CLAIMS

What is claimed is:

1. A compound comprising formula (I), or a salt, geometric isomer, stereoisomer, or solvate thereof:

$$[Ab]_{k'}—[CON]_{h}—[Linker]_{i}—[CON]_{h'}—[CRBM]_{j'} \quad (I),$$

wherein:

the Ab is an antibody that binds to an extracellular protein;

the CRBM is a cellular receptor binding moiety that binds to at least one receptor on the surface of a degrading cell in a subject, whereby binding of (I) leads to endocytosis and degradation of the extracellular protein;

each CON is independently a bond or a group that covalently links an Ab to an CRBM, an Ab to a Linker, and/or a Linker to a CRBM;

the Linker is a group having a valence ranging from 1 to 15;

k' is an integer ranging from 1 to 15;

h is an integer ranging from 0 to 15;

i is an integer ranging from 0 to 15;

h' is an integer ranging from 0 to 15;

j is an integer ranging from 1 to 15.

2. The compound of claim 1, wherein the valence of the Linker is 1, 2, or 3.

3. The compound of claim 1, wherein k' is 1, 2, or 3.

4. The compound of claim 1, wherein j is 1, 2, or 3.

5. The compound of claim 1, wherein h is 1, 2, or 3.

6. The compound of claim 1, wherein h' is 1, 2, or 3.

7. The compound of claim 1, wherein i is 1, 2, or 3.

8. The compound of claim 1, wherein at least one of h, h', and i is at least 1.

9. The compound of claim 1, wherein k', j', h, h', and i are each independently 1, 2, or 3.

10. The compound of claim 1, wherein k' is 1, and j' is 1, 2, or 3.

11. The compound of claim 1, which is:

$$[Ab]—[CON]_{0\text{-}1}—[Linker]—[CON]_{0\text{-}1}—[CRBM] \quad (Ia).$$

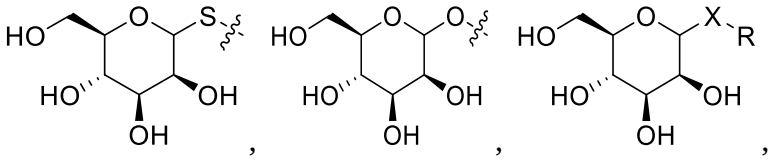
12. The compound of claim 1, wherein the degrading cell comprises a hepatocyte.

13. The compound of claim 1, wherein the CRBM is a folic acid (folate) receptor binder, mannose receptor binder, mannose-6-phosphate (M6P) receptor binder, low density lipoprotein receptor-related protein 1 (LRP1) receptor binder, low density lipoprotein receptor (LDLR) binder, FcγRI receptor binder, transferrin receptor binder, macrophage scavenger receptor binder, G-Protein coupled receptor binder, or asialoglycoprotein receptor (ASGPR) binder.

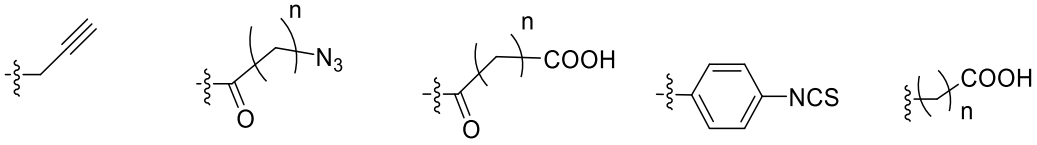
14. The compound of claim 1, wherein the CRBM is:

(a) a folic acid (folate) receptor binder comprising at least one of folic acid, methotrexate, premetrexed, or a biologically active fragment thereof;

(b) a mannose receptor binder comprising at least one of:



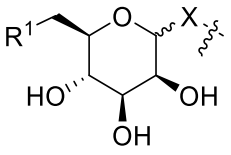
wherein: X is S or O, R is selected from the group consisting of:

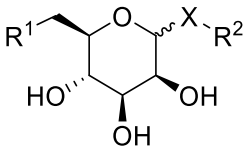


and each occurrence of 'n' is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20; and

a polymeric molecule illustrated in FIGs. 1-7;

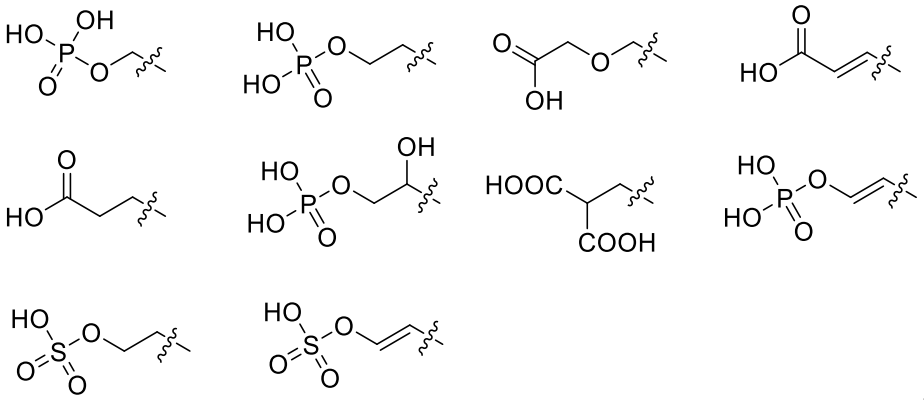
(c) a mannose-6-phosphate (M6P) receptor binder comprising at least one of:



and


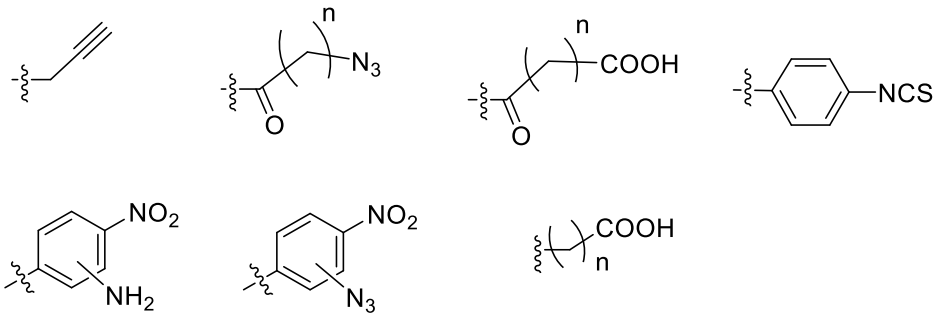
,

wherein X is O or S, R^1 is selected from the group consisting of:



,

R^2 is selected from the group consisting of:

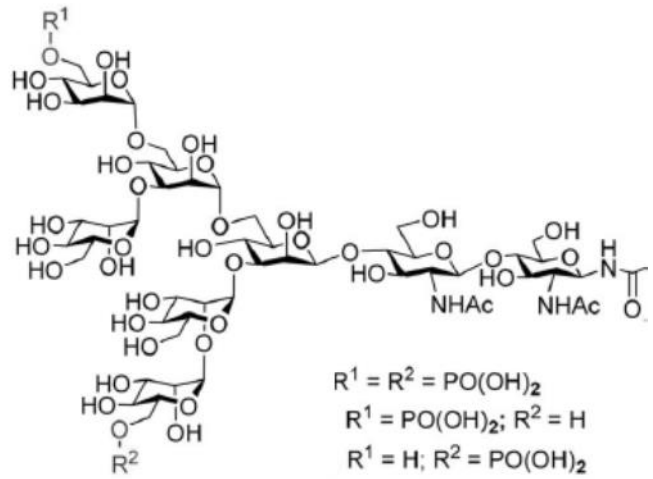


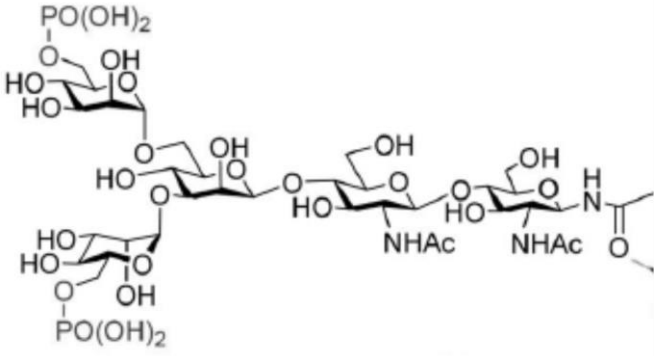
,

and each occurrence of 'n' is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20;

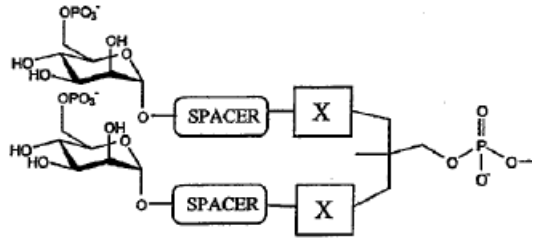
a polymeric molecule illustrated in FIG. 8;

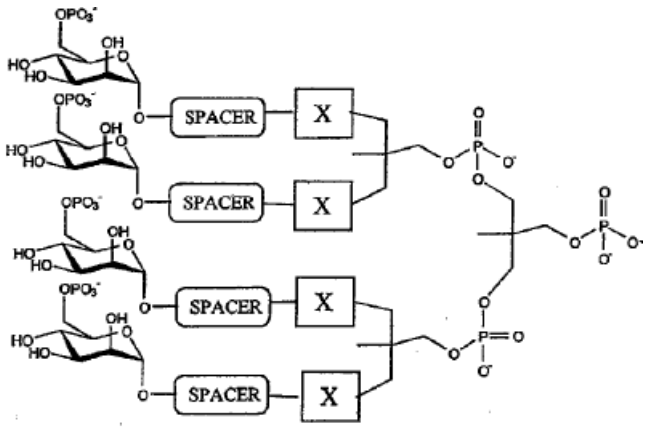
a compound selected from:

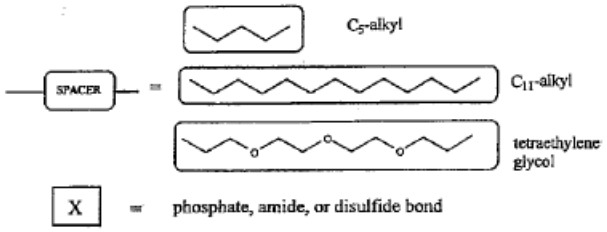




a compound selected from:







;

(d) a low density lipoprotein receptor-related protein 1 (LRP1) receptor binder comprising at least one amino acid sequence of SEQ ID NOs:1-9;

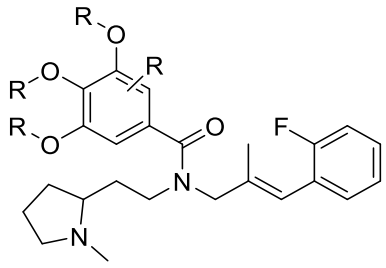
(e) a low density lipoprotein receptor (LDLR) binder comprising at least one amino acid sequence of SEQ ID NOs:10-35;

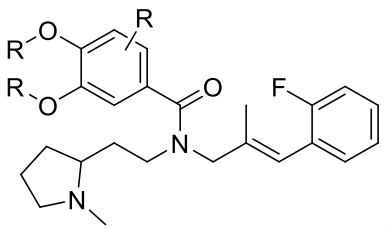
(f) a FcγRI receptor binder comprising at least one amino acid sequence of SEQ ID NOs:36-52;

(g) a transferrin receptor binder comprising at least one amino acid sequence of SEQ ID NOs:53-59 and 67;

(h) a macrophage scavenger receptor binder comprising at least one amino acid sequence of SEQ ID NOs:60-65;

(i) a G-protein coupled receptor binder comprising at least one of:

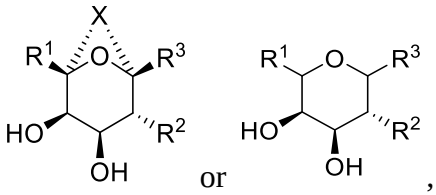


or


,

wherein each occurrence of R is independently H or C_1-C_6 alkyl;

(j) an asialoglycoprotein receptor (ASGPR) binder comprising:



wherein:

X is a linker of 1-4 atoms in length and comprises O, S, $N(R^{N1})$, or $C(R^{N1})(R^{N1})$ groups, such that:

when X is a linker of 1 atom in length, X is O, S, $N(R^{N1})$, or $C(R^{N1})(R^{N1})$,

when X is a linker of 2 atoms in length, no more than 1 atom of X is O, S, or $N(R^{N1})$,

when X is a linker of 3 or 4 atoms in length, no more than 2 atoms of X are independently O, S, or $N(R^{N1})$;

wherein each occurrence of R^{N1} is independently H or C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups;

R^1 and R^3 are each independently H, $-(CH_2)_KOH$, $-(CH_2)_KO(C_1$-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, C_1-C_4 alkyl optionally substituted with 1-3 independently selected halogens, $-(CH_2)_K$(vinyl), $-O(CH_2)_K$(vinyl), $-(CH_2)_K$(alkynyl), $-(CH_2)_KCOOH$, $-(CH_2)_KC(=O)O(C_1$-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, $-OC(=O)(C_1$-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or $-C(=O)(C_1$-C_4 alkyl) optionally substituted with 1-3 independently selected halogens; or

R^1 and R^3 are each independently $Ph(CH_2)_K$-, which is optionally substituted with: 1-3 independently selected halogens; C_1-C_4 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups; or C_1-C_4 alkoxy optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups; or

R^1 and R^3 are each independently a group of structure:

$$-O-(CH_2)_{K'}-CH(OH)-(CH_2)K'-R^7,$$

wherein:

R^7 is: C_1-C_4 alkoxy optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxy groups; $-NR^{N3}R^{N4}$; or $-(CH_2)_{K'}-O-(CH_2)_K-CH_2-CH=CH_2$;

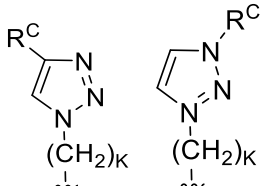
K is 0, 1, 2, 3, or 4;

K' is 1, 2, 3, or 4;

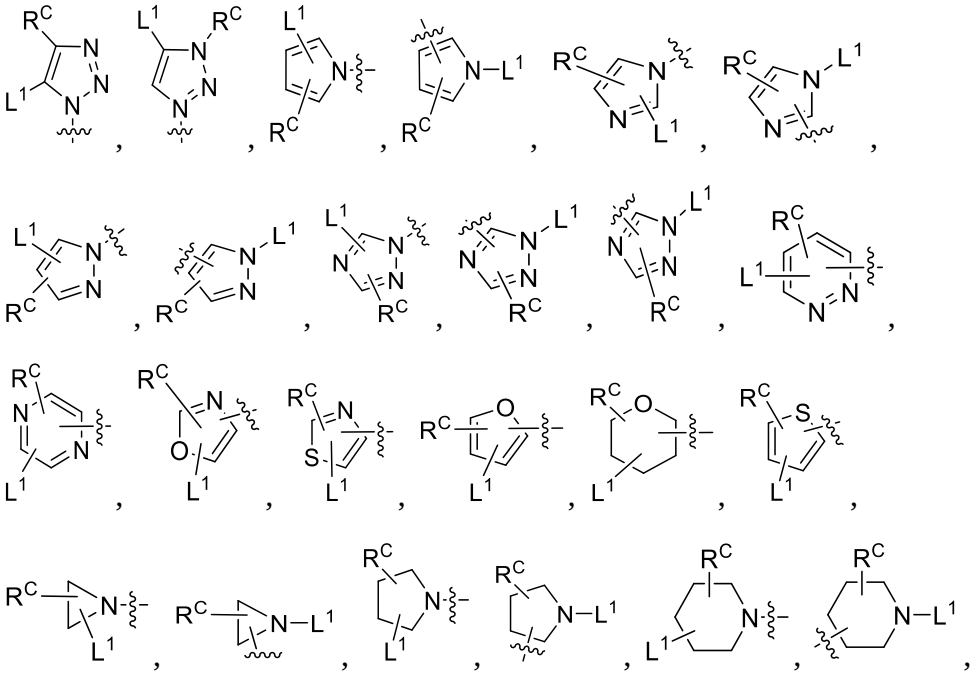
each occurrence of R^{N3} is independently H or C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups;

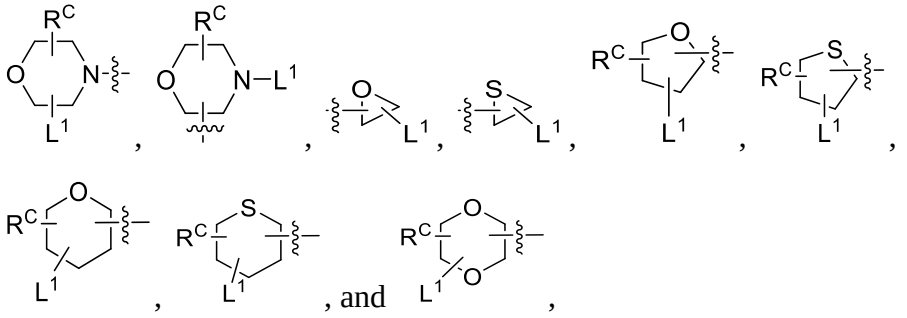
each occurrence of R^{N4} is independently H, C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups, or Ph-$(CH_2)_K$-; or

R^1 and R^3 are each independently selected from the group consisting of:



$-(CH_2)_KOH$, , , L^1-≡-, L^1-$(CH_2)_K$-, and CYC-$(CH_2)_K$-, wherein CYC is selected from the group consisting of:



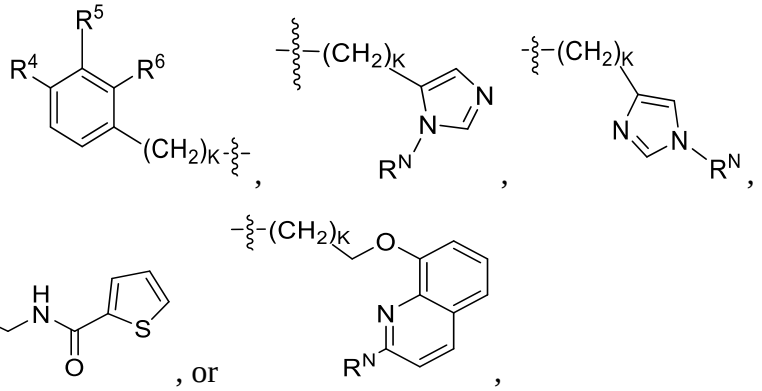


wherein:

the bond marked with ~~~ indicating the site on CYC whereto -$(CH_2)_K$ is connected;

L^1 is a bond, -Linker, -CON-Linker, or -CON-Linker-CON;

R^C is absent, H, C_1-C_4 alkyl optionally substituted with 1-3 optionally substituted halogens and/or 1-2 hydroxyl groups, or a group of structure:



wherein:

R^4, R^5, and R^6 are each independently H, F, Cl, Br, I, CN, $NR^{N1}R^{N2}$, -$(CH_2)_K$OH, -$(CH_2)_K$O(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens, C_1-C_3-alkoxy optionally substituted with 1-3 independently selected halogens, -$(CH_2)_K$COOH, -$(CH_2)_K$C(=O)O-(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, O-C(=O)-(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or -C(=O)-(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens;

each occurrence of R^N is independently H or C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups;

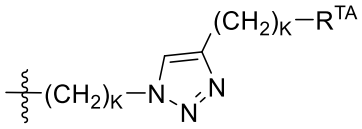
each occurrence of R^{N2} is independently H or C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups;

or

R^1 and R^3 are each independently (C_3-C_8 saturated carbocyclic)-$(CH_2)_K$-, wherein the carbocyclic is further substituted with -L^1 and -R^C;

R^2 is -$(CH_2)_K$-$N(R^{N1})$-$C(=O)R^{AM}$, wherein:

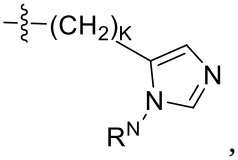
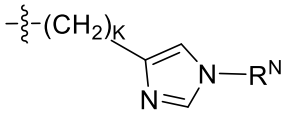
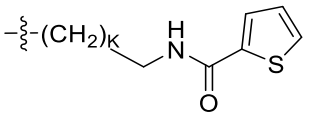
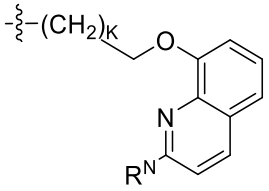
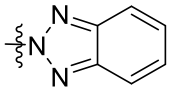
R^{AM} is H, C_1-C_4 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups, -$(CH_2)_K$COOH, -$(CH_2)_K$C(=O)O(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, -OC(=O)(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, -C(=O)(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or -$(CH_2)_K$-$NR^{N3}R^{N4}$; or

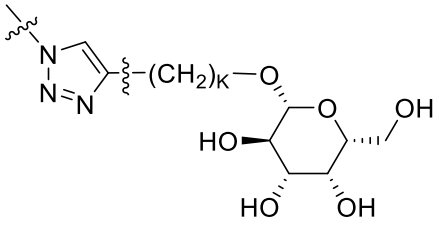
R^2 is , wherein:

R^{TA} is H, CN, $NR^{N1}R^{N2}$, -$(CH_2)_K$OH, -$(CH_2)_K$O(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, C_1-C_4 alkyl optionally substituted with 1-3 independently selected halogens, -$(CH_2)_K$COOH, -$(CH_2)_K$C(=O)O(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, -OC(=O)(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or -C(=O)(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or

R^{TA} is C_3-C_{10} aryl or a 3- to 10-membered heteroaryl group containing 1-5 non-carbon ring atoms, each of the aryl or heteroaryl groups being optionally substituted with 1-3 groups independently selected from CN, $NR^{N1}R^{N2}$, -$(CH_2)_K$OH, -$(CH_2)_K$O(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, C_1-C_3 alkyl optionally substituted with 1-3 independently selected halogens and/or 1-2 hydroxyl groups, -(C_1-C_3-alkoxy) optionally substituted from 1-3 independently selected halogens, -$(CH_2)_K$COOH, -$(CH_2)_K$C(=O)O-(C_1-C_4 alkyl) optionally substituted with 1-3

independently selected halogens, -OC(=O)(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or -$(CH_2)_K$C(=O)-(C_1-C_4 alkyl) optionally substituted with 1-3 independently selected halogens, or

R^{TA} is , , , , or  optionally substituted with 1-3 C_1-C_3 alkyl groups optionally substituted with 1-3 independently selected halogens, or

R^{TA} is , wherein each -$(CH_2)_K$ group is optionally substituted with 1-4 C_1-C_3 alkyl groups optionally substituted with 1-3 fluoro groups or 1-2 hydroxyl groups.

15. The compound of claim 14, wherein:

the X in ASGPRBM is -O-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-O-, -S-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-S-, -N(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-N(R^{N1})-, or -C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, when X is 2 atoms in length;

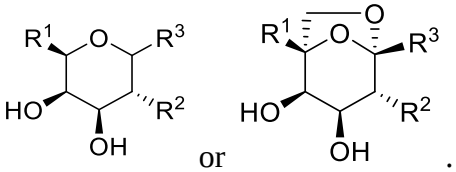
the X in ASGPRBM is -O-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-O-C(R^{N1})(R^{N1})-, -O-C(R^{N1})(R^{N1})-O-, -O-C(R^{N1})(R^{N1})-S-, -O-C(R^{N1})(R^{N1})-N(R^{N1})-, -S-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-S-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-S, -S-C(R^{N1})(R^{N1})-S-, -S-C(R^{N1})(R^{N1})-O-, -S-C(R^{N1})(R^{N1})-N(R^{N1})-, -N(R^{N1})-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-N(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-N(R^{N1})-, -N(R^{N1})-C(R^{N1})(R^{N1})-N(R^{N1})-, or -C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})- C(R^{N1})(R^{N1}), when X is 3 atoms in length; or

the X in ASGPRBM is -O-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, -C(R^{N1})(R^{N1})-O-C(R^{N1})(R^{N1})-C(R^{N1})(R^{N1})-, -O-C(R^{N1})(R^{N1})-O-C(R^{N1})(R^{N1})-, -S-C(R^{N1})(R^{N1})-

$C(R^{N1})(R^{N1})$-$C(R^{N1})(R^{N1})$-, -$C(R^{N1})(R^{N1})$-S-$C(R^{N1})(R^{N1})$-$C(R^{N1})(R^{N1})$-, -$C(R^{N1})(R^{N1})$-$C(R^{N1})(R^{N1})$-S-$C(R^{N1})(R^{N1})$-, -S-$C(R^{N1})(R^{N1})$-S-$C(R^{N1})(R^{N1})$-, -$N(R^{N1})$-$C(R^{N1})(R^{N1})$-$C(R^{N1})(R^{N1})$- $C(R^{N1})(R^{N1})$-, or -$C(R^{N1})(R^{N1})$-$N(R^{N1})$-$C(R^{N1})(R^{N1})$-$C(R^{N1})(R^{N1})$-, when X is 4 atoms in length.

16. The compound of claim 14, wherein X is OCH_2 and R^{N1} is H, or wherein X is CH_2O and R^{N1} is H.

17. The compound of claim 14, wherein the ASGPRBM comprises the structure:



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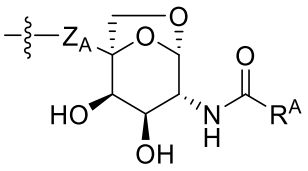
18. The compound of claim 14, wherein the ASGPRBM group comprises:



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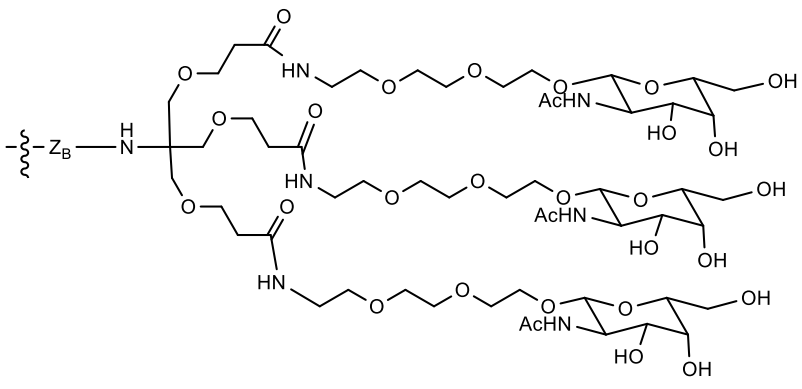


;

wherein:

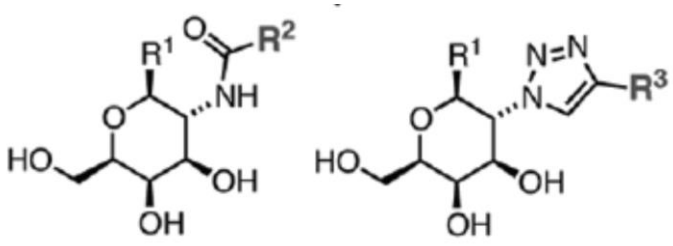
R^A is C_1-C_3 alkyl optionally substituted with 1-5 independently selected halogens;

Z_A is -$(CH_2)_{IM}$-, -O-$(CH_2)_{IM}$-, -S-$(CH_2)_{IM}$-, -NR^M-$(CH_2)_{IM}$-, -C(=O)-$(CH_2)_{IM}$-, a PEG group containing from 1 to 8 ethylene glycol residues, or -$C(O)(CH_2)_{IM}NR^M$-;

Z_B is absent, -$(CH_2)_{IM}$-, -C(=O)-$(CH_2)_{IM}$-, or -C(=O)$(CH_2)_{IM}$-NR^M-;

R^M is H or C_1-C_3 alkyl optionally substituted with 1-2 hydroxyl groups; and

each occurrence of IM is independently 0, 1, 2, 3, 4, 5, or 6;

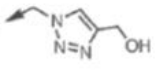


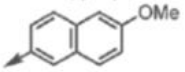
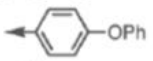
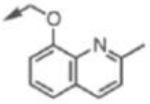
3

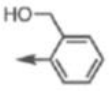
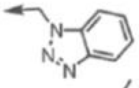
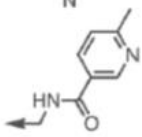
4

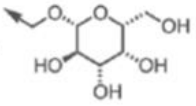
	R¹
a	Me
b	4-OMePh

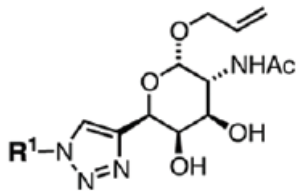
#	R²
1	Me
2	*n*-C_3H_7
3	*i*-Pr
4	*t*-Bu
5	CCl_3
6	CF_3
7	O*t*-Bu
8	CH_2CO_2H

#	R²
9	CH_2NH_2
10	CH_2CF_3
11	2-furyl
12	Ph
13	4-OMePh
14	3-OMePh
15	4-CNPh
16	3-pyridyl
17	

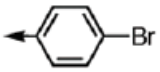
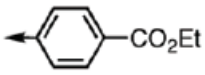
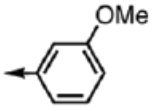
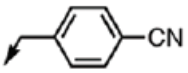
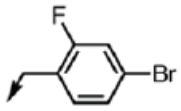
#	R³
1	Ph
2	4-OMePh
3	3-OMePh
4	3-NH_2Ph
5	4-NMe_2Ph
6	2-pyridyl
7	
8	
9	

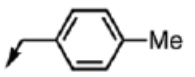
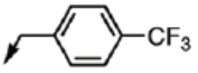
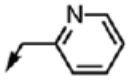
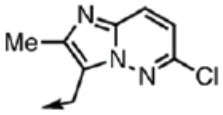
#	R³
10	
11	
12	
13	

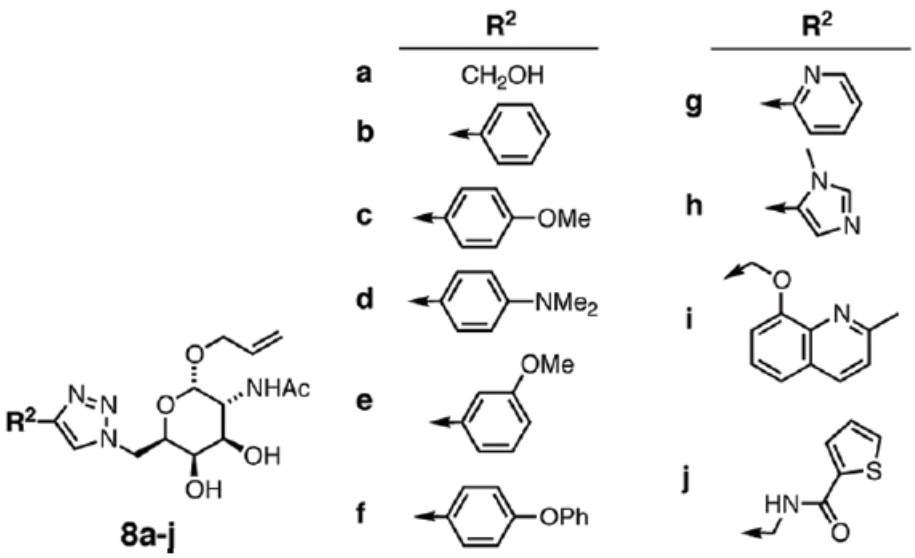
#	R³
14	
15	CH_2OH
16	CH_2NH_2
17	CH_2NHMe
18	CH_2NMe_2
19	CO_2H
20	$CH_2NHCOPh$
21	$CH_2NHCOMe$

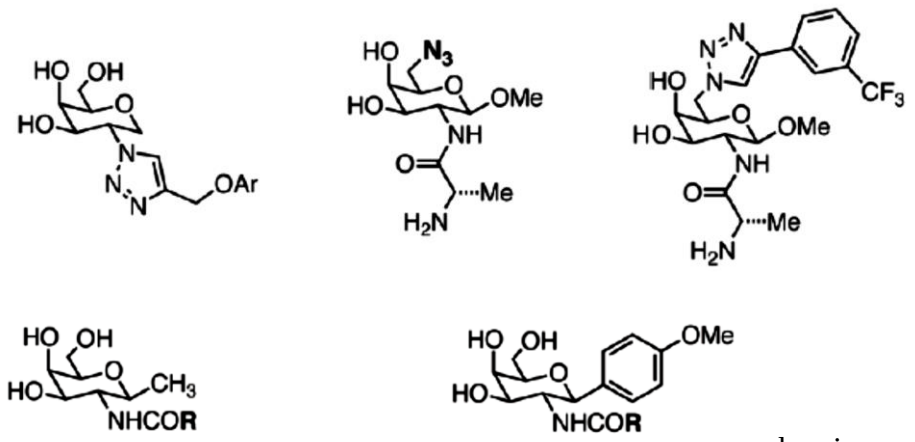


6a-j

	R¹
a	Me
b	
c	
d	
e	
f	

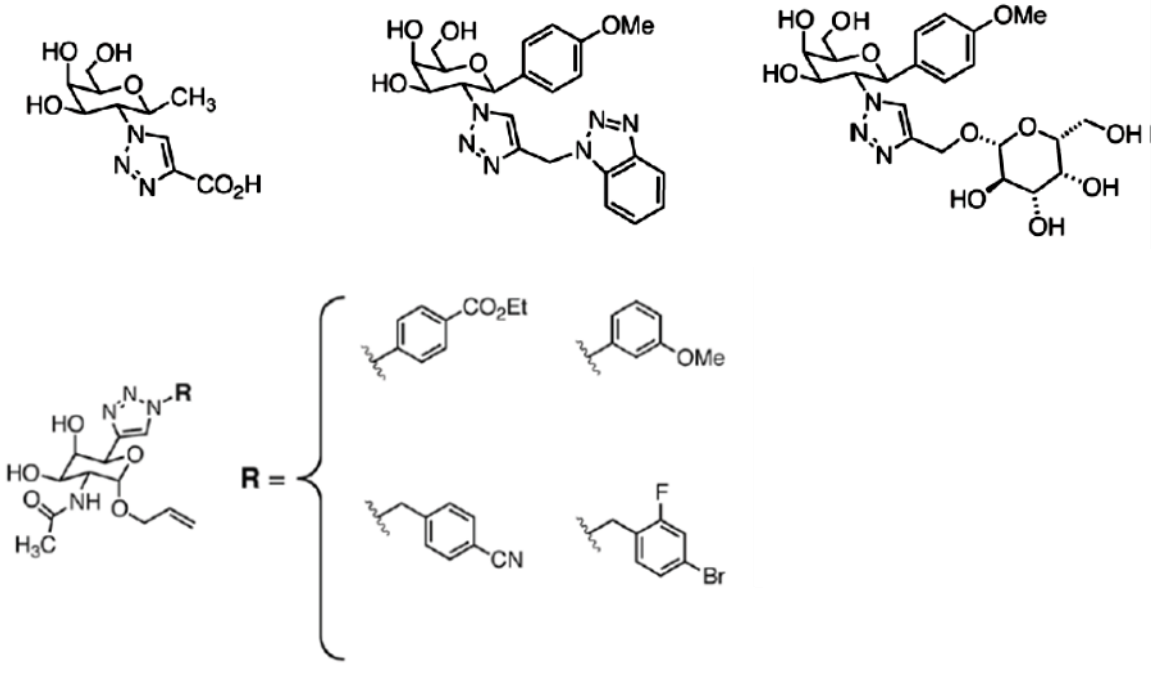
	R¹
g	
h	
i	
j	



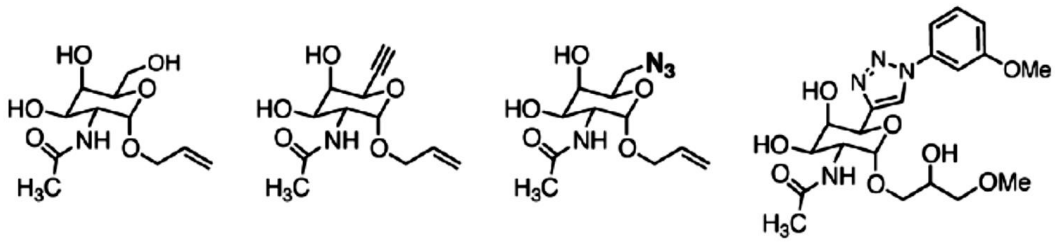


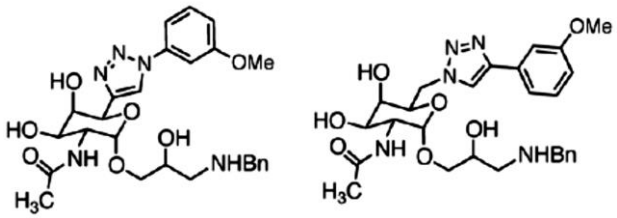
wherein

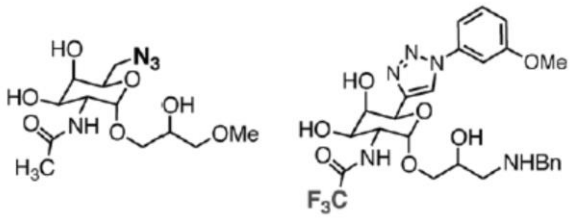
R = CH_3, CF_3, or CH_2CF_3;











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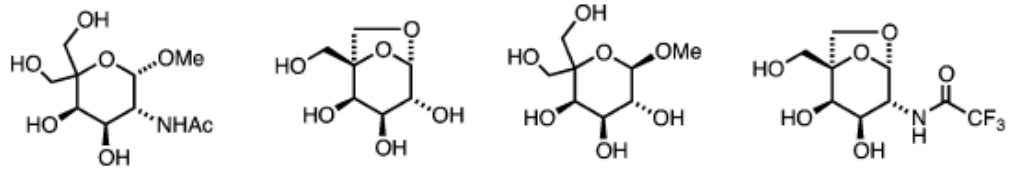
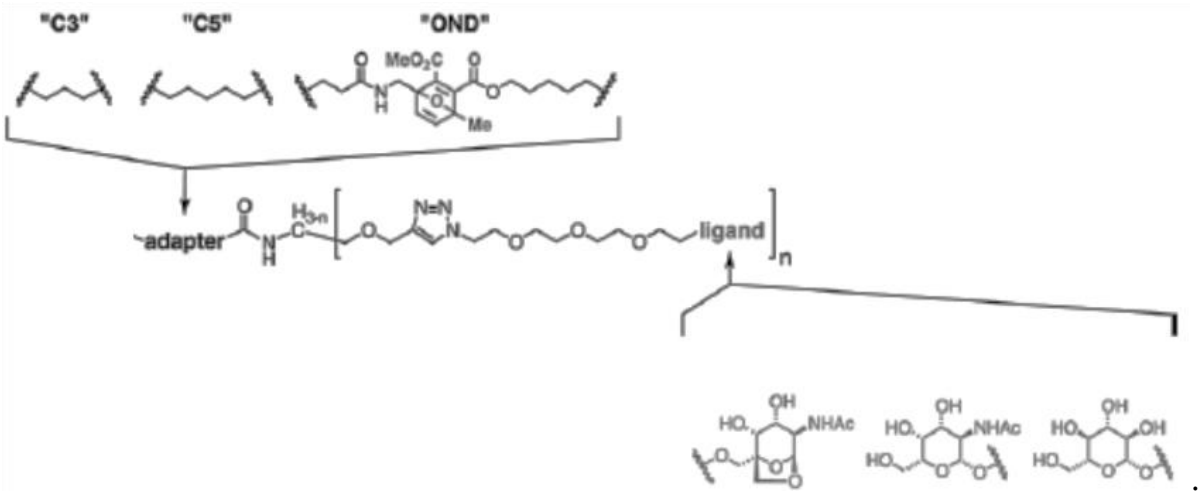


	R
16a	Et
16b	*n*-C_3H_7
16c	*n*-C_4H_9
16d	*n*-C_5H_{11}
16e	*n*-C_6H_{13}
16f	$(CH_2CH_2O)_4Me$

, or



19. The compound of claim 1, wherein the Linker is a polyethylene glycol containing linker having 1-12 ethylene glycol residues.

20. The compound of claim 1,

wherein the Linker comprises the structure:

$-CH_2CH_2(OCH_2CH_2)_mOCH_2-$, $-(CH_2)_mCH_2-$, $-[N(R^a)-CH(R^b)(C=O)]_m-$,

or a polypropylene glycol or polypropylene-co-polyethylene glycol group containing 1-100 alkylene glycol units;

wherein each R^a is independently H, C_1-C_3 alkyl, or C_1-C_6 alkanol, or combines with R^b to form a pyrrolidine or hydroxypyrroline group;

wherein each R^b is independently selected from the group consisting of hydrogen, methyl, isopropyl, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-(CH_2)_3$-guanidine, $-CH_2C(=O)NH_2$, $-CH_2C(=O)OH$, $-CH_2SH$, $-(CH_2)_2C(=O)NH_2$, $-(CH_2)_2C(=O)OH$, $-(CH_2)$imidazole, $-(CH_2)_4NH_2$, $-CH_2CH_2SCH_3$, benzyl, $-CH_2OH$, $-CH(OH)CH_3$, $-(CH_2)$imidazole, or $-(CH_2)$phenol; and

wherein m is an integer ranging from 1 to 15; or

wherein the Linker comprises the structure

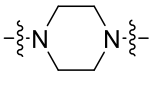
$-[N(R'-(CH_2)_{1\text{-}15}-C(=O)]-$,

wherein R' is H or a C_1-C_3 alkyl optionally substituted with 1-2 hydroxyl groups, and m is an integer ranging from 1 to 100; or

wherein the Linker comprises the structure:

-Z-D-Z'-,

wherein:

Z and Z' are each independently a bond, $-(CH_2)_i-O-$, $-(CH_2)_i-S-$, $-(CH_2)_i-N(R)-$,  , $-(CH_2)_i-C(R^2)=C(R^2)-$ (cis or trans), $-(CH_2)_i-\equiv-$, or -Y-C(=O)-Y-;

each R is independently H, C_1-C_3 alkyl, or C_1-C_6 alkanol;

each R^2 is independently H or C_1-C_3 alkyl;

each Y is independently a bond, O, S, or N(R);

each i is independently 0 to 100;

D is a bond, $-(CH_2)_i-Y-C(=O)-Y-(CH_2)_i-$, $-(CH_2)_{m'}-$, or $-[(CH_2)_n-X_1)]_j-$, with the proviso that Z, Z', and D are not each simultaneously bonds;

X^1 is O, S, or N(R);

j is an integer ranging from 1 to 100;

m' is an integer ranging from 1 to 100;

n is an integer ranging from 1 to 100; or

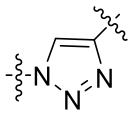
wherein the Linker comprises the structure:

$-CH_2-(OCH_2CH_2)_n-CH_2-$, $-(CH_2CH_2O)_{n'}CH_2CH_2-$, or $-(CH_2CH_2CH_2O)_n-$,

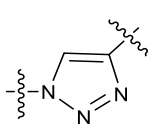
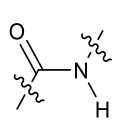
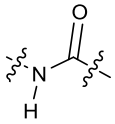
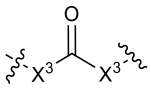
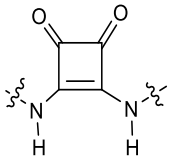
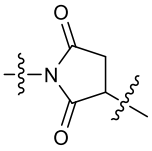
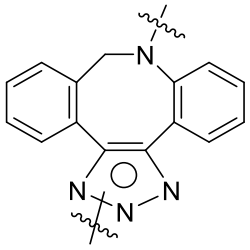
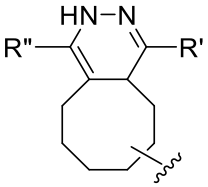
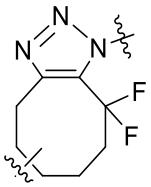
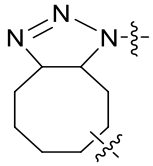
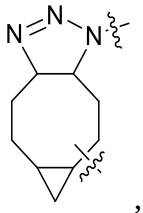
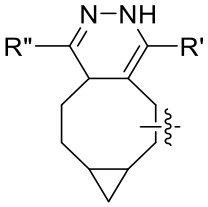
wherein each n and n' is independently an integer ranging from 1 to 25; or

wherein the Linker comprises a structure:

-PEG-CON-PEG-

wherein each PEG is independently a polyethylene glycol group containing from 1-12 ethylene glycol residues and CON is a triazole group  .

21. The compound of claim 1,

wherein the CON comprises a structure: , , , , , , , , , , , , , ; wherein R' and R" are each independently H, methyl, or a bond; or

wherein the CON comprises a structure:

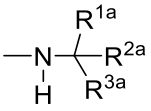
$$-C(=O)-N(R^1)-(CH_2)_{n''}-N(R^1)C(=O)-,$$

$$-N(R^1)-C(=O)(CH_2)_{n''}-C(=O)N(R^1)-, \text{ or}$$

$$-N(R^1)-C(=O)(CH_2)_{n''}-N(R^1)C(=O)\ -;$$

wherein each R^1 is independently H or C_1-C_3 alkyl, and n" is independently an integer from 0 to 8, in certain embodiments 1 to 7, in certain embodiments 1, 2, 3, 4, 5 or 6; or

wherein the CON comprises a structure:



wherein:

R^{1a}, R^{2a} and R^{3a} are each independently H, $-(CH_2)_{M1}-$, $-(CH_2)_{M2}C(=O)_{M3}(NR^4)_{M3}-(CH_2)_{M2}-$, $-(CH_2)_{M2}(NR^4)_{M3}C(O)_{M3}-(CH_2)_{M2}-$, or $-(CH_2)_{M2}O-(CH_2)_{M1}-C(O)NR^4-$, with the proviso that R^{1a}, R^{2a} and R^{3a} are not simultaneously H;

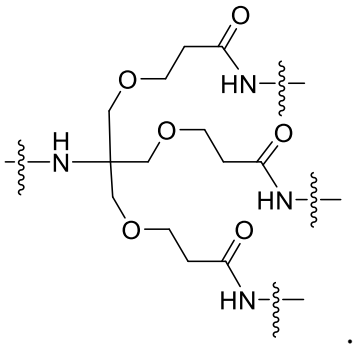
each M1 is independently 1, 2, 3, or 4;

each M2 is independently 0, 1, 2, 3, or 4;

each M3 is independently 0 or 1; and

each R^4 is independently H, C_1-C_3 alkyl, C_1-C_6 alkanol, or -C(=O)(C_1-C_3 alkyl), with the proviso that M2, and M3 within the same R^{1a}, R^{2a} and R^{3a} cannot all be simultaneously 0; or

wherein the CON comprises a structure:



22. The compound of claim 1, wherein the extracellular protein comprises 1-40-β-amyloid, 5'-nucleotidase, activated F9, F10, activin receptor-like kinase 1, alpha-fetoprotein, amyloid, angiopoietin 2, angiopoietin 3, anthrax toxin, AOC3, AOC3 (VAP-1), Bacillus anthracis anthrax, BAFF, beta amyloid, c-Met, C1s, C242 antigen, C5, CA-125, calcitonin, calcitonin gene-related peptide, calcitonin gene-related peptide alpha, Canis lupus familiaris IL31, carbonic anhydrase 9 (CA-IX), CEA, CEA-related antigen, CEACAM5, CFD, CGRP, clumping factor A, coagulation factor III, complement C5a, CSF1, MCSF, CSF2, dabigatran, E. coli shiga toxin type-1, E. coli shiga toxin type-2, EGFL7, endotoxin, episialin, FGF 23, fibrin II, beta chain, fibronectin extra domain-B, folate hydrolase, GDF-8, gelatinase B, GMCSF, growth differentiation factor 8, hemagglutinin, hemagglutinin HA, HGF, HIV-1, HNGF, Hsp90, human beta-amyloid, human scatter factor receptor kinase, human TNF, IFN-α, IFN-γ, IgE, IgE Fc region, IGF1, IGF2, IGHE, IL 17A, IL 17A and IL 17F, IL 20, IL-1, IL-12, IL-23, IL-13, IL-17, IL-1β, IL-22, IL-4, IL-5, IL-6, IL17A and IL17F, IL1A, IL2, IL23, IL23A, IL31RA, IL6, IL6R, IL9, ILGF2, Influenza A hemagglutinin, influenza A virus hemagglutinin, influenza A virus hemagglutinin HA, interferon gamma, interferon gamma-induced protein, interleukin 1 alpha, interleukin 13, interleukin 17 alpha, interleukin 17 alpha, TNF, interleukin 17A, kallikrein, LOXL2, LRRC15, LTA, MASP-2, MCP-1, MIF, MST1R (aka RON), MUC1, myostatin, NACP, NCA-90 (granulocyte antigen), neural apoptosis-regulated proteinase 1, NGF, NOGO-A, Notch 1, NRP1, oxLDL, PCSK9, PD-L1, phosphatidylserine, RANKL, RGMA, root plate-specific spondin 3, RTN4, sclerostin, SDC1, serum amyloid A protein, serum amyloid P

component, SOST, Staphylococcus aureus alpha toxin, tau protein, TFPI, TGF beta 1, TGF beta 2, TGF-β, TNF-α, TROP-2, TSLP, VEGF-A, VEGF-A and Ang-2, VEGFA, or VWF.

23. The compound of claim 1, wherein the Ab is a monoclonal antibody.

24. The compound of claim 1, wherein the antibody comprises: Abagovomab, Abrezekimab, Adalimumab, Aducanumab, Afasevikumab, Afelimomab, Alirocumab, Altumomab, Altumomab pentetate, Andecaliximab, Anrukinzumab, Arcitumomab, Ascrinvacumab, Atezolizumab, Atidortoxumab, Atinumab, Avelumab, Bapineuzumab, Bavituximab, Belimumab, Bermekimab, Besilesomab, Bevacizumab, Biciromab, Bimekizumab, Birtamimab, Blosozumab, Bococizumab, Brazikumab, Briakinumab, Brodalumab, Brolucizumab, Brontictuzumab, Burosumab, Cabiralizumab, Canakinumab, Cantuzumab, Cantuzumab ravtansine, Caplacizumab, Carlumab, Cergutuzumab, Cergutuzumab amunaleukin, Certolizumab, Certolizumab pegol, Cibisatamab, Clazakizumab, Clivatuzumab, Clivatuzumab tetraxetan, Concizumab, Crenezumab, Dectrekumab, Denosumab, Dezamizumab, Diridavumab, Domagrozumab, Dorlimomab, Dorlimomab aritox, Durvalumab, Dusigitumab, Eculizumab, Edobacomab, Efungumab, Eldelumab, Elezanumab, Elsilimomab, Emactuzumab, Emapalumab, Emicizumab, Enokizumab, Epitumomab, Epitumomab cituxetan, Eptinezumab, Erenumab, Evinacumab, Evolocumab, Faricimab, Fasinumab, Fezakinumab, Ficlatuzumab, Firivumab, Fletikumab, Fontolizumab, Fremanezumab, Fresolimumab, Frovocimab, Frunevetmab, Fulranumab, Galcanezumab, Gantenerumab, Gatipotuzumab, Gedivumab, Gevokizumab, Gimsilumab, Girentuximab, Golimumab, Gosuranemab, Guselkumab, Idarucizumab, Igovomab, Imalumab, Indatuximab, Indatuximab ravtansine, Infliximab, Istiratumab, Ixekizumab, Labetuzumab, Lacnotuzumab, Lampalizumab, Lanadelumab, Landogrozumab, Lebrikizumab, Lemalesomab, Lendalizumab, Lenzilumab, Lerdelimumab, Lesofavumab, Ligelizumab, Lodelcizumab, Lokivetmab, Lutikizumab, Marstacimab, Mepolizumab, Metelimumab, Mirikizumab, Nacolomab, Nacolomab tafenatox, Namilumab, Narnatumab, Navivumab, Naxitamab, Nebacumab, Nemolizumab, NEOD, Nerelimomab, Nesvacumab, Netakimab, Nofetumomab, Nofetumomab merpentan, Obiltoxaximab, Oleclumab, Olendalizumab, Olokizumab, Omalizumab, OMS, Onartuzumab, Oregovomab, Orticumab, Otilimab, Ozanezumab, Ozoralizumab, Parsatuzumab, Pascolizumab, Pasotuxizumab, Pateclizumab, Pemtumomab, Perakizumab, Pexelizumab, Placulumab, Ponezumab, Prasinezumab, Pritoxaximab, Quilizumab, Radretumab, Ralpancizumab, Ranevetmab,

Ranibizumab, Ravulizumab, Raxibacumab, REGN-EB, Remtolumab, Reslizumab, Rilotumumab, Risankizumab, Romilkimab, Romosozumab, Rontalizumab, Rosmantuzumab, Sacituzumab, Sacituzumab govitecan, Samrotamab, Samrotamab vedotin, Sarilumab, Secukinumab, Setoxaximab, Setrusumab, Sifalimumab, Siltuximab, Simtuzumab, Sirukumab, Sofituzumab, Sofituzumab, Sofituzumab vedotin, Solanezumab, Sontuzumab, Stamulumab, Sulesomab, Sutimlimab, Suvizumab, Suvratoxumab, Tabalumab, Tacatuzumab, Tacatuzumab tetraxetan, Talizumab, Tanezumab, Tefibazumab, Telimomab, Telimomab aritox, Tesidolumab, Tezepelumab, Tibulizumab, Tildrakizumab, Timolumab, Tisotumab, Tisotumab vedotin, Tralokinumab, Trevogrumab, Urtoxazumab,Ustekinumab, Vanucizumab, Vapaliximab, Varisacumab, Vepalimomab, Vesencumab, Vobarilizumab, Vunakizumab, or Xentuzumab.

25. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and at least one compound of claim 1.

26. The pharmaceutical composition of claim 25, further comprising another therapeutically active compound.

27. The compound of claim 1 for use in the treatment of ~~A method of treating~~ a disease or disorder in a subject, ~~the method comprising administering~~wherein a therapeutically effective amount of at least one compound of claim 1 is to be administered to the subject.

28. Use of the compound of claim 1 in the manufacture of a medicament for the treatment of a disease or disorder in a subject,~~The method of claim 27,~~ wherein the disease or disorder comprises an autoimmune disease, cancer, or inflammation~~.~~, and wherein a therapeutically effective amount of at least one compound of claim 1 is to be administered to the subject.

29. The ~~method~~ use of claim 28, wherein the autoimmune disease comprises Addison's Disease, Autoimmune polyendodrine syndrome (APS) types 1, 2 and 3, autoimmune pancreatitis (AIP), diabetes mellitus type 1, autoimmune thyroiditis, Ord's thyroiditis, Grave's disease, autoimmune oophoritis, endometriosis, autoimmune orchitis, Sjogren's syndrome, autoimmune enteropathy, coeliac disease, Crohn's disease, microscopic colitis, ulcerative colitis, autophospholipid syndrome (APlS), aplastic anemia, autoimmune hemolytica anemia, autoimmune lymphoproliferative syndrome, autoimmune neutropenia, autoimmune

thrombocytopenic purpura, cold agglutinin disease, essential mixed cryoglulinemia, Evans syndrome, pernicious anemia, pure red cell aplasia, thrombocytopenia, adiposis dolorosa, adult-onset Still's disease, ankylosing spondylitis, CREST syndrome, drug-induced lupus, enthesitis-related arthritis, esosinophilic fasciitis, Felty syndrome, AgG4-related disease, juvenile arthritis, Lyme disease (chronic), mixed connective tissue disease (MCTD), palindromic rheumatism, Parry Romberg syndrome, Parsonage-Turner syndrome, psoriatic arthritis, reactive arthritis, relapsing polychondritis, retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis, sarcoidosis, Schnitzler syndrome, systemic lupus erythematosus, undifferentiated connective tissue disease (UCTD), dermatomyositis, fibromyalgia, myositis, inclusion body myositis, myasthenia gravis, neuromyotonia, paraneoplastic cerebellar degeneration, polymysositis, acute disseminated encephalomyelitis (ADEM), acute motor axonic neuropathy, anti-NMDA receptor encephalitis, Balo concentric sclerosis, Bickerstaff's encephalitis, chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome, Hashimoto's encephalopathy, idiopathic inflammatory demyelinating diseases, Lambert-Eaton myasthenic syndrome, multiple sclerosis, pattern II, Oshtoran Syndrome, Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS), progressive inflammatory neuropathy, restless leg syndrome, stiff person syndrome, Syndenham chorea, transverse myelitis, autoimmune retinopathy, autoimmune uveitis, Cogan syndrome, Graves ophthalmopathy, intermediate uveitis, ligneous conjunctivitis, Mooren's ulcer, neuromyelitis optica, opsoclonus myoclonus syndrome, optic neuritis, scleritis, Susac's syndrome, sympathetic ophthalmia, Tolosa-Hunt syndrome, autoimmune inner ear disease (AIED), Méniére's disease, Behçet's disease, Eosinophilic granulomatosis with polyangiitis (EGPA), giant cell arteritis, granulomatosis with polyangiitis (GPA), IgA vasculitis (IgAV), IgA nephropathy, Kawasaki's disease, leukocytoclastic vasculitis, lupus vasculitis, rheumatoid vasculitis, microscopic polyangiitis (MPA), polyarteritis nodosa (PAN), polymyalgia rheumatica, urticarial vasculitis, vasculitis, primary immune deficiency, chronic fatigue syndrome, complex regional pain syndrome, eosinophilic esophagitis, gastritis, interstitial lung disease, POEMS syndrome, Raynaud's syndrome, primary immunodeficiency, or pyoderma gangrenosum.

30. The ~~method~~ use of claim 28, wherein the cancer comprises prostate cancer, metastatic prostate cancer, stomach cancer, colon cancer, rectal cancer, liver cancer, pancreatic cancer, lung cancer, breast cancer, cervix uteri cancer, corpus uteri cancer, ovary cancer, testis cancer, bladder cancer, renal cancer, brain/CNS cancer, head and neck cancer, throat cancer,

Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, leukemia, melanoma, non-melanoma skin cancer, acute lymphocytic leukemia, acute myelogenous leukemia, Ewing's sarcoma, small cell lung cancer, choriocarcinoma, rhabdomyosarcoma, Wilms' tumor, neuroblastoma, hairy cell leukemia, mouth/pharynx, oesophagus, larynx, kidney cancer, or lymphoma.

31. The ~~method~~ use of claim 28, wherein the inflammation comprises inflammatory diseases of neurodegeneration, diseases of compromised immune response causing inflammation, chronic inflammatory diseases, hyperglycemic disorders, diabetes (I and II), pancreatic β-cell death and related hyperglycemic disorders, liver disease, renal disease, cardiovascular disease, muscle degeneration and atrophy, low grade inflammation, gout, silicosis, atherosclerosis and associated conditions, stroke and spinal cord injury, or arteriosclerosis.

32. The ~~method~~ use of claim ~~27~~28, wherein ~~the subject is further administered~~ at least one additional therapeutic agent that treats or prevents the disease or disorder is to be administered to the subject.

33. The ~~method~~ use of claim ~~27~~28, wherein the subject is a mammal.

34. The ~~method~~ use of claim ~~27~~28, wherein the subject is a human.