SUMMARY ~~OF THE INVENTION~~

In one aspect~~embodiment~~, the disclosure~~invention~~ provides N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in solid crystalline form.

In one aspect~~embodiment~~, the disclosure~~invention~~ provides N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in solid crystalline form.

In a further embodiment, the disclosure~~invention~~ provides a crystal polymorph of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate characterized herein and designated dihydrogen citrate Form I.

In one aspect, the disclosure provides the compound N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ.

In a further embodiment, the disclosure~~invention~~ provides hydrated forms of dihydrogen citrate Form I, including the monohydrate form.

In a further embodiment, the disclosure~~invention~~ provides a crystal polymorph of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate characterized herein and designated hydrogen citrate Form II.

In one aspect, the disclosure provides the compound N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ.

In a further embodiment, the disclosure~~invention~~ provides hydrated forms of hydrogen citrate Form II, including the monohydrate form.

There is further provided a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate Form I and one or more pharmaceutically acceptable excipients.

There is further provided a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate Form II and one or more pharmaceutically acceptable excipients.

There is further provided process for preparing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate Form I comprising providing a mixture comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea, water, acetone, and citric acid, and causing the N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate Form I to exist in the mixture.

There is further provided process for preparing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate Form II comprising providing a mixture comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea, water, tetrahydrofuran, and citric acid, and causing the N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate Form II to exist in the mixture.

In one aspect, the disclosure provides a process for preparing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I as defined herein, comprising:

a) providing a mixture comprising (i) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea, water, tetrahydrofuran, and citric acid;

b) causing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate crystalline Form II to exist in the mixture.

In a further embodiment, the disclosure~~invention~~ provides a method for treating cancer in a mammal comprising administering to a subject having the disease therapeutically effective amount of citrate salts of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea in a solid crystalline form, wherein the crystalline form is Form I or II, or (b) a pharmaceutical composition comprising citrate salts of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea in a solid crystalline form, wherein the crystalline form is Form I or II, one or more pharmaceutically acceptable excipients. Examples of such cancers include myelodysplastic syndrome, acute myeloid leukemia, colorectal cancer, non-small cell lung cancer, and ovarian cancer.

There is still further provided a method for treating cancer in a mammal comprising dissolving N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, in a pharmaceutically acceptable solvent or mixture of solvents, and administering the resulting solution in a therapeutically effective amount to subject having the disease.

There is still further provided a method for treating cancer in a mammal comprising dissolving N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, in a pharmaceutically acceptable solvent or mixture of solvents, and administering the resulting solution in a therapeutically effective amount to subject having the disease.

There is still further provided a method for treating cancer in a mammal comprising dispersing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, in a pharmaceutically acceptable polymeric carrier, and

administering the resulting solid dispersion in a therapeutically effective amount to subject having the disease.

There is still further provided a method for treating cancer in a mammal comprising dissolving N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, in a pharmaceutically acceptable solvent or mixture of solvents, and administering the resulting solution in a therapeutically effective amount to subject having the disease.

In another aspect, there is provided the use of a therapeutically effective amount of (a) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihyrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ or (b) a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ and one or more pharmaceutically acceptable excipients in the manufacture of a medicament for treating cancer in a mammal.

In another aspect, there is provided the use of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ, dissolved in a pharmaceutically acceptable solvent or mixture of solvents in the manufacture of a medicament for treating cancer in a mammal.

In another aspect, there is provided the use of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ, dispersed in a pharmaceutically acceptable polymeric carrier in the manufacture of a medicament for treating cancer in a mammal.

In another aspect, there is provided the use of a therapeutically effective amount of (a) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ or (b) a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ and one or more pharmaceutically acceptable excipients in the manufacture of a medicament for treating cancer in a mammal.

In another aspect, there is provided the use of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ, dissolved in a pharmaceutically acceptable solvent or mixture of solvents in the manufacture of a medicament for treating cancer in a mammal.

In another aspect, there is provided the use of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ, dispersed in a pharmaceutically acceptable polymeric carrier in the manufacture of a medicament for treating cancer in a mammal.

Additional embodiments of the disclosure~~invention~~, including more particular aspects of those provided above, will be found in, or will be evident from, the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 is a PXRD scan of crystal polymorph Form I N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate.

Fig. 2 is a PXRD scan of crystal polymorph Form II N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate.

DETAILED DESCRIPTION

The invention encompasses crystalline forms of citrate salts of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea. N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea free base is prepared, illustratively, as described in Example 1 of above-cited U.S. Patent Application No. 12/632183, the entire disclosure of which is incorporated by reference herein. The term "free base" is used for convenience herein to refer to N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea parent compound as distinct from any salt thereof.

Those skilled in the art will also understand that the term "monohydrate" when referring to N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea means that there is one water molecule for every molecule of N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea.

8. The process of claim 7, further comprising isolating N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I.

9. ~~A method for treating cancer in a mammal comprising administering to a subject having the disease~~Use of a therapeutically effective amount of (a) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihyrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ or (b) a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ and one or more pharmaceutically acceptable excipients in the manufacture of a medicament for treating cancer in a mammal.

10. The use~~method~~ of claim 9, wherein the crystalline N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate Form I or pharmaceutical composition is to be administered by an oral, parenteral, sublingual, buccal, intranasal, pulmonary, topical, transdermal, intradermal, ocular, otic, rectal, vaginal, intragastric, intracranial, intrasynovial, or intra-articular route.

11. The use~~method~~ of claim 9, wherein the cancer is myelodysplastic syndrome, acute myeloid leukemia, colorectal cancer, non-small cell lung cancer, and ovarian cancer.

12. Use of~~A method for treating cancer in a mammal comprising dissolving~~ N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ, dissolved in a pharmaceutically acceptable solvent or mixture of solvents~~, and administering the resulting solution in a therapeutically effective amount to subject having the disease~~ in the manufacture of a medicament for treating cancer in a mammal.

13. Use of~~A method for treating cancer in a mammal comprising dispersing~~ N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 11.80, 14.59, 15.95, 21.38, 26.12° 2θ, ± 0.2° 2θ, dispersed in a pharmaceutically acceptable polymeric carrier~~, and administering the resulting solid dispersion in a therapeutically effective amount to subject having the disease~~ in the manufacture of a medicament for treating cancer in a mammal.

14. The compound N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form.

15. The compound N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ.

16. The compound of claim 15, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at each of said positions.

17. The compound of claim 15, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at each of said positions: 5.71, 6.30, 7.27, 8.65, 9.80, 13.06, 14.31, 15.18, 15.92, 16.68, 17.71, 20.17, 21.98, 23.30, 24.47, 26.11, 28.02° 2θ, ± 0.2° 2θ.

18. The compound of any of claims 14-17, wherein the crystalline form is a hydrate.

19. A pharmaceutical composition comprising the compound of any of claims 14-18 and one or more pharmaceutically acceptable excipients.

20. A process for preparing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea dihydrogen citrate in a solid crystalline form, wherein the crystalline form is Form I of any of claims 14-18, comprising:

a) providing a mixture comprising (i) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea, water, tetrahydrofuran, and citric acid;

b) causing N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate crystalline Form II to exist in the mixture.

21. The process of claim 20, further comprising isolating N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II.

22. Use of~~A method for treating cancer in a mammal comprising administering to a subject having the disease~~ a therapeutically effective amount of (a) N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ or (b) a pharmaceutical composition comprising N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ and one or more pharmaceutically acceptable excipients in the manufacture of a medicament for treating cancer in a mammal.

23. The use~~method~~ of claim 22, wherein the crystalline N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate Form II or pharmaceutical composition is to be administered by an oral, parenteral, sublingual, buccal, intranasal, pulmonary, topical, transdermal, intradermal, ocular, otic, rectal, vaginal, intragastric, intracranial, intrasynovial, or intra-articular route.

24. The use~~method~~ of claim 22, wherein the cancer is myelodysplastic syndrome, acute myeloid leukemia, colorectal cancer, non-small cell lung cancer, and ovarian cancer.

25. Use of~~A method for treating cancer in a mammal comprising dissolving~~ N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-

fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ, dissolved in a pharmaceutically acceptable solvent or mixture of solvents~~, and administering the resulting solution in a therapeutically effective amount to subject having the disease~~ in the manufacture of a medicament for treating cancer in a mammal.

26. Use of~~A method for treating cancer in a mammal comprising dispersing~~ N-(4-{4-amino-7-[1-(2-hydroxyethyl)-1H-pyrazol-4-yl]thieno[3,2-c]pyridin-3-yl}phenyl)-N'-(3-fluorophenyl)urea hydrogen citrate in a solid crystalline form, wherein the crystalline form is Form II, characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 8.65, 15.18, 24.47, 28.02° 2θ, ± 0.2° 2θ, dispersed in a pharmaceutically acceptable polymeric carrier~~, and administering the resulting solid dispersion in a therapeutically effective amount to subject having the disease~~ in the manufacture of a medicament for treating cancer in a mammal.