CLAIMS

What is claimed is:

1. Use of a multifunctional molecule in the manufacture of a medicament for treating cancer in a human subject in need thereof,

   wherein the multifunctional molecule comprises:

   (a) a TCRβV6-binding moiety, and

   (b) an interleukin-2 (IL-2) or a functional fragment or a functional variant thereof, and

   wherein the multifunctional molecule is to be administered to the human subject at a first dose of from 0.001 mg/kg to 10 mg/kg; thereby treating the cancer in the human subject.

2. The use of claim 1, wherein the multifunctional molecule is to be administered at a second dose to the human subject.

3. The use of claim 1 or 2, wherein the first dose is from 0.001 mg/kg to 1 mg/kg, from 0.01 mg/kg to 1 mg/kg, or from 0.05 mg/kg to 1 mg/kg.

4. The use of claim 3, wherein the first dose is about 0.08 mg/kg.

5. The use of any one of claims 2-4, wherein the second dose is from 0.001 mg/kg to 1 mg/kg, from 0.01 mg/kg to 1 mg/kg, or from 0.05 mg/kg to 1 mg/kg.

6. The use of any one of claims 2-5, wherein the second dose is about 0.08 mg/kg.

7. The use of any one of claims 2-6, wherein the second dose is to be administered at least 7 days, 13 days, or 14 days after administration of the first dose.

8. The use of any one of claims 1-7, wherein the multifunctional molecule is to be administered to the human subject once every two weeks.

9. The use of any one of claims 1-8, wherein the multifunctional molecule is to be administered at a dose of from 0.01 mg/kg to 1 mg/kg to the human subject once every two weeks.

10. The use of any one of claims 1-7, wherein the multifunctional molecule is to be administered to the human subject once every week.

11. The use of any one of claims 1-10, wherein the multifunctional molecule is to be administered via intravenous infusion.

12. The use of any one of claims 1-11, wherein the human subject is at least 18 years old.

13. The use of any one of claims 1-12, wherein the human subject:

(i) does not have a history of autoimmune disease;

(ii) does not have a major surgery or traumatic injury within 8 weeks before a first administration of the multifunctional molecule or the subject does not have an unhealed wound from surgery or injury;

(iii) is not treated with >10 mg per day of an immune-suppressive drug within 7 days prior to a first administration of the multifunctional molecule;

(iv) is not previously treated with a cytotoxic chemotherapy, a small molecule inhibitor, radiation, or an interventional radiology procedure with 2 weeks prior to a first administration of the multifunctional molecule;

(v) is not previously treated with a monoclonal antibody, an antibody-drug conjugate, a radioimmunoconjugate within 6 weeks prior to a first administration of the multifunctional molecule;

(vi) does not have an inflammatory process that is not resolved within 4 weeks before a first administration of the multifunctional molecule;

(vii) does not have a clinically significant pulmonary compromise; or

(viii) does not have an active viral, bacterial, or systemic fungal infection requiring parenteral treatment within 7 days of a first administration of the multifunctional molecule.

14. The use of any one of claims 1-13, wherein the human subject is characterized as having a solid tumor, and wherein the solid tumor is selected from the group consisting of a high mutational burden (TMB-H) tumor, microsatellite instability/DNA mismatch repair (MSI-H/dMMR), a virally associated tumor, metastatic triple-negative breast cancer (mTNBC), relapsed and refractory epithelial ovarian cancer, metastatic castration-resistant prostate cancer (mCRPC), colorectal cancer (CRC), and non-small cell lung cancer (NSCLC).

15. The use of any one of claims 1-14, wherein at least one additional therapeutic agent or therapy is to be further administered to the human subject.

16. The use of any one of claims 1-15, wherein the multifunctional molecule comprises a first polypeptide, a second polypeptide, and a third polypeptide,

wherein the first polypeptide, the second polypeptide and the third polypeptide are non-contiguous; and wherein:

(i) the first polypeptide comprises an Fc domain linked to a first portion of the TCRβV6-binding moiety, the first portion of the TCRβV6-binding moiety comprising a VH of the TCRβV6-binding moiety;

(ii) the second polypeptide comprises an Fc domain covalently linked to the IL-2 or functional fragment or functional variant thereof; and

(iii) the third polypeptide comprises a second portion of the TCRβV6-binding moiety, the second portion of the TCRβV6-binding moiety comprising a VL of the TCRβV6-binding moiety.

17. The use of claim 16, wherein

(a) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3517, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3521, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3518;

(b) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4000, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4002, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3518;

(c) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4004, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4030, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4005;

(d) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4006, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4007, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4005;

(e) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4008, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3521, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4009;

(f) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4010, the second polypeptide comprises a sequence with at least 90%

sequence identity to SEQ ID NO: 4003, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4009;

(g) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4011, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4013, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4012;

(h) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4014, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4015, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4012;

(i) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4016, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 3521, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4017; or

(j) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4018, the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4002, and the third polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4017.

18. The use of any one of claims 1-17, wherein the multifunctional molecule comprises a first polypeptide and a second polypeptide,

wherein the first polypeptide and the second polypeptide are non-contiguous, and wherein:

(i) the first polypeptide comprises an Fc domain linked to the TCRβV6-binding moiety; and

(ii) the second polypeptide comprises an Fc domain covalently linked to the IL-2 or functional fragment or functional variant thereof.

19. The use of claim 18, wherein

(a) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4019, and the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4020;

(b) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4021, and the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4022;

(c) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4023, and the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4024;

(d) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4025, and the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4026; or

(e) the first polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4027, and the second polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4028.

20. Use of a pharmaceutical composition comprising a multifunctional molecule in the manufacture of a medicament for treating cancer in a human subject in need thereof, wherein the multifunctional molecule comprises:

(a) a TCRβV6-binding moiety, and

(b) an interleukin-2 (IL-2) or a functional fragment or a functional variant thereof, and

wherein the pharmaceutical composition comprising the multifunctional molecule is to be administered to the human subject, wherein the multifunctional molecule is to be administered to the human subject at a first dose of from 0.001 mg/kg to 10 mg/kg; thereby treating the cancer in the human subject, and wherein the pharmaceutical composition further comprises a pharmaceutically acceptable excipient, carrier or diluent.

21. The use of claim 20, wherein the pharmaceutical composition comprises a pharmaceutically acceptable diluent that is a saline solution, optionally wherein the pharmaceutically acceptable diluent is 0.9% saline solution.

22. The use of claim 20, wherein the multifunctional molecule is present in the pharmaceutical composition at a concentration of from 0.02 mg/mL to 15 mg/mL.

23. The use of claims 20-22, wherein the multifunctional molecule is present in the pharmaceutical composition at a concentration of from 0.02 mg/mL to 1.5 mg/mL.

24. A dose of a pharmaceutical composition comprising a multifunctional molecule, wherein the multifunctional molecule comprises:

(a) a TCRβV6-binding moiety, and

(b) an interleukin-2 (IL-2) or a functional fragment or variant thereof; and

wherein the dose is from 0.001 mg/kg to 10 mg/kg of the multifunctional molecule.

25. A pharmaceutical composition comprising a multifunctional molecule and a pharmaceutically acceptable diluent,

wherein the multifunctional molecule comprises:

(a) a TCRβV6-binding moiety, and

(b) an interleukin-2 (IL-2) or a functional fragment or variant thereof;

wherein the pharmaceutically acceptable diluent is a 0.9% saline solution; and

wherein the multifunctional molecule is present in the pharmaceutical composition at a concentration of from 0.02 mg/mL to 15 mg/mL.