

Summary

In one aspect of the present disclosure, there is provided a compound which is 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate.

5 In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate and one or more pharmaceutically acceptable carriers, diluents, or excipients.

10 In a further aspect of the present disclosure, there is provided a use of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate in the manufacture of a medicament for treating cancer.

In another aspect of the present disclosure, there is provided a compound which is 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate for use in the treatment of cancer.

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Description

The present invention provides a novel, pharmaceutically acceptable salt of an aminopyrazole compound that inhibits Chk1/2 and provides several advantages over previously disclosed aminopyrazole compounds.

20 The present invention provides a compound which is 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate. The present invention also provides 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate in isolation.

25 The present invention provides 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate in crystalline form. The present invention also provides 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-

pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate in crystalline form characterized by an X-ray powder diffraction pattern (CuK α radiation, $\lambda = 1.54060 \text{ \AA}$) comprising a peak at 12.6, and one or more peaks at 24.8, 25.5, 8.1, 6.6, 12.3, and 16.3 ($2\theta \pm 0.2^\circ$).

5 The present invention provides a pharmaceutical composition comprising 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate and one or more of a pharmaceutically acceptable carrier, diluent, or excipient.

10 The present invention provides a method of treating cancer, comprising administering to a patient in need thereof an effective amount of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate. In addition, the present invention also provides a method of treating cancer, comprising administering to a patient in need thereof an effective amount of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate and ionizing radiation. The present invention provides a method of treating cancer, comprising administering to a patient in need thereof an effective amount of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate and one or more chemotherapy agents. The present invention provides a method of treating cancer, comprising administering to a patient in need thereof an effective amount of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate, one or more chemotherapy agents, and ionizing radiation.

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WE CLAIM:

1. A compound which is 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate.
- 5 2. The compound according to claim 1, wherein the compound is in crystalline form characterized by a X-ray powder diffraction pattern (CuK α radiation, $\lambda = 1.54060$ Å) comprising a peak at 12.6, and one or more peaks at 24.8, 25.5, 8.1, 6.6, 12.3, and 16.3 ($2\theta \pm 0.2^\circ$).
- 10 3. A pharmaceutical composition comprising 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate and one or more pharmaceutically acceptable carriers, diluents, or excipients.
- 15 4. The pharmaceutical composition of claim 3, wherein 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate is in crystalline form characterized by a X-ray powder diffraction pattern (CuK α radiation, $\lambda = 1.54060$ Å) comprising a first peak at 12.6, and one or more peaks at 24.8, 25.5, 8.1, 6.6, 12.3, and 16.3 ($2\theta \pm 0.2^\circ$).

5. Use of 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate in the manufacture of a medicament for treating cancer.

6. The use according to claim 5, wherein 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate is in crystalline form characterized by a X-ray powder diffraction pattern (CuK α radiation, $\lambda = 1.54060 \text{ \AA}$) comprising a peak at 12.6, and one or more peaks at 24.8, 25.5, 8.1, 6.6, 12.3, and 16.3 ($2\theta \pm 0.2^\circ$).

7. The use according to claim 5 or 6, with one or more pharmaceutically acceptable carriers, diluents, or excipients.

8. The use according to any one of claims 5-7, in combination with ionizing radiation.

9. The use according to any one of claims 5-8, in combination with one or more chemotherapy agents.

10. The use according to any one of claims 5-9, in combination with a chemotherapy agent selected from 5-fluorouracil, hydroxyurea, gemcitabine, methotrexate, pemetrexed, doxorubicin, etoposide, cetuximab, cisplatin, taxol, and combinations thereof.

11. A compound which is 5-(5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3-ylamino)pyrazine-2-carbonitrile (S)-lactate monohydrate for use in the treatment of cancer.

12. The compound of claim 11, wherein the compound is in crystalline form characterized by a X-ray powder diffraction pattern (CuK α radiation, $\lambda = 1.54060 \text{ \AA}$) comprising a peak at 12.6, and one or more peaks at 24.8, 25.5, 8.1, 6.6, 12.3, and 16.3 ($2\theta \pm 0.2^\circ$).

13. The compound of claim 11 or 12, wherein the compound is for use with one or more pharmaceutically acceptable carriers, diluents, or excipients.

14. The compound of any one of claims 11-13, wherein the compound is for use in simultaneous, separate, or sequential combination with ionizing radiation.

5 15. The compound of any one of claims 11-14, wherein the compound is for use in simultaneous, separate, or sequential combination with one or more chemotherapy agents.

10 16. The compound of any one of claims 11-15, wherein the compound is for use in simultaneous, separate, or sequential combination with a chemotherapy agent selected from 5-fluorouracil, hydroxyurea, gemcitabine, methotrexate, pemetrexed, doxorubicin, etoposide, cetuximab, cisplatin, taxol, and combinations thereof.