**WHAT IS CLAIMED IS:**

1. ~~A method of treating cancer in a subject comprising administering an effective amount of poziotinib to the subject~~A use of an effective amount of poziotinib in the manufacture of a medicament for treating cancer in a subject, wherein the subject has a tumor that has been determined to have one or more EGFR exon 20 insertion mutations, wherein the mutations comprise an insertion of 1–6 amino acids between amino acids 763-778.

~~2. The method of claim 1, wherein the one or more EGFR exon 20 mutations are further defined as EGFR 20 insertion mutations.~~

~~3. The method of claim 1, wherein the one or more EGFR exon 20 mutations comprise a point mutation, insertion, and/or deletion of 3-18 nucleotides between amino acids 763-778.~~

2~~4~~. The use~~method~~ of claim 1, wherein the subject has been determined to have 2, 3, or 4 EGFR exon 20 insertion mutations.

3~~5~~. The use~~method~~ of claim 1~~3~~, wherein the one or more EGFR exon 20 insertion mutations are at one or more residues selected from the group consisting of A763, A767, S768, V769, D770, N771, P772, and H773.

4~~6~~. The use~~method~~ of claim 1, wherein the subject has been determined to not have a C797 or T790M EGFR mutation~~an EGFR mutation at residue C797~~.

5~~7~~. The use~~method~~ of claim 1, wherein the one or more exon 20 insertion mutations are selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, N771del insGY, N771del insFH, and N771dupNPH.

6~~8~~. The use~~method~~ of claim 1, wherein the exon 20 insertion mutation is D770insNPG.

~~9. The method of claim 1, wherein the subject was determined to have an EGFR exon 20 mutation by analyzing a genomic sample from the patient.~~

~~10. The method of claim 10, wherein the genomic sample is isolated from saliva, blood, urine, normal tissue, or tumor tissue.~~

~~11. The method of claim 1, wherein the presence of an EGFR exon 20 mutation is determined by nucleic acid sequencing or PCR analyses~~

712. The usemethod of claim 1, further comprising administering an additional anti-cancer therapy.

813. The usemethod of claim 712, wherein the additional anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or immunotherapy.

914. The usemethod of claim 712, wherein the poziotinib and/or anti-cancer therapy are administered intravenously, subcutaneously, intraosseously, orally, transdermally, in sustained release, in controlled release, in delayed release, as a suppository, or sublingually.

~~15. The method of claim 12, wherein administering the poziotinib and/or anti-cancer therapy comprises local, regional or systemic administration.~~

106. The usemethod of claim 712, wherein the poziotinib and/or anti-cancer therapy are administered dailytwo or more times.

117. The usemethod of claim 1, wherein the cancer is non-small cell lung cancer, oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer.

128. The usemethod of claim 1, wherein the exon 20 insertion mutation is V769insASVcancer is non-small cell lung cancer.

139. The usemethod of claim 1, wherein the exon 20 insertion mutation is A763insFQEApatient is human.

14~~20~~. The use of claim 1, wherein the exon 20 insertion mutation is D770insSVD~~A pharmaceutical composition comprising poziotinib for use in a subject determined to have one or more EGFR exon 20 mutations~~.

~~2~~15. The use of claim 7, wherein the additional anti-cancer therapy is an mTOR inhibitor~~The composition of claim 20, wherein the one or more EGFR exon 20 mutations are further defined as EGFR 20 insertion mutations~~.

16~~22~~. The use of claim 15, wherein the mTOR inhibitor is selected from the group consisting of rapamycin, temsirolimus, everolimus, ridaforolimus and MLN4924~~The composition of claim 20, wherein the one or more EGFR exon 20 mutations comprise a point mutation, insertion, and/or deletion of 3-18 nucleotides between amino acids 763-778~~.

17~~23~~. The use of claim 15, wherein the mTOR inhibitor is everolimus~~The composition of claim 20, wherein the subject has been determined to have 2, 3, or 4 EGFR exon 20 mutations~~.

18~~24~~. The use of claim 7, wherein the additional anti-cancer therapy is trastuzumab emtansine~~The composition of claim 22, wherein the one or more EGFR exon 20 insertion mutations are at one or more residues selected from the group consisting of A763, A767, S768, V769, D770, N771, P772, and H773~~.

~~25. The composition of claim 20, wherein the subject has been determined to not have an EGFR mutation at residue C797.~~

~~26. The composition of claim 20, wherein the one or more exon 20 mutations are selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, N771del insGY, N771del insFH, and N771dupNPH.~~

~~27. The composition of claim 20, wherein the subject is being treated with an anti-cancer therapy.~~

~~28. A method of predicting a response to poziotinib alone or in combination with a second anti-cancer therapy in a subject having a cancer comprising detecting an EGFR exon 20 mutation in a genomic sample obtained from said patient, wherein if the sample is positive for the presence of the EGFR exon 20 mutation, then the patient is predicted to have a favorable response to the poziotinib alone or in combination with an anti-cancer therapy.~~

~~29. The method of claim 28, wherein the EGFR exon 20 mutation is further defined as an exon 20 insertion mutation.~~

~~30. The method of claim 28, wherein the genomic sample is isolated from saliva, blood, urine, normal tissue, or tumor tissue.~~

~~31. The method of claim 28, wherein the presence of a EGFR exon 20 mutation is determined by nucleic acid sequencing or PCR analyses.~~

~~32. The method of claim 31, wherein the EGFR exon 20 mutation comprises a point mutation, insertion, and/or deletion of 3-18 nucleotides between amino acids 763-778.~~

~~33. The method of claim 32, wherein the EGFR exon 20 mutation is at residue A763, H773, A767, S768, V769, D770, N771, and/or D773.~~

~~34. The method of claim 28, wherein the EGFR exon 20 mutation is selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, H773insNPH, N771del insGY, N771del insFH, and N771dupNPH.~~

~~35. The method of claim 28, wherein a favorable response to poziotinib alone or in combination with an anti-cancer therapy comprises reduction in tumor size or burden, blocking of tumor growth, reduction in tumor-associated pain, reduction in cancer associated pathology, reduction in cancer associated symptoms, cancer non-progression, increased disease free interval, increased time to progression, induction of remission, reduction of metastasis, or increased patient survival.~~

~~36. The method of claim 28, further comprising administering poziotinib alone or in combination with a second anti-cancer therapy to said patient predicted to have a favorable response.~~

~~37. A method of treating cancer in a subject comprising administering an effective amount of poziotinib or afatinib to the subject, wherein the subject has been determined to have one or more HER2 exon 20 mutations selected from the group consisting of A775insV G776C, A775insYVMA, G776V, G776C V777insV, G776C V777insC, G776del insVV, G776del insVC, and P780insGSP.~~

~~38. The method of claim 37, wherein the one or more HER2 exon 20 mutations further comprise one or more point mutations, insertions, and/or deletions of 3-18 nucleotides between amino acids 770-785.~~

~~39. The method of claim 38, wherein the one or more HER2 exon 20 mutations are at residue A775, G776, S779, and/or P780.~~

~~40. The method of claim 37, wherein the HER exon 20 mutation is further defined as a HER2 exon 20 insertion mutation.~~

41. The method of claim 40, wherein the HER exon 20 insertion mutation is A775insYVMA.

42. The method of claim 37, further comprising administering an mTOR inhibitor.

43. The method of claim 42, wherein the mTOR inhibitor is rapamycin, temsirolimus, everolimus, ridaforolimus or MLN4924.

44. The method of claim 42, wherein the mTOR inhibitor is everolimus.

45. The method of claim 42, wherein the poziotinib or afatinib and/or the mTOR inhibitor are administered intravenously, subcutaneously, intraosseously, orally, transdermally, in sustained release, in controlled release, in delayed release, as a suppository, or sublingually.

46. The method of claim 37, wherein the subject was determined to have a HER2 exon 20 mutation by analyzing a genomic sample from the patient.

47. The method of claim 46, wherein the genomic sample is isolated from saliva, blood, urine, normal tissue, or tumor tissue.

48. The method of claim 37, wherein the presence of an HER2 exon 20 mutation is determined by nucleic acid sequencing or PCR analyses.

49. The method of claim 37, further comprising administering an additional anti-cancer therapy.

50. The method of claim 37, wherein the additional anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or immunotherapy.

51. The method of claim 37, wherein the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head

~~and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer.~~

~~52. The method of claim 37, wherein the cancer is non-small cell lung cancer.~~

~~53. The method of claim 37, wherein the subject is human.~~

~~54. A pharmaceutical composition comprising poziotinib or afatinib for use in a subject determined to have one or more HER2 exon 20 mutations selected from the group consisting of A775insV G776C, A775insYVMA, G776C V777insC, G776del insVV, G776del insVC, and P780insGSP.~~

~~55. The composition of claim 54, wherein the HER2 exon 20 mutation is further defined as a HER2 exon 20 insertion mutation.~~

~~56. The composition of claim 54, wherein the HER2 exon 20 mutation further comprises one or more point mutations, insertions, and/or deletions of 3-18 nucleotides between amino acids 770-785.~~

~~57. The composition of claim 56, wherein the one or more HER2 exon 20 mutations are at residue A775, G776, S779, and/or P780.~~

~~58. The pharmaceutical composition of claim 49, wherein the patient is being treated with an anti-cancer therapy.~~

~~59. A method of predicting a response to poziotinib or afatinib alone or in combination with an anti-cancer therapy in a subject having a cancer comprising detecting an HER2 exon 20 mutation selected from the group consisting of A775insV G776C, A775insYVMA, G776C V777insC, G776del insVV, G776del insVC, and P780insGSP in a genomic sample obtained from said subject, wherein if the sample is positive for the presence of the HER2 exon 20 mutation, then the patient is predicted to have a favorable response to the poziotinib or afatinib alone or in combination with an anti-cancer therapy.~~

~~60. The method of claim 59, wherein the HER2 exon 20 mutation is further defined as a HER2 exon 20 insertion mutation.~~

61. The method of claim 59, wherein the genomic sample is isolated from saliva, blood, urine, normal tissue, or tumor tissue.

62. The method of claim 59, wherein the presence of a HER2 exon 20 mutation is determined by nucleic acid sequencing or PCR analyses.

63. The method of claim 59, wherein the anti-cancer therapy is an mTOR inhibitor.

64. The method of claim 59, wherein a favorable response to poziotinib or afatinib inhibitor alone or in combination with an anti-cancer therapy comprises reduction in tumor size or burden, blocking of tumor growth, reduction in tumor-associated pain, reduction in cancer associated pathology, reduction in cancer associated symptoms, cancer non-progression, increased disease free interval, increased time to progression, induction of remission, reduction of metastasis, or increased patient survival.

65. The method of claim 58, further comprising administering poziotinib or afatinib alone or in combination with a second anti-cancer therapy to said subject predicted to have a favorable response.

66. A composition comprising:

(a) nucleic acids isolated from human cancer cells; and

(b) a primer pair that can amplify at least a first portion of exon 20 of a human EGFR or HER2 coding sequence.

67. The composition of claim 66, further comprising a labeled probe molecule that can specifically hybridize to the first portion of exon 20 of the human EGFR or HER coding sequence when there is a mutation in the sequence.

68. The composition of claim 66, further comprising a thermostable DNA polymerase.

69. The composition of claim 66, further comprising dNTPS.

70. The composition of claim 67, wherein the labeled probe hybridizes to the first portion of exon 20 of the human EGFR coding sequence when there is a mutation selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, N771del insGY, N771del insFH, and N771dupNPH.

~~71. The composition of claim 67, wherein the labeled probe hybridizes to the first portion of exon 20 of the human HER2 coding sequence when there is a mutation selected from the group consisting of A775insV G776C, A775insYVMA, G776V, G776C V777insV, G776C V777insC, G776del insVV, G776del insVC, and P780insGSP.~~

~~72. An isolated nucleic acid encoding a mutant EGFR protein, wherein said mutant protein differs from wild-type human EGFR by one or more EGFR exon 20 mutations comprising a point mutation, insertion, and/or deletion of 3-18 nucleotides between amino acids 763-778.~~

~~73. The isolated nucleic acid of claim 72, wherein the one or more EGFR exon 20 mutations are at one or more residues selected from the group consisting of A763, A767, S768, V769, D770, N771, P772, and H773.~~

~~74. The isolated nucleic acid of claim 72, wherein the one or more exon 20 mutations are selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, N771del insGY, N771del insFH, and N771dupNPH.~~

~~75. The isolated nucleic acid of claim 72, wherein the nucleic acid comprises the sequence of SEQ ID NO:8, 9, 10, 11, or 12.~~

~~76. An isolated nucleic acid encoding a mutant HER2 protein, wherein said mutant protein differs from wild-type human HER2 by one or more HER2 exon 20 mutations comprising one or more point mutations, insertions, and/or deletions of 3-18 nucleotides between amino acids 770-785.~~

~~77. The isolated nucleic acid of claim 76, wherein the one or more HER2 exon 20 mutations are at residue A775, G776, S779, and/or P780.~~

~~78. The isolated nucleic acid of claim 76, wherein the one or more HER2 exon 20 mutations are selected from the group consisting of A775insV G776C, A775insYVMA, G776V, G776C V777insV, G776C V777insC, G776del insVV, G776del insVC, and P780insGSP.~~

~~79. The isolated nucleic acid of claim 76, wherein the nucleic acid comprises the sequence of SEQ ID NO:14, 15, 16, 17, or 18.~~