**WHAT IS CLAIMED IS:**

1. Use of an effective amount of poziotinib in the manufacture of a medicament for the treatment of cancer in a subject, wherein the medicament is to be administered to the subject, and wherein the subject has been determined to have one or more HER2 exon 21 mutations.

2. The use of claim 1, wherein the poziotinib is further defined as poziotinib hydrochloride salt.

3. The use of any one of claims 1-2, wherein the one or more HER2 exon 21 mutations comprise a point mutation, insertion, and/or deletion of 1-18 nucleotides between amino acids 832-883.

4. The use of any one of claims 1-3, wherein the subject has been determined to have 2, 3, or 4 HER exon 21 mutations.

5. The use of any one of claims 1-4, wherein the subject has been previously administered a tyrosine kinase inhibitor.

6. The use of claim 5, wherein the subject is resistant to the previously administered tyrosine kinase inhibitor.

7. The use of claim 3, wherein the one or more HER2 exon 21 mutations are at one or more residues selected from the group consisting of V842, R868, and L869.

8. The use of claim 3, wherein the one or more HER2 exon 21 mutations are at residues V842 and/or R868.

9. The use of any one of claims 1-8, wherein the subject has been determined to not have an EGFR mutation at residue C797.

10. The use of any one of claims 1-9, wherein the one or more HER2 exon 21 mutations are selected from the group consisting of V842I, R868W, and L869R.

11. The use of any one of claims 1-10, wherein the one or more HER2 exon 21 mutations are V842I and/or R868W.

12. The use of any one of claims 1-11, wherein the poziotinib is to be administered at a dose of 8 mg, 12 mg, or 16 mg.

13. The use of any one of claims 1-12, wherein an additional anti-cancer therapy is to be further administered to the subject.

14. The use of any one of claims 1-13, 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.

15. The use of any one of claims 1-14, wherein the cancer is non-small cell lung cancer.