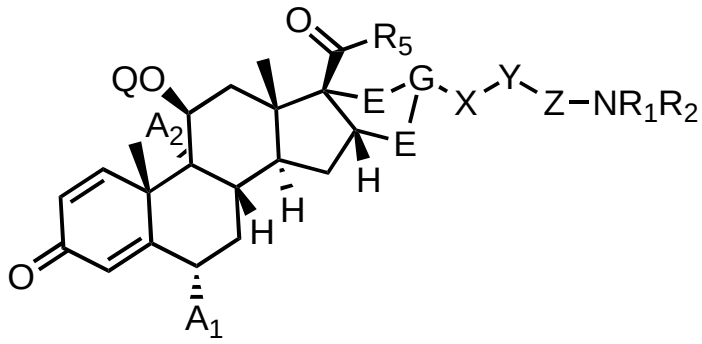
CLAIMS

1. A glucocorticoid agonist having the following structure of **Formula (I)**:



Formula (I)

wherein

X is selected from phenyl, spiro[3.3]heptane, 5- or 6-membered heteroaryl, 3-6 membered heterocycle, cycloalkyl, spiro-alkyl, spiro-heterocycloalkyl, bicyclic alkyl, heterobicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, N, S, and O, each of which ring structure may contain at least one skeletal heteroatom selected from N, S, and O;

Y is selected from CHR_1, O, S, and NR_1;

Z is selected from phenyl, spiro[3.3]heptane, 3-6 membered heterocycle, cycloalkyl, spiro-alkyl, spiro-heterocycloalkyl, bicyclic alkyl, heterobicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, N, S, and O, each of which ring structure may contain at least one skeletal heteroatom selected from N, S, and O;

E is O and G is CH, or E is CH_2 and G is N;

with the proviso that when G is CH and X is phenyl or 5- or 6-membered heteroaryl, Z is not phenyl;

the linkage of G to X is selected from a bond, C_{1-3} alkyl and ethylene oxide, each of which may be substituted with 1-4 heteroatoms independently selected from N, S, and O and are optionally further substituted with 1-4 C_{1-3} alkyl;

the linkage of X to Y may occupy any available position on X;

the linkage of Y to Z may occupy any available position on Z;

substituent NR_1R_2 may occupy any available position on Z;

R_1 is selected from H, linear or branched alkyl of 1-8 carbons, aryl, and heteroaryl groups wherein said aryl and heteroaryl groups may be substituted with functional groups selected from alkyl, haloalkyl, halogen, biphenyl, nitro, nitrile, -OH, -O-alkyl, $-NH_2$, alkylamino,

dialkylamino, thiol, thioalkyl, guanidine, urea, carboxylic acid, alkoxyl, carboxamide, carboxylic ester, alkyl-C(O)O-, alkylamino-C(O)- and dialkylamino-C(O)-;

R_2 is selected from H, linear or branched alkyl of 1-8 carbons, aryl, and heteroaryl, wherein said aryl and heteroaryl groups may be substituted with functional groups selected from alkyl, haloalkyl, halogen, biphenyl, nitro, nitrile, -OH, -O-alkyl, $-NH_2$, alkylamino, dialkylamino, thiol, thioalkyl, guanidine, urea, carboxylic acid, alkoxyl, carboxamide, carboxylic ester, alkyl-C(O)O-, alkylamino-C(O)- and dialkylamino-C(O)- , and

a functional group selected from

$[(C=O)CH(W)NH]_m$-$[C=O]$-$[V]_k$-J,

$(C=O)OCH_2$-*p*-aminophenyl-*N*-V-J,

$(C=O)OCH_2$-*p*-aminophenyl-*N*-$[(C=O)CH(W)NH]_m$-$[C=O]$-$[V]_k$-J, and

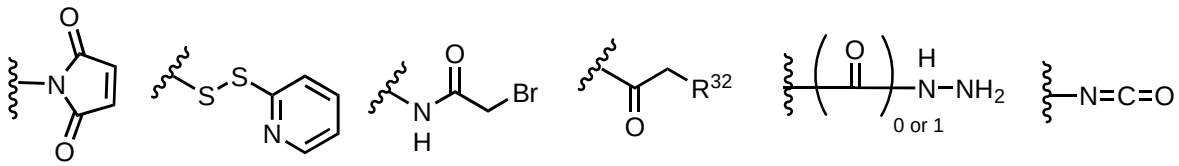
$[V]_k$-$(C=O)OCH_2$-*p*-aminophenyl-*N*-$[(C=O)CH(W)NH]_m$-$[C=O]$-J,

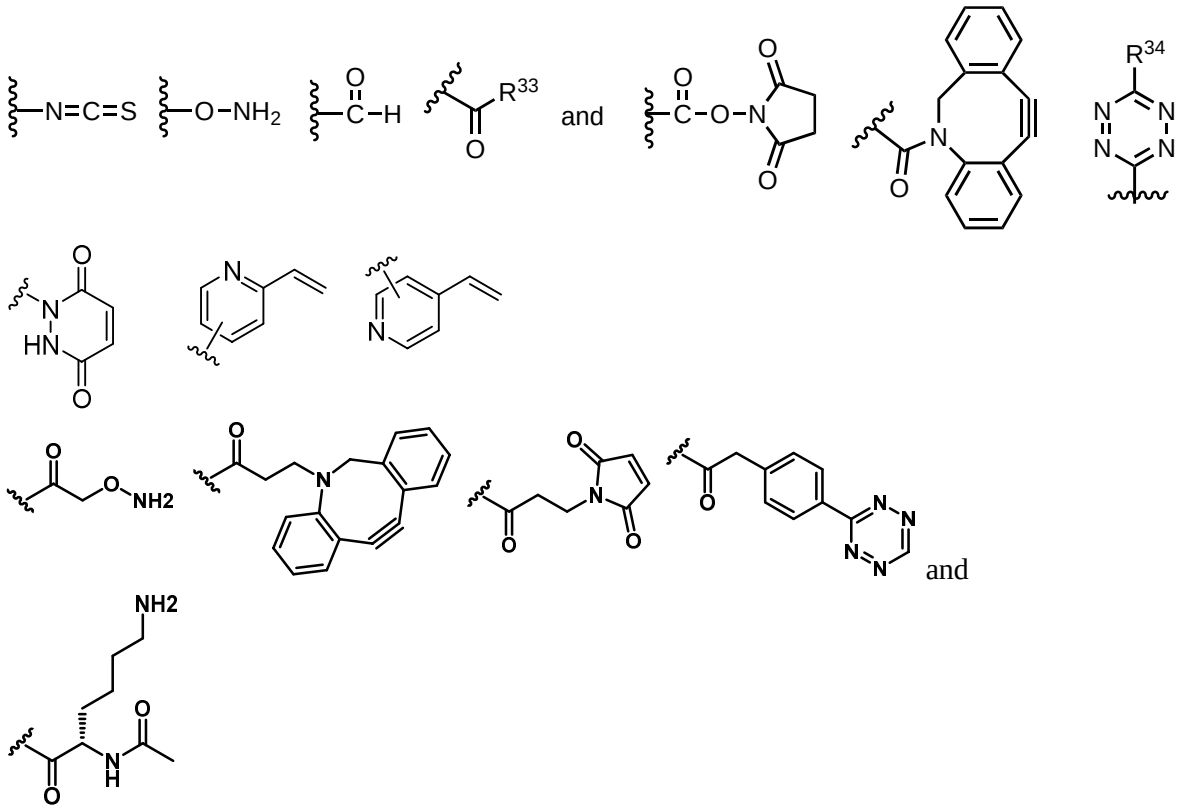
wherein m = 1-6, k = 0-1, and each permutation of W is selected from H, $[(CH_2)_nR_3]$ where n = 1-4, a branched alkyl chain terminating in R_3, and a linear or branched polyethylene oxide group comprising 1-13 units;

R_3 is selected from H, methyl, ethyl, isopropyl, OH, O-alkyl, NH_2, NH-alkyl, N-dialkyl, SH, S-alkyl, guanidine, urea, carboxylic acid, carboxamide, carboxylic ester, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, wherein said aryl and heteroaryl substituents may be selected from alkyl, haloalkyl, halogen, biphenyl, nitro, nitrile, -OH, -O-alkyl, $-NH_2$, alkylamino, dialkylamino, thiol, thioalkyl, guanidine, urea, carboxylic acid, alkoxyl, carboxamide, carboxylic ester, alkyl-C(O)O-, alkylamino-C(O)-, and dialkylamino-C(O)-;

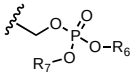
V is selected from an alkylene chain of 1-8 carbons; a linear or branched polyethylene oxide group comprising 1-13 units; linear or branched alkylene group comprising 1-8 carbons; -O-alkyl; carboxylic acid; carboxamide; carboxylic ester; alkyl-C(O)O-; alkylamino-C(O)-; dialkylamino-C(O)-; glucuronic acid (GlcA); a 1-3 amino acid sequence wherein each amino acid is independently selected from Glu, Gly, Asn, Asp, Gln, Leu, Lys, Ala, beta-Ala, Phe, Val, and Cit; Glu-Gly; aryl; and heteroaryl groups wherein said aryl and heteroaryl groups may be substituted with functional groups selected from alkyl, haloalkyl, halogen, biphenyl, nitro, nitrile, -OH, $-NH_2$, alkylamino, dialkylamino, thiol, thioalkyl, guanidine, urea, carboxylic acid, alkoxyl, carboxamide, carboxylic ester, alkyl-C(O)O-, alkylamino-C(O)-, dialkylamino-C(O)-;

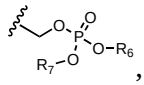
J is a reactive group selected from $-NH_2$, N_3, -SH, cyclooctyne, -OH, $-CO_2H$, trans-cyclooctene, alkynyl, propargyl,





where R_{32} is selected from Cl, Br, F, mesylate, and tosylate and R_{33} is selected from Cl, Br, I, F, OH, -O-N-succinimidyl, -O-(4-nitrophenyl), -O-pentafluorophenyl or -O-tetrafluorophenyl R_{34} is H, Me, tetrazine-H, and tetrazine-Me;

R_5 is selected from the group consisting of $-CH_2OH$, $-CH_2SH$, $-CH_2Cl$, $-SCH_2Cl$, $-SCH_2F$, $-SCH_2CF_3$, hydroxy, $-OCH_2CN$, $-OCH_2Cl$, $-OCH_2F$, $-OCH_3$, $-OCH_2CH_3$, $-SCH_2CN$, and ;

Q is H, , $C(O)R_8$, or $(C=O)NR_4CH_nNR_4(C=O)OCH_2$-$(V)_n$-J, or $P(O)OR_4$;

where n=1-4 and R_4 =H, alkyl or branched alkyl; R_6 and R_7 are independently selected from hydrogen and $C_{1\text{-}10}$ alkyl; R_8 is linear or branched alkyl of 1-8 carbons; A_1 and A_2 are independently selected from H and F.

2. The glucocorticoid agonist **according to claim 1**, wherein:

X is phenyl;

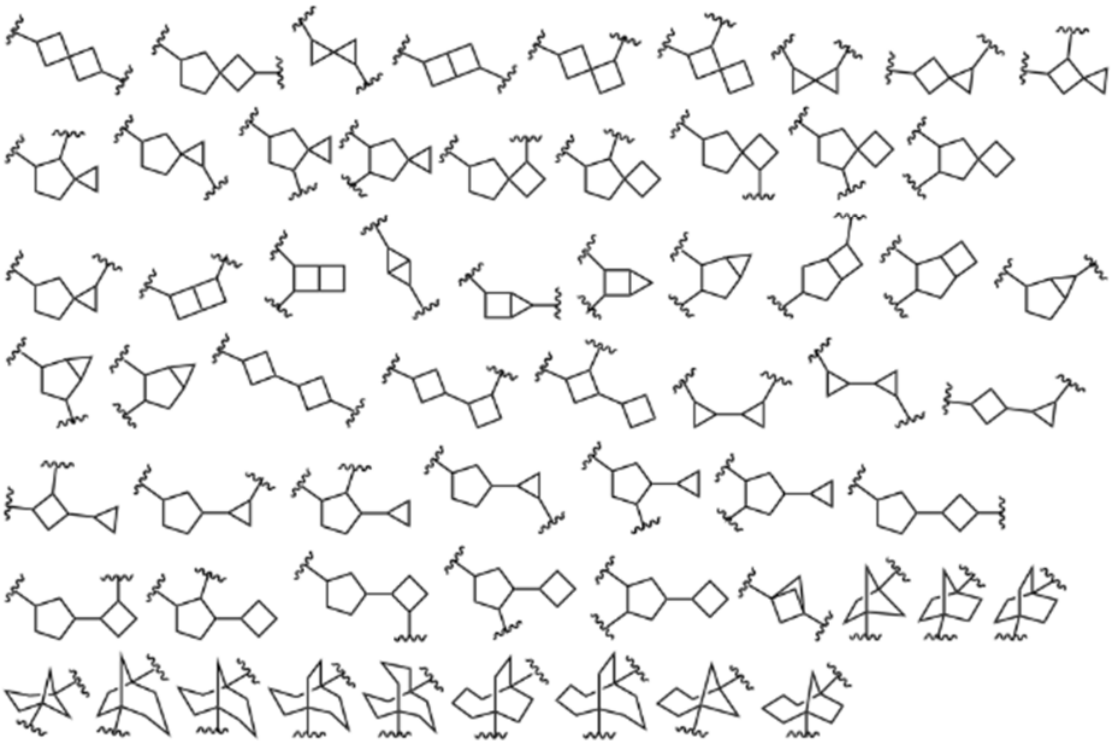
Y is CH_2 and O;

Z is selected from phenyl, spiro[3.3]heptane, [1.1.1]bicyclopentane, and bicyclo [2.2.2]octane; and

permutations of W are independently selected from $CH_2CH_2CO_2H$ and H.

3. The glucocorticoid agonist of **claim 1**, wherein:

Z is selected from



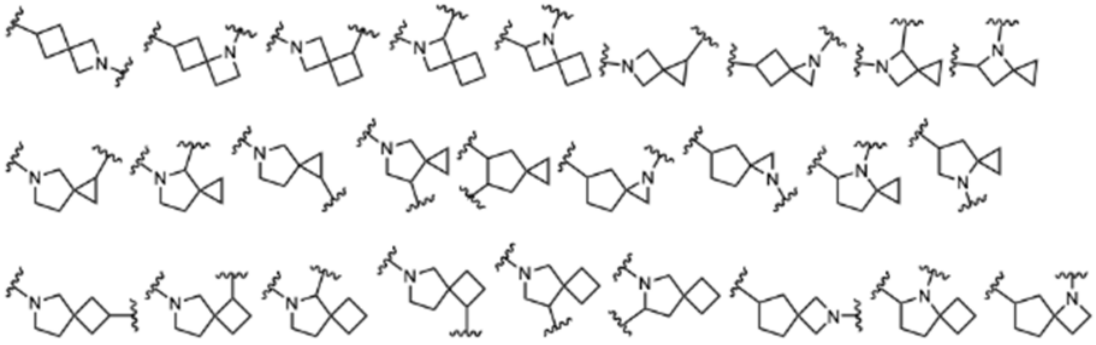
wherein

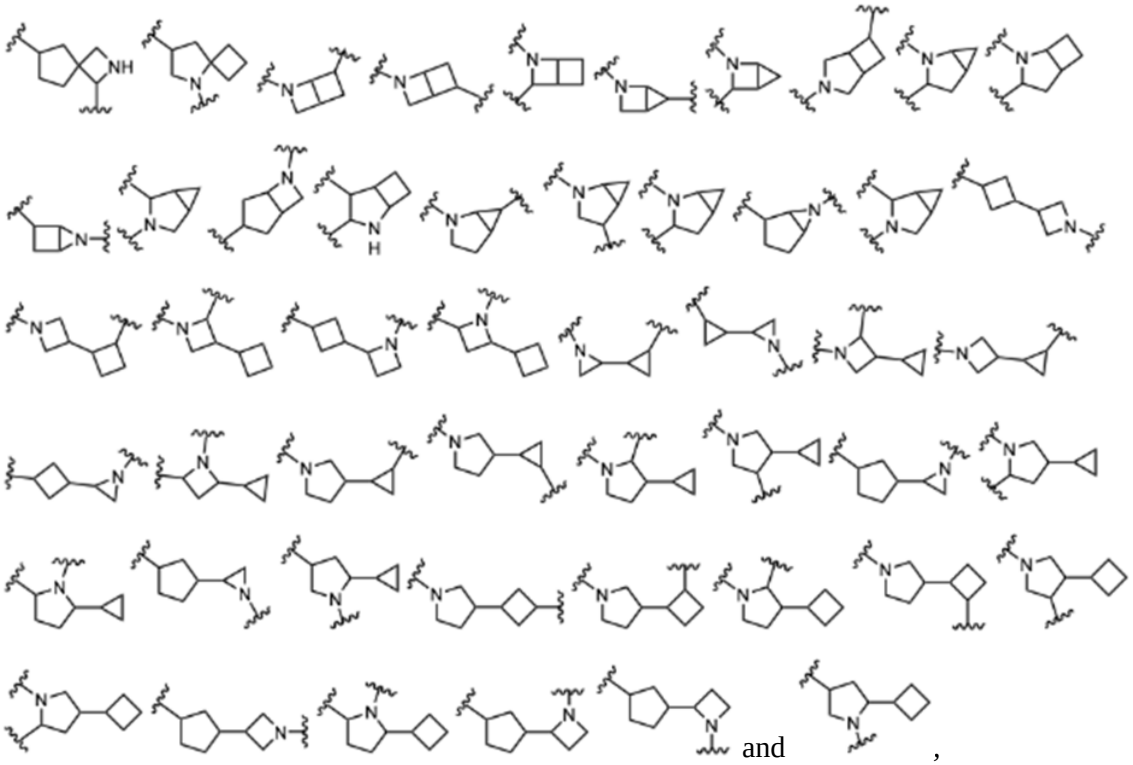
each of which may be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, N, S, and O, and are optionally further substituted with 1-4 C_{1-3} alkyl or C_{1-3} perfluoroalkyl groups;

each of which ring structure may contain at least one additional skeletal heteroatom selected from N, S, and O; and

each  indicates a point of attachement to the rest of the formula and each of said points of attachment may be covalently bonded to the rest of the formula via an additional heteroatom selected from N, S, and O; or

Z-NR_1 is selected from:





and ,

wherein

each of which may be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, N, S, and O, and are optionally further substituted with 1-4 C_{1-3} alkyl or C_{1-3} perfluoroalkyl groups;

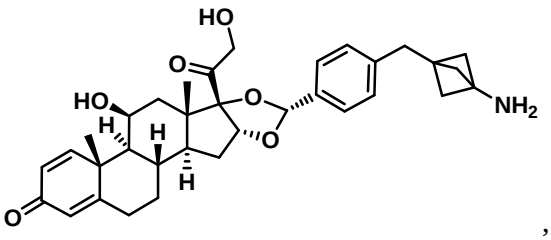
each of which ring structure may contain at least one additional skeletal heteroatom selected from N, S, and O; and

each  indicates a point of attachement to the rest of the formula and each of said points of attachment may be covalently bonded to the rest of the formula via an additional heteroatom selected from N, S, and O.

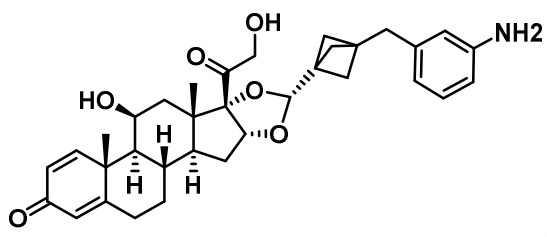
4. The glucocorticoid agonist **according to claim 1**, selected from:

(i) any of the glucocorticoid agonists disclosed in **Figure 118A-G**; or

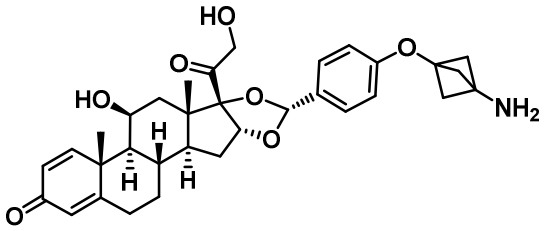
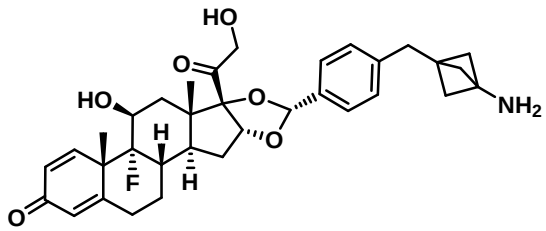
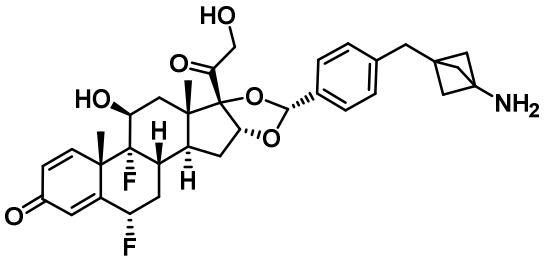
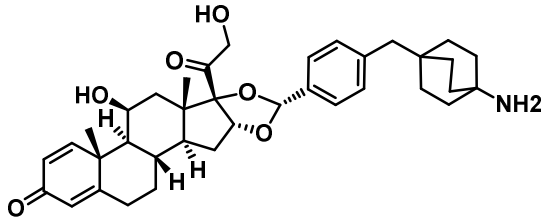
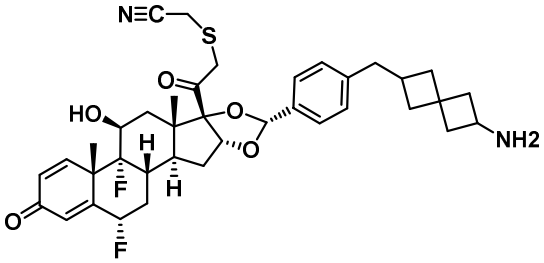
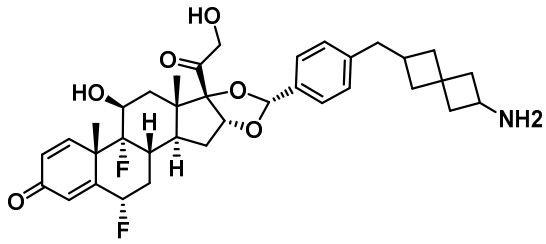
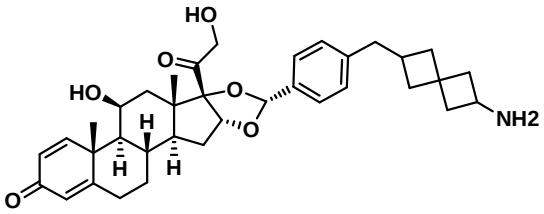
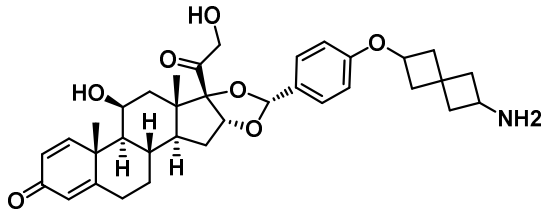
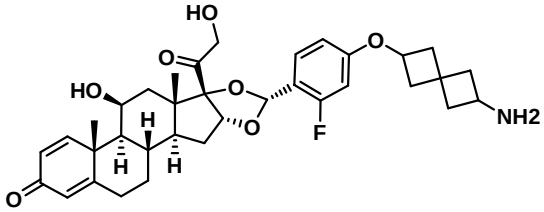
(ii) one having a structure selected from:



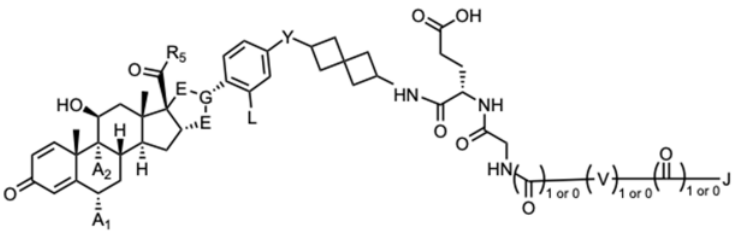
,



,










and .

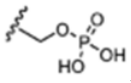
5. The glucocorticoid agonist according to **claim 1**, having the structure of **Formula (II)**:


Formula (II),

wherein:

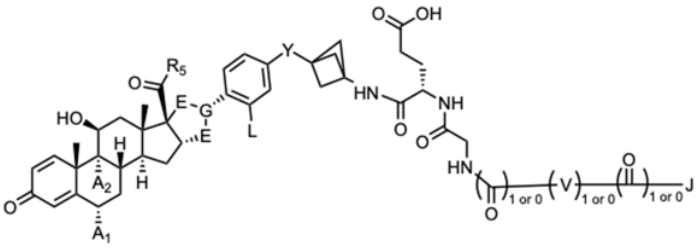
Y is selected from CH_2 and O;

L is selected from H and F;

R_5 is selected from $-CH_2OH$, $-SCH_2F$ and ; and

V is selected from aminobenzyloxycarbonyl (AB), p-aminobenzyloxycarbonyl (PAB), Glu-Gly, Val-Cit, Val-Ala, Val-Gly, Val-Gln, Ala-Val, Cit-Cit, Lys-Val-Cit, Asp-Val-Ala, Ala-Ala-Asn, Asp-Val-Ala, Ala-Val-Cit, Ala-Asn-Val, beta-Ala-Leu-Ala-Leu, Lys-Val-Ala, Val-Leu-Lys, Asp-Val-Cit, Val-Ala-Val, Ala-Ala-Asn, AB-beta-Ala, AB-GlcA, AB-GlcA-beta-Ala; PAB-GlcA, and PAB-Glu-Gly.

6. The glucocorticoid agonist according to **claim 1**, having the structure of **Formula (III)**:

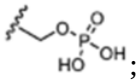


Formula (III),

wherein

Y is selected from CH_2 and O;

L is selected from H and F;

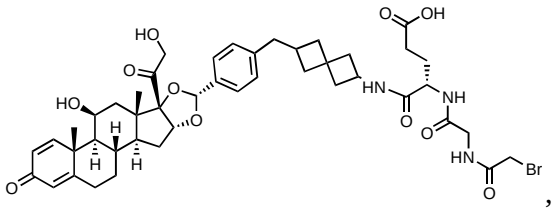
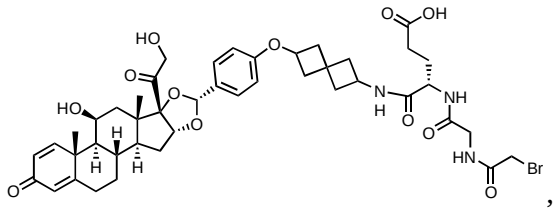
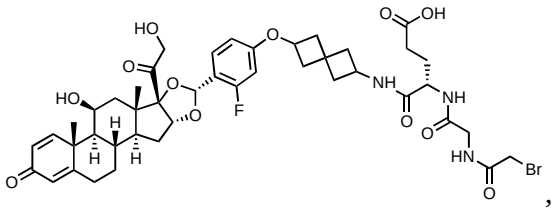
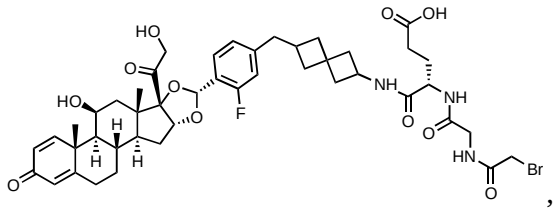
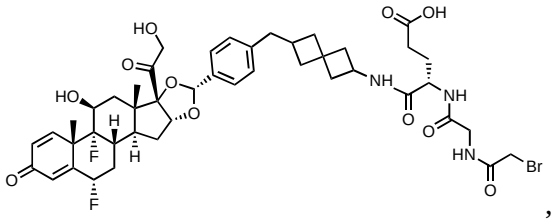
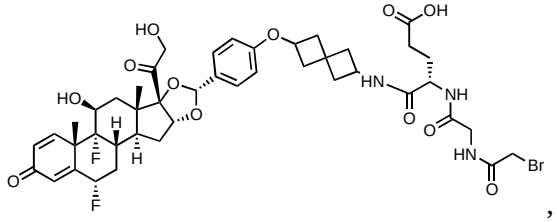
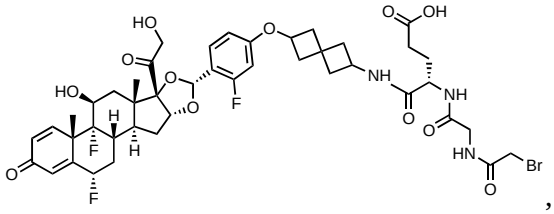
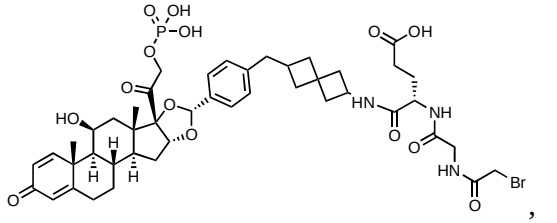
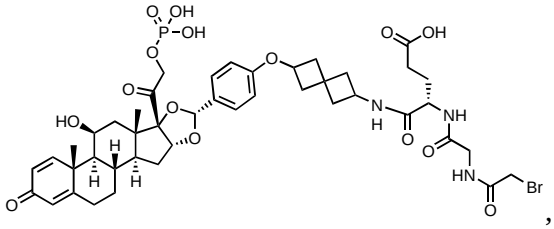
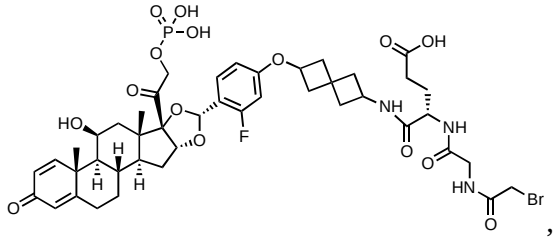
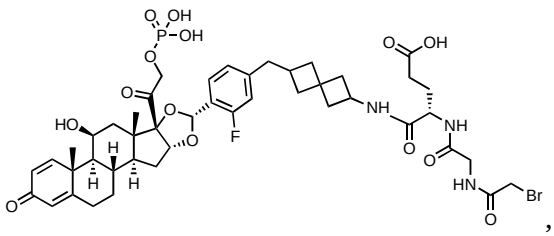
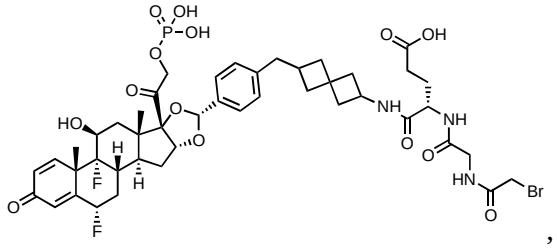
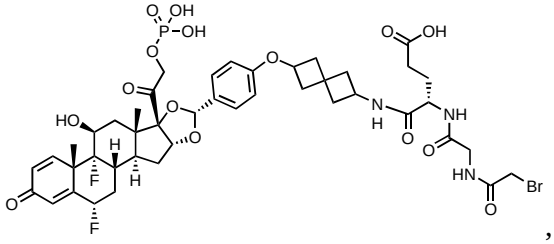
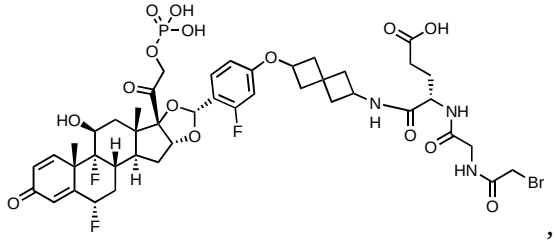
R_5 is selected from $-CH_2OH$, $-SCH_2F$ and ;

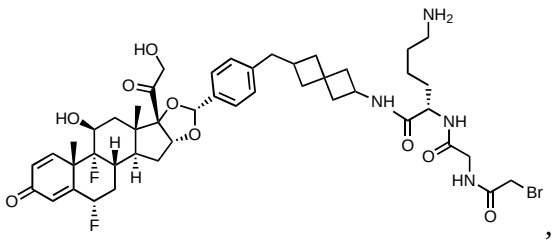
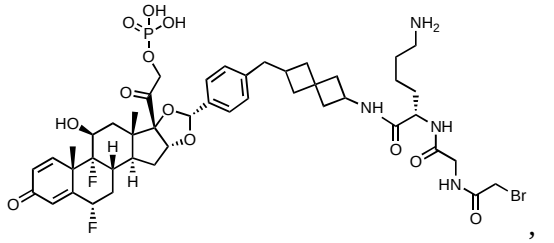
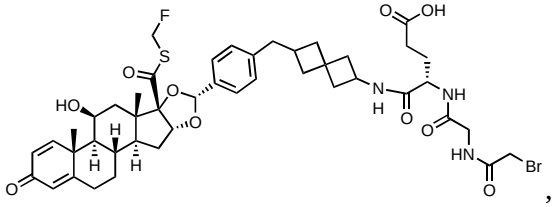
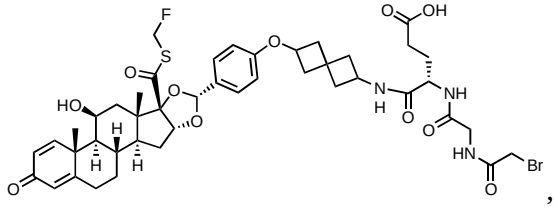
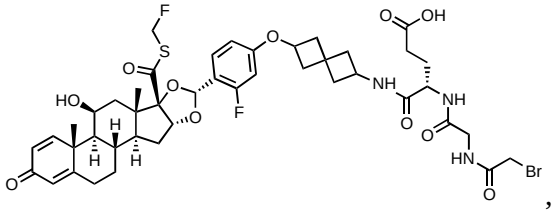
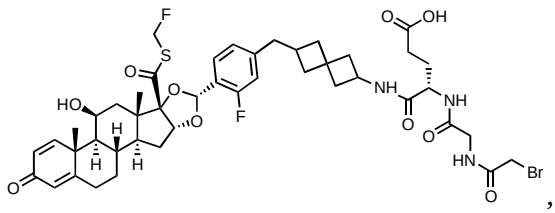
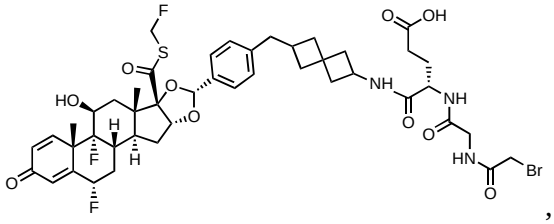
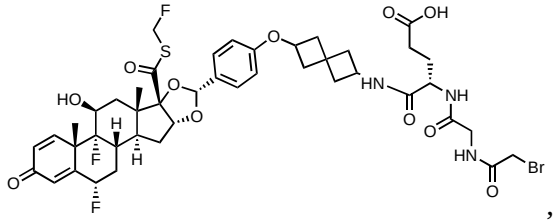
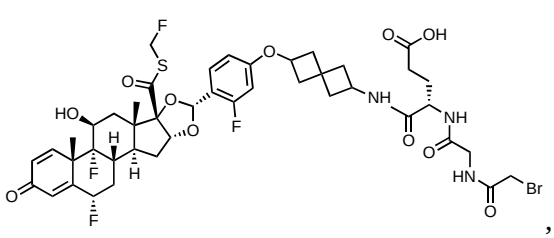
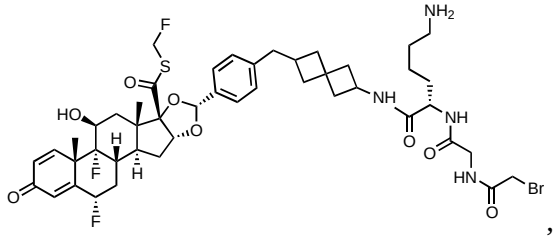
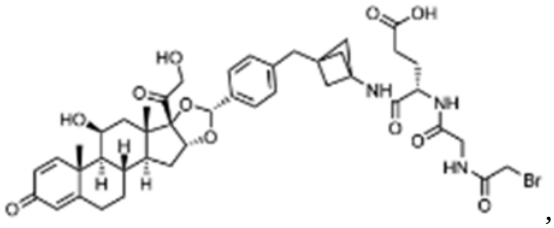
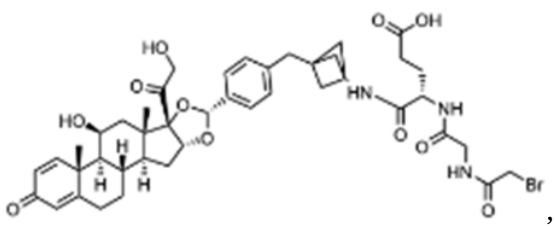
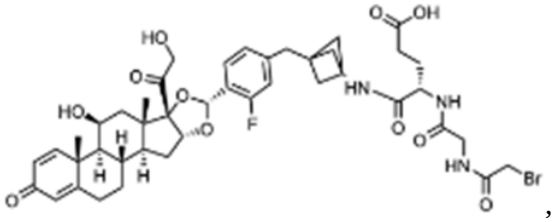
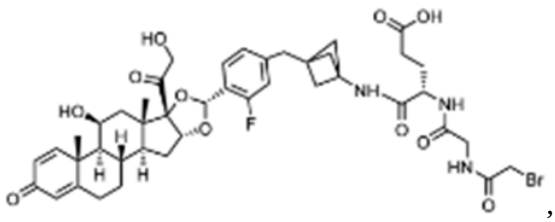
V is selected from aminobenzyloxycarbonyl (AB), p-aminobenzyloxycarbonyl (PAB), Glu-Gly, Val-Cit, Val-Ala, Val-Gly, Val-Gln, Ala-Val, Cit-Cit, Lys-Val-Cit, Asp-Val-Ala, Ala-Ala-Asn, Asp-Val-Ala, Ala-Val-Cit, Ala-Asn-Val, beta-Ala-Leu-Ala-Leu, Lys-Val-Ala, Val-Leu-Lys, Asp-Val-Cit, Val-Ala-Val, Ala-Ala-Asn, AB-beta-Ala, AB-GlcA, AB-GlcA-beta-Ala; PAB-GlcA, and PAB-Glu-Gly.

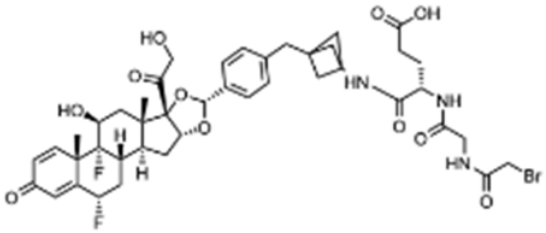
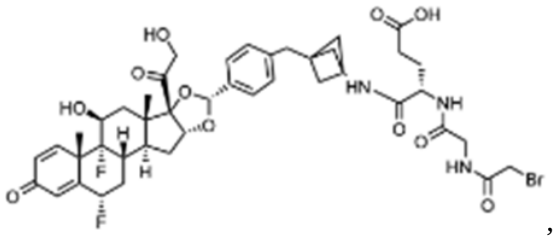
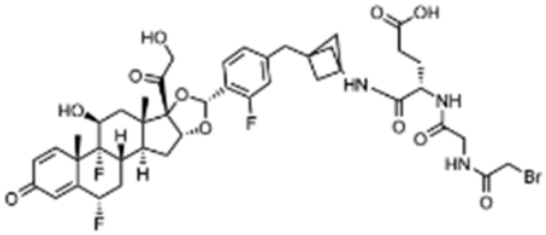
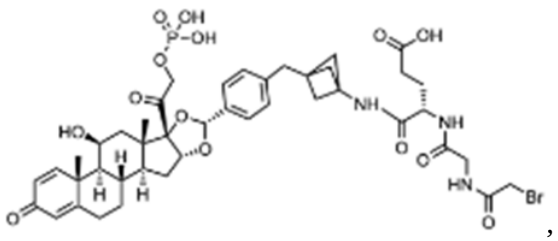
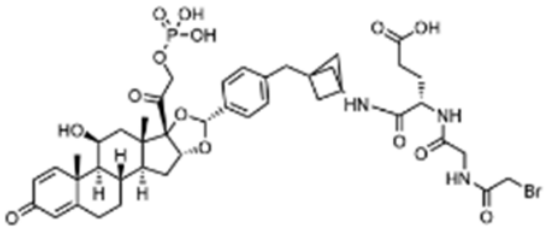
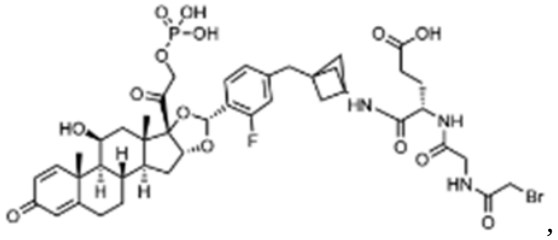
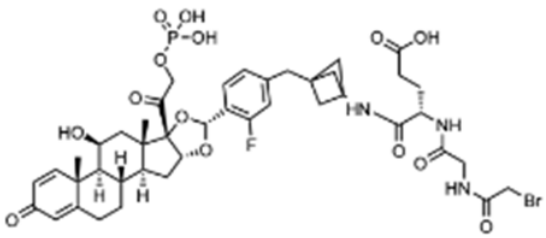
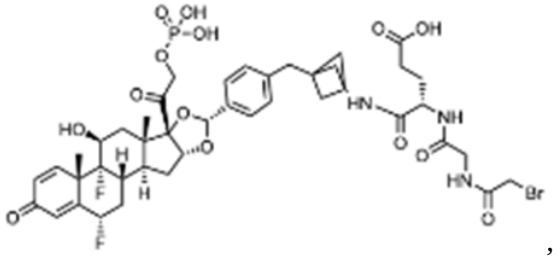
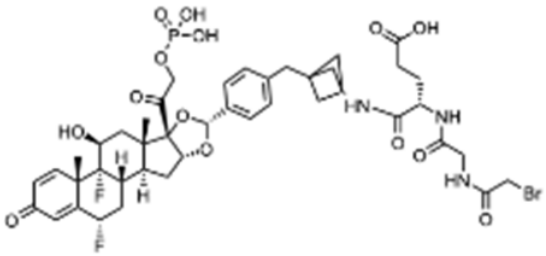
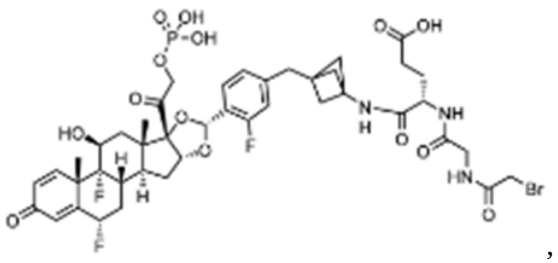
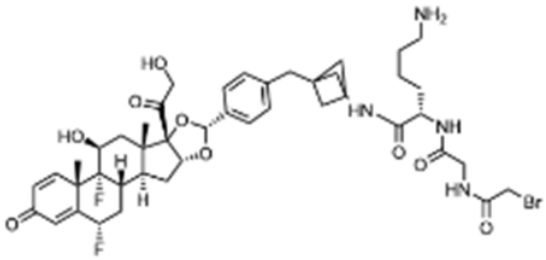
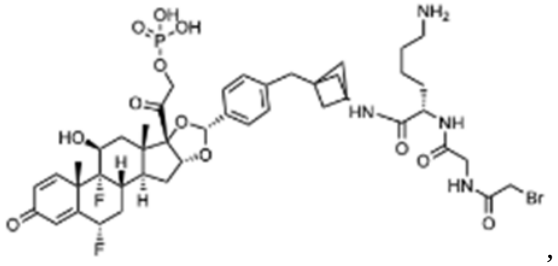
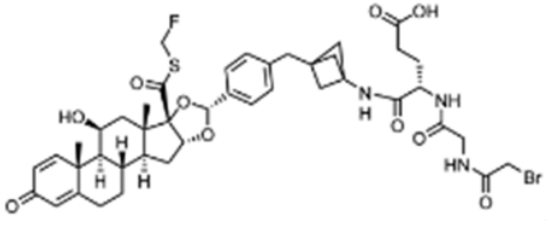
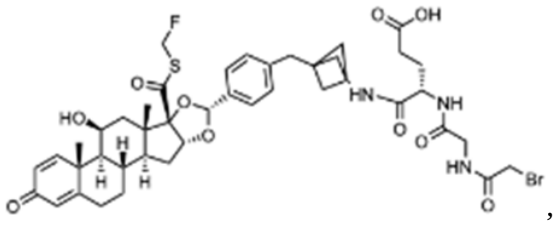
7. The glucocorticoid agonist according to **claim 1**, which is selected from the following:

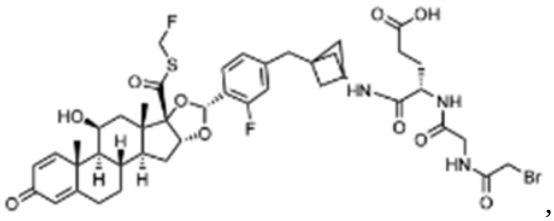
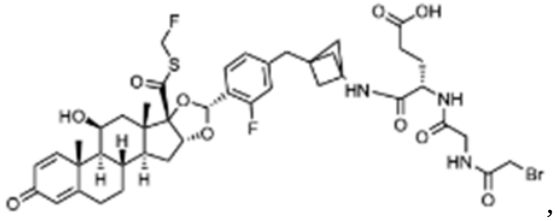
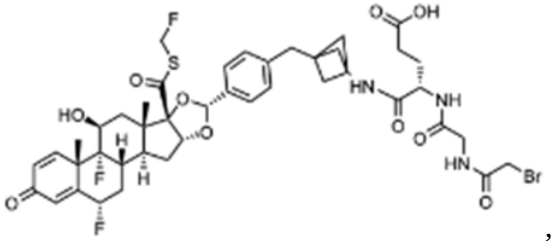
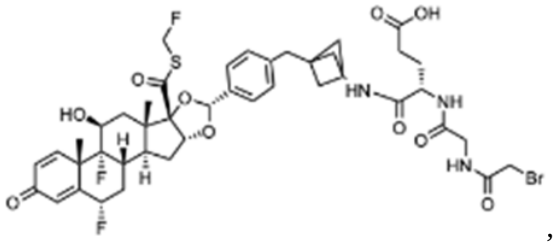
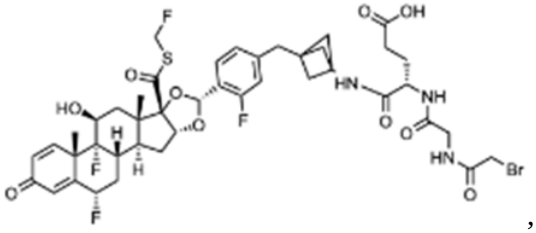
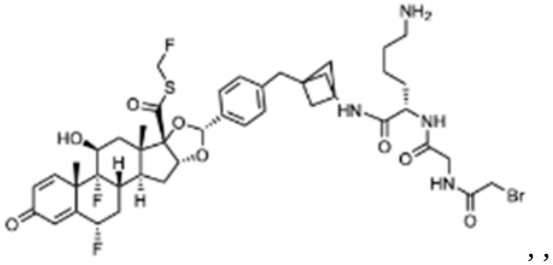
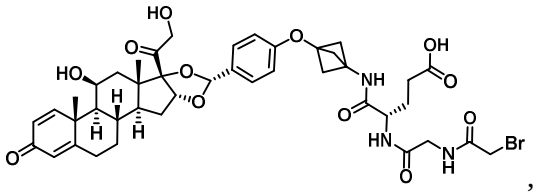
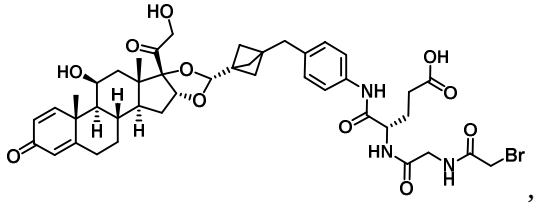
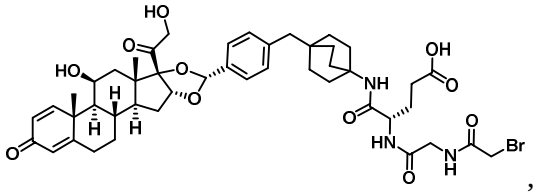
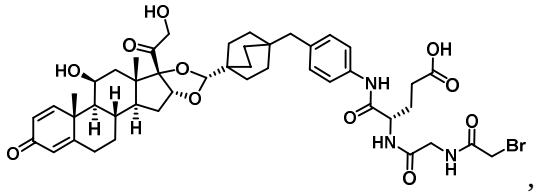
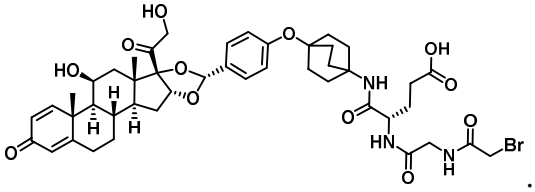
(i) any of the glucocorticoid agonists disclosed in **Figure 118H-O**; or

(ii) having a structure selected from:


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8. The glucocorticoid agonist **according to any one of claims 1-7**, wherein:

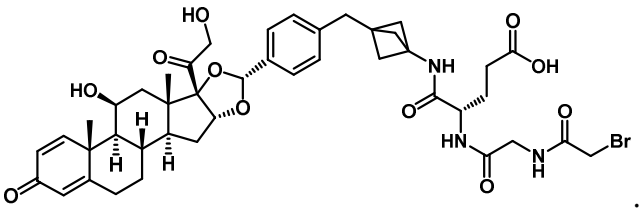
(i) R_2 comprises at least one immolative linker or at least one cleavable linker which is susceptible to one or more of acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage;

(ii) R_2 is a non-cleavable linker, which is resistant to acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage;

(iii) V comprises at least one immolative linker or cleavable linker; or

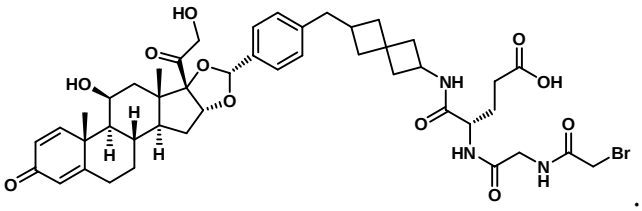
(iv) V is a non-cleavable linker.

9. The glucocorticoid agonist **of claim 1**, having the structure



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10. The glucocorticoid agonist **of claim 1**, having the structure



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11. A payload-linker conjugate having the structure of **(Formula IV)**:

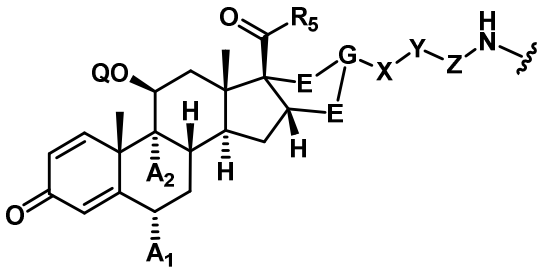
J-L-NHPayload **(Formula IV)**

wherein:

J is a reactive group according to **claim 1** which is suitable for reacting with a complementary functional group on an antibody (Ab) to form an antibody-drug conjugate;

L is a linker comprising aminobenzyloxycarbonyl (AB), p-aminobenzyloxycarbonyl (PAB), glucuronic acid (GlcA), AB-GlcA, PAB-GlcA, an amino acid, a peptide comprising 1-12 amino acids, or any combination thereof,

NHPayload is a glucocorticoid agonist according to **claim 1** and having the structure of



.

12. The payload-linker conjugate according to **claim 11,** wherein:

(i) L comprises at least one immolative linker or at least one cleavable linker which is susceptible to one or more of acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage; or

(ii) L is a non-cleavable linker, which is resistant to acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage.

13. The payload-linker conjugate according to **claim 11 or 12**, wherein:

(i) L comprises AB, PAB, AB-GlcA, or PAB-GlcA;

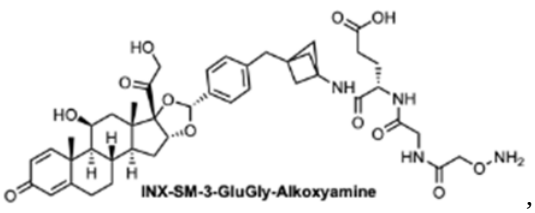
(ii) L comprises said amino acid or peptide selected from a peptide comprising 1-12 amino acids, a dipeptide, a tripeptide, a tetrapeptide, a pentapeptide, Gly, Glu, beta-Ala, Asn, Asp, Gln, Leu, Lys, Ala, Phe, Cit, Val, Glu-Gly, Val-Cit, Val-Ala, Val-Gly, Val-Gln, Ala-Val, Cit-Cit, Lys-Val-Cit, Asp-Val-Ala, Ala-Ala-Asn, Asp-Val-Ala, Ala-Val-Cit, Ala-Asn-Val, beta-Ala-Leu-Ala-Leu, Lys-Val-Ala, Val-Leu-Lys, Asp-Val-Cit, Val-Ala-Val, and Ala-Ala-Asn;

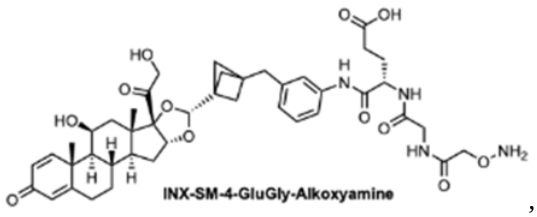
(iii) L is Glu-Gly, PAB-Glu-Gly, or AB-GlcA-beta-Ala; or

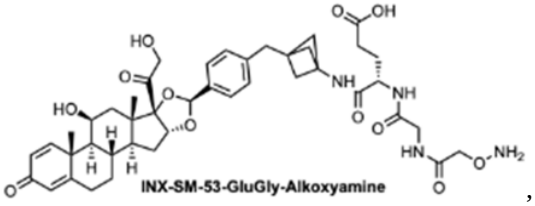
(iv) any combination thereof.

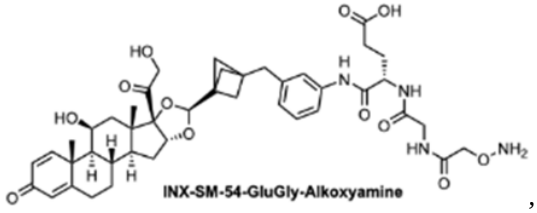
14. The payload-linker conjugate **according to any one of claims 11-13**, which is selected from:

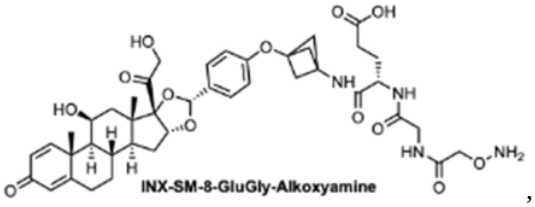
(i) the list of Glu-Gly-Alkoxyamines consisting of

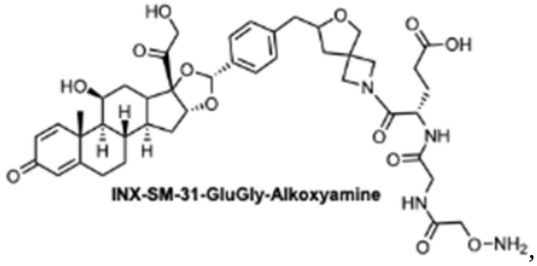


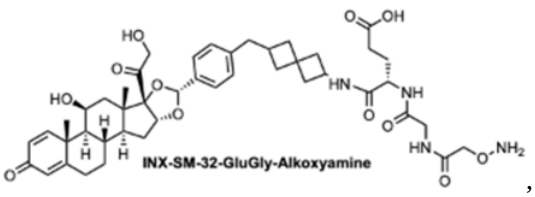
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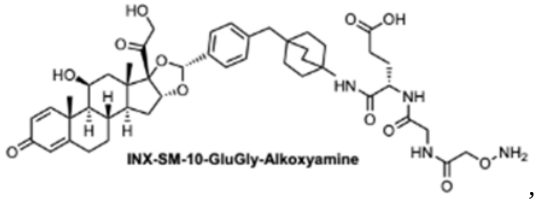
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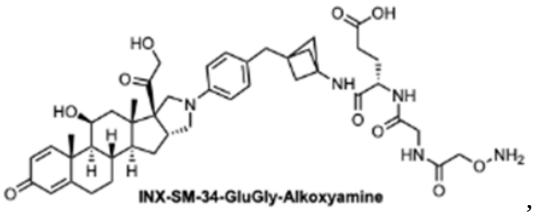
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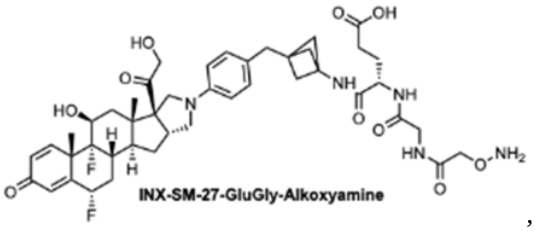
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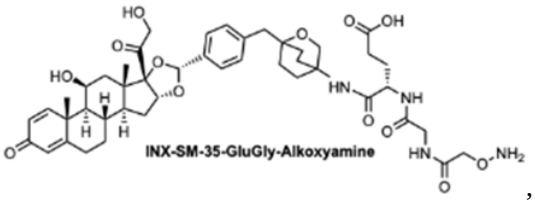
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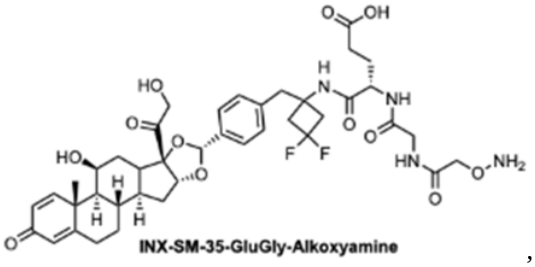
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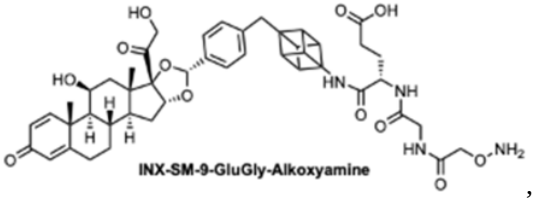
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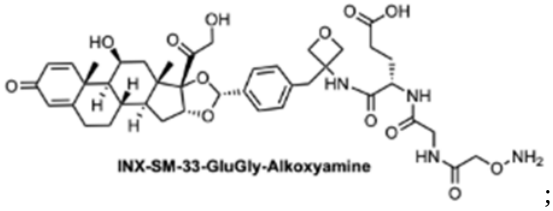

INX-SM-34-GluGly-Alkoxyamine

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INX-SM-27-GluGly-Alkoxyamine

, 
INX-SM-35-GluGly-Alkoxyamine

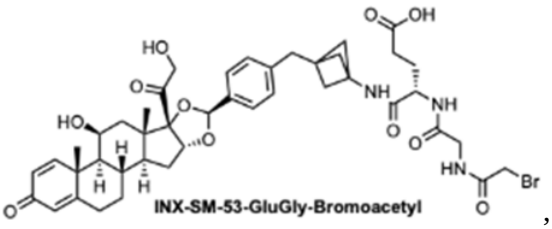
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INX-SM-35-GluGly-Alkoxyamine

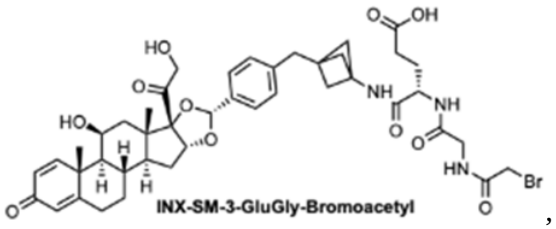
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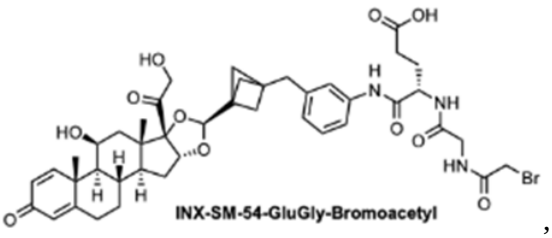
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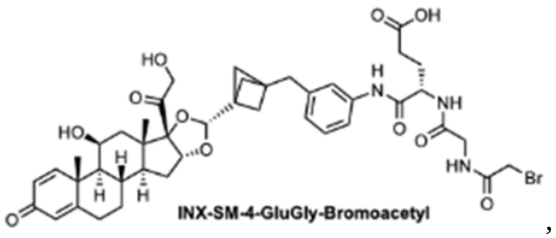
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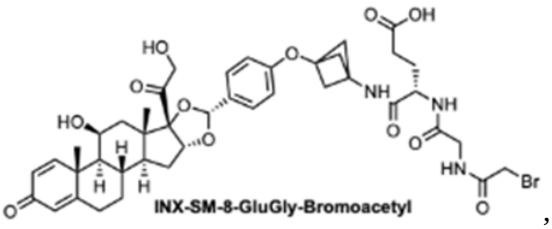
(ii) the list of Glu-Gly-Bromoacetyls consisting of

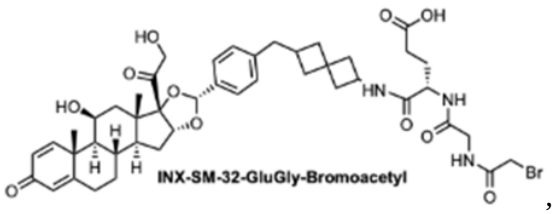

INX-SM-53-GluGly-Bromoacetyl

, 
INX-SM-3-GluGly-Bromoacetyl

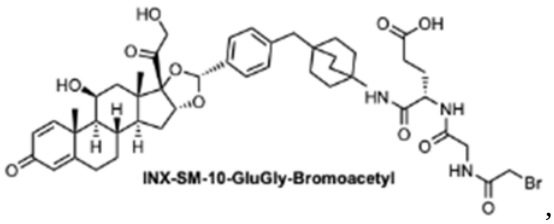
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INX-SM-54-GluGly-Bromoacetyl

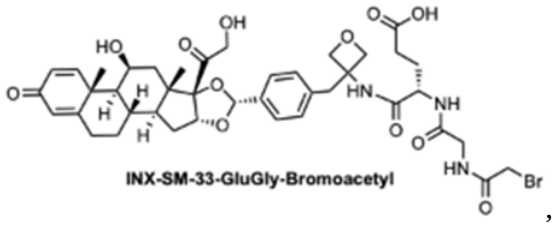
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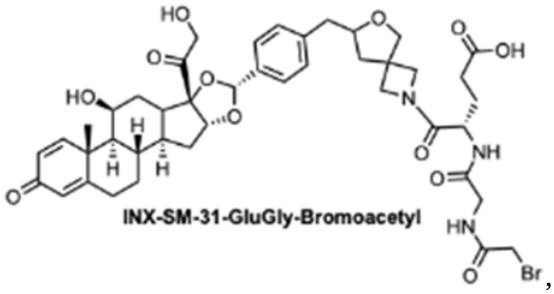
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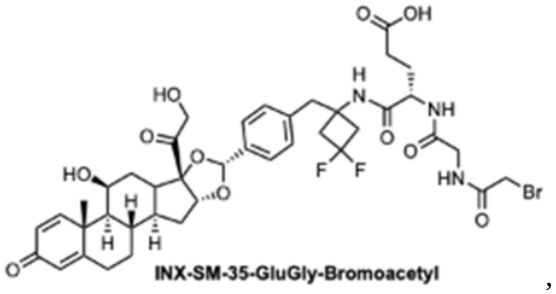
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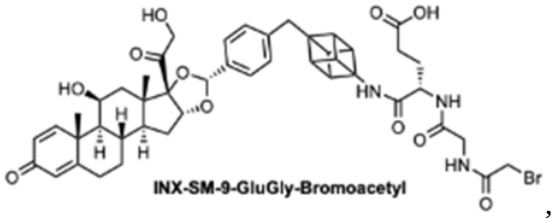
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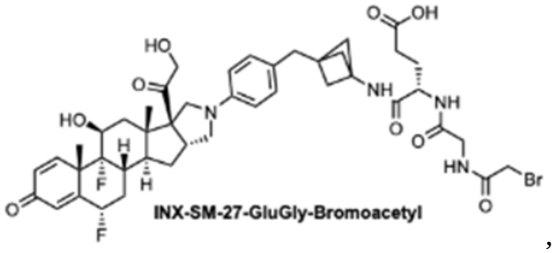


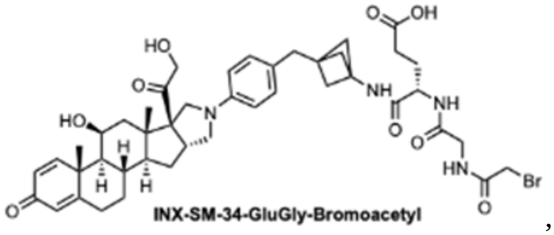
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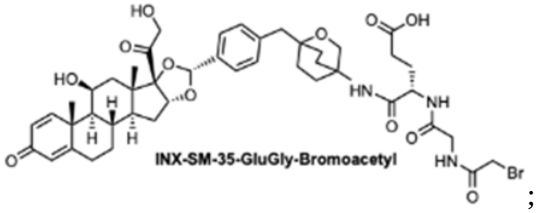
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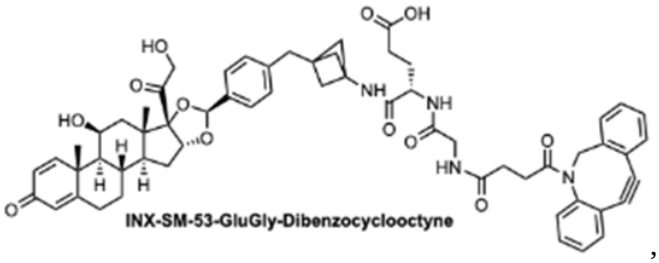
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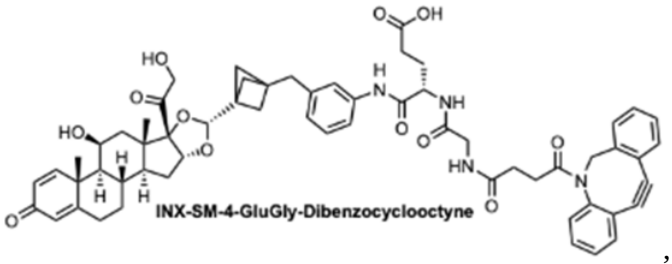
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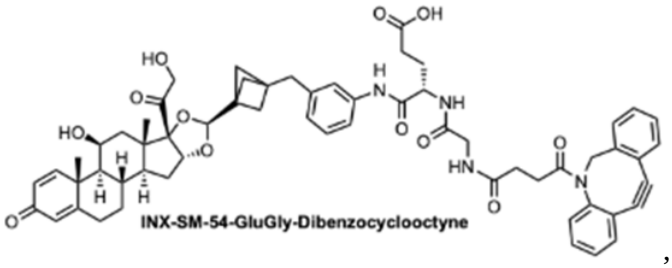
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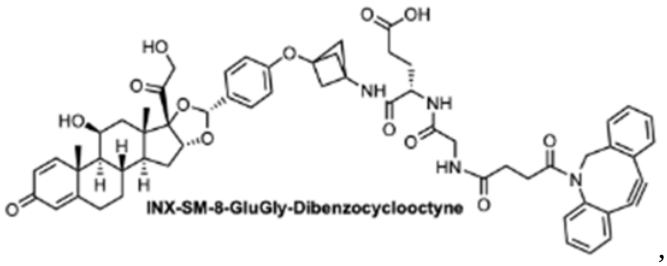
(iii) the list of Glu-Gly-Dibenzocyclooctynes consisting of

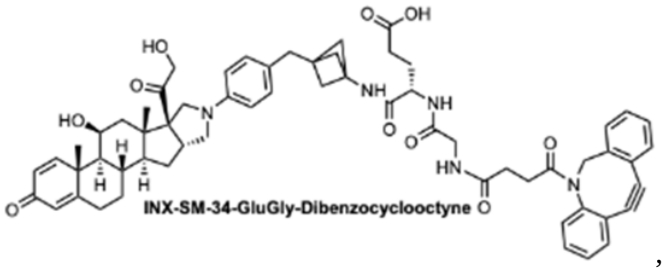


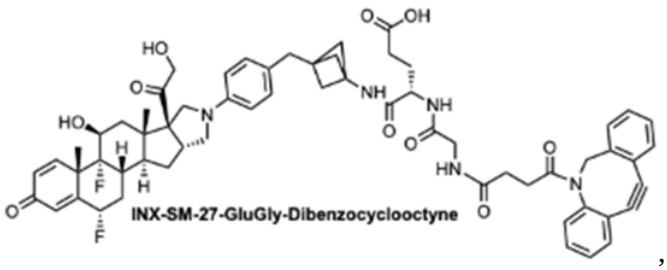
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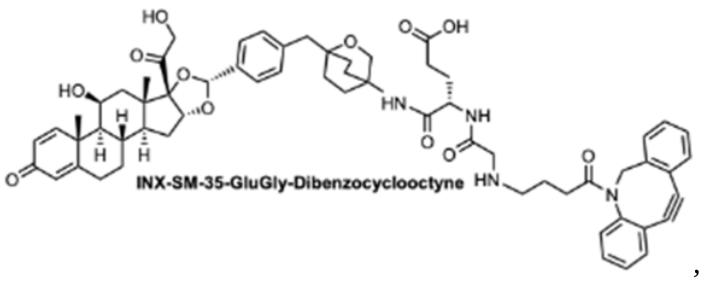

INX-SM-4-GluGly-Dibenzocyclooctyne
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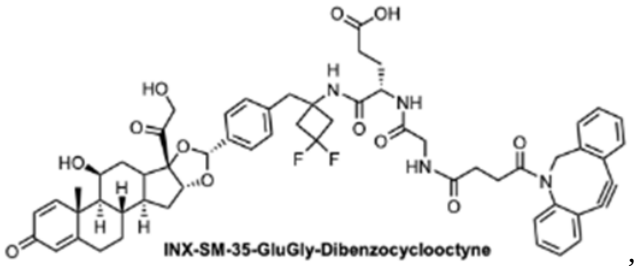

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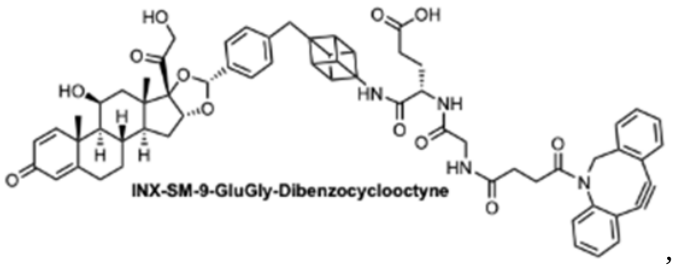

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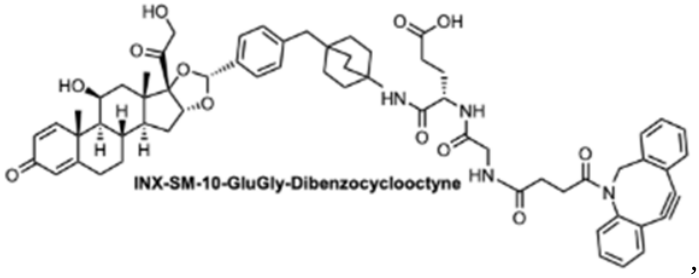

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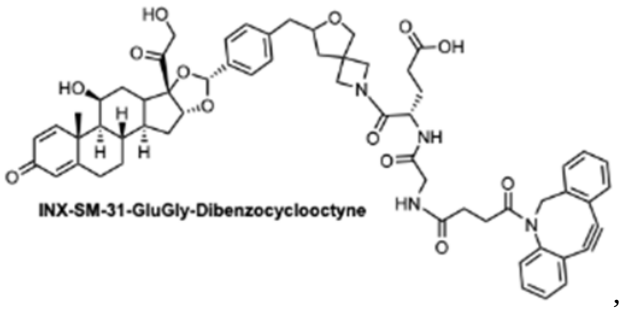

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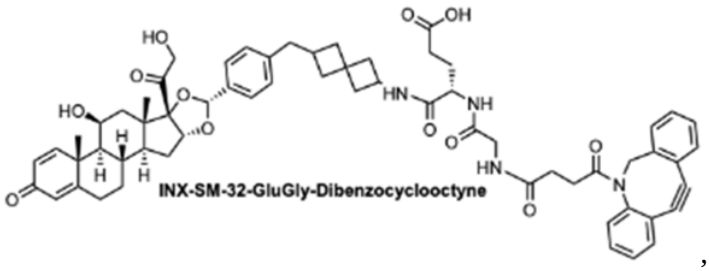

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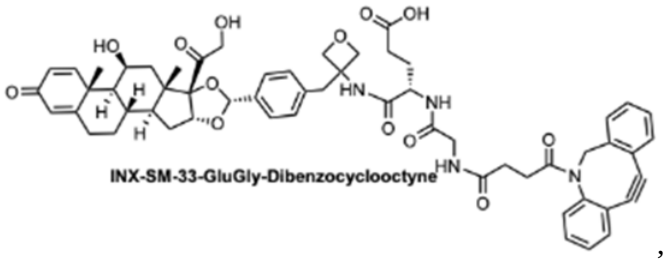

INX-SM-35-GluGly-Dibenzocyclooctyne
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INX-SM-9-GluGly-Dibenzocyclooctyne
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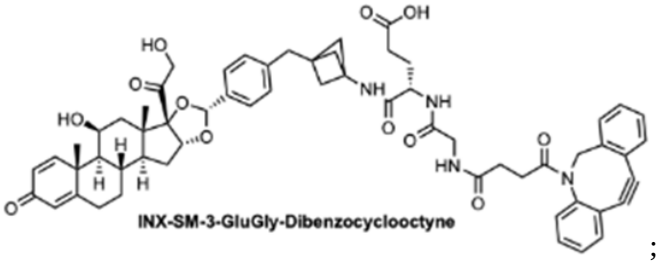

INX-SM-10-GluGly-Dibenzocyclooctyne
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INX-SM-31-GluGly-Dibenzocyclooctyne
,


INX-SM-32-GluGly-Dibenzocyclooctyne
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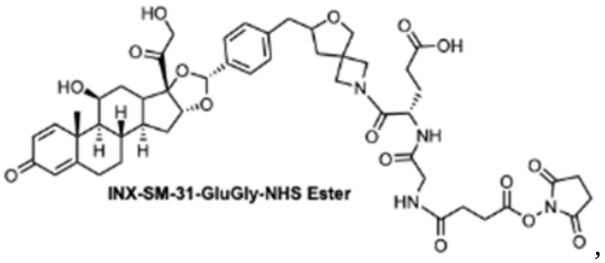


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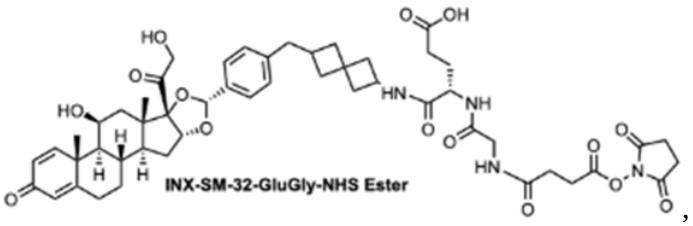


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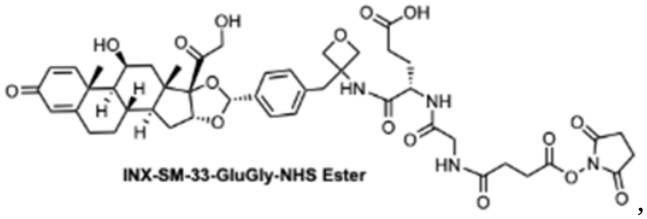
(iv) the list of Glu-Gly-NHS esters consisting of



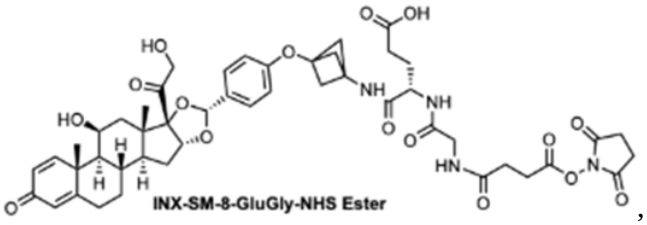
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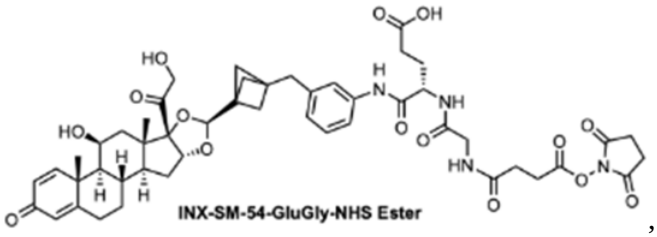
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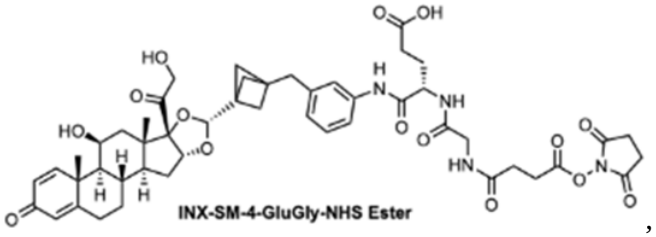


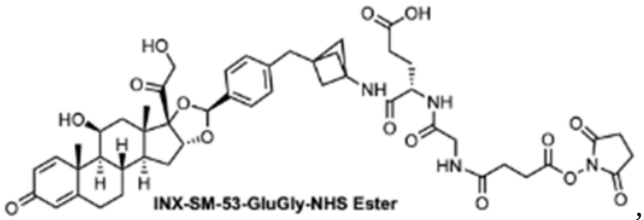
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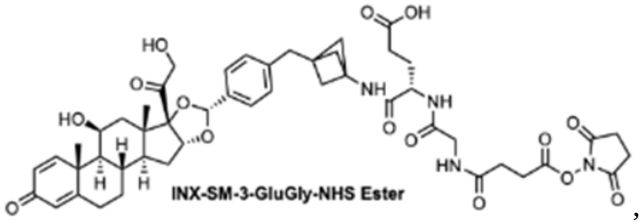


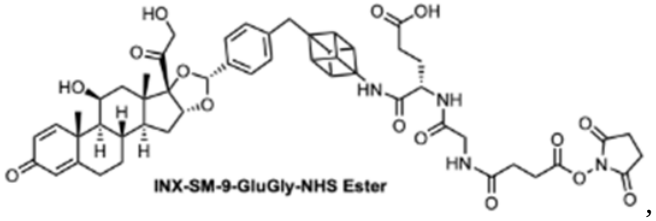
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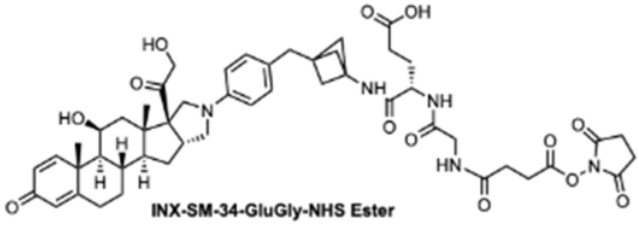

INX-SM-54-GluGly-NHS Ester ,

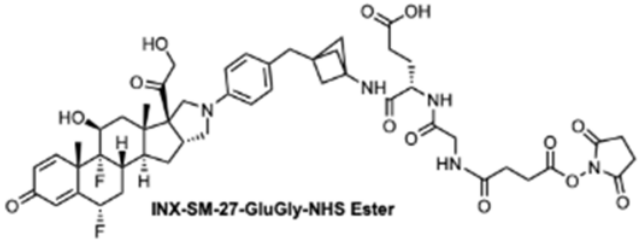

INX-SM-4-GluGly-NHS Ester ,

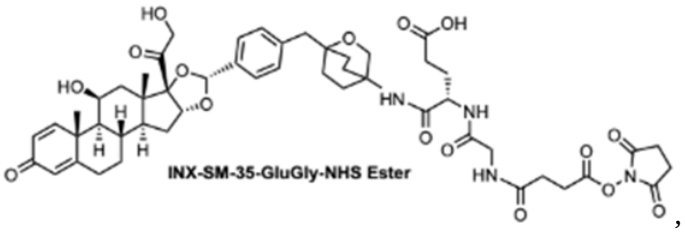

INX-SM-53-GluGly-NHS Ester ,


INX-SM-3-GluGly-NHS Ester ,

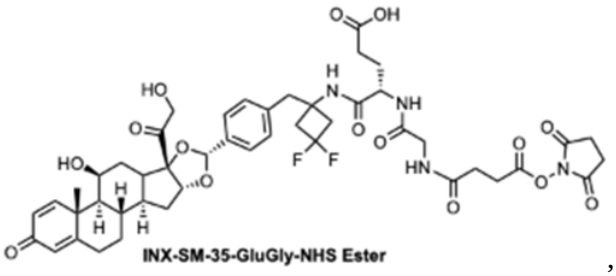

INX-SM-9-GluGly-NHS Ester ,


INX-SM-34-GluGly-NHS Ester ,

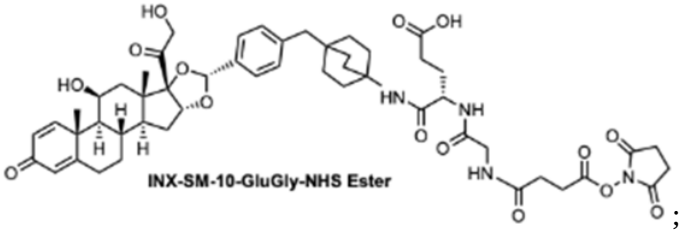

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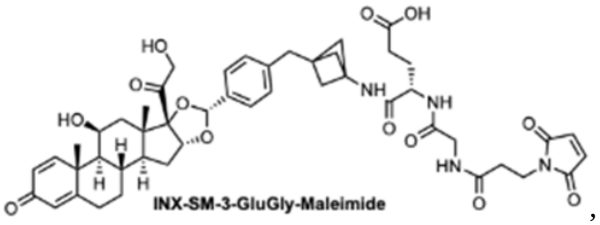


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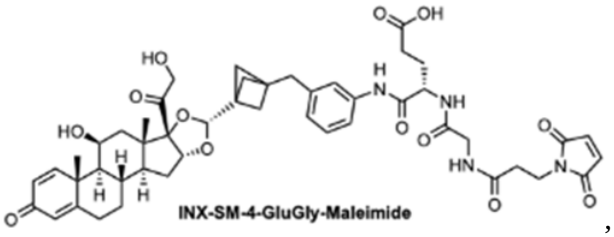


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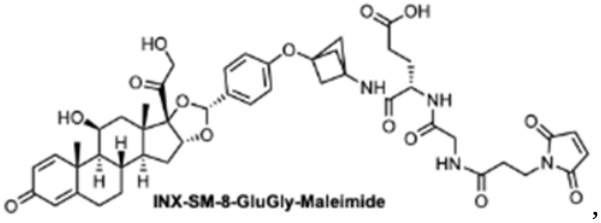
(v) the list of Glu-Gly-Maleimides consisting of



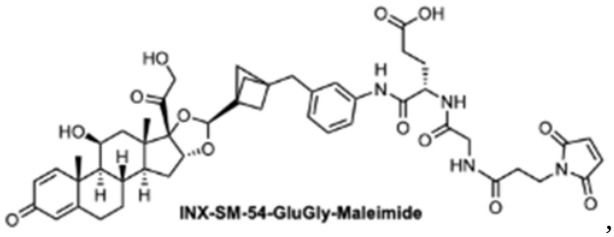
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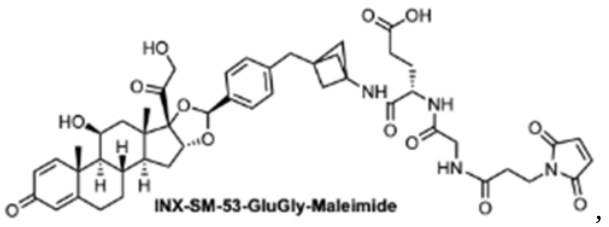


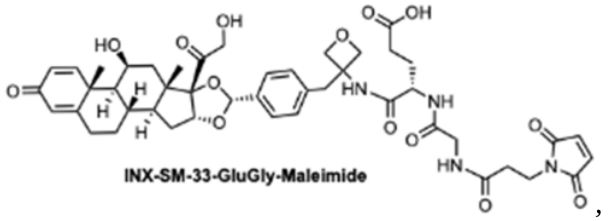
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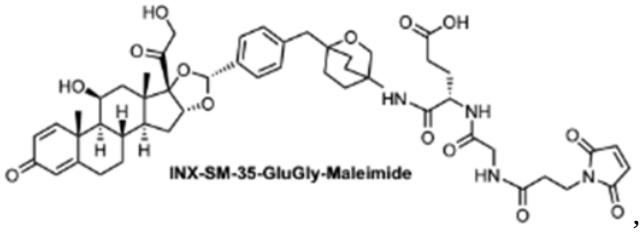


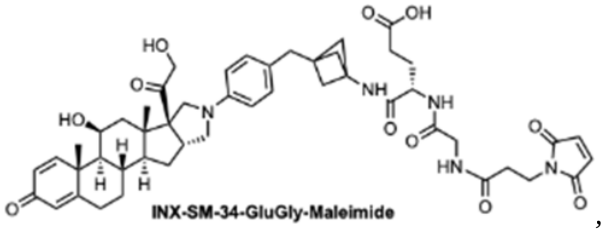
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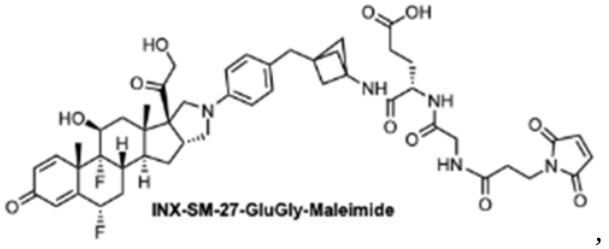

INX-SM-54-GluGly-Maleimide
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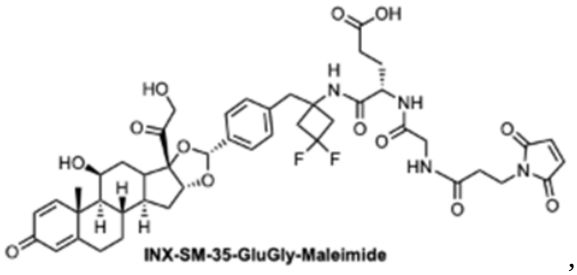

INX-SM-53-GluGly-Maleimide
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INX-SM-33-GluGly-Maleimide
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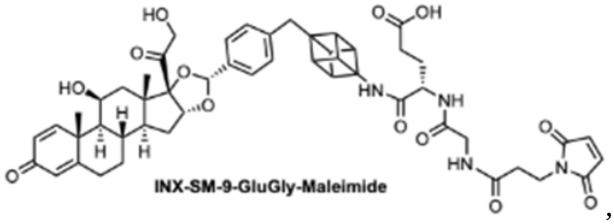

INX-SM-35-GluGly-Maleimide
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INX-SM-34-GluGly-Maleimide
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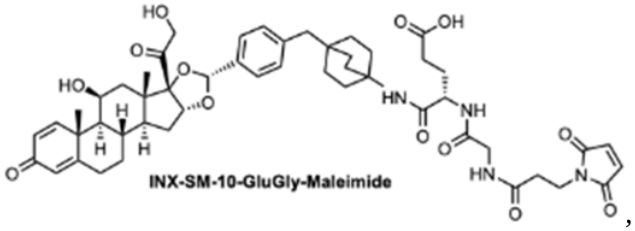

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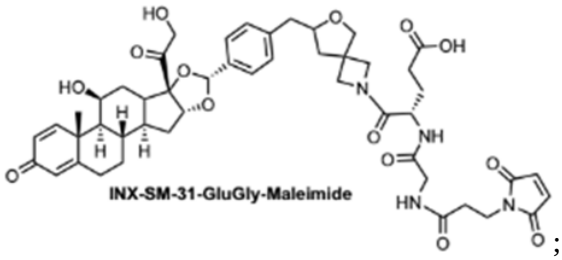
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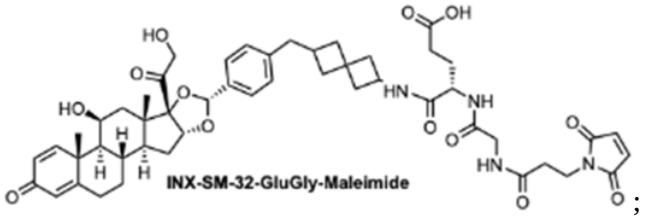
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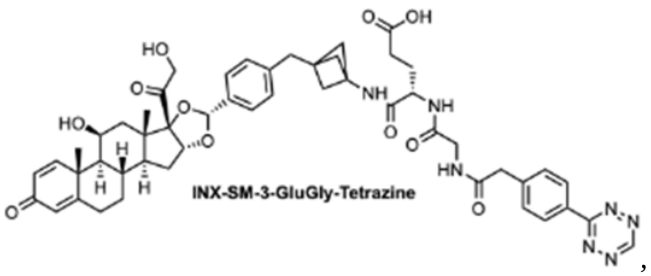


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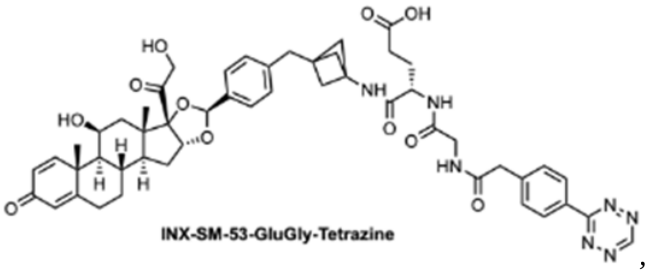


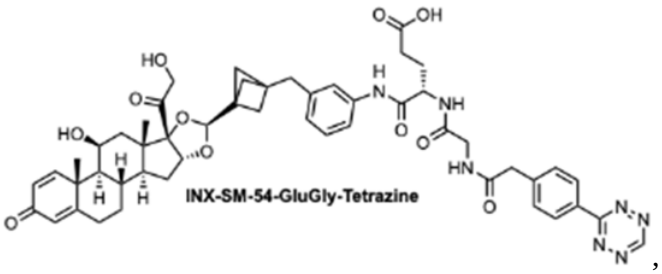
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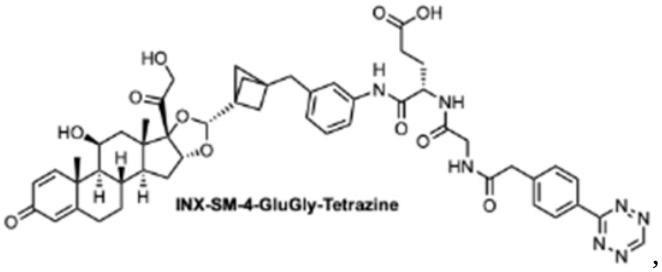
(vi) the list of Glu-Gly-Tetrazines selected from

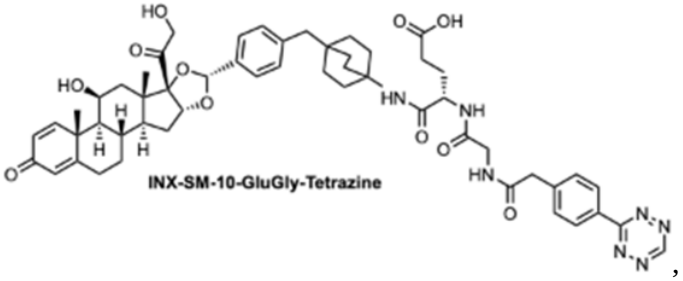


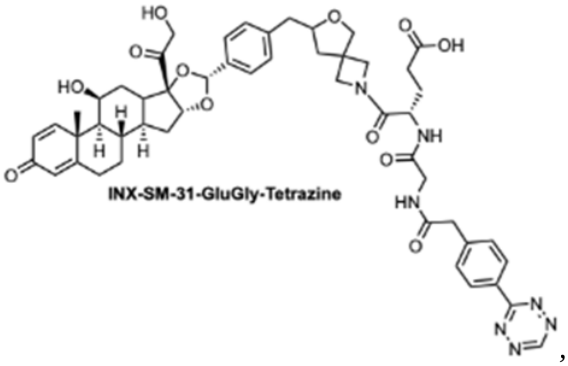
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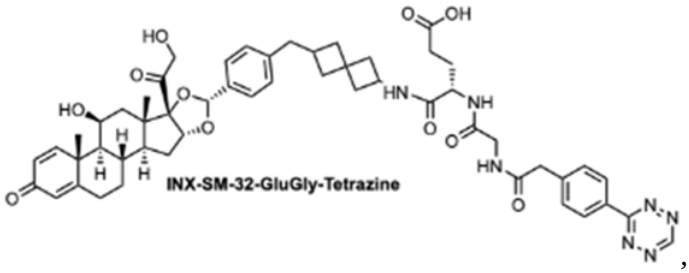

INX-SM-53-GluGly-Tetrazine
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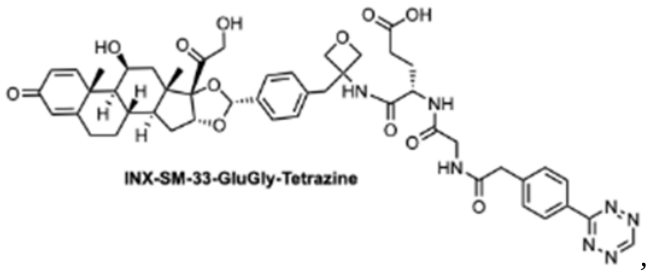

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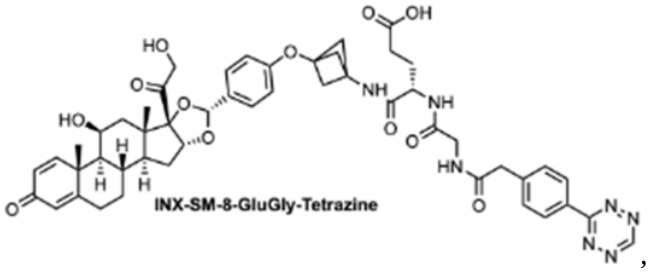

INX-SM-4-GluGly-Tetrazine
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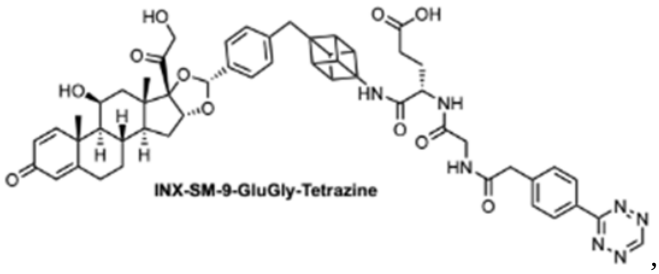

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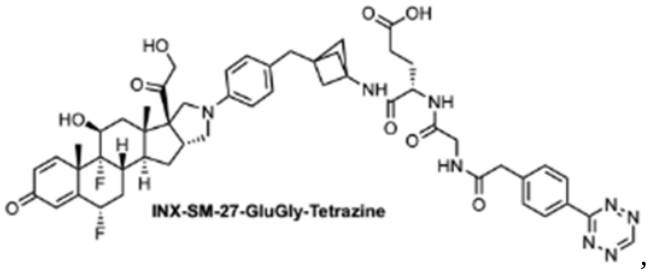

INX-SM-31-GluGly-Tetrazine
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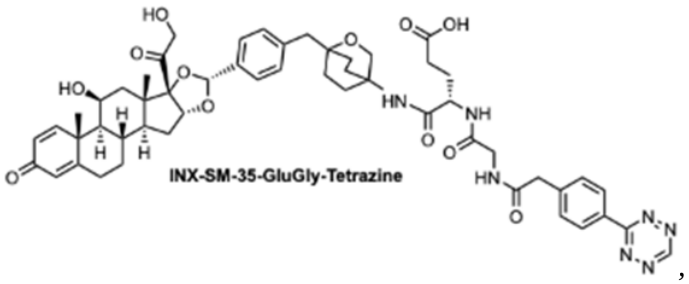

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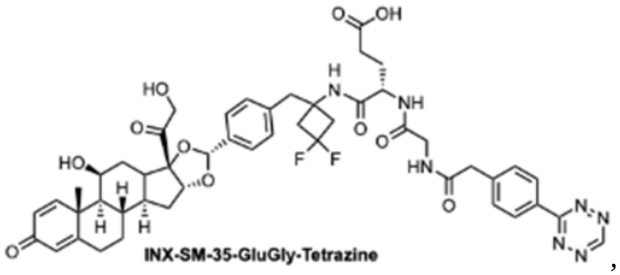

INX-SM-33-GluGly-Tetrazine
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INX-SM-8-GluGly-Tetrazine
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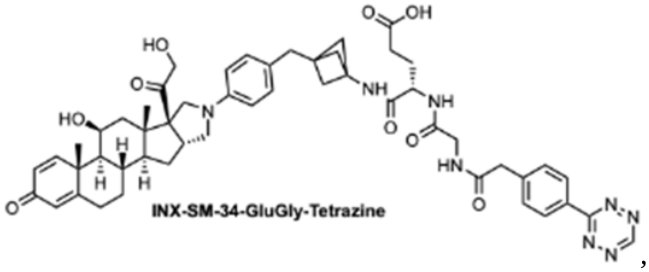

INX-SM-9-GluGly-Tetrazine
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INX-SM-27-GluGly-Tetrazine
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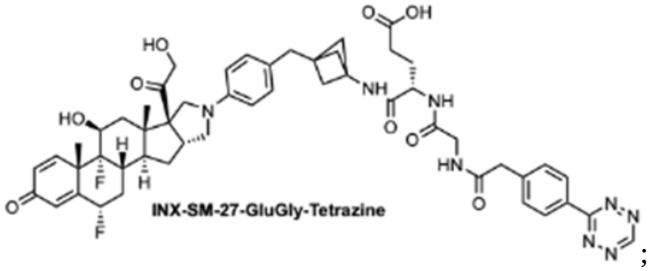

INX-SM-35-GluGly-Tetrazine
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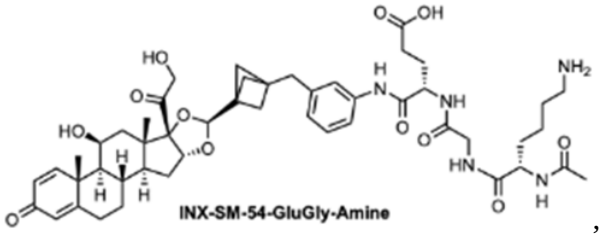


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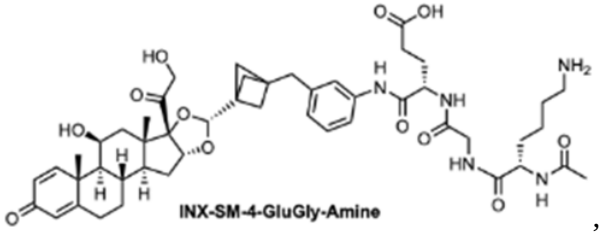


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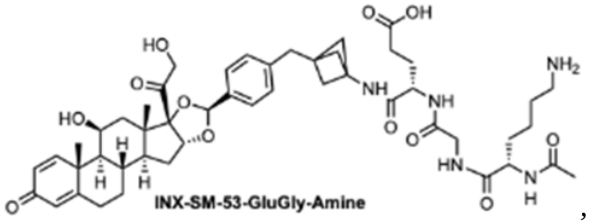
(vii) the list of Glu-Gly-Amines selected from



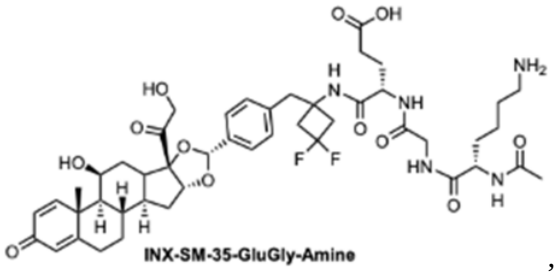
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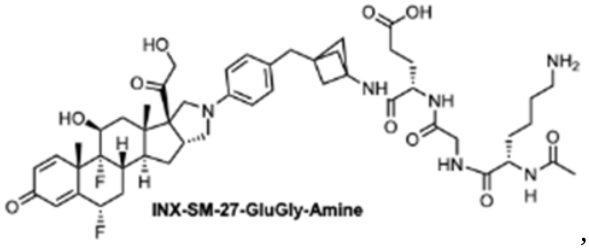


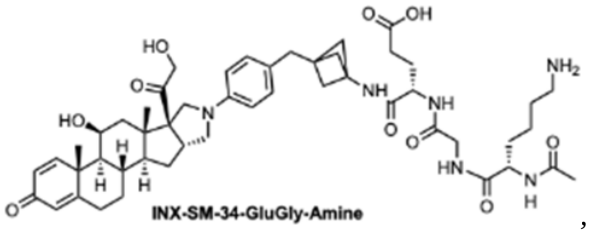
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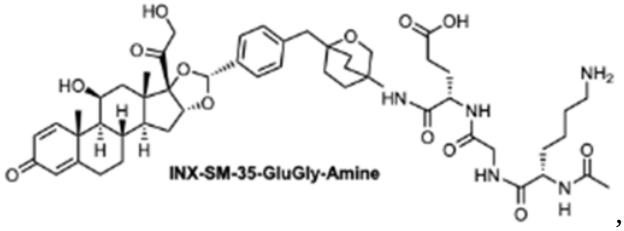


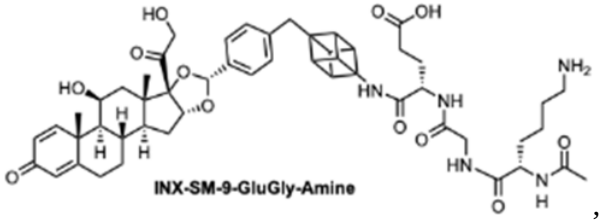
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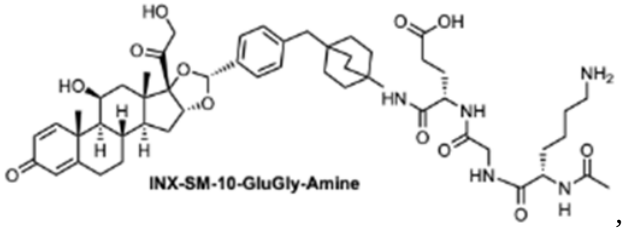

INX-SM-35-GluGly-Amine
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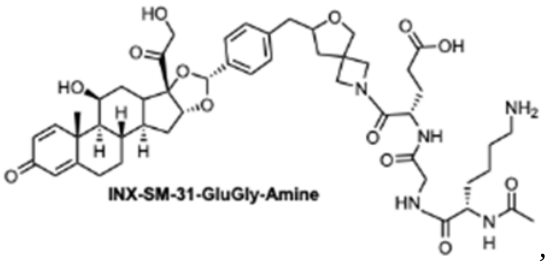

INX-SM-27-GluGly-Amine
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INX-SM-34-GluGly-Amine
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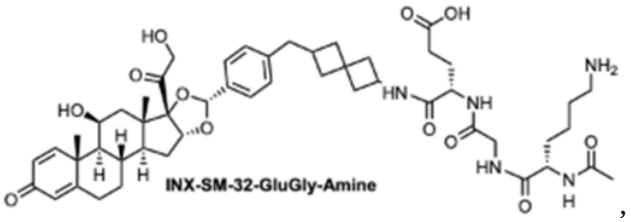

INX-SM-35-GluGly-Amine
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INX-SM-9-GluGly-Amine
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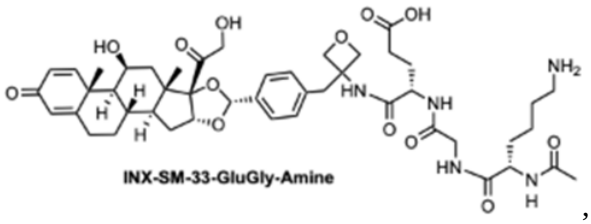

INX-SM-10-GluGly-Amine
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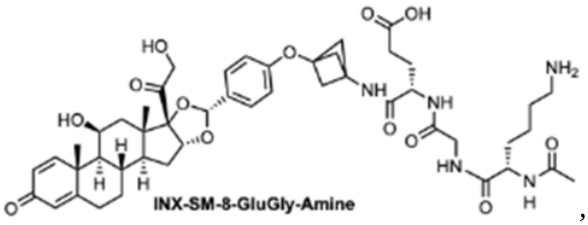
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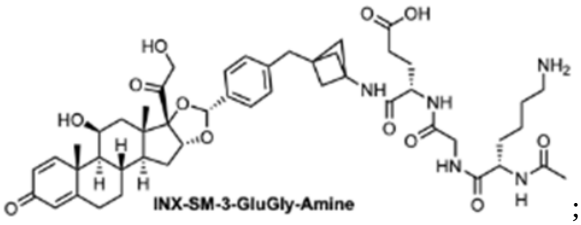
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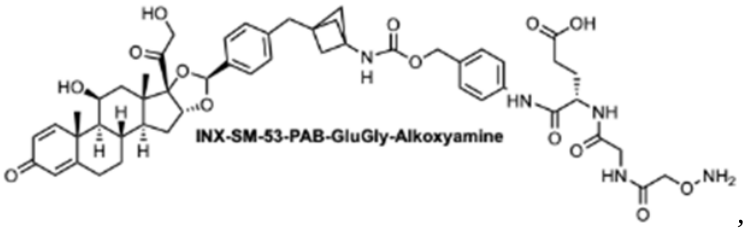


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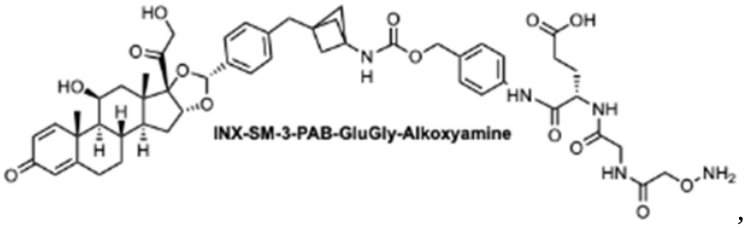


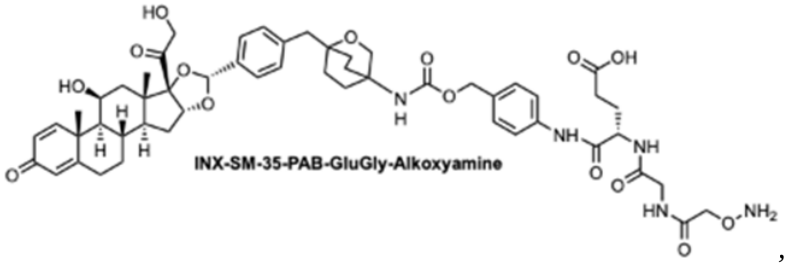
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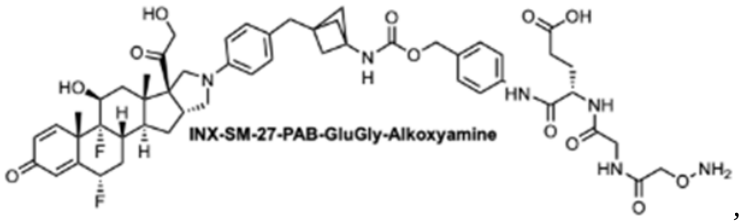
(viii) the list of PAB-Glu-Gly-Alkoxyamines selected from

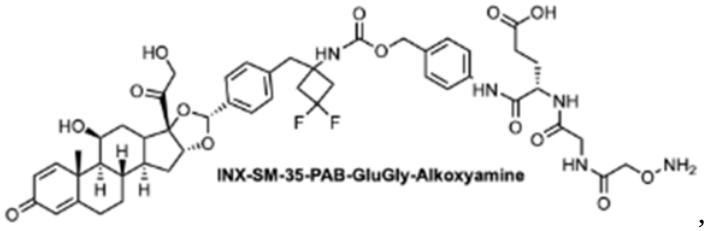


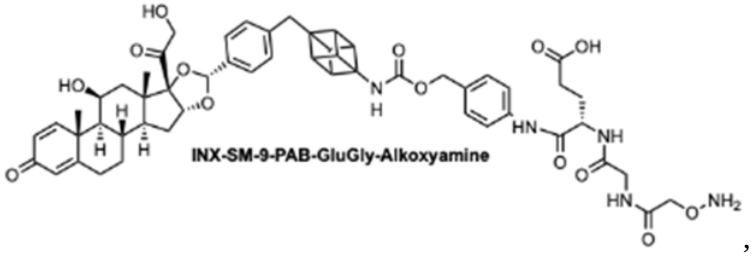
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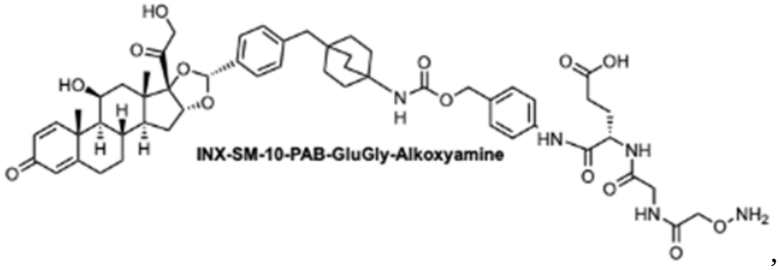

INX-SM-3-PAB-GluGly-Alkoxyamine
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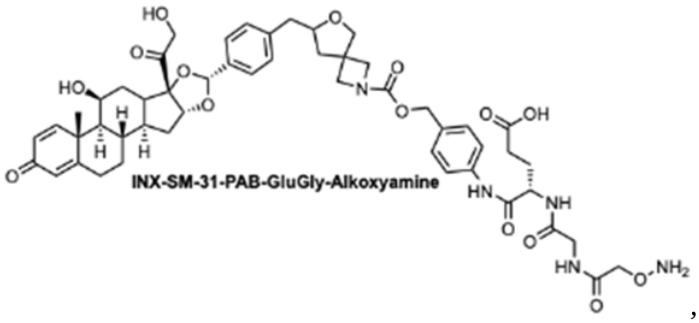

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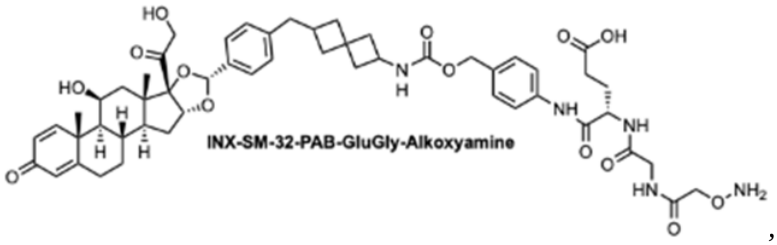

INX-SM-27-PAB-GluGly-Alkoxyamine
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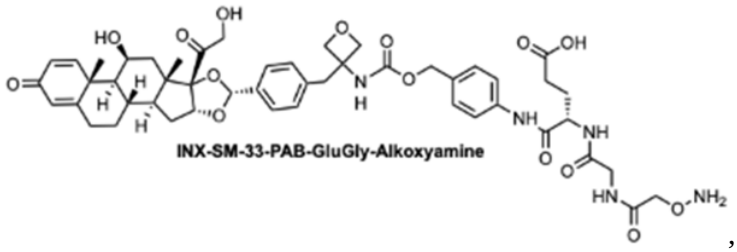

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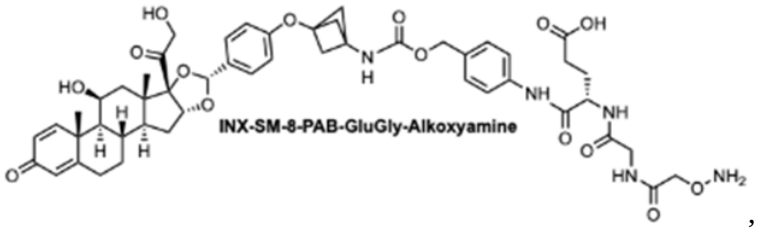

INX-SM-9-PAB-GluGly-Alkoxyamine
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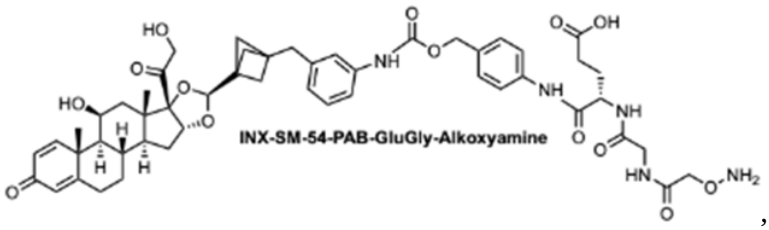

INX-SM-10-PAB-GluGly-Alkoxyamine
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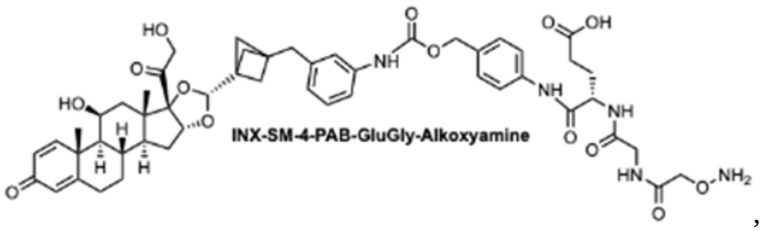

INX-SM-31-PAB-GluGly-Alkoxyamine
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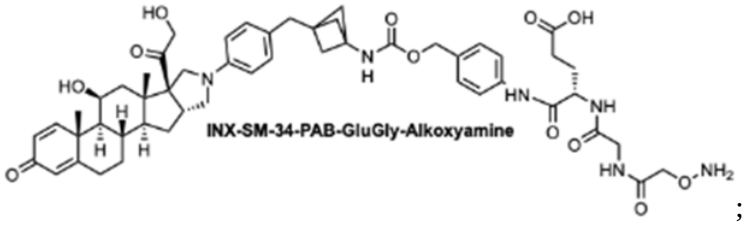

INX-SM-32-PAB-GluGly-Alkoxyamine
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INX-SM-33-PAB-GluGly-Alkoxyamine
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INX-SM-8-PAB-GluGly-Alkoxyamine
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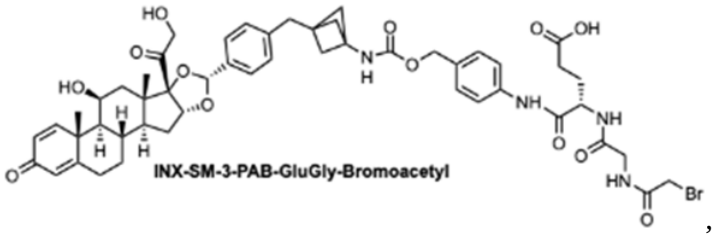

INX-SM-54-PAB-GluGly-Alkoxyamine
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INX-SM-4-PAB-GluGly-Alkoxyamine
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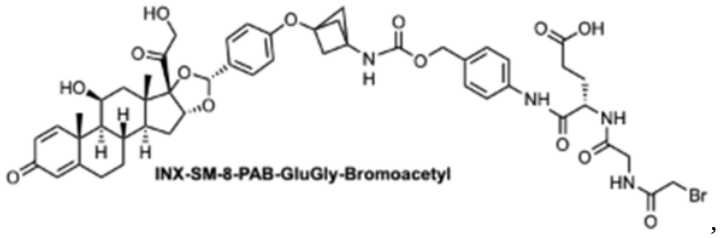


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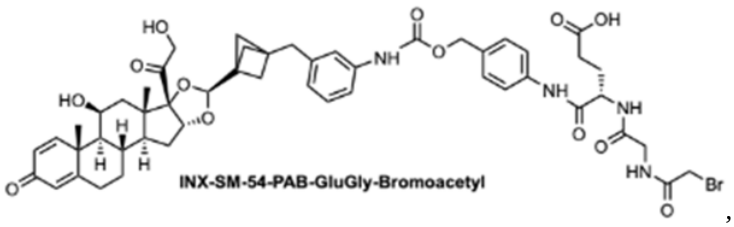
(ix) the list of PAB-Glu-Gly-Bromoacetyls selected from



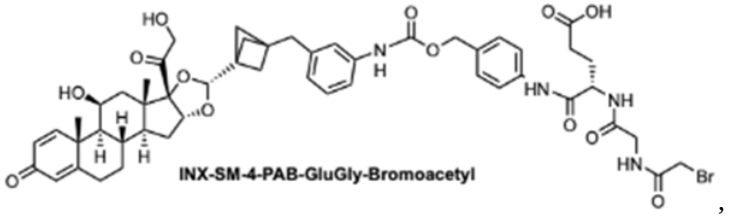
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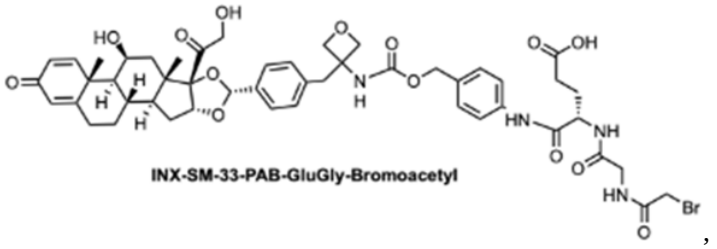
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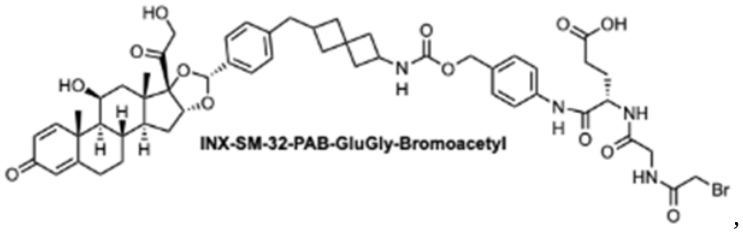
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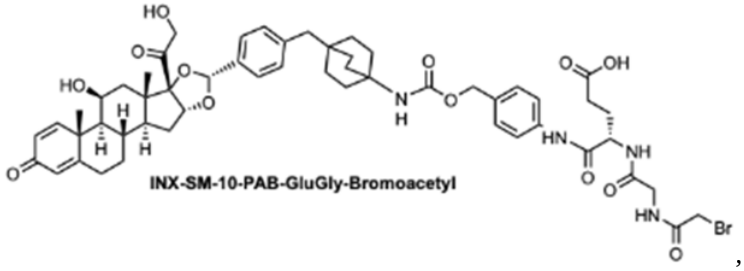


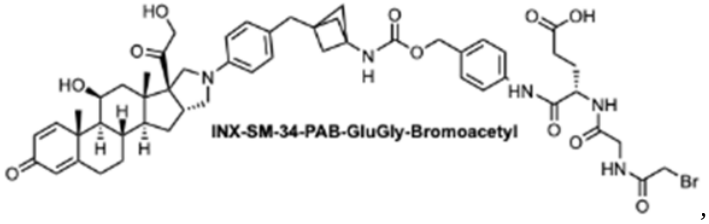
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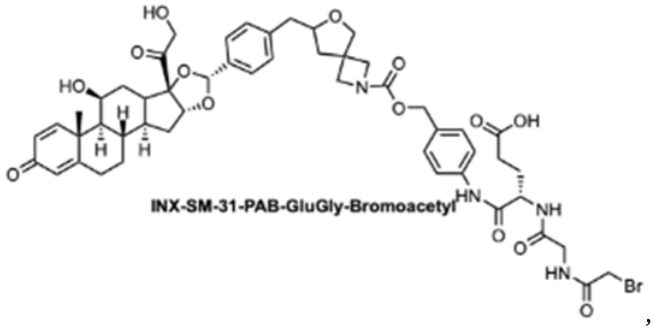


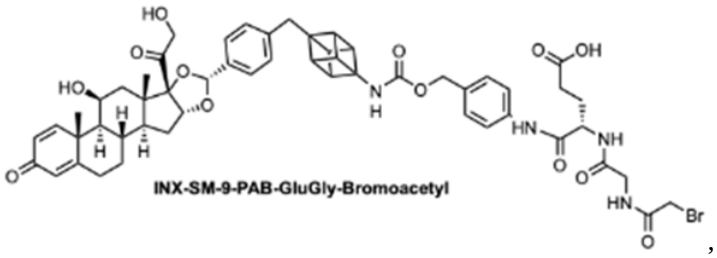
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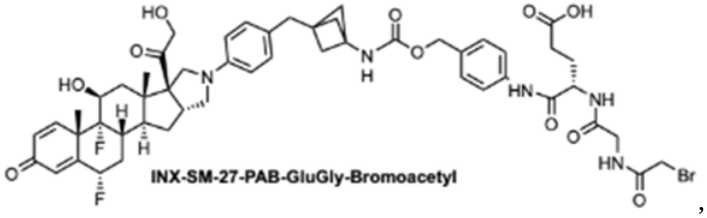

INX-SM-32-PAB-GluGly-Bromoacetyl
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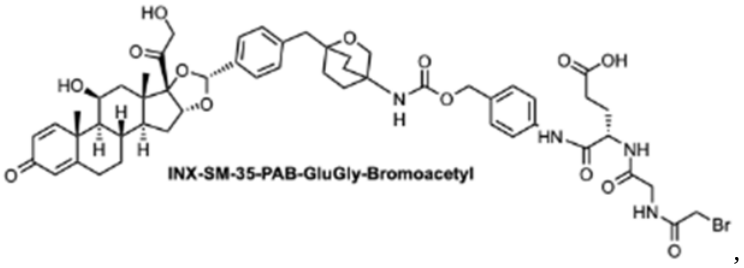

INX-SM-10-PAB-GluGly-Bromoacetyl
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INX-SM-34-PAB-GluGly-Bromoacetyl
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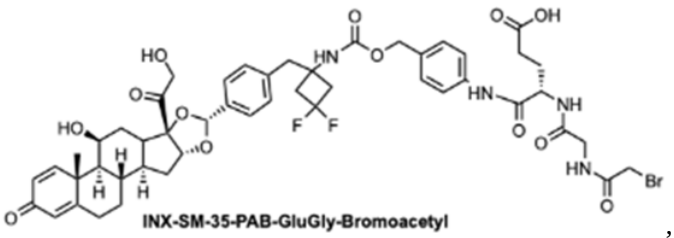

INX-SM-31-PAB-GluGly-Bromoacetyl
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INX-SM-9-PAB-GluGly-Bromoacetyl
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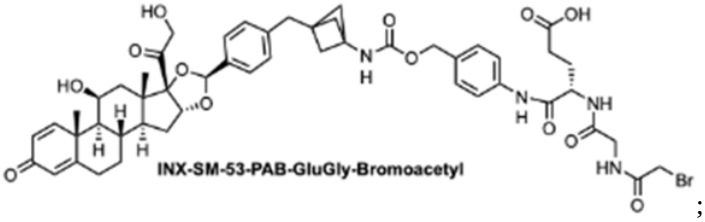

INX-SM-27-PAB-GluGly-Bromoacetyl
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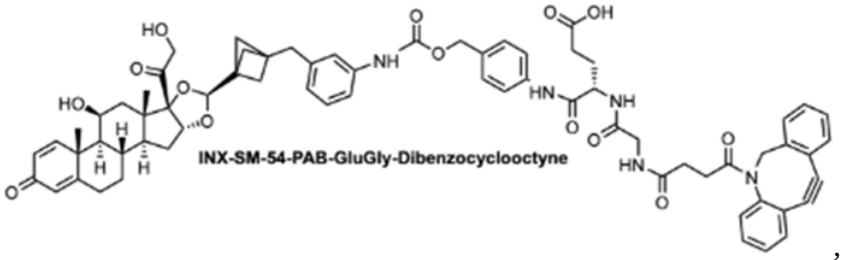


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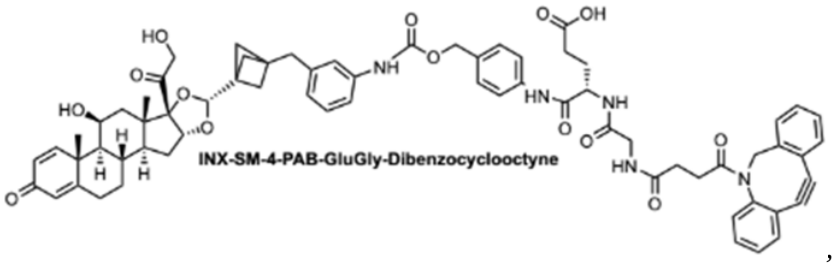


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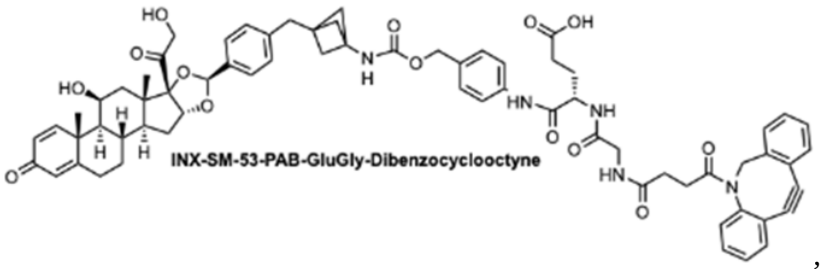
(x) the list of PAB-Glu-Gly-Dibenzocyclooctynes selected from



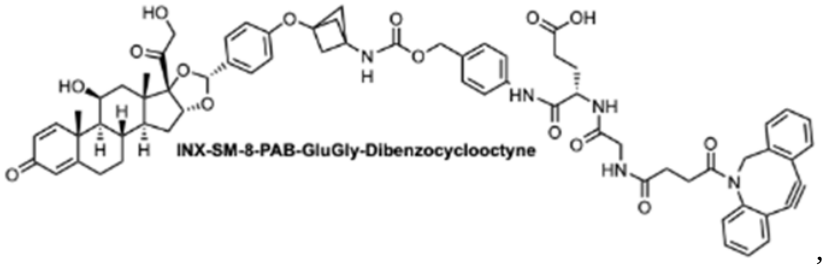
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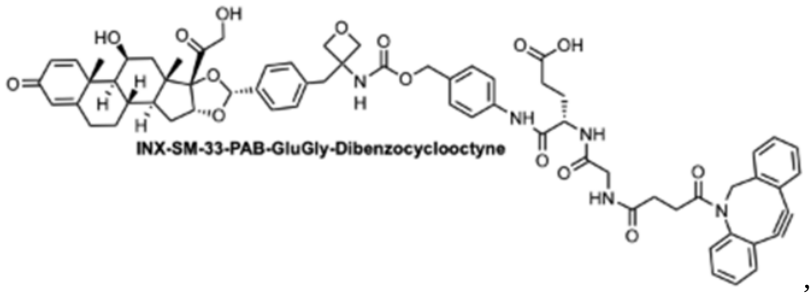
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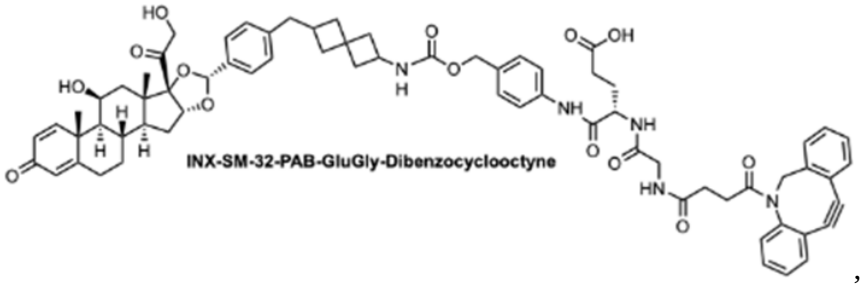
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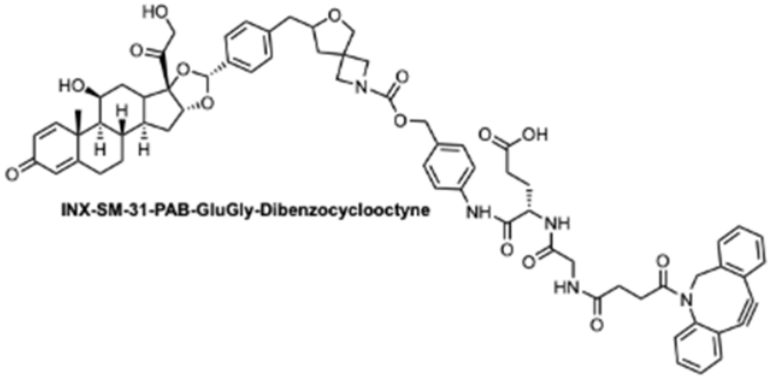
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INX-SM-33-PAB-GluGly-Dibenzocyclooctyne

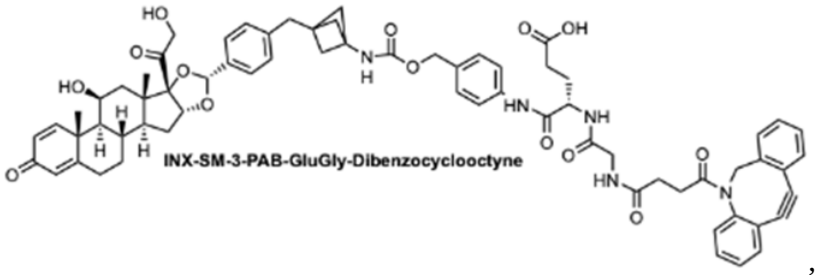
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INX-SM-32-PAB-GluGly-Dibenzocyclooctyne

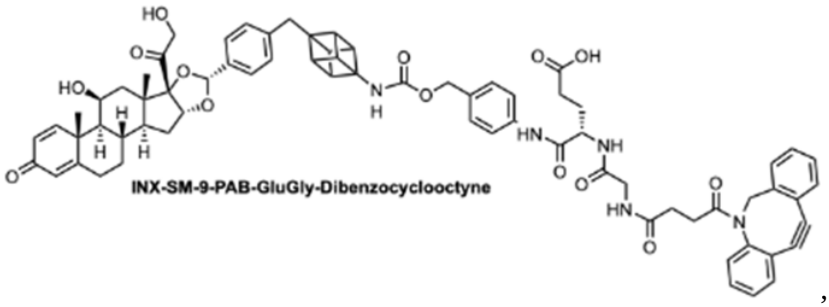
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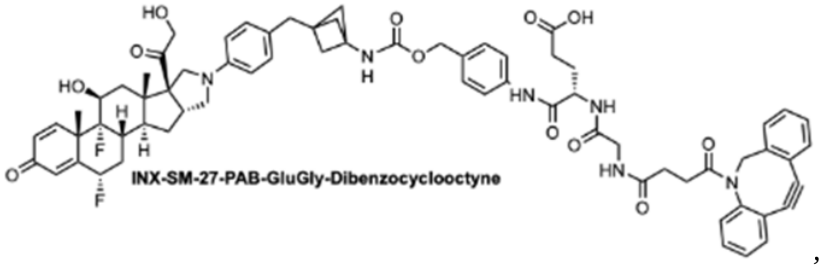

INX-SM-31-PAB-GluGly-Dibenzocyclooctyne

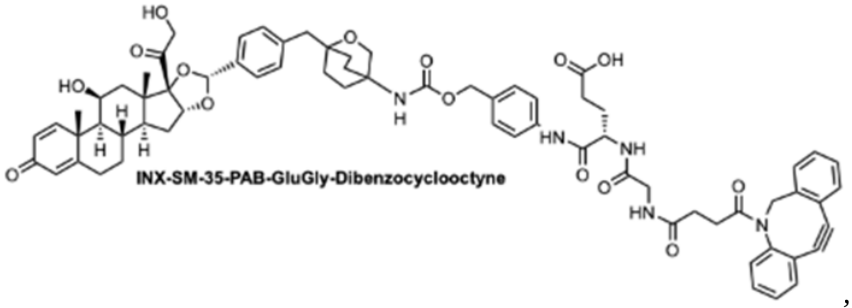
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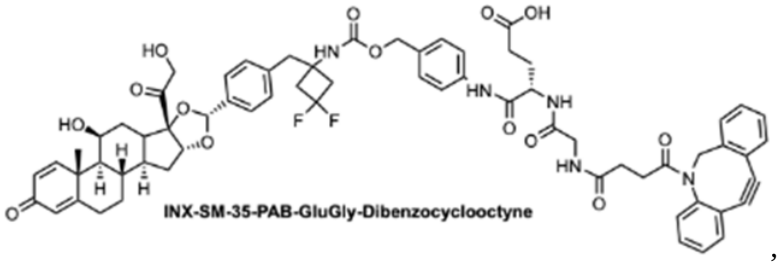

INX-SM-3-PAB-GluGly-Dibenzocyclooctyne

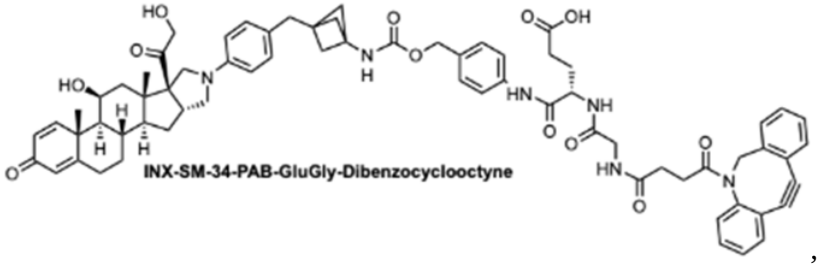
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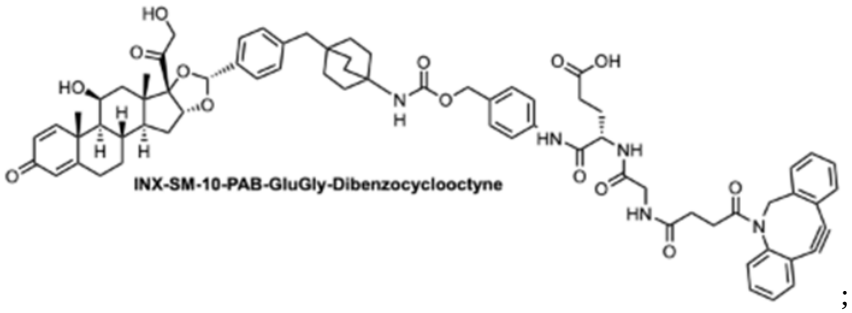

INX-SM-9-PAB-GluGly-Dibenzocyclooctyne
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INX-SM-27-PAB-GluGly-Dibenzocyclooctyne
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INX-SM-35-PAB-GluGly-Dibenzocyclooctyne
,

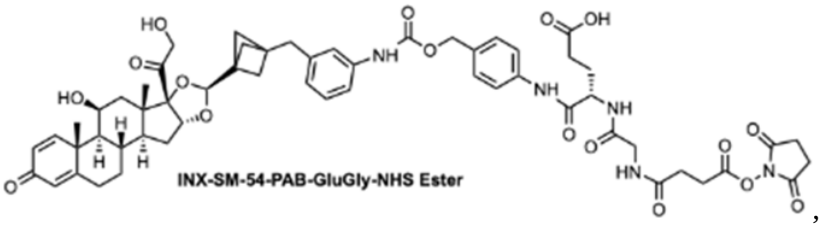

INX-SM-35-PAB-GluGly-Dibenzocyclooctyne
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INX-SM-34-PAB-GluGly-Dibenzocyclooctyne
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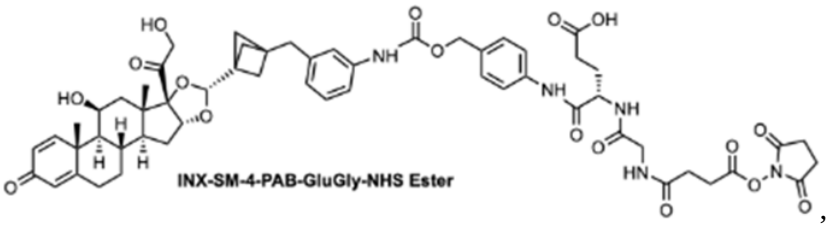


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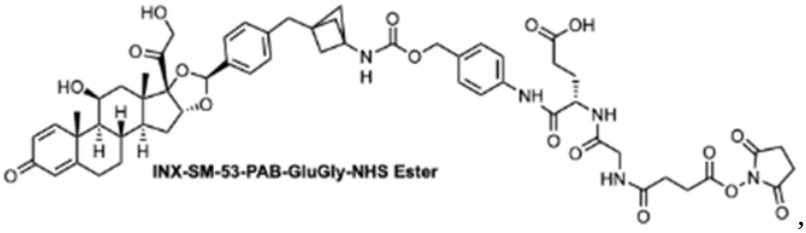
(xi) the list of PAB-Glu-Gly-NHS esters selected from



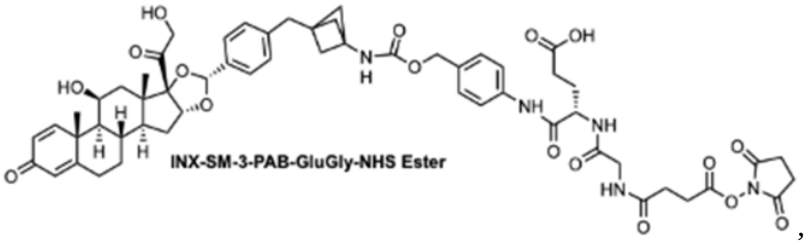
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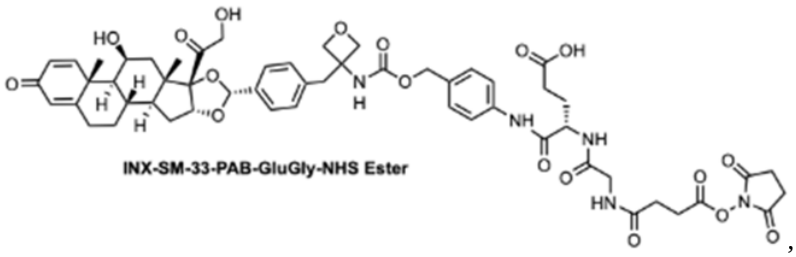
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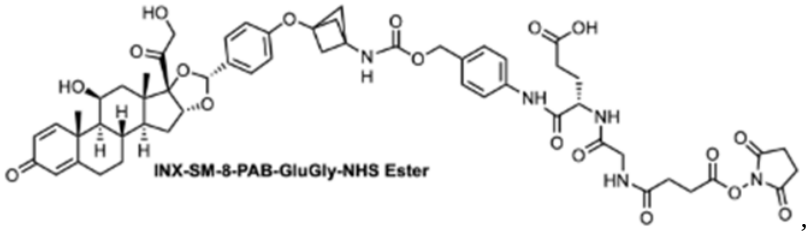
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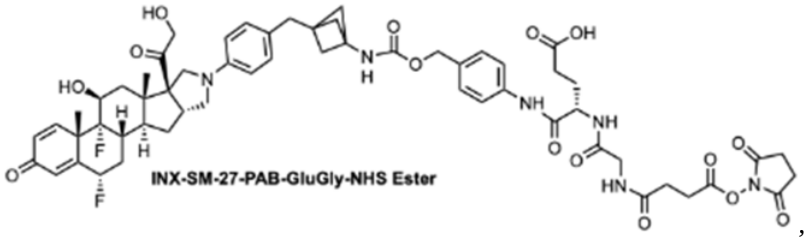


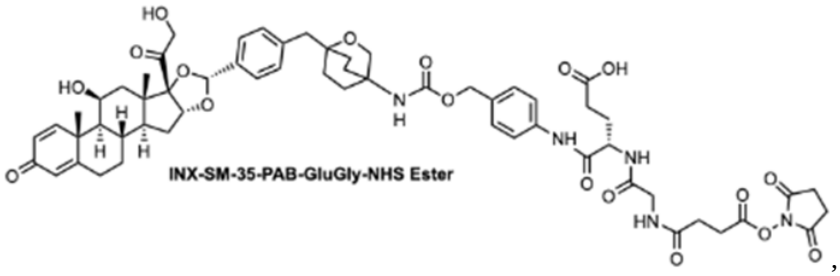
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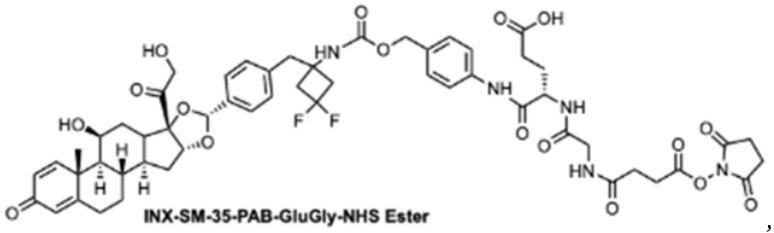


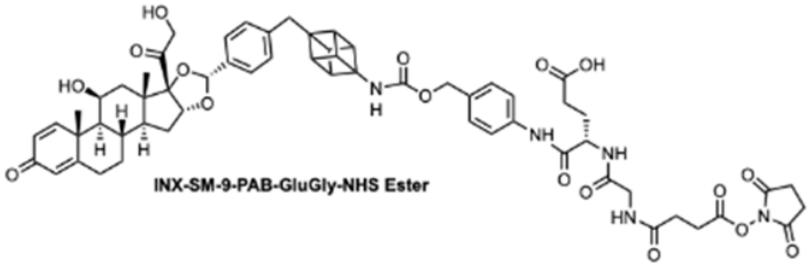
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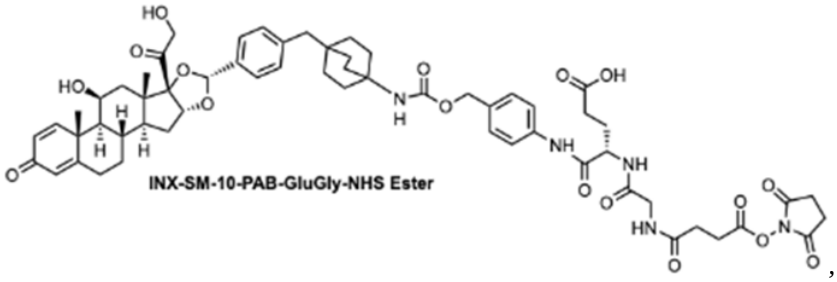

INX-SM-8-PAB-GluGly-NHS Ester

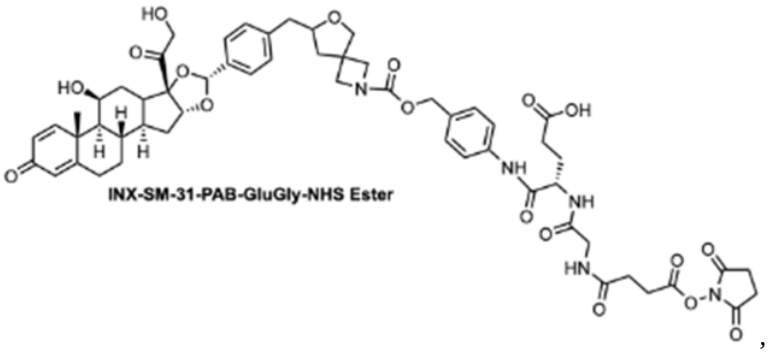

INX-SM-27-PAB-GluGly-NHS Ester


INX-SM-35-PAB-GluGly-NHS Ester

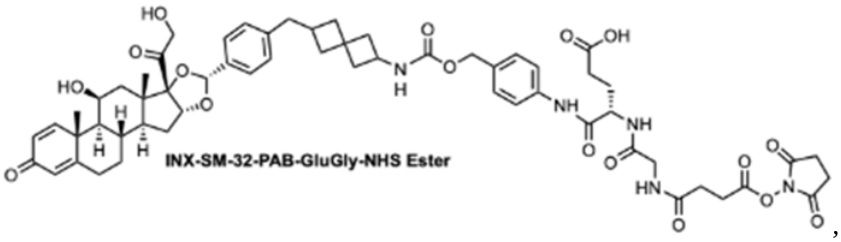

INX-SM-35-PAB-GluGly-NHS Ester


INX-SM-9-PAB-GluGly-NHS Ester

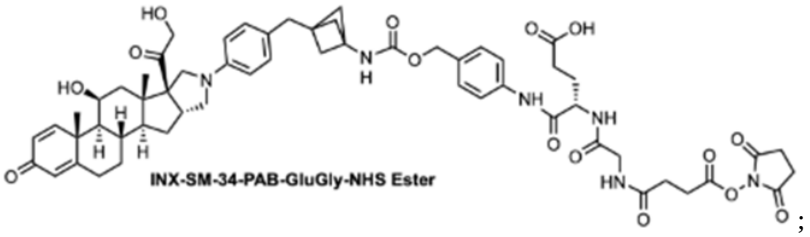

INX-SM-10-PAB-GluGly-NHS Ester



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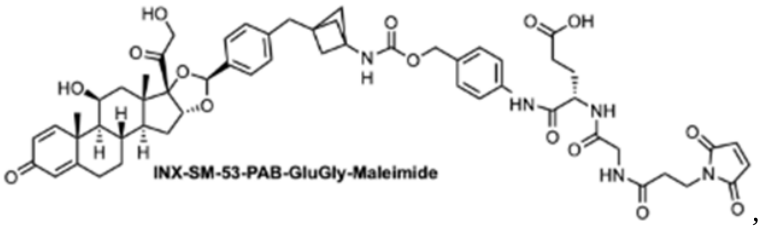


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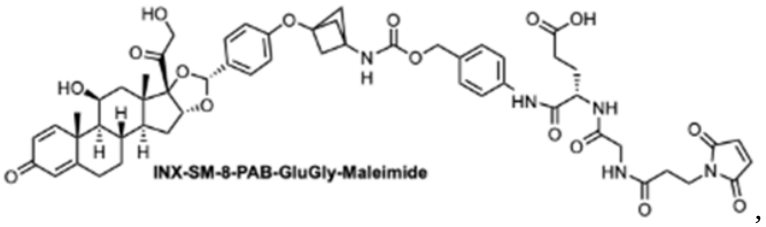


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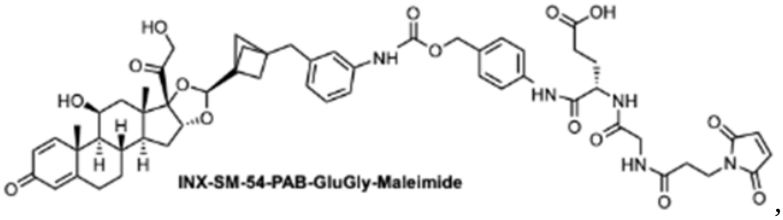
(xii) the list of PAB-Glu-Gly-Maleimides selected from



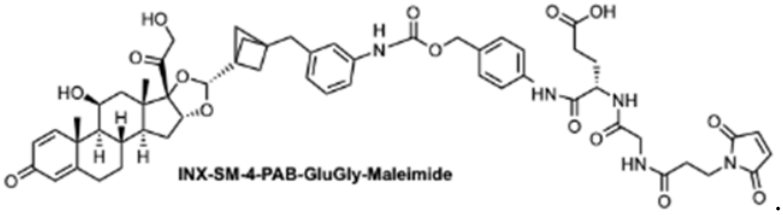
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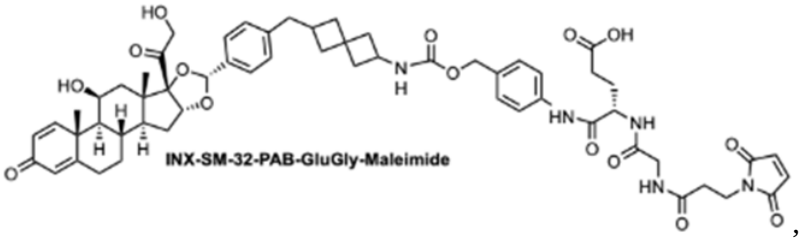


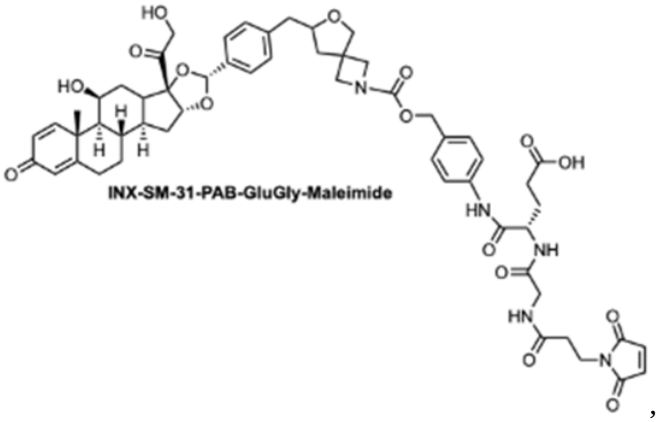
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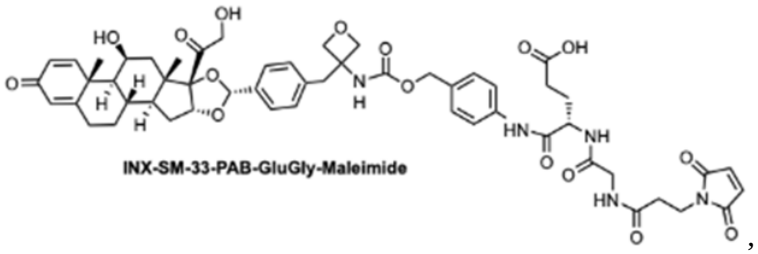


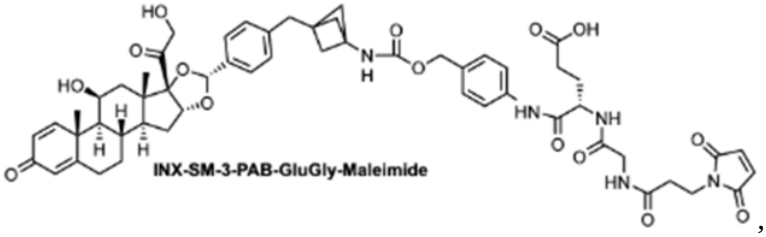
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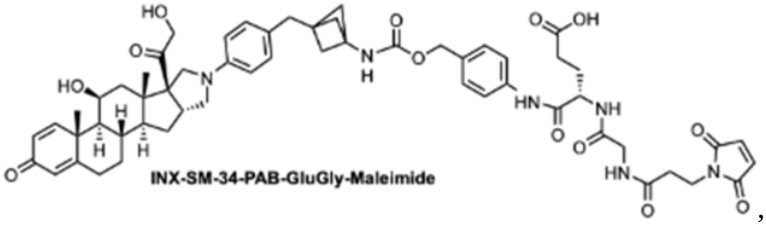

INX-SM-4-PAB-GluGly-Maleimide

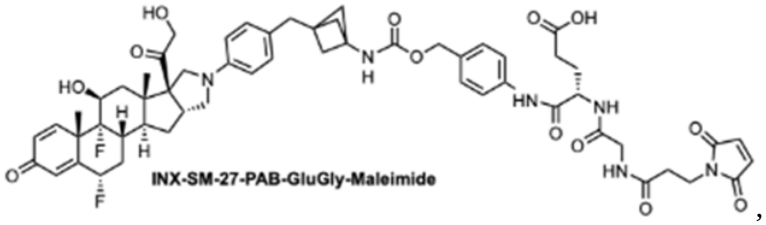

INX-SM-32-PAB-GluGly-Maleimide


INX-SM-31-PAB-GluGly-Maleimide

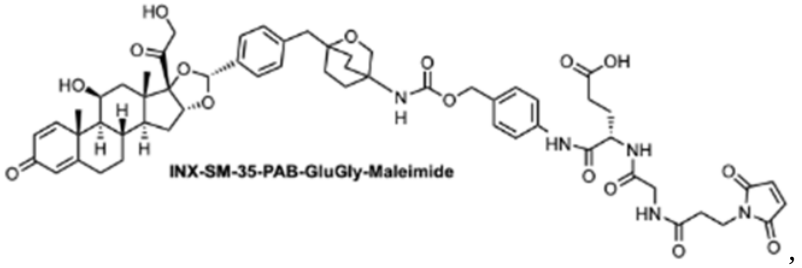

INX-SM-33-PAB-GluGly-Maleimide


INX-SM-3-PAB-GluGly-Maleimide

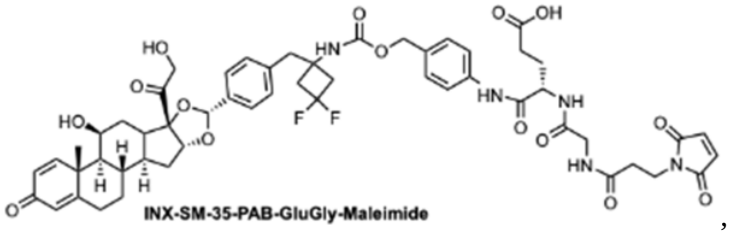

INX-SM-34-PAB-GluGly-Maleimide



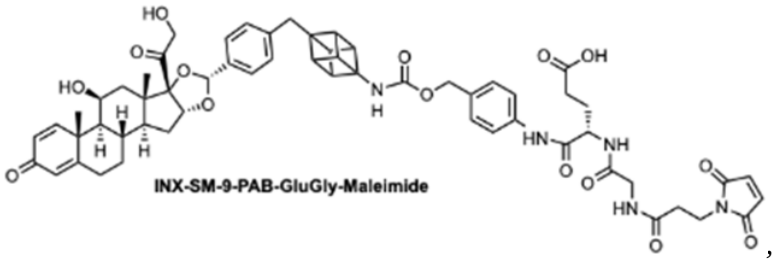
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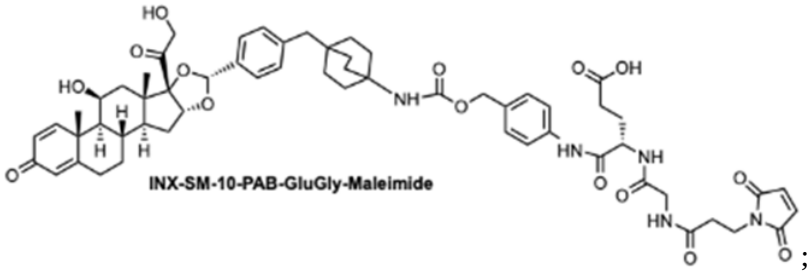
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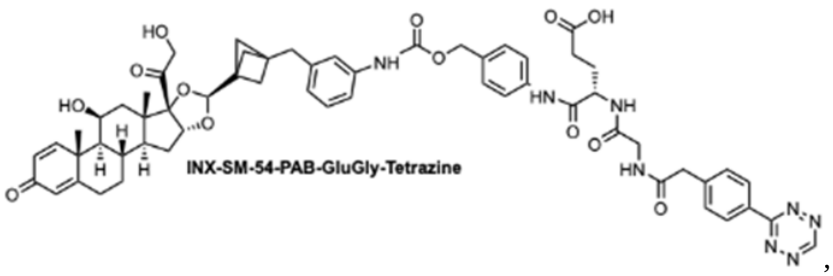


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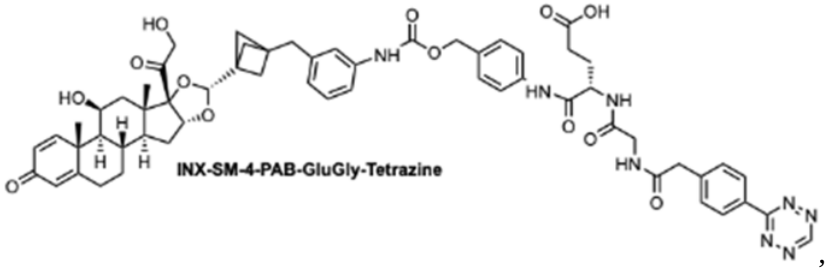


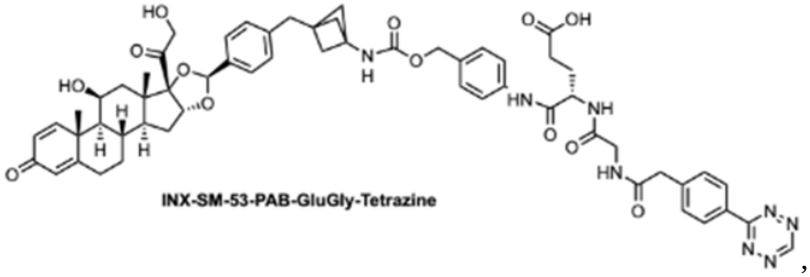
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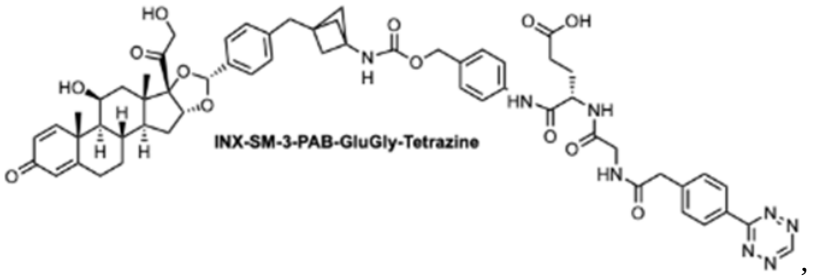
(xiii) the list of PAB-Glu-Gly-Tetrazines selected from

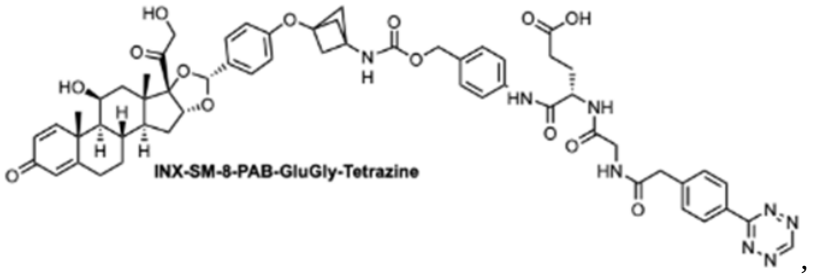


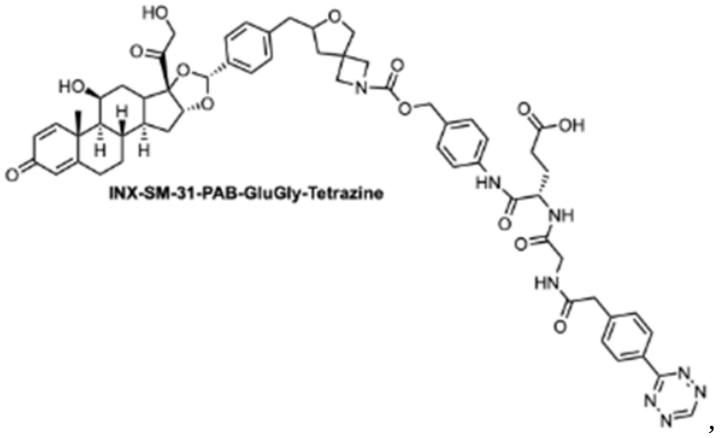
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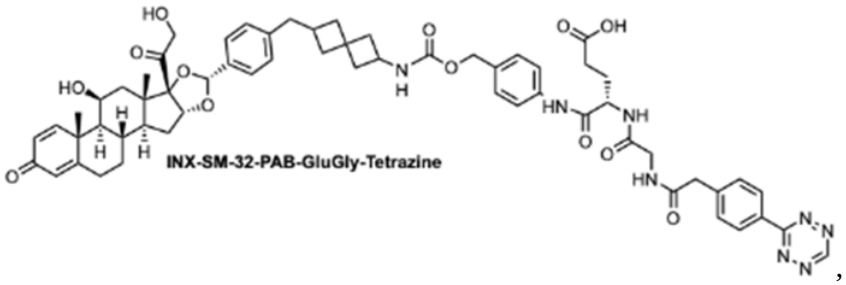

INX-SM-4-PAB-GluGly-Tetrazine,


INX-SM-53-PAB-GluGly-Tetrazine,

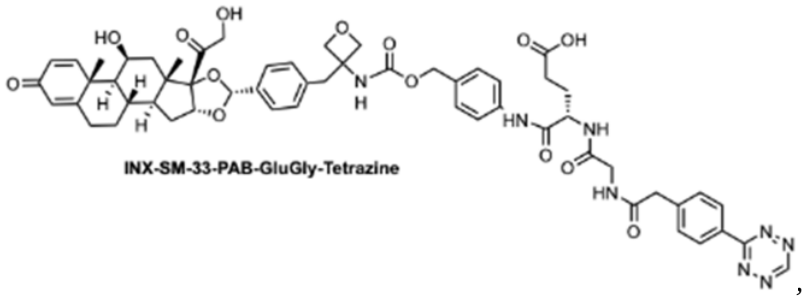

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INX-SM-8-PAB-GluGly-Tetrazine,

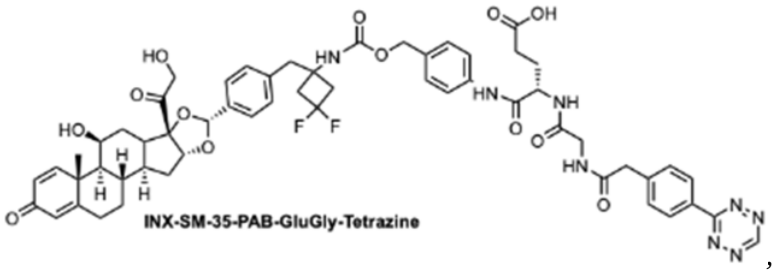

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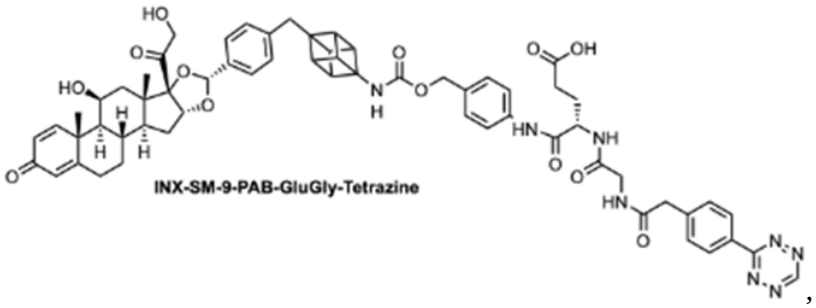
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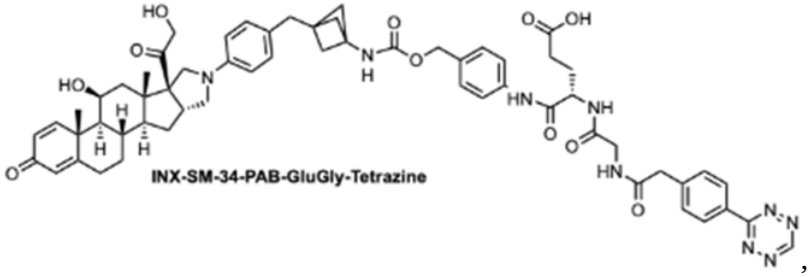
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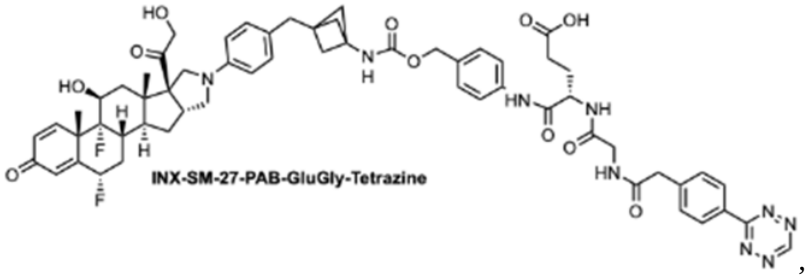
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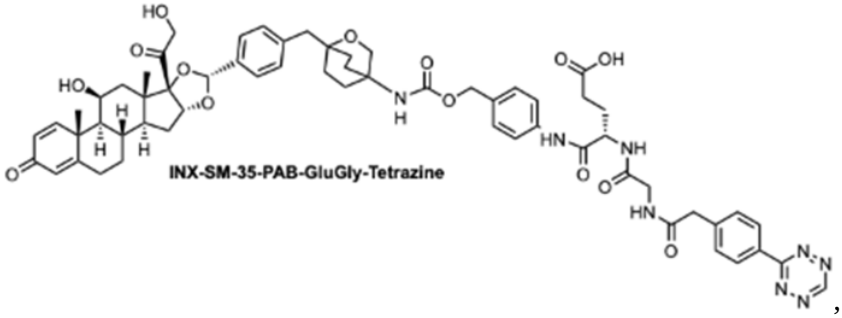
INX-SM-9-PAB-GluGly-Tetrazine,



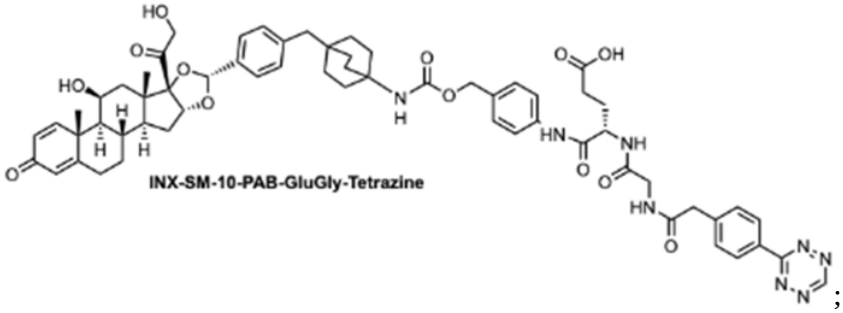
INX-SM-34-PAB-GluGly-Tetrazine,



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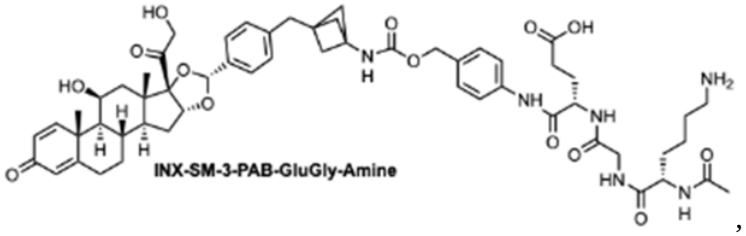


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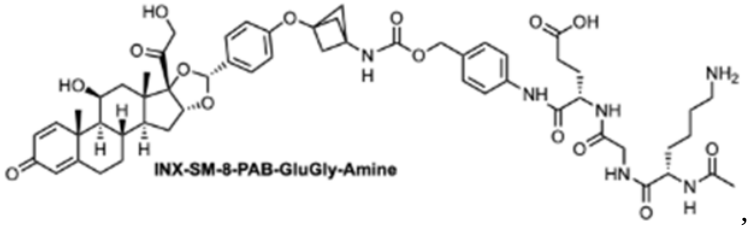


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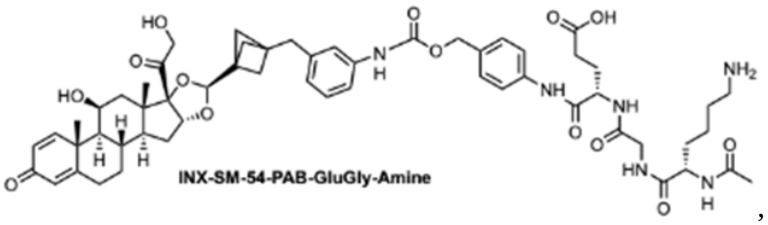
(xiv) the list of PAB-Glu-Gly-Amines selected from

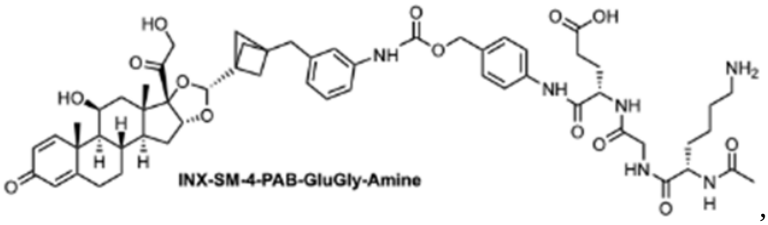


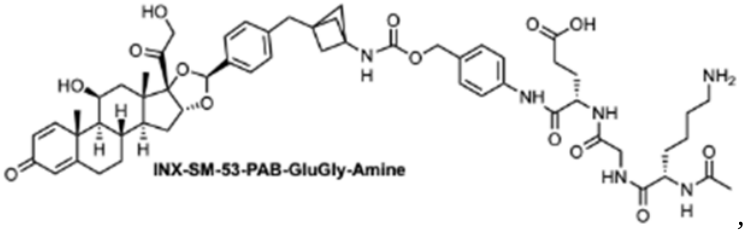
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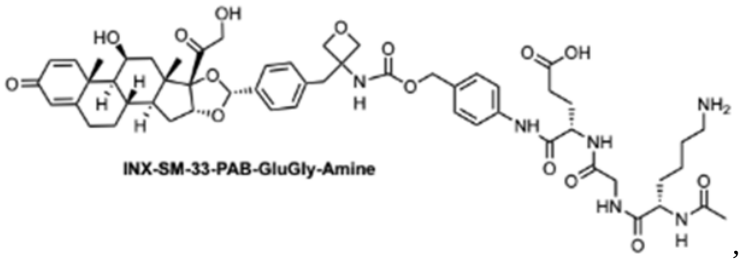


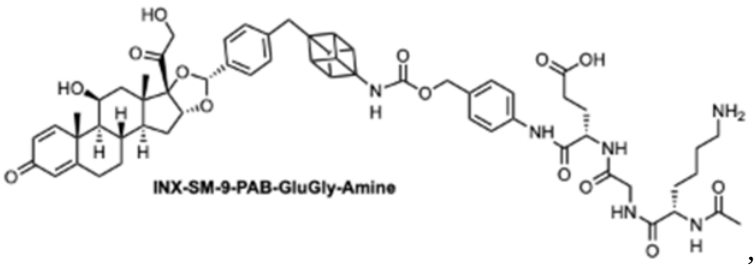
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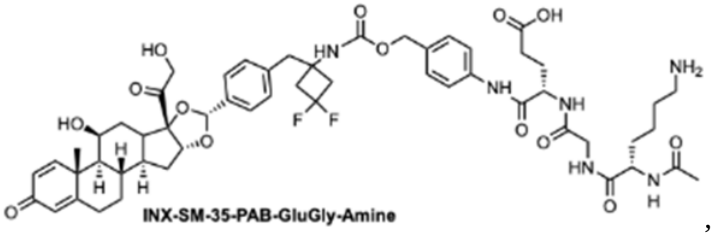

INX-SM-54-PAB-GluGly-Amine ,

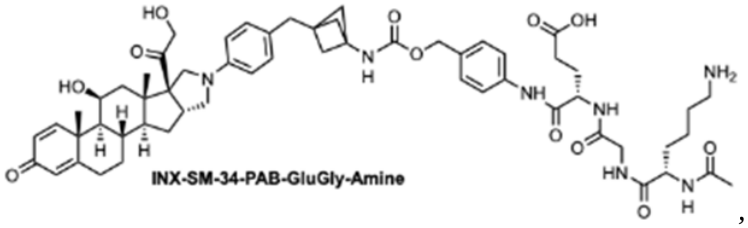

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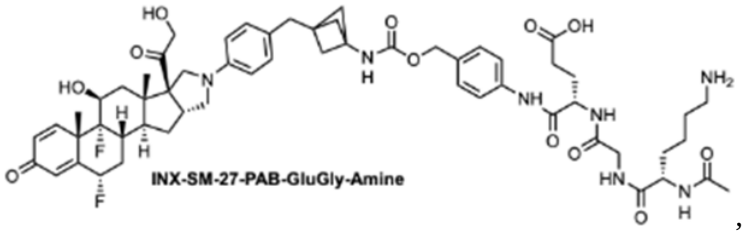

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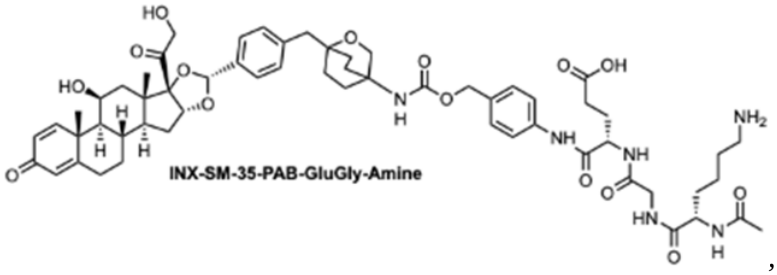

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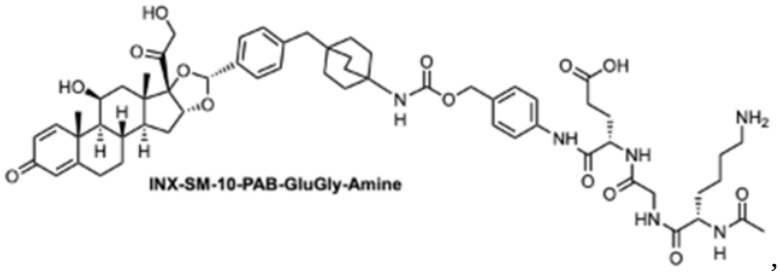

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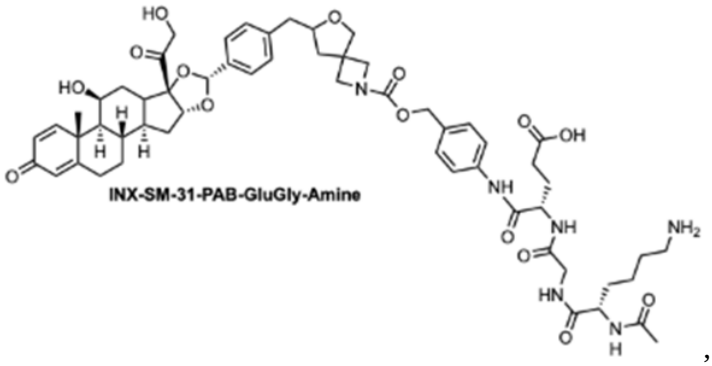

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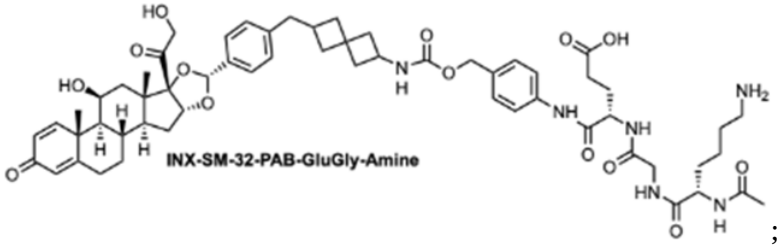

INX-SM-34-PAB-GluGly-Amine
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INX-SM-27-PAB-GluGly-Amine
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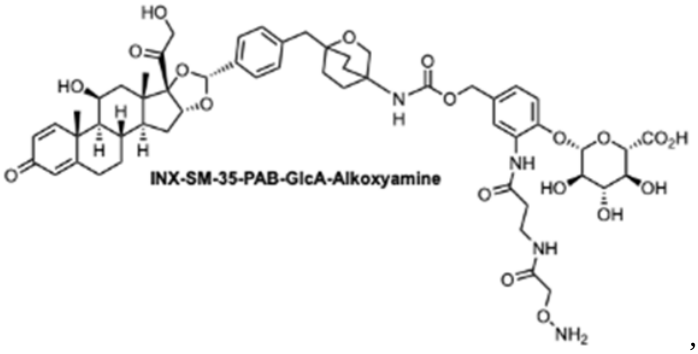

INX-SM-35-PAB-GluGly-Amine
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INX-SM-10-PAB-GluGly-Amine
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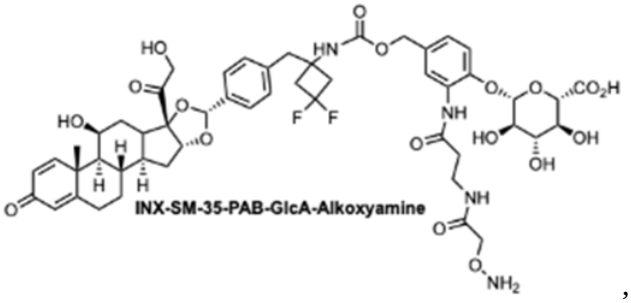

INX-SM-31-PAB-GluGly-Amine
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INX-SM-32-PAB-GluGly-Amine
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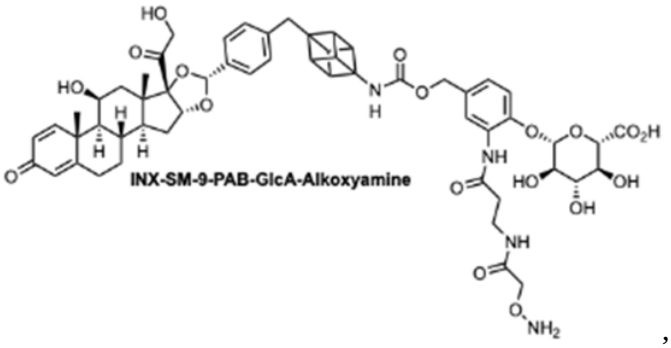
(xv) the list of AB-GlcA-beta-Ala-Alkoxyamines selected from



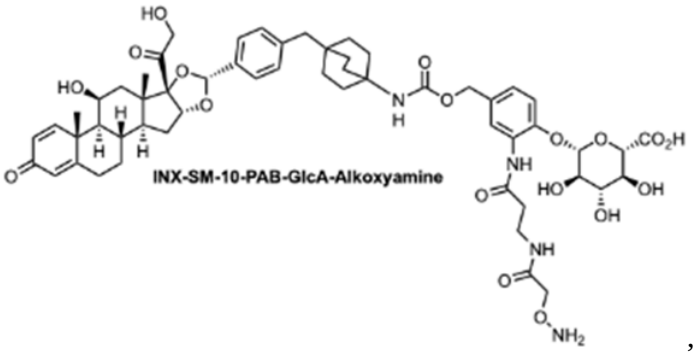
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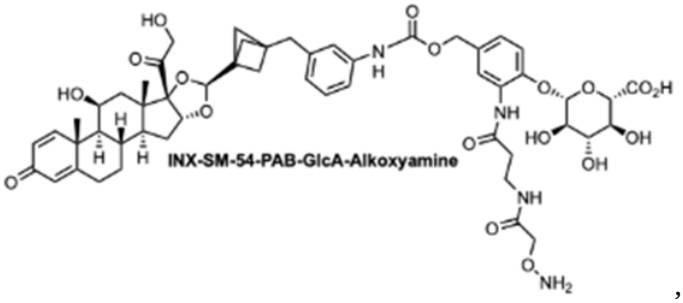
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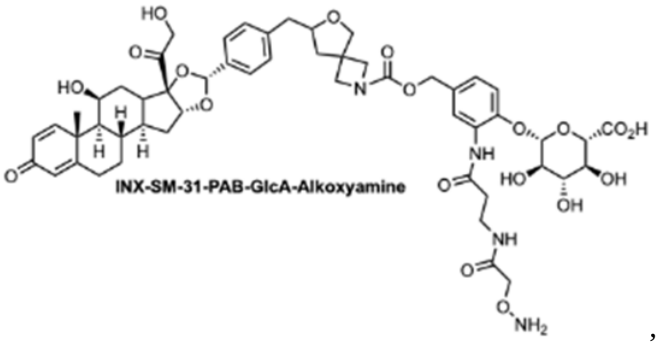
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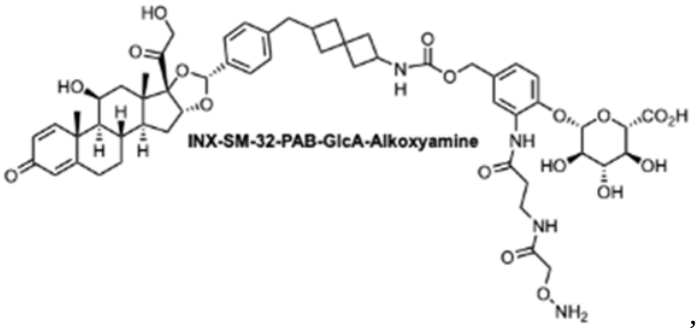
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INX-SM-54-PAB-GlcA-Alkoxyamine

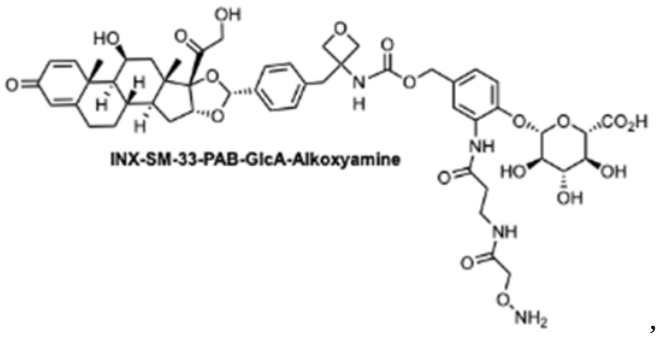
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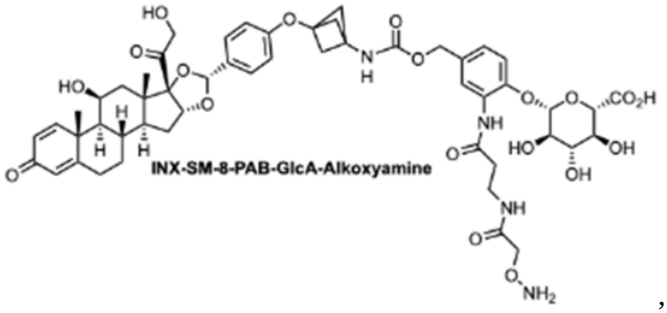
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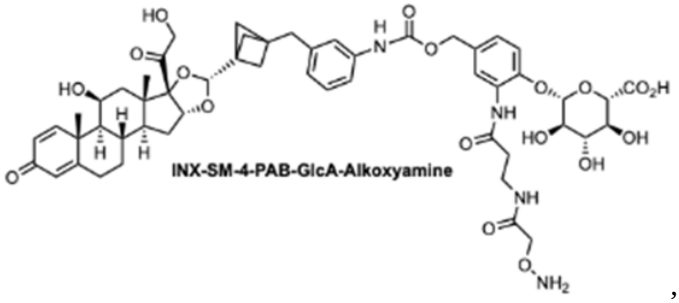
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INX-SM-33-PAB-GlcA-Alkoxyamine

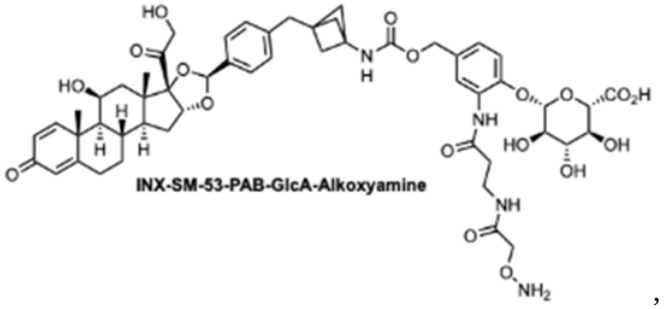
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INX-SM-8-PAB-GlcA-Alkoxyamine

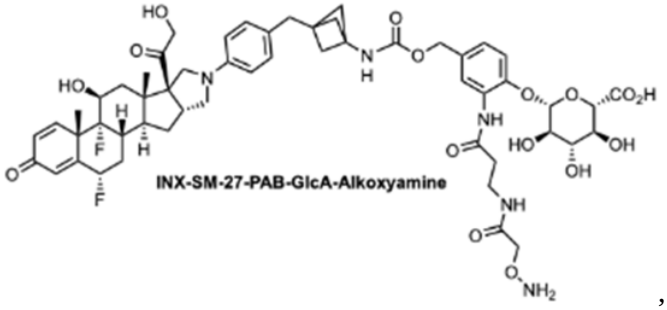
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INX-SM-4-PAB-GlcA-Alkoxyamine

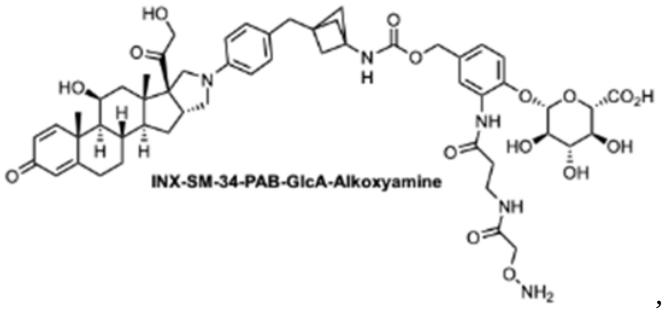
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INX-SM-53-PAB-GlcA-Alkoxyamine

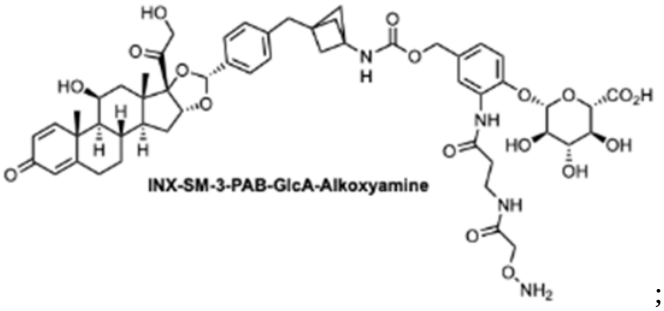
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INX-SM-27-PAB-GlcA-Alkoxyamine

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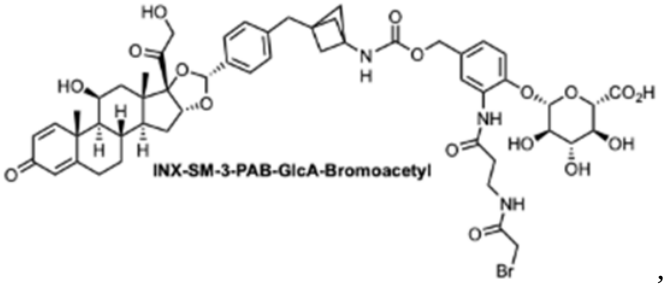

INX-SM-34-PAB-GlcA-Alkoxyamine

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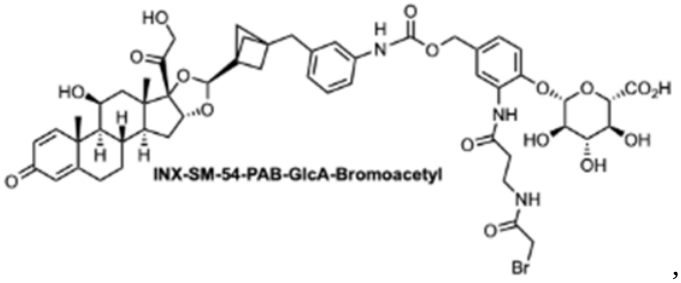


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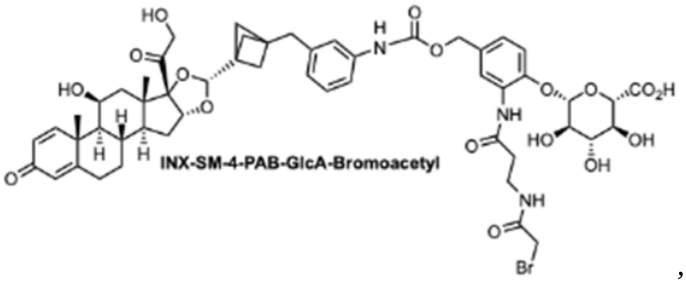
(xvi) the list of AB-GlcA-beta-Ala-Bromoacetyls selected from



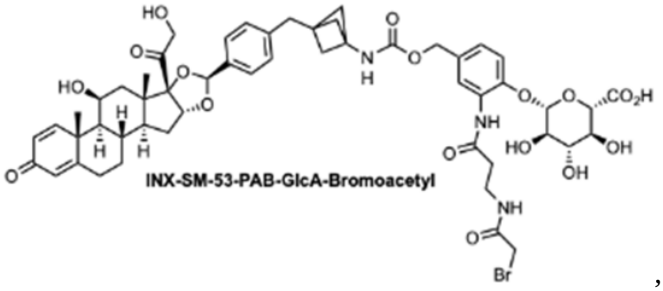
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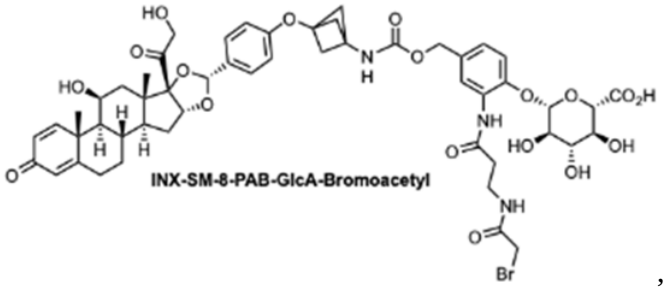
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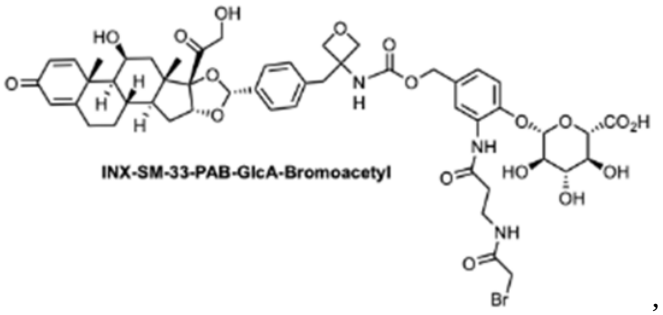
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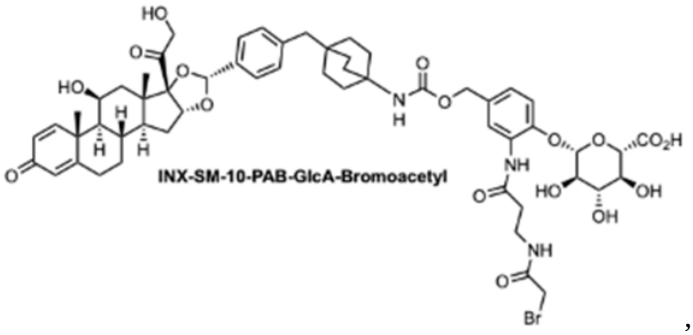
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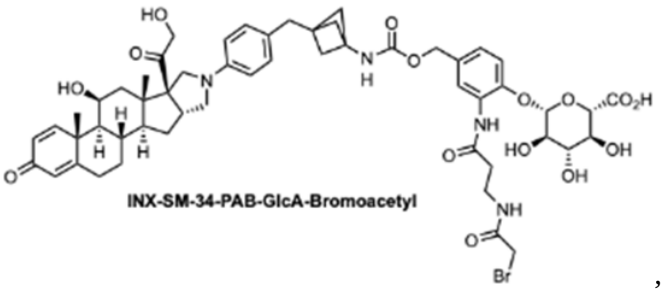
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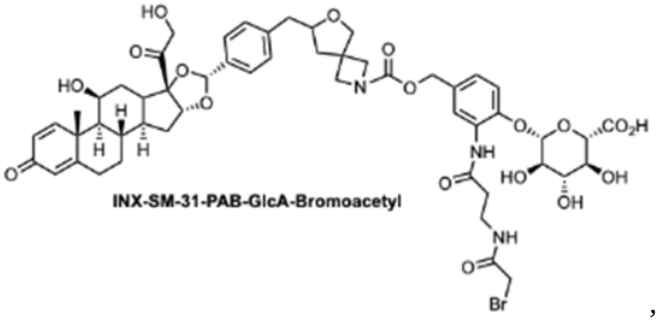
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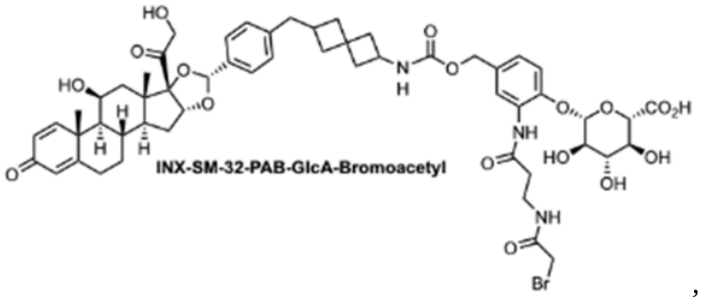
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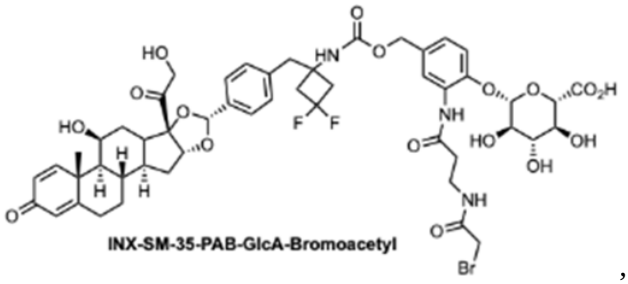
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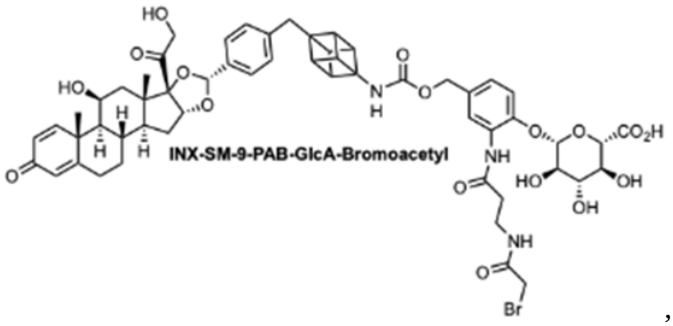
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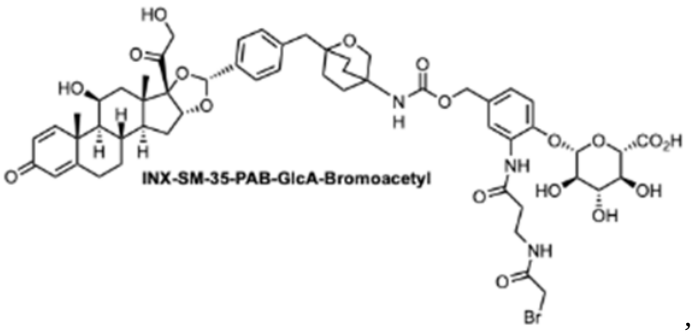
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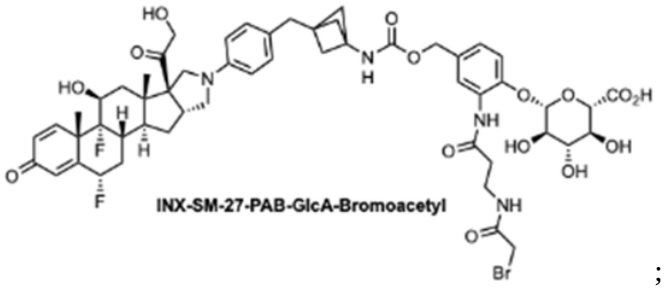
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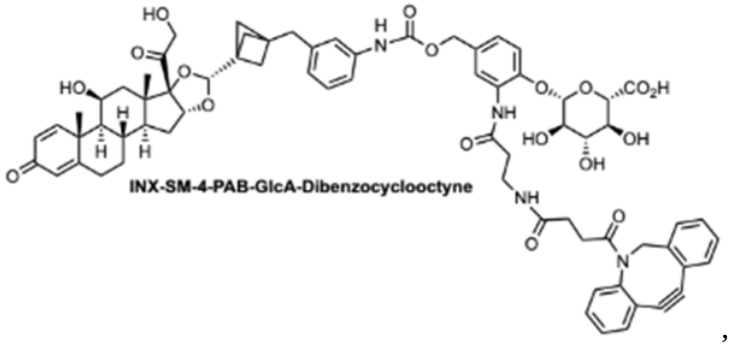


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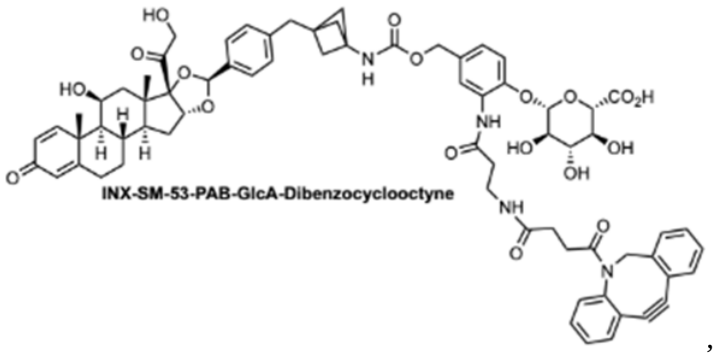


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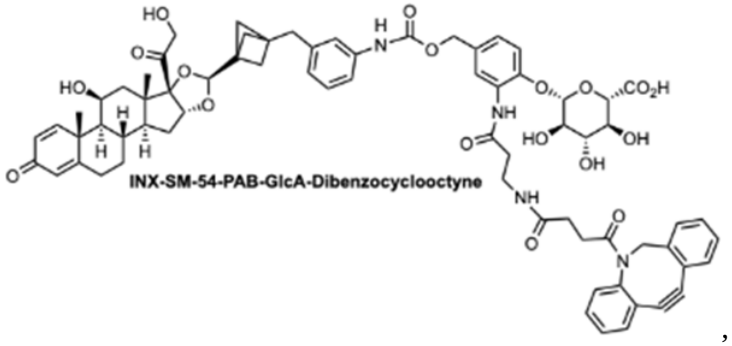
(xvii) the list of AB-GlcA-beta-Ala-Dibenzocyclooctynes selected from


INX-SM-4-PAB-GlcA-Dibenzocyclooctyne

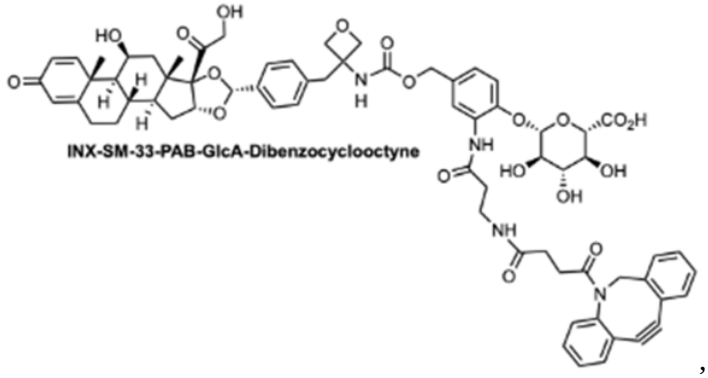
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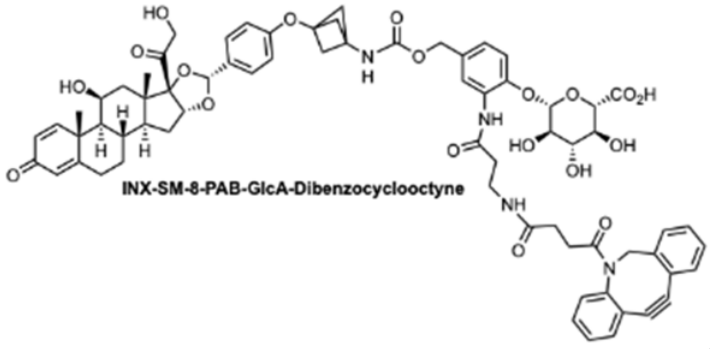
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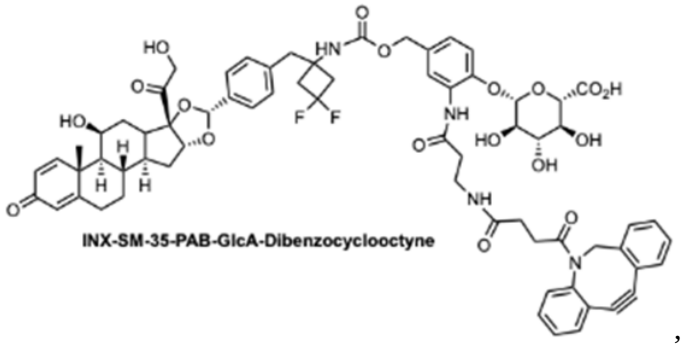

INX-SM-33-PAB-GlcA-Dibenzocyclooctyne

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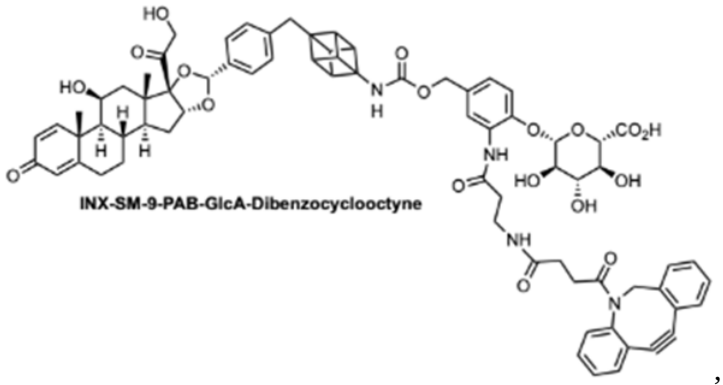
INX-SM-8-PAB-GlcA-Dibenzocyclooctyne

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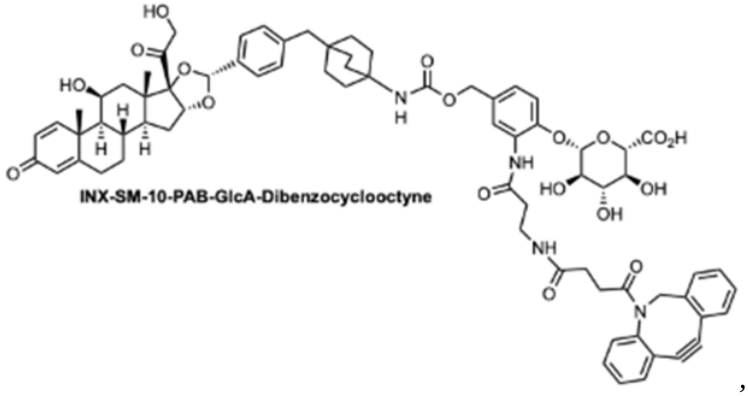
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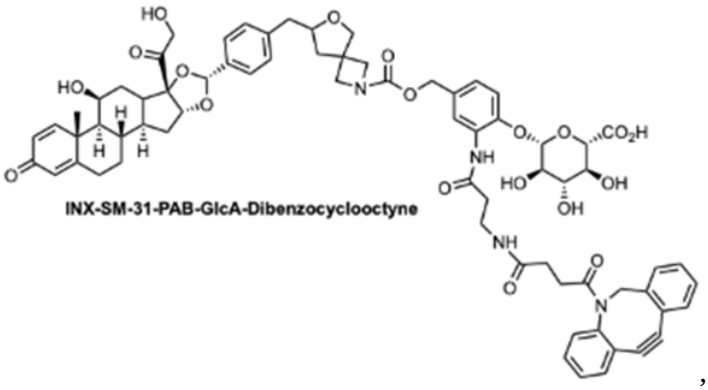
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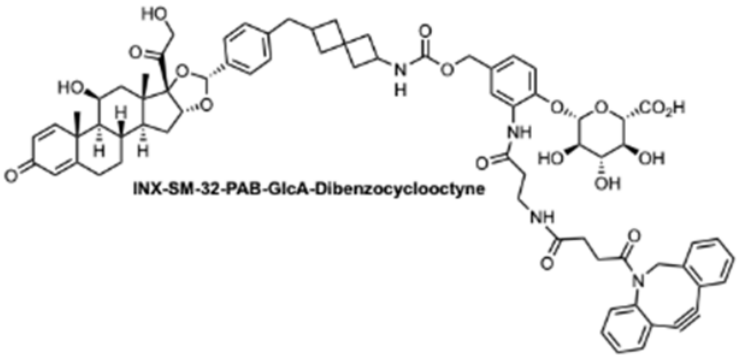
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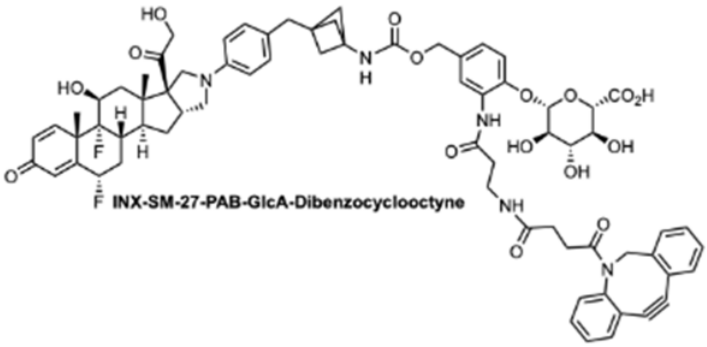
INX-SM-31-PAB-GlcA-Dibenzocyclooctyne

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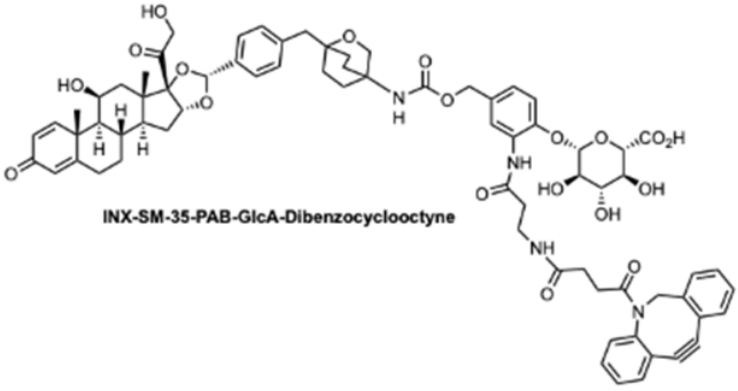
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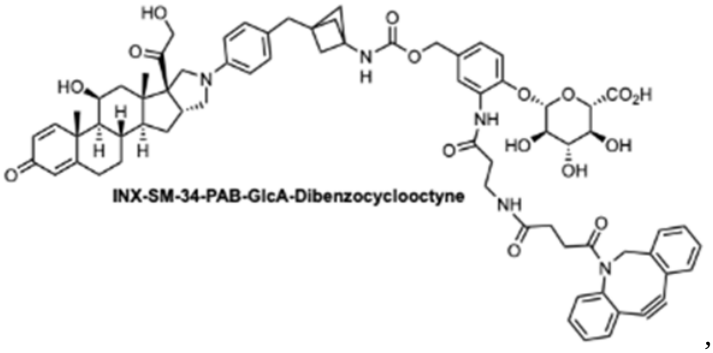
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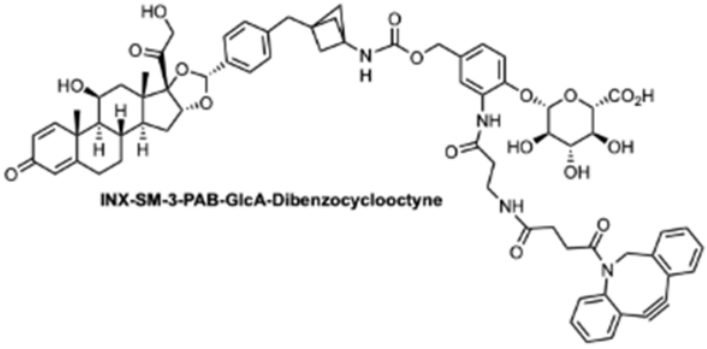


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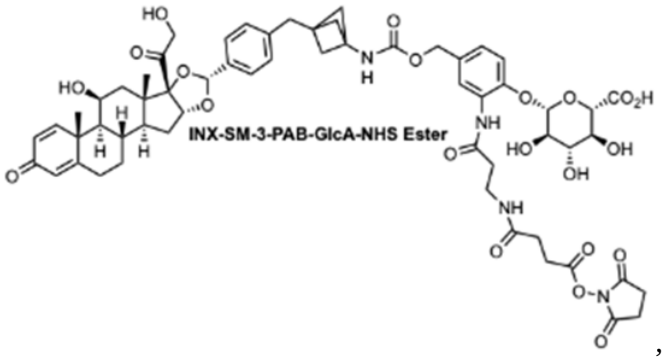


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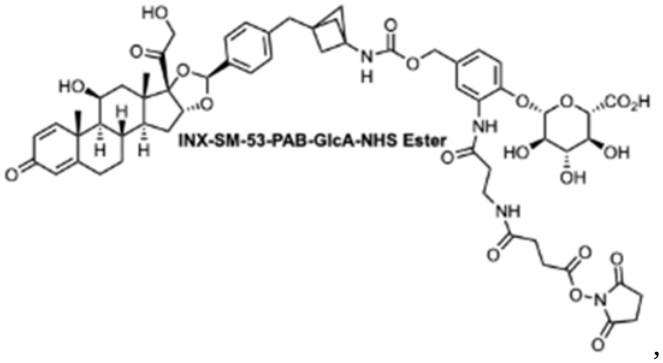


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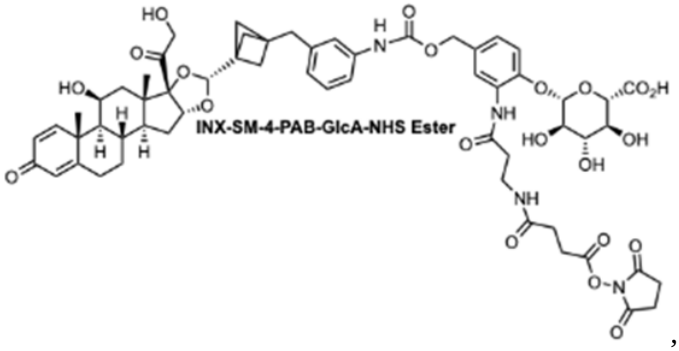
(xviii) the list of AB-GlcA-beta-Ala-NHS Esters selected from



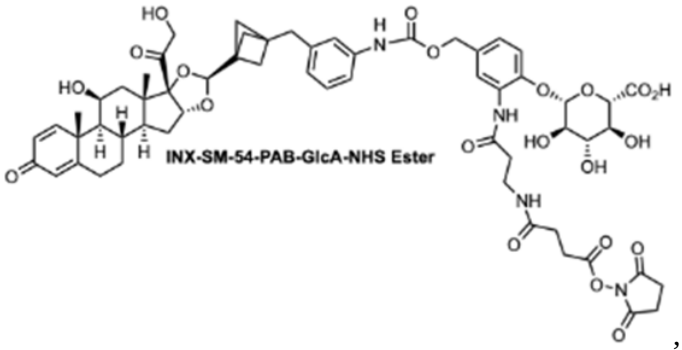
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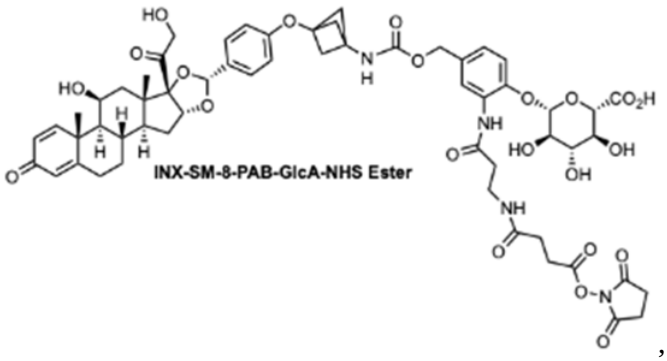
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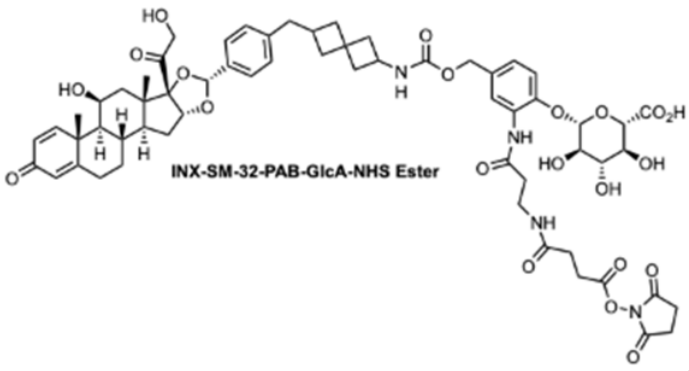
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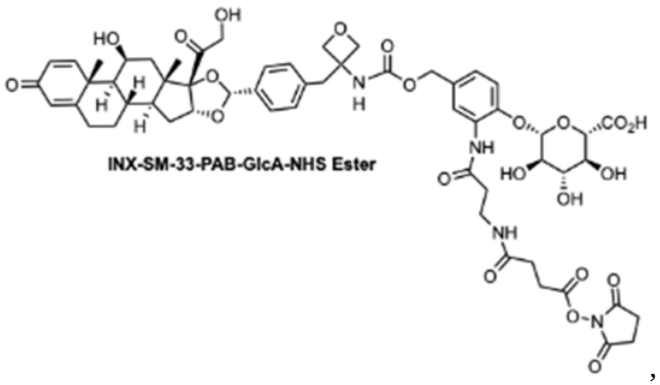
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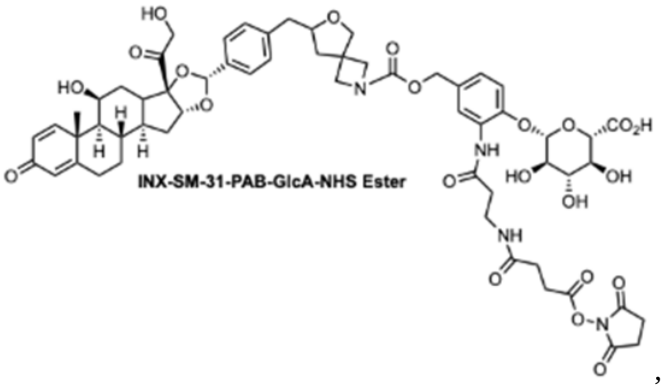
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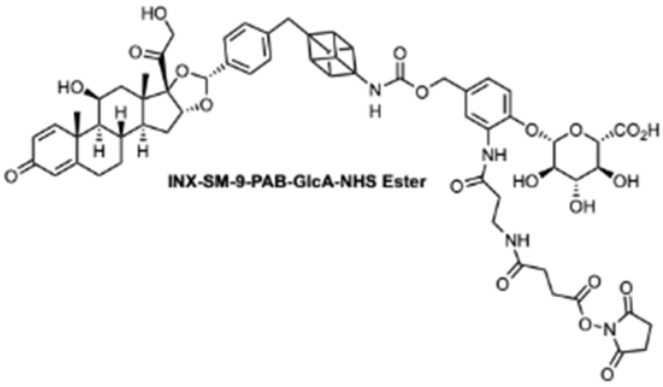
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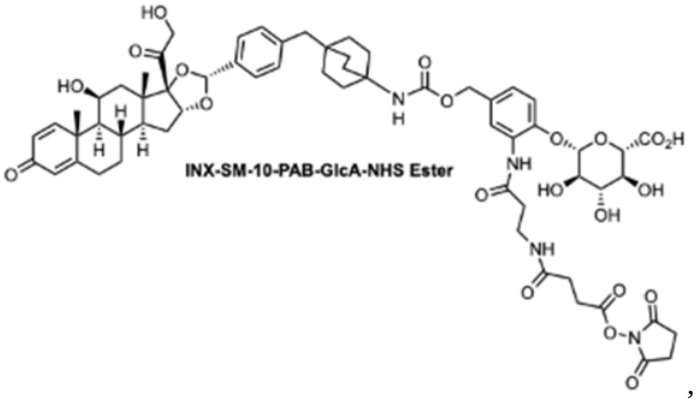
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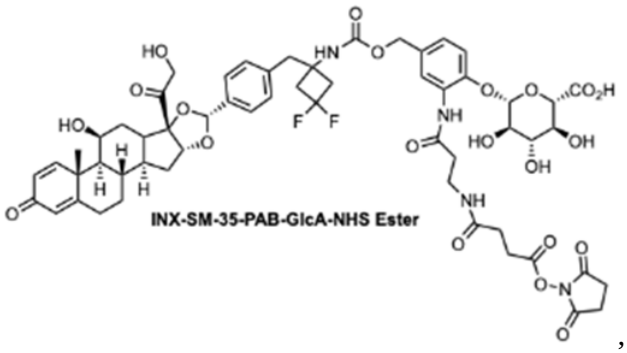
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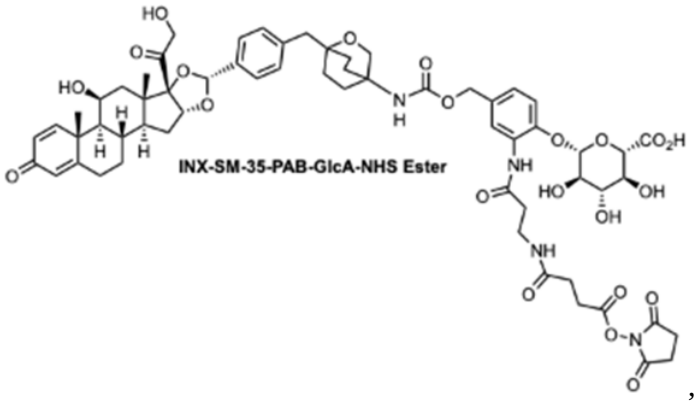
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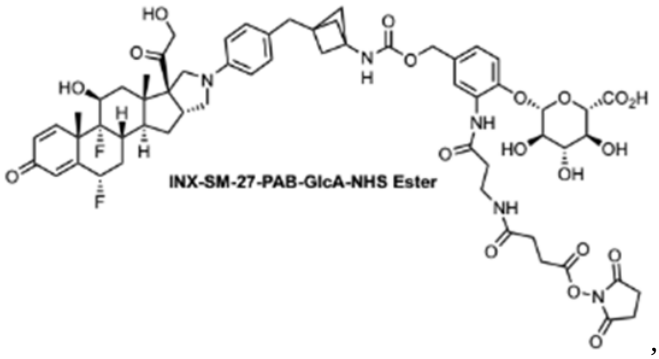
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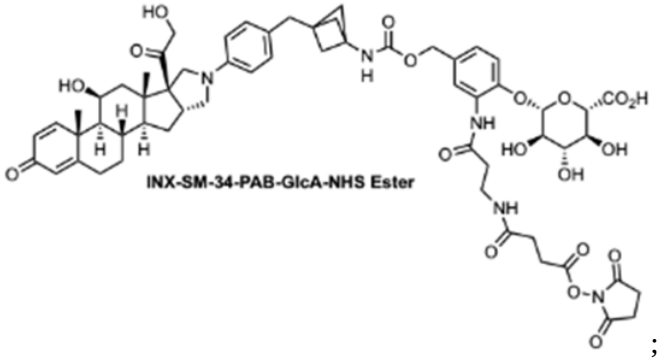
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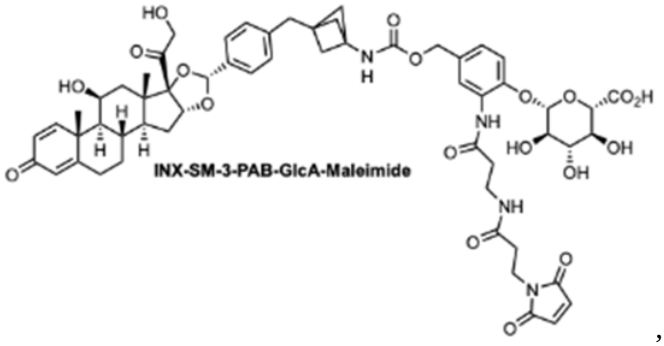


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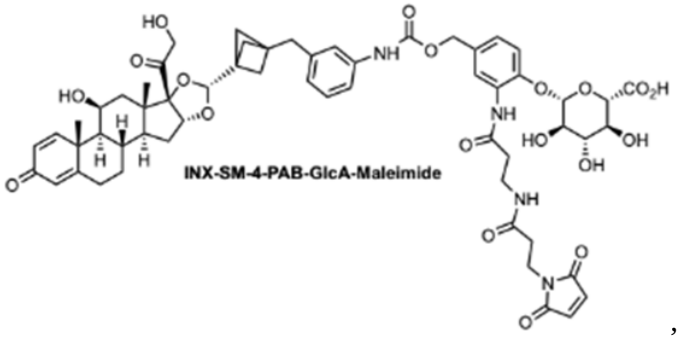


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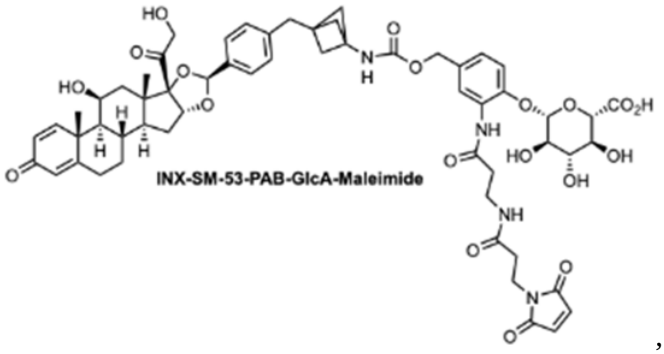
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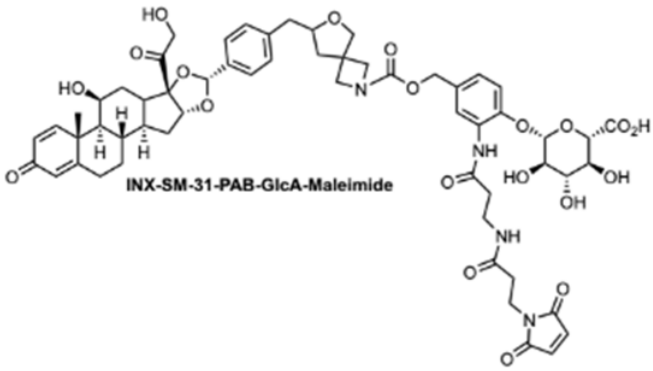
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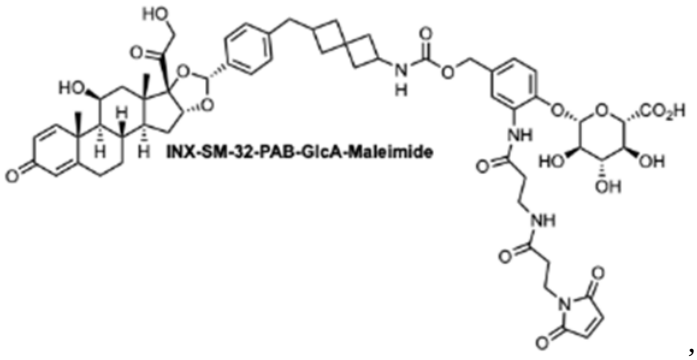
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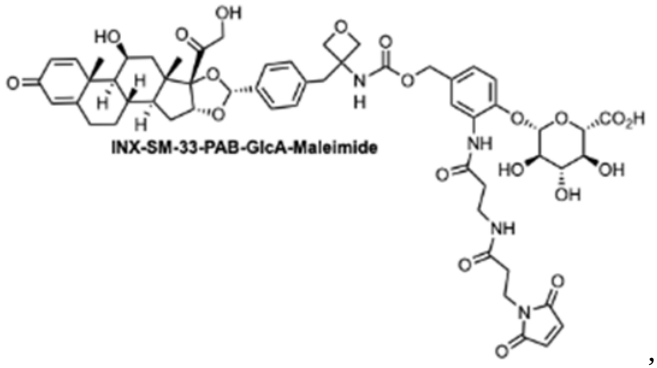
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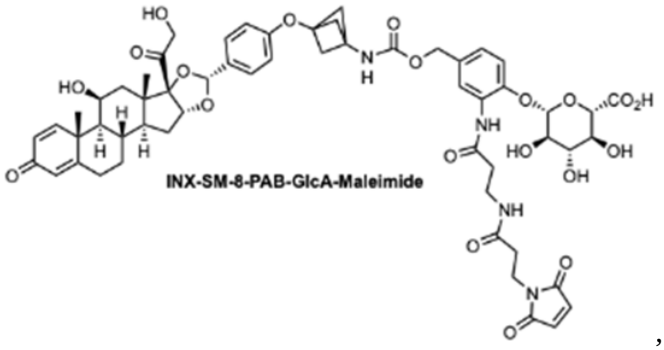
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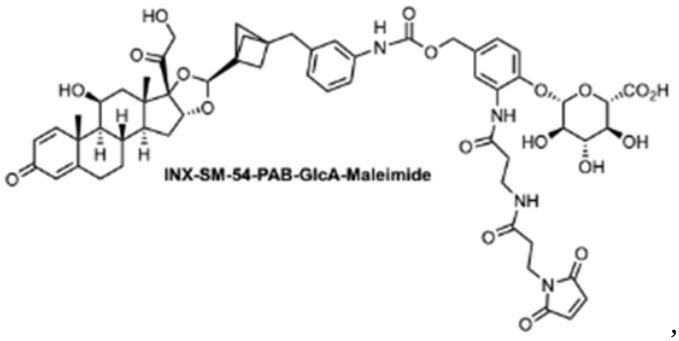
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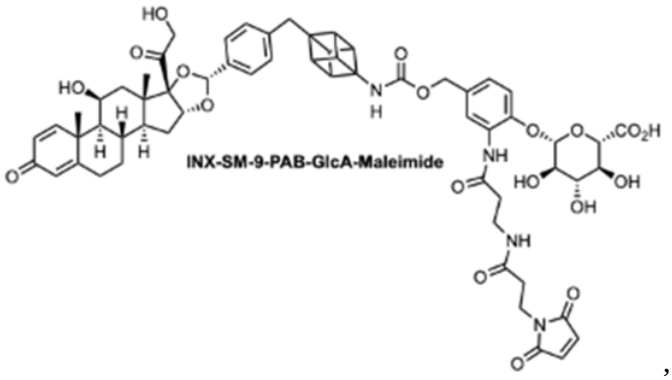
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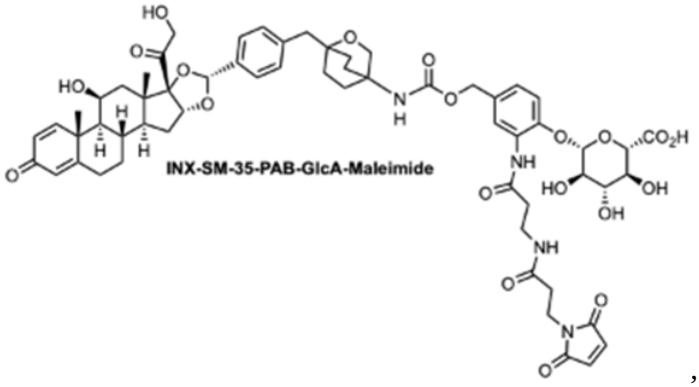
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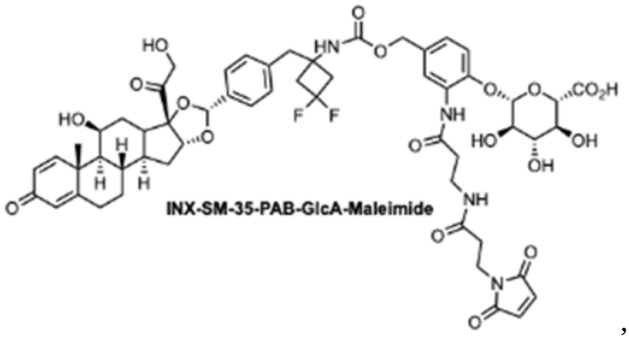
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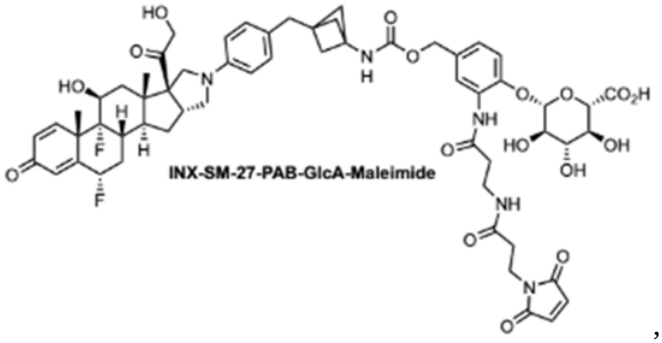
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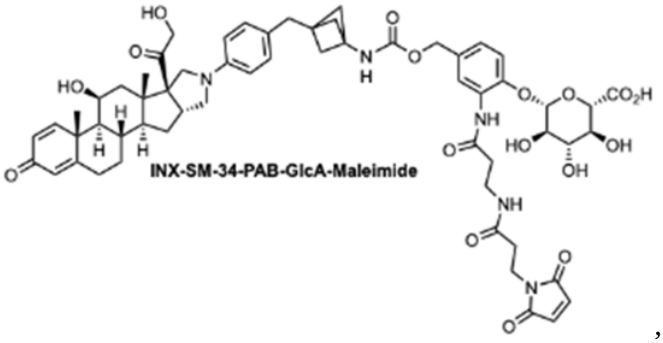
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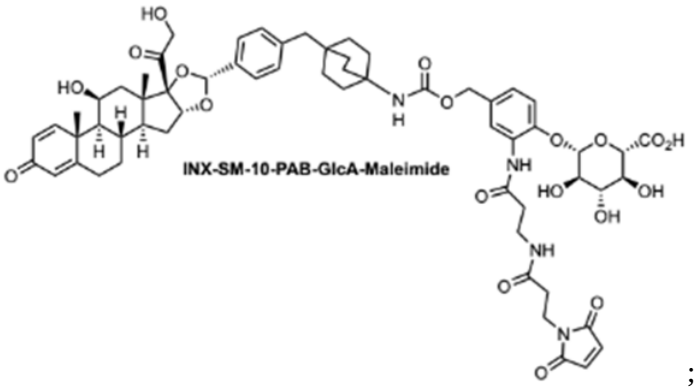
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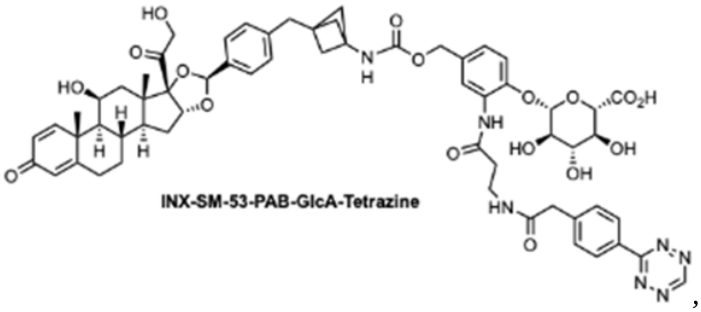


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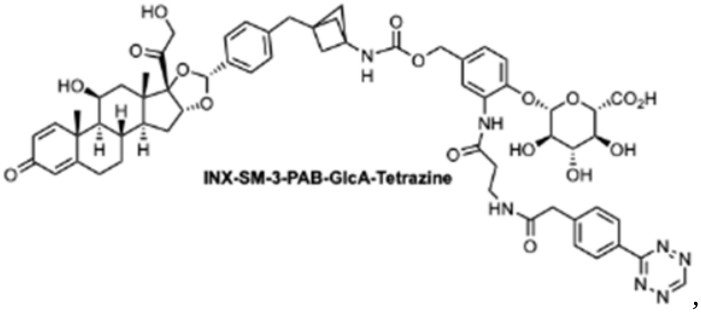


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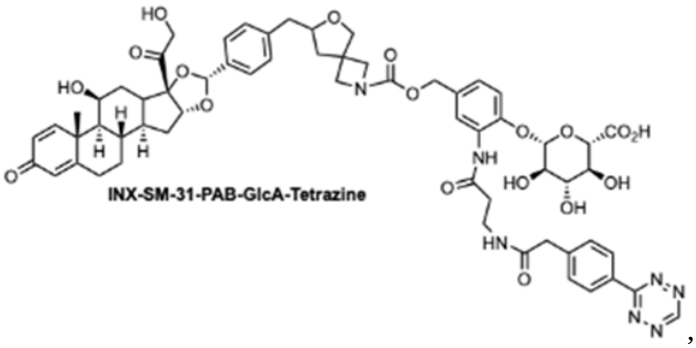
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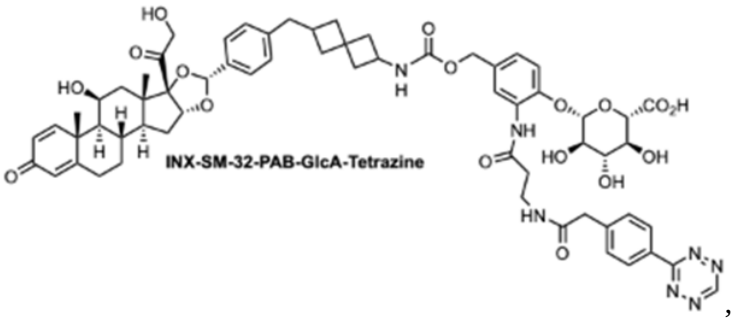


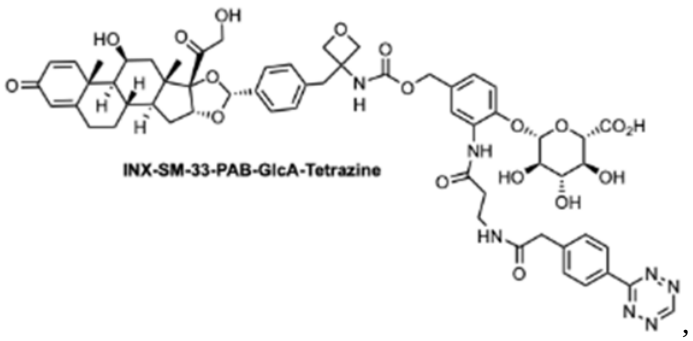
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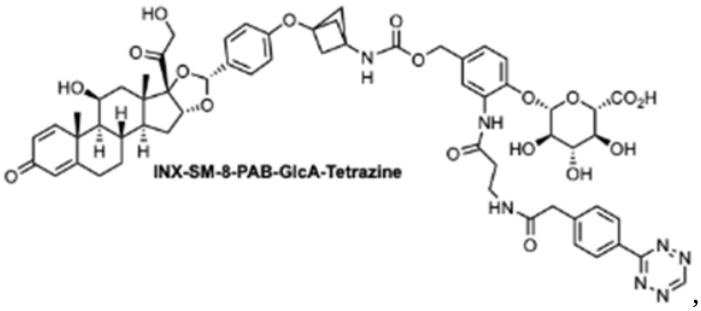


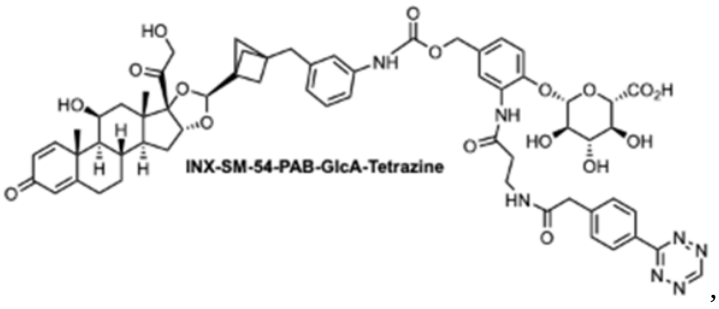
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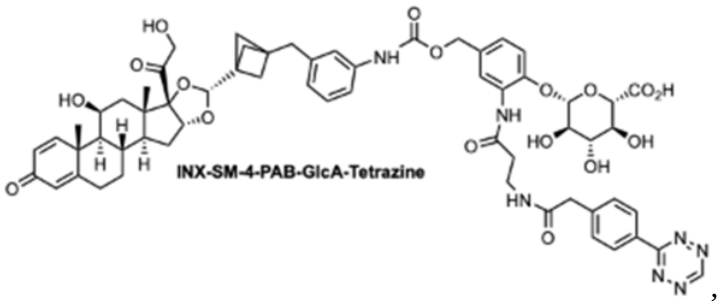

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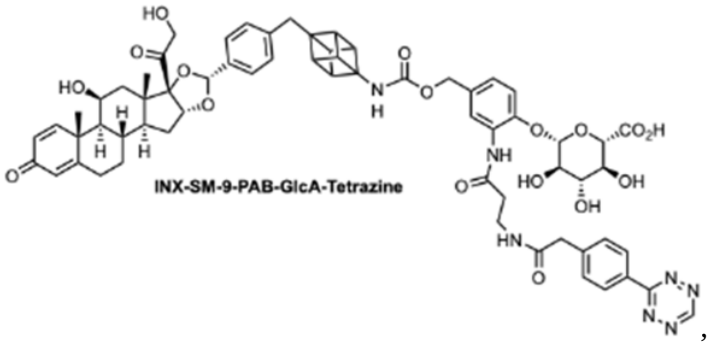

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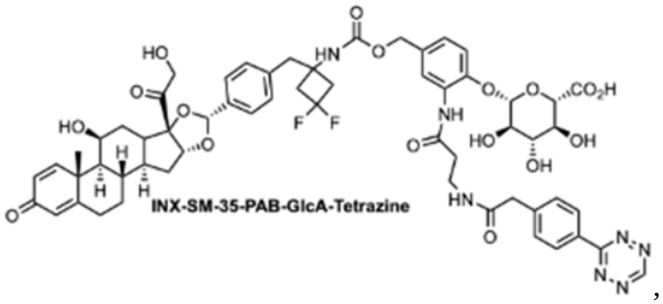

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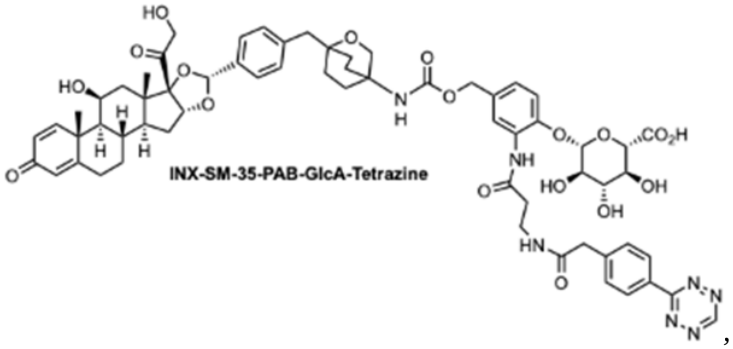

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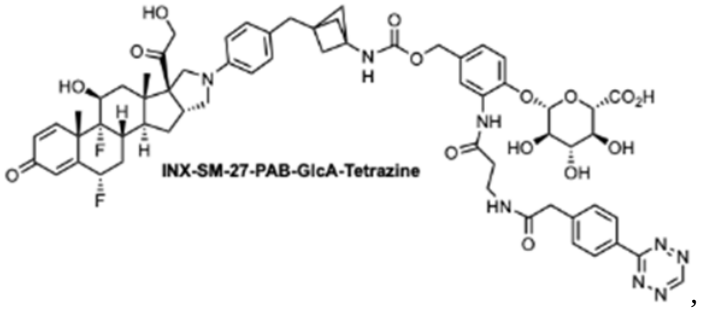

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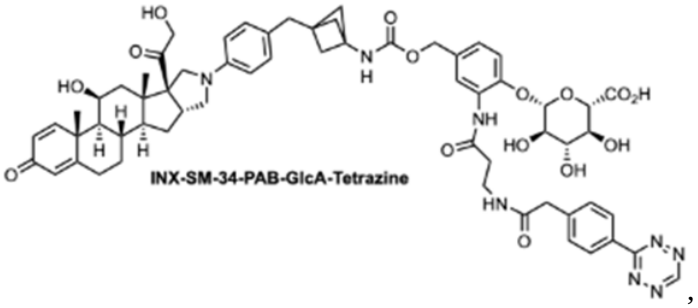

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INX-SM-9-PAB-GlcA-Tetrazine

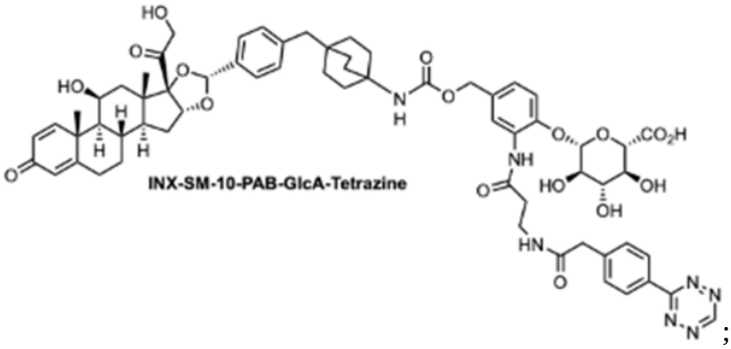

INX-SM-35-PAB-GlcA-Tetrazine


INX-SM-35-PAB-GlcA-Tetrazine


INX-SM-27-PAB-GlcA-Tetrazine

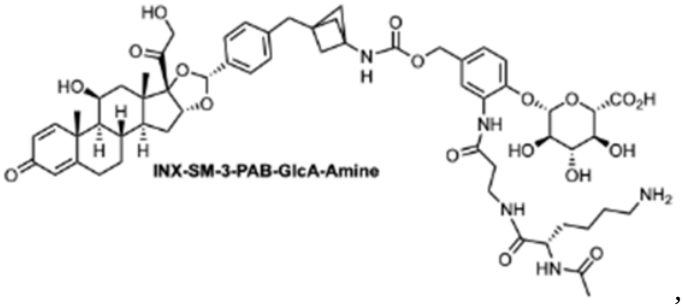


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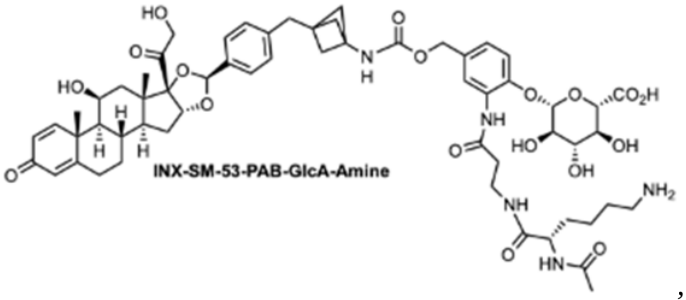


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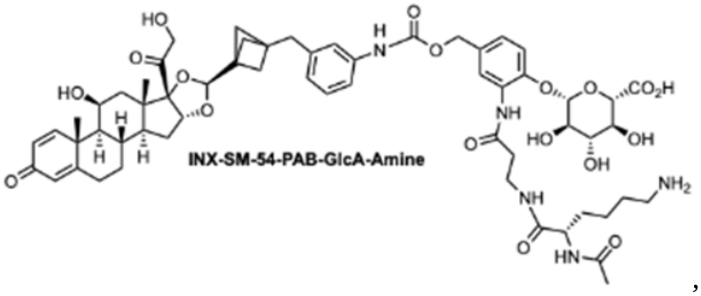
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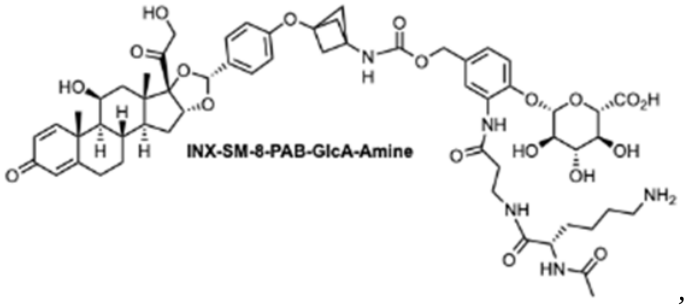
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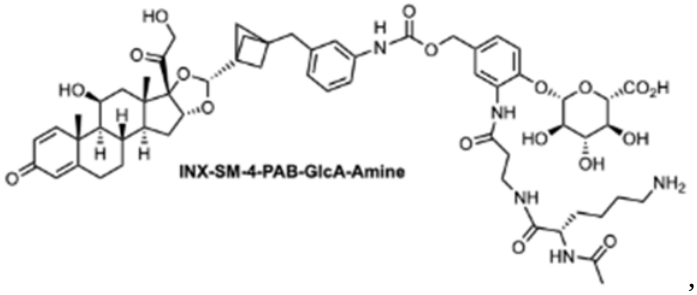
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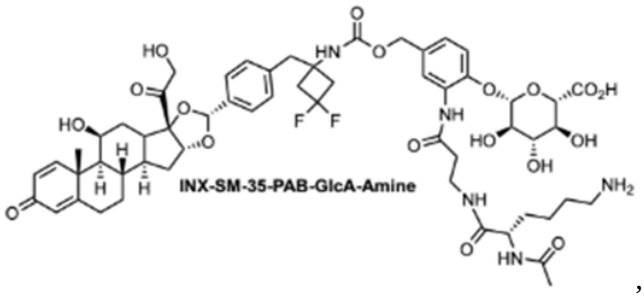
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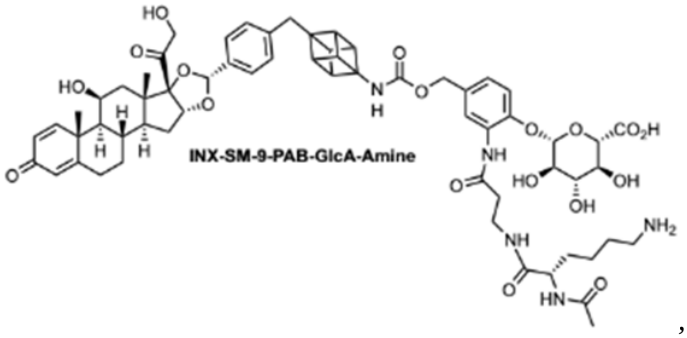
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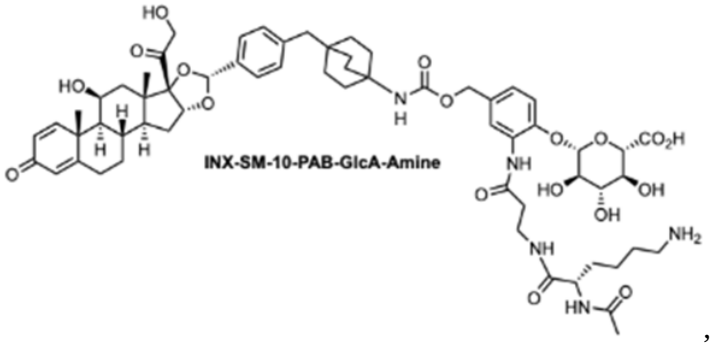
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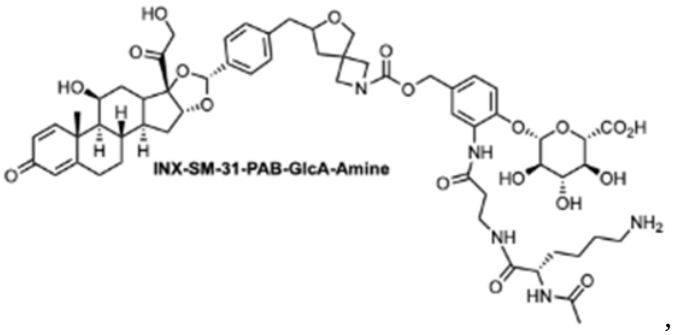
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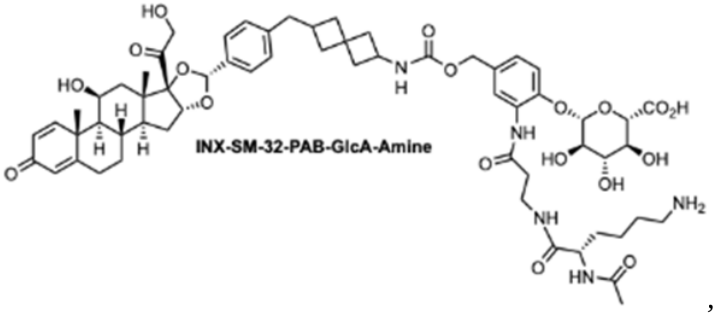

INX-SM-9-PAB-GlcA-Amine

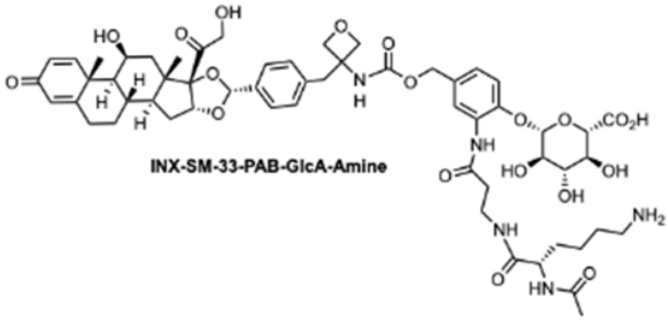
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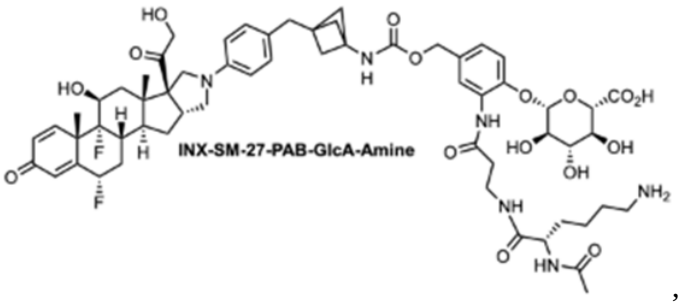

INX-SM-10-PAB-GlcA-Amine

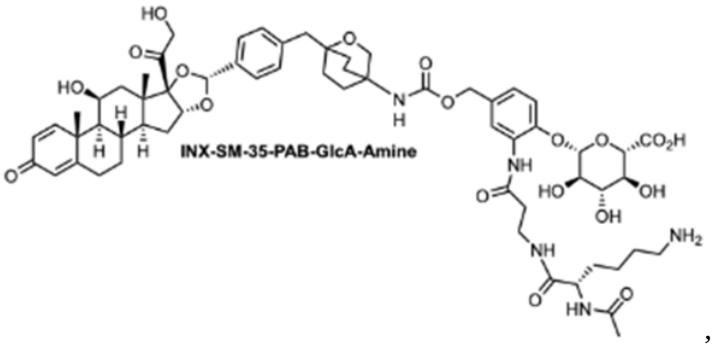
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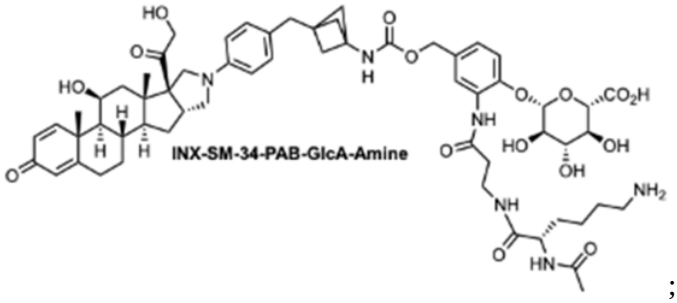

INX-SM-31-PAB-GlcA-Amine
,


INX-SM-32-PAB-GlcA-Amine
,


INX-SM-33-PAB-GlcA-Amine
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INX-SM-27-PAB-GlcA-Amine
,


INX-SM-35-PAB-GlcA-Amine
, and



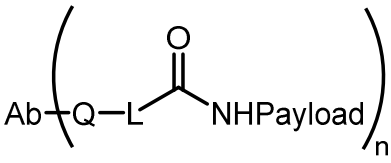
;

15. An antibody drug conjugate (ADC) comprising a glucocorticoid agonist **according to any of claims 1-10** or a payload-linker conjugate **according to any of claims 11-14**, wherein:

said glucocorticoid agonist or payload-linker conjugate is conjugated to an antibody or antigen-binding fragment thereof (**Ab**) by a linkage wherein the reactive group **J** has been reacted with a complementary functional group on **Ab** to form the ADC; and

the ADC has a drug antibody ratio (DAR) of 1:1-12:1; wherein DAR refers to the number of said glucocorticoid agonists per Ab group.

16. An antibody drug conjugate (ADC) having the structure of **Formula (V)**:



Formula (V);

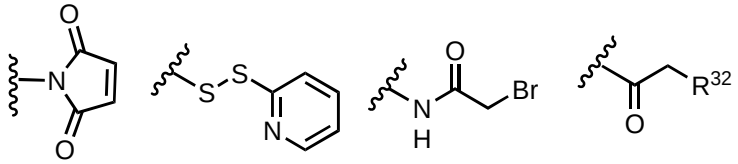
wherein:

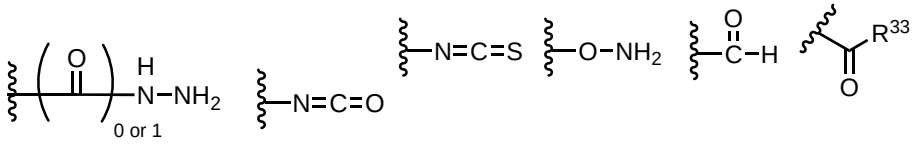
Ab is an antibody or antigen-binding fragment thereof;

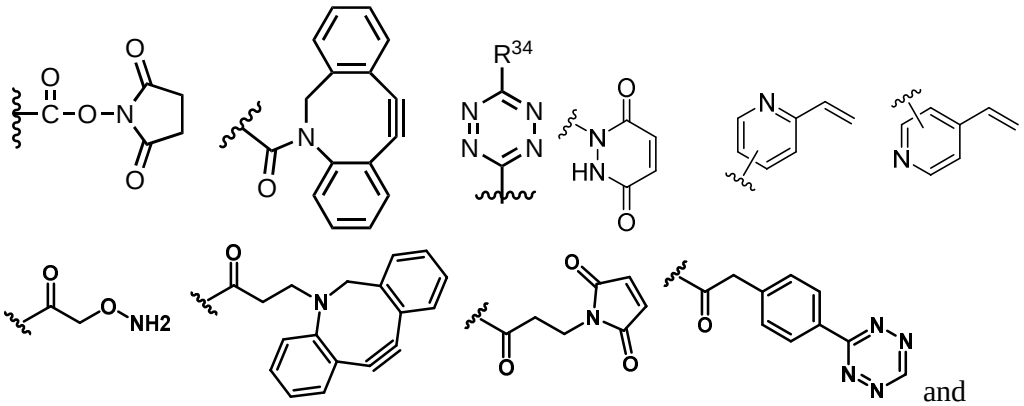
L is a linker comprising p-aminobenzyloxycarbonyl (PAB), an amino acid, a peptide comprising 1-12 amino acids, or any combination thereof,

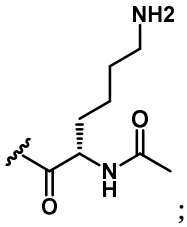
Q is a chemical moiety used to connect Ab to L, and Q comprises a reactive group J, which has been reacted with a complementary functional group on Ab to form the ADC,

where J is a reactive group selected from -NH_2, N_3, thiol, cyclooctyne, -OH, -CO_2H, trans-cyclooctene, alkynyl, propargyl,



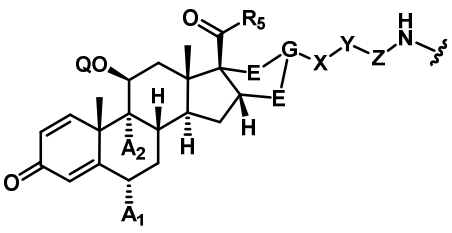



and


;

where R_{32} is selected from Cl, Br, F, mesylate, and tosylate and R_{33} is selected from Cl, Br, I, F, OH, -O-N-succinimidyl, -O-(4-nitrophenyl), -O-pentafluorophenyl or -O-tetrafluorophenyl R_{34} is H, Me, tetrazine-H, and tetrazine-Me;

NHPayload is a glucocorticoid agonist having the following structure

NHPayload = 

where

X is selected from phenyl, 5- or 6-membered heteroaryl, spiro[3.3]heptane, cycloalkyl, spiro-alkyl, bicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane, each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, $-NH_2$, -SH, and -OH;

Y is selected from CHR_1, O, S, and NR_1;

Z is selected from phenyl, 5- or 6-membered heteroaryl, spiro[3.3]heptane, cycloalkyl, spiro-alkyl, bicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, $-NH_2$, -SH, and -OH;

E is O and G is CH, or E is CH_2 and G is N;

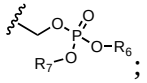
with the proviso that when X is phenyl or 6-membered heteroaryl, Z is not phenyl;

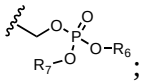
the linkage of G to X is selected from a bond, C_{1-3} alkyl, and ethylene oxide, each of which may be substituted with 1-4 heteroatoms independently selected from $-NH_2$, -SH, and -OH and are optionally further substituted with 1-4 C_{1-3} alkyl;

the linkage of X to Y may occupy any available position on X;

the linkage of Y to Z may occupy any available position on Z;

substituent NH_2 may occupy any available position on Z;

R_5 is selected from the group consisting of $-CH_2OH$, $-CH_2SH$, $-CH_2Cl$, $-SCH_2Cl$, $-SCH_2F$, $-SCH_2CF_3$, hydroxy, $-OCH_2CN$, $-OCH_2Cl$, $-OCH_2F$, $-OCH_3$, $-OCH_2CH_3$, $-SCH_2CN$, and ;

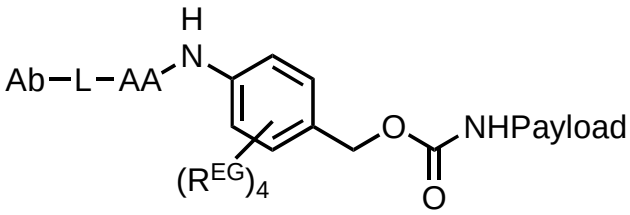
Q is H, ; $C(O)R_8$; or $P(O)OR_4$;

where R_4 =H, alkyl or branched alkyl; R_6 and R_7 are independently selected from hydrogen and C_{1-10} alkyl; and R_8 is linear or branched alkyl of 1-8 carbons; and

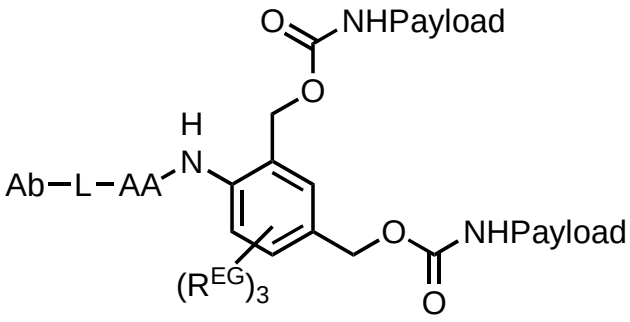
A_1 and A_2 are independently selected from H and F; and

the ADC has a drug antibody ratio (DAR) of 1:1-12:1; wherein DAR refers to the number of said NHPayload groups per Ab group.

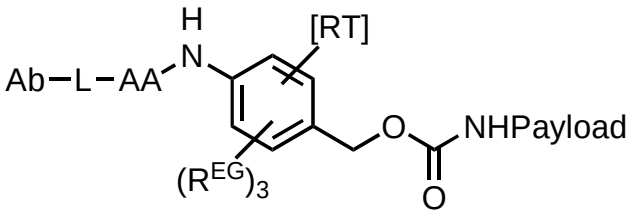
17. An antibody drug conjugate (ADC) having a structure selected from any one of **Formulas (VI)-(X)**:



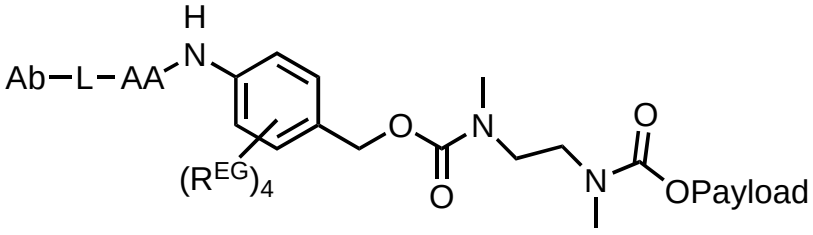
Formula (VI);



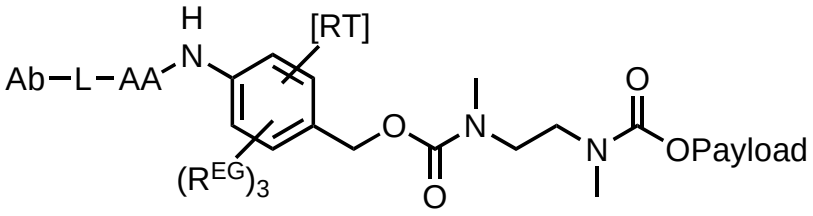
Formula (VII);



Formula (VIII);



Formula (IX); or



Formula (X);

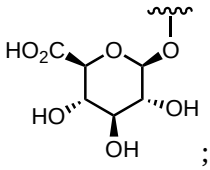
wherein,

Ab is an antibody or antigen-binding fragment thereof;

L is a linker that is conjugated to Ab by a functional group suitable for reacting with a complementary functional group on the Ab;

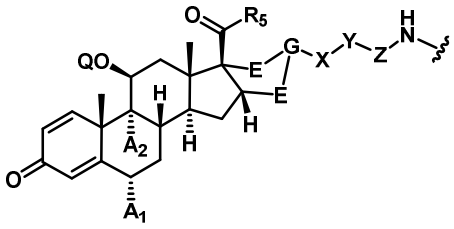
AA is a single, double, or triple amino acid sequence, or is not present;

R^{EG} is independently selected from the group consisting of hydrogen, alkyl, biphenyl, $-CF_3$, $-NO_2$, -CN, fluoro, bromo, chloro, alkoxyl, alkylamino, dialkylamino, alkyl-C(O)O-, alkylamino-C(O)- and dialkylamino-C(O)-;

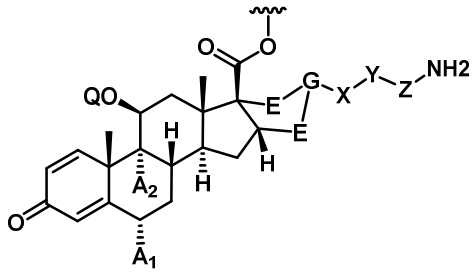
RT= AA or 

;

NHPayload and OPayload are glucocorticoid agonists having the following structures

NHPayload = 

; and

OPayload =  ;

where

X is selected from phenyl, 5- or 6-membered heteroaryl, spiro[3.3]heptane, cycloalkyl, spiro-alkyl, bicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane, each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, $-NH_2$, -SH, and -OH;

Y is selected from CHR_1, O, S, and NR_1;

Z is selected from phenyl, 5- or 6-membered heteroaryl, spiro[3.3]heptane, cycloalkyl, spiro-alkyl, bicyclic alkyl, [1.1.1]bicyclopentane, bicyclo [2.2.2]octane, adamantane, and cubane each of which can be substituted with 1-4 heteroatoms independently selected from F, Cl, Br, I, $-NH_2$, -SH, and -OH;

E is O and G is CH, or E is CH_2 and G is N;

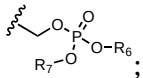
with the proviso that when X is phenyl or 6-membered heteroaryl, Z is not phenyl;

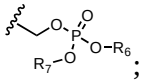
the linkage of G to X is selected from a bond, C_{1-3} alkyl, and ethylene oxide, each of which may be substituted with 1-4 heteroatoms independently selected from $-NH_2$, -SH, and -OH and are optionally further substituted with 1-4 C_{1-3} alkyl;

the linkage of X to Y may occupy any available position on X;

the linkage of Y to Z may occupy any available position on Z;

substituent NH_2 may occupy any available position on Z;

R_5 is selected from the group consisting of $-CH_2OH$, $-CH_2SH$, $-CH_2Cl$, $-SCH_2Cl$, $-SCH_2F$, $-SCH_2CF_3$, hydroxy, $-OCH_2CN$, $-OCH_2Cl$, $-OCH_2F$, $-OCH_3$, $-OCH_2CH_3$, $-SCH_2CN$, and ;

Q is H, ; $C(O)R_8$; or $P(O)OR_4$;

where R_4 =H, alkyl or branched alkyl; R_6 and R_7 are independently selected from hydrogen and C_{1-10} alkyl; and R_8 is linear or branched alkyl of 1-8 carbons; and

A_1 and A_2 are independently selected from H and F; and

the ADC has a drug antibody ratio (DAR) of 1:1-12:1; wherein DAR refers to the number of said NHPayload and OPayload groups per Ab group.

18. The ADC according to **any of claims 15-17**, wherein L:

(i) comprises at least one immolative linker or at least one cleavable linker which is susceptible to one or more of acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage; or

(ii) is a non-cleavable linker, which is resistant to acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage.

19. The ADC **according to any of claims 15-18**, wherein L comprises:

(i) AB, PAB, AB-GlcA, PAB-GlcA or,

(ii) said amino acid or peptide selected from a peptide comprising 1-12 amino acids, a dipeptide, a tripeptide, a tetrapeptide, a pentapeptide, Gly, Glu, beta-Ala, Asn, Asp, Gln, Leu, Lys, Ala, Phe, Cit, Val, Glu-Gly, Val-Cit, Val-Ala, Val-Gly, Val-Gln, Ala-Val, Cit-Cit, Lys-Val-Cit, Asp-Val-Ala, Ala-Ala-Asn, Asp-Val-Ala, Ala-Val-Cit, Ala-Asn-Val, beta-Ala-Leu-Ala-Leu, Lys-Val-Ala, Val-Leu-Lys, Asp-Val-Cit, Val-Ala-Val, and Ala-Ala-Asn;

(iii) Glu-Gly, PAB-Glu-Gly, AB-GlcA-beta-Ala; or

(iv) any combination thereof.

20. The ADC **according to any of claims 15-19**, wherein said Ab:

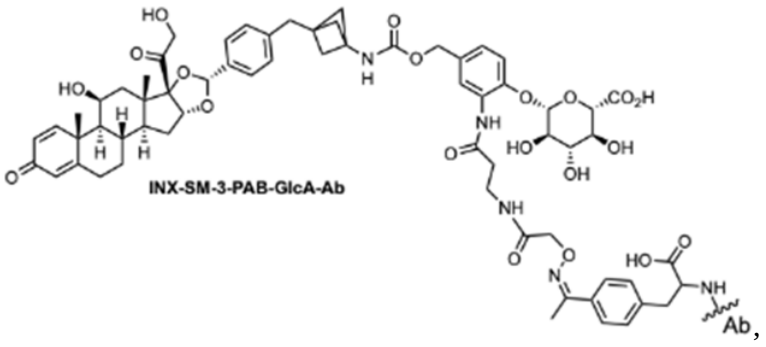
(i) binds to human immune cells;

(ii) binds to an antigen expressed on a human immune cell;

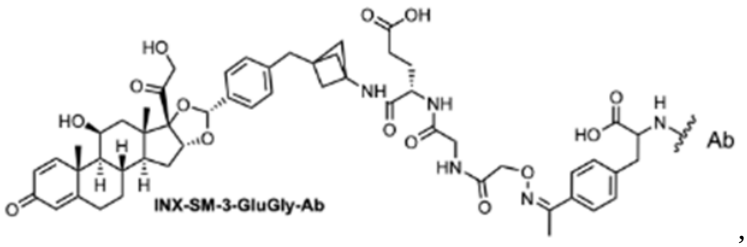
(iii) is an anti-V-domain Ig Suppressor of T cell Activation (VISTA) antibody or fragment thereof, which binds to human VISTA antigen; or

(iv) is an anti-VISTA antibody or fragment thereof, which binds to a human VISTA antigen expressed on a human immune cell.

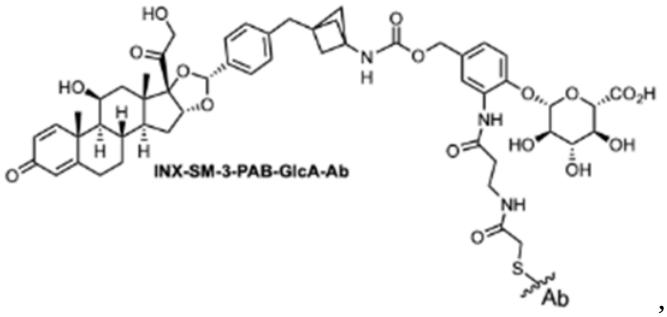
21. The ADC **according to any of claims 15-20**, which is selected from the following structures:



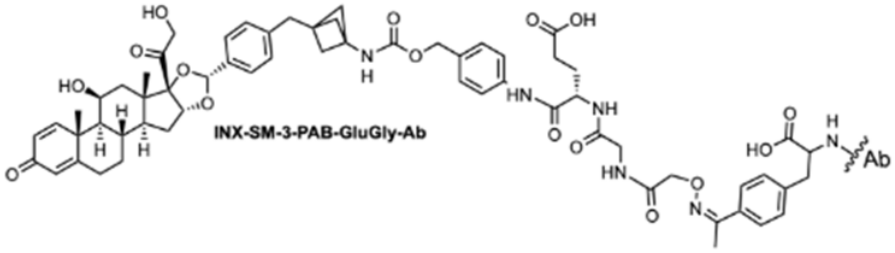
INX-SM-3-PAB-GlcA-Ab


INX-SM-3-GluGly-Ab
Ab

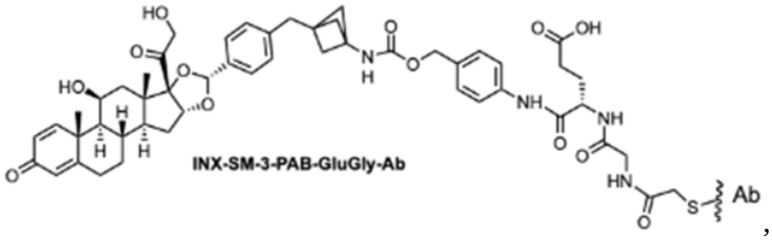
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INX-SM-3-PAB-GlcA-Ab
Ab

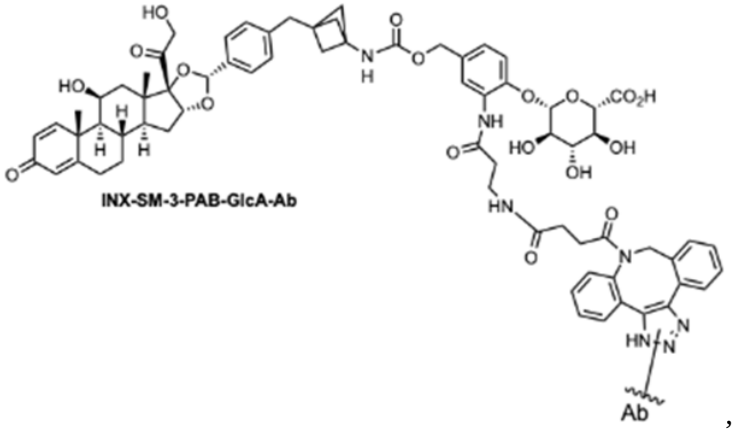
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INX-SM-3-PAB-GluGly-Ab
Ab

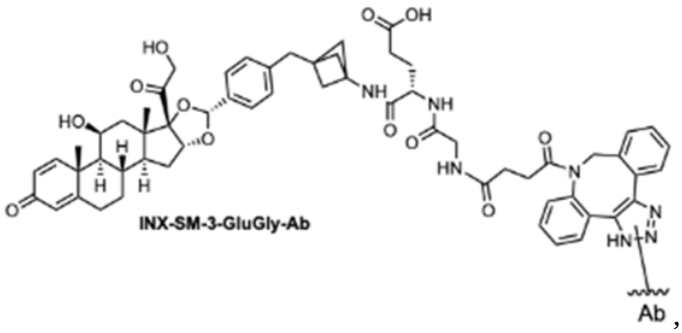
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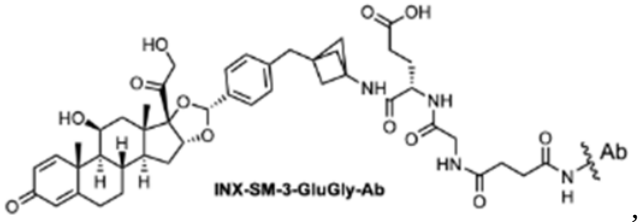

INX-SM-3-PAB-GluGly-Ab
Ab

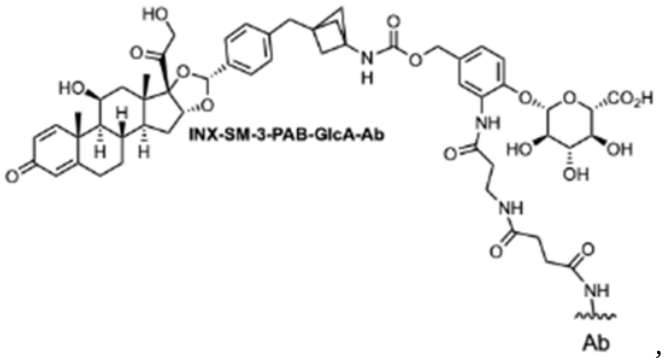
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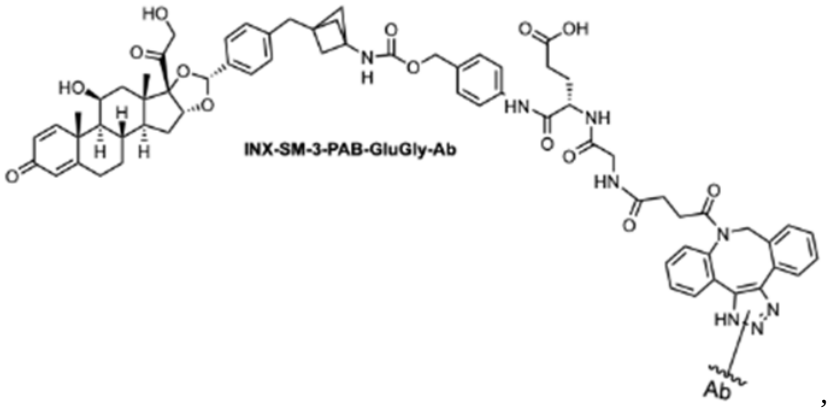

INX-SM-3-PAB-GlcA-Ab
Ab

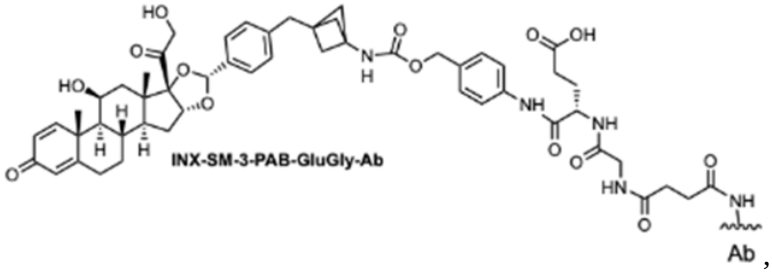
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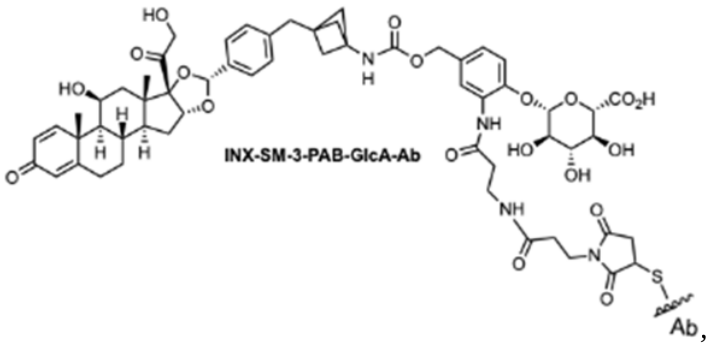

INX-SM-3-GluGly-Ab
Ab
,

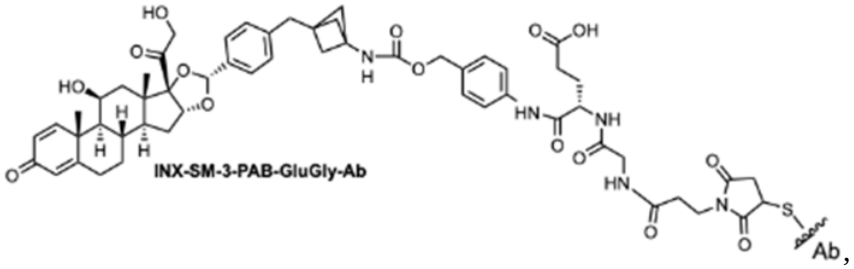

INX-SM-3-GluGly-Ab
Ab
,

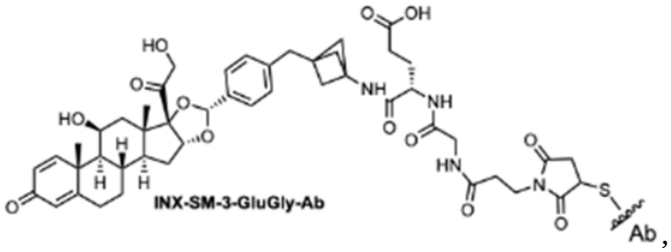

INX-SM-3-PAB-GlcA-Ab
Ab
,

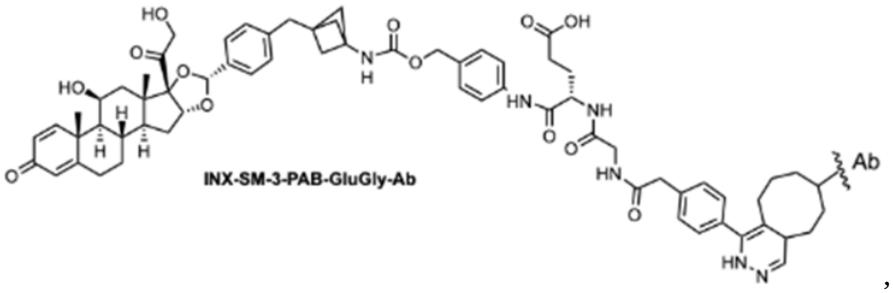

INX-SM-3-PAB-GluGly-Ab
Ab
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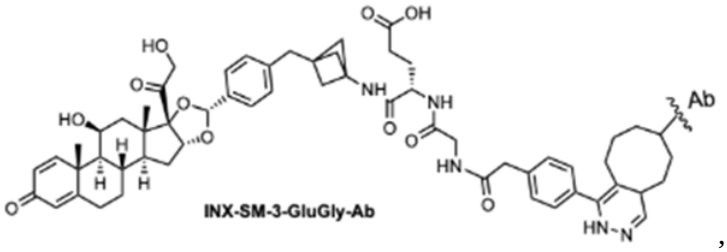

INX-SM-3-PAB-GluGly-Ab
Ab
,

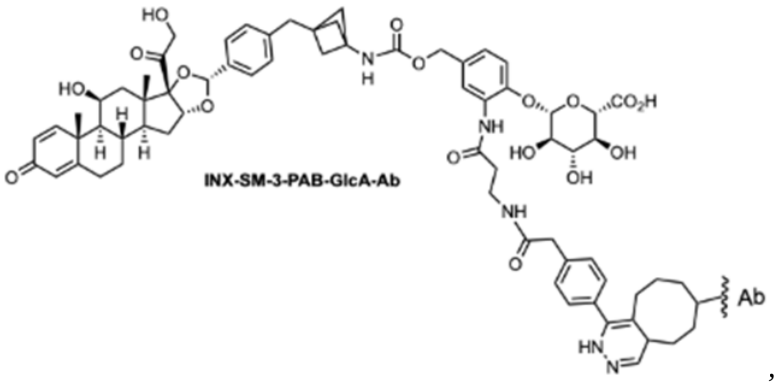

INX-SM-3-PAB-GlcA-Ab
Ab
,


INX-SM-3-PAB-GluGly-Ab
Ab
,

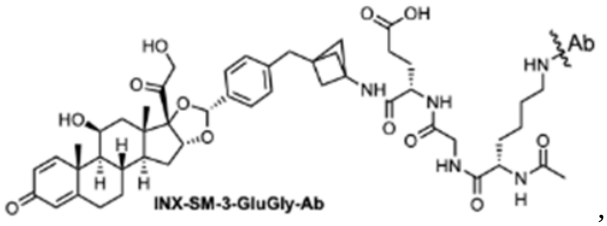

INX-SM-3-GluGly-Ab
Ab
,


INX-SM-3-PAB-GluGly-Ab
Ab
,

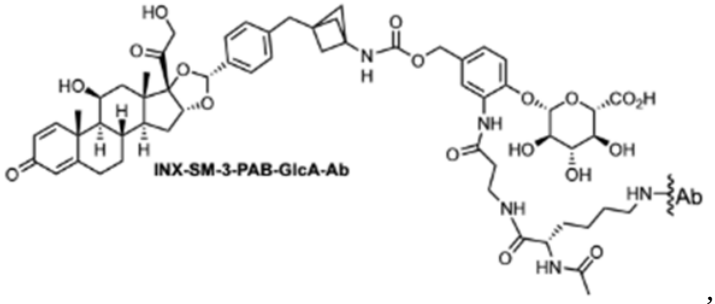

INX-SM-3-GluGly-Ab
Ab
,



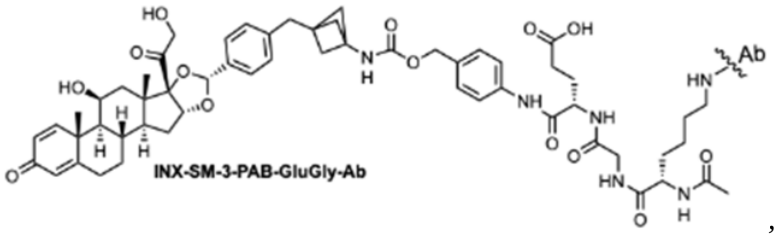
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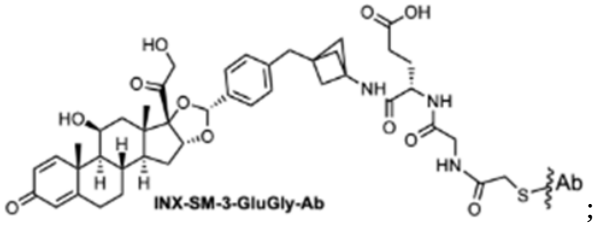
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, and



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wherein Ab is said antibody or antigen binding fragment thereof, which:

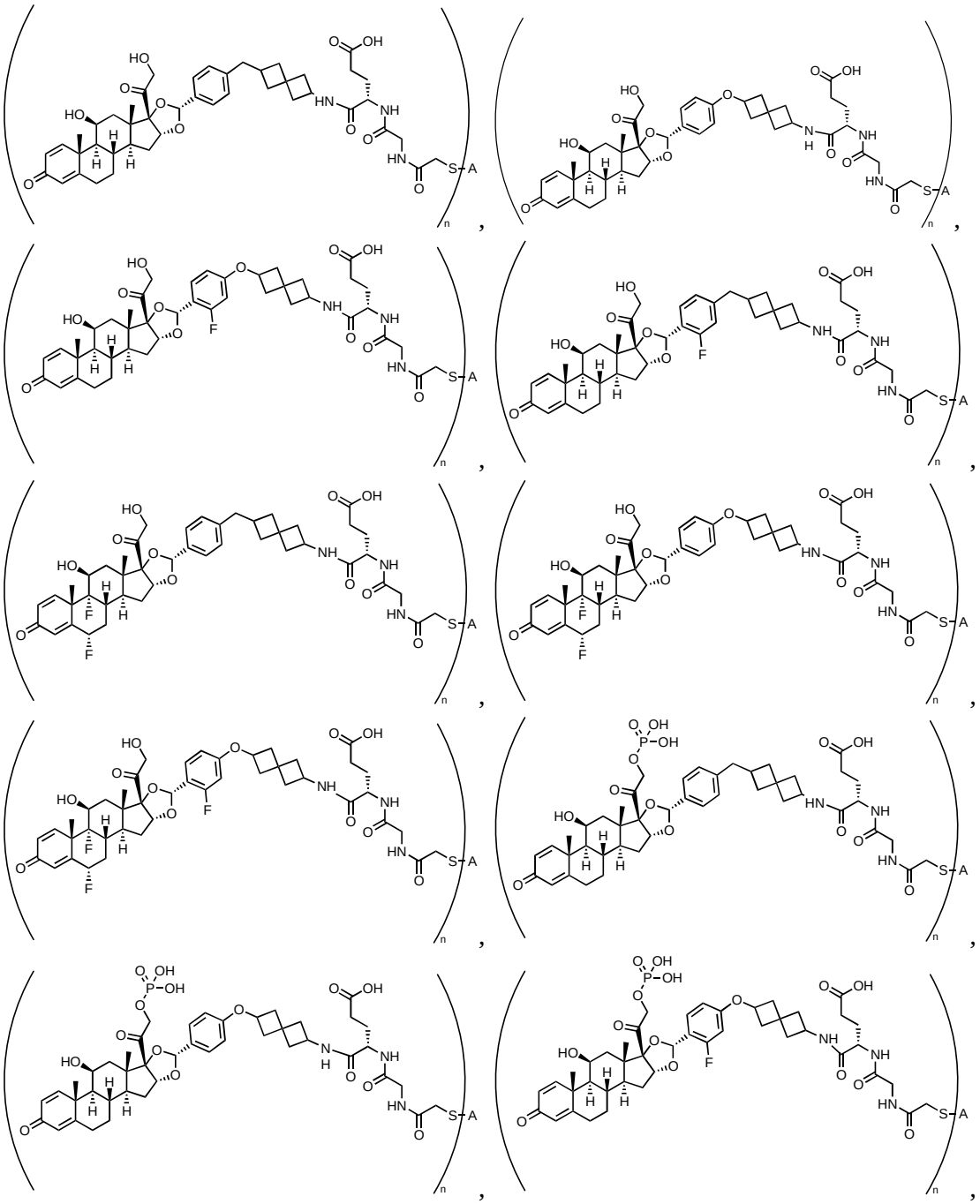
binds to an antigen expressed on an immune cell;

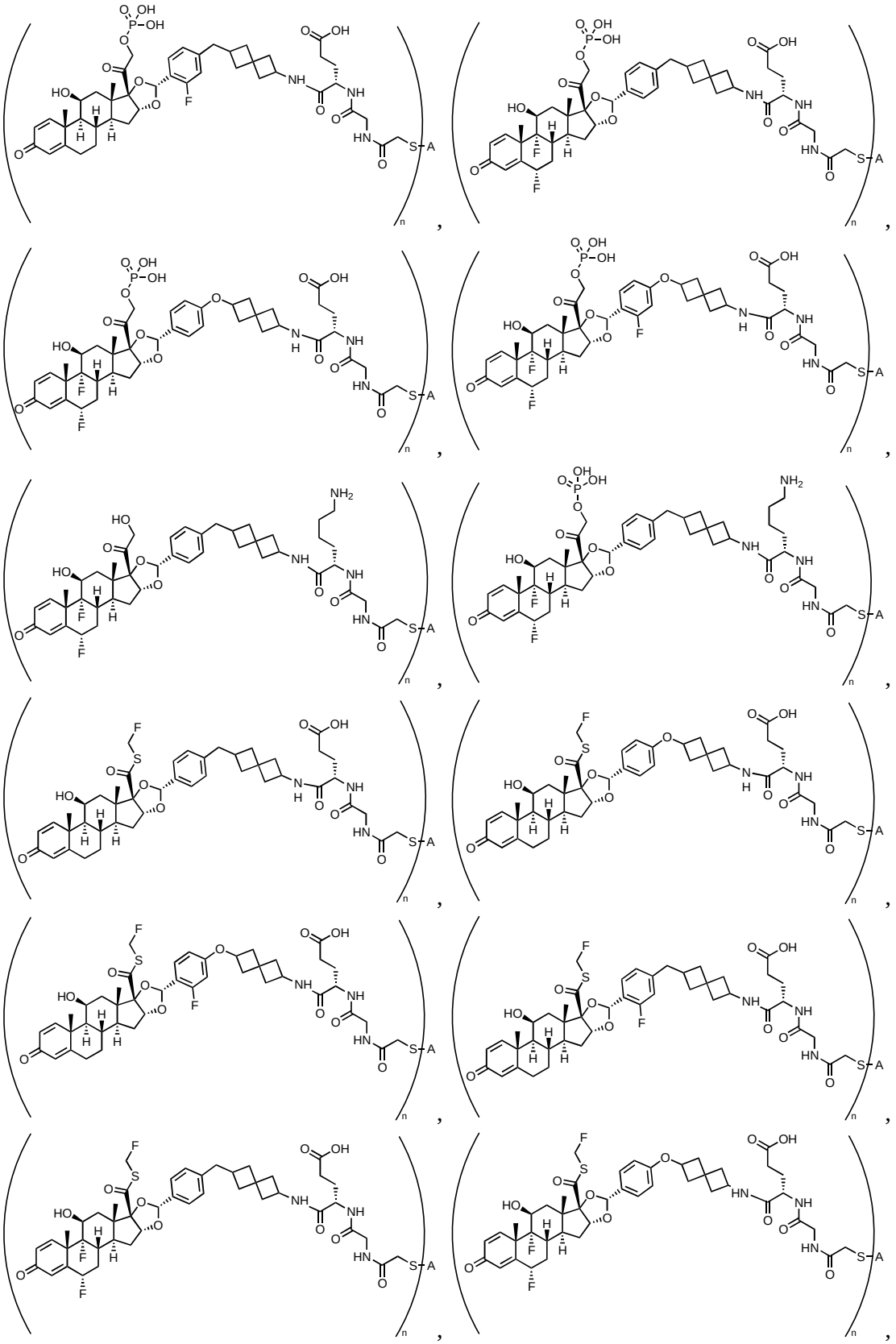
binds to an antigen expressed on a human immune cell;

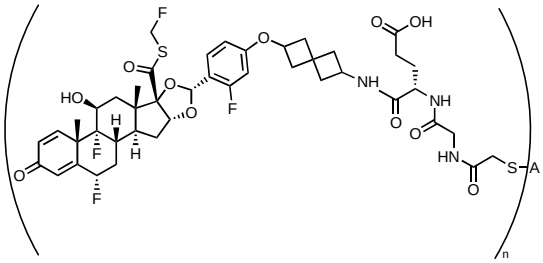
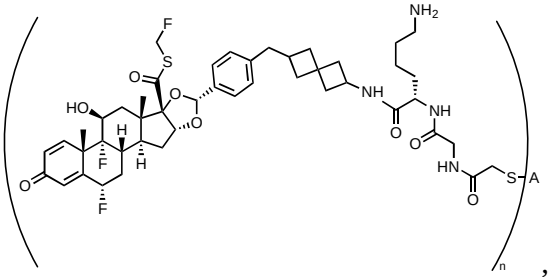
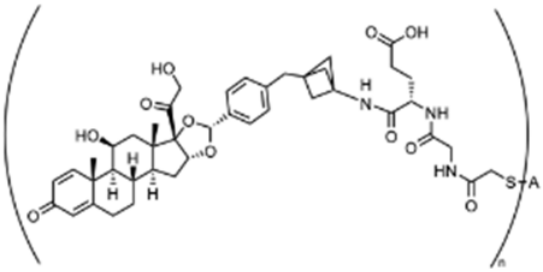
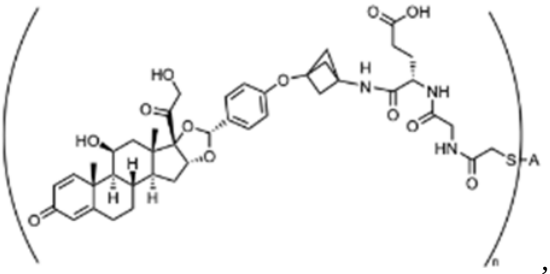
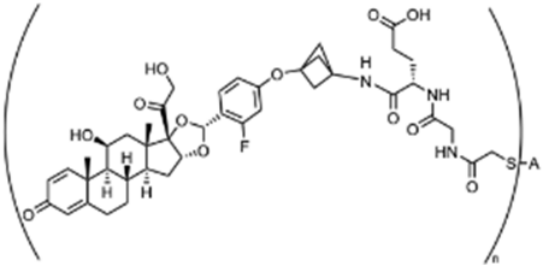
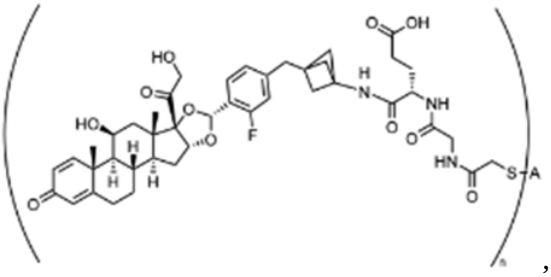
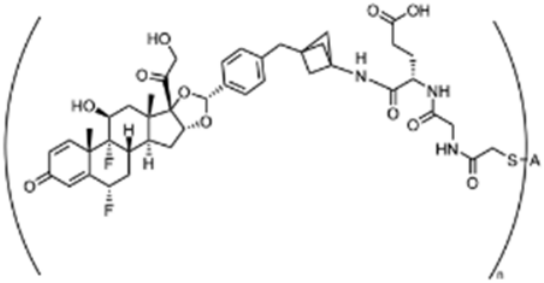
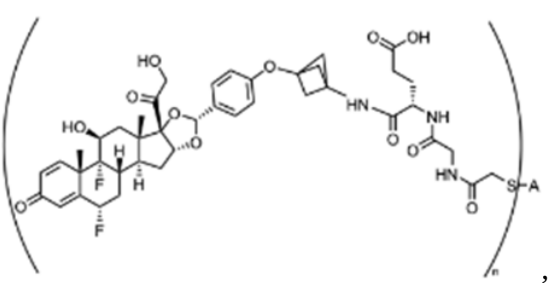
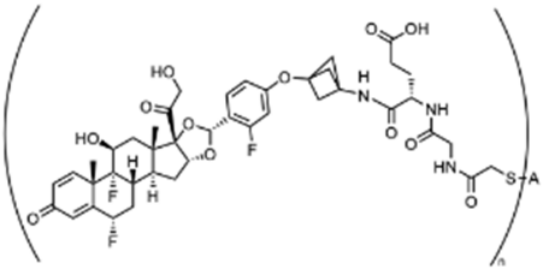
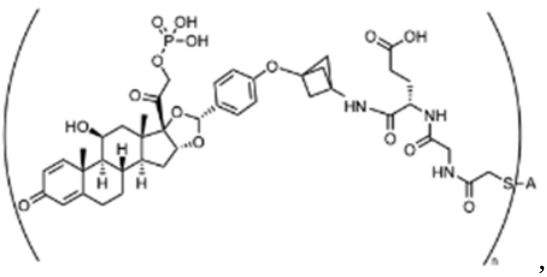
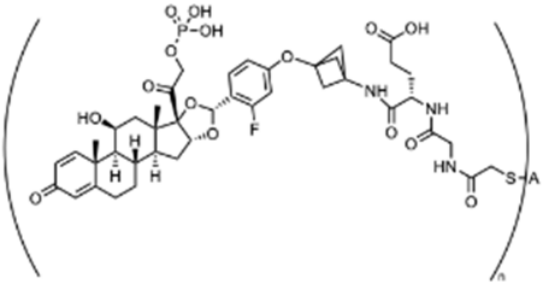
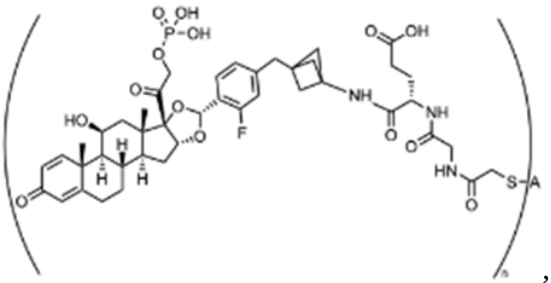
is an anti- human VISTA antibody or fragment thereof, which binds to a human VISTA antigen; or

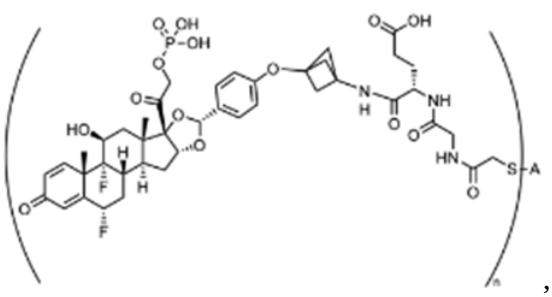
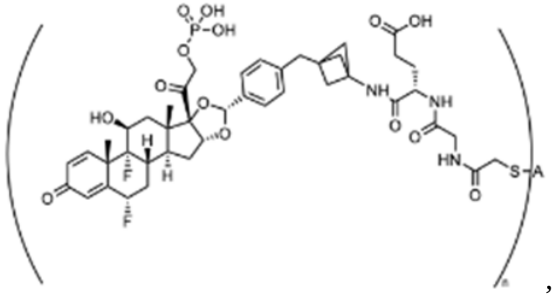
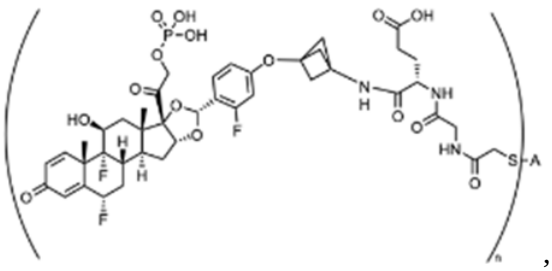
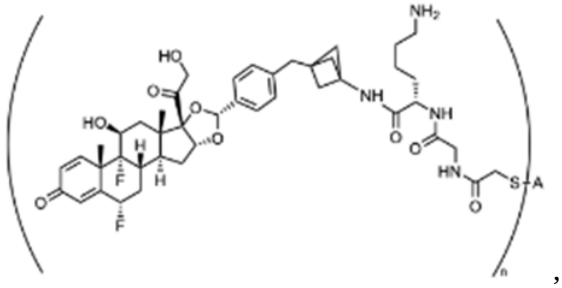
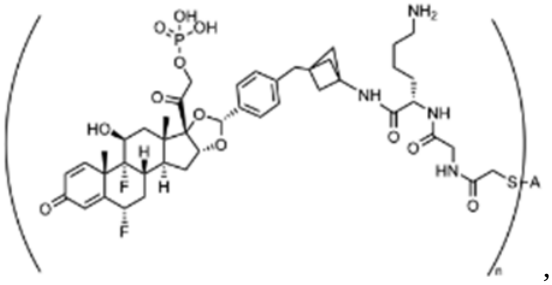
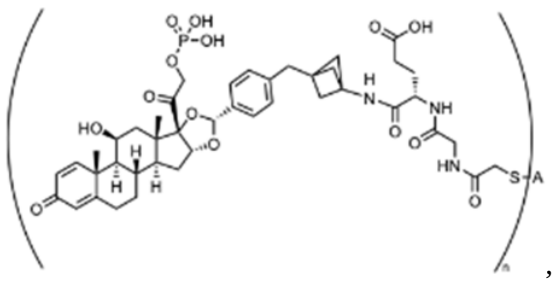
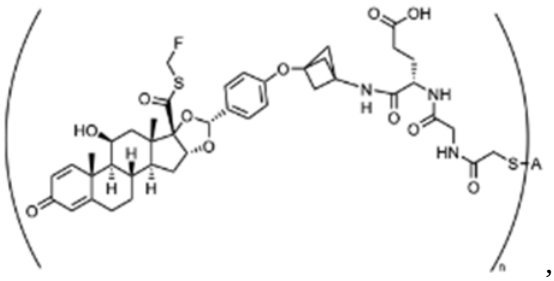
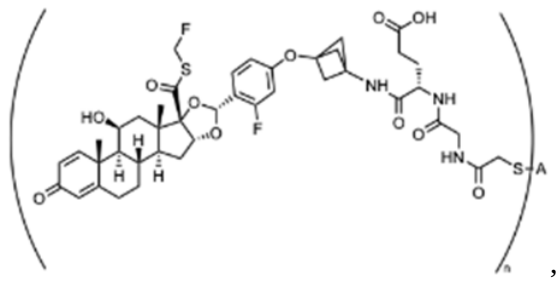
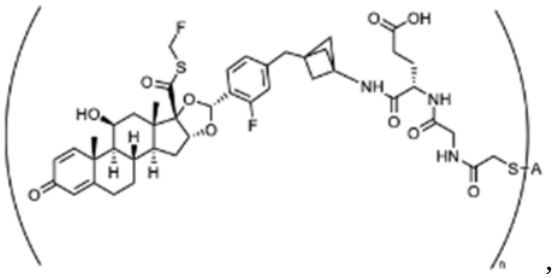
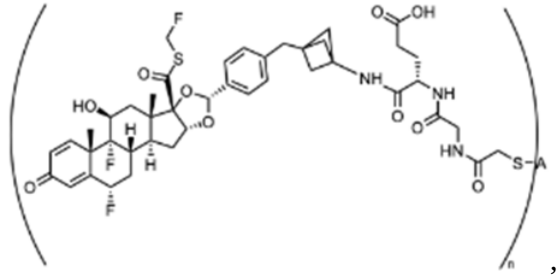
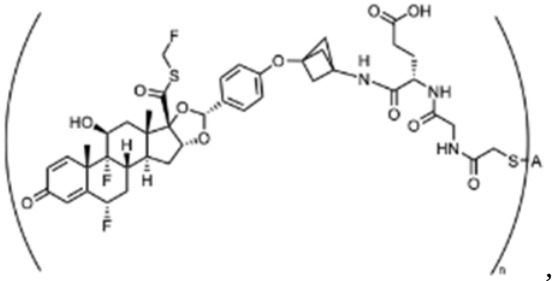
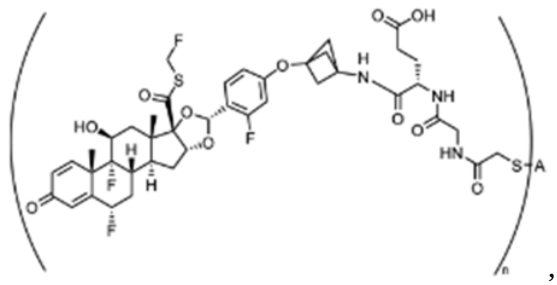
is an anti-human VISTA antibody or fragment thereof, which binds to a human VISTA antigen expressed on a human immune cell.

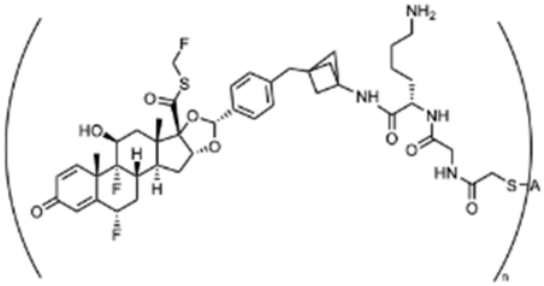
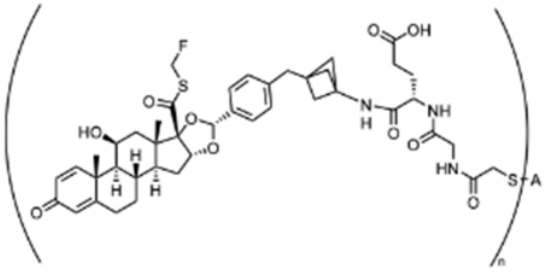
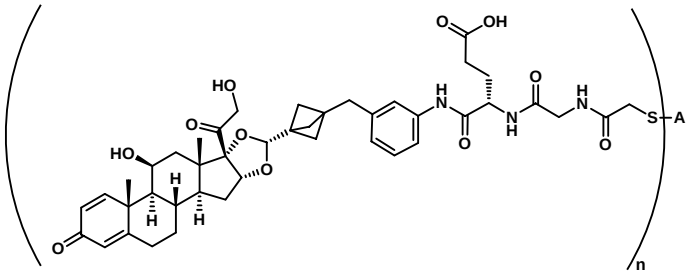
22. The ADC **according to any of claims 15-21**, which is selected from:






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and ,

wherein n = 2-12 and A is said antibody or antigen binding fragment thereof (Ab), which:

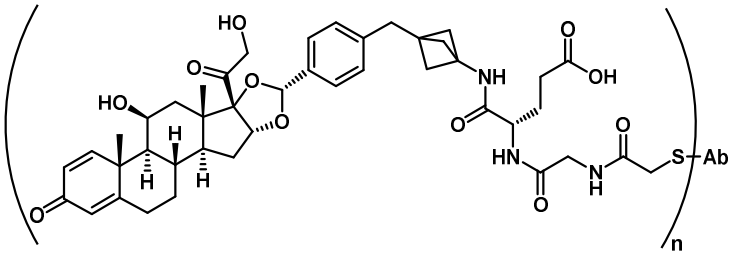
binds to an antigen expressed by an immune cell;

binds to an antigen expressed on a human immune cell;

is an anti-human VISTA antibody or fragment thereof, which binds to a human VISTA antigen; or

is an anti-human VISTA antibody or fragment thereof, which binds to a human VISTA antigen expressed on a human immune cell.

23. The ADC of **any one of claims 15-22**, having the structure

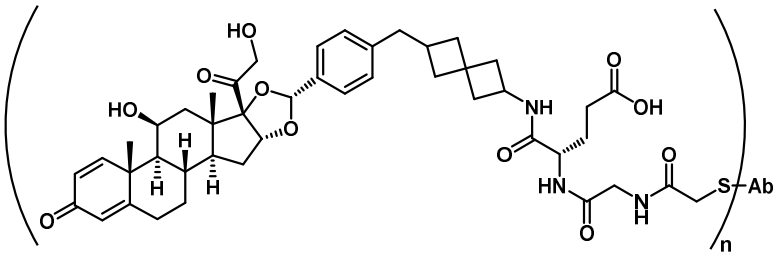


wherein:

n = 1-12; and

Ab is an antibody or antigen binding fragment comprising an antigen binding region that specifically binds to human V-domain Ig Suppressor of T cell Activation (VISTA).

24. The ADC of **any one of claims 15-23**, having the structure



wherein:

n = 1-12; and

Ab is an antibody or comprising an antigen binding region that specifically binds to human V-domain Ig Suppressor of T cell Activation (VISTA).

25. The ADC of **any one of claims 15-24**, wherein said Ab comprises an anti-human VISTA antibody or antigen binding fragment thereof selected from one that:

(i) comprises the V_H CDRs of SEQ ID NO:100, 101 and 102 and the V_L CDRs of SEQ ID NO:103, 104 and 105;

(ii) comprises the V_H CDRs of SEQ ID NO:110, 111 and 112 and the V_L CDRs of SEQ ID NO:113, 114 and 115;

(iii) comprises the V_H CDRs of SEQ ID NO:120, 121 and 122 and the V_L CDRs of SEQ ID NO:123, 124 and 125;

(iv) comprises the V_H CDRs of SEQ ID NO:130, 131 and 132 and the V_L CDRs of SEQ ID NO:133, 134 and 135;

(v) comprises the V_H CDRs of SEQ ID NO:140, 141 and 142 and the V_L CDRs of SEQ ID NO:143, 144 and 145;

(vi) comprises the V_H CDRs of SEQ ID NO:150, 151 and 152 and the V_L CDRs of SEQ ID NO:153, 154 and 155;

(vii) comprises the V_H CDRs of SEQ ID NO:160, 161 and 162 and the V_L CDRs of SEQ ID NO:163, 164 and 165;

(viii) comprises the V_H CDRs of SEQ ID NO:170, 171 and 172 and the V_L CDRs of SEQ ID NO:173, 174 and 175;

(ix) comprises the V_H CDRs of SEQ ID NO:180, 181 and 182 and the V_L CDRs of SEQ ID NO:183, 184 and 185;

(x) comprises the V_H CDRs of SEQ ID NO:190, 191 and 192 and the V_L CDRs of SEQ ID NO:193, 194 and 195;

(xi) comprises the V_H CDRs of SEQ ID NO:200, 201 and 202 and the V_L CDRs of SEQ ID NO:203, 204 and 205;

(xii) comprises the V_H CDRs of SEQ ID NO:210, 211 and 212 and the V_L CDRs of SEQ ID NO:213, 214 and 215;

(xiii) comprises the V_H CDRs of SEQ ID NO:220, 221 and 222 and the V_L CDRs of SEQ ID NO:223, 224 and 225;

(xiv) comprises the V_H CDRs of SEQ ID NO:230, 231 and 232 and the V_L CDRs of SEQ ID NO:233, 234 and 235;

(xv) comprises the V_H CDRs of SEQ ID NO:240, 241 and 242 and the V_L CDRs of SEQ ID NO:243, 244 and 245;

(xvi) comprises the V_H CDRs of SEQ ID NO:250, 251 and 252 and the V_L CDRs of SEQ ID NO:253, 254 and 255;

(xvii) comprises the VH CDRs of SEQ ID NO:260, 261 and 262 and the V_L CDRs of SEQ ID NO:263, 264 and 265;

(xviii) comprises the V_H CDRs of SEQ ID NO:270, 271 and 272 and the V_L CDRs of SEQ ID NO:273, 274 and 275;

(xix) comprises the V_H CDRs of SEQ ID NO:280, 281 and 282 and the V_L CDRs of SEQ ID NO:283, 284 and 285;

(xx) comprises the V_H CDRs of SEQ ID NO:290, 291 and 292 and the V_L CDRs of SEQ ID NO:293, 294 and 295;

(xxi) comprises the V_H CDRs of SEQ ID NO:300, 301 and 302 and the V_L CDRs of SEQ ID NO:303, 304 and 305;

(xxii) comprises the V_H CDRs of SEQ ID NO:310, 311 and 312 and the V_L CDRs of SEQ ID NO:313, 314 and 315;

(xxiii) comprises the V_H CDRs of SEQ ID NO:320, 321 and 322 and the V_L CDRs of SEQ ID NO:323, 324 and 325;

(xxiv) comprises the V_H CDRs of SEQ ID NO:330, 331 and 332 and the V_L CDRs of SEQ ID NO:333, 334 and 335;

(xxv) comprises the V_H CDRs of SEQ ID NO:340, 341 and 342 and the V_L CDRs of SEQ ID NO:343, 344 and 345;

(xxvi) comprises the V_H CDRs of SEQ ID NO:350, 351 and 352 and the V_L CDRs of SEQ ID NO:353, 354 and 355;

(xxvii) comprises the V_H CDRs of SEQ ID NO:360, 361 and 362 and the V_L CDRs of SEQ ID NO:363, 364 and 365;

(xxviii) comprises the V_H CDRs of SEQ ID NO:370, 371 and 372 and the V_L CDRs of SEQ ID NO:373, 374 and 375;

(xxix) comprises the V_H CDRs of SEQ ID NO:380, 381 and 382 and the V_L CDRs of SEQ ID NO:383, 384 and 385;

(xxx) comprises the V_H CDRs of SEQ ID NO:390, 391 and 392 and the V_L CDRs of SEQ ID NO:393, 394 and 395;

(xxxi) comprises the V_H CDRs of SEQ ID NO:400, 401 and 402 and the V_L CDRs of SEQ ID NO:403, 404 and 405;

(xxxii) comprises the V_H CDRs of SEQ ID NO:410, 411 and 412 and the V_L CDRs of SEQ ID NO:413, 414 and 415;

(xxxiii) comprises the V_H CDRs of SEQ ID NO:420, 421 and 422 and the V_L CDRs of SEQ ID NO:423, 424 and 425;

(xxxiv) comprises the V_H CDRs of SEQ ID NO:430, 431 and 432 and the V_L CDRs of SEQ ID NO:433, 434 and 435;

(xxxv) comprises the V_H CDRs of SEQ ID NO:440, 441 and 442 and the V_L CDRs of SEQ ID NO:443, 444 and 445;

(xxxvi) comprises the V_H CDRs of SEQ ID NO:450, 451 and 452 and the V_L CDRs of SEQ ID NO:453, 454 and 455;

(xxxvii) comprises the V_H CDRs of SEQ ID NO:460, 461 and 462 and the V_L CDRs of SEQ ID NO:463, 464 and 465;

(xxxviii) comprises the V_H CDRs of SEQ ID NO:470, 471 and 472 and the V_L CDRs of SEQ ID NO:473, 474 and 475;

(xxxix) comprises the V_H CDRs of SEQ ID NO:480, 481 and 482 and the V_L CDRs of SEQ ID NO:483, 484 and 485;

(xl) comprises the V_H CDRs of SEQ ID NO:490, 491 and 492 and the VL CDR polypeptides of SEQ ID NO:493, 494 and 495;

(xli) comprises the V_H CDRs of SEQ ID NO:500, 501 and 502 and the VL CDR polypeptides of SEQ ID NO:503, 504 and 505;

(xlii) comprises the V_H CDRs of SEQ ID NO:510, 511 and 512 and the VL CDR polypeptides of SEQ ID NO:513, 514 and 515;

(xliii) comprises the V_H CDRs of SEQ ID NO:520, 521 and 522 and the VL CDR polypeptides of SEQ ID NO:523, 524 and 525;

(xliv) comprises the V_H CDRs of SEQ ID NO:530, 531 and 532 and the VL CDR polypeptides of SEQ ID NO:533, 534 and 535;

(xlv) comprises the V_H CDRs of SEQ ID NO:540, 541 and 542 and the VL CDR polypeptides of SEQ ID NO:543, 544 and 545;

(xlvi) comprises the V_H CDRs of SEQ ID NO:550, 551 and 552 and the VL CDR polypeptides of SEQ ID NO:553, 554 and 555;

(xlvii) comprises the V_H CDRs of SEQ ID NO:560, 561 and 562 and the V_L CDRs of SEQ ID NO:563, 564 and 565;

(xlviii) comprises the V_H CDRs of SEQ ID NO:570, 571 and 572 and the V_L CDRs of SEQ ID NO:573, 574 and 575;

(xlix) comprises the V_H CDRs of SEQ ID NO:580, 581 and 582 and the V_L CDRs of SEQ ID NO:583, 584 and 585;

(l) comprises the V_H CDRs of SEQ ID NO:590, 591 and 592 and the V_L CDRs of SEQ ID NO:593, 594 and 595;

(li) comprises the V_H CDRs of SEQ ID NO:600, 601 and 602 and the V_L CDRs of SEQ ID NO:603, 604 and 605;

(lii) comprises the V_H CDRs of SEQ ID NO:610, 611 and 612 and the V_L CDRs of SEQ ID NO:613, 614 and 615;

(liii) comprises the V_H CDRs of SEQ ID NO:620, 621 and 622 and the V_L CDRs of SEQ ID NO:623, 624 and 625;

(liv) comprises the V_H CDRs of SEQ ID NO:630, 631 and 632 and the V_L CDRs of SEQ ID NO:633, 634 and 635;

(lv) comprises the V_H CDRs of SEQ ID NO:640, 641 and 642 and the V_L CDRs of SEQ ID NO:643, 644 and 645;

(lvi) comprises the V_H CDRs of SEQ ID NO:650, 651 and 652 and the V_L CDRs of SEQ ID NO:653, 654 and 655;

(lvii) comprises the V_H CDRs of SEQ ID NO:660, 661 and 662 and the V_L CDRs of SEQ ID NO:663, 664 and 665;

(lviii) comprises the V_H CDRs of SEQ ID NO:670, 671 and 672 and the V_L CDRs of SEQ ID NO:673, 674 and 675;

(lix) comprises the V_H CDRs of SEQ ID NO:680, 681 and 682 and the V_L CDRs of SEQ ID NO:683, 684 and 685;

(lx) comprises the V_H CDRs of SEQ ID NO:690, 691 and 692 and the V_L CDRs of SEQ ID NO:693, 694 and 695;

(lxi) comprises the V_H CDRs of SEQ ID NO:700, 701 and 702 and the V_L CDRs of SEQ ID NO:703, 704 and 705;

(lxii) comprises the V_H CDRs of SEQ ID NO:710, 711 and 712 and the V_L CDRs of SEQ ID NO:713, 714 and 715;

(lxiii) comprises the V_H CDRs of SEQ ID NO:720, 721 and 722 and the V_L CDRs of SEQ ID NO:723, 724 and 725;

(lxiv) comprises the V_H CDRs of SEQ ID NO:730, 731 and 732 and the V_L CDRs of SEQ ID NO:733, 734 and 735;

(lxv) comprises the V_H CDRs of SEQ ID NO:740, 741 and 742 and the V_L CDRs of SEQ ID NO:743, 744 and 745;

(lxvi) comprises the V_H CDRs of SEQ ID NO:750, 751 and 752 and the V_L CDRs of SEQ ID NO:753, 754 and 755;

(lxvii) comprises the V_H CDRs of SEQ ID NO:760, 761 and 762 and the V_L CDRs of SEQ ID NO:763, 764 and 765;

(lxviii) comprises the V_H CDRs of SEQ ID NO:770, 771 and 772 and the V_L CDRs of SEQ ID NO:773, 774 and 775;

(lxix) comprises the V_H CDRs of SEQ ID NO:780, 781 and 782 and the V_L CDRs of SEQ ID NO:783, 784 and 785;

(lxx) comprises the V_H CDRs of SEQ ID NO:790, 791 and 792 and the V_L CDRs of SEQ ID NO:793, 794 and 795;

(lxxi) comprises the V_H CDRs of SEQ ID NO:800, 801 and 802 and the V_L CDRs of SEQ ID NO:803, 804 and 805; or

(lxxii) comprises the V_H CDRs of SEQ ID NO:810, 811 and 812 and the V_L CDRs of SEQ ID NO: 813, 814 and 815.

26. The ADC of **any one of claims 15-25**, wherein Ab comprises an anti-VISTA antibody or antigen binding fragment thereof that comprises:

(i) the same CDRs as an antibody having the sequences in **Figure 8, 10** or **12**;

(ii) the same CDRS as any one of VSTB92, VSTB56, VSTB95, VSTB103 and VSTB66; or

(iii) the V_H CDRs of SEQ ID NO: 200, 201 and 202 and the V_L CDRs of SEQ ID NO: 203, 204 and 205.

27. The ADC of **any one of claims 15-26**, wherein said Ab comprises an anti-VISTA antibody or antigen binding fragment thereof that comprises a V_H polypeptide and a V_L polypeptide which respectively possess at least 90%, 95% or 100% sequence identity to those of an antibody comprising the following V_H polypeptide and a V_L polypeptides and further the CDRs are not modified:

(i) one comprising the V_H polypeptide of SEQ ID NO:106 identity and the V_L polypeptide of SEQ ID NO:108;

(ii) one comprising the V_H polypeptide of SEQ ID NO:116 and the V_L polypeptide of SEQ ID NO:118;

(iii) one comprising the V_H polypeptide of SEQ ID NO:126 and the V_L polypeptide of SEQ ID NO:128;

(iv) one comprising the V_H polypeptide of SEQ ID NO:136 and the V_L polypeptide f SEQ ID NO:138;

(v) one comprising the V_H polypeptide of SEQ ID NO:146 and the V_L polypeptide of SEQ ID NO:148;

(vi) one comprising the V_H polypeptide of SEQ ID NO:156 and the V_L polypeptide of SEQ ID NO:158;

(vii) one comprising the V_H polypeptide of SEQ ID NO:166 and the V_L polypeptide of SEQ ID NO:168;

(viii) one comprising the V_H polypeptide of SEQ ID NO:176 and the V_L polypeptide of SEQ ID NO:178;

(ix) one comprising the V_H polypeptide of SEQ ID NO:186 and the V_L polypeptide of SEQ ID NO:188;

(x) one comprising the V_H polypeptide of SEQ ID NO:196 and the V_L polypeptide of SEQ ID NO:198;

(xi) one comprising the V_H polypeptide of SEQ ID NO:206 and the V_L polypeptide of SEQ ID NO:208;

(xii) one comprising the V_H polypeptide of SEQ ID NO:216 and the V_L polypeptide of SEQ ID NO:218;

(xiii) one comprising the V_H polypeptide of SEQ ID NO:226 and the V_L polypeptide of SEQ ID NO:228;

(xiv) one comprising the V_H polypeptide of SEQ ID NO:236 and the V_L polypeptide of SEQ ID NO:238;

(xv) one comprising the V_H polypeptide of SEQ ID NO:246 and the V_L polypeptide of SEQ ID NO:248;

(xvi) one comprising the V_H polypeptide of SEQ ID NO:256 and the V_L polypeptide of SEQ ID NO:258;

(xvii) one comprising the V_H polypeptide of SEQ ID NO:266 and the V_L polypeptide of SEQ ID NO:268;

(xviii) one comprising the V_H polypeptide of SEQ ID NO:276 and the VL polypeptide of SEQ ID NO:278;

(xix) one comprising the V_H polypeptide of SEQ ID NO:286 and the V_L polypeptide of SEQ ID NO:288;

(xx) one comprising the V_H polypeptide of SEQ ID NO:296 and the V_L polypeptide of SEQ ID NO:298;

(xxi) one comprising the V_H polypeptide of SEQ ID NO:306 and the V_L polypeptide of SEQ ID NO:308;

(xxii) one comprising the V_H polypeptide of SEQ ID NO:316 and the V_L polypeptide of SEQ ID NO:318;

(xxiii) one comprising the V_H polypeptide of SEQ ID NO:326 and the V_L polypeptide of SEQ ID NO:328;

(xxiv) one comprising the V_H polypeptide of SEQ ID NO:336 and the V_L polypeptide of SEQ ID NO:338;

(xxv) one comprising the V_H polypeptide of SEQ ID NO:346 and the V_L polypeptide of SEQ ID NO:348;

(xxvi) one comprising the V_H polypeptide of SEQ ID NO:356 and the V_L polypeptide of SEQ ID NO:358;

(xxvii) one comprising the V_H polypeptide of SEQ ID NO:366 and the V_L polypeptide of SEQ ID NO:368;

(xxviii) one comprising the V_H polypeptide of SEQ ID NO:376 and the V_L polypeptide of SEQ ID NO:378;

(xxix) one comprising the V_H polypeptide of SEQ ID NO:386 and the V_L polypeptide of SEQ ID NO:388;

(xxx) one comprising the V_H polypeptide of SEQ ID NO:396 and the V_L polypeptide of SEQ ID NO:398;

(xxxi) one comprising the V_H polypeptide of SEQ ID NO:406 and the V_L polypeptide of SEQ ID NO:408;

(xxxii) one comprising the V_H polypeptide of SEQ ID NO:416 and the V_L polypeptide of SEQ ID NO:418;

(xxxiii) one comprising the V_H polypeptide of SEQ ID NO:426 and the V_L polypeptide of SEQ ID NO:428;

(xxxiv) one comprising the V_H polypeptide of SEQ ID NO:436 and the V_L polypeptide of SEQ ID NO:438;

(xxxv) one comprising the V_H polypeptide of SEQ ID NO:446 and the V_L polypeptide of SEQ ID NO:448;

(xxxvi) one comprising the V_H polypeptide of SEQ ID NO:456 and the V_L polypeptide of SEQ ID NO:458;

(xxxvii) one comprising the V_H polypeptide of SEQ ID NO:466 and the V_L polypeptide of SEQ ID NO:468;

(xxxviii) one comprising the V_H polypeptide of SEQ ID NO:476 and the V_L polypeptide of SEQ ID NO:478;

(xxxix) one comprising the V_H polypeptide of SEQ ID NO:486 and the V_L polypeptide of SEQ ID NO:488;

(xl) one comprising the V_H polypeptide of SEQ ID NO:496 and the V_L polypeptide of SEQ ID NO:498;

(xli) one comprising the V_H polypeptide of SEQ ID NO:506 and the V_L polypeptide of SEQ ID NO:508;

(xlii) one comprising the V_H polypeptide of SEQ ID NO:516 and the V_L polypeptide of SEQ ID NO:518;

(xliii) one comprising the V_H polypeptide of SEQ ID NO:526 and the V_L polypeptide of SEQ ID NO:528;

(xliv) one comprising the V_H polypeptide of SEQ ID NO:536 and the V_L polypeptide of SEQ ID NO:533, 534 and 535;

(xlv) one comprising the V_H polypeptide of SEQ ID NO:546 and the V_L polypeptide of SEQ ID NO:548;

(xlvi) one comprising the V_H polypeptide of SEQ ID NO:556 and the V_L polypeptide of SEQ ID NO:558;

(xlvii) one comprising the V_H polypeptide of SEQ ID NO:566 and the V_L polypeptide of SEQ ID NO:568;

(xlviii) one comprising the V_H polypeptide of SEQ ID NO:576 and the V_L polypeptide of SEQ ID NO:578;

(xlix) one comprising the V_H polypeptide of SEQ ID NO:586 and the V_L polypeptide of SEQ ID NO:588;

(l) one comprising the V_H polypeptide of SEQ ID NO:596 and the V_L polypeptide of SEQ ID NO:598;

(li) one comprising the V_H polypeptide of SEQ ID NO:606 and the V_L polypeptide of SEQ ID NO:608;

(lii) one comprising the V_H polypeptide of SEQ ID NO:616 and the V_L polypeptide of SEQ ID NO:618;

(liii) one comprising the V_H polypeptide of SEQ ID NO:626 and the V_L polypeptide of SEQ ID NO:628;

(liv) one comprising the V_H polypeptide of SEQ ID NO:636 and the V_L polypeptide of SEQ ID NO:638;

(lv) one comprising the V_H polypeptide of SEQ ID NO:646 and the V_L polypeptide of SEQ ID NO:648;

(lvi) one comprising the V_H polypeptide of SEQ ID NO:656 and the V_L polypeptide of SEQ ID NO:658;

(lvii) one comprising the V_H polypeptide of SEQ ID NO:666 and the V_L polypeptide of SEQ ID NO:668;

(lviii) one comprising the V_H polypeptide of SEQ ID NO:676 and the V_L polypeptide of SEQ ID NO:678;

(lix) one comprising the V_H polypeptide of SEQ ID NO:686 and the V_L polypeptide of SEQ ID NO:688;

(lx) one comprising the V_H polypeptide of SEQ ID NO:696 and the V_L polypeptide of SEQ ID NO:698;

(lxi) one comprising the V_H polypeptide of SEQ ID NO:706 and the V_L polypeptide of SEQ ID NO:708;

(lxii) one comprising the V_H polypeptide of SEQ ID NO:716 and the V_L polypeptide of SEQ ID NO:718;

(lxiii) one comprising the V_H polypeptide of SEQ ID NO:726 and the V_L polypeptide of SEQ ID NO:728;

(lxiv) one comprising the V_H polypeptide of SEQ ID NO:736 and the V_L polypeptide of SEQ ID NO:738;

(lxv) one comprising the V_H polypeptide of SEQ ID NO:746 and the V_L polypeptide of SEQ ID NO:748;

(lxvi) one comprising the V_H polypeptide of SEQ ID NO:756 and the V_L polypeptide of SEQ ID NO:758;

(lxvii) one comprising the V_H polypeptide of SEQ ID NO:766 and the V_L polypeptide of SEQ ID NO:768;

(lxviii) one comprising the V_H polypeptide of SEQ ID NO:776 and the V_L polypeptide of SEQ ID NO:778;

(lxix) one comprising the V_H polypeptide of SEQ ID NO:786 and the V_L polypeptide of SEQ ID NO:788;

(lxx) one comprising the V_H polypeptide of SEQ ID NO:796 and the V_L polypeptide of SEQ ID NO:798;

(lxxi) one comprising the V_H polypeptide of SEQ ID NO:806 and the V_L polypeptide of SEQ ID NO:808; and

(lxxii) one comprising the V_H polypeptide of SEQ ID NO:816 and the V_L polypeptide of SEQ ID NO: 818.

28. The ADC of **any one of claims 15-27**, wherein said Ab comprises an anti-human VISTA antibody or antigen binding fragment thereof that comprises:

(i) the same variable regions as an antibody having the sequences in **Figure 8, 10** or **12**;

(ii) the same variable regions as one of VSTB92, VSTB56, VSTB95, VSTB103 and VSTB66; or

(ii) the V_H polypeptide of SEQ ID NO:206 and the V_L polypeptide of SEQ ID NO:208.

29. The ADC of **any one of claims 15-28**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, wherein the anti-human VISTA antibody comprises an Fc region having impaired FcR binding or intact FcR binding.

30. The ADC of **any one of claims 15-29**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, wherein the antibody or antibody fragment comprises a human IgG1, IgG2, IgG3 or IgG4 Fc region having impaired FcR binding.

31. The ADC of **any one of claims 15-30**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, comprising a human IgG1, IgG2, IgG3 or IgG4 Fc region wherein endogenous FcR binding is not impaired.

32. The ADC of **any one of claims 15-31**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment wherein the antibody or antibody fragment comprises a human IgG1 Fc region having impaired FcR binding.

33. The ADC of **any one of claims 15-32**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, comprising a native (unmodified) human IgG2 Fc region.

34. The ADC of **any one of claims 15-33**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, comprising a human or non-human primate constant or Fc region which is modified to impair or eliminate binding to at least 2 native human Fc gamma receptors.

35. The ADC of **any one of claims 15-34**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, comprising a human or non-human primate constant or Fc region modified to impair or eliminate binding to any one, two, three, four or all five of the following FcRs:

hFcγRI(CD64), FcyRIIA or hFcyRIIB, (CD32 or CD32A) and FcγRlllA (CD16A) or FcγRlllB (CD16B).

36. The ADC of **any one of claims 15-35**, wherein said Ab comprises an anti-human VISTA antibody or antigen binding fragment thereof comprising a human IgG2 kappa backbone with V234A/G237A/P238S/H268A/V309L/A330S/P331S silencing mutations in the Fc region.

37. The ADC of **any one of claims 15-36**, wherein said Ab comprises an anti-human VISTA antibody antigen binding fragment thereof comprising a human IgG1 kappa backbone with L234A/L235A silencing mutations in the Fc region.

38. The ADC of **any one of claims 15-37**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, comprising a human IgG1/kappa backbone, optionally with L234A/L235A silencing mutations and E269R and E233A mutations in the Fc region.

39. The ADC of **any one of claims 15-38**, wherein said Ab comprises an anti-human VISTA antibody antigen binding fragment thereof, which comprises a Fab, F(ab')2, or scFv antigen binding fragment.

40. The ADC of **any one of claims 15-39**, wherein the linker is a positive, negative or neutral charged cleavable peptide.

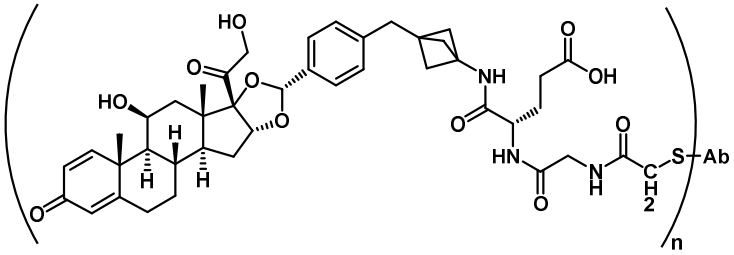
41. The ADC of **any one of claims 15-40**, which comprises said cleavable linker that is susceptible to one or more of acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage, and disulfide bond cleavage.

42. The ADC of **any one of claims 15-41**, which comprises said cleavable linker that is susceptible to peptidase-induced and/or esterase-induced cleavage.

43. The ADC of **any one of claims 15-42**, which comprises said non-cleavable linker that is substantially resistant to one or more of acid-induced cleavage, photo-induced cleavage, peptidase-induced cleavage, esterase-induced cleavage and disulfide bond cleavage.

44. The ADC of **any one of claims 15-43**, wherein the glucocorticosteroid agonist or the payload- linker conjugate is conjugated to Ab via its interchain disulfides.

45. The ADC of **any of claims 15-17**, having the structure



wherein:

n = 8;

Ab is an anti-VISTA antibody or antibody fragment that comprises

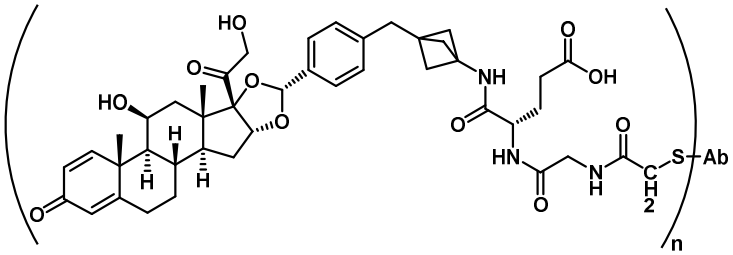
the V_H CDRs of SEQ ID NO: 200, 201 and 202 and the V_L CDRs of SEQ ID NO: 203, 204 and 205; and/or

the V_H polypeptide of SEQ ID NO: 206 and the V_L polypeptide of SEQ ID NO: 208; and

human heavy and light chain IgG1 constant regions optionally mutated to reduce FcR binding; and

linkage of CH_2 to S-Ab was formed by reduction of interchain disulfides on Ab followed by haloacetyl conjugation to the resulting cysteine-SH to form the ADC.

46. The ADC of **any of claims 15-17**, having the structure



wherein:

n = 8;

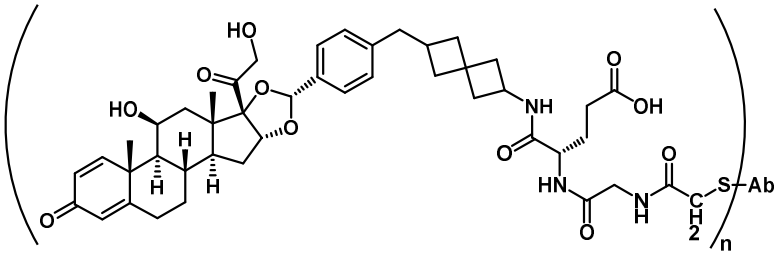
Ab is an anti-VISTA antibody or antibody fragment that comprises:

the variable heavy chain polypeptide of SEQ ID NO: 206, and the variable light chain polypeptide of SEQ ID NO: 208; and

human heavy and light chain IgG1 constant regions optionally mutated to reduce FcR binding; and

linkage of CH_2 to S-Ab was formed by reduction of interchain disulfides on Ab followed by haloacetyl conjugation to the resulting cysteine-SH to form the ADC.

47. The ADC of **any of claims 15-17**, having the structure



wherein:

n = 8;

Ab is an anti-VISTA antibody or antibody fragment that comprises

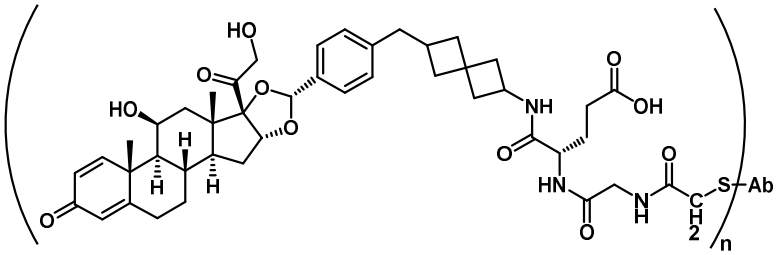
the V_H CDRs of SEQ ID NO: 200, 201 and 202 and the V_L CDRs of SEQ ID NO: 203, 204 and 205; and/or

the V_H polypeptide of SEQ ID NO: 206 and the V_L polypeptide of SEQ ID NO: 208; and

human heavy and light chain IgG1 constant regions optionally mutated to reduce FcR binding; and

linkage of CH_2 to S-Ab was formed by reduction of interchain disulfides on Ab followed by haloacetyl conjugation to the resulting cysteine-SH to form the ADC.

48. The ADC of **any one of claims 15-17**, having the structure



wherein:

n = 8;

Ab is an anti-VISTA antibody or antibody fragment that comprises:

the variable heavy chain polypeptide of SEQ ID NO: 206, and the variable light chain polypeptide of SEQ ID NO: 208; and

human heavy and light chain IgG1 constant regions optionally mutated to reduce FcR binding; and

linkage of CH_2 to S-Ab was formed by reduction of interchain disulfides on Ab followed by haloacetyl conjugation to the resulting cysteine-SH to form the ADC.

49. The ADC of **any one of claims 15-48**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, wherein the antibody or antigen binding fragment binds to VISTA with a K_D ranging from.0001 nM to 10.0 nM, 0.001 to 1.0 nM, or 0.01 to 0.7 or less determined by surface plasmon resonance (SPR) at 24 °C or 37 °C.

50. The ADC of **any one of claims 15-49**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, wherein the antibody or antigen binding fragment binds to VISTA with a K_D of 0.13 to 0.64 nM determined by surface plasmon resonance (SPR) at 24° C or 37 °C.

51. A composition comprising at least one glucocorticoid agonist **according to any of claims 1-10**, at least one payload-linker conjugate **according to any of claims 11-14**, or at least one ADC **according to any of claims 15-50** and a pharmaceutically acceptable carrier.

52. The composition of **claim 51**, which is suitable for *in vivo* administration to a subject in need thereof.

53. The composition of **claim 51 or claim 52**, which comprises at least one excipient.

54. The composition of **claim 51, 52, or 53**, which comprises at least one stabilizer or buffer.

55. The composition **of any one of claims 51-54,** which is suitable for parenteral administration, optionally by injection.

56. The composition **of any one of claims 51-55**, which is suitable for injection to a subject in need thereof, optionally via intravenous, subcutaneous, intramuscular, intratumoral, intranodal, intranasal, or intrathecal.

57. The composition **of any one of claims 51-56**, which is subcutaneously administrable.

58. The composition **of any one of claims 51-57**, which is comprised in a device that provides for subcutaneous administration selected from the group consisting of a syringe, an injection device, an infusion pump, an injector pen, a needleless device, an autoinjector, and a subcutaneous patch delivery system.

59. The composition of **claim 58**, wherein said device delivers a fixed dose of the glucocorticoid agonist, the payload-linker conjugate. or the ADC to a patient.

60. A pharmaceutical composition comprising a therapeutically effective amount of at least one glucocorticosteroid agonist **according to any of claims 1-10**, at least one payload-linker conjugate **according to any of claims 11-14**, or at least one ADC **according to any of claims 15-50**; and a pharmaceutically acceptable carrier.

61. The pharmaceutical composition of **claim 60**, which is administrable via an injection route, optionally intravenous, intramuscular, intrathecal, or subcutaneous.

62. The pharmaceutical composition of **claim 60 or 61**, which is subcutaneously administrable.

63. The pharmaceutical composition **of any one of claims 60-62**, which is comprised in a device that provides for subcutaneous administration selected from the group consisting of a syringe, an injection device, an infusion pump, an injector pen, a needleless device, an autoinjector, and a subcutaneous patch delivery system.

64. The pharmaceutical composition of **claim 63**, wherein said device delivers a fixed dose of the glucocorticoid agonist, the payload-linker conjugate. or the ADC to a patient.

65. A device comprising the glucocorticosteroid agonist, payload-linker conjugate, ADC, composition, or pharmaceutical composition of **any of claims 1-64**, that provides for subcutaneous administration selected from the group consisting of a syringe, an injection

device, an infusion pump, an injector pen, a needleless device, an autoinjector, and a subcutaneous patch delivery system.

66. The device of **claim 65**, which delivers to a patient a fixed dose of the glucocorticoid receptor agonist, or a functional derivative thereof.

67. A kit comprising the device of **claim 65 or 66**, which further comprises instructions informing the patient how to administer the ADC composition comprised therein and the dosing regimen.

68. *Ex vivo* use of a glucocorticosteroid agonist, payload-linker conjugate, ADC, composition, or pharmaceutical composition of **any of claims 1-64**, wherein human immune cells from a patient or donor are contacted with said glucocorticosteroid agonist, payload-linker conjugate, ADC, composition, or pharmaceutical composition.

69. An *ex vivo* method for effecting internalization of a glucocorticosteroid agonist into cells, the method comprising contacting human immune cells obtained from a patient or donor with a glucocorticosteroid agonist, payload-linker conjugate, ADC, composition, or pharmaceutical composition of **any of claims 1-64**.

70. The method of **claim 69**, wherein said human immune cells:

(i) comprise one or more types of immune cells selected from B cells, T cells, CD4 T cells, CD8 T cells, Tregs, NK cells, Neutrophils, monocytes, myeloid cells, Dendritic cells, eosinophils, mast cells, and macrophages; or

(ii) is a purified or enriched composition comprising said one or more types of immune cells.

71. The glucocorticoid agonist, payload-linker conjugate, ADC, composition, pharmaceutical composition, device, or kit **according to any one of claims 1-67**, for use in treating, preventing or inhibiting inflammation or autoimmunity in a subject or patient in need thereof.

72. Use of a glucocorticoid agonist, payload-linker conjugate, ADC, composition, or pharmaceutical composition **according to any of claims 1-67** in the preparation of a medicament for the treatment, prevention or inhibition of inflammation or autoimmunity or an allergic reaction in a subject or patient in need thereof.

73. The use **according to claim 72**, wherein the glucocorticoid agonist, payload-linker conjugate, ADC, composition, pharmaceutical composition:

(i) is comprised in a device according to **claim 65 or 66**;

(ii) is comprised in a kit according to **claim 67**;

(iii) has been contacted with human immune cells according to **claim 68**; and/or

(iv) has been internalized into human immune cells according to **claim 69 or 70**.

74. The use **according to claim 72 or 73**, wherein the medicament is to be administered to said patient in need thereof.

75. The use **according to any one of claims 72-74**, wherein the medicament is for the treatment of allergy, autoimmunity, transplant, gene therapy, inflammation, GVHD or sepsis, or to treat or prevent inflammatory, autoimmune, or allergic side effects associated with any of the foregoing conditions in a human subject.

76. The use **according to any one of claims 72-75**, wherein the medicament is for acute use.

77. The use **according to any one of claims 72-76**, wherein the medicament is for chronic use.

78. The use **according to any one of claims 72-77**, wherein the medicament is for maintenance therapy.

79. The use **according to any one of claims 72-78**, wherein the medicament is for the treatment or prophylaxis of acute or chronic inflammation and autoimmune and inflammatory indications associated therewith.

80. The use **according to claim 79**, wherein the conditions are selected from Acquired aplastic anemia +, Acquired hemophilia +, Acute disseminated encephalomyelitis (ADEM) +, Acute hemorrhagic leukoencephalitis (AHLE) / Hurst's disease +, Agammaglobulinemia, primary +, Alopecia areata +, Ankylosing spondylitis (AS), Anti-NMDA receptor encephalitis +, Antiphospholipid syndrome (APS) +, Arteriosclerosis, Autism spectrum disorders (ASD), Autoimmune Addison's disease (AAD) +, Autoimmune dysautonomia / Autoimmune autonomic ganglionopathy (AAG), Autoimmune encephalitis +**,** Autoimmune gastritis, Autoimmune hemolytic anemia (AIHA) +, Autoimmune hepatitis (AIH) +,Autoimmune hyperlipidemia, Autoimmune hypophysitis / lymphocytic hypophysitis +, Autoimmune inner ear disease (AIED) +, Autoimmune lymphoproliferative syndrome (ALPS) +, Autoimmune myocarditis, Autoimmune oophoritis +, Autoimmune orchitis +, Autoimmune pancreatitis (AIP) / Immunoglobulin G4-Related Disease (IgG4-RD) +, Autoimmune polyglandular syndromes, Types I, II, & III +, Autoimmune progesterone dermatitis +, Autoimmune sudden sensorineural hearing loss (SNHL)Achalasia, Addison's disease, Adult Still's disease, Agammaglobulinemia, Alopecia areata, Amyloidosis, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune angioedema, Autoimmune dysautonomia, Autoimmune encephalomyelitis, Autoimmune hepatitis, Autoimmune inner ear disease (AIED), Autoimmune myocarditis, Autoimmune oophoritis, Autoimmune orchitis, Autoimmune pancreatitis, Autoimmune retinopathy, Autoimmune urticaria, Axonal & neuronal neuropathy (AMAN), Baló disease, Behcet's disease, Benign mucosal pemphigoid, Bullous pemphigoid, Castleman disease (CD), Celiac disease, Chagas disease, Chronic inflammatory demyelinating polyneuropathy (CIDP), Chronic recurrent multifocal osteomyelitis (CRMO), Churg-Strauss Syndrome (CSS) or Eosinophilic Granulomatosis (EGPA), Cicatricial pemphigoid, Cogan's syndrome, Cold agglutinin disease, Congenital heart block, Coxsackie myocarditis, CREST syndrome, Diabetes, type 1, Dermatitis herpetiformis, Dermatomyositis, Devic's disease (neuromyelitis optica). Discoid lupus, Dressler's syndrome, Endometriosis, Eosinophilic esophagitis (EoE), Eosinophilic fasciitis, Erythema nodosum, Essential mixed cryoglobulinemia, Evans syndrome, Fibromyalgia, Fibrosing alveolitis, Fibrosing alveolitis, Giant cell myocarditis,

Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis, Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura (HSP), Herpes gestationis or pemphigoid gestationis (PG), Hidradenitis Suppurativa (HS) (Acne Inversa), Hypogammalglobulinemia, IgA Nephropathy, IgG4-related sclerosing disease, Immune thrombocytopenic purpura (ITP), Inclusion body myositis (IBM), Interstitial cystitis (IC), Juvenile arthritis, Juvenile diabetes (Type 1 diabetes), Juvenile myositis (JM), Kawasaki disease, Lambert-Eaton syndrome, Leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, Linear IgA disease (LAD), Lupus (including nephritis and cutaneous), Lyme disease chronic, Meniere's disease, Microscopic polyangiitis (MPA), Mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, Multifocal Motor Neuropathy (MMN) or MMNCB, Multiple sclerosis, Myasthenia gravis, Myelin Oligodendrocyte Glycoprotein Antibody Disorder, Myositis, Narcolepsy, Neonatal Lupus, Neuromyelitis optica, Neutropenia, Ocular cicatricial pemphigoid, Optic neuritis,Opsoclonus-myoclonus syndrome (OMS), Palindromic rheumatism (PR), PANDAS, Paraneoplastic cerebellar degeneration (PCD), Paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Pars planitis (peripheral uveitis), Parsonage-Turner syndrome, Pemphigus, Peripheral neuropathy, Perivenous encephalomyelitis, Pernicious anemia (PA), POEMS syndrome, Polyarteritis nodosa, Polyglandular syndromes type I, II, III, Polymyalgia rheumatica, Polymyositis, Postmyocardial infarction syndrome, Postpericardiotomy syndrome, Primary Biliary Cholangitis, Primary sclerosing cholangitis, Progesterone dermatitis, Psoriasis, Psoriatic arthritis, Pure red cell aplasia (PRCA), Pyoderma gangrenosum, Raynaud's phenomenon, Reactive Arthritis, Reflex sympathetic dystrophy, Relapsing polychondritis, Restless legs syndrome (RLS), Retroperitoneal fibrosis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Schmidt syndrome, Scleritis, Scleroderma, Sjögren's syndrome, Sperm & testicular autoimmunity, Stiff person syndrome (SPS), Subacute bacterial endocarditis (SBE), Susac's syndrome, Sympathetic ophthalmia (SO), Takayasu's arteritis, Temporal arteritis/Giant cell arteritis, Thrombocytopenic purpura (TTP), Thyroid eye disease (TED), Tolosa-Hunt syndrome (THS), Transverse myelitis, Type 1 diabetes, Undifferentiated connective tissue disease (UCTD), Uveitis, Vasculitis, Vitiligo, and Vogt-Koyanagi-Harada Disease.

81. The use **according to claim 79**, wherein the conditions are selected from Severe asthma, Giant cell arteritis, ANKA vasculitis, and IBD (Colitis and Crohn's).

82. The use **according to any one of claims 72-81**, wherein the medicament is for the treatment or prophylaxis of a condition selected from rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, pediatric Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa, uveitis, Bechet's disease, a spondyloarthropathy, or psoriasis.

83. The use **according to any one of claims 72-82**, wherein the medicament is for treatment or prophylaxis in said patient who comprises one or more of the following:

(i) a chronic, acute, episodic allergic, inflammatory or inflammatory condition, e.g., chronic, acute, episodic, remitting/relapsing;

(ii) a condition primarily only effectively treatable with high doses of steroids, optionally polymyalgia rheumatica and/or giant cell arteritis, which patient optionally has been treated or is undergoing treatment with high steroid doses;

(iii) a condition with a comorbidity limiting steroid use, optionally diabetes mellitis, nonalcoholic steatohepatitis (NASH), morbid obesity avascular necrosis/osteonecrosis (AVN), glaucoma. Steroid-induced hypertension, severe skin fragility, and/or osteoarthritis;

(iv) a condition wherein safe long-term treatment agents are available, but wherein several months of induction with high-doses of steroids is desired, optionally AAV, polymyositis, dermatomyositis, lupus, inflammatory lung disease, autoimmune hepatitis, inflammatory bowel disease, immune thrombocytopenia, autoimmune hemolytic anemia, gout patients wherein several months of induction with high-doses of steroids is therapeutically warranted;

(v) dermatologic conditions that require short/long-term treatment, optionally of uncertain treatment or duration and/or no effective alternative to steroid administration, optionally Stevens Johnson, other severe drug eruption conditions, conditions involving extensive contact dermatitis, other severe immune-related dermatological conditions such as PG, LCV, Erythroderma and the like;

(vi) conditions treated with high-dose corticosteroids for flares/reoccurrences, optionally COPD, asthma, lupus, gout, pseudogout;

(vii) immune-related neurologic diseases such as small-fiber neuropathy, MS (subset), chronic inflammatory demyelinating polyneuropathy, myasthenia gravis and the like;

(viii) hematological/oncology indications, optionally wherein high doses of steroids would potentially be therapeutically warranted or beneficial;

(ix) ophthalmologic conditions, optionally uveitis, iritis, scleritis, and the like;

(x) conditions associated with permanent or very prolonged adrenal insufficiency or secondary adrenal insufficiency, optionally iatrogenic Addisonian crisis;

(xi) conditions often treated with long term, low dose steroids, optionally lupus, RA, psA, vasculitis, and the like; and

(xii) special classes of patients such as pregnant/breast-feeding women, pediatric patients optionally those with growth impairment or cataracts.

84. The use **according to any one of claims 72-83**, wherein the patient is further being treated with another active agent.

85. The use **according to any one of claims 72-84**, wherein the patient is further being treated with an immunomodulatory antibody or fusion protein which is selected from immunoinhibitory antibodies or fusion proteins targeting one or more of CTLA4, PD-1, PDL-

1, LAG-3, TIM-3, BTLA, B7-H4, B7-H3, VISTA, and/or agonistic antibodies or fusion protein targeting one or more of CD40, CD137, OX40, GITR, CD27, CD28 or ICOS.

86. The use **according to any one of claims 72-85,** wherein the ADC comprises an antibody or antigen binding fragment comprising an antigen binding region that specifically binds to human V-domain Ig Suppressor of T cell Activation (human VISTA) ("A"), wherein the ADC is to be administered to a subject in need thereof, and is preferentially to be delivered to VISTA expressing immune cells, optionally one or more of monocytes, myeloid cells, T cells, Tregs, NK cells, Neutrophils, Dendritic cells, macrophages, eosinophils, and endothelial cells, and results in the functional internalization of the anti-inflammatory agent into one or more of said immune cells.

87. The use **of any one of claims 72-86**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment that preferentially binds to VISTA expressing cells at physiological pH (≈7.5); which optionally has a PK of at most 70 hours in a human VISTA knock-in rodent.

88. The use **of any one of claims 72-87**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, which binds to VISTA expressing cells at physiologic pH, and which has a PK of at most 3.5 ±0.5 days, more typically at most 48 hours, at most 24 hours, at most 18 hours or at most 12 hours in a Cynomolgus macaque or a human at physiologic pH.

89. The use **any one of claims 72-88**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, which has a PK of at most 2.8 or 2.3 or 1.5 days or 1 day or 12 hours or 8 hours ±.5 days in Cynomolgus macaque or in a human at physiologic pH.

90. The use **of any one of claims 72-89**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, which has a PK of at most 6-12 hours in a human VISTA rodent at physiologic pH.

91. The use of **any one of claims 72-90**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, which comprises a linker which upon internalization of the ADC into VISTA-expressing immune cells, optionally one or more of T cells, Tregs, NK cells, neutrophils, monocytes, myeloid cells, dendritic cells, macrophages, eosinophils, and endothelial cells, is cleaved resulting in the release of a therapeutically effective amount of an anti-inflammatory agent in the immune cell, wherein it elicits anti-inflammatory activity.

92. The use **of any one of claims 72-91**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment the anti-VISTA antibody or antigen binding fragment has an *in vivo* serum half-life of about 2.3 days in a primate, optionally Cynomolgus macaque at physiological pH (~pH 7.5).

93. The use **of any one of claims 72-92**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, wherein the anti-VISTA antibody or antigen binding fragment has an *in vivo* serum half-life in serum at physiological pH (~pH 7.5) in a human VISTA knock-in rodent of no more than 70 hours, no more than 60 hours, no more than 50 hours, no more than 40 hours, no more than 30 hours, no more than 24 hours, no more than 22-24

hours, no more than 20-22 hours, no more than 18-20 hours, no more than 16-18 hours, no more than 14-16 hours, no more than 12-14 hours, no more than 10-12 hours, no more than 8-10 hours, no more than 6-8 hours, no more than 4-6 hours, no more than 2-4 hours, no more than 1-2 hours, no more than 0.5 to 1.0 hours, or no more than 0.1-0.5 hours.

94. The use **of any one of claims 72-93**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, wherein the PD/PK ratio of the ADC when used *in vivo* is at least 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 12:1, 13:1, 14:1, 28:1 or greater in a human VISTA knock-in rodent or in a human or non-human primate, optionally Cynomolgus macaque.

95. The use **of any one of claims 72-94**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment, wherein the PD of the ADC is at least 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 28 days, 2-3 weeks, 1 month, 2 months, or longer in any one of a rodent or in a human or non-human primate, optionally Cynomolgus macaque.

96. The use **of any one of claims 72-95**, wherein the ADC comprises an anti-human VISTA antibody or antibody fragment wherein the binding of the anti-VISTA antibody or antigen binding fragment to VISTA expressing immune cells does not directly agonize or antagonize VISTA-mediated effects on immunity.

97. The use **of any one of claims 72-96**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, which internalizes into one or more of monocytes, myeloid cells, T cells, Tregs, CD4 T cells, CD8 T cells, macrophages, NK cells, macrophages, eosinophils, mast cells, B cells, and neutrophils.

98. The use **of any one of claims 72-97**, wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, which does not appreciably internalize into B cells.

99. The use **of any one of claims 72-98,** wherein the ADC comprises an antibody or antibody fragment, optionally an anti-human VISTA antibody or antibody fragment, which when administered to a subject in need thereof promotes the efficacy and/or reduces adverse side effects such as toxicity associated with the anti-inflammatory agent, compared to the same dosage of anti-inflammatory agent administered in naked (non-conjugated) form.

100. The use **of any one of claims 72-99**, wherein the inflammation is associated with cancer, or an infection, optionally a viral or bacterial infection.

101. The use according to **any one of claims 72-100**, wherein the medicament is for the treatment of an inflammatory or autoimmune or allergic condition involving one or more of any of B cells, T cells, Tregs, NK cells, Neutrophils, monocytes, myeloid cells, dendritic cells, eosinophils, mast cells, and macrophages, and wherein the ADC is to be administered to a subject in need thereof.