

What is claimed is:

1. A pharmaceutical formulation comprising a DR5-binding polypeptide, wherein the formulation comprises 20-70 mg/mL DR5-binding polypeptide, 5-20 mM histidine, 7-10% w/v sucrose, and 0.1-0.8% poloxamer P188 at a pH of 5.3-6.7; and wherein the DR5-binding polypeptide comprises at least one VHH domain comprising a CDR1 comprising the amino acid sequence of SEQ ID NO: 1, a CDR2 comprising the amino acid sequence of SEQ ID NO: 2, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 3.
2. The pharmaceutical formulation of claim 1, wherein the formulation comprises 30-60 mg/mL DR5-binding polypeptide, optionally wherein the formulation comprises 50 mg/mL DR5-binding polypeptide.
3. The pharmaceutical formulation of claim 1 or 2, wherein the formulation comprises 7-15 mM histidine, optionally wherein the formulation comprises 10 mM histidine.
4. The pharmaceutical formulation of any one of claims 1-3, wherein the histidine is histidine HCl.
5. The pharmaceutical formulation of any one of claims 1-4, wherein the formulation comprises 8-9% sucrose, optionally wherein the formulation comprises 8% sucrose or 9% sucrose.
6. The pharmaceutical formulation of any one of claims 1-5, wherein the formulation comprises 0.2-0.4% poloxamer P188, optionally wherein the formulation comprises 0.2% poloxamer P188.
7. The pharmaceutical formulation of any one of claims 1-6, wherein the formulation comprises 1-10 mM, 2-8 mM, 3-7 mM, or 4-6 mM methionine, optionally wherein the formulation comprises 5 mM methionine.
8. The pharmaceutical formulation of any one of claims 1-7, wherein the pH of the formulation is 5.4-6.6, 5.5-6.5, 5.6-6.4, 5.7-6.3, or 5.8-6.2, optionally wherein the pH of the formulation is about 6.
9. The pharmaceutical formulation of any one of claims 1-8, wherein the formulation comprises 50 mg/mL DR5-binding polypeptide, 10 mM histidine HCl, 8% sucrose, and 0.2% poloxamer P188, and wherein the pH of the formulation is about 6.

10. The pharmaceutical formulation of claim 9, wherein the formulation consists essentially of 50 mg/mL DR5-binding polypeptide, 10 mM histidine HCl, 8% sucrose, 0.2% poloxamer P188, and water, and wherein the pH of the formulation is about 6.
11. The pharmaceutical formulation of any one of claims 1-10, wherein the DR5-binding polypeptide comprises a VHH domain comprising the amino acid sequence of SEQ ID NO: 4.
12. The pharmaceutical formulation of any one of claims 1-11, wherein the DR5-binding polypeptide comprises an Fc region.
13. The pharmaceutical formulation of claim 12, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 6.
14. The pharmaceutical formulation of any one of claims 1-13, wherein the DR5-binding polypeptide has the structure VHH-linker-VHH-linker-Fc.
15. The pharmaceutical formulation of claim 14, wherein the VHH-linker-VHH comprises the amino acid sequence of SEQ ID NO: 5.
16. The pharmaceutical formulation of any one of claims 1-15, wherein the DR5-binding polypeptide comprises the amino acid sequence of SEQ ID NO: 7.
17. The pharmaceutical formulation of any one of claims 1-16, wherein the DR5-binding polypeptide consists of the amino acid sequence of SEQ ID NO: 7.
18. A lyophilized formulation comprising a DR5-binding polypeptide, wherein the DR5-binding polypeptide comprises at least one VHH domain comprising a CDR1 comprising the amino acid sequence of SEQ ID NO: 1, a CDR2 comprising the amino acid sequence of SEQ ID NO: 2, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 3; and wherein upon reconstitution of the lyophilized formulation in water to form an aqueous formulation, the aqueous formulation comprises 20-70 mg/mL DR5-binding polypeptide, 5-20 mM histidine, 7-10% sucrose, and 0.1-0.5% poloxamer P188, pH 5.3-6.7.
19. The lyophilized formulation of claim 18, wherein upon reconstitution of the lyophilized formulation in water to form an aqueous formulation, the aqueous formulation is a pharmaceutical formulation of any one of claims 1-17.
20. A lyophilized formulation formed by lyophilizing the pharmaceutical formulation of any one of claims 1-17.

21. The lyophilized formulation of any one of claims 18-20, wherein following storage at 2-8 °C for up to 3 months, up to 6 months, up to 9 months, up to 12 months, or more than 12 months, the lyophilized formulation is an off-white, uniform and elegant cake without any visible impurities.

22. The lyophilized formulation of any one of claims 18-21, wherein following storage at 2-8 °C for up to 3 months, up to 6 months, up to 9 months, up to 12 months, or more than 12 months, upon reconstitution of the formulation in water to form an aqueous formulation, the aqueous formulation is practically free of visible particles.

23. The lyophilized formulation of any one of claims 18-22, wherein following storage at 2-8 °C for up to 3 months, up to 6 months, up to 9 months, up to 12 months, or more than 12 months, upon reconstitution of the formulation in water to form an aqueous formulation, less than 3% or less than 2% of the DR5-binding polypeptide present in the aqueous formulation is aggregated, as measured by size-exclusion chromatography.

24. The lyophilized formulation of claim 23, wherein less than 1% or less than 0.5% of the DR5-binding polypeptide present in the aqueous formulation is degraded, as measured by size-exclusion chromatography.

25. A pharmaceutical formulation formed by reconstituting the lyophilized formulation of any one of claims 18-24.

26. Use of the pharmaceutical formulation of any one of claims 1-17 and 25 in the manufacture of a medicament for treating cancer in a subject with cancer.

27. The use of claim 26, wherein the cancer is chondrosarcoma, mesothelioma, colorectal cancer, Ewing sarcoma, or pancreatic adenocarcinoma.