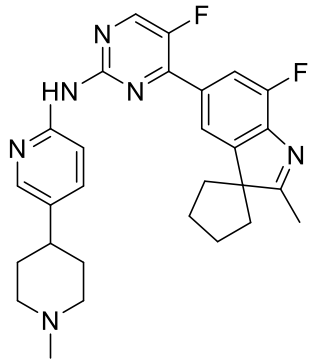
CLAIMS

1. A salt of the compound represented by Formula I:



Formula I

the salt is selected from fumarate, maleate, adipate or succinate.

2. The salt according to claim 1, wherein the molar ratio of fumarate ion, maleate ion, adipate ion or succinate ion to free base in the salt is each independently n:1, wherein n ≥ 0.5, preferably n is 0.5, 1 or 2, more preferably n is 1;

and/or, the salt comprises one or more crystal forms, preferably the salt is present in one crystal form or a mixture of multiple crystal forms, particularly preferably the salt is present in one crystal form; and/or, the salt contains solvent molecules， preferably the salt contains solvent molecules with a variable content, further preferably the salt contains water molecules, preferably water molecules with a variable content.

3. The salt according to claim 1 or 2, wherein the fumarate comprises one or more of the following crystal forms of fumarate, preferably the fumarate is present in any one of the following crystal forms of fumarate or a mixture of multiple crystal forms of the fumarate, and particularly preferably the fumarate is any one of the following crystal forms of fumarate:

the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2° at least comprises:

(1) characteristic diffraction peaks shown at 7.0°, 13.9°, 18.4°, 21.8°

and 24.1°; or

(2) characteristic diffraction peaks shown at 4.5°, 10.5°, 18.3°, 20.6° and 23.9°; or

(3) characteristic diffraction peaks shown at 5.9°, 14.4°, 18.6°, 23.6° and 23.9°;

preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2° at least comprises:

(1) characteristic diffraction peaks shown at 5.5°, 7.0°, 9.2°, 10.6°, 13.9°, 18.4°, 21.8° and 24.1°; or

(2) characteristic diffraction peaks shown at 4.5°, 8.9°, 10.5°, 17.9°, 18.3°, 20.6°, 22.5°, and 23.9°; or

(3) characteristic diffraction peaks shown at 5.9°, 14.4°, 17.6°, 18.6°, 21.6°, 23.6°, 23.9° and 28.4°;

more preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2° at least comprises:

(1) characteristic diffraction peaks shown at 5.5°, 7.0°, 9.2°, 10.6°, 13.9°, 15.7°, 17.2°, 18.4°, 21.8° and 24.1°; or

(2) characteristic diffraction peaks shown at 4.5°, 8.9°, 10.5°, 17.1°, 17.9°, 18.3°, 20.6°, 22.5°, 23.9°, and 27.5°; or

(3) characteristic diffraction peaks shown at 5.9°, 11.7°, 14.4°, 17.6°, 18.6°, 21.6°, 23.6°, 23.9°, 25.0° and 28.4°;

and particularly preferably, the crystal form of the fumarate has XRPD data and/or a XRPD pattern selected from any one of the following (1) to (3):

(1) XRPD data substantially as shown in Table 1; and/or a XRPD pattern substantially as shown in FIG. 2;

(2) XRPD data substantially as shown in Table 2; and/or a XRPD pattern substantially as shown in FIG. 5; and

(3) XRPD data substantially as shown in Table 3; and/or a XRPD

pattern substantially as shown in FIG. 8.

4. The salt according to claim 1 or 2, wherein the maleate comprises one or more of the following crystal forms of maleate, preferably the maleate is present in any one of the following crystal forms of maleate or a mixture of multiple crystal forms of the maleate, particularly preferably the maleate is any one of the following crystal forms of maleate:

the X-ray powder diffraction pattern of the crystal form of the maleate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 7.8º, 9.0º, 15.7º, 18.4º and 22.7º; or

(2) characteristic diffraction peaks shown at 5.7º, 13.7º, 17.9º, 18.9º and 23.6º;

preferably, the X-ray powder diffraction pattern of the crystal form of the maleate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 7.3º, 7.8º, 9.0º, 15.7º, 17.9º, 18.4º, 20.7º and 22.7º; or

(2) characteristic diffraction peaks shown at 5.7º, 13.7º, 17.6º, 17.9º, 18.9º, 21.9º, 23.6º and 24.8º;

more preferably, the X-ray powder diffraction pattern of the crystal form of the maleate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 7.3º, 7.8º, 9.0º, 13.6º, 15.7º, 17.9º, 18.4º, 20.7º, 22.7º, and 24.1º; or

(2) characteristic diffraction peaks shown at 5.7º, 13.7º, 14.1º, 17.2º, 17.6º, 17.9º, 18.9º, 21.9º, 23.6º and 24.8º;

particularly preferably, the crystal form of the maleate has XRPD data and/or a XRPD pattern selected from any one of the following (1) to (2):

(1) XRPD data substantially as shown in Table 4; and/or a XRPD pattern substantially as shown in FIG. 11; and

(2) XRPD data substantially as shown in Table 5; and/or a XRPD

pattern substantially as shown in FIG. 14.

5. The salt according to claim 1 or 2, wherein the adipate comprises the following crystal forms of adipate or is only present in the following crystal forms of adipate, the X-ray powder diffraction pattern of the crystal form of the adipate represented by the diffraction angle of 2θ ± 0.2° at least comprises: characteristic diffraction peaks shown at 4.3°, 8.5°, 15.7°, 21.7° and 28.2°;

preferably, the X-ray powder diffraction pattern of the crystal form of the adipate represented by the diffraction angle of 2θ ± 0.2° at least comprises: characteristic diffraction peaks shown at 4.3°, 8.5°, 13.0°, 15.7°, 18.2°, 19.9°, 21.7° and 28.2°;

more preferably, the X-ray powder diffraction pattern of the crystal form of the adipate represented by the diffraction angle of 2θ ± 0.2° at least comprises: characteristic diffraction peaks shown at 4.3°, 8.5°, 13.0°, 15.3°, 15.7°, 18.2°, 19.4°, 19.9°, 21.7° and 28.2°;

particularly preferably, the crystal form of the adipate has XRPD data substantially as shown in Table 6, and/or, a XRPD pattern substantially as shown in FIG. 17.

6. The salt according to claim 1 or 2, wherein the succinate comprises the following crystal forms of succinate or is only present in the following crystal forms of succinate, the X-ray powder diffraction pattern of the crystal form of the succinate represented by the diffraction angle of 2θ ± 0.2° at least comprises:

characteristic diffraction peaks shown at 5.4°, 13.9°, 16.0°, 21.1° and 24.3°;

preferably, the X-ray powder diffraction pattern of the crystal form of the succinate represented by the diffraction angle of 2θ ± 0.2° at least comprises:

characteristic diffraction peaks shown at 5.4°, 9.5°, 10.1°, 13.9°, 16.0°, 18.6°, 21.1° and 24.3°;

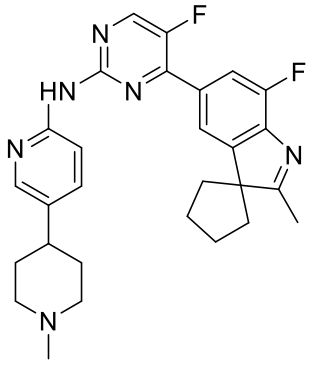
more preferably, the X-ray powder diffraction pattern of the crystal

form of the succinate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

characteristic diffraction peaks shown at 5.4º, 9.5º, 10.1º, 13.4º, 13.9º, 16.0º, 17.7º, 18.6º, 21.1º and 24.3º;

particularly preferably, the crystal form of the succinate has XRPD data substantially as shown in Table 8, and/or a XRPD pattern substantially as shown in FIG. 22.

7. A crystal form of the fumarate of the compound represented by formula I:



Formula I

wherein, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 7.0º, 13.9º, 18.4º, 21.8º and 24.1º; or

(2) characteristic diffraction peaks shown at 4.5º, 10.5º, 18.3º, 20.6º and 23.9º; or

(3) characteristic diffraction peaks shown at 5.9º, 14.4º, 18.6º, 23.6º and 28.4º;

preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 5.5º, 7.0º, 9.2º, 10.6º, 13.9º, 18.4º, 21.8º and 24.1º;

(2) characteristic diffraction peaks shown at 4.5º, 8.9º, 10.5º, 17.9º, 18.3º, 20.6º, 22.5º, and 23.9º; or

(3) characteristic diffraction peaks shown at 5.9º, 14.4º, 17.6º, 18.6º, 21.6º, 23.6º, 23.9º and 28.4º;

more preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

(1) characteristic diffraction peaks shown at 5.5º, 7.0º, 9.2º, 10.6º, 13.9º, 15.7º, 17.2º, 18.4º, 21.8º and 24.1º; or

(2) characteristic diffraction peaks shown at 4.5º, 8.9º, 10.5º, 17.1º, 17.9º, 18.3º, 20.6º, 22.5º, 23.9º, and 27.5º; or

(3) characteristic diffraction peaks shown at 5.9º, 11.7º, 14.4º, 17.6º, 18.6º, 21.6º, 23.6º, 23.9º, 25.0º and 28.4º;

particularly preferably, the crystal form of the fumarate has XRPD data and/or a XRPD pattern selected from any one of the following (1) to (3):

(1) XRPD data substantially as shown in Table 1; and/or a XRPD pattern substantially as shown in FIG. 2;

(2) XRPD data substantially as shown in Table 2; and/or a XRPD pattern substantially as shown in FIG. 5; and

(3) XRPD data substantially as shown in Table 3; and/or a XRPD pattern substantially as shown in FIG. 8.

8. The crystal form of the fumarate according to claim 7, wherein the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

characteristic diffraction peaks shown at 7.0º, 13.9º, 18.4º, 21.8º and 24.1º;

preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

characteristic diffraction peaks shown at 5.5º, 7.0º, 9.2º, 10.6º, 13.9º, 18.4º, 21.8º and 24.1º;

more preferably, the X-ray powder diffraction pattern of the crystal form of the fumarate represented by the diffraction angle of 2θ ± 0.2º at least comprises:

characteristic diffraction peaks shown at 5.5º, 7.0º, 9.2º, 10.6º, 13.9º, 15.7º, 17.2º, 18.4º, 21.8º and 24.1º;

and particularly preferably, the crystal form of the fumarate has XRPD data substantially as shown in Table 1; and/or a XRPD pattern substantially as shown in FIG. 2.

9. The preparation method of the crystal form of the fumarate according to claim 8, comprising allowing 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine to react with fumaric acid in a reaction solvent, the reaction solvent is an organic solvent or an aqueous solution of the organic solvent;

preferably, the organic solvent is a polar organic solvent;

further preferably, the organic solvent is selected from one or more of alcohol, ketone, halogenated alkane, ether and ester;

more preferably, the organic solvent is selected from one or more of C_1-C_5 linear or branched alkanol, acetone, THF, ethyl acetate, dichloromethane, and chloroform; particularly preferably, the organic solvent is selected from one or more of methanol, ethanol, propanol, isopropanol, acetone, dichloromethane and chloroform; more preferably, the organic solvent is selected from one or more of methanol, ethanol, dichloromethane and chloroform; most preferably, the organic solvent is ethanol, dichloromethane, or a combination of the both.

10. The method according to claim 9, wherein the method further comprises slowly adding fumaric acid dropwise into 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine for mixing; and/or

allowing 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-

amine to react with fumaric acid at a temperature ranging from 20°C to a temperature at which the reaction solvent is refluxed; and/or

the method further comprises: dissolving 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine before reacting with fumaric acid.

11. The method according to claim 10, wherein the solvent used for dissolving 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine comprises a first solvent and a second solvent, wherein the first solvent is selected from one or more of a ketone, an ether, an ester and an alcohol, preferably selected from one or more alcohols, more preferably the first solvent is selected from one or more of C_1-C_5 linear and branched alkanols, particularly preferably selected from one or more of methanol, ethanol, propanol and isopropanol; the second solvent is dichloromethane, chloroform or a combination of the both;

preferably, the mixing volume ratio of the first solvent to the second solvent is 1:(0.1-10), preferably 1:(1-3), and most preferably 1:1.

12. The method according to any one of claims 9 to 11, wherein the method further comprises: after dissolving 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine, subjecting the resulting solution to filtration; and/or

the method further comprises: evaporating the solvent used for dissolving 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine before reacting with fumaric acid; and/or

the method further comprises: cooling the reaction system to a temperature of 10°C to 35°C, preferably cooling to a temperature of 20°C to 30°C after the reaction of 5-fluoro-4-(7'-fluoro-2'-methylspiro[cyclopentane-1,3'-indol]-5'-yl)-N-(5-(1-methylpiperidin-4-yl)pyridin-2-yl)pyrimidine-2-amine with fumaric acid is completed.

13. A pharmaceutical composition, comprising a therapeutically effective amount of the salt according to any one of claims 1 to 6 or the crystal form of the fumarate according to any one of claims 7 to 8; preferably, the pharmaceutical composition also comprises a pharmaceutically acceptable adjuvant; more preferably, the pharmaceutically acceptable adjuvant includes at least one of a carrier, a diluent, and an excipient.

14. The pharmaceutical composition according to claim 13, wherein the pharmaceutical composition comprises one or more other biologically active substances;

preferably, the other biologically active substances are selected from one or more of an anticancer agent, an immunosuppressive agent and an anti-viral agent;

more preferably, the other biologically active substances are selected from one or more of an alkylating agent, an antineoplastic antimetabolite drug, a platinum complexing agent, an antibiotic antineoplastic drug, a naturally-derived antineoplastic drug, a hormonal antineoplastic drug, a VEGFR or EGFR inhibitor, an antineoplastic antibody drug, an mTOR inhibitor, and a drug for treating brain tumors;

particularly preferably,

the alkylating agent is selected from one or more of cyclophosphamide, ifosfamide, thiotepa, semustine, mechlorethamine hydrochloride, busulfan, chlorambucil, melphalan, nitrocaphane, formylmelphalan, carmustine, lomustine, altretamine, dibromomannitol, and temozolomide;

the antineoplastic antimetabolite drug is selected from one or more of cytarabine, fluorouracil, methotrexate, hydroxyurea, tegafur, Meisoindigo and mercaptopurine;

the platinum complexing agent is selected from one or more of cisplatin, carboplatin, and oxaliplatin;

the antibiotic antineoplastic drug is selected from one or more of actinomycin D, mitomycin, doxorubicin, pingyangmycin, epirubicin,

pirarubicin, daunorubicin, and bleomycin;

the naturally-derived antineoplastic drug is selected from one or more of homoharringtonine and its derivatives, vincristine and its derivatives, hydroxycamptothecin and its derivatives, etoposide and its derivatives, vindesine and its derivatives, vinblastine and its derivatives, vinorelbine tartrate, taxol and its derivatives, colchicine and its derivatives, and elemene and its derivatives;

the hormonal antineoplastic drug is selected from one or more of aminoglutethimide, tamoxifen, dexamethasone, dutasteride, flutamide, gonadorelin, leuprolide acetate, and letrozole;

the VEGFR or EGFR inhibito is selected from one or more of sunitinib, sorafenib, imatinib, gefitinib, erlotinib, vandetanib, pazopanib, lapatinib, canertinib, afatinib, mubritinib, dasatinib, and neratinib;

the antineoplastic antibody drug is selected from one or more of trastuzumab, pertuzumab, rituximab, panitumumab, bevacizumab, ipilimumab, ofatumumab, and ramucirumab; the mTOR inhibitor comprises everolimus, sirolimus, and zotarolimus; and

the drug for treating brain tumors comprises temozolomide.

15. A kit, comprising the salt according to any one of claims 1 to 6 or the crystal form of the fumarate according to any one of claims 7 to 8, and one or more of other biologically active substances; preferably, thekit further comprises a pharmaceutically acceptable adjuvant; more preferably, the pharmaceutically acceptable adjuvant includes at least one of a carrier, a diluent, and an excipient;

preferably, the other biologically active substances are selected from one or more of an anticancer agent, an immunosuppressive agent and an anti-viral agent;

more preferably, the other biologically active substances are selected from one or more of an alkylating agent, an antineoplastic antimetabolite drug, a platinum complexing agent, an antibiotic antineoplastic drug, a naturally-derived antineoplastic drug, a hormonal antineoplastic drug, a

VEGFR or EGFR inhibitor, an antineoplastic antibody drug, an mTOR inhibitor, and a drug for treating brain tumors;

particularly preferably,

the alkylating agent is selected from one or more of cyclophosphamide, ifosfamide, thiotepa, semustine, mechlorethamine hydrochloride, busulfan, chlorambucil, melphalan, nitrocaphane, formylmelphalan, carmustine, lomustine, altretamine, dibromomannitol, and temozolomide;

the antineoplastic antimetabolite drug is selected from one or more of cytarabine, fluorouracil, methotrexate, hydroxyurea, tegafur, Meisoindigo and mercaptopurine;

the platinum complexing agent is selected from one or more of cisplatin, carboplatin, and oxaliplatin;

the antibiotic antineoplastic drug is selected from one or more of actinomycin D, mitomycin, doxorubicin, pingyangmycin, epirubicin, pirarubicin, daunorubicin, and bleomycin;

the naturally-derived antineoplastic drug is selected from one or more of homoharringtonine and its derivatives, vincristine and its derivatives, hydroxycamptothecin and its derivatives, etoposide and its derivatives, vindesine and its derivatives, vinblastine and its derivatives, vinorelbine tartrate, taxol and its derivatives, colchicine and its derivatives, and elemene and its derivatives;

the hormonal antineoplastic drug is selected from one or more of aminoglutethimide, tamoxifen, dexamethasone, dutasteride, flutamide, gonadorelin, leuprolide acetate, and letrozole;

the VEGFR or EGFR inhibitor is selected from one or more of sunitinib, sorafenib, imatinib, gefitinib, erlotinib, vandetanib, pazopanib, lapatinib, canertinib, afatinib, mubritinib, dasatinib, and neratinib;

the antineoplastic antibody drug is selected from one or more of trastuzumab, pertuzumab, rituximab, panitumumab, bevacizumab, ipilimumab, ofatumumab, and ramucirumab; the mTOR inhibitor comprises everolimus, sirolimus, and zotarolimus; and

the drug for treating brain tumors comprises temozolomide.

16. The kit according to claim 15, wherein the other biologically active substance is temozolomide.

17. Use of the salt according to any one of claims 1 to 6, the crystal form of the fumarate according to any one of claims 7 to 8, the pharmaceutical composition according to claim 13-14, or the kit according to any one of claims 15 to 16 in the preparation of a medicament for the treatment of diseases responsive to the inhibition of a cyclin dependent kinase~~.~~

~~18. The use according to claim 17~~, wherein the diseases are selected from a brain tumor, a breast cancer, an urogenital cancer, a lung cancer, a gastrointestinal cancer, an epidermoid cancer, a melanoma, an ovarian cancer, a pancreatic cancer, a neuroblastoma, a head and neck cancer or a bladder cancer; a leukemia, a hyperplasia, a gastric cancer, a colon cancer, a laryngeal cancer, a lymphatic system cancer, a genitourinary tract cancer, a bone cancer, a prostate cancer, a small cell lung cancer, a glioma cancer, a colorectal cancer, a kidney cancer, an epithelial cancer, a liver cancer, an esophageal cancer, a hematopoietic system cancer, a lymphoma, a myeloma, a follicular thyroid cancer; a tumor of mesenchymal origin; a tumor of the central or peripheral nervous system; a seminoma; a teratocarcinoma; an osteosarcoma; xeroderma pigmentosum; a keratoacanthoma; a follicular thyroid cancer; Kaposi's sarcoma, chronic lymphocytic leukemia, mantle cell lymphoma, or large B-cell lymphoma;

preferably, the tumor of mesenchymal origin is a fibrosarcoma or a rhabdomyosarcoma; and the tumor of the central or peripheral nervous system is an astrocytoma, a neuroblastoma, a glioma, or a schwannomas.

~~19~~18. The salt according to any one of claims 1 to 6, the crystal form of the fumarate according to any one of claims 7 to 8, the pharmaceutical composition according to claim 13 to 14, or the kit according to any one of claims 15 to 16, for use in the treatment of diseases responsive to the inhibition of a cyclin dependent kinase~~.~~

~~20. The salt, crystal form of fumarate, pharmaceutical composition or kit for the uses according to claim 19~~, wherein the diseases are selected from a brain tumor, a breast cancer, an urogenital cancer, a lung cancer, a gastrointestinal cancer, an epidermoid cancer, a melanoma, an ovarian cancer, a pancreatic cancer, a neuroblastoma, a head and neck cancer or a bladder cancer; a leukemia, a hyperplasia, a gastric cancer, a colon cancer, a laryngeal cancer, a lymphatic system cancer, a genitourinary tract cancer, a bone cancer, a prostate cancer, a small cell lung cancer, a glioma cancer, a colorectal cancer, a kidney cancer, an epithelial cancer, a liver cancer, an esophageal cancer, a hematopoietic system cancer, a lymphoma, a myeloma, a follicular thyroid cancer; a tumor of mesenchymal origin; a tumor of the central or peripheral nervous system; a seminoma; a teratocarcinoma; an osteosarcoma; xeroderma pigmentosum; a keratoacanthoma; a follicular thyroid cancer; Kaposi's sarcoma, chronic lymphocytic leukemia, mantle cell lymphoma, and large B-cell lymphoma;

preferably, the tumor of mesenchymal origin is a fibrosarcoma or a rhabdomyosarcoma; and the tumor of the central or peripheral nervous system is an astrocytoma, a neuroblastoma, a glioma, or a schwannomas.