CLAIMS

1. An aqueous formulation comprising an Aqueous Stable DVD-Ig (AS-DVD-Ig) protein and a buffer having a molarity of about 5 to about 50 mM, wherein the formulation has a pH of about 4.5 to about 7.5.

2. The aqueous formulation of claim 1, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 15% loss in relative percentage monomers as determined by size exclusion chromatography (SEC) when formulated in a histidine or citrate phosphate buffer at a concentration of at least about 50 mg/ml, following 14 days storage at about 40 degrees C.

3. The aqueous formulation of claim 1, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 10% loss in relative percentage monomers as determined by SEC when formulated in a histidine or citrate phosphate buffer at a concentration of at least about 50 mg/ml, following 14 days storage at about 40 degrees C.

4. The aqueous formulation of claim 1, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 5% loss in relative percentage monomers as determined by SEC when formulated in a histidine or citrate phosphate buffer at a concentration of at least about 50 mg/ml, following 14 days storage at about 40 degrees C.

5. The aqueous formulation of claim 1, wherein the formulation comprises about 6% or less aggregation as determined by SEC analysis.

6. The aqueous formulation of claim 1, wherein the formulation comprises about 5% or less aggregation as determined by SEC analysis.

7. The aqueous formulation of any one of claims 1-6, wherein the formulation has a pH of about 5 to about 6.5.

8. The aqueous formulation of any one of claims 1-7, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having about a 10% relative (rel.) peak area or less change in monomers at about 40 °C after 21 days of storage at a concentration of about 100 mg/ml in an aqueous formulation at a pH between about 5.5 to about 6.5.

9. The aqueous formulation of any one of claims 1-8, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having about a 1% rel. peak area or less

change in monomers at about 5 °C after 21 days of storage at a concentration of about 100 mg/ml at a pH between about 5.5 to about 6.5 in an aqueous formulation.

10. The aqueous formulation of any one of claims 1-9, further comprising at least one component selected from a surfactant, a polyol, and combinations thereof.

11. The aqueous formulation of claim 10, wherein the polyol is selected from the group consisting of sorbitol, mannitol, and sucrose.

12. The aqueous formulation of claim 11, wherein the polyol is mannitol and wherein the concentration of mannitol is selected from the group consisting of about 10 to about 100 mg/ml, about 20 to about 80, about 20 to about 70, about 30 to about 60, and about 30 to about 50 mg/ml.

13. The aqueous formulation of claim 11, wherein the polyol is sorbitol.

14. The aqueous formulation of claim 13, wherein the concentration of sorbitol is selected from the group consisting of about 20 to about 60 mg/ml, about 25 to about 55 mg/ml, about 30 to about 50 mg/ml, and about 35 to about 45 mg/ml.

15. The aqueous formulation of claim 11, wherein the polyol is sucrose.

16. The aqueous formulation of claim 15, wherein the concentration of sucrose is selected from the group consisting of about 60 to about 100 mg/ml, about 65 to about 95 mg/ml, about 70 to about 90 mg/ml, and about 75 to about 85 mg/ml.

17. The aqueous formulation of any one of claims 10-16, wherein the surfactant is a polysorbate.

18. The aqueous formulation of claim 17, wherein the concentration of polysorbate is selected from the group consisting of about 0.001% to about 1%, about 0.005% to about 0.05%, about 0.005% to about about 0.02%, about 0.01% to about 0.05%, and about 0.1%.

19. The aqueous formulation of claim 17 or claim 18, wherein the polysorbate is polysorbate 80 or polysorbate 20.

20. The aqueous formulation of claim 19, wherein the polysorbate 80 or the polysorbate 20 has a concentration of about 0.005% to about 0.02%.

21. The formulation of any one of claims 1-20, wherein the buffer is selected from the group consisting of acetate, histidine, glycine, arginine, phosphate, and citrate.

22. The aqueous formulation of any one of claims 1-21, wherein the molarity of the buffer ranges from 10 to 20 mM.

23. The aqueous formulation of any one of claims 1-22, wherein the AS-DVD-Ig protein has a concentration of about 1 to about 200 mg/ml.

24. The aqueous formulation of claim 23, wherein the AS-DVD-Ig protein has a concentration selected from the group consisting of about 20 to about 100 mg/ml, about 1 to about 250 mg/ml, about 10 to about 230 mg/ml, about 20 to about 210 mg/ml, about 30 to about 190 mg/ml, about 40 to about 170 mg/ml, about 50 to about 150 mg/ml, about 60 to about 130 mg/ml, about 70 to about 110 mg/ml, and about 80 to about 105 mg/ml of the AS-DVD-Ig protein.

25. An aqueous formulation comprising a Aqueous Stable DVD-Ig (AS-DVD-Ig) protein, a buffer having a molarity of about 5 to about 50 mM, a surfactant, and a polyol, wherein the formulation has a pH of about 4.5 to about 7.5.

26. The aqueous formulation of claim 25, wherein the polyol is selected from the group consisting of sorbitol, mannitol, and sucrose.

27. The aqueous formulation of claim 26, wherein the polyol is sorbitol.

28. The aqueous formulation of claim 27, wherein the concentration of sorbitol is about 30 to about 50 mg/ml.

29. The aqueous formulation of claim 26, wherein the polyol is sucrose.

30. The aqueous formulation of claim 29, wherein the sucrose has a concentration of about 70 to about 90 mg/ml.

31. The aqueous formulation of any one of claims 25-30, wherein the buffer is selected from the group consisting of acetate, histidine, glycine, arginine, phosphate, and citrate.

32. The aqueous formulation of any one of claims 25-31, wherein the molarity of the buffer ranges from about 10 to about 20 mM.

33. The aqueous formulation of any one of claims 25-32, wherein the AS-DVD-Ig protein has a concentration of about 1 to about 200 mg/ml.

34. The aqueous formulation of any one of claims 25-32, wherein the AS-DVD-Ig protein has a concentration selected from the group consisting of about 20 to about 100 mg/ml, about 1 to about 250 mg/ml, about 10 to about 230 mg/ml, about 20 to about 210 mg/ml, about 30 to about 190 mg/ml, about 40 to about 170 mg/ml, about 50 to about 150 mg/ml, about 60 to about 130 mg/ml, about 70 to about 110 mg/ml, and about 80 to about 105 mg/ml of the AS-DVD-Ig protein.

35. An aqueous formulation comprising an AS-DVD-Ig protein, a polyol, buffer, and a surfactant, wherein said formulation has a pH of about 5 to about 7, and wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 15% loss in relative percentage monomers as determined by SEC when formulated in a histidine or citrate phosphate buffer at a concentration of about 60 mg/ml following 14 days storage at about 40 degrees C.

36. The aqueous formulation of claim 35, wherein the polyol is selected from the group consisting of sorbitol, mannitol, and sucrose.

37. The aqueous formulation of claim 35 or 36, wherein the buffer is selected from the group consisting of acetate, histidine, glycine, arginine, phosphate, and citrate.

38. The aqueous formulation of any one of claims 35-38, wherein the surfactant is a polysorbate.

39. The aqueous formulation of claim 38, wherein the polysorbate is polysorbate 80 or polysorbate 20.

40. The aqueous formulation of claim 39, wherein the polysorbate 80 or the polysorbate 20 has a concentration of about 0.005% to about 0.02%.

41. An aqueous formulation comprising an AS-DVD-Ig protein, a polyol, histidine buffer, and a polysorbate, wherein said formulation has a pH of about 5 to about 7, and wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 15% aggregation as determined by SEC when formulated in a histidine or citrate phosphate buffer at a concentration of about60 mg/ml following 14 days storage at about 40 degrees C.

42. The formulation of any one of claims 1-41, wherein the AS-DVD-Ig protein comprises first and second polypeptide chains, each independently comprising VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first variable domain;

VD2 is a second variable domain;

C is a constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region;

n is 0 or 1,

wherein the VD1 domains on the first and second polypeptide chains form a first functional target binding site and the VD2 domains on the first and second polypeptide chains form a second functional target binding site.

43. The formulation of claim 42, wherein the first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region;

n is 0 or 1, and

wherein the second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region;

n is 0 or 1,

wherein the VD1 domains on the first and second polypeptide chains form a first functional target binding site and the VD2 domains on the first and second polypeptide chains form a second functional target binding site.

44. The formulation of claim 42 or 43, comprising two first polypeptide chains and two second polypeptide chains, wherein the binding protein comprises four functional target binding sites.

45. The formulation of any one of claims 42-44, wherein X1 is not CL.

46. The formulation of any one of claims 42-45, wherein the AS-DVD-Ig protein comprises three CDRs from the variable light or heavy chain amino acid sequences as set forth in SEQ ID NOs: 28 to 75.

47. The formulation of any one of claims 42-46, wherein the AS-DVD-Ig protein comprises a light or heavy chain amino acid sequence as set forth in SEQ ID NOs: 28 to 75.

48. The formulation of any one of claims 42-47, wherein the AS-DVD-Ig protein has a binding specificity selected from the group consisting of CD20/CD80, VEGF/Her2, TNF/RANKL, TNF/DKK, CD20/RANKL, DLL4/PLGF, TNF/SOST, IL-9/IgE, IL-12/IL-18, TNF/IL-17, TNF/PGE2, IL1α/IL1β, and DLL4/VEGF.

49. The formulation of any one of claims 42-47, wherein the AS-DVD-Ig protein has a binding specificity selected from the group consisting of IL4/IL13, IL1α/IL1β, and TNFα / IL17.

50. The formulation of claim 48, wherein the AS-DVD-Ig protein has a binding specificity for TNF and IL-17.

51. The formulation of claim 50, wherein the TNFα / IL17 specific AS-DVD-Ig protein is DVD A (SEQ ID NOs: 62 and 63).

52. The formulation of claim 48, wherein the AS-DVD-Ig protein has a binding specificity for IL1α/IL1β.

53. The formulation of claim 52, wherein the IL1α/IL1β specific AS-DVD-Ig protein is DVD C (SEQ ID NOs: 66 and 67).

54. The formulation of claim 48, wherein the AS-DVD-Ig protein has a binding specificity for IL-12/IL-18.

55. The formulation of any one of claims 1 to 54, wherein the formulation is a pharmaceutical formulation.

56. A pharmaceutical composition comprising an Aqueous Stable DVD-Ig (AS-DVD-Ig) protein and a buffer having a molarity of about 5 to about 50 mM, wherein the AS-DVD-Ig protein is characterized as a DVD-Ig protein having less than about 10% loss in relative percentage monomers as determined by SEC when formulated in a histidine or citrate phosphate buffer at a concentration of about 60 mg/ml, following 14 days storage at about 40 degrees C, and the formulation has a pH of 4.5 to 7.5.

57. The pharmaceutical composition of claim 56, further comprising at least one component selected from a surfactant, a polyol, and combinations thereof.

58. Use of the pharmaceutical composition of claim 56 or 57, in the manufacture of a medicament for treating a disorder.

59. A lyophilized formulation comprising a Lyophilized-Stable DVD-Ig (LS-DVD-Ig) protein, wherein when said formulation is reconstituted, it comprises about 1 to about 100 mg/ml of the LS-DVD-Ig protein, about 10 to about 50 mM of a buffer, a polyol, about 0.01 to about 0.2 mg/ml of a polysorbate, and has a pH of about 5 to about 7

60. The lyophilized formulation of claim 59, wherein the formulation has a pH of about 5.5 to about 6.5.

61. The lyophilized formulation of claim 59 or 60, wherein the LS-DVD-Ig protein has more than 10% rel. peak area change in monomers observed, following accelerated storage at a pH between about 5.5 and about 6.5 in an aqueous formulation for 21 days at about 40°C, when formulated at a concentration over about 100 mg/ml.

62. The lyophilized formulation of any one of claims 59-61, wherein the LS-DVD-Ig protein comprises first and second polypeptide chains, each independently comprising VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first variable domain;

VD2 is a second variable domain;

C is a constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region;

n is 0 or 1,

wherein the VD1 domains on the first and second polypeptide chains form a first functional target binding site and the VD2 domains on the first and second polypeptide chains form a second functional target binding site.

63. The lyophilized formulation of claim 62, wherein the first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region;

n is 0 or 1, and

wherein the second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region;

n is 0 or 1,

wherein the VD1 domains on the first and second polypeptide chains form a first functional target binding site and the VD2 domains on the first and second polypeptide chains form a second functional target binding site.

64. The lyophilized formulation of claim 62 or 63, comprising two first polypeptide chains and two second polypeptide chains, wherein the binding protein comprises four functional target binding sites.

65. The lyophilized formulation of any one of claims 62-64, wherein X1 is not CL.

66. The lyophilized formulation of any one of claims 62-65, wherein the LS-DVD-Ig protein comprises three CDRs from the variable light or heavy chain amino acid sequences as set forth in SEQ ID NOs: 28 to 75.

67. The lyophilized formulation of any one of claims 61-64, wherein the LS-DVD-Ig protein comprises a light or heavy chain amino acid sequence as set forth in SEQ ID NOs: 28 to 75.

68. The lyophilized formulation of any one of claims claims 59-67, wherein the LS-DVD-Ig protein has a binding specificity selected from the group consisting of CD20/CD80, VEGF/Her2, TNF/RANKL, TNF/DKK, CD20/RANKL, DLL4/PLGF, TNF/SOST, IL-9/IgE, IL-12/IL-18, TNF/IL-17, TNF/PGE2, IL1α/IL1β, or DLL4/VEGF.

69. The lyophilized formulation of claim 68, wherein the LS-DVD-Ig protein has a binding specificity for TNF and IL-17.

70. The lyophilized formulation of claim 68, wherein the LS-DVD-Ig protein has a binding specificity for IL1α/IL1β.

71. The lyophilized formulation of claim 68, wherein the LS-DVD-Ig protein has a binding specificity for IL-12/IL-18.

72. A lyophilized formulation prepared by lyophilizing an aqueous formulation comprising a LS-DVD-Ig protein, a buffer have a molarity of about 5 to about 50 mM, a surfactant, and a polyol, wherein the formulation has a pH of about 4.5 to about 7.5.

73. The lyophilized formulation of claim 72, wherein the buffer is selected from the group consisting of histidine, succinate, and citrate and/or phosphate.

74. The lyophilized formulation of claim 72 to 73, wherein the polyol is selected from the group consisting of mannitol, sorbitol, sucrose, and trehalose.

75. A formulation comprising an anti-TNF/IL-17 DVD-Ig protein and a buffer, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

76. A formulation comprising an anti-TNF/IL-17 DVD-Ig protein and a surfactant, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

77. A formulation comprising an anti-TNF/IL-17 DVD-Ig protein and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

78. A formulation comprising an anti-TNF/IL-17 DVD-Ig protein and two or more components selected from a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

79. The formulation of any one of claims 75-78, wherein the formulation is an aqueous formulation.

80. The formulation of any one of claims 75-78, wherein the formulation is a lyophilized formulation.

81. An aqueous formulation comprising an anti-TNF/IL-17 DVD-Ig protein, a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

82. A lyophilized formulation comprising an anti-TNF/IL-17 DVD-Ig protein, a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 62 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 63.

83. The formulation of any one of claims 75, 78, 81 or 82, wherein the buffer is histidine or acetate.

84. The formulation of any one of claims 77, 78, 81, or 82, wherein the polyol is sucrose or sorbitol.

85. The formulation of any one of claims 76, 78, 81, or 82, wherein the surfactant is a polysorbate.

86. The formulation of claim 85, wherein the polysorbate is polysorbate 80.

87. A formulation comprising an anti-IL1α/IL1β DVD-Ig protein and a buffer, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

88. A formulation comprising an anti-IL1α/IL1β DVD-Ig protein and a surfactant, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

89. A formulation comprising an anti-IL1α/IL1β DVD-Ig protein and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

90. A formulation comprising an anti-IL1α/IL1β DVD-Ig protein and two or more components selected from a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

91. The formulation of any one of claims 87-90, wherein the formulation is an aqueous formulation.

92. The formulation of any one of claims 87-90, wherein the formulation is a lyophilized formulation.

93. An aqueous formulation comprising an anti-IL1α/IL1β DVD-Ig protein, a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

94. A lyophilized formulation comprising an anti-IL1α/IL1β DVD-Ig protein, a buffer, a surfactant, and a polyol, wherein the DVD-Ig protein comprises a heavy chain comprising the amino acid sequence set forth as SEQ ID NO: 66 and a light chain comprising the amino acid sequence set forth as SEQ ID NO: 67.

95. The formulation of any one of claims 87, 90, 93, or 94, wherein the buffer is histidine.

96. The formulation of any one of claims 87, 89, 93, or 94, wherein the polyol is sucrose.

97. The formulation of any one of claims 87, 88, 93, or 94, wherein the surfactant is a polysorbate.

98. The formulation of claim 98, wherein the polysorbate is polysorbate 80.

CLAIMS

1. An aqueous formulation comprising about 50 to about 150 mg/ml DVD C DVD-Ig protein (SEQ ID NOs: 66 and 67), about 10 to about 20 mM of histidine buffer, about 30 to about 50 mg/ml sorbitol, and about 0.005% to about 0.02% polysorbate 80, wherein said formulation has a pH of about 5 to about 7.

2. The formulation of claim 1 comprising about 15 mM of histidine buffer, about 35 to about 45 mg/ml sorbitol, and about 0.01% polysorbate 80, wherein said formulation has a pH of about 5.5 to about 6.5.

3. The formulation of claim 1 or claim 2 comprising about 70 to about 110 mg/ml DVD C DVD-Ig protein.

4. The formulation of claim 1 or claim 2 comprising about 100 mg/ml DVD C DVD-Ig protein.