ANTIBODIES TARGETING B-CELL MATURATION ANTIGEN AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Patent Application Serial No. 62/088,246, filed December 5, 2014, the content of which is incorporated by reference in its entirety, and to which priority is claimed.

FIELD OF THE INVENTION

The presently disclosed subject matter relates to antibodies that bind to B-cell maturation antigen (BCMA), and methods of using the same.

BACKGROUND

BCMA is involved in B cell differentiation and signaling and is known to be expressed on non-malignant differentiated B cells and plasma cells. Several groups have confirmed surface expression of BCMA on multiple myeloma (MM), with one group finding it as an alternative to CD138 as a FACS marker for malignant plasma cells from fresh or frozen patient bone marrow samples with mean relative mean fluorescence intensity (MFI) between 9-16 (n=35) (Frigyesi, I., et al. Robust isolation of malignant plasma cells in multiple myeloma. Blood 123, 1336-1340 (2014); Tai, Y.T., et al. Novel afucosylated anti-B cell maturation antigen-monomethyl auristatin F antibody-drug conjugate (GSK2857916) induces potent and selective anti-multiple myeloma activity. Blood (2014)). Given the significant role for BCMA in multiple myeloma, antibodies that recognize BCMA, and methods of using such agents, are desired.

SUMMARY

In one aspect, the present disclosure refers to an anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising:

(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: 34, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 35, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 36;

(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 refers to an anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising:

(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.

In another aspect, the present disclosure refers to a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, and a pharmaceutically acceptable carrier.

In another aspect, the present disclosure refers to an immunoconjugate comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, linked to a therapeutic agent.

In yet another aspect, the present disclosure refers to a bispecific molecule comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, linked to a second functional moiety.

In yet another aspect, the present disclosure refers to a nucleic acid molecule that encodes an anti-BCMA antibody or antigen-binding fragment thereof as described herein.

In yet another aspect, the present disclosure refers to a method for detecting BCMA in a whole cell or tissue, comprising:

contacting a cell or tissue with the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, wherein the antibody or antigen-binding fragment thereof comprises a detectable label; and

determining the amount of the labeled antibody or antigen-binding fragment thereof bound to the cell or tissue by measuring the amount of detectable

label associated with the cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of BCMA in the cell or tissue.

In yet another aspect, the present disclosure refers to a use of a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein for the manufacture of a medicament for treating a tumor in a subject.

In yet another aspect, the present disclosure refers to a kit for treating a tumor, comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein.

In yet another aspect, the present disclosure refers to the composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein for use as a therapy.

The presently disclosed subject matter provides antibodies that bind to a B-cell maturation antigen (BCMA), and methods of using the same.

In certain examples, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising 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%, 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,

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 the sequence set forth in SEQ ID NO:65, and a light chain variable region comprising amino acids having a 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 the sequence set forth in SEQ ID NO:66, wherein the antibody or antigen-binding portion thereof specifically binds to human BCMA.

In certain examples, the antibody or antigen-binding fragment 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

In certain examples, the heavy chain variable region and light chain variable region CDR2 domains the antibody or antigen-binding portion thereof are selected from the group consisting of:

(a) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:90 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 93 and conservative modifications thereof;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 96 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 99 and conservative modifications thereof;

(c) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 102 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 105 and conservative modifications thereof;

(d) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 108 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 111and conservative modifications thereof;

(e) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 114 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 117 and conservative modifications thereof;

(f) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 123 and conservative modifications thereof;

(g) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 126 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 129 and conservative modifications thereof;

(h) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 132 and conservative modifications thereof;

and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183 and conservative modifications thereof; and

(q) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189 and conservative modifications thereof.

In certain examples, the heavy chain variable region and light chain variable region CDR1 domains of the antibody or antigen-binding portion thereof are selected from the group consisting of:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:89 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 92 and conservative modifications thereof;

(b) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:95 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:98 and conservative modifications thereof;

(c) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:101 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:104 and conservative modifications thereof;

(d) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:107 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:110 and conservative modifications thereof;

(e) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:113 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:116 and conservative modifications thereof;

(f) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:119 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122 and conservative modifications thereof;

(o) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:173 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:176 and conservative modifications thereof;

(p) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:179 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:182 and conservative modifications thereof; and

(q) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:185 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:188 and conservative modifications thereof.

In certain examples, one or more of the CDR sequences have up to about 3 amino acid substitutions. In certain examples, one or more of the CDR sequences have up to about 5 amino acid substitutions.

Furthermore, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding portion thereof, comprising:

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 91;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 97;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 103;

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 antibody or antigen-binding portion thereof binds to human BMCA with a binding affinity (K_D) of from about 1 x 10^{-9} M to about 1 x 10^{-8} M. In certain examples, the antibody, or antigen-binding portion thereof binds to a human BCMA comprising the amino acid sequence set forth in SEQ ID NO: 71. In certain examples, the antibody or antigen-binding portion thereof binds to an epitope region comprising amino acids 14-22 of SEQ ID NO:71. For example, the antibody or antigen-binding portion thereof 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, For example, the antibody or antigen-binding portion thereof 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.

The presently disclosed subject matter provides an isolated antibody, or an antigen-binding portion thereof, which cross-competes for binding to human

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 cross-competing antibody, or antigen-binding portion thereof binds to a human BCMA comprising the amino acid sequence set forth in SEQ ID NO: 71. In certain examples, the cross-competing antibody, or

antigen-binding portion thereof binds to an epitope region comprising amino acids 14-22 of SEQ ID NO:71. For example, the reference antibody or antigen-binding portion thereof 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, For example, the reference antibody or antigen-binding portion 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.

The presently disclosed subject matter also provides an isolated antibody, or antigen-binding fragment thereof, comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 72-88.

In certain examples, the antibody or antigen-binding fragment thereof comprises a human variable region framework region. In certain examples, the antibody or antigen-binding fragment thereof is fully human or an antigen-binding fragment thereof. In certain examples, the antibody or antigen-binding fragment thereof is a chimeric antibody or an antigen-binding fragment thereof. In certain examples, the antibody or antigen-binding portion thereof is a humanized antibody or an antigen-binding fragment thereof. In certain examples, the antigen-binding fragment of the antibody is an Fab, Fab', F(ab')2, Fv or single chain Fv (scFv).

The presently disclosed subject matter also provides a composition comprising the antibody or antigen-binding fragment thereof disclosed herein, and a pharmaceutically acceptable carrier.

In addition, the presently disclosed subject matter provides an immunoconjugate comprising the antibody or antigen-binding fragment thereof disclosed herein, linked to a therapeutic agent. In certain examples, the therapeutic agent is a drug, cytotoxin, or a radioactive isotope. The presently disclosed subject matter also provides a composition comprising such immunoconjugate and a pharmaceutically acceptable carrier.

Furthermore, the presently disclosed subject matter provides a bispecific molecule comprising the antibody or antigen-binding fragment thereof disclosed herein, linked to a second functional moiety. In certain examples, the second functional moiety has a different binding specificity than the antibody or antigen binding fragment thereof. In certain examples, the second functional moiety has a binding specificity for an immune cell. In certain examples, the second functional moiety has a binding specificity for CD3. The presently disclosed subject matter also provides a composition comprising such bispecific molecule and a pharmaceutically acceptable carrier.

In addition, the presently disclosed subject matter provides an isolated nucleic acid that encodes the antibody or antigen-binding fragment thereof disclosed herein, an expression vector comprising such nucleic acid molecule, and a host cell comprising such expression vector.

Furthermore, the presently disclosed subject matter provides a method for detecting BCMA in a whole cell or tissue. In certain examples, the method comprises: contacting a cell or tissue with the antibody or antigen-binding fragment thereof disclosed herein, wherein said antibody or antigen-binding fragment thereof comprises a detectable label; and determining the amount of the labeled antibody or antigen-binding fragment thereof bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of BCMA in said cell or tissue.

Furthermore, the presently disclosed subject matter provides a method of treating a tumor in a subject. In certain examples, the method comprises: administering an effective amount of the antibody or antigen-binding fragment thereof disclosed herein to the subject, thereby inducing death of a tumor cell in the subject. In certain examples, the method reduces the number of the tumor cells. In certain examples, the method reduces the tumor size. In certain examples, the method eradicates the tumor in the subject. In certain examples, the subject is a human.

In addition, the presently disclosed subject matter provides use of the antibody or antigen-binding fragment disclosed herein for the treatment of a tumor,

and the antibody or antigen-binding fragment thereof disclosed herein for use in treating a tumor in a subject.

Furthermore, the presently disclosed subject matter provides a kit for treating a tumor, comprising the antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the kit further comprises written instructions for using the antibody or antigen-binding fragment thereof for treating a subject having a tumor.

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.

BRIEF DESCRIPTION OF THE FIGURES

The following Detailed Description, given by way of example, but not intended to limit the invention to specific embodiments described, may be understood in conjunction with the accompanying drawings.

Figure 1 depicts the human BCMA expression in various tissues.

Figure 2 depicts epitope mapping of ET140-3.

Figure 3 depicts epitope mapping of ET140-24.

Figure 4 depicts epitope mapping of ET140-54.

Figure 5 depicts epitope mapping of ET140-3, ET140-24, and ET140-54.

Figure 6 depicts ELISA screening data of ET140-3, ET140-24, ET140-37, ET140-40, and ET140-54.

Figure 7 depicts FCAS screening data of ET140-3, ET140-24, ET140-37, ET140-40, and ET140-54.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

All publications, patents and other references cited herein are incorporated by reference in their entirety into the present disclosure.

In practicing the presently disclosed subject matter, many conventional techniques in molecular biology, microbiology, cell biology, biochemistry, and immunology are used, which are within the skill of the art. These techniques are described in greater detail in, for example, Molecular Cloning: a Laboratory Manual 3rd edition, J.F. Sambrook and D.W. Russell, ed. Cold Spring Harbor Laboratory

WHAT IS CLAIMED IS:

1. An anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising:

(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: 34, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 35, and a

CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 36;

(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.

2. An anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising:

(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.

3. The anti-BCMA antibody or antigen-binding fragment thereof 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 anti-BCMA antibody or antigen-binding fragment thereof 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 anti-BCMA antibody or antigen-binding fragment thereof 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 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 the light chain variable region comprises 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.

6. The anti-BCMA antibody or antigen-binding fragment thereof 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 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 the light chain variable region comprises 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.

7. The anti-BCMA antibody or antigen-binding fragment thereof 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 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 the light chain variable region comprises 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.

8. The anti-BCMA antibody or antigen-binding fragment thereof 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 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 the light chain variable region comprises 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.

9. The anti-BCMA antibody or antigen-binding fragment thereof 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 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 the light chain variable region comprises 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.

10. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the heavy chain variable region comprises comprising 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 anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4 and 6, wherein the heavy chain variable region comprises comprising 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 anti-BCMA antibody or antigen-binding fragment thereof 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 anti-BCMA antibody or antigen-binding fragment thereof 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 anti-BCMA antibody or antigen-binding fragment thereof 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 anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein the antigen-binding fragment of the antibody is an antigen-binding fragment (Fab), a Fab', a $F(ab')_2$, a variable fragment (Fv) or a single chain variable fragment (scFv).

16. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-15, comprising a linker positioned between the heavy chain variable region and the light chain variable region.

17. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-16, wherein the antigen-binding fragment thereof is a single chain variable fragment (scFv).

18. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-17, comprising 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.

19. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-18, comprising 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.

20. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-5, 10 and 15-19, comprising the amino acid sequence set forth in SEQ ID NO:77.

21. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4, 6, 11 and 15-19, comprising the amino acid sequence set forth in SEQ ID NO:88.

22. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4, 7, 12 and 15-19, comprising the amino acid sequence set forth in SEQ ID NO:87.

23. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4, 8, 13 and 15-19, comprising the amino acid sequence set forth in SEQ ID NO:86.

24. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4, 9 and 14-19, comprising the amino acid sequence set forth in SEQ ID NO:85.

25. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-24, wherein the antibody comprises a human variable region framework region.

26. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-25, which is a fully human or an antigen-binding fragment thereof.

27. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-25, which is a chimeric antibody or an antigen-binding fragment thereof.

28. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-25, which is a humanized antibody or an antigen-binding fragment thereof.

29. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-24, wherein the antigen-binding fragment is a human single chain variable fragment (scFv).

30. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-16 and 18-28, wherein the antigen-binding fragment is an antigen-binding fragment (Fab).

31. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-16 and 18-28, wherein the antigen-binding fragment is a $F(ab')_2$.

32. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 15-31,

wherein the one or more of the scFv, the Fab and the $F(ab')_2$ are comprised in a fusion protein with a heterologous sequence to form the extracellular antigen-binding domain.

33. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-32, wherein the antibody or antigen-binding fragment binds to B cell maturation antigen (BCMA) with a dissociation constant (K_d) of from about 1×10^{-9} M to about 1×10^{-6} M.

34. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-33, wherein the antibody or antigen-binding fragment binds to B cell maturation antigen (BCMA) with a dissociation constant (K_D) of from about 1×10^{-9} M to about 1×10^{-8} M.

35. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-34, wherein the antibody or antigen-binding fragment binds to a non-linear epitope of BCMA.

36. A composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, and a pharmaceutically acceptable carrier.

37. An immunoconjugate comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, linked to a therapeutic agent.

38. The immunoconjugate of claim 37, wherein the therapeutic agent is a drug, a cytotoxin, or a radioactive isotope.

39. A composition comprising the immunoconjugate of claim 37 or 38, and a pharmaceutically acceptable carrier.

40. A bispecific molecule comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, linked to a second functional moiety.

41. The bispecific molecule of claim 40, wherein the second functional moiety has a different binding specificity than the antibody or antigen binding fragment thereof.

42. The bispecific molecule of claim 40 or claim 41, wherein the second functional moiety has a binding specificity for an immune cell.

43. The bispecific molecule of any one of claims 40-42, wherein the second functional moiety has a binding specificity for CD3.

44. A composition comprising the bispecific molecule of any one of claims 40-43, and a pharmaceutically acceptable carrier.

45. A nucleic acid molecule that encodes an anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35.

46. An expression vector comprising the nucleic acid molecule of claim 45.

47. A host cell comprising the expression vector of claim 46.

48. A method for detecting BCMA in a whole cell or tissue, comprising:

contacting a cell or tissue with the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, wherein the antibody or antigen-binding fragment thereof comprises a detectable label; and

determining the amount of the labeled antibody or antigen-binding fragment thereof bound to the cell or tissue by measuring the amount of detectable label associated with the cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of BCMA in the cell or tissue.

49. Use of a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35 for the manufacture of a medicament for treating a tumor in a subject.

50. The use of claim 49, wherein the medicament reduces the number of the tumor cells.

51. The use of claim 49 or claim 50, wherein the medicament reduces the tumor size.

52. The use of any one of claims 49-51, wherein the medicament eradicates the tumor in the subject.

53. The use of any one of claims 49-52, 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.

54. The use of any one of claims 49-53, wherein the tumor is multiple myeloma.

55. The use of any one of claims 49-54, wherein the subject is a human.

56. A kit for treating a tumor, comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35.

57. The kit of claim 56, wherein the kit comprises written instructions for using the antibody or antigen-binding fragment thereof for treating a subject having a tumor.

58. The kit of claim 56 or claim 57, wherein the tumor is multiple myeloma.

59. The composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35 for use as a therapy.