

What is claimed is:

1. A crystalline polymorph of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
2. A pharmaceutical composition comprising said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1.
3. The pharmaceutical composition of claim 2, wherein said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is suspended in a carrier matrix, wherein said carrier matrix comprises at least one surfactant.
4. The pharmaceutical composition of claim 2, wherein said carrier matrix further comprises at least one oil.
5. The pharmaceutical composition according to claim 2, comprising about 1 to about 50% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
6. The pharmaceutical composition according to claim 2, comprising about 1 to about 40% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
7. The pharmaceutical composition according to claim 2, comprising about 1 to about 30% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
8. The pharmaceutical composition according to claim 2, comprising about 20 to about 50% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
9. The pharmaceutical composition according to claim 2, comprising about 20 to about 40% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
10. The pharmaceutical composition according to claim 2, comprising about 25% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-

indazol-5-yloxy)benzyl)urea hydrochloride Form B.

11. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 10:90.

12. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 15:85.

13. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 25:75.

14. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 33:67.

15. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 50:50.

16. The pharmaceutical composition according to claim 4, further comprising one or more release modifiers.

17. The pharmaceutical composition according to claim 16, wherein said release modifier is selected from:

Vitamin E Succinate;

Cellulose derivatives;

Polyvinylpyrrolidones having molecular weights greater than 58,000;

Long chain (C12-C28) triglycerides, long chain (C12-C28) diglycerides, long chain (C12-C28) monoglycerides, and combinations thereof;

Long chain alcohols;

Castor wax;

High molecular weight polyethylene glycols;

Poloxamers; and

Long chain (C12-C28) fatty acids.

18. The pharmaceutical composition according to claim 17, wherein said release modifier is selected from Vitamin E succinate, glyceryl behenate, hydroxypropyl methylcellulose, and stearyl alcohol.

19. The pharmaceutical composition according to claim 18, comprising from at least 0.5% up to 20% by weight of each of said one or more release modifiers.

20. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprises 0-60% w/w of an oil and 40-100% w/w of a surfactant and said Form B is present in a range from about 1-50% w/w relative to the weight of the composition, wherein said composition has a dissolution profile in a dissolution media in which within 45 minutes about 40-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

21. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprising 0-60% w/w of an oil and 40-100% w/w of a surfactant and said Form B is present in a range from about 1-50% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 60 minutes about 50-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

22. The pharmaceutical composition according to claim 3, wherein said surfactant is a non-ionic surfactant.

23. The pharmaceutical composition according to claim 22, wherein said non-ionic surfactant is selected from D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate, polyethylene glycol-15-hydroxystearate, polyoxyl 35 castor oil, polyoxyl 40 hydrogenated castor oil, polyethylene glycol sorbitan monostearate, polyoxyethylene 20 sorbitan monooleate, caprylocaproyl polyoxylglycerides, lauroyl polyoxylglycerides, stearyl polyoxylglycerides, polyethylene glycol hexadecyl ether, polyoxyethylene (20) oleyl ether, polyethylene glycol

hexadecyl ether, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monooleate, a synthetic copolymer of ethylene and propylene oxides, a synthetic copolymer of ethylene and propylene oxides, phospholipids, zwitterionic surfactants, soy lecithin, phosphatidyl choline, phosphatidyl inositol, phosphatidyl ethanolamine, and cocamidopropyl betaine, and mixtures thereof.

24. The pharmaceutical composition according to claim 23, wherein said non-ionic surfactant is selected from D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate, polyethylene glycol-15-hydroxystearate, polyoxyl 40 hydrogenated castor oil, caprylacaproyl polyoxylglycerides, and lauroyl polyoxylglycerides.

25. The pharmaceutical composition according to claim 24, wherein said non-ionic surfactant is D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate.

26. The pharmaceutical composition according to claim 4, wherein said oil is a medium chain triglyceride.

27. The pharmaceutical composition of claim 26, wherein said medium chain triglyceride is selected from caprylic acid/capric acid triglycerides and medium chain fatty acids.

28. The pharmaceutical composition according to claim 27, wherein said medium chain triglyceride is caprylic acid/capric acid triglyceride.

29. The pharmaceutical composition according to claim 4, wherein said oil is a long chain triglyceride.

30. The pharmaceutical composition of claim 29, wherein the long chain triglyceride is glyceryl behenate.

31. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprises either D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate or a mixture of caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70 and 33:67 and said Form B is present in a range from about 20-40% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 45 minutes about 70-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

32. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B, wherein said carrier matrix comprises either D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate or a mixture of caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70 and 33:67 and wherein said Form B is present in a range from about 20-40% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 60 minutes about 80-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

33. The pharmaceutical composition according to claim 2, wherein said composition comprises 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B suspended in a carrier matrix, wherein said carrier matrix comprises a medium chain triglyceride and a non-ionic surfactant in a ratio selected from 10:90, 15:85 30:70 and 33:67 and said Form B is present in a range from about 20-50% w/w relative to the weight of said composition, wherein said composition optionally further comprises an antioxidant.

34. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 300 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

35. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 100 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

36. The pharmaceutical composition according claim 33, wherein said composition

comprises less than or equal to 55 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

37. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 100 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 25 °C/60% relative humidity for 1 year.

38. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 70 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 25 °C/60% relative humidity for 1 year.

39. The pharmaceutical composition according to claim 33, wherein said medium chain triglyceride is caprylic acid/capric acid triglyceride and said non-surfactant is D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate.

40. The pharmaceutical composition according to claim 39, wherein the ratio of said caprylic acid/capric acid triglyceride to said D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate is about 15:85.

41. The pharmaceutical composition according to claim 2, further comprising an anti-oxidant.

42. The pharmaceutical composition of claim 41, wherein said antioxidant is 2,6-di-*tert*-butyl-4-methylphenol.

43. The pharmaceutical composition according to claim 2, comprising about 213 mg of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yl)oxy)benzyl)urea hydrochloride Form B suspended in a carrier matrix, wherein said carrier matrix comprises caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70, and 33:67 and said Form B is present in a range from about 20-50% w/w relative to the weight of said composition, wherein said composition optionally further comprises an antioxidant.

44. The pharmaceutical composition according to claim 43, wherein the ratio of said caprylic acid/capric acid triglyceride to said D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate is about 15:85.

45. The pharmaceutical composition according to claim 43, wherein said composition comprises about 25% w/w of said Form B.

46. The pharmaceutical composition according to claim 45, wherein a single dose of the pharmaceutical composition when orally administered to a healthy human subject in the fasted state has less variability in  $C_{\max}$  relative to a single dose of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea when orally administered to a healthy human subject as a powder in capsule in the fasted state, wherein a single dose of said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B is about 426 mg and a single dose of said amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea is about 400 mg.

47. The pharmaceutical composition according to claim 45, wherein a single dose of the pharmaceutical composition when orally administered to a healthy human subject in the fasted state has less variability in  $AUC_{\text{inf}}$  relative to a single dose of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea when orally administered to a healthy human subject as a powder in capsule in the fasted state, wherein a single dose of said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B is about 426 mg and a single dose of said amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea is about 400 mg.

48. The pharmaceutical composition according to claim 45, wherein a single dose of the pharmaceutical composition when orally administered to a healthy human subject in the fasted state has less variability in  $T_{\max}$  relative to a single dose of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea when orally administered to a healthy human subject as a powder in capsule in the fasted state, wherein a single dose of said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B is about 426 mg and a single dose of said amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea is about 400 mg.

49. The pharmaceutical composition according to claim 45, wherein a single dose of the pharmaceutical composition when orally administered to a healthy human subject in the fasted state has increased exposure and increased relative bioavailability relative to a single dose

of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea when orally administered to a healthy human subject as a powder in capsule in the fasted state, wherein a single dose of said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B is about 426 mg and a single dose of said amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea is about 400 mg.

50. The pharmaceutical composition of claim 45, wherein said composition provides an  $AUC_{inf}$  that is about 4-fold greater than the  $AUC_{inf}$  for the powder in capsule formulation of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea.

51. The pharmaceutical composition of claim 45, wherein said composition provides  $C_{max}$  that is about 8-fold greater than the  $C_{max}$  for the powder in capsule formulation of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea.

52. The pharmaceutical composition according to claim 4, prepared by the method comprising:

- (i) stirring a mixture of said surfactant and said oil at a temperature sufficient to provide a liquefied homogeneous carrier matrix optionally in a nitrogen atmosphere; and
- (ii) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B to the carrier matrix with stirring at a temperature sufficient to maintain said carrier matrix in a liquefied state and optionally under a nitrogen atmosphere, thereby providing said pharmaceutical composition comprising a liquefied homogeneous suspension of said Form B in said carrier matrix.

53. The pharmaceutical composition according to claim 52, wherein said method further comprises (iv) transferring aliquots of said molten homogenous suspension obtained in step (iii) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

54. The pharmaceutical composition according to claim 4, prepared by the method comprising (i) homogenizing said oil at a temperature sufficient to melt the oil optionally under a

nitrogen atmosphere; (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant optionally under a nitrogen atmosphere; (iii) combining said molten oil and molten surfactant with stirring at a temperature that maintains the combination in a molten state and optionally under a nitrogen atmosphere to form a molten homogenous carrier matrix; and (iv) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to said molten homogenous carrier matrix with stirring at a temperature that maintains said carrier matrix in a molten state and optionally under a nitrogen atmosphere, thereby providing said composition comprising a molten homogeneous suspension of said Form B in said carrier matrix.

55. The pharmaceutical composition according to claim 54, wherein said method further comprises (v) transferring aliquots of said molten homogenous suspension obtained in step (iv) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

56. The pharmaceutical composition according to claim 4, prepared by the method comprising (i) homogenizing said oil at a temperature sufficient to melt the oil; (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant; and (iii) combining said molten oil, said molten surfactant, and said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B with stirring at a temperature that maintains said combination in a molten state, thereby providing said composition comprising a molten homogeneous suspension of said Form B in a carrier matrix.

57. The pharmaceutical composition according to claim 56, wherein said method further comprises (iv) transferring aliquots of said molten homogenous suspension obtained in step (iii) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

58. The pharmaceutical composition according to claim 4, wherein said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is micronized.

59. The polymorph according to claim 1, characterized by having at least one specific XRPD diffraction peak ( $2\theta$  degrees  $\pm 0.3$ ) at about 15.9.

60. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 12.3, 13.0, 15.9, 16.9 and 17.6.

61. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 23.4, 27.0 and 27.3.

62. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 20.4, 21.5, 21.9, 22.4, 23.4, 25.9, 27.0 and 27.3.

63. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 19.8, 20.4, 20.8, 21.5, 21.9, 22.4, 23.4, 23.9, 24.6, 25.2, 25.9, 27.0 and 27.3.

64. The polymorph according to claim 1, characterized by having substantially the same XRPD pattern as shown in Figure 3.

65. The polymorph according to claim 1, characterized by having an XRPD pattern that substantially includes the peaks in Table 2.

66. The polymorph according to claim 1, wherein 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is in substantially pure form.

67. The polymorph according to claim 1, characterized by having a DSC thermogram which comprises an endothermic event having a melt maxima temperature at about  $185 \pm 5$  °C.

68. A method for treating a myelodysplastic syndrome comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 2.

69. A method of administering 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to a healthy human subject such that the bioavailability of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea is increased, said method comprising orally administering a composition comprising about 20 to 50% w/w of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-

yloxy)benzyl)urea hydrochloride Form B suspended in a carrier matrix, said carrier matrix comprising caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85 30:70 and 33:67.

70. The method of claim 69, whereby said composition contacts the biological fluids of the gastro-intestinal tract and dissolves said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B, thereby increasing the bioavailability of said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea.

71. The method according to claim 69, wherein said composition comprises 25% w/w of said Form B.

72. A process for preparing a pharmaceutical composition of claim 4, comprising:

- (i) stirring a mixture of said surfactant and said oil at a temperature sufficient to provide a liquefied homogeneous carrier matrix, optionally under a stream of nitrogen; and
- (ii) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to the carrier matrix with stirring at a temperature sufficient to maintain said carrier matrix in a liquefied state, optionally under a stream of nitrogen, to provide a liquefied homogeneous suspension of said Form B in said carrier matrix

73. The process of claim 72, further comprising adding an antioxidant in step (i) or step (ii).

74. The process of claim 72, further comprising adding one or more release modifiers in step (ii).

75. A process for preparing a pharmaceutical composition of claim 4, comprising:

- (i) homogenizing said oil at a temperature sufficient to melt the oil, optionally under a stream of nitrogen;
- (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant, optionally under a stream of nitrogen;
- (iii) combining said molten oil and molten surfactant with stirring at a temperature that maintains the combination in a molten state, optionally under a stream of nitrogen, to form a molten homogenous carrier matrix; and

(iv) adding 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to said molten homogenous carrier matrix with stirring at a temperature that maintains said carrier matrix in a molten state, optionally under a stream of nitrogen, to provide a molten homogeneous suspension of said Form B in said carrier matrix.

76. The process of claim 75, further comprising adding an antioxidant in step (iii) or step (iv).

77. The process of claim 75, further comprising adding one or more release modifiers in step (iii) or (iv).

78. A process for preparing a pharmaceutical composition of claim 4, comprising:

(i) homogenizing said oil at a temperature sufficient to melt the oil, optionally under a stream of nitrogen;

(ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant, optionally under a stream of nitrogen; and

(iii) combining said molten oil, said molten surfactant, and 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B with stirring at a temperature that maintains said combination in a molten state, optionally under a stream of nitrogen, to form to provide a molten homogeneous suspension of said Form B in a carrier matrix.

79. The process of claim 78, further comprising adding an antioxidant in step (iii).

80. The process of claim 78, further comprising adding one or more release modifiers in step (iii).

81. The process according to claim 72, further comprising transferring aliquots of said liquefied or molten homogenous suspension into capsules and allowing said suspension to cool in said capsules, thereby providing a liquid, solid semi-solid or solid form of the suspension within the capsules.

82. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-

(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in MTBE with at least 1.5 equivalents of hydrochloric acid in 1,4-dioxane for a sufficient time to convert 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

- (b) allowing said Form B to crystallize from said solution; and
- (c) isolating said Form B.

83. A process for preparing 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in a solvent selected from ethyl acetate, isopropyl acetate, acetonitrile, acetone, isopropyl alcohol and ethanol with at least a stoichiometric amount of (i) HCl in 1,4-dioxane, (ii) HCl in acetone, or (iii) concentrated HCl, for a sufficient time to convert said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

- (b) allowing said Form B to crystallize from said solution; and
- (c) isolating said Form B.

84. A process for preparing 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in isopropanol with at least a stoichiometric amount of an aqueous solution of hydrochloric acid for a sufficient time to convert 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

(b) seeding said solution from step (a) with a suspension of 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea

hydrochloride Form B in isopropanol to allow said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to crystallize from said solution; and

(c) isolating said Form B.

85. The process according to claim 83, wherein about 1.05 equivalents of HCl are added.

86. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) heating a mixture of 2-(5-(2-(aminomethyl)-4-fluorophenoxy)-1H-indazol-1-yl)ethanol and phenyl 3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-ylcarbamate in an organic solvent at 35-40 °C for 5 hours to form 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea;

(b) cooling said mixture to ambient temperature;

(c) filtering said mixture;

(d) adding at least a stoichiometric amount of aqueous HCl to said mixture;

(e) allowing said Form B to crystallize from said solution; and

(f) isolating said Form B.

87. The process of claim 86, further comprising (d1) seeding said mixture in step (d) with 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B either as a solid or as a suspension in the solvent used in step (a).

88. A crystalline polymorph of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form A.

89. The crystalline polymorph of claim 88, characterized by having at least ten specific XRPD diffraction peaks ( $2\theta$  degrees  $\pm$  0.3) at about 6.9, 7.8, 13.9, 15.6, 16.7, 17.1, 19.2, 22.4, 22.8 and 26.6.

90. The crystalline polymorph of claim 88, characterized by substantially the same XRPD pattern as shown in Figure 1.

91. The crystalline polymorph of claim 88, characterized by having a DSC

thermogram which comprises a melt maxima temperature of about  $131 \pm 5$  °C.

92. A method for treating a myelodysplastic syndrome comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 43.

93. A method for treating a myelodysplastic syndrome comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 44.

94. A method for treating a myelodysplastic syndrome comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 45.

95. The method according to claim 94, wherein said pharmaceutical composition is formulated for oral administration.

96. The pharmaceutical composition according to claim 43 formulated for oral administration.

97. The pharmaceutical composition according to claim 44 formulated for oral administration.

98. The pharmaceutical composition according to claim 45 formulated for oral administration.

What is claimed is:

1. A crystalline polymorph of 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
2. A pharmaceutical composition comprising said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1.
3. The pharmaceutical composition of claim 2, wherein said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is suspended in a carrier matrix, wherein said carrier matrix comprises at least one surfactant.
4. The pharmaceutical composition of claim 3, wherein said carrier matrix further comprises at least one oil.
5. The pharmaceutical composition according to claim 2, comprising about 1 to about 50% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
6. The pharmaceutical composition according to claim 2, comprising about 1 to about 40% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
7. The pharmaceutical composition according to claim 2, comprising about 1 to about 30% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
8. The pharmaceutical composition according to claim 2, comprising about 20 to about 50% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
9. The pharmaceutical composition according to claim 2, comprising about 20 to about 40% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B.
10. The pharmaceutical composition according to claim 2, comprising about 25% w/w of said 1-(3-*tert*-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-

indazol-5-yloxy)benzyl)urea hydrochloride Form B.

11. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 10:90.

12. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 15:85.

13. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 25:75.

14. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 33:67.

15. The pharmaceutical composition according to claim 4, wherein the ratio of the oil to the surfactant is about 50:50.

16. The pharmaceutical composition according to claim 4, further comprising one or more release modifiers.

17. The pharmaceutical composition according to claim 16, wherein said release modifier is selected from:

Vitamin E Succinate;

Cellulose derivatives;

Polyvinylpyrrolidones having molecular weights greater than 58,000;

Long chain (C12-C28) triglycerides, long chain (C12-C28) diglycerides, long chain (C12-C28) monoglycerides, and combinations thereof;

Long chain alcohols;

Castor wax;

High molecular weight polyethylene glycols;

Poloxamers; and

Long chain (C12-C28) fatty acids.

18. The pharmaceutical composition according to claim 17, wherein said release modifier is selected from Vitamin E succinate, glyceryl behenate, hydroxypropyl methylcellulose, and stearyl alcohol.

19. The pharmaceutical composition according to claim 18, comprising from at least 0.5% up to 20% by weight of each of said one or more release modifiers.

20. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprises 0-60% w/w of an oil and 40-100% w/w of a surfactant and said Form B is present in a range from about 1-50% w/w relative to the weight of the composition, wherein said composition has a dissolution profile in a dissolution media in which within 45 minutes about 40-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

21. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprising 0-60% w/w of an oil and 40-100% w/w of a surfactant and said Form B is present in a range from about 1-50% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 60 minutes about 50-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

22. The pharmaceutical composition according to claim 3, wherein said surfactant is a non-ionic surfactant.

23. The pharmaceutical composition according to claim 22, wherein said non-ionic surfactant is selected from D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate, polyethylene glycol-15-hydroxystearate, polyoxyl 35 castor oil, polyoxyl 40 hydrogenated castor oil, polyethylene glycol sorbitan monostearate, polyoxyethylene 20 sorbitan monooleate, caprylocaproyl polyoxylglycerides, lauroyl polyoxylglycerides, stearyl polyoxylglycerides, polyethylene glycol hexadecyl ether, polyoxyethylene (20) oleyl ether, polyethylene glycol

hexadecyl ether, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monooleate, a synthetic copolymer of ethylene and propylene oxides, a synthetic copolymer of ethylene and propylene oxides, phospholipids, zwitterionic surfactants, soy lecithin, phosphatidyl choline, phosphatidyl inositol, phosphatidyl ethanolamine, and cocamidopropyl betaine, and mixtures thereof.

24. The pharmaceutical composition according to claim 23, wherein said non-ionic surfactant is selected from D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate, polyethylene glycol-15-hydroxystearate, polyoxyl 40 hydrogenated castor oil, caprylocaproyl polyoxylglycerides, and lauroyl polyoxylglycerides.

25. The pharmaceutical composition according to claim 24, wherein said non-ionic surfactant is D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate.

26. The pharmaceutical composition according to claim 4, wherein said oil is a medium chain triglyceride.

27. The pharmaceutical composition of claim 26, wherein said medium chain triglyceride is selected from caprylic acid/capric acid triglycerides and medium chain fatty acids.

28. The pharmaceutical composition according to claim 27, wherein said medium chain triglyceride is caprylic acid/capric acid triglyceride.

29. The pharmaceutical composition according to claim 4, wherein said oil is a long chain triglyceride.

30. The pharmaceutical composition of claim 29, wherein the long chain triglyceride is glyceryl behenate.

31. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B suspended in a carrier matrix, wherein said carrier matrix comprises either D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate or a mixture of caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70 and 33:67 and said Form B is present in a range from about 20-40% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 45 minutes about 70-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

32. The pharmaceutical composition according to claim 2, wherein said composition comprises about 1 to about 213 mg of said Form B, wherein said carrier matrix comprises either D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate or a mixture of caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70 and 33:67 and wherein said Form B is present in a range from about 20-40% w/w relative to the weight of said composition, wherein said composition has a dissolution profile in a dissolution media in which within 60 minutes about 80-100% of said Form B is dissolved,

wherein said dissolution media comprises a 0.1 M HCl aqueous solution at pH 1 containing about 0.05% cetyl trimethylammonium bromide,

wherein said dissolution is measured by placing said composition in about 900 mL of said dissolution media, optionally using spiral wire capsule sinkers when said formulation is in capsule form, and using a USP II apparatus with a 75 rpm paddle speed.

33. The pharmaceutical composition according to claim 2, wherein said composition comprises 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B suspended in a carrier matrix, wherein said carrier matrix comprises a medium chain triglyceride and a non-ionic surfactant in a ratio selected from 10:90, 15:85 30:70 and 33:67 and said Form B is present in a range from about 20-50% w/w relative to the weight of said composition, wherein said composition optionally further comprises an antioxidant.

34. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 300 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

35. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 100 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

36. The pharmaceutical composition according claim 33, wherein said composition

comprises less than or equal to 55 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 40 °C/75% relative humidity for 4 weeks.

37. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 100 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 25 °C/60% relative humidity for 1 year.

38. The pharmaceutical composition according claim 33, wherein said composition comprises less than or equal to 70 ppm of 3-(*tert*-butyl)-1-(*p*-tolyl)-1H-pyrazol-5-amine after storage at 25 °C/60% relative humidity for 1 year.

39. The pharmaceutical composition according to claim 33, wherein said medium chain triglyceride is caprylic acid/capric acid triglyceride and said non-surfactant is D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate.

40. The pharmaceutical composition according to claim 39, wherein the ratio of said caprylic acid/capric acid triglyceride to said D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate is about 15:85.

41. The pharmaceutical composition according to claim 2, further comprising an anti-oxidant.

42. The pharmaceutical composition of claim 41, wherein said antioxidant is 2,6-di-*tert*-butyl-4-methylphenol.

43. The pharmaceutical composition according to claim 2, comprising about 213 mg of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yl)oxy)benzyl)urea hydrochloride Form B suspended in a carrier matrix, wherein said carrier matrix comprises caprylic acid/capric acid triglyceride and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate in a ratio selected from 10:90, 15:85, 30:70, and 33:67 and said Form B is present in a range from about 20-50% w/w relative to the weight of said composition, wherein said composition optionally further comprises an antioxidant.

44. The pharmaceutical composition according to claim 43, wherein the ratio of said caprylic acid/capric acid triglyceride to said D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate is about 15:85.

45. The pharmaceutical composition according to claim 43, wherein said composition comprises about 25% w/w of said Form B.

46. The pharmaceutical composition of claim 45, wherein said composition provides an  $AUC_{inf}$  that is about 4-fold greater than the  $AUC_{inf}$  for the powder in capsule formulation of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea.

47. The pharmaceutical composition of claim 45, wherein said composition provides  $C_{max}$  that is about 8-fold greater than the  $C_{max}$  for the powder in capsule formulation of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea.

48. The pharmaceutical composition according to claim 4, prepared by the method comprising:

- (i) stirring a mixture of said surfactant and said oil at a temperature sufficient to provide a liquefied homogeneous carrier matrix optionally in a nitrogen atmosphere; and
- (ii) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-indazol-5-yloxy)benzyl)urea hydrochloride Form B to the carrier matrix with stirring at a temperature sufficient to maintain said carrier matrix in a liquefied state and optionally under a nitrogen atmosphere, thereby providing said pharmaceutical composition comprising a liquefied homogeneous suspension of said Form B in said carrier matrix.

49. The pharmaceutical composition according to claim 48, wherein said method further comprises (iv) transferring aliquots of said molten homogenous suspension obtained in step (iii) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

50. The pharmaceutical composition according to claim 4, prepared by the method comprising (i) homogenizing said oil at a temperature sufficient to melt the oil optionally under a nitrogen atmosphere; (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant optionally under a nitrogen atmosphere; (iii) combining said molten oil and molten surfactant with stirring at a temperature that maintains the combination in a molten state and optionally under a nitrogen atmosphere to form a molten homogenous carrier matrix; and (iv) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1*H*-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1*H*-

indazol-5-yloxy)benzyl)urea hydrochloride Form B to said molten homogenous carrier matrix with stirring at a temperature that maintains said carrier matrix in a molten state and optionally under a nitrogen atmosphere, thereby providing said composition comprising a molten homogeneous suspension of said Form B in said carrier matrix.

51. The pharmaceutical composition according to claim 50, wherein said method further comprises (v) transferring aliquots of said molten homogenous suspension obtained in step (iv) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

52. The pharmaceutical composition according to claim 4, prepared by the method comprising (i) homogenizing said oil at a temperature sufficient to melt the oil; (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant; and (iii) combining said molten oil, said molten surfactant, and said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B with stirring at a temperature that maintains said combination in a molten state, thereby providing said composition comprising a molten homogeneous suspension of said Form B in a carrier matrix.

53. The pharmaceutical composition according to claim 52, wherein said method further comprises (iv) transferring aliquots of said molten homogenous suspension obtained in step (iii) into capsules and allowing said suspension to cool in said capsules to provide said composition comprising a liquid, solid semi-solid or solid form of the suspension within the capsules.

54. The pharmaceutical composition according to claim 4, wherein said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is micronized.

55. The polymorph according to claim 1, characterized by having at least one specific XRPD diffraction peak ( $2\theta$  degrees  $\pm 0.3$ ) at about 15.9.

56. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 12.3, 13.0, 15.9, 16.9 and 17.6.

57. The polymorph according to claim 1, characterized by having XRPD diffraction

peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 23.4, 27.0 and 27.3.

58. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 20.4, 21.5, 21.9, 22.4, 23.4, 25.9, 27.0 and 27.3.

59. The polymorph according to claim 1, characterized by having XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 10.0, 12.3, 13.0, 15.9, 16.9, 17.6, 18.5, 19.8, 20.4, 20.8, 21.5, 21.9, 22.4, 23.4, 23.9, 24.6, 25.2, 25.9, 27.0 and 27.3.

60. The polymorph according to claim 1, characterized by having substantially the same XRPD pattern as shown in Figure 3.

61. The polymorph according to claim 1, characterized by having an XRPD pattern that substantially includes the peaks in Table 2.

62. The polymorph according to claim 1, wherein 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B is in substantially pure form.

63. The polymorph according to claim 1, characterized by having a DSC thermogram which comprises an endothermic event having a melt maxima temperature at about  $185 \pm 5$  °C.

64. A process for preparing a pharmaceutical composition of claim 4, comprising:  
(i) stirring a mixture of said surfactant and said oil at a temperature sufficient to provide a liquefied homogeneous carrier matrix, optionally under a stream of nitrogen; and  
(ii) adding said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to the carrier matrix with stirring at a temperature sufficient to maintain said carrier matrix in a liquefied state, optionally under a stream of nitrogen, to provide a liquefied homogeneous suspension of said Form B in said carrier matrix

65. The process of claim 64, further comprising adding an antioxidant in step (i) or step (ii).

66. The process of claim 64, further comprising adding one or more release modifiers in step (ii).

67. A process for preparing a pharmaceutical composition of claim 4, comprising:  
(i) homogenizing said oil at a temperature sufficient to melt the oil, optionally under

a stream of nitrogen;

- (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant, optionally under a stream of nitrogen;
- (iii) combining said molten oil and molten surfactant with stirring at a temperature that maintains the combination in a molten state, optionally under a stream of nitrogen, to form a molten homogenous carrier matrix; and
- (iv) adding 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to said molten homogenous carrier matrix with stirring at a temperature that maintains said carrier matrix in a molten state, optionally under a stream of nitrogen, to provide a molten homogeneous suspension of said Form B in said carrier matrix.

68. The process of claim 67, further comprising adding an antioxidant in step (iii) or step (iv).

69. The process of claim 67, further comprising adding one or more release modifiers in step (iii) or (iv).

70. A process for preparing a pharmaceutical composition of claim 4, comprising:

- (i) homogenizing said oil at a temperature sufficient to melt the oil, optionally under a stream of nitrogen;
- (ii) homogenizing said surfactant at a temperature sufficient to melt the surfactant, optionally under a stream of nitrogen; and
- (iii) combining said molten oil, said molten surfactant, and 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B with stirring at a temperature that maintains said combination in a molten state, optionally under a stream of nitrogen, to form to provide a molten homogeneous suspension of said Form B in a carrier matrix.

71. The process of claim 70, further comprising adding an antioxidant in step (iii).

72. The process of claim 70, further comprising adding one or more release modifiers in step (iii).

73. The process according to claim 64, further comprising transferring aliquots of said liquefied or molten homogenous suspension into capsules and allowing said suspension to cool

in said capsules, thereby providing a liquid, solid semi-solid or solid form of the suspension within the capsules.

74. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in MTBE with at least 1.5 equivalents of hydrochloric acid in 1,4-dioxane for a sufficient time to convert 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

(b) allowing said Form B to crystallize from said solution; and

(c) isolating said Form B.

75. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in a solvent selected from ethyl acetate, isopropyl acetate, acetonitrile, acetone, isopropyl alcohol and ethanol with at least a stoichiometric amount of (i) HCl in 1,4-dioxane, (ii) HCl in acetone, or (iii) concentrated HCl, for a sufficient time to convert said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

(b) allowing said Form B to crystallize from said solution; and

(c) isolating said Form B.

76. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) combining a solution of amorphous 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea in isopropanol with at least a

stoichiometric amount of an aqueous solution of hydrochloric acid for a sufficient time to convert 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea to 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B;

(b) seeding said solution from step (a) with a suspension of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B in isopropanol to allow said 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B to crystallize from said solution; and

(c) isolating said Form B.

77. The process according to claim 75, wherein about 1.05 equivalents of HCl are added.

78. A process for preparing 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B according to claim 1, comprising:

(a) heating a mixture of 2-(5-(2-(aminomethyl)-4-fluorophenoxy)-1H-indazol-1-yl)ethanol and phenyl 3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-ylcarbamate in an organic solvent at 35-40 °C for 5 hours to form 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea;

(b) cooling said mixture to ambient temperature;

(c) filtering said mixture;

(d) adding at least a stoichiometric amount of aqueous HCl to said mixture;

(e) allowing said Form B to crystallize from said solution; and

(f) isolating said Form B.

79. The process of claim 78, further comprising (d1) seeding said mixture in step (d) with 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form B either as a solid or as a suspension in the solvent used in step (a).

80. A crystalline polymorph of 1-(3-*tert*-butyl-1-*p*-tolyl-1H-pyrazol-5-yl)-3-(5-fluoro-2-(1-(2-hydroxyethyl)-1H-indazol-5-yloxy)benzyl)urea hydrochloride Form A.

81. The crystalline polymorph of claim 80, characterized by having at least ten specific XRPD diffraction peaks ( $2\theta$  degrees  $\pm 0.3$ ) at about 6.9, 7.8, 13.9, 15.6, 16.7, 17.1, 19.2, 22.4, 22.8 and 26.6.

82. The crystalline polymorph of claim 80, characterized by substantially the same XRPD pattern as shown in Figure 1.

83. The crystalline polymorph of claim 80, characterized by having a DSC thermogram which comprises a melt maxima temperature of about  $131 \pm 5$  °C.

84. The pharmaceutical composition according to claim 43 formulated for oral administration.

85. The pharmaceutical composition according to claim 44 formulated for oral administration.

86. The pharmaceutical composition according to claim 45 formulated for oral administration.