CLAIMS

What is claimed is:

1. A capsule suitable for oral administration comprising an admixture of (i) a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate, wherein the admixture is contained in the capsule.

2. The capsule of claim 1, wherein the capsule contains about 10 mg to about 500 mg of the compound, wherein the specified weight is the free base moiety weight of the compound.

3. The capsule of claim 2, wherein the capsule contains about 10 mg, about 40 mg, about 100 mg, or about 200 mg of the compound.

4. The capsule of claim 3, wherein the capsule contains about 100 mg of the compound.

5. The capsule of any one of claims 1-4, wherein the weight ratio of the compound to microcrystalline cellulose in the admixture is between about 1:1.5 to about 1:15, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

6. The capsule of any one of claims 1-5, wherein the weight ratio of the compound to sodium stearyl fumarate in the admixture is between about 5:1 to about 50:1, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

7. The capsule of any one of claims 1-6, wherein microcrystalline cellulose is silicified microcrystalline cellulose.

8. The capsule of any one of claims 1-7, wherein the compound is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

9. The capsule of claim 8, wherein the capsule contains an admixture of about 12 mg of *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 122 mg of silicified microcrystalline cellulose, and about 1 mg of sodium stearyl fumarate.

10. The capsule of claim 8, wherein the capsule contains an admixture of about 47 mg of *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 448 mg of silicified microcrystalline cellulose, and about 5 mg of sodium stearyl fumarate.

11. The capsule of claim 8, wherein the capsule contains an admixture of about 117 mg of *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

12. The capsule of claim 8, wherein the capsule contains an admixture of about 235 mg of *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 357 mg of silicified microcrystalline cellulose, and about 6 mg of sodium stearyl fumarate.

13. The capsule of any one of claims 1-8, wherein sodium stearyl fumarate is about 1% w/w of capsule fill weight.

14. The capsule of claim 7 or 8, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:1.5.

15. The capsule of claim 7 or 8, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:9.

16. The capsule of any one of claims 1-15, wherein the capsule is a hard gelatin capsule.

17. A unit dosage form comprising an admixture of (i) a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate.

18. The unit dosage form of claim 17, wherein the unit dosage form is for treatment of myelofibrosis in a subject.

19. The unit dosage form of claim 17 or 18, wherein the unit dosage form is in the form of a capsule, and the admixture is contained in the capsule.

20. The unit dosage form of any one of claims 17-19, wherein the unit dosage form comprises about 10 mg to about 500 mg of the compound, wherein the specified weight is the free base moiety weight of the compound.

21. The unit dosage form of claim 20, wherein the unit dosage form comprises about 10 mg, about 40 mg, about 100 mg, about 200 mg, about 300 mg, about 400 mg, or about 500 mg of the compound.

22. The unit dosage form of claim 21, wherein the unit dosage form comprises about 400 mg or about 500 mg of the compound.

23. The unit dosage form of any one of claims 17-22, wherein the weight ratio of the compound to microcrystalline cellulose in the admixture is between about 1:1.5 to about 1:15, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

24. The unit dosage form of any one of claims 17-23, wherein the weight ratio of the compound to sodium stearyl fumarate in the admixture is between about 5:1 to about 50:1, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

25. The unit dosage form of any one of claims 17-24, wherein the compound is N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

26. A method of treating myelofibrosis in a subject, comprising orally administering a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, and wherein the compound is in an admixture of (i) the compound, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate.

27. A method of treating myelofibrosis in a subject, comprising administering to the subject an effective amount of a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, wherein the subject has previously received another myelofibrosis therapy with a JAK2 inhibitor which is not *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-

pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof.

28. The method of claim 27, wherein the previous therapy comprises administration of INCB018424 (ruxolitinib).

29. The method of claim 27 or 28, wherein the subject is unresponsive to the previous therapy.

30. The method of any one of claims 27-29, wherein the compound is administered orally.

31. The method of any one of claims 27-30, wherein the compound is in an admixture of (i) the compound, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate.

32. The method of any one of claims 26-31, wherein the compound is in a capsule.

33. The method of any one of claims 26-32, wherein the compound is in a unit dosage form.

34. The method of any one of claims 26-33, wherein the subject has high risk myelofibrosis.

35. The method of any one of claims 26-33, wherein the subject has intermediate risk level 2 myelofibrosis.

36. The method of any one of claims 26-35, wherein the subject has spleen of at least 5cm below costal margin as measured by palpation.

37. The method of any one of claims 26-36, wherein the subject has primary myelofibrosis.

38. The method of any one of claims 26-36, wherein the subject has post-polycythemia vera myelofibrosis.

39. The method of any one of claims 26-36, wherein the subject has post-essential thrombocythemia myelofibrosis.

40. The method of any one of claims 26-39, wherein the compound is administered daily.

41. The method of any one of claims 26-40, wherein the compound is administered at a dose of about 240 mg per day to about 680 mg per day, and wherein the specified weight is the free base moiety weight of the compound.

42. The method of claim 41, wherein the compound is administered at a dose of about 300 mg per day to about 500 mg per day, and wherein the specified weight is the free base moiety weight of the compound.

43. The method of claim 42, wherein the compound is administered at a dose of about 400 mg per day, and wherein the specified weight is the free base moiety weight of the compound.

44. The method of claim 42, wherein the compound is administered at a dose of about 500 mg per day, and wherein the specified weight is the free base moiety weight of the compound.

45. The method of any one of claims 26-44, wherein the compound is administered over a period of at least 1 cycle, at least 6 cycles, at least 10 cycles, or at least 15 cycles of a 28-day treatment cycle.

46. The method of any one of claims 26 and 31-45, wherein the weight ratio of the compound to microcrystalline cellulose in the admixture is between about 1:1.5 to about 1:15, and wherein the weight for the compound is the free base moiety weight of the compound.

47. The method of any one of claims 26 and 31-46, wherein the weight ratio of the compound to sodium stearyl fumarate in the admixture is between about 5:1 to about 50:1, and wherein the weight for the compound is the free base moiety weight of the compound.

48. The method of any one of claims 26-47, wherein the subject is a human.

49. The method of any one of claims 26 and 31-48, wherein, upon administration of the compound to a human subject, the Cmax of the compound is achieved within about 2 to about 4 hours post-dose.

50. The method of any one of claims 26 and 31-49, wherein upon administration of the compound to a human subject, the elimination half life of the compound is about 16 to about 34 hours.

51. The method of any one of claims 26 and 31-50, wherein the mean AUC of the compound increases more than proportionally with increasing doses ranging from about 30 mg to about 800 mg per day.

52. The method of any one of claims 26 and 31-51, wherein the accumulation of the compound is about 1.25 to about 4.0 fold at steady state when the compound is dosed once daily.

53. The method of any one of claims 26-52, wherein the compound is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

54. A method of preparing a capsule drug product comprising a) blending a lubricant with a compound that is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof to generate granules; and b) mixing the granules of a) with an excipient.

55. The method of claim 54, wherein the lubricant is sodium stearyl fumarate.

56. The method of claim 54 or 55, wherein the excipient is silicified microcrystalline cellulose.

57. The method of claim 55 or 56, wherein sodium stearyl fumarate is about 1% w/w of capsule fill weight.

58. The method of claim 56 or 57, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:1.5.

59. The method of claim 56 or 57, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:9.

60. The method of any one of claims 54-59, wherein the capsule is a hard gelatin capsule.

61. An article of manufacture comprising (a) an admixture of (i) a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate, and (b) a package insert or a label indicating that the admixture is useful for treating myelofibrosis in a subject.

62. The article of manufacture of claim 61, wherein the package insert or a label indicates that, upon administration of the admixture to a human subject, the Cmax of the compound is achieved within about 2 to about 4 hours post-dose.

63. The article of manufacture of claim 61 or 62, wherein the package insert or a label indicates that, upon administration of the compound to a human subject, the elimination half life of the compound is about 16 to about 34 hours.

64. The article of manufacture of any one of claims 61-63, wherein the mean AUC of the compound increases more than proportionally with increasing doses ranging from about 30 mg to about 800 mg per day.

65. The article of manufacture of any one of claims 61-64, wherein the accumulation of the compound is about 1.25 to about 4.0 fold at steady state when the compound is dosed once daily.

66. An article of manufacture comprising (a) a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutical salt thereof or a hydrate thereof, and (b) a package insert or a label indicating that the compound can be used for treating myelofibrosis in a subject, wherein the subject has previously received another myelofibrosis therapy with a JAK2 inhibitor which is not *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof.

67. The article of manufacture of any one of claims 61-66, wherein the package insert or the label is in a position which is visible to prospective purchasers.

68. The article of manufacture of any one of claims 61-67, wherein the compound is in a capsule form.

69. The article of manufacture of any one of claims 61-68, wherein the compound is in unit dosage form.

CLAIMS

1. A capsule suitable for oral administration comprising an admixture of (i) a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate, wherein the admixture is contained in the capsule.

2. The capsule of claim 1, wherein the capsule contains about 10 mg to about 500 mg of the compound, wherein the specified weight is the free base moiety weight of the compound.

3. The capsule of claim 2, wherein the capsule contains about 10 mg, about 40 mg, about 100 mg, or about 200 mg of the compound.

4. The capsule of claim 3, wherein the capsule contains about 100 mg of the compound.

5. The capsule of any one of claims 1-4, wherein the weight ratio of the compound to microcrystalline cellulose in the admixture is between about 1:1.5 to about 1:15, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

6. The capsule of any one of claims 1-5, wherein the weight ratio of the compound to sodium stearyl fumarate in the admixture is between about 5:1 to about 50:1, wherein the weight for the compound in the weight ratio is the free base moiety weight of the compound.

7. The capsule of any one of claims 1-6, wherein microcrystalline cellulose is silicified microcrystalline cellulose.

8. The capsule of any one of claims 1-7, wherein the compound is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

9. The capsule of claim 8, wherein the capsule contains an admixture of about 12 mg of N-*tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 122 mg of silicified microcrystalline cellulose, and about 1 mg of sodium stearyl fumarate.

10. The capsule of claim 8, wherein the capsule contains an admixture of about 47 mg of N-*tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 448 mg of silicified microcrystalline cellulose, and about 5 mg of sodium stearyl fumarate.

11. The capsule of claim 8, wherein the capsule contains an admixture of about 117 mg of N-*tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

12. The capsule of claim 8, wherein the capsule contains an admixture of about 235 mg of N-*tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate, about 357 mg of silicified microcrystalline cellulose, and about 6 mg of sodium stearyl fumarate.

13. The capsule of any one of claims 1-8, wherein sodium stearyl fumarate is about 1% w/w of capsule fill weight.

14. The capsule of claim 7 or 8, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:1.5.

15. The capsule of claim 7 or 8, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:9.

16. The capsule of any one of claims 1-15, wherein the capsule is a hard gelatin capsule.

17. Use of a compound which is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof in the manufacture of a medicament for treating myelofibrosis in a subject, wherein the compound is in an admixture of (i) the compound, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate; and wherein said medicament is formulated for oral administration.

18. The use of claim 17, wherein the medicament is a capsule.

19. The use of claim 17, wherein the medicament is a unit dosage form.

20. The use of any one of claims 17-19, wherein the subject has primary myelofibrosis.

21. The use of any one of claims 17-19, wherein the subject has post-polycythemia vera myelofibrosis.

22. The use of any one of claims 17-21, wherein the subject has post-essential thrombocythemia myelofibrosis.

23. The use of any one of claims 17-22, wherein the medicament is formulated for daily administration.

24. The use of any one of claims 17-23, wherein the weight ratio of the compound to microcrystalline cellulose in the admixture is between about 1:1.5 to about 1:15, and wherein the weight for the compound is the free base moiety weight of the compound.

25. The use of any one of claims 17-24, wherein the weight ratio of the compound to sodium stearyl fumarate in the admixture is between about 5:1 to about 50:1, and wherein the weight for the compound is the free base moiety weight of the compound.

26. The use of any one of claims 17-25, wherein the subject is a human.

27. The use of any one of claims 17-26, wherein the compound is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate.

28. A method of preparing a capsule drug product comprising a) blending sodium stearyl fumarate with a compound that is *N-tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof to generate granules; and b) mixing the granules of a) with silicified microcrystalline cellulose.

29. The method of claim 28, wherein sodium stearyl fumarate is about 1% w/w of capsule fill weight.

30. The method of claim 28 or 29, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:1.5.

31. The method of claim 28 or 29, wherein the weight ratio of the compound to silicified microcrystalline cellulose is about 1:9.

32. The method of any one of claims 28-31, wherein the capsule is a hard gelatin capsule.

33. A capsule prepared by the method of any one of claims 28-32.

34. An article of manufacture comprising (a) an admixture of (i) a compound which is N-*tert*-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide or a pharmaceutically acceptable salt thereof or a hydrate thereof, (ii) a microcrystalline cellulose, and (iii) sodium stearyl fumarate, and (b) a package insert or a label indicating that the admixture is useful for treating myelofibrosis in a subject.

35. The article of manufacture of claim 34, wherein the package insert or the label is in a

position which is visible to prospective purchasers.

36. The article of manufacture of claim 34 or 35, wherein the compound is in a capsule form.

37. The article of manufacture of any one of claims 34-36, wherein the compound is in unit dosage form.