[0005] There are no approved therapeutic interventions for ACH or HCH in North America, Europe, or Australia, and no widely accepted consensus about treatment (Unger). Current treatment options are nontargeted, ineffective, or painful interventions aimed at preventing or treating complications of ACH (FDA Background Document. Joint meeting of the Pediatric Advisory Committee and Endocrinologic and Metabolic Drugs Advisory Committee. 11 May 2018. Available at: https://www.fda.gov/downloads/AdvisoryCommittees/; Unger).

[0006] No clear growth effects have been shown after treatment with recombinant human growth hormone (r-hGH). An increase in growth velocity was noted (height increase from −5.0 to −4.0 standard deviations over 5 years), but no clear benefit was established for long-term treatment (Miccoli M, Bertelloni S, Massart F., Horm. Res. Paediatr., 2016, 86, 27–34); it is generally not a recommended treatment option for ACH (Horton; FDA).

[0007] Limb-lengthening procedures can provide 15–30 cm of additional height (~20% increased length of bone segment), but the procedures are painful, often require repeat procedures, and have high complication rates (Horton). Furthermore, the growth rate of the growth plate can be disturbed by these procedures, and the cosmetic effect of long legs and short arms may not be suitable for some patients (FDA). Clinicians who consider limb lengthening now typically require psychological evaluations and require that children be old enough to provide assent for the procedure (Wright MJ, Irving MD., Arch. Dis. Child., 2012, 97(2), 129-134).

[0008] Therefore, there remains an unmet need to develop novel therapeutic strategies for treating children with skeletal dysplasias such as achondroplasia and hypochondroplasia.

SUMMARY

[0008a] In an aspect of the present disclosure, there is provided a use of infigratinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating achondroplasia or hypochondroplasia in a pediatric patient in need thereof, wherein about 0.01 milligrams per kilogram (mg/kg) to about 0.51 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the pediatric patient.

[0008b] In another aspect of the present disclosure, there is provided a use of infigratinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a pediatric patient suffering from achondroplasia or hypochondroplasia, wherein about 0.1 mg to about 8 mg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the pediatric patient.

[0008c] In a further aspect of the present disclosure, there is provided a minitablet for orally delivering 1 mg of infigratinib, comprising:

infigratinib monophosphate, in an amount to deliver 1 mg of infigratinib, and

a pharmaceutically acceptable excipient.

[0008d] In another aspect of the present disclosure, there is provided a minitablet for orally delivering 0.1 mg of infigratinib, comprising:

infigratinib monophosphate, in an amount to deliver 0.1 mg of infigratinib, and

a pharmaceutically acceptable excipient.

[0008e] In a further aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 1% w/w to about 20% w/w of infigratinib monophosphate; and

about 30% w/w to about 95% w/w of a filler.

[0008f] In another aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 1% w/w to about 20% w/w of infigratinib monophosphate;

about 30% w/w to about 60% w/w of mannitol; and

about 30% w/w to about 45% w/w of microcrystalline cellulose.

[0008g] In a further aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 10% w/w to about 20% w/w of infigratinib monophosphate;

about 30% w/w to about 45% w/w of mannitol; and

about 30% w/w to about 40% w/w of microcrystalline cellulose.

[0008h] In another aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 1% w/w to about 5% w/w of infigratinib monophosphate;

about 45% w/w to about 60% w/w of mannitol; and

about 30% w/w to about 40% w/w of microcrystalline cellulose.

[0008i] In a further aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 1.2 mg of infigratinib monophosphate;

about 3 mg to about 4 mg of mannitol; and

about 2 mg to about 4.4 mg of microcrystalline cellulose.

[0008j] In another aspect of the present disclosure, there is provided a minitablet for oral delivery, comprising:

about 0.12 mg of infigratinib monophosphate;

about 3 mg to about 4 mg of mannitol; and

about 2 mg to about 3 mg of microcrystalline cellulose.

[0009] The present disclosure provides methods of treating skeletal dysplasias using an FGFR inhibitor, namely, infigratinib.

[0010] In one ~~aspect~~example, provided herein are methods of treating a skeletal dysplasia such as hypochondroplasia or achondroplasia in a pediatric patient in need thereof, the method generally comprises orally administering daily to the pediatric patient about 0.01 mg/kg to about 0.51 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof.

[0011] In certain ~~embodiment~~examples, the method comprises administering to the pediatric patient about 0.01 mg/kg to about 0.3 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples, the method comprises administering to the pediatric patient

about 0.01 mg/kg to about 0.15 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples, the method comprises administering to the pediatric patient about 0.015 mg/kg to about 0.13 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples, the method comprises administering to the pediatric patient about 0.016 mg/kg, about 0.032 mg/kg, about 0.064 mg/kg, about 0.128 mg/kg, about 0.256 mg/kg, or about 0.51 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof.

[0012] In another ~~aspect~~example, provided herein are methods of treating a pediatric patient suffering from a skeletal dysplasia such as hypochondroplasia or achondroplasia, the method generally comprising orally administering daily to the patient about 0.1 mg to about 8 mg of infigratinib, or a pharmaceutically acceptable salt thereof.

[0013] In certain ~~embodiment~~examples, the method comprises administering to the pediatric patient about 1 mg to about 7 mg of infigratinib, or a pharmaceutically acceptable salt thereof.

[0014] In certain ~~embodiment~~examples, the pediatric patient has a FGFR3 mutation. In certain ~~embodiment~~examples, the FGFR3 mutation is a G380R mutation.

[0015] In certain ~~embodiment~~examples, the infigratinib, or a pharmaceutically acceptable salt thereof, is administered as minitablets each having about 0.1 mg or about 1 mg of infigratinib, or a pharmaceutically acceptable salt thereof.

[0016] In certain ~~embodiment~~examples, the infigratinib is present in the minitablets as infigratinib monophosphate. In certain ~~embodiment~~examples, the infigratinib monophosphate is present as an anhydrous crystalline form. In certain ~~embodiment~~examples, the anhydrous crystalline form of infigratinib monophosphate is characterized by an XRPD peak (2 theta) at 15.0° ± 0.2°.

[0017] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits increased height velocity relative to baseline. In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase in absolute height velocity.

[0018] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in an anthropometric measurement selected from the group consisting of standing height, sitting height, upper and lower arm length, thigh length, knee height, arm span, and combinations thereof. In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an

absolute increase in an anthropometric measurement selected from the group consisting of standing height, sitting height, upper and lower arm length, thigh length, knee height, arm span, and combinations thereof.

[0019] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in weight. In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute decrease in weight.

[0020] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a proportional increase, relative to baseline, in head circumference. In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute proportional increase in head circumference.

[0021] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a normalization, relative to baseline, of a body proportion measurement ratio. In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute normalization of a body proportion measurement ratio. In certain ~~embodiment~~examples, the body proportion measurement ratio is selected from the group consisting of upper to lower body segment ratio, upper arm to forearm ratio, upper leg to lower leg length ratio, arm span to standing height ratio, head circumference to standing height ratio, and combinations thereof.

[0022] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in a biomarker of bone turnover selected from the group consisting of type X collagen degradation fragment, collagen X marker, and combinations thereof.

[0023] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in mobility.

[0024] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in the number of episodes of otitis media.

[0025] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in the number of episodes and/or severity of sleep apnea.

[0026] In certain ~~embodiment~~examples, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase in quality of life, wherein quality of life is assessed using the Pediatric Quality of Life Inventory.

[0027] In certain ~~embodiment~~examples, the pediatric patient is no more than 12 years of age. In certain ~~embodiment~~examples, the pediatric patient is 3 to 11 years of age. In certain ~~embodiment~~examples, the pediatric patient is less than 8 years of age. In certain ~~embodiment~~examples, the pediatric patient is 8 years of age or older.

[0028] In another ~~aspect~~example, provided herein are minitablets for orally delivering about 1 mg of infigratinib, the minitablets generally comprise: infigratinib monophosphate, in an amount to deliver about 1 mg of infigratinib, and a pharmaceutically acceptable excipient.

[0029] In another ~~aspect~~example, provided herein are minitablets for orally delivering about 0.1 mg of infigratinib, the minitablets generally comprise: infigratinib monophosphate, in an amount to deliver about 0.1 mg of infigratinib, and a pharmaceutically acceptable excipient.

[0030] In certain ~~embodiment~~examples, the pharmaceutically acceptable excipient is selected from the group consisting of mannitol, microcrystalline cellulose, a polyvinylpyrrolidone, a cross-linked polyvinylpyrrolidone, magnesium stearate, croscarmellose sodium, and combinations thereof.

[0031] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 1% w/w to about 20% w/w of infigratinib monophosphate; and about 30% w/w to about 95% w/w of a filler.

[0032] In certain ~~embodiment~~examples, the filler is selected from the group consisting of microcrystalline cellulose, lactose, mannitol, and combinations thereof. In certain ~~embodiment~~examples, the filler comprises microcrystalline cellulose and mannitol.

[0033] In certain ~~embodiment~~examples, the minitablet further comprises about 5% w/w to about 10% w/w of a binder. In certain ~~embodiment~~examples, the binder is selected from the group consisting of a sugar, a gelatin, a natural gum, sorbitol, maltodextrin, an alginate, an alginate derivative, a polyvinylpyrrolidone, a cellulose, a cellulose derivative, and combinations thereof.

[0034] In certain ~~embodiment~~examples, the minitablet further comprises about 5% w/w to about 10% w/w of a disintegrant. In certain ~~embodiment~~examples, the disintegrant is selected from the group

consisting of a starch, a starch derivative, a clay, a cross-linked cellulose, a cross-linked cellulose derivative, a cross-linked polyvinylpyrrolidone, and combinations thereof.

[0035] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 1% w/w to about 20% w/w of infigratinib monophosphate; about 30% w/w to about 60% w/w of mannitol; and about 30% w/w to about 45% w/w of microcrystalline cellulose.

[0036] In certain ~~embodiment~~examples, the minitablet comprises about 10% w/w to about 20% w/w of infigratinib monophosphate. In certain ~~embodiment~~examples, the minitablet comprises about 1% w/w to about 5% w/w of infigratinib monophosphate.

[0037] In certain ~~embodiment~~examples, the minitablet comprises about 30% w/w to about 45% w/w of mannitol. In certain ~~embodiment~~examples, the minitablet comprises about 45% w/w to about 60% w/w of mannitol. In certain ~~embodiment~~examples, the minitablet comprises about 35% w/w to about 40% w/w of microcrystalline cellulose.

[0038] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 10% w/w to about 20% w/w of infigratinib monophosphate; about 30% w/w to about 45% w/w of mannitol; and about 30% w/w to about 40% w/w of microcrystalline cellulose.

[0039] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 1% w/w to about 5% w/w of infigratinib monophosphate; about 45% w/w to about 60% w/w of mannitol; and about 30% w/w to about 40% w/w of microcrystalline cellulose.

[0040] In certain ~~embodiment~~examples, the minitablet further comprises about 5% w/w to about 10% w/w of a polyvinylpyrrolidone. In certain ~~embodiment~~examples, the minitablet further comprises about 5% w/w to about 10% w/w of a cross-linked polyvinylpyrrolidone. In certain ~~embodiment~~examples, about 2% w/w to about 6% w/w of croscarmellose sodium.

[0041] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 1.2 mg of infigratinib monophosphate; about 3 mg to about 4 mg of mannitol; and about 2 mg to about 4.4 mg of microcrystalline cellulose.

[0042] In certain ~~embodiment~~examples, the minitablet further comprises about 0.6 mg to about 0.8 mg of a polyvinylpyrrolidone. In certain ~~embodiment~~examples, the minitablet further comprises about 0.5 mg to about 0.7 mg of a cross-linked polyvinylpyrrolidone.

[0043] In another ~~aspect~~example, provided herein are minitablets for oral delivery, the minitablets comprising: about 0.12 mg of infigratinib monophosphate; about 3 mg to about 4 mg of mannitol; and about 2 mg to about 3 mg of microcrystalline cellulose.

[0044] In certain ~~embodiment~~examples, the minitablet further comprises about 0.4 mg to about 0.6 mg of a polyvinylpyrrolidone. In certain ~~embodiment~~examples, the minitablet further comprises about 0.3 mg to about 0.5 mg of a cross-linked polyvinylpyrrolidone. In certain ~~embodiment~~examples, about 0.2 mg to about 0.4 mg of croscarmellose sodium.

DETAILED DESCRIPTION

[0045] As generally described herein, the present disclosure provides methods of treating a skeletal dysplasia such as hypochondroplasia or achondroplasia in a pediatric patient in need thereof. The methods generally comprise administering an effective amount of infigratinib (e.g., 0.01 milligrams per kilogram (mg/kg) to about 0.51 mg/kg) to the pediatric patient. In addition, a minitablet for delivering the effective amount of infigratinib to the pediatric patient is provided, for example, where the minitablet comprises infigratinib monophosphate and one or more pharmaceutically acceptable excipients (e.g., a filler, a binder, a disintegrant, a lubricant).

Definitions

[0046] To facilitate an understanding of the present invention, a number of terms and phrases are defined below.

[0047] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. The abbreviations used herein have their conventional meaning within the chemical and biological arts. The chemical structures and formulae set forth herein are constructed according to the standard rules of chemical valency known in the chemical arts.

[0048] Throughout the description, where compositions and kits are described as having, including, or comprising specific components, or where processes and methods are described as having, including, or comprising specific steps, it is contemplated that, additionally, there are compositions and kits of the present invention that consist essentially of, or consist of, the recited components, and that there are processes and methods according to the present invention that consist essentially of, or consist of, the recited processing steps.

CLAIMS

We claim:

1. ~~A method of~~ Use of infigratinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating achondroplasia or hypochondroplasia in a pediatric patient in need thereof, ~~comprising orally administering daily to the pediatric patient~~ wherein about 0.01 milligrams per kilogram (mg/kg) to about 0.51 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the pediatric patient.

2. The ~~method~~ use of claim 1, ~~comprising administering to the pediatric patient~~wherein about 0.01 mg/kg to about 0.3 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered to the pediatric patient.

3. The ~~method~~ use of claim 1, ~~comprising administering to the pediatric patient~~wherein about 0.01 mg/kg to about 0.15 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered to the pediatric patient.

4. The ~~method~~ use of claim 1, ~~comprising administering to the pediatric patient~~wherein about 0.015 mg/kg to about 0.13 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered to the pediatric patient.

5. The ~~method~~ use of claim 1, ~~comprising administering to the pediatric patient~~wherein about 0.016 mg/kg, about 0.032 mg/kg, about 0.064 mg/kg, about 0.128 mg/kg, about 0.256 mg/kg, or about 0.51 mg/kg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered to the pediatric patient.

6. ~~A method of~~ Use of infigratinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a pediatric patient suffering from achondroplasia or hypochondroplasia, ~~comprising orally administering daily to the patient~~wherein about 0.1 mg to about 8 mg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the pediatric patient.

7. The ~~method~~ use of claim 6, ~~comprising administering to the pediatric patient~~wherein about 1 mg to about 7 mg of infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered to the pediatric patient.

8. The ~~method~~ use of any one of claims 1-7, wherein the pediatric patient has a FGFR3 mutation.

9. The ~~method~~ use of claim 8, wherein the FGFR3 mutation is a G380R mutation.

10. The ~~method~~ use of any one of claims 1-9, wherein the infigratinib, or a pharmaceutically acceptable salt thereof, is to be administered as minitablets each having 0.1 mg or about 1 mg of infigratinib, or a pharmaceutically acceptable salt thereof.

11. The ~~method~~ use of claim 10, wherein the infigratinib is present in the minitablets as infigratinib monophosphate.

12. The ~~method~~ use of claim 11, wherein the infigratinib monophosphate is present as an anhydrous crystalline form.

13. The ~~minitablet~~ use of claim 12, wherein the anhydrous crystalline form of infigratinib monophosphate is characterized by an XRPD peak (2 theta) at 15.0° ± 0.2°.

14. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits increased height velocity relative to baseline.

15. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase in absolute height velocity.

16. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in an anthropometric measurement selected from the

group consisting of standing height, sitting height, upper and lower arm length, thigh length, knee height, arm span, and combinations thereof.

17. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute increase in an anthropometric measurement selected from the group consisting of standing height, sitting height, upper and lower arm length, thigh length, knee height, arm span, and combinations thereof.

18. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in weight.

19. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute decrease in weight.

20. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a proportional increase, relative to baseline, in head circumference.

21. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute proportional increase in head circumference.

22. The ~~method~~use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a normalization, relative to baseline, of a body proportion measurement ratio.

23. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an absolute normalization of a body proportion measurement ratio.

24. The ~~method~~ use of claim 22 or 23, wherein the body proportion measurement ratio is selected from the group consisting of upper to lower body segment ratio, upper arm to forearm ratio, upper leg to lower leg length ratio, arm span to standing height ratio, head circumference to standing height ratio, and combinations thereof.

25. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in a biomarker of bone turnover selected from the group consisting of type X collagen degradation fragment, collagen X marker, and combinations thereof.

26. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase, relative to baseline, in mobility.

27. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in the number of episodes of otitis media.

28. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits a decrease, relative to baseline, in the number of episodes and/or severity of sleep apnea.

29. The ~~method~~ use of any one of claims 1-13, wherein, after daily administration of the dose of infigratinib, or a pharmaceutically acceptable salt thereof, the pediatric patient exhibits an increase in quality of life, wherein quality of life is assessed using the Pediatric Quality of Life Inventory.

30. The ~~method~~ use of any one of claims 1-29, wherein the pediatric patient is no more than 12 years of age.

31. The ~~method~~ use of any one of claims 1-30, wherein the pediatric patient is 3 to 11 years of age.

32. The ~~method~~ use of any one of claims 1-30, wherein the pediatric patient is less than 8 years of age.

33. The ~~method~~ use of any one of claims 1-29, wherein the pediatric patient is 8 years of age or older.

34. A minitablet for orally delivering 1 mg of infigratinib, comprising:
infigratinib monophosphate, in an amount to deliver 1 mg of infigratinib, and
a pharmaceutically acceptable excipient.

35. A minitablet for orally delivering 0.1 mg of infigratinib, comprising:
infigratinib monophosphate, in an amount to deliver 0.1 mg of infigratinib, and
a pharmaceutically acceptable excipient.

36. The minitablet of claim 34 or 35, wherein the pharmaceutically acceptable excipient is selected from the group consisting of mannitol, microcrystalline cellulose, a polyvinylpyrrolidone, a cross-linked polyvinylpyrrolidone, magnesium stearate, croscarmellose sodium, and combinations thereof.

37. A minitablet for oral delivery, comprising:
about 1% w/w to about 20% w/w of infigratinib monophosphate; and
about 30% w/w to about 95% w/w of a filler.

38. The minitablet of claim 37, wherein the filler is selected from the group consisting of microcrystalline cellulose, lactose, mannitol, and combinations thereof.

39. The minitablet of claim 37 or 38, wherein the filler comprises microcrystalline cellulose and mannitol.

40. The minitablet of any one of claims 37-39, further comprising about 5% w/w to about 10% w/w of a binder.

41. The minitablet of claim of 40, wherein the binder is selected from the group consisting of a sugar, a gelatin, a natural gum, sorbitol, maltodextrin, an alginate, an alginate derivative, a polyvinylpyrrolidone, a cellulose, a cellulose derivative, and combinations thereof.

42. The minitablet of any one of claims 37-41, further comprising about 5% w/w to about 10% w/w of a disintegrant.

43. The minitablet of claim of 40, wherein the disintegrant is selected from the group consisting of a starch, a starch derivative, a clay, a cross-linked cellulose, a cross-linked cellulose derivative, a cross-linked polyvinylpyrrolidone, and combinations thereof.

44. A minitablet for oral delivery, comprising:
about 1% w/w to about 20% w/w of infigratinib monophosphate;
about 30% w/w to about 60% w/w of mannitol; and
about 30% w/w to about 45% w/w of microcrystalline cellulose.

45. The minitablet of claim 44, comprising about 10% w/w to about 20% w/w of infigratinib monophosphate.

46. The minitablet of claim 44, comprising about 1% w/w to about 5% w/w of infigratinib monophosphate.

47. The minitablet of claim 44, comprising about 30% w/w to about 45% w/w of mannitol.

48. The minitablet of claim 44, comprising about 45% w/w to about 60% w/w of mannitol.

49. The minitablet of any one of claims 44-48, comprising about 35% w/w to about 40% w/w of microcrystalline cellulose.

50. A minitablet for oral delivery, comprising:
about 10% w/w to about 20% w/w of infigratinib monophosphate;
about 30% w/w to about 45% w/w of mannitol; and

about 30% w/w to about 40% w/w of microcrystalline cellulose.

51. A minitablet for oral delivery, comprising:
about 1% w/w to about 5% w/w of infigratinib monophosphate;
about 45% w/w to about 60% w/w of mannitol; and
about 30% w/w to about 40% w/w of microcrystalline cellulose.

52. The minitablet of claim 50 or 51, further comprising about 5% w/w to about 10% w/w of a polyvinylpyrrolidone.

53. The minitablet of any one of claims 50-52, further comprising about 5% w/w to about 10% w/w of a cross-linked polyvinylpyrrolidone.

54. The minitablet of any one of claims 50-53, further comprising about 2% w/w to about 6% w/w of croscarmellose sodium.

55. A minitablet for oral delivery, comprising:
about 1.2 mg of infigratinib monophosphate;
about 3 mg to about 4 mg of mannitol; and
about 2 mg to about 4.4 mg of microcrystalline cellulose.

56. The minitablet of claim 55, further comprising about 0.6 mg to about 0.8 mg of a polyvinylpyrrolidone.

57. The minitablet of claim 55, further comprising about 0.5 mg to about 0.7 mg of a cross-linked polyvinylpyrrolidone.

58. A minitablet for oral delivery, comprising:
about 0.12 mg of infigratinib monophosphate;
about 3 mg to about 4 mg of mannitol; and
about 2 mg to about 3 mg of microcrystalline cellulose.

59. The minitablet of claim 58, further comprising about 0.4 mg to about 0.6 mg of a polyvinylpyrrolidone.

60. The minitablet of claim 58 or 59, further comprising about 0.3 mg to about 0.5 mg of a cross-linked polyvinylpyrrolidone.

61. The minitablet of any one of claims 55-60, further comprising about 0.2 mg to about 0.4 mg of croscarmellose sodium.

62. The minitablet of any one of claims 34-61, wherein the infigratinib monophosphate is present as an anhydrous crystalline form.

63. The minitablet of claim 62, wherein the anhydrous crystalline form of infigratinib monophosphate is characterized by an XRPD peak (2 theta) at 15.0° ± 0.2°.