

CLAIMS

What is claimed is:

1. A monospecific binding protein that binds a CD38 polypeptide, wherein the monospecific binding protein comprises:

(a) an antibody heavy chain that comprises an antibody heavy chain variable (VH) domain comprising a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYA (SEQ ID NO:37), a CDR-H2 sequence comprising the amino acid sequence of IYPGQGGT (SEQ ID NO:38), and a CDR-H3 sequence comprising the amino acid sequence of ARTGGLRRAYFTY (SEQ ID NO:33); and

(b) an antibody light chain comprising an antibody light chain variable (VL) domain comprising a CDR-L1 sequence comprising the amino acid sequence of QSVSSYGQGF (SEQ ID NO:39), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:40), and a CDR-L3 sequence comprising the amino acid sequence of QQNKEDPWT (SEQ ID NO:36).

2. The monospecific binding protein of claim 1, wherein the VH domain comprises the sequence, from N-terminus to C-terminus, FR1—CDR-H1—FR2—CDR-H2—FR3—CDR-H3—FR4; wherein FR1 comprises the sequence QVQLVQSGAEVVKPGASVKVSCCKAS (SEQ ID NO:86), QVQLVQSGAEVVKSGASVKVSCCKAS (SEQ ID NO:87), or QVQLVQSGAEVVKPGASVKMSCKAS (SEQ ID NO:88); wherein FR2 comprises the sequence MHWVKEAPGQRLEWIGY (SEQ ID NO:90) or MHWVKEAPGQGLEWIGY (SEQ ID NO:91); wherein FR3 comprises the sequence NYNQKFQGRATLTADTSASTAYMELSSLRSEDNAVYFC (SEQ ID NO:93) or NYNQKFQGRATLTADTSASTAYMEISSLRSEDNAVYFC (SEQ ID NO:94); and wherein FR4 comprises the sequence WGQGTLVTVSS (SEQ ID NO:96).

3. The monospecific binding protein of claim 1, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:13, and the VL domain comprises the amino acid sequence of SEQ ID NO:14.

4. The monospecific binding protein of claim 3, wherein the antibody heavy chain comprises the amino acid sequence of SEQ ID NO:15, and the antibody light chain comprises the amino acid sequence of SEQ ID NO:16.
5. The monospecific binding protein of any one of claims 1-4, wherein the binding protein cross-reacts with an extracellular domain of a human CD38 polypeptide and an extracellular domain of a cynomolgus monkey CD38 polypeptide.
6. The monospecific binding protein of claim 5, wherein the binding protein binds a human CD38 polypeptide comprising the amino acid sequence of SEQ ID NO:1.
7. The monospecific binding protein of claim 6, wherein the binding protein binds the human CD38 polypeptide comprising the amino acid sequence of SEQ ID NO:1 with an equilibrium dissociation constant (K_D) of 2.1nM or less.
8. The monospecific binding protein of claim 5, wherein the binding protein binds a human isoform E CD38 polypeptide comprising the amino acid sequence of SEQ ID NO:105.
9. The monospecific binding protein of any one of claims 5-8, wherein the binding protein binds a cynomolgus monkey CD38 polypeptide comprising the amino acid sequence of SEQ ID NO:30.
10. The monospecific binding protein of claim 9, wherein the binding protein binds the cynomolgus monkey CD38 polypeptide comprising the amino acid sequence of SEQ ID NO:30 with an equilibrium dissociation constant (K_D) of 1.3nM or less.
11. The monospecific binding protein of any one of claims 1-10, wherein the binding protein is a chimeric or humanized antibody.
12. The monospecific binding protein of any one of claims 1-11, wherein the binding protein is a monoclonal antibody.
13. The monospecific binding protein of any one of claims 1-12, wherein the binding protein comprises one or more full-length antibody heavy chains comprising an Fc region.

14. The monospecific binding protein of claim 13, wherein the Fc region is a human Fc region, and wherein the binding protein induces antibody-dependent cellular cytotoxicity of a cell expressing CD38 on its cell surface.
15. The monospecific binding protein of claim 13 or claim 14, wherein the Fc region is a human IgG1 Fc region.
16. A polynucleotide encoding the monospecific binding protein of any one of claims 1-15.
17. A vector comprising the polynucleotide of claim 16.
18. A host cell comprising the polynucleotide of claim 16 or the vector of claim 17.
19. A method of producing a monospecific binding protein, the method comprising culturing the host cell of claim 18 such that the monospecific binding protein is produced.
20. The method of claim 19, further comprising recovering the monospecific binding protein from the host cell.
21. A pharmaceutical composition comprising the monospecific binding protein of any one of claims 1-15 and a pharmaceutically acceptable carrier.