CLAIMS

1. A bispecific binding molecule comprising a monoclonal antibody that is an immunoglobulin that binds to HER2, wherein said immunoglobulin is mutated in its Fc region to destroy a glycosylation site, said immunoglobulin comprising two identical heavy chains and two identical light chains, said light chains being a first light chain and a second light chain, wherein the first light chain is fused to a first single chain variable fragment (scFv), via a peptide linker, to create a first light chain fusion polypeptide, and wherein the second light chain is fused to a second scFv, via a peptide linker, to create a second light chain fusion polypeptide, wherein the first and second scFv (i) are identical, and (ii) bind to CD3, and wherein the first and second light chain fusion polypeptides are identical;

wherein the heavy chains comprise a V_H domain present in any of SEQ ID NOs: 23, 27, 62 or 63;

wherein the light chains comprise a V_L domain present in SEQ ID NO: 25;

wherein the first and second scFvs comprise a V_H domain having a sequence selected from the group consisting of SEQ ID NOs: 15, 17 and 64, and a V_L domain having a sequence selected from the group consisting of SEQ ID NOs: 16 and 65; and

wherein the first scFv is fused to the carboxyl end of the first light chain, and wherein the second scFv is fused to the carboxyl end of the second light chain

2. The bispecific binding molecule of claim 1, wherein

(a) the sequence of each heavy chain is SEQ ID NO: 23, 27 or 62;

(b) the sequence of each light chain is SEQ ID NO: 25;

(c) the sequence of the peptide linker is any one of SEQ ID NO: 14 and 35-41; and/or

(d) the sequence of an intra-scFv peptide linker between the V_H domain and the V_L domain in the first scFv is any of SEQ ID NO: 14 and 35-41.

3. The bispecific binding molecule of claim 1 or claim 2, wherein (a) the sequence of the first scFv is SEQ ID NO: 19 and 48-59, or (b) the sequence of the first light chain fusion polypeptide is any of SEQ ID NOs: 29, 34, 42-47, and 60.

4. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 27, and wherein the sequence of the first light chain is SEQ ID NO: 25.

5. The bispecific binding molecule of claim 1 or 4, wherein the peptide linker is 5-30, 5-25, 5-15, 10-30, 10-20, 10-15, 15-30, or 15-25 amino acids in length.

6. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 27, wherein the sequence of the first light chain is SEQ ID NO: 25, and wherein the sequence of the first scFv is SEQ ID NO: 52.

7. The bispecific binding molecule of claim 1, wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 60.

8. The bispecific binding molecule of claim 1, wherein (a) the sequence of each heavy chain is SEQ ID NO: 62 and wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 60, or (b) the sequence of each heavy chain is SEQ ID NO: 27 and wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 47.

9. The bispecific binding molecule of claim 1, wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 47.

10. The bispecific binding molecule of claim 1, wherein the sequence of the heavy chain is SEQ ID NO: 27 and wherein the sequence of each light chain fusion polypeptide is SEQ ID NO: 47.

11. The bispecific binding molecule of claim 1, wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 29.

12. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 27 and wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 29.

13. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 27 and wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 34.

14. The bispecific binding molecule of any one of claims 1 to 13, wherein the glycosylation site is an N-linked glycosylation site.

15. The bispecific binding molecule of any of claims 1 to 14, wherein the K_D is between 70nM and 1 μM for CD3.

16. The bispecific binding molecule of any of claims 1 to 15, wherein the bispecific binding molecule does not bind an Fc receptor in its soluble or cell-bound form.

17. The bispecific binding molecule of claim 14, wherein the heavy chain has an amino acid substitution to replace an asparagine that is an N-linked glycosylation site, with an amino acid that does not function as a glycosylation site.

18. The bispecific binding molecule of any of claims 1 to 17, wherein the heavy chain has been mutated to destroy a C1q binding site.

19. The bispecific binding molecule of any of claims 1 to 17, wherein the bispecific binding molecule does not activate complement.

20. The bispecific binding molecule of any of claims 1 to 19, wherein the first scFv is disulfide stabilized.

21. A polynucleotide comprising nucleotide sequences encoding a light chain fusion polypeptide comprising an immunoglobulin light chain fused to a scFv, via a peptide linker, wherein the scFv is fused to the C-terminus of the light chain; wherein [[an]] the immunoglobulin light chain binds to HER2 and comprises a V_L domain present in SEQ ID NO: 25; and wherein the scFv binds to CD3 and comprises a V_H domain having a sequence selected from the group consisting of SEQ ID NOs: 15, 17 and 64, and a VL domain having a sequence selected from the group consisting of SEQ ID NOs: 16 and 65; and

wherein optionally.

(a) the sequence of the light chain is SEQ ID NO: 25, wherein optionally the nucleotide sequence encoding the light chain is SEQ ID NO: 24;

(b) the sequence of the scFv is SEQ ID NO: 52;

(c) the sequence of the scFv is SEQ ID NO: 19; wherein optionally the nucleotide sequence encoding the scFv is SEQ ID NO: 18;

(d) the sequence of the light chain is SEQ ID NO: 25, and the sequence of the scFv is SEQ ID NO: 52;

(e) the sequence of the light chain is SEQ ID NO: 25, and the sequence of the scFv is SEQ ID NO: 19, wherein optionally the nucleotide sequence encoding the light chain is SEQ ID NO: 24, and the nucleotide sequence encoding the scFv is SEQ ID NO: 18;

(f) the peptide linker is 5-30, 5-25, 5-15, 10-30, 10-20, 10-15, 15-30, or 15-25 amino acids in length, wherein optionally the sequence of the peptide linker is SEQ ID NO: 14, wherein optionally the nucleotide sequence encoding the peptide linker is SEQ ID NO: 13; or

(g) the sequence of the light chain fusion polypeptide is SEQ ID NO: 34 or SEQ ID NO: 29, wherein optionally the nucleotide sequence encoding the light chain fusion polypeptide of SEQ ID NO: 29 is SEQ ID NO: 28.

22. A vector comprising the polynucleotide of claim 21 operably linked to a promoter.

23. An *ex vivo* cell comprising the polynucleotide of claim 21 operably linked to a promoter.

24. An *ex vivo* cell comprising the vector of claim 22.

25. A vector comprising (i) a first polynucleotide of claim 21 operably linked to a first promoter, and (ii) a second polynucleotide encoding an immunoglobulin heavy chain that binds to HER2 operably linked to a second promoter.

26. An *ex vivo* cell comprising the vector of claim 25.

27. A method of producing a bispecific binding molecule comprising (i) culturing the cell of claim 26 to express the first and second polynucleotides such that a bispecific binding molecule comprising said light chain fusion polypeptide and said immunoglobulin heavy chain is expressed, and (ii) recovering the bispecific binding molecule.

28. A mixture of polynucleotides comprising (i) a first polynucleotide of claim 21 operably linked to a first promoter, and (ii) a second polynucleotide encoding an immunoglobulin heavy chain that binds to HER2 operably linked to a second promoter.

29. The mixture of polynucleotides of claim 28, wherein the sequence of the heavy chain is SEQ ID NO: 27.

30. The mixture of polynucleotides of claim 28, wherein the nucleotide sequence encoding the heavy chain is SEQ ID NO: 26.

31. An *ex vivo* cell comprising the mixture of polynucleotides of any of claims 28-30.

32. A method of producing a bispecific binding molecule, comprising (i) culturing the cell of claim 31 to express the first and second polynucleotides such that a bispecific binding molecule comprising said light chain fusion polypeptide and said immunoglobulin heavy chain is produced, and (ii) recovering the bispecific binding molecule.

33. A method of producing a bispecific binding molecule, comprising (i) expressing the mixture of polynucleotides of any of claims 28-30 such that a bispecific binding molecule comprising said first light chain fusion polypeptide and said immunoglobulin heavy chain is produced, and (ii) recovering the bispecific binding molecule.

34. A pharmaceutical composition comprising a therapeutically effective amount of the bispecific binding molecule of any of claims 1 to 20 and a pharmaceutically acceptable carrier.

35. A pharmaceutical composition comprising a therapeutically effective amount of (i) a first polynucleotide of claim 21 operably linked to a first promoter, and (ii) a second polynucleotide encoding an immunoglobulin heavy chain that binds to HER2 operably linked to a second promoter.

36. A pharmaceutical composition comprising a therapeutically effective amount of a vector comprising (i) a first polynucleotide of claim 21 operably linked to a first promoter, and (ii) a second polynucleotide encoding an immunoglobulin heavy chain that binds to HER2 operably linked to a second promoter.

37. The bispecific binding molecule of any of claims 1 to 20 for use in the treatment of a HER2-positive cancer in a subject in need thereof.

38. The bispecific binding molecule of claim 37, wherein the HER2-positive cancer is breast cancer, gastric cancer, an osteosarcoma, desmoplastic small round cell cancer, squamous cell carcinoma of head and neck cancer, ovarian cancer, prostate cancer, pancreatic cancer, glioblastoma multiforme, gastric junction adenocarcinoma, gastroesophageal junction adenocarcinoma, cervical cancer, salivary gland cancer, soft tissue sarcoma, leukemia, melanoma, Ewing's sarcoma, rhabdomyosarcoma, neuroblastoma, or any other neoplastic tissue that expresses the HER2 receptor.

39. The bispecific binding molecule of any of claims 37 to 38, wherein the HER2-positive cancer is a primary tumor or a metastatic tumor.

40. The bispecific binding molecule of any of claims 37 to 39, wherein the bispecific binding molecule is to be administered intravenously to the subject.

41. The bispecific binding molecule of any of claims 37 to 39, wherein the bispecific binding molecule is to be administered intraperitoneally, intrathecally, intraventricularly in the brain, or intraparenchymally in the brain.

42. The bispecific binding molecule of any of claims 37 to 41, wherein the bispecific binding molecule is to be administered in combination with doxorubicin, cyclophosphamide, paclitaxel, docetaxel, and/or carboplatin.

43. The bispecific binding molecule of any of claims 37 to 41, wherein the bispecific binding molecule is to be administered in combination with external beam or radioimmunotherapy.

44. The bispecific binding molecule of any of claims 37 to 43, wherein the HER2-positive cancer is resistant to treatment with trastuzumab, cetuximab, lapatinib, or erlotinib.

45. The bispecific binding molecule of any of claims 37 to 44, wherein the bispecific binding molecule is not bound to a T cell.

46. The bispecific binding molecule of any of claims 37 to 45, wherein the bispecific binding molecule is to be administered in combination with T cells.

47. The bispecific binding molecule of claim 46, wherein the T cells are bound to molecules identical to said bispecific binding molecule.

48. The bispecific binding molecule of any of claims 37 to 47, wherein the subject is a human.

49. A pharmaceutical composition comprising T cells bound to the bispecific binding molecule of any of claims 1 to 20 and a pharmaceutically acceptable carrier.

50. A method of making a therapeutic T cell, comprising binding the bispecific binding molecule of any of claims 1 to 20 to a T cell.

51. The method of claim 50, wherein the T cell is a human T cell.

52. The method of claim 50 or 51, wherein the binding is noncovalent.