CLAIMS

We claim:

1. An antibody or antigen-binding fragment thereof comprising at least one modified glycan comprising at least one moiety of Formula (IV):

-Gal-Sia-C(H)=N-Q-CON-X

Formula (IV),

wherein:

A) Q is NH or O;

B) CON is a linker moiety; and

C) X is an effector moiety selected from the group consisting of a cytotoxin, a detection agent and a targeting moiety;

D) Gal is a galactose moiety; and

E) Sia is a sialic acid moiety.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the modified glycan is a biantennary glycan.

3. The antibody or antigen-binding fragment thereof of claims 1 or 2, wherein the biantennary glycan is fucosylated or non-fucosylated.

4. The antibody or antigen-binding fragment thereof of any one of the preceding claims, said modified glycan comprising at least two moieties of Formula (IV), wherein Sia is present in only one of the two moieties.

5. The antibody or antigen-binding fragment thereof of any one of claims 1-3, said modified glycan comprising at least two moieties of Formula (IV), wherein Sia is present in both of the two moieties.

6. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the modified glycan is N-linked to the binding polypeptide.

7. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the binding polypeptide comprises an Fc domain.

8. The antibody or antigen-binding fragment thereof of claim 7, 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.

9. The antibody or antigen-binding fragment thereof of claim 8, 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. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the Fc domain is human.

11. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the binding polypeptide comprises a CH1 domain.

12. The antibody or antigen-binding fragment thereof of claim 11, 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.

13. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the effector moiety is a cytotoxin.

14. The antibody or antigen-binding fragment thereof of claim 13, wherein the cytotoxin is selected from the group consisting of the cytotoxins listed in Table 1.

15. The antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein the effector moiety is a detection agent.

16. The antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein the effector moiety is a targeting moiety.

17. The antibody or antigen-binding fragment thereof of claim 16, wherein the targeting moiety is a carbohydrate or glycopeptide.

18. The antibody or antigen-binding fragment thereof of claim 16, wherein the targeting moiety is a glycan.

19. The antibody or antigen-binding fragment thereof of any one of the previous claims, wherein the linker moiety comprises a pH-sensitive linker, disulfide linker, enzyme-sensitive linker or other cleavable linker moiety.

20. The antibody or antigen-binding fragment thereof of any one of the previous claims, wherein the linker moiety is selected from the group of linker moieties depicted in Table 2 or 14.

21. The antibody or antigen-binding fragment thereof of any one of the preceding claims which is an IgG antibody or immunoadhesin.

22. A composition comprising an antibody or antigen-binding fragment thereof of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.

23. The composition of claim 22, wherein the ratio of therapeutic or diagnostic effector moiety to antibody or antigen-binding fragment thereof is less than 4.

24. The composition of claim 23, wherein the ratio of therapeutic or diagnostic effector moiety to antibody or antigen-binding fragment thereof is about 2.

25. An isolated polynucleotide encoding the antibody or antigen-binding fragment thereof of any one of claims 1-21.

26. A vector comprising the polynucleotide of claim 25.

27. A host cell comprising the polynucleotide or vector of claims 25 or 26.

28. A method of making an antibody or antigen-binding fragment thereof of any one of the preceding claims, the method comprising reacting an effector moiety of Formula (I):

NH2-Q-CON-X

Formula (I),

wherein:

A) Q is NH or O;

B) CON is a linker moiety; and

C) X is an effector moiety selected from the group consisting of a cytotoxin, a detection agent and a targeting moiety,

with an altered antibody or antigen-binding fragment thereof comprising a glycan comprising an oxidized sialic acid moiety.

29. The method of claim 28, further comprising reacting an antibody or antigen-binding fragment thereof comprising a glycan comprising a sialic acid moiety with an oxidizing agent.

30. The method of claim 29, wherein the oxidizing agent is sodium periodate.

31. The method of claim 30, wherein less than 1mM sodium periodate is employed.

32. The method of claim 29, wherein the oxidizing agent is galactose oxidase.

33. The method of any of claims 28-32, wherein the antibody or antigen-binding fragment thereof comprising the glycan comprises one or two terminal sialic acid moieties.

34. The method of claim 33, further comprising treating an antibody or antigen-binding fragment thereof comprising the glycan with a sialyltransferase or combination of sialyltransferase and galactosyltransferase to introduce one or two terminal sialic acid moiety(ies).

35. The antibody or antigen-binding fragment thereof of any of the preceding claims, wherein the antibody or antigen-binding fragment thereof binds human epidermal growth factor receptor 2 (HER2) or fibroblast activation protein (FAP).

36. An antibody or antigen-binding fragment thereof comprising at least one modified glycan comprising at least one moiety of Formula (IV):

-Gal-Sia-C(H)=N-Q-CON-X

Formula (IV),

wherein:

A) Q is O;

B) CON is Cys-MC-VC-PABC;

C) X is MMAE;

D) Gal is a galactose moiety; and

E) Sia is a sialic acid moiety.

37. An antibody or antigen-binding fragment thereof comprising at least one modified glycan comprising at least one moiety of Formula (IV):

-Gal-Sia-C(H)=N-Q-CON-X

Formula (IV),

wherein:

A) Q is NH or O;

B) CON is a linker moiety;

C) X is an effector moiety selected from the group consisting of a cytotoxin, a detection agent and a targeting agent;

D) Gal is a galactose moiety; and

E) Sia is a sialic acid moiety;

wherein the glycan is selected from the group consisting of one or any combination of a biantennary glycan, a glycan comprising at least two moieties of Formula (IV), and a glycan that is N-linked to the antibody or antigen-binding fragment thereof.

38. An antibody or antigen-binding fragment thereof comprising at least one glycan comprising at least one moiety of Formula (IV):

-Gal-Sia-C(H)=N-Q-CON-X

Formula (IV),

wherein:

A) Q is NH or O;

B) CON is a linker moiety;

C) X is an effector moiety selected from the group consisting of a cytotoxin, a detection agent and a targeting agent;

D) Gal is a galactose moiety; and

E) Sia is a sialic acid moiety;

wherein the antibody or antigen-binding fragment binds HER2 or FAP.