

Claims

1. A stable aqueous pharmaceutical composition comprising:
 - a) a concentration of about 7.5 mg/mL to about 12.5 mg/mL of a bispecific B-cell mature antigen (BCMA)/cluster of differentiation 3 (CD3) antibody or antigen-binding fragment thereof, the bispecific BCMA/CD3 antibody or antigen-binding fragment thereof comprising:
 - (1) a first heavy chain (HC1) comprising a HC1 variable region 1 (VH1), wherein the VH1 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:1, 2, and 3, respectively;
 - (2) a first light chain (LC1) comprising a LC1 variable region (VL1), wherein the VL1 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively;
 - (3) a second heavy chain (HC2) comprising a HC2 variable region 2 (VH2), wherein the VH2 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:11, 12, and 13, respectively; and
 - (4) a second light chain (LC2) comprising a LC2 variable region 2 (VL2), wherein the VL2 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs:14, 15, and 16, respectively;
 - b) about 10 mM to about 20 mM of acetate and/or pharmaceutically acceptable acetate salt;
 - c) about 6% (w/v) to about 10% (w/v) of sucrose;
 - d) about 16 µg/mL to about 24 µg/mL of ethylenediaminetetraacetic acid (EDTA);
 - e) about 0.01% to about 0.07% polysorbate 20; and
 - f) a pH from about 4.7 to about 5.7.
2. A stable aqueous pharmaceutical composition comprising:

- a) a concentration of about 76.5 mg/mL to about 103.5 mg/mL of a bispecific B-cell mature antigen (BCMA)/cluster of differentiation 3 (CD3) antibody or antigen-binding fragment thereof, the bispecific BCMA/CD3 antibody or antigen-binding fragment thereof comprising:
- (1) a first heavy chain (HC1) comprising a HC1 variable region 1 (VH1), wherein the VH1 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:1, 2, and 3, respectively;
 - (2) a first light chain (LC1) comprising a LC1 variable region (VL1), wherein the VL1 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively;
 - (3) a second heavy chain (HC2) comprising a HC2 variable region 2 (VH2), wherein the VH2 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:11, 12, and 13, respectively; and
 - (4) a second light chain (LC2) comprising a LC2 variable region 2 (VL2), wherein the VL2 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs:14, 15, and 16, respectively;
- b) about 10 mM to about 20 mM of acetate and/or pharmaceutically acceptable acetate salt;
- c) about 6% (w/v) to about 10% (w/v) of sucrose;
- d) about 16 µg/mL to about 24 µg/mL of ethylenediaminetetraacetic acid (EDTA);
- e) about 0.01% to about 0.07% polysorbate 20; and
- f) a pH from about 4.7 to about 5.7.
3. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the bispecific BCMA/CD3 antibody comprises a VH1 having the amino acid sequence of SEQ ID NO:7, and a VL1 having the amino acid sequence of SEQ ID NO:8.

4. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the bispecific BCMA/CD3 antibody comprising a HC having the amino acid sequence of SEQ ID NO:9, and a LC1 having the amino acid sequence of SEQ ID NO:10.
5. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the bispecific BCMA/CD3 antibody comprises a VH2 having the amino acid sequence of SEQ ID NO:17, and a VL2 having the amino acid sequence of SEQ ID NO:18.
6. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the bispecific BCMA/CD3 antibody comprises a HC2 having the amino acid sequence of SEQ ID NO:19, and a LC2 having the amino acid sequence of SEQ ID NO:20.
7. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the bispecific BCMA/CD3 antibody is teclistamab.
8. The stable aqueous pharmaceutical composition of claim 1, wherein the bispecific BCMA/CD3 antibody has a concentration of about 8 mg/mL to about 12 mg/mL.
9. The stable aqueous pharmaceutical composition of claim 8, wherein the bispecific BCMA/CD3 antibody has a concentration of about 9 mg/mL to about 11 mg/mL.
10. The stable aqueous pharmaceutical composition of claim 9, wherein the bispecific BCMA/CD3 antibody has a concentration of about 10 mg/mL.
11. The stable aqueous pharmaceutical composition of claim 2, wherein the bispecific BCMA/CD3 antibody has a concentration of about 85 mg/mL to about 95 mg/mL.
12. The stable aqueous pharmaceutical composition of claim 11, wherein the bispecific BCMA/CD3 antibody has a concentration of about 87 mg/mL to about 93 mg/mL.

13. The stable aqueous pharmaceutical composition of claim 12, wherein the bispecific BCMA/CD3 antibody has a concentration of about 90 mg/mL.
14. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 12 mM to about 18 mM of acetate and/or pharmaceutically acceptable acetate salt.
15. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 14 mM to about 16 mM of acetate and/or pharmaceutically acceptable acetate salt.
16. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 15 mM of acetate and/or pharmaceutically acceptable acetate salt.
17. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 7% (w/v) to about 9% (w/v) of sucrose.
18. The stable aqueous pharmaceutical composition of claim 17, wherein the composition comprises about 8% (w/v) of sucrose.
19. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 18 µg/mL to about 22 µg/mL of EDTA.
20. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 20 µg/mL of EDTA.
21. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 0.02% to about 0.06% of PS-20.
22. The stable aqueous pharmaceutical composition of claim 21, wherein the composition comprises about 0.03 to about 0.05% of PS-20.

23. The stable aqueous pharmaceutical composition of claim 22, wherein the composition comprises about 0.04% of PS-20.
24. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the pH is about 4.8 to about 5.6.
25. The stable aqueous pharmaceutical composition of claim 23, wherein the pH is about 4.9 to about 5.5.
26. The stable aqueous pharmaceutical composition of claim 25, wherein the pH is about 5.2.
27. The stable aqueous pharmaceutical composition of claim 1, wherein the composition comprises 10 mg/mL of the bispecific BCMA/CD3 antibody, 15 mM of acetate and/or pharmaceutically acceptable acetate salt, 8% (w/v) sucrose, 20 µg/mL of EDTA, 0.04% PS 20, and a pH of 5.2.
28. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein the stable aqueous pharmaceutical composition is stable at a temperature of about 2-8°C for at least two years.
29. The stable aqueous pharmaceutical composition of claim 1 or 2, wherein stability is defined based on color of solution, pH, turbidity, percentage of purity, percentage of new peaks, percentage of main component, percentage of high molecular weight species (HWMS), percentage of low molecular weight species (LMWS), percentage of sum of acidic peaks, percentage of sum of basic peaks, protein concentration, percentage of T cell activation, percentage of PS 20 (w/v), or any combination thereof.
30. Use of the stable aqueous pharmaceutical composition of claim 1 or claim 2 for the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the bispecific BCMA/CD3 antibody is to be administered to a subject.

31. The use of claim 30, wherein the bispecific BCMA/CD3 antibody is to be subcutaneously administered.

32. A method for preparing a stable aqueous pharmaceutical composition of a bispecific B-cell mature antigen (BCMA)/cluster of differentiation 3 (CD3) antibody or antigen-binding fragment thereof, the bispecific BCMA/CD3 antibody or antigen-binding fragment thereof comprising:

- (1) a first heavy chain (HC1) comprising a HC1 variable region 1 (VH1), wherein the VH1 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:1, 2, and 3, respectively;
- (2) a first light chain (LC1) comprising a LC1 variable region (VL1), wherein the VL1 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively;
- (3) a second heavy chain (HC2) comprising a HC2 variable region 2 (VH2), wherein the VH2 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:11, 12, and 13, respectively; and
- (4) a second light chain (LC2) comprising a LC2 variable region 2 (VL2), wherein the VL2 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs:14, 15, and 16, respectively;

the method comprising combining a composition comprising about 10 mg/mL of the bispecific BCMA/CD3 antibody, about 15 mM of acetate and/or a pharmaceutically acceptable acetate salt, about 8% (w/v) sucrose, about 20 mg/mL of EDTA, and about 0.04% polysorbate (PS) 20, wherein the stable aqueous pharmaceutical composition has a pH of about 5.2.

33. A method for preparing a stable aqueous pharmaceutical composition of a bispecific B-cell mature antigen (BCMA)/cluster of differentiation 3 (CD3) antibody or antigen-binding fragment thereof, the bispecific BCMA/CD3 antibody or antigen-binding fragment thereof comprising:

- (1) a first heavy chain (HC1) comprising a HC1 variable region 1 (VH1), wherein the VH1 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:1, 2, and 3, respectively;
- (2) a first light chain (LC1) comprising a LC1 variable region (VL1), wherein the VL1 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively;
- (3) a second heavy chain (HC2) comprising a HC2 variable region 2 (VH2), wherein the VH2 comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3 having the amino acid sequences of SEQ ID NOs:11, 12, and 13, respectively; and
- (4) a second light chain (LC2) comprising a LC2 variable region 2 (VL2), wherein the VL2 comprises a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3 having the amino acid sequences of SEQ ID NOs:14, 15, and 16, respectively;

the method comprising combining a composition comprising about 90 mg/mL of the bispecific BCMA/CD3 antibody, about 15 mM of acetate and/or a pharmaceutically acceptable acetate salt, about 8% (w/v) sucrose, about 20 mg/mL of EDTA, and about 0.04% polysorbate (PS) 20, wherein the stable aqueous pharmaceutical composition has a pH of about 5.2.

34. The method of claim 32 or 33, wherein the bispecific BCMA/CD3 antibody comprises a VH1 having the amino acid sequence of SEQ ID NO:7, and a VL1 having the amino acid sequence of SEQ ID NO:8.

35. The method of claim 32 or 33, wherein the bispecific BCMA/CD3 antibody comprising a HC having the amino acid sequence of SEQ ID NO:9, and a LC1 having the amino acid sequence of SEQ ID NO:10.
36. The method of claim 32 or 33, wherein the bispecific BCMA/CD3 antibody comprises a VH2 having the amino acid sequence of SEQ ID NO:17, and a VL2 having the amino acid sequence of SEQ ID NO:18.
37. The method of claim 32 or 33, wherein the bispecific BCMA/CD3 antibody comprises a HC2 having the amino acid sequence of SEQ ID NO:19, and a LC2 having the amino acid sequence of SEQ ID NO:20.
38. The method of claim 32 or 33, wherein the bispecific BCMA/CD3 antibody is teclistamab.
39. A kit comprising the stable aqueous pharmaceutical composition of claim 1 or 2 and instructions for use.
40. An article of manufacture comprising a container holding the stable aqueous pharmaceutical composition of claim 1 or 2.
41. The article of manufacture of claim 40, wherein the container is a vial with a stopper pierceable by a syringe.
42. The stable aqueous pharmaceutical composition of claim 1 or 2 for use in the treatment of cancer.
43. The stable aqueous pharmaceutical composition of claim 1 or 2 for use in the preparation of a medicament for the treatment of cancer.

44. Use of the stable aqueous pharmaceutical composition of claim 1 or 2 for treating in a subject in need thereof, the use comprising the stable aqueous pharmaceutical composition to be administered to the subject in need thereof.

45. The use of claim 44, wherein the administration is subcutaneous.