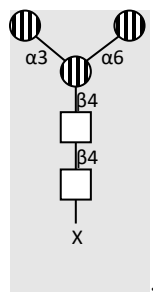


WHAT IS CLAIMED IS:

1. A bifunctional binding protein comprising a first moiety that specifically binds to a target protein and a second moiety comprising a glycan comprising the structure:



wherein the square represents an N-acetylglucosamine residue and the black striped circle represents a mannose residue, and wherein X represents an amino acid residue of the bifunctional binding protein.

2. The bifunctional binding protein of claim 1, wherein the glycan further comprises a fucose residue at the N-acetylglucosamine that is directly attached to X, optionally wherein X is an asparagine residue in the bifunctional binding protein.
3. The bifunctional binding protein of claim 1, wherein the glycan consists of the structure of claim 1.
4. The bifunctional binding protein of claim 1, wherein the target protein comprises HER2, EGFR, HER3, VEGFR, CD20, CD19, CD22, $\alpha\text{v}\beta 3$ integrin, CEA, CXCR4, MUC1, LCAM1, EphA2, PD-1, PD-L1, TIGIT, TIM3, CTLA4, VISTA, Notch receptors, EGF, c-MET, Frizzled receptors, Wnt, LRP5/6, CD38, CD73, TGF- β , Bombesin R, CAIX, CD13, CD44, v6, CXCR4, ErbB-2, Her2, Emmprin, Endoglin, EpCAM, EphA2, FAP- α , Folate R, GRP78, IGF-1R, Matriptase, Mesothelin, sMET/HGFR, MT1-MMP, MT6-MMP, Muc-1, PSCA, PSMA, Tn antigen, and uPAR, TSHR α , AChR- $\alpha 1$, noncollagen domain 1 of the $\alpha 3$ chain of type IV collagen ($\alpha 3\text{NC1}$), ADAMTS13, Desmoglein-1/3, or GPIb/IX, GPIIb/IIIa, GPIa/IIa, NMDA receptor, glutamic acid decarboxylase (GAD), amphiphysin and gangliosides GM1, GD3, GQ1B, MOG, SIRP α , CCR2, CSF-1R, LILRB1, LILRB2, VEGF-R, CXCR4, CCL2, CXCL12, CSF-1, CD47,

or misfolded light chain and misfolded transthyretin; preferably wherein the target protein comprises PD-L1, SIRP α or CD47.

5. The bifunctional binding protein of claim 1, wherein the second moiety specifically binds to: (i) a mannose 3 receptor, a Cluster of Differentiation 206 (CD206) receptor, a DC-SIGN (Cluster of Differentiation 209 or CD209) receptor, a C-Type Lectin Domain Family 4 Member G (LSECTin) receptor, a macrophage inducible Ca²⁺-dependent lectin receptor (Mincle); or (ii) any endocytic carbohydrate-binding receptor recognizing Man3GlcNAc2 structure; preferably wherein the second moiety specifically binds to a Cluster of Differentiation 206 (CD206) receptor.

6. The bifunctional binding protein of claim 1, wherein the first moiety comprises: (i) a heavy chain variable region or a light chain variable region; or (ii) a Fab region of a monoclonal antibody.

7. The bifunctional binding protein of claim 1, wherein the bifunctional binding protein is an antibody, optionally wherein the antibody is: (i) a monoclonal or polyclonal antibody; or (ii) recombinant; or (iii) humanized, chimeric or fully human.

8. The bifunctional binding protein of claim 7, wherein:

(a) the antibody has a glycan to protein ratio of 2 to 1, 4 to 1, 6 to 1, 8 to 1, or 10 to 1; and/or

(b) the antibody is glycosylated at a predetermined and specific residue.

9. The bifunctional binding protein of claim 1, wherein the bifunctional binding protein is an autoantigen.

10. The bifunctional binding protein any one of claims 1 to 9, wherein at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% the glycans of the bifunctional binding protein have the structure of the glycan of claim 1.

11. The bifunctional binding protein of claim 1, wherein the target protein is a cell surface molecule or a non-cell surface molecule, optionally wherein the cell surface molecule is a receptor, and optionally wherein the non-cell surface molecule is an extracellular protein.

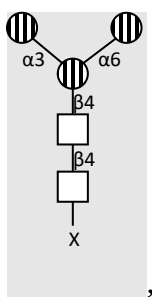
12. The bifunctional binding protein of claim 11, wherein the target protein is bound by the first moiety.
13. Use of the bifunctional binding protein of any one of claims 1 to 12 in the manufacture of a medicament for delivering a target protein to liver macrophages, wherein the delivery comprises contacting the target protein with the bifunctional binding protein under conditions suitable to mediate endocytosis of the target protein.
14. Use of the bifunctional binding protein of any one of claims 1 to 12 in the manufacture of a medicament for degrading a target protein, wherein the degrading comprises contacting the target protein with the bifunctional binding protein under conditions suitable to mediate lysosomal degradation of the target protein by a host cell.
15. The use of claim 14, wherein the target protein is upregulated in cancer or involved in cancer progression, optionally wherein the target protein upregulated in cancer or involved in cancer progression comprises HER2, EGFR, HER3, VEGFR, CD20, CD19, CD22, $\alpha\text{v}\beta 3$ integrin, CEA, CXCR4, MUC1, LCAM1, EphA2, PD-1, PD-L1, TIGIT, TIM3, CTLA4, VISTA, Notch receptors, EGF, c-MET, CCL2, CCR2, Frizzled receptors, Wnt, LRP5/6, CSF-1R, SIRP α , LILRB1, LILRB2, CD38, CD73, or TGF- β .
16. The use of claim 14, wherein the target protein is an autoantibody of an autoimmune disease or an autoantigen in an autoimmune disease, optionally wherein the autoantibody in the autoimmune disease is an antibody binding to MOG, TSHR α , AChR- $\alpha 1$, noncollagen domain 1 of the $\alpha 3$ chain of type IV collagen ($\alpha 3\text{NC1}$), ADAMTS13, Desmoglein-1/3, GPIb/IX, GPIIb/IIIa, GPIa/IIa, NMDA receptor, glutamic acid decarboxylase (GAD), amphiphysin, or gangliosides GM1, GD3 or GQ1B.
17. The use of claims 14, wherein the target protein is upregulated or expressed in a neurodegenerative disease, optionally wherein the target protein upregulated or expressed in a neurodegenerative disease is alpha-synuclein, amyloid beta or complement cascade component.

18. The use of claim 14, wherein the host cell is a myeloid cell, an immune cell, an endothelial cell, a parenchymal cell, or an epithelial cell, optionally wherein the immune cell is a dendritic cell, a macrophage, a monocyte, a microglia cell, a granulocyte or a B lymphocyte.
19. The use of claim 14, wherein said bifunctional binding protein enhances degradation of the target protein relative to degradation of the target protein in the presence of a bifunctional binding protein comprising a different second moiety.
20. The use of claim 14, wherein said degradation is mediated by endocytosis or phagocytosis.
21. A pharmaceutical composition comprising the bifunctional binding protein of any one of claims 1 to 12 and a pharmaceutically acceptable carrier.
22. Use of the bifunctional binding protein of any one of claims 1 to 12 or the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating or preventing a disease in a patient.
23. The use of claim 22, wherein the disease is an autoimmune disease, a cancer or tumor, a liver disease, an inflammatory disorder, or a blood coagulation disorder.
24. The use of claim 23, wherein
 - a. the autoimmune disease is selected from MOGAD (Myelin oligodendrocyte glycoprotein antibody-associated disease), Graves' Disease, Myasthenia Gravis, Anti-GBM Disease, Immune Thrombotic Thrombocytopenic Purpura, Acquired Pemphigus Vulgaris, Immune Thrombocytopenia, autoimmune encephalitis, and Guillain-Barré Syndrome; or
 - b. the cancer is selected from lung cancer, breast cancer, gastric cancer, colorectal cancer, bladder cancer, malignant melanoma, multiple myeloma, and Hodgkin's lymphoma.
25. The use of claim 24, wherein treatment comprises reprogramming tumor associated macrophages (TAMs) by administering the bifunctional binding protein under conditions to mediate endocytosis of a target protein.

26. The use of claim 25, wherein the target protein is upregulated or expressed in TAMs, optionally wherein the target protein upregulated or expressed in TAMs comprises SIRP α , CCR2, CSF-1R, LILRB1, LILRB2, VEGF-R, CXCR4, CCL2, CXCL12, CSF-1 or CD47.

27. A kit comprising the bifunctional binding protein of any one of claims 1 to 12, or the pharmaceutical composition of claim 21 and instructions for administering the bifunctional molecule or pharmaceutical composition to an individual in need thereof.

28. A bifunctional binding protein, wherein the bifunctional binding protein (i) specifically binds to a target protein and (ii) comprises an N-glycan of the structure:



wherein the square represents an N-acetylglucosamine residue and the black striped circle represents a mannose residue, and wherein X represents an amino acid residue of the bifunctional binding protein, wherein the N-glycan is linked to the bifunctional binding protein at 1, 2, 3, 4 or 5 N-glycosylation sites.

29. The bifunctional binding protein of claim 28, wherein the glycan further comprises a fucose residue at the N-acetylglucosamine that is directly attached to X, optionally wherein X is an asparagine residue in the bifunctional binding protein.

30. A population of bifunctional binding proteins according to claim 29, wherein for at least one of the N-glycosylation sites at a specified amino acid position of the bifunctional binding protein, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or 99% of N-glycosylation sites in the population are glycosylated with the N-glycan specified in claim 29.

31. The bifunctional binding protein of claim 29 or the population of claim 30, wherein the N-glycosylation site comprises one or more asparagine residues, wherein the asparagine residues are within a canonical consensus sequence N-X-S/T, N-X-C motifs, and non-canonical consensus motifs.

32. The bifunctional binding protein of claim 29 or the population of claim 30, wherein the N-glycosylation site is introduced into the bifunctional protein by recombinant engineering, optionally wherein the recombinant engineering is performed adding an amino acid, deleting an amino acid, substituting an amino acid, or adding a glycotag.

33. The bifunctional binding protein of claim 29 or the population of claim 30 wherein the glycan consists of the structure of claim 29.

34. The bifunctional binding protein of claim 29 or the population of claim 30, wherein the bifunctional proteins binds to an endocytic carbohydrate-binding receptor, specifically binds to a mannose 3 receptor, a Cluster of Differentiation 206 (CD206) receptor, a DC-SIGN (Cluster of Differentiation 209 or CD209) receptor, a C-Type Lectin Domain Family 4 Member G (LSECTin) receptor, a macrophage inducible Ca^{2+} -dependent lectin receptor (Mincle).

35. The bifunctional binding protein of claim 29 or the population of claim 30, wherein the bifunctional binding protein is an antibody, optionally wherein the antibody has a glycan to protein ratio of 2 to 1, 4 to 1, 6 to 1, 8 to 1, or 10 to 1.

36. The bifunctional binding protein of claim 35, wherein the antibody comprises an N-glycosylation site in:

(a) the Fc domain and wherein the N-glycan is linked to the N-glycosylation site in the Fc domain; and/or

(b) the heavy chain variable regions and/or light chain variable regions and wherein the N-glycan is linked to the N-glycosylation site in the heavy chain variable regions and/or light chain variable regions.

37. Use of the bifunctional binding protein or population of any one of claims 29 to 36 in the manufacture of a medicament for:

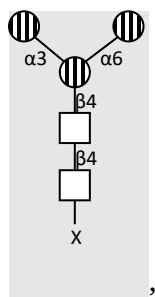
(a) delivering a target protein to liver macrophages, wherein the delivery comprises contacting the target protein with the bifunctional binding protein or population under conditions suitable to mediate endocytosis of the target protein; or

(b) degrading a target protein, wherein the degrading comprises contacting the target protein with the bifunctional binding protein or population under conditions suitable to mediate lysosomal degradation of the target protein by a host cell.

38. A pharmaceutical composition comprising the bifunctional binding protein or population of any one of claims 29 to 36 and a pharmaceutically acceptable carrier.

39. Use of the bifunctional binding protein or population of any one of claims 29 to 36 in the manufacture of a medicament for treating or preventing a disease in a patient.

40. Use of a bifunctional binding protein of any one of the preceding claims in the manufacture of a medicament for treating an acute or chronic condition associated with increased levels of a target protein, wherein the treating comprises administering the bifunctional binding protein to a patient in need of treatment, wherein the bifunctional binding protein (i) specifically binds to the target protein and (ii) comprises an N-glycan of the structure



wherein the square represents an N-acetylglucosamine residue and the black striped circle represents a mannose residue, and wherein X represents an amino acid residue of the bifunctional binding protein, wherein the N-glycan is linked to the bifunctional binding protein at a number of N-glycosylation sites that results in a half-life of the target protein of at most 5 minutes, 15 minutes,

30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, or 6 hours in a patient after administration of the bifunctional binding protein to the patient, or that results in a half-life of the target protein of at most 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 75%, 80%, or at most 90% of the half-life of the target protein in the patient in the absence of any treatment, and optionally wherein the bifunctional protein carries the N-glycan at three or more N-glycosylation sites.