

regulatory T cells (Tregs), enhances the efficacy of adoptive T cell therapy,^{4,12} as such, the immediate post-autologous transplant period could be an optimal time to administer T cells, and myeloma is one of the few diseases where autologous stem cell transplantation is the standard of care. Third, the immunomodulatory drug lenalidomide may improve CAR based therapy, as has been shown in mice,¹³ and lenalidomide is commonly used to treat MM. Fourth, adoptive T cell therapy works best in bone marrow predominant disease such as ALL,^{6,7} when compared to solid tumors or extra-medullary CLL,⁴ and similar to ALL, myeloma is a disease of the bone marrow.

While there are various reasons to expect that adoptive T cell therapy may work well in MM, expanding adoptive T cell therapy to myeloma also poses unique challenges. Unlike other B-cell malignancies, CD19 expression is seen in only 2% of myeloma patients.¹⁴ Furthermore, unlike CD19, the common extracellular immunophenotypic markers in myeloma (CD138, CD38, and CD56) are all co-expressed on other essential cell types, and we predict CARs to any of these targets would lead to unacceptable “off tumor, on target” toxicity⁶ which can be fatal even in targets where antibodies are well tolerated, as was the case with a HER2 targeted CAR.¹⁵ Accordingly, there are needs for novel therapeutic strategies to design CARs targeting antigens that are highly expressed in MM cells and limited expression in normal tissues for treating multiple myeloma, which strategies capable of inducing potent tumor eradication with minimal toxicity and immunogenicity.

SUMMARY

In one aspect, the present disclosure provides a chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that specifically binds to B cell maturation antigen (BCMA), a transmembrane domain, and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:53, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:54;

(b) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:65, and a light

chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:66;

(c) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:1, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:2;

(d) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:5, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:6;

(e) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:9, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:10;

(f) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:13, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:14;

(g) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:17, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:18;

(h) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:21, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:22;

(i) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:25, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:26;

(j) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:29, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:30;

(k) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:33, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:34;

5 (l) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:37, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:38;

(m) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3
10 of the heavy chain variable region sequence set forth in SEQ ID NO:41, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:42;

(n) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3
15 of the heavy chain variable region sequence set forth in SEQ ID NO:45, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:46;

(o) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3
20 of the heavy chain variable region sequence set forth in SEQ ID NO:49, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:50;

(p) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3
of the heavy chain variable region sequence set forth in SEQ ID NO:57, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:58; or

25 (q) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:61, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:62.

In another aspect, the present disclosure provides a chimeric antigen receptor
30 (CAR), comprising an extracellular antigen-binding domain that binds to B cell maturation antigen (BCMA), a transmembrane domain, and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 167, a CDR2 comprising the amino acid

sequence set forth in SEQ ID NO: 168, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 169; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 170, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 171, and a CDR3
5 comprising the amino acid sequence set forth in SEQ ID NO: 172;

(b) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 185, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 186, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 187; and a light chain variable region comprising a
10 CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 188, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 189, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 190;

(c) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 89, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 90, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 91; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 92, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 93, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 94;
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(d) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 95, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 96, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 97; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 98, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 99, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 100;
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(e) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 101, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 102, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 103; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 104, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 105, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 106;
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(f) a heavy chain variable region comprising a CDR1 comprising the amino

acid sequence set forth in SEQ ID NO: 107, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 108, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 109; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 110, a CDR2
5 comprising the amino acid sequence set forth in SEQ ID NO: 111, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 112;

(g) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 113, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 114, and a CDR3 comprising the amino acid
10 sequence set forth in SEQ ID NO: 115; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 116, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 117, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 118;

(h) a heavy chain variable region comprising a CDR1 comprising the amino
15 acid sequence set forth in SEQ ID NO: 119, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 120, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 121; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 122, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 123, and a CDR3
20 comprising the amino acid sequence set forth in SEQ ID NO: 124;

(i) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 125, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 127; and a light chain variable region comprising a
25 CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 128, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 129, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 130;

(j) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 131, a CDR2 comprising the amino acid
30 sequence set forth in SEQ ID NO: 132, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 133; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 134, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 135, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 136;

(k) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 137, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 138, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 139; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 140, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 141, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 142;

(l) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 143, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 145; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 146, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 147, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 148;

(m) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 149, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 150, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 151; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 152, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 153, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 154;

(n) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 155, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 156, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 157; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 158, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 159, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 160;

(o) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 161, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 162, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 163; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 164, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 165, and a CDR3

comprising the amino acid sequence set forth in SEQ ID NO: 166;

(p) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 173, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 174, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 175; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 176, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 177, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 178; or

(q) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 179, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 180, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 181; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 182, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 183, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 184.

In another aspect, the present disclosure provides an immunoresponsive cell comprising the CAR as described herein.

In another aspect, the present disclosure provides a T cell comprising the CAR as described herein.

In another aspect, the present disclosure provides a nucleic acid molecule encoding the CAR as described herein.

In another aspect, the present disclosure provides a vector comprising the nucleic acid molecule as described herein.

In another aspect, the present disclosure provides an immunoresponsive cell comprising the nucleic acid molecule as described herein.

In another aspect, the present disclosure provides a use of the cell as described herein in the manufacture of a medicament for reducing tumor burden in a subject.

In another aspect, the present disclosure provides a use of the cell as described herein in the manufacture of a medicament for increasing or lengthening survival of a subject having a tumor.

In another aspect, the present disclosure provides a method for producing an immunoresponsive cell that binds to B cell maturation antigen (BCMA), comprising introducing into the immunoresponsive cell a nucleic acid sequence that encodes a chimeric antigen receptor (CAR) as described herein.

In another aspect, the present disclosure provides a pharmaceutical composition comprising an effective amount of the cell as described herein and a pharmaceutically acceptable excipient.

5 In yet another aspect, the present disclosure provides a kit for treating a tumor, comprising the cell as described herein.

In yet another aspect, the present disclosure provides the cell as described herein for use in therapy.

The presently disclosed subject matter generally provides chimeric antigen receptors (CARs) that specifically target B-cell maturation antigen (BCMA),
10 immunoresponsive cells comprising such CARs, and uses of these CARs and immunoresponsive cells for treating multiple myeloma.

The presently disclosed subject matter provides CARs. In one non-limiting example, the CAR comprises an extracellular antigen-binding domain, a transmembrane domain and an intracellular domain, where the extracellular antigen-
15 binding domain is a human single-chain variable fragment (scFv) that specifically binds to B cell maturation antigen (BMCA). In certain examples, the human scFv specifically binds to BCMA with a binding affinity (K_D) of from about 1×10^{-9} M to

about 3×10^{-6} M. In certain examples, the human scFv specifically binds to BCMA with a binding affinity (K_D) of from about 1×10^{-9} M to about 1×10^{-8} M.

In certain examples, the human scFv comprises a heavy chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%,
5 about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%,
about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%,
about 97%, about 98% or about 99% homologous to an amino acid sequence selected
from the group consisting of SEQ ID NOS: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45,
49, 53, 57, 61, and 65.

10 In certain examples, the human scFv comprises a light chain variable region
comprising an amino acid sequence that is at least about 80%, about 81%, about 82%,
about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%,
about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%,
about 97%, about 98% or about 99% homologous to an amino acid sequence selected
15 from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46,
50, 54, 58, 62, and 66.

In certain examples, the human scFv comprises (a) a heavy chain variable
region comprising an amino acid sequence that is at least about 80%, about 81%,
about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%,
20 about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%,
about 96%, about 97%, about 98% or about 99% homologous to an amino acid
sequence selected from the group consisting of SEQ ID NO: 1, 5, 9, 13, 17, 21, 25,
29, 33, 37, 41, 45, 49, 53, 57, 61, and 65; and (b) a light chain variable region
comprising an amino acid sequence that is at least about 80%, about 81%, about 82%,
25 about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%,
about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%,
about 97%, about 98% or about 99% homologous to an amino acid sequence selected
from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46,
50, 54, 58, 62, and 66.

30 In certain examples, the human scFv comprises a heavy chain variable region
comprising an amino acid sequence selected from the group consisting of SEQ ID
NOS: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65, and
conservative modifications thereof.

In certain examples, the human scFv comprises a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, and 66, and conservative modifications thereof.

5 In certain examples, the human scFv comprises (a) a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65, and conservative modifications thereof, and (b) a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10,
10 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, and 66, and conservative modifications thereof.

 In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having a sequence selected from the group consisting of: SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65. In
15 certain examples, the human scFv comprises a light chain variable region comprising amino acids having a sequence selected from the group consisting of: SEQ ID NOS:2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, and 66. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:21. In certain examples, the human scFv
20 comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:53. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:57. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:61. In
25 certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:65. In certain examples, the human scFv comprises a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:22. In certain examples, the human scFv comprises a light chain variable region comprising amino acids having
30 the sequence set forth in SEQ ID NO:54. In certain examples, the human scFv comprises a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:58. In certain examples, the human scFv comprises a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:62. In certain examples, the human scFv comprises a light chain variable

region comprising amino acids having the sequence set forth in SEQ ID NO:66. In certain examples, the extracellular antigen-binding domain comprises (a) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:1, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:2; (b) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:5, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:6; (c) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:9, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:10; (d) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:13, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:14; (e) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:17, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:18; (f) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:21, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:22; (g) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:25, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:26; (h) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:29, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:30; (i) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:33, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:34; (j) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:37, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:38; (k) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:41, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:42; (l) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:45, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:46; (m) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:49, and a light chain variable region comprising amino acids having a sequence

set forth in SEQ ID NO:50; (n) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:53, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:54; (o) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:57, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:58; (p) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:61, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:62; or (q) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:65, and a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:66. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:21; and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:22. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:53; and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:54. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:57; and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:58. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:61; and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:62. In certain examples, the human scFv comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:65; and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:66.

In certain non-limiting examples, the human scFv comprises both of said heavy and light chains, optionally with a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain variable region. For example, in certain non-limiting examples, the human scFv comprises (i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:53 and (ii) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:54, optionally with (iii) a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain

variable region. In certain examples, the human scFv comprises (i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:21 and (ii) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:22, optionally with (iii) a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain variable region. In certain examples, the human scFv comprises (i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:57 and (ii) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:58, optionally with (iii) a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain variable region. In certain examples, the human scFv comprises (i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:61 and (ii) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:62, optionally with (iii) a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain variable region. In certain examples, the human scFv comprises (i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:65 and (ii) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:66, optionally with (iii) a linker sequence, for example a linker peptide, between the heavy chain variable region and the light chain variable region.

In certain examples, the human scFv comprises (a) a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 91, 97, 103, 109, 115, 121, 127, 133, 139, 145, 151, 157, 163, 169, 175, 181, and 187; and (b) a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 94, 100, 106, 112, 118, 124, 130, 136, 142, 148, 154, 160, 166, 172, 178, 184, and 190.

In certain examples, the human scFv comprises (a) a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 90, 96, 102, 108, 114, 120, 126, 132, 138, 144, 150, 156, 162, 168, 174, 180, and 186, and conservative modifications thereof; and (b) a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 93, 99, 105, 111, 117, 123, 129, 135, 141, 147, 153, 159, 165, 171, 177, 183, and 189, and conservative modifications thereof.

In certain examples, the human scFv comprises (a) a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 89, 95, 101, 107, 113, 119, 125, 131, 137, 143, 149, 155, 161, 167, 173, 179, and 185, and conservative modifications thereof; and (b) a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 92, 98, 104, 110, 116, 122, 128, 134, 140, 146, 152, 158, 164, 170, 176, 182, and 188, and conservative modifications thereof. In certain examples, the human scFv comprises: (a) a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 89, 95, 101, 107, 113, 119, 125, 131, 137, 143, 149, 155, 161, 167, 173, 179, and 185; (b) a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 90, 96, 102, 108, 114, 120, 126, 132, 138, 144, 150, 156, 162, 168, 174, 180, and 186; (c) a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 91, 97, 103, 109, 115, 121, 127, 133, 139, 145, 151, 157, 163, 169, 175, 181, and 187; (d) a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 92, 98, 104, 110, 116, 122, 128, 134, 140, 146, 152, 158, 164, 170, 176, 182, and 188; (e) a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 93, 99, 105, 111, 117, 123, 129, 135, 141, 147, 153, 159, 165, 171, 177, 183, and 189; and (f) a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 94, 100, 106, 112, 118, 124, 130, 136, 142, 148, 154, 160, 166, 172, 178, 184, and 190. In certain examples, the human scFv comprises (a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 89 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 90 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 91 or conservative modifications thereof; (b) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 95 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 96 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:

97 or conservative modifications thereof; (c) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 101 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 102 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 103 or conservative modifications thereof; (d) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 107 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 108 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 109 or conservative modifications thereof; (e) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 113 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 114 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 115 or conservative modifications thereof; (f) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 119 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121 or conservative modifications thereof; (g) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 125 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 126 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 127 or conservative modifications thereof; (h) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 131 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 132 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 133 or conservative modifications thereof; (i) a heavy chain variable region CDR1

comprising amino acids having the sequence set forth in SEQ ID NO: 137 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 138 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 139 or conservative modifications thereof; (j) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 143 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 144 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 145 or conservative modifications thereof; (k) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 149 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151 or conservative modifications thereof; (l) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 155 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157 or conservative modifications thereof; (m) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 161 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163 or conservative modifications thereof; (n) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169 or conservative modifications thereof; (o) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 173 or

conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175 or conservative modifications thereof; (p) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181 or conservative modifications thereof; or (q) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185 or conservative modifications thereof; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186 or conservative modifications thereof; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187 or conservative modifications thereof. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 119; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 173; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181. In

certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186; and a heavy chain variable region CDR3 comprising amino acids
5 having the sequence set forth in SEQ ID NO: 187.

In certain examples, the human scFv comprises (a) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 92 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:93 or
10 conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 94 or conservative modifications thereof; (b) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 98 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids
15 having the sequence set forth in SEQ ID NO:99 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 100 or conservative modifications thereof; (c) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 104 or conservative modifications thereof; a light chain variable region CDR2
20 comprising amino acids having the sequence set forth in SEQ ID NO:105 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 106 or conservative modifications thereof; (d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 110 or conservative
25 modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:111 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 112 or conservative modifications thereof; (e) a light chain variable region CDR1 comprising amino acids having the sequence set
30 forth in SEQ ID NO: 116 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:117 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 118 or conservative modifications thereof; (f) a light chain variable region CDR1 comprising

amino acids having the sequence set forth in SEQ ID NO: 122 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124 or conservative modifications thereof; (g) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 128 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:129 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 130 or conservative modifications thereof; (h) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 134 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:135 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 136 or conservative modifications thereof; (i) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 140 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:141 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 142 or conservative modifications thereof; (j) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 146 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:147 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 148 or conservative modifications thereof; (k) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:153 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154 or conservative modifications thereof; (l) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 158 or conservative

modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:159 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160 or conservative modifications thereof; (m) a

5 light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:165 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 166 or

10 conservative modifications thereof; (n) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the

15 sequence set forth in SEQ ID NO: 172 or conservative modifications thereof; (o) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177 or conservative modifications thereof; and a light chain variable region CDR3

20 comprising amino acids having the sequence set forth in SEQ ID NO: 178 or conservative modifications thereof; (p) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183 or conservative modifications

25 thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184 or conservative modifications thereof; or (q) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188 or conservative modifications thereof; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:

30 189 or conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190 or conservative modifications thereof. In certain examples, the human scFv comprises: a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 122; a light chain variable region CDR2 comprising amino acids

having the sequence set forth in SEQ ID NO: 123; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124. In certain examples, the human scFv comprises: a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172. In certain examples, the human scFv comprises: a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178. In certain examples, the human scFv comprises: a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184. In certain examples, the human scFv comprises: a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190.

In certain examples, the human scFv comprises: (a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 89; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 90; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 91; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 92; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 93; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 94; (b) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 95; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 96; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 97; a light chain variable region

CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 98; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 99; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 100; (c) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 101; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 102; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 103; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 104; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 105; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 106; (d) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 107; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 108; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 109; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 110; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 111; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 112; (e) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 113; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 114; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 115; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 116; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 117; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 118; (f) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 119; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 122; a light chain variable region CDR2 comprising amino acids

having the sequence set forth in SEQ ID NO: 123; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124; (g) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 125; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 126; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 127; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 128; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 129; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 130; (h) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 131; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 132; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 133; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 134; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 135; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 136; (i) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 137; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 138; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 139; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 140; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 141; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 142; (j) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 143; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 144; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 145; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 146; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SE ID NO: 147; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 148; (k)

a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 149; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151; a

5 light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 153; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154; (l)

10 a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 155; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157; a

15 light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 158; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 159; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160; (m)

20 a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 161; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163; a

light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 165; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 166; (n)

25 a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169; a

30 light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172; (o)

a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 173; a heavy chain variable region CDR2 comprising amino

acids having the sequence set forth in SEQ ID NO: 174; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178; (p) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184; or (q) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 119; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 122; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 123; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168; a heavy

chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 173; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184. In certain examples, the human scFv comprises: a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185; a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186; a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187; a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188; a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190.

In certain examples, the BCMA comprises the amino acid sequence set forth in SEQ ID NO:71. In certain examples, the human scFv binds to an epitope region

comprising amino acids 14-22 of SEQ ID NO:71. In certain examples, the human scFv that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO:71 comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:21 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:22, In certain examples, the human scFv that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO:71 comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:119, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:120, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:121, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:124.

In accordance with the presently disclosed subject matter, the extracellular antigen-binding domain is covalently joined to a transmembrane domain. The extracellular antigen-binding domain can comprise a signal peptide that is covalently joined to the 5' terminus of the extracellular antigen-binding domain. In certain examples, the transmembrane domain of the CAR comprises a CD8 polypeptide, a CD28 polypeptide, a CD3 ζ polypeptide, a CD4 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a CTLA-4 polypeptide, a PD-1 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, a synthetic peptide (not based on a protein associated with the immune response), or a combination thereof. In certain examples, the transmembrane domain comprises a CD8 polypeptide. In certain examples, the transmembrane domain comprises a CD28 polypeptide.

In accordance with the presently disclosed subject matter, the intracellular domain comprises a CD3 ζ polypeptide. In certain examples, the intracellular domain further comprises at least one signaling region. In certain examples, the at least one signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, a PD-1 polypeptide, a CTLA-4 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, a synthetic peptide (not based on a protein associated with the immune response), or a combination thereof. In certain examples, the signaling region is a co-stimulatory signaling region. In certain examples, the co-stimulatory signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide,

a DAP-10 polypeptide, or a combination thereof. In certain examples, the at least one co-stimulatory signaling region comprises a CD28 polypeptide. In certain examples, the at least one signaling region comprises a 4-1BB polypeptide. In one specific non-limiting example, the transmembrane domain comprises a CD28 polypeptide, the intracellular domain comprises a CD3 ζ polypeptide, and the at least one signaling domain comprises a CD28 polypeptide.

In certain examples, the CAR is recombinantly expressed. The CAR can be expressed from a vector. In certain examples, the vector is a γ -retroviral vector.

The presently disclosed subject matter also provides isolated immunoresponsive cells comprising the above-described CARs. In certain examples, the isolated immunoresponsive cell is transduced with the CAR, for example, the CAR is constitutively expressed on the surface of the immunoresponsive cell. In certain examples, the isolated immunoresponsive cell is further transduced with at least one co-stimulatory ligand such that the immunoresponsive cell expresses the at least one co-stimulatory ligand. In certain examples, the at least one co-stimulatory ligand is selected from the group consisting of 4-1BBL, CD80, CD86, CD70, OX40L, CD48, TNFRSF14, and combinations thereof. In certain examples, the isolated immunoresponsive cell is further transduced with at least one cytokine such that the immunoresponsive cell secretes the at least one cytokine. In certain examples, the at least one cytokine is selected from the group consisting of IL-2, IL-3, IL-6, IL-7, IL-11, IL-12, IL-15, IL-17, IL-21, and combinations thereof. In certain examples, the isolated immunoresponsive cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a human embryonic stem cell, a lymphoid progenitor cell, a T cell-precursor cell, and a pluripotent stem cell from which lymphoid cells may be differentiated. In certain examples, the immunoresponsive cell is a T cell.

The presently disclosed subject matter further provides nucleic acid molecules encoding the presently disclosed CARs, vectors comprising the nucleic acid molecules, and host cells expressing such nucleic acid molecules. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:207. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:208. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:209. In certain examples, the nucleic acid molecule comprises nucleic

acids having the sequence set forth in SEQ ID NO:229. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:230. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:231. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:232. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:233. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:234. In certain examples, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:235. In certain examples, the vector is a γ -retroviral vector. In certain examples, the host cell is a T cell.

Furthermore, the presently disclosed subject matter provides methods of using the above-described immunoresponsive cell for reducing tumor burden in a subject. For example, the presently disclosed subject matter provides methods of reducing tumor burden in a subject, where the method comprises administering an effective amount of the presently disclosed immunoresponsive cell to the subject, thereby inducing tumor cell death in the subject. In certain examples, the method reduces the number of tumor cells. In another example, the method reduces the tumor size. In yet another example, the method eradicates the tumor in the subject. In certain examples, the tumor is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia. In certain examples, the tumor is multiple myeloma. In certain examples, the subject is a human. In certain examples, the immunoresponsive cell is a T cell.

Furthermore, the presently disclosed subject matter provides methods of using the above-described immunoresponsive cell for increasing or lengthening survival of a subject having neoplasia. For example, the presently disclosed subject matter provides methods of increasing or lengthening survival of a subject having neoplasia, where the method comprises administering an effective amount of the presently disclosed immunoresponsive cell to the subject, thereby increasing or lengthening survival of the subject. In certain examples, the neoplasia is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's

Macroglobulinemia. In certain examples, the neoplasia is multiple myeloma. In certain examples, the method reduces or eradicates tumor burden in the subject.

The presently disclosed subject matter also provides methods for producing an immunoresponsive cell that binds to BCMA. In one non-limiting example, the method comprises introducing into the immunoresponsive cell a nucleic acid sequence that encodes a chimeric antigen receptor (CAR), which comprises an extracellular antigen-binding domain, a transmembrane domain and an intracellular domain, wherein the extracellular antigen-binding domain comprises a human scFv that specifically binds to BCMA.

The presently disclosed subject matter further provides pharmaceutical compositions comprising an effective amount of the presently disclosed immunoresponsive cells and a pharmaceutically acceptable excipient. In certain examples, the pharmaceutical compositions are for treating a neoplasia. In certain examples, the neoplasia is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia. In certain examples, the neoplasia is multiple myeloma.

The presently disclosed subject matter further provides kits for treating a neoplasia, comprising the presently disclosed immunoresponsive cells. In certain examples, the kit further include written instructions for using the immunoresponsive cell for treating a neoplasia. In certain examples, the neoplasia is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia. In certain examples, the neoplasia is multiple myeloma.

What is claimed is:

1. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that specifically binds to B cell maturation antigen (BCMA), a transmembrane domain, and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:53, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:54;

(b) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:65, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:66;

(c) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:1, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:2;

(d) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:5, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:6;

(e) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:9, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:10;

(f) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:13, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:14;

(g) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:17, and a light chain variable

region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:18;

(h) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:21, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:22;

(i) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:25, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:26;

(j) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:29, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:30;

(k) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:33, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:34;

(l) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:37, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:38;

(m) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:41, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:42;

(n) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:45, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:46;

(o) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the

heavy chain variable region sequence set forth in SEQ ID NO:49, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:50;

(p) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:57, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:58; or

(q) a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:61, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:62.

2. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that binds to B cell maturation antigen (BCMA), a transmembrane domain, and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 167, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 168, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 169; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 170, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 171, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 172;

(b) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 185, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 186, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 187; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 188, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 189, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 190;

(c) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 89, a CDR2 comprising the amino acid sequence set forth

in SEQ ID NO: 90, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 91; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 92, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 93, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 94;

(d) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 95, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 96, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 97; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 98, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 99, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 100;

(e) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 101, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 102, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 103; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 104, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 105, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 106;

(f) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 107, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 108, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 109; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 110, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 111, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 112;

(g) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 113, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 114, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 115; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 116, a CDR2 comprising the amino acid sequence set

forth in SEQ ID NO: 117, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 118;

(h) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 119, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 120, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 121; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 122, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 123, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 124;

(i) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 125, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 127; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 128, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 129, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 130;

(j) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 131, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 132, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 133; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 134, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 135, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 136;

(k) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 137, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 138, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 139; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 140, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 141, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 142;

(l) a heavy chain variable region comprising a CDR1 comprising the amino acid

sequence set forth in SEQ ID NO: 143, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 145; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 146, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 147, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 148;

(m) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 149, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 150, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 151; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 152, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 153, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 154;

(n) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 155, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 156, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 157; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 158, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 159, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 160;

(o) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 161, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 162, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 163; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 164, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 165, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 166;

(p) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 173, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 174, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 175; and a light chain variable region comprising a CDR1 comprising the amino acid

sequence set forth in SEQ ID NO: 176, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 177, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 178; or

(q) a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 179, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 180, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 181; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 182, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 183, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 184.

3. The CAR of claim 1 or claim 2, wherein:

(a) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:53, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:54;

(b) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:65, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:66;

(c) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:1, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:2;

(d) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:5, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:6;

(e) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:9, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence

identity to the sequence set forth in SEQ ID NO:10;

(f) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:13, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:14;

(g) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:17, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:18;

(h) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:21, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:22;

(i) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:25, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:26;

(j) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:29, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:30;

(k) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:33, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:34;

(l) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:37, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:38;

(m) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:41, and the light

chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:42;

(n) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:45, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:46;

(o) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:49, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:50;

(p) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:57, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:58; or

(q) the heavy chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:61, and the light chain variable region comprises an amino acid sequence that has at least about 90% sequence identity to the sequence set forth in SEQ ID NO:62.

4. The CAR of any one of claims 1-3, wherein:

(a) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:53, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:54;

(b) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66;

(c) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:1, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:2;

(d) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:5, and the light chain variable region comprises the amino acid sequence set

forth in SEQ ID NO:6;

(e) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:9, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:10;

(f) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:13, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:14;

(g) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:17, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:18;

(h) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:21, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:22;

(i) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:25, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:26;

(j) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:29, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:30;

(k) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:33, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:34;

(l) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:37, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:38;

(m) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:41, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:42;

(n) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:45, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:46;

(o) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:49, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:50;

(p) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:57, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:58; or

(q) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:61, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:62.

5. The CAR of any one of claims 1-4, wherein the heavy chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 119, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 120, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 121; and the light chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 122, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 123, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 124.

6. The CAR of any one of claims 1-4, wherein the heavy chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 185, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 186, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 187; and the light chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 188, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 189, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 190.

7. The CAR of any one of claims 1-4, wherein the heavy chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 179, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 180, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 181; and the light chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 182, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 183, and a CDR3 comprising the amino acid

sequence set forth in SEQ ID: 184.

8. The CAR of any one of claims 1-4, wherein the heavy chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 173, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 174, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 175; and the light chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 176, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 177, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 178.

9. The CAR of any one of claims 1-4, wherein the heavy chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 167, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 168, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 169; and the light chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID: 170, a CDR2 comprising the amino acid sequence set forth in SEQ ID: 171, and a CDR3 comprising the amino acid sequence set forth in SEQ ID: 172.

10. The CAR of any one of claims 1-5, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:21, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:22.

11. The CAR of any one of claims 1-4 and 6, wherein heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66.

12. The CAR of any one of claims 1-4 and 7, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 61, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 62.

13. The CAR of any one of claims 1-4 and 8, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 57; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 58.

14. The CAR of any one of claims 1-4 and 9, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 53; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 54.
15. The CAR of any one of claims 1-14, wherein the extracellular antigen-binding domain is a single chain variable fragment (scFv), an antigen-binding fragment (Fab), or a F(ab')₂.
16. The CAR of any one of claims 1-15, wherein the extracellular antigen-binding domain comprises the amino acid sequence set forth in SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, or SEQ ID NO: 88.
17. The CAR of any one of claims 1-15, wherein the extracellular antigen-binding domain comprises the amino acid sequence set forth in SEQ ID NO: 77; SEQ ID NO: 88; SEQ ID NO: 87; SEQ ID NO: 86; or SEQ ID NO: 85.
18. The CAR of any one of claims 1-17, wherein the extracellular antigen-binding domain binds to B cell maturation antigen (BCMA) with a binding affinity (K_d) of from about 1×10^{-9} M to about 3×10^{-6} M or of from about 1×10^{-9} M to about 1×10^{-8} M.
19. The CAR of any one of claims 1-18, wherein the extracellular antigen-binding domain binds to a non-linear epitope of BCMA.
20. The CAR of any one of claims 1-19, wherein the BCMA comprises the amino acid sequence set forth in SEQ ID NO:71.
21. The CAR of any one of claims 1-20, wherein the transmembrane domain comprises a CD8 polypeptide, a CD28 polypeptide, a CD3 ζ polypeptide, a CD4 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a CTLA-4 polypeptide, a PD-1 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, a synthetic peptide, or a combination thereof.

22. The CAR of claim 21, wherein the transmembrane domain comprises a CD8 polypeptide or a CD28 polypeptide.
23. The CAR of any one of claims 1-22, wherein the intracellular domain comprises a CD3 ζ polypeptide.
24. The CAR of any one of claims 1-23, wherein the intracellular domain further comprises at least one signaling region.
25. The CAR of claim 24, wherein the at least one signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, a PD-1 polypeptide, a CTLA-4 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, a synthetic peptide, or a combination thereof.
26. The CAR of claim 24, wherein the at least one signaling region is a co-stimulatory signaling region.
27. The CAR of claim 26, wherein the at least one co-stimulatory signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, or a combination thereof.
28. The CAR of claim 26, wherein the at least one co-stimulatory signaling region comprises a CD28 polypeptide or a 4-1BB polypeptide.
29. The CAR of any one of claims 24-28, wherein:
- (a) the transmembrane domain comprises a CD28 polypeptide, and the intracellular domain comprises a CD3 ζ polypeptide and the at least one co-stimulatory signaling region that comprises a CD28 polypeptide; or
 - (b) the transmembrane domain comprises a CD8 polypeptide, and the intracellular domain comprises a CD3 ζ polypeptide and the at least one co-stimulatory signaling region that comprises a 4-1BB polypeptide.

30. The CAR of any one of claims 24-28, wherein the transmembrane domain comprises a CD28 polypeptide, and the intracellular domain comprises a CD3 ζ polypeptide and the at least one co-stimulatory signaling region that comprises a 4-1BB polypeptide.
31. The CAR of any one of claims 1-29, wherein the CAR is recombinantly expressed.
32. The CAR of any one of claims 1-31, wherein the CAR is expressed from a γ -retroviral vector or a lentiviral vector.
33. An immunoresponsive cell comprising the CAR of any one of claims 1-32.
34. The immunoresponsive cell of claim 33, wherein the immunoresponsive cell is transduced with the CAR.
35. The immunoresponsive cell of claim 33 or claim 34, wherein the CAR is constitutively expressed on the surface of the immunoresponsive cell.
36. The immunoresponsive cell of any one of claims 33-35, wherein
- (a) the immunoresponsive cell is further transduced with at least one co-stimulatory ligand such that the immunoresponsive cell expresses the at least one co-stimulatory ligand, wherein the at least one co-stimulatory ligand is selected from the group consisting of 4-1BBL, CD80, CD86, CD70, OX40L, CD48, TNFRSF14, and combinations thereof; and/or
 - (b) the immunoresponsive cell is further transduced with at least one cytokine such that the immunoresponsive cell secretes the at least one cytokine, wherein the at least one cytokine is selected from the group consisting of IL-2, IL-3, IL-6, IL-7, IL-11, IL-12, IL-15, IL-17, IL-21, and combinations thereof.
37. The immunoresponsive cell of any one of claims 33-36, wherein the immunoresponsive cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a human embryonic stem

cell, a lymphoid progenitor cell, a T cell-precursor cell, and a pluripotent stem cell from which a lymphoid cell may be differentiated.

38. The immunoresponsive cell of claim 37, wherein the immunoresponsive cell is a T cell.

39. A T cell comprising the CAR of any one of claims 1-32.

40. A nucleic acid molecule encoding the CAR of any one of claims 1-32.

41. The nucleic acid molecule of claim 40, comprising the nucleotide sequence set forth in SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, or SEQ ID NO:235.

42. A vector comprising the nucleic acid molecule of claim 40 or claim 41.

43. The vector of claim 42, wherein the vector is a γ -retroviral vector or a lentiviral vector.

44. An immunoresponsive cell comprising the nucleic acid molecule of claim 40 or claim 41.

45. The immunoresponsive cell of claim 44, wherein the immunoresponsive cell is a T cell.

46. Use of the cell of any one of claims 33-39, 44, and 45 in the manufacture of a medicament for reducing tumor burden in a subject.

47. The use of claim 46, wherein the medicament reduces the number of tumor cells, reduces tumor size, and/or eradicates the tumor in the subject.

48. The use of claim 46 or claim 47 wherein the tumor is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia.
49. The use of any one of claims 46-48, wherein the tumor is multiple myeloma.
50. Use of the cell of any one of claims 33-39, 44, and 45 in the manufacture of a medicament for increasing or lengthening survival of a subject having a tumor.
51. The use of claim 50, wherein the tumor is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia.
52. The use of claim 50 or claim 51, wherein the tumor is multiple myeloma.
53. The use of any one of claims 50-52, wherein the medicament reduces the number of tumor cells, reduces tumor size, and/or eradicates the tumor in the subject.
54. A method for producing an immunoresponsive cell that binds to B cell maturation antigen (BCMA), comprising introducing into the immunoresponsive cell a nucleic acid sequence that encodes a chimeric antigen receptor (CAR) of any of claims 1-32.
55. A pharmaceutical composition comprising an effective amount of the cell of any one of claims 33-39, 44, and 45 and a pharmaceutically acceptable excipient.
56. The pharmaceutical composition of claim 55, wherein the pharmaceutical composition is for treating a tumor.
57. The pharmaceutical composition of claim 56, wherein the tumor is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma,

Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia.

58. The pharmaceutical composition of claim 57, wherein the tumor is multiple myeloma.
59. A kit for treating a tumor, comprising the cell of any one of claims 33-39, 44, and 45.
60. The kit of claim 59, wherein the kit further comprises written instructions for using the cell for treating a subject having the tumor.
61. The kit of claim 59 or claim 60, wherein the tumor is selected from the group consisting of multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia.
62. The kit of any one of claims 59-61, wherein the tumor is multiple myeloma.
63. The cell of any one of claims 33-39, 44, and 45 for use in therapy.