CLAIMS

1. A lyophilized formulation of an antibody, comprising

(a) a humanized antibody or antigen binding fragment thereof, comprising:

(i) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 6, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11; or

(ii) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 12, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11;

(b) L-histidine;

(c) L-histidine HCl monohydrate;

(d) trehalose; and

(e) polysorbate 20,

in such amounts, which upon reconstitution yield an aqueous solution wherein:

(i) the antibody or antigen binding fragment thereof is present at a concentration of about 10 mg/mL;

(ii) a histidine buffer is present at a concentration of about 25 mM;

(iii) the trehalose is present at a concentration of about 230 mM;

(iv) the polysorbate 20 is present at a concentration of about 0.2 g/L; and

wherein the aqueous solution has a pH of about 6.5.

2. The lyophilized formulation of claim 1, comprising:

(a) about 100 mg of the antibody or antigen binding fragment thereof;

(b) about 27.2 mg L-histidine;

(c) about 15.7 mg L-histidine HCl monohydrate;

(d) about 870.2 mg trehalose dihydrate; and

(e) about 2 mg polysorbate 20.

3. A lyophilized formulation of an antibody, comprising

(a) a humanized antibody or antigen binding fragment thereof, comprising:

(i) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 6, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11; or

(ii) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 12, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11;

(b) L-histidine;

(c) L-histidine HCl monohydrate;

(d) trehalose; and

(e) polysorbate 20,

in such amounts, which upon reconstitution yield an aqueous solution wherein:

(i) the antibody or antigen binding fragment thereof is present at a concentration of about 50 mg/mL;

(ii) a histidine buffer is present at a concentration of about 25 mM;

(iii) the trehalose is present at a concentration of about 230 mM;

(iv) the polysorbate 20 is present at a concentration of about 0.2 g/L; and

wherein the aqueous solution has a pH of about 6.5.

4. The lyophilized formulation of claim 3, comprising:

(a) about 500 mg of the antibody or antigen binding fragment thereof;

(b) about 27.2 mg L-histidine;

(c) about 15.7 mg L-histidine HCl monohydrate;

(d) about 870.2 mg trehalose dihydrate; and

(e) about 2 mg polysorbate 20.

5. The lyophilized formulation of any one of claims 1-4, wherein the antibody or antigen binding fragment thereof comprises a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 6, 7, and 8, and a heavy chain variable region comprising three CDRs set forth as SEQ ID NOs: 9, 10, and 11.

6. The lyophilized formulation of any one of claims 1-4, wherein the antibody or antigen binding fragment thereof comprises a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 12, 7, and 8, and a heavy chain variable region comprising three CDRs set forth as SEQ ID NOs: 9, 10, and 11.

7. The lyophilized formulation of any one of claims 1-4, wherein the antibody or antigen binding fragment thereof comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 4 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 5.

8. The lyophilized formulation of any one of claims 1-4, wherein the antibody or antigen binding fragment thereof comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as any one of SEQ ID NOs: 14-16.

9. The lyophilized formulation of any one of claims 1-4, wherein the antibody or antigen binding fragment thereof comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 15.

10. A nucleic acid comprising a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 13.

11. The nucleic acid of claim 10 comprising the nucleotide sequence of SEQ ID NO: 19.

12. The nucleic acid of claim 11 comprising the nucleotide sequence of SEQ ID NO: 20.

13. A nucleic acid comprising a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as any one of SEQ ID NOs: 14-16.

14. The nucleic acid of claim 13 comprising a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 15.

15. The nucleic acid of claim 14 comprising the nucleotide sequence of SEQ ID NO: 22.

16. The nucleic acid of claim 15 comprising the nucleotide sequence of SEQ ID NO: 23.

17. A vector comprising the nucleic acid of any one of claims 10-16.

18. A vector comprising the nucleic acids of claims 10 and 14.

19. A vector comprising the nucleic acids of claims 11 and 15.

20. A vector comprising the nucleic acids of claims 12 and 16.

21. A host cell having stably incorporated into its genome the nucleic acid of any one of claims 10-16.

22. The host cell of claim 21, wherein the host cell is a CHO cell.

23. The host cell of claim 21 having stably incorporated into its genome a nucleic acid comprising the nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 13 and a nucleic acid comprising the nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as any one of SEQ ID NOs: 14-16.

24. The host cell of claim 21 having stably incorporated into its genome a nucleic acid comprising the nucleotide sequence set forth as SEQ ID NO: 19 and a nucleic acid comprising the nucleotide sequence set forth as SEQ ID NO: 22.

25. The host cell of claim 21 having stably incorporated into its genome a nucleic acid comprising the nucleotide sequence set forth as SEQ ID NO: 20 and a nucleic acid comprising the nucleotide sequence set forth as SEQ ID NO: 23.

26. The host cell of any one of claims 23-25, wherein the host cell is a CHO cell.

27. A method of making a lyophilized formulation comprising:

(a) culturing mammalian cells having stably incorporated into their genome one or more nucleic acids encoding an antibody or antigen binding fragment thereof so that the cells secrete the antibody or antigen binding fragment thereof into the cell culture media, wherein the antibody or antigen binding fragment thereof comprises:

(i) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 6, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11, or

(ii) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 12, 7, and 8 and a heavy chain variable region comprising three CDRS set forth as SEQ ID NOs: 9, 10, and 11;

(b) purifying the antibody or antigen binding fragment thereof from the cell culture media; and

(c) preparing the lyophilized formulation of any one of claims 1-9.

28. The method of claim 27, wherein the nucleic acid encoding the antibody or antigen binding fragment thereof comprises a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 13, and wherein the nucleic acid encoding the heavy chain of the antibody or antigen binding fragment thereof comprises a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as any one of SEQ ID NOs: 14-16.

29. The method of claim 28, wherein the nucleic acid encoding the light chain of the antibody or antigen binding fragment thereof comprises a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 13, and wherein the

nucleic acid encoding the heavy chain of the antibody or antigen binding fragment thereof comprises a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence set forth as SEQ ID NO: 15.

30. The method of claim 28, wherein the nucleic acid encoding the light chain of the antibody or antigen binding fragment thereof comprises the nucleotide sequence of SEQ ID NO: 19, and wherein the nucleic acid encoding the heavy chain of the antibody or antigen binding fragment thereof comprises the nucleotide sequence of SEQ ID NO: 22.

31. The method of claim 30, wherein the nucleic acid encoding the light chain of the antibody or antigen binding fragment thereof comprises the nucleotide sequence of SEQ ID NO: 20, and wherein the nucleic acid encoding the heavy chain of the antibody or antigen binding fragment thereof comprises the nucleotide sequence of SEQ ID NO: 23.

32. The method of any one of claims 27-31, further comprising evaluating at least one property of the antibody or antigen binding fragment thereof in the formulation selected from the group consisting of the physical stability, chemical stability and biological activity.

33. The method of any one of claims 27-32, wherein the mammalian cells are CHO cells.

34. Use of a lyophilized formulation according to any one of claims 1-9 for the manufacture of a medicament for the treatment of amyloidosis in a human patient characterized by the presence of amyloid protein fibrils.

35. The use of claim 34, wherein the human patient has amyloid A amyloidosis characterized by the presence of amyloid A protein fibrils.

36. The use of claim 34, wherein the human patient has AL amyloidosis characterized by the presence of amyloid light chain-type protein fibrils.

37. The use of claim 36, wherein the AL amyloidosis is associated with a dyscrasia of the B lymphocyte lineage.

38. The use of claim 37, wherein the dyscrasia is a malignancy.

39. The use of claim 38, wherein the malignancy is multiple myeloma.

40. The use of any one of claims 34-39, wherein the medicament is administrable with at least one second drug selected from the group consisting of melphalan, bortezomib, lenolidomide and carfilzomib.

41. The use of claim 40, wherein the at least one second drug is bortezomib.

42. The use of any one of claims 34-41, wherein the medicament is administrable to the human patient at a frequency of daily to annually.

43. The use of any one of claims 34-42, wherein the medicament is administrable to the human patient once every twenty-eight days.

44. The use of any one of claims 40-43, wherein the at least one second drug is administrable to the human patient at a frequency of daily to annually.

45. The use of any one of claims 40-44, wherein the at least one second drug is administrable to the human patient once every seven days.

46. The use of any one of claims 34-45, wherein the medicament is administrable to the human patient in a dose ranging from about 0.5 mg of the antibody per kg body weight of the human patient to about 30 mg of the antibody per kg of body weight of the human patient.

47. The use of any one of claims 34-46, wherein the medicament is administrable to the human patient in a dose ranging from about 20 mg of the antibody per kg body weight of the human patient to about 30 mg of the antibody per kg of body weight of the human patient.

48. The use of any one of claims 34-47, wherein the medicament is administrable to the human patient in a dose of about 25 mg of the antibody per kg body weight of the human patient.

49. The use of any one of claims 34-48, wherein the medicament is administrable to the human patient in a dose ranging from about 10 mg of the antibody to about 5000 mg of the antibody.

50. The use of any one of claims 34-49, wherein the medicament is administrable to the human patient in a dose ranging from about 30 mg of the antibody to about 2500 mg of the antibody.

51. A lyophilized formulation according to any one of claims 1-9 for use in the manufacture of a medicament for the treatment of amyloidosis in a human patient characterized by the presence of amyloid protein fibrils.

52. The lyophilized formulation of claim 51, wherein the human patient has amyloid A amyloidosis characterized by the presence of amyloid A protein fibrils.

53. The lyophilized formulation of claim 51, wherein the human patient has AL amyloidosis characterized by the presence of amyloid light chain-type protein fibrils.

54. The lyophilized formulation of claim 53, wherein the AL amyloidosis is associated with a dyscrasia of the B lymphocyte lineage.

55. The lyophilized formulation of claim 54, wherein the dyscrasia is a malignancy.

56. The lyophilized formulation of claim 55, wherein the malignancy is multiple myeloma.

57. The lyophilized formulation of any one of claims 51-56, wherein the medicament is administrable with at least one second drug selected from the group consisting of melphalan, bortezomib, lenolidomide and carfilzomib.

58. The lyophilized formulation of claim 57, wherein the at least one second drug is bortezomib.

59. The lyophilized formulation of any one of claims 51-58, wherein the medicament is administrable to the human patient at a frequency of daily to annually.

60. The lyophilized formulation of any one of claims 51-59, wherein the medicament is administrable to the human patient once every twenty-eight days.

61. The lyophilized formulation of any one of claims 57-60, wherein the at least one second drug is administrable to the human patient at a frequency of daily to annually.

62. The lyophilized formulation of any one of claims 57-61, wherein the at least one second drug is administrable to the human patient once every seven days.

63. The lyophilized formulation of any one of claims 51-62, wherein the medicament is administrable to the human patient in a dose ranging from about 0.5 mg of the antibody per kg body weight of the human patient to about 30 mg of the antibody per kg of body weight of the human patient.

64. The lyophilized formulation of any one of claims 51-63, wherein the medicament is administrable to the human patient in a dose ranging from about 20 mg of the antibody per kg body weight of the human patient to about 30 mg of the antibody per kg of body weight of the human patient.

65. The lyophilized formulation of any one of claims 51-64, wherein the medicament is administrable to the human patient in a dose of about 25 mg of the antibody per kg body weight of the human patient.

66. The lyophilized formulation of any one of claims 51-65, wherein the medicament is administrable to the human patient in a dose ranging from about 10 mg of the antibody to about 5000 mg of the antibody.

67. The lyophilized formulation of any one of claims 51-66, wherein the medicament is administrable to the human patient in a dose ranging from about 30 mg of the antibody to about 2500 mg of the antibody.

68. A pharmaceutical product, comprising:

(a) a vial comprising an antibody, L-histidine, trehalose and polysorbate 20 in powder form;

(b) instructions for reconstitution of the antibody; and

(c) instructions for preparing the reconstituted antibody for infusion,

wherein:

(i) the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as any one of SEQ ID NOs: 14-16;

(ii) the vial comprises about 100 mg of the antibody, about 27.2 mg L-histidine, about 15.7 mg L-histidine HCl monohydrate, about 870.2 mg trehalose dehydrate, and about 2 mg polysorbate 20; and

(ii) the reconstitution instructions require reconstitution with water for injection to an extractable volume of 10 mL.

69. A pharmaceutical product, comprising:

(a) a vial comprising an antibody, L-histidine, trehalose and polysorbate 20 in powder form;

(b) instructions for reconstitution of the antibody; and

(c) instructions for preparing the reconstituted antibody for infusion,

wherein:

(i) the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as any one of SEQ ID NOs: 14-16;

(ii) the vial comprises 500 mg of the antibody, 27.2 mg L-histidine, 15.7 mg L-histidine HCl monohydrate, 870.2 mg trehalose dehydrate, and 2 mg polysorbate 20; and

(iii) the reconstitution instructions require reconstitution with water for injection to an extractable volume of 10 mL.