

WHAT IS CLAIMED IS:

1. An anti-BCMA binding moiety comprising a heavy chain variable region (VH) comprising a HCDR1, a H, and a HCDR3, and a light chain variable region (VL) comprising a LCDR1, a L, and a LCDR3, wherein the VH comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VH amino acid sequence set forth in any one of SEQ ID NOS:260-285 and 1582-1600; and the VL comprises the LCDR1, the LCDR2, and the LCDR3 contained within the VL amino acid sequence set forth in any one of SEQ ID NOS:541-566 and 1677-1695.

2. The anti-BCMA binding moiety of claim 1, wherein the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOS:260-285 and 1582-1600, and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOS:541-566 and 1677-1695.

3. The anti-BCMA binding moiety of claim 1 or claim 2, wherein the VH comprises the amino acid sequence set forth in any one of SEQ ID NOS:260-285 and 1582-1600, and the VL comprises the amino acid sequence set forth in any one of SEQ ID NOS:541-566 and 1677-1695.

4. The anti-BCMA binding moiety of any one of claims 1-3, wherein:

(a) the VH comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VH amino acid sequence set forth in SEQ ID NO:268, and the VL comprises the LCDR1, the LCDR2, and the LCDR3 contained within the VL amino acid sequence set forth in SEQ ID NO:549;

(b) the VH comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VH amino acid sequence set forth in SEQ ID NO:270, and the VL comprises the LCDR1, the LCDR2, and the LCDR3 contained within the VL amino acid sequence set forth in SEQ ID NO:551;

(c) the VH comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VH amino acid sequence set forth in SEQ ID NO:1600, and the VL comprises the LCDR1, the

LCDR2, and the LCDR3 contained within the VL amino acid sequence set forth in SEQ ID NO:1695; or

(d) the VH comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VH amino acid sequence set forth in SEQ ID NO:1586, and the VL comprises the LCDR1, the LCDR2, and the LCDR3 contained within the VL amino acid sequence set forth in SEQ ID NO:1681.

5. The anti-BCMA binding moiety of any one of claims 1-4, wherein:

(a) the VH comprises an amino acid sequence having at least 90% sequence identity to the VH amino acid sequence set forth in SEQ ID NO:268, and the VL comprises an amino acid sequence having at least 90% sequence identity to the VL amino acid sequence set forth in SEQ ID NO:549;

(b) the VH comprises an amino acid sequence having at least 90% sequence identity to the VH amino acid sequence set forth in SEQ ID NO:270, and the VL comprises an amino acid sequence having at least 90% sequence identity to the VL amino acid sequence set forth in SEQ ID NO:551;

(c) the VH comprises an amino acid sequence having at least 90% sequence identity to the VH amino acid sequence set forth in SEQ ID NO:1600, and the VL comprises an amino acid sequence having at least 90% sequence identity to the VL amino acid sequence set forth in SEQ ID NO:1695; or

(d) the VH comprises an amino acid sequence having at least 90% sequence identity to the VH amino acid sequence set forth in SEQ ID NO:1586, and the VL comprises an amino acid sequence having at least 90% sequence identity to the VL amino acid sequence set forth in SEQ ID NO:1681.

6. The anti-BCMA binding moiety of any one of claims 1-5, wherein:

(a) the VH comprises the amino acid sequence set forth in SEQ ID NO:268, and the VL comprises the amino acid sequence set forth in SEQ ID NO:549;

(b) the VH comprises the amino acid sequence set forth in SEQ ID NO:270, and the VL comprises the amino acid sequence set forth in SEQ ID NO:551;

(c) the VH comprises the amino acid sequence set forth in SEQ ID NO:1600, and the VL comprises the amino acid sequence set forth in SEQ ID NO:1695; or

(d) the VH comprises the amino acid sequence set forth in SEQ ID NO:1586, and the VL comprises the amino acid sequence set forth in SEQ ID NO:1681.

7. The anti-BCMA binding moiety of any one of claims 1-6, wherein the anti-BCMA binding moiety is a single-chain variable fragment (scFv), a Fv, a Fab, or a F(ab')₂.

8. The anti-BCMA binding moiety of any one of claims 1-7, wherein the VH and VL are joined by a linker.

9. The anti-BCMA binding moiety of claim 8, wherein the linker comprises the amino acid sequence set forth in SEQ ID NO:1388 or SEQ ID NO:2388.

10. The anti-BCMA binding moiety of any one of claims 1-9 wherein the anti-BCMA binding moiety is a single-chain variable fragment (scFv).

11. The anti-BCMA binding moiety of claim 10, wherein the VH is N-terminal of the VL.

12. The anti-BCMA binding moiety of claim 10 or claim 11, wherein the scFv comprises the amino acid sequence set forth in any one of SEQ ID NOS:593-618.

13. The anti-BCMA binding moiety of claim 10, wherein the VL is N-terminal of the VH.

14. The anti-BCMA binding moiety of claim 10 or claim 13 wherein the scFv comprises the amino acid sequence set forth in any one of SEQ ID NOS:671-696.

15. An anti-BCMA binding moiety comprising a first heavy chain variable region (VHH1), wherein the VHH1 comprises a HCDR1, a HCDR2, and a HCDR3 contained within the VHH1 amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

16. The anti-BCMA binding moiety of claim 15, wherein the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

17. The anti-BCMA binding moiety of claim 15 or claim 16, wherein the VHH1 comprises the amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

18. The anti-BCMA binding moiety of any one of claims 15-17, wherein:

(a) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3264;

(d) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3265;

(e) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3271; or

(f) the VHH1 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH1 amino acid sequence set forth in SEQ ID NO:3273.

19. The anti-BCMA binding moiety of any one of claims 15-18, wherein:

(a) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3264;

(d) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3265;

(e) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3271; or

(f) the VHH1 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3273.

20. The anti-BCMA binding moiety of any one of claims 15-18, wherein:

(a) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3264;

(d) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3265;

(e) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3271; or

(f) the VHH1 comprises the amino acid sequence set forth in SEQ ID NO:3273.

21. The anti-BCMA binding moiety of any one of claims 15-20, further comprising a second heavy chain variable region (VHH2), wherein the VHH2 comprises a HCDR1, a HCDR2, and a HCDR3 contained within the VHH2 amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

22. The anti-BCMA binding moiety of claim 21, wherein the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

23. The anti-BCMA binding moiety of claim 21 or claim 22, wherein the VHH2 comprises the amino acid sequence set forth in any one of SEQ ID NOS:3255-3277.

24. The anti-BCMA binding moiety of any one of claims 21-23, wherein:

(a) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3264;

(d) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3265;

(e) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3271; or

(f) the VHH2 comprises the HCDR1, the HCDR2, and the HCDR3 contained within the VHH2 amino acid sequence set forth in SEQ ID NO:3273.

25. The anti-BCMA binding moiety of any one of claims 21-24, wherein:

(a) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3264;

(d) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3265;

(e) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3271; or

(f) the VHH2 comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:3273.

26. The anti-BCMA binding moiety of any one of claims 21-25, wherein:

(a) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3262;

(b) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3263;

(c) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3264;

- (d) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3265;
- (e) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3271; or
- (f) the VHH2 comprises the amino acid sequence set forth in SEQ ID NO:3273.

27. The anti-BCMA binding moiety of any one of claims 21-26, wherein the VHH1 and the VHH2 are joined by a linker.

28. The anti-BCMA binding moiety of claim 27, wherein the linker comprises the amino acid sequence set forth in SEQ ID NO:1388 or SEQ ID NO:2388.

29. The anti-BCMA binding moiety of any one of claims 21-28 comprising, wherein the anti-BCMA binding moiety comprises the amino acid sequence set forth in any one of SEQ ID NOS:3324-3346.

30. A BCMA-directed chimeric antigen receptor (CAR) comprising:

- (a) the anti-BCMA binding moiety of any one of Claims 1-29;
- (b) a hinge domain;
- (c) a transmembrane domain; and
- (d) an intracellular signaling domain comprising a co-stimulatory subdomain and a CD3 ζ subdomain.

31. The BCMA-directed CAR of claim 30, wherein the co-stimulatory subdomain comprises an OX40 subdomain, a CD28 subdomain, or a 4-1BB subdomain.

32. The BCMA-directed CAR of claim 30 or claim 31, wherein the BCMA-directed CAR is encoded by a nucleic acid sequence that also encodes a membrane-bound interleukin 15 (mbIL15).

33. A polynucleotide encoding the anti-BCMA binding moiety of any one of claims 1-29 or the CAR of any one of claims 30-33.

34. A vector comprising the polynucleotide of claim 33.
35. An immune cell comprising an anti-BCMA binding moiety of any one of claims 1-29, a BCMA-directed CAR of any one of claims 30-33, a polynucleotide of claim 33, or a vector of claim 34.
36. The immune cell of claim 35, wherein the immune cell is a natural killer (NK) cell or T cell.
37. A composition comprising the immune cells of claim 35 or claim 36.
38. The composition of claim 37 for use in treating a cancer.
39. The composition for use of claim 38, wherein the cancer is multiple myeloma.
40. Use of the composition of claim 37 in the manufacture of a medicament for the treatment of a cancer.