

CLAIMS

1. Use of a pharmaceutical composition comprising an anti-CD38 antibody in the manufacture of a medicament for treating a patient having light chain amyloidosis (AL),
2. The use of claim 1, wherein the patient is resistant to treatment with a proteasome inhibitor, cyclophosphamide and/ or a corticosteroid.
3. The use of claim 2, wherein the proteasome inhibitor is Velcade® (bortezomib).
4. The use of claim 2, wherein the corticosteroid is dexamethasone.
5. The use of claim 1 or claim 2, wherein the anti-CD38 antibody is to be administered in combination with a second therapeutic agent.
6. The use of claim 5, wherein the second therapeutic agent is a proteasome inhibitor, cyclophosphamide or a corticosteroid.
7. The use of claim 5, wherein the second therapeutic agent is Velcade® (bortezomib), NINLARO® (ixazomib), Kyprolis® (carfilzomib), Farydak® (panobinostat), cyclophosphamide, Alkeran® (melphalan), Thalomid® (thalidomide), Revlimid® (lenalidomide), Pomalyst® (pomalidomide), dexamethasone or interferon alpha.
8. The use of claim 1, wherein the anti-CD38 antibody is to be administered in combination with a proteasome inhibitor, cyclophosphamide and a corticosteroid.
9. The use of claim 6 or claim 8, wherein the proteasome inhibitor is Velcade® (bortezomib) or NINLARO® (ixazomib).
10. The use of claim 6 or claim 8, wherein the corticosteroid is dexamethasone.

11. The use of claim 8, wherein the proteasome inhibitor is Velcade® (bortezomib) or NINLARO® (ixazomib) and the corticosteroid is dexamethasone.
12. The use of claim 5, wherein the anti-CD38 antibody and the second therapeutic agent are to be administered simultaneously, sequentially or separately.
13. The use of claim 8, wherein the proteasome inhibitor, cyclophosphamide and the corticosteroid are to be administered simultaneously, sequentially or separately.
14. The use of claim 1, wherein AL is cardiac stage I, cardiac stage II, cardiac stage III, relapsed or refractory.
15. The use of claim 1, wherein the patient is to undergo hematopoietic stem cell transplantation (HSCT).
16. The use of claim 15, wherein the HSCT is allogeneic, autologous or syngeneic.
17. The use of claim 16, wherein the HSCT comprises transplantation of blood stem cells derived from bone marrow, blood or amniotic fluid.
18. The use of claim 17, wherein the anti-CD38 antibody is to be administered prior to, during or after HSCT.
19. The use of claim 18, wherein the patient has completed chemotherapy and/or radiation therapy prior to HSCT.
20. The use of claim 1, wherein the patient is to be further treated with radiotherapy.

21. The use of claim 1, wherein the anti-CD38 antibody does not mediate killing of CD34-positive hematopoietic progenitor cells by complement dependent cytotoxicity (CDC).
22. The use of claim 1, wherein the anti-CD38 antibody induces killing of CD38 positive plasma cells by antibody -dependent cell-mediated cytotoxicity (ADCC), antibody -dependent cellular phagocytosis (ADCP), complement dependent cytotoxicity (CDC), apoptosis, or modulation of CD38 enzymatic activity.
23. The use of claim 1, wherein the anti-CD38 antibody competes for binding to CD38 with an antibody comprising a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5.
24. The use of claim 23, wherein the anti-CD38 antibody binds at least to the region SKRNIQFSCCKNIYR (SEQ ID NO: 2) and the region EKVQTTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
25. The use of claim 24, wherein the anti-CD38 antibody comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NOs: 6, 7 and 8, respectively, and a light chain complementarity determining region 1 (LCDR1), a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively.
26. The use of claim 25, wherein the anti-CD38 antibody comprises the VH comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 4 and the VL comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 5.
27. The use of claim 26, wherein the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.

28. The use of claim 25, wherein the anti-CD38 antibody comprises a heavy chain comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 12 and a light chain comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 13.
29. The use of claim 28, wherein the anti-CD38 antibody comprises the heavy chain of SEQ ID NO: 12 and the light chain of SEQ ID NO: 13.
30. The use of claim 1, wherein the anti-CD38 antibody comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:
- a. the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b. the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c. the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d. the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21, wherein the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 are defined by Kabat, Chothia, or IMGT.
31. The use of claim 30, wherein the anti-CD38 antibody comprises
- a. the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b. the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c. the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d. the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
32. The use of claim 1 or 31, wherein the anti-CD38 antibody is to be ~~is~~ administered intravenously.
33. The use of claim 1, wherein the anti-CD38 antibody is to be administered subcutaneously and further comprises a hyaluronidase.
34. The use of claim 33, wherein the hyaluronidase is rHuPH20 of SEQ ID NO: 22.

35. The use of claim 31, wherein the anti-CD38 antibody is to be administered subcutaneously and which further comprises a hyaluronidase.
36. The use of claim 35, wherein the hyaluronidase is rHuPH20 of SEQ ID NO: 22.
37. Use of a pharmaceutical composition comprising an anti-CD38 antibody in the manufacture of a medicament for the treatment of a patient having a CD38-positive hematological malignancy, wherein the patient is about to undergo hematopoietic stem cell transplantation (HSCT).
38. The use of claim 37, wherein the anti-CD38 antibody competes for binding to CD38 with an antibody comprising a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5.
39. The use of claim 38, wherein the CD38-positive hematological malignancy is light chain amyloidosis (AL), multiple myeloma (MM), acute lymphoblastic leukemia (ALL), non-Hodgkin's lymphoma (NHL), diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma (BL), follicular lymphoma (FL) or mantle-cell lymphoma (MCL).
40. The use of claim 38, wherein the CD38-positive hematological malignancy is a plasma cell disease.
41. The use of claim 40, wherein the plasma cell disease is light chain amyloidosis (AL), multiple myeloma (MM) or Waldenstrom's macroglobulinemia.
42. The use of claim 41, wherein the plasma cell disease is AL or MM.
43. The use of claim 42, wherein AL is cardiac stage I, cardiac stage II, cardiac stage III, relapsed or refractory.

44. The use of claim 37, wherein the HSCT is allogeneic, autologous or syngeneic.
45. The use of claim 44, wherein the HSCT comprises transplantation of blood stem cells derived from bone marrow, blood or amniotic fluid.
46. The use of claim 45, wherein the anti-CD38 antibody is to be administered prior to, during or after HSCT.
47. The use of claim 46, wherein the patient has completed chemotherapy and/or radiation therapy prior to HSCT.
48. The use of claim 37, wherein the anti-CD38 antibody is to be administered in combination with a second therapeutic agent.
49. The use of claim 48, wherein the second therapeutic agent is bortezomib, ixazomib, carfilzomib, panobinostat, cyclophosphamide, melphalan, thalidomide, lenalidomide, pomalidomide, dexamethasone or interferon alpha.
50. The use of claim 48, wherein the anti-CD38 antibody and the second therapeutic agent are to be administered simultaneously, sequentially or separately.
51. The use of claim 37, wherein the patient is to be further treated with radiotherapy.
52. The use of claim 37, wherein the anti-CD38 antibody does not mediate killing of CD34-positive hematopoietic progenitor cells by complement dependent cytotoxicity (CDC).
53. The use of claim 37, wherein the anti-CD38 antibody induces killing of CD38 expressing plasma cells by antibody -dependent cell-mediated cytotoxicity (ADCC),

antibody -dependent cellular phagocytosis (ADCP), complement dependent cytotoxicity (CDC), apoptosis, or modulation of CD38 enzymatic activity.

54. The use of claim 37, wherein the anti-CD38 antibody competes for binding to CD38 with an antibody comprising a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5.
55. The use of claim 54, wherein the anti-CD38 antibody binds at least to the region SKRNIQFSCCKNIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
56. The use of claim 55, wherein the anti-CD38 antibody comprises a heavy chain complementarity determining region 1 (HCDR1), a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NOs: 6, 7 and 8, respectively, and a light chain complementarity determining region 1 (LCDR1), a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively.
57. The use of claim 56 wherein the anti-CD38 antibody comprises the VH comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 4 and the VL comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 5.
58. The use of claim 57, wherein the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
59. The use of claim 56, wherein the anti-CD38 antibody comprises a heavy chain comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 12 and a light chain comprising an amino acid sequence that is 95%, 96%, 97%, 98%, 99% or 100% identical to that of SEQ ID NO: 13.

60. The use of claim 59, wherein the anti-CD38 antibody comprises the heavy chain of SEQ ID NO: 12 and the light chain of SEQ ID NO: 13.
61. The use of claim 37, wherein the anti-CD38 antibody comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:
- a. the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b. the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c. the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or d. the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21, wherein the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 are defined by Kabat, Chothia, or IMGT.
62. The use of claim 61, wherein the anti-CD38 antibody comprises
- a. the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b. the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c. the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or d. the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
63. The use of claim 37, wherein the anti-CD38 antibody is humanized or human.
64. The use of claim 63, wherein the anti-CD38 antibody is of IgG1, IgG2, IgG3 or IgG4 isotype.
65. The use of claim 1 or claim 30 or claim 61, wherein the anti-CD38 antibody is humanized or human.
66. The use of claim 65, wherein the anti-CD38 antibody is of IgG1, IgG2, IgG3 or IgG4 isotype.
67. The use of claim 37 or 62, wherein the anti-CD38 antibody is to be administered intravenously.

68. The use of claim 37, wherein the anti-CD38 antibody is to be administered subcutaneously and further comprises a hyaluronidase.
69. The use of claim 68, wherein the hyaluronidase is rHuPH20 of SEQ ID NO: 22.
70. The use of claim 62, wherein the anti-CD38 antibody is to be administered subcutaneously and further comprises a hyaluronidase.
71. The use of claim 70, wherein the hyaluronidase is rHuPH20 of SEQ ID NO: 22.
72. A pharmaceutical composition comprising an anti-CD38 antibody for use in the treatment of a patient having light chain amyloidosis (AL),
73. A pharmaceutical composition for use in the treatment of a patient having a CD38-positive hematological malignancy, comprising an anti-CD38 antibody wherein the patient is undergoing hematopoietic stem cell transplantation (HSCT).