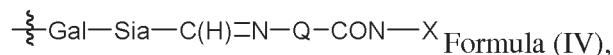


CLAIMS

We claim:

1. A binding polypeptide comprising at least one modified glycan, wherein the glycan
5 comprises at least one moiety of Formula (IV):



wherein:

A) Q is NH or O;

B) CON is a connector moiety;

10 C) X is a targeting moiety;

D) Gal is a component derived from galactose; and

E) Sia is a component derived from sialic acid, wherein Sia is present or absent, and
wherein the targeting moiety binds to a cell.

15 2. The binding polypeptide of claim 1, wherein the cell is a mammalian cell.

3. The binding polypeptide of claim 2, wherein the mammalian cell is selected from an
immune cell, a liver cell, a tumor cell, a vascular cell, an epithelial cell, or a mesenchymal
cell.

20

4. The binding polypeptide of claim 2, wherein the mammalian cell is selected from a B
cell, a T cell, a dendritic cell, a natural killer (NK) cell, a macrophage, a neutrophil, a
hepatocyte, a liver sinusoidal endothelial cell, or a hepatoma cell.

25 5. The binding polypeptide of claim 1, wherein the binding polypeptide is internalized
by the cell.

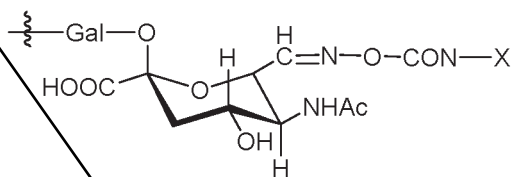
6. The binding polypeptide of claim 5, wherein the amount of the binding polypeptide
internalized by the cell is greater than the amount of a reference binding polypeptide lacking
30 a targeting moiety internalized by the cell.

7. The binding polypeptide of claim 1, wherein the targeting moiety binds to a mannose 6 phosphate receptor on the cell.
8. The binding polypeptide of claim 7, wherein the targeting moiety comprises a mannose 6 phosphate moiety.
9. The binding polypeptide of claim 1, wherein the targeting moiety binds to a sialic acid-binding immunoglobulin-type lectin (Siglec) on the cell.
10. The binding polypeptide of claim 9, wherein the Siglec is sialoadhesin (Siglec-1), CD22 (Siglec-2), CD33 (Siglec-3), myelin-associated glycoprotein (MAG (Siglec-4)), Siglec-5, Siglec-6, Siglec-7, Siglec-8, Siglec-9, Siglec-10, Siglec-11, Siglec-12, Siglec-14, or Siglec-15.
11. The binding polypeptide of claim 9, wherein the targeting moiety comprises an α 2,3-, α 2,6-, or α 2,8-linked sialic acid residue.
12. The binding polypeptide of claim 11, wherein the targeting moiety comprises an α 2,3-siallylactose moiety or an α 2,6-siallylactose moiety.
13. The binding polypeptide of claim 1, wherein the targeting moiety binds to a C-type lectin receptor, a galectin, or a L-type lectin receptor.
14. The binding polypeptide of claim 13, wherein the targeting moiety binds to DEC-205 (CD205; lymphocyte antigen 75), macrophage mannose receptor (MMR; CD206), Dectin-1, Dectin-2, macrophage-inducible C-type lectin (Mincle), dendritic cell-specific ICAM3-grabbing nonintegrin (DC-SIGN, CD209), DC NK lectin group receptor-1 (DNGR-1), Langerin (CD207), a lectican, an asialoglycoprotein receptor (ASGPR), C-lectin receptor dendritic cell immunoreceptor (CLEC4A; CLECSF6; DCIR), macrophage galactose-type lectin (MGL), a DC receptor, a collectin, a selectin, an NK-cell receptor, a multi- C-type lectin domain (CTLD) endocytic receptor, a Reg group (type VII) lectin, chondrolectin, tetranectin, polycystin, attractin (ATRN), eosinophil major basic protein (EMBP), DiGeorge

Syndrome Critical Region Gene 2 (DGCR2), Thrombomodulin, Bimlec, a group XVI lectin (SEEC), or a group XVII lectin (CBCP/Frem1/QBRICK).

15. The binding polypeptide of claim 1, wherein Q is O.

16. The binding polypeptide of claim 1, wherein the glycan comprises at least one moiety of the following structural formula:

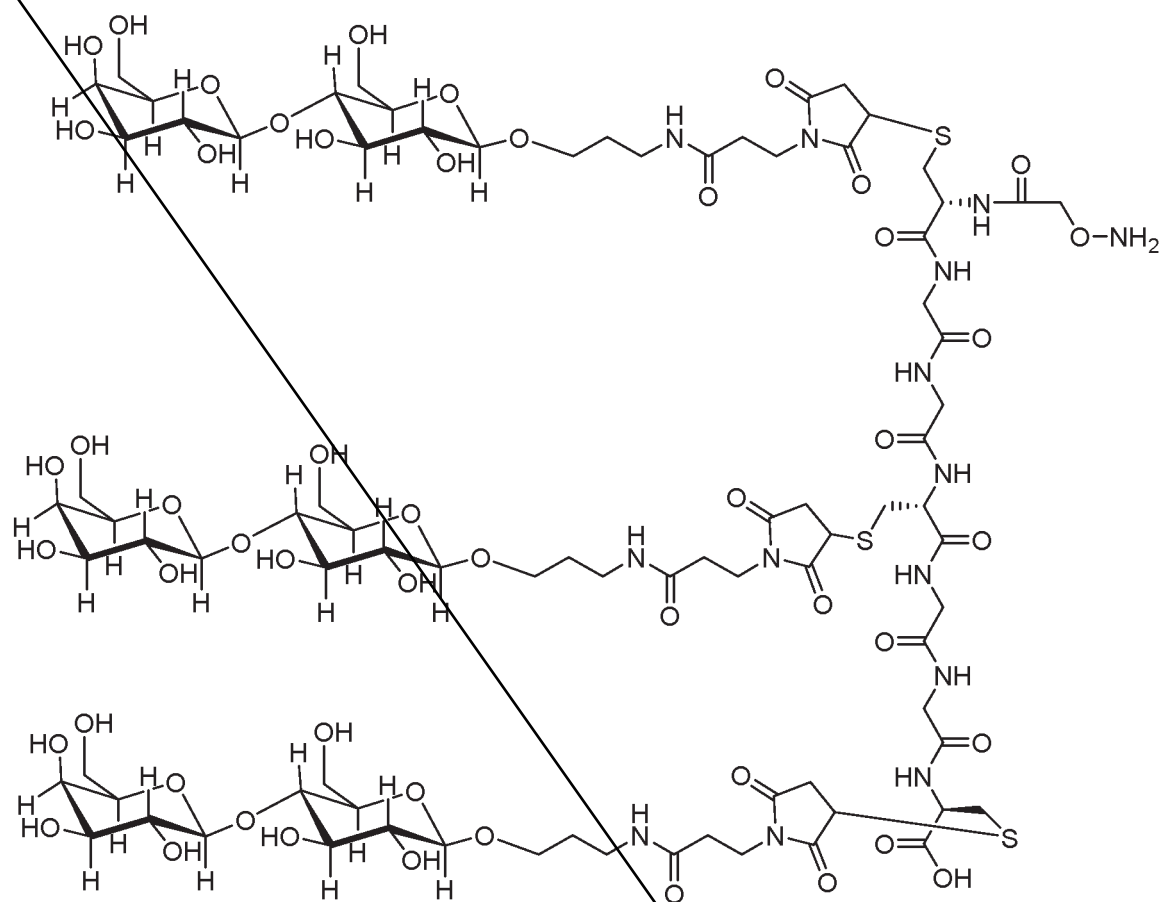


17. The binding polypeptide of claim 16, wherein the targeting moiety is a trivalent GalNAc glycan moiety.

18. The binding polypeptide of claim 1, wherein the targeting moiety is a glycopeptide capable of binding an asialoglycoprotein receptor (ASGPR) on a cell.

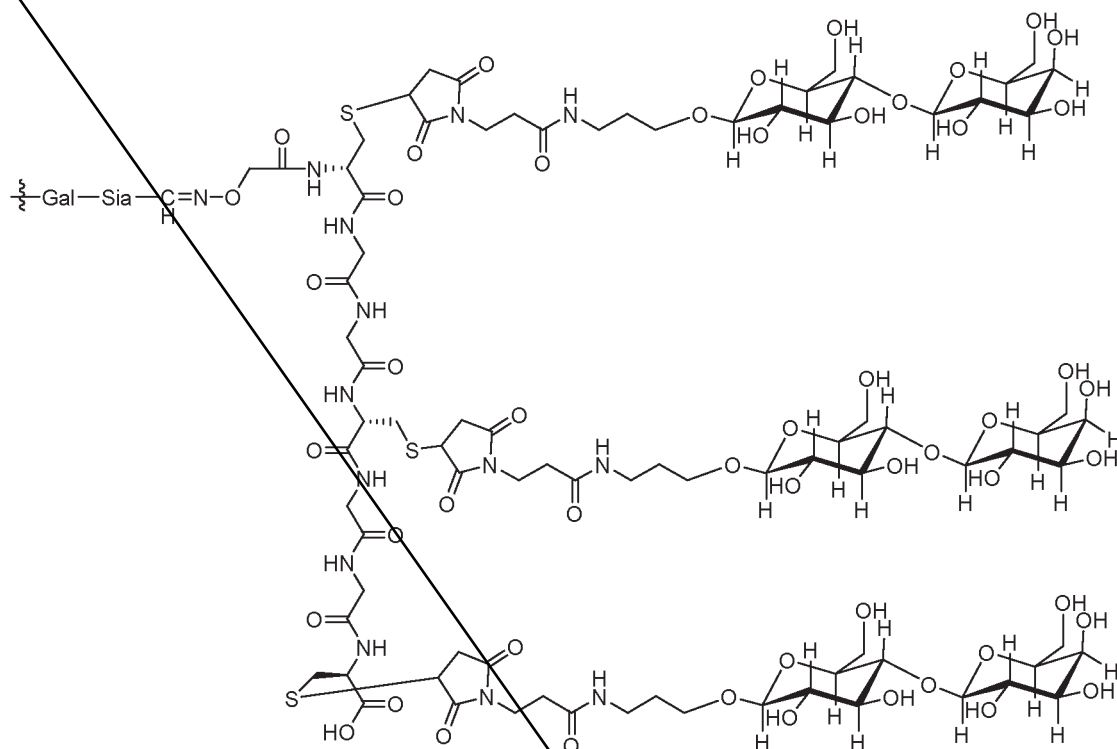
19. The binding polypeptide of claim 17, wherein the targeting moiety is a tri-galactosylated glycopeptide or lactose₃-Cys₃Gly₄.

20. The binding polypeptide of claim 19, wherein Sia is present and the lactose₃-Cys₃Gly₄ moiety is represented by Formula V:

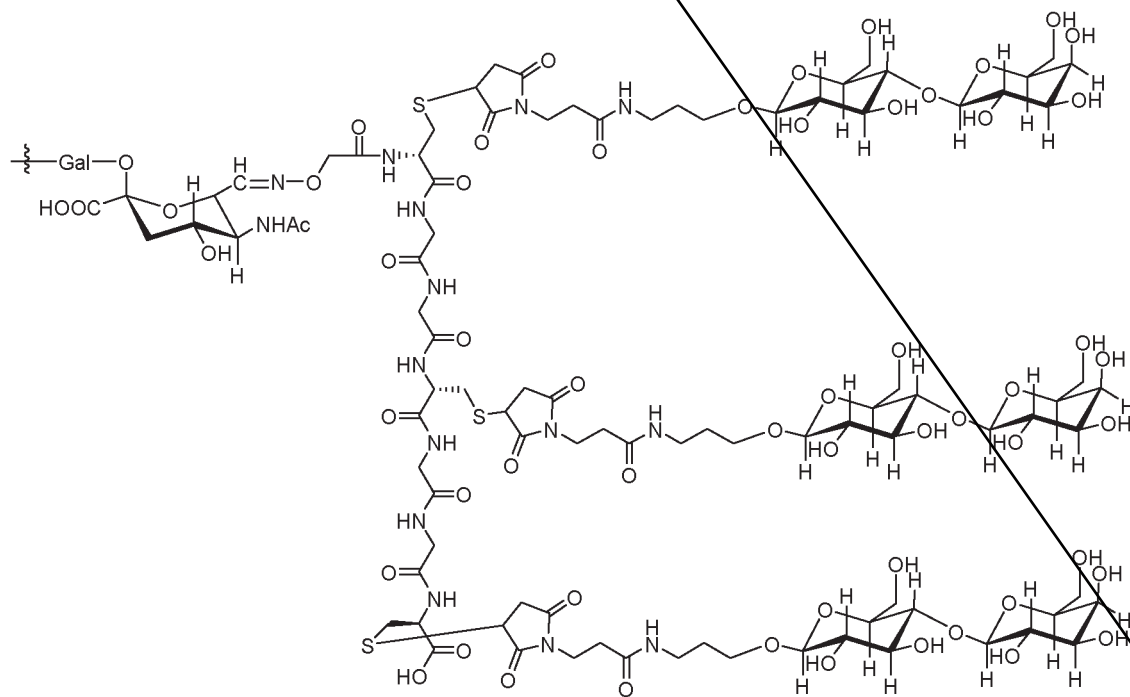


[Formula V].

21. The binding polypeptide of claim 20, wherein the glycan comprises at least one moiety
5 of the following structural formula:

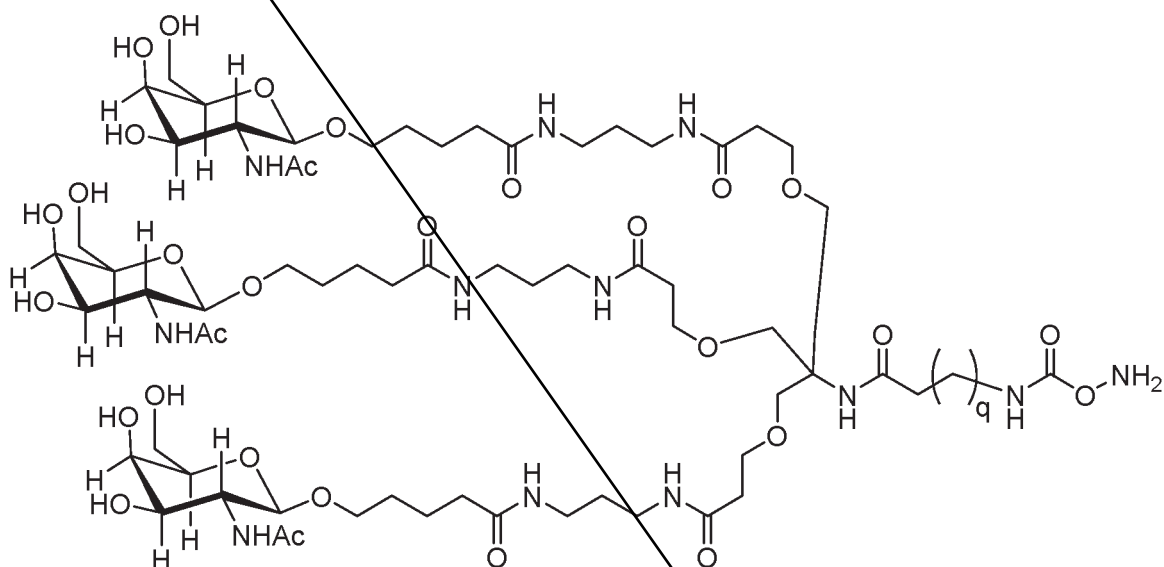


22. The binding polypeptide of claim 20, wherein the glycan comprises at least one moiety of the following structural formula:



23. The binding polypeptide of claim 18, wherein the targeting moiety is a trivalent GalNAc glycan moiety.

- 5 24. The binding polypeptide of claim 23, wherein Sia is present and the trivalent GalNAc glycan moiety is represented by Formula VIII:



- 10 [Formula VIII], wherein q is an integer between 1 and 29 inclusive.

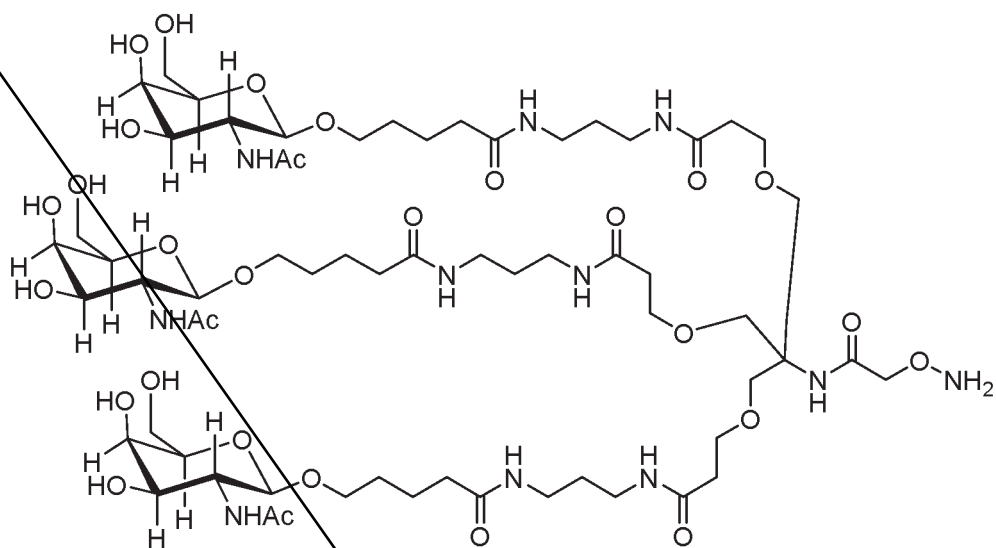
25. The binding polypeptide of claim 23, wherein the glycan comprises at least one moiety having the following structural formula:



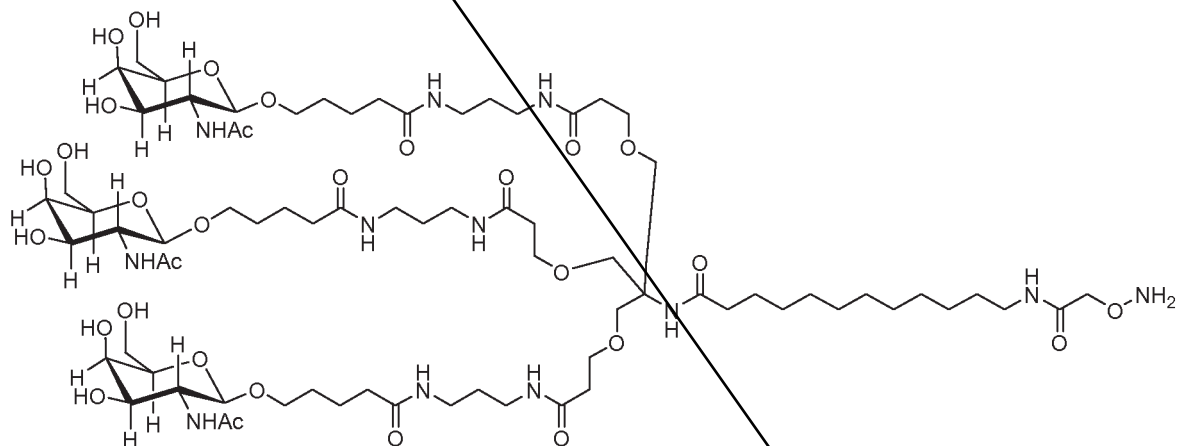
5 moiety having the following structural formula:



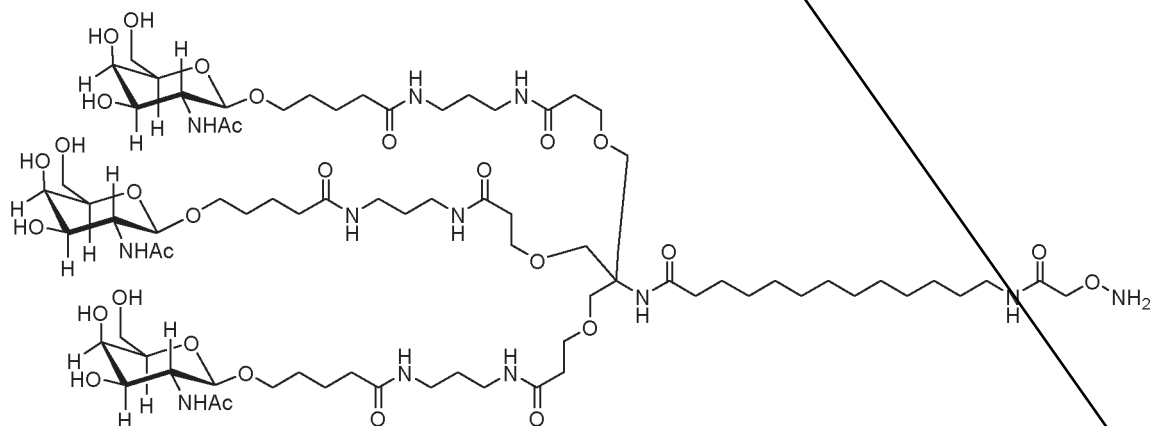
10 represented by Formula VII, Formula XIII, or Formula XIV:



[Formula VII];

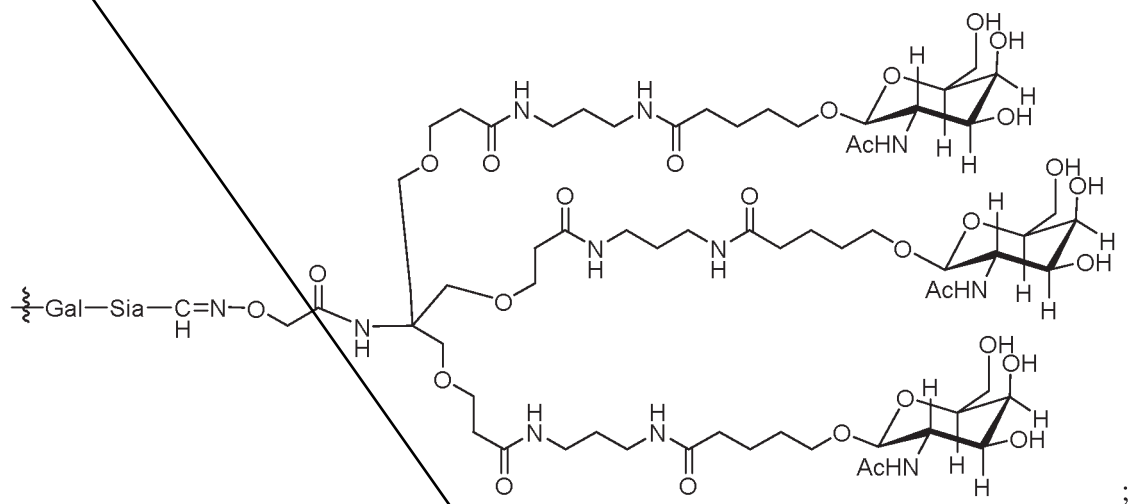
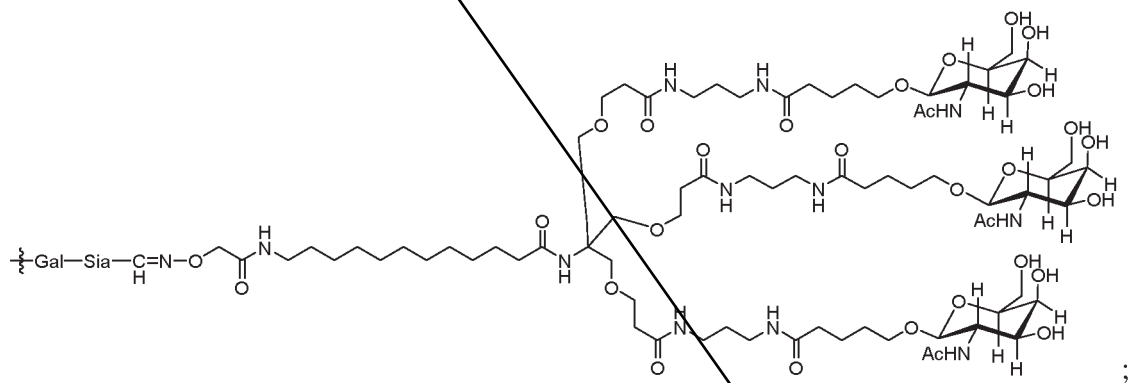


[Formula XIII]; or

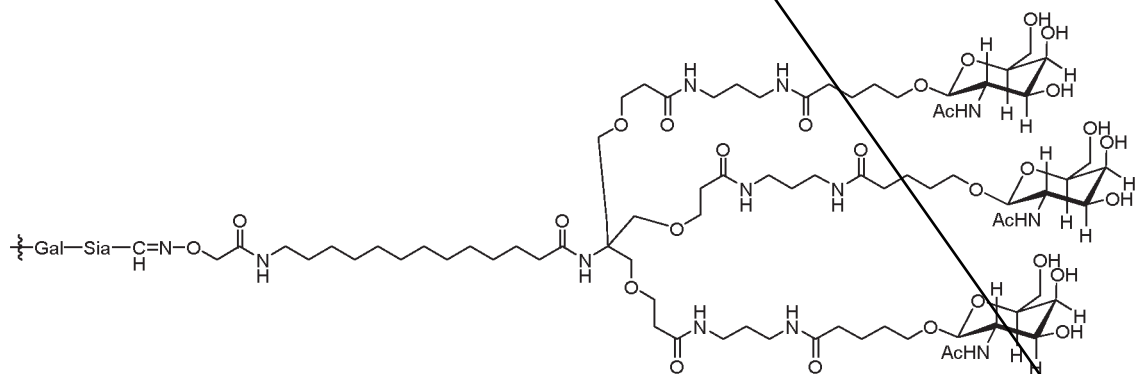


[Formula XIV].

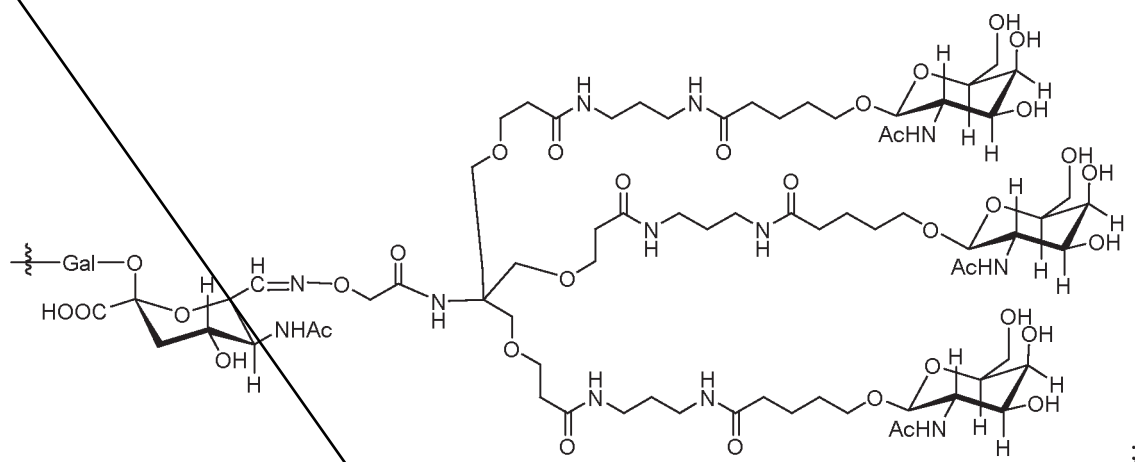
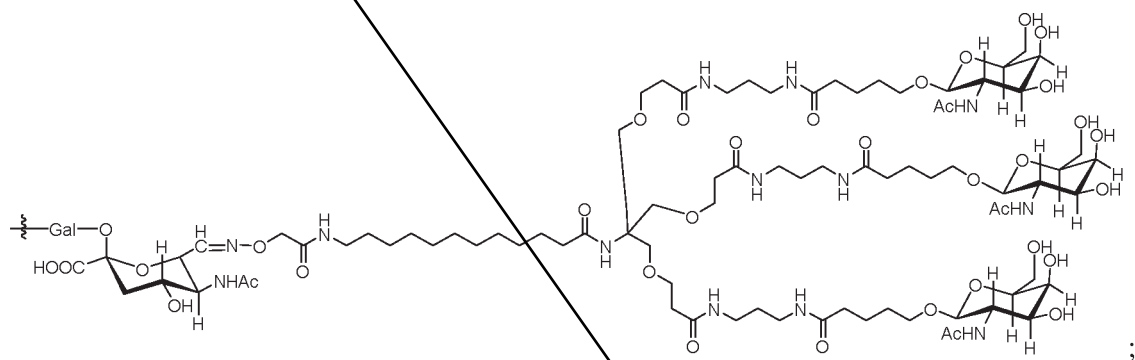
28. The binding polypeptide of claim 23, wherein the glycan comprises at least one moiety selected from the following structural formulae:



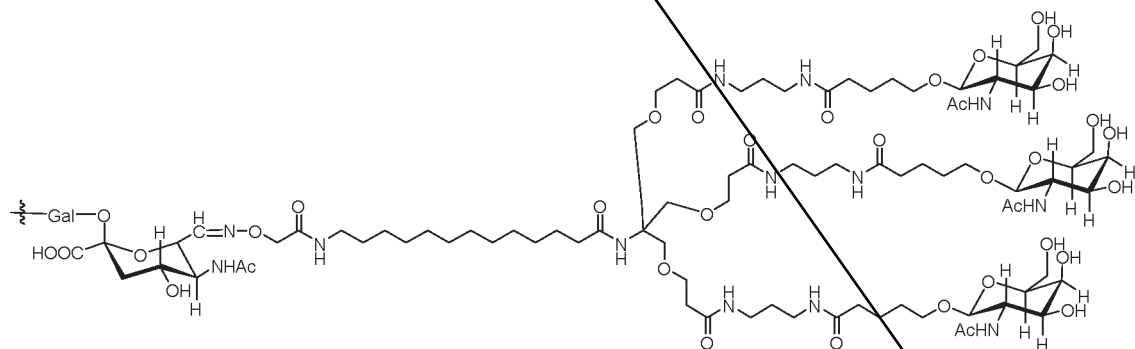
5 or



29. The binding polypeptide of claim 23, wherein the glycan comprises at least one moiety selected from the following structural formulae:



or



5

30. The binding polypeptide of any one of the preceding claims, wherein the binding polypeptide comprises an Fc domain.

31. The binding polypeptide of claim 30, wherein the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 297 of the Fc domain, according to EU numbering.

5 32. The binding polypeptide of claim 30, wherein the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 298 of the Fc domain, according to EU numbering.

10 33. The binding polypeptide of any one of the preceding claims, wherein the Fc domain is human.

34. The binding polypeptide of any one of the preceding claims, wherein the binding polypeptide comprises a CH1 domain.

15 35. The binding polypeptide of claim 34, wherein the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 114 of the CH1 domain, according to Kabat numbering.

20 36. The binding polypeptide of any one of the preceding claims, wherein the connector moiety comprises a pH-sensitive linker, disulfide linker, enzyme-sensitive linker or other cleavable linker moiety.

25 37. The binding polypeptide of any one of the preceding claims, wherein the connector moiety comprises a linker moiety selected from the group consisting of linker moieties depicted in Table 2 and 14.

38. The binding polypeptide of any one of the preceding claims which is an antibody or immunoadhesin.

39. A method of making the binding polypeptide of any one of the preceding claims, the method comprising reacting an effector moiety of Formula (I):



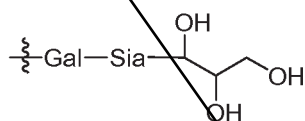
Formula (I),

wherein:

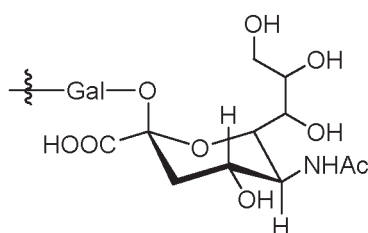
- A) Q is NH or O;
- B) CON is a connector moiety; and
- C) X is a targeting moiety,

with a precursor binding polypeptide comprising an oxidized glycan.

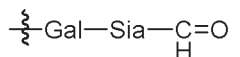
40. The method of claim 39, wherein the initial binding polypeptide comprises at least one moiety of the following structural formula:



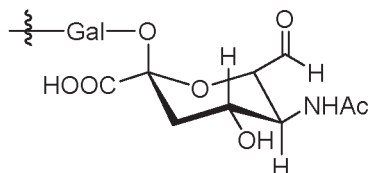
41. The method of claim 39, wherein the initial binding polypeptide comprises at least one moiety of the following structural formula:



42. The method of claim 39, wherein the precursor binding polypeptide comprises an oxidized glycan comprises at least one moiety of the following structural formula:



43. The method of claim 39, wherein the precursor binding polypeptide comprises an oxidized glycan comprises at least one moiety of the following structural formula:



44. The method of claim 39, wherein the precursor binding polypeptide comprising an oxidized glycan is generated by reacting an initial binding polypeptide comprising a glycan with a mildly oxidizing agent.

45. The method of claim 44, wherein the mildly oxidizing agent is sodium periodate.

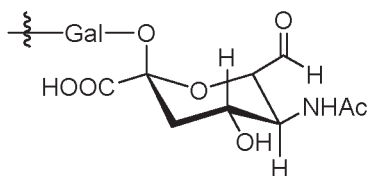
46. The method of claim 45, wherein less than 1mM sodium periodate is employed.

47. The method of claim 44, wherein the mildly oxidizing agent is periodate or galactose oxidase.

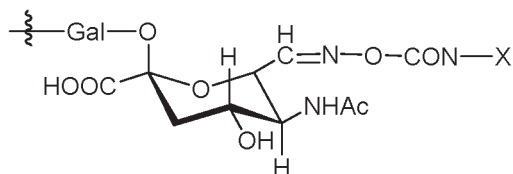
48. The method of claim 39 comprising reacting an effector moiety of the following structural formula:



with the precursor binding polypeptide comprising an oxidized glycan comprising at least one moiety of the following structural formula:



to form a binding polypeptide of the following structural formula:



49. The method of claim 48, wherein the targeting moiety is a trivalent GalNAc glycan moiety.

5 50. The method of claim 44, wherein the reacting step is conducted in the presence of a salt comprising a metal ion.

51. The method of claim 50, wherein the metal ion is a copper ion.

10 52. The method of claim 50 or 51, wherein the salt is copper acetate.

53. The method of any of claims 50-52, wherein the salt comprising a metal ion is present at a concentration of at least 0.1 mM.

15 54. The method of any of any one of the preceding claims, wherein the binding polypeptide comprising the glycan comprises one or two terminal sialic acid residues.

55. The method of claim 54, where the terminal sialic acid residues are introduced by treatment of the binding polypeptide with a sialyltransferase or combination of
20 sialyltransferase and galactosyltransferase.

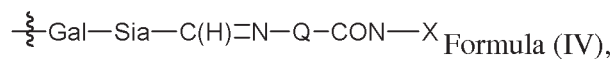
56. A composition comprising a binding polypeptide of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.

25 57. The composition of claim 56, wherein the ratio of targeting moiety to binding polypeptide is equal to or more than about 4.

58. The composition of claim 57, wherein the ratio of targeting moiety to binding polypeptide is at least about 2.

30 59. A method of treating a patient in need thereof comprising administering an effective amount of the composition of claims 56-58.

60. A binding polypeptide comprising at least one modified glycan comprising at least one moiety of Formula (IV):

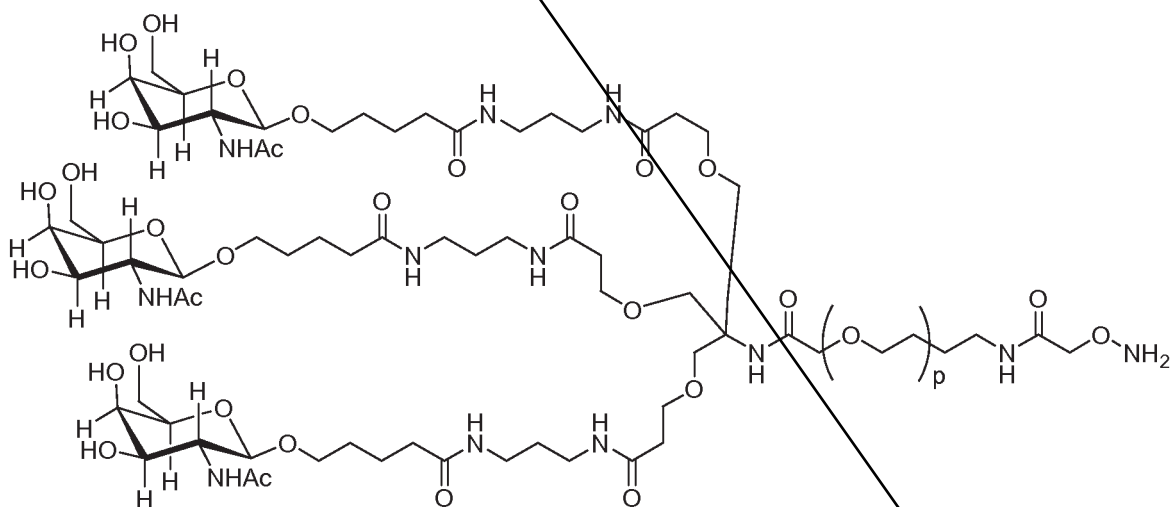


5 wherein:

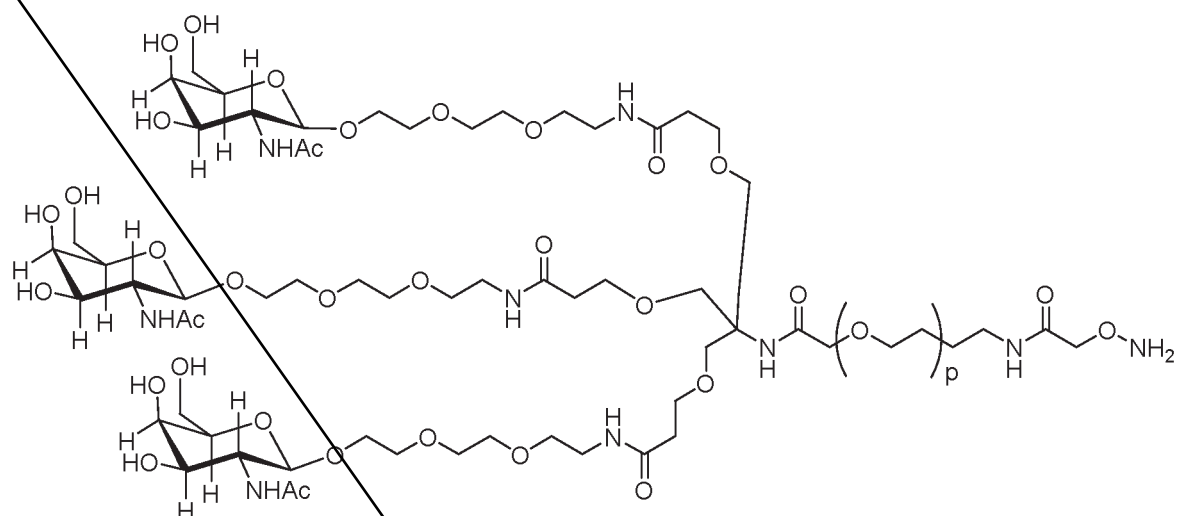
- A) Q is NH or O;
- B) CON is a connector moiety;
- C) X is a moiety comprising PEG;
- D) Gal is a component derived from galactose; and
- 10 E) Sia is a component derived from sialic acid,

wherein Sia is present or absent.

61. The binding polypeptide of claim 60, wherein the glycan comprises at least one moiety represented by Formula IX or Formula XI:

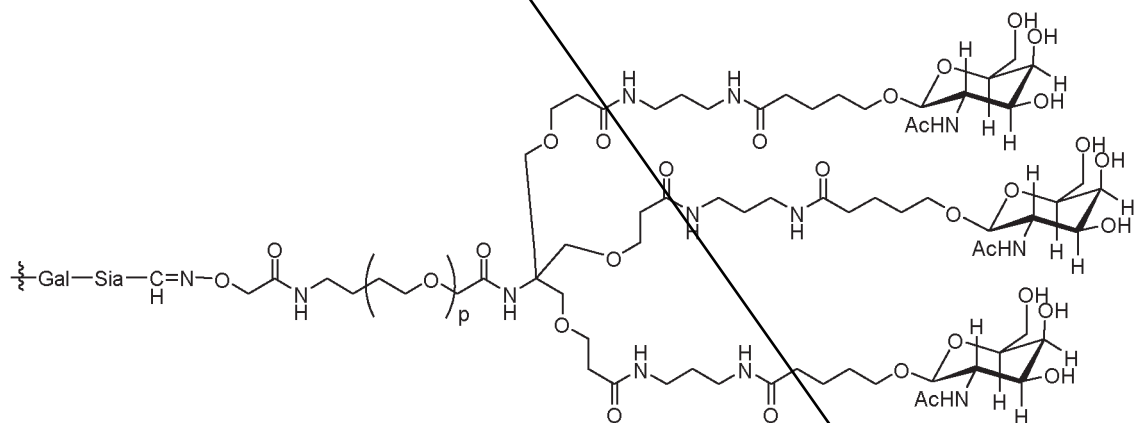


15 [Formula IX], wherein p has a value of 1 to 32; or

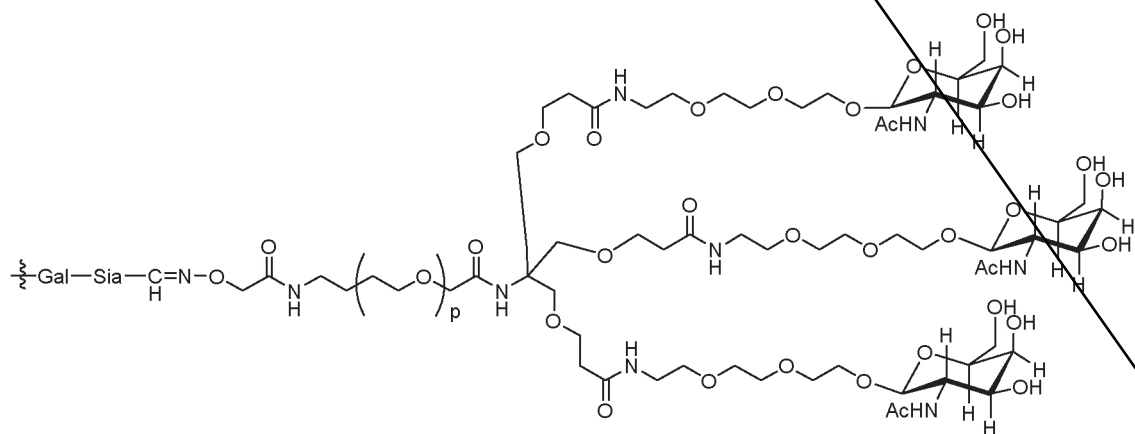


[Formula XI], wherein p has a value of 1 to 32.

62. The binding polypeptide of claim 60, wherein the glycan comprises at least one moiety selected from the following structural formulae:

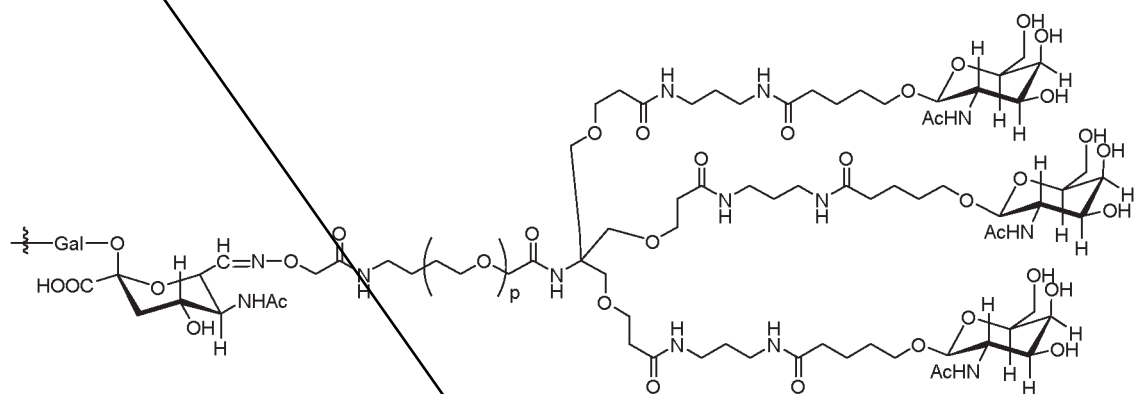


wherein p has a value of 1 to 32; or

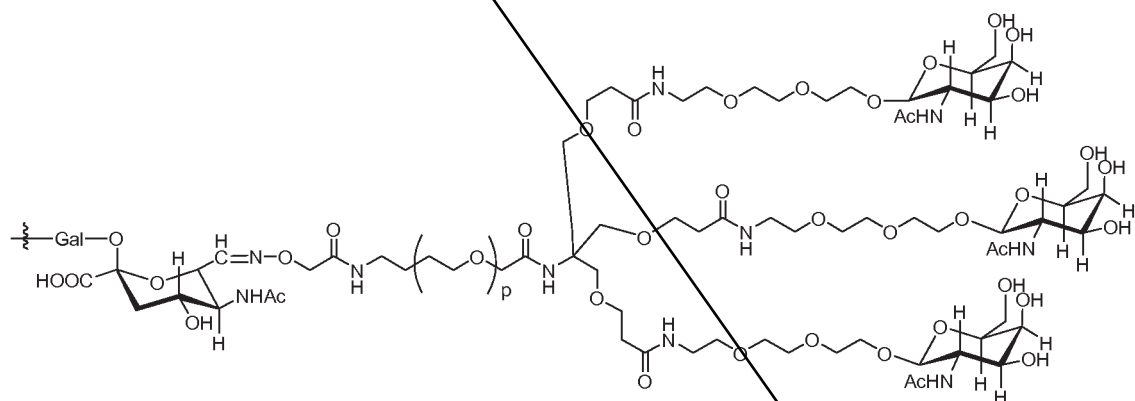


wherein p has a value of 1 to 32.

63. The binding polypeptide of claim 60, wherein the glycan comprises at least one moiety selected from the following structural formulae:

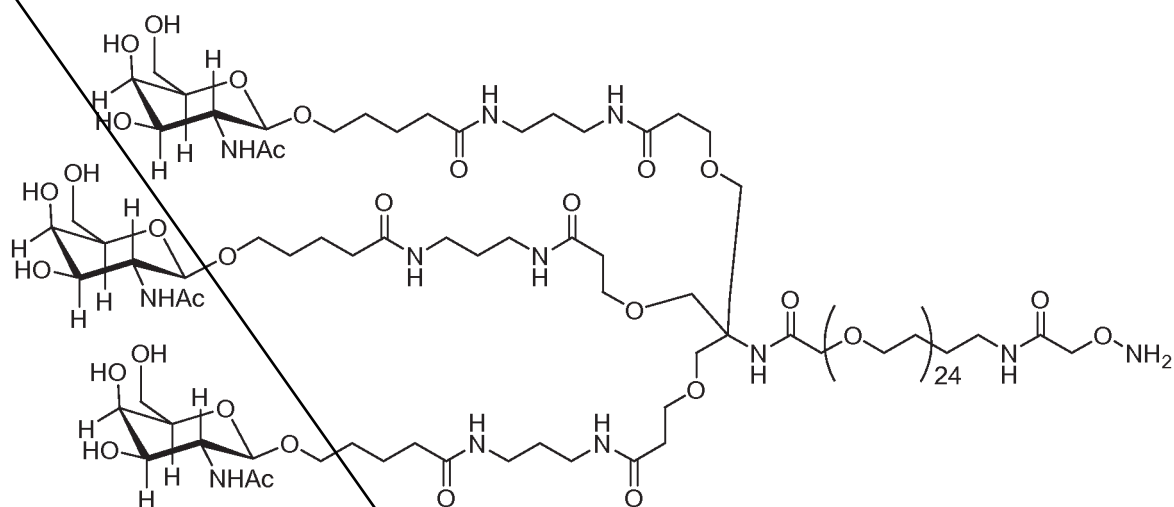
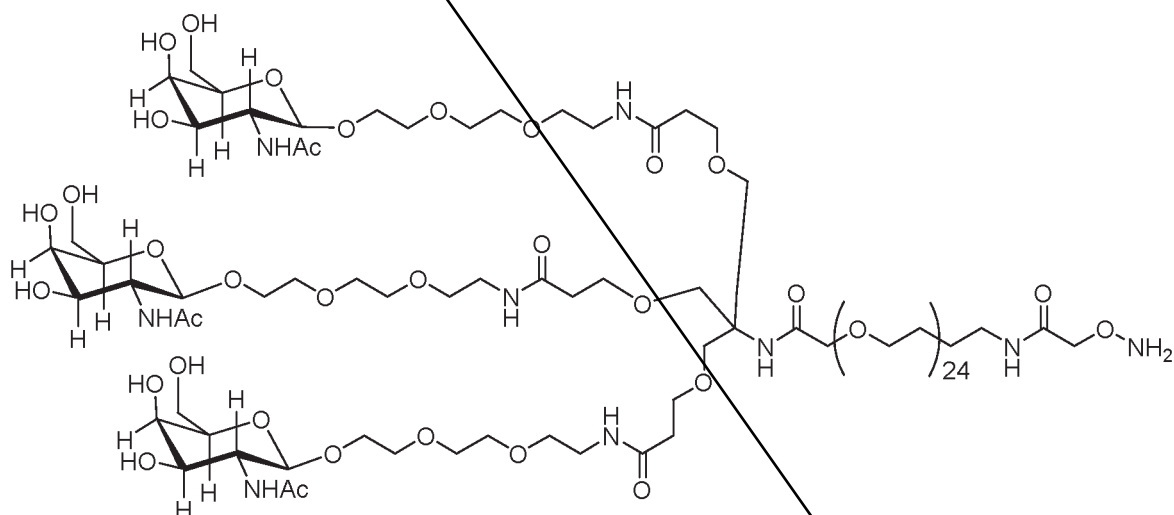


wherein p has a value of 1 to 32; or



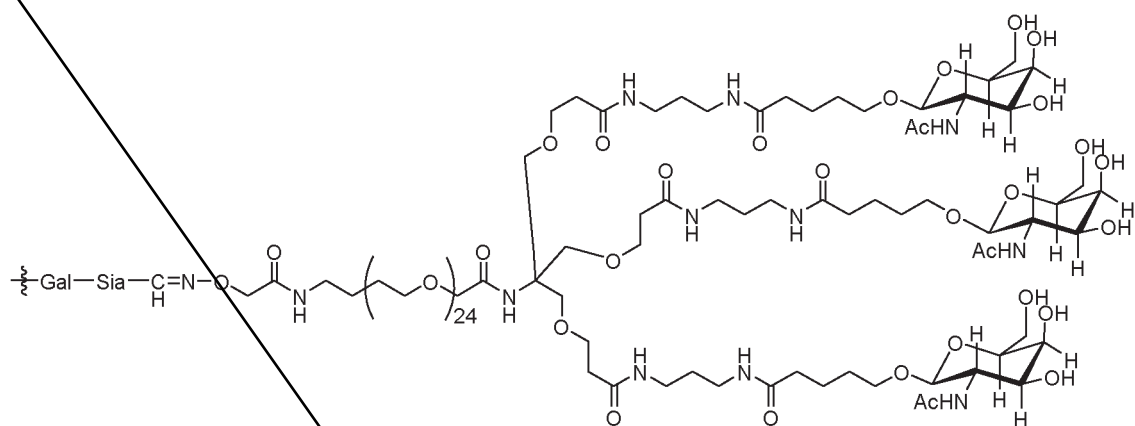
wherein p has a value of 1 to 32.

64. The binding polypeptide of claim 60, wherein the targeting moiety comprises PEG and is represented by Formula X or Formula XII:

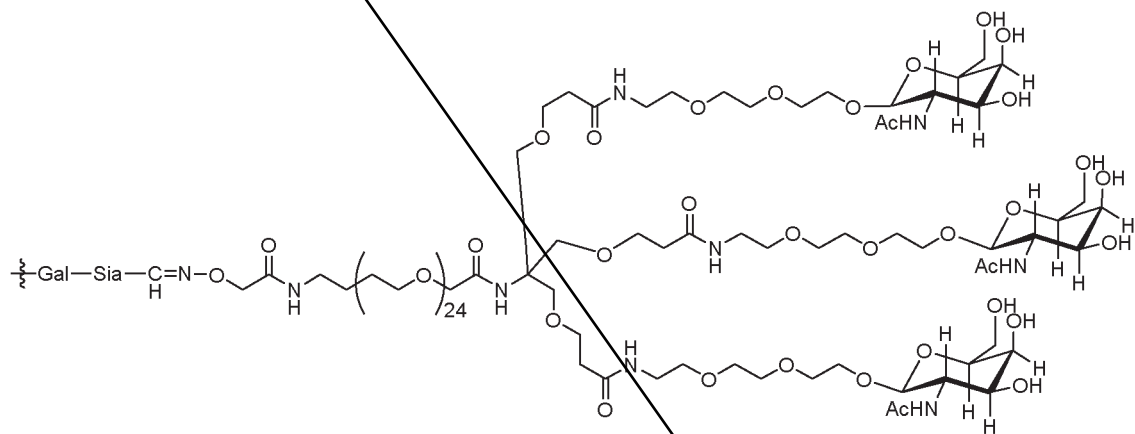


5 [Formula XII].

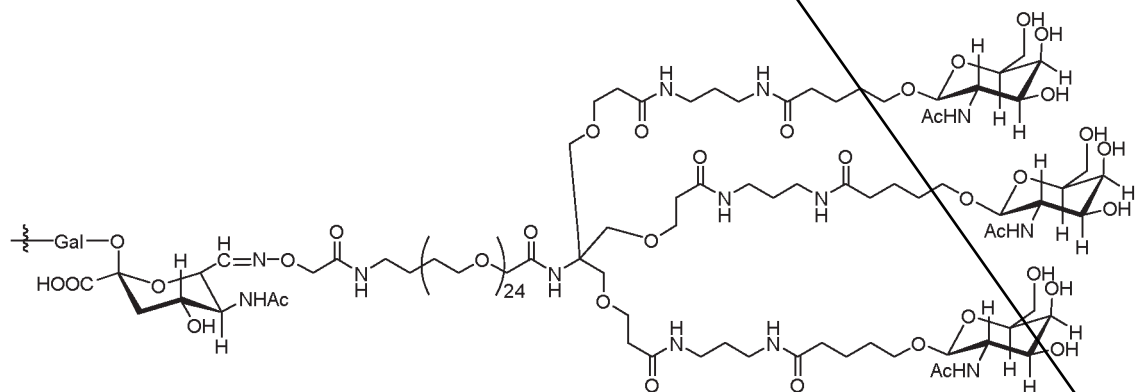
65. The binding polypeptide of claim 60, wherein the glycan comprises at least one moiety selected from the following structural formulae:



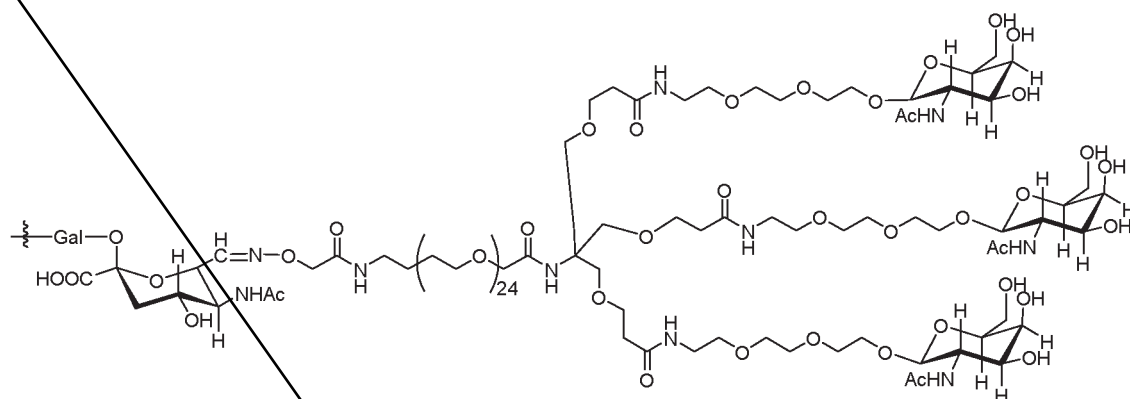
or



- 5 66. The binding polypeptide of claim 60, wherein the glycan comprises at least one moiety selected from the following structural formulae:



or



67. The binding polypeptide of claim 60, wherein the PEG comprises mono-PEG, bi-PEG,
5 or tri-PEG.

68. The binding polypeptide of claim 60 or 67, wherein the PEG comprises 3 to 3.5 PEG.

69. The binding polypeptide of claims 60, 67, or 68, wherein the binding polypeptide is
10 an antibody or immunoadhesin.

70. A method of making a PEGylated binding polypeptide, wherein the method
comprises:

- 15 (a) reacting a binding polypeptide comprising at least one glycan with a mildly oxidizing agent in the presence of a salt comprising a metal ion to generate an oxidized binding polypeptide comprising at least one oxidized glycan, and
(b) conjugating the oxidized binding polypeptide with at least one moiety comprising PEG, thereby generating the PEGylated binding polypeptide.

20 71. The method of claim 70, wherein the metal ion is a copper ion.

72. The method of claim 70 or 71, wherein the salt is copper acetate.

73. The method of claims 70-72, wherein the salt comprising a metal ion is present at a
25 concentration of at least 0.1 mM.

74. The method of claims 70-73, wherein the mildly oxidizing agent is periodate oxidase or galactose oxidase.

5 75. The method of claims 70-74, wherein the at least one glycan is a modified glycan.

76. The binding polypeptide of claim 1, wherein the binding protein comprises an N-glycan glycoform selected from the group consisting of: a G0 glycoform, a G1 glycoform, and a G2 glycoform.

10

77. The binding polypeptide of claim 76, wherein the N-glycan glycoform is selected from the group consisting of: a G1S1 glycoform, a G2S1 glycoform, and a G2S2 glycoform.

78. The binding polypeptide of claim 76, wherein the N-glycan glycoform is selected from the group consisting of: a G1F glycoform, a G2F glycoform, a G1S1F glycoform, a G2S1F glycoform, and a G2S2F glycoform.

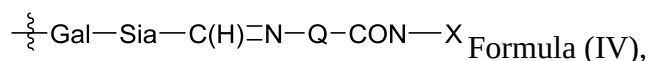
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CLAIMS

We claim:

1. A binding polypeptide comprising at least one modified glycan, wherein the glycan comprises at least one moiety of Formula (IV):

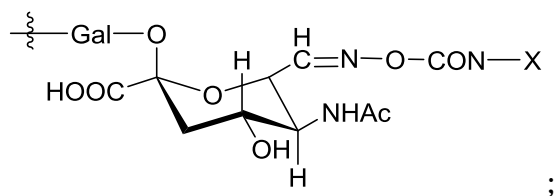


wherein:

- A) Q is NH or O;
- B) CON is a connector moiety;
- C) X is a targeting moiety;
- D) Gal is a component derived from galactose; and
- E) Sia is a component derived from sialic acid, wherein Sia is present or absent, and wherein the targeting moiety binds to a cell.

2. The binding polypeptide of claim 1, wherein one or more of the following conditions are met:

- a) the cell is a mammalian cell;
- b) the binding polypeptide is internalized by the cell;
- c) the targeting moiety binds to a mannose 6 phosphate receptor on the cell;
- d) the targeting moiety binds to a sialic acid-binding immunoglobulin-type lectin (Siglec) on the cell;
- e) the targeting moiety binds to a C-type lectin receptor, a galectin, or a L-type lectin receptor;
- f) Q is O;
- g) the glycan comprises at least one moiety of the following structural formula:



- h) the targeting moiety is a glycopeptide capable of binding an asialoglycoprotein receptor (ASGPR) on a cell;
 - i) the binding protein comprises an N-glycan glycoform selected from the group consisting of: a G0 glycoform, a G1 glycoform, and a G2 glycoform;
 - j) the N-glycan glycoform is selected from the group consisting of: a G1S1 glycoform, a G2S1 glycoform, and a G2S2 glycoform; and
 - k) the N-glycan glycoform is selected from the group consisting of: a G1F glycoform, a G2F glycoform, a G1S1F glycoform, a G2S1F glycoform, and a G2S2F glycoform.
3. The binding polypeptide of claim 2, wherein one or more of the following conditions are met:
- a) the mammalian cell is selected from an immune cell, a liver cell, a tumor cell, a vascular cell, an epithelial cell, or a mesenchymal cell;
 - b) the amount of the binding polypeptide internalized by the cell is greater than the amount of a reference binding polypeptide lacking a targeting moiety internalized by the cell;
 - c) the targeting moiety comprises a mannose 6 phosphate moiety;
 - d) the Siglec is sialoadhesin (Siglec-1), CD22 (Siglec-2), CD33 (Siglec-3), myelin-associated glycoprotein (MAG (Siglec-4)), Siglec-5, Siglec-6, Siglec-7, Siglec-8, Siglec-9, Siglec-10, Siglec-11, Siglec-12, Siglec-14, or Siglec-15;
 - e) the targeting moiety comprises an α 2,3-, α 2,6-, or α 2,8-linked sialic acid residue;
 - f) the targeting moiety binds to DEC-205 (CD205; lymphocyte antigen 75), macrophage mannose receptor (MMR; CD206), Dectin-1, Dectin-2, macrophage-inducible C-type lectin (Mincle), dendritic cell-specific ICAM3-grabbing nonintegrin (DC-SIGN, CD209), DC NK lectin group receptor-1 (DNGR-1), Langerin (CD207), a lectican, an asialoglycoprotein receptor (ASGPR), C-lectin receptor dendritic cell immunoreceptor (CLEC4A; CLECSF6; DCIR), macrophage galactose-type lectin (MGL), a DC receptor, a collectin, a selectin, an NK-cell receptor, a multi- C-type lectin domain (CTLD) endocytic receptor, a Reg group (type VII) lectin, chondrolectin, tetranectin, polycystin, attractin (ATRN), eosinophil major basic protein (EMBP), DiGeorge Syndrome Critical

Region Gene 2 (DGCR2), Thrombomodulin, Bimlec, a group XVI lectin (SEEC), or a group XVII lectin (CBCP/Frem1/QBRICK); and

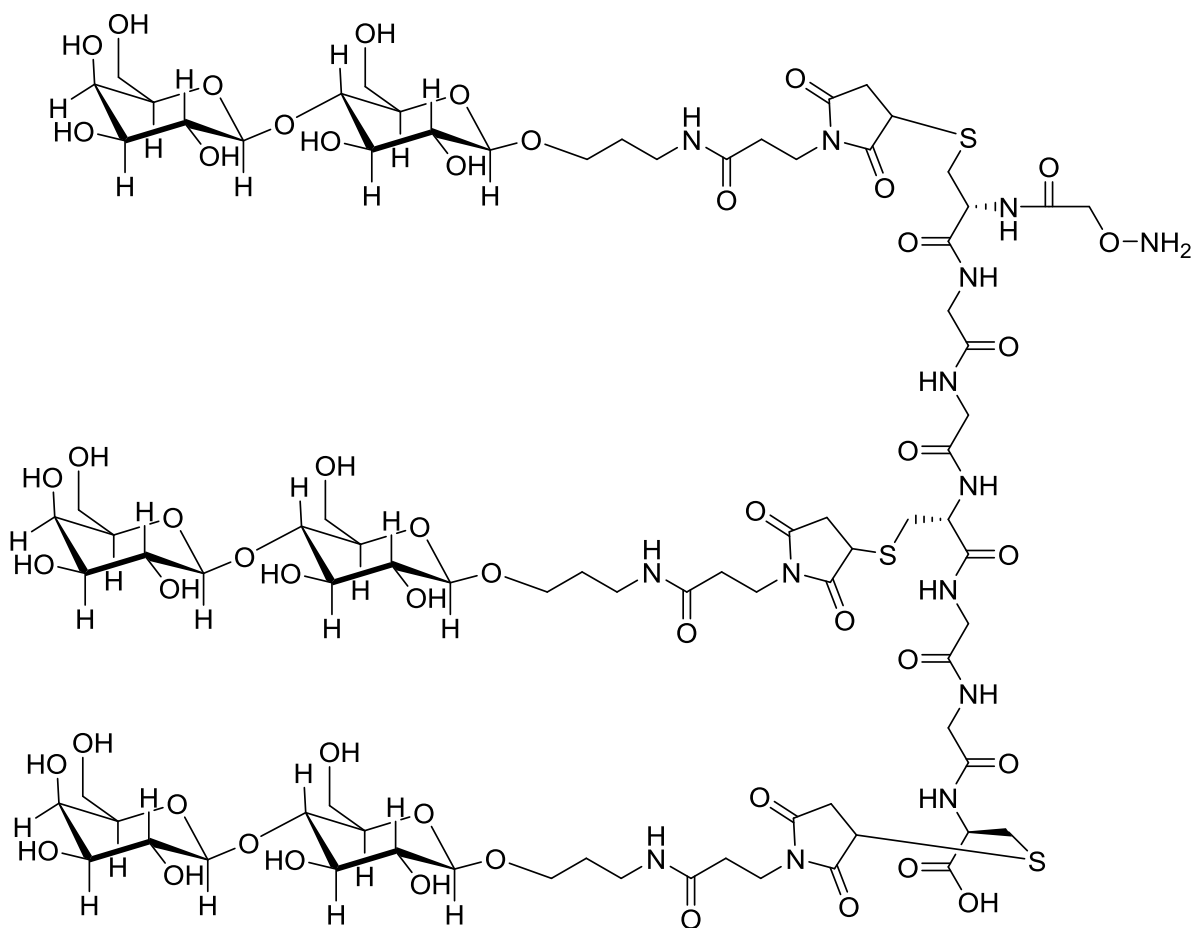
g) the targeting moiety is a trivalent GalNAc glycan moiety.

4. The binding polypeptide of claim 2, wherein the mammalian cell is selected from a B cell, a T cell, a dendritic cell, a natural killer (NK) cell, a macrophage, a neutrophil, a hepatocyte, a liver sinusoidal endothelial cell, or a hepatoma cell.

5. The binding polypeptide of claim 3,

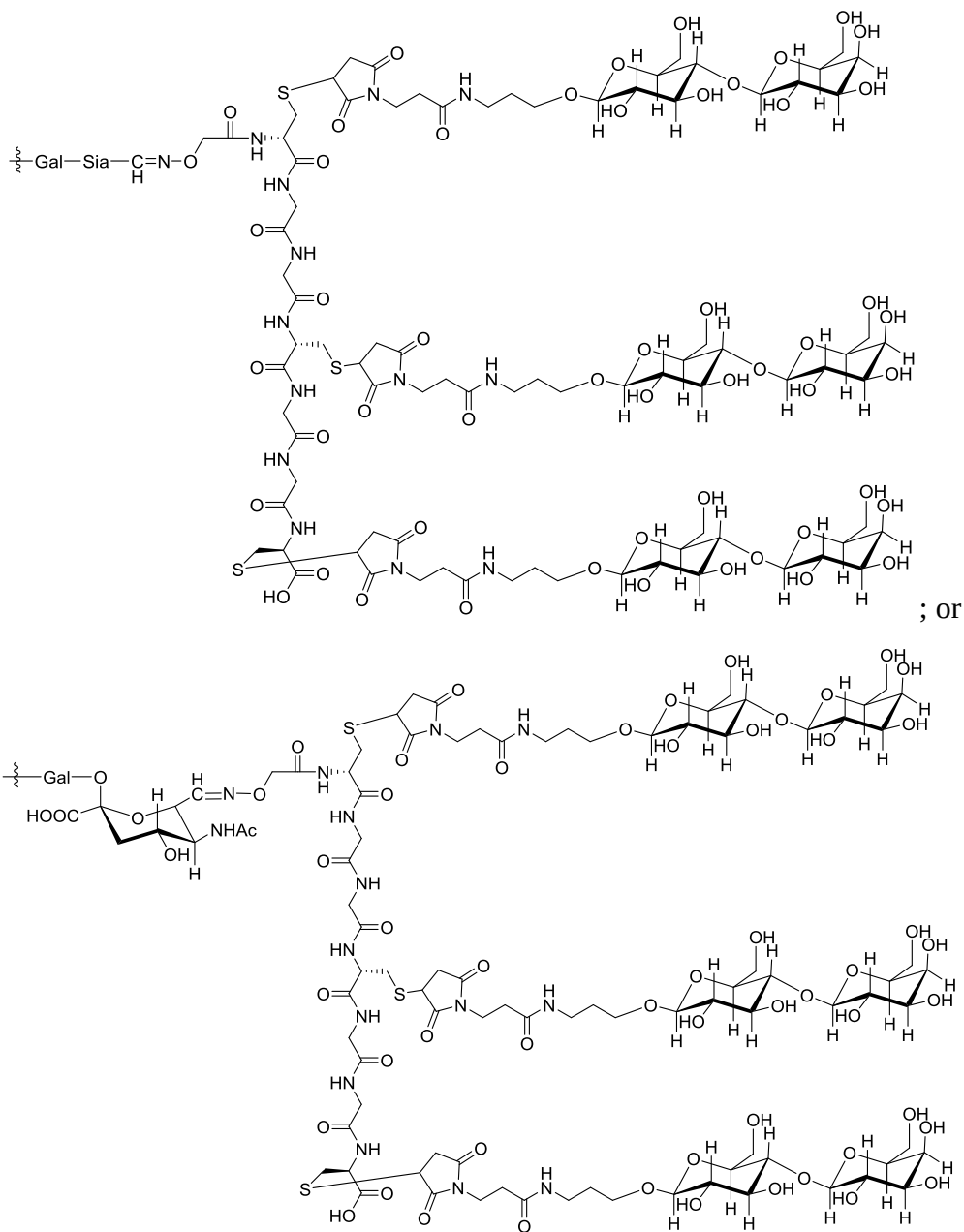
wherein the targeting moiety comprises an α 2,3-siallylactose moiety or an α 2,6-siallylactose moiety, or

wherein the targeting moiety is a tri-galactosylated glycopeptide or lactose₃-Cys₃Gly₄, optionally wherein Sia is present and the lactose₃-Cys₃Gly₄ moiety is represented by Formula V:



Formula V

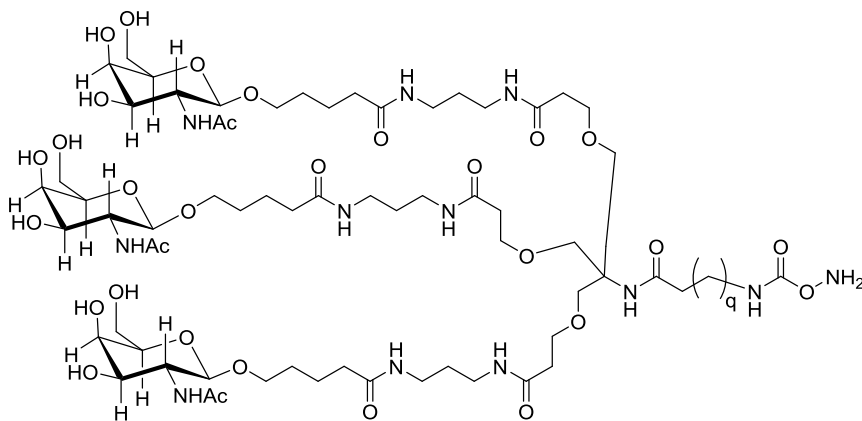
6. The binding polypeptide of claim 5, wherein the glycan comprises at least one moiety selected from the following structural formulae:



7. The binding polypeptide of claim 2, wherein the targeting moiety is a trivalent GalNAc glycan moiety.

8. The binding polypeptide of claim 7, wherein one or more of the following conditions are met:

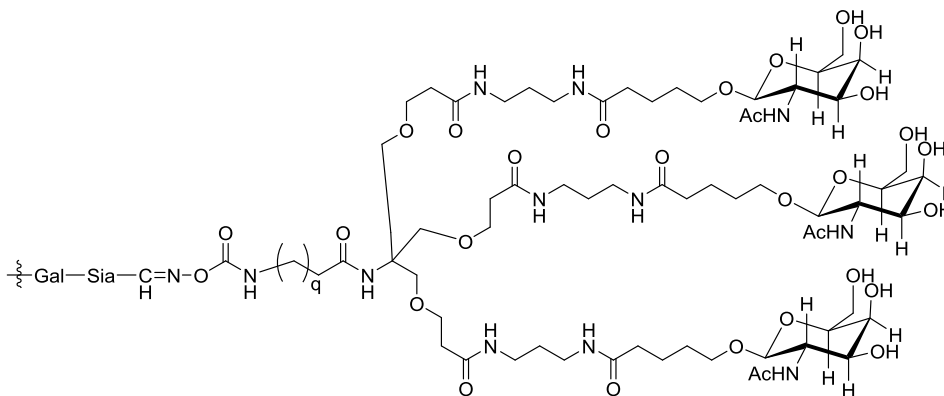
a) Sia is present and the trivalent GalNAc glycan moiety is represented by Formula VIII:



Formula VIII

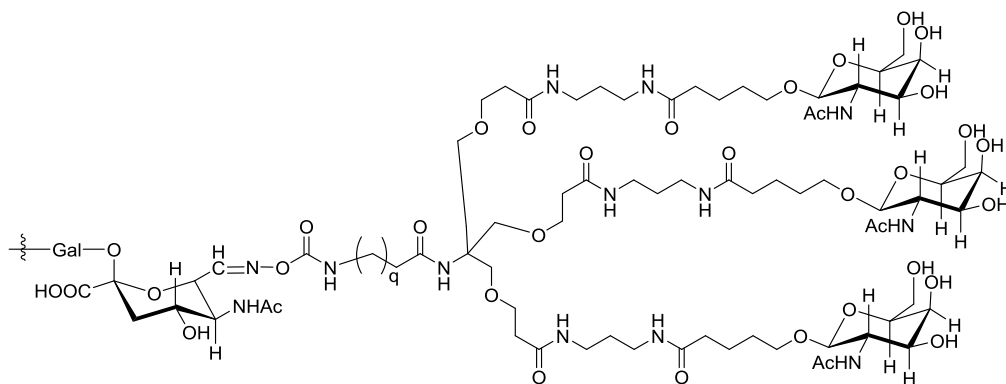
wherein q is an integer between 1 and 29 inclusive;

b) the glycan comprises at least one moiety having the following structural formula:



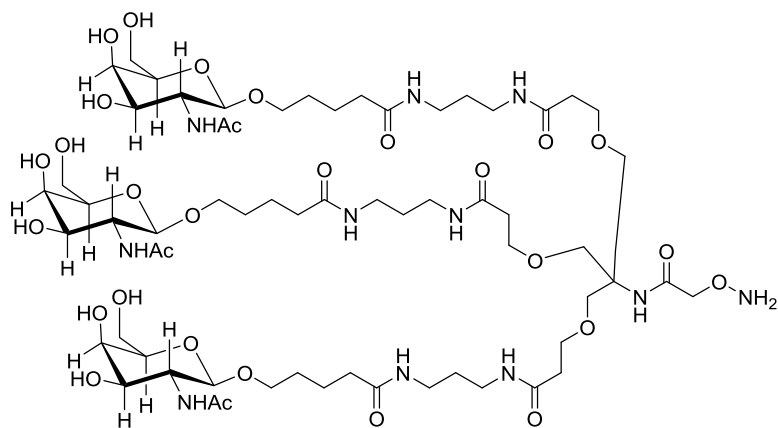
wherein q is an integer between 1 and 29 inclusive;

c) the glycan comprises at least one moiety having the following structural formula:

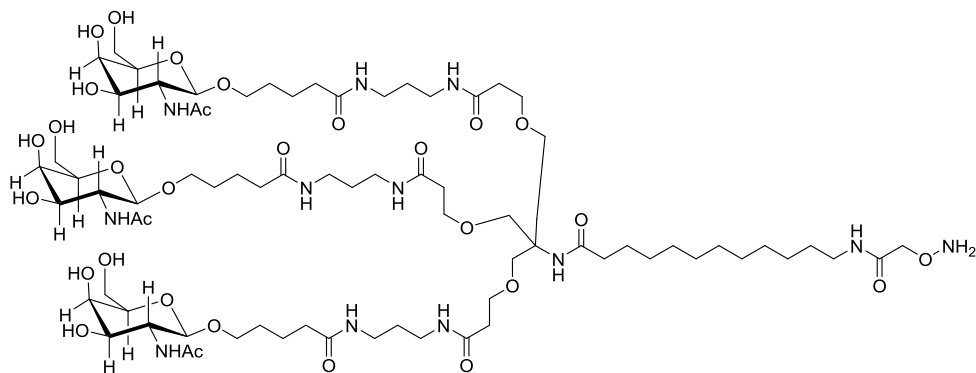


wherein q is an integer between 1 and 29 inclusive;

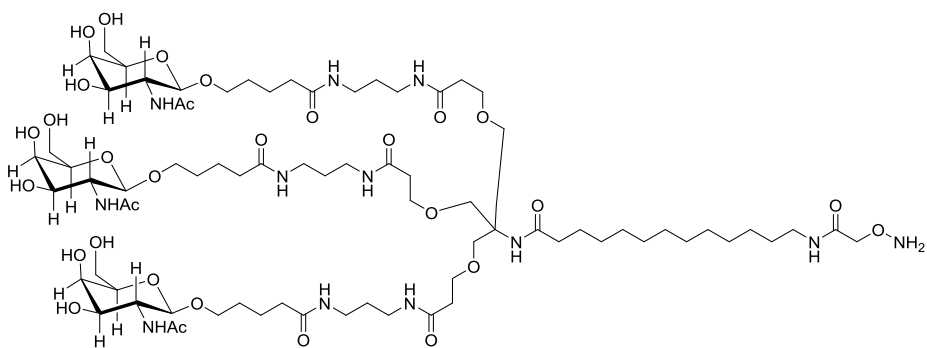
d) the trivalent GalNAc glycan moiety is represented by Formula VII, Formula XIII, or Formula XIV:



Formula VII

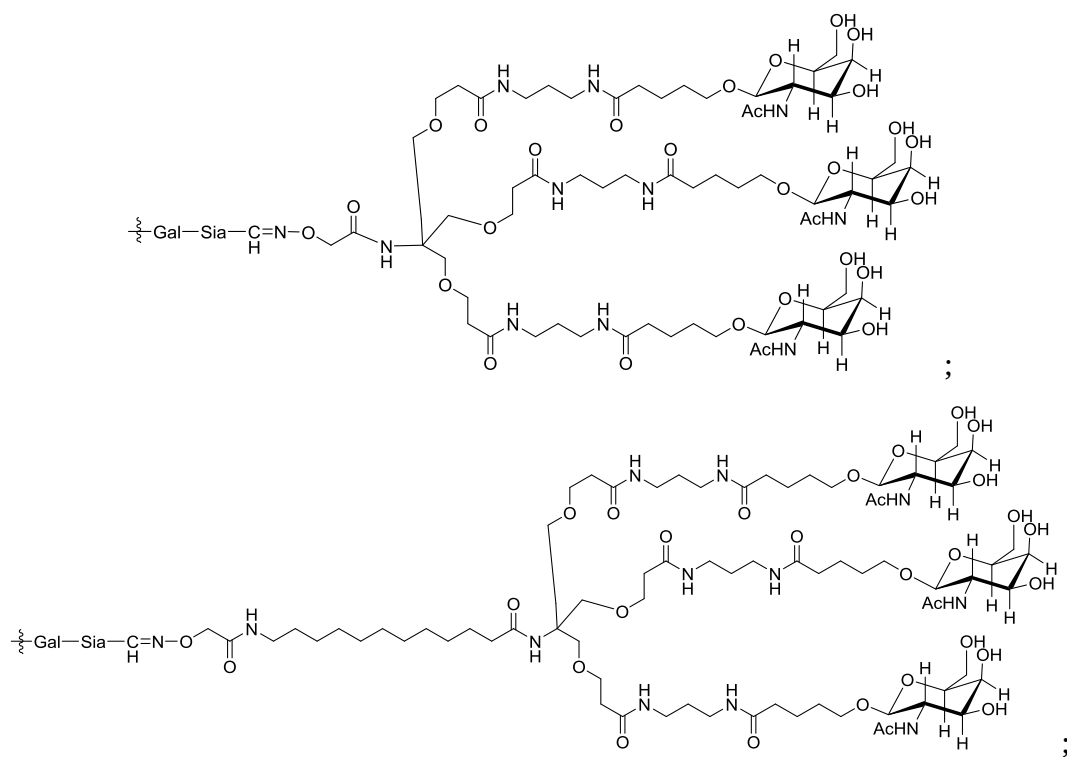


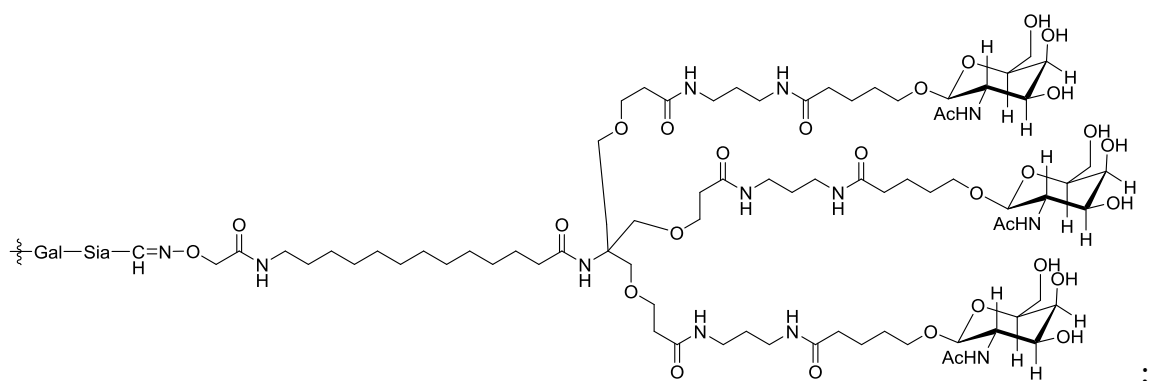
Formula XIII or



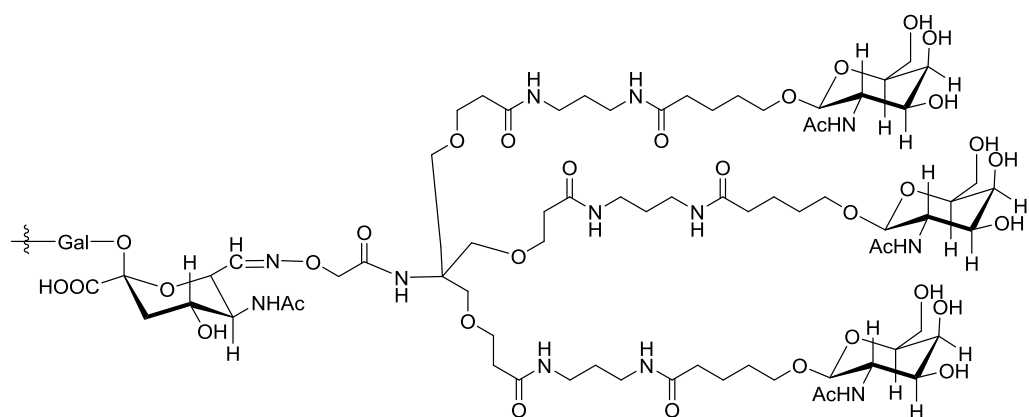
Formula XIV; and

e) the glycan comprises at least one moiety selected from the following structural formulae:

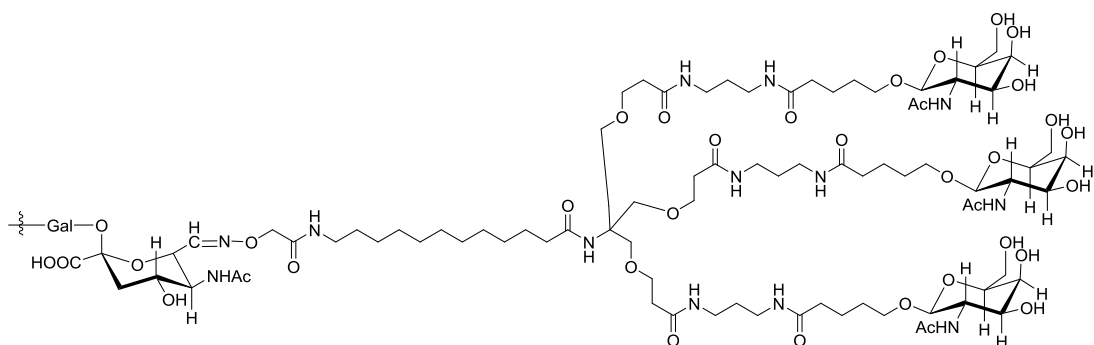




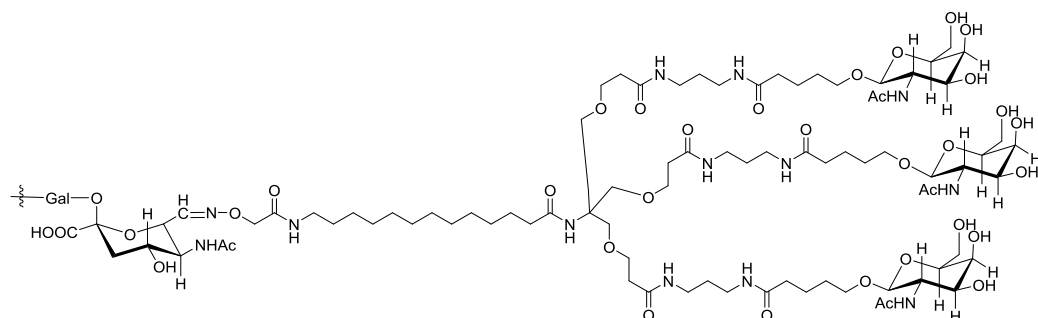
;



;



; or

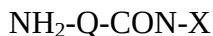


9. The binding polypeptide of any one of the preceding claims, wherein one or more of the

following conditions are met:

- a) the binding polypeptide comprises an Fc domain, wherein the Fc domain is optionally human;
- b) the binding polypeptide comprises a CH1 domain;
- c) the connector moiety comprises a pH-sensitive linker, disulfide linker, enzyme-sensitive linker or other cleavable linker moiety;
- d) the connector moiety comprises a linker moiety selected from the group consisting of linker moieties depicted in Table 2 and 14;
- e) the binding polypeptide is an antibody or immunoadhesin;
- f) the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 297 of the Fc domain, according to EU numbering;
- g) the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 298 of the Fc domain, according to EU numbering; and
- h) the modified glycan is N-linked to the binding polypeptide via an asparagine residue at amino acid position 114 of the CH1 domain, according to Kabat numbering.

10. A method of making the binding polypeptide of any one of the preceding claims, the method comprising reacting an effector moiety of Formula (I):



Formula (I),

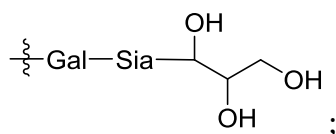
wherein:

- A) Q is NH or O;
- B) CON is a connector moiety; and
- C) X is a targeting moiety,

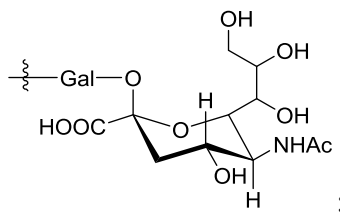
with a precursor binding polypeptide comprising an oxidized glycan.

11. The method of claim 10, wherein one or more of the following conditions are met:

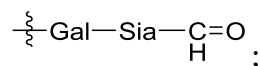
- a) the initial binding polypeptide comprises at least one moiety of the following structural formula:



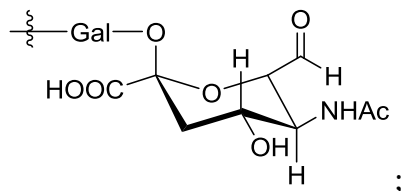
b) the initial binding polypeptide comprises at least one moiety of the following structural formula:



c) the precursor binding polypeptide comprises an oxidized glycan comprises at least one moiety of the following structural formula:



d) the precursor binding polypeptide comprises an oxidized glycan comprises at least one moiety of the following structural formula: and

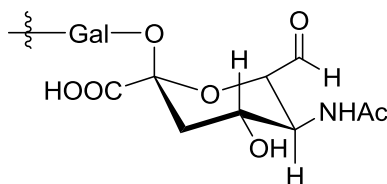


e) the precursor binding polypeptide comprising an oxidized glycan is generated by reacting an initial binding polypeptide comprising a glycan with a mildly oxidizing agent, optionally wherein the mildly oxidizing agent is sodium periodate, wherein less than 1mM sodium periodate is employed, or wherein the mildly oxidizing agent is periodate or galactose oxidase.

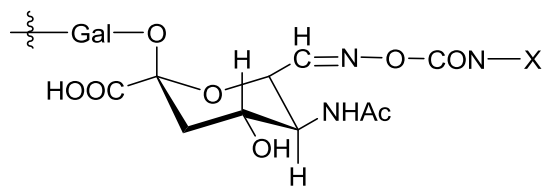
12. The method of claim 10 comprising reacting an effector moiety of the following structural formula:



with the precursor binding polypeptide comprising an oxidized glycan comprising at least one moiety of the following structural formula:

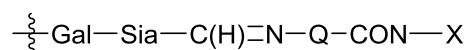


to form a binding polypeptide of the following structural formula:



wherein the targeting moiety is optionally a trivalent GalNAc glycan moiety.

13. The method of claim 11, wherein the reacting step is conducted in the presence of a salt comprising a metal ion, optionally wherein
 - the metal ion is a copper ion,
 - the salt is copper acetate, or
 - the salt comprises a metal ion present at a concentration of at least 0.1 mM.
14. The method of any of any one of the preceding claims wherein the binding polypeptide comprising the glycan comprises one or two terminal sialic acid residues, optionally wherein the one or two terminal sialic acid residues are introduced by treatment of the binding polypeptide with a sialyltransferase or combination of sialyltransferase and galactosyltransferase.
15. A composition comprising a binding polypeptide of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient, optionally wherein the ratio of targeting moiety to binding polypeptide is at least about 2 or equal to or more than about 4.
16. Use of an effective amount of the composition of claim 15 in the manufacture of a medicament for the treatment of neoplastic disorders in a patient in need thereof.
17. A binding polypeptide comprising at least one modified glycan comprising at least one moiety of Formula (IV):



Formula (IV)

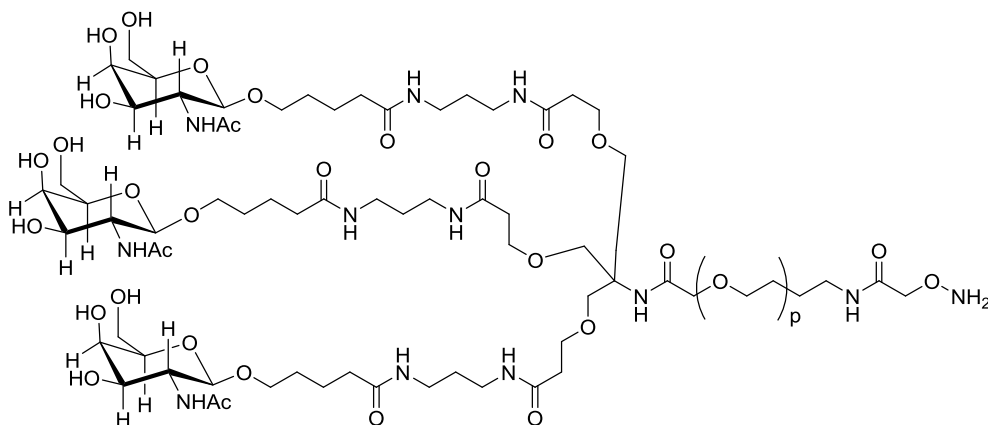
wherein:

- A) Q is NH or O;
- B) CON is a connector moiety;
- C) X is a moiety comprising PEG;
- D) Gal is a component derived from galactose; and
- E) Sia is a component derived from sialic acid,

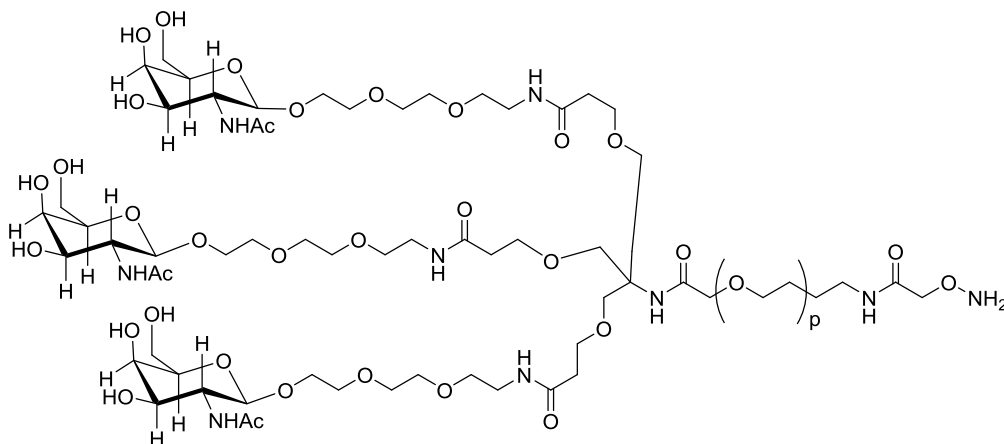
wherein Sia is present or absent.

18. The binding polypeptide of claim 17, wherein one or more of the following conditions are met:

a) the glycan comprises at least one moiety represented by Formula IX or Formula XI:

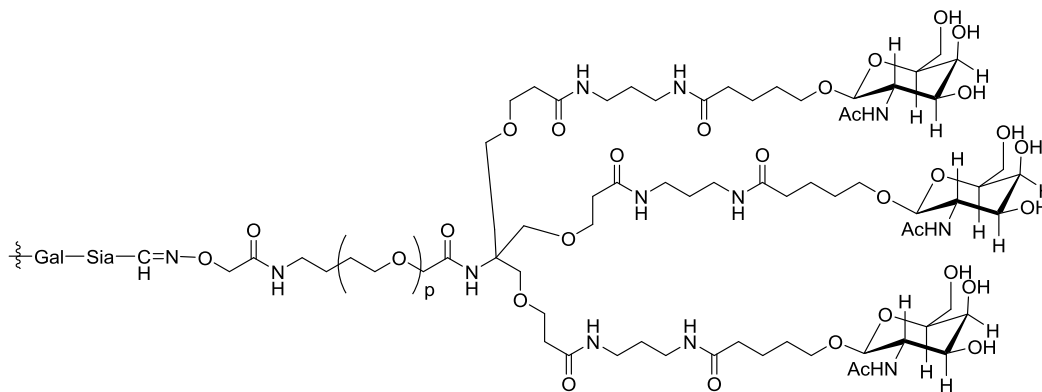


[Formula IX], wherein p has a value of 1 to 32; or

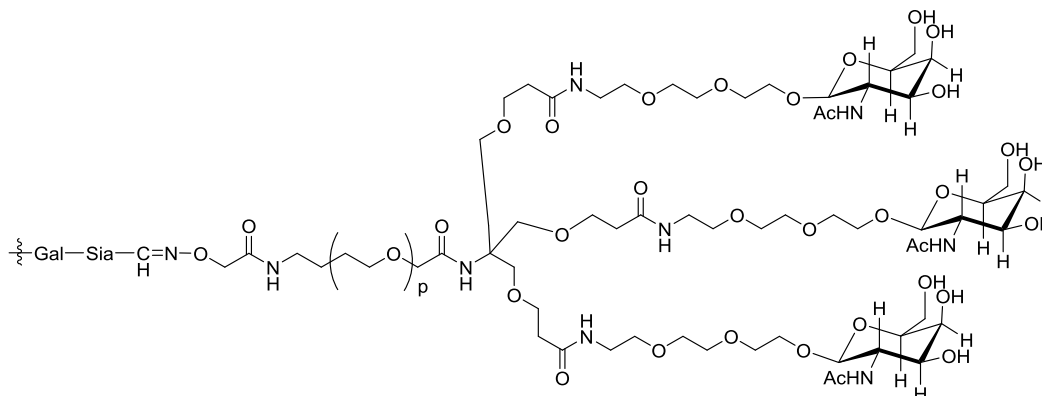


[Formula XI], wherein p has a value of 1 to 32;

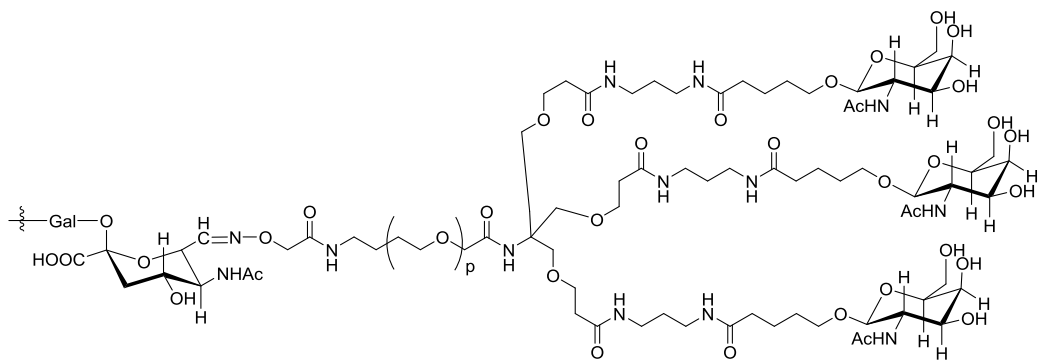
b) the glycan comprises at least one moiety selected from the following structural formulae:



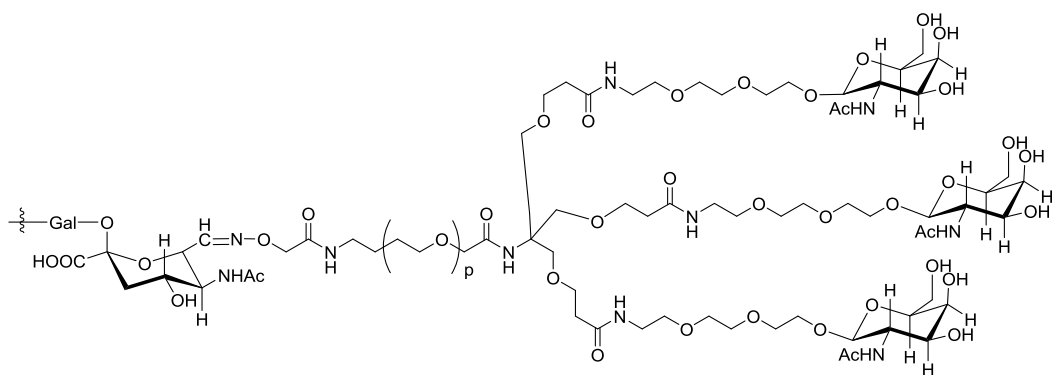
wherein p has a value of 1 to 32;



wherein p has a value of 1 to 32;

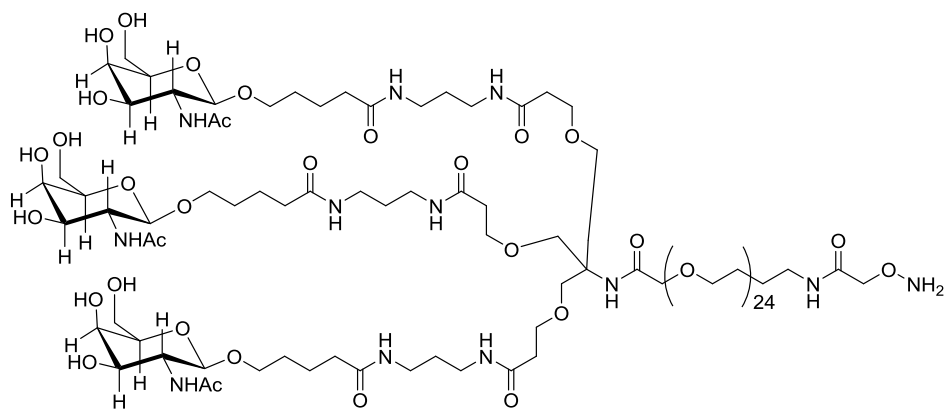


wherein p has a value of 1 to 32; or

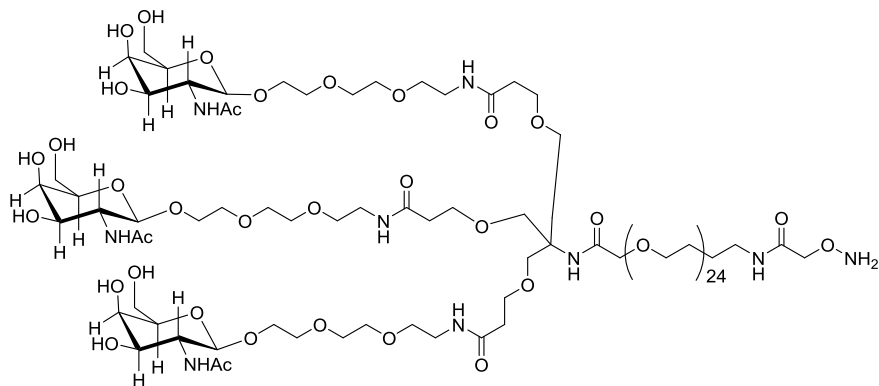


wherein p has a value of 1 to 32;

c) the targeting moiety comprises PEG and is represented by Formula X or Formula XII:

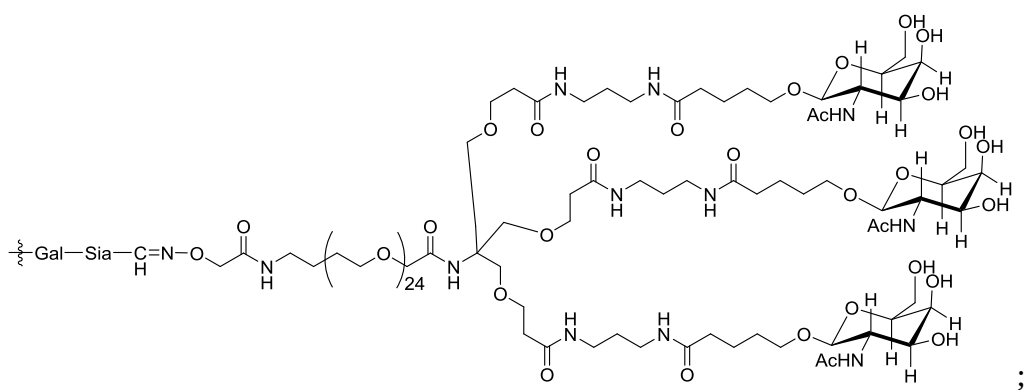
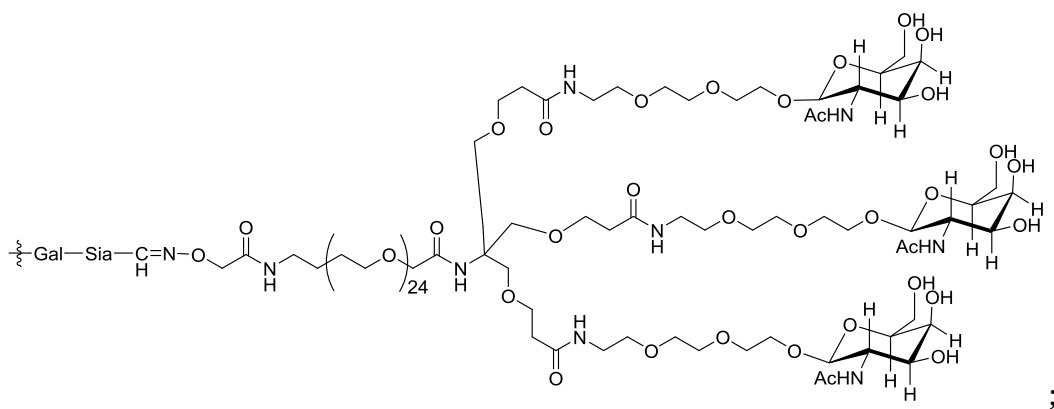
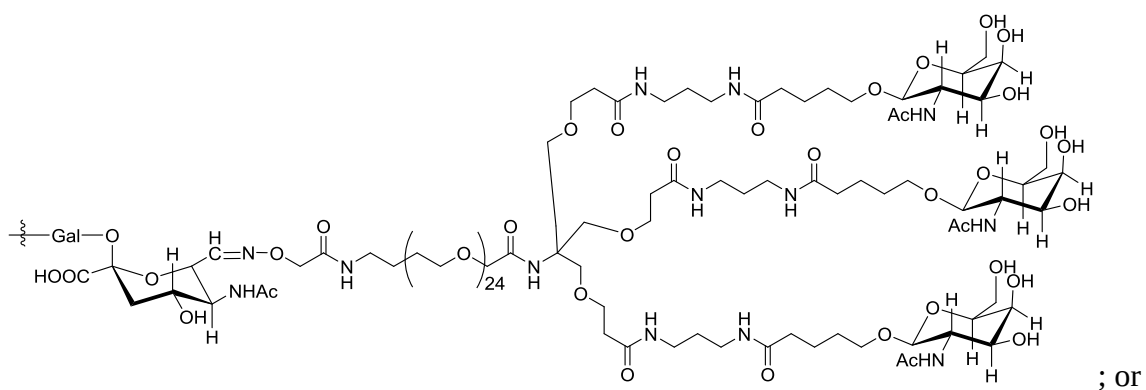
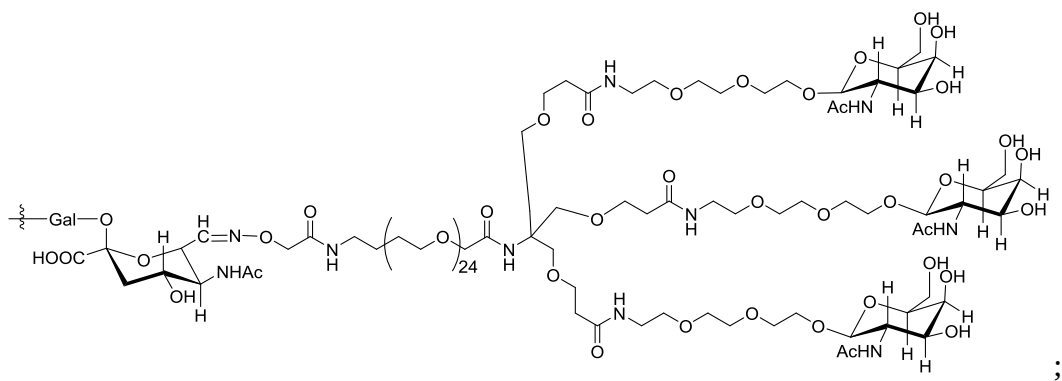


[Formula X]; or



[Formula XII];

d) the glycan comprises at least one moiety selected from the following structural formulae:



e) the PEG comprises mono-PEG, bi-PEG, or tri-PEG, wherein

- the PEG optionally comprises 3 to 3.5 PEG; and
- f) the binding polypeptide is an antibody or immunoadhesin.
18. A method of making a PEGylated binding polypeptide, wherein the method comprises:
- (a) reacting a binding polypeptide comprising at least one glycan with a mildly oxidizing agent in the presence of a salt comprising a metal ion to generate an oxidized binding polypeptide comprising at least one oxidized glycan, and
 - (b) conjugating the oxidized binding polypeptide with at least one moiety comprising PEG, thereby generating the PEGylated binding polypeptide.
19. The method of claim 18, wherein one or more of the following conditions are met:
- a) the metal ion is a copper ion;
 - b) the salt is copper acetate;
 - c) the salt comprising a metal ion is present at a concentration of at least 0.1 mM;
 - d) the mildly oxidizing agent is periodate oxidase or galactose oxidase; and
 - e) the at least one glycan is a modified glycan.