

What is claimed is:

1. Use of a bispecific antibody in the manufacture of a medicament for treating a BCMA+ cancer in a subject in need thereof, wherein the bispecific antibody comprises a first antigen-binding domain that specifically binds a human B-cell maturation antigen (BCMA) on a target tumor cell, and a second antigen-binding domain that specifically binds human CD3, wherein the medicament is to be administered to the subject at a dose of at least 1 mg of the bispecific antibody weekly, and wherein:

the first antigen-binding domain comprises:

(a) three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 66; and

(b) three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:82; and

the second antigen-binding domain comprises:

(a) three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 90 or SEQ ID NO: 98; and

(b) three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:82.

2. The use of claim 1, wherein the BCMA+ cancer is multiple myeloma.

3. The use of claim 1 or 2, wherein the first antigen-binding domain comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO:68, a HCDR2 comprising the amino acid sequence of SEQ ID NO:70, and a HCDR3 comprising the amino acid sequence of SEQ ID NO:72.

4. The use of claim 3, wherein the first antigen-binding domain comprises a LCDR1 comprising the amino acid sequence of SEQ ID NO:84, a LCDR2 comprising the amino acid sequence of SEQ ID NO:86, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:88.

5. The use of any one of claims 1-4, wherein the first antigen-binding domain comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 66, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82.

6. The use of any one of claims 1-5, wherein the second antigen-binding domain comprises:

(a) a HCDR1 comprising the amino acid sequence of SEQ ID NO: 92 or SEQ ID NO: 100;

(b) a HCDR2 comprising the amino acid sequence of SEQ ID NO: 94 or SEQ ID NO: 102; and

(c) a HCDR3 comprising the amino acid sequence of SEQ ID NO: 96 or SEQ ID NO: 104.

7. The use of claim 6, wherein the second antigen-binding domain comprises a LCDR1 comprising the amino acid sequence of SEQ ID NO:84, a LCDR2 comprising the amino acid sequence of SEQ ID NO:86, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:88.

8. The use of claim 7, wherein the second antigen-binding domain comprises:

(a) HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 92, 94, 96; and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88; or

(b) HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 100, 102, 104; and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88.

9. The use of claim 8, wherein the second antigen-binding domain comprises:

(a) a HCVR comprising the amino acid sequence of SEQ ID NO: 90, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82; or

(b) a HCVR comprising the amino acid sequence of SEQ ID NO: 98, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82.

10. The use of claim 1 or 2, wherein the bispecific antibody comprises:

(a) a first antigen-binding domain that comprises HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88; and

(b) a second antigen binding domain that comprises HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 92, 94, 96, and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88.

11. The use of claim 1 or 2, wherein the bispecific antibody comprises:

(a) a first antigen-binding domain that comprises HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88; and

(b) a second antigen binding domain that comprises HCDR1, HCDR2, HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 100, 102, 104, and LCDR1, LCDR2, LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 84, 86, 88.

12. The use of claim 1 or 2, wherein the bispecific antibody comprises: a first antigen binding domain that comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 66, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82; and a second antigen binding domain that comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 90, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82.

13. The use of claim 1 or 2, wherein the bispecific antibody comprises: a first antigen binding domain that comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 66, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82; and a second antigen binding domain that comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 98, and a LCVR comprising the amino acid sequence of SEQ ID NO: 82.

14. The use of claim 1 or 2, wherein the bispecific antibody comprises a first heavy chain comprising the amino acid sequence of SEQ ID NO: 126, a second heavy chain

comprising the amino acid sequence of SEQ ID NO: 127, and a common light chain comprising the amino acid sequence of SEQ ID NO: 129.

15. The use of claim 1 or 2, wherein the bispecific antibody comprises a first heavy chain comprising the amino acid sequence of SEQ ID NO: 126, a second heavy chain comprising the amino acid sequence of SEQ ID NO: 128, and a common light chain comprising the amino acid sequence of SEQ ID NO: 129.

16. Use of a bispecific antibody in the manufacture of a medicament for treating multiple myeloma in a subject in need thereof, wherein the bispecific antibody comprises a first heavy chain and common light chain pair comprising a first antigen-binding domain that specifically binds a human B-cell maturation antigen (BCMA), and a second heavy chain and common light chain pair comprising a second antigen-binding domain that specifically binds human CD3, wherein the first antigen-binding domain comprises three heavy chain complementarity determining regions (CDRs) and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, 84, 86, and 88, respectively, the second antigen-binding domain comprises three heavy chain CDRs and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 92, 94, 96, 84, 86, and 88, respectively and wherein the medicament is to be administered to the subject at a dose of at least 1 mg of the bispecific antibody weekly.

17. The use of claim 16, wherein the first heavy chain comprises a first heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 66, the second heavy chain comprises a second heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 90, and the common light chain comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 82.

18. The use of claim 17, wherein the first heavy chain comprises the amino acid sequence of SEQ ID NO: 126, the second heavy chain comprises the amino acid sequence of SEQ ID NO: 127, and the common light chain comprises the amino acid sequence of SEQ ID NO: 129.

19. Use of a bispecific antibody in the manufacture of a medicament for treating multiple myeloma in a subject in need thereof, wherein the bispecific antibody comprises a first heavy chain and common light chain pair comprising a first antigen-binding domain that specifically binds a human B-cell maturation antigen (BCMA), and a second

heavy chain and common light chain pair comprising a second antigen-binding domain that specifically binds human CD3, wherein the first antigen-binding domain comprises three heavy chain complementarity determining regions (CDRs) and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, 84, 86, and 88, respectively, the second antigen-binding domain comprises three heavy chain CDRs and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 100, 102, 104, 84, 86, and 88, respectively and wherein the medicament is to be administered to the subject at a dose of at least 1 mg of the bispecific antibody weekly.

20. The use of claim 19, wherein the first heavy chain comprises a first heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 66, the second heavy chain comprises a second heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 98, and the common light chain comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 82.

21. The use of claim 20, wherein the first heavy chain comprises the amino acid sequence of SEQ ID NO: 126, the second heavy chain comprises the amino acid sequence of SEQ ID NO: 128, and the common light chain comprises the amino acid sequence of SEQ ID NO: 129.

22. The use of any one of claims 1-21, wherein the subject has been previously treated with an anti-CD38 antibody therapy, a proteasome inhibitor, or an immunomodulatory drug.

23. The use of any one of claims 2-22, wherein the subject has been diagnosed with a multiple myeloma immune subtype selected from immunoglobulin G, immunoglobulin A, lambda light chain, or kappa light chain, or the subject has an extramedullary plasmacytoma.

24. The use of any one of claims 2-22, wherein the multiple myeloma is relapsed or refractory multiple myeloma.

25. The use of any one of claims 1-24, wherein the subject is at least triple-refractory to prior therapies.

26. The use of claim 25, wherein the subject is quad-refractory or penta-refractory to prior therapies.

27. Use of a bispecific antibody in the manufacture of a medicament for use in a dosing regimen for treating multiple myeloma in a subject in need thereof, wherein the medicament is to be administered to the subject in a dosing regimen at an initial dose during week one of the dosing regimen, at a secondary dose during week two of the dosing regimen, and at a tertiary dose during week three of the dosing regimen, wherein the tertiary dose is equal to or greater than the secondary dose, and the secondary dose is greater than the initial dose,

wherein the bispecific antibody comprises:

a first heavy chain and common light chain pair comprising a first antigen-binding domain that specifically binds a human B-cell maturation antigen (BCMA), and a second heavy chain and common light chain pair comprising a second antigen-binding domain that specifically binds human CD3, wherein the first antigen-binding domain comprises three heavy chain complementarity determining regions (CDRs) and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, 84, 86, and 88, respectively, the second antigen-binding domain comprises three heavy chain CDRs and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 92, 94, 96, 84, 86, and 88, respectively.

28. Use of a bispecific antibody in the manufacture of a medicament for use in a dosing regimen for treating multiple myeloma in a subject in need thereof, wherein the medicament is to be administered to the subject in a dosing regimen at an initial dose during week one of the dosing regimen, at a secondary dose during week two of the dosing regimen, and at a tertiary dose during week three of the dosing regimen, wherein the tertiary dose is equal to or greater than the secondary dose, and the secondary dose is greater than the initial dose,

wherein the bispecific antibody comprises: a first heavy chain and common light chain pair comprising a first antigen-binding domain that specifically binds a human B-cell maturation antigen (BCMA), and a second heavy chain and common light chain pair comprising a second antigen-binding domain that specifically binds human CD3, wherein the first antigen-binding domain comprises three heavy chain complementarity determining regions (CDRs) and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 68, 70, 72, 84, 86, and 88, respectively, the second antigen-binding domain comprises three heavy chain CDRs and three light chain CDRs comprising the amino acid sequences of SEQ ID NOs: 100, 102, 104, 84, 86, and 88, respectively.

29. The use of any one of claims 1-28, wherein the medicament is to be administered to the subject in a dosing regimen comprising: (a) a single dose of 5 mg of the bispecific antibody to be administered during week one of the dosing regimen; (b) a single dose of 25 mg of the bispecific antibody to be administered during week two of the dosing regimen; and (c) a single dose of 50 mg to 200 mg of the bispecific antibody to be administered during week three of the dosing regimen.

30. The use of claim 29, wherein the medicament is to be administered to the subject in a dosing regimen comprising: (a) a single dose of 5 mg of the bispecific antibody to be administered during week one of the dosing regimen; (b) a single dose of 25 mg of the bispecific antibody to be administered during week two of the dosing regimen; and (c) a single dose of 200 mg of the bispecific antibody to be administered during week three of the dosing regimen.