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.

2. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 23 or 27.

3. The bispecific binding molecule of claim 1 or 2, wherein the sequence of each light chain is SEQ ID NO: 25.

4. The bispecific binding molecule of any of claims 1 to 3, wherein the sequence of the peptide linker is SEQ ID NO: 14.

5. The bispecific binding molecule of any of claims 1 to 4, wherein the sequence of a VH domain in the first scFv is SEQ ID NO: 15 or 17.

6. The bispecific binding molecule of any of claims 1 to 5, wherein the sequence of an intra-scFv peptide linker between a VH domain and a VL domain in the first scFv is SEQ ID NO: 14.

7. The bispecific binding molecule of any of claims 1 to 6, wherein the sequence of a VL domain in the first scFv is SEQ ID NO: 16.

8. The bispecific binding molecule of any of claims 1 to 4, wherein the sequence of the first scFv is SEQ ID NO: 19.

9. The bispecific binding molecule of any of claims 1 to 3, wherein the sequence of the first light chain fusion polypeptide is SEQ ID NO: 29.

10. The bispecific binding molecule of claim 1, wherein the sequence of each heavy chain is SEQ ID NO: 27 or 62.

11. The bispecific binding molecule of claim 1 or 10, wherein the sequence of the first light chain is SEQ ID NO: 25.

12. The bispecific binding molecule of any of claims 1, 10, and 11, wherein the sequence of the peptide linker is any of SEQ ID NOs: 14 and 35-41.

13. The bispecific binding molecule of any of claims 1 and 10 to 12, wherein the sequence of a V_H domain in the first scFv is any of SEQ ID NOs: 15, 17 and 64.

14. The bispecific binding molecule of any of claims 1 and 10 to 13, wherein the sequence of an intra-scFv peptide linker between a V_H domain and a V_L domain in the first scFv is any of SEQ ID NOs: 14 and 35-41.

15. The bispecific binding molecule of any of claims 1 and 10 to 12, wherein the sequence of a V_L domain in the first scFv is SEQ ID NO: 16 or 65.

16. The bispecific binding molecule of any of claims 1 and 10 to 12, wherein the sequence of the first scFv is any of SEQ ID NOs: 19 and 48-59.

17. The bispecific binding molecule of any of claims 1, 10, and 11, wherein the sequence of the first light chain fusion polypeptide is any of SEQ ID NOs: 29, 34, 42-47, and 60.

18. 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.

19. The bispecific binding molecule of claim 1 or 18, 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.

20. 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.

21. The bispecific binding molecule of claim 1 or 18, wherein the sequence of the peptide linker is SEQ ID NO: 14.

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

23. 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.

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

25. 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.

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

27. 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.

28. 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.

29. The bispecific binding molecule of any one of claims 1 to 28, wherein the glycosylation site is an N-linked glycosylation site.

30. A bispecific binding molecule comprising a heavy chain-aglycosylated monoclonal antibody that is an immunoglobulin that binds to HER2, 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.

31. The bispecific binding molecule of claim 30, wherein

(a) the sequence of each heavy chain is any of SEQ ID NOs: 23, 27, 62 and 63;

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

(c) the sequence of the peptide linker is any of SEQ ID NOs: 14 and 35-41;

(d) the sequence of a V_H domain in the first scFv is any of SEQ ID NOs: 15, 17 and 64;

(e) the sequence of an intra-scFv peptide linker between a V_H domain and a V_L domain in the first scFv is any of SEQ ID NOs: 14 and 35-41;

(f) the sequence of a V_L domain in the first scFv is SEQ ID NO: 16 or 65;

(g) the sequence of the first scFv is any of SEQ ID NOs: 19 and 48-59; and/or

(h) the sequence of the first light chain fusion polypeptide is any of SEQ ID NOs: 29, 34, 42-47, and 60.

32. The bispecific binding molecule of claim 30, wherein 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.

33. The bispecific binding molecule of any one of claims 30 to 31, 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.

34. The bispecific binding molecule of claim 30, 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.

35. The bispecific binding molecule of any one of claims 30-34, wherein the heavy chain has been mutated to destroy an N-linked glycosylation site.

36. The bispecific binding molecule of any one of claims 1 to 35 wherein the monoclonal antibody is aglycosylated.

37. A bispecific binding molecule comprising a heavy chain and a light chain fusion polypeptide, wherein the heavy chain comprises the sequence set forth in SEQ ID NO: 27 and the light chain fusion polypeptide comprises the sequence set forth in SEQ ID NO: 34.

38. The bispecific binding molecule of any of claims 1 to 37, wherein the K_D is between 70nM and 1 μM for CD3.

39. The bispecific binding molecule of any of claims 1 to 38, wherein the bispecific binding molecule does not bind an Fc receptor in its soluble or cell-bound form.

40. The bispecific binding molecule of claim 29 or 35, 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.

41. The bispecific binding molecule of any of claims 1 to 40, wherein the heavy chain has been mutated to destroy a C1q binding site.

42. The bispecific binding molecule of any of claims 1 to 40, wherein the bispecific binding molecule does not activate complement.

43. The bispecific binding molecule of any of claims 1 to 42, wherein the first scFv is disulfide stabilized.

44. The bispecific binding molecule of claim 1, 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.

45. 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 an immunoglobulin comprising the light chain binds to HER2 and wherein the scFv binds to CD3.

46. The polynucleotide of claim 45, wherein the sequence of the light chain is SEQ ID NO: 25.

47. The polynucleotide of claim 45, wherein the nucleotide sequence encoding the light chain is SEQ ID NO: 24.

48. The polynucleotide of claim 45, wherein the sequence of the scFv is SEQ ID NO: 19.

49. The polynucleotide of claim 45, wherein the nucleotide sequence encoding the scFv is SEQ ID NO: 18.

50. The polynucleotide of claim 45, wherein the sequence of the light chain is SEQ ID NO: 25, and wherein the sequence of the scFv is SEQ ID NO: 19.

51. The polynucleotide of claim 45, wherein the nucleotide sequence encoding the light chain is SEQ ID NO: 24, and wherein the nucleotide sequence encoding the scFv is SEQ ID NO: 18.

52. The polynucleotide of any of claims 45 to 50, 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.

53. The polynucleotide of any of claims 45 to 50, wherein sequence of the peptide linker is SEQ ID NO: 14.

54. The polynucleotide of any of claims 45 to 50, wherein nucleotide sequence encoding the peptide linker is SEQ ID NO: 13.

55. The polynucleotide of claim 45, wherein the sequence of the light chain fusion polypeptide is SEQ ID NO: 29.

56. The polynucleotide of claim 45, wherein the nucleotide sequence encoding the light chain fusion polypeptide is SEQ ID NO: 28.

57. A vector comprising the polynucleotide of any of claims 45 to 56 operably linked to a promoter.

58. An *ex vivo* cell comprising the polynucleotide of any of claims 45 to 56 operably linked to a promoter.

59. An *ex vivo* cell comprising the vector of claim 57.

60. A vector comprising (i) a first polynucleotide of any of claims 45 to 56 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.

61. An *ex vivo* cell comprising the vector of claim 60.

62. A method of producing a bispecific binding molecule comprising (i) culturing the cell of claim 61 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.

63. A mixture of polynucleotides comprising (i) a first polynucleotide of any of claims 45 to 56 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.

64. The mixture of polynucleotides of claim 63, wherein the sequence of the heavy chain is SEQ ID NO: 27.

65. The mixture of polynucleotides of claim 63, wherein the nucleotide sequence encoding the heavy chain is SEQ ID NO: 26.

66. An *ex vivo* cell comprising the mixture of polynucleotides of any of claims 63-65.

67. A method of producing a bispecific binding molecule, comprising (i) culturing the cell of claim 66 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.

68. A method of producing a bispecific binding molecule, comprising (i) expressing the mixture of polynucleotides of any of claims 63-65 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.

69. A pharmaceutical composition comprising a therapeutically effective amount of the bispecific binding molecule of any of claims 1 to 44 and a pharmaceutically acceptable carrier.

70. A pharmaceutical composition comprising a therapeutically effective amount of (i) a first polynucleotide of any of claims 45 to 56 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.

71. A pharmaceutical composition comprising a therapeutically effective amount of a vector comprising (i) a first polynucleotide of any of claims 45 to 56 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.

72. The bispecific binding molecule of any of claims 1 to 44 for use in the treatment of a HER2-positive cancer in a subject in need thereof.

73. The bispecific binding molecule of claim 72, 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.

74. The bispecific binding molecule of any of claims 72 to 73, wherein the HER2-positive cancer is a primary tumor or a metastatic tumor.

75. The bispecific binding molecule of any of claims 72 to 74, wherein the bispecific binding molecule is to be administered intravenously to the subject.

76. The bispecific binding molecule of any of claims 72 to 74, wherein the bispecific binding molecule is to be administered intraperitoneally, intrathecally, intraventricularly in the brain, or intraparenchymally in the brain.

77. The bispecific binding molecule of any of claims 72 to 76, wherein the bispecific binding molecule is to be administered in combination with doxorubicin, cyclophosphamide, paclitaxel, docetaxel, and/or carboplatin.

78. The bispecific binding molecule of any of claims 72 to 76, wherein the bispecific binding molecule is to be administered in combination with external beam or radioimmunotherapy.

79. The bispecific binding molecule of any of claims 72 to 78, wherein the HER2-positive cancer is resistant to treatment with trastuzumab, cetuximab, lapatinib, erlotinib, or any other small molecule or antibody that targets the HER family of receptors.

80. The bispecific binding molecule of any of claims 72 to 79, wherein the bispecific binding molecule is not bound to a T cell.

81. The bispecific binding molecule of any of claims 72 to 80, wherein the bispecific binding molecule is to be administered in combination with T cells.

82. The bispecific binding molecule of claim 81, wherein the T cells are bound to molecules identical to said bispecific binding molecule.

83. The bispecific binding molecule of any of claims 72 to 82, wherein the subject is a human.

84. A pharmaceutical composition comprising T cells bound to the bispecific binding molecule of any of claims 1 to 44 and a pharmaceutically acceptable carrier.

85. A method of making a therapeutic T cell, comprising binding the bispecific binding molecule of any of claims 1 to 44 to a T cell.

86. The method of claim 85, wherein the T cell is a human T cell.

87. The method of claim 85 or 86, wherein the binding is noncovalent.