

CLAIMS

1. Use of an anti-CD38 antibody in the manufacture of a medicament for treating multiple myeloma in a human individual, wherein at least a first, a second, and a third intravenous infusion of the anti-CD38 antibody is to be administered to the individual, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg, wherein the dose of the anti-CD38 antibody is in a volume of 250 ml,

wherein the first intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 25 mL/hour for a first hour, and wherein the infusion rate is increased by 25 mL/hour every 30 minutes after the first hour to a maximum infusion rate of 150 mL/hour until the 250 ml volume is infused,

wherein the second intravenous infusion of anti-CD38 antibody is to be administered to the individual at an infusion rate of 50 mL/hour for a first 30 minutes, wherein the infusion rate is increased by 50 ml/hour a second 30 minutes, and wherein the infusion rate is increased by 100 mL/hour every 30 minutes after the second 30 minutes to a maximum infusion rate of 200 mL/hour until the 250 ml volume is infused,

wherein the third intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 200 ml/hour until the 250 ml volume is infused, and

wherein the anti-CD38 antibody comprises (a) a heavy chain variable domain (VH) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (VL) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6).

2. The use of claim 1 wherein the anti-CD38 antibody is isatuximab.

3. The use of claim 1 or 2, comprising a fourth intravenous infusion of the anti-CD38 antibody that is to be administered to the individual, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml.

4. The use of claim 3, wherein the fourth intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 200 ml/hour until the 250 ml volume infused.

5. The use of claim 3, wherein the fourth intravenous infusion of the anti-CD38 antibody is to be

administered to the individual at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml volume is infused.

6. The use of any one of claims 3-5, wherein the anti-CD38 antibody is to be administered in a first 28-day cycle, wherein the first intravenous infusion of the anti-CD38 antibody is to be administered on Day 1, the second intravenous infusion of the anti-CD38 antibody is to be administered on Day 8, the third intravenous infusion of the anti-CD38 antibody is to be administered on Day 15, and the fourth intravenous infusion of the anti-CD38 antibody is to be administered on Day 22 the first 28-day cycle.

7. The use of any one of claims 3-6, wherein one or more subsequent intravenous infusions of the anti-CD38 antibody are to be administered to the individual following the fourth intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml for each of the one or more subsequent intravenous infusions.

8. The use of claim 7, wherein each of the one or more subsequent intravenous infusions of the anti-CD38 antibody following the fourth intravenous infusion is to be administered to the individual at an infusion rate of 200 ml/hour until the 250 ml volume infused.

9. The use of claim 7, wherein each of the one or more subsequent intravenous infusions of the anti-CD38 antibody following the fourth intravenous infusion is to be administered to the individual at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml volume is infused.

10. The use of any one of claims 7-9, wherein the anti-CD38 antibody is to be administered in one or more subsequent 28-day cycles following the first 28-day cycle, wherein each of the one or more subsequent intravenous infusions of the anti-CD38 antibody following the fourth intravenous infusion is to be administered on Days 1 and 15 of each of the one or more subsequent 28-day cycles following the first 28-day cycle.

11. Use of an anti-CD38 antibody in the manufacture of a medicament for treating multiple myeloma in a human individual, wherein at least three intravenous infusions of the anti-CD38 antibody are to be administered to the individual, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg, wherein the dose of the anti-CD38 antibody is in a volume of 250 ml, and wherein the anti-CD38 antibody comprises (a) a heavy chain variable domain (VH) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2

comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (VL) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6) ;

wherein the first intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 25 mL/hour for a first hour, and wherein the infusion rate is increased by 25 mL/hour every 30 minutes after the first hour to a maximum infusion rate of 150 mL/hour until the 250 ml volume is infused;

wherein the second intravenous infusion of the anti-CD38 is to be administered to the individual at an infusion rate of 50 mL/hour for a first 30 minutes, wherein the infusion rate is increased by 50 ml/hr a second 30 minutes, and wherein the infusion rate is increased by 100 mL/hour every 30 minutes after the second 30 minutes to a maximum infusion rate of 200 mL/hour until the 250 ml volume is infused; and

wherein the third intravenous infusion of the anti-CD38 is to be administered to the individual at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml volume is infused.

12. The use of claim 11, wherein the anti-CD38 antibody is isatuximab.

13. The use of claim 11 or 12, wherein one or more subsequent intravenous infusions of the anti-CD38 antibody are to be administered following the third intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml for each of the one or more subsequent intravenous infusions.

14. The use of claim 13, wherein each of the one or more subsequent intravenous infusions of the anti-CD38 antibody following the third intravenous infusion is to be administered to the individual at an infusion rate of 200 ml/hour until the 250 ml volume infused.

15. Use of an anti-CD38 antibody in the manufacture of a medicament for treating multiple myeloma in an individual, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion comprising at least a first, a second, and a third intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg, wherein the volume of each dose of the anti-CD38 antibody is 250 ml,

wherein the first intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 25 mL/hour for a first hour, and wherein the infusion rate is

increased by 25 mL/hour every 30 minutes after the first hour to a maximum infusion rate of 150 mL/hour until the 250 ml volume is infused,

wherein the second intravenous infusion of anti-CD38 antibody is to be administered to the individual at an infusion rate of 50 mL/hour for a first 30 minutes, wherein the infusion rate is increased by 50 ml/hour a second 30 minutes, and wherein the infusion rate is increased by 100 mL/hour every 30 minutes after the second 30 minutes to a maximum infusion rate of 200 mL/hour until the 250 ml volume is infused,

wherein the third intravenous infusion of the anti-CD38 antibody is to be administered to the individual at an infusion rate of 200 ml/hour until the 250 ml volume is infused, and

wherein the anti-CD38 antibody comprises (a) a heavy chain variable domain (VH) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (VL) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6).

16. The use of claim 15, wherein the anti-CD38 antibody is isatuximab.

17. The the use of claim 15 or 16, wherein the anti-CD38 antibody is to be administered in a first 28-day cycle, and wherein the anti-CD38 antibody is to be administered on Days 1, 8, 15, and 22 of the first 28-day cycle.

18. The use of claim 17, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 1 of the first 28 day cycle at an infusion rate of 25 mL/hour for a first hour, and wherein the infusion rate is increased by 25 mL/hour every 30 minutes after the first hour to a maximum infusion rate of 150 mL/hour until the 250 ml dose of the anti-CD38 antibody is infused.

19. The use of claim 17, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 1 of the first 28 day cycle at an infusion rate of 12.5 mL/hour for a first 30 minutes, and wherein the infusion rate is increased by 25 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.

20. The use of any one of claims 17-19, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 8 of the first 28 day cycle at an infusion rate of 50 mL/hour for a first 30 minutes, wherein the infusion rate is increased by 50 ml/hr for an second 30

minutes, and wherein the infusion rate is increased by 100 mL/hour every 30 minutes after the second 30 minutes to a maximum infusion rate of 200 mL/hour until the 250 ml volume is infused.

21. The use of any one of claims 17-19, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 8 of the first 28 day cycle at an infusion rate of 50 mL/hour for a first 30 minutes, 100 mL/hour for a second 30 minutes, 200 mL for the third 30 minutes, and 300 mL/hour after the third 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.

22. The use of any one of claims 17-19, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 8 of the first 28 day cycle at an infusion rate of 25 mL/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.

23. The use of any one of claims 17-22, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 15 of the first 28-day cycle at an infusion rate of 200 ml/hour until the 250 ml dose of the anti-CD38 antibody is infused.

24. The use of any one of claims 17-22, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 15 of the first 28 day cycle at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.

25. The use of any one of claims 17-24, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 22 of the first 28-day cycle at an infusion rate of 200 ml/hour until the 250 ml dose of the anti-CD38 antibody is infused.

26. The use of any one of claims 17-24, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 22 of the first 28 day cycle at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.

27. The use of any one of claims 17-26, wherein the anti-CD38 antibody is to be further administered in one or more subsequent 28-day cycles, and wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg on Days 1 and 15 of each subsequent 28 day cycle, wherein the volume of each dose of the anti-CD38 antibody to be administered in the one or more subsequent cycles is 250 ml.

28. The use of claim 27, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 1 of each subsequent 28-day cycle at an infusion rate of 200 ml/hour until the 250 ml dose of the anti-CD38 antibody is infused.
29. The use of claim 27, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 1 of each subsequent 28-day cycle at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.
30. The use of any one of claims 27-29, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 15 of each subsequent 28-day cycle at an infusion rate of 200 ml/hour until the 250 ml dose of the anti-CD38 antibody is infused.
31. The use of any one of claims 27-29, wherein the anti-CD38 antibody is to be administered to the individual via intravenous infusion on Day 15 of each subsequent 28 day cycle at an infusion rate of 100 ml/hour for a first 30 minutes, and wherein the infusion rate is increased by 50 mL/hour every 30 minutes after the first 30 minutes until the 250 ml dose of the anti-CD38 antibody is infused.
32. Use of an anti-CD38 antibody in the manufacture of a medicament for treating multiple myeloma in a human individual, wherein at least a first dose of the anti-CD38 antibody is to be administered to the individual via intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml, wherein the first dose is infused over a duration between 1.5 and 6.5 hours, and wherein the anti-CD38 antibody comprises (a) a heavy chain variable domain (VH) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (VL) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6).
33. The use of claim 32, wherein the anti-CD38 antibody is isatuximab.
34. The use of claim 32 or 33, wherein at least a second dose of the anti-CD38 antibody is to be administered to the individual via intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml, wherein the second dose is infused over a

duration between 0.5 and 3.5 hours.

35. The the use of any one of claims 27-30, wherein at least a third dose of the anti-CD38 antibody is to be administered to the individual via intravenous infusion, wherein the anti-CD38 antibody is to be administered at a dose of 10 mg/kg in a volume of 250 ml, wherein the third dose is infused over a duration between 0.5 and 1.5 hours.

36. The use of any one of claims 1-35, wherein the administration of the anti-CD38 antibody does not result in the individual experiencing an infusion reaction (IR).

37. The use of any one of claims 1-35, wherein the administration of the anti-CD38 antibody does not result in the individual experiencing an IR greater than Grade 1 in severity.

38. The use of any one of claims 1-35, wherein the administration of the anti-CD38 antibody does not result in the individual experiencing an IR of Grade 2 or greater in severity.

39. The the use of any one of claims 1-38, wherein the 10 mg/kg dose of the anti-CD38 antibody in the volume of 250 ml further comprises 0.9% sodium chloride or 5% dextrose.

40. The the use of any one of claims 1-39, wherein the individual does not receive premedication with one or more of an analgesic, an antacid, an anti-inflammatory agent, an antihistamine prior for the purpose of preventing or minimizing an infusion reaction prior to the administration of the anti-CD38 antibody via intravenous infusion.

41. The use of any one of claims 1-40, wherein the multiple myeloma is relapsed/refractory multiple myeloma.

42. The use of any one of claims 1-41, wherein the individual was refractory to the most recent prior therapy for multiple myeloma.

43. The use of any one of claims 1-42, wherein the individual is refractory to lenalidomide.

44. The use of any one of claims 1-43, wherein the most recent prior therapy was lenalidomide.

45. The use of any one of claims 1-44, wherein the individual is refractory to a proteasome inhibitor.

46. The use of any one of claims 1-45, wherein the most recent prior therapy was a proteasome inhibitor.
47. The use of claim 45 or 46, wherein the proteasome inhibitor is selected from the group consisting of: bortezomib, carfilzomib, marizomib, oprozomib, and ixazomib.
48. The use of any one of claims 42-47, wherein the lenalidomide and the proteasome inhibitor were administered in combination.
49. The use of any one of claims 1-48, wherein the individual has a respiratory disorder, thoracic disorder, and/or mediastinal disorder.
50. The use of claim 49, wherein the respiratory disorder is chronic obstructive pulmonary disorder (COPD).
51. The use of claim 49, wherein the respiratory disorder is asthma.
52. The use of claim 49, wherein the respiratory disorder is bronchospasm.
53. The use of any one of claims 1-52, wherein the individual has received at least two prior therapies for multiple myeloma.
54. The use of any one of claims 1-53, wherein the individual has received at least three prior therapies for multiple myeloma.
55. The use of any one of claims 1-54, wherein the anti-CD38 antibody is to be administered in conjunction with at least one additional agent.
56. The use of claim 55, wherein the at least one additional agent comprises an immunomodulatory drug.
57. The use of claim 56, wherein the immunomodulatory drug is lenalidomide or pomalidomide.
58. The use of any one of claims 3-10, 13-14, 17-31, and 34-57, wherein the at least one additional agent comprises a proteasome inhibitor.
59. The use of claim 58, wherein the proteasome inhibitor is bortezomib, carfilzomib, marizomib,

oprozomib, and ixazomib.

60. The use of any one of claims 5-21, 26-27, 32-46, and 51-81, wherein the at least one additional agent comprises a corticosteroid.

61. The use of claim 60, wherein the corticosteroid is dexamethasone.