

mantle cell lymphoma, Hodgkin's Lymphoma (HL), plasma cell myeloma, precursor B cell lymphoblastic leukemia/lymphoma, plasmacytoma, giant cell myeloma, plasma cell myeloma, heavy-chain myeloma, light chain or Bence-Jones myeloma, lymphomatoid granulomatosis, post-transplant lymphoproliferative disorder, an immunoregulatory disorder, rheumatoid arthritis, myasthenia gravis, idiopathic thrombocytopenia purpura, anti-phospholipid syndrome, Chagas' disease, Grave's disease, Wegener's granulomatosis, poly-arteritis nodosa, Sjogren's syndrome, pemphigus vulgaris, scleroderma, multiple sclerosis, anti-phospholipid syndrome, ANCA associated vasculitis, Goodpasture's disease, Kawasaki disease, autoimmune hemolytic anemia, and rapidly progressive glomerulonephritis, heavy-chain disease, primary or immunocyte-associated amyloidosis, and monoclonal gammopathy of undetermined significance.

[0069a] The present disclosure provides a use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment as described herein in the manufacture of a medicament for treating a subject having a disease associated with BCMA over-expression or a BCMA-positive cancer.

[0069b] The present disclosure provides a use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment as described herein in the manufacture of a medicament for treating a subject having a BCMA-positive cancer, wherein the BCMA-positive cancer comprises a B-cell leukemia, B-cell lymphoma or B-cell myeloma.

[0069c] The present disclosure provides use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment as described herein in the manufacture of a medicament for treating a subject having a disease associated with BCMA expression, wherein the disease associated with BCMA expression is a multiple myeloma (MM), non-Hodgkin's lymphoma (NHL) including Burkitt's lymphoma (BL), B chronic lymphocytic leukemia (B-CLL), systemic lupus erythematosus (SLE), B and T acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), diffuse large B cell lymphoma, chronic myelogenous leukemia (CML), hairy cell leukemia (HCL), follicular lymphoma, Waldenstrom's Macroglobulinemia, mantle cell lymphoma, Hodgkin's Lymphoma (HL), plasma cell myeloma, precursor B cell lymphoblastic leukemia/lymphoma, plasmacytoma, giant cell myeloma, plasma cell myeloma, heavy-chain myeloma, light chain or Bence-Jones myeloma, lymphomatoid granulomatosis, post-transplant lymphoproliferative disorder, an

immunoregulatory disorder, rheumatoid arthritis, myasthenia gravis, idiopathic thrombocytopenia purpura, anti-phospholipid syndrome, Chagas' disease, Grave's disease, Wegener's granulomatosis, poly-arteritis nodosa, Sjogren's syndrome, pemphigus vulgaris, scleroderma, multiple sclerosis, anti-phospholipid syndrome, ANCA associated vasculitis, Goodpasture's disease, Kawasaki disease, autoimmune hemolytic anemia, and rapidly progressive glomerulonephritis, heavy-chain disease, primary or immunocyte-associated amyloidosis, or monoclonal gammopathy of undetermined significance.

[0069d] The present disclosure provides a composition comprising the antibody or antigen-binding fragment as described herein use in therapy.

DESCRIPTION OF THE DRAWINGS

- [0070]** **Figure 1** shows an SPR sensorgram of binding kinetics of BCA7 antibody.
- [0071]** **Figure 2** shows an SPR sensorgram of binding kinetics of GSK J6M0 antibody.
- [0072]** **Figure 3** shows an SPR sensorgram of binding kinetics of BC4C9 antibody.
- [0073]** **Figure 4** shows an SPR sensorgram of binding kinetics of BC5C5 antibody.
- [0074]** **Figure 5** shows an SPR sensorgram of binding kinetics of BCA7-2C5 antibody.
- [0075]** **Figure 6** shows an SPR sensorgram of binding kinetics of BCA7-2D11 antibody.
- [0076]** **Figure 7** shows an SPR sensorgram of binding kinetics of BCA7-2G2 antibody.
- [0077]** **Figure 8** shows an SPR sensorgram of binding kinetics of BCA7-2E1 antibody.
- [0078]** **Figure 9** shows an SPR sensorgram of binding kinetics of BCA7-2D8 antibody.
- [0079]** **Figure 10** shows an SPR sensorgram of binding kinetics of BCA7-2E81 antibody.
- [0080]** **Figure 11A** shows an SPR sensorgram of binding kinetics of BCA7-2C5 antibody to human BCMA protein.
- [0081]** **Figure 11B** shows an SPR sensorgram of binding kinetics of BCA7-2E1 antibody to human BCMA protein.
- [0082]** **Figure 12A** shows an SPR sensorgram of binding kinetics of BCA7-2C5 antibody to cynomolgus BCMA protein.
- [0083]** **Figure 12B** shows an SPR sensorgram of binding kinetics of BCA7-2E1 antibody to cynomolgus BCMA protein.

WHAT IS CLAIMED:

1. A fully human anti-BCMA antibody, or an antigen-binding fragment thereof, comprising a heavy chain and a light chain,
wherein **(a)** the heavy chain comprises: a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO:29, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:30, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:31; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:32, a light chain CDR2 having the amino acid sequence of SEQ ID NO:33, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:34;
wherein **(b)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:35, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:36, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:37; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:38, a light chain CDR2 having the amino acid sequence of SEQ ID NO:39, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:40;
wherein **(c)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:41, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:42, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:43; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:44, a light chain CDR2 having the amino acid sequence of SEQ ID NO:45, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:46;
wherein **(d)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:47, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:48, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:49; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:50, a light chain CDR2 having the amino acid sequence of SEQ ID NO:51, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:52;
wherein **(e)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:53, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:54, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:55;

and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:56, a light chain CDR2 having the amino acid sequence of SEQ ID NO:57, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:58;

wherein **(f)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:59, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:60, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:61; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:62, a light chain CDR2 having the amino acid sequence of SEQ ID NO:63, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:64;

wherein **(g)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:65, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:66, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:67; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:68, a light chain CDR2 having the amino acid sequence of SEQ ID NO:69, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:70;

wherein **(h)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:71, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:72, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:73; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:74, a light chain CDR2 having the amino acid sequence of SEQ ID NO:75, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:76;

wherein **(i)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:77, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:78, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:79; and the light chain comprises: a light chain CDR1 having the amino acid sequence of SEQ ID NO:80, a light chain CDR2 having the amino acid sequence of SEQ ID NO:81, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:82;

wherein **(j)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:83, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:84, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:85; and the light chain comprises: a light chain CDR1 having the amino acid sequence of

SEQ ID NO:86, a light chain CDR2 having the amino acid sequence of SEQ ID NO:87, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:88; or wherein **(k)** the heavy chain comprises: a heavy chain CDR1 having the amino acid sequence of SEQ ID NO:53, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:54, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:55; and the light chain comprises: a lambda light chain CDR1 having the amino acid sequence of SEQ ID NO:89, a lambda light chain CDR2 having the amino acid sequence of SEQ ID NO:90, and a lambda light chain CDR3 having the amino acid sequence of SEQ ID NO:91.

2. A fully human anti-BCMA antibody, or antigen-binding fragment thereof, comprising a heavy chain and a light chain, the heavy chain variable region having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8, 10, 12, 14 or 22, and the light chain variable region having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 9, 11, 13, 15, 16, 17, 18, 19, 20, 21 or 23.
3. A fully human anti-BCMA antibody, or the 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 comprise the amino acid sequences of SEQ ID NOS:8 and 9 (herein called BCA7); SEQ ID NOS:10 and 11 (herein called BC4C9); SEQ ID NOS:12 and 13 (herein called CD5C4); SEQ ID NOS:14 and 15 (herein called BC6G8); SEQ ID NOS:8 and 16 (herein called BCA7-2C5); SEQ ID NOS:8 and 17 (herein called BCA7-2E1); SEQ ID NOS:8 and 18 (herein called BCA7-2D11); SEQ ID NOS:8 and 19 (herein called BCA7-2G2); SEQ ID NOS:8 and 20 (herein called BCA7-2D8); SEQ ID NOS:8 and 21 (herein called BCA7-2E8); or SEQ ID NOS:22 and 23 (herein called BCA7-2C5 full length).
4. The antigen-binding fragment of claim 2, comprising a Fab fragment having a variable domain region from a heavy chain and a variable domain region from a light chain, wherein the variable domain region from the heavy chain comprises a sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8, 10, 12, 14 or

- 22, and wherein the variable domain region from the light chain comprises a sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 9, 11, 13, 15, 16, 17, 18, 19, 20, 21 or 23.
5. The antigen-binding fragment of claim 2, comprising a single chain antibody comprising a variable domain region from a heavy chain and a variable domain region from a light chain joined together with a peptide linker, wherein the variable domain region from the heavy chain comprises a sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8, 10, 12, 14 or 22, and wherein the variable domain region from the light chain comprises a sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 9, 11, 13, 15, 16, 17, 18, 19, 20, 21 or 23.
 6. The fully human anti-BCMA antibody of claim 2 or 3, comprising an IgG1, IgG2, IgG3 or IgG4 class antibody.
 7. The antibody or antigen-binding fragment of any one of the preceding claims, that blocks binding between APRIL (**A** **P**roliferation-**I**nducing **L**igand; also known as TNF13 and CD256) protein and BCMA protein.
 8. The antibody or antigen-binding fragment of any one of the preceding claims, that binds to BCMA proteins from human, cynomolgus and mouse.
 9. The antibody or antigen-binding fragment of any one of the preceding claims, that binds to cells expressing BCMA protein.
 10. The antibody or antigen-binding fragment of any one of the preceding claims, that binds to human myeloma cells expressing BCMA protein.
 11. A pharmaceutical composition, comprising the antibody or antigen-binding fragment of any one of the preceding claims and a pharmaceutically-acceptable excipient.
 12. A first nucleic acid encoding a first polypeptide comprising the antibody heavy chain variable region of claim 2, wherein the amino acid sequence of the antibody heavy chain

variable region has at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8, 10, 12, 14 or 22, and a second nucleic acid encoding a second polypeptide comprising the antibody light chain variable region of claim 2, wherein the amino acid sequence of the antibody light chain variable region has at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 9, 11, 13, 15, 16, 17, 18, 19, 20, 21 or 23.

13. One or more nucleic acids encoding the antibody or antigen-binding fragment of any one of claims 1-10.
14. One or more expression vectors comprising one or more promoters operably linked to the first and second nucleic acids of claim 12.
15. One or more expression vectors comprising one or more promoters operably linked to the one or more nucleic acids of claim 13.
16. A host cell harboring the one or more expression vectors of claim 13 or 15.
17. A method for preparing the first polypeptide comprising the antibody heavy chain variable region and the second polypeptide comprising the antibody light chain variable region or the antibody or antigen-binding fragment, the method comprising: culturing a population (a plurality) of the host cell of claim 16 under conditions suitable for expressing the first polypeptide and the second polypeptide or the antibody or antigen-binding fragment.
18. The method of claim 17, further comprising: recovering from the population of the host cell of claim 16 the expressed first polypeptide and the expressed second polypeptide or the expressed antibody or antigen-binding fragment.
19. An *in vitro* method for killing BCMA-expressing cells, comprising: contacting (i) a population of effector cells with (ii) a population of target cells which express BCMA (iii) in the presence of the antibody or antigen-binding fragment of any one of claims 1-10, under conditions that are suitable for killing the BCMA-expressing cells.

20. Use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment of any one of claims 1-10 in the manufacture of a medicament for treating a subject having a disease associated with BCMA over-expression or a BCMA-positive cancer.
21. Use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment of any one of claims 1-10 in the manufacture of a medicament for treating a subject having a BCMA-positive cancer, wherein the BCMA-positive cancer comprises a B-cell leukemia, B-cell lymphoma or B-cell myeloma.
22. Use of an effective amount of a therapeutic composition comprising the antibody or antigen-binding fragment of any one of claims 1-10 in the manufacture of a medicament for treating a subject having a disease associated with BCMA expression, wherein the disease associated with BCMA expression is a multiple myeloma (MM), non-Hodgkin's lymphoma (NHL) including Burkitt's lymphoma (BL), B chronic lymphocytic leukemia (B-CLL), systemic lupus erythematosus (SLE), B and T acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), diffuse large B cell lymphoma, chronic myelogenous leukemia (CML), hairy cell leukemia (HCL), follicular lymphoma, Waldenstrom's Macroglobulinemia, mantle cell lymphoma, Hodgkin's Lymphoma (HL), plasma cell myeloma, precursor B cell lymphoblastic leukemia/lymphoma, plasmacytoma, giant cell myeloma, plasma cell myeloma, heavy-chain myeloma, light chain or Bence-Jones myeloma, lymphomatoid granulomatosis, post-transplant lymphoproliferative disorder, an immunoregulatory disorder, rheumatoid arthritis, myasthenia gravis, idiopathic thrombocytopenia purpura, anti-phospholipid syndrome, Chagas' disease, Grave's disease, Wegener's granulomatosis, poly-arteritis nodosa, Sjogren's syndrome, pemphigus vulgaris, scleroderma, multiple sclerosis, anti-phospholipid syndrome, ANCA associated vasculitis, Goodpasture's disease, Kawasaki disease, autoimmune hemolytic anemia, and rapidly progressive glomerulonephritis, heavy-chain disease, primary or immunocyte-associated amyloidosis, or monoclonal gammopathy of undetermined significance.

23. A composition comprising the antibody or antigen-binding fragment of any one of claims 1-10
for use in therapy.