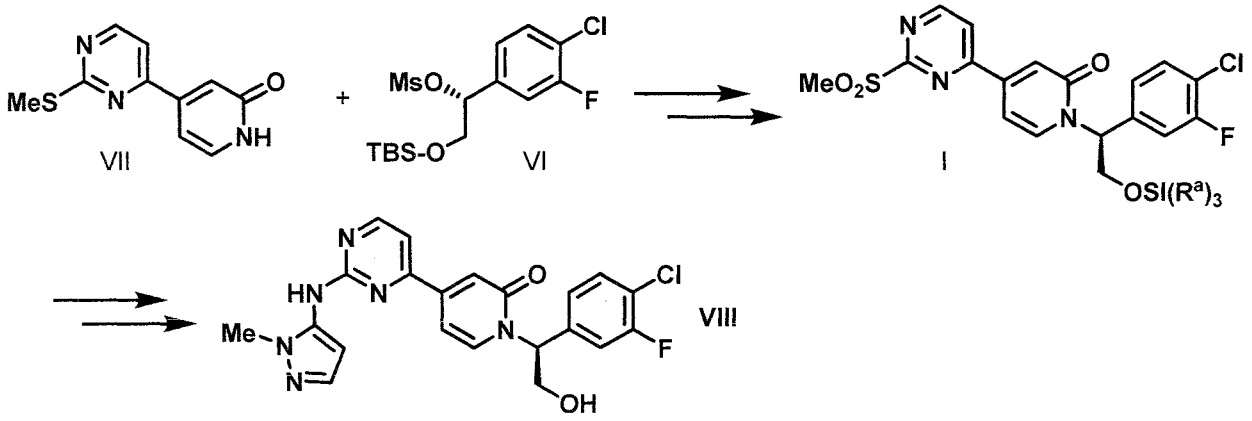
yl)pyridin-2(1H)-one is set forth in WO 2013/130976.

SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ provides processes for the manufacture of **I** which is a useful intermediate that can be used in the manufacture **VIII.** (WO2013/130976) Compound **VIII** is an ERK inhibitor and a useful medicament for treating hyperproliferative disorders. The process provides an efficient route to **VIII** and to the useful intermediates **VI** and **VII**. Alkylation of **VII** with **VI** affords **I,** which ultimately is condensed with 1-methyl-1H-pyrazol-5-amine (**XIV**). (SCHEME A)

SCHEME A

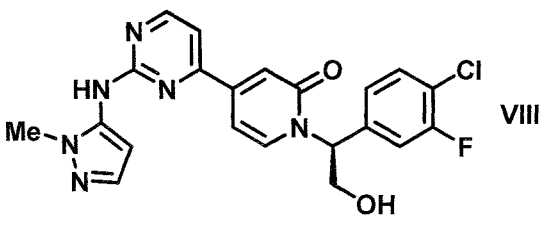


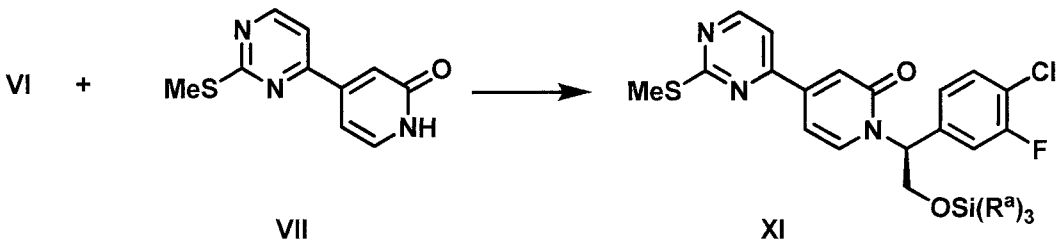
The present disclosure~~invention~~ further provides an asymmetric enzymatic reduction which permits the stereospecific reduction of 1-(4-chloro-3-fluorophenyl)-2-hydroxyethanone to afford (*R*)-1-(4-chloro-3-fluorophenyl)ethan-1,2-diol (**IV**).

The present disclosure~~invention~~ also provides an improved process to prepare 4-(2-(methylthio)pyrimidin-4-yl)pyridin-2(1H)-one (**VII**).

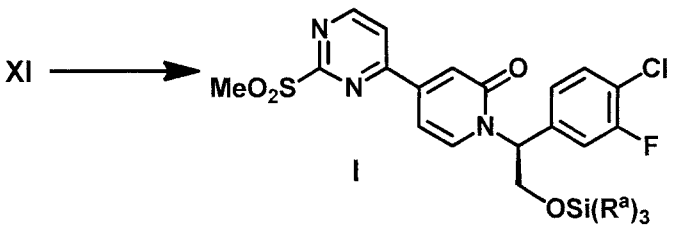
The present disclosure~~invention~~ provides a crystalline besylate salt **(VIIIb)** with desirable physical properties that permit ready formulation and good bioavailability.

In ~~embodiment~~ aspect 1, the present invention provides processes for the preparation of a compound of formula **VIII,** the processes comprising the steps of:

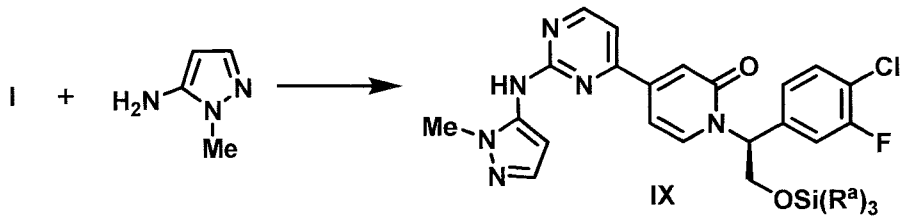




(*f*) treating **XI** with an oxidizing agent to afford **I**;



(*g*) treating 1-methyl-1H-pyrazol-5-amine with a strong base in an aprotic solvent at reduced temperature and adding the compound of formula **I** to afford **IX**; and,



(*h*) contacting **IX** with a de-silylating agent to afford **VIII**.

In embodiment ~~2~~1, the present disclosure~~invention~~ provides processes according to ~~embodiment~~ aspect 1 wherein the ketoreductase in step (c) affords an enantiomeric excess at least about 98%.

In embodiment ~~3~~2, the present disclosure~~invention~~ provides processes of embodiment ~~2~~1 wherein the ketoreductase in step (c) is KRED-NADH-112.

In embodiment ~~4~~3, the present disclosure~~invention~~ provides processes of embodiment ~~2~~1 wherein step (c) further comprises NADH or NADPH as a cofactor.

In embodiment ~~5~~4, the present disclosure~~invention~~ provides processes of embodiment ~~4~~3 wherein the cofactor is regenerated with a cosubstrate selected from a secondary alcohol or from an additional enzyme selected from alcohol dehydrogenase, glucose dehydrogenase, formatted dehydrogenase, glucose-6-phosphate dehydrogenase, phosphite dehydrogenase or hydrogenase.

In embodiment ~~6~~5, the present disclosure~~invention~~ provides processes of any of embodiment ~~2~~ 1 to ~~5~~ 4 wherein the ketoreductase step is performed in an aqueous medium in the presence of organic cosolvent at a temperature between 1 and 50 ^{0}C.

In embodiment ~~7~~6, the present disclosure~~invention~~ provides processes of embodiment ~~6~~ 5 wherein the ketoreductase step produces a homogeneous suspension.

In embodiment ~~8~~7, the present disclosure~~invention~~ provides processes of ~~embodiment~~ aspect 1 wherein the silyl chloride is *tert*-butyldimethylsilyl chloride, the sulfonyl chloride is methanesulfonyl chloride, the bases in step (d) are DMAP and TEA and the non-polar aprotic solvent is DCM and in step (e) the organic solvent is dioxane.

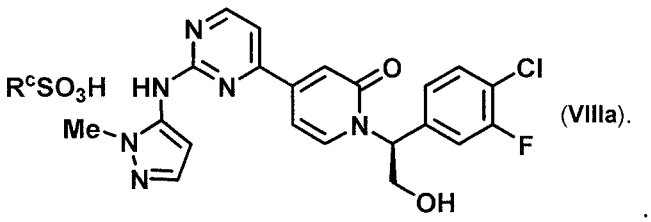
In embodiment ~~9~~8, the present disclosure~~invention~~ provides processes of ~~embodiment~~ aspect 1 wherein $(\mathbf{R}^a)_3Si$ is *tert*-butyldimethylsilyl, $\mathbf{R}^b$ is methyl, and in step (e) the strong base is potassium hexamethyldisilazane and the organic solvent is diglyme.

In embodiment ~~10~~9, the present disclosure~~invention~~ provides processes of ~~embodiment~~ aspect 1 wherein in step (a) the metallating agent is *i*-PrMgCl and LiCl and the solvent is THF, in step (c) the ketoreductase is KRED-NADH-112 and step (c) further comprises the cofactor NAD and the cofactor recycling agent glucose dehydrogenase, in step (d) $(\mathbf{R}^a)_3Si$ is *tert*-butyldimethylsilyl, $\mathbf{R}^b$ is methyl, the bases are DMAP and TEA and the non-polar aprotic solvent is DCM, and in step (e) the strong base is potassium hexamethyldisilazane and the organic solvent is diglyme.

In embodiment ~~11~~10, the present disclosure~~invention~~ provides processes of ~~embodiment~~ aspect 1 wherein in step (a) the metallating agent is *i*-PrMgCl and LiCl and the solvent is THF, in step (c) the ketoreductase is KRED-NADH-112 and step (c) further comprises the cofactor NAD and the cofactor recycling agent is glucose dehydrogenase, in step (d) $(\mathbf{R}^a)_3Si$ is *tert*-butyldimethylsilyl, $\mathbf{R}^b$ is methyl, the bases are DMAP and TEA and the non-polar aprotic solvent is DCM, in step (e) the strong base is potassium hexamethyldisilazane and the organic solvent is diglyme, and in step (g) the strong base is potassium hexamethyldisilazane and the aprotic solvent is THF.

In embodiment ~~12~~11, the present disclosure~~invention~~ provides processes of ~~embodiment~~ aspect 1 wherein in step (a) the metallating agent is *i*-PrMgCl and LiCl and the solvent is THF, in step (c) the ketoreductase is KRED-NADH-112 and step (c) further comprises the cofactor NAD and cofactor recycling agent is glucose dehydrogenase, in step (d) $(\mathbf{R}^a)_3Si$ is *tert*-butyldimethylsilyl, $\mathbf{R}^b$ is methyl, the bases are DMAP and TEA and the non-polar aprotic solvent is DCM, in step (e) the strong base is potassium hexamethyldisilazane and the organic solvent is diglyme, in step (g) the strong base is potassium hexamethyldisilazane and the aprotic solvent is THF, and in step (h) the desilylating agent is methanolic HCl.

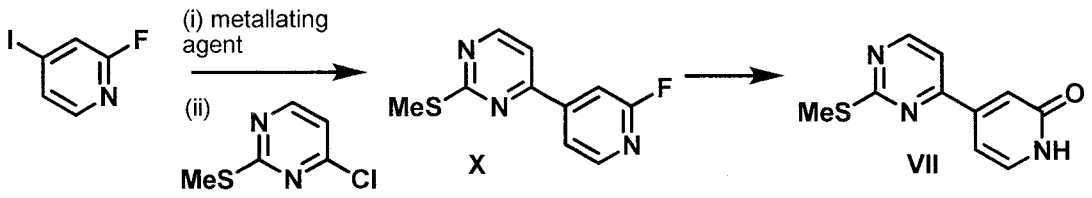
In embodiment ~~13~~12, the present disclosure~~invention~~ provides processes according to ~~embodiment~~ aspect 1 wherein the compound **VIII** from step h is contacted with a sulfonic acid in an organic solvent and water to afford a salt of **VIIIa** where $\mathbf{R^c}$ is an aryl sulfonic acid



(VIIIa).

In embodiment ~~14~~13, the present disclosure~~invention~~ provides processes according to embodiment ~~13~~12 wherein $\mathbf{R^c}SO_3H$ is benzenesulfonic acid and the solvent is methyl ethyl ketone and water to afford the besylate salt **VIIIb**.

In ~~embodiment~~ aspect 2~~15~~, the present invention provides processes for the preparation of 4-(2-(methylsulfonyl)pyrimidin-4-yl)pyridin-2(1H)-one (**VII**) comprising the steps of:



(*a*) contacting 2-fluoro-4-iodopyridine with a metallating agent in an aprotic organic solvent to afford an organomagnesium compound, which is reacted with 4-chloro-2(methylthio)pyrimidine in the presence of a palladium catalyst to afford 4-(2-fluoropyridin-4-yl)-2-(methylthio)pyrimidine (**X**);

(b) treating **X** with potassium *tert*-butoxide in THF and subsequently with an aqueous acid to afford 4-(2-(methylsulfonyl)pyrimidin-4-yl)pyridin-2(1H)-one (**VII**).

In embodiment ~~16~~14, the present disclosure~~invention~~ provides processes according to ~~embodiment 15~~aspect 2 wherein the palladium catalyst is (1,3-diisopropylimidazol-2-ylidene)(3-chloropyridyl)palladium(II) dichloride, the metallating agent is *i*-PrMgCl and LiCl, and the aprotic solvent is THF.

In ~~embodiment~~ aspect ~~17~~3, the present invention provides the compound (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate.

In ~~embodiment~~ aspect ~~184~~, the present invention provides pharmaceutical compositions comprising (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~195~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate.

In ~~embodiment~~ aspect ~~206~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an X-ray powder diffraction pattern comprising peaks at 6.16 ± 0.2, 7.46 ± 0.2, 16.36 ± 0.2, 25.76 ± 0.2 and 25.98 ± 0.2 2~~θ~~

In ~~embodiment~~ aspect ~~217~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an X-ray powder diffraction pattern substantially as shown in Figure 1.

In ~~embodiment~~ aspect ~~228~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an ^{13}C NMR pattern substantially as shown in Figure 19.

In ~~embodiment~~ aspect ~~239~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an ^{19}F NMR pattern substantially as shown in Figure 20.

In ~~embodiment~~ aspect ~~2410~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an ^{13}C NMR pattern substantially as shown in Figure 19 and a ^{19}F NMR pattern substantially as shown in Figure 20.

In ~~embodiment~~ aspect ~~2511~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an ^{19}F NMR pattern comprising peaks at -111.1 ± 0.4 ppm and -115.4 ± 0.4 ppm relative to $CFCl_3$ (at 293 K).

In ~~embodiment~~ aspect ~~2612~~, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an ^{13}C NMR pattern comprising peaks at 157.7 ± 0.2 ppm, 129.6 ± 0.2 ppm, 125.8 ± 0.2 ppm, and 117.0 ± 0.2 ppm relative to tetramethylsilane (at 293 K).

In ~~embodiment~~ aspect ~~27~~13, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having a DSC pattern substantially as shown in Figure 2.

In ~~embodiment~~ aspect ~~28~~14, the present invention provides pharmaceutical compositions comprising crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate in accordance with any one of ~~embodiments 19 to 27~~aspects 5 to 13 and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~29~~15, the present invention provides the compound (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid.

In ~~embodiment~~ aspect ~~30~~16, the present invention provides pharmaceutical compositions comprising (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~31~~17, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid.

In ~~embodiment~~ aspect ~~32~~18, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form A.

In ~~embodiment~~ aspect ~~33~~19, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form A having an X-ray powder diffraction pattern comprising peaks at. 5.76 ± 0.2, 13.44 ± 0.2, 15.64± 0.2, 19.40± 0.2 2Θ.

In ~~embodiment~~ aspect ~~34~~20, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form A having an X-ray powder diffraction pattern substantially as shown in Figure 12.

In ~~embodiment~~ aspect ~~35~~21, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form A having a DSC pattern substantially as shown in Figure 13.

In ~~embodiment~~ aspect ~~36~~22, the present invention provides pharmaceutical compositions comprising crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form A in accordance with any one of ~~claims 31 to 35~~aspects 17 to 21 and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~37~~23, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form B.

In ~~embodiment~~ aspect ~~38~~24, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form B. having an X-ray powder diffraction pattern comprising peaks at 7.02 ± 0.2, 16.30 ± 0.2, 17.30 ± 0.2, 21.86 ± 0.2 2Θ.

In ~~embodiment~~ aspect ~~39~~25, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form B having an X-ray powder diffraction pattern substantially as shown in Figure 15.

In ~~embodiment~~ aspect ~~40~~26, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form B having a DSC pattern substantially as shown in Figure 16.

In ~~embodiment~~ aspect ~~41~~27, the present invention provides pharmaceutical compositions comprising crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one *p*-toluenesulfonic acid Form B in accordance with any one of ~~embodiments 37 to 40~~aspects 23 to 26 and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~42~~28, the present invention provides the compound (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid.

In ~~embodiment~~ aspect ~~43~~29, the present invention provides pharmaceutical compositions comprising (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~44~~30, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid.

In ~~embodiment~~ aspect ~~45~~31, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form I.

In ~~embodiment~~ aspect ~~46~~32, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form I having an X-ray powder diffraction pattern comprising peaks at 12.50 ± 0.2, 13.86 ± 0.2 2Θ.

In ~~embodiment~~ aspect ~~47~~33, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form I having an X-ray powder diffraction pattern substantially as shown in Figure 6.

In ~~embodiment~~ aspect ~~48~~34, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form I having a DSC pattern substantially as shown in Figure 7.

In ~~embodiment~~ aspect ~~49~~35, the present invention provide pharmaceutical compositions comprising crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form I in accordance with any one of ~~embodiments 44 to 48~~aspects 30 to 34 and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~50~~36, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form II.

In ~~embodiment~~ aspect ~~51~~37, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form II having an X-ray powder diffraction pattern comprising peaks at 12.80 ± 0.2, 22.42 ± 0.2, 24.92 ± 0.2 2Θ.

In ~~embodiment~~ aspect ~~52~~38, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form II having an X-ray powder diffraction pattern substantially as shown in Figure 8.

In ~~embodiment~~ aspect ~~53~~39, the present invention provides crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form II having a DSC pattern substantially as shown in Figure 9.

In ~~embodiment~~ aspect ~~54~~40, the present invention provides pharmaceutical compositions comprising crystalline (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one naphthalenedisulfonic acid Form II in accordance with any one of ~~claims 50 to 53~~aspects 36 to 39 and a pharmaceutically acceptable excipient.

In ~~embodiment~~ aspect ~~55~~41, the present invention provides amorphous (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate.

In ~~embodiment~~ aspect ~~56~~42, the present invention provides amorphous (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having an X-ray powder diffraction pattern substantially as shown in Figure 21.

In ~~embodiment~~ aspect ~~57~~43, the present invention provides amorphous (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate having a DSC pattern substantially as shown in Figure 22.

In ~~embodiment~~ aspect ~~58~~44, the present invention provides pharmaceutical compositions comprising amorphous (S)-1-(1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one benzenesulfonate in accordance with any one of ~~embodiments 55 to 57~~aspects 41 to 43 and a pharmaceutically acceptable excipient.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows the XRPD pattern of VIII crystalline besylate form A.

Figure 2 shows the DSC and TGA analysis of VIII crystalline besylate form A.

Figure 3 shows the single crystal structure analysis of VIII crystalline besylate form A.

Figure 4 shows the XRPD pattern of VIII free base.

Figure 5 shows the DSC analysis of VIII free base.

Figure 6 shows the XRPD pattern of VIII naphthalenedisulfonic acid form I.

Figure 7 shows the DSC analysis of VIII naphthalenedisulfonic acid form I.