CLAIMS

What is claimed is:

1. A method for treating cancer in a subject comprising administering a therapeutically effective amount of tucatinib, or salt or solvate thereof, to the subject, wherein the cancer has been determined to express a mutant form of HER2.

2. A method for treating cancer in a subject comprising administering a therapeutically effective amount of tucatinib, or salt or solvate thereof, to the subject, wherein the cancer expresses a mutant form of HER2.

3. The method of claim 1 or claim 2, wherein the mutant form of HER2 is determined by DNA sequencing.

4. The method of claim 1 or claim 2, wherein the mutant form of HER2 is determined by determining RNA sequencing.

5. The method of any one of claims 1-4, wherein the mutant form of HER2 is determined by nucleic acid sequencing.

6. The method of claim 5, wherein the nucleic acid sequencing is next-generation sequencing (NGS).

7. The method of claim 1 or claim 2, wherein the mutant form of HER2 is determined by polymerase chain reaction (PCR).

8. The method of any one of claims 1-7, wherein the mutant form of HER2 is determined by analyzing a sample obtained from the subject.

9. The method of claim 8, wherein the sample obtained from the subject is a cell-free plasma sample.

10. The method of claim 8, wherein the sample obtained from the subject is a tumor biopsy.

11. The method of any one of claims 1-10, wherein the cancer does not have HER2 amplification, and wherein the absence of HER2 amplification is determined by immunohistochemistry (IHC).

12. The method of any one of claims 1-10, wherein the cancer has a HER2 amplification score of 0 or 1+, and wherein the HER2 amplification score is determined by immunohistochemistry (IHC).

13. The method of any one of claims 1-11, wherein the cancer has less than a 2 fold increase in HER2 protein levels.

14. The method of any one of claims 1-13, wherein the mutant form of HER2 comprises at least one amino acid substitution, insertion, or deletion compared to the amino acid sequence of SEQ ID NO:1.

15. The method of any one of claims 1-14, wherein the mutation in HER2 is an activating mutation.

16. The method of any one of claims 1-15, wherein the mutant form of HER2 comprises the amino acid substitution L755S.

17. The method of any one of claims 1-16, wherein the mutant form of HER2 comprises the amino acid substitution V777L.

18. The method of any one of claims 1-17, wherein the mutant form of HER2 comprises the amino acid substitution S310Y.

19. The method of any one of claims 1-18, wherein the mutant form of HER2 comprises a G776 YVMA insertion (G776 ins YVMA).

20. The method of any one of claims 1-19, wherein the cancer is selected from the group consisting of gastric cancer, colorectal cancer, lung cancer, gall bladder cancer, and breast cancer.

21. The method of claim 20, wherein the lung cancer is non-small cell lung cancer.

22. The method of claim 20, wherein the breast cancer is a HER2 positive breast cancer.

23. The method of any one of claims 1-22, wherein the tucatinib, or salt or solvate thereof, is administered to the subject at a dose of about 150 mg to about 650 mg.

24. The method of claim 23, wherein the tucatinib, or salt or solvate thereof, is administered to the subject at a dose of about 300 mg.

25. The method of claim 23 or 24, wherein the tucatinib, or salt or solvate thereof, is administered once or twice per day.

26. The method of claim 25, wherein the tucatinib, or salt or solvate thereof, is administered to the subject at a dose of about 300 mg twice per day.

27. The method of any one of claims 1-26, wherein the tucatinib is administered to the subject orally.

28. The method of any one of claims 1-27, further comprising administering one or more additional therapeutic agents to the subject to treat the cancer.

29. The method of claim 28, wherein the one or more additional therapeutic agents is selected from the group consisting of capecitabine and an anti-HER2 antibody.

30. The method of claim 28, wherein the one or more additional therapeutic agents is capecitabine.

31. The method of claim 28, wherein the one or more additional therapeutic agents is trastuzumab.

32. The method of claim 28, wherein the one or more additional therapeutic agents are capecitabine and trastuzumab.

33. The method of claim 30 or 32, wherein the capecitabine is administered to the subject at a dose of about 500 mg/m^2 to about 1500 mg/m^2.

34. The method of claim 33, wherein the capecitabine is administered to the subject at a dose of about 1000 mg/m^2.

35. The method of claim 33 or 34, wherein the capecitabine is administered to the subject orally.

36. The method of any one of claims 32-35, wherein the capecitabine is administered to the subject twice per day.

37. The method of claim 31 or 32, wherein the trastuzumab is administered to the subject at a dose of about 400 mg to about 800 mg.

38. The method of claim 37, wherein the trastuzumab is administered to the subject at a dose of about 600 mg.

39. The method of claim 37 or 38, wherein the trastuzumab is administered to the subject subcutaneously.

40. The method of claim 31 or 32, wherein the trastuzumab is administered to the subject intraperitoneally.

41. The method of claim 31 or 32, wherein the trastuzumab is administered to the subject at a dose of about 4 mg/kg to about 10 mg/kg.

42. The method of claim 41, wherein the trastuzumab is administered to the subject at a dose of about 6 mg/kg.

43. The method of claim 41, wherein the trastuzumab is administered to the subject at a dose of about 8 mg/kg.

44. The method of claim 41, wherein the trastuzumab is administered to the subject at an initial dose of about 8 mg/kg followed by subsequent doses of about 6 mg/kg.

45. The method of any one of claims 41-44, wherein the trastuzumab is administered intravenously.

46. The method of any one of claims 37-45, wherein the trastuzumab is administered once about every 1 week, once about every 2 weeks, once about every 3 weeks, or once about every 4 weeks.

47. The method of claim 46, wherein the trastuzumab is administered once about every 3 weeks.

48. The method of claim 47, wherein the tucatinib, capecitabine and trastuzumab are administered to the subject on a 21 day treatment cycle.

49. The method of claim 48, wherein the tucatinib is administered to the subject twice per day on each day of the 21 day treatment cycle.

50. The method of claim 48 or 49, wherein the capecitabine is administered to the subject twice per day on each of days 1-14 of the 21 day treatment cycle.

51. The method of any one of claims 48-50, wherein the trastuzumab is administered to the subject once per 21 day treatment cycle.

52. The method of claim 51, wherein the dose of trastuzumab during the first 21 day treatment cycle is 8 mg/kg and the dose of trastuzumab during the subsequent 21 day treatment cycles is 6 mg/kg.

53. The method of any one of claims 1-52, wherein treating the subject results in a tumor growth inhibition (TGI) index of at least about 85%.

54. The method of any one of claims 1-52, wherein treating the subject results in a TGI index of about 100%.

55. The method of any one of claims 1-54, wherein one or more therapeutic effects in the subject is improved after administration of tucatinib to the subject relative to a baseline.

56. The method of claim 55, 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.

57. The method of any one of claims 1-56, 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 tucatinib to the subject.

58. The method of any one of claims 1-57, 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%.

59. The method of any one of claims 1-58, 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 tucatinib to the subject.

60. The method of any one of claims 1-59, 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 tucatinib to the subject.

61. The method of any one of claims 1-60, wherein the duration of response to tucatinib 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 tucatinib to the subject.

62. The method of any one of claims 1-61, wherein the subject is a human.

63. Use of a therapeutically effective amount of tucatinib, or salt or solvate thereof, for the manufacture of a medicament for use in the method for treating cancer of any one of claims 1-62.

64. Tucatinib, or a salt or solvate thereof, for use in the method for treating cancer of any one of claims 1-62.

65. A pharmaceutical composition for treating cancer in a subject, the composition comprising tucatinib, or salt or solvate thereof, wherein the composition is for use in the method of any one of claims 1-62.

66. A kit comprising tucatinib, or salt or solvate thereof, and instructions for using the kit in the method of any one of claims 1-62.