

CLAIMS

1. A crystal form of (S)-4-(8-amino-3-(1-(but-2-ynoyl)pyrrolidin-2-yl)imidazo[1,5-a]pyrazin-1-yl)-N-(pyridin-2-yl)benzamide characterized by a reflection X-ray powder diffraction pattern comprising peaks at $6.4^{\circ} \pm 0.2^{\circ} 2\theta$, $8.6^{\circ} \pm 0.2^{\circ} 2\theta$, $10.5^{\circ} \pm 0.2^{\circ} 2\theta$, $11.6^{\circ} \pm 0.2^{\circ} 2\theta$ and $15.7^{\circ} \pm 0.2^{\circ} 2\theta$.

2. The crystal form of claim 1, wherein the reflection X-ray powder diffraction pattern further comprises peaks at $10.9^{\circ} \pm 0.2^{\circ} 2\theta$, $12.7^{\circ} \pm 0.2^{\circ} 2\theta$, $13.4^{\circ} \pm 0.2^{\circ} 2\theta$, $14.3^{\circ} \pm 0.2^{\circ} 2\theta$, $14.9^{\circ} \pm 0.2^{\circ} 2\theta$ and $18.2^{\circ} \pm 0.2^{\circ} 2\theta$.

3. The crystal form of claim 2, wherein the reflection X-ray powder diffraction pattern comprises one or more peaks at $11.3^{\circ} \pm 0.2^{\circ} 2\theta$, $15.1^{\circ} \pm 0.2^{\circ} 2\theta$, $16.1^{\circ} \pm 0.2^{\circ} 2\theta$, $17.3^{\circ} \pm 0.2^{\circ} 2\theta$, $19.2^{\circ} \pm 0.2^{\circ} 2\theta$, $19.4^{\circ} \pm 0.2^{\circ} 2\theta$, $19.8^{\circ} \pm 0.2^{\circ} 2\theta$, $20.7^{\circ} \pm 0.2^{\circ} 2\theta$, $21.1^{\circ} \pm 0.2^{\circ} 2\theta$, $21.4^{\circ} \pm 0.2^{\circ} 2\theta$, $21.6^{\circ} \pm 0.2^{\circ} 2\theta$, $21.9^{\circ} \pm 0.2^{\circ} 2\theta$, $22.6^{\circ} \pm 0.2^{\circ} 2\theta$, $23.3^{\circ} \pm 0.2^{\circ} 2\theta$, $23.6^{\circ} \pm 0.2^{\circ} 2\theta$, $24.9^{\circ} \pm 0.2^{\circ} 2\theta$, $25.2^{\circ} \pm 0.2^{\circ} 2\theta$, $25.4^{\circ} \pm 0.2^{\circ} 2\theta$, $25.7^{\circ} \pm 0.2^{\circ} 2\theta$, $26.1^{\circ} \pm 0.2^{\circ} 2\theta$, $26.4^{\circ} \pm 0.2^{\circ} 2\theta$, $26.8^{\circ} \pm 0.2^{\circ} 2\theta$, $26.9^{\circ} \pm 0.2^{\circ} 2\theta$, $27.7^{\circ} \pm 0.2^{\circ} 2\theta$, $28.6^{\circ} \pm 0.2^{\circ} 2\theta$, $29.1^{\circ} \pm 0.2^{\circ} 2\theta$, $29.4^{\circ} \pm 0.2^{\circ} 2\theta$, $30.1^{\circ} \pm 0.2^{\circ} 2\theta$, $30.5^{\circ} \pm 0.2^{\circ} 2\theta$, $31.7^{\circ} \pm 0.2^{\circ} 2\theta$, $31.9^{\circ} \pm 0.2^{\circ} 2\theta$, $32.2^{\circ} \pm 0.2^{\circ} 2\theta$, $32.6^{\circ} \pm 0.2^{\circ} 2\theta$, $33.1^{\circ} \pm 0.2^{\circ} 2\theta$, $33.4^{\circ} \pm 0.2^{\circ} 2\theta$, $34.5^{\circ} \pm 0.2^{\circ} 2\theta$, $35.9^{\circ} \pm 0.2^{\circ} 2\theta$, $36.1^{\circ} \pm 0.2^{\circ} 2\theta$, $36.8^{\circ} \pm 0.2^{\circ} 2\theta$, $37.4^{\circ} \pm 0.2^{\circ} 2\theta$, $38.1^{\circ} \pm 0.2^{\circ} 2\theta$, $38.9^{\circ} \pm 0.2^{\circ} 2\theta$ and $39.5^{\circ} \pm 0.2^{\circ} 2\theta$.

4. The crystal form of claim 2, wherein the reflection X-ray powder diffraction pattern further comprises peaks at $11.3^{\circ} \pm 0.2^{\circ} 2\theta$, $15.1^{\circ} \pm 0.2^{\circ} 2\theta$, $16.1^{\circ} \pm 0.2^{\circ} 2\theta$, $17.3^{\circ} \pm 0.2^{\circ} 2\theta$, $19.2^{\circ} \pm 0.2^{\circ} 2\theta$, $19.4^{\circ} \pm 0.2^{\circ} 2\theta$, $19.8^{\circ} \pm 0.2^{\circ} 2\theta$, $20.7^{\circ} \pm 0.2^{\circ} 2\theta$, $21.1^{\circ} \pm 0.2^{\circ} 2\theta$, $21.4^{\circ} \pm 0.2^{\circ} 2\theta$, $21.6^{\circ} \pm 0.2^{\circ} 2\theta$, $21.9^{\circ} \pm 0.2^{\circ} 2\theta$, $22.6^{\circ} \pm 0.2^{\circ} 2\theta$, $23.3^{\circ} \pm 0.2^{\circ} 2\theta$, $23.6^{\circ} \pm 0.2^{\circ} 2\theta$, $24.9^{\circ} \pm 0.2^{\circ} 2\theta$, $25.2^{\circ} \pm 0.2^{\circ} 2\theta$, $25.4^{\circ} \pm 0.2^{\circ} 2\theta$, $25.7^{\circ} \pm 0.2^{\circ} 2\theta$, $26.1^{\circ} \pm 0.2^{\circ} 2\theta$, $26.4^{\circ} \pm 0.2^{\circ} 2\theta$, $26.8^{\circ} \pm 0.2^{\circ} 2\theta$, $26.9^{\circ} \pm 0.2^{\circ} 2\theta$, $27.7^{\circ} \pm 0.2^{\circ} 2\theta$, $28.6^{\circ} \pm 0.2^{\circ} 2\theta$, $29.1^{\circ} \pm 0.2^{\circ} 2\theta$, $29.4^{\circ} \pm 0.2^{\circ} 2\theta$, $30.1^{\circ} \pm 0.2^{\circ} 2\theta$, $30.5^{\circ} \pm 0.2^{\circ} 2\theta$, $31.7^{\circ} \pm 0.2^{\circ} 2\theta$, $31.9^{\circ} \pm 0.2^{\circ} 2\theta$, $32.2^{\circ} \pm 0.2^{\circ} 2\theta$, $32.6^{\circ} \pm 0.2^{\circ} 2\theta$, $33.1^{\circ} \pm 0.2^{\circ} 2\theta$, $33.4^{\circ} \pm 0.2^{\circ} 2\theta$, $34.5^{\circ} \pm 0.2^{\circ} 2\theta$, $35.9^{\circ} \pm 0.2^{\circ} 2\theta$, $36.1^{\circ} \pm 0.2^{\circ} 2\theta$, $36.8^{\circ} \pm 0.2^{\circ} 2\theta$, $37.4^{\circ} \pm 0.2^{\circ} 2\theta$, $38.1^{\circ} \pm 0.2^{\circ} 2\theta$, $38.9^{\circ} \pm 0.2^{\circ} 2\theta$ and $39.5^{\circ} \pm 0.2^{\circ} 2\theta$.

5. The crystal form of claim 2, wherein the crystal form is a crystalline anhydrate.

6. The crystal form of claim 1, 2, 3, 4 or 5, wherein the peaks are present when the reflection x-ray powder diffraction is carried out using Cu-K α radiation.

7. The crystal form of claim 1, 2, 3, 4 or 5, wherein the peaks are present when the reflection x-ray powder diffraction is carried out using a Bruker D8 Advance powder X-ray diffractometer equipped with a LynxEye detector and operating in Bragg-Brentano reflection geometry, a tube voltage of 40 kV and current of 40 mA, a variable divergence slit with a 3° window, a step size of 0.02° 2 θ , sample rotation of 0.5 rps, and a step time of 37 seconds.

8. A pharmaceutical composition comprising the crystal form of any of claims 1, 2, 3, 4 or 5 and at least one pharmaceutically acceptable excipient.

9. The pharmaceutical composition of claim 8, wherein the pharmaceutical composition further comprises an extragranular acidulant.

10. The pharmaceutical composition of claim 9, wherein the extragranular acidulant is selected from the group consisting of fumaric acid, succinic acid, D-tartaric acid, L-tartaric acid, ($\pm$)-tartaric acid, ascorbic acid, isoascorbic acid, alginic acid, a salt of alginic acid, Protacid F 120 NM, Protacid AR 1112 and Carbopol 971P, and a combination thereof.

11. The pharmaceutical composition of claim 9, wherein the extragranular acidulant is selected from the group consisting of alginic acid, a sodium salt of alginic acid and a potassium salt of alginic acid.

12. The pharmaceutical composition of claim 8 for use in the treatment of a hyperproliferative disease, wherein the hyperproliferative disease is selected from the group consisting of chronic lymphocytic leukemia, non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, mantle cell lymphoma, follicular lymphoma, B-cell lymphoproliferative disease, B cell acute lymphoblastic leukemia, Waldenström's macroglobulinemia, Burkitt's leukemia, Hodgkin's disease, multiple myeloma, acute myeloid leukemia, juvenile myelomonocytic leukemia, hairy cell leukemia, mast cell leukemia, mastocytosis, myeloproliferative disorders (MPDs), myeloproliferative neoplasms, polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), myelodysplastic syndrome, chronic myelogenous leukemia (BCR-ABL1-positive), chronic neutrophilic leukemia, chronic eosinophilic leukemia, primary central nervous system (CNS) lymphoma, primary multifocal lymphoma of peripheral nervous system (PNS), thymus cancer, brain cancer, glioblastoma, lung cancer, squamous cell cancer, skin cancer (*e.g.*, melanoma), eye cancer, retinoblastoma, intraocular melanoma, oral cavity and oropharyngeal cancers, bladder cancer, gastric cancer, stomach cancer, pancreatic cancer, breast cancer, cervical cancer, head and neck cancer, renal cancer, kidney cancer, liver cancer, ovarian cancer, prostate cancer, colorectal cancer, bone cancer (*e.g.*, metastatic bone cancer), esophageal cancer, testicular cancer, gynecological cancer, thyroid cancer, epidermoid cancer, AIDS-related cancer (*e.g.*, lymphoma), viral-induced cervical carcinoma (human papillomavirus), nasopharyngeal carcinoma (Epstein-Barr virus), Kaposi's sarcoma, primary effusion lymphoma (Kaposi's sarcoma herpesvirus), hepatocellular carcinoma (hepatitis B and hepatitis C viruses), T-cell leukemias (Human T-cell leukemia virus-1), benign hyperplasia of the skin, restenosis, benign prostatic hypertrophy, and tumor angiogenesis.

13. The pharmaceutical composition of claim 8 for use in the treatment of diffuse large B-cell lymphoma (DLBCL).

14. The pharmaceutical composition of claim 8 for use in the treatment of chronic lymphocytic leukemia (CLL).

15. The pharmaceutical composition of claim 8 for use in the treatment of small lymphocytic lymphoma (SLL).

16. The pharmaceutical composition of claim 8 for use in the treatment of mantle cell lymphoma (MCL).

17. The pharmaceutical composition of claim 8 for use in the treatment of Waldenstrom's macroglobulinemia.