

Claims

1. A pharmaceutical composition comprising an anti-CD38 antibody and a hyaluronidase, wherein:
 - a) the anti-CD38 antibody is of an IgG1 isotype and comprises a complementarity determining region 1 (HCDR1), HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 6, 7 and 8, respectively, and a light chain complementarity determining region 1 (LCDR1), LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively;
 - b) the hyaluronidase is rHuPH20 recombinant hyaluronidase; and
 - c) the pharmaceutical composition comprises about 1,800 mg of the anti-CD38 antibody and about 30,000 U of the hyaluronidase.
2. The pharmaceutical composition of claim 1, further comprising a pharmaceutically acceptable carrier.
3. The pharmaceutical composition of claim 1 or 2, which is a fixed combination or a non-fixed combination.
4. The pharmaceutical composition of any of the claims 1-3, comprising from 1 mg/mL to 180 mg/mL of the anti-CD38 antibody.
5. The pharmaceutical composition of any of the claims 1-4, comprising
 - a) from 10 mg/mL to 180 mg/mL of the anti-CD38 antibody;
 - b) from 20 mg/mL to 160 mg/mL of the anti-CD38 antibody;
 - c) from 20 mg/mL to 140 mg/mL of the anti-CD38 antibody;
 - d) from 20 mg/mL to 120 mg/mL of the anti-CD38 antibody;
 - e) from 40 mg/mL to 120 mg/mL of the anti-CD38 antibody;
 - f) from 60 mg/mL to 120 mg/mL of the anti-CD38 antibody;
 - g) from 80 mg/mL to 120 mg/mL of the anti-CD38 antibody; or
 - h) from 100 mg/mL to 120 mg/mL of the anti-CD38 antibody.
6. The pharmaceutical composition of any of the claims 1-5, comprising
 - a) about 20 mg/mL of the anti-CD38 antibody;
 - b) about 100 mg/mL of the anti-CD38 antibody; or

- c) about 120 mg/mL of the anti-CD38 antibody.
7. The pharmaceutical composition of any of the claims 1-6, comprising from 50 U/ml to 5,000 U/ml of the hyaluronidase.
8. The pharmaceutical composition of any of the claims 1-7, comprising
- a) from 50 U/ml to 5,000 U/ml of the hyaluronidase;
 - b) from 500 U/ml to 5,000 U/ml of the hyaluronidase;
 - c) from 1,000 U/ml to 5,000 U/ml of the hyaluronidase;
 - d) from 2,000 U/ml to 5,000 U/ml of the hyaluronidase;
 - e) from 50 U/ml to 2,000 U/ml of the hyaluronidase;
 - f) from 500 U/ml to 2,000 U/ml of the hyaluronidase; or
 - g) from 1,000 U/ml to 2,000 U/ml of the hyaluronidase.
9. The pharmaceutical composition of any of the claims 1-8, comprising
- a) about 50 U/ml of the hyaluronidase;
 - b) about 500 U/ml of the hyaluronidase;
 - c) about 2,000 U/ml of the hyaluronidase; or
 - d) about 5,000 U/ml of the hyaluronidase.
10. The pharmaceutical composition of any of the claims 1-9, wherein the anti-CD38 antibody comprises
- a) a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5; and/or
 - b) a heavy chain of SEQ ID NO: 12 and a light chain of SEQ ID NO: 13.
11. The pharmaceutical composition of claim 10, comprising
- a) from 20 mg/mL to 120 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5 in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mM mannitol and about 0.04% w/v polysorbate-20 (PS-20); at pH about 5.5; and

- b) about 30,000 U of the hyaluronidase in 10 mM L-histidine, 130 mM NaCl, 10 mM L-methionine, 0.02% w/v Polysorbate-80, pH 6.5.
- 12. The pharmaceutical composition of any of the claims 1-9, 14 and 16, which is a non-fixed combination.
- 13. The pharmaceutical composition of claim 10, comprising
 - a) about 20 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5 in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mM mannitol and about 0.04% w/v polysorbate-20 (PS-20); at pH about 5.5; and
 - b) about 30,000 U of the hyaluronidase in 10 mM L-histidine, 130 mM NaCl, 10 mM L-methionine, 0.02% w/v Polysorbate-80, pH 6.5.
- 14. The pharmaceutical composition of claim 10, comprising
 - a) from 1 mg/mL to 180 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;
 - b) from 50 U/ml to 5,000 U/ml of the hyaluronidase;
 - c) from 5 mM to 50 mM histidine; and
 - d) from 50 mM to 400 mM sorbitol.
- 15. The pharmaceutical composition of claim 14, further comprising
 - a) from 0.01% w/v to 0.1% w/v polysorbate-20 (PS-20); and/or
 - b) from 0.1 mg/mL to 2.5 mg/mL methionine.
- 16. The pharmaceutical composition of claim 14, comprising
 - a) from 100 mg/mL to 120 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;

- b) from 50 U/ml to 5,000 U/ml of the hyaluronidase;
 - c) about 10 mM histidine; and
 - d) from 100 mM to 300 mM sorbitol.
17. The pharmaceutical composition of claim 16, further comprising
- a) from 0.01% w/v to 0.04% w/v polysorbate-20 (PS-20); and
 - b) from 1 mg/mL to 2 mg/mL methionine.
18. The pharmaceutical composition of claim 17, comprising
- a) about 120 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;
 - b) about 2,000 U/ml of rHuPH20;
 - c) about 10 mM histidine;
 - d) about 300 mM sorbitol;
 - e) about 0.04% w/v polysorbate-20 (PS-20); and
 - f) about 1 mg/mL methionine; pH about 5.5.
19. Use of a pharmaceutical composition comprising an anti-CD38 antibody and a hyaluronidase in the manufacture of a medicament for the treatment of multiple myeloma (MM) in a subject, wherein the medicament is to be subcutaneously administered to the subject in need thereof, wherein:
- a) the anti-CD38 antibody is of an IgG1 isotype and comprises a complementarity determining region 1 (HCDR1), HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 6, 7 and 8, respectively, and a light chain complementarity determining region 1 (LCDR1), LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively;
 - b) the hyaluronidase is rHuPH20 recombinant hyaluronidase; and
 - c) the pharmaceutical composition comprises about 1,800 mg of the anti-CD38 antibody and about 30,000 U of the hyaluronidase.

20. The use of claim 19, wherein the pharmaceutical composition is a fixed combination or a non-fixed combination.
21. The use of claim 20, wherein the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
22. The use of claim 21, wherein the pharmaceutical composition comprises from 10 mg/mL to 180 mg/mL, from 20 mg/mL to 160 mg/mL, from 20 mg/mL to 140 mg/mL, from 20 mg/mL to 120 mg/mL, from 40 mg/mL to 120 mg/mL, from 60 mg/mL to 120 mg/mL, from 80 mg/mL to 120 mg/mL, from 100 mg/mL to 120 mg/mL, about 20 mg/mL, about 100 mg/mL or about 120 mg/mL of the anti-CD38 antibody.
23. The use of claim 22, wherein the pharmaceutical composition comprises from 50 U/ml to 5,000 U/ml, from 500 U/ml to 5,000 U/ml, from 1,000 U/ml to 5,000 U/ml, from 2,000 U/ml to 5,000 U/ml, from 50 U/ml to 2,000 U/ml, from 500 U/ml to 2,000 U/ml, from 1,000 U/ml to 2,000 U/ml, about 50 U/ml, about 500 U/ml, about 2,000 U/ml or about 5,000 U/ml of the hyaluronidase.
24. The use of claim 19, wherein the pharmaceutical composition comprises about 20 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5, about 30,000 U of the hyaluronidase, about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mM mannitol; and about 0.04% w/v polysorbate-20 (PS-20), pH about 5.5.
25. The use of claim 19, wherein the pharmaceutical composition comprises from 1 mg/mL to 180 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5, from 50 U/ml to 5,000 U/ml of the hyaluronidase, from 5 mM to 50 mM histidine and from 50 mM to 400 mM sorbitol, optionally further comprising from 0.01% w/v to 0.1% w/v polysorbate-20 (PS-20) and/or from 0.1 mg/mL to 2.5 mg/mL methionine.

26. The use of claim 25, wherein the pharmaceutical composition comprises from 100 mg/mL to 120 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5, from 50 U/ml to 5,000 U/ml of the hyaluronidase, 10 mM histidine and from 100 mM to 300 mM sorbitol, optionally further comprising from 0.01% w/v to 0.04% w/v polysorbate-20 (PS-20) and/or from 1 mg/mL to 2 mg/mL methionine.
27. The use of claim 26, wherein the pharmaceutical composition comprises about 120 mg/mL of the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5, about 2,000 U/ml of the hyaluronidase, about 10 mM histidine, about 300 mM sorbitol, about 0.04% w/v PS-20 and about 1 mg/mL methionine; pH about 5.5.
28. The use of claim 19, wherein a second therapeutic agent is also to be administered.
29. The use of claim 28, wherein the second therapeutic agent is a proteasome inhibitor, an alkylating agent or a glutamic acid derivative, or combinations thereof, wherein the glutamic acid derivative is lenalidomide, thalidomide or pomalidomide.
30. The use of claim 29, wherein
- a) the proteasome inhibitor is bortezomib, carfilzomib or ixazomib; and
 - b) the alkylating agent is busulfan, cyclophosphamide, bendamustine, chlorambucil, carboplatin, cisplatin, temozolomide, melphalan, carmustine, lomustine, dacarbazine, oxaliplatin, ifosfamide, mechlorethamine, thiotepa, trabectedin or streptozocin.
31. The use of claim 30, wherein a corticosteroid is also to be administered.
32. The use of claim 31, wherein the corticosteroid is dexamethasone or prednisone.
33. The use of claim 32, wherein the corticosteroid is dexamethasone.
34. A unit dosage form, comprising
- a) an anti-CD38 antibody of an IgG1 isotype comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5 in an amount of about 1,800 mg;

- b) a hyaluronidase in an amount of about 30,000 U, wherein the hyaluronidase is rHuPH20 recombinant hyaluronidase;
 - c) histidine at a concentration of from 5 mM to 15 mM;
 - d) sorbitol at a concentration of from 100 mM to 300 mM;
 - e) polysorbate-20 (PS-20) at a concentration of from 0.01% w/v to 0.04 % w/v; and
 - f) methionine at a concentration of from 1 mg/mL to 2 mg/mL, at a pH of about 5.5.
35. The unit dosage form of claim 34, wherein histidine is present at a concentration of about 10 mM.
36. The unit dosage form of claim 35, wherein sorbitol is present at a concentration of about 300 mM.
37. The unit dosage form of claim 36, wherein polysorbate is present at a concentration of about 0.04% w/v.
38. The unit dosage form of claim 37, wherein methionine is present at a concentration of about 1 mg/mL.
39. The unit dosage form of claim 38, comprising sucrose at a concentration of from 100 mM to 200 mM.
40. A container comprising the unit dosage form of claim 39.
41. The unit dosage form of claim 34, comprising
- a) the anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5 in an amount of about 1,800 mg;
 - b) a hyaluronidase in an amount of about 30,000 U;
 - c) histidine at a concentration of about 10 mM;
 - d) sorbitol at a concentration of about 300 mM;
 - e) polysorbate-20 (PS-20) at a concentration of about 0.04 % w/v; and
 - f) methionine at a concentration of about 1 mg/mL, at a pH of about 5.5.

42. A container comprising the unit dosage form of claim 41.
43. A pharmaceutical composition comprising an anti-CD38 antibody and a hyaluronidase for use in treating multiple myeloma (MM), wherein the composition is to be administered subcutaneously to the subject in need thereof for a time sufficient to treat the cancer, wherein:
- a) the anti-CD38 antibody is of an IgG1 isotype and comprises a complementarity determining region 1 (HCDR1), HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 6, 7 and 8, respectively, and a light chain complementarity determining region 1 (LCDR1), LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively
 - b) the hyaluronidase is rHuPH20 recombinant hyaluronidase; and
 - c) the pharmaceutical composition comprises about 1,800 mg of the anti-CD38 antibody and about 30,000 U of the hyaluronidase.
44. A unit dosage form, comprising
- a) an anti-CD38 antibody of an IgG1 isotype comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5 in an amount of about 1,800 mg;
 - b) a hyaluronidase in an amount of ~~from~~ about 30,000 U, wherein the hyaluronidase is rHuPH20 recombinant hyaluronidase;
 - c) histidine at a concentration of from 5 mM to 15 mM;
 - d) sorbitol at a concentration of from 100 mM to 300 mM;
 - e) polysorbate-20 (PS-20) at a concentration of from 0.01% w/v to 0.04 % w/v; and
 - f) methionine at a concentration of from 0.1 mg/mL to 2.5 mg/mL, at a pH of about 5.5.