

CLAIMS

1. A cell comprising a chimeric antigen receptor (CAR) comprising:
 - (a) an ectodomain comprising an antigen recognition region, wherein the antigen recognition region comprises at least one VH that specifically binds to B-Cell Maturation Antigen (BCMA);
 - (b) a transmembrane domain, and
 - (c) an endodomain comprising at least one costimulatory domain;wherein the VH comprises:
 - a complementarity determining region 1 (CDR1) comprising an amino acid sequence of SEQ ID NO: 18056;
 - a complementarity determining region 2 (CDR2) comprising an amino acid sequence of SEQ ID NO: 18060; and
 - a complementarity determining region 3 (CDR3) comprising an amino acid sequence of SEQ ID NO: 18064.
2. The cell of claim 1, wherein the VH comprises or consists of a recombinant or chimeric sequence.
3. The cell of claim 1, wherein the VH comprises or consists of a human or humanized sequence.
4. The cell of any one of claims 1-3, wherein the ectodomain of (a) further comprises a signal peptide.
5. The cell of any one of claims 1-4, wherein the ectodomain of (a) further comprises a hinge between the antigen recognition region and the transmembrane domain.
6. The cell of claim 4 or 5, wherein the signal peptide comprises a sequence encoding a human CD2, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD8 α , CD19, CD28, 4-1BB or GM-CSFR signal peptide.

7. The cell of claim 6, wherein the signal peptide comprises a sequence encoding a human CD8 α signal peptide.
8. The cell of claim 7, wherein the human CD8 α signal peptide comprises an amino acid sequence of SEQ ID NO: 18012.
9. The cell of any one of claims 1-8, wherein the transmembrane domain comprises a sequence encoding a human CD2, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD8 α , CD19, CD28, 4-1BB or GM-CSFR transmembrane domain.
10. The cell of claim 9, wherein the transmembrane domain comprises a sequence encoding a human CD8 α transmembrane domain.
11. The cell of claim 10, wherein the human CD8 α transmembrane domain comprises an amino acid sequence of SEQ ID NO: 18014.
12. The cell of any one of claims 1-11, wherein the endodomain comprises a human CD3 ζ endodomain.
13. The cell of any one of claims 1-12, wherein the at least one costimulatory domain comprises a human 4-1BB, CD28, CD40, ICOS, MyD88, OX-40 intracellular segment, or any combination thereof.
14. The cell of claim 13, wherein the at least one costimulatory domain comprises a human-4-1BB costimulatory domain.
15. The cell of claim 12, wherein the human CD3 ζ endodomain comprises an amino acid sequence of SEQ ID NO: 18016.
16. The cell of claim 14, wherein the human 4-1BB costimulatory domain comprises an amino acid sequence of SEQ ID NO: 18018.
17. The cell of claim 5, wherein the hinge comprises a sequence derived from a human CD8 α , IgG4, CD4 or any combination thereof.

18. The cell of claim 17, wherein the hinge comprises a sequence derived from a human CD8 α .
19. The cell of claim 18, wherein the sequence derived from a human CD8 α comprises an amino acid sequence of SEQ ID NO: 18020.
20. The cell of any one of claims 1-19, wherein the cell is an immune cell.
21. The cell of claim 20, wherein the immune cell is a T-cell, a Natural Killer (NK) cell, a Natural Killer (NK)-like cell, a Cytokine Induced Killer (CIK) cell, a hematopoietic progenitor cell, a peripheral blood (PB) derived T cell or an umbilical cord blood (UCB) derived T-cell.
22. The cell of any one of claims 1-21, wherein the cell is autologous.
23. The cell of any one of claims 1-21, wherein the cell is allogeneic.
24. The cell of any one of claims 1-23, wherein the VH comprises an amino acid sequence of SEQ ID NO: 18051.
25. The cell of any one of claims 1-23, comprising the amino acid sequence of SEQ ID NO: 18006.
26. An isolated cell comprising a CAR comprising:
- (a) an ectodomain comprising a human CD8 α signal peptide and an antigen recognition region, wherein the antigen recognition region comprises at least one VH that specifically binds to BCMA and wherein the VH comprises an amino acid sequence of SEQ ID NO: 18051;
 - (b) a hinge domain comprising a human CD8 α hinge domain;
 - (c) a transmembrane domain comprising a human CD8 α transmembrane domain;
- and
- (d) an endodomain comprising a human 4-1BB costimulatory domain and a human CD3 ζ endodomain.

27. The cell of claim 26, wherein the human CD8 α signal peptide comprises the amino acid sequence of SEQ ID NO: 18012, wherein the human CD8 α hinge domain comprises the amino acid sequence of SEQ ID NO: 18020, wherein the human CD8 α transmembrane domain comprises the amino acid sequence of SEQ ID NO: 18014, wherein the human 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 18018, and wherein the human CD3 ζ endodomain comprises the amino acid sequence of SEQ ID NO: 18016.
28. A composition comprising the cell of any one of claims 1-27 and at least one pharmaceutically acceptable carrier.
29. A composition comprising a population of cells, wherein a plurality of cells of the population comprises the cell of any one of claims 1-27.
30. Use of the composition of claim 28 or claim 29 in the manufacture of a medicament for the treatment of a BCMA-associated cancer in a subject in need thereof.
31. The use of claim 30, wherein the cancer is multiple myeloma.