CLAIMS

We claim:

1. Use of a pharmaceutically acceptable formulation comprising as an active ingredient a heterodimeric hIL12Fc mutein in the manufacture of medicament for treating a mammal suffering from a neoplastic disease, wherein the heterodimeric hIL12Fc mutein comprises a first polypeptide having the sequence of any one of SEQ ID NOs: 80, 83, 85, 86, 88, 90, 92, 121, 129, 132, 135, 138, 141, 144, 147, 150, and 153; and

a second polypeptide having the sequence of any one of SEQ ID NOs: 81, 82, 84, 87, 89, 91, 93, and 124; and

wherein the mammal is to be contacted with the pharmaceutically acceptable formulation.

2. The use of claim 1, wherein the dose of the heterodimeric hIL12Fc mutein provided to the mammal is from 10 µg/kg to 500 µg/kg.

3. The use of any one of claim 1, wherein the mammal is to be contacted with the pharmaceutically acceptable formulation in combination with one or more supplementary therapeutic agents.

4. The use of claim 3, wherein the one or more supplementary therapeutic agents is selected from the group consisting of checkpoint inhibitors, cytokines, or a therapeutic antibody.

5. The use of claim 1, wherein the neoplastic disease characterized by a tumor with T cell infiltration.

6. The use of claim 1, wherein the neoplastic disease is selected from the group consisting of melanoma, renal cell carcinoma (RCC), ovarian cancer, cervical cancer, non-small cell lung cancer (NSCLC), head and neck cancer, pancreatic cancer, and microsatellite instability (MSI) high cancers.

7. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 80 and the second polypeptide has the sequence of SEQ ID NO: 81.

8. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 121 and the second polypeptide has the sequence of SEQ ID NO: 124.

9. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 83 and the second polypeptide has the sequence of SEQ ID NO: 82.

10. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 141 and the second polypeptide has the sequence of SEQ ID NO: 124.

11. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO:144 and the second polypeptide has the sequence of SEQ ID NO: 124.

12. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 129 and the second polypeptide has the sequence of SEQ ID NO: 124.

13. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 147 and the second polypeptide has the sequence of SEQ ID NO: 82.

14. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 150 and the second polypeptide has the sequence of SEQ ID NO: 82.

15. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 153 and the second polypeptide has the sequence of SEQ ID NO: 82.

16. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 135 and the second polypeptide has the sequence of SEQ ID NO: 124.

17. The use of claim 1, wherein the first polypeptide has the sequence of SEQ ID NO: 138 and the second polypeptide has the sequence of SEQ ID NO: 124.

18. The use of claim 1, wherein the first polypeptide and the second polypeptide are linked by at least one interchain disulfide bond.

19. The use of claim 1, wherein the heterodimeric hIL12Fc mutein is PEGylated.