CLAIMS

1. An isolated bispecific antigen-binding molecule, comprising:

(a) a first antigen-binding domain that binds human CD28 and comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 20, 22, and 24, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 12, 14, and 16; and

(b) a second antigen binding domain specifically binds a human mucin 16 membrane antigen (MUC16) and comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 4, 6, and 8, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 12, 14, and 16.

2. An isolated bispecific antigen-binding molecule, comprising:

(a) a first antigen-binding domain that binds human CD28 and comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 44, 46, and 48, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 36, 38, and 40; and

(b) a second antigen binding domain specifically binds a human mucin 16 membrane antigen (MUC16) and comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 28, 30, and 32, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 36, 38, and 40.

3. The isolated bispecific antigen-binding molecule of claim 1, comprising:

(a) a first antigen binding domain that binds human CD28 and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 18, and a LCVR comprising the amino acid sequence of SEQ ID NO: 10; and

(b) a second antigen binding domain that specifically binds MUC16 and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 2, and a LCVR comprising the amino acid sequence of SEQ ID NO: 10.

4. The isolated bispecific antigen-binding molecule of claim 2~~1~~, comprising:

(a) a first antigen binding domain that binds human CD28 and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 42, and a LCVR comprising the amino acid sequence of SEQ ID NO: 34; and

(b) a second antigen binding domain that specifically binds MUC16 and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 26, and a LCVR comprising the amino acid sequence of SEQ ID NO: 34.

5. The isolated bispecific antigen binding molecule of any one of claims 1-4, wherein:

(a) the bispecific antigen binding molecule binds to the surface of human T cells with an EC_{50} of less than about 10^{-5} M as measured by an *in vitro* FACS binding assay;

(b) the bispecific antigen binding molecule binds to the surface of cynomolgus T cells with an EC_{50} of less than about $6x10^{-6}$ M as measured by an *in vitro* FACS binding assay;

(c) the bispecific antigen binding molecule binds to the surface of cell lines expressing MUC16 with an EC_{50} of less than about 10^{-9} M as measured by an *in vitro* FACS binding assay; or

(d) the bispecific antigen binding molecule demonstrates a costimulatory effect when used in conjunction with an anti-MUC16xCD3 bispecific antibody and tested on target cells expressing MUC16.

6. The isolated bispecific antigen binding molecule of claim 5(d), wherein the costimulatory effect is shown by one or more of the following: (a) the ability to activate and direct human T cells to kill a target cell expressing MUC16; (b) the ability to upregulate PD-1 on T cells; (c) the ability to increase the release of the cytokines IFN gamma from PBMC; (d) the ability to deplete tumor cells; (f) the ability to enhance tumor clearance; (g) the lack of inducing systemic T cell activation; and/or (h) measurement of IL-2 cytokine production using a primary $CD4^{+}$T cell/APC functional assay.

7. The isolated bispecific antigen-binding molecule of any one of claims 1-6 that is a bispecific antibody.

8. The isolated bispecific antigen-binding molecule of claim 7, wherein the bispecific antibody comprises a human IgG heavy chain constant region.

9. The isolated bispecific antigen-binding molecule of claim 8, wherein the human IgG heavy chain constant region of the bispecific antibody is isotype IgG1 or IgG4.

10. The isolated bispecific antigen-binding molecule of any one of claims 7-9, wherein the bispecific antibody comprises a chimeric hinge that alters Fc receptor binding.

11. A pharmaceutical composition comprising the bispecific antigen-binding molecule of any one of claims 1-10, and a pharmaceutically acceptable carrier or diluent.

12. A nucleic acid molecule comprising a nucleotide sequence encoding a bispecific antigen-binding molecule of any one of claims 1-10.

13. An expression vector comprising the nucleic acid molecule of claim 12.

14. A host cell comprising the expression vector of claim 13.

15. Use of the isolated bispecific antigen-binding molecule of any one of claims 1-10, or the pharmaceutical composition of claim 11, in the manufacture of a medicament for treating a MUC16-expressing tumor in a subject.

16. The use of claim 15, wherein the MUC16-expressing tumor is ovarian cancer.

17. The use of claim 15 or 16, wherein the medicament is for treating a MUC16-expression tumor in combination with a second therapeutic agent.

18. The use of claim 17, wherein the second therapeutic agent comprises an anti-tumor agent, radiotherapy, an antibody drug conjugate, a bispecific antibody conjugated to an anti-tumor agent, a checkpoint inhibitor, or combinations thereof.

19. The use of claim 17, wherein the second therapeutic agent is an anti-PD-1 antibody~~, optionally wherein the anti-PD-1 antibody is cemiplimab~~.

20. The use of claim 19, wherein the anti-PD-1 antibody is cemiplimab.

21~~20~~. The use of claim 17, wherein the second therapeutic agent is an anti-MUC16 x anti-CD3 bispecific antibody.