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 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.

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

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 another aspect, the present disclosure refers to a composition comprising the immunoconjugate as described herein, and a pharmaceutically acceptable carrier.

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 composition comprising the bispecific molecule as described herein, and a pharmaceutically acceptable carrier.

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 an expression vector comprising the nucleic acid molecule as described herein.

In yet another aspect, the present disclosure refers to a host cell comprising the expression vector 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,

25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65, wherein the antibody, or an antigen-binding fragment thereof specifically binds to human BCMA. The presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising 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 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, wherein the antibody or antigen-binding fragment thereof specifically binds to human BCMA. Furthermore, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising (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%, 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; and (b) 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 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, wherein the antibody or antigen-binding fragment thereof specifically binds to human BCMA.

In addition, 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 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, 65, and conservative modifications thereof, wherein the antibody or antigen-binding fragment thereof specifically binds to human BCMA. The presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising 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, 66, and conservative modifications thereof, wherein the antibody, or antigen-binding fragment thereof specifically binds to human BCMA. Furthermore, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising (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, 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: , 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, and conservative modifications thereof, wherein the antibody, or antigen-binding fragment thereof specifically binds to human BCMA.

The presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region and the light chain variable region are selected from the group consisting of: (a) a heavy 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:1, 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:2; (b) a heavy 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:5, 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:6; (c) a heavy 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:9, 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:10; (d) a heavy 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:13, 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:14; (e) a heavy 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:17, 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:18; (f) a heavy 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:21, 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:22; (g) a heavy 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:25, 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:26; (h) a heavy 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:29, 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:30; (i) a heavy 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:33, 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:34; (j) a heavy 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:37, 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:38; (k) a heavy 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:41, 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:42; (l) a heavy 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:45, 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:46; (m) a heavy 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:49, 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:50; (n) a heavy 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:53, 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:54; (o) a heavy 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:57, 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:58; (p) a heavy 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:61, 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:62; and (q) a heavy 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: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

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.

The presently disclosed subject matter also provides an isolated antibody or antigen-binding fragment thereof comprising a heavy chain variable region that comprises CDR1, CDR2, and CDR3 domains; and a light chain variable region that comprises CDR1, CDR2, and CDR3 domains, wherein the heavy chain variable region and light chain variable region CDR3 domains are selected from the group consisting of:

(a) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 91 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 94 and conservative modifications thereof;

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

light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 100 and conservative modifications thereof;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 103 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:106 and conservative modifications thereof;

(d) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 109 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 112 and conservative modifications thereof;

(e) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:115 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:118 and conservative modifications thereof;

(f) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124 and conservative modifications thereof;

(g) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 127 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 130 and conservative modifications thereof;

(h) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 133 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:136 and conservative modifications thereof;

(i) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 139 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 142 and conservative modifications thereof;

(j) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:145 and conservative modifications thereof; and a

light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:148 and conservative modifications thereof;

(k) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154 and conservative modifications thereof;

(l) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:160 and conservative modifications thereof;

(m) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 166 and conservative modifications thereof;

(n) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172 and conservative modifications thereof;

(o) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178 and conservative modifications thereof;

(p) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184 and conservative modifications thereof; and

(q) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:187 and conservative modifications thereof; and a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:190 and conservative modifications thereof;

wherein the antibody or antigen-binding portion thereof specifically binds to BCMA.

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: 135 and conservative modifications thereof;

(i) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 138 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 141 and conservative modifications thereof;

(j) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:144 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:147 and conservative modifications thereof;

(k) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 153 and conservative modifications thereof;

(l) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:156 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:159 and conservative modifications thereof;

(m) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:162 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:165 and conservative modifications thereof;

(n) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171 and conservative modifications thereof;

(o) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174 and conservative modifications thereof; and a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177 and conservative modifications thereof;

(p) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180 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;

(g) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:125 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:128 and conservative modifications thereof;

(h) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:131 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:134 and conservative modifications thereof;

(i) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:137 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:140 and conservative modifications thereof;

(j) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:143 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:146 and conservative modifications thereof;

(k) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:149 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:152 and conservative modifications thereof;

(l) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:155 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:158 and conservative modifications thereof;

(m) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:161 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:164 and conservative modifications thereof;

(n) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:167 and conservative modifications thereof; and a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:170 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;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 109;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 115;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 127;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 133;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 139;

(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; and a

heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 145;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151;

(l) 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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157;

(m) 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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163;

(n) 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;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175;

(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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181; 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; and a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187.

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

(a) 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 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 SEQ ID NO: 100;

(c) 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 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 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 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 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 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 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 SEQ ID NO: 136;

(i) 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 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 SEQ 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 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) a 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) 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) 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;

(o) 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 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 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.

The presently disclosed subject matter also 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; 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 SE 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 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) 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 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) 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) 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;

(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 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

BCMA with any of the above-described antibody or antigen-binding portion thereof. The presently disclosed subject matter provides an isolated antibody, or an antigen-binding portion thereof, which binds to the same epitope on human BCMA as any of the above-described antibody or antigen-binding portion thereof.

Furthermore, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding portion thereof, which cross-competes for binding to human BCMA with a reference antibody or reference antigen-binding portion thereof comprising: (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 addition, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding portion thereof, which binds to the same epitope on human BCMA as a reference antibody or reference antigen-binding portion thereof comprising: (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 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

Press 2001 ; Recombinant Antibodies for Immunotherapy, Melvyn Little, ed. Cambridge University Press 2009; Oligonucleotide Synthesis" (M. J. Gait, ed., 1984); "Animal Cell Culture" (R. I. Freshney, ed., 1987); "Methods in Enzymology" (Academic Press, Inc.); "Current Protocols in Molecular Biology" (F. M. Ausubel et al., eds., 1987, and periodic updates); "PCR: The Polymerase Chain Reaction", (Mullis et al., ed., 1994); "A Practical Guide to Molecular Cloning" (Perbal Bernard V., 1988); "Phage Display: A Laboratory Manual" (Barbas et al., 2001). The contents of these references and other references containing standard protocols, widely known to and relied upon by those of skill in the art, including manufacturers' instructions are hereby incorporated by reference as part of the present disclosure.

Definitions

In the description that follows, certain conventions will be followed as regards the usage of terminology. Generally, terms used herein are intended to be interpreted consistently with the meaning of those terms as they are known to those of skill in the art.

An "antigen-binding protein" is a protein or polypeptide that comprises an antigen-binding region or antigen-binding portion, that is, has a strong affinity to another molecule to which it binds. Antigen-binding proteins encompass antibodies, chimeric antigen receptors (CARs) and fusion proteins.

"Antibody" and "antibodies" as those terms are known in the art refer to antigen binding proteins of the immune system. The term "antibody" as referred to herein includes whole, full length antibodies having an antigen-binding region, and any fragment thereof in which the "antigen-binding portion" or "antigen-binding region" is retained, or single chains, for example, single chain variable fragment (scFv), thereof. A naturally occurring "antibody" is a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as V_H) and a heavy chain constant (CH) region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as V_L) and a light chain constant C_L region. The light chain constant region is comprised of one domain, C_L. The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more

conserved, termed framework regions (FR). Each V_H and V_L is composed of three CDRs and four FRs arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1 q) of the classical complement system.

The term "human antibody", as used herein, is intended to include antibodies having variable regions in which both the framework and CDR regions are derived from human germline immunoglobulin sequences. Furthermore, if the antibody contains a constant region, the constant region also is derived from human germline immunoglobulin sequences. The human antibodies of the presently disclosed subject matter may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation *in vivo*).

The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical and/or bind the same epitope, except for possible variant antibodies, e.g., containing naturally occurring mutations or arising during production of a monoclonal antibody preparation, such variants generally being present in minor amounts. In contrast to polyclonal antibody preparations, which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody of a monoclonal antibody preparation is directed against a single determinant on an antigen. Thus, the modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the presently disclosed subject matter may be made by a variety of techniques, including but not limited to the hybridoma method, recombinant DNA methods, phage-display methods, and methods utilizing transgenic animals containing all or part of the human immunoglobulin loci,

such methods and other exemplary methods for making monoclonal antibodies being described herein.

The term "recombinant human antibody", as used herein, includes all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as (a) antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom (described further below), (b) antibodies isolated from a host cell transformed to express the human antibody, e.g., from a transfectoma, (c) antibodies isolated from a recombinant, combinatorial human antibody library, and (d) antibodies prepared, expressed, created or isolated by any other means that involve splicing of human immunoglobulin gene sequences to other DNA sequences. Such recombinant human antibodies have variable regions in which the framework and CDR regions are derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies can be subjected to in vitro mutagenesis (or, when an animal transgenic for human Ig sequences is used, in vivo somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline V_H and V_L sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

The term "humanized antibody" is intended to refer to antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences. Additional framework region modifications may be made within the human framework sequences.

The term "chimeric antibody" is intended to refer to antibodies in which the variable region sequences are derived from one species and the constant region sequences are derived from another species, such as an antibody in which the variable region sequences are derived from a mouse antibody and the constant region sequences are derived from a human antibody.

As used herein, an antibody that "specifically binds to human BCMA" is intended to refer to an antibody that binds to human BCMA with a K_D of about 5×10^{-7} M or less, about 1×10^{-7} M or less, about 5×10^{-8} M or less, about 1×10^{-8} M or

less, about 5 x 10^{-9} M or less, about 1 x 10^{-9} M or less, about 5 x 10^{-10} M or less, about 1 x 10^{-10} M or less, about 5 x 10^{-11} M or less, or about 1 x 10^{-11} M or less.

An "antibody that competes for binding" or "antibody that cross-competes for binding" with a reference antibody for binding to an antigen, e.g., BCMA, refers to an antibody that blocks binding of the reference antibody to the antigen (e.g., BCMA) in a competition assay by 50% or more, and conversely, the reference antibody blocks binding of the antibody to the antigen (e.g., BCMA) in a competition assay by 50% or more. An exemplary competition assay is described in "Antibodies", Harlow and Lane (Cold Spring Harbor Press, Cold Spring Harbor, NY).

As used herein, "isotype" refers to the antibody class (e.g., IgM or IgGl) that is encoded by the heavy chain constant region genes.

The phrases "an antibody recognizing an antigen" and "an antibody specific for an antigen" are used interchangeably herein with the term "an antibody which binds specifically to an antigen (e.g., a BMCA polypeptide)."

The term "antigen-binding portion" or "antigen-binding region" of an antibody, as used herein, refers to that region or portion of the antibody that binds to the antigen and which confers antigen specificity to the antibody; fragments of antigen-binding proteins, for example, antibodies includes one or more fragments of an antibody that retain the ability to specifically bind to an antigen (e.g., a BCMA polypeptide). It has been shown that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody. Examples of antigen-binding fragments encompassed within the term "antibody fragments" of an antibody include a Fab fragment, a monovalent fragment consisting of the V_L, V_H, C_L and CH1 domains; a $F(ab)_2$ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the V_H and CH1 domains; a Fv fragment consisting of the V_L and V_H domains of a single arm of an antibody; a dAb fragment (Ward et al., 1989 Nature 341 :544-546), which consists of a V_H domain; and an isolated complementarity determining region (CDR).

Furthermore, although the two domains of the Fv fragment, V_L and V_H, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the V_L and V_H regions pair to form monovalent molecules. These are known as single chain Fv (scFv); see e.g., Bird et al., 1988 Science 242:423-426; and Huston et al., 1988

Proc. Natl. Acad. Sci. 85:5879-5883. These antibody fragments are obtained using conventional techniques known to those of skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

An "isolated antibody" or "isolated antigen-binding protein" is one which has been identified and separated and/or recovered from a component of its natural environment. "Synthetic antibodies" or "recombinant antibodies" are generally generated using recombinant technology or using peptide synthetic techniques known to those of skill in the art.

The terms "BCMA" and "B-cell maturation antigen" are used interchangeably, and include variants, isoforms, species homologs of human BCMA, and analogs having at least one common epitope with BCMA (e.g., human BCMA). An exemplary human BCMA sequence can be found under Entrez Gene Accession No.: NP_001183.

As used herein, the term "single-chain variable fragment" or "scFv" is a fusion protein of the variable regions of the heavy (V_H) and light chains (V_L) of an immunoglobulin (e.g., mouse or human) covalently linked to form a V_H::V_L heterodimer. The heavy (V_H) and light chains (V_L) are either joined directly or joined by a peptide-encoding linker (e.g., 10, 15, 20, 25 amino acids), which connects the N-terminus of the V_H with the C-terminus of the V_L, or the C-terminus of the V_H with the N-terminus of the V_L. The linker is usually rich in glycine for flexibility, as well as serine or threonine for solubility. The linker can link the heavy chain variable region and the light chain variable region of the extracellular antigen-binding domain. Non-limiting examples of linkers are disclosed in Shen et al., Anal. Chem. 80(6):1910-1917 (2008) and WO 2014/087010, the contents of which are hereby incorporated by reference in their entireties. In certain embodiments, the linker is a G4S linker. In certain embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:191 as provided below:

GGGGSGGGGSGGGGS [SEQ ID NO: 191].

In certain embodiments, the nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:191 is set forth in SEQ ID NO:192, which is provided below:

GGTGGAGGTGGATCAGGTGGAGGTGGATCTGGTGGAGGTGGAT CT [SEQ ID NO:192].

In certain embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69 as provided below.

SRGGGGSGGGGSGGGGSLEMA [SEQ ID NO:69]

In certain embodiments, the nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:69 is set forth in SEQ ID NO:70, which is provided below:

tctagaggtggtggtggtagcggcggcggcggctctggtggtggtggatccctcgagatggcc [SEQ ID NO:70]

In certain embodiments, the linker comprises amino acids having the following sequence GGGGS [SEQ ID NO:193].

In certain embodiments, the linker comprises amino acids having the following sequence SGGSGGS [SEQ ID NO:194].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGS [SEQ ID NO:195].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGS [SEQ ID NO:196].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGSGGGGGGGS [SEQ ID NO:197].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGSGGGGSGGGGS [SEQ ID NO:198].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGSGGGGSGGGGSGGGGS [SEQ ID NO:199].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS [SEQ ID NO:200].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS [SEQ ID NO:201].

In certain embodiments, the linker comprises amino acids having the following sequence EPKSCDKTHTCPPCP [SEQ ID NO:202].

In certain embodiments, the linker comprises amino acids having the following sequence GGGGSGGGSEPKSCDKTHTCPPCP [SEQ ID NO:203].

In certain embodiments, the linker comprises amino acids having the following sequence

ELKTPLGDTTHTCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCP EPKSCDTPPPCPRCP [SEQ ID NO:204].

In certain embodiments, the linker comprises amino acids having the following sequence GSGSGS [SEQ ID NO:205].

In certain embodiments, the linker comprises amino acids having the following sequence AAA [SEQ ID NO:206].

Despite removal of the constant regions and the introduction of a linker, scFv proteins retain the specificity of the original immunoglobulin. Single chain Fv polypeptide antibodies can be expressed from a nucleic acid comprising V_H - and V_L -encoding sequences as described by Huston, et al. (Proc. Nat. Acad. Sci. USA, 85:5879-5883, 1988). See, also, U.S. Patent Nos. 5,091,513, 5,132,405 and 4,956,778; and U.S. Patent Publication Nos. 20050196754 and 20050196754. Antagonistic scFvs having inhibitory activity have been described (see, e.g., Zhao et al., Hyrbidoma (Larchmt) 2008 27(6):455-51; Peter et al., J Cachexia Sarcopenia Muscle 2012 August 12; Shieh et al., J Imunol2009 183(4):2277-85; Giomarelli et al., Thromb Haemost 2007 97(6):955-63; Fife eta., J Clin Invst 2006 116(8):2252-61; Brocks et al., Immunotechnology 1997 3(3):173-84; Moosmayer et al., Ther Immunol 1995 2(10:31-40). Agonistic scFvs having stimulatory activity have been described (see, e.g., Peter et al., J Bioi Chern 2003 25278(38):36740-7; Xie et al., Nat Biotech 1997 15(8):768-71; Ledbetter et al., Crit Rev Immunol1997 17(5-6):427-55; Ho et al., BioChim Biophys Acta 2003 1638(3):257-66).

As used herein, "F(ab)" refers to a fragment of an antibody structure that binds to an antigen but is monovalent and does not have a Fc portion, for example, an antibody digested by the enzyme papain yields two F(ab) fragments and an Fc fragment (e.g., a heavy (H) chain constant region; Fc region that does not bind to an antigen).

As used herein, "$F(ab')_2$" refers to an antibody fragment generated by pepsin digestion of whole IgG antibodies, wherein this fragment has two antigen binding (ab') (bivalent) regions, wherein each (ab') region comprises two separate amino acid chains, a part of a H chain and a light (L) chain linked by an S-S bond for

binding an antigen and where the remaining H chain portions are linked together. A "F(ab')2" fragment can be split into two individual Fab' fragments.

As used herein, the term "vector" refers to any genetic element, such as a plasmid, phage, transposon, cosmid, chromosome, virus, virion, etc., which is capable of replication when associated with the proper control elements and which can transfer gene sequences into cells. Thus, the term includes cloning and expression vehicles, as well as viral vectors and plasmid vectors.

""CDRs" are defined as the complementarity determining region amino acid sequences of an antibody which are the hypervariable regions of immunoglobulin heavy and light chains. See, e. g., Kabat et al., Sequences of Proteins of Immunological Interest, 4th U. S. Department of Health and Human Services, National Institutes of Health (1987). The term "hypervariable region" or "HVR" as used herein refers to each of the regions of an antibody variable domain which are hypervariable in sequence ("complementarity determining regions" or "CDRs") and/or form structurally defined loops ("hypervariable loops") and/or contain the antigen-contacting residues ("antigen contacts"). Generally, antibodies comprise three heavy chain and three light chain CDRs or CDR regions in the variable region. CDRs provide the majority of contact residues for the binding of the antibody to the antigen or epitope.

An "isolated antibody" is one which has been separated from a component of its natural environment. In certain embodiments, an antibody is purified to greater than 95% or 99% purity as determined by, for example, electrophoretic (e.g., SDS-PAGE, isoelectric focusing (IEF), capillary electrophoresis) or chromatographic (e.g., ion exchange or reverse phase HPLC). For review of methods for assessment of antibody purity, see, e.g., Flatman et al., *J. Chromatogr. B* 848:79-87 (2007).

An "isolated nucleic acid" refers to a nucleic acid molecule that has been separated from a component of its natural environment. An isolated nucleic acid includes a nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location.

An "isolated nucleic acid encoding an antibody" (including references to a specific antibody, e.g. an anti-KLB antibody) refers to one or more nucleic acid

molecules encoding antibody heavy and light chains (or fragments thereof), including such nucleic acid molecule(s) in a single vector separate vectors, and such nucleic acid molecule(s) present at one or more locations in a host cell.

The term "vector," as used herein, refers to a nucleic acid molecule capable of propagating another nucleic acid to which it is linked. The term includes the vector as a self-replicating nucleic acid structure as well as the vector incorporated into the genome of a host cell into which it has been introduced. Certain vectors are capable of directing the expression of nucleic acids to which they are operatively linked. Such vectors are referred to herein as "expression vectors."

An "immunoconjugate" is an antibody conjugated to one or more heterologous molecule(s), including, but not limited to, a cytotoxic agent.

An "effective amount" of an agent, e.g., an anti-BCMA antibody or an antigen-binding fragment thereof, a pharmaceutical composition comprising thereof, refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result, e.g., treating a tumor (e.g., multiple myeloma).

An "individual" or "subject" is a mammal. Mammals include, but are not limited to, domesticated animals (e.g., cows, sheep, cats, dogs, and horses), primates (e.g., humans and non-human primates such as monkeys), rabbits, and rodents (e.g., mice and rats). In certain embodiments, the individual or subject is a human.

As used herein, "treatment" (and grammatical variations thereof such as "treat" or "treating") refers to clinical intervention in an attempt to alter the natural course of the individual being treated, and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include, but are not limited to, preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In certain embodiments, antibodies of the presently disclosed subject matter are used to delay development of a disease or to slow the progression of a disease, e.g., a tumor (multiple myeloma).

As used herein, the term "about" or "approximately" means within an acceptable error range for the particular value as determined by one of ordinary skill

in the art, which will depend in part on how the value is measured or determined, *i.e.*, the limitations of the measurement system. For example, "about" can mean within 3 or more than 3 standard deviations, per the practice in the art. Alternatively, "about" can mean a range of up to 20%, preferably up to 10%, more preferably up to 5%, and more preferably still up to 1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, preferably within 5-fold, and more preferably within 2-fold, of a value.

As described herein, any concentration range, percentage range, ratio range or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated.

Anti-BCMA Antibodies

The antibodies of the presently disclosed subject matter are characterized by particular functional features or properties of the antibodies. For example, the antibodies bind specifically to BCMA (e.g., bind to human BCMA and may cross-react with BCMA from other species, such as mouse). In certain embodiments, an antibody of the presently disclosed subject matter binds to BCMA with high affinity, for example with a K_D of 1 x 10^{-6} M or less, e.g., about 1 x 10^{-7} M or less, about 1 x 10^{-8} M or less, about 1 x 10^{-9} M or less, about 1 x 10^{-10} M or less, or about 1 x 10^{-11} M or less. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of from about 1 x 10^{-11} M to about 1 x 10^{-6} M, e.g., from about 1 x 10^{-11} M to about 1 x 10^{-10} M, from about 1 x 10^{-10} M to about 1 x 10^{-9} M, from 1 x 10^{-9} M to about 1 x 10^{-8} M, from about 1 x 10^{-8} M to about 1 x 10^{-7} M, or from about 1 x 10^{-7} M to about 1 x 10^{-6} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 1 x 10^{-8} M or less. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of from about 1 x 10^{-9} M to about 1 x 10^{-8} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of from about 1 x 10^{-9} M to about 1.5 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 1.2 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of from about 4 x 10^{-9} M to

about 5 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 5 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 4.8 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of from about 8 x 10^{-9} M to about 9 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 8 x 10^{-9} M. In certain embodiments, a presently disclosed anti-BCMA antibody binds to BCMA (e.g., human BCMA) with a K_D of about 8.1 x 10^{-9} M.

The heavy and light chains of an antibody of the presently disclosed subject matter can be full-length (*e.g.,* an antibody can include at least one (e.g., one or two) complete heavy chains, and at least one (e.g., one or two) complete light chains) or can include an antigen-binding portion (a Fab, $F(ab')_2$, Fv or a single chain Fv fragment ("scFv")). In certain embodiments, the antibody heavy chain constant region is chosen from, e.g., IgG1 , IgG2, IgG3, IgG4, IgM, IgA1 , IgA2, IgD, and IgE, particularly chosen from, *e.g.*, IgG1 , IgG2, IgG3, and IgG4, more particularly, IgG1 (e.g., human IgG1). In another embodiment, the antibody light chain constant region is chosen from, e.g., kappa or lambda, particularly kappa.

1. Single-chain variable fragments (scFvs)

In some embodiments, the presently disclosed subject matter includes antibodies that have the scFv sequence fused to one or more constant domains to form an antibody with an Fc region of a human immunoglobulin to yield a bivalent protein, increasing the overall avidity and stability of the antibody. In addition, the Fc portion allows the direct conjugation of other molecules, including but not limited to fluorescent dyes, cytotoxins, radioisotopes etc. to the antibody for example, for use in antigen quantitation studies, to immobilize the antibody for affinity measurements, for targeted delivery of a therapeutic agent, to test for Fc-mediated cytotoxicity using immune effector cells and many other applications.

The results presented here highlight the specificity, sensitivity and utility of the antibodies of the invention in targeting a BCMA polypeptide.

The molecules of the invention are based on the identification and selection of single chain variable fragments (scFvs) using phage display, the amino acid sequence of which confers the molecules' specificity for a BCMA polypeptide of

interest and forms the basis of all antigen binding proteins of the disclosure. The scFv, therefore, can be used to design a diverse array of "antibody" molecules, including, for example, full length antibodies, fragments thereof, such as Fab and $F(ab')_2$, minibodies, fusion proteins, including scFv-Fc fusions, multivalent antibodies, that is, antibodies that have more than one specificity for the same antigen or different antigens, for example, bispecific antibodies, tribodies, etc. (see Cuesta et al., Multivalent antibodies: when design surpasses evolution. Trends in Biotechnology 28:355-362 2010).

In certain embodiments, the antigen-binding protein is a full length antibody, the heavy and light chains of an antibody of the presently disclosed subject matter can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding portion (a Fab, $F(ab')_2$, Fv or a single chain Fv fragment ("scFv")). In certain embodiments, the antibody heavy chain constant region is chosen from, e.g., IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In certain embodiments, the immunoglobulin isotype is selected from IgG1, IgG2, IgG3, and IgG4, more particularly, IgG1 (e.g., human IgG1). The choice of antibody isotype can depend on the immune effector function that the antibody is designed to elicit.

In constructing a recombinant immunoglobulin, appropriate amino acid sequences for constant regions of various immunoglobulin isotypes and methods for the production of a wide array of antibodies are known to those of skill in the art.

In certain embodiments, the antibody or other antigen binding protein is an anti- BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO: 72 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71 provided below, or fragments thereof), which is designated as ET140-192 (also referred to as "ET140-42").

MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASV
TNSVKGTNAILWTCLGLSLIISLAVFVLMFLLRKINSEPLKDEFKNTGSGLLGM
ANIDLEKSRTGDEIILPRGLEYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGA
TILVTTKTNDYCKSLPAALSATEIEKSISAR [SEQ ID NO:71]

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:1 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:2, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:1, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:2, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:1 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:2, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:89 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:90 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:91 or conservative modifications thereof, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:92 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:93 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:94 or conservative modifications thereof, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:89 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:90 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:91or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:92 or conservative modifications thereof, a V_L

CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:93 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:94 or conservative modifications thereof, as shown in Table 1. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:89, a V_H CDR2 mprising amino acids having the sequence set forth in SEQ ID NO:90, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:91, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:92, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:93, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:94.

Table 1

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	VSSNSAAWN [SEQ ID NO:89]	YRSKWYN [SEQ ID NO:90]	ARQGYSYYGYSD V [SEQ ID NO:91]
V_L	SSNIGHND [SEQ ID NO:92]	FDD [SEQ ID NO:93	AAWDGSLNAFV [SEQ ID NO:94]
Full V_H	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRT YYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARQGYSY YGYSDVWGQGTLVTVSS [SEQ ID NO:1]		
DNA	Caggtacagctgcagcagtcaggtccaggactggtgaagccctcgcagaccctctcactcacctgtgccatctccggggac agtgtctctagcaacagtgctgcttggaactggatcaggcagtccccatcgagaggccttgagtggctgggaaggacatact acaggtccaagtggtataatgattatgcagtatctgtgaaaagtcgaataaccatcaacccagacacatccaagaaccagttct ccctgcagctgaactctgtgactcccgaggacacggctgtgtattactgtgcgcgccagggttactcttactacggttactctga tgtttggggtcaaggtactctggtgaccgtctcctca [SEQ ID NO:3]		
Full V_L	QSVLTQPPSVSVAPRQRVTISCSGSSSNIGHNDVSWYQHLPGKAPRLLIYFDDLL PSGVSDRFSASKSGTSASLAISGLQSEDEADYYCAAWDGSLNAFVFGTGTKVT VLG [SEQ ID NO:2]		
DNA	Cagtctgtgctgactcagccaccctcggtgtctgtagcccccaggcagagggtcaccatctcgtgttctggaagcagctccaa catcggacataatgatgtaagctggtaccagcatctcccagggaaggctcccagactcctcatctattttgatgacctgctgccg tcaggggtctctgaccgattctctgcctccaagtctggcacctcagcctccctggccatcagtgggctccagtctgaggatgag gctgattattactgtgcagcatgggatggcagcctgaatgcctttgtcttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:4]		
scFv	QSVLTQPPSVSVAPRQRVTISCSGSSSNIGHNDVSWYQHLPGKAPRLLIYFDDLL PSGVSDRFSASKSGTSASLAISGLQSEDEADYYCAAWDGSLNAFVFGTGTKVT VLGSRGGGGSGGGGSGGGGSLEMAQVQLQQSGPGLVKPSQTLSLTCAISGDSV SSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQF SLQLNSVTPEDTAVYYCARQGYSYYGYSDVWGQGTLVTVSS [SEQ ID NO:72]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:73 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the

amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-197 (also referred to as "ET140-47").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:5 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:6, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:5, as shown in Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:6, as shown in Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:5 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:6, as shown in Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:95 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:96 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:97 or conservative modifications thereof, as shown in Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:98 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:99 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:100 or conservative modifications thereof, as shown in Table 2. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:95 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:96 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:97 or

conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:98 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:99 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:100 or conservative modifications thereof, as shown in Table 2. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:95, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:96, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:97, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:98, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:99, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:100.

Table 2

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	VSSNSAAWN [SEQ ID NO:95]	YRSKWYN [SEQ ID NO:96]	ARYGFSGSRFYDT [SEQ ID NO:97]
V_L	SSNIGNNA [SEQ ID NO:98]	FDD [SEQ ID NO:99]	AAWDDSLNGYV [SEQ ID NO:100]
Full V_H	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRTY YRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARYGFSGSR FYDTWGQGTLVTVSS [SEQ ID NO:5]		
DNA	Caggtacagctgcagcagtcaggtccaggactggtgaagccctcgcagaccctctcactcacctgtgccatctccggggaca gtgtctctagcaacagtgctgcttggaactggatcaggcagtccccatcgagaggccttgagtggctgggaaggacatactaca ggtccaagtggtataatgattatgcagtatctgtgaaaagtcgaataaccatcaacccagacacatccaagaaccagttctccctg cagctgaactctgtgactcccgaggacacggctgtgtattactgtgcgcgctacggtttctctggttctcgtttctacgatacttggg gtcaaggtactctggtgaccgtctcctca [SEQ ID NO:7]		
Full V_L	QPVLTQPPSVSEAPRQRVTISCSGSSSNIGNNAVNWYQQLPGKAPKLLIYFDDLL SSGVSDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGYVFGTGTKVTV LG [SEQ ID NO:6]		
DNA	Cagcctgtgctgactcagccaccctcggtgtctgaagcccccaggcagagggtcaccatctcctgttctggaagcagctccaa catcggaaataatgctgtaaactggtaccagcagctcccaggaaaggctcccaaactcctcatctattttgatgatctgctgtcctc aggggtctctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtgggctccagtctgaagatgaggct gattattactgtgcagcatgggatgacagcctgaatggttatgtcttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:8]		
scFv	QPVLTQPPSVSEAPRQRVTISCSGSSSNIGNNAVNWYQQLPGKAPKLLIYFDDLL SSGVSDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGYVFGTGTKVTV LGSRGGGGSGGGGSGGGGSLEMAQVQLQQSGPGLVKPSQTLSLTCAISGDSVSS NSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSL QLNSVTPEDTAVYYCARYGFSGSRFYDTWGQGTLVTVSS [SEQ ID NO:73]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-

binding region that comprises the amino acid sequence of SEQ ID NO:74 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-180 (also referred to as "ET140-30").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:9 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:10, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:9, as shown in Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:10, as shown in Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:9 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:10, as shown in Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:101 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:102 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:103 or conservative modifications thereof, as shown in Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:104 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:105 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:106 or conservative modifications thereof, as shown in Table 3. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:101 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the

sequence set forth in SEQ ID NO:102 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:103 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:104 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:105 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:106 or conservative modifications thereof, as shown in Table 3. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:101, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:102, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:103, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:104, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:105, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:106.

Table 3

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGTFSSYA [SEQ ID NO:101]	IIPILGIA [SEQ ID NO:102]	ARSGYSKSIVSYMDY [SEQ ID NO:103]
V_L	SSNIGSNV [SEQ ID NO:104]	RNN [SEQ ID NO:105]	AAWDDSLSGYV [SEQ ID NO:106]
Full V_H	EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTMTEDTSTDTAYMELSSLRSEDTAVYYCARSGYSKSIVSYMDYWGQGTLVTVSS [SEQ ID NO:9]		
DNA	Gaggtccagctggtgcagtctggagctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcttctggaggcaccttcagcagctatgctatcagctgggtgcgacaggccccctggacaagggcttgagtggatgggaaggatcatccctatcctttggtatagcaaactacgcacagaagttccagggcagagtcaccatgaccgaggacacatctacagacacagcctacatggagctgagcagcctgagatctgaggacacggccgtgtattactgtgcgcgctctggttactctaaatctatcgtttcttacatggattactgggtcaaggtactctggtgaccgtctcctca [SEQ ID NO:11]		
Full V_L	LPVLTQPPSTSGTPGQRVTVSCSGSSSNIGSNVVFWYQQLPGTAPKLVIYRNNQRPSGVPDRFSVSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGYVFGTGTKVTVLG [SEQ ID NO:10]		
DNA	Ctgcctgtgctgactcagccccctccacgtctgggaccccgggcagagggtcaccgtctcttgttctggaagcagctccaacatcggaagtaatgttgtattctggtaccagcagctcccaggcacggccccaaacttgtcatctataggaataatcaacggccctcaggggtccctgaccgattctctgtctccaagtctggcacctcagcctccctggccatcagtgggctccggtccgaggacgaggctgattattattgtgcagcttgggatgacagcctgagtggttatgtcttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:12]		
scFv	LPVLTQPPSTSGTPGQRVTVSCSGSSSNIGSNVVFWYQQLPGTAPKLVIYRNNQRPSGVPDRFSVSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGYVFGTGTKVTVLGSRGGGGSGGGGSGGGGSLEMAEVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTMTEDTSTDTAYMELSSLRSEDTAVYYCARSGYSKSIVSYMDYWGQGTLVTVSS [SEQ ID NO:74]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:75 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-172 (also referred to as "ET140-22").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:13 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:14, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 4. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:13, as shown in Table 4. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:14, as shown in Table 4. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:13 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:14, as shown in Table 4. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:107 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:108 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:109 or conservative modifications thereof, as shown in Table 4. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:110 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:111 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:112 or conservative modifications thereof, as shown in Table 4. In certain embodiments, the anti-BCMA scFv

comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:107 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:108 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:109 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:110 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:111 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:112 or conservative modifications thereof, as shown in Table 4. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:107, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:108, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:109, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:110, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:111, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:112.

Table 4

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFTSYY [SEQ ID NO:107]	INPSGGST [SEQ ID NO:108]	ARSQWGGVLDY [SEQ ID NO:109]
V_L	SSNIGARYD [SEQ ID NO:110]	GNN [SEQ ID NO: 111]	QSYDSSLSASV [SEQ ID NO: 112]
Full V_H	EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIIN PSGGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARSQWGGVL DYWGQGTLVTVSS [SEQ ID NO:13]		
DNA	Gaggtccagctggtacagtctggggctgaggtgaagaagcctggggcctcagtgaaggtttcctgcaaggcatctggataca ccttcaccagctactatatgcactgggtgcgacaggcccctggacaagggcttgagtggatgggaataatcaaccctagtggtg gtagcacaagctacgcacagaagttccagggcagagtcaccatgaccagggacacgtccacgagcacagtctacatggagct gagcagcctgagatctgaggacacggccgtgtattactgtgcgcgctctcagtggggtggtgttctggattactggggtcaagg tactctggtgaccgtctcctca [SEQ ID NO:15]		
Full V_L	QSVVTQPPSVSGAPGQRVTISCSGSSSNIGARYDVQWYQQLPGTAPKLLIFGNNN RPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDSSLSASVFGGGTKLTV LG [SEQ ID NO:14]		
DNA	Cagtctgtcgtgacgcagccgccctcagtgtctggggccccagggcagagggtcaccatctcctgcagtgggagcagctcca acatcggggcacgttatgatgttcagtggtaccagcagcttccaggaacagccccaaactcctcatctttggtaacaacaatcg gccctcaggggtccctgaccgattctctggctccaagtctggcacgtcagcctccctggccatcactgggctccaggctgagga tgaggctgattattactgccagtcctatgacagcagcctgagtgcttcggtgttcggcggagggaccaagctgaccgtcctaggt [SEQ ID NO:16]		
scFv	QSVVTQPPSVSGAPGQRVTISCSGSSSNIGARYDVQWYQQLPGTAPKLLIFGNNN RPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDSSLSASVFGGGTKLTV		

	LGSRGGGGSGGGGSGGGGSLEMAEVQLVQSGAEVKKPGASVKVSCKASGYTF TSYYMHWVRQAPGQGLEWMGIINPSGGSTSYAQKFQGRVTMTRDTSTSTVYM ELSSLRSEDTAVYYCARSQWGGVLDYWGQGTLVTVSS [SEQ ID NO:75]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:76 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof),, which is designated as ET140-157 (also referred to as "ET140-7").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:17 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:18, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:17, as shown in Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:18, as shown in Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:17 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:18, as shown in Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:113 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:114 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:115 or conservative modifications thereof, as shown in Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:116 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:117 or conservative modifications thereof, and a V_L CDR3 comprising amino

acids having the sequence set forth in SEQ ID NO:118 or conservative modifications thereof, as shown in Table 5. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:113 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:114 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:115 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:116 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:117 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:118 or conservative modifications thereof, as shown in Table 5. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:113, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:114, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:115, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:116, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:117, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:118.

Table 5

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGTFSSYA [SEQ ID NO:113]	IIPILGIA [SEQ ID NO:114]	ARTGYESWGSYEVI DR [SEQ ID NO:115]
V_L	SSNIGSNT [SEQ ID NO:116]	SNN [SEQ ID NO:117]	AAWDDSLNGVV [SEQ ID NO:118]
Full V_H	QVQLVESGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGRIIPI LGIANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARTGYESWGSYE VIDRWGQGTLVTVSS [SEQ ID NO:17]		
DNA	Caggtgcagctggtggagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcttctggaggca ccttcagcagctatgctatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggaaggatcatccctatcctg gtatagcaaactacgcacagaagttccagggcagagtcacgattaccgcggacgaatccacgagcacagcctacatggagct gagcagcctgagatctgaggacacggccgtatattactgtgcgcgcactggttacgaatcttggggttcttacgaagttatcgatc gttggggtcaaggtactctggtgaccgtctcctca [SEQ ID NO:19]		
Full V_L	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYRQLPGTAPKLLIYSNNQR PSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGVVFGGGTKLTV LG [SEQ ID NO:18]		
DNA	Caggctgtgctgactcagccaccctcagcgtctgggaccccccgggcagagggtcaccatctcttgttctggaagcagctccaa catcggaagtaatactgtaaactggtaccggcagctcccaggaacggccccccaaactcctcatctatagtaataatcagcggcc ctcaggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtgggctccagtctgaggatga ggctgattattactgtgcagcatgggatgacagcctgaatggtgtggtattcggcggagggaccaagctgaccgtcctaggt		

	[SEQ ID NO:20]
scFv	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYRQLPGTAPKLLIYSNNQR PSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGVVFGGGTKLTV LGSRGGGGSGGGGSGGGGSLEMAQVQLVESGAEVKKPGSSVKVSCKASGGTFS SYAISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADESTSTAYMELSS LRSEDTAVYYCARTGYESWGSYEVIDRWGQGTLVTVSS [SEQ ID NO:76]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:77 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-153 (also referred to as "ET140-3")..

In certain embodiments, the anti-BCMA scFv antibody 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, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 6. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:21, as shown in Table 6. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:22, as shown in Table 6. In certain embodiments, the anti-BCMA scFv 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, as shown in Table 6. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:119 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:120 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:121 or conservative modifications thereof, as shown in Table 6. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122 or conservative modifications

thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:124 or conservative modifications thereof, as shown in Table 6. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:119 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:120 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:121 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:124 or conservative modifications thereof, as shown in Table 6. In certain embodiments, the extracellular antigen-binding domain 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.

Table 6

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGTFSSYA [SEQ ID NO:119]	IIPILGIA [SEQ ID NO:120]	ARGGYYSHDMWS ED [SEQ ID NO:121]
V_L	SSNIGSNS [SEQ ID NO:122]	SNN [SEQ ID NO:123]	ATWDDNLNVHYV [SEQ ID NO:124]
Full V_H	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGRIIP ILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGGYYSHDM WSEDWGQGTLVTVSS [SEQ ID NO:21]		
DNA	Caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcttctggaggc accttcagcagctatgctatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggaaggatcatccctatcct tggtatagcaaactacgcacagaagttccagggcagagtcacgattaccgcggacaaatccacgagcacagcctacatgga gctgagcagcctgagatctgaggacacggccgtgtattactgtgcgcgcggtggttactactctcatgacatgtggtctgaaga ttggggtcaaggtactctggtgaccgtctcctca [SEQ ID NO:23]		
Full V_L	LPVLTQPPSASGTPGQRVTISCSGRSSNIGSNSVNWYRQLPGAAPKLLIYSNNQR PPGVPVRFSGSKSGTSASLAISGLQSEDEATYYCATWDDNLNVHYVFGTGTKV TVLG [SEQ ID NO:22]		

DNA	Ctgcctgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggacgcagttccaa catcgggagtaattctgttaactggtatcgacaactcccaggagcggccccaaactcctcatctatagtaataatcagcggcc cccaggggtccctgtgcgattctctggctccaagtctggcacctcagcctccctggccatcagtgggctccagtctgaagatg aggccacttattactgtgcaacatgggatgacaatctgaatgttcactatgtcttcggaactgggaccaaggtcaccgtcctagg t [SEQ ID NO:24]
scFv	LPVLTQPPSASGTPGQRVTISCSGRSSNIGSNSVNWYRQLPGAAPKLLIYSNNQR PPGVPVRFSGSKSGTSASLAISGLQSEDEATYYCATWDDNLNVHYVFGTGTKV TVLGSRGGGGSGGGGSGGGGSLEMAQVQLVQSGAEVKKPGSSVKVSCKASGG TFSSYAISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYM ELSSLRSEDTAVYYCARGGYYSHDMWSEDWGQGTLVTVSS [SEQ ID NO:77]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:78 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-201 (also referred to as "ET140-51").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:25 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:26, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 7. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:25, as shown in Table 7. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:26, as shown in Table 7. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:25 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:26, as shown in Table 7. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:125 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:126 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:127 or conservative modifications thereof, as shown in Table 7. In

certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:128 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:129 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:130 or conservative modifications thereof, as shown in Table 7. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:125 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:126 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:127 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:128 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:129 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:130 or conservative modifications thereof, as shown in Table 7. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:125, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:126, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:127, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:128, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:129, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:130.

Table 7

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGSISNSNW [SEQ ID NO:125]	IYHSGST [SEQ ID NO: 126]	ARRDNWKTPTTKID GFDI [SEQ ID NO:127]
V_L	SGYSNYK [SEQ ID NO:128]	VGTGGIVG [SEQ ID NO:129]	GADHGSGSNFVYV SEQ ID NO:130]
Full V_H	QVQLQESGPGLVKPSGTLSLTCGVSGGSISNSNWWSWVRQPPGKGLEWIGEIYH SGSTKYNPSLRSRVTISVDKSKNQFSLKLSSVTAADTAVYYCARRDNWKTPTTK IDGFDIWGQGTMVTVSS [SEQ ID NO:25]		
DNA	Caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggggaccctgtccctcacctgcggtgtctctggtggct ccatcagcaatagtaactggtggagttgggtccgccagccccccgggaaggggctggagtggattggggaaatctatcatagt gggagcaccaagtacaacccgtccctcaggagtcgagtcaccatatcagtagacaagtccaagaaccagttctccctaaaattg agctctgtgaccgccgcggacacggccgtatattactgtgcgagacgagataactggaagacccccactaccaaaattgatgg ttttgatatctggggccaagggacaatggtcaccgtctcttca [SEQ ID NO:27]		

Full V_L	QPVLTQPPSASASLGASVTLTCTLSSGYSNYKVDWYQQRPGKGPRFVMRVGTG GIVGSKGDGIPDRFSVLGSGLNRYLTIKNIQEEDEGDYHCGADHGSGSNFVYVFG TGTKVTVLG [SEQ ID NO:26]
DNA	Cagcctgtgctgactcagccaccttctgcatcagcctccctgggagcctcggtcacactcacctgcaccctgagcagcggcta cagtaattataaagtggactggtaccagcagagaccagggaagggcccccggtttgtgatgcgagtgggcactggtgggattg tgggatccaaggggatggcatccctgatcgcttctcagtcttgggctcaggcctgaatcggtacctgaccatcaagaacatcc aggaagaagatgagggtgactatcactgtggggcagaccatggcagtgggagcaacttcgtgtatgtcttcggaactgggacc aaggtcaccgtcctaggt [SEQ ID NO:28]
scFv	QPVLTQPPSASASLGASVTLTCTLSSGYSNYKVDWYQQRPGKGPRFVMRVGTG GIVGSKGDGIPDRFSVLGSGLNRYLTIKNIQEEDEGDYHCGADHGSGSNFVYVFG TGTKVTVLGSRGGGGSGGGGSGGGGSLEMAQVQLQESGPGLVKPSGTLSLTCG VSGGSISNSNWWSWVRQPPGKGLEWIGEIYHSGSTKYNPSLRSRVTISVDKSKN QFSLKLSSVTAADTAVYYCARRDNWKTPTTKIDGFDIWGQGTMVTVSS [SEQ ID NO:78]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:79 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-167 (also referred to as "ET140-17").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:29 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:30, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 8. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:29, as shown in Table 8. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:30, as shown in Table 8. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:29 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:30, as shown in Table 8. In certain embodiments, the anti-BCMA comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:131 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:132 or conservative modifications thereof, and a V_H

CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:133 or conservative modifications thereof, as shown in Table 8. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:134 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:135 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:136 or conservative modifications thereof, as shown in Table 8. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:131 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:132 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:133 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:134 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:135 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:136 or conservative modifications thereof, as shown in Table 8. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:131, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:132, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:133, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:134, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:135, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:136.

Table 8

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFTGYY [SEQ ID NO:131]	INPNSGGT [SEQ ID NO: 132]	ARSQWGSSWDY [SEQ ID NO: 133]
V_L	QSISSY [SEQ ID NO: 134]	AAS [SEQ ID NO: 135]	QQSYSTPPT [SEQ ID NO: 136]
Full V_H	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWI NPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARSQWGSS WDYWGQGTLVTVSS [SEQ ID NO:29]		
DNA	Caggtccagctggtacagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggataca ccttcaccggctactatatgcactgggtgcgacaggccccctggacaagggcttgagtggatgggatggatcaaccctaacagt		

	ggtggcacaaactatgcacagaagtttcagggcagggtcaccatgaccagggacacgtccatcagcacagcctacatggagc tgagcaggctgagatctgacgacacggccgtgtattactgtgcgcgctctcagtggggttcttcttgggattactggggtcaagg tactctggtgaccgtctcctca [SEQ ID NO:31]
Full V_L	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKR [SEQ ID NO:30]
DNA	Gacatccagttgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcagagc attagcagctatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctatgctgcatccagtttgcaaagtgg ggtcccatcaaggttcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacctgaagattttgcaactt actactgtcaacagagttacagtaccctccgacgttcggccaagggaccaaggtggagatcaaacgt [SEQ ID NO:32]
scFv	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKRSRGG GGSGGGGSGGGGSLEMAQVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMH WVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLR SDDTAVYYCARSQWGSSWDYWGQGTLVTVSS [SEQ ID NO:79]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:80 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-163 (also referred to as "ET140-13").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:33 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:34, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:33, as shown in Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:34, as shown in Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:33 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:34, as shown in Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ

ID NO:137 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:138 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:139 or conservative modifications thereof, as shown in Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:140 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:141 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:142 or conservative modifications thereof, as shown in Table 9. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:137 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:138 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:139 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:140 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:141 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:142 or conservative modifications thereof, as shown in Table 9. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:137, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:138, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:139, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:140, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:141, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:142.

Table 9

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFTGYY [SEQ ID NO:137]	INPNSGGT [SEQ ID NO:138]	ARSSYHLYGYDS [SEQ ID NO:139]
V_L	NDYTNYK [SEQ ID NO:140]	VGPGGIVG [SEQ ID NO:141]	GADHGTGSNFVYV [SEQ ID NO:142]
Full V_H	EVQLVESGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWI		

	NPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARSSYHLY GYDSWGQGTLVTVSS [SEQ ID NO:33]
DNA	Gaggtgcagctggtggagtccggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggatac accttcaccggctactatatgcactgggtgcgacaggcccctggacaagggcttgagtggatgggatggatcaaccctaacag tggtggcacaaactatgcacagaagtttcagggcagggtcaccatgaccagggacacgtccatcagcacagcctacatggag ctgagcaggctgagatctgacgcacggccgtatattactgtgcgcgctcttcttaccatctgtacggttacgattcttggggtcaa ggtactctggtgaccgtctcctca [SEQ ID NO:35]
Full V_L	QPVLTQPPSASASLGASVTLTCTLSNDYTNYKVDWYQQRPGKGPRFVMRVGPG GIVGSKGDGIPDRFSVLGSGLNRYLTIKNIQEEDESDYHCGADHGTGSNFVYVFG GGTKLTVLG [SEQ ID NO:34]
DNA	Cagcctgtgctgactcagccaccttctgcatcagcctccctgggagcctcggtcactctcacctgcaccctgagcaacgactac actaattataaagtggactggtaccagcagagaccagggaagggccccggtttgtgatgcgagtgggccctggtgggattgt gggatccaaggggatggcatccctgatcgcttctcagtcttgggctcaggcctgaatcgatacctgaccatcaagaacatcca ggaggaggatgagagtgactaccactgtggggcggaccatggcaccgggagcaacttcgtgtacgtgttcggcggagggac caagctgaccgtcctaggt [SEQ ID NO:36]
scFv	QPVLTQPPSASASLGASVTLTCTLSNDYTNYKVDWYQQRPGKGPRFVMRVGPG GIVGSKGDGIPDRFSVLGSGLNRYLTIKNIQEEDESDYHCGADHGTGSNFVYVFG GGTKLTVLGSRGGGGSGGGGSGGGGSLEMAEVQLVESGAEVKKPGASVKVSC KASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRD TSISTAYMELSRLRSDDTAVYYCARSSYHLYGYDSWGQGTLVTVSS [SEQ ID NO:80]

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:81 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-207 (also referred to as "ET140-57").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:37 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:38, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:98. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:37, as shown in Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:38, as shown in Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:37 and a V_L comprising amino acids having the sequence set forth in SEQ ID

NO:38, as shown in Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:143 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:144 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:145 or conservative modifications thereof, as shown in Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:146 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:147 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:148 or conservative modifications thereof, as shown in Table 10. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:143 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:144 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:145 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:146 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:147 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:148 or conservative modifications thereof, as shown in Table 10. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:143, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:144, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:145, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:146, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:147, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:148.

Table 10

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGTFSSYA [SEQ ID NO:143]	IIPIFSTA [SEQ ID NO:144]	ARQPWTWYSPYDQ [SEQ ID NO:145]
V_L	SGYSNYK [SEQ ID NO:146]	VDTGGIVG [SEQ ID NO:147]	GADHGSGSNFVWV [SEQ ID NO:148]
Full V_H	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFSTANYAQKFQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARQPWTWYSPYDQWGQGTLVTVSS [SEQ ID NO:37]		
DNA	Caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcttctggaggcaccttcagcagctatgctatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggagggatcatccctatcttta gtacagcaaactacgcacagaagttccagggcagagtcaccatgaccacagacacatccacgagcacagcctacatggagct gaggagcctgagatctgacgacacggccgtgtattactgtgcgcgccagccgtggacttggtactctccgtacgatcagtggg gtcaaggtactctggtgaccgtctcctca [SEQ ID NO:39]		
Full V_L	QPVLTQPPSASASLGASVTLTCTLSSGYSNYKVDWYQQRPGKGPRFLMRVDTGGIVGSKGDGIPDRFSVSGSGLNRYLTIKNIQEEDESDYHCGADHGSGSNFVWVFGGGTKLTVLG [SEQ ID NO:38]		
DNA	Cagcctgtgctgactcagccaccttctgcatcagcctccctgggagcctcggtcacactcacctgcaccctgagcagcggcta cagtaattataaagtggactggtatcaacagagaccagggaagggccccggtttctgatgcgagtagacaccggtgggattgt gggatccaaggggatggcatccctgatcgcttctcagtctcgggctcaggtctgaatcggtacctgaccatcaagaacattca ggaagaggatgagagtgactaccactgtggggcagaccatggcagtgggagcaacttcgtgtgggtgttcggcggagggac caagctgaccgtcctaggt [SEQ ID NO:40]		
scFv	QPVLTQPPSASASLGASVTLTCTLSSGYSNYKVDWYQQRPGKGPRFLMRVDTGGIVGSKGDGIPDRFSVSGSGLNRYLTIKNIQEEDESDYHCGADHGSGSNFVWVFGGGTKLTVLGSRGGGGSGGGGSGGGGSLEMAQVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFSTANYAQKFQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARQPWTWYSPYDQWGQGTLVTVSS [SEQ ID NO:81]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:82 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-165 (also referred to as "ET140-15").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:41 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:42, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID

NO:41, as shown in Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:42, as shown in Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:41 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:42, as shown in Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:149 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151 or conservative modifications thereof, as shown in Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 153 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154 or conservative modifications thereof, as shown in Table 11. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 147 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 153 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154 or conservative modifications thereof, as shown in Table 11. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 149, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152, a V_L CDR2 comprising amino

acids having the sequence set forth in SEQ ID NO: 153, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154.

Table 11

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GFTFSTYA [SEQ ID NO: 149]	ITPGGDRT [SEQ ID NO: 150]	ARYYGYMIDM [SEQ ID NO: 151]
V_L	QSLLHSNGYNY [SEQ ID NO: 152]	LGS [SEQ ID NO: 153]	MQALQTPLT [SEQ ID NO:154]
Full V_H	EVQLVETGGGLVQPGGSLRLSCAASGFTFSTYAMTWVRQAPGKGLEWVSAITP GGDRTYYADSVKGRFTISRDNSRNTLYLQMNSLRAEDTAVYYCARYYGYMID MWGQGTLVTVSS [SEQ ID NO:41]		
DNA	Gaggtgcagctggtggagactgggggaggcctggtacagcctgggggtccctgagactctcctgtgctgcctctggattca cctttagcacctatgccatgacctgggtccgccaggctccagggaaggggctggagtgggtctcagctattactcctggtggtg atcgcacatactacgcagactccgtgaagggccgtttcactatctccagagacaattccaggaacacgctgtatctgcaaatgaa cagcctgagagccgaggacacggccgtatattactgtgcgcgctactacggttacatgatcgatatgtggggtcaaggtactct ggtgaccgtctcctca [SEQ ID NO:43]		
Full V_L	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYL GSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKV EIKR [SEQ ID NO:42]		
DNA	Gatgttgtgatgactcagtctccactctccctgcccgtcacccctggagagccggcctccatctcctgcaggtctagtcagagcc tcctgcatagtaatggatacaactatttggattggtacctgcagaagccagggcagtctccacagctcctgatctatttgggttctaa tcgggcctccggggtccctgacaggttcagtggcagtggatcaggcacagattttacactgaaaatcagcagagtggaggctg aggatgttggggtttattactgcatgcaagctctacaaactcctctcactttcggcggagggaccaaggtggaaatcaaacgt [SEQ ID NO:44]		
scFv	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYL GSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKV EIKRSRGGGGSGGGGSGGGGSLEMAEVQLVETGGGLVQPGGSLRLSCAASGFTF STYAMTWVRQAPGKGLEWVSAITPGGDRTYYADSVKGRFTISRDNSRNTLYLQ MNSLRAEDTAVYYCARYYGYMIDMWGQGTLVTVSS [SEQ ID NO:82]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:83 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-188 (also referred to as "ET140-38").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:45 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:46, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions

or CDRs selected from Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:45, as shown in Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:46, as shown in Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:45 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:46, as shown in Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:155 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157 or conservative modifications thereof, as shown in Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 158 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 159 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160 or conservative modifications thereof, as shown in Table 12. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 155 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 158 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 159 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160 or conservative modifications thereof, as shown in Table 12. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 155, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157, a V_L CDR1 comprising amino acids

having the sequence set forth in SEQ ID NO: 158, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 159, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160.

Table 12

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFTGYY [SEQ ID NO: 155]	INPNSGGT [SEQ ID NO: 156]	ARSQWGGTYDY [SEQ ID NO: 157]
V_L	SSNIGSNT [SEQ ID NO: 158]	SNN [SEQ ID NO: 159]	AAWDDSLNGWV [SEQ ID NO:160]
Full V_H	QMQLVQSGAEVKKPGASVKVSCKASGYTFTGYYVHWLRQAPGQGLEWMGWI NPNSGGTNNAQEFQGRITMTRDTSINTAYMELSRLRSDDTAVYYCARSQWGGT YDYWGQGTLVTVSS [SEQ ID NO:45]		
DNA	Cagatgcagctggtgcagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggataca ccttcaccggctattatgtacactggttgcgacaggccccctggacaagggcttgagtggatgggttggatcaaccctaacagtg gcggcacaaacaatgcacaggagtttcaaggcaggatcaccatgaccagggacacgtccatcaacacagcctacatggagct gagcaggctgagatctgacgacacggccgtgtattactgtgcgcgctctcagtggggtggtacttacgattactggggtcaagg tactctggtgaccgtctcctca [SEQ ID NO:47]		
Full V_L	SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQVPGTAPKLLIYSNNQR PSGVPDRFSGSKSGASASLAISWLQSEDEADYYCAAWDDSLNGWVFGGGTKLT VLG [SEQ ID NO:46]		
DNA	Tcctatgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagctccaac atcggaagtaatactgtaaactggtaccagcaggtcccaggaacggcccccaaactcctcatctatagtaataatcagcggccct caggggtccctgaccgattctctggctccaagtctggcgcctcagcctccctggccatcagttggctccagtctgaggatgagg ctgattattactgtgcagcatgggatgacagcctgaatggttgggtgttcggcggagggaccaagctgaccgtcctaggt [SEQ ID NO:48]		
scFv	SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQVPGTAPKLLIYSNNQR PSGVPDRFSGSKSGASASLAISWLQSEDEADYYCAAWDDSLNGWVFGGGTKLT VLGSRGGGGSGGGGSGGGGSLEMAQMQLVQSGAEVKKPGASVKVSCKASGYT FTGYYVHWLRQAPGQGLEWMGWINPNSGGTNNAQEFQGRITMTRDTSINTAY MELSRLRSDDTAVYYCARSQWGGTYDYWGQGTLVTVSS [SEQ ID NO:83]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:84 and specifically binds to a BCMApolypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-196 (also referred to as "ET140-46").

In certain embodiments, the anti-BCMA scFv antibody comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:49 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:50, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv

antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:49, as shown in Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:50, as shown in Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:49 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:50, as shown in Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:161 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163 or conservative modifications thereof, as shown in Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:165 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:166 or conservative modifications thereof, as shown in Table 13. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 161 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:165 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:166 or conservative modifications thereof, as shown in Table 13. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 161, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162, a V_H CDR3 comprising amino acids having

the sequence set forth in SEQ ID NO: 163, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:165, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:166.

Table 13

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYDFTTYW [SEQ ID NO: 161]	IYPGDSDT [SEQ ID NO: 162]	ARMWTFSQDG [SEQ ID NO: 163]
V_L	SSNIGSYT [SEQ ID NO: 164]	SNN [SEQ ID NO:165]	AAWDDSLNGYV [SEQ ID NO:166]
Full V_H	EVQLVQSGAEVKKPGESLKISCKGSGYDFTTYWIGWVRQMPGKGLEWMGIIYP GDSDTRYSPSVRGRVTISADKSINTAYLQWSSLEASDTAMYYCARMWTFSQDG WGQGTLVTVSS [SEQ ID NO:49]		
DNA	gaggtgcagctggtgcagtctggagcagaggtgaaaaagccgggggagtctctgaagatctcctgtaagggttctggatatga ctttaccacctactggatcgggtgggtgcgccagatgcccgggaagggcctggagtggatggggatcatctatcctggtgactc tgataccagatacagcccgtccgtccgaggccgggtcaccatctcagccgacaagtccatcaacaccgcctatttgcagtgga gtagcctggaggcctccgacaccgccatgtattactgtgcgcgcatgtggactttctctcaggatggttggggtcaaggtactct ggtgaccgtctcctca [SEQ ID NO:51]		
Full V_L	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSYTVSWYQQLPGTAPKFLIYSNNQRP SGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGYVFGTGTKVTVL G [SEQ ID NO:50]		
DNA	Caggctgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagctccaa catcggaagttatactgtaagctggtaccagcaactcccaggaacggcccccaaattcctcatctattctaataatcagcggccct caggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtgggctccagtctgaggatgagg ctgattattactgtgctgcatgggatgacagcctgaatggttatgtcttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:52]		
scFv	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSYTVSWYQQLPGTAPKFLIYSNNQRP SGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGYVFGTGTKVTVL GSRGGGGSGGGGSGGGGSLEMAEVQLVQSGAEVKKPGESLKISCKGSGYDFTT YWIGWVRQMPGKGLEWMGIIYPGDSDTRYSPSVRGRVTISADKSINTAYLQWSS LEASDTAMYYCARMWTFSQDGWGQGTLVTVSS [SEQ ID NO:84]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:85 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-204 (also referred to as "ET140-54").

In certain embodiments, the anti-BCMA scFv antibody 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, 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 embodiments, the linker comprises amino acids having the

sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:53, as shown in Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:54, as shown in Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:53 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:54, as shown in Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:167 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:168 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:169 or conservative modifications thereof, as shown in Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172 or conservative modifications thereof, as shown in Table 14. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172 or conservative modifications thereof, as shown in Table 14. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167, a V_H CDR2 comprising amino acids having the

sequence set forth in SEQ ID NO: 168, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172.

Table 14

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFIDYY [SEQ ID NO: 167]	INPNSGGT [SEQ ID NO: 168]	ARSQRDGYMDY [SEQ ID NO: 169]
V_L	ISCTGTSSD [SEQ ID NO: 170]	EDS [SEQ ID NO: 171]	SSNTRSSTLV [SEQ ID NO: 172]
Full V_H	EVQLVQSGAEMKKPGASLKLSCKASGYTFIDYYVYWMRQAPGQGLESMGWIN PNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAMYYCARSQRDGY MDYWGQGTLVTVSS [SEQ ID NO:53]		
DNA	Gaagtgcagctggtgcagtctggggctgagatgaagaagcctggggcctcactgaagctctcctgcaaggcttctggatacac cttcatcgactactatgtatactggatgcgacaggcccctggacaagggcttgagtccatgggatggatcaaccctaacagtggt ggcacaaactatgcacagaagtttcagggcagggtcaccatgaccagggacacgtccatcagcacagcctacatggagctga gcaggctgagatctgacgacaccgccatgtattactgtgcgcgctcccagcgtgacggttacatggattactggggtcaaggta ctctggtgaccgtctcctca [SEQ ID NO:55]		
Full V_L	QSALTQPASVSASPGQSIAISCTGTSSDVGWYQQHPGKAPKLMIYEDSKRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSNTRSSTLVFGGGTKLTVLG [SEQ ID NO:54]		
DNA	Caatctgccctgactcagcctgcctccgtgtctgcgtctcctggacagtcgatcgccatctcctgcactggaaccagcagtgac gttggttggtatcaacagcacccaggcaaagccccaaactcatgatttatgaggacagtaagcggccctcaggggtttctaatc gcttctctggctccaagtctggcaacacggcctccctgaccatctctgggctccaggctgaggacgaggctgattattactgcag ctcaaatacaagaagcagcactttggtgttcggcggagggaccaagctgaccgtcctaggt [SEQ ID NO:56]		
scFv	QSALTQPASVSASPGQSIAISCTGTSSDVGWYQQHPGKAPKLMIYEDSKRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSNTRSSTLVFGGGTKLTVLGSRGGG GSGGGGSGGGGSLEMAEVQLVQSGAEMKKPGASLKLSCKASGYTFIDYYVYW MRQAPGQGLESMGWINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSD DTAMYYCARSQRDGYMDYWGQGTLVTVSS [SEQ ID NO:85]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:86 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-190 (also referred to as "ET140-40").

In certain embodiments, the anti-BCMA scFv antibody 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, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:57, as shown in Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:58, as shown in Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:57 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:58, as shown in Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:173 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175 or conservative modifications thereof, as shown in Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178 or conservative modifications thereof, as shown in Table 15. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 173 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178 or conservative modifications thereof, as shown in Table 15. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence

set forth in SEQ ID NO: 173, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178.

Table 15

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYTFTDYY [SEQ ID NO: 173]	INPNSGGT [SEQ ID NO: 174]	ARSPYSGVLDK [SEQ ID NO: 175]
V_L	SSNIGAGFD [SEQ ID NO: 176]	GNS [SEQ ID NO: 177]	QSYDSSLSGYV [SEQ ID NO: 178]
Full V_H	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQRLEWMGWIN PNSGGTNYAQKFQDRITVTRDTSSNTGYMELTRLRSDDTAVYYCARSPYSGVLD KWGQGTLVTVSS [SEQ ID NO:57]		
DNA	Caggtccagctggtacagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggatacac cttcaccgactactatatgcactgggtgcgacaggccccctggacaacggcttgagtggatgggatggatcaaccctaacagtggt ggcacaaactatgcacagaagtttcaggacaggatcaccgtgaccagggacacctccagcaacacaggctacatggagctgac caggctgagatctgacgacacggccgtgtattactgtgcgcgctctccgtactctggtgttctggataaatggggtcaaggtactct ggtgaccgtctcctca [SEQ ID NO:59]		
Full V_L	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGAGFDVHWYQQLPGTAPKLLIYGNSNR PSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDSSLSGYVFGTGTKVTVL G [SEQ ID NO:58]		
DNA	Cagtctgtgctgacgcagccgccctcagtgtctggggccccagggcagagggtcaccatctcctgcactgggagcagctccaa catcggggcaggttttgatgtacactggtaccagcagcttccaggaacagccccccaaactcctcatctatggtaacagcaatcggc cctcaggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcactgggctccaggctgaggatga ggctgattattactgccagtcctatgacagcagcctgagtggttatgtcttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:60]		
scFv	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGAGFDVHWYQQLPGTAPKLLIYGNSNR PSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDSSLSGYVFGTGTKVTVL GSRGGGGSGGGGSGGGGSLEMAQVQLVQSGAEVKKPGASVKVSCKASGYTFTD YYMHWVRQAPGQRLEWMGWINPNSGGTNYAQKFQDRITVTRDTSSNTGYMEL TRLRSDDTAVYYCARSPYSGVLDKWGQGTLVTVSS [SEQ ID NO:86]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO: 87 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-187 (also referred to as "ET140-37").

In certain embodiments, the anti-BCMA scFv antibody 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, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:61, as shown in Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:62, as shown in Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:61 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:62, as shown in Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:179 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181 or conservative modifications thereof, as shown in Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184 or conservative modifications thereof, as shown in Table 16. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184 or conservative modifications thereof, as shown in Table 16. In certain embodiments, the extracellular antigen-

binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183 and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184.

Table 16

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GGTFSSYA [SEQ ID NO: 179]	IIPILGTA [SEQ ID NO: 180]	ARSGYGGSYRWED S [SEQ ID NO: 181]
V_L	SSNIGSNY [SEQ ID NO: 182]	SNN [SEQ ID NO: 183]	AAWDDSLSASYV [SEQ ID NO: 184]
Full V_H	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGRIIPIL GTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARSGYGSYRWEDS WGQGTLVTVSS [SEQ ID NO:61]		
DNA	Caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcttctggaggcac cttcagcagctatgctatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggaaggatcatccctatccttggt acagcaaactacgcacagaagttccagggcagagtcacgattaccgcggacgaatccacgagcacagcctacatggagctga gcagcctgagatctgaggacacggccgtgtattactgtgcgcgctctggttacggttcttaccgttgggaagattcttggggtcaag gtactctggtgaccgtctcctca [SEQ ID NO:63]		
Full V_L	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVFWYQQLPGTAPKLLIYSNNQRP SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSASYVFGTGTKVTVL G [SEQ ID NO:62]		
DNA	Caggctgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagctccaac atcggaagtaattacgtattctggtaccagcagctcccaggaacggccccaaactcctcatctatagtaataatcagcggccctc aggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtgggctccggtccgaggatgaggct gattattactgtgcagcatgggatgacagcctgagtgccttatgttttcggaactgggaccaaggtcaccgtcctaggt [SEQ ID NO:64]		
scFv	QAVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVFWYQQLPGTAPKLLIYSNNQRP SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSASYVFGTGTKVTVL GSRGGGGSGGGGSGGGGSLEMAQVQLVQSGAEVKKPGSSVKVSCKASGGTFSS YAISWVRQAPGQGLEWMGRIIPILGTANYAQKFQGRVTITADESTSTAYMELSSL RSEDTAVYYCARSGYGSYRWEDSWGQGTLVTVSS [SEQ ID NO:87]		

In certain embodiments, the antibody or other antigen binding protein is an anti-BCMA scFv or an antigen-binding fragment thereof having an antigen-binding region that comprises the amino acid sequence of SEQ ID NO:88 and specifically binds to a BCMA polypeptide (e.g., a BCMA polypeptide having the amino acid sequence SEQ ID NO:71, or fragments thereof), which is designated as ET140-174 (also referred to as "ET140-24").

In certain embodiments, the anti-BCMA scFv antibody 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, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, the anti-BCMA scFv antibody is a scFv-Fc fusion protein or full length human IgG with V_H and V_L regions or CDRs selected from Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:65, as shown in Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:66, as shown in Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_H comprising amino acids having the sequence set forth in SEQ ID NO:65 and a V_L comprising amino acids having the sequence set forth in SEQ ID NO:66, as shown in Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:185 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187 or conservative modifications thereof, as shown in Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190 or conservative modifications thereof, as shown in Table 17. In certain embodiments, the anti-BCMA scFv comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190 or conservative modifications

thereof, as shown in Table 17. In certain embodiments, the extracellular antigen-binding domain comprises a V_H CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190.

Table 17

Antigen	A BCMA polypeptide having the amino acid sequence of SEQ ID NO:71		
CDRs	1	2	3
V_H	GYSFTSYW [SEQ ID NO: 185]	IYPGDSDT [SEQ ID NO: 186]	ARYSGSFDN [SEQ ID NO: 187]
V_L	SSNIGSHS [SEQ ID NO: 188]	TNN [SEQ ID NO: 189]	AAWDGSLNGLV [SEQ ID NO: 190]
Full V_H	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYP GDSDTRYSPSFQGHVTISADKSISTAYLQWSSLKASDTAMYYCARYSGSFDNWG QGTLVTVSS [SEQ ID NO:65]		
DNA	Gaggtgcagctggtgcagtctggagcagaggtgaaaaagcccggggagtctctgaagatcctcctgtaagggttctggataca gctttaccagctactggatcggctgggtgcgccagatgcccgggaaaggcctggagtggatggggatcatctatcctggtgact ctgataccagatacagcccgtccttccaaggccacgtcaccatctcagctgacaagtccatcagcactgcctacctgcagtgga gcagcctgaaggcctcggacaccgccatgtattactgtgcgcgctactctggttctttcgataactggggtcaaggtactctggtg accgtctcctca [SEQ ID NO:67]		
Full V_L	SYELTQPPSASGTPGQRVTMSCSGTSSNIGSHSVNWYQQLPGTAPKLLIYTNNQR PSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDGSLNGLVFGGGTKLTV LG [SEQ ID NO:66]		
DNA	Tcctatgagctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatgtcttgttctggaaccagctccaa catcggaagtcactctgtaaactggtaccagcagctcccaggaacggcccccaaactcctcatctatactaataatcagcggcc ctcaggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtggcctccagtctgaggatga ggctgattattactgtgcagcatgggatggcagcctgaatggtctggtattcggcggagggaccaagctgaccgtcctaggt [SEQ ID NO:68]		
scFv	SYELTQPPSASGTPGQRVTMSCSGTSSNIGSHSVNWYQQLPGTAPKLLIYTNNQR PSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDGSLNGLVFGGGTKLTV LGSRGGGGSGGGGSGGGGSLEMAEVQLVQSGAEVKKPGESLKISCKGSGYSFTS YWIGWVRQMPGKGLEWMGIIYPGDSDTRYSPSFQGHVTISADKSISTAYLQWSS LKASDTAMYYCARYSGSFDNWGQGTLVTVSS [SEQ ID NO:88]		

The presently disclosed subject matter further provides anti-BCMA scFv antibodies comprising a heavy chain variable region, a light chain variable region, a linker peptide between the heavy chain variable region and the light chain variable region, and an His-tag and an HA-tag. In certain embodiments, the amino acid sequence of the His-tag and HA-tag comprises the amino acid sequence of SEQ ID NO:246,which is provided below:

TSGQAGQHHHHHHGAYPYDVPDYAS [SEQ ID NO: 246]

The nucloetide sequence encoding SEQ ID NO: 246 is SEQ ID NO: 247, which is provided below:

ACTAGTGGCCAGGCCGGCCAGCACCATCACCATCACCATGGCG CATACCCGTACGACGTTCCGGACTACGCTTCT [SEQ ID NO: 247]

2. Monoclonal Antibodies

The presently disclosed subject matter provides human antibodies (e.g., human monoclonal antibodies) that specifically bind to BCMA (*e.g.*, human BCMA) and were isolated and structurally characterized as described in Example 2. The V_H amino acid sequences of human anti-BCMA antibodies ET140-192 (also referred to as "ET140-42"), ET140-197 (also referred to as "ET140-47"), ET140-180 (also referred to as "ET140-30"), ET140-172 (also referred to as "ET140-22"), ET140-157 (also referred to as "ET140-7"), ET140-153 (also referred to as "ET140-3"), ET140-201 (also referred to as "ET140-51"), ET140-167 (also referred to as "ET140-17"), ET140-163 (also referred to as "ET140-13"), ET140-207 (also referred to as "ET140-57"), ET140-165 (also referred to as "ET140-15"), ET140-188 (also referred to as "ET140-38"), ET140-196 (also referred to as "ET140-46"), ET140-204 (also referred to as "ET140-54"), ET140-190 (also referred to as "ET140-40"), ET140-187 (also referred to as "ET140-37"), and ET140-174 (also referred to as "ET140-24") are shown in SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65, respectively. The V_L amino acid sequences of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, and 66, respectively.

Given that each of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies can bind to BCMA, the V_H and V_L sequences can be "mixed and matched" to create other anti-BCMA binding molecules. BCMA binding of such "mixed and matched" antibodies can be tested using the binding assays known in the art, including for example, ELISAs, Western blots, RIAs, Biacore analysis. Preferably, when V_H and V_L chains are mixed and matched, a V_H sequence from a particular V_H/V_L pairing is replaced with a structurally similar V_H sequence. Likewise, a V_L

sequence from a particular V_H/V_L pairing is replaced with a structurally similar V_L sequence.

In certain embodiments, the presently disclosed subject matter provides an isolated antibody, or antigen-binding portion thereof comprising: (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 (b) 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; wherein the antibody specifically binds BCMA, e.g., human BCMA.

Preferred heavy and light chain combinations include:

(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; or

(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 embodiments, the presently disclosed subject matter provides antibodies that comprise the heavy chain and light chain CDR1s, CDR2s and CDR3s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-

201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies. The amino acid sequences of the V_H CDR1s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 89, 95, 101, 107, 113, 119, 125, 131, 137, 143, 149, 155, 161, 167, 173, 179, and 185, respectively. The amino acid sequences of the V_H CDR2s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies are shown in SEQ ID NOs: 90, 96, 102, 108, 114, 120, 126, 132, 138, 144, 150, 156, 162, 168, 174, 180, and 186, respectively. The amino acid sequences of the V_H CDR3s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 91, 97, 103, 109, 115, 121, 127, 133, 139, 145, 151, 157, 163, 169, 175, 181, and 187, respectively.

The amino acid sequences of the V_L CDR1s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 92, 98, 104, 110, 116, 122, 128, 134, 140, 146, 152, 158, 164, 170, 176, 182, and 188, respectively. The amino acid sequences of the V_L CDR2s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 93, 99, 105, 111, 117, 123, 129, 135, 141, 147, 153, 159, 165, 171, 177, 183, and 189, respectively. The amino acid sequences of the V_L CDR3s of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 are shown in SEQ ID NOs: 94, 100, 106, 112, 118, 124, 130, 136, 142, 148, 154, 160, 166, 172, 178, 184, and 190, respectively. The CDR regions are delineated using the Kabat system (Kabat, E.

A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242).

Given that each of these antibodies can bind to BCMA and that antigen-binding specificity is provided primarily by the CDR1, CDR2, and CDR3 regions, the V_H CDR1, CDR2, and CDR3 sequences and V_L CDR1, CDR2, and CDR3 sequences can be "mixed and matched" (i.e., CDRs from different antibodies can be mixed and match, although each antibody must contain a V_H CDR1, CDR2, and CDR3 and a V_L CDR1, CDR2, and CDR3) to create other anti-BCMA binding molecules. BCMA binding of such "mixed and matched" antibodies can be tested using the binding assays described above. When V_H CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular V_H sequence is replaced with a structurally similar CDR sequence(s). Likewise, when V_L CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular V_L sequence preferably is replaced with a structurally similar CDR sequence(s). It will be readily apparent to the ordinarily skilled artisan that novel V_H and V_L sequences can be created by substituting one or more V_H and/or V_L CDR region sequences with structurally similar sequences from the CDR sequences of the antibodies disclosed herein ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174.

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

(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;

wherein the antibody specifically binds BCMA, e.g., human BCMA.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 89;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 90;

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

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 92;

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

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 94.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 95;

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

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

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 98;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 99; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 100.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 101;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 102;

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

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 104;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 105; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 106.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 107;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 108;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 109;

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

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 111; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 112.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 113;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 114;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 115;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 116;

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

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 118.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 119;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 120;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 121;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 122;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 123; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 124.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 125;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 126;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 127;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 128;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 129; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 130.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 131;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 132;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 133;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 134;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 135; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 136.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 137;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 138;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 139;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 140;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 141; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 142.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 143;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 144;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 145;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 146;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 147; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 148.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 149;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 150;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 151;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 152;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 153; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 154.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 155;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 156;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 157;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 158;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 159; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 160.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 161;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 162;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 163;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 164;

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

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 166.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 167;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 168;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 169;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 170;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 171; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 172.

In certain embodiments, the antibody comprises:

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

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 174;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 175;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 176;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 177; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 178.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 179;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 180;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 181;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 182;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 183; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 184.

In certain embodiments, the antibody comprises:

(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 185;

(b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 186;

(c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 187;

(d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO: 188;

(e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO: 189; and

(f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 190.

The constant region/framework region of the anti-BCMA antibodies disclosed herein can be altered, for example, by amino acid substitution, to modify the properties of the antibody (e.g., to increase or decrease one or more of: antigen binding affinity, Fc receptor binding, antibody carbohydrate, for example, glycosylation, fucosylation etc, the number of cysteine residues, effector cell function, effector cell function, complement function or introduction of a conjugation site).

In certain embodiments, a presently disclosed anti-BCMA antibody is a fully-human antibody, e.g., any one of ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174. Fully-human mAbs are preferred for therapeutic use in humans because murine antibodies cause an immunogenicity reaction, known as the HAMA (human anti-mouse antibodies) response (Azinovic I, et al. Survival benefit associated with human anti-mouse antibody (HAMA) in patients with B-cell malignancies. Cancer Immunol Immunother 2006; 55(12):1451-8; Tjandra JJ, et al. Development of human anti-murine antibody (HAMA) response in patients. Immunol Cell Biol 1990; 68(6):367-76), when administered to humans, causing serious side effects, including anaphylaxis and hypersensitivity reactions. This immunogenicity reaction is triggered by the human immune system recognizing the murine antibodies as foreign because of slightly different amino acid sequences from natural human antibodies. Humanization methods known in the art (Riechmann L, et al. Reshaping human antibodies for therapy. Nature 1988; 332 (6162): 332:323; Queen C, et al. A humanized antibody that binds to the interleukin 2 receptor. Proc Natl Acad Sci USA 1989; 86 (24): 10029-33) can be employed to reduce the immunogenicity of murine-derived antibodies (Gerd R, et al. Serological Analysis of Human Anti-Human Antibody Responses in Colon Cancer Patients Treated with Repeated Doses of Humanized Monoclonal Antibody A33. Cancer Res 2001; 61, 6851–6859).

The use of phage display libraries has made it possible to select large numbers of Ab repertoires for unique and rare Abs against very defined epitopes (for

more details on phage display see McCafferty et al., Phage antibodies: filamentous phage displaying antibody variable domains. Nature, 348: 552-554.) The rapid identification of human Fab or single chain Fv (scFV) fragments highly specific for tumor antigen-derived peptide-MHC complex molecules has thus become possible (19-22). Recently, immuno-toxins, generated by fusing TCR-like Fab specific for melanoma Ag MART-1 26-35/A2 or gp100 280-288/A2 to a truncated form of Pseudomonas endotoxin, have been shown to inhibit human melanoma growth both in vitro and in vivo (Klechevsky E, et al. Antitumor activity of immunotoxins with T-cell receptor-like specificity against human melanoma xenografts. Cancer Res 2008; 68 (15): 6360- 6367). In addition, by engineering full-length mAb using the Fab fragments, it is possible to directly generate a therapeutic human mAb, bypassing months of time-consuming work, normally needed for developing therapeutic mAbs. The presently disclosed subject matter involves the development of a fully human mAb that recognizes, for example, a human BCMA polypeptide (e.g., a polypeptide having the amino acid sequence set forth in SEQ ID NO:71) for cancer therapy.

3. Homologous Antibodies

In certain embodiments, an antibody of the presently disclosed subject matter comprises heavy and light chain variable regions comprising amino acid sequences that are homologous to the amino acid sequences of the antibodies described herein (e.g., ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies), and wherein the antibodies retain the desired functional properties of the anti-BMCA antibodies of the presently disclosed subject matter.

For example, the presently disclosed subject matter provides an isolated antibody, or antigen-binding portion thereof, comprising a heavy chain variable region and a light chain variable region, wherein:

(a) the heavy chain variable region comprises 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, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, and 65;

(b) the light chain variable region comprises 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: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, and 66; and

wherein the antibody binds to human BCMA with a K_D of 1 x 10^{-7} M or less.

In certain embodiments, the V_H and/or V_L amino acid sequences can be 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 sequences set forth above. An antibody having V_H and V_L regions having high (i.e., 80% or greater) homology to the V_H and V_L regions of the sequences set forth above, can be obtained by mutagenesis (e.g., site-directed or PCR-mediated mutagenesis), followed by testing of the encoded altered antibody for retained function (i.e., the binding affinity) using the binding assays described herein.

As used herein, the percent homology between two amino acid sequences is equivalent to the percent identity between the two sequences. The percent identity or homology between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology = # of identical positions/total # of positions x 100), taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm, as described in the non-limiting examples below.

The percent homology between two amino acid sequences can be determined using the algorithm of E. Meyers and W. Miller (Comput. Appl. Biosci., 4:11-17 (1988)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. In addition, the percent homology between two amino acid sequences can be determined using the Needleman and Wunsch (J. Mol. Biol. 48:444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250

matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6.

Additionally or alternatively, the protein sequences of the presently disclosed subject matter can further be used as a "query sequence" to perform a search against public databases to, for example, identify related sequences. Such searches can be performed using the XBLAST program (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to the antibody molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. (See www.ncbi.nlm.nih.gov).

4. Antibodies with Conservative Modifications

In certain embodiments, an antibody of the presently disclosed subject matter comprises a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences and a light chain variable region comprising CDR1, CDR2 and CDR3 sequences, wherein one or more of these CDR sequences comprise specified amino acid sequences based on the preferred antibodies described herein (e.g., ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies), or conservative modifications thereof, and wherein the antibodies retain the desired functional properties of the anti-BCMA antibodies of the presently disclosed subject matter. The presently disclosed subject matter provides an isolated antibody, or antigen-binding portion thereof, comprising a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences and a light chain variable region comprising CDR1, CDR2, and CDR3 sequences, wherein:

(a) the heavy chain variable region CDR3 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequences of SEQ ID NOs: 91, 97, 103, 109, 115, 121, 127, 133, 139, 145, 151, 157, 163, 169, 175, 181, and 187, and conservative modifications thereof;

(b) the light chain variable region CDR3 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequence of SEQ ID NOs: 94, 100, 106, 112, 118, 124, 130, 136, 142, 148, 154, 160, 166, 172, 178, 184, and 190, and conservative modifications thereof; and the antibody binds to human BCMA with a K_D of 1 x 10^{-7} M or less.

In certain embodiments, the heavy chain variable region CDR2 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequences 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 the light chain variable region CDR2 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequences 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 embodiments, the heavy chain variable region CDR1 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequences 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 the light chain variable region CDR1 sequence comprises an amino acid sequence selected from the group consisting of amino acid sequences 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.

As used herein, the term "conservative sequence modifications" is intended to refer to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis.

Conservative amino acid substitutions are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. Exemplary conservative amino acid substitutions are shown in Table 18. Amino acid substitutions may be introduced into an antibody of interest and the products screened

for a desired activity, e.g., retained/improved antigen binding, decreased immunogenicity, or improved ADCC or CDC. In certain embodiments, a sequence disclosed herein, e.g., a CDR sequence, a VH sequence or a VL sequence, can have up to about one, up to about two, up to about three, up to about four, up to about five, up to about six, up to about seven, up to about eight, up to about nine or up to about ten amino acid residues that are modified and/or substituted.

Table 18

Original Residue	**Exemplary conservative amino acid Substitutions**
Ala (A)	Val; Leu; Ile
Arg (R)	Lys; Gln; Asn
Asn (N)	Gln; His; Asp, Lys; Arg
Asp (D)	Glu; Asn
Cys (C)	Ser; Ala
Gln (Q)	Asn; Glu
Glu (E)	Asp; Gln
Gly (G)	Ala
His (H)	Asn; Gln; Lys; Arg
Ile (I)	Leu; Val; Met; Ala; Phe
Leu (L)	Ile; Val; Met; Ala; Phe
Lys (K)	Arg; Gln; Asn
Met (M)	Leu; Phe; Ile
Phe (F)	Trp; Leu; Val; Ile; Ala; Tyr
Pro (P)	Ala
Ser (S)	Thr
Thr (T)	Val; Ser
Trp (W)	Tyr; Phe
Tyr (Y)	Trp; Phe; Thr; Ser
Val (V)	Ile; Leu; Met; Phe; Ala

Amino acids may be grouped according to common side-chain properties:

- hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;
- neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
- acidic: Asp, Glu;

- basic: His, Lys, Arg;
- residues that influence chain orientation: Gly, Pro;
- aromatic: Trp, Tyr, Phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class.

5. Anti-BCMA Antibodies that Cross-compete for Binding to BCMA with Anti-BCMA Antibodies of the Invention

The presently disclosed subject matter provides antibodies that cross-compete with any of the disclosed anti-BCMA antibodies for binding to BCMA (e.g., human BCMA). For example, and not by way of limitation, the cross-competing antibodies can bind to the same epitope region, e.g., same epitope, adjacent epitope, or overlapping as any of the anti-BCMA antibodies of the presently disclosed subject matter. In certain embodiments, the reference antibody for cross-competition studies can be any one of the anti-BCMA antibodies disclosed herein, e.g., ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies.

In certain embodiments, the cross-competing antibody binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71. In certain embodiments, the cross-competing antibody binds to one, two, three, four, five, six, or seven epitope region selected from the group consisting of amino acids 8-22, 9-23, 10-24, 11-25, 12-26, 13-27, 14-28, and 8-28 of SEQ ID NO: 71.

Such cross-competing antibodies can be identified based on their ability to cross-compete with any one of the presently disclosed anti-BCMA antibodies in standard BCMA binding assays. For example, Biacore analysis, ELISA assays or flow cytometry can be used to demonstrate cross-competition with the antibodies of the presently disclosed subject matter. The ability of a test antibody to inhibit the binding of, for example, any one of the presently disclosed anti-BMCA antibodies (e.g., ET140-192, ET140-197, ET140-180, ET140-172, ET140-157, ET140-153, ET140-201, ET140-167, ET140-163, ET140-207, ET140-165, ET140-188, ET140-196, ET140-204, ET140-190, ET140-187, and ET140-174 antibodies) to human BCMA demonstrates that the test antibody can compete with any one of the presently disclosed anti-BCMA antibodies for binding to human BCMA and thus binds to the

same epitope region on human BCMA as any one of the presently disclosed anti-BCMA antibodies. In certain embodiments, the cross-competing antibody binds to the same epitope on human BCMA as any one of the presently disclosed anti-BCMA antibodies.

6. Characterization of Antibody Binding to Antigen

Antibodies of the presently disclosed subject can be tested for binding to BCMA by, for example, standard ELISA. To determine if the selected anti-BCMA antibodies bind to unique epitopes, each antibody can be biotinylated using commercially available reagents (Pierce, Rockford, IL). Competition studies using unlabeled monoclonal antibodies and biotinylated monoclonal antibodies can be performed using BCMA coated-ELISA plates as described above. Biotinylated mAb binding can be detected with a strep-avidin-alkaline phosphatase probe.

To determine the isotype of purified antibodies, isotype ELISAs can be performed using reagents specific for antibodies of a particular isotype. Anti-BCMA human IgGs can be further tested for reactivity with BCMA antigen by Western blotting.

In certain embodiments, K_D is measured by a radiolabeled antigen binding assay (RIA). In certain embodiments, an RIA is performed with the Fab version of an antibody of interest and its antigen. For example, solution binding affinity of Fabs for antigen is measured by equilibrating Fab with a minimal concentration of (^{125}I)-labeled antigen in the presence of a titration series of unlabeled antigen, then capturing bound antigen with an anti-Fab antibody-coated plate (see, e.g., Chen et al., *J. Mol. Biol.* 293:865-881(1999)).

In certain embodiments, K_D is measured using a BIACORE® surface plasmon resonance assay. For example, an assay using a BIACORE®-2000 or a BIACORE®-3000 (BIAcore, Inc., Piscataway, NJ)

Epitope Mapping

In certain embodiments, a presently disclosed anti-BCMA antibody binds to a human BCMA polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 71. In certain embodiments, a presently disclosed anti-BCMA antibody binds to one or more portion of the amino acid sequence set forth in SEQ ID NO: 71. In certain embodiments, a presently disclosed anti-BCMA antibody binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71. In certain embodiments, a

presently disclosed anti-BCMA antibody binds to one, two, three, four, five, six, or seven epitope region selected from the group consisting of amino acids 8-22, 9-23, 10-24, 11-25, 12-26, 13-27, 14-28, and 8-28 of SEQ ID NO: 71. In certain embodiments, a presently disclosed anti-BCMA antibody that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71 comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:9 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:10, 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 embodiments, the linker comprises amino acids having the sequence set forth in SEQ ID NO:69. In certain embodiments, a presently disclosed anti-BCMA antibody that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71 comprises a V_H comprising an amino acid sequence that is at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homologous to the amino acid sequence set forth in SEQ ID NO:21. In certain embodiments, a presently disclosed anti-BCMA antibody 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. In certain embodiments, a presently disclosed anti-BCMA antibody that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71 comprises a V_L comprising an amino acid sequence that is at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homologous to the amino acid sequence set forth in SEQ ID NO:22. In certain embodiments, a presently disclosed anti-BCMA antibody that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71 comprises a V_L comprising amino acids having the sequence set forth in SEQ ID NO:22. In certain embodiments, a presently disclosed anti-BCMA antibody 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 embodiments, a presently disclosed anti-BCMA antibody 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 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:120 or conservative modifications thereof, and a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:121 or conservative modifications thereof. In certain embodiments, a presently disclosed anti-BCMA antibody that binds to an epitope region comprising amino acids 14-22 of SEQ ID NO: 71 comprises a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:124 or conservative modifications thereof. In certain embodiments, a presently disclosed anti-BCMA antibody 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 or conservative modifications thereof, a V_H CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:120 or conservative modifications thereof, a V_H CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:121 or conservative modifications thereof, a V_L CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:122 or conservative modifications thereof, a V_L CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:123 or conservative modifications thereof, and a V_L CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:124 or conservative modifications thereof. In certain embodiments, a presently disclosed anti-BCMA antibody 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 certain embodiments, a presently disclosed anti-BCMA antibody is ET140-3 (or "ET140-153").

7. Immunoconjugates

The presently disclosed subject provides an anti-BCMA antibody, or a fragment thereof, conjugated to a therapeutic moiety, such as a cytotoxin, a drug (e.g., an immunosuppressant) or a radiotoxin. Such conjugates are referred to herein as "immunoconjugates". Immunoconjugates that include one or more cytotoxins are referred to as "immunotoxins." A cytotoxin or cytotoxic agent includes any agent that is detrimental to (e.g., kills) cells. Examples include taxol (such as ricin, diphtheria, gelonin), cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents also include, for example, calecheamicin, aureastatin, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

Other examples of therapeutic cytotoxins that can be conjugated to an anti-BCMA antibody disclosed herein include duocarmycins, calicheamicins, maytansines and auristatins, and derivatives thereof. An example of a calicheamicin antibody conjugate is commercially available (Mylotarg™; Wyeth-Ayerst).

Cytotoxins can be conjugated to anti-BCMA antibody disclosed herein using linker technology available in the art. Examples of linker types that have been used to conjugate a cytotoxin to an antibody include, but are not limited to, hydrazones, thioethers, esters, disulfides and peptide-containing linkers. A linker can be chosen that is, for example, susceptible to cleavage by low pH within the lysosomal compartment or susceptible to cleavage by proteases, such as proteases preferentially expressed in tumor tissue such as cathepsins (e.g., cathepsins B, C, D). For further discussion of types of cytotoxins, linkers and methods for conjugating therapeutic agents to antibodies, see also Saito, G. et al. (2003) Adv. Drug Deliv. Rev. 55:199-215; Trail, P.A. et al. (2003) Cancer Immunol. Immunother. 52:328-337;

Payne, G. (2003) Cancer Cell 3:207-212; Allen, T.M. (2002) Nat. Rev. Cancer 2:750-763; Pastan, I. and Kreitman, R. J. (2002) Curr. Opin. Investig. Drugs 3:1089-1091; Senter, P.D. and Springer, C.J. (2001) Adv. Drug Deliv. Rev. 53:247-264.

Anti-BCMA antibodies of the presently disclosed subject matter also can be conjugated to a radioactive isotope to generate cytotoxic radiopharmaceuticals, also referred to as radioimmunoconjugates. Examples of radioactive isotopes that can be conjugated to antibodies for use diagnostically or therapeutically include, but are not limited to, ^{90}Y, ^{131}I, ^{225}Ac, ^{213}Bi, ^{223}Ra and ^{227}Th. Methods for preparing radioimmunconjugates are established in the art. Examples of radioimmunoconjugates are commercially available, including Zevalin™ (IDEC Pharmaceuticals) and Bexxar™ (Corixa Pharmaceuticals), and similar methods can be used to prepare radioimmunoconjugates using the antibodies of the invention.

The antibody conjugates of the presently disclosed subject matter can be used to modify a given biological response, and the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, an enzymatically active toxin, or active fragment thereof, such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor (TNF) or interferon-γ; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, e.g., Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And

Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev., 62:119-58 (1982).

8. Bispecific Molecules

The presently disclosed subject matter provides bispecific molecules comprising an anti-BCMA antibody, or a fragment thereof, disclosed herein. An antibody of the presently disclosed subject matter, or antigen-binding portions thereof, can be derivatized or linked to another functional molecule, e.g., another peptide or protein (e.g., another antibody or ligand for a receptor) to generate a bispecific molecule that binds to at least two different binding sites or target molecules. The antibody of the presently disclosed subject matter can in fact be derivatized or linked to more than one other functional molecule to generate multispecific molecules that bind to more than two different binding sites and/or target molecules; such multispecific molecules are also intended to be encompassed by the term "bispecific molecule" as used herein. To create a bispecific molecule, a presently disclosed anti-BCMA antibody can be functionally linked (e.g., by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other binding molecules, such as another antibody, antibody fragment, peptide or binding mimetic, such that a bispecific molecule results.

The presently disclosed subject matter provides bispecific molecules comprising at least a first binding specificity for BCMA and a second binding specificity for a second target epitope. The second target epitope can be a BCMA epitope, or a non-BCMA epitope, e.g., a different antigen. In certain embodiments, the bispecific molecule is multispecific, the molecule can further include a third binding specificity. Where a first portion of a bispecific antibody binds to an antigen on a tumor cell for example and a second portion of a bispecific antibody recognizes an antigen on the surface of a human immune effector cell, the antibody is capable of recruiting the activity of that effector cell by specifically binding to the effector antigen on the human immune effector cell. In certain embodiments, bispecific antibodies, therefore, are able to form a link between effector cells, for example, T cells and tumor cells, thereby enhancing effector function. In certain embodiments, a bispecific antibody of the present disclosure comprises at least a first binding to BCMA and at least a second binding to an immune cell. For example, and not by way of limitation, a bispecific antibody of the present disclosure comprises at least a first

binding to BCMA and at least a second binding to a receptor present on the surface of an immune cell, e.g., CD3.

The bispecific molecules of the presently disclosed subject matter can be prepared by conjugating the constituent binding specificities using methods known in the art. For example, each binding specificity of the bispecific molecule can be generated separately and then conjugated to one another. When the binding specificities are proteins or peptides, a variety of coupling or cross-linking agents can be used for covalent conjugation. Examples of cross-linking agents include protein A, carbodiimide, N-succinimidyl-S-acetyl-thioacetate (SATA), 5, 5'-dithiobis(2-nitrobenzoic acid) (DTNB), o-phenylenedimaleimide (oPDM), N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), and sulfosuccinimidyl 4-(N-maleimidomethyl) cyclohaxane-1-carboxylate (sulfo-SMCC) (see e.g., Karpovsky et al. (1984) J. Exp. Med. 160:1686; Liu, MA et al. (1985) Proc. Natl. Acad. Sci. USA 82:8648). Other methods include those described in Paulus (1985) Behring Ins. Mitt. No. 78, 118-132; Brennan et al. (1985) Science 229:81-83), and Glennie et al. (1987) J. Immunol. 139: 2367-2375). Preferred conjugating agents are SATA and sulfo-SMCC, both available from Pierce Chemical Co. (Rockford, IL).

When the binding specificities are antibodies, they can be conjugated via sulfhydryl bonding of the C-terminus hinge regions of the two heavy chains. In certain embodiments, the hinge region is modified to contain an odd number of sulfhydryl residues, preferably one, prior to conjugation.

Alternatively, both binding specificities can be encoded in the same vector and expressed and assembled in the same host cell. This method is particularly useful where the bispecific molecule is a mAb x mAb, mAb x Fab, Fab x $F(ab')_2$ or ligand x Fab fusion protein.

Binding of the bispecific molecules to their specific targets can be confirmed by, for example, enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), FACS analysis, bioassay (e.g., growth inhibition), or Western Blot assay. Each of these assays generally detects the presence of protein-antibody complexes of particular interest by employing a labeled reagent (e.g., an antibody) specific for the complex of interest. Alternatively, the complexes can be detected using any of a variety of other immunoassays. For example, the antibody can be radioactively labeled and used in a radioimmunoassay (RIA) (see, for example,

Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986, which is incorporated by reference herein). The radioactive isotope can be detected by such means as the use of a γ counter or a scintillation counter or by autoradiography.

9. Selecting a high affinity ScFv against a BCMA polypeptide

The next step is to the selection of phage that bind to the target antigen of interest with high affinity, from phage in a human phage display library that either does not bind or that binds with lower affinity. This is accomplished by iterative binding of phage to the antigen, which is bound to a solid support, for example, beads or mammalian cells followed by removal of non-bound phage and by elution of specifically bound phage. In certain embodiments, antigens are first biotinylated for immobilization to, for example, streptavidin-conjugated Dynabeads M-280. The phage library is incubated with the cells, beads or other solid support and non binding phage is removed by washing. Clones that bind are selected and tested.

Once selected, positive scFv clones are tested for their binding to BCMA (human BCMA) on live 3T3 cell surfaces by flow cytometry. Briefly, phage clones are incubated with 3T3 cells over-expressing BCMA. The cells are washed and then with a mouse anti-M13 coat protein mAb. Cells are washed again and labeled with a FITC-goat anti-mouse Ig prior to flow cytometry.

In other embodiments, the anti-BCMA antibodies can comprise one or more framework region amino acid substitutions designed to improve protein stability, antibody binding, expression levels or to introduce a site for conjugation of therapeutic agents. These scFv are then used to produce recombinant human monoclonal Igs in accordance with methods known to those of skill in the art.

10. Engineering full length mAb using the selected ScFv fragments

Phage display technology allows for the rapid selection and production of antigen-specific scFv and Fab fragments, which are useful in and of themselves, or which can be further developed to provide complete antibodies, antigen binding proteins or antigen binding fragments thereof. Complete mAbs with Fc domains have a number of advantages over the scFv and Fab antibodies. First, only full length Abs exert immunological function such as CDC and ADCC mediated via Fc domain. Second, bivalent mAbs offer stronger antigen-binding affinity than monomeric Fab Abs. Third, plasma half-life and renal clearance will be different with the Fab and

bivalent mAb. The particular features and advantages of each can be matched to the planned effector strategy. Fourth, bivalent mAb may be internalized at different rates tha scFv and Fab, altering immune function or carrier function. Alpha emitters, for example, do not need to be internalized to kill the targets, but many drugs and toxins will benefit from internalization of the immune complex. In certain embodiments, therefore, once scFv clones specific for BCMA were obtained from phage display libraries, a full length IgG mAb using the scFv fragments was produced.

To produce recombinant human monoclonal IgG in Chinese hamster ovary (CHO) cells, a full length IgG mAb can be engineered based on a method known to those of skill in the art (Tomomatsu et al., Production of human monoclonal antibodies against FceRIa by a method combining in vitro immunization with phage display. Biosci Biotechnol Biochem 73(7): 1465-1469 2009). Briefly, antibody variable regions can be subcloned into mammalian expression vectors, with matching Lambda or Kappa light chain constant sequences and IgG1 subclass Fc (for example) (Lidija P, et al. An integrated vector system for the eukaryotic expression of antibodies or their fragments after selection from phage display libraries. Gene 1997; 187(1): 9-18; Lisa JH, et al. Crystallographic structure of an intact lgG1 monoclonal antibody. Journal of Molecular Biology 1998; 275 (5): 861-872). Kinetic binding analysis (Yasmina NA, et al. Probing the binding mechanism and affinity of tanezumab, a recombinant humanized anti-NGF monoclonal antibody, using a repertoire of biosensors. Protein Science 2008; 17(8): 1326-1335) can be used to confirm specific binding of full length IgG to BCMA, with a K_D in nanomolar range.

Pharmaceutical Compositions and Methods of Treatment

Anti-BCMA antibodies of the presently disclosed subject matter can be administered for therapeutic treatments to a patient suffering from a tumor (e.g., multiple myeloma) in an amount sufficient to prevent, inhibit, or reduce the progression of the tumor. Progression includes, e.g., the growth, invasiveness, metastases and/or recurrence of the tumor. Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's own immune system. Dosing schedules will also vary with the disease state and status of the patient, and will typically range from a single bolus dosage or continuous infusion to multiple administrations per day (e.g., every 4-6 hours), or as indicated by the treating physician and the patient's condition.

The identification of medical conditions treatable by anti-BCMA antibodies of the presently disclosed subject matter is well within the ability and knowledge of one skilled in the art. For example, human individuals who are either suffering from multiple myeloma or who are at risk of developing multiple myeloma are suitable for administration of the presently disclosed anti-BCMA antibodies. A clinician skilled in the art can readily determine, for example, by the use of clinical tests, physical examination and medical/family history, if an individual is a candidate for such treatment.

In certain embodiments, the presently disclosed subject matter provides a method of treating a tumor by administering a presently disclosed anti-BCMA antibody in combination with one or more other agents. For example, the presently disclosed subject matter provides a method of treating a tumor by administering a presently disclosed anti-BCMA antibody with an antineoplastic agent. The anti-BCMA antibody can be chemically or biosynthetically linked to one or more of the antineoplastic agents.

Non-limiting examples of suitable tumors include multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, and Waldenstrom's Macroglobulinemia. In certain embodiments, the tumor is multiple myeloma.

Any suitable method or route can be used to administer a presently disclosed anti-BCMA antibody, and optionally, to co-administer antineoplastic agents. Routes of administration include, for example, oral, intravenous, intraperitoneal, subcutaneous, or intramuscular administration. It should be emphasized, however, that the presently disclosed subject matter is not limited to any particular method or route of administration.

It is noted that presently disclosed anti-BCMA antibody can be administered as a conjugate, which binds specifically to the receptor and delivers a toxic, lethal payload following ligand-toxin internalization.

It is understood that anti-BCMA antibodies of the presently disclosed subject matter can be administered in the form of a composition additionally comprising a pharmaceutically acceptable carrier. Suitable pharmaceutically acceptable carriers include, for example, one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations

thereof. Pharmaceutically acceptable carriers may further comprise minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives or buffers, which enhance the shelf life or effectiveness of the binding proteins. The compositions of the injection can, as is well known in the art, be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the mammal.

The presently disclosed subject matter also provides use of antibodies and nucleic acids that encode them for treatment of a tumor (e.g., multiple myeloma), for diagnostic and prognostic applications as well as use as research tools for the detection of BCMA in cells and tissues. Pharmaceutical compositions comprising the disclosed antibodies and nucleic acids are encompassed by the presently disclosed subject matter. Vectors comprising the nucleic acids of the presently disclosed subject matter for antibody-based treatment by vectored immunotherapy are also contemplated by the presently disclosed subject matter. Vectors include expression vectors which enable the expression and secretion of antibodies, as well as vectors which are directed to cell surface expression of the antigen binding proteins, such as chimeric antigen receptors.

Cells comprising the nucleic acids, for example cells that have been transfected with the vectors of the invention are also encompassed by the presently disclosed subject matter.

Kits

The presently disclosed subject matter provides kits for the treatment or prevention of a tumor (e.g., multiple myeloma). In certain embodiments, the kit comprises a therapeutic composition containing an effective amount of an anti-BCMA antibody in unit dosage form. In some embodiments, the kit comprises a sterile container which contains a therapeutic or prophylactic vaccine; such containers can be boxes, ampules, bottles, vials, tubes, bags, pouches, blister-packs, or other suitable container forms known in the art. Such containers can be made of plastic, glass, laminated paper, metal foil, or other materials suitable for holding medicaments.

If desired, the anti-BCMA antibody is provided together with instructions for administering the cell to a subject having or at risk of developing a tumor (e.g., multiple myeloma). The instructions will generally include information about the use

of the composition for the treatment or prevention of a tumor (e.g., multiple myeloma). In other embodiments, the instructions include at least one of the following: description of the therapeutic agent; dosage schedule and administration for treatment or prevention of a neoplasia (e.g., multiple myeloma) or symptoms thereof; precautions; warnings; indications; counter-indications; overdosage information; adverse reactions; animal pharmacology; clinical studies; and/or references. The instructions may be printed directly on the container (when present), or as a label applied to the container, or as a separate sheet, pamphlet, card, or folder supplied in or with the container.

Methods

Flow cytometry analysis. For cell surface staining, cells can be incubated with appropriate mAbs for 30 minutes on ice, washed, and incubated with secondary antibody reagents when necessary. Flow cytometry data can be collected on a FACS Calibur (Becton Dickinson) and analyzed with FlowJo V8.7.1 and 9.4.8 software.

Selection and characterization of scFv specific for BCMA. A human scFv antibody phage display library is used for the selection of mAb clones. In brief, biotinylated antigens can be first mixed with the huma scFv phage library, then the antigen-scFv antibody complexes can be pulled down by streptavidin-conjugated Dynabeads M-280 through a magnetic rack. Bound clones can be then eluted and used to infect *E.Coli* XL1 -Blue. The scFv phage clones expressed in the bacteria can be purified (Yasmina NA, et al. Probing the binding mechanism and affinity of tanezumab, a recombinant humanized anti-NGF monoclonal antibody, using a repertoire of biosensors. Protein Science 2008; 17(8): 1326-1335; Roberts WK, et al. Vaccination with CD20 peptides induces a biologically active, specific immune response in mice. Blood 2002: 99 (10): 3748-3755). Panning can be performed for 3-4 cycles to enrich scFv phage clones binding to BCMA specifically. Positive clones can be determined by standard ELISA method against biotinylated single chain BCMA. Positive clones can be further tested for their binding to BCMA on live cell surfaces by flow cytometry, using a $BCMA^+$ cell line, 3T3. The cells can be washed, and the staining can be performed in following steps.

The cells can be first stained with purified scFv phage clones, and followed by staining with a mouse anti-M13 mAb, and finally the goat anti-mouse

Ig's conjugate to FITC. Each step of the staining can be done between 30-60 minutes on ice and the cells were washed twice between each step of the staining.

Engineering full length mAb using the selected ScFv fragments. Full-length human IgG1 of the selected phage clones can be produced in HEK293 and Chinese hamster ovary (CHO) cell lines, as described (Caron PC, Class K, Laird W, Co MS, Queen C, Scheinberg DA. Engineered humanized dimeric forms of IgG are more effective antibodies. J Exp Med 176:1 191 -1 195. 1992). In brief, antibody variable regions can be subcloned into mammalian expression vectors, with matching human lambda or kappa light chain constant region and human lgG constant region sequences. Molecular weight of the purified full length IgG antibodies can be measured under both reducing and non-reducing conditions by electrophoresis.

Characterization of the full-length human IgG for BCMA. Initially, specificities of the fully human IgG mAbs for the BMCA can be determined by staining 3T3 cells transduced to overexpress BCMA, followed by secondary goat anti-human IgG mAb conjugate to PE or FITC. The fluorescence intensity can be measured by flow cytometry. The same method can be used to determine the binding of the mAbs to fresh tumor cells and cell lines.

Antibody-dependent cellular cytotoxicity (ADCC). Target cells used for ADCC can be 3T3 cells over-expressing BCMA. Anti-BCMA antibody or its control human IgG at various concentrations can be incubated with target cells and fresh PBMCs at different effector:target (E:T) ratio for 16 hrs. The supernatant can be harvested and the cytotoxicity can be measured by LDH release assay using Cytotox 96 nonradioactive kit from Promega following their instruction. Cytotoxicity can also be measured by standard 4 hours 51 Cr-release assay.

EXAMPLES

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the antibodies, bispecific antibodies, compositions comprising thereof, screening, and therapeutic methods of the presently disclosed subject matter, and are not intended to limit the scope of what the inventors regard as their presently disclosed subject matter. It is understood that various other embodiments may be practiced, given the general description provided above.

Example 1 –BCMA Expression in various tissues

The Expression of human BCMA was evaluated in various malignant and normal tissues by investigating gene expression profiles in databases such as the cancer cell line encyclopedia and BioGPS. As shown in Figure 1, human BCMA was highly expressed in lymphoma and multiple myeloma, but not in other malignant tissues. Normal expression appeared limited to B-cells and plasma cells. Potential BCMA targeted CAR T cell eradication of these normal cell types may not have significant adverse effects based on inventors' patient experience with CD19 targeted CAR T cells. Any lack of physiologic antibody production can be addressed with intravenous immunoglobulin treatment.

Example 2 – Selection of scFv specific for BCMA using a fully human phage display library.

Phage display against BCMA was performed for 3 panning rounds to enrich the scFv phage clones binding to BCMA specifically. Independent pannings with 12 different phage libraries were carried out against BCMA overexpressing 3T3 cells identifying 186 clones. Individual scFv phage clones positive for the BCMA were determined by ELISA and the clones that possessed unique DNA coding sequences were subjected to further characterization. To test if the scFv bound to BCMA on live cells, the positive phage clones were tested for binding to a BCMA-positive cell line, 3T3. After sequencing, 57 unique and BCMA-Fc positive clones were found out of 79 sequenced positive clones; the unique clone rate was 72%. FACS analysis of phage antibody clones against BCMA-3T3 and parental 3T3 cell lines resulted in confirming 25 unique positive clones.

Example 3 – Screening Data for Anti-BCMA Antibodies

ELISA Screening: Figure 6 shows the representative results of protein ELISA screening against BCMA antigen using specific scFv phage antibody clones (ET140-3, ET140-24, ET140-37, ET140-40 and ET140-54). ELISA plates were coated with human BCMA ECD-Fc fusion protein, control-Fc fusion protein, or PBS alone as blank control, respectively. Individual phage clones from enriched phage display panning pools against BCMA ECD-Fc fusion protein were incubated in the coated plates. Binding of the phage clones was detected by HRP-conjugated anti-M13 antibodies and developed using TMB substrate. The absorbance was read at 450nm.

FACS Screening: Figure 7 shows a representative figure of a FACS analysis of the BCMA-specific phage antibody clones ET140-3, ET140-24, ET140-37, ET140-40 and ET140-54. Phage clones were incubated with 3T3-BCMA cell line, then with anti-M13 mouse antibody. Finally APC-labeled anti-mouse IgG 2nd antibody was added to the reaction after washing again. The binding was measured by FACS and expressed as mean fluorescence intensity (MFI). Cells incubated with 2nd antibody alone, M13 K07 helper phage and cells only were used as negative controls.

Example 4 — Epitope mapping of Anti-BCMA Antibodies

BCMA peptides were ordered based on the ECD sequence with N-terminal Biotin + SGSG linker + 15 amino acids with 1 amino acid space. The peptide library is shown in Table 19.

Table 19

ET140-p1	SGSGLQMAGQCSQNEYFDS [SEQ ID NO: 207]	ET140-p21	SGSGIPCQLRCSSNTPPLT [SEQ ID NO: 227]
ET140-p2	SGSGQMAGQCSQNEYFDSL [SEQ ID NO: 208]	ET140-p22	SGSGPCQLRCSSNTPPLTC [SEQ ID NO: 228]
ET140-p3	SGSGMAGQCSQNEYFDSLL [SEQ ID NO: 209]	ET140-p23	SGSGCQLRCSSNTPPLTCQ [SEQ ID NO: 229]
ET140-p4	SGSGAGQCSQNEYFDSLLH [SEQ ID NO: 210]	ET140-p24	SGSGQLRCSSNTPPLTCQR [SEQ ID NO: 230]
ET140-p5	SGSGGQCSQNEYFDSLLHA [SEQ ID NO: 211]	ET140-p25	SGSGLRCSSNTPPLTCQRY [SEQ ID NO: 231]
ET140-p6	SGSGQCSQNEYFDSLLHAC [SEQ ID NO: 212]	ET140-p26	SGSGRCSSNTPPLTCQRYC [SEQ ID NO: 232]
ET140-p7	SGSGCSQNEYFDSLLHACI [SEQ ID NO: 213]	ET140-p27	SGSGCSSNTPPLTCQRYCN [SEQ ID NO: 233]
ET140-p8	SGSGSQNEYFDSLLHACIP [SEQ ID NO: 214]	ET140-p28	SGSGSSNTPPLTCQRYCNA [SEQ ID NO: 234]
ET140-p9	SGSGQNEYFDSLLHACIPC [SEQ ID NO: 215]	ET140-p29	SGSGSNTPPLTCQRYCNAS [SEQ ID NO: 235]
ET140-p10	SGSGNEYFDSLLHACIPCQ [SEQ ID NO: 216]	ET140-p30	SGSGNTPPLTCQRYCNASV [SEQ ID NO: 236]
ET140-p11	SGSGEYFDSLLHACIPCQL [SEQ ID NO: 217]	ET140-p31	SGSGTPPLTCQRYCNASVT [SEQ ID NO: 237]
ET140-p12	SGSGYFDSLLHACIPCQLR [SEQ ID NO: 218]	ET140-p32	SGSGPPLTCQRYCNASVTN [SEQ ID NO: 238]
ET140-p13	SGSGFDSLLHACIPCQLRC [SEQ ID NO: 219]	ET140-p33	SGSGPLTCQRYCNASVTNS [SEQ ID NO: 239]
ET140-p14	SGSGDSLLHACIPCQLRCS [SEQ ID NO: 220]	ET140-p34	SGSGLTCQRYCNASVTNSV [SEQ ID NO: 240]
ET140-p15	SGSGSLLHACIPCQLRCSS [SEQ ID NO: 221]	ET140-p35	SGSGTCQRYCNASVTNSVK [SEQ ID NO: 241]
ET140-p16	SGSGLLHACIPCQLRCSSN [SEQ ID NO: 222]	ET140-p36	SGSGCQRYCNASVTNSVKG [SEQ ID NO: 242]
ET140-p17	SGSGLHACIPCQLRCSSNT [SEQ ID NO: 223]	ET140-p37	SGSGQRYCNASVTNSVKGT [SEQ ID NO: 243]
ET140-p18	SGSGHACIPCQLRCSSNTP [SEQ ID NO: 224]	ET140-p38	SGSGRYCNASVTNSVKGTN [SEQ ID NO: 244]
ET140-p19	SGSGACIPCQLRCSSNTPP [SEQ ID NO: 225]	ET140-p39	SGSGYCNASVTNSVKGTNA [SEQ ID NO: 245]
ET140-p20	SGSGCIPCQLRCSSNTPPL [SEQ ID NO: 226]		

The peptides were coated onto Streptavidin plates at 2 ug/mL in PBST (PBS+ 0.05% Tween-20). After washing and blocking with 3% BSA. After washing, 1 ug/mL ET140-3, ET140-24, ET140-54 or ET901 mIgG1 was added to the wells, respectively. "mIgG1" used in all Examples represents that the variable region is fully human and the Fc part is mouse IgG1. Then HRP anti-mouse IgG detection antibody was added to each well. Finally, the color was developed using TMB substrate. A450 was recorded for data analysis. The results are shown in Figures 2-5. As shown in Figures 2 and 5, ET140-3 bound to peptidese 7-13 (i.e., amino acids 8-22, 9-23, 10-24, 11-25, 12-26, 13-27, and 14-28) of SEQ ID NO:71. As shown in Figures 3 and 4, no linear epitopes found for ET140-24 or ET140-54.

Summary: 3 ET140 antibodies (mIgG1) were tested together with isotype control ET901 mIgG1 for their binding epitope towards BCMA-ECD. A peptide library consisting of 39 peptides (N-terminal biotin+ SGSG linker+ 15 amino acids, with 1 amino acid offset) was used for epitope mapping ELISA. This allows to search for the linear binding epitope of BCMA-ECD. ET901 mIgG1 was used as background reference for each peptide. Only ET140-3 can be identified for its epitope region: a region comprising amino acids 14-22 of SEQ ID NO:71, e.g., amino acids 8-28 of SEQ ID NO: 71.

ET140-24 and ET140-54 did not show any significant binding towards peptide library. This indicated that these two antibodies may recognize conformational epitope rather than linear epitope of BCMA.

Example 5 – Anti-BCMA Antibodies recombinant antigen by Surface Plasmon Resonance

Kinetics of interaction between ET140-153 mIgG1 (or "ET140-3 mIgG1"), ET140-174 mIgG1 (or "ET140-24 mIgG1"), ET140-204 mIgG1 (or "ET140-54 mIgG1") and BCMA recombinant antigen was measured using a BIAcore X100 instrument. In brief, 50 μg/mL of modified streptavidin was immobilized onto a Sensor Chip CAP by flowing the Biotin CAPture Reagent through the flow cells at 2 μL/min for 5 minutes. 10 ug/mL biotinylated BCMA-Fc protein was loaded onto the flow cell at a rate of 30 μL/min for 3 minutes. Following the standard protocol for kinetics, a series of injection of ESK1 was performed between 0.6 and 15 μg/mL, each step consisting of a 3 minute injection at 30 μL/min and 3 minute disassociation. Afterwards, the surface was regenerated for 2 minutes with a solution consisting of 75%v/v of 8M guanidine-HCl and 25%v/v 1M NaOH. Kinetic constants were derived by the global fitting (1:1 Langmuir binding model) using BIAcore X100 Evaluation Software (Version 2.0.1). The binding affinity data are shown in Table 20.

Table 20

Protein	KD
ET140-24 mIgG1	KD: 4.8 nM (BiaCore)
ET140-54 mIgG1	KD: 8.1 nM (BiaCore)
ET140-3 mIgG1	KD: 1.2nM (BiaCore)

Although the foregoing presently disclosed subject matter has been described in some detail by way of illustration and example for purposes of clarity of understanding, the descriptions and examples should not be construed as limiting the scope of the presently disclosed subject matter. The disclosures of all patent and scientific literature cited herein are expressly incorporated in their entirety by reference.

WHAT IS CLAIMED IS:

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

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

3. The anti-BCMA antibody or antigen-binding fragment thereof of claim 1 or claim 2, wherein the heavy chain variable region comprises an amino acid sequence that has at least 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 90% sequence identity to the sequence set forth in SEQ ID NO:54.

4. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-3, 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.

5. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-4, 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).

6. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-5, comprising a linker positioned between the heavy chain variable region and the light chain variable

region.

7. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antigen-binding fragment thereof is a single chain variable fragment (scFv).

8. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-7, comprising the amino acid sequence set forth in SEQ ID NO:85.

9. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antibody comprises a human variable region framework region.

10. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-9, which is a fully human or an antigen-binding fragment thereof.

11. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-9, which is a chimeric antibody or an antigen-binding fragment thereof.

12. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-9, which is a humanized antibody or an antigen-binding fragment thereof.

13. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antigen-binding fragment is a human single chain variable fragment (scFv).

14. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-6 and 8-12, wherein the antigen-binding fragment is an antigen-binding fragment (Fab).

15. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-6 and 8-12, wherein the antigen-binding fragment is a $F(ab')_2$.

16. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 5-15, 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.

17. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-16, wherein the antibody or antigen-binding fragment binds to B cell maturation antigen (BCMA) with a dissociation constant (K_d) of from 1×10^{-9} M to 1×10^{-6} M.

18. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-17, wherein the antibody or antigen-binding fragment binds to B cell maturation antigen (BCMA) with a dissociation constant (K_D) of from 1×10^{-9} M to 1×10^{-8} M.

19. The anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment binds to a non-linear epitope of BCMA.

20. A composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19, and a pharmaceutically acceptable carrier.

21. An immunoconjugate comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19, linked to a therapeutic agent.

22. The immunoconjugate of claim 21, wherein the therapeutic agent is a drug, a cytotoxin, or a radioactive isotope.

23. A composition comprising the immunoconjugate of claim 21 or 22, and a pharmaceutically acceptable carrier.

24. A bispecific molecule comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19, linked to a second functional moiety.

25. The bispecific molecule of claim 24, wherein the second functional moiety has a different binding specificity than the antibody or antigen binding fragment thereof.

26. The bispecific molecule of claim 24 or claim 25, wherein the second functional moiety has a binding specificity for an immune cell.

27. The bispecific molecule of any one of claims 24-26, wherein the second functional moiety has a binding specificity for CD3.

28. A composition comprising the bispecific molecule of any one of claims 24-27, and a pharmaceutically acceptable carrier.

29. A nucleic acid molecule that encodes an anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19.

30. An expression vector comprising the nucleic acid molecule of claim 29.

31. A host cell comprising the expression vector of claim 30.

32. 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 1-19, 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.

33. Use of a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19 for the manufacture of a medicament for treating a tumor in a subject.

34. The use of claim 33, wherein the medicament reduces the number of the tumor cells.

35. The use of claim 33 or claim 34, wherein the medicament reduces the tumor size.

36. The use of any one of claims 33-35, wherein the medicament eradicates the tumor in the subject.

37. The use of any one of claims 33-36, 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.

38. The use of any one of claims 33-37, wherein the tumor is multiple myeloma.

39. The use of any one of claims 33-38, wherein the subject is a human.

40. A kit for treating a tumor, comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19.

41. The kit of claim 40, wherein the kit comprises written instructions for using the antibody or antigen-binding fragment thereof for treating a subject having a tumor.

42. The kit of claim 40 or claim 41, wherein the tumor is multiple myeloma.

43. The composition comprising the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-19 for use as a therapy.