

CLAIMS

1. A composition comprising a multispecific protein, a buffer, an excipient and a surfactant, wherein

(a) the multispecific protein is a dimer of two identical polypeptides, wherein each polypeptide comprises, in order from amino-terminus to carboxyl-terminus, or in order from carboxyl-terminus to amino-terminus:

(i) a first binding domain selected from a CD3 binding domain, a 4-1-BB binding domain, an OX40 binding domain, or a tumor antigen binding domain which binds to CD123, PSMA, CD19, CD33, or HER2,

(ii) a hinge region,

(iii) an immunoglobulin constant region, and

(iv) a second binding domain selected from a CD3 binding domain, a 4-1-BB binding domain, an OX40 binding domain, or a tumor antigen binding domain which binds to CD123, PSMA, CD19, CD33, or HER2;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

2. The composition of claim 1, wherein the composition comprises about 5 mM succinate or a pharmaceutically acceptable salt or acid thereof.

3. The composition of claim 1 or 2, wherein the sugar is sucrose.

4. The composition of claim 3, wherein the composition comprises about 6.5% (w/v) of the sugar.

5. The composition of any one of claims 1-4, wherein the composition comprises about 0.02% w/v polysorbate 80.

6. The composition of any one of claims 1-5, wherein the composition comprises from 0.1 mg/ml to 10 mg/ml of the multispecific protein, optionally wherein the

composition comprises from 1 mg/ml to 5 mg/ml of the multispecific protein, and optionally wherein the composition comprises about 2 mg/ml of the multispecific protein.

7. The composition of any one of claims 1-6, wherein the composition comprises about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80.

8. The composition of any one of claims 1-7, wherein the composition has a pH from 4.0 to 5.5, and optionally wherein the composition has a pH of about 4.8.

9. The composition of any one of claims 1-8, wherein the immunoglobulin constant region is a human Fc domain, and optionally wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.

10. The composition of any one of claims 1-9,

(i) wherein the first binding domain is a CD3 binding domain and the second binding domain is a tumor antigen binding domain, and optionally wherein the polypeptide comprises, from N-terminus to C-terminus, the CD3 binding domain, the hinge region, the immunoglobulin constant region, and the tumor antigen binding domain; or

(ii) wherein the first domain is a tumor antigen binding domain, and the second binding domain is a CD3 binding domain, and optionally wherein the polypeptide comprises, from N-terminus to C-terminus, the tumor antigen binding domain, the hinge region, the immunoglobulin constant region, and the CD3 binding domain.

11. The composition of any one of claims 1-9,

(i) wherein the first binding domain is a 4-1-BB binding domain and the second binding domain is a tumor antigen binding domain, and optionally wherein the polypeptide comprises, from N-terminus to C-terminus, the 4-1-BB binding domain, the hinge region, the immunoglobulin constant region, and the tumor antigen binding domain; or

(ii) wherein the first binding domain is a tumor antigen binding domain, and the second binding domain is a 4-1-BB binding domain, and optionally wherein the polypeptide comprises, from N-terminus to C-terminus, tumor antigen binding domain, the hinge region, the immunoglobulin constant region, and the 4-1-BB binding domain.

12. The composition of any one of claims 1-9,

(i) wherein the first binding domain or the second binding domain is a 4-1BB binding domain;

(ii) wherein the first binding domain or the second binding domain is an OX40 binding domain;

(iii) wherein the first binding domain is a 4-1BB binding domain and wherein the second binding domain is an OX40 binding domain, optionally wherein the 4-1BB binding domain is an scFv and the OX40 binding domain is an scFv;

(iv) wherein the first binding domain is an OX40 binding domain and wherein the second binding domain is a 4-1BB binding domain optionally wherein the 4-1BB binding domain is an scFv and the OX40 binding domain is an scFv;

(v) wherein the first binding domain is an OX40 binding domain and the second binding domain is a tumor antigen binding domain; or

(vi) wherein the first binding domain is a tumor antigen binding domain and the second binding domain is an OX40 binding domain.

13. The composition of any one of claims 1-12, wherein at least one of the first binding domain and the second binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

14. The composition of any one of claims 1-13, wherein at least one of the first binding domain and the second binding domain is a single chain variable fragment (scFv), optionally wherein the light chain variable region of the scFv is carboxy-terminal to the heavy chain variable region of the scFv or wherein the light chain variable region of the scFv is amino-terminal to the heavy chain variable region of the scFv; optionally wherein the scFv comprises a linker polypeptide; optionally wherein the linker polypeptide is between the light chain variable region and the heavy chain variable region of the scFv; optionally wherein the linker polypeptide comprises a Gly₄Ser (SEQ ID NO: 128) linker; and optionally wherein the linker polypeptide comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).

15. The composition of any one of claims 10-11,

(i) wherein the tumor antigen binding domain is an anti-CD123 scFv comprising:
a HCDR1 that comprises SEQ ID NO: 10, a HCDR2 that comprises SEQ ID NO: 11, and a HCDR3 that comprises SEQ ID NO: 12; and

a LCDR1 that comprises SEQ ID NO: 13, a LCDR2 that comprises SEQ ID NO: 14, and a LCDR3 that comprises SEQ ID NO: 15;

(ii) wherein the tumor antigen binding domain is an anti-CD123 scFv comprising a VH comprising SEQ ID NO: 136, and a VL comprising SEQ ID NO: 134; or

(iii) wherein the tumor antigen binding domain is an anti-CD123 scFv, and wherein the scFv comprises SEQ ID NO: 27.

16. The composition of claim 10,

(i) wherein the CD3 binding domain is an anti-CD3 scFv comprising:
a HCDR1 that comprises SEQ ID NO: 19, a HCDR2 that comprises SEQ ID NO: 20, and a HCDR3 that comprises SEQ ID NO: 21; and

a LCDR1 that comprises SEQ ID NO: 22, a LCDR2 that comprises SEQ ID NO: 23, and a LCDR3 that comprises SEQ ID NO: 24;

(ii) wherein the CD3 binding domain is an anti-CD3 scFv that comprises a VH comprising SEQ ID NO: 383 or 387, and a VL comprising SEQ ID NO: 384; or

(iii) wherein the CD3 binding domain is an anti-CD3 scFv that comprises SEQ ID NO: 27.

17. The composition of any one of claims 10 or 16, wherein each polypeptide comprises SEQ ID NO: 31.

18. The composition of any one of claims 1-17,

(i) wherein the immunoglobulin constant region comprises one, two, three or more amino acid substitutions compared to a wild-type immunoglobulin constant region to reduce or prevent binding to FcγR1, FcγRIIa, FcγRIIb, FcγRIIa, and FcγRIIIb;

(ii) wherein the immunoglobulin constant region comprises one, two, three or more amino acid substitutions compared to a wild-type immunoglobulin constant region to prevent or reduce Fc-mediated T-cell activation;

(iii) wherein the immunoglobulin constant region comprises one, two, three or more amino acid substitutions compared to a wild-type immunoglobulin constant region to prevent or reduce CDC activity; or

(iv) wherein the immunoglobulin constant region comprises one, two, three or more amino acid substitutions compared to a wild-type immunoglobulin constant region to prevent or reduce ADCC activity.

19. The composition of any one of claims 1-18, wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain with one, two, three or more amino acid substitutions compared to a wild-type human IgG1 CH2 domain.

20. The composition of any one of claims 1-19,

(i) wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions L234A, L235A, G237A, and K322A, according to

the EU numbering system, optionally wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions L234A, L235A, G237A, E318A, K320A and K322A, according to the EU numbering system; or

(ii) wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions E233P, L234A, L235A, G237A, and K322A and a deletion of G236, according to the EU numbering system.

21. The composition of any one of claims 1-20, wherein the hinge region is derived from an immunoglobulin hinge region.

22. The composition of any one of claims 1-21, wherein each polypeptide comprises an Fc-binding domain linker between the immunoglobulin constant region, and the second binding domain; optionally wherein the Fc-binding domain linker comprises a Gly₄Ser (SEQ ID NO: 128) sequence; and optionally wherein the Fc-binding domain linker comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).

23. A composition comprising a fusion protein, a buffer, an excipient and a surfactant, wherein:

(a) the fusion protein is a dimer of two identical polypeptides, wherein each polypeptide comprises, in order from amino-terminus to carboxyl-terminus:

- (i) a first binding domain that specifically binds to CD123,
- (ii) a hinge region,
- (iii) an immunoglobulin constant region, and
- (iv) a second binding domain that specifically binds to CD3;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

24. The composition of claim 23, wherein the composition comprises about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80.

25. The composition of claim 23 or 24, wherein the composition comprises from 0.1 mg/ml to 10 mg/ml of the multispecific protein; optionally wherein the composition comprises from 1 mg/ml to 5 mg/ml of the multispecific protein; and optionally wherein the composition comprises about 2 mg/ml of the multispecific protein.

26. The composition of any one of claims 23-25, wherein the composition has a pH from 4.0 to 5.5; and optionally wherein the composition has a pH of about 4.8.

27. The composition of any one of claims 23-26, wherein the immunoglobulin constant region is a human Fc domain; and optionally wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.

28. The composition of any one of claims 1-27, wherein the CH2 domain is a human IgG1 CH2 domain with one, two, three or more amino acid substitutions compared to a wild-type human IgG1 CH2 domain.

29. The composition of any one of claims 23-28,

(i) wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions L234A, L235A, G237A, and K322A, according to the EU numbering system, optionally wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions L234A, L235A, G237A, E318A, K320A and K322A, according to the EU numbering system; or

(ii) wherein the immunoglobulin constant region comprises a human IgG1 CH2 domain comprising the substitutions E233P, L234A, L235A, G237A, and K322A and a deletion of G236, according to the EU numbering system.

30. The composition of any one of claims 23-29, wherein the hinge region is derived from an immunoglobulin hinge region.

31. The composition of any one of claims 23-30, wherein each polypeptide comprises an Fc-binding domain linker between the immunoglobulin constant region and the second binding domain; optionally wherein the Fc-binding domain linker comprises a Gly₄Ser (SEQ ID NO: 128) sequence; and optionally wherein the Fc-binding domain linker comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).

32. The composition of any one of claims 23-31, wherein at least one of the first binding domain and the second binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

33. The composition of any one of claims 23-32, wherein at least one of the first binding domain and the second binding domain is a single chain variable fragment (scFv); optionally wherein the light chain variable region of the scFv is carboxy-terminal to the heavy chain variable region of the scFv, or wherein the light chain variable region of the scFv is amino-terminal to the heavy chain variable region of the scFv; optionally wherein the scFv comprises a linker polypeptide; optionally wherein the linker polypeptide is between the light chain variable region and the heavy chain variable region of the scFv; optionally wherein the linker polypeptide comprises a Gly₄Ser (SEQ ID NO: 128) linker; and optionally wherein the linker polypeptide comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).

34. The composition of any one of claims 23-33,

(i) wherein the first binding domain is an anti-CD123 scFv comprising:

a HCDR1 comprising the sequence of SEQ ID NO: 10, a HCDR2 comprising the sequence of SEQ ID NO: 11, and a HCDR3 comprising the sequence of SEQ ID NO: 12; and

a LCDR1 comprising the sequence of SEQ ID NO: 13, a LCDR2 comprising the sequence of SEQ ID NO: 14, and a LCDR3 comprising the sequence of SEQ ID NO: 15;

(ii) wherein the first binding domain is an anti-CD123 scFv comprising a VH comprising SEQ ID NO: 136, and a VL comprising SEQ ID NO: 134; or

(iii) wherein the first binding domain is an anti-CD123 scFv comprising SEQ ID NO: 18.

35. The composition of any one of claims 23-34,

(i) wherein the second binding domain is an anti-CD3 scFv comprising:

a HCDR1 comprising the sequence of SEQ ID NO: 19, a HCDR2 comprising the sequence of SEQ ID NO: 20, and a HCDR3 comprising the sequence of SEQ ID NO: 21; and

a LCDR1 comprising the sequence of SEQ ID NO: 22, a LCDR2 comprising the sequence of SEQ ID NO: 23, and a LCDR3 comprising the sequence of SEQ ID NO: 24;

(ii) wherein the second binding domain is an anti-CD3 scFv comprising a VH that comprises SEQ ID NO: 383 or 387, and a VL that comprises SEQ ID NO: 384; or

(iii) wherein the second binding domain is an anti-CD3 scFv comprising SEQ ID NO: 27.

36. The composition of any one of claims 23-34, wherein each polypeptide comprises the sequence of SEQ ID NO: 31.

37. The composition of any one of claims 23-34, wherein:

the first binding domain is an anti-CD123 scFv comprising an immunoglobulin heavy chain variable region (VH) comprising a HCDR1 of SEQ ID NO: 10, a HCDR2 of SEQ ID NO: 11, and a HCDR3 of SEQ ID NO: 12, and an immunoglobulin light chain variable region (VL) comprising a LCDR1 of SEQ ID NO: 13, a LCDR2 of SEQ ID NO: 14, and a LCDR3 of SEQ ID NO: 15, and

the second binding domain is an anti-CD3 scFv comprising an immunoglobulin heavy chain variable region (VH) comprising a HCDR1 of SEQ ID NO: 19, a HCDR2

of SEQ ID NO: 20, and a HCDR3 of SEQ ID NO: 21, and an immunoglobulin light chain variable region (VL) comprising a LCDR1 of SEQ ID NO: 22, a LCDR2 of SEQ ID NO: 23, and a LCDR3 of SEQ ID NO: 24.

38. The composition of any one of claims 1 to 37, wherein the composition is for intravenous or subcutaneous administration.

39. The composition of any one of claims 1 to 38, wherein the composition substantially prevents degradation of the multispecific protein; optionally wherein the composition slows or reduces the degradation of the multispecific protein as compared to an identical multispecific protein stored in histidine buffer under identical storage conditions; and optionally wherein the composition is substantially stable for at least 1 year at 4°C.

40. The composition of any one of claims 1 to 39, wherein the composition is substantially resistant to formation of aggregates of multispecific protein; and optionally wherein the composition forms fewer aggregates as compared to an identical multispecific protein stored in histidine buffer under identical storage conditions.

41. A composition comprising a fusion protein, a buffer, an excipient and a surfactant, wherein

(a) the fusion protein comprises:

(i) a first binding domain that specifically binds to CD123,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 10, HCDR2 of SEQ ID NO: 11, and HCDR3 of SEQ ID NO: 12; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 13, LCDR2 of SEQ ID NO: 14, and LCDR3 of SEQ ID NO: 15; and

(ii) a second binding domain that specifically binds to CD3, wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 19, HCDR2 of SEQ ID NO: 20, and HCDR3 of SEQ ID NO: 21; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 22, LCDR2 of SEQ ID NO: 23, and LCDR3 of SEQ ID NO: 24;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

42. A composition comprising a fusion protein, about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80, wherein the fusion protein comprises a Fab, Fab', F(ab')₂, scFv, disulfide linked Fv, scFv x scFv (BiTE), scFv-Fc (SMIP), scFv-Fc-scFv, quadroma, K λ -body, dAbs, diabody, nanobody, DOCK-AND-LOCKS® (DNLs®), CrossMab Fabs, CrossMab VH-VL, strand-exchange engineered domain bodies (SEEDbodies), Affibodies, Fynomers, Kunitz Domains, Albu-dabs, two engineered Fv fragments with exchanged VHs (e.g., a dual-affinity re-targeting molecules (D.A.R.T.s)), DVD-IG, Covx-body, peptibody, SVD-Igs, dAb-Igs, Knobs-in-Holes, IgG1 antibodies comprising matched mutations in the CH3 domain (e.g., DuoBody antibody) and triomAb.

43. A composition comprising a fusion protein, about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80, wherein

(a) the fusion protein comprises:

(i) a first binding domain that specifically binds to CD123,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 10, HCDR2 of SEQ ID NO: 11, and HCDR3 of SEQ ID NO: 12; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 13, LCDR2 of SEQ ID NO: 14, and LCDR3 of SEQ ID NO: 15; and

(ii) a second binding domain that specifically binds to CD3,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 19, HCDR2 of SEQ ID NO: 20, and HCDR3 of SEQ ID NO: 21; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 22, LCDR2 of SEQ ID NO: 23, and LCDR3 of SEQ ID NO: 24.

44. A composition comprising a fusion protein, a buffer, an excipient and a surfactant, wherein

(a) the fusion protein comprises:

(i) a first binding domain that specifically binds to CD123,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising SEQ ID NO: 136; and an immunoglobulin light chain variable region (VL) comprising SEQ ID NO: 134; and

(ii) a second binding domain that specifically binds to CD3,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising SEQ ID NO: 383 or 387; and an immunoglobulin light chain variable region (VL) comprising SEQ ID NO: 384;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

45. A composition comprising a fusion protein, a buffer, an excipient and a surfactant, wherein

(a) the fusion protein comprises:

(i) a first binding domain that specifically binds to CD123, wherein the first binding domain comprises SEQ ID NO: 18; and

(ii) a second binding domain that specifically binds to CD3, wherein the second binding domain comprises SEQ ID NO: 27;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

46. A composition comprising a fusion protein, a buffer, an excipient and a surfactant, wherein

(a) the fusion protein is a dimer of two identical polypeptides, wherein each polypeptide comprises, in order from amino-terminus to carboxyl-terminus, or in order from carboxyl-terminus to amino-terminus:

(i) a first binding domain that specifically binds to CD123,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 10, HCDR2 of SEQ ID NO: 11, and HCDR3 of SEQ ID NO: 12; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 13, LCDR2 of SEQ ID NO: 14, and LCDR3 of SEQ ID NO: 15,

(ii) a hinge region of SEQ ID NO: 47,

(iii) an immunoglobulin constant region of SEQ ID NO: 131,

(iv) a Fc-binding domain linker of SEQ ID NO: 132, and

(v) a second binding domain that specifically binds to CD3,

wherein the second binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 19, HCDR2 of SEQ ID NO: 20, and HCDR3 of SEQ ID NO: 21; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 22, LCDR2 of SEQ ID NO: 23, and LCDR3 of SEQ ID NO: 24;

(b) the buffer comprises or consists of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof;

(c) the excipient comprises or consists of from 1% weight/volume (w/v) to 12% w/v of a sugar; and

(d) the surfactant comprises or consists of polysorbate 80.

47. A composition comprising a fusion protein, about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80, wherein:

the fusion protein is a dimer of two identical polypeptides, wherein each polypeptide comprises, in order from amino-terminus to carboxyl-terminus:

(i) a first binding domain that specifically binds to CD123,

wherein the binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 10, HCDR2 of SEQ ID NO: 11, and HCDR3 of SEQ ID NO: 12; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 13, LCDR2 of SEQ ID NO: 14, and LCDR3 of SEQ ID NO: 15,

- (ii) a hinge region of SEQ ID NO: 47,
- (iii) an immunoglobulin constant region of SEQ ID NO: 131,
- (iv) a Fc-binding domain linker of SEQ ID NO: 132, and
- (v) a second binding domain that specifically binds to CD3,

wherein the second binding domain comprises an immunoglobulin heavy chain variable region (VH) comprising HCDR1 of SEQ ID NO: 19, HCDR2 of SEQ ID NO: 20, and HCDR3 of SEQ ID NO: 21; and an immunoglobulin light chain variable region (VL) comprising LCDR1 of SEQ ID NO: 22, LCDR2 of SEQ ID NO: 23, and LCDR3 of SEQ ID NO: 24.

48. A composition comprising a fusion protein, about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80,

wherein the fusion protein comprises or consists of SEQ ID NO: 31;

wherein the composition comprises about 2 mg/ml of the fusion protein; and

wherein the composition has a pH of about 4.8.

49. Use of the composition of any one of claims 1-48 in the manufacture of a medicament for treating an autoimmune disorder.

50. The use of claim 49, wherein the autoimmune disorder is irritable bowel syndrome, inflammatory bowel disease, psoriasis, rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, asthma, multiple sclerosis, dermatomyositis, polymyositis, pernicious anaemia, primary biliary cirrhosis, acute disseminated encephalomyelitis (ADEM), Addison's disease, ankylosing spondylitis, antiphospholipid antibody syndrome (aPL), autoimmune hepatitis, diabetes mellitus type 1, Goodpasture's syndrome, Graves' disease, Guillain-Barré syndrome (GBS), Hashimoto's disease, idiopathic thrombocytopenic purpura, pemphigus vulgaris, Sjögren's syndrome, temporal arteritis, autoimmune hemolytic anemia, bullous pemphigoid, vasculitis, celiac disease, endometriosis, hidradenitis suppurativa, interstitial cystitis, morphea, scleroderma, narcolepsy, neuromyotonia, vitiligo, autoimmune inner ear disease or myasthenia gravis.

51. Use of the composition of any one of claims 1 to 48 in the manufacture of a medicament for treating cancer.

52. The use of claim 51, wherein the cancer is selected from a carcinoma or sarcoma; optionally wherein the cancer is selected from a melanoma, kidney cancer, pancreatic cancer, lung cancer, intestinal cancer, prostate cancer, breast cancer, liver cancer, brain cancer, colon cancer, ovarian cancer, or a hematological cancer; and optionally wherein the hematological cancer is an acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), hairy cell leukemia (HCL), blastic plasmacytoid dendritic cell neoplasm, B-cell acute lymphoblastic leukemia (ALL), and chronic myeloid leukemia (CML).

53. The composition of any one of claims 1-48 for use in treating an autoimmune disorder.

54. The composition of any one of claims 1-48 for use in treating cancer.

55. Use of a composition comprising a multispecific protein comprising a CD123 binding domain and a CD3 binding domain, a buffer comprising or consisting of from 1 mM to 10 mM succinate or a pharmaceutically acceptable salt or acid thereof, an excipient comprising or consisting of from 1% weight/volume (w/v) to 12% w/v of a sugar; and a surfactant comprising or consisting of polysorbate 80, in the manufacture of a medicament for treating a cancer selected from acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS), wherein the composition is to be administered to the subject by IV infusion at a dose of 0.3, 1, 3, 6, 9, 12, 18, 20, 24, 30, 36, 48, 50, 60, 75, or 100 µg.

56. Use of a composition of any one of claims 15-17, 34-37, and 43-46 in the manufacture of a medicament for treating a cancer selected from acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS), wherein the composition is to be administered to a patient by IV infusion at a dose of 0.3, 1, 3, 6, 9, 12, 18, 20, 24, 30, 36, 48, 60, 50, 75, or 100 µg.

57. The use of claim 55 or 56, wherein the first dose of the composition is to be administered to the patient by IV infusion over a 20-24 hour period of time; optionally wherein a second dose of the composition is to be administered to the patient by IV infusion over an 8 hour period of time, wherein the second dose is the same as the

first dose; optionally wherein a third dose of the composition is to be administered to the patient by IV infusion over a 6 hour period of time, wherein the third dose is the same as the first and the second dose; and optionally wherein the fourth dose and subsequent doses of the composition are to be administered to the patient by IV infusion over a 2 to a 4 hour period of time.

58. The use of any one of claims 55-56, wherein the composition is to be administered to the patient by continuous IV infusion up to 72 hours.

59. The use of any one of claims 55-58, wherein the composition is to be administered on days 1, 8, 15, and 22; and optionally

(i) wherein 6 μg is to be administered on day 1, 9 μg is to be administered on day 8, 12 μg is to be administered on day 15, and 12 μg is to be administered on day 22;

(ii) wherein 6 μg is to be administered on day 1, 9 μg is to be administered on day 8, 12 μg is to be administered on day 15, and 18 μg is to be administered on day 22;

(iii) wherein 6 μg is to be administered on day 1, 9 μg is to be administered on day 8, 9 μg is to be administered on day 15, and 9 μg is to be administered on day 22;

(iv) wherein 9 μg is to be administered on day 1, 12 μg is to be administered on day 8, 12 μg is to be administered on day 15, and 12 μg is to be administered on day 22; or

(v) wherein 12 μg is to be administered on day 1, 18 μg is to be administered on day 8, 18 μg is to be administered on day 15, and 18 μg is to be administered on day 22.

60. The use of any one of claims 55-58, wherein the composition is to be administered to a patient by IV according to the following weekly treatment schedule:

(i)

Week 1 dosage: 6 µg;
Week 2 dosage: 9 µg;
Week 3 dosage: 12 µg; and
Week 4 dosage and subsequent week dosages: 12 µg;

(ii)

Week 1 dosage: 6 µg;
Week 2 dosage: 9 µg;
Week 3 dosage: 12 µg; and
Week 4 dosage and subsequent week dosages: 18 µg;

(iii)

Week 1 dosage: 6 µg;
Week 2 dosage: 12 µg;
Week 3 dosage: 12 µg; and
Week 4 dosage and subsequent week dosages: 12 µg;

(iv)

Week 1 dosage: 6 µg;
Week 2 dosage: 12 µg;
Week 3 dosage: 18 µg; and
Week 4 dosage and subsequent week dosages: 24 µg;

(v)

Week 1 dosage: 6 µg;
Week 2 dosage: 12 µg;
Week 3 dosage: 18 µg; and
Week 4 dosage and subsequent week dosages: 36 µg;

(vi)

Week 1 dosage: 6 µg;
Week 2 dosage: 12 µg;
Week 3 dosage: 18 µg; and
Week 4 dosage and subsequent week dosages: 48 µg;

(vii)

Week 1 dosage: 6 µg;

Week 2 dosage: 12 µg;

Week 3 dosage: 18 µg; and

Week 4 dosage and subsequent week dosages: 60 µg;

(viii)

Week 1 dosage: 6 µg; and

Week 2 and subsequent week dosages: 9 µg;

(ix)

Week 1 dosage: 9 µg; and

Week 2 and subsequent week dosages: 12 µg; or

(x)

Week 1 dosage: 12 µg; and

Week 2 and subsequent week dosages: 18 µg.

61. The use of any one of claims 55-58, wherein the composition is to be administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is to be administered on day 1, 9 µg of the multispecific protein is to be administered on day 2, 12 µg of the multispecific protein is to be administered on day 3, 18 µg of the multispecific protein is to be administered on day 4, 18 µg of the multispecific protein is to be administered on day 8, 18 µg of the multispecific protein is to be administered on day 11, 36 µg of the multispecific protein is to be administered on day 15, and 36 µg of the multispecific protein is to be administered on day 22 of the first 28-day cycle; and optionally wherein the multispecific protein is to be further administered to the patient during at least one additional 28-day cycle, wherein 36 µg of the multispecific protein is to be administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

62. The use of any one of claims 55-58, wherein the composition is to be administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific

protein is to be administered on day 1, 12 µg of the multispecific protein is to be administered on day 2, 18 µg of the multispecific protein is to be administered on day 3, 24 µg of the multispecific protein is to be administered on day 4, 24 µg of the multispecific protein is to be administered on day 8, 24 µg of the multispecific protein is to be administered on day 11, 48 µg of the multispecific protein is to be administered on day 15, and 48 µg of the multispecific protein is to be administered on day 22 of the first 28-day cycle; and optionally wherein the multispecific protein is to be further administered to the patient during at least one additional 28-day cycle, wherein 48 µg of the multispecific protein is to be administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

63. The use of any one of claims 55-58, wherein the composition is to be administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is to be administered on day 1, 12 µg of the multispecific protein is to be administered on day 2, 24 µg of the multispecific protein is to be administered on day 3, 36 µg of the multispecific protein is to be administered on day 4, 36 µg of the multispecific protein is to be administered on day 8, 36 µg of the multispecific protein is to be administered on day 11, 60 µg of the multispecific protein is to be administered on day 15, and 60 µg of the multispecific protein is to be administered on day 22 of the first 28-day cycle; and optionally wherein the multispecific protein is to be further administered to the patient during at least one additional 28-day cycle, wherein 60 µg of the multispecific protein is to be administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

64. The use of any one of claims 55-58, wherein the composition is to be administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is to be administered on day 1, 12 µg of the multispecific protein is to be administered on day 2, 24 µg of the multispecific protein is to be administered on day 3, 36 µg of the multispecific protein is to be administered on day 4, 48 µg of the multispecific protein is to be administered on day 8, 48 µg of the multispecific protein is to be administered on day 11, 100 µg of the multispecific protein is to be administered on day 15, and 100 µg of the multispecific protein is to be administered on day 22 of the first 28-day cycle; and optionally wherein the multispecific protein is to be further administered to the patient during at least one additional 28-day cycle,

wherein 100 µg of the multispecific protein is to be administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

65. The use of any one of claims 55-58, (i) wherein the composition is to be administered to a patient by IV and the dosage is increased each week for the first weeks; or (ii) wherein the patient is to be administered the composition once, twice, three, or four times each week.