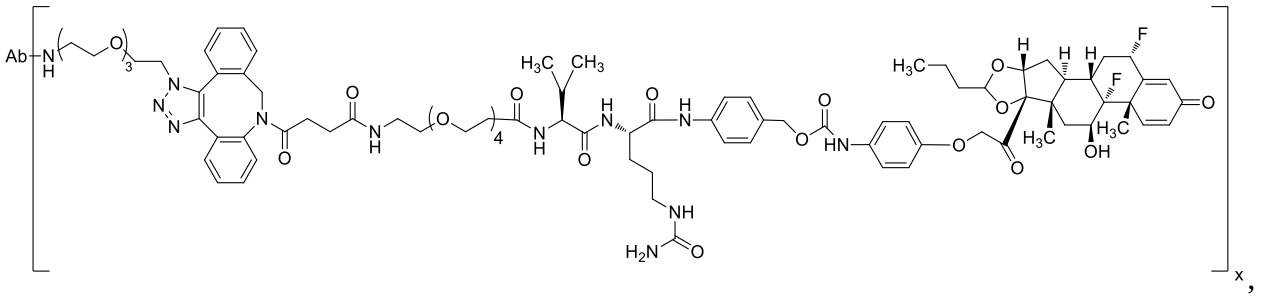


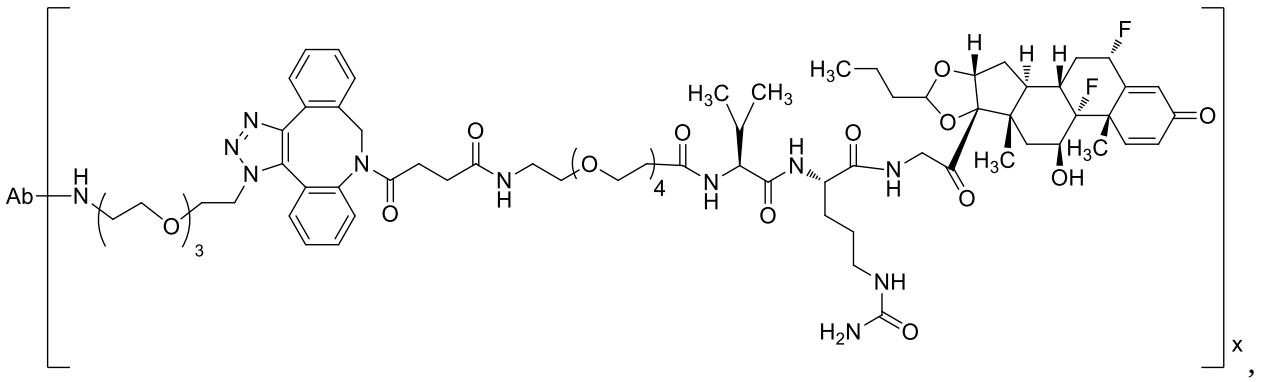


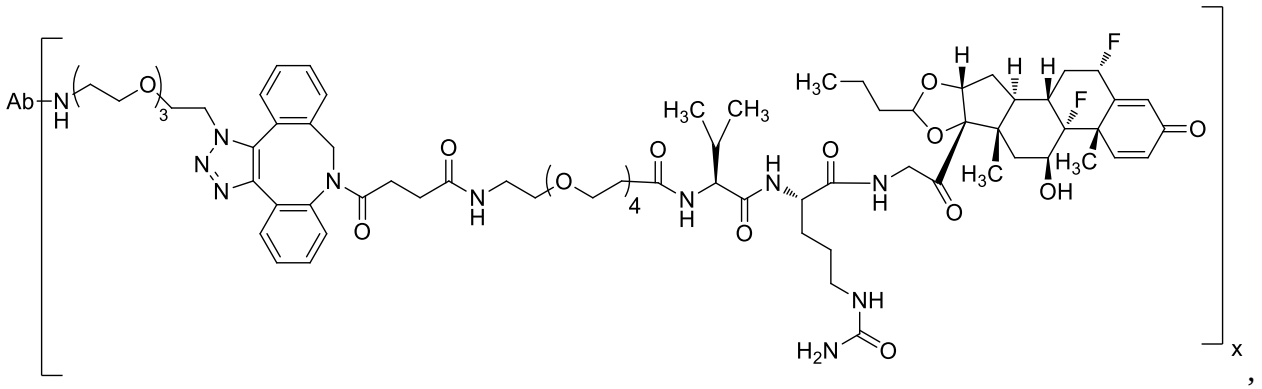


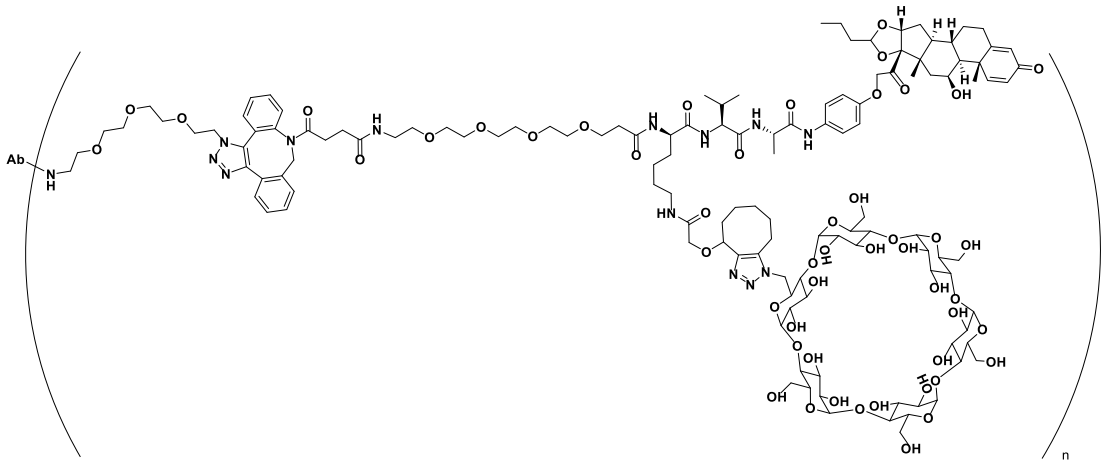


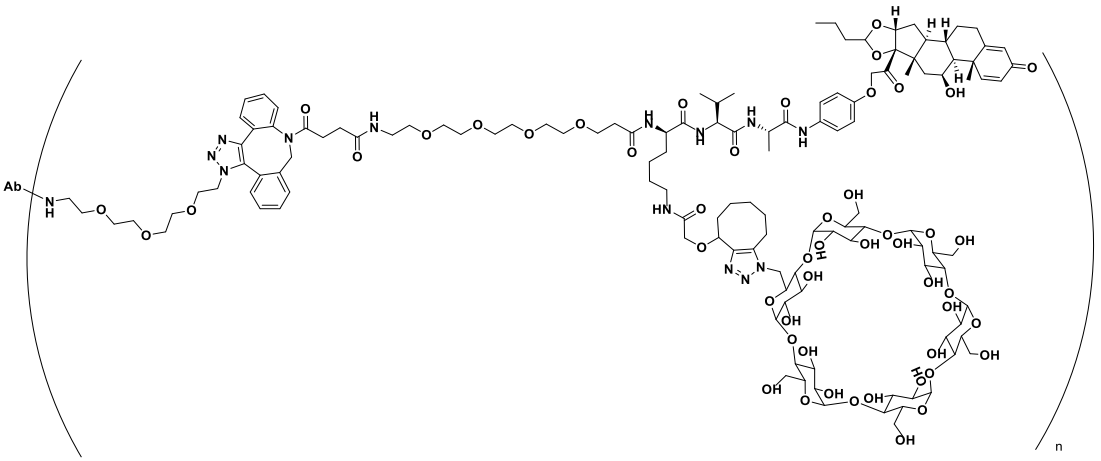


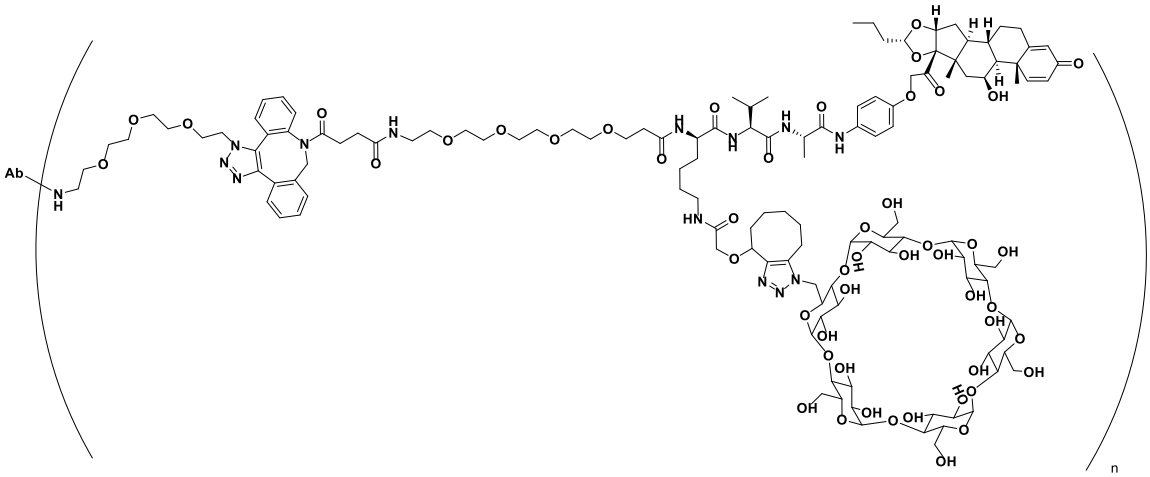


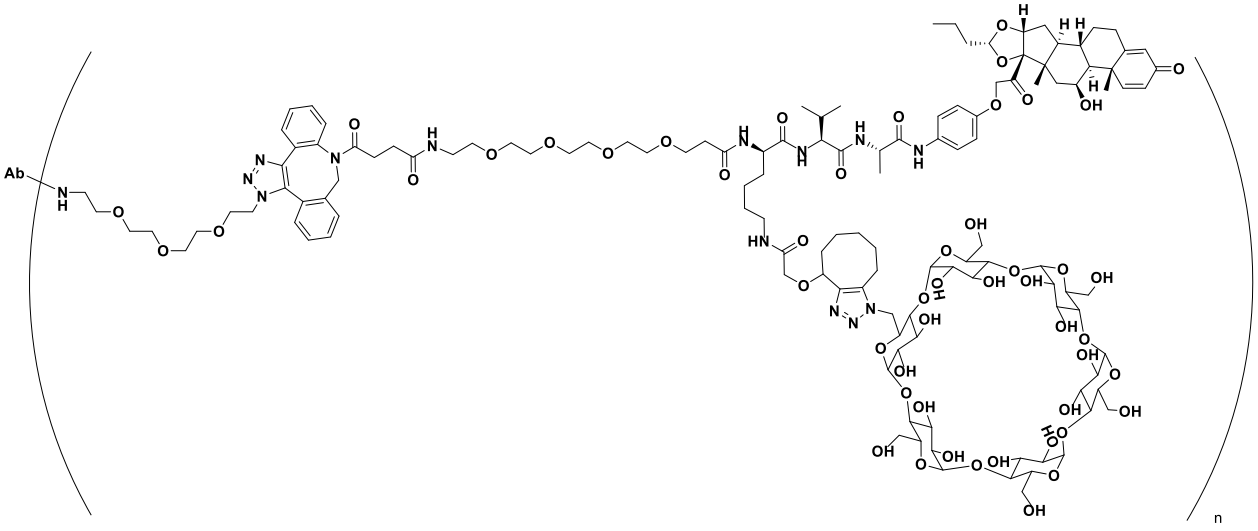


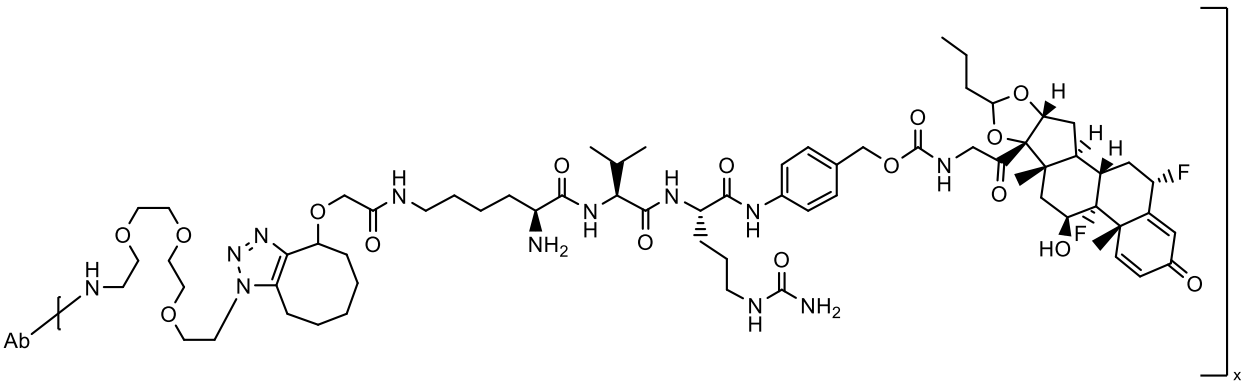




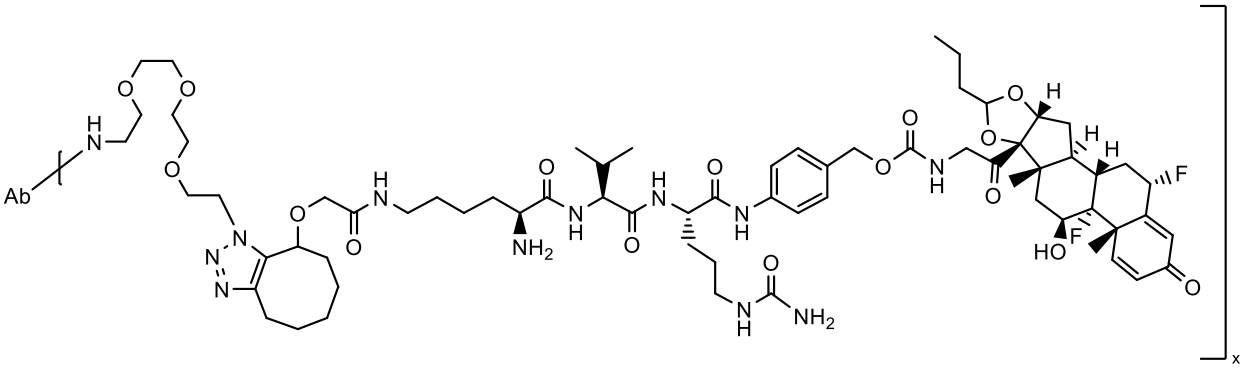




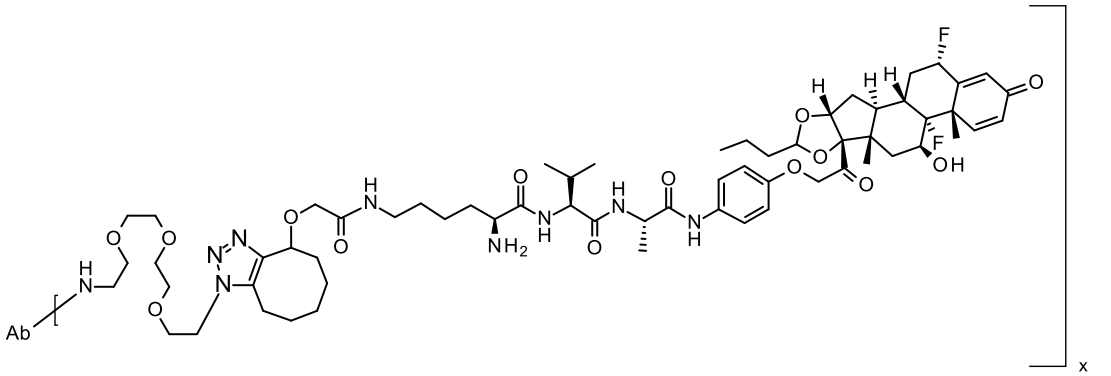




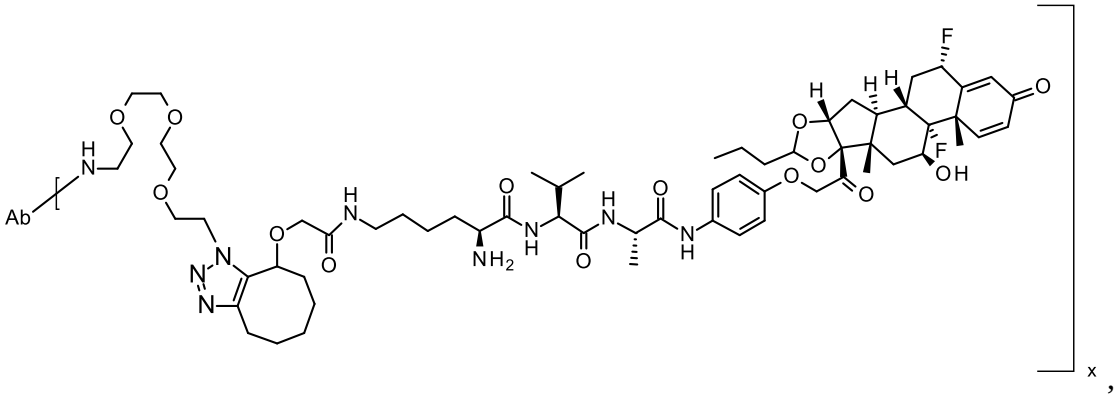
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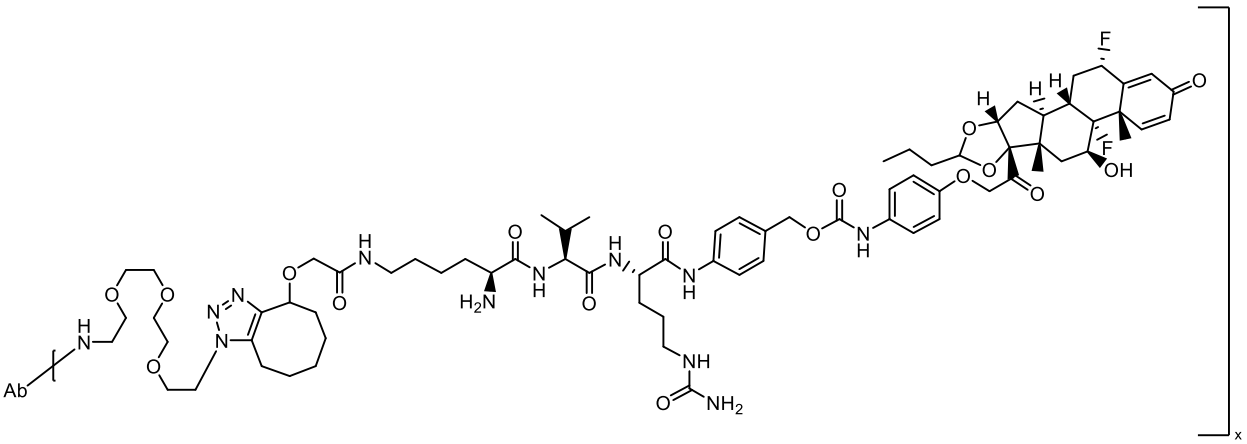
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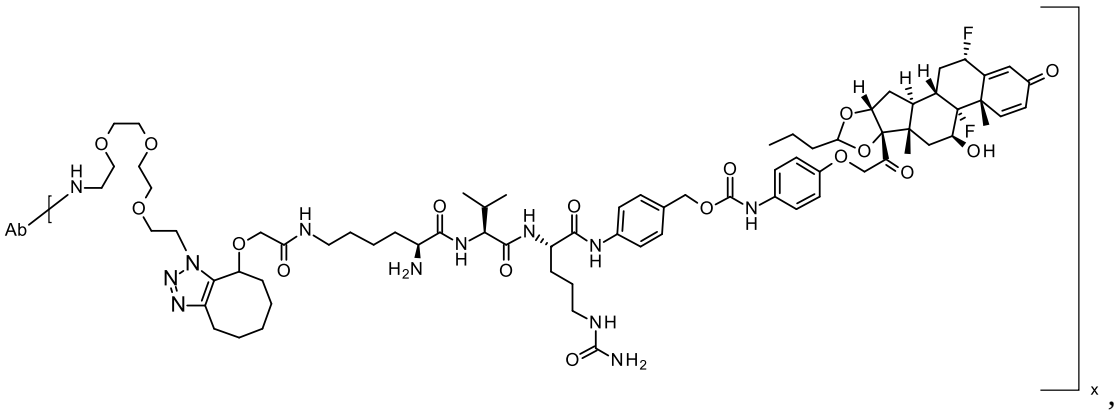
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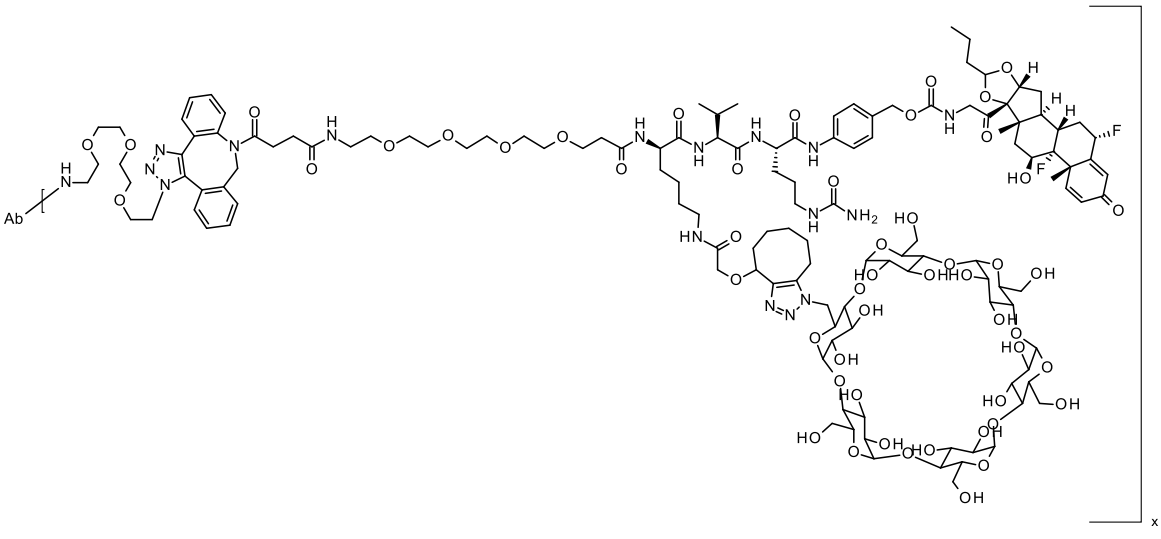
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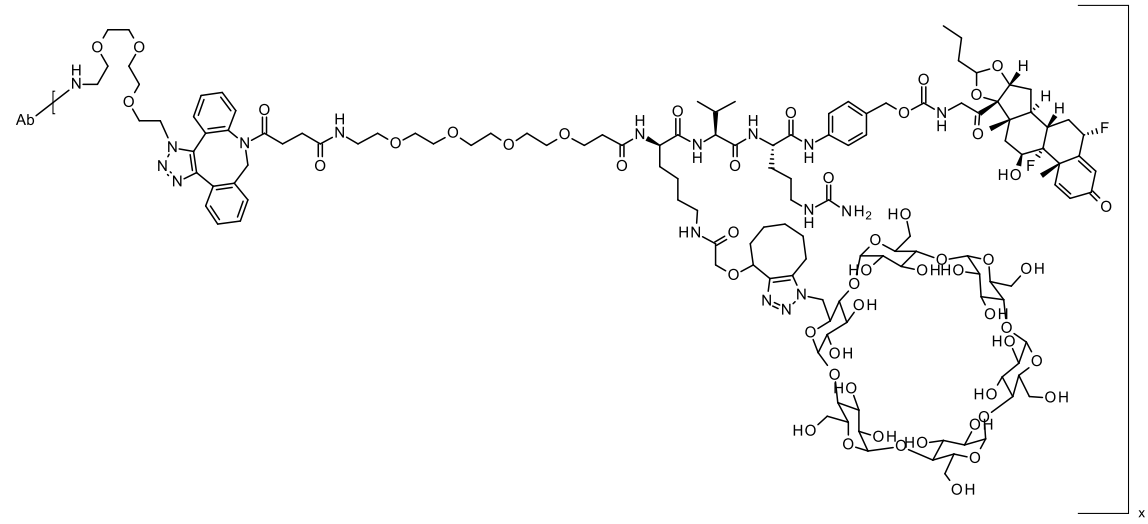
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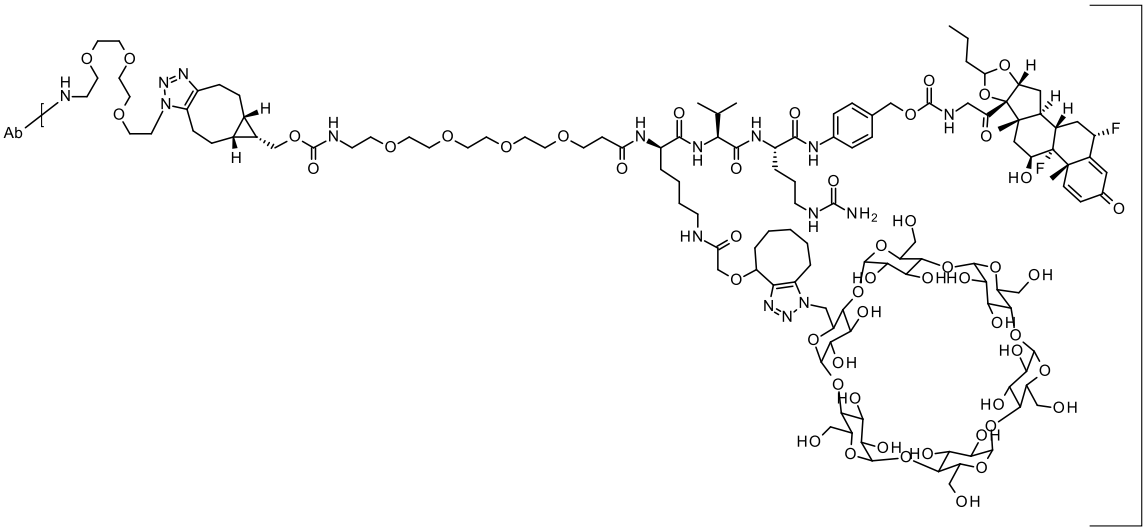


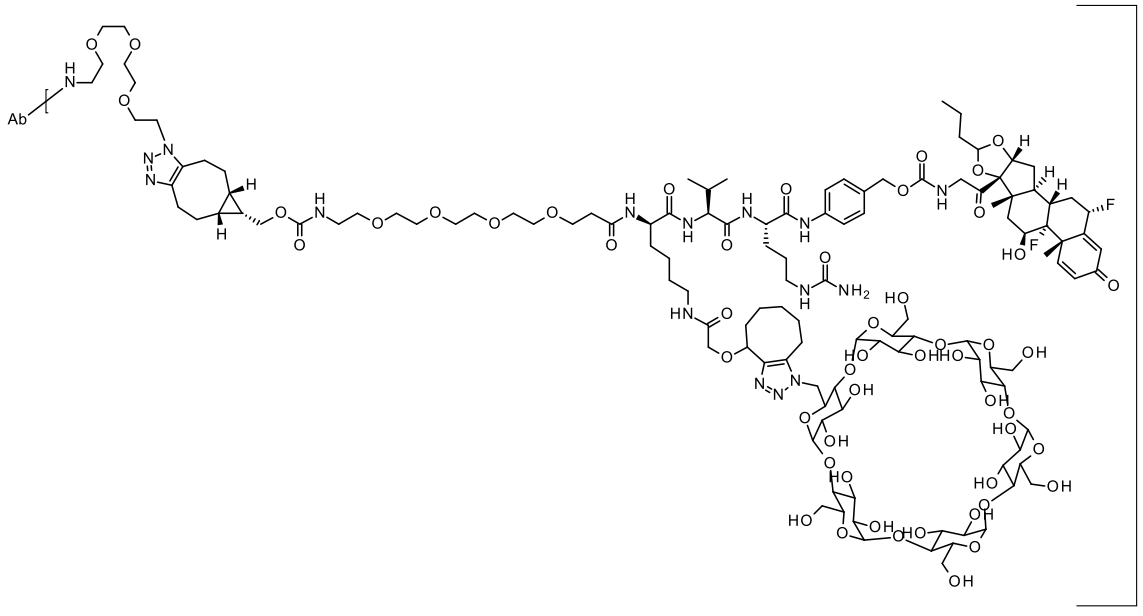
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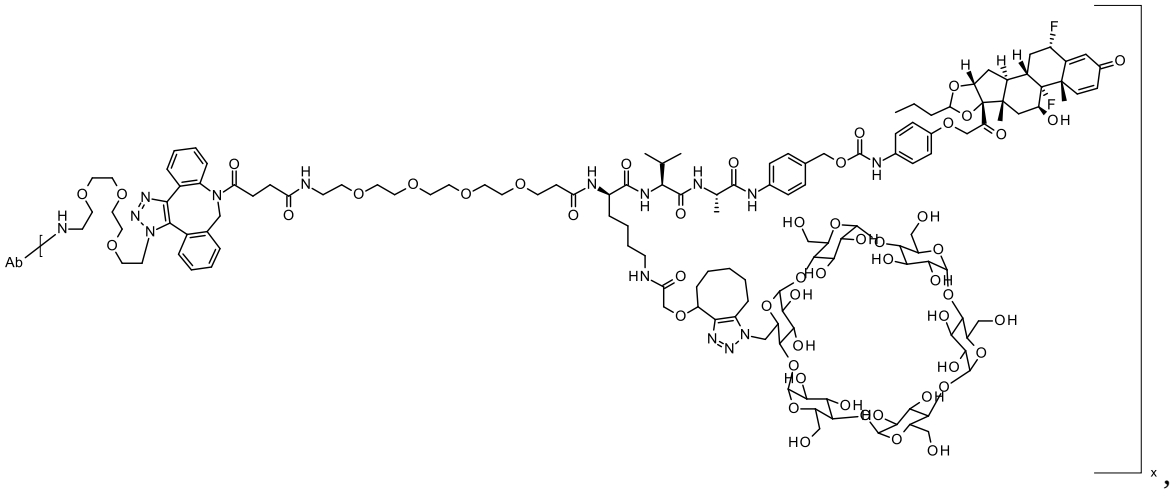


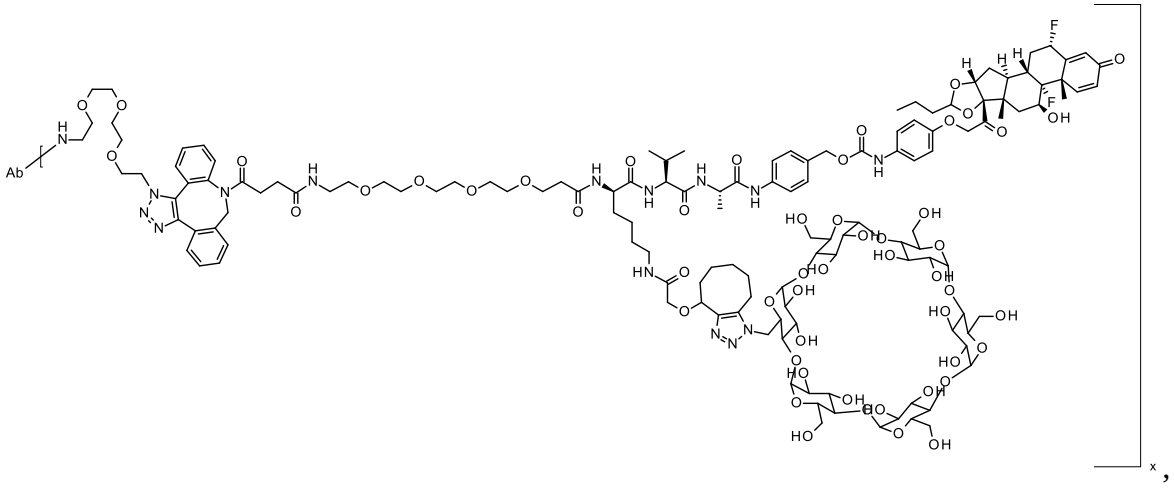
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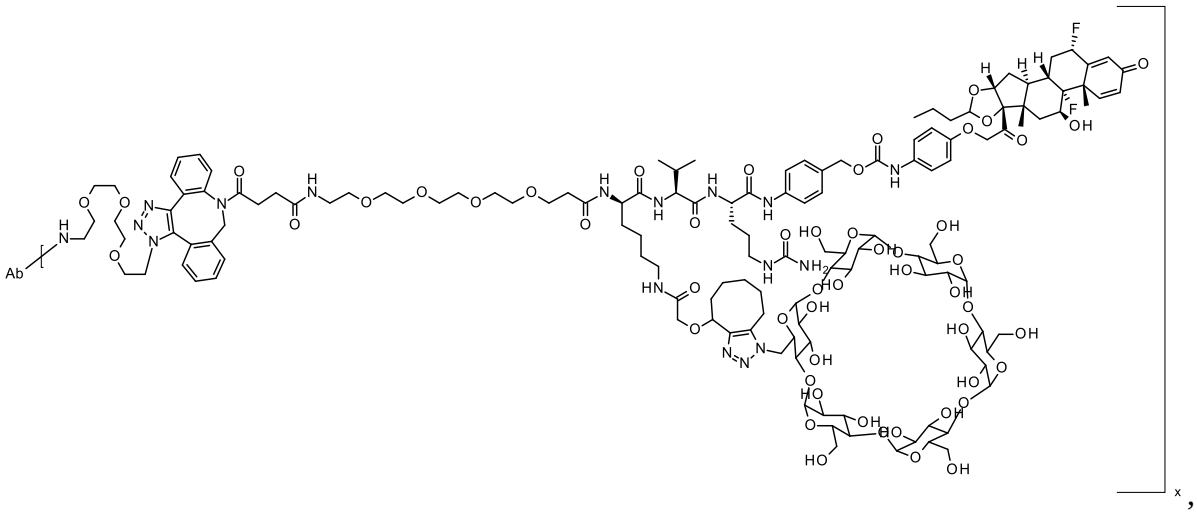


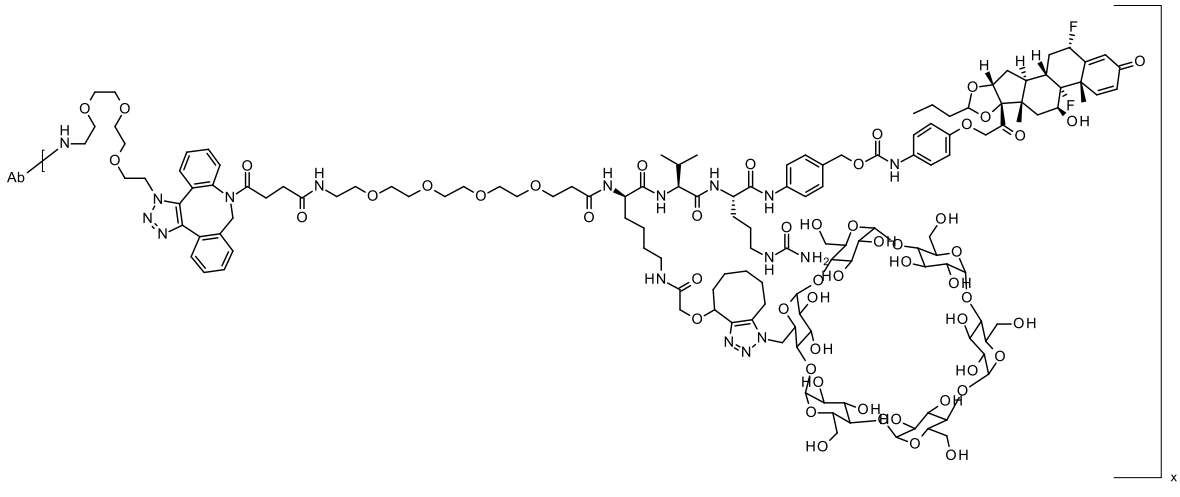


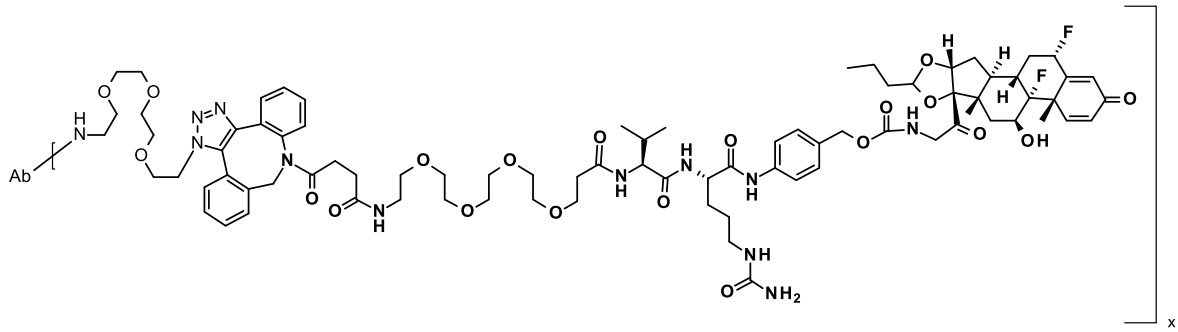


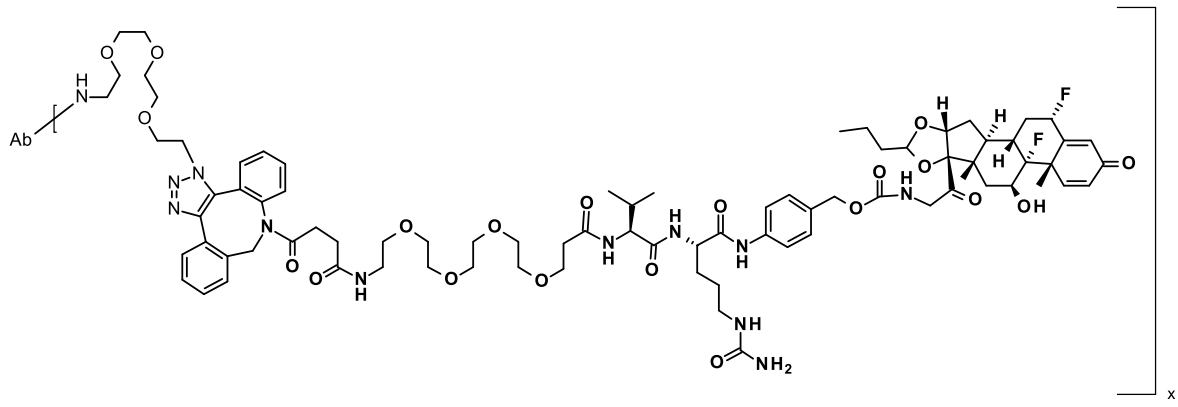


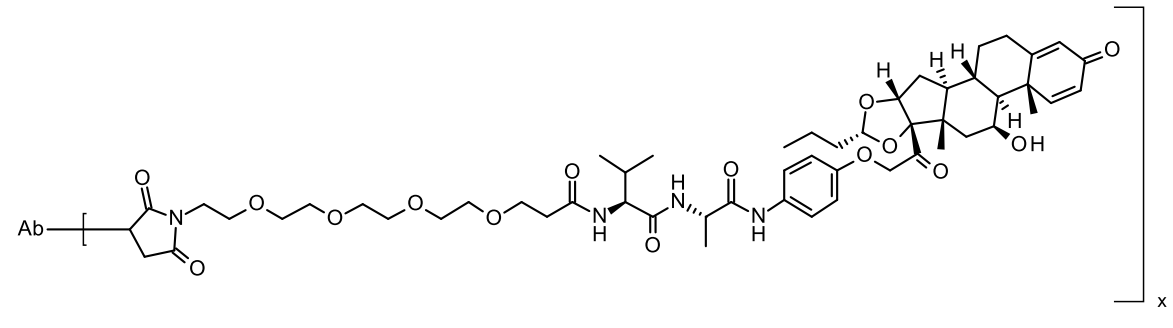


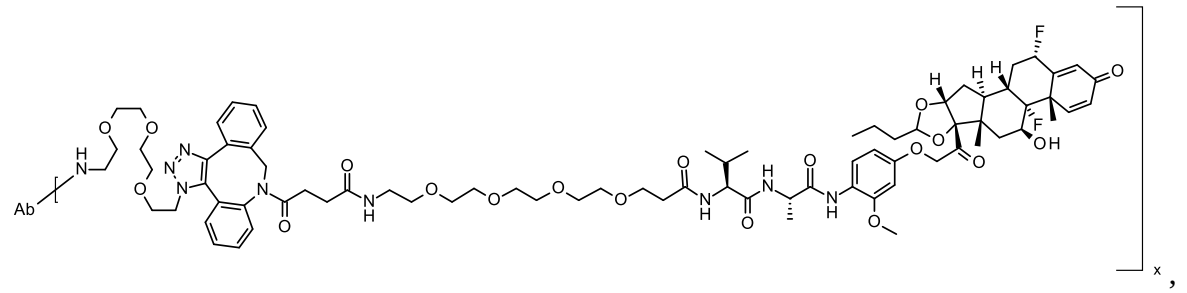


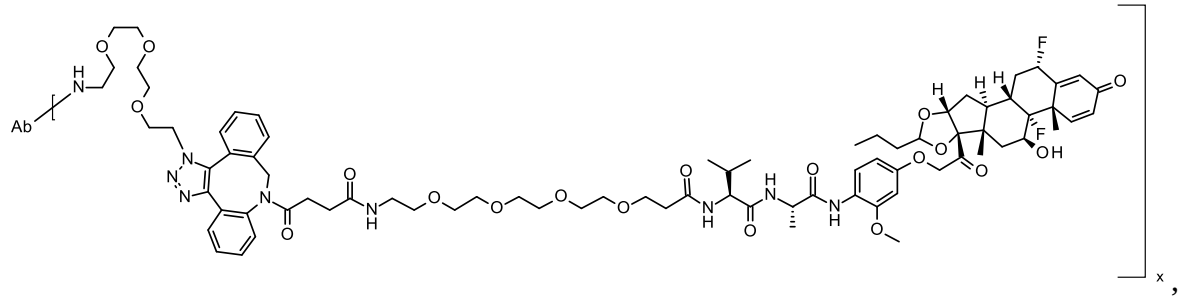


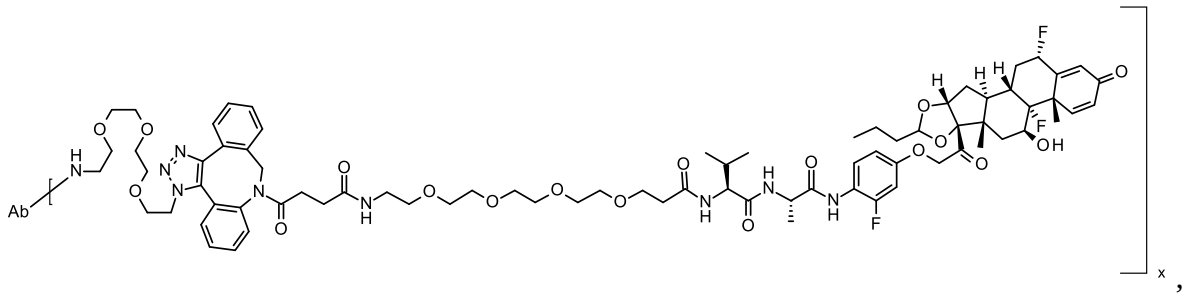


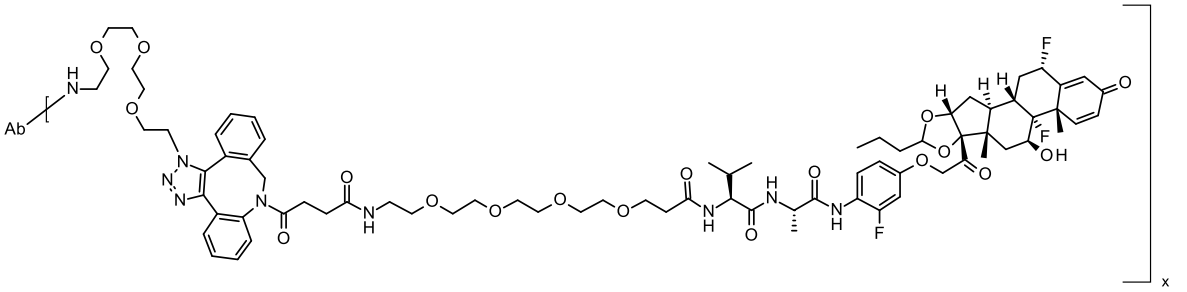


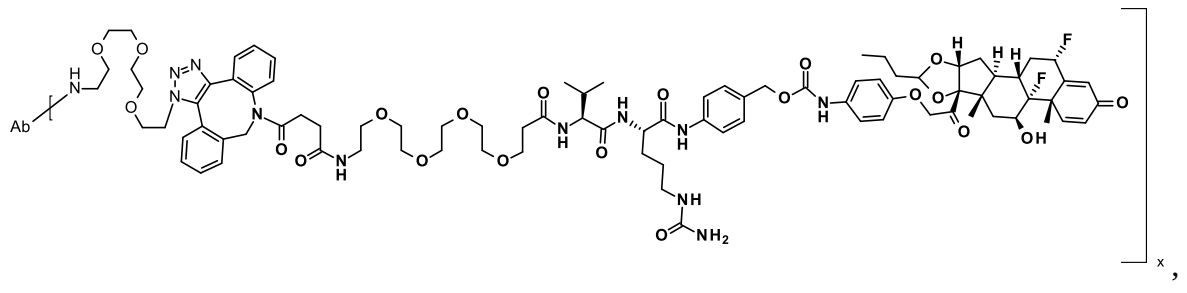


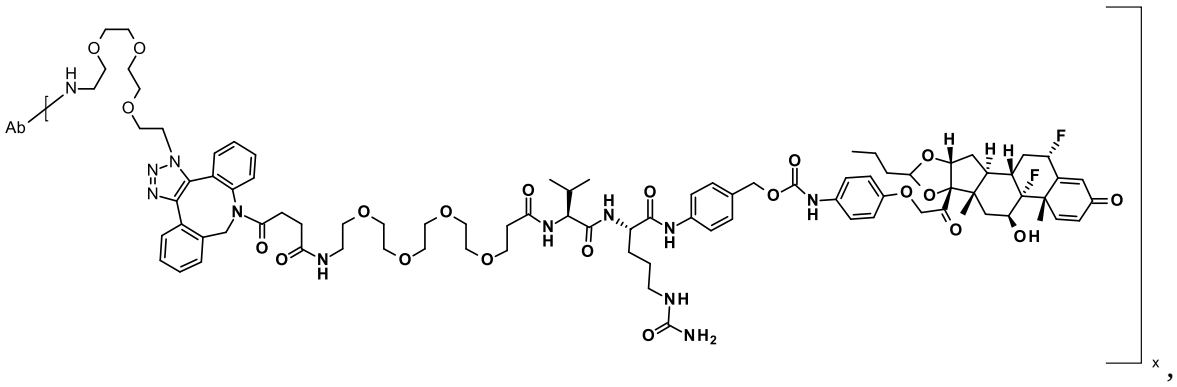












wherein x is an integer from 1 to 30; and n is an integer from 1 to 30;
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

38. Use of the compound of any of claims 1-26 or the conjugate compound of any one of claims 27-37 for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling comprising administering to a patient having said disease, disorder, or condition.

39. The use of claim 38, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

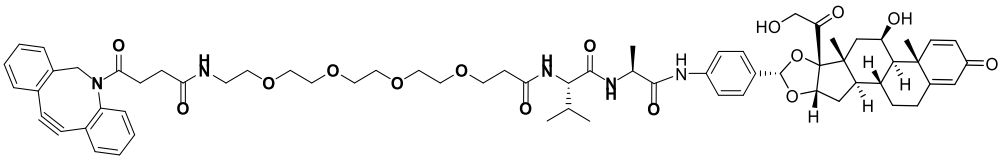
40. The use of claim 39, wherein a compound of any one of claims 12-16 is administered.

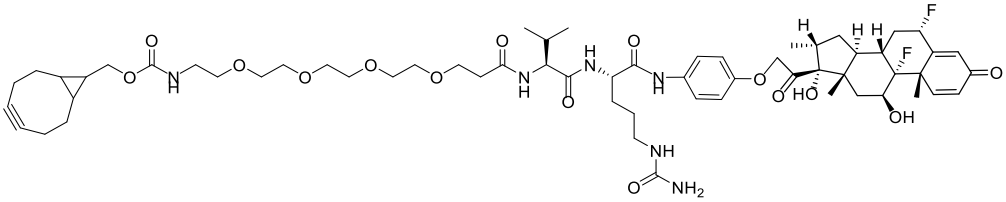
41. The use of claim 40, wherein side effects associated with administration of the unconjugated steroid payload of said compound are reduced.

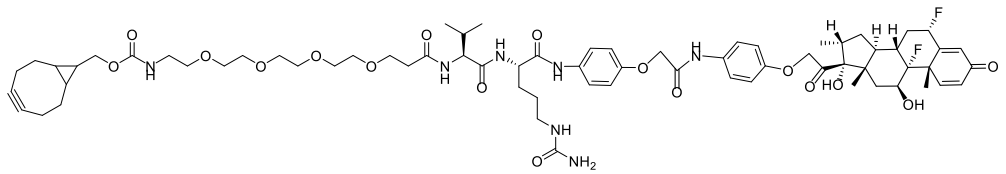
42. A *in vitro* method of delivering a compound of claim 1 to a cell comprising contacting said cell with a protein conjugate of said compound, wherein said protein conjugate comprises an antibody or antigen binding fragment thereof that binds a surface antigen of said cell.

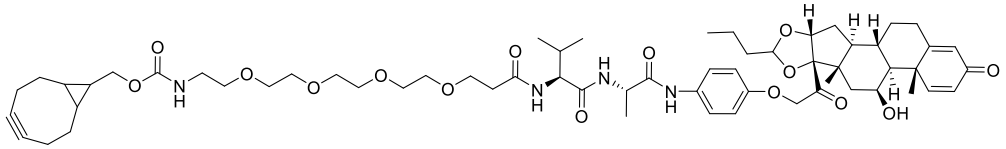
43. A linker-payload compound comprising the compound of any of claims 1-26 linked to a reactive group, optionally via a linker.

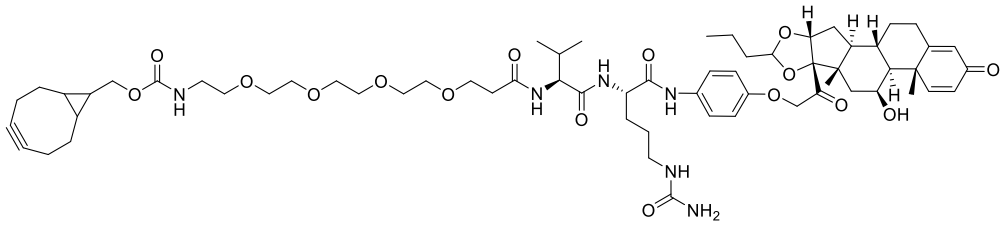
44. The linker-payload compound of claim 43 selected from the group consisting of:

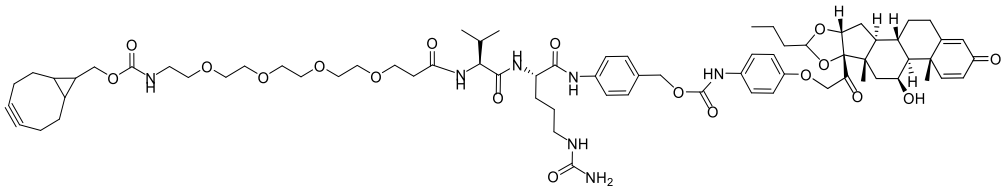


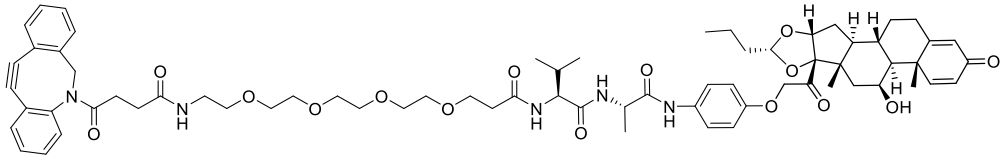


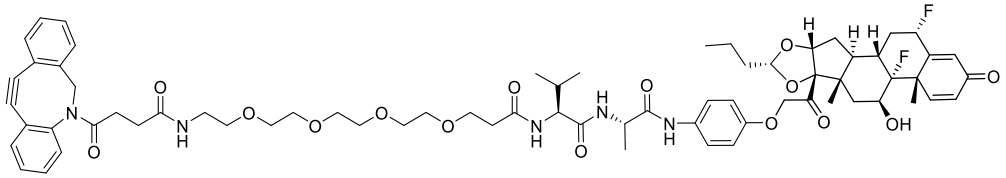


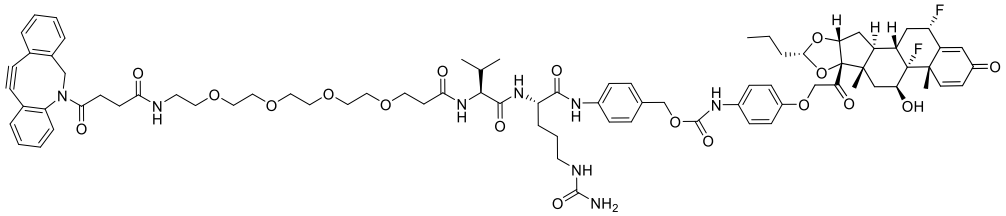


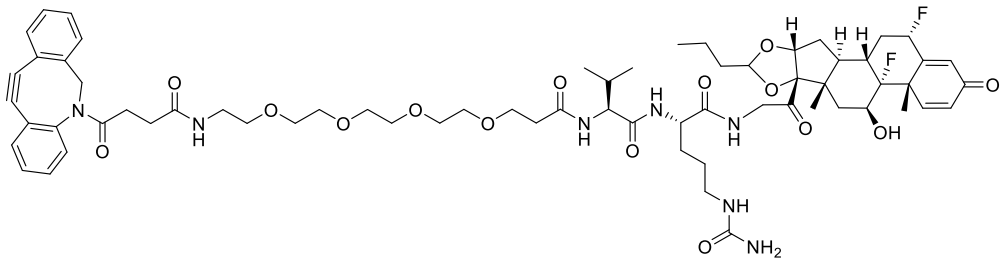


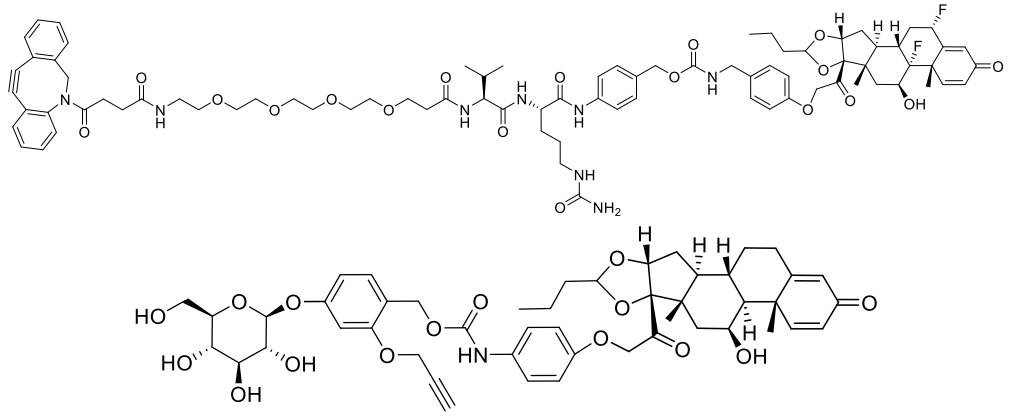


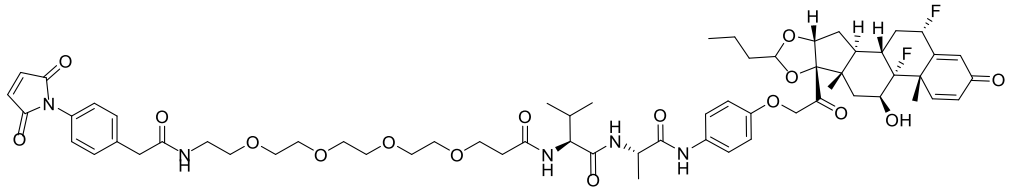


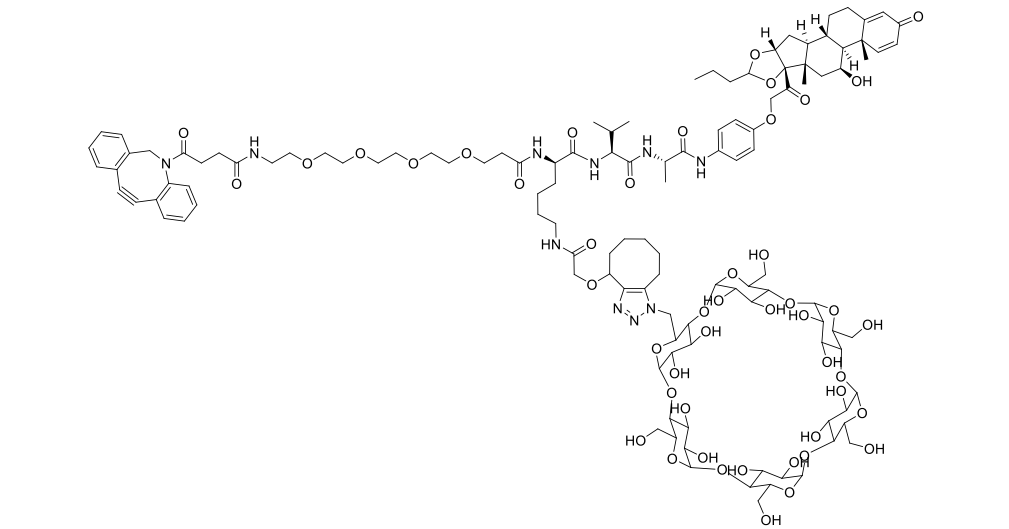


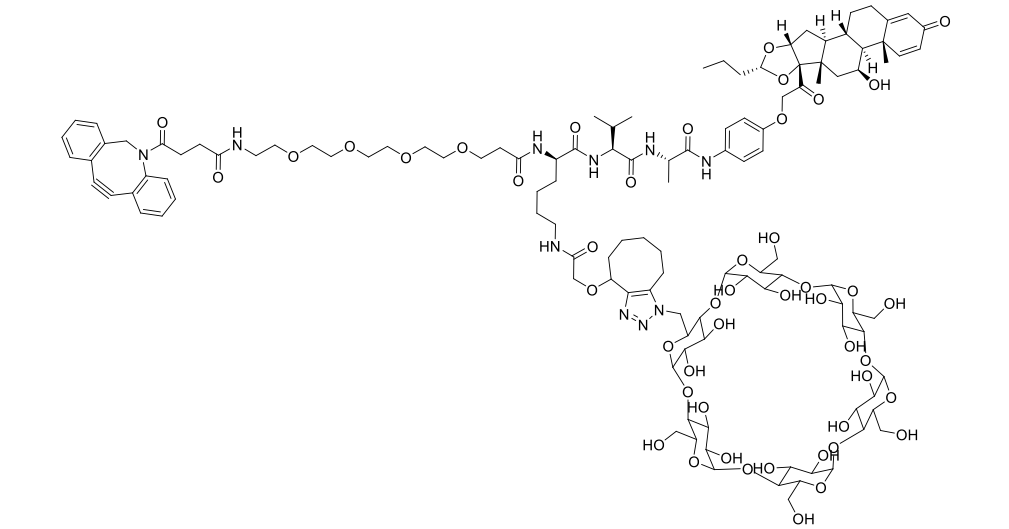


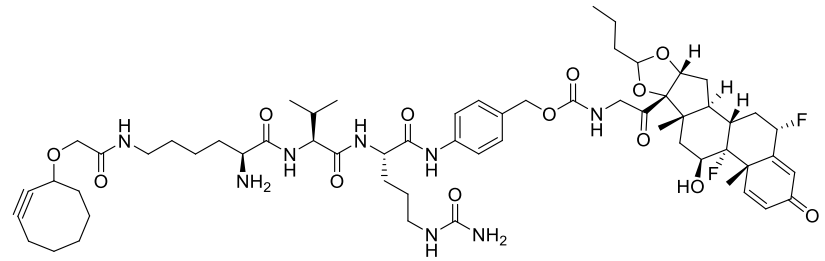


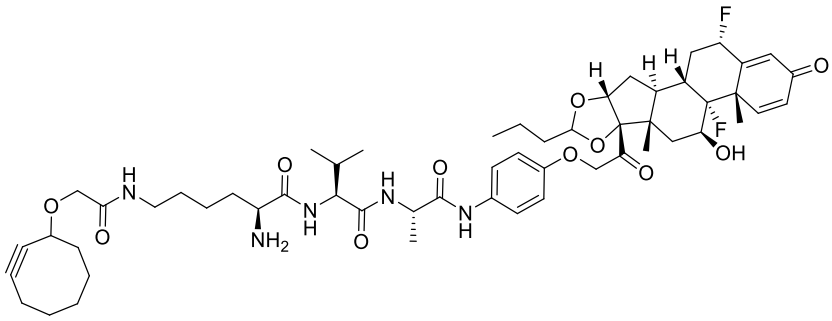


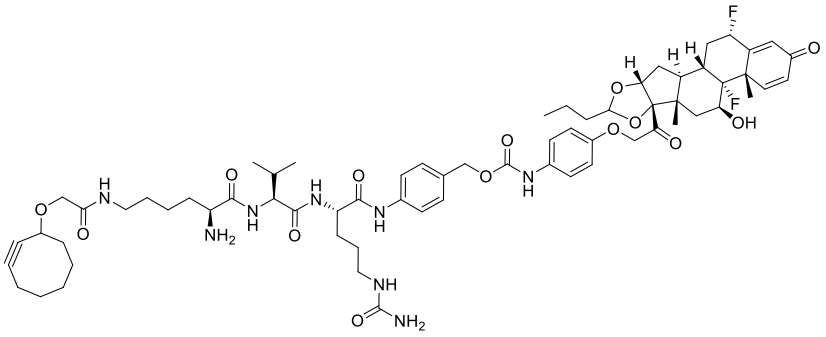


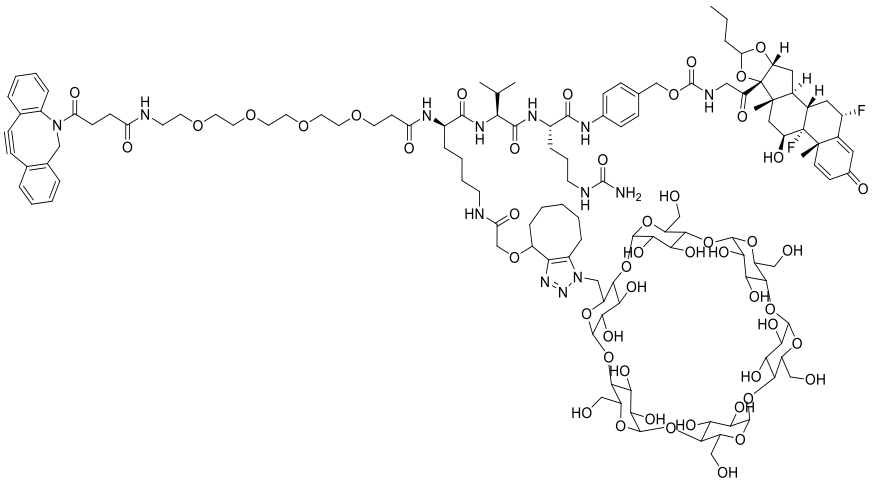


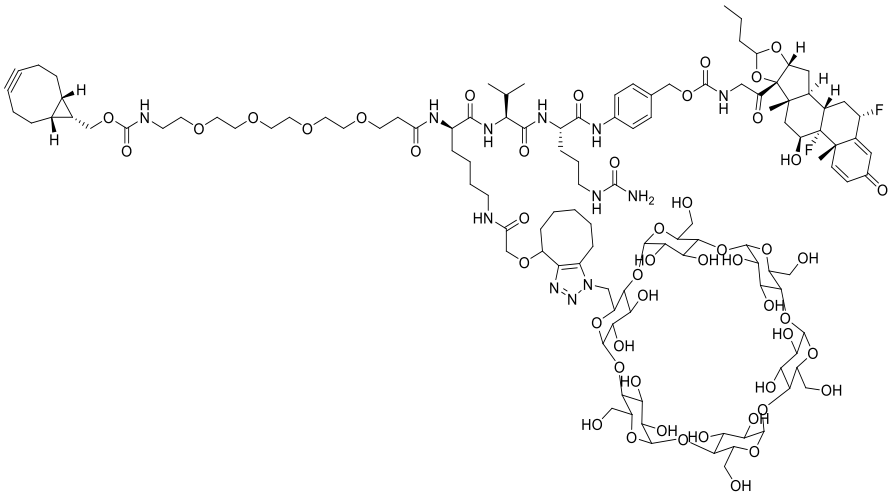


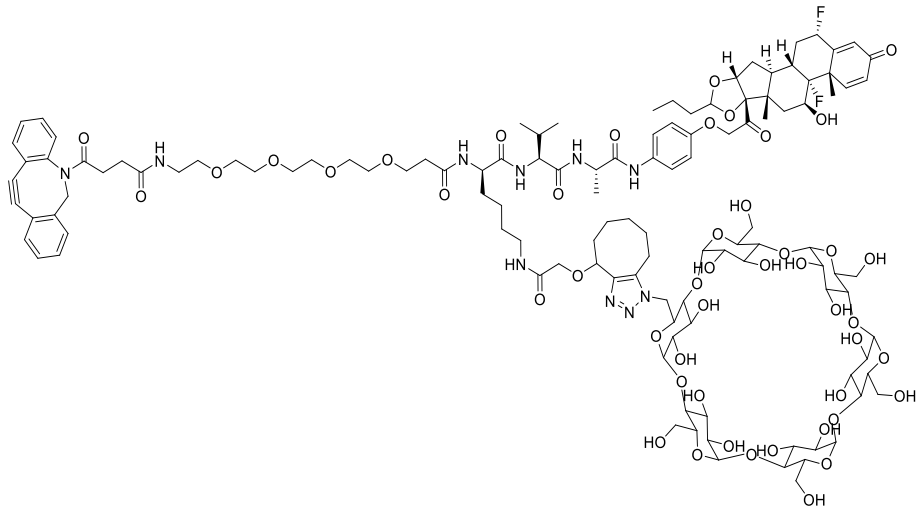


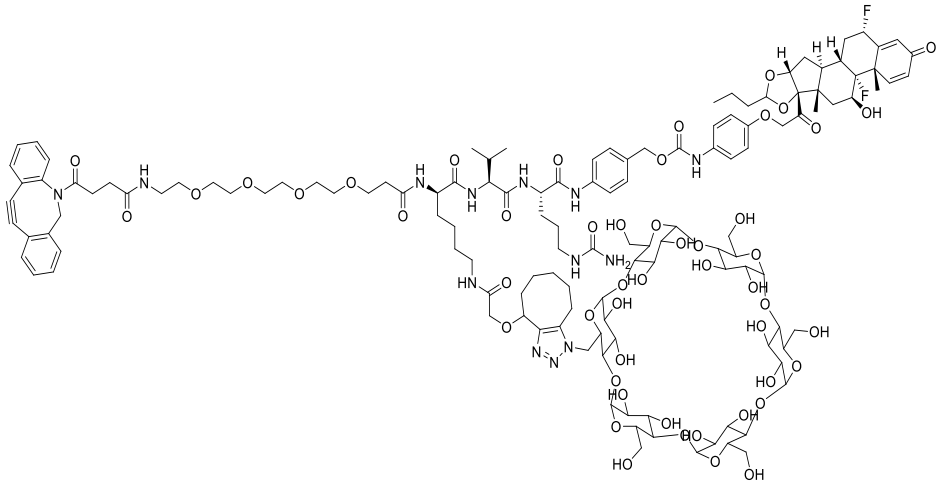


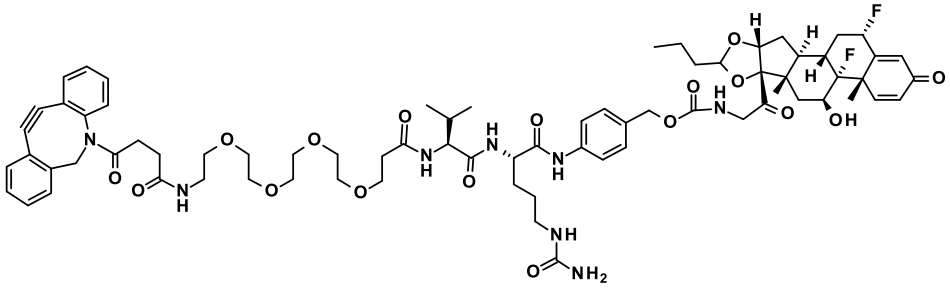


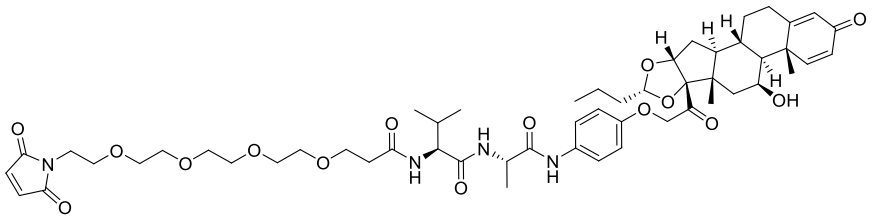


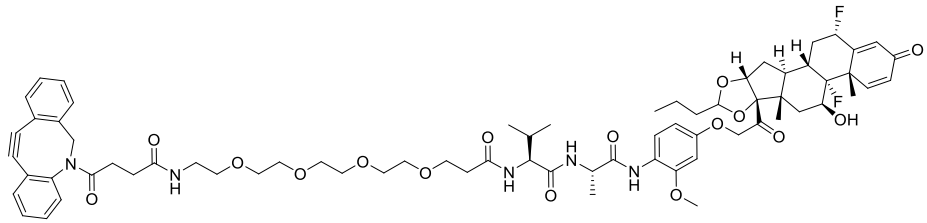


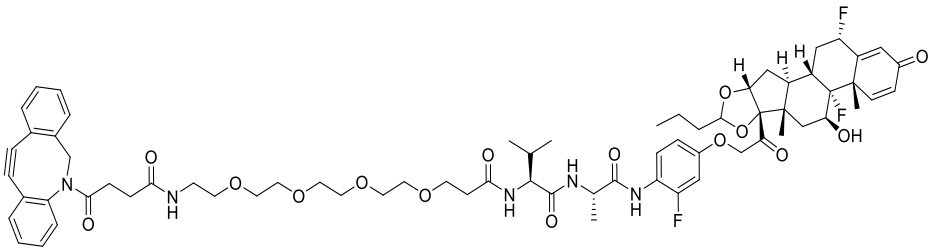




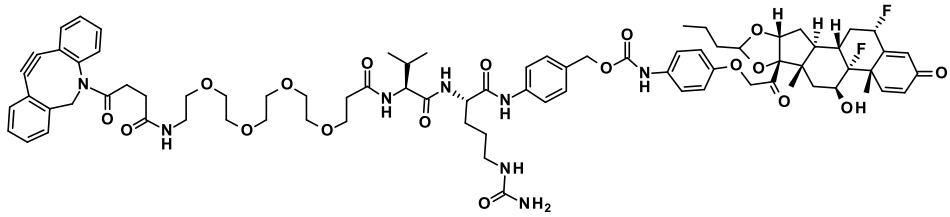








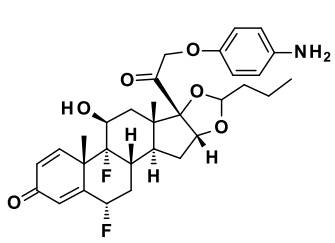
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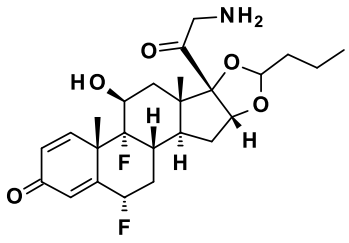
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45. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1-26 or the conjugate compound of any one of claims 27-37.

46. The compound of claim 26, wherein the compound is one of the following:

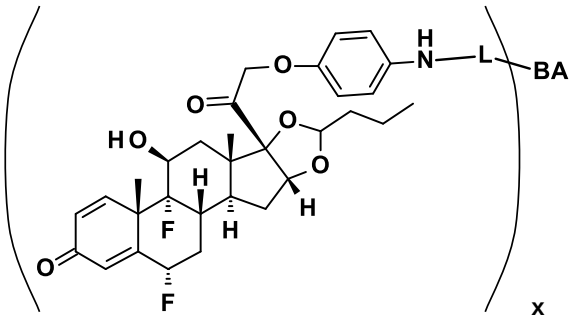


and

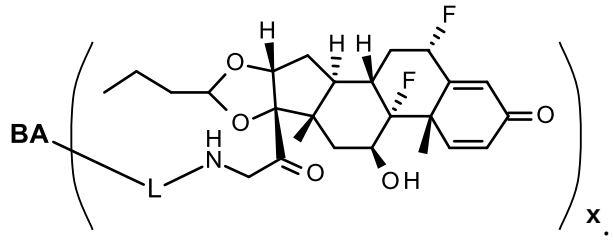


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47. The conjugate compound of claim 36, wherein the conjugate compound is one of the following:



and



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48. The conjugate compound of claim 33, wherein BA is an antibody modified with one or more H_2N-LL-N_3 groups, wherein LL is divalent polyethylene glycol.