CLAIMS

1. Polymorph E of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide.

2. The polymorph of claim 1, wherein the polymorph exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-Theta at angles of 18.3° ± 0.3° and 24.4° ± 0.3°.

3. The polymorph of any one of claims 1-2, wherein the polymorph exhibits characteristic peaks at angles of 18.8° ± 0.3° and 23.7° ± 0.3°.

4. The polymorph of any one of claims 1-3, wherein the polymorph exhibits characteristic peaks at angles of 10.1° ± 0.3° and 28.3° ± 0.3°.

5. The polymorph of any one of claims 1-4, wherein the polymorph exhibits characteristic peaks at angles of 9.8° ± 0.3° and 23.2° ± 0.3°.

6. The polymorph of any one of claims 1-5, wherein the polymorph exhibits characteristic peaks at angles of 9.8° ± 0.3°, 10.1° ± 0.3°, 18.3° ± 0.3°, 18.8° ± 0.3°, 23.2° ± 0.3°, 23.7° ± 0.3°, 28.3° ± 0.3° and 24.4° ± 0.3°.

7. The polymorph of any one of claims 1-6, wherein the polymorph exhibits an X-ray powder diffraction pattern substantially in accordance with Figure 1 and Table 1.

8. The polymorph of any one of claims 1-7, wherein the polymorph exhibits an FT-IR spectrum having characteristic peaks expressed in units of cm-1 at values of about 1682, about 1296 and about 1136.

9. The polymorph of any one of claims 1-8, wherein the polymorph exhibits an FT-IR spectrum substantially in accordance with Figure 2.

10. The polymorph of any one of claims 1-9, wherein the polymorph exhibits a differential scanning calorimetry thermogram having a characteristic peak at a temperature of 232.6 ± 2°C.

11. The polymorph of any one of claims 1-10, wherein the polymorph exhibits a differential scanning calorimetry thermogram substantially in accordance with Figure 3.

12. The polymorph of any one of claims 1-11, wherein the polymorph exhibits a melting point of about 230-235°C.

13. The polymorph of claim 12, wherein the polymorph has an enthalpy of fusion of about 114 J/g.

14. The polymorph of any one of claims 1-13, wherein the polymorph exhibits a thermogravimetry curve substantially in accordance with Figure 5.

15. The polymorph of claim 1, containing less than 1% by weight total impurities.

16. The polymorph of claim 1, containing less than 0.1% by weight total impurities.

17. A mixed DMAC/toluene solvate of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide, wherein said solvate exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-Theta at angles of 18.3° ± 0.3°, 22.0° ± 0.3° and 27.6° ± 0.3°.

18. The solvate of claim 17, wherein the solvate exhibits an X-ray powder diffraction pattern substantially in accordance with Figure 13 and Table 3.

19. A DMSO solvate of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide, wherein said solvate exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-Theta at angles of 7.6° ± 0.3°, 18.6° ± 0.3° and 19.8° ± 0.3°.

20. The solvate of claim 19, wherein the solvate exhibits an X-ray powder diffraction pattern substantially in accordance with Figure 16 and Table 4.

21. A pharmaceutical composition comprising the polymorph of claim 1, and a pharmaceutically acceptable carrier or diluent.

22. The pharmaceutical composition of claim 21, further comprising a polymorph of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in a crystalline, solvate, hydrate or amorphous form other than polymorph E.

23. The pharmaceutical composition of claim 22, further comprising polymorph A.

24. The pharmaceutical composition of claim 22, further comprising pseudo-polymorph B.

25. The pharmaceutical composition of any one of claims 21-24, wherein the composition comprises less than 1% by weight of polymorph E based on the total weight of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in the composition.

26. The pharmaceutical composition of any one of claims 21-25, wherein the composition comprises at least 50.0% by weight of polymorph E based on the total weight of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in the composition.

27. The pharmaceutical composition of any one of claims 21-26, wherein the composition comprises at least 99.0% by weight of polymorph E based on the total weight of the compound of formula 1 in the composition.

28. The pharmaceutical composition of any one of claims 21-27, wherein the composition is formulated for oral administration in the form of a pill, capsule, lozenge or tablet.

29. The pharmaceutical composition of any one of claims 21-27, wherein the composition is in the form of a suspension.

30. A process for the preparation of a compound according to any one of claims 1-20, which comprises the following steps: (a) dissolving *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in a first solvent, (b) optionally adding a second solvent, and (c) optionally seeding the mixture, such that said polymorph is formed.

31. The process of claim 30, which comprises the following steps: (a) dissolving *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in THF, (b) concentrating the mixture, (c) reducing the temperature of the mixture, (d) adding ethanol to the mixture, (e) seeding the mixture, and (f) lowering the temperature of the mixture, such that said polymorph is formed.

32. The process of claim 30, which comprises the following steps: (a) dissolving *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in dimethylacetamide, (b) adding toluene, (c) lowering the temperature of the mixture, (d) filtering solids from the mixture and washing the solids, (e) suspending the filtered solids in ethanol, and (f) seeding the mixture, such that said polymorph is formed.

33. The process of claim 30, which comprises the following steps: (a) dissolving *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in DMSO, (b) adding ethanol to the mixture, (c) filtering solids from the mixture, (d) suspending the solids in ethanol, and (e) seeding the mixture, such that said polymorph is formed.

34. A method for the treatment of disorders mediated by PI3K, comprising administering to a patient in need of such treatment an effective amount of the polymorph of any one of claims 1-20 or a pharmaceutical composition of any one of claims 21-29.

35. The method of claim 34, wherein the disorder is a cellular proliferative disease.

36. The method of any one of claims 34-35, wherein the disorder is selected from breast cancer, colorectal cancer, endometrial cancer, gastric carcinoma, glioblastoma, hepatocellular carcinoma, small cell lung cancer, non-small cell lung cancer, melanoma, ovarian cancer, pancreatic cancer, prostate carcinoma, and thyroid carcinoma.

37. The method of claim 36, wherein a pharmaceutical composition comprising polymorph E of *N*-(3-{[(2*Z*)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1*H*)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide is administered.

38. Use of a polymorph of any one of claims 1-20 for the preparation of a medicament for the treatment of disorders mediated by PI3K.

39. The use of claim 40, wherein the disorder is a cellular proliferative disease.

40. The use of any one of claims 38-39, wherein the disorder is selected from the group consisting of breast cancer, colorectal cancer, endometrial cancer, gastric carcinoma, glioblastoma, hepatocellular carcinoma, small cell lung cancer, non-small cell lung cancer, melanoma, ovarian cancer, pancreatic cancer, prostate carcinoma and thyroid carcinoma.

41. Use of a polymorph of any one of claims 1-20 for the preparation of a medicament for the treatment a disorder selected from the group consisting of breast cancer, colorectal cancer, endometrial cancer, gastric carcinoma, glioblastoma, hepatocellular carcinoma, small cell lung cancer, non-small cell lung cancer, melanoma, ovarian cancer, pancreatic cancer, prostate carcinoma and thyroid carcinoma.

CLAIMS

1. Polymorph E of N-(3- {[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide .

2. The polymorph of claim 1 , wherein the polymorph exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-Theta at angles of 18.3° ± 0.3° and 24.4° ± 0.3°.

3. The polymorph of claim 1, wherein the polymorph exhibits characteristic peaks at angles of 18.8° ± 0.3° and 23.7° ± 0.3°.

4. The polymorph of claim 1, wherein the polymorph exhibits characteristic peaks at angles of 10.1 ° ± 0.3° and 28.3° ± 0.3°.

5. The polymorph of claim 1, wherein the polymorph exhibits characteristic peaks at angles of 9.8° ± 0.3° and 23.2° ± 0.3°.

6. The polymorph of claim 1, wherein the polymorph exhibits characteristic peaks at angles of 9.8° ± 0.3°, 10.1 ° ± 0.3°, 18.3° ± 0.3°, 18.8° ± 0.3°, 23.2° ± 0.3°, 23.7° ± 0.3°, 28.3° ± 0.3° and 24.4° ± 0.3°.

7. The polymorph of claim 1, wherein the polymorph exhibits an X-ray powder diffraction pattern in accordance with FIG. 1.

8. The polymorph of claim 1, wherein the polymorph exhibits a Fourier transform infrared spectrum having characteristic peaks expressed in units of cm^{-1} at values of 1682, about 1296 and about 1 136.

9. The polymorph of claim 1, wherein the polymorph exhibits a Fourier transform infrared spectrum in accordance with FIG. 2.

10. The polymorph of claim 1, wherein the polymorph exhibits a differential scanning calorimetry thermogram having a characteristic peak at a temperature of 232.6 ± 2°C.

11. The polymorph of claim 1, wherein the polymorph exhibits a differential scanning calorimetry thermogram in accordance with FIG. 3.

12. The polymorph of claim 1, wherein the polymorph exhibits a melting point of about 230-235°C.

13. The polymorph of claim 12, wherein the polymorph has an enthalpy of fusion of 114 J/g.

14. The polymorph of claim 1, wherein the polymorph exhibits a thermogravimetry curve in accordance with FIG. 5.

15. The polymorph of claim 1, containing less than 1 % by weight total impurities.

16. The polymorph of claim 1, containing less than 0.1 % by weight total impurities.

17. A pharmaceutical composition comprising the polymorph of claim 1, and a pharmaceutically acceptable carrier or diluent.

18. The pharmaceutical composition of claim 17, the composition comprises at least 50.0% by weight of polymorph E based on the total weight of N-(3-{[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in the composition.

19. The pharmaceutical composition of claim 17, the composition comprises at least 99.0% by weight of polymorph E based on the total weight of N-(3-{[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in the composition.

20. The pharmaceutical composition of claim 17, wherein the composition is formulated for oral administration in the form of a pill, capsule, lozenge or tablet.

21. The pharmaceutical composition of claim 17, wherein the composition is in the form of a suspension.

22. A process for the preparation of the polymorph according to claim 1, which comprises the following steps: (a) dissolving N-(3- {[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)-ylidene]sulfamoyl}phenyl)-2-methylalaninamide in a first solvent, (b) optionally adding a second solvent, and (e) optionally seeding the mixture.

23. The process of claim 22, which comprises the following steps: (a) dissolving N-(3-{[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)ylidene] sulfamoyl}phenyl)-2-methylalaninamide in tetrahydrofuran, (b) concentrating the mixture, (c) reducing the temperature of the mixture, (d) adding ethanol to the mixture, (e) seeding the mixture, and (f) lowering the temperature of the mixture.

24. The process of claim 22, which comprises the following steps: (a) dissolving N-(3-{[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)ylidene] sulfamoyl}phenyl)-2-methylalaninamide in dimethylacetamide, (b) adding toluene, (c) lowering the temperature of the mixture, (d) filtering solids from the mixture and washing the solids, (e) suspending the filtered solids in ethanol, and (f) seeding the mixture.

25. The process of claim 22, which comprises the following steps: (a) dissolving N-(3-{[(2Z)-3-[(2-chloro-5-methoxyphenyl)amino]quinoxalin-2(1H)ylidene] sulfamoyl}phenyl)-2-methylalaninamide in dimethylsulfoxide, (b) adding ethanol to the mixture, (c) filtering solids from the mixture, (d) suspending the solids in ethanol, and (e) seeding the mixture.