

WHAT IS CLAIMED IS:

1. An article of manufacture comprising a single dose vial containing a single fixed dose of a HER2 antibody comprising the variable light chain and variable heavy chain amino acid sequences of SEQ ID Nos. 7 and 8, respectively, wherein the fixed dose is about 600 mg or about
5 1200 mg.
2. The article of manufacture of claim 1, wherein the HER2 antibody is pertuzumab.
3. The article of manufacture of claim 2 comprising two single dose vials, wherein a first vial contains a single fixed dose of about 1200 mg of pertuzumab, and a second vial contains a single fixed dose of about 600 mg of pertuzumab.
- 10 4. The article of manufacture of claim 2 comprising two single dose vials, wherein the first vial contains a single fixed dose of about 600 mg of pertuzumab and the second vial contains a single fixed dose of about 600 mg of trastuzumab.
5. The article of manufacture of claim 2 comprising two single dose vials, wherein the first vial contains a single fixed dose of about 1200 mg of pertuzumab and a second vial comprising a
15 single fixed dose of 600 mg of trastuzumab.
6. The article of manufacture of any one of claims 1-5 wherein at least one of said single dose vials contains said fixed dose(s) in a liquid formulation for subcutaneous administration.
7. The article of manufacture of claim 6, wherein each of said single dose vials contains said fixed dose(s) in a liquid formulation for subcutaneous administration.
- 20 8. The article of manufacture of claim 6 or claim 7 wherein said liquid formulation further comprises a hyaluronidase enzyme.
9. The article of manufacture of claim 8 wherein the hyaluronidase enzyme is recombinant human hyaluronidase (rHuPH20).
10. The article of manufacture of claim 9 wherein the rHuPH20 is present in an amount
25 sufficient to result in an increase in the dispersion of the pertuzumab or trastuzumab contained in the same liquid formulation during subcutaneous administration.
11. The article of manufacture of claim 10, wherein the rHuPH20 is present in the trastuzumab containing liquid formulation at a concentration of between about 150 U/ml and 16,000 U/ml.
- 30 12. The article of manufacture of claim 11, wherein the rHuPH20 is present in the trastuzumab containing liquid formulation at a concentration of between about 600 U/ml and about 16,000 U/ml.
13. The article of manufacture of claim 12, wherein the rHuPH20 is present in the trastuzumab containing liquid formulation at a concentration of between about 1,000 U/ml and about

2,000 U/ml.

14. The article of manufacture of claim 13, wherein the rHuPH20 is present in the trastuzumab containing liquid formulation at a concentration of about 2,000 U/ml.

15. The article of manufacture of any one of claims 10 to 14, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of at least about 600 U/mL.

16. The article of manufacture of claim 15, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of between about 600 U/ml and about 2,000 U/ml.

17. The article of manufacture of claim 16, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of about 600 U/mL.

18. The article of manufacture of claim 16, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of about 667 U/ml.

19. The article of manufacture of claim 16, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of about 1,000 U/mL.

20. The article of manufacture of claim 16, wherein the rHuPH20 is present in the pertuzumab containing liquid formulation at a concentration of about 2,000 U/mL.

21. The article of manufacture of claim 2, wherein said single dose vial further comprises a single fixed dose of trastuzumab.

22. The article of manufacture of claim 21 wherein the single fixed dose of pertuzumab and the single fixed dose of trastuzumab is contained in a single liquid formulation for subcutaneous administration.

23. The article of manufacture of claim 22 wherein said liquid formulation contains a single fixed dose of about 600 mg of pertuzumab and a single fixed dose of about 600 mg of trastuzumab.

24. The article of manufacture of claim 22 wherein said liquid formulation contains a single fixed dose of about 1200 mg of pertuzumab and a single fixed dose of about 600 mg of trastuzumab.

25. The article of manufacture of any one of claims 22-24, wherein said liquid formulation further comprises a hyaluronidase enzyme.

26. The article of manufacture of claim 25, wherein said hyaluronidase enzyme is recombinant human hyaluronidase (rHuPH20).

27. The article of manufacture of claim 26, wherein the rHuPH20 is present in said liquid formulation in an amount sufficient to result in an increase in the dispersion of the pertuzumab

and trastuzumab contained in the same liquid formulation during subcutaneous administration.

28. The article of manufacture of claim 27, wherein the rHuPH20 is present in said liquid formulation at a concentration of at least about 600 U/mL.

29. The article of manufacture of claim 28, wherein the rHuPH20 is present in said
5 liquid formulation at a concentration of between about 600 U/ml and about 2,000 U/ml.

30. The article of manufacture of claim 29, wherein the rHuPH20 is present in said liquid formulation at a concentration of about 1,000 U/mL.

31. The article of manufacture of any one of claims 1 to 3 further comprising a package insert instructing the user to administer the fixed dose(s) subcutaneously to a patient with HER2
10 positive cancer.

32. The article of manufacture of any one of claims 4 to 20 further comprising a package insert instructing the user to administer the fixed doses of pertuzumab and trastuzumab subcutaneously to a patient with HER2 positive cancer.

33. The article of manufacture of claim 32 wherein the package insert further instructs
15 the user to co-administer the fixed dose pertuzumab and the fixed dose of trastuzumab subcutaneously as two separate subcutaneous injections.

34. The article of manufacture of claim 32 wherein the package insert further instructs the user to administer the fixed dose pertuzumab co-mixed with the fixed-dose trastuzumab, as a single subcutaneous injection.

20 35. The article of manufacture of any one of claims 21 to 31 further comprising a package insert with instructions to administer the fixed doses of pertuzumab and trastuzumab subcutaneously to a patient with HER2 positive cancer.

36. The article of manufacture of any one of claims 31-35, wherein the HER2 positive cancer is selected from the group consisting of breast cancer, peritoneal cancer, fallopian tube cancer,
25 lung cancer, colorectal cancer, biliary cancer and bladder cancer.

37. The article of manufacture of claim 36, wherein the HER2 positive cancer is early breast cancer (EBC) or metastatic breast cancer (MBC).

38. An article of manufacture comprising a 10-mL or 20-mL vial holding a single fixed dose of a HER2 antibody comprising the variable light and variable heavy amino acid sequences in
30 SEQ ID Nos. 7 and 8, respectively, wherein the fixed dose is about 600 mg or about 1200 mg of the HER2 antibody, and a package insert instructing the user to administer the fixed dose subcutaneously to a patient with HER2 positive cancer.

39. The article of manufacture of claim 38 wherein the HER2 antibody is pertuzumab.

40. The article of manufacture of claim 39, wherein the fixed dose of pertuzumab is

contained in a liquid formulation for subcutaneous administration.

41. The article of manufacture of claim 40, wherein said liquid formulation comprises the pertuzumab at a concentration of about 100-150 mg/mL.

42. The article of manufacture of claim 41, wherein said liquid formulation comprises the pertuzumab at a concentration of about 120 mg/mL.

43. The article of manufacture of any one of claims 40-42, wherein said liquid formulation further comprises recombinant human hyaluronidase (rHuPH20) in amount sufficient to result in an increase in the dispersion of the pertuzumab during subcutaneous administration.

44. The article of manufacture of claim 43, wherein the liquid formulation contains the rHuPH20 at a concentration of about 2,000 U/mL.

45. The article of manufacture of claim 43, wherein the liquid formulation contains the rHuPH20 at a concentration of about 1,000 U/mL.

46. The article of manufacture of any one of claims 40-45 further comprising one of more excipients selected from the group consisting of buffering agents, stabilizers and surfactants.

47. The article of manufacture of claim 46, wherein the buffering agent is suitable to adjust the pH to about 5.0 to 6.0.

48. The article of manufacture of claim 47, wherein the buffering agent is a histidine buffer.

49. The article of manufacture of claim 48, wherein the histidine buffer is L-histidine acetate.

50. The article of manufacture of claim 49, wherein the pH is about 5.5 to 5.7.

51. The article of manufacture of claim 50, wherein the pH is about 5.5.

52. The article of manufacture of any one of claims 46-51, wherein the stabilizer comprises sucrose.

53. The article of manufacture of claim 53, wherein the stabilizer further comprises methionine.

54. The article of manufacture of claim 52 or claim 53, wherein the stabilizer further comprises trehalose.

55. The article of manufacture of any one of claims 46-54, wherein the surfactant is polysorbate 20.

56. An aqueous formulation for subcutaneous administration comprising pertuzumab at a concentration of about 120 mg/mL, rHuPH20 at a concentration of about 1000-2000 U/mL, an L-histidine buffer to adjust to pH to about 5.5-5.7, sucrose, methionine and polysorbate 20.

57. The aqueous solution of claim 56, wherein the rHuPH20 is present at a concentration

of about 1000 U/mL.

58. The aqueous solution of claim 56, wherein the rHuPH20 is present at a concentration of about 2000 U/mL.

59. The aqueous solution of any one of claims 56-58, wherein the pH is 5.7.

5 60. A liquid subcutaneous pharmaceutical composition comprising a fixed dose of pertuzumab and a fixed dose of trastuzumab co-formulated in an aqueous solution further comprising rHuPH20, a buffering agent suitable to adjust the pH to about 5.0 to 6.0, a stabilizer and a surfactant.

61. The liquid subcutaneous pharmaceutical composition of claim 60, wherein the buffering agent is a histidine buffer.

10 62. The liquid subcutaneous pharmaceutical composition of claim 61 wherein the buffering agent is L-histidine acetate.

63. The liquid subcutaneous pharmaceutical composition of any one of claims 60-62, wherein the pH is 5.5-5.7.

15 64. The liquid subcutaneous pharmaceutical composition of claim 63, wherein the pH is 5.5 or 5.7.

65. The liquid subcutaneous pharmaceutical composition of claim 63, wherein the pH is 5.5.

66. The liquid pharmaceutical composition of any one of claims 60-65, comprising sucrose as a stabilizer.

20 67. The liquid pharmaceutical composition of claim 66 further comprising methionine as a stabilizer.

68. The liquid pharmaceutical composition of claim 66 further comprising trehalose as a stabilizer.

25 69. A liquid pharmaceutical composition comprising 600 mg pertuzumab at a concentration of 60 mg/ml, 600 mg trastuzumab at a concentration of 60 mg/ml, 1,000 U/mL rHuPH20, 20 mM His-HCl pH 5.5, 105 mM trehalose, 100 mM sucrose, 0.04% polysorbate 20, 10 mM methionine, and sterile water for injection up to a total volume of 10 ml.

70. The liquid pharmaceutical composition of claim 69 contained in a 15-ml vial.

30 71. A liquid pharmaceutical composition comprising 1,200 mg pertuzumab at a concentration of 80 mg/ml, 600 mg trastuzumab at a concentration of 40 mg/ml, 1,000 U/mL rHuPH20, 20 mM His-HCl pH 5.5, 70 mM trehalose, 133 mM sucrose, 0.04% polysorbate 20, 10 mM methionine, and sterile water for injection up to a total volume of 15 ml.

72. The liquid pharmaceutical composition of claim 71 contained in a 20-ml vial.

73. An article of manufacture comprising a liquid pharmaceutical composition of any

one of claims 69-72.

74. The article of manufacture of claim 73 further comprising a package insert with instructions to subcutaneously administer the liquid pharmaceutical composition contained therein to a human subject with HER2 positive cancer.

5 75. The article of manufacture of claim 74, wherein the HER2 positive cancer is selected from the group consisting of breast cancer, peritoneal cancer, fallopian tube cancer, lung cancer, colorectal cancer, biliary cancer and bladder cancer.

76. The article of manufacture of claim 75, wherein the cancer is breast cancer.

77. The article of manufacture of claim 76, wherein the breast cancer is early breast
10 cancer (EBC) or metastatic breast cancer (MBC).

78. A method for treating cancer comprising subcutaneously administering to a human subject with a HER2 positive cancer one or more fixed dose(s) of a HER2 antibody comprising the variable light and variable heavy amino acid sequences in SEQ ID Nos. 7 and 8, respectively, in an amount effective to treat the cancer, wherein the fixed dose is about 600 mg and/or about 1200 mg.

15 79. The method of claim 78, wherein the HER2 antibody is pertuzumab.

80. The method of claim 79, comprising administering to said human subject pertuzumab at a fixed loading dose of about 1200 mg followed by at least one maintenance dose of about 600 mg.

81. The method of claim 80, wherein the administration of the loading dose is followed
20 by administration of multiple maintenance doses.

82. The method of claim 80 or 81 wherein the first maintenance dose of pertuzumab is administered to said human subject approximately two weeks or approximately three weeks after administration of the loading dose of pertuzumab.

83. The method of any one of claims 80-82, wherein the fixed doses of pertuzumab are
25 administered to said human subject approximately every 2 weeks or approximately every 3 weeks.

84. The method of claim 83 wherein the fixed doses of pertuzumab are administered approximately every 3 weeks.

85. The method of any one of claims 78-84, wherein the cancer is HER2 positive cancer.

86. The method of claim 85, wherein the cancer is selected from the group consisting of
30 breast cancer, peritoneal cancer, fallopian tube cancer, lung cancer, colorectal cancer, biliary cancer and bladder cancer.

87. The method of claim 86, wherein the cancer is breast cancer.

88. The method of claim 87, wherein the cancer is early breast cancer (EBC) or metastatic breast cancer (MBC).

89. The method of any one of claims 78-88, comprising administering a second therapeutic agent to the patient.
90. The method of claim 89, wherein the second therapeutic agent is a different HER2 antibody.
- 5 91. The method of claim 90, wherein the second therapeutic agent is trastuzumab.
92. The method of claim 91, wherein the fixed dose pertuzumab is administered subcutaneously in combination with subcutaneously administered trastuzumab.
93. The method of claim 92, wherein the fixed dose pertuzumab and the trastuzumab are co-administered subcutaneously as two separate subcutaneous injections.
- 10 94. The method of claim 92, wherein the fixed dose pertuzumab is co-mixed with fixed dose trastuzumab, and administered as a single subcutaneous injection.
95. The method of claim 92 wherein fixed dose pertuzumab and fixed dose trastuzumab are administered as a single co- formulation for subcutaneous administration.
96. The method of claim 95, wherein the co-formulation is a liquid pharmaceutical composition of any one of claims 69-72.
- 15 97. The method of claim 89, wherein the further therapeutic agent is a chemotherapeutic agent.
98. The method of claim 97, wherein the chemotherapeutic agent is selected from the group consisting of taxanes and anthracyclines.
- 20 99. The method of claim 98, wherein the taxane is paclitaxel or docetaxel.
100. The method of claim 98 wherein the anthracycline comprises daunorubicin, doxorubicin, or epirubicin.