

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,
 - (ii) a hinge region,
 - (iii) an immunoglobulin constant region, and
 - (iv) a second binding domain; and
 - (b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.
2. The composition of claim 1, wherein the composition comprises from about 1 mM to about 10 mM succinate or a pharmaceutically acceptable salt or acid thereof.
3. The composition of claim 2, wherein the composition comprises about 5 mM succinate or a pharmaceutically acceptable salt or acid thereof.
4. The composition of any one of claims 1-3, wherein the excipient comprises or consists of a sugar.
5. The composition of claim 4, wherein the sugar is sucrose.
6. The composition of claim 4 or 5, wherein the composition comprises from about 1% weight/volume (w/v) to about 12% w/v of the sugar.
7. The composition of claim 6, wherein the composition comprises about 6.5% (w/v) of the sugar.
8. The composition of any one of claims 1-7, wherein the surfactant comprises or consists of polysorbate 80.

9. The composition of claim 8, wherein the composition comprises about 0.02% w/v polysorbate 80.
10. The composition of any one of claims 1-9, wherein the composition comprises from about 0.1 mg/ml to about 10 mg/ml of the multispecific protein.
11. The composition of claim 10, wherein the composition comprises from about 1 mg/ml to about 5 mg/ml of the multispecific protein.
12. The composition of claim 11, wherein the composition comprises about 2 mg/ml of the multispecific protein.
13. The composition of any one of claims 1-12, wherein the composition comprises about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80.
14. The composition of any one of claims 1-13, wherein the composition has a pH from about 4.0 to about 5.5.
15. The composition of claim 14, wherein the composition has a pH of about 4.8.
16. The composition of any one of claims 1-15, wherein the immunoglobulin constant region is a human Fc domain.
17. The composition of any one of claims 1-16, wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.
18. The composition of any one of claims 1-17 wherein the first binding domain is a CD3 binding domain and the second binding domain is a tumor antigen binding domain.
19. The composition of claim 18, 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.

20. The composition of any one of claims 1-17 wherein the first domain is a tumor antigen binding domain, and the second binding domain is a CD3 binding domain.
21. The composition of claim 20, 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.
22. The composition of any one of claims 1-17 wherein the first binding domain is a 4-1-BB binding domain and the second binding domain is a tumor antigen binding domain.
23. The composition of claim 22, 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.
24. The composition of any one of claims 1-17 wherein the first binding domain is a tumor antigen binding domain, and the second binding domain is a 4-1-BB binding domain.
25. The composition of claim 24, 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.
26. The composition of any one of claims 18-25, wherein the tumor antigen binding domain binds to CD123, PSMA, CD19, CD33, or HER2.
27. The composition of any one of claims 1-17, wherein the first binding domain or the second binding domain is a 4-1BB binding domain.
28. The composition of any one of claims 1-17, wherein the first binding domain or the second binding domain is an OX40 binding domain.
29. The composition of any one of claims 1-17, wherein the first binding domain is a 4-1BB binding domain and wherein the second binding domain is an OX40 binding domain.

30. The composition of any one of claims 1-17, wherein the first binding domain is an OX40 binding domain and wherein the second binding domain is a 4-1BB binding domain.
31. The composition of claim 29 or 30, wherein the 4-1BB binding domain is an scFv and the OX40 binding domain is an scFv.
32. The composition of any one of claims 1-17, wherein the first binding domain is an OX40 binding domain and the second binding domain is a tumor antigen binding domain.
33. The composition of any one of claims 1-17, wherein the first binding domain is a tumor antigen binding domain and the second binding domain is an OX40 binding domain.
34. The composition of any one of claims 1-33, 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.
35. The composition of any one of claims 1-34, wherein at least one of the first binding domain and the second binding domain is a single chain variable fragment (scFv).
36. The composition of claim 35, wherein the light chain variable region of the scFv is carboxy-terminal to the heavy chain variable region of the scFv.
37. The composition of claim 35, wherein the light chain variable region of the scFv is amino-terminal to the heavy chain variable region of the scFv.
38. The composition of any one of claims 35-37, wherein the scFv comprises a linker polypeptide.

39. The composition of claim 38, wherein the linker polypeptide is between the light chain variable region and the heavy chain variable region of the scFv.
40. The composition of any one of claims 38-39, wherein the linker polypeptide comprises a Gly₄Ser (SEQ ID NO: 128) linker.
41. The composition of claim 40, wherein the linker polypeptide comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).
42. The composition of any one of claims 18-26, 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.
43. The composition of any one of claims 18-26, wherein the tumor antigen binding domain is an anti-CD123 scFv comprising a VH comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 136, and a VL comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 134.
44. The composition of any one of claims 18-26, wherein the tumor antigen binding domain is an anti-CD123 scFv, and wherein the scFv comprises a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 27.
45. The composition of any one of claims 18 to 21, 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.
46. The composition of any one of claims 18-21, wherein the CD3 binding domain is an anti-CD3 scFv that comprises a VH comprising a sequence at least 90%, at least

95%, or 100% identical to SEQ ID NO: 383 or 387, and a VL comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 384.

47. The composition of any one of claims 18-21, wherein the CD3 binding domain is an anti-CD3 scFv that comprises a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 27.

48. The composition of any one of claims 18-21 or 45-47, wherein each polypeptide comprises a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 31.

49. The composition of any one of claims 1-48, 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, FcγRIIIa, and FcγRIIIb.

50. The composition of any one of claims 1-48, 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.

51. The composition of any of claims 1-48, 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.

52. The composition of any one of claims 1-48, 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.

53. The composition of any one of claims 1-52, 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.

54. The composition of any one of claims 1-53, 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.

55. The composition of any one of claim 54, 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.

56. The composition of any one of claims 1-53, 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.

57. The composition of any one of claims 1-56, wherein the hinge region is derived from an immunoglobulin hinge region.

58. The composition of any one of claims 1-57, wherein each polypeptide comprises an Fc-binding domain linker between the immunoglobulin constant region, and the second binding domain.

59. The composition of claim 58, wherein the Fc-binding domain linker comprises a Gly₄Ser (SEQ ID NO: 128) sequence.

60. The composition of claim 59, wherein the Fc-binding domain linker comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).

61. The composition of any one of claims 1-60, wherein the composition is for intravenous or subcutaneous administration.

62. The composition of any one of claims 1 to 61, wherein the composition substantially prevents degradation of the multispecific protein.

63. The composition of any one of claims 1-62, 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.

64. The composition of any one of claims 1 to 63, wherein the composition is substantially stable for at least 1 year at 4°C.
65. The composition of any one of claims 1 to 64, wherein the composition is substantially resistant to formation of aggregates of multispecific protein.
66. The composition of any one of claims 1-65, wherein the composition forms fewer aggregates as compared to an identical multispecific protein stored in histidine buffer under identical storage conditions.
67. 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; and
 - (b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.
68. The composition of claim 67, wherein the composition comprises about 5 mM succinate, about 6.5% weight/volume (w/v) sucrose and about 0.02% w/v polysorbate 80.
69. The composition of claim 67 or 68, wherein the composition comprises from about 0.1 mg/ml to about 10 mg/ml of the multispecific protein.
70. The composition of claim 69, wherein the composition comprises from about 1 mg/ml to about 5 mg/ml of the multispecific protein.
71. The composition of claim 70, wherein the composition comprises about 2 mg/ml of the multispecific protein.

72. The composition of any one of claims 67-71, wherein the composition has a pH from about 4.0 to about 5.5.
73. The composition of claim 72, wherein the composition has a pH of about 4.8.
74. The composition of any one of claims 67-73, wherein the immunoglobulin constant region is a human Fc domain.
75. The composition of any one of claims 67-74, wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.
76. The composition of any one of claims 1-75, 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.
77. The composition of any one of claims 67-76, 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.
78. The composition of any one of claims 67-77, 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.
79. The composition of any one of claims 67-76, 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.
80. The composition of any one of claims 67-79, wherein the hinge region is derived from an immunoglobulin hinge region.

81. The composition of any one of claims 67-80, wherein each polypeptide comprises an Fc-binding domain linker between the immunoglobulin constant region and the second binding domain.
82. The composition of claim 81, wherein the Fc-binding domain linker comprises a Gly₄Ser (SEQ ID NO: 128) sequence.
83. The composition of claim 82, wherein the Fc-binding domain linker comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).
84. The composition of any one of claims 67-83, wherein the composition is for intravenous or subcutaneous administration.
85. The composition of any one of claims 67-84, 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.
86. The composition of any one of claims 67-85, wherein at least one of the first binding domain and the second binding domain is a single chain variable fragment (scFv).
87. The composition of claim 86, wherein the light chain variable region of the scFv is carboxy-terminal to the heavy chain variable region of the scFv.
88. The composition of claim 86, wherein the light chain variable region of the scFv is amino-terminal to the heavy chain variable region of the scFv.
89. The composition of any one of claims 86-88, wherein the scFv comprises a linker polypeptide.
90. The composition of claim 89, wherein the linker polypeptide is between the light chain variable region and the heavy chain variable region of the scFv.

91. The composition of claim 89 or 90, wherein the linker polypeptide comprises a Gly₄Ser (SEQ ID NO: 128) linker.
92. The composition of claim 91, wherein the linker polypeptide comprises the formula (Gly₄Ser)_n, wherein n = 1-5 (SEQ ID NO: 129).
93. The composition of any one of claims 67-92, 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 HDCR3 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.
94. The composition of any one of claims 67-92, wherein the first binding domain is an anti-CD123 scFv comprising a VH comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 136, and a VL comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 134.
95. The composition of any one of claims 67-92, wherein the first binding domain is an anti-CD123 scFv comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 18.
96. The composition of any one of claims 67-95, 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 HDCR3 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.

97. The composition of any one of claims 67-95, wherein the second binding domain is an anti-CD3 scFv comprising a VH that comprises a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 383 or 387, and a VL that comprises a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 384.

98. The composition of any one of claims 67-95, wherein the second binding domain is an anti-CD3 scFv comprising a sequence at least 90%, at least 95%, or 100% identical to SEQ ID NO: 27.

99. The composition of any one of claims 67-95, wherein each polypeptide comprises the sequence of SEQ ID NO: 31, or comprises a sequence at least 90%, at least 95%, or at least 98% identical to SEQ ID NO: 31.

100. The composition of any one of claims 67-95, 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.

101. The composition of any one of claims 67 to 100, wherein the composition substantially prevents degradation of the multispecific protein.

102. The composition of any one of claims 67 to 101, 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.

103. The composition of any one of claims 67 to 102, wherein the composition is substantially stable for at least 1 year at 4°C.

104. The composition of any one of claims 67 to 103, wherein the composition is substantially resistant to formation of aggregates of multispecific protein.

105. The composition of any one of claims 67 to 104, wherein the composition forms fewer aggregates as compared to an identical multispecific protein stored in histidine buffer under identical storage conditions.

106. 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; and

(b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.

107. 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.

108. 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.

109. 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; and

and

(b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.

110. 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; and

(b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.

111. 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; and

(b) the buffer comprises or consists of succinate or a pharmaceutically acceptable salt or acid thereof.

112. 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.

113. 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.

114. A method for treating an autoimmune disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the composition of any one of claims 1-113.

115. The method of claim 114, 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.

116. A method for treating cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the composition of any one of claims 1-113.

117. The method of claim 116, wherein the cancer is selected from a carcinoma or sarcoma.

118. The method of claim 116 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.

119. The method of claim 118, 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).

120. Use of the composition of any one of claims 1-113 for treating autoimmune disorder in a subject.

121. Use of the composition of any one of claims 1-113 in the manufacture of a medicament for treating an autoimmune disorder.

122. Use of the composition of any one of claims 1-113 for treating cancer in a subject.

123. Use of the composition of any one of claims 1-113 in the manufacture of a medicament for treating cancer.

124. A method of treating a cancer in a subject comprising administering a composition comprising a multispecific protein comprising a CD123 binding domain and a CD3 binding domain 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.

125. A method of treating a cancer in a subject comprising administering a composition of any one of claims 42-48, 93-100, and 108-111 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.

126. The method of claim 124 or 125, wherein the first dose of the composition is administered to the patient by IV infusion over a 20-24 hour period of time.

127. The method of claim 126, wherein a second dose of the composition is 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.

128. The method of claim 127, wherein a third dose of the composition is 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.

129. The method of any one of claims 124-128, wherein the fourth dose and subsequent doses of the composition are administered to the patient by IV infusion over about a 2 to about a 4 hour period of time.

130. The method of any one of claims 124-125, wherein the composition is administered to the patient by continuous IV infusion up to 72 hours.

131. The method of any one of claims 124-130, wherein the composition is administered on days 1, 8, 15, and 22.

132. The method of claim 131, wherein 6 μg is administered on day 1, 9 μg is administered on day 8, 12 μg is administered on day 15, and 12 μg is administered on day 22.

133. The method of claim 131, wherein 6 μg is administered on day 1, 9 μg is administered on day 8, 12 μg is administered on day 15, and 18 μg is administered on day 22.

134. The method of claim 131, wherein 6 μg is administered on day 1, 9 μg is administered on day 8, 9 μg is administered on day 15, and 9 μg is administered on day 22.

135. The method of claim 131, wherein 9 μg is administered on day 1, 12 μg is administered on day 8, 12 μg is administered on day 15, and 12 μg is administered on day 22.

136. The method of claim 131, wherein 12 μg is administered on day 1, 18 μg is administered on day 8, 18 μg is administered on day 15, and 18 μg is administered on day 22.

137. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

138. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

139. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

140. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

141. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

142. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

143. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

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 .

144. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

Week 1 dosage: 6 µg; and

Week 2 and subsequent week dosages: 9 µg.

145. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

Week 1 dosage: 9 µg; and

Week 2 and subsequent week dosages: 12 µg.

146. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV according to the following weekly treatment schedule:

Week 1 dosage: 12 µg; and

Week 2 and subsequent week dosages: 18 µg.

147. The method of any one of claims 124-130, wherein the composition is administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is administered on day 1, 9 µg of the multispecific protein is administered on day 2, 12 µg of the multispecific protein is administered on day 3, 18 µg of the multispecific protein is administered on day 4, 18 µg of the multispecific protein is administered on day 8, 18 µg of the multispecific protein is administered on day 11, 36 µg of the multispecific protein is administered on day 15, and 36 µg of the multispecific protein is administered on day 22 of the first 28-day cycle.

148. The method of claim 147, wherein the method further comprises administering the multispecific protein to the patient during at least one additional 28-day cycle, wherein 36 µg of the multispecific protein is administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

149. The method of any one of claims 124-130, wherein the composition is administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is administered on day 1, 12 µg of the multispecific protein is administered on day 2, 18 µg of the multispecific protein is administered on day 3, 24 µg of the multispecific protein is administered on day 4, 24 µg of the multispecific protein is

administered on day 8, 24 µg of the multispecific protein is administered on day 11, 48 µg of the multispecific protein is administered on day 15, and 48 µg of the multispecific protein is administered on day 22 of the first 28-day cycle.

150. The method of claim 149, wherein the method further comprises administering the multispecific protein to the patient during at least one additional 28-day cycle, wherein 48 µg of the multispecific protein is administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

151. The method of any one of claims 124-130, wherein the composition is administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is administered on day 1, 12 µg of the multispecific protein is administered on day 2, 24 µg of the multispecific protein is administered on day 3, 36 µg of the multispecific protein is administered on day 4, 36 µg of the multispecific protein is administered on day 8, 36 µg of the multispecific protein is administered on day 11, 60 µg of the multispecific protein is administered on day 15, and 60 µg of the multispecific protein is administered on day 22 of the first 28-day cycle.

152. The method of claim 151, wherein the method further comprises administering the multispecific protein to the patient during at least one additional 28-day cycle, wherein 60 µg of the multispecific protein is administered on each of days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

153. The method of any one of claims 124-130, wherein the composition is administered to a patient during a first 28-day cycle, wherein 6 µg of the multispecific protein is administered on day 1, 12 µg of the multispecific protein is administered on day 2, 24 µg of the multispecific protein is administered on day 3, 36 µg of the multispecific protein is administered on day 4, 48 µg of the multispecific protein is administered on day 8, 48 µg of the multispecific protein is administered on day 11, 100 µg of the multispecific protein is administered on day 15, and 100 µg of the multispecific protein is administered on day 22 of the first 28-day cycle.

154. The method of claim 153, wherein the method further comprises administering the multispecific protein to the patient during at least one additional 28-day cycle,

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

155. The method of any one of claims 124-130, wherein the composition is administered to a patient by IV and the dosage is increased each week for the first weeks.

156. The method of any one of claims 124-130, wherein the patient is administered the composition once, twice, three, or four times each week.

157. The method of any one of claims 124-156, wherein the composition is administered to the patient with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS).