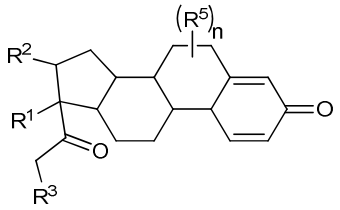
SUMMARY

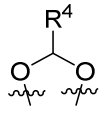
[0005] Provided herein are compounds and methods useful for the treatment of various diseases, disorders, or conditions. Provided herein is a compound of Formula (**A**):



(**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 –OH, R^Z-C(O)-X–, heteroalkyl, piperidinyl, $–NR^aR^b$, -oxyaryl–NR^aR^b or $-Z-A(R^P)_t$;

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

R^Z is alkyl;

X is O or NR^a;

Z is S, S(O), $S(O)_2$, SO_2NR^a, O, $C(O)NR^a$, C(O), or NR^a;

A is aryl, arylalkyl, or heteroaryl;

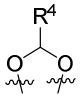
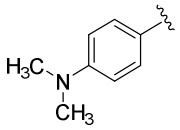
R^P is, independently in each instance, halo, optionally substituted alkyl, –OH, or $-NR^aR^b$;

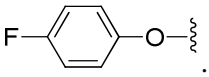
R^a and R^b are, independently in each instance, –H, optionally substituted alkyl, or optionally subtitued aryl;

n is an integer from 0-19; and

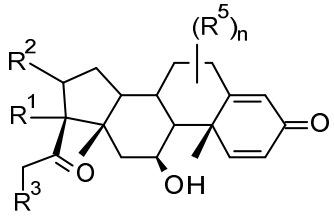
t is an integer from 1-3;

with the proviso that:

(1) R^3 is not –OH (a) when R^1 is –OH or (b) when R^1 and R^2 together form  , wherein R^4 is $C_{1\text{-}9}$alkyl or  and

(2) R^3 is not  .

[0005a] In one aspect, provided herein is a compound of Formula (**1000**):



1000

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

wherein:

R^1 and R^2 together form  ,

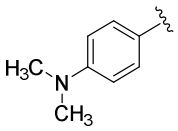
R^3 is -OH,

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

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

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;

n is an integer from 0-19; with the proviso that

R^4 is not  .

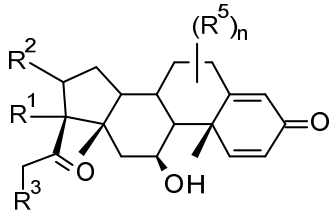
[0006] Provided herein are compounds that are protein-drug conjugates, *e.g.*, antibody-drug conjugates, comprising an antigen-binding protein, *e.g.*, antibody and a compound of Formula (**A**).

[0006a] In another aspect, provided herein is a conjugate compound comprising a binding agent conjugated to a compound as defined herein.

[0007] Provided herein are compounds that are protein-drug conjugates, *e.g.*, antibody-drug conjugates, comprising an antigen-binding protein, *e.g.*, antibody, a compound of Formula (**A**), and a cyclodextrin moiety.

[0007a] In another aspect, provided herein is a conjugate compound comprising a binding agent conjugated to a compound as defined herein and a cyclodextrin (**CD**).

[0007b] In another aspect, provided herein is a conjugate compound comprising a binding agent conjugated to a compound of Formula (**1000**) and a cyclodextrin (**CD**):



1000

or a pharmaceutically acceptable salt, solvate, or stereoisomer 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 -OH,

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

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;

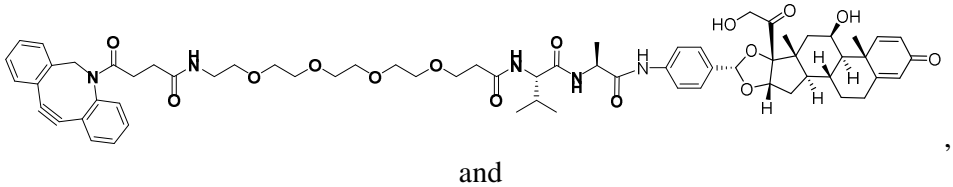
n is an integer from 0-19.

[0007c] In another aspect, provided herein is use of a compound as defined herein or a conjugate compound as defined herein in the manufacture of medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

[0007d] In another aspect, provided herein is an *in vitro* method of delivering a compound as defined herein to a cell comprising contacting said cell with a protein steroid conjugate of said compound, wherein said protein conjugate comprises an antibody or antigen binding fragment thereof that binds a surface antigen of said cell.

[0007e] In another aspect, provided herein is a linker-payload comprising the compound as defined herein linked to a reactive group via a linker.

[0007f] In another aspect, provided herein is a linker-payload selected from the group consisting of:


HO
O
OH
H
H
H
H
O
O
O

[0007g] In another aspect, provided herein is a pharmaceutical composition comprising a therapeutically effective amount of a compound as defined herein or a conjugate compound as defined herein.

BRIEF DESCRIPTIONS OF THE DRAWINGS

[0008] FIG. 1. shows a sequence for synthesizing the certain steroids described herein.

[0009] FIG. 2. shows a sequence for modifying the primary alcohol position of budesonide.

[0010] FIG. 3. shows a sequence for modifying the primary alcohol position of Flumethasone.

[0011] FIG. 4. shows a sequence for modifying the primary alcohol position of dexamethasone.

[0012] FIG. 5 shows a two–dimensional nuclear Overhauser effect (NOE) magnetic resonance spectrum (hereinafter "2D–NOESY") for compound 7-1*R* in Table 1.

[0013] FIG. 6 shows a 2D–NOESY for compound 7-1*S* in Table 1.

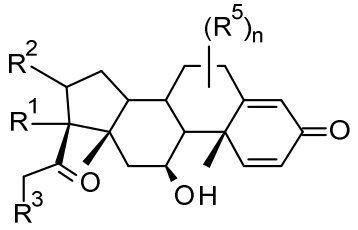
[0014] FIG. 7 shows a 2D–NOESY spectrum for 11-5*R* in Table 1.

[0015] FIG. 8 shows a 2D–NOESY spectrum for compound 11-5*S* in Table 1.

CLAIMS

What is claimed is:

1. A compound of Formula (**1000**):



1000

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

wherein:

R^1 and R^2 together form  ,

R^3 is -OH,

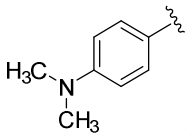
R^4 is selected from the group consisting of -alkylene-NR^aR^b,

-X-arylene-Y-NR^aR^b, and -X-heteroarylene-Y-NR^aR^b; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

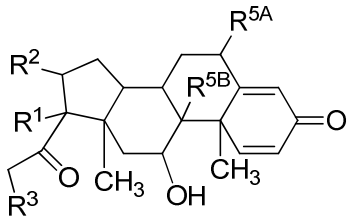
R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; and each R^5 is positioned on any ring atom; and

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;

n is an integer from 0-19; with the proviso that

R^4 is not  .

2. The compound of claim 1, wherein the compound of Formula (**1000**) has the structure of Formula (**A[1]**):

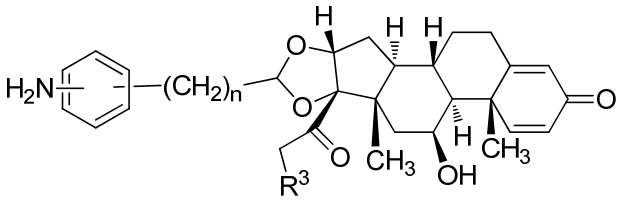


(**A[1]**)

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 $-NR^aR^b$.

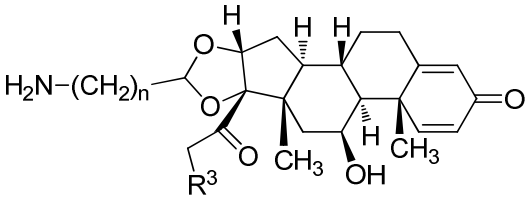
4. The compound of claim 1 according to Formula (**A[2]**)



(**A[2]**)

wherein n is an integer from 0 to 4.

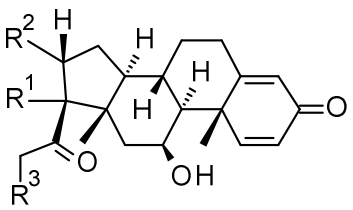
5. The compound of claim 1 according to Formula (**A[3]**):



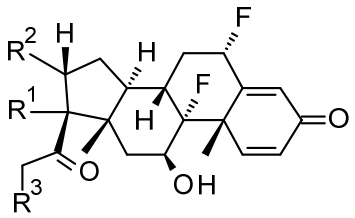
(**A[3]**)

wherein n is an integer from 1-4.

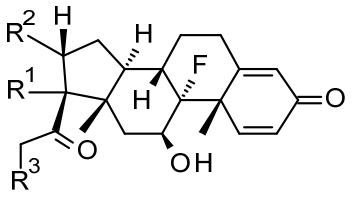
6. The compound of claim 1 according to Formula **1010**, **1020**, **1030**, or **1040**:



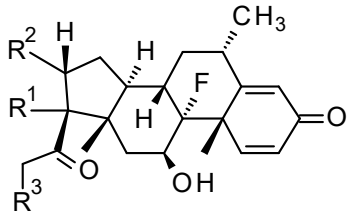
1010



1020



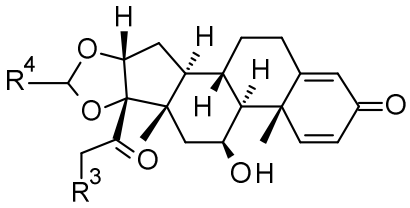
1030



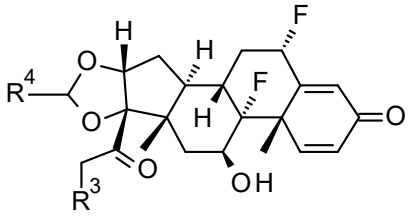
1040

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

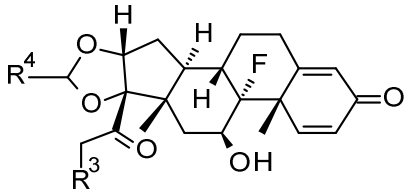
7. The compound of claim 1 according to Formula **1110**, **1120**, **1130**, or **1140**:



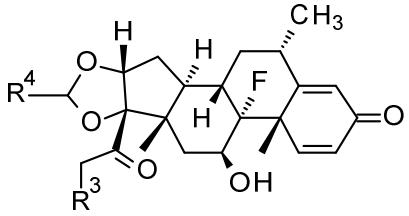
1110



1120

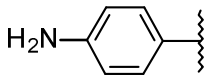


1130

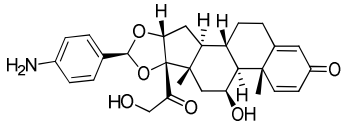


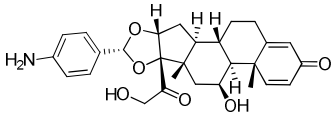
1140

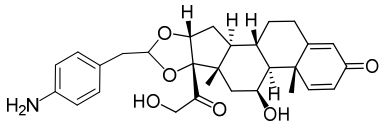
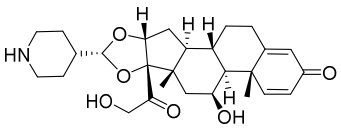
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

8. The compound of claim 7, wherein R^4 is $H_2NCH_2CH_2$- or  .

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





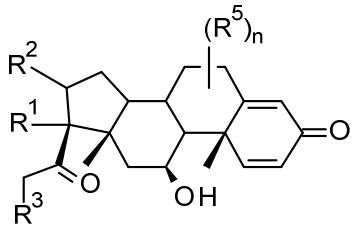



or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

10. A conjugate compound comprising a binding agent conjugated to a compound of any of claims 1-9.

11. A conjugate compound comprising a binding agent conjugated to a compound of claim 10 and a cyclodextrin (**CD**).

12. A conjugate compound comprising a binding agent conjugated to a compound of Formula (**1000**) and a cyclodextrin (**CD**):



1000

or a pharmaceutically acceptable salt, solvate, or stereoisomer 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 $-NR^aR^b$;

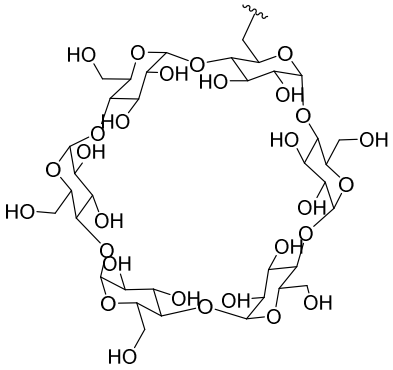
R^3 is -OH,

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

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;

n is an integer from 0-19.

13. The conjugate compound of claim 11 or 12, wherein **CD** is selected from the group consisting of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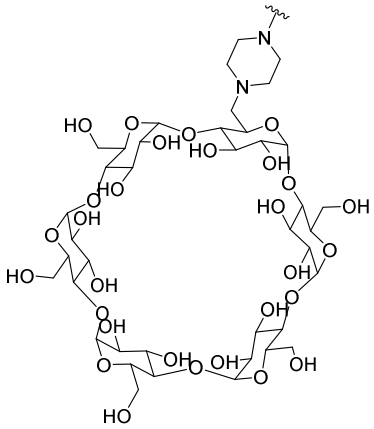
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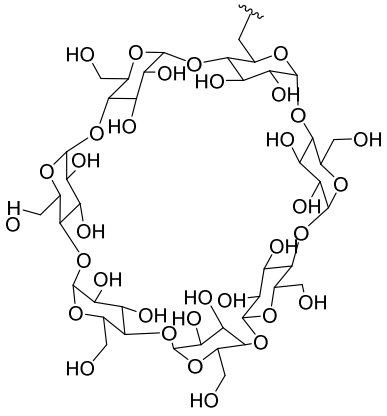
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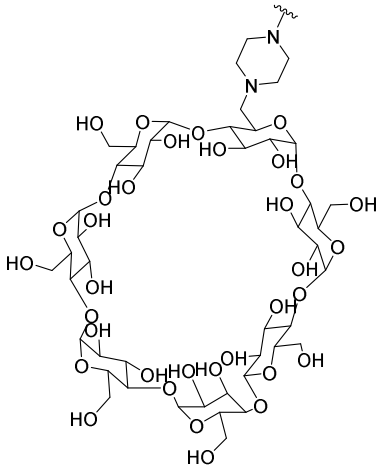
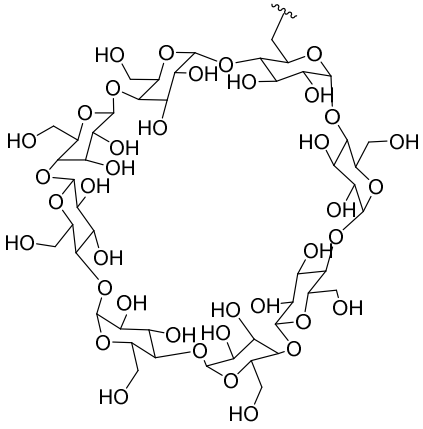
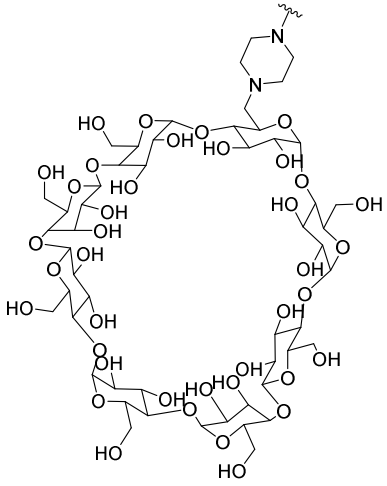

,



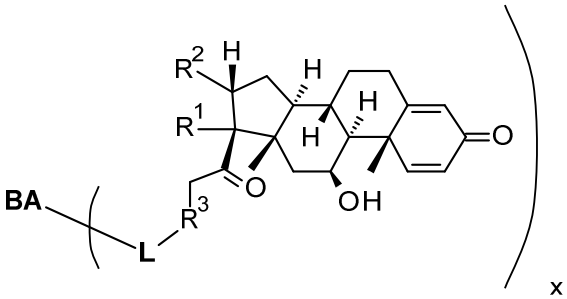
, and



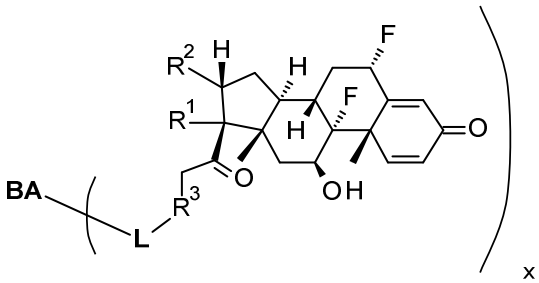
, wherein  indicates the bond through which the CD is linked to the conjugate compound.

14. The conjugate compound of any one of claims 10 to 13, wherein the binding agent is an antibody or antigen binding fragment thereof..

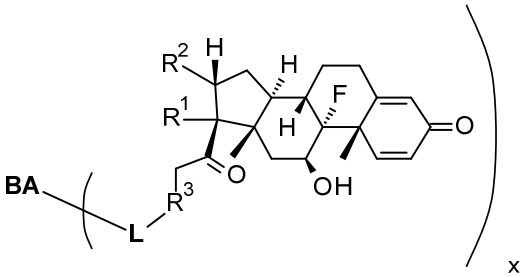
15. The conjugate compound of claim 10 according to Formula **1210**, **1220**, **1230**, or **1240**:



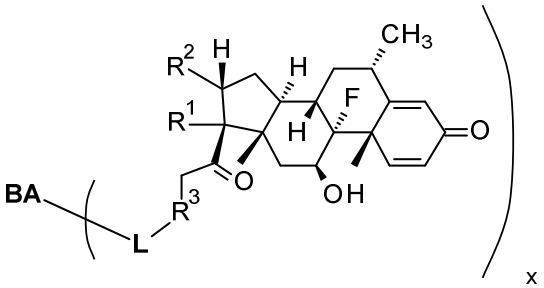
1210



1220



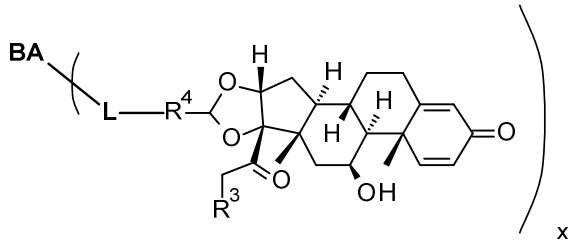
1230



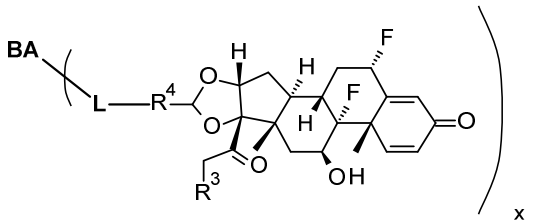
1240

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;
wherein R^3 is covalently bonded to L or BA.

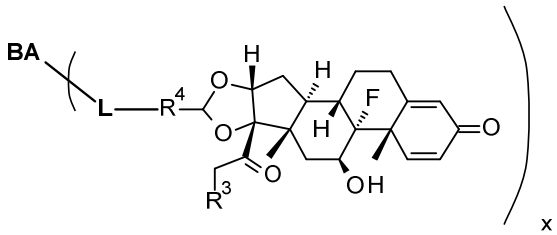
16. The conjugate compound of claim 10 according to Formula **1310**, **1320**, **1330**, or **1340**:



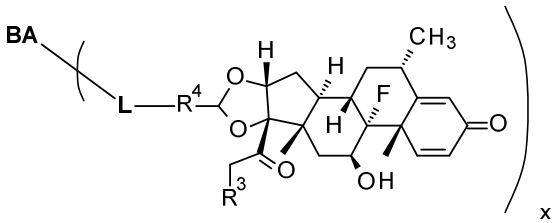
1310



1320



1330

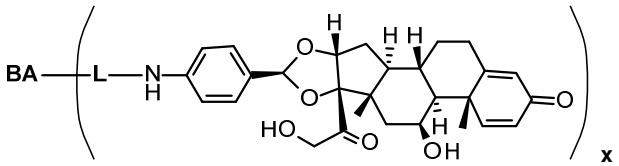


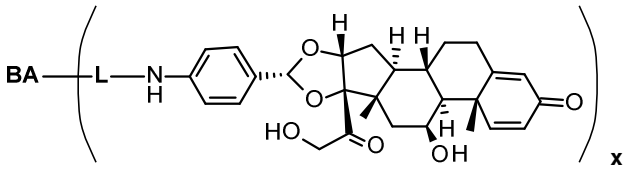
1340

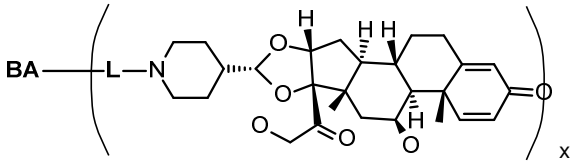
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;

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

17. The conjugate compound of claim 10 selected from the group consisting of:







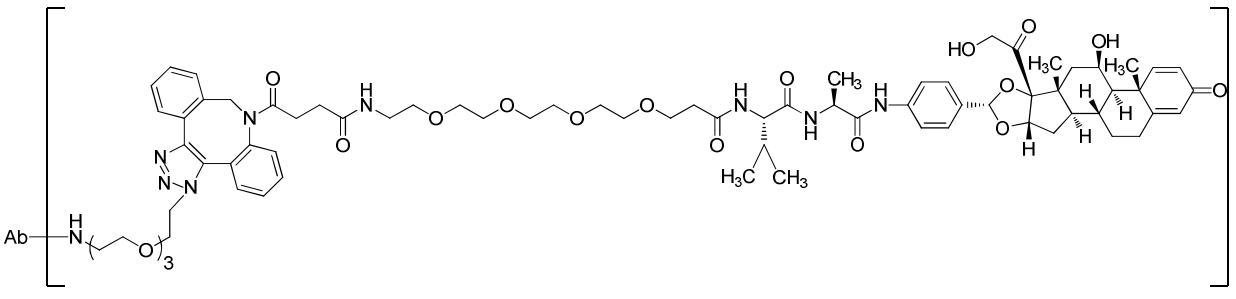
and pharmaceutically acceptable salts, solvates, and stereoisomers thereof;

wherein each L is an optional linker;

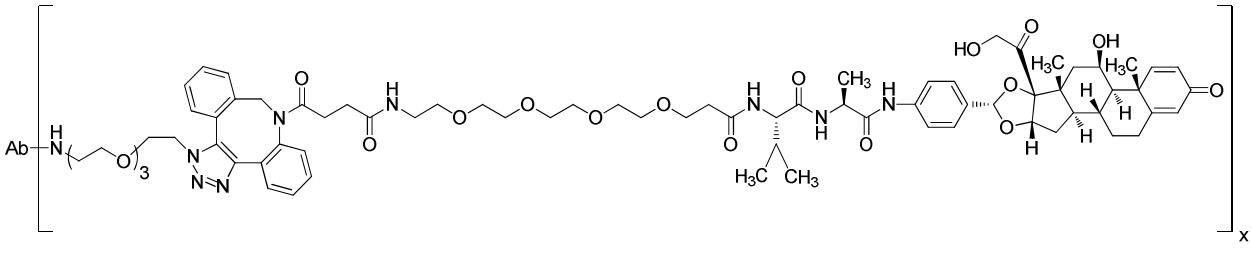
each BA is a binding agent; and

each x is an integer from 1 to 30.

18. The conjugate compound of claim 10 selected from the group consisting of:



or



,

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

19. Use of a compound of any of claims 1-9 or a conjugate compound of any one of claims 10-18 in the manufacture of a medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

20. The use of claim 19, wherein the disease, disorder, or condition, is asthma.

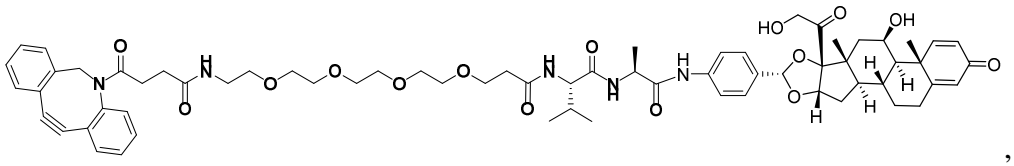
21. The use of claim 20, wherein the compound is a compound of any one of claims 6-8.

22. The use of claim 21, wherein side effects associated with administration of the unconjugated steroid payload of said compound are reduced.

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

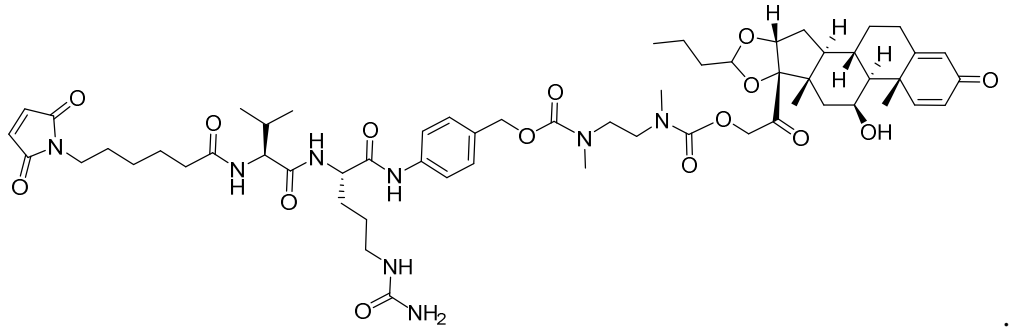
24. A linker-payload comprising the compound of any of claims 1-9 or the conjugate compound of claim 10 linked to a reactive group via a linker.

25. A linker-payload selected from the group consisting of:



,

and



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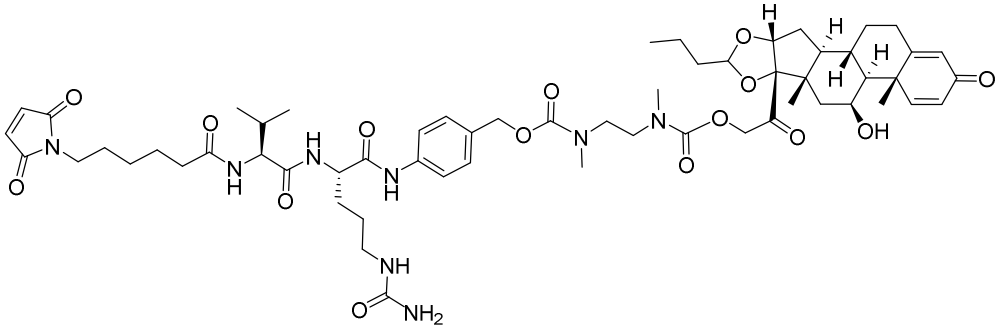
26. The conjugate compound of claim 12 wherein the binding agent is conjugated to budesonide.

27. The linker-payload of claim 25, wherein the linker-payload is



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28. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-9 or a conjugate compound of any one of claims 10-18.