WHAT IS CLAIMED IS:

1. Use of a combination therapy in the manufacture of a medicament for treating or ameliorating the effects of a HER2 positive cancer in a subject, wherein the combination therapy comprises an anti-HER2 antibody and tucatinib, and

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

2. Use of an anti-HER2 antibody and tucatinib in the manufacture of a medicament for combination therapy to treat a HER2 positive cancer in a subject;

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

3. Use of an anti-HER2 antibody in the manufacture of a first medicament and use of tucatinib in the manufacture of a second medicament;

wherein the first and second medicaments are to be used in combination therapy to treat a HER2 positive cancer in a subject; and

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

4. Use of tucatinib in the manufacture of a medicament for use in combination therapy for treating disease a HER2 positive cancer in a subject;

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof;

and wherein said medicament is to be administered in combination with an anti-HER2 antibody.

5. The use of any one of claims 1-4, wherein the combination therapy further comprises a chemotherapeutic agent.

6. The use of claim 5, wherein the chemotherapeutic agent is an antimetabolite.

7. The use of claim 6, wherein the antimetabolite is a member selected from the group consisting of capecitabine, carmofur, doxidluridine, fluorouracil, tegafur, and a combination thereof.

8. The use of claim 7, wherein the antimetabolite is capecitabine.

9. The use of any one of claims 1-8, wherein the cancer is selected from the group consisting of colorectal cancer, esophageal cancer, gastric cancer, cholangiocarcinoma, non-small cell lung cancer, bladder cancer, and biliary cancer, and a combination thereof.

10. The use of any one of claims 1-9, wherein the cancer is an unresectable locally advanced cancer or a metastatic cancer.

11. The use of any one of claims 1-10, wherein the cancer is colorectal cancer, gastric cancer, lung cancer, biliary cancers, or esophageal cancer.

12. The use of any one of claims 1-11, wherein the subject had prior treatment with trastuzumab, pertuzumab, and T-DM1.

13. The use of any one of claims 1-11, wherein the anti-HER2 antibody is a member selected from the group consisting of trastuzumab, pertuzumab, ado-trastuzumab emtansine, margetuximab, and a combination thereof.

14. The use of any one of claims 1-13, wherein the anti-HER2 antibody is trastuzumab.

15. The use of any one of claims 1-13, wherein the anti-HER2 antibody is a combination of trastuzumab and pertuzumab.

16. The use of any one of claims 10-15, wherein the antimetabolite is capecitabine.

17. The use of any one of claims 1-16, wherein the anti-HER2 antibody is to be administered before, during, or after the administration of tucatinib.

18. The use of any one of claims 1-17, wherein the cancer comprises a cell that has a wild-type *KRAS* exon 2 genotype.

19. The use of any one of claims 1-18, wherein the cancer comprises a cell that has a wild-type *NRAS* genotype.

20. The use of any one of claims 1-19, wherein the cancer comprises a cell that has a wild-type *BRAF* genotype.

21. The use of any one of claims 1-20, wherein the subject has a cancer which is relapsed or refractory to a standard of care.

22. The use of any one of claims 1-21, wherein treating the subject results in a tumor growth inhibition (TGI) index of at least about 85%.

23. The use of any one of claims 1-22, wherein treating the subject results in a TGI index of about 100%.

24. The use of any one of claims 1-23, wherein the combination of the anti-HER2 antibody and tucatinib is synergistic.

25. The use of any one of claims 1-24, wherein treating the subject results in a TGI index that is greater than the TGI index observed when using an anti-HER2 antibody or tucatinib alone.

26. The use of any one of claims 1-25, wherein a dose of tucatinib is 3 to 7 mg per kg of the subject's body weight twice daily.

27. The use of any one of claims 1-25, wherein a dose of tucatinib is about 300 mg twice per day.

28. The use of any one of claims 1-27, wherein a dose of the anti-HER2 antibody is 6 mg to 8 mg per kg of the subject's body weight once every three weeks.

29. The use of any one of claims 1-27, wherein a dose of the anti-HER2 antibody is about 600 mg once every three weeks.

30. The use of any one of claims 1-29, wherein the tucatinib or the anti-HER2 antibody is to be administered orally.

31. The use of any one of claims 6-30, wherein the antimetabolite is to be administered orally.

32. The use of claim 31, wherein a dose of the antimetabolite is about 1,000 mg per m^2 of the subject's body surface area twice per day.

33. The use of claim 31 or 32, wherein the anti-HER2 antibody is to be administered intravenously or subcutaneously.

34. The use of any one of claims 1-33, wherein one or more therapeutic effects in the subject is improved after administration of the combination therapy relative to a baseline.

35. The use of claim 34, wherein the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival.

36. The use of claim 35, wherein the size of a tumor derived from the cancer is reduced by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% relative to the size of the tumor derived from the cancer before administration of the combination therapy.

37. The use of claim 35, wherein the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%.

38. The use of claim 35, wherein the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the combination therapy.

39. The use of claim 35, wherein the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the combination therapy.

40. The use of claim 35, wherein the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the combination therapy.

41. The use of any one of claims 1-40, wherein the subject has one or more adverse events and is to be further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events.

42. The use of any one of claims 1-41, wherein the subject is at risk of developing one or more adverse events and is to be further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events.

43. The use of claim 41 or 42, wherein the one or more adverse events is a grade 2 or greater adverse event.

44. The use of claim 43, wherein the one or more adverse events is a grade 3 or greater adverse event.

45. The use of any one of claims 41-44, wherein the one or more adverse events is a serious adverse event.

46. The use of any one of claims 1-45, wherein the subject is a human.

47. Use of a combination therapy comprising an anti-HER2 antibody and tucatinib in the manufacture of medicament for treating a HER2 positive cancer in a subject that has exhibited an adverse event after starting treatment with the combination therapy at an initial dosage level, wherein the medicament is to be administered at a reduced dosage level;

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

48. Use of an anti-HER2 antibody and tucatinib in the manufacture of a medicament for combination therapy for treating a HER2 positive cancer in a subject that has exhibited an adverse event after starting treatment with the combination therapy at an initial dosage level, wherein the medicament is to be administered at a reduced dosage level;

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

49. Use of an anti-HER2 antibody in the manufacture of a first medicament and use of tucatinib in the manufacture of a second medicament;

wherein the first and second medicaments are to be used in combination therapy for treating a HER2 positive cancer in a subject that has exhibited an adverse event after starting treatment with the combination therapy at an initial dosage level, wherein the medicament is to be administered at a reduced dosage level; and

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof.

50. Use of tucatinib in the manufacture of a medicament for use in combination therapy for treating a HER2 positive cancer in a subject that has exhibited an adverse event after starting treatment with the combination therapy at an initial dosage level, wherein the medicament is to be administered at a reduced dosage level;

wherein the HER2 positive cancer is selected from the group consisting of colorectal cancer, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, head and neck cancer, uterine cancer, cervical cancer, and a combination thereof;

and wherein said medicament is to be administered in combination with an anti-HER2 antibody.

51. The use of any one of claims 47-50, wherein the combination therapy further comprises a chemotherapeutic agent.

52. The use of claim 51, wherein the chemotherapeutic agent is an antimetabolite.

53. The use of claim 52, wherein the antimetabolite is a member selected from the group consisting of capecitabine, carmofur, doxidluridine, fluorouracil, tegafur, and a combination thereof.

54. The use of claim 53, wherein the antimetabolite is capecitabine.

55. The use of any one of claims 47-54, wherein the one or more adverse events is a grade 2 or greater adverse event.

56. The use of claim 55, wherein the one or more adverse events is a grade 3 or greater adverse event.

57. The use of any one of claims 47-56, wherein the adverse event is hepatotoxicity.

58. The use of any one of claims 47-56, wherein the adverse event is left ventricular dysfunction.

59. The use of any one of claims 47-56, wherein the adverse event is prolongation of the QTc interval.

60. The use of any one of claims 47-59, wherein the cancer is an unresectable locally advanced cancer or a metastatic cancer.

61. The use of any one of claims 47-60, wherein the cancer is colorectal cancer, gastric cancer, lung cancer, biliary cancers, or esophageal cancer.

62. The use of any one of claims 47-61, wherein the subject had prior treatment with trastuzumab, pertuzumab, and T-DM1.

63. The use of any one of claims 47-62, wherein the initial dosage level of tucatinib is about 300 mg twice daily.

64. The use of any one of claims 47-63, wherein the reduced dosage level of tucatinib is about 250 mg twice daily.

65. The use of any one of claims 47-64, wherein the reduced dosage level of tucatinib is about 200 mg twice daily.

66. The use of any one of claims 47-64, wherein the reduced dosage level of tucatinib is about 150 mg twice daily.

67. A pharmaceutical composition comprising an anti-HER2 antibody, tucatinib, a chemotherapeutic agent, and a pharmaceutically acceptable carrier.

68. The pharmaceutical composition of claim 67, wherein the anti-HER2 antibody is a member selected from the group consisting of trastuzumab, pertuzumab, ado-trastuzumab emtansine, margetuximab, and a combination thereof.

69. The pharmaceutical composition of claim 67 or 68, wherein the anti-HER2 antibody is trastuzumab.

70. The pharmaceutical composition of claim 67 or 68, wherein the anti-HER2 antibody is a combination of trastuzumab and pertuzumab.

71. The pharmaceutical composition of any one of claims 67-70, wherein the chemotherapeutic agent is capecitabine.

72. A kit for treating or ameliorating the effects of a HER2 positive cancer in a subject, the kit comprising the pharmaceutical composition of any one of claims 67-71.

73. The kit of claim 72, further comprising instructions for use.

74. The kit of claim 72 or 73, further comprising one or more reagents.