

What is claimed is:

1. A pharmaceutical formulation comprising
 - (a) a bispecific antibody construct,
 - (b) a saccharide,
 - (c) a surfactant,
 - (d) a buffer, and
 - (e) methionine present at a molar ratio of methionine to bispecific antibody construct of about 10X to about 5000X;
wherein the pH of the formulation is from about 4 to about 7.
2. The formulation of claim 1, wherein the pH of the formulation is about 4.2.
3. The formulation of claim 1 or claim 2, wherein the saccharide is a monosaccharide or a disaccharide.
4. The formulation of any one of claims 1-3, wherein the saccharide is glucose, galactose, fructose, xylose, sucrose, lactose, maltose, trehalose, sorbitol, mannitol, or xylitol.
5. The formulation of claim 4, wherein the saccharide is sucrose.
6. The formulation of any one of claims 1-5, wherein the surfactant is a nonionic surfactant.
7. The formulation of any one of claims 1-6, wherein the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, poloxamer 188, poloxamer 407, or Triton™ x-100.
8. The formulation of claim 7, wherein the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, or polysorbate 80.
9. The formulation of claim 7, wherein the surfactant is polysorbate 80.
10. The formulation of any one of claims 1-9, wherein the buffer is an acetate buffer, a glutamate buffer, a citrate buffer, a lactic buffer, a succinate buffer, a tartrate buffer, a fumarate buffer, a maleate buffer, a histidine buffer, or a phosphate buffer.
11. The formulation of claim 10, wherein the buffer is a glutamate buffer.
12. The formulation of any one of claims 1-11, wherein the formulation comprises the bispecific antibody construct at a concentration of from about 1 mg/ml to about 20 mg/ml.
13. The formulation of any one of claims 1-12, wherein the formulation comprises methionine at molar ratio of methionine to bispecific antibody construct of about 50X to about 5000X.
14. The formulation of any one of claims 1-12, wherein the formulation comprises about 10 mM to about 200 mM methionine.
15. The formulation of any one of claims 1-14, wherein the formulation is frozen.
16. The formulation of any one of claims 1-14, wherein the formulation is a thawed formulation.

17. The formulation of any one of claims 1-14, wherein the formulation is lyophilized.
18. The formulation of any one of claims 1-17, which comprises at least about 10% less high molecule weight (HMW) species compared to a matched formulation not comprising methionine when stored for four weeks at -15°C.
19. The formulation of claim 18, which comprises at least about 25% to about 85% less high molecule weight (HMW) species compared to a matched formulation not comprising methionine when stored for four weeks at -15°C.
20. A frozen pharmaceutical formulation comprising about 1 mg/mL to about 20 mg/mL bispecific antibody construct, sucrose, glutamic acid, polysorbate 80, and about 10 mM to about 200 mM methionine, wherein the pH of the formulation is from about 4 to about 7.
21. The formulation of any one of claims 1-20, wherein the bispecific antibody construct comprises a first binding domain that binds to a target cell surface antigen and a second binding domain that binds to human CD3 on the surface of a T cell.
22. The formulation of claim 21, further comprising a third domain comprising, in an amino to carboxyl order, hinge-CH2 domain-CH3 domain-linker-hinge-CH2 domain-CH3 domain.
23. The formulation of claim 22, wherein each of the first and second binding domains comprise a VH region and a VL region.
24. The formulation of claim 22 or claim 23, wherein the bispecific antibody construct is a single chain antibody construct.
25. The formulation of any one of claims 21-24, wherein the target cell surface antigen is CDH19, MSLN, DLL3, FLT3, EGFR, EGFRvIII, BCMA, PSMA, CD33, CD19, CD70, MUC17, or CLDN18.2.
26. The formulation of any one of claims 21-25, wherein the bispecific antibody construct comprises the amino acid sequence set forth in SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 33, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 55, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 87, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 131, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 156, SEQ ID NO: 165, SEQ ID NO: 174, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, or SEQ ID NO: 188.
27. The formulation of any one of claims 1-26, wherein the formulation comprises methionine at molar ratio of methionine to bispecific antibody construct of about 105X to about 5000X, and the bispecific antibody construct comprises the amino acid sequence set forth in SEQ ID NO: 77.
28. A method of treating cancer in a subject in need thereof comprising administering the formulation of any one of claims 1-26 to the subject.
29. The method of claim 28, wherein the formulation is frozen and the method further comprises thawing the formulation prior to administration to the subject.
30. The method of claim 27 or 28, wherein the method comprises intravenously administering the formulation to the subject.

31. The method of any one of claims 28-30, wherein the formulation comprises methionine at molar ratio of methionine to bispecific antibody construct of about 105X to about 5000X, and the bispecific antibody construct comprises the amino acid sequence set forth in SEQ ID NO: 77.

32. A method comprising

(a) preparing a formulation comprising a bispecific antibody construct, methionine, and a buffer, wherein the methionine is present at a molar ratio of methionine to bispecific antibody construct of about 10X to about 5000X;

(b) freezing the formulation of (a); and

(c) storing the formulation of (b) at a temperature of about -10°C to about -40°C.

30. The method of claim 29, wherein the method further comprises

(d) thawing the formulation of (c); and

(e) lyophilizing the formulation of (d).

33. The method of claim 32, wherein the formulation of (a) further comprises a saccharide, and comprises pH of from about 4 to about 7.

34. The method of claim 33, wherein between step (d) and (e) a buffer exchange step is performed to produce a pharmaceutical formulation comprising the bispecific antibody construct, a saccharide, a surfactant, a buffer, and methionine present at a molar ratio of methionine to bispecific antibody construct of about 10X to about 5000X; wherein the pH of the formulation is from about 4 to about 7.

35. The method of any one of claims 32-34, wherein steps (b) and (c) are performed at a temperature of about -20°C to about -35°C.

36. The method of any one of claims 32-35, wherein step (c) comprises storing the formulation for at least one month.

37. The method of any one of claims 32-36, wherein the formulation comprises methionine present at molar ratio of methionine to bispecific antibody construct of about 50X to about 5000X

38. The method of any one of claims 32-37, wherein the formulation comprises about 10 mM to about 200 mM methionine.

39. The method of any one of claims 33-38, wherein the saccharide is a monosaccharide or a disaccharide.

40. The method of any one of claims 33-39, wherein the saccharide is glucose, galactose, fructose, xylose, sucrose, lactose, maltose, trehalose, sorbitol, mannitol, or xylitol.

41. The method of claim 40, wherein the saccharide is sucrose.

42. The method of any one of claims 34-41, wherein the surfactant is a nonionic surfactant.

43. The method of any one of claims 34-42, wherein the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, poloxamer 188, poloxamer 407, or Triton™ x-100.

44. The method of claim 43, wherein the surfactant is polysorbate 80.

45. The method of any one of claims 32-44, wherein the buffer is an acetate buffer, a glutamate buffer, a citrate buffer, a lactic buffer, a succinate buffer, a tartrate buffer, a fumarate buffer, a maleate buffer, a histidine buffer, or a phosphate buffer.

46. The method of claim 45, wherein the buffer is a glutamate buffer.

47. The method of any one of claims 31-46, wherein the formulation comprises the bispecific antibody construct at a concentration of from about 1 mg/ml to about 20 mg/ml.

48. The method of any one of claims 31-47, wherein the bispecific antibody construct comprises a first binding domain that binds to a target cell surface antigen and a second binding domain that binds to human CD3 on the surface of a T cell.

49. The method of claim 48, further comprising a third domain comprising, in an amino to carboxyl order, hinge-CH2 domain-CH3 domain-linker-hinge-CH2 domain-CH3 domain.

50. The method of claim 49, wherein each of the first and second binding domains comprise a VH region and a VL region.

51. The method of claim 49 or claim 50, wherein the bispecific antibody construct is a single chain antibody construct.

52. The method of any one of claims 48-51, wherein the target cell surface antigen is CDH19, MSLN, DLL3, FLT3, EGFR, EGFRvIII, BCMA, PSMA, CD33, CD19, CD70, MUC17, or CLDN18.2.

53. The method of any one of claims 48-52, wherein the bispecific antibody construct comprises the amino acid sequence set forth in SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 33, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 55, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 87, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 131, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 156, SEQ ID NO: 165, SEQ ID NO: 174, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, or SEQ ID NO: 188.

54. The method of claim 53, wherein the formulation comprises methionine at molar ratio of methionine to bispecific antibody construct of about 105X to about 5000X, and the bispecific antibody construct comprises the amino acid sequence set forth in SEQ ID NO: 77.