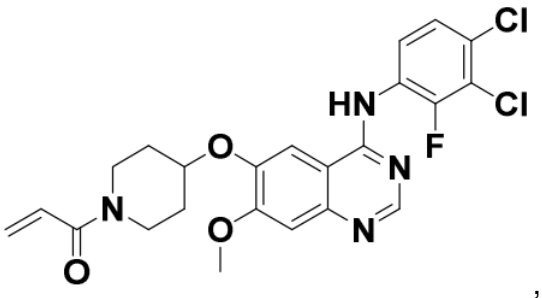
CLAIMS

What is claimed is:

1. A kit for treating cancer comprising a crystalline form derived from a compound of Chemical formula (1):

[Chemical formula (1)]



,

wherein the chemical purity of the crystalline form is greater than about 80%, and wherein the crystalline form is selected from the group consisting of

(a) a dihydrate ($2H_2O$) crystalline form of the compound of Chemical Formula (1) and the crystalline form has an X-ray powder diffraction (XRPD) pattern comprising peaks at diffraction angle 2θ values of 9.4° ± 0.2°, 13.0° ± 0.2° and 18.5° ± 0.2° when irradiated with a Cu-Kα light source;

(b) an anhydrous Form I of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2 values θ of 6.0° ± 0.2°, 18.3° ± 0.2° and 22.7° ± 0.2° when irradiated with a Cu-Kα light source;

(c) an anhydrous Form II of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2θ values of 4.9° ± 0.2°, 5.9° ± 0.2° and 11.8° ± 0.2° when irradiated with a Cu-Kα light source;

(d) a monohydrochloride monohydrate ($1HCl{\cdot}1H_2O$) crystalline form of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2θ values of 8.9° ± 0.2°, 13.4° ± 0.2°, 21.1° ± 0.2° and 23.5° ± 0.2° when irradiated with a Cu-Kα light source; and

(e) an anhydrous monohydrochloride crystalline form of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2 values θ of 9.5° ± 0.2°, 23.0° ± 0.2°, 23.2° ± 0.2° and 23.5° ± 0.2° when irradiated with a Cu-Kα light source.

2. The kit of claim 1, wherein the chemical purity of the crystalline form is greater than 95%.

3. The kit of claim 1, wherein the crystalline form is as described in (a).

4. The kit of claim 1, wherein the crystalline form is as described in (b).

5. The kit of claim 1, wherein the crystalline form is as described in (c).

6. The kit of claim 1, wherein the crystalline form is as described in (d).

7. The kit of claim 1, wherein the crystalline form is as described in (e).

8. The kit of claim 1, wherein the crystalline form is as described in (a), and wherein the crystalline form has a ^{13}C solid state nuclear magnetic resonance (ssNMR) spectrum comprising peaks at the following chemical shifts: 147.7 ± 0.5, 156.2 ± 0.5 and 165.4 ± 0.5 ppm.

9. The kit of claim 1, wherein the crystalline form is as described in (b), and wherein the crystalline form has a ^{13}C ssNMR spectrum comprising peaks at the following chemical shifts: 54.3 ± 0.5, 127.3 ± 0.5, 146.9 ± 0.5 and 156.7 ± 0.5 ppm.

10. The kit of claim 1, wherein the crystalline form is as described in (c), and wherein the crystalline form has a ^{13}C ssNMR spectrum comprising peaks at the following chemical shifts: 129.2 ± 0.5, 153.1 ± 0.5, 156.7 ± 0.5 and 165.2 ± 0.5 ppm.

11. The kit of claim 1, wherein the crystalline form is as described in (d), and wherein the crystalline form has a ^{13}C ssNMR spectrum comprising peaks at the following chemical shifts: 145.8 ± 0.5, 157.8 ± 0.5 and 164.5 ± 0.5 ppm.

12. The kit of claim 1, wherein the crystalline form is as described in (e), and wherein the crystalline form has a ^{13}C ssNMR spectrum comprising peaks at the following chemical shifts: 146.9 ± 0.5, 158.7 ± 0.5 and 163.0 ± 0.5 ppm.

13. The kit of claim 1, further comprising at least one cytotoxic agent and/or at least one molecularly targeted agent, as the active ingredient, wherein the at least one cytotoxic agent is selected from the group consisting of taxanes, base analogs, VEGF inhibitors, platinum-based antineoplastic drugs and vinca alkaloids, and wherein the at least one molecularly targeted agent is selected from the group consisting of at least one epidermal growth factor receptor (EGFR) family inhibitor.

14. The kit of claim 13, comprising the EGFR family inhibitor which is an anti-EGFR family antibody selected from the group consisting of trastuzumab, T-DM1, margetuximab cetuximab, matuzumab, panitumumab, necitumumab, and pertuzumab.

15. The kit of claim 13, comprising the VEGF inhibitor selected from the group consisting of pegaptanib, bevacizumab, ranibizumab, lapatinib, sorafenib, sunitinib, axitinib, pazopanib, aflibercept and ramucirumab.

16. The kit of claim 13, comprising the taxane selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

17. The kit of claim 13, comprising the base analog selected from the group consisting of 5-fluorouracil, 6-mercaptopurine, capecitabine, gemcitabine, pemetrexed, methotrexate, cladribine, cytarabine, doxifludine, floxuridine, fludarabine and decarbazine.

18. The kit of claim 13, comprising the platinum-based antineoplastic drug selected from the group consisting of cisplatin, carboplatin, dicycloplatin, eptaplatin, lobaplatin, miriplatin, nedaplatin, oxaliplatin, picoplatin, and satraplatin.

19. The kit of claim 13, comprising the vinca alkaloid selected from the group consisting of vinblastine, vincristine, vinflunine, vinorelbine, vincaminol, vinburnine, vineridine and vindesine

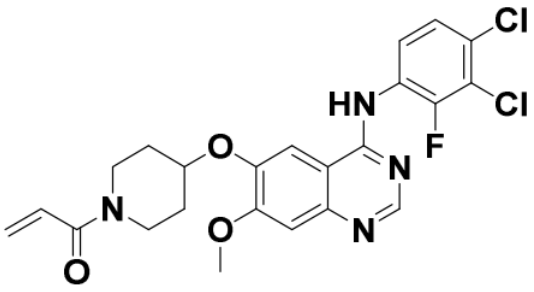
20. The kit of claim 13, wherein the EGFR family inhibitor is a mTOR inhibitor selected from the group consisting of zotarolimus, umirolimus, temsirolimus, sirolimus, sirolimus NanoCrystal, sirolimus TransDerm, sirolimus-PNP, everolimus, biolimus A9,

ridaforolimus, rapamycin, TCD-10023, DE-109, MS-R001, MS-R002, MS-R003, Perceiva, XL-765, quinacrine, PKI-587, PF-04691502, GDC-0980, dactolisib, CC-223, PWT-33597, P-7170, LY-3023414, INK-128, GDC-0084, DS-7423, DS-3078, CC-115, CBLC-137, AZD-2014, X-480, X-414, EC-0371, VS-5584, PQR-401, PQR-316, PQR-311, PQR-309, PF-06465603, NV-128, nPT-MTOR, BC-210, WAY-600, WYE-354, WYE-687, LOR-220, HMPL-518, GNE-317, EC-0565, CC-214, ABTL-0812, and pharmaceutically acceptable salts thereof or combinations thereof.

21. The kit of claim 13, comprising the cytotoxic agent selected from the group consisting of paclitaxel, cisplatin, 5-fluorouracil, vinorelbine and any combinations thereof.

22. The kit of claim 13, comprising the molecularly targeted agent selected from the group consisting of cetuximab, trastuzumab, T-DM1 and any combinations thereof.

23. Use of a crystalline form derived from a compound of Chemical formula (1) in the manufacture of a medicament for treating a neoplasm in a subject:



Formula I

wherein the chemical purity of the crystalline form is greater than about 80%, and wherein the crystalline form is selected from the group consisting of

(a) a dihydrate ($2H_2O$) of the compound of Chemical Formula (1) and the crystalline form has an X-ray powder diffraction (XRPD) pattern comprising peaks at diffraction angle 2θ values of 9.4° ± 0.2°, 13.0° ± 0.2° and 18.5° ± 0.2° when irradiated with a Cu-Kα light source;

(b) an anhydrous Form I of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2 values θ of 6.0° ± 0.2°, 18.3° ± 0.2° and 22.7° ± 0.2° when irradiated with a Cu-Kα light source;

(c) an anhydrous Form II of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2θ values of 4.9° ± 0.2°, 5.9° ± 0.2° and 11.8° ± 0.2° when irradiated with a Cu-Kα light source;

(d) a monohydrochloride monohydrate ($1HCl \cdot 1H_2O$) of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2θ values of 8.9° ± 0.2°, 13.4° ± 0.2°, 21.1° ± 0.2° and 23.5° ± 0.2° when irradiated with a Cu-Kα light source;

(e) an anhydrous monohydrochloride of the compound of Chemical Formula (1) having an XRPD pattern comprising peaks at diffraction angle 2 values θ of 9.5° ± 0.2°, 23.0° ± 0.2°, 23.2° ± 0.2° and 23.5° ± 0.2° when irradiated with a Cu-Kα light source.

24. Use of claim 23, wherein the neoplasm is non-small cell lung cancer, breast cancer, stomach cancer, colon cancer, pancreatic cancer, prostate cancer, myeloma, head and neck cancer, ovarian cancer, esophageal cancer, or metastatic cell carcinoma.

25. Use of claim 23, wherein the use further comprises at least one cytotoxic agent and/or at least one molecularly targeted agent, as the active ingredient, wherein the at least one cytotoxic agent is selected from the group consisting of taxanes, base analogs, platinum-based antineoplastic drugs and vinca alkaloids, and wherein the at least one molecularly targeted agent is selected from the group consisting of at least one epidermal growth factor receptor (EGFR) family inhibitor.