

CLAIMS

1. A chimeric antigen receptor (CAR) comprising a polypeptide comprising:
 - (a) an extracellular antigen binding domain comprising a first BCMA binding moiety and a second BCMA binding moiety, wherein the first BCMA binding moiety is a first anti-BCMA single domain antibody (sdAb), and the second BCMA binding moiety is a second anti-BCMA sdAb;
 - (b) a transmembrane domain; and
 - (c) an intracellular signaling domain;wherein the first anti-BCMA sdAb and the second anti-BCMA sdAb are each independently an sdAb comprising a CDR1, a CDR2 and a CDR3 as set forth in a single anti-BCMA sdAb comprising the amino acid sequence of any one of SEQ ID NOs: 115-152.
2. The CAR of claim 1, wherein:
 - (i) the first anti-BCMA sdAb comprises a CDR1, a CDR2 and a CDR3 as set forth in the anti-BCMA sdAb comprising the amino acid sequence of SEQ ID NO: 124, and
 - (ii) the second anti-BCMA sdAb comprises a CDR1, a CDR2, and a CDR3 as set forth in the anti-BCMA sdAb comprising the amino acid sequence of SEQ ID NO: 117.
3. An anti-BCMA single domain antibody (sdAb) comprising a CDR1, a CDR2 and a CDR3 as set forth in a single anti-BCMA sdAb comprising the amino acid sequence of any one of SEQ ID NOs: 115-152.
4. The anti-BCMA sdAb of claim 3, wherein the anti-BCMA sdAb is a camelid antibody, or wherein the anti-BCMA sdAb is a chimeric antibody.
5. The anti-BCMA sdAb of claim 3, wherein the anti-BCMA sdAb is a V_HH fragment.
6. A chimeric antigen receptor (CAR) comprising a polypeptide comprising:

(a) an extracellular antigen binding domain comprising an anti-BCMA sdAb of any one of claims 3-5;

(b) a transmembrane domain; and

(c) an intracellular signaling domain.

7. The CAR of any one of claims 1-2 and 6, wherein the transmembrane domain is from a molecule selected from the group consisting of CD8 α , CD4, CD28, CD137, CD80, CD86, CD152, and PD1.

8. The CAR of claim 7, wherein the transmembrane domain is from CD8 α or CD28.

9. The CAR of any one of claims 1-2 and 6-8, wherein the intracellular signaling domain comprises a primary intracellular signaling domain of an immune effector cell.

10. The CAR of claim 9, wherein the primary intracellular signaling domain is from CD3 ζ .

11. The CAR of any one of claims 1-2 and 6-10, wherein the intracellular signaling domain comprises a co-stimulatory signaling domain.

12. The CAR of claim 11, wherein the co-stimulatory signaling domain is from a co-stimulatory molecule selected from the group consisting of CD27, CD28, CD137, OX40, CD30, CD40, CD3, LFA-1, ICOS, CD2, CD7, LIGHT, NKG2C, B7-H3, ligands of CD83, and combinations thereof.

13. The CAR of claim 12, wherein the co-stimulatory signaling domain comprises a cytoplasmic domain of CD28 and/or a cytoplasmic domain of CD137.

14. The CAR of any one of claims 1-2 and 6-13, further comprising a hinge domain located between the C-terminus of the extracellular antigen binding domain and the N-terminus of the transmembrane domain.

15. The CAR of claim 14, wherein the hinge domain is from CD8 α .
16. The CAR of any one of claims 1-2 and 6-15, further comprising a signal peptide located at the N-terminus of the polypeptide.
17. The CAR of claim 16, wherein the signal peptide is from CD8 α .
18. A chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 216-256 and 299.
19. An isolated nucleic acid comprising a nucleic acid sequence encoding the CAR of any one of claims 1-2 and 6-18 or the anti-BCMA sdAb of any one of claims 3-5.
20. A vector comprising the isolated nucleic acid of claim 19.
21. An engineered immune effector cell, comprising the CAR of any one of claims 1-2 and 6-18, the isolated nucleic acid of claim 19, or the vector of claim 20.
22. The engineered immune effector cell of claim 21, wherein the immune effector cell is a T cell.
23. A pharmaceutical composition, comprising the engineered immune effector cell of claim 21 or 22, the CAR of any one of claims 1-2 and 6-18, or the anti-BCMA sdAb of any one of claims 3-5, and a pharmaceutically acceptable carrier.
24. Use of the engineered immune effector cell of claim 21 or 22, the CAR of any one of claims 1-2 and 6-18, or the anti-BCMA sdAb of any one of claims 3-5 in the manufacture of a medicament for treating cancer in an individual, wherein the cancer comprises a cell expressing BCMA.
25. The use of claim 24, wherein the cancer is multiple myeloma.

26. The use of claim 25, wherein the cancer is refractory or relapsed multiple myeloma.